JACC Vol. 27, No. 4
March 15, 1996:779–86

Development and Validation of a Bayesian Model for Perioperative Cardiac Risk Assessment in a Cohort of 1,081 Vascular Surgical Candidates

GILBERT J. L'ITALIEN, PHD, SUMITA D. PAUL, MD, MPH, FACC,
ROBERT C. HENDEL, MD, FACC,* JEFFREY A. LEPPO, MD, FACC,†
MYLAN C. COHEN, MD, MPH, FACC,‡ LEE A. FLEISHER, MD, FACC,§
KENNETH A. BROWN, MD, FACC,‖ STUART W. ZARICH, MD, FACC,‡
RICHARD P. CAMBRIA, MD, BRUCE S. CUTLER, MD,† KIM A. EAGLE, MD, FACC¶

Objectives. **This study sought to develop and validate a Bayesian risk prediction model for vascular surgery candidates.**

Background. **Patients who require surgical treatment of peripheral vascular disease are at increased risk of perioperative cardiac morbidity and mortality. Existing prediction models tend to underestimate risk in vascular surgery candidates.**

Methods. **The cohort comprised 1,081 consecutive vascular surgery candidates at five medical centers. Of these, 567 patients from two centers ("training" set) were used to develop the model, and 514 patients from three centers were used to validate it ("validation" set). Risk scores were developed using logistic regression for clinical variables: advanced age (>70 years), angina, history of myocardial infarction, diabetes mellitus, history of congestive heart failure and prior coronary revascularization. A second model was developed from dipyridamole–thallium predictors of myocardial infarction (i.e., fixed and reversible myocardial defects and ST changes). Model performance was assessed by comparing observed event rates with risk estimates and by performing receiver–operating characteristic curve (ROC) analysis.**

Results. **The postoperative cardiac event rate was 8% for both sets. Prognostic accuracy (i.e., ROC area) was 74 ± 3% (mean ± SD) for the clinical and 81 ± 3% for the clinical and dipyridamole–thallium models. Among the validation sets, areas were 74 ± 9%, 72 ± 7% and 76 ± 5% for each center. Observed and estimated rates were comparable for both sets. By the clinical model, the observed rates were 3%, 8% and 18% for patients classified as low, moderate and high risk by clinical factors ($p < 0.0001$). The addition of dipyridamole–thallium data reclassified >80% of the moderate risk patients into low (3%) and high (19%) risk categories ($p < 0.0001$) but provided no stratification for patients classified as low or high risk according to the clinical model.**

Conclusions. **Simple clinical markers, weighted according to prognostic impact, will reliably stratify risk in vascular surgery candidates referred for dipyridamole–thallium testing, thus obviating the need for the more expensive testing. Our prediction model retains its prognostic accuracy when applied to the validation sets and can reliably estimate risk in this group.**

(J Am Coll Cardiol 1996;27:779–86)

Patients who require surgical treatment of peripheral vascular disease are at increased risk of perioperative cardiac morbidity and mortality related both to the surgical procedure and to concomitant coronary atherosclerosis (1–10). To reduce the incidence of perioperative cardiac events among vascular surgery candidates, clinicians have sought methods to stratify cardiac risk in individual patients. Patient management may thus be influenced by the patient's risk classification. For example, surgical treatment may be deferred or modified to a less invasive therapy in high risk patients. Others, deemed to be at moderate risk of early events, may be further classified into more specific risk categories by conducting diagnostic tests for the detection of coronary disease. Finally, low risk patients might avoid further testing and undergo operation directly, thus reducing cost, test-related morbidity and possible unnecessary coronary angiography.

According to Detsky et al. (11,12) and Eagle and Boucher (13), the first step in the assessment of risk is to consider the average risk of a major perioperative cardiac event among vascular surgery candidates. Factors such as referral patterns, general patient characteristics, surgical expertise and patient management will determine this level of risk for a particular

From the Cardiac Unit, Department of Medicine and Vascular Unit, Department of Surgery, Massachusetts General Hospital, Boston and Harvard Medical School, Cambridge, Massachusetts; †Department of Nuclear Medicine and Department of Vascular Surgery, University of Massachusetts Medical Center, Worcester, Massachusetts; *Divisions of Cardiology and Critical Care, Northwestern University, Chicago, Illinois; ‡Cardiovascular Division and Institute for Prevention of Cardiovascular Disease, Deaconess Hospital, Boston and Harvard Medical School, Cambridge, Massachusetts; §Department of Anesthesiology, Johns Hopkins University, Baltimore, Maryland; ‖Cardiology Unit, University of Vermont College of Medicine, Burlington, Vermont; and ¶Heart Care Program, University of Michigan Medical Center, Ann Arbor, Michigan. This study was completed in partial fulfillment of the doctoral degree requirement in epidemiology and biostatistics, Boston University School of Public Health, Boston, Massachusetts (Dr. L'Italien).

Manuscript received August 14, 1995; revised manuscript received October 24, 1995, accepted November 10, 1995.

Address for correspondence: Gilbert J. L'Italien, Vascular Unit, Massachusetts General Hospital, Wang ACC 458, 15 Parkman Street, Boston, Massachusetts 02114.

Published by Elsevier Science Inc.

0735-1097/96/$15.00
0735-1097(95)00566-8

medical institution. This value, referred to as the complication rate or, in Bayesian terms, the *prior probability*, may be regarded as unique to a given institution and as such should be supplied by the clinician who wishes to compute a patient's risk estimate. Subsequently, using a Bayesian approach (14), clinicians should then perform "tests" for each patient, which include gathering clinical data and conducting noninvasive stress testing. The goal of these tests is to revise the prior probability to a *posttest probability* that is more representative of the patient's characteristics. To be practical, these revised risk estimates should be easily obtainable by the clinician "in the field."

Although Bayesian models of cardiac risk assessment (e.g., the Modified Clinical Risk Index of Detsky et al. [11]) have been developed for general surgical populations, such models tend to underestimate risk in vascular surgery candidates because of their higher prevalence of underlying coronary disease. In response to these concerns, Eagle et al. (15) developed a non-Bayesian predictor algorithm from a cohort of vascular surgery candidates that incorporates a series of clinical risk factors and the results of a pharmacologic stress test using dipyridamole–thallium scintigraphy (16). Dipyridamole–thallium scintigraphy is a sensitive predictor of major perioperative cardiac morbidity (17–23). However, the initial criteria used were based simply on the number of predictors present. In the early model (15), each factor's quantitative contribution to risk (i.e., weight) was not considered. Although this approach was later modified to incorporate the weighted value of each predictor (24), the actual risk computation proved cumbersome. In addition, the outcome of interest was defined as a cardiac ischemic event (including unstable angina) rather than the "hard" end points of nonfatal myocardial infarction or cardiac death.

Accordingly, we sought to develop a simplified Bayesian method for the assessment of the risk of postoperative myocardial infarction or cardiac death in vascular surgery candidates. No computation other than simple addition is required. The clinician can readily obtain a perioperative risk estimate that incorporates the patient's clinical or test status, or both, with the prior probability of a serious cardiac event.

Methods

Training set. The model was developed from a "training" set of 606 consecutive vascular surgery candidates referred to the cardiac nuclear laboratory for dipyridamole–thallium testing before major elective vascular surgery at two university hospitals (246 from Massachusetts General Hospital, Boston, and 360 from the University of Massachusetts Medical Center, Worcester) between August 1984 and December 1991, as previously described (19,24). Thirty nine patients were excluded because vascular surgery was postponed or canceled because of severity of coronary disease. The remaining 567 patients who received prompt vascular surgery comprised the cohort.

Validation set. The validation set included an additional 547 patients from three university medical centers: 167 from Deaconess Hospital, Boston, 175 patients from Medical Center Hospital of Vermont, Burlington, and 172 patients from Yale University, New Haven. Consistent with the training set, all subjects were consecutive elective vascular surgery candidates referred to their institution's respective nuclear cardiology laboratories for dipyridamole–thallium testing from January 1988 to September 1991. A total of 33 patients were excluded because vascular surgery was postponed or canceled for severity of coronary disease.

The total study cohort is therefore 1,081 patients.

Risk factor selection. Variables identified as independent predictors of major perioperative cardiac events (i.e., nonfatal myocardial infarction or cardiac death) by consensus of the study investigators and supported by data from published reports (17–28) were selected for inclusion into the logistic models. These were the presence of the following: advanced age (>70 years), history of angina, history of myocardial infarction or electrocardiographic (ECG) Q waves, history of diabetes mellitus and history of congestive heart failure. Additionally, coronary revascularization that occurred 1 month to 5 years (mean 2.4 ± 0.8 years) before the current hospital period and was shown to be protective for postoperative myocardial infarction in the current cohort and elsewhere (29,30). For the training set, clinical and historical information was obtained retrospectively from the medical record by investigators who reviewed records up to, but not including, the operative chart. For the validation sets, clinical and historical information was obtained prospectively, that is, before operation. Clinically relevant dipyridamole–thallium results were described as 1) ischemic ECG changes, defined as a ≥1 mm ST segment depression compared with baseline levels; 2) planar myocardial scintigraphic images that on review by two experienced observers showed fixed defects; and 3) images showing defects that partially or completely redistributed on delayed (>3 h) imaging.

Outcome determination. At all centers, outcomes were assessed by medical record review and or interview of the treating physicians, the patients and their families. Outcomes of interest were nonfatal or fatal myocardial infarction or cardiac death. All patients were monitored by daily ECGs and serum cardiac enzyme levels (creatinine kinase-MB fraction [CK-MB]) for 72 h after operation. For the definition of myocardial infarction, the University of Minnesota criteria were used: new ECG Q wave ≥1 mm or CK-MB ≥5% or both. Fatal cardiac events were defined as sudden death directly attributable to myocardial infarction, congestive failure or ventricular arrhythmia. All reported fatal events were confirmed by review of hospital records, autopsy findings and death certificates. All reported nonfatal events were confirmed by medical record review for the ECG or enzyme criteria, or both, cited previously.

Model development. Two specified logistic regression models were developed using BMDP LR (BMDP Statistical Software, Inc.) software: clinical and dipyridamole–thallium vari-

Table 1. Distribution of Study Variables According to Perioperative Event Rate

	Training Set				Validation Set			
	Event (n = 46)	No Event (n = 521)	OR (95% CI)	p Value	Event (n = 39)	No Event (n = 475)	OR (95% CI)	p Value
Clinical								
Age >70 yr	21 (46%)	176 (34%)	1.6 (0.9–3.0)	0.104	18 (46%)	194 (41%)	1.2 (0.6–2.4)	0.517
Male	32 (70%)	348 (67%)	1.1 (0.6–2.2)	0.702	14 (36%)	210 (44%)	0.7 (0.4–1.4)	0.490
Hx of MI/Q wave	24 (52%)	195 (37%)	1.8 (1.1–3.3)	0.049	33 (85%)	255 (54%)	4.8 (2.0–12.0)	0.000
Hx of angina	21 (46%)	127 (24%)	2.6 (1.4–4.8)	0.002	12 (31%)	135 (28%)	1.1 (0.5–2.3)	0.755
Hx of diabetes	17 (37%)	105 (20%)	2.3 (1.3–4.4)	0.008	27 (69%)	251 (53%)	2.0 (1.0–4.1)	0.048
Hx of CHF	10 (22%)	49 (9%)	2.7 (1.3–5.7)	0.009	15 (38%)	77 (16%)	3.2 (1.6–6.4)	0.000
Prior CABG	1 (2%)	67 (13%)	0.2 (0.1–0.9)	0.033	5 (13%)	51 (11%)	1.2 (0.5–3.3)	0.600
Dipyridamole–thallium								
Fixed defects	32 (70%)	229 (44%)	2.9 (1.5–5.6)	0.001	18 (46%)	153 (32%)	1.8 (0.9–3.4)	0.076
Reversible defects	37 (80%)	224 (43%)	5.5 (2.6–11.6)	0.000	23 (59%)	167 (35%)	2.6 (1.4–5.2)	0.003
Ischemic ST changes	14 (30%)	45 (9%)	4.6 (2.3–9.3)	0.000	9 (23%)	47 (10%)	2.7 (1.2–6.1)	0.011

CABG = coronary artery bypass graft surgery; CHF = congestive heart failure; CI = confidence interval; Event = nonfatal myocardial infarction (MI) or cardiac death; Hx = history; OR = odds ratio.

ables were regressed separately because it was anticipated that in practice the models would be applied to patients who had not yet undergone dipyridamole–thallium testing and for whom these variables would be undefined. Appropriate interaction terms were also considered among the clinical variables, such as the possible interaction between advanced age and any of the cardiac or diabetic variables.

A Bayesian framework for the analysis permits the clinician to consider both the average risk (prior probability) and the patient-specific predictive diagnostic information, which is referred to as the likelihood ratio (31). A likelihood ratio is typically computed for each clinical variable or test result from the proportion of patients with a particular result who experience an event divided by the proportion who do not experience the event. Likelihood ratios >1 yield a patient risk estimate greater than the average risk. Conversely, likelihood ratios <1 imply that the patient's risk is below the average. One of the advantages to the use of likelihood ratios is that risk estimates can be revised sequentially, first by the likelihood ratios obtained for the set of clinical factors alone, then by the dipyridamole–thallium results if necessary. In this study, likelihood ratios were derived from logistic regression analyses using a previously described method (32–37).

Model validation. Ultimately, any predictive model should be validated by comparing risk estimates to observed event rates in both the challenge and validation sets. Validation procedures are typically designed to assess discrimination (38) and calibration (39) performance. *Calibration* refers to comparability between observed and estimated rates. *Discrimination* describes a model's ability to separate a population into those who will experience the event and those who will not. Typically, "goodness of fit" tests (39) and receiver–operating characteristic (ROC) curves (38) are used to evaluate a model's calibration and discrimination, respectively.

Results

Distribution of risk factors according to outcome. The distributions of clinical and dipyridamole–thallium variables according to outcome is shown in Table 1 for perioperative events (all patients). There were 46 events (30 nonfatal, 16 fatal) among the 567 training set patients (8%) and 39 events (27 nonfatal, 12 fatal) among 514 validation set patients (8%). With the exception of gender and perhaps advanced age, all clinical and all dipyridamole–thallium variables in the training set were more prevalent among those patients with than without an event. The computed odds ratios also indicate a significant association between clinical and dipyridamole–thallium variables and outcome. There is also evidence of a protective effect among patients who underwent a prior coronary bypass procedure within 5 years. Three of the six clinical variables (prior myocardial infarction, diabetes, congestive heart failure) in the validation set were associated with events, and all dipyridamole–thallium variables were associated with outcome.

The major cardiac complication rates (nonfatal myocardial infarction, cardiac death) classified according to type of vascular surgical procedure are shown in Table 2 for both the training and validation sets. These values thus correspond to the procedure-specific prior probability of a cardiac event. Event rates in the training set were significantly greater for infrainguinal (13%, 95% confidence interval [CI] 8% to 18%) than for aortic (6%, 95% CI 4% to 8%) or carotid (6%, 95% CI 1% to 16%) procedures (p = 0.012). Again, event rates in the validation set were greater for infrainguinal (10%, 95% CI 7% to 14%) than aortic (6%, 95% CI 2% to 12%) or carotid (6%, 95% CI 3% to 12%) procedures, although these differences were not statistically significant.

The logistic regression analyses are detailed in Table 3. Among the model 1 clinical variables, a history of diabetes, angina, and prior coronary revascularization remained strongly

Table 2. Complication Rates (prior probabilities) for Types of Vascular Surgery

	Training Set (n = 567)		Validation Set (n = 514)	
Procedure	No. (%) of Pts	95% CI	No. (%) of Pts	95% CI
Aortic	19/334 (6%)	4% to 8%	7/123 (6%)	2% to 14%
Infrainguinal	23/180 (13%)	8% to 18%	24/250 (10%)	2% to 12%
Carotid	3/53 (6%)	1% to 16%	8/131 (6%)	3% to 12%
Total	46/567 (8%)	6% to 10%	39/514 (8%)	6% to 11%

Complications include nonfatal myocardial infarction and cardiac death. CI = confidence interval; Pts = patients.

associated with outcome. No interaction terms were found to contribute to the model. All variables in the dipyridamole–thallium model (model 2) are significantly predictive of outcome.

Validation results. The ROC curves for the clinical and sequentially applied (clinical plus dipyridamole–thallium) models developed from the training set are shown in Figure 1. Prognostic accuracy, as expressed by the ROC areas, was 74 ± 3% for the clinical model and 81 ± 3% for the sequentially applied models.

Figure 2 displays the comparative prognostic accuracy of the training and individual validation set patients for the sequentially applied model according to ROC areas. Areas were 81 ± 3% for the training set, and 74 ± 9%, 72 ± 7% and 76 ± 5% for each of the three centers representing the validation set.

Calibration results are displayed graphically in Figure 3 for both the training and validation sets at four risk categories. Values for the Hosmer-Lemeshow goodness of fit statistic, C (39), computed from the observed and estimated event frequencies for the training set and each of the medical centers comprising the validation set, are 10.54 (p = 0.75) for the training set and 14.55 (p = 0.45), 23.68 (p = 0.1) and 8.2 (p = 0.85) for each of the individual validation sets (degrees of freedom 15). The observed and estimated risk for each of four risk categories among the training set are as follows: 3% versus 3%, 17% versus 14%, 23% versus 26% and 40% versus 54%. The observed and estimated risk for each risk category among the validation set are 4% versus 3%, 9% versus 12%, 15% versus 28% and 26% versus 42%.

The utility of stratification according to the models' risk estimates is illustrated in Figure 4. When the clinical model was applied to all 1,081 patients, the observed event rates were 3%, 8% and 18% for patients classified as low (0–5%), moderate (5–15%) and high risk (>15%), respectively, ($p < 0.0001$). The addition of dipyridamole–thallium data reclassified >80% of the moderate risk patients into low (3%) and high (19%) risk categories ($p < 0.0001$). However, dipyridamole–thallium testing provided no further risk discrimination among the patients defined as either low ($p = 0.610$) or high ($p = 0.11$) risk according to the clinical model.

Risk estimate tables. Table 4 lists the estimated risk (posttest probability) of a perioperative cardiac event computed from a range of complication rates (prior probability) and the patient's clinical risk score. These estimates were calculated using logistic regression-derived likelihood ratios (32–37). Table 5 provides risk estimates obtained from the dipyridamole–thallium risk score. The prior probability for this model is defined as the posttest probability of the clinical model. The procedure required for estimating a patient-specific risk estimate from these tables is detailed in the Appendix.

Table 3. Logistic Regression Model Coefficients

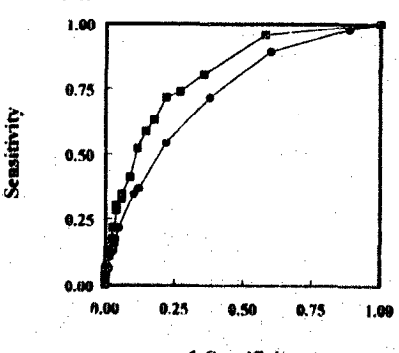
Term	Coefficient	SE	p Value
Model 1: Clinical Variables			
Age (≥ 70 yr)	0.500	0.324	0.125
Diabetes	0.747	0.341	0.027
Angina	0.786	0.347	0.025
CHF	0.550	0.425	0.209
MI	0.470	0.346	0.177
Prior CABG	−2.228	1.040	0.028
Constant	−3.249	0.306	
Model 2: Dipyridamole Thallium Variables			
Ischemic ST changes	1.234	0.373	0.001
Fixed defect	0.823	0.348	0.015
Reversible defect	1.329	0.396	0.0001
Constant	−3.958	0.395	

Abbreviations as in Table 2.

Discussion

The present analysis expands on our earlier model (24) for predicting cardiac events by making use of a larger, more diverse population of vascular surgery candidates and limiting outcome definition to the "hard" end points of myocardial

Figure 1. Receiver-operating characteristic curves for clinical and sequential Bayesian (i.e., clinical and dipyridamole–thallium) models derived from the training set. **Circles** = clinical model only, area 74 ± 3%; **squares** = sequential Bayesian (clinical plus dipyridamole thallium), area 81 ± 3%.



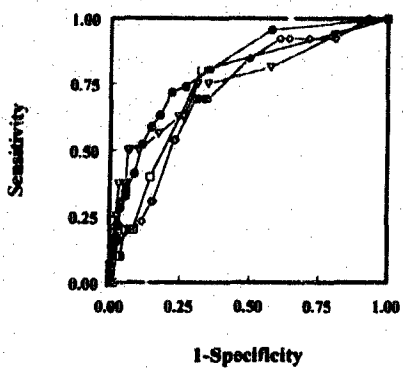


Figure 2. Receiver-operating characteristic curves for sequential Bayesian models derived from the training set and each of the three validation sets. **Circles** = training set (n = 567), area 81 ± 3%; **squares** = University of Vermont (n = 175), area 74 ± 9%; **diamonds** = Deaconess Hospital (n = 167), area 72 ± 7%; **inverse triangles** = Yale (n = 172), area 76 ± 5%.

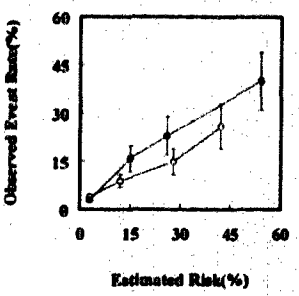


Figure 3. Calibration results from both the training set (**solid circles**, n = 567) and combined validation set (**open circles**, n = 514) (± SE of observed rate). The observed and estimated risk for each of four risk categories among the training set are as follows: 3% versus 3%, 17% versus 14%, 23% versus 26% and 40% versus 54%. The observed and estimated risk for each risk category among the validation set are 4% versus 3%, 9% versus 12%, 15% versus 28% and 26% versus 42%.

infarction or cardiac death. Furthermore, we used an improved method of risk estimation that combines elements of Bayes theorem and logistic regression, yet requires no calculation beyond addition and subtraction of the risk estimate from Tables 4 and 5. A clear advantage to this method is that it permits consideration of the procedure-specific institutional complication rate in the estimation of risk. Another advantage to the use of logistic regression to calculate likelihood ratios is that it is not necessary to assume independence between those variables included in each model (31). The logistic regression method used here has been successfully applied elsewhere (32–37) and is one of several related methods of deriving likelihood ratios using logistic regression (40–43). Logistic models have also been applied previously in a sequential Bayesian manner (44–46) to estimate cardiac risk in general populations.

In contrast to our earlier studies (19,24), we noted differences in the type of variables and the values of the coefficients found to be independently predictive of cardiac risk. This is probably a result of the larger size of our cohort and the selection of the "hard" end points of nonfatal myocardial infarction or cardiac death versus the softer end points of cardiac ischemic events (including unstable angina) used in one of the earlier studies (24). The prognostic accuracy of the models, as expressed by the ROC areas, is similar to values published elsewhere for patients undergoing noncardiac surgery: Detsky et al. (11) reported a ROC area of 81 ± 4% for a multifactorial risk index, which is identical to the value of 81 ± 3% obtained for our sequential Bayesian models. Also, as shown in Figure 4, risk stratification based on the clinical model alone could obviate the need for dipyridamole–thallium testing in nearly half the patients in this study. These patients could not be further stratified and therefore did not benefit from added testing in the operative setting. Dipyridamole–thallium testing provided further refined risk stratification only among the patients classified as moderate risk (according to the clinical model): >80% of these patients were reclassified as low or high risk. Thus, risk stratification according to the clinical model could reduce the need for further testing and may prevent the possible consequences of a false positive result (unnecessary coronary angiography). Given the relatively high cost of the thallium test, considerable savings are possible if its use is limited to patients deemed to be at moderate risk according to the clinical profile.

Validation assessments. The validation assessments indicate some loss of prognostic accuracy when the combined (clinical plus thallium) model was applied to the validation set and some loss of reliability between observed and estimated events. For example, as shown in Figure 4, the model tends to overestimate risk when applied to the challenge set, particularly at the higher risk levels (>20%). However, the goodness of fit p values indicate that overall the estimated risk does correspond to the observed rates for each of the validation sets. Although ROC areas are less for the validation set than the training set, these values indicate that good discrimination remains (i.e., all areas exceed 50%) and are superior to the external validation results reported elsewhere for a similar model (13). Such "shrinkage" may result from observed differences in the distribution of risk factors between the event and nonevent groups of patients between the training and validation sets (Table 1). However, it is reasonable to assume general comparability between training and validation sets for the following reasons: 1) all centers included in the study are relatively large urban teaching hospitals located in the northeastern United States; 2) both the training and validation sets included successive vascular surgery candidates referred to the respective institution's cardiac nuclear laboratory for dipyridamole–thallium testing before major elective vascular surgery; 3) ~6% of the training group and 6% of the validation set patients were excluded because vascular surgery was post-

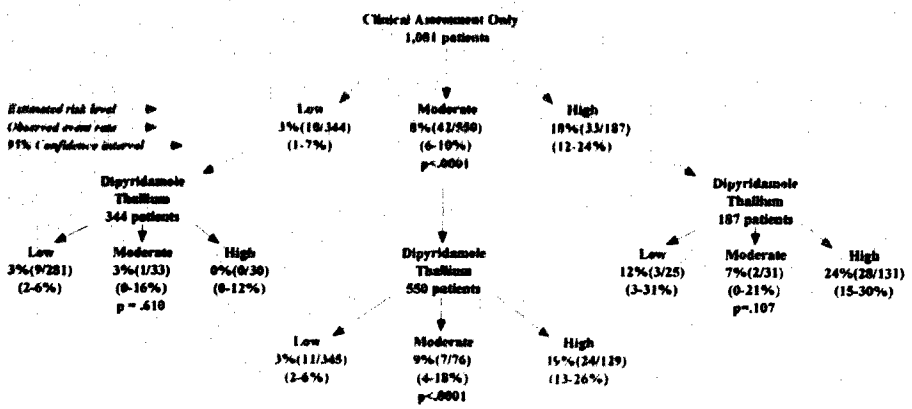


Figure 4. Suggested algorithm and results for using clinical variables and dipyridamole–thallium results sequentially to stratify risk in 1,081 patients. Values shown are the event rates (nonfatal myocardial infarction or cardiac death) and associated 95% confidence intervals. Clinical variables include advanced age (>70 years), history of angina, history of myocardial infarction, history of diabetes, history of congestive heart failure and prior coronary bypass grafting. Dipyridamole–thallium variables were ischemic electrocardiographic changes, fixed defects and reversible defects. Cut points defining low, moderate and high risk correspond to posttest probabilities of 0 to 5%, 5 to 15% and >15%, respectively, for both models. See text for detailed discussion of the algorithm.

poned because of the severity of coronary disease; 4) the overall event rates were identical between validation and training sets (8%).

Study limitations. The present study was restricted to successive vascular surgery candidates who underwent dipyridamole–thallium testing and prompt vascular surgery at major university medical centers. Because this is an observational study, the indication for thallium was based on the clinician's discretion, and as such, the patients in this study are at slightly higher risk than all vascular surgery candidates. Thus, our model may therefore not be generalizable to all vascular surgery candidates. Further, because the model is based on patients who have already been selected for vascular surgery, it cannot be used to decide who should undergo operation, that is, the model may be used to predict outcome among those patients who do undergo operation.

One major source of bias in this study is that preoperative dipyridamole–thallium results were made available to physicians caring for all patients and tended to influence operative management. For example, those patients with positive dipyridamole–thallium images were likely to be more carefully

Table 4. Estimated Risk of Perioperative Cardiac Event According to Complication Rate and Clinical Variables Risk Score Range

	Complication Rate							
Clinical Score Range	2%	4%	6%	8%	10%	12%	14%	16%
0.0–	1%	2%	3%	4%	5%	6%	7%	8%
0.5	1%	2%	3%	4%	5%	6%	7%	8%
>0.5–	1%	3%	4%	6%	7%	9%	11%	12%
1.0	2%	3%	5%	7%	8%	10%	12%	13%
>1.0–	3%	5%	8%	10%	13%	15%	18%	20%
1.5	4%	8%	11%	15%	18%	21%	24%	27%
>1.5–	4%	8%	12%	17%	19%	23%	26%	29%
2.0	6%	12%	17%	22%	27%	31%	35%	38%
>2.0–	7%	13%	19%	24%	29%	33%	37%	41%
2.5	10%	18%	25%	32%	37%	42%	47%	50%
>2.5–	11%	20%	27%	34%	40%	45%	49%	53%
3.0	15%	27%	36%	43%	50%	55%	59%	63%

To compute score, add weights corresponding to patient's clinical risk factors: age >70, 0.5; diabetes, 0.8; angina, 0.8; congestive heart failure, 0.6; prior infarction, 0.5; prior bypass (<5 years), 2.2. To estimate risk, find value (in table) corresponding to patient's risk score and institutional complication rate.

Table 5. Estimated Risk of Perioperative Cardiac Event According to Clinical Risk and Dipyridamole Thallium Risk Score Range

	Clinical Risk							
Thallium Score Range	2.5%	5.0%	7.5%	10.0%	12.5%	15.0%	17.5%	20.0%
0.0–	1%	1%	2%	2%	3%	4%	4%	5%
0.5	1%	1%	2%	3%	3%	4%	5%	6%
>0.5–	1%	2%	3%	4%	5%	6%	7%	8%
1.0	1%	2%	3%	4%	5%	7%	8%	9%
>1.0–	2%	3%	5%	7%	8%	10%	12%	14%
1.5	2%	5%	7%	10%	12%	15%	17%	20%
>1.5–	3%	5%	8%	11%	13%	16%	19%	21%
2.0	4%	7%	11%	15%	19%	22%	25%	29%
>2.0–	4%	8%	13%	16%	20%	24%	27%	31%
2.5	6%	12%	18%	23%	27%	32%	36%	40%
>2.5–	7%	13%	19%	24%	29%	34%	38%	42%
3.0	10%	18%	26%	33%	38%	43%	48%	52%
>3.0–	12%	21%	30%	37%	43%	48%	53%	57%
3.5	14%	24%	34%	42%	48%	53%	58%	62%

To compute score, add weights corresponding to patient's thallium test results: ischemic ST changes, 1.2; fixed defect, 0.8; reversible defect, 1.3. To estimate risk, find value (in table) corresponding to patient's thallium risk score and clinical risk estimate.

monitored during operation and subjected to longer postoperative intensive care stays.

Another potential bias may occur if risk factor assessment, obtained retrospectively from chart review, differs from risk factor determination by clinicians when the model is being applied. We recommend that every effort be made both to review the patient's history and to consult the patient's past medical record for confirmation of risk factor status.

Clinical implications. The suggested risk stratification scheme shown in Figure 4 demonstrates that a spectrum of clinical markers only, weighted according to prognostic impact, may significantly alter the prior probability of a postoperative cardiac event in a substantial number of patients referred for dipyridamole–thallium testing, thus obviating the need for the more expensive cardiac screening. Also, the performance of the clinical model indicates that it could be used by itself to estimate or stratify cardiac risk in patients not considered for further testing because of the urgency of the vascular procedure. However, it is also apparent from the thallium model that dipyridamole–thallium scanning reliably reclassifies a majority of intermediate risk patients into low or high risk categories.

The prediction models described in this report retain much of their prognostic accuracy when applied to the validation sets and can also reliably estimate risk in this group. The models are thus generalizable to vascular surgery candidates who present for elective operation at major university medical centers.

We acknowledge the contributions of the following to the development of the validation data sets: From Yale University, Stanley Rosenbaum, MD, Ann H. Nelson, RN, Diwaker Jain, MD, Frans J. Th. Wackers, MD, Barry L. Zaret, MD; from Deaconess Hospital, Steven E. Lane, MD, Stanley M. Lewis, MD, John J. Pippin, MD, Edward J. Kosinski, MD, David Campbell, MD, Richard W. Nesto, MD, Thomas Hill, MD.

Appendix

Example of Risk Estimation Procedure for Individual Patients

The clinician should first obtain an estimate of the institutional perioperative rate of nonfatal myocardial infarction or cardiac death for the required vascular surgery procedure, such as the values listed in Table 2. This estimate is computed from the number of events divided by the total number of patients. For our example we will use the perioperative cardiac complication rate for aortic procedures, which is 6%.

Second, the patient's medical record should be consulted to obtain information on all clinical variables listed at the bottom of Table 4. With this list, the patient's clinical risk score is obtained by summing the weights corresponding to each of the patient's clinical risk factors. For example, if the patient were a 69-year-old candidate for aortic surgery with a history of diabetes and angina, the risk score is

$$\text{Clinical score} = 0.8\ (\text{Diabetes}) + 0.8\ (\text{Angina}) = 1.6.$$

From Table 4, the estimated risk of a perioperative cardiac event that corresponds to an institutional complication rate of 6% and that falls within the clinical risk score range >1.5 to 2.0 is ~13%. Thus, the "average" risk of a complication (6%) is revised to ~13% for an individual patient who exhibits the given clinical risk factors.

Further risk discrimination based on dipyridamole–thallium results may be desired if the patient was subsequently tested and displayed the following results: positive ischemic electrocardiographic changes and a reversible myocardial defect. The weights from the dipyridamole–thallium model shown at the bottom of Table 5 corresponding to these predictors are 1.2 and 1.3, respectively, for a total score of 2.5:

$$\text{Thallium score} = 1.2\ (\text{Ischemic ST}) + 1.3\ (\text{Reversible defect}) = 2.5.$$

A revised cardiac risk estimate is obtained from Table 5 by using the estimated risk from the clinical model, (~13%), as the pretest probability for the dipyridamole-thallium model and the risk score range >2.0 to 2.5. A cardiac risk (posttest probability) of ~27% is now obtained for the patient, indicating a doubling of risk. However, if all dipyridamole-thallium results had been negative, (i.e., score = 0). This would yield a posttest probability of ~3% from Table 5, implying a substantial reduction of risk.

References

1. Vogt MT, Wolfson SK, Kuller LH. Lower extremity arterial disease and the aging process: a review. J Clin Epidemiol 1992;45:529–42.
2. Hertzer N, Beven E, Young J, et al. Coronary artery disease in peripheral vascular patients: a classification of 1000 coronary angiograms and results of surgical management. Ann Surg 1984;199:223–33.
3. Taylor LM, Yeager RA, Moneta GL, McConnell DB, Porter JM. The incidence of perioperative myocardial infarction in general vascular surgery. J Vasc Surg 1991;15:52–61.
4. Krupski WC, Layug EL, Reilly LM, Rapp JH, Mangano DT. Study of perioperative ischemia (SPI) research group. Comparison of cardiac morbidity between aortic and intrainguinal operations. J Vasc Surg 1992;15:354–65.
5. Yeager RA, Moneta GL, McConnell DB, Neuwelt EA, Taylor LM, Porter JM. Analysis of risk factors for myocardial infarction following carotid endarterectomy. Arch Surg 1989;124:1142–5.
6. Roger VL, Ballard DJ, Hallet JW, Osmundson PJ, Puetz PA, Gersh BJ. Influence of coronary artery disease on morbidity and mortality after abdominal aortic aneurysmectomy: a population-based study, 1971–1987. J Am Coll Cardiol 1989;14:1245–52.
7. Crawford ES, Saleh SA, Babb JW, Glaeser DH, Vaccaro PS, Silvers A. Infrarenal abdominal aortic aneurysm. Ann Surg 1981;193:492–8.
8. Cambria RP, Brewster DC, Abbott WM, L'Italien GJ, et al. The impact of selective use of dipyridamole-thallium scans and surgical factors on the current morbidity of aortic surgery. J Vasc Surg 1992;15:43–51.
9. Hertzer NR. Fatal myocardial infarction following lower extremity revascularization. Ann Surg 1981;193:492–8.
10. Ashton CM, Petersen NJ, Wray NP, et al. The incidence of perioperative myocardial infarction in men undergoing noncardiac surgery. Ann Intern Med 1993;118:502–10.
11. Detsky AS, Abrams HB, McLaughlin JR, et al. Predicting cardiac complications in patients undergoing non-cardiac surgery. J Gen Intern Med 1986;1:211–9.
12. Detsky AS, Abrams HB, Forbath N, et al. Cardiac assessment for patients undergoing noncardiac surgery. Arch Intern Med 1986;146:2131–4.
13. Eagle KA, Boucher CA. Cardiac risk of noncardiac surgery. N Engl J Med 1989;321:1330–2.
14. Van der Helm HJ, Hische EA. Application of Bayes theorem to results of quantitative clinical determinations. Clin Chem 1979;25:985–8.
15. Eagle KA, Singer DE, Brewster DC, Darling RC, Mulley AG, Boucher CA. Dipyridamole-thallium scanning in patients undergoing vascular surgery. JAMA 1987;257:2185–9.
16. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging. A diagnostic tool comes of age. Circulation 1991;83:363–81.
17. Boucher CA, Brewster DC, Darling RC, Okada RD, Strauss HW, Pohost GM. Determination of cardiac risk by dipyridamole-thallium imaging before peripheral vascular surgery. N Engl J Med 1985;312:389–94.
18. Brewster DC, Okada RD, Strauss HW, Abbott WM, Darling RC, Boucher CA. Selection of patients for perioperative coronary angiography: use of dipyridamole-stress thallium myocardial imaging. J Vasc Surg 1985;504–10.
19. Cutler BS, Hendel RC, Leppo JA. Dipyridamole-thallium scintigraphy predicts perioperative and long-term survival after major vascular surgery. J Vasc Surg 1992;15:972–81.
20. Kresowik TF, Bower TR, Garner SA, et al. Dipyrimadole thallium in patients being considered for vascular procedures. Arch Surg 1993;128:299–302.
21. Leppo J, Plaja J, Maurissa G, et al. Noninvasive evaluation of cardiac risk before elective vascular surgery. J Am Coll Cardiol 1987;9:269–76.
22. Mackey WC, O'Donnell TF, Callow AD. Cardiac risk in patients undergoing carotid endarterectomy: impact on perioperative and long-term mortality. J Vasc Surg 1990;11:226–34.
23. Younis LT, Aguirre F, Byers S, et al. Perioperative and long-term prognostic value of intravenous dipyridamole thallium scintigraphy in patients with peripheral vascular disease. Am Heart J 1990;119:1287–92.
24. 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 1989;110:859–66.
25. Crawford ES, Morris GC, Howell JF, Flynn WF, Moorhead DT. Operative risk in patients with previous coronary bypass. Ann Thorac Surg 1978;26:215–21.
26. Johnson KW. Multicenter prospective study of nonruptured abdominal aortic aneurysm. Part ii. variables predicting morbidity and mortality. J Vasc Surg 1989;9:437–47.
27. Suggs WD, Smith RB, Weintraub WS, et al. Selective screening for coronary artery disease in patients undergoing elective repair of abdominal aortic aneurysms. J Vasc Surg 1993;18:349–57.
28. Wong T, Detsky AS. Preoperative cardiac risk assessment for patients having peripheral vascular surgery. Ann Intern Med 1992;116:743–53.
29. Kalra M, Charlesworth D, Morris JA, Al-Khaffaf H. Myocardial infarction after reconstruction of the abdominal aorta. Br J Surg 1993;80:28–31.
30. Mahar LJ, Steen PA, Tinker JH, et al. Perioperative myocardial infarction in patients with coronary disease with and without coronary artery bypass grafts. J Thorac Cardiovasc Surg 1978;75:1–13.
31. Sackett DL, Haynes RB, Guyatt GH, Tugwell P. The Interpretation of Diagnostic Data in Clinical Epidemiology: A Basic Science for Clinical Medicine. Boston: Little Brown, 1991:69–152.
32. Albert A. On the use and computation of likelihood ratios in clinical chemistry. Clin Chem 1982;28:1113–9.
33. Lacher DA. Predictive value derived from likelihood ratios: a superior technic to interpret quantitative laboratory results. Am J Clin Pathol 1987;87:673–6.
34. Reibnegger G, Fuchs D, Hausen A, et al. Generalized likelihood ratio concept and logistic regression analysis for multiple diagnostic categories. Clin Chem 1989;35:990–4.
35. Reeves JM, Curtis CR, Salman MD, et al. Multivariable prediction model for the need for surgery in horses with colic. Am J Vet Res 1991;52:1903–7.
36. Bhutani VK, Abbasi S. Relative likelihood of bronchopulmonary dysplasia based on pulmonary mechanics measured in preterm neonates during the first week of life. J Pediatr 1992;120:605–13.
37. Royston P, Thompson SG. Model based screening by risk with application to Down's syndrome. Statist Med 1992;11:257–68.
38. Hanley JA, McNeil BJ. The meaning and use of the area under a receiver operating characteristic (ROC) curve. Radiology 1982;143:29–36.
39. Hosmer DW, Lemeshow S. Goodness-of-fit tests for the multiple logistic regression model. Commun Statist P A Theor Methods 1980;A9:1043–69.
40. Coughlin SS, Trock B, Criqui MH, et al. The logistic modelling of sensitivity, specificity and predictive value of a diagnostic test. J Clin Epidemiol 1992;45:1–7.
41. Simel DL, Samsa GP, Matchar DB. Likelihood ratios for continuous test results—making the clinician's job easier or harder? J Clin Epidemiol 1993;46:85–93.
42. Seymour DG, Green M, Vaz FG. Making better decisions: construction of clinical scoring systems by the Spiegelhalter-Knill-Jones approach. Br Med J 1990;300:223–6.
43. Knottnerus JA. Application of logistic regression to the analysis of diagnostic data. Med Decis Making 1992;12:93–108.
44. Morise AP, Duval RD. The estimation of post-test probability of coronary disease following exercise testing using the sequential application of two Bayesean methods. Am Heart J 1990;120:1292–7.
45. Morise AP, Detrano R, Bobbio M, Diamond GA. Development and validation of a logistic regression-derived algorithm for estimating the incremental probability of coronary artery disease before and after exercise testing. J Am Coll Cardiol 1992;20:1187–96.
46. Weintraub WS, Barr-Alderfer VA, Seelaas PA, et al. A sequential approach to the diagnosis of coronary artery disease using multivariate analysis. Am Heart J 1985;109:999–1005.