Rational Cardiac Risk Stratification Before Peripheral Vascular Surgery: Application of Evidence-Based Medicine and Bayesian Analysis

Srinivas Mantha, MD

The high prevalence of severe coronary artery disease (CAD) in patients who need vascular surgery is responsible for their high risk for both short- (30-days postoperatively) and long-term morbidity and mortality. Coronary revascularization before noncardiac surgery is virtually never indicated solely "to get a patient through" the perioperative period. Patients with 3-vessel CAD or left main artery disease and those with poor left ventricular function are a subgroup who may benefit from surgical coronary revascularization. After clinical evaluation, selective noninvasive testing with either dobutamine stress echocardiography or dipyridamole scintigraphy followed by coronary angiography, when these test results are positive, appears reasonable. Such evaluation may identify patients with coronary anatomy that need revascularization. Evidence-based medicine and Bayesian theory provide tools to evaluate these strategies. Copyright © 2000 by W.B. Saunders Company.

he prevalence of symptomatic and asymptomatic cor-I onary artery disease (CAD) in vascular surgery patients is high.¹⁻³ Patients are at risk for short-term (30-days postoperatively) and long-term cardiac-related morbidity and mortality. To limit morbidity and mortality, various preoperative strategies have been proposed. However, the recommendations of experts are variable, conflicting, and confusing, which makes choosing one strategy difficult. Thus, preoperative evaluation, risk stratification, and preparation before vascular surgery remain highly controversial.⁴ The cardiac risk of vascular surgery patients may be estimated for several reasons5; (1) to target those who might benefit from perioperative risk-reducing strategies, such as drug therapy, invasive monitoring, extra thermal care, and so on; (2) to identify patients who might benefit from preoperative myocardial revascularization. Finally, a conservative surgical procedure or no surgery at all may be an option for those at high risk and who are unlikely to

Copyright © 2000 by W.B. Saunders Company. 1089-2532/00/0404-0002\$10.00/0 doi:10.1053/scva.2000.19826 benefit from risk-reducing strategies or revascularization. In our cost-conscious medical environment, the primary goal of any strategy is to minimize cost while preserving or improving the quality of care with technology assessment,^{6,7} evidence-based medicine,⁸ and economic analysis.^{9,10} This review focuses on patients who need noncardiac peripheral vascular surgery, ie, repair of an abdominal aortic aneurysm (AAA) or aortic occlusion, lower extremity revascularization, or carotid endarterectomy.

Coronary Artery and Peripheral Vascular Disease

When coronary angiography was performed in 1,000 consecutive vascular patients, correctable CAD was identified in 31% of patients scheduled for aortic repair, 26% of patients for carotid endarterectomy, and 21% of patients with ischemia of the lower extremity.¹ Significant CAD (stenosis > 70%) was found in 37% of patients without clinical indications and in 78% with symptoms. When these data were pooled with 50 other series that represented more than 10,000 patients, evidence of CAD was found in approximately 50% (range 22%-70%) of patients scheduled for vascular surgery.² Significant CAD was found in approximately 60% of patients who underwent preoperative coronary angiography. Prevalence of CAD in patients with peripheral vascular disease varies from 16% to 92%, which depends on the method of evaluation and type of peripheral vascular disease.3 In another series of 125 patients who needed repair of AAA, angiography detected CAD that required revascularization in 26.5% of patients. The prevalence of diffuse inoperable CAD was 5.6%.11

Short-Term Morbidity and Mortality

Short-term morbidity and mortality after vascular surgery is higher than after other types of noncardiac surgery.¹²⁻¹⁵ Complications after vascular surgery include cardiac-related death, myocardial infarction (MI), cardiogenic pulmonary edema, ischemic ST-T changes, unstable angina, and dysrhythmias. The risk of these cardiac complications ranges from 5% to 40%.⁵ Reports of cardiac death and MI are usually consistent in risk stratification studies in vascu-

From the Department of Anesthesiology & Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad, India.

Address reprint requests to Srinivas Mantha, MD, Department of Anesthesiology & Intensive Care, Nizam's Institute of Medical Sciences, Hyderabad 500082, India.

lar surgery, but nonreporting of the other events does not necessarily mean that no event occurred.^{14,15} The rate of MI and cardiac-related death after vascular surgery ranges from 2% to 15%, which depends on the type of surgery and the clinical pathways. A meta-analysis of 20 studies (n = 1,891 patients), showed the following rates of postoperative cardiac-related morbidity and mortality: death, 0% to 8% of patients; MI, 0% to 15.3%; unstable angina, 0% to 10.4%; and pulmonary edema, 0% to 8.3%.¹³

In a prospective study, Krupski et al^{16} compared the rate of perioperative cardiac complications after aortic surgery (n = 53) or lower extremity vascular surgery (n = 87). The rates were 24% for aortic surgery and 28% for infrainguinal surgery; the rates of cardiac death were 2% and 3.5%, respectively. The percentage of patients who had a history of angina, congestive heart failure, diabetes mellitus, dysrhythmias, or digitalis therapy was significantly higher among patients in need of infrainguinal procedures. The investigators attributed the high morbidity after infrainguinal procedures to a higher likelihood of preoperative cardiac risk factors in that group.

Complications after carotid endarterectomy are generally less frequent, regardless of the presence or absence of known CAD.¹⁷ For example, in 177 patients who underwent carotid endarterectomy, the rates of cardiac-related death, MI, pulmonary edema, and ventricular tachycardia were 0%, 2%, 17%, and 3%, respectively, for patients without clinically recognized CAD (n = 93); rates were 0%, 3%, 5%, and 2%, respectively, for patients with CAD (n = 64); and 0%, 0%, 10%, and 0%, respectively, for patients who had myocardial revascularization (n = 20) before carotid endarterectomy.¹⁸

Long-Term Morbidity and Mortality

The presence of CAD decreases long-term survival substantially after vascular surgery. In 7,805 vascular surgery patients, the 5-year mortality rate was 20% for those with no overt CAD, 41% for those with suspected CAD, and 21% for those who had previous coronary artery bypass graft (CABG) surgery.² A population-based study with a 17-year follow-up reported long-term survival in 131 patients who had repair of AAA.¹⁹ Uncorrected CAD was associated with a nearly 2-fold increase in the risk of death hazard ratio, 1.79 (95% confidence interval, 1.06 to 3.00) and a 4-fold increase in the risk of adverse cardiac events.

In a prospective observational study of patients at high risk undergoing abdominal aortic or infrainguinal vascular operations, Krupski et al²⁰ found the incidence of longterm adverse cardiac outcomes was substantially greater after infrainguinal operations because of a greater prevalence of diabetes and CAD in that group. These results were similar to short-term perioperative outcomes.¹⁶ When the risk for cardiac morbidity and mortality was evaluated in 376 consecutive patients who had infrainguinal revascularization procedures, 129 patients (34.3%) had 183 cardiac events in the follow-up period (mean 5.9 years). Of these patients, 79 (61.2%) died and 13 (10.0%) required coronary angioplasty or bypass. The risk of cardiac events was 34% at 5 years and increased to 56% at 15 years. Age, cardiac disease, and impaired renal function at the time of operation were associated with an increased risk of cardiac events during follow-up. Independent predictors of cardiac death were age, cardiac disease, hypertension, diabetes, and impaired renal function.²¹ For another geographically-defined patient group (n = 173) after aortoiliac, aortofemoral, femoropopliteal, or infrapopliteal revascularization, the Kaplan-Meier survival rate at 5 and 10 years was 77% and 51%, respectively, for those without overt CAD and 54% and 24% for those with overt CAD (P < .01).²²

In another population-based study, the Kaplan-Meier estimate of 8-year survival after carotid endarterectomy was 89% for patients without overt CAD and 75% for those with overt CAD.¹⁸ Coronary rather than cerebrovascular disease was the most frequent cause of long-term morbidity and mortality.

When Yeager et al²³ compared 1,561 patients who did or did not have MI after peripheral vascular surgery, survival rates at 1 and 4 years were similar, but among those with MI, incidence of adverse cardiac events and coronary artery revascularization was higher.

In a study that comprised 547 vascular surgery patients (aortic, n = 321; infrainguinal, n = 177; carotid, n = 49), patients who had infrainguinal procedures had more than twice the risk for perioperative MI and a 3-fold risk for cardiac events (confidence interval 1.8 to 5.1, P = .005) compared with patients who had aortic surgery. The first value was reduced to insignificant levels and the second to 1.3 (95% confidence interval 0.8 to 2.3, P = .32) after adjustment for comorbid factors. Long-term risk among patients undergoing carotid artery surgery was less dramatically altered by risk factor adjustment. The investigators attributed the differences to CAD risk factors, not to the type of vascular surgery.²⁴

After analysis of the data from the Coronary Artery Surgery Registry on 1,834 patients who had both peripheral vascular disease and CAD and underwent either CABG (n = 986) or medical therapy (n = 848), the estimated probability of survival at 4, 8, 12, and 16 years after surgery was significantly (P < .001) higher for the CABG group (88%, 72%, 55%, and 41%, respectively) than for the medical group (73%, 57%, 44%, and 34%, respectively). The type of therapy was independently associated with survival (P < 0.0001). The benefits of surgical therapy were limited to patients with 3-vessel CAD and were inversely related to ejection fraction. The rate of survival free of MI was also significantly better for the surgical group. The investigators concluded that myocardial revascularization provides long-term benefits for patients who have both CAD and peripheral vascular disease.25

In several other studies²⁶⁻³⁰ of patients who underwent vascular surgery, adverse cardiac events and mortality were related to the severity of CAD documented at the time of surgery. The presence of diabetes mellitus is an additional risk factor that adversely affects the long-term survival of vascular surgery patients.^{18,20,21,22,26,29}

Thus, irrespective of the type of vascular surgical procedure, prior revascularization therapy for CAD before vascular surgery appears beneficial. Controversy persists as to whether identification of patients most likely to have myocardial ischemic events benefits patients. Invasive interventions, including CABG, may benefit patients with vascular disease but are generally more risky in these patients.^{31,32} Coronary revascularization may be a "survival test" that increases short-term morbidity33 or it may lead to better long-term survival.34 Patients who have survived coronary revascularization have fewer cardiac complications after vascular surgery.35 When 194 patients underwent percutaneous transluminal coronary angioplasty (PTCA) before vascular surgery, their perioperative cardiac complications were limited. The benefit was shown when coronary angioplasty was performed up to 18 months beforehand.36

Evidence-Based Medicine: Definition of Terms

Evidence-based medicine refers to conscientious, explicit, and judicious use of the best evidence in making decisions about the care of individual patients. Ideally, evidence must be provided by randomized, controlled, clinical trials. When a randomized clinical trial cannot be performed on ethical or logistical grounds, weaker forms of evidence are considered, such as prospective observational studies, retrospective studies, and case series.

The following guidelines are suggested for levels of evidence based on the study design from highest to lowest quality³⁷: Level I, large randomized trials with clear-cut results and low risk of (α) false-positive or (β) false-negative errors; Level II, small randomized trials with uncertain results and moderate-to-high risk of (α) false-positive or (β) false-negative error; Level III, nonrandomized trials with contemporaneous controls; Level IV, nonrandomized, historical controls and expert opinion; Level V, case series, uncontrolled studies, and expert opinion.

Synthesis of evidence by systematic review of the literature, meta-analysis, or decision analysis can resolve confusion in some controversial areas. Meta-analysis is a statistical method that synthesizes evidence from different but related studies. Decision analysis is an explicit analytic tool designed to facilitate complex therapeutic or diagnostic decisions in which many variables must be considered simultaneously. In policy applications, decision analysis is applied to society, populations, or groups of patients. The analysis involves constructing a decision tree and mapping all relevant courses of action and their associated out-

comes. The expected utility of each potential course of action is a function of both the probability of the outcome and its utility. Typical measures of utility can be lives saved, number of MIs averted, life expectancy, quality adjusted life expectancy, and costs. In decision analysis, Markov modeling is used to obtain the outcome in life years, quality adjusted life years (QALYs), and lifetime costs. Sensitivity analysis to assess the impact of variations in probabilities and utilities on the final decision enhances the flexibility of decision analysis. Decision analysis models also can be used to evaluate 2 or more mutually exclusive competing strategies. The analysis involves computing the incremental cost-effectiveness ratio and comparing it with some benchmark values. The numerator in the ratio is the difference in cost and the denominator is the difference in effectiveness (typically, QALYs) . A strategy is generally considered "cost-effective" if the ratio is between \$20,000 and \$40,000 (1991 US dollars) per QALY, because the range is consistent with other funded programs, such as hemodialysis and hypertension.³⁸ Other classifications are "very attractive" ratio, which is less than \$20,000 per QALY; "expensive" ratio, which is more than \$60,000; and "unattractive" ratio, which is more than \$100,000 per QALY.

The American College of Physicians provides grades when formulating guidelines for assessing and managing the perioperative risk from CAD associated with major noncardiac surgery. Strong quality equals are studies with a sample size of 100 or more, prospective evaluation, consecutive selection of patients, and double blinding. Fair quality equals are those with a sample size less than 100, prospective evaluation, consecutive selection of patients, single blinding or no blinding. Weak quality equals are studies based on retrospective chart reviews.¹⁵

The American Heart Association (AHA)/American College of Cardiology (ACC) uses the following codes to summarize recommendations for a particular strategy for perioperative cardiovascular evaluation for noncardiac surgery: class I, conditions for which there is evidence and or general agreement that a procedure be performed or a treatment is of benefit; class II, conditions for which there is a divergence of evidence and/or opinion about the treatment; class III, conditions for which there is evidence and/or general agreement that the procedure or treatment is not necessary.¹⁴

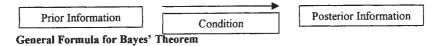
Principles of Diagnostic Test Selection

Clinical evaluation, noninvasive tests, and coronary angiography are used to identify the severity of CAD before vascular surgery or to predict perioperative cardiac complications. By applying the principles of Bayesian theory to diagnostic tests and risk stratification strategies, unnecessary tests that do not provide additional information can be eliminated. One application of Bayesian theory to diagnostic testing is the use of odds and the likelihood ratio. Unlike sensitivity, specificity, predictive values, or probabilities, likelihoods are expressed as odds. The likelihood ratio expresses the odds that the test result occurs in patients with the disease versus those without the disease. Thus, there is one likelihood ratio for a positive test and another for a negative test. If the probability of a particular event, like CAD is *P*, then the odds in favor of the event can be defined as P/(1 - P). The odds can be converted to probability with the formula: Probability = odds/(1 + odds).

Assuming a noninvasive diagnostic test has a sensitivity of 0.8 (80%) and a specificity of 0.9 (90%) to detect CAD that warrants therapeutic intervention, likelihood ratios for positive and negative test results are 8 (0.8 / (1 - 0.9)

and 0.22 (1 - 0.8)/0.9), respectively. If the test is used in 4 patient groups, posttest probabilities of CAD can be revised based on test results and the use of the formulas shown in Fig 1.

As shown in Table 1, limited information is obtained by testing individuals with very low or very high prior probability for the disease. For those with low prior probability of CAD, posttest probability is low even with a positive test result. For those with high probability of CAD, probability remains high even with a negative test result. Little is gained from a screening test for a high-risk patient because the test result is likely to be positive or suspect if negative.



Prior x Likelihood ration (LR) for the condition = Posterior

Bayes' Formula Applied to Diagnostic Testing

Odds for prevalence x LR for positive result = posttest odds with positive result Odds for prevalence x LR for negative result = posttest odds with negative test

Bayes' Formula Applied to Perioperative Risk Stratification

Pretest odds for		LR for a		Posttest odds for
Complications	x	stratification class	=	complications for the class

	Disease/Complication Positive	Disease/Complication Negative	Total
Positive Test	a	b	a + b
Negative Test	c	d	c + d
Total	a+c	b + d	n

Variable	Formula
Prior probability (prevalence)	$\mathbf{p} = (\mathbf{a} + \mathbf{c}) \div \mathbf{n}$
Prior odds (pre-test likelihood)	p ÷ (1-p)
Sensitivity	$a \div (a + c)$
Specificity	$d \div (b + d)$
Likelihood ratio (LR) for a positive test	(sensitivity) ÷ (1 – specificity)
Likelihood ration (LR) for a negative test	$(1 - \text{sensitivity}) \div (\text{specificity})$
Post-test likelihood after positive test	prior odds x LR for a positive test
Post-test likelihood after negative test	prior odds x LR for a negative test
Post-test probability	posterior odds \div (1 + posterior odds)
Predictive value of a positive test	$a \div (a + b)$
Predictive value of a negative test	$d \div (c + d)$
Odds ratio	$(a \times d) \div (b \times c)$

Figure 1. Application of Bayesian theory to diagnostic testing or perioperative risk stratification, which updates prior information based on condition to new posterior information. The prior is prevalence (prev) or pretest probability of disease, condition is test result (positive or negative), and posterior is posttest probability of the disease when the principle is applied to diagnostic testing. When applied to perioperative risk stratification, the prior is overall risk of complications, condition is risk stratification class, and posterior is the estimated risk of complications for the class that a patient is stratified (see text for details).

	Assumed Prior	Estimated Posttest Probability			
Patient Group	Probability of Significant CAD	When Test Result Is Positive	When Test Result Is Negative		
40-yr-old man with no risk factors	0.02	0.14	0.0045		
Patients with peripheral vascular disease Patients with peripheral vascular disease and 2	0.25	0.73	0.07		
other risk factors for CAD Patients > 70 yr with peripheral vascular disease	0.5	0.89	0.18		
and 3 other clinical risk factors for CAD	0.9	0.99	0.67		

 Table 1. Application of Bayes' Theorem to Diagnostic Tests With Dichotomous Results

The previously discussed principles can be applied for predicting perioperative cardiac complications from preoperative diagnostic test results. Pretest probability is the overall risk of complications and posttest is the estimated risk of complications for a risk class.^{5,15} Diagnostic test results or risk stratification need not necessarily be dichotomous when likelihood formulas are applied. Assuming risk stratification classes range from class 1 (no risk factors) to class 4 (most risk factors) and the number of patients suffering perioperative complications (eg, cardiac-related death and MI), the following likelihood ratios can be derived as in Table 2.

In Table 2, the prior probability of perioperative complications is 0.2 (20/100), a measure of overall risk of perioperative complications. The likelihood ratio for class 1 is 0.27 (0.1/0.375) and for class 4 is 4 (0.5/0.125). The prior odds 0.25 (0.2/0.8) can be revised based on likelihood ratios for each class. The pretest and posttest probabilities multiplied by 100 give the data in percentages. A likelihood ratio >1produces a posttest probability higher than the pretest probability. For a likelihood ratio <1, the posttest probability is less than the pretest probability. A likelihood ratio of 1 implies that the pretest and posttest probabilities are equal. Therefore, for a diagnostic tests with dichotomous results, the likelihood ratio must be >1 for a positive result and <1for a negative result. Similarly, for diagnostic tests with semiquantitative results (normal, weakly or strongly positive) or risk stratification classes, the ratio must ideally be <1 for normal and lower risk classes and >1 for strongly positive results or higher risk classes.5,15

If diagnostic tests or predictive systems are evaluated after a change in the test criterion for positivity, the sen-

sitivity and specificity change. For example, assume a new marker for myocardial ischemia represents values on a continuous scale and lets higher values of the marker represent severe abnormality. When the threshold value for diagnosis (positivity criterion) is changed to a higher value, sensitivity will decrease (more false-negatives) and specificity will increase (fewer false-positives). When the threshold is set at a lower level, sensitivity will increase and specificity will decrease. Similarly, when evaluating a noninvasive test to detect CAD that can assess abnormal regions of myocardium, the increase in the threshold to more regions for diagnosis decreases the test's sensitivity and increases its specificity. Analysis of receiver operating characteristic (ROC) curves identifies an ideal threshold value to make a quantitative evaluation of the test. The curve shows the relationship between the true-positive rate (sensitivity) and the false-positive rate (1 - specificity) as the decision threshold of a positive test varies. The conditional probability of a false-positive decision is depicted on the x-axis and that of a true-positive decision is depicted on the y-axis. The closer the curve is to the upper left corner of the graph, the more accurate it is, because the true-positive rate then approaches 1 while the false-positive rate remains near zero. Determination of the area under the curve, which ideally must be more than 0.5 and closer to 1, provides a quantitative measure of the test's predictive performance.39

Cardiac Risk Stratification for Vascular Surgery Patients

There are 3 components to risk stratification. The first is to segregate patients at high risk for perioperative myocardial

Table 2. Application of Bayes' Theorem to Multiclass Scoring System

	·····		0,		
Risk Class	Patients With Complications (n)	Proportion of Patients With Complications	Patients Without Complications (n)	Proportion of Patients Without Complications	Likelihooo Ratio
Class 1	2	Ó.1	30	0.375	0.27
Class 2	3	0.15	25	0.32	0.48
Class 3	5	0.25	15	0.188	1.33
Class 4	10	0.5	10	0.125	4
Total	20	1	80	1	

ischemia and infarction who might benefit from risk-reducing strategies. The patient's history, physical examination, electrocardiogram (ECG), and chest radiograph provide important prognostic information. Studies have identified known CAD, CHF, advanced age, severely limited exercise tolerance, chronic renal insufficiency, severe uncontrolled hypertension with left ventricular hypertrophy, and the use of digoxin as risk factors for perioperative cardiac morbidity. In most clinical series, CHF (whether diagnosed by an S3 gallop or basilar rales on physical examination or history) is associated with the highest risk.¹²

The clinician must also identify patients who have suffered an MI. The risk of reinfarction depends primarily on the amount of time that has passed since the last infarction.¹² It has been suggested that at least 6 months must elapse after an MI before a patient is eligible for elective noncardiac surgery. However, with thrombolytic therapy for acute MI and subsequent noninvasive identification of ischemic burden, this waiting period before surgery may no longer apply to most patients.⁴⁰

A prospective study of consecutive patients for all types of vascular surgery found that clinical parameters and scoring systems, including Goldman's risk index and Detsky's risk index, failed to reliably and consistently predict adverse cardiac outcomes.⁴¹ Thus, specialized testing to identify the extent of CAD seems logical. Given the costs and risk of coronary angiography, it is not practical to subject all patients undergoing vascular surgery to this test before the procedure. It is also difficult to obtain meaningful results from conventional exercise electrocardiography because claudication in the lower extremities of many patients undergoing vascular surgery prevents them from achieving an adequate exercise load. Therefore, interest has increased in cardiac risk stratification by other noninvasive preoperative tests.^{5,13-15,42-45} Noninvasive tests include conventional 2-dimensional echocardiography, ambulatory electrocardiography, radionuclide ventriculography, dipyridamole scintigraphy (DTS), and dobutamine stress echocardiography (DSE).

DTS

The DTS test is based on the principle of coronary steal. Dipyridamole is an antiplatelet drug and a coronary artery vasodilator. At rest, coronary arteries supplying the normal myocardium have a great vasodilatory reserve and are able to increase blood flow up to 10 times the normal amount to meet extra demand. In areas of critical stenosis, the coronary arteries are vasodilated in the nonstressed state and have diminished reserve. Dipyridamole can dilate only normal coronary arteries, not those in areas with stenosis. When the thallium radioisotope is injected, stenotic areas of myocardium have a lower concentration of the isotope (cold spot) after dipyridamole administration. When the effect of dipyridamole wears off, the isotope redistributes to ischemic zones. The areas with redistribution are considered ischemic but viable; those with persistent defects with no redistribution are infarcted. Although, both redistributed (reversible) and persistent (fixed) defects may be abnormal test results in DTS, reversible defects are more important in risk stratification.

In a fasting patient, dipyridamole (0.56 mg/kg body weight) is administered intravenously over a period of 4 minutes while heart rate, blood pressure, and ECG are monitored. After 2 additional minutes to allow the maximal action of dipyridamole, 2 mCi of thallium-201 is administered intravenously. Five minutes after thallium administration, initial images at different planes are obtained with the gamma camera. Images in the same planes are obtained 2 to 4 hours later. This test can be evaluated semiquantitatively by the number of segments with redistribution defects and their severity.41 To improve the predictive value of the test, images can be obtained after 24 hours to identify very late redistribution defects, lung uptake, left ventricular cavity dilation, and redistribution defect size. Large redistribution defects, defects in ≥ 2 coronary territories, or increased lung uptake are considered high-risk results. A new technique for imaging in DTS is single photon mission computerized tomography (SPECT). Adenosine can also be used for coronary vasodilation instead of dipyridamole. DTS is not suitable for patients with bronchospasm, critical carotid stenosis, or a condition that prevents their being withdrawn from theophylline preparations.

DSE

In this test the oxygen consumption of the heart is increased by slow and graded infusion of dobutamine to see whether new regional wall motion abnormalities develop. The infusion is continued until 85% of the maximum heart rate for the patient's age is achieved. The maximum predicted heart rate in men is 220 beats/min minus age and in women is 200 beats/min minus age. Dobutamine is infused at 10 μ g/kg body weight per minute for 3 minutes (stage I). The infusion rate is increased by 10 μ g/kg every 3 minutes to a maximum of 40 μ g/kg body weight (stage IV) and continued for 6 minutes. If signs and symptoms of ischemia do not develop during stage IV, atropine is administered in 0.25-mg increments to a maximum of 1 mg while the dobutamine infusion is continued. During the test, the 12-lead ECG is recorded each minute. Blood pressure is monitored with the patient at rest and at each stage of the protocol. The 2-dimensional echocardiogram is monitored continuously and recorded on videotape during the last minute of each stage. A quad-screen video display facilitates side-by-side comparison of rest and stress images. The test is stopped for any of the following: systolic blood pressure decreases greater than 40 mm Hg from the rest value or it is less than 100 mm Hg; severe hypertension $(\geq 240/120 \text{ mm Hg})$; significant tachyarrhythmias; severe chest pain; horizontal or downsloping of ST-segment depression ≥ 0.2 mV measured 80 milliseconds after the J point on ECG; ST segment elevation >0.2 mV; or evidence

of new wall motion abnormalities. Evaluation is based on the severity and number of myocardial segments manifesting new wall motion abnormalities. Patients are at highrisk if new regional wall motion abnormalities are found in \geq 3 regions or at the first stage of the test. The ischemic threshold is the heart rate at which new wall motion abnormalities occur divided by maximal age-related heart rate.

In a systematic review of 28 studies of DSE involving 2,246 patients, sensitivity for detecting CAD was 80% and specificity was 84%. Mean sensitivity for detecting 1-, 2-, and 3-vessel disease was 74%, 86%, and 92%, respectively.46 Investigators who verified the prediction of multi-vessel disease by echocardiography consistently reported a high specificity (range 90%-100%). However, the sensitivity of predicting multi-vessel disease decreased and varied from 8% to 71%. Low sensitivity with high specificity is not surprising when the criteria are stringent; that is, as a greater number of abnormal segments are set as the threshold for diagnosis. In the review, only 1 in approximately 2,000 patients had serious complications, such as ventricular fibrillation or MI. In another retrospective review of the charts of 90 patients with an AAA \geq 4 cm, DSE was safe and no patient suffered aneurysmal rupture.47 DSE is contraindicated in patients with severe hypertension or arrhythmias. When echocardiographic image quality is likely to be poor, as in patients with chronic obstructive pulmonary disease, DTS may be preferred.

In a meta-analysis of the usefulness of 4 preoperative tests to predict adverse cardiac outcomes after vascular surgery, the measure of predictive value was used as relative risk (Fig 2).¹³ Relative risk is the probability of a cardiac event when a test result is positive divided by the probability of an event when the test result is negative. A value greater than 1 implies predictive ability. The median relative risk and 95% confidence intervals (CIs) for the 4 tests are shown in Table 3. Although the DSE test appears to be the best of the 4, the data do not allow selection of an optimal test because of overlapping CIs.

In another meta-analysis of DTS and DSE, the odds ratio was used as a measure of the predictive value of the tests.⁴⁸ Again, an odds ratio greater than 1 implies predictive ability. The odds ratio for DTS was 3.9 (95% CI 2.5 to 5.6) and for DSE was 14.4 (95% CI 5.3 to 39.2). Pretest probability of coronary disease correlated with positive predictive value of the tests.

Table 4 summarizes the results of 4 studies published after 1994 that evaluated the usefulness of noninvasive tests to predict adverse cardiac outcomes after vascular surgery.⁴⁹⁻⁵² Test factors such as availability at a center, experience with interpretation, and limitations or contraindications also influence the choice of a test before vascular surgery. The expertise of the local laboratory in identifying advanced CAD is perhaps more important than the type of test.

Some investigators recommend testing only for symptomatic patients.⁵³⁻⁵⁶ An economic analysis of DTS for screening before aortic and infrainguinal surgical procedures in preventing 30-day postoperative cardiac death or MI yielded a cost-effectiveness ratio of \$392,253 per life saved and \$181,039 per MI averted. The investigators concluded that risk stratification with dipyridamole-thallium scanning may not be justified given the current trends of health care reform.⁵⁶

Although ambulatory echocardiography is a simple test, the value of the test is limited because of the high percentage of patients with baseline ECG abnormalities that obscure the diagnosis of myocardial ischemia. The diagnosis may be obscured by left ventricular hypertrophy with "strain," bundle branch block, pacemakers, the effects of digoxin, or nonspecific ST-segment changes caused by changes in body temperature, serum electrolytes, ventilation, or body position. Determination of systolic left ventricular function may provide prognostic information because of the association of CHF with morbid postoperative events. Radionuclide ventriculography can define systolic and diastolic function.⁴³ If ejection fraction does not increase at least 5% with exercise, myocardial ischemia is indicated.

Investigators are becoming aware that poor diastolic dysfunction is also a problem, particularly for hypertensive patients. Recently, radionuclide ventriculography has been supplanted by transthoracic echocardiography, which shows cardiac structure as well as function. In a prospective study of 250 consecutive patients, transthoracic 2-dimensional echocardiography predicted adverse cardiac outcomes in 9.2% of patients after vascular surgery.57 Using an ejection fraction less than 50%, the following estimates were made for predictive ability of the test: relative risk 10.03, odds ratio 13.4, likelihood for positive test 3.7, and likelihood for a negative test, 0.27. In other studies echocardiographic measurements had limited prognostic value for assessment of cardiac risk and suboptimal operating characteristics.58 Two-dimensional echocardiography is useful in patients with CHF or a history of CHF. The guidelines of the AHA do not recommend echocardiography as a routine test for cardiac risk stratification.14

Mangano et al⁵⁹ and Baron et al,⁶⁰ have challenged the usefulness of DTS for routine preoperative screening of patients undergoing vascular surgery. If one applies Bayes' theory to diagnostic testing, noninvasive testing is most beneficial for patients judged to be at moderate risk based on history and physical examination. According to Eagle's algorithm,⁶¹ patients are stratified into 3 classes by Q waves on ECG, history of ventricular ectopic activity, diabetes, age greater than 70, and angina. With none of these factors, a patient is at low risk; with 1 or 2 risk factors, at intermediate risk; and with 3 or more risk factors, at high risk. Eagle suggested that DTS is most beneficial for patients at intermediate risk. In patients at high risk, cardiac complications are expected, irrespective of test results.

Patients with 2 or more risk factors benefited from SPECT and DTS, which had greater predictive value than

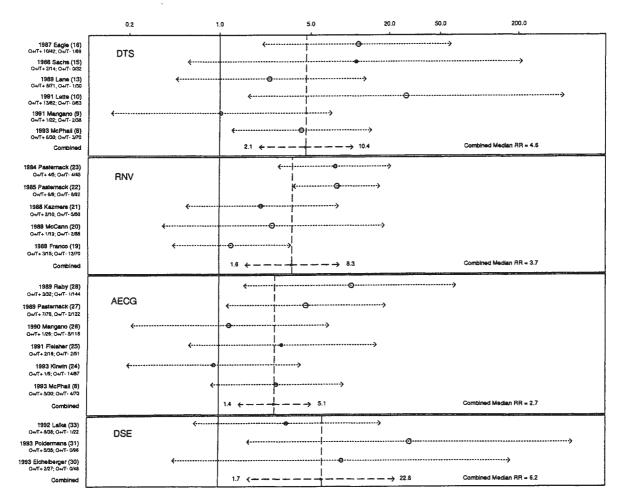


Figure 2. Meta-analysis of studies with no myocardial revascularization procedures before vascular surgery. Relative risk (RR) with 95% CIs for adverse cardiac outcome (cardiac death or MI) after vascular surgery in studies of 4 preoperative tests: DTS, ejection fraction estimation by radionuclide ventriculography (RNV), ambulatory electro-cardiography (AECG), and DSE. The center of the circle represents the point estimate of RR The area of a circle is proportional to the study sample size for the respective test group. The vertical solid line represents a RR of 1; outcome is similar whether the test result is positive or negative. The vertical interrupted line represents the combined median RR for the studies. Final conclusions were based on the data shown in this figure. O+, outcome positive; O-, outcome negative; T+, test positive; T-, test negative. Outcome refers to cardiac death or MI. Please note: The authors and citation numbers described in this figure refer to those cited in the original article. (Reprinted with permission from Mantha S, Roizen MF, Barnard J, et al: Relative effectiveness of four preoperative tests for predicting adverse cardiac outcome after vascular surgery: A meta-analysis. Anesth Analg 79:422-433, 1994.¹³)

echocardiographic or clinical evaluation.⁵¹ The risk factors were age \geq 70; history of MI, angina, CHF, or diabetes mellitus; hypertension with severe left ventricular hypertrophy; and Q waves or ischemic ST-segment abnormalities on ECG at rest.⁵¹ Eagle's criteria were also successfully applied to stratify risk when combined with DSE results.⁶²

In another Bayesian model of cardiac risk assessment⁶³ in a cohort of 1,081 vascular surgery patients, risk scores were developed using logistic regression analysis for clinical variables: age more than 70, angina, history of MI, diabetes mellitus, history of CHF and prior myocardial revascularization. A second model was developed using reversible defects, fixed defects, and ST changes after DTS

Table 3.	Median	Relative	Risk	of a	Meta-Analysis
of 4 Tests	5				

Test (No. of Studies)	Median Relative Risk (95% CI)
Ambulatory EKG (6) Radionuclide	2.7 (1.4-5.1)
ventriculography (5) DTS (6) DSE (3)	$\begin{array}{c} 3.7 \ (1.6\text{-}8.3) \\ 4.6 \ (2.1\text{-}10.4) \\ 6.2 \ (1.7\text{-}22.8) \end{array}$

Data from Mantha et al.13

		N. C	Quality	Death		Prevalence of Positive Criteria	n	Odds		lihood atio
Study (yr)	Test	No. of Patients	of Study*	or MI (%)	Criterion	(%)	Relative Risk	Ratio	Pos	Neg
Marshall et al (1995) ⁴⁹	Adenosine thallium scan	117	Weak	10.2	>1 reversible defect in 1 segment	30.8	3.15	3.67	2.11	0.58
Poldermans et al (1995) ⁵⁰	DSE	300	Fair	5.7	New RWMA in 1 segment	24.0	109.8†	144.1†	5.15	0
Vanzetto et al (1996) ⁵¹	SPECT-DTS	134	Strong	9	>1 reversible defect in 1 segment	35.8	19.7	25.3	3.02	0.12
Landesberg et al (1997) ⁵²	Preoperative 12- lead EKG	405	Fair	4.7	LVH by voltage criteria or ST-segment depression	33.1	7.6	8.4	2.56	0.30

Table 4. Noninvasive Tests to Predict MI and Cardiac Death After Vascular Surgery

Abbreviations: RWMA, regional wall motion abnormalities; LVH, left ventricular hypertrophy; Pos, positive; Neg, negative.

* As defined by the American College of Physicians.15

+ Value after 0.5 was added to all the cells because of a zero event in those with a negative test result. Without the correction the relative risk and odds ratio would be infinite.

tests. These models were validated in a separate set of patients by comparing event rates with risk estimates and by performing ROC analysis. The postoperative cardiac event rate was 8% for both sets. By the clinical model, the observed rates were 3%, 8%, and 18% for patients classified as at low, moderate, or high risk, respectively, by clinical risk factors. The addition of data from DTS tests reclassified more than 80% of patients from moderate-tolow (3%) or high (19%) risk. No reclassification was provided for patients at low or high risk.

Neural networks also are being considered for predicting outcomes. Neural networks are computer programs based on the principles of artificial intelligence and are typically used to model variable interactions and nonlinear relationships. When neural network scores were computed based on cardiac risk factors and DTS results and then converted into likelihood ratios for risk in 514 patients, the networks successfully estimated perioperative risk with better calibratio than comparable logistic regression models.⁶⁴

Perioperative Strategies in Patients at Moderate and High Risk

Patients at highest risk on the basis of noninvasive testing often undergo preoperative coronary revascularization as discussed later. For patients identified as having moderate risk for cardiac events after clinical stratification and selective testing, risk-reducing strategies are put in place. Perioperative beta-adrenergic blockade may be the most efficacious drug therapy for ischemia prophylaxis. The strategies may include drug therapy to prevent myocardial ischemia, invasive monitoring, stress-reducing anesthetic techniques, or a prolonged stay in the intensive care unit. When 200 patients were randomly allocated to receive either atenolol (n = 99) or placebo (n = 101) at least 30 minutes before and for 7 days after noncardiac surgery, mortality was significantly lower among the atenololtreated patients. Rates were 0% versus 8% (P < .001) 6 months after discharge, 3% versus 14%, (P = .005) after 1 year, 10% versus 21%, (P = .019) after 2 years. The principal effect was a reduction in deaths from cardiac causes during the first 6 to 8 months.65 Event-free survival throughout the 2-year study period was 68% in the placebo group and 83% in the atenolol group (P = .008). Incidence and severity of myocardial ischemia as assessed by Holter monitoring was reduced because of atenolol therapy.66 β-adrenergic blockers, like atenolol, reduce perioperative myocardial ischemia by controlling heart rate and improving myocardial oxygen supply-demand balance. More recently, perioperative beta-blockade therapy with bisoprolol significantly reduced affected 30-day mortality and MI in high-risk patients undergoing vascular surgery. Of 59 patients given bisoprolol, 2 (3.4%) died (both of cardiac causes), of 53 patients given standard care, 9 (17%, P = .02) died. There were 9 (17%) nonfatal MIs after standard care and none in the bisoprolol group (P <.001).67

The benefits of the α_2 -adrenergic agonist clonidine for controlling perioperative cardiovascular complications were evaluated in a double-blind, randomized, placebocontrolled trial.⁶⁸ The treatment group (n = 30) received premedication with transdermal clonidine (0.2 mg/d) the night before surgery. Clonidine reduced enflurane requirements, intraoperative tachycardia, and myocardial ischemia. In another double-blind, randomized, controlled trial in hypertensive patients who had abdominal aortic reconstruction, the treatment group (n = 11) received 6 µg/kg clonidine orally 120 minutes before induction and 3 µg/kg as an infusion over 60 minutes after complete circulatory stabilization from aortic declamping up to skin closure. Clonidine reduced anesthetic requirements and improved circulatory stability.⁶⁹

When the relationship between body temperature and perioperative cardiac morbidity was evaluated in a randomized controlled trial of 300 patients, perioperative maintenance of normothermia was associated with a reduced incidence of morbid cardiac events and ventricular tachycardia.⁷⁰ Spinal or epidural anesthetic techniques alone or combined with general anesthesia had several beneficial effects and improved outcome.⁷¹ In vascular

Study (yr)	Perioperative Intervention	No. of Patients	Level of Evidence	Reduced
Ellis et al (1994) ⁶⁸	Clonidine oral and transdermal	61	Level II	Enflurane requirements, intraoperative tachycardia, and myocardial ischemia
Mangano et al (1996) ⁶⁵	Atenolol	200	Level I	In-hospital mortality and incidence of long-term cardiac event
Quintin et al (1996) ⁶⁹	Clonidine—oral and intravenous*	21	Level II	Anesthetic requirements and circulatory instability
Frank et al (1997) ⁷⁰	Maintenance of normothermia	300	Level I	Incidence of morbid cardiac events and ventricular tachycardia
Poldermans et al (1999) ⁶⁷	Bisoprolol	112	Level I	Incidence of MI 30 days postoperatively and cardiac-related death

Table 5. Randomized Controlled Trials Evaluating Perioperative Cardiovascular Risk-Reducing Strategies in PatientsUndergoing Noncardiac Surgery

* In hypertensive patients undergoing vascular surgery.

surgery patients, there were beneficial effects on preload, afterload, coronary circulation, and adrenergic stress response; thromboembolic events were fewer.⁷²⁻⁷⁴ Unfortunately, improvement in cardiac outcomes was not shown. To evaluate the impact of anesthetic choice on overall mortality, MI, angina, and CHF, 423 patients, scheduled for femoral distal bypass graft surgery, were randomly assigned to receive general (n = 138), spinal anesthesia (n = 136), or epidural (n = 149) anesthesia. Complications after the 3 different anesthetics were comparable. The investigators concluded that anesthetic technique does not greatly influence cardiac morbidity in patients undergoing femoral distal bypass graft surgery.⁷⁵

Preoperative normalization of hemodynamic variables and hemodynamic monitoring with a pulmonary artery catheter (PAC) have been suggested as a means to improve outcomes. Preoperative admission to a surgical intensive care unit and hemodynamic monitoring using PAC were evaluated in patients who had extremity vascular surgery. Incidence of mortality, cardiovascular morbidity, and early graft occlusion was lower in patients monitored with PAC than with central venous pressure monitors.

However, patients monitored with PAC also received nitroglycerin and volume loading (which may reduce morbidity from vascular surgery), whereas the others did not. Bias may have affected diagnosis and treatment because the investigators were not blinded to the study groups.76 The prophylactic use of nitrates in this study may have contributed more to improved outcome than did the use of PACs. In a retrospective analysis of the effects of preoperative intensive care unit admission and invasive hemodynamic monitoring, including PAC, patients whose hemodynamic variables were normal or abnormal but normalized preoperatively experienced significantly fewer cardiovascular complications than those with abnormal hemodynamic variables.77 The patients had noncardiac surgery, and CAD was documented by history and cardiac imaging. PAC did not reduce the incidence of cardiac, renal, or other complications in another group of patients who had aortic surgery, and intraoperative complications were greater than PAC.⁷⁸ Even when CAD is documented, PAC should be reserved for the approximately 25% of patients with the most severe comorbidity. These conditions may include severe left ventricular dysfunction (ejec-

Table 6. C	Cardiac Risk	Stratification and	d Interventions i	n Patients S	Scheduled f	or Elective	Vascular Surgery
------------	--------------	--------------------	-------------------	--------------	-------------	-------------	------------------

Presentation	Interventions	Strength of Recommendation*
Unstable angina, recent MI ⁺ , decompensated CHF, significant arrhythmias (any one)	Coronary angiography ¹⁴	Class I
Mild angina pectoris, prior MI, compensated CHF or prior CHF, diabetes mellitus (1 or 2)	Noninvasive test by DTS or DSE14	Class I
Strongly positive results on DTS or DSE	Coronary angiography ¹⁴	Class I
Intermediate-risk results on DTS or DSE	Coronary angiography ¹⁴	Class II
"Critical" CAD or left main disease, $EF < 35\%$	CABG ^{14,25}	Class I
Documented CAD by clinical or noninvasive testing, and surgery without CABG first	Atenolol therapy or additional thermal care or both ^{65,70}	Class I

Abbreviation: EF, ejection fraction.

* Class I, conditions for which there is evidence and/or general agreement that a procedure be performed or a treatment is beneficial; Class II, conditions for which there is a divergence of evidence and/or opinion about the treatment.

† Recent MI, greater than 7 days but ≤ 1 month.

tion fraction 25%-30%), renal failure, diabetes mellitus with autonomic neuropathy, severe cor pulmonale and pulmonary hypertension. Table 5 summarizes the cardio-vascular risk-reducing interventions that have been tested by randomized controlled trials. Ultimately, the choice of risk-reducing strategies depends on the surgical procedure, the discretion of the anesthesiologist and surgeon, and institutional protocols (clinical pathways).

Myocardial Revascularization

The second goal of cardiac risk stratification is to determine which patients should undergo myocardial revascularization. Decision analysis was used to determine the need for coronary angiography and revascularization before noncardiac vascular surgery in patients who had no or mild angina or mild angina and a positive result on dipyridamole-thallium scan. Proceeding directly to vascular surgery without angiography led to lower morbidity, lower cost, and better outcomes.⁷⁹ The investigators suggested that coronary angiography be reserved for patients whose estimated mortality from vascular surgery is substantially higher than average. In another study of patients before abdominal aortic surgery, the investigators came to a similar conclusion: in patients with low probability of CAD, vascular surgery should be performed without cardiac screening.⁸⁰ That analysis shows the importance of local factors, particularly an institution's mortality rates after myocardial revascularization versus those after vascular surgery, in determining preoperative strategy. See Table 6.

When interpreting studies of preoperative coronary revascularization before vascular surgery, the time frame for analysis must be considered. If the time for analysis is anywhere from 30 days to 3 months, risk stratification and coronary revascularization may prove neither "effective" nor "cost-effective." Investigators who do not favor aggressive cardiac risk stratification and coronary revascularization argue that the current state of surgical, anesthetic, and perioperative care has reduced cardiac morbidity sufficiently to dispense with preoperative interventions. Those who favor aggressive risk stratification and myocardial revascularization argue that CAD represents a lifetime risk, and preoperative intervention affords an advantage for long-term survival. There is evidence that when results on DTS or DSE were positive, patients had more cardiac events after surgery than when results are negative.^{24,26,28-30,62} Therefore, the key factor is to identify the subgroup of patients with peripheral vascular disease who would receive long-term benefit from myocardial revascularization. Patients with critical 3-vessel CAD, left main arterial disease, or poor left ventricular function have been identified as such subgroups.25 A concordance between preoperative clinical risk and severity of CAD on angiography was found in patients who had vascular surgery.81 A simple algorithm based on history of angina, MI, CHF, or diabetes mellitus is proposed to exclude critical coronary

stenosis. See Fig 3. Critical stenosis is considered to be present when 3-vessels have $\geq 70\%$ stenosis in each or $\geq 70\%$ in the left main artery. The absence of critical stenosis can be predicted with 94% accuracy for those who do not have the risk factors.

Finally, cardiac risk stratification may guide the choice of surgical procedure in patients with severe inoperable CAD; a conservative surgical approach, such as limb amputation, may be planned in such patients.⁷⁹

The Limitations of Risk Stratification

Despite an enormous amount of literature on cardiac risk stratification for vascular surgery patients, the conclusions drawn in the studies vary and preclude definite recommendations. The difference in conclusions can be attributed to differences in the following factors: pretest selection criteria, pretest probability of CAD, experience in the interpretation of noninvasive screening tests, criteria for selecting patients for coronary angiography after initial screening with noninvasive tests, perioperative care, and different morbidity and mortality rates for myocardial revascularization at different institutions. Information from large databases, like the Medicare claims database, also failed to provide reliable answers. For example, Fleisher et al⁸² studied a 5% random sample of the Medicare population to identify a cohort of patients who had elective infrainguinal or abdominal aortic reconstruction surgery during an 18-month period. Thirty-day (perioperative) and 1-year mortality rates were reviewed with respect to preoperative testing and coronary revascularization. Mortality in the perioperative period was significantly greater after aortic surgery (209 of 2,865 or 7.3%) than after infrainguinal surgery (232 of 4,030 or 5.8%); however, mortality after 1 year was significantly greater after infrainguinal surgery (16.3% v 11.3%, P < .05). Stress testing, with or without coronary revascularization, was associated with improved survival after aortic surgery. Stress testing with coronary revascularization did not reduce perioperatively mortality after infrainguinal surgery, but stress testing alone did reduce mortality after 1 year. MI and cardiac-related mortality need not necessarily be caused by previously severely narrowed coronary arteries. Recent evidence suggests that the rupture of previously nonocclusive lipid-laden, macrophage-rich, coronary plaques can cause spasm and initiate unstable angina, acute MI, and sudden death. Therefore, testing that attempts to induce ischemia will miss some patients who have nonobstructive plaques that can rupture and cause transmural infarction.83

In 1996, the AHA and the ACC proposed guidelines for perioperative cardiovascular evaluation before noncardiac surgery.¹⁴ Table 3 summarizes the guidelines for vascular surgery patients. Bartels et al⁸⁴ followed these guidelines and evaluated their benefit for 203 patients scheduled for aortic surgery. The incidence of cardiac-related mortality and morbidity (MI, CHF, unstable angina, or arrhythmias) was 1% and 12.4%, respectively. They concluded that the

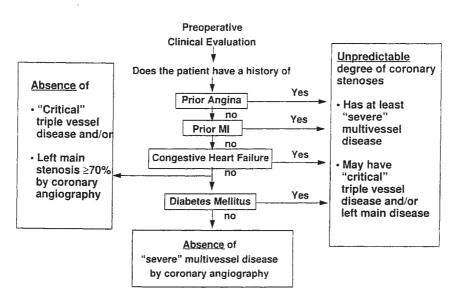


Figure 3. Clinical prediction rules. For excluding critical 3-vessel disease ($\geq 70\%$ stenosis in each) and/or left main stenosis $\geq 70\%$, the clinical history must exclude the first 3 markers. The presence of any one of these 3 markers makes the coronary angiogram unpredictable. To exclude severe multi-vessel disease, all 4 markers must be absent. With the presence of any of the 4 markers, one can make a reasonable prediction for the presence of severe coronary disease. "Severe" stenosis was defined as 3-vessel disease ($\geq 50\%$ stenosis in each), 2-vessel ($\geq 50\%$ stenosis in one when the other is $\geq 70\%$ stenosis of the left anterior descending), or left main disease ($\geq 50\%$). With the help of this algorithm, the absence of "critical" stenoses can be predicted with a positive predictive value of 96% and the absence of "severe" stenoses can be predicted with a positive predictive value of 96% and the absence of "severe" stenoses can be predicted with a positive predictive value of 94\%. (Reprinted with permission from Paul SD, Eagle KA, Kuntz KM, et al: Concordance of preoperative clinical risk with angiographic severity of coronary artery disease in patients undergoing vascular surgery. Circulation 94:1561-1566, 1996.⁸¹)

protocol was a safe strategy for preoperative evaluation before vascular surgery. In a recent decision analysis model, the long-term outcomes (5-year survival) and costeffectiveness for 1 of 3 possible cardiac screenings were reviewed in patients scheduled to undergo elective AAA repair.85 In the first strategy, all patients were screened with a dipyridamole-thallium test. In the second, all patients underwent coronary angiography. In the third, selective screening divided patients into high-, intermediate-, and low-risk groups by clinical criteria. High-risk patients underwent preoperative angiography. Patients at intermediate risk were screened noninvasively, and patients at low risk proceeded directly to surgery without further testing. Proceeding directly to vascular surgery resulted in the poorest 5-year survival rate, 77.4%. The rate with preoperative risk stratification followed by selective coronary revascularization and routine noninvasive testing was 86.1%; with selective testing, 86.0%; and with routine angiography, 87.9%. The incremental cost-effectiveness ratio for selective testing was significantly lower than for routine angiography (\$44,800/year of life saved [YLS] v \$93,300/ YLS; P < .02). Routine noninvasive testing was not costeffective. The investigators concluded that selective screening before vascular surgery may improve 5-year survival and be cost-effective.

The range of options for preoperative coronary revascularization continues to expand rapidly. The options include traditional surgical revascularization (CABG),

transmyocardial laser therapy, PTCA, excimer laser, rotablader, coronary stent placement, and endoscopic CABG. However, mortality rates associated with CABG are 2.4-fold higher in patients with peripheral vascular disease (7.7% v3.2%) than in patients without.³² Greater complication rates can be anticipated for the newer revascularization techniques when they are performed in patients with peripheral vascular disease.³¹ Patients who survive PTCA before vascular surgery do well.36 However, complications associated with PTCA are significant: emergency CABG, MI, early and late occlusion, and the need for chronic anticoagulation. If myocardial revascularization is indicated in a patient with diabetes, CABG is preferred to PTCA because of better long-term prognosis and less need for reinterventions.86 Once the patient has recovered from successful coronary revascularization (typically 1 week after angioplasty and 6-8 weeks after CABG), peripheral vascular surgery is performed. In some cases CABG can be combined with vascular surgery, most commonly with carotid endarterectomy. Elective AAA repair should probably be performed before, with, or within 2 weeks of CABG because of increased risk of aneurysm rupture after this period.87

Conclusion

The use of evidence-based medicine and Bayesian analysis can provide a rational framework for choosing diagnostic strategies and evaluating choices for therapeutic options in vascular surgery patients with suspected CAD. This framework must be evaluated in light of patient preferences and institutional resources and expertise. This calculus may change in the future, as vascular surgery (eg, endovascular), coronary revascularization, and medical comorbidities (eg, CHF) are managed with lower risks.

References

- Hertzer NR, Beven EG, Young JR, et al: Coronary artery disease in peripheral vascular patients. A classification of 1000 coronary angiograms and results of surgical management. Ann Surg 199:223-233, 1984
- Hertzer NR: Basic data concerning associated coronary disease in peripheral vascular patients. Ann Vasc Surg 1:616-620, 1987
- Gajraj H, Jamieson CW: Coronary artery disease in patients with peripheral vascular disease. Br J Surg 81:333-342, 1994
- 4. Mantha S, Fleisher LA, Roizen MF, et al: Cost-effectiveness and benefit of preoperative work-up and preparation for vascular surgery, in Youngberg JA (ed): Cardiac, Vascular, and Thoracic Anesthesia. New York, NY, Churchill Livingstone, 2000, pp 20-40
- Wong T, Detsky AS: Preoperative cardiac risk assessment for patients having peripheral vascular surgery. Ann Intern Med 116:743-753, 1992
- Fleisher LA, Mantha S, Roizen MF: Medical technology assessment: An overview. Anesth Analg 87:1271-1282, 1998
- Fleisher LA, Mantha S: Technology assessment and determination of cost-effectiveness. Prob Anesth 10:293-303, 1998
- Goodman NW: Anaesthesia and evidence-based medicine. Anaesthesia 53:353-368, 1998
- Kupersmith J, Holmes-Rovner M, Hogan A, et al: Cost-effectiveness analysis in heart disease, Part I: General principles. Prog Cardiovasc Dis 37:161-184, 1994
- Watcha MF, White PF: Economics of anesthetic practice. Anesthesiology 86:1170-1196, 1997
- Bayazit M, Gol MK, Battaloglu B, et al: Routine coronary arteriography before abdominal aortic aneurysm repair. Am J Surg 170:246-250, 1995
- Mangano DT: Perioperative cardiac morbidity. Anesthesiology 72:153-184, 1990
- Mantha S, Roizen MF, Barnard J, et al: Relative effectiveness of four preoperative tests for predicting adverse cardiac outcomes after vascular surgery: A meta-analysis. Anesth Analg 79:422-433, 1994
- 14. Eagle KA, Brundage BH, Chaitman BR, et al: Guidelines for perioperative cardiovascular evaluation for noncardiac surgery. Report of the American College of Cardiology/ American Heart Association Task Force on Practice Guidelines. Committee on Perioperative Cardiovascular Evaluation for Noncardiac Surgery. Circulation 93:1278-1317, 1996
- Palda VA, Detsky AS: Perioperative assessment and management of risk from coronary artery disease. Ann Intern Med 127:313-328, 1997
- Krupski WC, Layug EL, Reilly LM, et al: Comparison of cardiac morbidity between aortic and infrainguinal operations. Study of Perioperative Ischemia (SPI) Research Group. J Vasc Surg 15:354-363, 1992

- Wilke HJ, II, Ellis JE, McKinsey JF: Carotid endarterectomy: Perioperative and anesthetic considerations. J Cardiothorac Vasc Anesth 10:928-949, 1996
- Rihal CS, Gersh BJ, Whisnant JP, et al: Influence of coronary heart disease on morbidity and mortality after carotid endarterectomy: A population-based study in Olmsted County, Minnesota (1970-1988). J Am Coll Cardiol 19:1254-1260, 1992
- Roger VL, Ballard DJ, Hallett JW, Jr, et al: Influence of coronary artery disease on morbidity and mortality after abdominal aortic aneurysmectomy: A population-based study, 1971-1987. J Am Coll Cardiol 14:1245-1252, 1989
- Krupski WC, Layug EL, Reilly LM, et al: Comparison of cardiac morbidity rates between aortic and infrainguinal operations: Two-year follow-up. Study of Perioperative Ischemia Research Group. J Vasc Surg 18:609-615, 1993
- 21. Dawson I, van Bockel JH, Brand R: Late nonfatal and fatal cardiac events after infrainguinal bypass for femoropopliteal occlusive disease during a thirty-one-year period. J Vasc Surg 18:249-260, 1993
- 22. Farkouh ME, Rihal CS, Gersh BJ, et al: Influence of coronary heart disease on morbidity and mortality after lower extremity revascularization surgery: A population-based study in Olmsted County, Minnesota (1970-1987). J Am Coll Cardiol 24: 1290-1296, 1994
- Yeager RA, Moneta GL, Edwards JM, et al: Late survival after perioperative myocardial infarction complicating vascular surgery. J Vasc Surg 20:598-606, 1994
- 24. L'Italien GJ, Cambria RP, Cutler BS, et al: Comparative early and late cardiac morbidity among patients requiring different vascular surgery procedures. J Vasc Surg 21:935-944, 1995
- Rihal CS, Eagle KA, Mickel MC, et al: Surgical therapy for coronary artery disease among patients with combined coronary artery and peripheral vascular disease. Circulation 91:46-53, 1995
- 26. Stratmann HG, Younis LT, Wittry MD, et al: Dipyridamole technetium-99m sestamibi myocardial tomography in patients evaluated for elective vascular surgery: Prognostic value for perioperative and late cardiac events. Am Heart J 131:923-929, 1996
- 27. Koskas F, Kieffer E: Long-term survival after elective repair of infrarenal abdominal aortic aneurysm: Results of a prospective multicentric study. Association for Academic Research in Vascular Surgery (AURC). Ann Vasc Surg 11:473-481, 1997
- Poldermans D, Arnese M, Fioretti PM, et al: Sustained prognostic value of dobutamine stress echocardiography for late cardiac events after major noncardiac vascular surgery. Circulation 95:53-58, 1997
- Landesberg G, Wolf Y, Schechter D, et al: Preoperative thallium scanning, selective coronary revascularization, and longterm survival after carotid endarterectomy. Stroke 29:2541-2548, 1998
- 30. Cohen MC, Curran PJ, L'Italien GJ, et al: Long-term prognostic value of preoperative dipyridamole thallium imaging and clinical indexes in patients with diabetes mellitus undergoing peripheral vascular surgery. Am J Cardiol 83:1038-1042, 1999
- Muller DW, Shamir KJ, Ellis SG, et al: Peripheral vascular complications after conventional and complex percutaneous coronary interventional procedures. Am J Cardiol 69:63-68, 1992
- Birkmeyer JD, O'Connor GT, Quinton HB, et al: The effect of peripheral vascular disease on in-hospital mortality rates with

coronary artery bypass surgery. Northern New England Cardiovascular Disease Study Group. J Vasc Surg 21:445-452, 1995

- Galland RB: Preoperative cardiac assessment in patients with peripheral vascular disease: Is it worthwhile? Eur J Vasc Endovasc Surg 18:466-468, 1999
- 34. Gersh BJ, Rihal CS, Rooke TW, et al: Evaluation and management of patients with both peripheral vascular and coronary artery disease. J Am Coll Cardiol 18:203-214, 1991
- 35. Eagle KA, Rihal CS, Mickel MC, et al: Cardiac risk of noncardiac surgery: Influence of coronary disease and type of surgery in 3368 operations. CASS Investigators and University of Michigan Heart Care Program. Coronary Artery Surgery Study. Circulation 96:1882-1887, 1997
- 36. Gottlieb A, Banoub M, Sprung J, et al: Perioperative cardiovascular morbidity in patients with coronary artery disease undergoing vascular surgery after percutaneous transluminal coronary angioplasty. J Cardiothorac Vasc Anesth 12:501-506, 1998
- Hollenberg SM: Preoperative cardiac risk assessment. Chest 115:51S-57S, 1999 (suppl)
- Kupersmith J, Holmes Rovner M, Hogan A, et al: Cost-effectiveness analysis in heart disease, Part III: Ischemia, congestive heart failure, and arrhythmias. Prog Cardiovasc Dis 37:307-346, 1995
- Sackett DL, Haynes RB, Guyatt GH, et al: Clinical Epidemiology: A Basic Science for Clinical Medicine. Boston, MA, Little Brown, 1991
- Fleisher LA, Barash PG: Preoperative cardiac evaluation for noncardiac surgery: A functional approach. Anesth Analg 74:586-598, 1992
- 41. Lette J, Waters D, Lassonde J, et al: Multivariate clinical models and quantitative dipyridamole-thallium imaging to predict cardiac morbidity and death after vascular reconstruction. J Vasc Surg 14:160-169, 1991
- 42. Fleisher LA, Beattie C: Current practice in the preoperative evaluation of patients undergoing major vascular surgery: A survey of cardiovascular anesthesiologists. J Cardiothorac Vasc Anesth 7:650-654, 1993
- Fleisher LA, Hulyalkar A: Cardiovascular testing for the 1990s. Adv Anesth 11:27-64, 1994
- Berman DS, Germano G, Shaw LJ: The role of nuclear cardiology in clinical decision making. Semin Nucl Med 29:280-297, 1999
- Travain MI, Wexler JP: Pharmacological stress testing. Semin Nucl Med 29:298-318, 1999
- Geleijnse ML, Fioretti PM, Roelandt JR: Methodology, feasibility, safety and diagnostic accuracy of dobutamine stress echocardiography. J Am Coll Cardiol 30:595-606, 1997
- 47. Pellikka PA, Roger VL, Oh JK, et al: Safety of performing dobutamine stress echocardiography in patients with abdominal aortic aneurysm > or = 4 cm in diameter. Am J Cardiol 77:413-416, 1996
- 48. Shaw LJ, Eagle KA, Gersh BJ, et al: Meta-analysis of intravenous dipyridamole-thallium-201 imaging (1985 to 1994) and dobutamine echocardiography (1991 to 1994) for risk stratification before vascular surgery. J Am Coll Cardiol 27:787-798, 1996
- Marshall ES, Raichlen JS, Forman S, et al: Adenosine radionuclide perfusion imaging in the preoperative evaluation of patients undergoing peripheral vascular surgery. Am J Cardiol 76:817-821, 1995
- 50. Poldermans D, Arnese M, Fioretti PM, et al: Improved cardiac

risk stratification in major vascular surgery with dobutamineatropine stress echocardiography. J Am Coll Cardiol 26:648-653, 1995

- 51. Vanzetto G, Machecourt J, Blendea D, et al: Additive value of thallium single-photon emission computed tomography myocardial imaging for prediction of perioperative events in clinically selected high cardiac risk patients having abdominal aortic surgery. Am J Cardiol 77:143-148, 1996
- 52. Landesberg G, Einav S, Christopherson R, et al: Perioperative ischemia and cardiac complications in major vascular surgery: Importance of the preoperative twelve-lead electrocardiogram. J Vasc Surg 26:570-578, 1997
- 53. D'Angelo AJ, Puppala D, Farber A, et al: Is preoperative cardiac evaluation for abdominal aortic aneurysm repair necessary? J Vasc Surg 25:152-156, 1997
- 54. Itani KM, Miller CC, Guinn G, et al: Preoperative cardiac evaluation is unnecessary in most patients undergoing vascular operations. Am J Surg 176:671-675, 1998
- 55. Roghi A, Palmieri B, Crivellaro W, et al: Preoperative assessment of cardiac risk in noncardiac major vascular surgery. Am J Cardiol 83:169-174, 1999
- 56. Bry JD, Belkin M, O'Donnell TF, Jr, et al: An assessment of the positive predictive value and cost-effectiveness of dipyridamole myocardial scintigraphy in patients undergoing vascular surgery. J Vasc Surg 19:112-121, 1994
- Ouriel K, Green RM, DeWeese JA, et al: Outpatient echocardiography as a predictor of perioperative cardiac morbidity after peripheral vascular surgical procedures. J Vasc Surg 22:671-677, 1995
- Halm EA, Browner WS, Tubau JF, et al: Echocardiography for assessing cardiac risk in patients having noncardiac surgery. Study of Perioperative Ischemia Research Group. Ann Intern Med 125:433-441, 1996
- 59. Mangano DT, London MJ, Tubau JF, et al: Dipyridamole thallium-201 scintigraphy as a preoperative screening test. A reexamination of its predictive potential. Study of Perioperative Ischemia Research Group. Circulation 84:493-502, 1991
- 60. Baron JF, Mundler O, Bertrand M, et al: Dipyridamole-thallium scintigraphy and gated radionuclide angiography to assess cardiac risk before abdominal aortic surgery. N Engl J Med 330:663-669, 1994
- 61. Eagle KA, Coley CM, Newell JB, et al: Combining clinical and thallium data optimizes preoperative assessment of cardiac risk before major vascular surgery. Ann Intern Med 110:859-866, 1989
- Ballal RS, Kapadia S, Secknus MA, et al: Prognosis of patients with vascular disease after clinical evaluation and dobutamine stress echocardiography. Am Heart J 137:469-475, 1999
- 63. L'Italien GJ, Paul SD, Hendel RC, et al: Development and validation of a Bayesian model for perioperative cardiac risk assessment in a cohort of 1,081 vascular surgical candidates. J Am Coll Cardiol 27:779-786, 1996
- Lapuerta P, L'Italien GJ, Paul S, et al: Neural network assessment of perioperative cardiac risk in vascular surgery patients. Med Decis Making 18:70-75, 1998
- 65. Mangano DT, Layug El, Wallace A, et al: Effect of atenolol on mortality and cardiovascular morbidity after noncardiac surgery. Multicenter Study of Perioperative Ischemia Research Group. N Engl J Med 335:1713-1720, 1996
- 66. Wallace A, Layug B, Tateo I, et al: Prophylactic atenolol reduces postoperative myocardial ischemia. McSPI Research Group. Anesthesiology 88:7-17, 1998

- 67. Poldermans D, Boersma E, Bax JJ, et al: The effect of bisoprolol on perioperative mortality and myocardial infarction in high-risk patients undergoing vascular surgery. Dutch Echocardiographic Cardiac Risk Evaluation Applying Stress Echocardiography Study Group. N Engl J Med 341:1789-1794, 1999
- 68. Ellis JE, Drijvers G, Pedlow S, et al: Premedication with oral and transdermal clonidine provides safe and efficacious postoperative sympatholysis. Anesth Analg 79:1133-1140, 1994
- 69. Quintin L, Bouilloc X, Butin E, et al: Clonidine for major vascular surgery in hypertensive patients: A double-blind, controlled, randomized study. Anesth Analg 83:687-695, 1996
- Frank SM, Fleisher LA, Breslow MJ, et al: Perioperative maintenance of normothermia reduces the incidence of morbid cardiac events. A randomized clinical trial. JAMA 277:1127-1134, 1997
- Liu S, Carpenter RL, Neal JM: Epidural anesthesia and analgesia. Their role in postoperative outcome. Anesthesiology 82:1474-1506, 1995
- Tuman KJ, McCarthy RJ, March RJ, et al: Effects of epidural anesthesia and analgesia on coagulation and outcome after major vascular surgery. Anesth Analg 73:696-704, 1991
- 73. Christopherson R, Beattie C, Frank SM, et al: Perioperative morbidity in patients randomized to epidural or general anesthesia for lower extremity vascular surgery. Perioperative Ischemia Randomized Anesthesia Trial Study Group. Anesthesiology 79:422-434, 1993
- 74. Rosenfeld BA, Beattie C, Christopherson R, et al: The effects of different anesthetic regimens on fibrinolysis and the development of postoperative arterial thrombosis. Perioperative Ischemia Randomized Anesthesia Trial Study Group. Anesthesiology 79:435-443, 1993
- Bode RH Jr, Lewis KP, Zarich SW, et al: Cardiac outcome after peripheral vascular surgery. Comparison of general and regional anesthesia. Anesthesiology 84:3-13, 1996
- 76. Berlauk JF, Abrams JH, Gilmour IJ, et al: Preoperative optimization of cardiovascular hemodynamics improves outcome in peripheral vascular surgery. A prospective, randomized clinical trial. Ann Surg 214:289-299, 1991

- 77. Flancbaum L, Ziegler DW, Choban PS: Preoperative intensive care unit admission and hemodynamic monitoring in patients scheduled for major elective noncardiac surgery: A retrospective review of 95 patients. J Cardiothorac Vasc Anesth 12:3-9, 1998
- Valentine RJ, Duke ML, Inmari NH, et al: Effectiveness of pulmonary artery catheters in aortic surgery: A randomized trial. J Vasc Surg 27:230-212, 1998
- Mason JJ, Owens DK, Harris RA, et al: The role of coronary angiography and coronary revascularization before noncardiac vascular surgery. JAMA 273:1919-1925, 1995
- Fleisher LA, Skolnick ED, Holroyd KJ, et al: Coronary artery revascularization before abdominal aortic aneurysm surgery: A decision analytic approach. Anesth Analg 79:661-669, 1994
- Paul SD, Eagle KA, Kuntz KM, et al: Concordance of preoperative clinical risk with angiographic severity of coronary artery disease in patients undergoing vascular surgery. Circulation 94:1561-1566, 1996
- 82. Fleisher LA, Eagle KA, Shaffer T, et al: Perioperative- and long-term mortality rates after major vascular surgery: The relationship to preoperative testing in the medicare population. Anesth Analg 89:849-855, 1999
- Gutstein DE, Fuster V: Pathophysiology and clinical significance of atherosclerotic plaque rupture. Cardiovasc Res 41: 323-333, 1999
- Bartels C, Bechtel JF, Hossmann V, et al: Cardiac risk stratification for high-risk vascular surgery. Circulation 95:2473-2475, 1997
- Glance LG: Selective preoperative cardiac screening improves five-year survival in patients undergoing major vascular surgery: A cost-effectiveness analysis. J Cardiothorac Vasc Anesth 13:265-271, 1999
- 86. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. N Engl J Med 335:217-225, 1996
- Blackbourne LH, Tribble CG, Langenburg SE, et al: Optimal timing of abdominal aortic aneurysm repair after coronary artery revascularization. Ann Surg 219:693-696, 1994