Comparative early and late cardiac morbidity among patients requiring different vascular surgery procedures

Gilbert J. L'Italien, BS, Richard P. Cambria, MD, Bruce S. Cutler, MD, Jeffrey A. Leppo, MD, Sumita D. Paul, MD, MPH, David C. Brewster, MD, Robert C. Hendel, MD, William M. Abbott, MD, and Kim A. Eagle, MD, *Boston, Cambridge, and Worcester, Mass.*

Purpose: The evaluation of coronary artery disease (CAD) in patients undergoing vascular surgery can provide information with respect to perioperative and long-term risk for CAD-related events. However, the extent to which the required surgical procedure itself imparts additional risk beyond that dictated by the presence of CAD determinants remains in question. The purpose of this study was to quantify the relative contributions of specific vascular procedures and CAD markers on perioperative and long-term cardiac risk.
Methods: The study cohort comprised 547 patients undergoing vascular surgery from two medical centers who underwent clinical evaluation, dipyridamole thallium testing, and either aortic (n = 321), infrainguinal (n = 177), or carotid (n = 49) vascular surgery between 1984 and 1991. Perioperative and late cardiac risk of fatal or nonfatal myocardial infarction (MI) was compared for the three procedures before and after adjustment for the influence of comorbid factors. These adjusted estimates may be regarded as the component of risk because of type of surgery.
Results: Perioperative MI occurred in 6% of patients undergoing aortic and carotid artery surgery, and in 13% of patients undergoing infrainguinal procedures (p = 0.019). Significant ($p < 0.05$) predictors of MI were history of angina, fixed and reversible dipyridamole thallium defects, and ischemic ST depression during testing. Although patients undergoing infrainguinal procedures exhibited more than twice the risk for perioperative MI compared with patients undergoing aortic surgery (relative risk: 2.4[1.2 to 4.5, p = 0.008]), this value was reduced to insignificant levels (1.6[0.8 to 3.2, p = 0.189]) after adjustment for comorbid factors. There was little change in comparative risk between carotid artery and aortic procedures before (1.0[0.3 to 3.6, p = 0.95]) or after (0.6[0.2 to 2.3, p = 0.4]) covariate adjustment. The 4-year cumulative event-free survival rate was 90% ± 2% for aortic, 74% ± 5% for infrainguinal, and 78% ± 7% for carotid artery procedures (p = 0.0001). Predictors of late MI included history of angina, congestive heart failure, diabetes, fixed dipyridamole thallium defects, and perioperative MI. Patients undergoing infrainguinal procedures exhibited a threefold greater risk for late events compared with patients undergoing aortic procedures (relative risk: 3.0[1.8 to 5.1, p = 0.005]), but this value was reduced to 1.3(0.8 to 2.3, p = 0.32) after adjustment. Long-term risk among patients undergoing carotid artery surgery was less dramatically altered by risk factor adjustment.
Conclusion: In current practice, among patients referred for dipyridamole testing before operation, observed differences in cardiac risk of vascular surgery procedures may be primarily attributable to readily identifiable CAD risk factors rather than to the specific type of vascular surgery. Thus the cardiac and diabetic status of patients should be given careful consideration whenever possible, regardless of surgical procedure to be performed.
(J VASC SURG 1995;21:935-44.)

From the Division of Vascular Surgery, Department of Surgery, and the Cardiac Unit, Department of Medicine, Massachusetts General Hospital, Boston, Harvard Medical School, Cambridge, and the Department of Vascular Surgery, and the Department of Nuclear Medicine, University of Massachusetts Medical Center, Worcester.
Presented at the Twenty-first Annual Meeting of the New England Society for Vascular Surgery, Newport, R.I., Sept. 28-30, 1994.
This study was completed in partial fulfillment of the Doctoral Degree requirement in Epidemiology and Biostatistics, Boston University School of Public Health, Boston (G.J.L.).
Reprint requests: Gilbert J. L'Italien, BS, Division of Vascular Surgery, Department of Surgery, Massachusetts General Hospital, 15 Parkman St., ACC-4, Suite 458, Boston, MA 02114.

0741-5214/95/$3.00 + 0 24/6/63394

Table I. Distribution of clinical and DTHAL variables according to the type of surgical procedure

	Procedure					
	Aortic (n = 321)	*Infrainguinal (n = 177)*	*Carotid (n = 49)*	*Overall p value*	*Aortic vs infrainguinal p value*	*Carotid vs infrainguinal p value*
Variable						
Mean age	66 ± 10	68 ± 9	65 ± 8	0.787		
Advanced age (>70 yrs.)	110 (34%)	69 (39%)	15 (31%)	0.436		
Male	222 (69%)	116 (66%)	30 (61%)	0.455		
History of MI	111 (35%)	88 (50%)	15 (31%)	0.002	0.0009	0.017
History of angina	67 (21%)	55 (31%)	19 (39%)	0.004	0.011	0.309
History of CHF	19 (6%)	32 (18%)	3 (6%)	0.0001	0.00002	0.04
Diabetes mellitus	34 (11%)	67 (38%)	13 (27%)	0.0001	0.00001	0.14
Prior CABG	39 (12%)	24 (14%)	3 (6%)	0.367		
Dipyridamole thallium results						
Fixed defects	135 (42%)	99 (56%)	20 (41%)	0.009	0.003	0.06
Reversible defects	129 (40%)	95 (54%)	24 (49%)	0.013	0.003	0.56
Ischemic ST dep	27 (9%)	21 (12%)	8 (16%)	0.168		

CHF, Congestive heart failure; *ST dep*, ST depression.

Table II, A. Stepwise logistic regression results—predictors of perioperative outcomes*

Variable	*RR*	*95% Confidence interval*	*p Value*
History of angina	2.1	1.1-4.0	0.034
Fixed defects	2.1	1.1-4.3	0.030
Reversible defects	3.7	1.7-8.3	0.001
Ischemic ST dep	3.0	1.4-6.5	0.005
Prior CABG	0.1	0.2-0.9	0.035

ST dep, ST depression.
*Fatal or nonfatal MI.

A significant proportion of patients with peripheral vascular disease will harbor either occult or clinically evident coronary artery disease (CAD),[1] and it is common knowledge that such associated CAD is the principal source of perioperative and late cardiac morbidity and death. The logical posture that perioperative risk is related to both the extent of CAD and the magnitude of the surgical procedure is reflected in the literature emphasizing cardiac risk in aortic surgery.[2-5] Recently, however, cardiac complications are being reported with equal or greater frequency among patients undergoing infrainguinal or carotid artery surgery. Krupski et al.[6] demonstrated that cardiac morbidity rates at 2 years were greater for infrainguinal versus abdominal aortic procedures among 140 male patients. The observed differences were attributed to diabetic and other coronary risk factors. Burnham et al.[7] ascribed differences in cardiac morbidity rates between aortic and femoropopliteal procedures to advanced age among the latter group. In a related earlier study, Cutler et al.[8] also reported increased morbidity rates for infrainguinal versus aortic procedures. The authors speculated that the differences were due to more intensive screening of patients undergoing aortobifemoral procedures, diabetic risk factors, and the observation by Kallero et al.[9] of the association between lower extremity and three-vessel CAD.

Although these studies reported differences in complication rates among surgical procedures, the distinction between procedure-specific risk and that attributable to the spectrum of CAD risk factors remains ill defined. The purpose of this study was to quantify the perioperative and late risk of myocardial infarction (MI) for major vascular procedures and to determine the relative contributions of the specific procedure and clinical and dipyrimadole thallium variables to short- and long-term cardiac risk.

METHODS

The study group was selected from a cohort of 606 consecutive patients receiving dipyridamole thallium before vascular surgery at two university hospitals (Massachusetts General Hospital, Boston, and University of Massachusetts Medical Center, Worcester) between August 1984 and December 1991. In 39 patients, vascular surgery was cancelled because of severe CAD. An additional 20 patients

Table II, B. Stepwise Cox regression results—predictors of long-term outcomes*

Variable	*RR*	*95% Confidence interval*	*p Value*
Diabetes mellitus	1.8	1.1-3.1	0.030
History of angina	1.7	1.0-2.9	0.049
History of CHF	3.6	2.0-6.4	0.0001
Fixed defects	2.6	1.5-4.4	0.001
Prior CABG	0.5	0.2-1.0	0.049
Perioperative nonfatal MI	5.5	3.1-9.8	0.0001

CHF, Congestive heart failure.
*Fatal or nonfatal MI.

Table III, A. Perioperative outcomes according to surgical procedure

	Procedure								
	Aortic (n = 321)		*Infrainguinal (n = 177)*		*Carotid (n = 49)*				
Variable	*No.*	*%*	*No.*	*%*	*No.*	*%*	*Overall p value*	*Ao vs Inf p value*	*Car vs Inf p value*
Fatal/nonfatal MI	19	6	23	13	3	6	0.019	0.006	0.18
All cause of death	16	5	6	3	0	0	0.222		
Nonfatal MI	9	3	18	10	3	6	0.003	0.0005	0.38

Ao, Aortic; *Inf*, infrainguinal; *Car*, carotid artery.

who underwent miscellaneous vascular procedures were also excluded. The remaining 547 patients who underwent prompt abdominal aortic (n = 321), infrainguinal (n = 177), and carotid artery (n = 49) reconstructive procedures comprised the study group. The proportion of all patients undergoing vascular surgery referred for dipyridamole thallium testing was approximately 30% for both aortic and infrainguinal (femoropopliteal, femorotibial) procedures, and 10% for carotid artery surgery at both medical centers.

Clinical and historical patient information was obtained retrospectively through careful medical record review by investigators who were not involved in the patients' clinical care. These variables included the presence of the following: advanced age (>70 years), a history of angina, a history of myocardial infarction or Q wave on electrocardiography, a history of diabetes mellitus, and a history of congestive heart failure and coronary revascularization before the current hospitalization.

The administration of intravenous dipyridamole and thallium was supervised by a cardiologist who recorded changes in pulse, blood pressure, and electrocardiography results. Ischemic electrocardiographic changes were defined as 1 mm or greater of horizontal or downsloping ST segment depression compared with baseline tracings. Planar thallium imaging was used. Initial images were obtained in three standard views (anterior, left anterior oblique, and lateral) immediately after the administration of dipyridamole and thallium, and delayed images were obtained 3 hours later. Positive results were described as planar myocardial scintigraphic images that, on review by two experienced observers, showed fixed defects or images showing defects that partially or completely redistributed on delayed (3-hour) imaging. The thallium scans were qualitatively interpreted by an experienced nuclear cardiologist who was unaware of the patients' clinical course. Thallium reinjection or quantitation of the degree of redistribution was not performed. Dipyridamole thallium results were made available to all treating physicians.

Outcomes were assessed by careful medical record review or interview of the treating physicians, the patients, and their families by cardiology research fellows who were not involved in the patients' clinical care. Outcomes were defined as nonfatal MI or heart-related death. For the definition of nonfatal MI, the University of Minnesota criteria were used: a new Q wave on electrocardiography of 1 mm or greater, creatine-kinase-MB of 5% or greater, or both. Fatal events were defined as sudden death directly attributable to MI or congestive heart failure. 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 of the electrocardiograms or enzyme criteria cited previously. No patients were lost to follow-up or could not have study events confirmed. Perioperative events were defined as those occurring

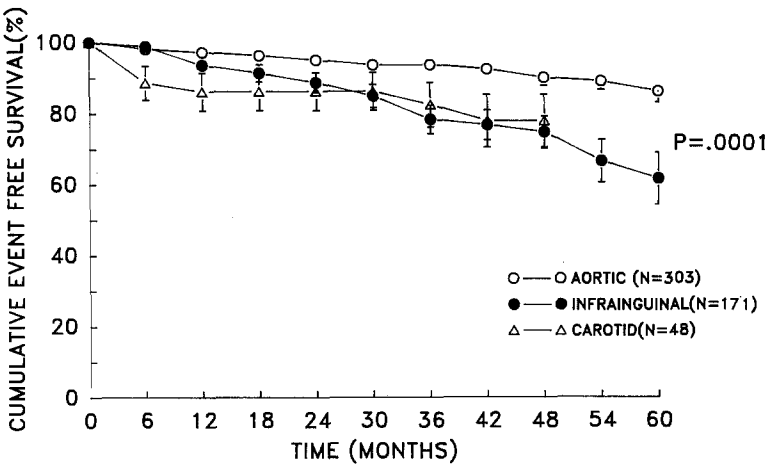

Fig. 1. Cumulative event (fatal/nonfatal MI) free survival rates according to type of surgical procedure.

Table III, B. No CAD risk factors (n = 148)

	Aortic (n = 98)	*Infrainguinal* (n = 38)	*Carotid* (n = 12)	*Overall p value*
Fatal/nonfatal MI	1 (1%)	0 (0%)	0 (0%)	0.700
All cause of death	2 (2%)	0 (0%)	0 (0%)	0.596
Nonfatal MI	0 (0%)	0 (0%)	0 (0%)	1.00

0 to 30 days after vascular surgery. Long-term events were defined as those occurring 31 days or more after surgery.

Statistical analysis A popular statistical package (BMDP Statistical Software, Los Angeles, Calif.) was used for univariate (BMDP4f), logistic (BMDPLR), survival (BMDP11), and Cox (BMDP21) analyses. The distribution of clinical, historical, and dipyridamole thallium factors was first compared among the three procedures by use of chi-square and Fisher exact tests where appropriate. Univariate predictors of perioperative and long-term adverse events were similarly determined. Variables associated with poor outcomes or unequally distributed between surgical treatment groups at the p value < 0.10 were chosen for inclusion into the multivariate models.

For the multivariate analyses, stepwise logistic and Cox regressions were first performed to identify significant ($p < 0.05$), independent predictors of perioperative and late outcomes, respectively. Second, nonstepwise regression analyses were conducted with use of these predictors plus variables comparing the type of surgery (i.e., "infrainguinal vs aortic" and "carotid versus aortic"). To derive these variables, it is necessary that one of the surgical categories be arbitrarily designated as a reference group (e.g., aortic surgery). This method permits the estimation of a "surgical relative risk" adjusted for the influence of the nonsurgical factors.[10] The magnitude of this adjusted risk is indicative of the contribution of surgical factors to the adverse outcome. Finally, these adjusted relative risks were compared with the crude or unadjusted relative risks computed from the simple ratio of event rates for the particular surgical category and the designated reference group (aortic surgery).

To further examine the impact of CAD risk factors on morbidity, patients were stratified according to the presence or absence of predictors identified by the regression models. Perioperative event rates and cumulative event-free survival rates were then calculated and compared by use of chi-square and Mantel-Cox tests, respectively. Non-heart-related deaths were treated as censored observations for the survival analyses. However, separate analyses were performed for all causes of death, heart-related death, and nonfatal MI.

RESULTS

The distribution of clinical, historical, and dipyridamole thallium variables according to operative procedure is illustrated in Table I. The prevalence of

Table III, C. One or more CAD risk factors (n = 399)*

	Aortic (n = 223)	*Infrainguinal (n = 139)*	*Carotid (n = 37)*	*Overall p value*	*Ao vs Inf p value*	*Car vs Inf p value*
Fatal/nonfatal MI	18 (8%)	23 (17%)	3 (8%)	0.039	0.004	0.18
All cause of death	14 (6%)	6 (4%)	0 (0.0%)	0.236	–	–
Nonfatal MI	9 (4%)	18 (13%)	3 (8%)	0.008	0.0005	0.387

Ao, Aortic; *Inf*, infrainguinal; *Car*, carotid artery.
*History of angina, fixed and reversible dipyridamole thallium defects, ischemic ST depression during testing.

Table IV, A. Crude and adjusted surgical RR for perioperative cardiac events* according to the type of surgical procedure

Variable	*Crude RR (95% CI)*	*p Value*	*Adjusted RR (95% CI)†*	*p Value*
Infrainguinal (vs aortic)	2.4 (1.2-4.5)	0.008	1.6 (0.8-3.2)	0.189
Carotid (vs aortic)	1.0 (0.3-3.6)	0.95	0.6 (0.2-2.3)	0.400

*Fatal or nonfatal MI.
†Adjusted for history of angina, fixed defects, reversible dipyridamole thallium defects, ischemic ST depression during dipyridamole thallium.

cardiac risk factors, such as a history of MI, congestive heart failure, fixed and reversible dipyridamole thallium defects, and diabetes are all significantly greater among patients undergoing infrainguinal procedures compared with patients undergoing aortic procedures, and to a lesser extent, among patients undergoing carotid artery surgery, except for a history of angina. The other variables, namely, age, sex, prior coronary artery bypass grafting (CABG), and ischemic ST changes during dipyridamole thallium were evenly distributed between groups.

The results of the logistic regression analysis are detailed in Table II, *A*. The stepwise regression identified a history of angina, fixed and reversible dipyridamole thallium defects, and ischemic ST changes during dipyridamole thallium as independent predictors of perioperative fatal or nonfatal MI; prior CABG was protective. Cox regression (Table II, *B*) identified a history of angina, congestive heart failure, diabetes, fixed dipyridamole thallium defects, and nonfatal perioperative MI as predictors of long-term adverse events, again with prior CABG demonstrating a protective effect.

Perioperative outcomes classed according to operative procedure are illustrated in Table III. There were a total of 45 cardiac events, 30 of which were nonfatal MI (67%). Both heart-related event rates were significantly greater for infrainguinal (13%) compared with aortic (6%) ($p = 0.006, p = 0.0001$, respectively) procedures but not for infrainguinal compared with carotid artery procedures (6%) ($p = 0.18, p = 0.38$, respectively). Furthermore, all cause of mortality rates did not differ according to procedure ($p = 0.222$).

Among 148 patients lacking risk factors identified by logistic regression, there were no procedural differences ($p = 0.7$ to 1) and virtual freedom from adverse outcome; that is, there was only one event among this subset. Among the 399 patients exhibiting one or more risk factors, all event rates were elevated with patients undergoing infrainguinal procedures at significantly higher risk compared with patients undergoing aortic surgery, particularly for nonfatal cardiac events ($p = 0.0005$). There were a total of 44 events in this subset. The overall MI event rate among the 148 "low" risk patients (< 1%) versus the 399 "high" risk patients (11%) was significantly different ($p = 0.002$).

Fig. 1 illustrates the cumulative event (fatal/nonfatal MI) free survival according to procedure for patients undergoing 303 aortic, 171 infrainguinal, and 48 carotid artery procedures. Median follow-up time for the entire cohort was 5 ± 0.5 years. In contrast to the perioperative events, 65% of late outcomes were due to fatal MI. By 24 months, procedural differences became apparent: the cumulative event-free survival rate at 2 years was 95% ± 2% for 210 patients undergoing aortic procedures, 88% ± 2% for 101 patients undergoing infrainguinal procedures, and 86% ± 5% for 25 patients undergoing carotid artery surgery. Among patients undergoing infrainguinal surgery, there is a further decline in the survival rate at 3 years. By 48 months, cumulative rates were 90% ± 2%,

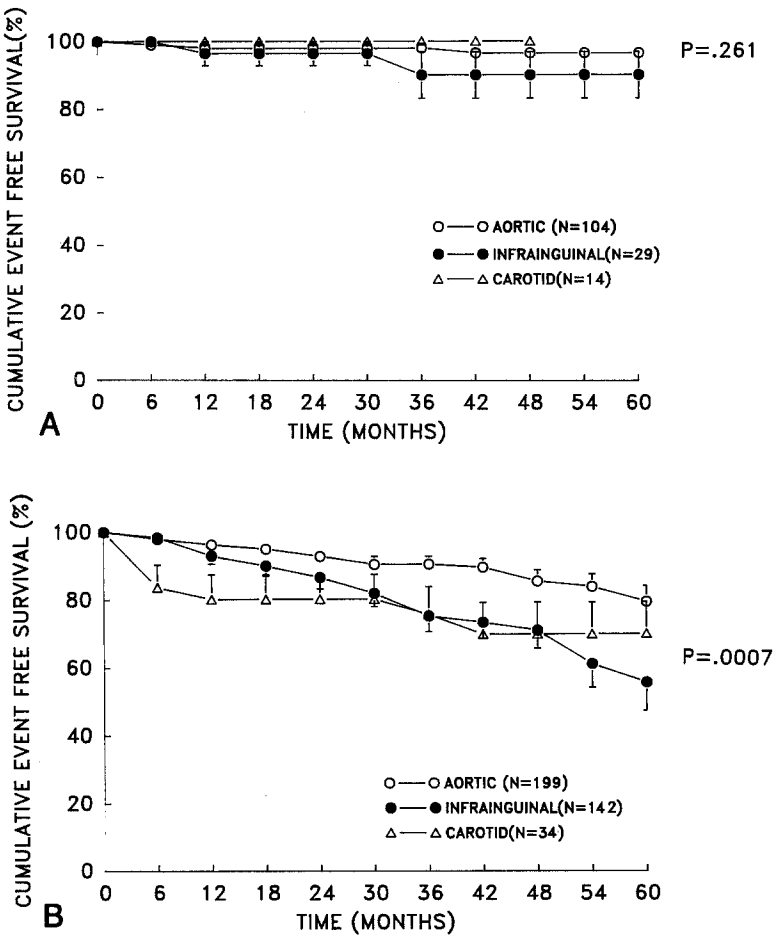

Fig. 2. A, Cumulative event-free survival rates for 147 patients exhibiting no preoperative CAD risk factors. **B,** Cumulative event-free survival rates among 375 patients exhibiting one or more preoperative risk factors (i.e., history of angina, history of diabetes, history of CHF, fixed dipyridamole thallium defects).

74% ± 5% and 78% ± 7% for 96 aortic, 35 infrainguinal, and 11 carotid artery procedures, respectively. These differences persisted for the remainder of the follow-up period (Mantel-Cox *p* value of 0.0001).

The influence of CAD risk factors on procedural differences in cumulative event-free survival is illustrated by the stratified results shown in Fig. 2. Among 147 patients exhibiting no CAD factors, there are no risk differences across procedures, and increased event free survival, up to 36 months; there were only five events in this subset. At 36 months, the rates are 98% ± 1%, 90% ± 7%, and 100% ± 0% for aortic, infrainguinal, and carotid artery procedures, respectively (overall *p* value of 0.261).

Among 375 patients exhibiting one or more CAD factors (Fig. 2, *B*) the procedural differences in event-free survival are again apparent, and rates are lower than the unstratified data shown previously, particularly for infrainguinal and carotid artery procedures. At 48 months, the cumulative event-free survival rate is 85% ± 3% for aortic, 71% ± 5% for infrainguinal, and 70% ± 9% for carotid artery procedures (overall p value of 0.0007). There were 64 events in this subset.

Overall survival according to procedure is illustrated in Fig. 3. More than half of the fatal events were heart related (60%). Differences between aortic and infrainguinal procedures do not become apparent until 36 months, whereas the survival pattern among patients undergoing carotid artery surgery is similar to that shown in Fig. 1. At 36 months, cumulative survival rates are 91% ± 2%, 81% ± 4%, and 81% ± 6% for patients undergoing aortic, infrainguinal, and carotid artery procedures, respectively (Overall p value 0.002).

Table IV details the results of the quantitative

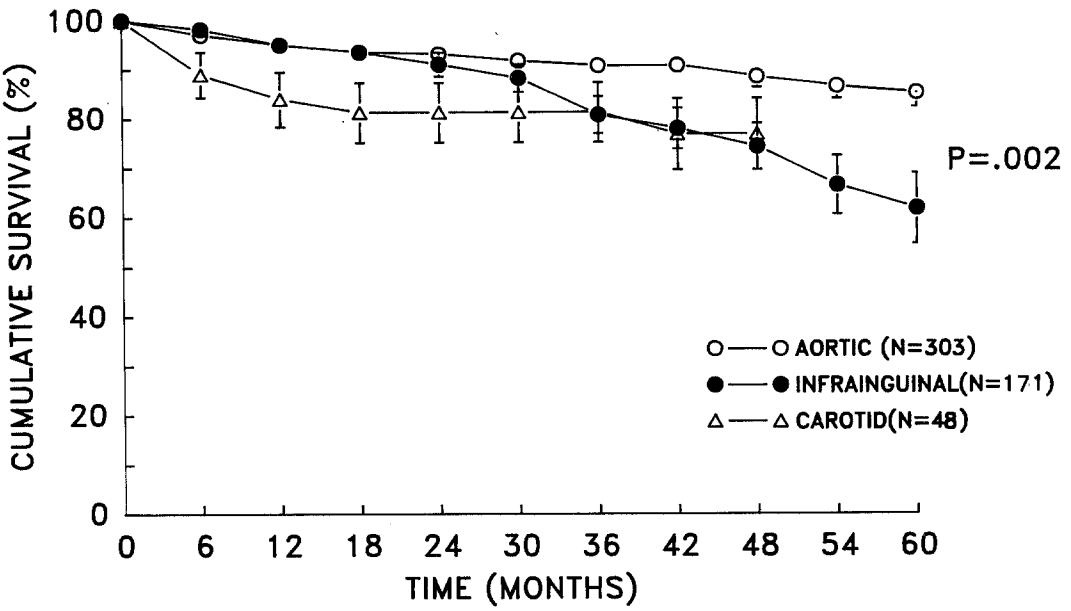

Fig. 3. Cumulative survival rates according to type of surgical procedure.

assessment of procedure-specific risk. Adjusted surgical relative risks (RR) were obtained from the regression models shown in Table II, *A* and II, *B* and compared with the crude (univariate) estimates. These adjusted estimates may be regarded as that component of risk caused by the type of surgery required. Although patients undergoing infrainguinal procedures exhibited more than twice the risk for perioperative events versus patients undergoing aortic surgery (crude RR 2.4, $p = 0.008$), this value was reduced to 1.6 ($p = 0.189$) after adjustment for the CAD risk factors. There was little change in comparative risk between carotid and aortic procedures before (crude RR 1.0, $p = 0.95$) or after (RR 0.6, $p = 0.4$) covariate adjustment.

Patients undergoing infrainguinal surgery exhibited a threefold greater risk for long-term events compared with patients undergoing aortic surgery (crude RR 3.0, $p = 0.005$); however, this value was considerably reduced to 1.3 ($p = 0.32$) after adjustment for comorbid factors. Long-term cardiac risk for patients undergoing carotid artery surgery was similarly elevated (crude RR 2.9, $p = 0.0001$) but was reduced somewhat after covariate adjustment (RR 2.1, $p = 0.07$).

DISCUSSION

This analysis corroborates and expands on our earlier finding[8] of the significantly higher incidence of both perioperative and late adverse cardiac events among patients undergoing infrainguinal versus aortic procedures. Patients undergoing lower extremity procedures exhibited a twofold to threefold greater risk for fatal or nonfatal MI compared with patients undergoing aortic surgery. Long-term risk was also elevated among patients undergoing carotid surgery. Although previous authors have made similar observations,[6-9] this is the first large, diverse study to report quantitative relative risks for major vascular procedures, adjusted for the influence of clinical markers of CAD.

Our results further indicate that these observed procedural risk differences are primarily attributable to a spectrum of CAD factors, which are more prevalent among patients undergoing infrainguinal and, to a lesser extent, carotid artery surgery compared with patients undergoing aortic procedures. Among 148 patients who exhibited no cardiac or diabetic risk factors, procedural risk differences were virtually eliminated, perioperative events were rare (0% to 1%), and cumulative event-free survival was considerably improved. Also, the independent effect of surgery, as indicated by the adjusted surgical RR, appears to be negligible for both perioperative and late MI incidence, particularly among patients undergoing infrainguinal procedures. Thus our results imply that surgery itself imparts minimal perioperative and long-term cardiac risk *on average*. Obviously, factors related to the surgery itself and unknown before operation will still play an important role in

Table IV, B. Crude and adjusted surgical RR for late cardiac events* according to the type of surgical procedure

Variable	*Crude RR (95% CI)*	*p Value*	*Adjusted RR (95% CI)†*	*p Value*
Infrainguinal (vs aortic)	2.9 (1.8-4.6)	0.0001	1.3 (0.8-2.3)	0.32
Carotid (vs aortic)	3.0 (1.5-5.9)	0.005	2.1 (0.9-4.9)	0.07

CHF, Congestive heart failure.
*Fatal or nonfatal MI.
†Adjusted for history of angina, history of diabetes, history of CHF, fixed dipyridamole thallium defects.

determining individual risk. In an earlier report,[2] we demonstrated that prolonged operative time was independently predictive of adverse events after aortic surgery despite a seemingly modest postoperative mortality rate of 2%.

The results of other studies corroborate our finding that lower extremity procedures are associated with a higher than expected morbidity rate, even when the indication for surgery is claudication. Krupski et al.[6] reported perioperative and 2-year cardiac morbidity rates of 25% and 8% for 87 infrainguinal versus 53 age-matched patients undergoing aortic surgery, respectively. As seen in this study, the observed differences in morbidity rates between aortic and infrainguinal procedures were attributed primarily to concommittent cardiac or diabetic factors, and most perioperative and late deaths were heart related. Dawson et al.[11] reported a 5-year cumulative incidence of 34% among 129 patients undergoing infrainguinal bypass, which is similar to this study. These authors also demonstrated that a spectrum of readily obtainable CAD markers was related to fatal cardiac events. Taylor and Porter[12] demonstrated a correlation between the severity of lower extremity ischemia and late death. The reported 5-year survival rate for patients with claudication (67%) was similar to our infrainguinal group (62% ± 7%). Last, recent epidemiologic studies have shown that intermittent claudication doubles the risk of death in most populations.[13-15]

One partial explanation for the observed procedural differences in morbidity rates may be selection bias. Preoperative dipyridamole thallium results were made available to physicians caring for all patients and tended to influence operative management. It is thus possible that candidates for aortic surgery as a result of aortoiliac occlusive disease (AIOD) may have had surgery postponed or cancelled because of severe CAD as indicated by an abnormal scan result. If selection bias was operative, it is reasonable to expect fewer abnormal dipyridamole thallium scan results among patients with AIOD undergoing prompt vascular surgery. However, the percentage of abnormal dipyridamole thallium results was similar for the 256 patients with abdominal aortic aneurysm and 67 patients with AIOD in the current study (60% vs 65%, respectively, $p = 0.450$).

Our aortic surgery results are similar to those reported elsewhere. For example, LaChappelle et al.[16] reported an overall cardiac mortality rate of 3.4% among 146 patients undergoing elective abdominal aortic aneurysm repair. When patients were classed according to CAD risk status, the rates were 1.8% and 9.5% for low- and high-risk groups, respectively. Karla et al.[17] found a perioperative cardiac morbidity rate of 6.3% among 555 patients who underwent elective abdominal aortic surgery, with an overall mortality rate of 2.2%. Last, Johnston and Skobie[3] reported an overall mortality rate of 4.8% among 666 patients undergoing surgery for nonruptured aortic aneurysm. Most of these deaths were due to heart-related causes (67%), as seen in this study.

Although we did not observe differences between the crude and adjusted perioperative relative risk for carotid artery versus aortic procedures, the late adjusted surgical RR remained somewhat elevated, although it was not statistically significant. This may be due to the fact that carotid atherosclerosis itself seems to be an independent predictor for late events,[18,19] because the surgical effects would be expected to be more pronounced during the perioperative interval. The association between carotid atherosclerosis and late MI may also account for the diminished survival seen for patients undergoing carotid artery surgery during the first 2 years of follow-up. Our late results were similar to those of Cohen et al.,[20] who reported a 4-year mortality rate of 35% for 211 carotid endarterectomies. As seen here, most of the late deaths were due to heart-related causes.

It is important to emphasize that our study was restricted to successive patients undergoing vascular surgery who underwent dipyridamole thallium testing *and* prompt vascular surgery. The study is thus limited to those patients for whom the cardiac risk factor status could be reliably determined with both

clinical and dipyridamole thallium information,[21] which minimizes misclassification bias. Furthermore, it is apparent that the indication for dipyridamole thallium testing was based on a clinical impression of elevated cardiac risk rather than the type of surgery required because only a fraction of all patients were tested regardless of procedure. For example, if *all* patients undergoing aortic surgery had been tested compared with a proportion of patients undergoing infrainguinal procedures, selection bias would be operative. However, this was not the case. Although our results may not be generalizable to all patients undergoing vascular surgery, it may be argued that cardiac risk would be inconsequential among the greater population of patients undergoing vascular surgery.[2]

We have demonstrated that all dipyridamole thallium results, including fixed and reversible myocardial defects, ischemic electrocardiographic changes during testing, and one clinical marker, (i.e., a history of angina) independently identify patients who will have development of a perioperative MI. The findings that fixed defects are also independently predictive of perioperative events is unique to this study and may be attributable to the larger size of our cohort. We have further demonstrated that a similar spectrum of readily identifiable CAD markers such as diabetes, angina, congestive heart failure, and fixed dipyridamole thallium defects identify patients who are nearly two to four times more likely to experience a late MI compared with those who do not. In particular, patients who survived a perioperative MI had nearly a sixfold increase in the rate of subsequent cardiac events that were predominantly fatal. This finding has important implications for the assessment of cardiac risk beyond the operative period (i.e., after recovery from vascular surgery) and may warrant long-term follow-up and subsequent treatment of underlying CAD for patients who survive a perioperative MI.

In conclusion, the incidence of heart-related complications among patients undergoing vascular surgery with concurrent CAD or diabetes remains high and is primarily due to these readily identifiable factors rather than the nature of the surgical intervention that is required. This implies that a careful assessment of the patient's preoperative clinical status is vital to the determination of cardiac risk *regardless* of the type of surgical procedure indicated. The presence of significant risk factors may influence anesthetic management, perioperative monitoring, and the need for antiischemic therapy. Last, long-term follow up of patients who exhibit significant CAD markers, as well as those who survive a perioperative MI, is warranted because these individuals are at substantially elevated risk for late cardiac events.

REFERENCES

1. Hertzer NP, Beven EG, Young JR, et al. Coronary artery disease in peripheral vascular surgery patients: a classification of 1000 coronary angiograms and results of surgical management. Ann Surg 1984;199:223-33.
2. Cambria RP, Brewster DC, Abbott WM, 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.
3. Johnston KW, Scobie KT. Multicenter prospective study of nonruptured abdominal aortic aneurysm: part i—population and operative management. J VASC SURG 1988;7:69-81.
4. Johnson KW. Multicenter prospective study of nonruptured abdominal aortic aneurysm. part ii. variables predicting morbidity and mortality. J VASC SURG 1989;9:437-47.
5. Golden MA, Whittemore AD, Donaldson MC, et al. Selective evaluation and management of coronary artery disease in patients undergoing repair of abdominal aortic aneurysms: a 16-year experience. Ann Surg 1990;212:415-20.
6. Krupski WC, Layug EL, Reilly LM, et al. Comparison of cardiac morbidity rates between aortic and infrainguinal operations: two year follow-up. J VASC SURG 1993;18:609-17.
7. Burnham SJ, Johnson G, Furri JA. Mortality risks for survivors of vascular reconstructive procedures. Surgery 1982;92:1072-6.
8. 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.
9. Kallero KS. Bergqvist D, Cederholm C, et al. Arteriosclerosis in popliteal artery trifurcation as a predictor for myocardial infarction after arterial reconstructive operation. Surg Gynecol Obstet 1984;159:133-8.
10. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic research: principles and quantitative methods. Wadsworth, Inc. 1982.
11. Dawson I, Hajo van Bockel J, Brand R. Late nonfatal and fatal cardiac events after infrainguinal bypass for femoropopliteal occlusive disease during a thirty-one year period. J VASC SURG 1993;18:249-60.
12. Taylor LM, Porter JM. Clinical and anatomic considerations for surgery in femoropopliteal disease and the results of surgery. Circulation 1991;83[suppl I]:163-9.
13. Johanson T, Ringqvist I. Mortality and morbidity in patients with intermittent claudication in relation to the location of the occlusive atherosclerosis in the leg. Angiology 1985;36: 310-4.
14. Jelnes R, Gaardstring O, Hougard JK, et al. Fate in intermittent claudication: outcome and risk factors. Br Med J 1986;293:1137-40.
15. Kannel WB, McGee DL. Update on some epidemiologic features of intermittent claudication: the framingham study. J Am Geriatr Soc 1985;33:13-8.
16. LaChappelle K, Graham AM, Symes JF. Does the clinical evaluation of the cardiac status predict outcome in patients with abdominal aortic aneurysms. J VASC SURG 1992;15: 964-71.

17. Kalra M, Charlesworth D, Morris JA, Al-Khaffaf. Myocardial infarction after reconstruction of the abdominal aorta. Br J Surg 1993;80:28-31.
18. Callow A, Mackey W. Long-term follow-up of surgically managed carotid bifurcation atherosclerosis. Ann Surg 1989; 210:308-15.
19. Mackey W, O'Donnell T, Callow A. Cardiac risk in patients undergoing carotid endarterectomy: impact on perioperative and long term mortality. J VASC SURG 1990;11:226-34.
20. Cohen SN, Hobson RW, Weiss DG, et al. Death associated with asymptomatic carotid artery stenosis: long-term clinical evaluation. J VASC SURG 1993;18:1002-11.
21. Eagle KA, Coley CM, Newell JB, et al. Combining clinical and thallium data optimizes peroperative assessment of cardiac risk before major vascular surgery. Ann Int Med 1989;110:859-66.

Submitted Oct. 6, 1994; accepted Jan. 15, 1995.

DISCUSSION

Dr. Martha McDaniel (White River Junction, Vt.). Operative risk prediction is a difficult and important task. Contributions to our knowledge of the topic are voluminous.

With sound methods in two institutions and a large group of patients, you have given us three important messages that are worth repeating. The first thing we heard is that, all other things (cardiac risk factors) being equal, the risk of having an MI is about the same in association with infrainguinal bypass as with aortic surgery. Do not let the anesthesiologists or anyone else underestimate the risks of those "subcutaneous" operations characterized by ICD-9 code 39.29. The second thing we heard is that the chance that an MI sustained at the time of a vascular reconstruction will be fatal is about one in three. This is a much more stable estimate than we have been able to obtain hitherto. The third thing worth noting is the importance of attention to the big picture. Having addressed a patient's immediate vascular problem, we must not forget that the long-term cardiac risk is substantial in this population. The next step is to consider whether attention to the coronary anatomy would improve the patient's quality or quantity of life.

In the world of shared medical decision-making, our job is to help patients arrive at an accurate answer to their very important question: "What are my chances?" Your model incorporates the results of an expensive and time-consuming test, dipyridamole thallium scanning (DTHAL), to try to predict operative and long-term risk. In the past, one of your coauthors (Kim Eagle) has pointed out that diabetes is an independent risk factor for predicting operative morbidity.[21] Would you please tell us what we would lose in predictive value from your model if we incorporated only in expensive or free information, such as angina by history, the presence of diabetes, or electrocardiographic changes?

Mr. Gilbert J. L'Italien. The issue of risk stratification has also occupied our interest for some time. Using the same patients as in this study, we developed a predictive model for perioperative outcomes with logistic regression–weighted scores for the type and number of clinical markers; these were history of angina, MI, diabetes, congestive heart failure, and advanced age. Applying this model, we found it possible to discriminate between low- and high-risk categories of patients. The observed event rate among 215 patients estimated to be at low risk was 2%, and for 35 patients at high risk it was 29%. We found that DTHAL added very little to the predictive value of the model in these patients at low and high risk. The patients at low risk could thus proceed directly to surgery, and the high-risk subset might require more conservative management or perioperative monitoring. Thus we could make these decisions based on clinical markers alone, without the need for DTHAL, in nearly half of the study group. This would save considerable expense. One would also improve the predictive value of DTHAL by restricting the test to the 300 or so patients at moderate risk. I want to emphasize that a weighted scoring system is preferable to merely counting the number or types of markers.

Dr. John Herrmann (Worcester, Mass.). Do you separate your aortic aneurysm cases from your patients with occlusive disease? My bias is that the patients with occlusive disease would probably have about the same risk factors as the patients undergoing infrainguinal and carotid artery procedures.

Mr. L'Italien. We found no difference in the prevalence of abnormal DTHAL results, that is, fixed or reversible defects, among patients with aortic disease whose indication for surgery was aneurysm compared with those undergoing operation for occlusive disease. Based on that result, we did not believe it was necessary to consider these two surgical groups separately. However, this result may be due to some selection bias: some of the patients with occlusive disease may have been screened out. This is a possibility in a retrospective study. However, I do not believe there would be enough bias to account for all of the observed differences in the prevalence of risk factors or in the event rate between patients undergoing infrainguinal and aortic procedures.