Preoperative and Long-term Cardiac Risk Assessment

Predictive Value of 23 Clinical Descriptors, 7 Multivariate Scoring Systems, and Quantitative Dipyridamole Imaging in 360 Patients

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A total of 360 patients underwent preoperative cardiac risk assessment using 23 clinical parameters, seven multivariate clinical scoring systems, and quantitative dipyridamole-thallium imaging to predict postoperative and long-term myocardial infarction and cardiac death after noncardiac surgery. There were 30 postoperative and an additional 13 cumulative long-term cardiac events after an average follow-up of 15 months. Clinical descriptors were not useful in predicting the outcome of individual patients. The postoperative and long-term cardiac event rates were 1% and 3.5%, respectively, in patients with normal scans or fixed perfusion defects, and 17.5% and 22% in patients with reversible defects. Using quantitative indices reflecting the amount of jeopardized myocardium, patients could be stratified by dipyridamole imaging into multiple scintigraphic subsets, with corresponding postoperative and 1-year coronary morbidity and mortality rates ranging from 0.5% to 100% (p = 0.0001). Thus, postoperative and long-term cardiac events cannot be predicted clinically, whereas quantitative dipyridamole imaging accurately identifies high-risk patients who require preoperative coronary angiography.

Myocardial infarction and sudden death are the most common causes of complications and death in coronary patients after major general and vascular surgery.[1-3] If a patient has a good exercise tolerance, and the standard treadmill test is clinically and electrically negative at 85% of the maximal predicted heart rate, the postoperative and long-term outlooks are good.[4-6] Dipyridamole-thallium imaging is routinely used for preoperative cardiac risk assessment in patients who cannot increase their heart rate sufficiently on the treadmill because of physical limitations or beta-blocker drugs. Patients with normal scans can undergo surgery safely.[7] Most authors recommend preoperative coronary angiography in patients with reversible defect or defects.[8-18]

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Accepted for publication December 20, 1991.

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The current study was designed to compare the accuracy of 23 individual clinical descriptors of seven multivariate clinical scoring systems and of dipyridamole myocardial perfusion imaging to predict postoperative and long-term outcome after vascular and major general surgery. Quantitative scintigraphic indices were developed to assess the amount of jeopardized myocardium and to restrict the requirement of preoperative coronary angiography to a small subset of high-risk coronary patients.

Materials and Methods

Patient Population

The study population consisted of 360 consecutive patients referred for dipyridamole-thallium imaging before vascular or major general surgery. The surgical procedures are listed in Table 1. An adequate level of stress on the standard treadmill test could not be achieved either because of physical limitations or because of beta-blocker usage.

Clinical evaluation. Medical charts were reviewed and Dripps-American Surgical Association score,[19] Goldman Cardiac Risk Index score and class,[20] Detsky Modified Risk Index score and class,[21] Eagle's low-risk criteria,[22] Yeager's low-risk criteria,[23] Cooperman event probability,[24] and the statistical significance of the parameters of the Eagle equation[25] were determined for each patient. The scoring systems are described in Table 2.

Dipyridamole infusion protocol. The dipyridamole infusion protocol is described in detail in a previous report.[26] Briefly, patients were studied in the fasting state, having

TABLE 1. *Surgical Procedures*

Vascular surgery: 66% (236/360)
Elective aortic replacement for aortoiliac disease (73), resection of an abdominal (71) or thoracoabdominal (5) aortic aneurysm, ileofemoral and infrainguinal vascular reconstruction (63), aortic endarterectomy (1), aortorenal bypass (12), carotid surgery (9), splenorenal bypass (1)
Major general surgery: 15% (54/360)
Esophageal, gastric, and bowel surgery and various intra-abdominal procedures (37), renal transplantation (7), neck dissection (9), mastectomy (1)
Urology: 3.6% (13/360)
Nephrectomy (5), bladder surgery (4), radical prostatectomy (2), ureteral reconstruction (1)
Orthopedic surgery: 9% (32/360)
Total hip (12) or knee (9) prosthesis, amputation (3), discoidectomy (7), hip arthroplasty (1)
Lung surgery: 3.9% (14/360)
Gynecologic surgery (hysterectomy or major vaginal surgery) 2.8% (10/360)
Neurosurgery for brain tumor: 0.3% (1/360)

avoided coffee, tea, soft drinks, and chocolate for 24 hours, and all theophylline derivatives were discontinued for 48 hours before the test. A 20-gauge cannula was installed in a large antecubital vein, and the cardiac rhythm was continuously monitored with a II lead. Baseline and once-a-minute heart rate and blood pressure measurements were recorded. Dipyridamole was infused at a rate of 0.14 mg/kg/minute over 4 minutes. After the infusion, the patient stood up and walked in place for 2 minutes. At that point, 3.0 mCi thallium-201 were injected as a compact bolus into the cannula, rapidly followed by a 10-mL bolus of normal saline solution. The patient continued walking on the spot for 2 minutes, then lay under the scintillation camera, and imaging was begun. During each study, aminophylline 125 mg was available to reverse any serious adverse effects of dipyridamole. Patients who developed symptomatic myocardial ischemia responded quickly to intravenous aminophylline. The mean variations in heart rate and systolic blood pressure after dipyridamole infusion were 11 ± 16 beats/minute and 18 ± 14 mmHg, respectively.

Thallium-201 myocardial imaging. The thallium imaging protocol, our definition of a fixed defect, and the quantification method are described in detail in a previous report.[27] The first image was acquired in the best septal view, followed by the left anterior oblique 70 degrees (with breast support in female patients), and the anterior view. Delayed images were obtained 4 hours after thallium injection, and the patient was instructed to eat lightly during that time. Preset 8-minute images were acquired in each of the three views (initial and delayed images) with a photopeak set at 80 keV with a 20% window. Care was taken to position the patients identically for the initial and redistribution studies. For each scintigraphic study, the following images were displayed: analog images, interpolated background-subtracted images, circumferential profiles, and washout rate analysis. All myocardial scintigraphic images were interpreted by two experienced observers without prior knowledge of patient history, coronary anatomy, or postoperative or long-term outcome.

Definition of a fixed defect. Because of the high reported incidence of viable but "stunned" myocardium in fixed defects,[28] we injected a supplementary 1-mCi dose of thallium before the redistribution images, or acquired either delayed 24-hour resting thallium images or a radionuclide gated equilibrium ventriculogram (MUGA scan) under continuous intravenous nitroglycerin infusion.

Infrequent disagreements in interpretation were resolved by consensus.

Quantification of the severity and extent of reversible perfusion defects. Scans were divided into seven segments, which were reduced to five myocardial perfusion regions, taking into account anatomic overlap (Fig. 1). All regional perfusion defects were graded according to a three-point scale: grade 0/3 being normal and grade 3/3 the most severe. Both immediate postdipyridamole and delayed (4 hours) images were evaluated. The quantitative indices used to assess the extent and severity of reversible defects and the amount of jeopardized and infarcted myocardium are described in Table 3.

Left Ventricular Cavitary Dilation

The left ventricular (LV) cavity was measured in the best septal view on the immediate postdipyridamole and redistribution analog images. A patient was considered to show transient cavitary dilation when the cavity size on the early images was >15% larger than on the delayed images.

Study end points: postoperative outcome. Only cardiac death (acute myocardial infarction or sudden unexpected death) and acute myocardial infarction before discharge from the hospital were accepted as end points. Acute myocardial infarction was diagnosed when at least two of the following three criteria were met: (1) a recent episode of characteristic chest pain that lasted longer than 30 minutes; (2) a transient increase above the upper limit of normal of total serum creatinine kinase and its myocardial isoenzyme subfraction, related temporally to the episode of chest pain; and (3) Minnesota code criteria for definite or probable myocardial infarction accompanied by evolving ST and T wave changes.[29,30] The results of thallium studies were made available to referring physicians, and the decision to refer the patient for coronary angiography or directly to surgery was left up to them. Patients with redistribution were usually monitored with a Swan-Ganz catheter during surgery, transferred to the intensive care unit after operation, and followed by the consulting cardiologist after operation.

TABLE 2. *Clinical Scoring Systems*

Test	No. of Points	Test
Goldman Cardiac Operative Risk Index[8]		Total score: 0–120
History		Detsky classification — Total points
Age >70 yr	5	1 — 0–15
Myocardial infarction <6 mo	10	2 — 16–30
Aortic stenosis	3	3 — >30
Physical examination		Eagle vascular surgery low-risk clinical markers[10]
Third heart sound, S3 gallop, or signs of congestive heart failure	11	The patient is considered to be at low risk for surgery if the following five clinical markers are absent: history of angina, clinical or electrocardiographic evidence of prior myocardial infarction, diabetes, and congestive heart failure.
Electrocardiogram		
Any rhythm other than sinus	7	
>5 premature ventricular contractions/min	7	Cooperman equation[11]
Poor general medical condition	3	$P = \text{antilog}_2 [C_1 * X_1 + (C_2 * X_2) + \ldots\ldots\ldots + C]$
P_{O_2} <60		X_1 = angina (C_1 = 0.46)
P_{CO_2} >50		X_2 = congestive heart failure (C_2 = 1.02)
K^+ <3		X_3 = arrhythmia (C_3 = 0.62)
BUN >50		X_4 = previous myocardial infarction (C_4 = 0.64)
Creatinine >3 (>260 mmol/L)		X_5 = cerebrovascular accident (C_6 = 1.15)
Bedridden		X_6 = abnormal electrocardiogram (C_5 = 1.25)
Operation		Dripps-American Surgical Association Physical Status Score[7]
Emergency	4	1 = normal healthy patient for elective operation
Intrathoracic or intra-abdominal or aortic	3	2 = mild systemic disease
Total points = 0–53		3 = severe systemic disease with limited activity but not incapacitated
Goldman classification — Total points		
1 — 0–5		4 = incapacitating systemic disease that is a constant threat to life
2 — 6–12		5 = moribund patient not expected to survive 24 hr with or without operation
3 — 13–25		
4 — >25		Eagle equation
Detsky Modified Multifactorial Risk Index[9]		
Coronary artery disease		Probability of postoperative event = $\frac{e^{score}}{1 + e^{score}}$
Myocardial infarction <6 mo	10	
Myocardial infarction >6 mo	5	Calculation of score
Canadian Cardiovascular Society angina		0.077 × age − 10
Class III	10	+ 1 if history of angina
Class IV	20	+ 1.4 if Q-wave on electrocardiogram
Unstable angina <6 mo	10	+ 1.2 if history of ventricular ectopic activity
Alveolar pulmonary edema		+ 1.0 if diabetes
Within 1 wk	10	+ 1.3 if ischemic electrocardiographic changes during dipyridamole infusion
Ever	5	
Valvular disease		+ 2.3 if redistribution of thallium
Suspected critical aortic stenosis	20	Total = score
Arrhythmias		Yeager clinical markers of low cardiac risk
Rhythm other than sinus (may have APB)	5	The patient is considered to be at low risk if the following three preoperative clinical markers are absent
>5 PVC before surgery	5	
Poor general medical status	5	History of angina
Age >70 yr	5	History of myocardial infarction
Emergency operation	10	History of congestive heart failure

Study End Points: Outpatient Follow-up

All patients were contacted by phone by a trained research assistant unless it was clearly recorded in the hospital chart that the patient had been referred for coronary revascularization or had sustained a cardiac event. All reported cardiac events were verified by the main investigator (J.L.) before being entered into the database.

Statistical Analysis

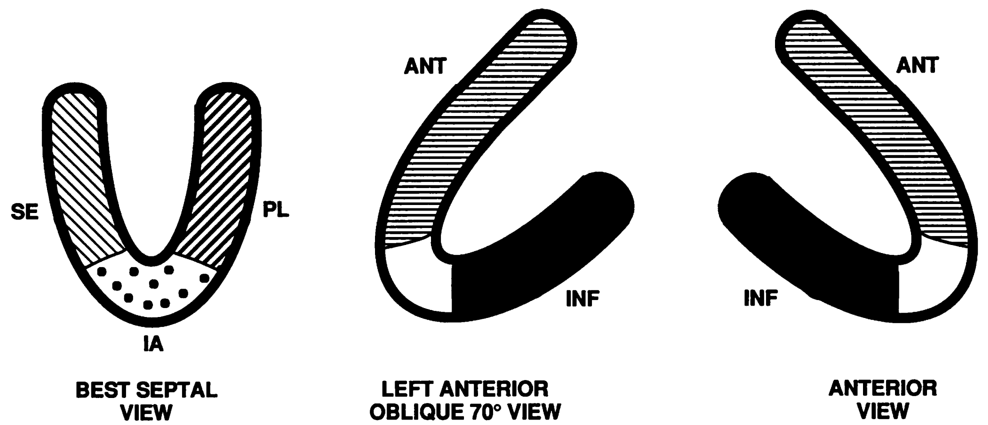
Correlation between clinical parameters and scoring systems, results of dipyridamole-thallium imaging, and cardiac events was done using chi square and analysis of variance. All values are mean ± standard deviation. Multivariate stepwise logistic regression analysis was carried out by the maximal likelihood ratio method.

Results

Clinical Features and Postoperative Outcome

The clinical features of the 360 patients are listed in Table 4. There were 30 postoperative cardiac events: 19 coronary deaths (13 fatal myocardial infarctions and six sudden deaths) and 11 nonfatal myocardial infarctions. The events occurred an average of 4 days after surgery.

FIG. 1. Division of myocardium into five regions. Scans were divided into seven segments, which were reduced to five myocardial perfusion regions, taking into account anatomic overlap. When scintigraphic indices for overlapping segments differed in magnitude, the segment with the most severe and reversible perfusion defect was considered as representative of the region.



Postoperative Outcome: Predictive Value of Clinical Parameters

The correlation between individual clinical parameters, multivariate scoring systems, quantitative perfusion indices, and postoperative outcome are shown in Tables 4, 5, and 6, respectively. Age ($p = 0.015$), history of coronary artery disease ($p = 0.016$), and diabetes ($p = 0.001$) attained statistical significance by univariate analysis. Interestingly, the Goldman ($p = 0.0008$) and Detsky ($p = 0.005$) "scores" correlated with the occurrence of postoperative cardiac complications, but of the patients who sustained cardiac events after operation, most had been classified as low risk according to the Goldman and Detsky "classes" that are used for risk stratification in clinical practice. The Cooperman equation correlated with postoperative outcome ($p = 0.04$) for the population as a whole, but there was too much individual variation to be of any practical use.

Postoperative Outcome: Predictive Value of Dipyridamole-Thallium Imaging Interpreted as Either "Positive" (Reversible Defect) or "Negative" (Normal Scan or Fixed Defect)

There was one fatal myocardial infarction (with normal coronary arteries at autopsy) and one nonfatal myocardial infarction in the 200 patients with either normal scans or fixed perfusion defects as defined in this study. The cardiac event rate was 17.5% in 160 patients with reversible defects.

TABLE 3. *Definition of Indices for Severity and Extent*

1. Extent: Reversible extent (RE): the myocardium is divided into five anatomic regions. The extent refers to the number of regions that display a given characteristic (range 1–5).
2. Reversibility score: the difference in the severity of the perfusion defect in a given anatomic region between the immediate postdipyridamole and the delayed images (range 0–3; measured for each of the five regions).
   Summed reversibility index (SR): the sum of the reversibility scores measured for each of the five regions (range 0–15).
   Maximal reversibility index (MR): the highest reversibility score among the five regions (range 0–3).
3. Amount of infarcted myocardium
   Infarcted myocardium index (IM): the amount of nonischemic, nonjeopardized myocardium calculated as the sum of severity scores in each anatomic region on the redistribution images.

Postoperative Outcome: Predictive Value of Dipyridamole-Thallium Imaging Based on the Severity and Extent of Reversible Perfusion Defects

There was a strong correlation between the scintigraphic indices of severity and extent of reversible defects and postoperative cardiac events ($p = 0.0001$), as shown in Table 6. There is a clear demarcation in severity and extent of thallium redistribution between patients with and without postoperative events, as illustrated in Figures 2, 3A, and 3B. Reversible left ventricular cavitary dilatation was observed in 53% (10/19) of patients who sustained a postoperative cardiac event.

Postoperative Outcome: Stepwise Logistic Regression Multivariate Analysis

Only two variables predicted postoperative outcome by stepwise logistic regression analysis: age and the summed reversibility index (a reflection of the amount of jeopardized myocardium). The regression coefficients and a simple predictive index derived from our model are shown in Table 7. A three-dimensional graphic representation of the statistical model is depicted in Figure 4A.

Outpatient Follow-up

Patient outcomes. A follow-up was obtained in 98.6% (355/360) of patients. The average follow-up was 15 months. There were 278 uneventful outcomes, 19 nonfatal myocardial infarctions, 24 coronary deaths, 25 noncardiac deaths, and nine patients underwent coronary revascularization after the noncardiac surgery. The clinical features of patients in the different categories are depicted in Table 8. Causes for cardiac deaths include cancer (10), cerebrovascular accidents (five), terminal valvular heart disease (one), chronic renal failure (two), sepsis (four),

TABLE 4. *Postoperative Outcome: Individual Clinical Descriptors*

	Uneventful Outcome (n = 330)	Postoperative Event (n = 30)	p	Significance
No. of men	195 (59)	23 (77)	0.06	NS
Age (yr)	63 ± 10	67.5 ± 5	0.015	†
Vascular surgery	212 (64)	21 (70)	0.53	NS
Site of surgery			0.4	NS
Intra-abdominal	222 (67)	20 (67)		
Intrathoracic	90 (27)	10 (33)		
Cerebrovascular disease	74 (22)	9 (30)	0.47	NS
COPD			0.08	NS
Mild	48 (15)	9 (30)		
Moderate	28 (8)	4 (13)		
Severe	8 (2)	1 (3)		
Renal failure*	31 (9)	4 (13)	0.7	NS
History of coronary artery disease	183 (55)	24 (80)	0.016	†
No. of risk factors	1.9 ± 1	2 ± 0.95	0.76	NS
Smoking	253 (77)	23 (77)	0.82	NS
High blood pressure	171 (52)	12 (40)	0.3	NS
Diabetes	63 (19)	14 (47)	0.001	†
Family history	79 (24)	6 (20)	0.8	NS
Anginal syndrome			0.7	NS
Asymptomatic	174 (53)	16 (53)		
Grade 1/4	24 (7)	1 (3)		
Grade 2/4	65 (20)	8 (27)		
Grade 3/4	10 (3)	0		
Atypical chest pain	57 (17)	5 (17)		
Unstable angina in past 6 mo	11 (3)	0	0.64	NS
MI in past 6 mo	7 (2)	2 (7)	0.36	NS
Previous MI	123 (37)	15 (50)	0.24	NS
History of CHF	19 (6)	5 (17)	0.56	NS
Clinical CHF	5 (2)	2 (7)	0.2	NS
Resting ECG				
LBBB	8 (2)	2 (7)	0.44	NS
LVH	47 (14)	7 (23)	0.3	NS
ST segment abnormality	132 (40)	17 (57)	0.11	NS
Arrhythmia	29 (9)	4 (13)	0.62	NS
Dipyridamole-induced chest pain	41 (12)	7 (23)	0.16	NS

* Renal failure involves hemodialysis, renal transplant, or peritoneal dialysis patient.
† Significant ($p < 0.05$).
Mean ± SD or N (%).

COPD, chronic obstructive lung disease; MI, myocardial infarction; CHF, congestive heart failure; ECG, electrocardiogram; LBBB, left bundle branch block; LVH, left ventricular hypertrophy.

TABLE 5. *Postoperative Outcome: Clinical Scoring Systems*

	Uneventful Outcome (n = 330)	Postoperative Event (n = 30)	p	Significance
Dripps-ASA class			0.4	NS
Class 1	18 (5)	1 (3)		
Class 2	212 (64)	18 (60)		
Class 3	98 (30)	10 (33)		
Class 4	2 (0.6)	1 (3)		
Goldman index total score	4.6 ± 3.6	7 ± 6	0.0008	*
			0.005	*
Class 1	231 (70)	15 (50)		
Class 2	82 (25)	9 (30)		
Class 3	17 (5)	6 (20)		
Detsky index total score	5 ± 6	8.3 ± 8	0.005	*
			0.1	NS
Class 1	308 (93)	25 (83)		
Class 2 or 3	22 (7)	5 (17)		
Eagle low-risk criteria	91 (28)	3 (10)		
Yeager low-risk criteria	96 (29)	7 (23)		
Cooperman probability	36 ± 38	52 ± 58	0.04	*

Mean ± SD or N (%).

* Significant ($p < 0.05$).

TABLE 6. *Postoperative Outcome: Quantitative Myocardial Perfusion Indices*

	Uneventful Outcome (n = 330)	Postoperative Event (n = 30)	p	Significance
Segmental reversibility indices				
Anterior	0.1 ± 0.4	0.9 ± 1.1	0.0001	†
Septal	0.2 ± 0.6	1.2 ± 1.7	0.0001	†
Inferoposterior	0.3 ± 0.7	1.2 ± 1	0.0001	†
Inferoapical	0.15 ± 0.5	1.4 ± 1.2	0.0001	†
Posterolateral	0.2 ± 0.5	1 ± 1	0.0001	†
Indices of severity and extent				
Reversible extent	0.67 ± 1	3 ± 1.4	0.0001	†
Maximal reversibility	0.6 ± 0.9	2.2 ± 0.9	0.0001	†
Summed reversibility	1 ± 1.7	6 ± 3.3	0.0001	†
Infarcted myocardium	0.9 ± 2	1.5 ± 1.9	0.154	NS
Transient left ventricle cavitary dilatation*	9 (3)	10 (33)	0.0001	†

Mean ± SD or N (%).
† Significant ($p < 0.05$).
* Transient dipyridamole-induced left ventricle cavitary dilatation.

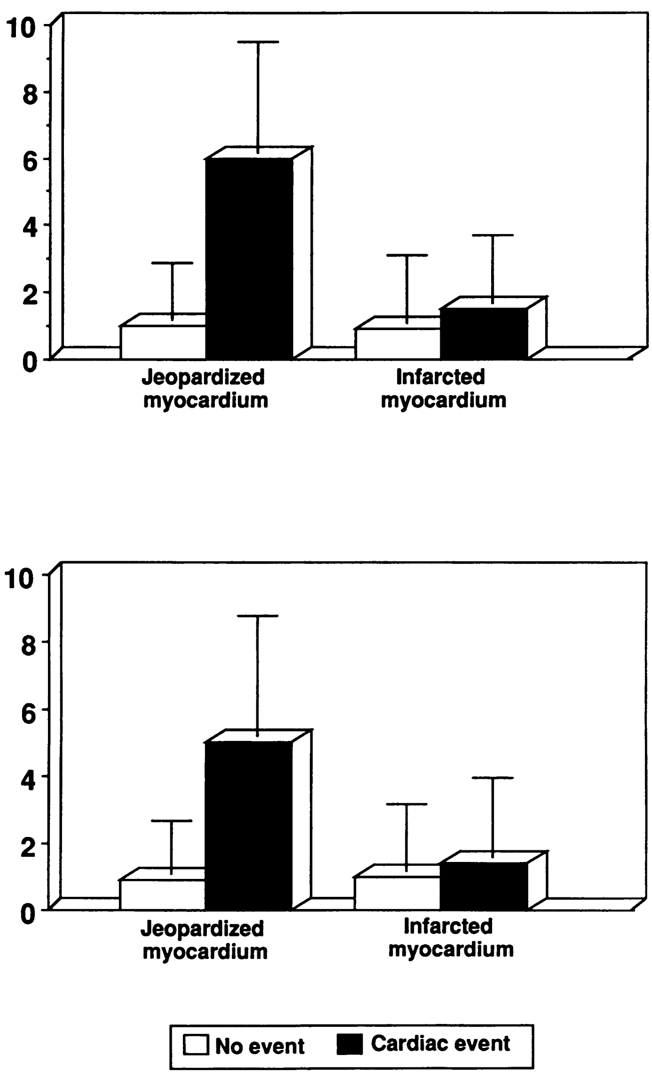


FIG. 2. Average amount of jeopardized (summed reversibility index) (p = 0.0001) and infarcted (infarcted myocardium index) (NS) myocardium in patients with and without postoperative and long-term cardiac events.

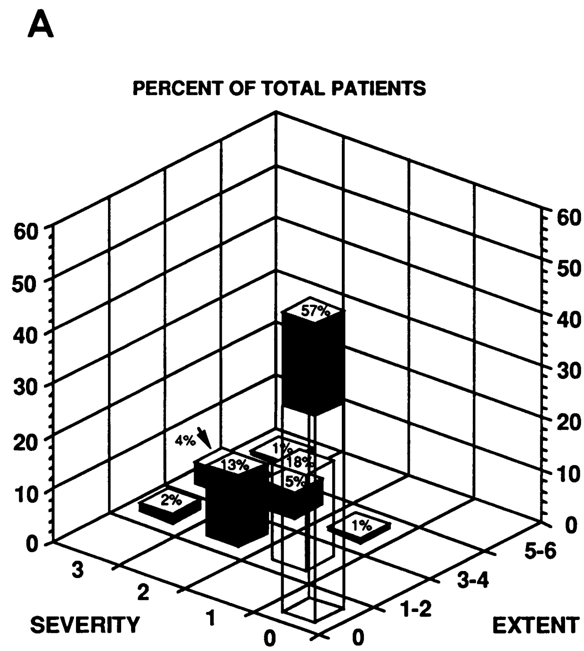
pulmonary embolism (one), adult respiratory distress syndrome (one), and hemorrhagic shock (one).

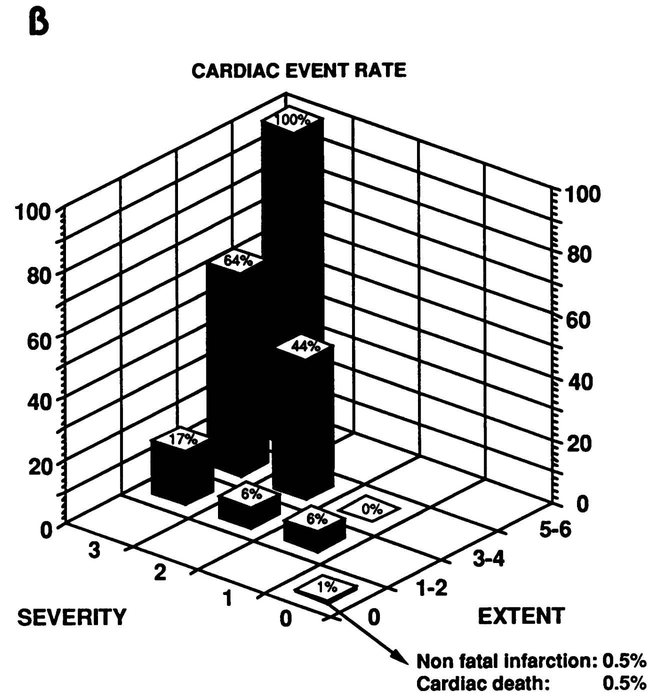
Clinical predictors. The correlations between individual clinical parameters and long-term outcome and between quantitative perfusion indices and long-term outcome are shown in Tables 8 and 9, respectively. Age (p = 0.003), history of coronary artery disease (p = 0.01), diabetes (p = 0.001), presence of congestive heart failure (p = 0.0006), and presence of ST segment abnormalities on the resting electrocardiogram (p = 0.004) attained statistical significance by univariate analysis.

Dipyridamole imaging. The long-term cumulative cardiac event rate was 3.5% (3% nonfatal infarctions and 0.5% cardiac deaths) for patients with normal scans or fixed defects, and 22% (7% nonfatal infarctions and 15% cardiac deaths) for patients with reversible perfusion defects. There was a strong correlation between the scintigraphic indices of severity and extent of reversible defects and long-term cardiac events (p = 0.0001), as shown in Table 9. There is a clear demarcation in severity and extent of thallium redistribution between patients with and without postoperative events, as illustrated in Figures 2, 3C, and 5. The 1-year total cardiac event rate escalates as the severity and extent of reversible defects on the dipyridamole-thallium scans increase. Patients can be stratified into multiple scintigraphic subsets, with corresponding postoperative and 1-year cumulative coronary morbidity and mortality rates ranging from 3.5% to 100% (Figs. 3C and 5). The proportion of patients with transient dipyridamole-induced left ventricular cavitary dilation who survived event-free over time is illustrated in Figure 5.

Long-term Outcome: Stepwise Logistic Regression Multivariate Analysis

A total of four variables predicted long-term outcome by stepwise logistic regression multivariate analysis: age,





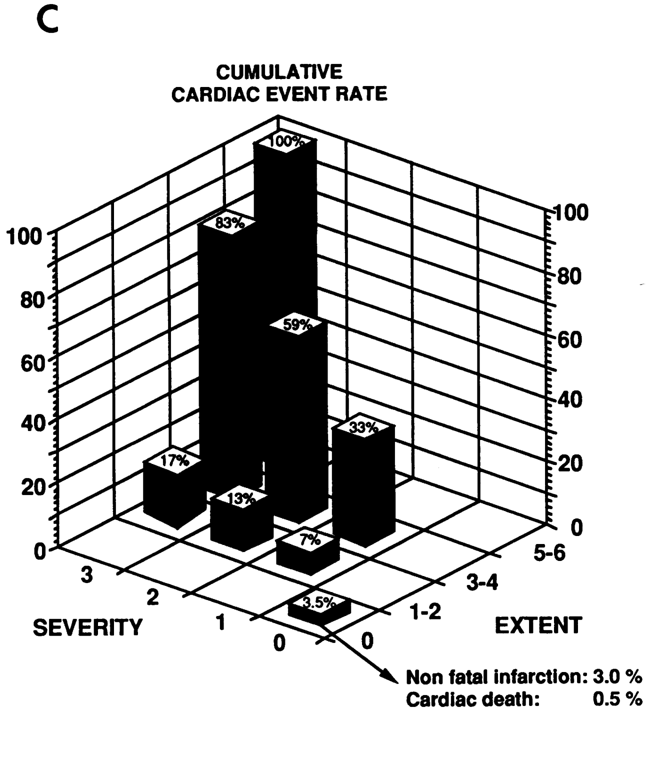


FIG. 3. (A) Distribution of patients in scintigraphic subsets according to the severity and extent of dipyridamole-induced reversible perfusion defects. (B) Postoperative and (C) long-term cardiac event rates in the various scintigraphic subsets. It is apparent that a relatively small number of patients with multiple and severe reversible perfusion defects (high-risk scintigraphic subsets) account for most postoperative cardiac events.

presence of congestive heart failure, presence of dipyridamole-induced left ventricular cavitary dilation, and the summed reversibility index (a reflection of the amount of jeopardized myocardium). The regression coefficients and a simple predictive index derived are shown in Table 10. A three-dimensional graphic representation of the long-term statistical model is depicted in Figure 4B.

Discussion

Why Assess Cardiac Risk Before Operation?

Preoperative cardiac risk assessment should identify three patient subgroups: those without significant coronary artery disease, those with coronary stenoses who can safely undergo noncardiac surgery with anti-ischemic medica-

TABLE 7. *Postoperative Outcome*

Logistic Regression Analysis: Clinical and Scintigraphic Predictors

Variable	Coefficients	Standard Error	PI	Odds Ratio	95% Confidence Interval
Age	0.07	0.03	0.022	1.07	1.006–1.14
SR	0.649	0.09	0.00001	1.914	1.58–2.32

PI, predictive index (probability of a postoperative cardiac event)

$$p = \frac{e^u}{1 + e^u}$$

where e = base of natural logarithm
$u = -8.9435 + (0.6491^* SR) + (0.07^* age)$

Operating characteristics of the predictive model
Sensitivity = 80%
Specificity = 83.3%
* SR, summed reversibility index (amount of jeopardized myocardium).

tion, and the small group of high-risk coronary patients who require preoperative coronary angiography and frequently revascularization. Therefore, risk assessment is distinct from diagnostic screening for coronary artery disease, which pigeonholes patients into two categories: positive or negative. In addition to the perioperative and postoperative course, preoperative cardiac risk assessment obviously should be concerned with long-term cardiac mortality rate to insure that those who undergo major noncardiac surgery live long enough to benefit from the procedure.

Pitfalls of Basing Individual Patient Management on Multivariate Clinical Models

Of 23 separate clinical descriptors studied, only history of coronary artery disease (p = 0.016), age (p = 0.015), and diabetes (p = 0.001) correlated with the occurrence of postoperative cardiac events. This is of little practical use, however: the expression "history of coronary artery disease" is too imprecise, and, of the patients who sustained cardiac complications, 56% were younger than age 70, and 53% did not have diabetes. Remarkably, the presence and severity of angina pectoris had no bearing on either the postoperative or the long-term outcome, which underscores the difficulty in evaluating clinically patients with a low exercise tolerance.[31]

The area of preoperative cardiac risk assessment provides a unique opportunity to examine the perils of basing individual patient management on statistically derived clinical scoring systems. Although the "clinical scores" derived from multivariate models correlated strongly with postoperative events, most patients who sustained cardiac events had in fact been categorized as low risk (Table 5). For example, the Goldman et al.[20] (p = 0.0008) and Detsky et al.[21] (p = 0.005) scores both correlated strongly with postoperative outcome, but mislabeled as "low risk" 80% (Goldman class 1 or 2) and 83% (Detsky class 1) of patients who sustained postoperative events. On closer examination, these multivariate models appear to add little to basic clinical common sense: the sicker a population of patients, the higher the incidence of postoperative complications, or, in candid terms, the sicker the patient, the higher the risk. In addition, clinical scoring systems based on multivariate analysis are not transportable between institutions[12,13,18] and are not reproducible within the same institution.[32]

Risk Assessment Based on the Resting Preoperative Ejection Fraction

There is a high reported incidence of postoperative and long-term cardiac complications in patients with a low left ventricular ejection fraction (35% or less), leading some authors to recommend preoperative radionuclide ventriculography as a tool for identifying high-risk patients.[33–37] Such a quick and simple approach is appealing but ignores a basic precept of clinical cardiology: patients with severe coronary disease, a large ischemic burden, and a normal ejection fraction at rest are at high risk.[38,39] For example, who would suggest that a patient with a 90% left main coronary artery stenosis and normal ventriculogram is at low risk? Conversely, it is misleading to lump all patients with a low ejection fraction into a high-risk category, irrespective of the amount of residual ischemia: a substantial number of these patients have a good long-term outlook and should not be denied surgery solely on the basis of a low ejection fraction.[40] In our study, the amount of jeopardized myocardium correlated strongly with postoperative outcome, whereas the amount of infarcted myocardium did not (Tables 6 and 9; Fig. 2). We are developing objective criteria combining resting ejection fraction and stress myocardial perfusion data to stratify patients with a low ejection fraction into high- and low-risk subgroups.

The Conventional Interpretation of Dipyridamole Images and its Limitations

The introduction of dipyridamole imaging was greeted with enthusiasm because of the low event rate in patients with normal studies or fixed defects.[1–7] In our study, a negative dipyridamole-thallium test was reported in 195 patients and indicated a very good prognosis: after operation, 0.5% (1/195) sustained a nonfatal myocardial infarction and 0.5% (1/195) sustained a fatal myocardial infarction (with normal coronary arteries at autopsy). The 1-year outlook was also good: of the 194 patients with

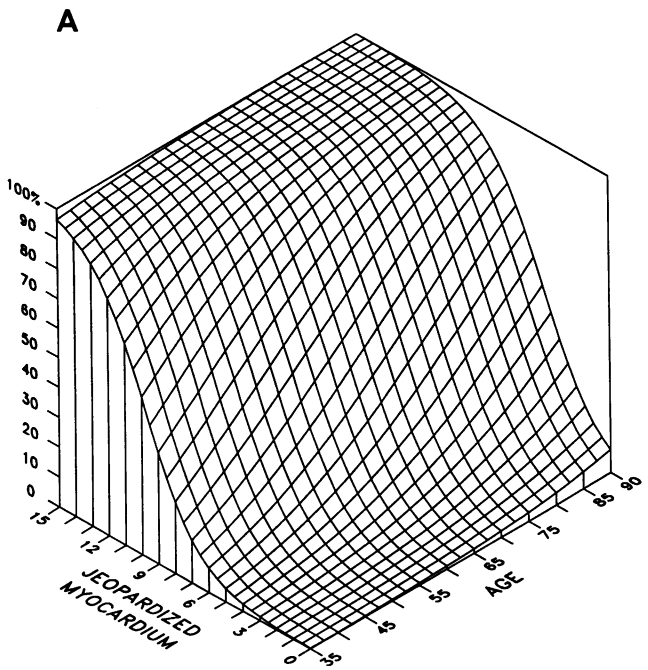


FIG. 4. (A) Three-dimensional graphic representation of the surgical risk (including the postoperative outcome) in 360 patients. There is an exponential escalation in cardiac risk as the amount of jeopardized myocardium (summed reversibility index) increases, as opposed to the relatively minor effect of age, which is the only other significant predictor. (B) Three-dimensional graphic representation of the long-term risk (including the postoperative outcome) in the same patients. There were four predictors of long-term outcome, namely, amount of jeopardized myocardium, presence of congestive heart failure (bottom), presence of transient dipyridamole-induced left ventricular cavitary dilatation (right), and age.

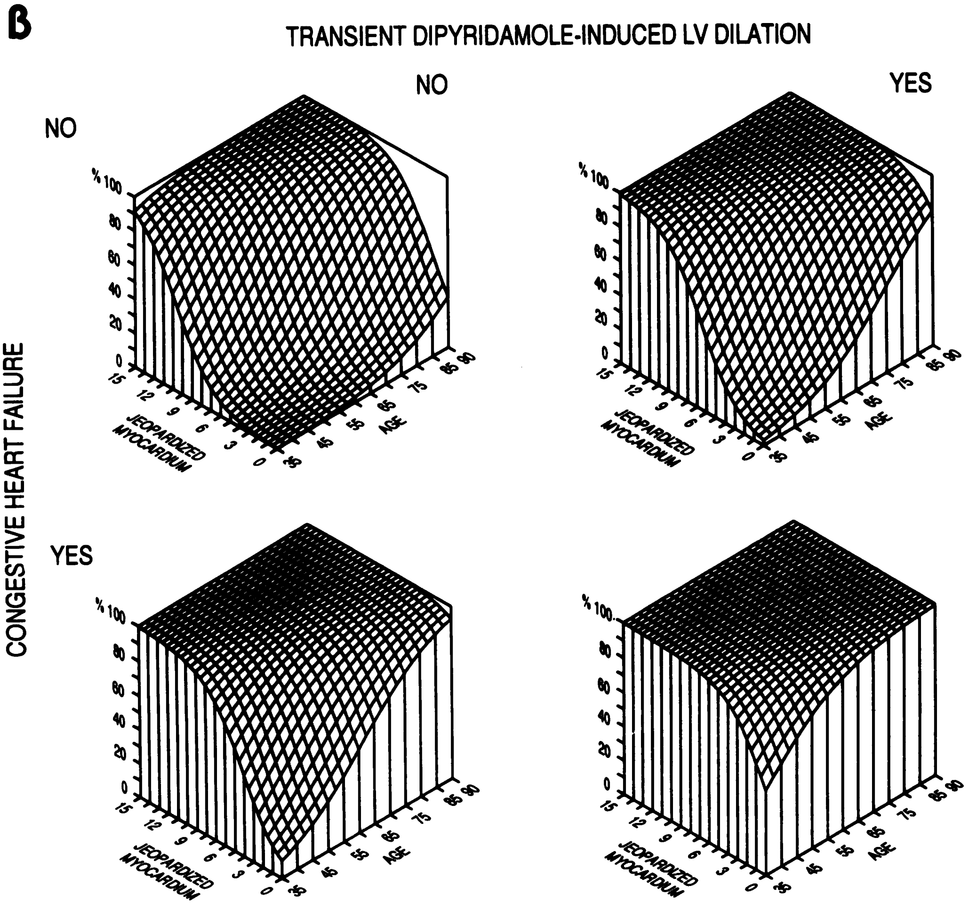


TABLE 8. *Long-term Outcome: Clinical Descriptors*

	No Cardiac Event (n = 303)	Cardiac Event (n = 43)	Coronary Revascularization (n = 9)	p	Significance
No. of men	177	31	6	0.12	NS
Age (yr)	63 ± 10	68 ± 7	60 ± 10	0.003	†
Cerebrovascular disease	69 (23)	11 (26)	3 (33)	0.82	NS
COPD				0.1	NS
Mild	43 (14)	12 (28)	1 (11)		
Moderate	26 (9)	5 (12)	1 (11)		
Severe	8 (3)	1 (2)	0		
Renal failure*	15 (5)	2 (5)	2 (22)	0.77	NS
High blood pressure	158 (52)	17 (40)	6 (67)	0.16	NS
Diabetes	57 (19)	18 (42)	2 (22)	0.001	†
History of coronary artery disease	167 (55)	33 (77)	5 (56)	0.01	†
Previous MI	112 (37)	21 (49)	2 (22)	0.18	NS
CHF	2 (1)	4 (9)	1 (11)	0.0006	†
Anginal syndrome				0.95	NS
Asymptomatic	161 (53)	21 (49)	6 (67)		
Grade 1/4	22 (7)	3 (7)	0		
Grade 2/4	61 (20)	11 (26)	0		
Grade 3/4	8 (3)	1 (2)	1 (11)		
Atypical chest pain	51 (17)	7 (16)	2 (22)		
Electrocardiogram					
LBBB	8 (3)	2 (5)	0	0.8	NS
LVH	42 (14)	10 (23)	1 (11)	0.17	NS
ST segment abnormality	117 (39)	27 (63)	4 (44)	0.004	†
Dipyridamole-induced chest pain	36 (12)	9 (21)	2 (22)	0.16	NS

Values are mean ± SD or N (%).
* Renal failure involves hemodialysis, renal transplant, or peritoneal dialysis patient.
† Significant at $p < 0.05$.

COPD, chronic obstructive lung disease; MI, myocardial infarction; LBBB, left bundle branch block; LVH, left ventricular hypertrophy; NS, not significant.

normal tests who were discharged from hospital after surgery, none died and 2.6% (5/194) sustained a nonfatal myocardial infarction. The low mortality rate is comparable to that previously reported in patients with mild nonobstructive (less than 50%) coronary stenoses.[41,42]

Most investigators lump all patients with reversible defects into a high-risk category and recommend coronary angiography.[8–18] Because the test was initially designed to screen for coronary artery disease, this would result in angiography performed and coronary revascularization considered in approximately 85% of coronary patients referred for noncardiac surgery. This approach is not supported by a previous large multicenter study that showed a low overall surgical risk in coronary patients undergoing noncardiac surgery,[43] and underscores the confusion created by taking a diagnostic procedure designed to screen for coronary artery disease and applying it blindly to risk stratification.

TABLE 9. *Long-term Outcome: Quantitative Myocardial Perfusion Indices*

	No Cardiac Event (n = 303)	Cardiac Event (n = 43)	Coronary Revascularization (n = 9)	p	Significance
Segmental reversibility indices					
Anterior	0.1 ± 0.4	0.8 ± 1	0.2 ± 0.7	0.0001	*
Septal	0.2 ± 0.6	1 ± 1	0.8 ± 1	0.0001	*
Inferoposterior	0.3 ± 0.7	1.1 ± 1	0.9 ± 1	0.0001	*
Inferoapical	0.1 ± 0.5	1.2 ± 1.2	0.6 ± 1	0.0001	*
Posterolateral	0.2 ± 0.5	0.9 ± 1	0.1 ± 0.3	0.0001	*
Indices of severity and extent					
Reversible extent	0.6 ± 0.9	2.5 ± 1.6	1.5 ± 1.2	0.0001	*
Maximal reversibility	0.6 ± 0.9	1 ± 0.2	1 ± 0.4	0.0001	*
Summed reversibility	0.9 ± 1.6	5 ± 3.6	3 ± 1	0.0001	*
Infarcted myocardium	1 ± 2	1.4 ± 2.4	0.7 ± 1.9	0.5	NS
Transient left ventricle cavitary dilatation	3 (1)	14 (33)	2 (22)	0.0001	*

Mean ± SD or N (%).

* Significant ($p < 0.05$).

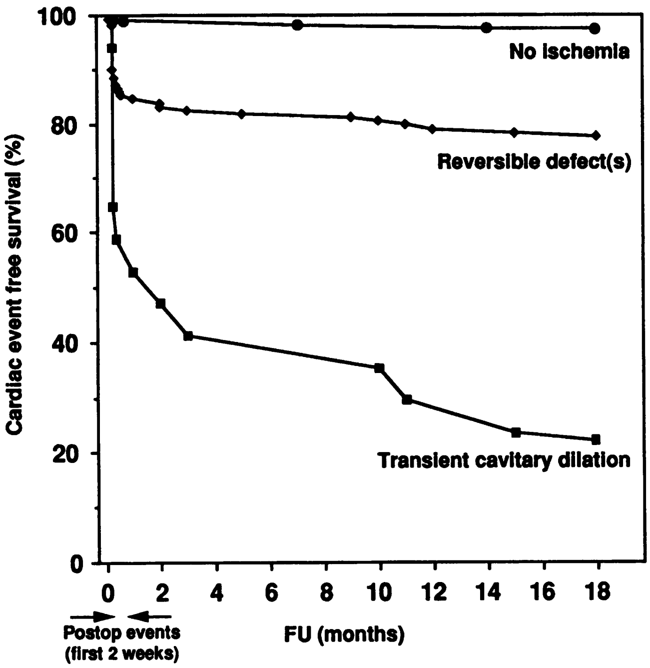


FIG. 5. Proportion of patients who remained cardiac event-free with normal scans or fixed defects (upper curve), reversible perfusion defect(s) (middle curve), and transient dipyridamole-induced left ventricular cavitary dilatation (lower curve). Patients with normal scans or fixed defects have an excellent prognosis; patients with reversible defect(s) are at an increased risk but clearly cannot be labeled as high risk. For patients with transient dipyridamole-induced left ventricular cavitary dilatation, the postoperative cardiac event rate is high, and most patients who survive the surgery eventually sustained a cardiac event on long-term follow-up, usually within the first 3 months after the surgery.

Thus, whereas clinical models failed to identify high-risk patients, dipyridamole-thallium testing displaced the problem, exposing large numbers of coronary patients to the risk of systematic preoperative coronary angiography and prophylactic revascularization: in this study, only 17.5% of patients with reversible defects developed postoperative cardiac complications; 22.5% sustained long-term cardiac events, including 14.4% who died of coronary disease. Furthermore, as preoperative dipyridamole-thallium imaging is being routinely performed, its predictive accuracy is gradually declining. This early referral bias in favor of more severe coronary patients is well illustrated by our own previous account of a 43% postoperative cardiac event rate in patients with reversible defects.[27]

The "Risk" of Preoperative Cardiac Risk Assessment

By "risk" of cardiac risk assessment, we refer to the significant increase in total morbidity and mortality rates from widespread preoperative coronary arteriography and prophylactic revascularization. Blombery et al.[44] report a mortality rate as high as 2.4% from coronary arteriography alone in multilevel vascular patients, and Hertzer et al.[45] report an operative mortality rate in excess of 5% from prophylactic coronary revascularization before vascular surgery. In addition, the delay in performing the noncardiac surgery increases the total risk to the patient: we have observed a few instances of critical lower limb ischemia due to the delay in the initially planned vascular surgery while patients undergo extensive cardiac investigation. Some patients are simply overwhelmed by the thought of coronary revascularization followed by major noncardiac surgery and refuse all procedures *en bloc.*

Only myocardial infarction and sudden coronary death were accepted as end points in our study. Unstable angina, ischemic pulmonary edema, cardiac arrhythmias, and other reversible conditions that uniformly respond to medical therapy initially do not justify the added morbidity and mortality from preoperative coronary revascularization.

Risk Stratification Based on the Severity and Extent of Dipyridamole-induced Perfusion Defects

The quantitative perfusion indices, which reflect the amount of potentially ischemic myocardium, correlated strongly with both the postoperative and long-term outcome (Tables 5, 6, and 9; Figs. 2, 3, and 4). Hence, using

TABLE 10. *Long-term Outcome*

Logistic Regression Analysis: Clinical and Scintigraphic Predictors

Variable	Coefficients	Standard Error	PI	Odds Ratio	95% Confidence Interval
Age	0.0809	0.0283	0.0026	1.084	1.02–1.14
CHF	1.7061	0.5433	0.0044	5.507	1.85–16.32
LVdil	1.088	0.4166	0.0073	2.968	1.29–6.82
SR*	0.5463	0.0885	0.00001	1.727	1.44–2.06

PI, predictive index (probability of a long-term cardiac event)

$$P = \frac{e^u}{1 + e^u}$$

where e = base of natural logarithm
$u = (-6.1994) + (0.0897^* \text{Age}) + (1.7061^* \text{CHF}) + (1.088^* \text{LVdil}) + (0.5463^* \text{SR})$

CHF and LVdil are equal to 0 or 1.
Operating characteristics of the predictive model
Sensitivity = 81%
Specificity = 80.5%
* SR = summed reversibility index = amount of jeopardized myocardium.
CHF, congestive heart failure; LVdil, transient dipyridamole-induced left ventricular cavitary dilatation.

quantitative indices, it is possible to convert a test initially designed to screen for coronary artery disease into a true simple and noninvasive risk stratification procedure. Patients can be stratified into multiple scintigraphic subgroups with differing amounts of jeopardized myocardium and corresponding postoperative and long-term coronary morbidity and mortality rates ranging from 0.5% to 100% (Fig. 3). This allows both the consulting cardiologist and the surgeon to tailor the decision either to proceed with surgery or to consider preoperative coronary angiography and revascularization to individual patient's age, general health, and the overall risk profile (operative risk, 1-year myocardial infarction, and coronary death rates). In fact, using quantification, only 13% (45/360) of patients are truly at high risk (*versus* 194/360 = 45% of patients labeled as "high risk" when the test is interpreted conventionally).

Obviously, no single test can substitute for good clinical judgment, but it may facilitate the clinician's task. For example, a dipyridamole-thallium scintigraphic pattern predicting an 8% postoperative cardiac event rate and a 20% 1-year cardiac mortality rate would be unacceptable in a young otherwise healthy patient undergoing elective surgery, but might be acceptable in an elderly patient with multisystem disease or multilevel arteriosclerosis, and a large aortic aneurysm. If, however, the latter patient had multiple severe reversible defects and predicted postoperative and 1-year cardiac mortality rates on the order of 60% and 90%, respectively, heroic measures including sequential or combined cardiac and vascular surgery may well be justified.

Example of a High-risk Scintigraphic Subset

When the amount of jeopardized myocardium is taken into account during risk stratification, it is clear that most postoperative and long-term cardiac events occur in small scintigraphic high-risk subgroups (Figs. 3, 6). For example, in a previous report, we described the occurrence of transient dipyridamole-induced ischemic left ventricular cavitary dilation, and showed that it is simple to recognize, is associated with a large amount of jeopardized myocardium and severe underlying coronary artery disease, and denotes a grim prognosis. In the current study, transient ischemic dilation was observed in only 4.5% (16/360) of the total patient population. This small subset of patients could not be identified clinically: 69% (11/16) denied any history of angina pectoris. They sustained a dreadful 63% (10/16) postoperative cardiac event rate, however, a 79% 1-year cardiac event rate, and they accounted for 33% (10/30) of all postoperative cardiac events.

Future Prospects

There is ongoing research at our institution to further simplify risk stratification based on dipyridamole imaging. Preliminary results suggest that postoperative and long-term outcome are determined primarily by perfusion in only three myocardial segments (anterior, posterolateral, and inferoposterior).

Acknowledgment

The authors thank Ms. Christiane Lussier, Ms. Mary Morello, Mrs. Nicole Choinière, Mr. Mao, Mrs. Maryrose Fontana, and Ms. Cheetah Peltz-Fraser for their assistance in preparing the manuscript, and Mr. Martin Dufresne for conceiving the three-dimensional graphic representation of the multivariate statistical models.

References

1. Calvin JE, Kieser TM, Walley VM, et al. Cardiac mortality and morbidity after vascular surgery. Can J Surg 1986; 29:93–97.
2. Deron SJ, Kotler MN. Noncardiac surgery in the cardiac patient. Am Heart J 1988; 116:831–838.
3. Hertzer NR, Beven EG, Young JR, et al. Fatal myocardial infarction following peripheral vascular operations: a study of 951 patients followed 6 to 11 years postoperatively. Cleve Clin Q 1982; 49: 1–11.
4. Gage AA, Bhayana JN, Balu V, et al. Assessment of cardiac risk in surgical patients. Ann Surg 1977; 112:1488–1492.
5. Arous EJ, Baum PL, Cutler BS. The ischemic exercise test in patients with peripheral vascular disease. Implications for management. Arch Surg 1984; 119:780–783.
6. McCabe CJ, Reidy NC, Abbott WM, et al. The value of electrocardiogram monitoring during treadmill testing for peripheral vascular disease. Surgery 1981; 89:183–186.
7. Iskandrian AS, Heo J, Askenase A, et al. Dipyridamole cardiac imaging. Am Heart J 1988; 115:432–443.
8. Eagle KA, Strauss HW, Boucher CA. Dipyridamole myocardial perfusion imaging for coronary heart disease. Am J Cardiac Imaging 1988; 2:292–303.
9. Eagle KA, Singer DE, Brewster DC, et al. Dipyridamole-thallium scanning in patients undergoing vascular surgery. JAMA 1987; 257:2185–2189.
10. Sachs RN, Tellier P, Larmignat P, et al. Assessment by dipyridamole-thallium-201 myocardial scintigraphy of coronary risk before peripheral vascular surgery. Surgery 1988; 5:584–587.
11. Cutler BS, Leppo JA. Dipyridamole thallium-201 scintigraphy to detect coronary artery disease before abdominal aortic surgery. J Vasc Surg 1987; 5:91–100.
12. Boucher CA, Brewster DC, Darling RC, et al. Determination of cardiac risk by dipyridamole-thallium imaging before peripheral vascular disease. N Engl J Med 1985; 312:389–394.
13. Fletcher JP, Antico VF, Gruenewald S, Kershaw LZ. Dipyridamole-thallium imaging for screening of coronary artery disease prior to vascular surgery. J Cardiovasc Surg 1988; 29:666–669.
14. Leppo J, Boucher CA, Okada RD, et al. Serial thallium-201 myocardial imaging after dipyridamole infusion: diagnostic utility in detecting coronary stenoses and relationship to regional wall motion. Circulation 1982; 3:649–657.
15. Younis LT, Aguirre F, Byers S, et al. Perioperative and long-term prognostic value of intravenous dipyridamole scintigraphy in patients with peripheral vascular disease. Am Heart J 1990; 119: 1287–1292.
16. Camp AD, Garvin PJ, Hoff J, et al. Prognostic value of intravenous dipyridamole-thallium imaging in patients with diabetes mellitus considered for renal transplantation. Am J Cardiol 1990; 65:1459–1463.
17. Brewster DC, Okada RD, Strauss W, et al. Selection of patients for preoperative coronary angiography: use of dipyridamole-stress-thallium myocardial imaging. J Vasc Surg 1985; 2:504–510.
18. Gillet T, Lecorff G, Scemama J, et al. Approche diagnostique de la coronarographie en chirurgie vasculaire. J Mal Vasc 1990; 15: 55–62.
19. Dripps RD, Lamont A, Eckenhoff JE. The role of anaesthesia in surgical mortality. JAMA 1961; 178:261–266.

20. Goldman L, Caldera DL, Nussbaum SR, et al. Multifactorial index of cardiac risk in noncardiac surgical procedures. N Engl J Med 1977; 297:845–850.
21. Detsky AS, Abrams HB, McLaughlin JR. Predicting cardiac complications in patients undergoing noncardiac surgery. J Gen Intern Med 1986; 1:211–219.
22. Eagle KA, Singer DE, Brewster DC, et al. Dipyridamole-thallium scanning in patients undergoing vascular surgery. JAMA 1987; 257:2185–2189.
23. Yeager RA, Weigel RM, Murphy ES, et al. Application of clinically valid cardiac risk factors to aortic aneurysm surgery. Arch Surg 1986; 121:278–281.
24. Cooperman M, Pflug B, Martin EW, Evans WE. Cardiovascular risk factors in patients with peripheral vascular disease. Surgery 1978; 84:505–509.
25. 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; 110:859–866.
26. Taillefer R, Lette J, Phaneuf DC, et al. Thallium-201 myocardial imaging during pharmacologic coronary vasodilation: comparison of oral and intravenous administration of dipyridamole. J Am Coll Cardiol 1986; 8:76–83.
27. Lette J, Waters D, Lapointe J, et al. Usefulness of the severity and extent of reversible defects during thallium dipyridamole imaging for cardiac risk assessment before non cardiac surgery. Am J Cardiol 1989; 64:276–281.
28. Braunwald E, Kloner RA. The stunned myocardium: prolonged, postischemic ventricular dysfunction. Circulation 1982; 66:1146–1149.
29. Blackburn H, Keys A, Simonson E, et al. The electrocardiogram in population studies: a classification system. Circulation 1960; 21: 1160–1175.
30. Rose GA, Blackburn H. Cardiovascular survey methods. Geneva: World Health Organization Monograph, 1968, p 56.
31. Goldman L, Cook F, Mitchell N, et al. Pitfalls in the serial assessment of cardiac functional status: how a reduction in "ordinary" activity may reduce the apparent degree of cardiac compromise and give a misleading impression of improvement. J Chronic Dis 1982; 35:763–771.
32. Lette J, Waters DD, Lassonde J, et al. Postoperative myocardial infarction and cardiac death: predictive value of dipyridamole-thallium imaging and five clinical scoring systems based on multifactorial analysis. Ann Surg 1990; 211:84–90.
33. Pasternak PF, Imparato AM, Bear G, et al. The value of radionuclide angiography as a predictor of perioperative myocardial infarction in patients undergoing abdominal aortic resection. J Vasc Surg 1984; 1:320–325.
34. Mosley JG, Clarke JMF, Ell PJ, Marston A. Assessment of myocardial function before aortic surgery by radionuclide angiocardiography. Br J Surg 1985; 72:886–887.
35. Fletcher JP, Antico VF, Gruenewald S, Kershaw LZ. Risk of aortic aneurysm surgery as assessed by preoperative gated heart pool scan. Br J Surg 1989; 76:26–28.
36. Kazmers A, Cerqueira MD, Zierler RE. Perioperative and late outcome in patients with left ventricular ejection fraction of 35% or less who require major vascular surgery. J Vasc Surg 1988; 8: 307–315.
37. Kazmers A, Moneta GL, Cerqueira MD, et al. The role of preoperative radionuclide ventriculography in defining outcome after revascularization of the extremity. Surg Gynecol Obstet 1990; 171:481–488.
38. Severi S, Michelassi C. Prognostic impact of stress testing in coronary artery disease. Circulation 1991; 83(5 Suppl III):82–88.
39. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging: a diagnostic tool comes of age. Circulation 1991; 83: 363–381.
40. Pilote L, Silberberg J, Lisbona R, Sniderman A. Prognosis in patients with low left ventricular ejection fraction after myocardial infarction. Circulation 1989; 80:1636–1641.
41. Proudfit WL, Bruschke AVG, Sones FM. Clinical course of patients with normal or slightly abnormal coronary arteriograms: 10 years follow-up of 521 patients. Circulation 1980; 62:712–717.
42. Kemp HG, Kronmal RA, Vlietstra RE, et al. Seven year survival of patients with normal or near normal coronary arteriograms: a CASS registry study. J Am Coll Cardiol 1986; 7:479–483.
43. Foster ED, Davis KB, Carpenter JA, et al. Risk of noncardiac operation in patients with defined coronary disease: the Coronary Artery Surgery Study (CASS) Registry experience. Ann Thorac Surg 1986; 41:42–50.
44. Blombery PA, Ferguson IA, Rosengarten DS, et al. The role of coronary artery surgery in complications of abdominal aortic aneurysm surgery. Surgery 1987; 101:150–155.
45. 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 1984; 199:223–233.