The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812 DECEMBER 30, 2004 VOL. 351 NO. 27

Coronary-Artery Revascularization before Elective Major Vascular Surgery

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ABSTRACT

BACKGROUND

The benefit of coronary-artery revascularization before elective major vascular surgery is unclear.

METHODS

We randomly assigned patients at increased risk for perioperative cardiac complications and clinically significant coronary artery disease to undergo either revascularization or no revascularization before elective major vascular surgery. The primary end point was long-term mortality.

RESULTS

Of 5859 patients scheduled for vascular operations at 18 Veterans Affairs medical centers, 510 (9 percent) were eligible for the study and were randomly assigned to either coronary-artery revascularization before surgery or no revascularization before surgery. The indications for a vascular operation were an expanding abdominal aortic aneurysm (33 percent) or arterial occlusive disease of the legs (67 percent). Among the patients assigned to preoperative coronary-artery revascularization, percutaneous coronary intervention was performed in 59 percent, and bypass surgery was performed in 41 percent. The median time from randomization to vascular surgery was 54 days in the revascularization group and 18 days in the group not undergoing revascularization ($P<0.001$). At 2.7 years after randomization, mortality in the revascularization group was 22 percent and in the no-revascularization group 23 percent (relative risk, 0.98; 95 percent confidence interval, 0.70 to 1.37; $P=0.92$). Within 30 days after the vascular operation, a postoperative myocardial infarction, defined by elevated troponin levels, occurred in 12 percent of the revascularization group and 14 percent of the no-revascularization group ($P=0.37$).

CONCLUSIONS

Coronary-artery revascularization before elective vascular surgery does not significantly alter the long-term outcome. On the basis of these data, a strategy of coronary-artery revascularization before elective vascular surgery among patients with stable cardiac symptoms cannot be recommended.

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N Engl J Med 2004;351:2795-804.

THE OPTIMAL TREATMENT OF PATIENTS undergoing elective vascular surgery has not been clearly defined. Because the prevalence of coronary artery disease among these patients approaches 50 percent,[1] the incidence of perioperative cardiac complications is high, leading to a rigorous process of risk stratification.[2-5] In the absence of any outcome-based studies, panels of experts have recommended that preoperative coronary-artery revascularization be reserved for subgroups of patients with unstable cardiac symptoms or for whom coronary-artery bypass grafting (CABG) offers a long-term survival benefit.[6,7] Despite these published guidelines, there is substantial variability among clinicians concerning the recommendations for preoperative cardiac intervention,[8] which reflects in part, the absence of any randomized studies.

In support of the aggressive treatment of coronary artery disease before vascular surgery, retrospective data indicate that revascularization improves long-term outcomes.[9] In addition, among the cohort of patients from the Coronary Artery Surgery Study with peripheral vascular disease, the survival after 3.5 years in the surgically treated group was better than that in the group receiving medical therapy.[10] In support of a conservative management plan, retrospective data from a large registry of patients who had undergone vascular surgery show that procedure-related complications among patients undergoing preoperative revascularization are frequent, often leading to critical delays in the intended vascular surgery.[11] Therefore, we undertook the Coronary Artery Revascularization Prophylaxis (CARP) trial to assess the long-term benefit of preoperative coronary-artery revascularization among patients with stable coronary artery disease who are scheduled for elective vascular surgery.

METHODS

STUDY PATIENTS

Patients were eligible for the study if they were scheduled for an elective vascular operation for either an expanding abdominal aortic aneurysm or severe symptoms of arterial occlusive disease involving the legs. The exclusion criteria were a need for urgent or emergency surgery, a severe coexisting illness, or prior revascularization without evidence of recurrent ischemia.[12]

Coronary angiography was recommended for eligible patients if the patient was considered by a cardiology consultant to be at increased risk for a perioperative cardiac complication. Guidelines for coronary angiography were provided for each site on the basis of combined clinical risk factors and the presence or absence of ischemia on a noninvasive stress imaging study.[4] During the study, cardiology consultants were also influenced by other recognized risk factors including a prior stroke, insulin-dependent diabetes, and renal failure,[13] as well as by a greater reliance on stress imaging.[14]

On the basis of the coronary angiogram, a patient was eligible for the study if one or more major coronary arteries had a stenosis of at least 70 percent and were suitable for revascularization. Local investigators decided which revascularization procedure to use, either percutaneous coronary intervention or CABG. Although percutaneous coronary intervention and CABG are considered equivalent before major noncardiac operations,[15] the potential long-term advantage of CABG among patients with diabetes and multivessel disease was recognized.[16] Anatomical exclusion criteria were a stenosis of the left main coronary artery of at least 50 percent, a left ventricular ejection fraction of less than 20 percent, and severe aortic stenosis.

Study patients were recruited for a 12-month feasibility trial (from August 1997 through July 1998) involving five Veterans Affairs (VA) medical centers. Enrollment for the main study, involving 18 VA medical centers, occurred from March 1999 through February 2003. As planned, the efficacy results from the pilot study were not evaluated at its completion so that they could be combined with the results of the main study. Follow-up ended on February 28, 2004. The human rights committee of the VA Cooperative Studies Program and the institutional review board at each participating VA medical center approved the study.

RANDOMIZATION AND TREATMENT

We used a stratified randomization process with permuted blocks. The stratification factors were the hospital and, because intraabdominal and infrainguinal operations have different outcomes, the proposed vascular surgery.[17] After randomization, we expected the intended procedure (either cardiac or vascular) to be performed within three weeks. If CABG was planned, we expected the vascular operation to occur within three months. If percutaneous coronary intervention was planned, we expected the vascular operation to be delayed for at least two weeks, owing to an increased risk of an in-stent cor-

onary-artery thrombus.[18] For three days after vascular surgery, blood was collected and sampled for cardiac enzymes and an electrocardiogram was obtained. Three months after surgery, the left ventricular ejection fraction was determined with the use of radionuclide angiography. All patients who underwent randomization had follow-up visits at the local site every three months for the first year and every six months for the remainder of the study.

OUTCOMES

The primary end point was long-term mortality and was ascertained through follow-up and by means of the Veterans Affairs Beneficiary Identification and Records Locator Subsystem. Secondary end points included myocardial infarction, stroke, limb loss, and dialysis. Eighty-six percent of patients in the revascularization group and 85 percent of patients in the no-revascularization group had follow-up visits within one year before the end of the study. After revascularization (CABG or percutaneous coronary intervention), myocardial infarction was diagnosed on the basis of a combination of elevated levels of cardiac enzymes and changes in the electrocardiogram. A myocardial infarction after the vascular surgery was diagnosed on the basis of elevated levels of cardiac enzymes and was characterized by associated ischemic changes on the electrocardiogram. The end-points committee, which was independent of the study and blinded to the assigned treatment, validated all outcomes.

STATISTICAL ANALYSIS

We predicted mortality on the basis of the outcomes of patients from the Coronary Artery Surgery Study registry who had peripheral vascular disease.[10] A 5 percent one-sided log-rank test was used, indicating that a sample of 559 patients would be needed to provide the study with 90 percent power to detect differences in the 3.5-year survival rates of 75 percent in one group and 85 percent in the other. Because recruitment was slower than expected in the main study, the three-year enrollment period, with a minimal follow-up of two years, was changed to a four-year enrollment period, with a one-year follow-up. Total recruitment was 510 patients (of whom 98 percent were male), who were randomly assigned to one of the two study groups.

Intention-to-treat analyses provided information about survival, from the time of randomization. Survival curves were generated with the use of Kaplan–Meier product-limit estimates, and intergroup differences were evaluated by the log-rank test. The Cox proportional-hazards model was used to calculate estimates of relative risk and 95 percent confidence intervals, comparing treatments within high-risk subgroups of patients. Data are expressed as means ±SD, or as medians with interquartile range when specified. All tests were two-sided.

RESULTS

SCREENING

Of 5859 patients scheduled for vascular surgery, 4669 (80 percent) were initially excluded. The main reasons were insufficient cardiac risk (1654 patients), an urgent need for vascular surgery (1025), prior CABG or percutaneous coronary intervention without ischemia (626), and a severe coexisting illness (731). The patient's decision not to participate and ineligibility because of participation in other research studies accounted for 633 exclusions. Of the patients who underwent coronary angiography without any clinical exclusions, 680 were excluded for reasons that were specified in the protocol. The primary reason was either nonobstructive coronary arteries (363 patients) or coronary artery disease that was not considered amenable to successful revascularization (215). Other anatomical reasons for exclusion included a stenosis of the left main coronary artery of at least 50 percent (54 patients), a left ventricular ejection fraction of less than 20 percent (11), and severe aortic stenosis (8). Refusal to participate, by either the patient or the referring physician, accounted for 29 exclusions.

STUDY PATIENTS

Of the 510 patients (9 percent of the 5859 originally screened) who underwent randomization, 258 were assigned to a strategy of preoperative coronary-artery revascularization, and 252 to no revascularization. There were no significant differences in the baseline characteristics of the two groups (Table 1). According to the criteria of Eagle and colleagues regarding preoperative assessment of cardiac risk,[4] 28 percent had three or more clinical risk factors, and 65 percent had either three or more clinical risk factors or one or two risk factors with ischemia, as demonstrated on a stress test. According to the Revised Cardiac Risk Index, 49 percent had two or more risk factors, and 13 percent had three or more risk factors.[13] Nuclear stress imaging was performed in 316 (62 percent) of the study patients. The size of the reversible defect relative to total my-

Table 1. Baseline Clinical Variables According to the Assigned Treatment before the Elective Major Vascular Surgery.*

Variable	Revascularization (N=258)	No Revascularization (N=252)	P Value
Age — yr	65.6±11.1	67.2±10.4	0.10
Angina — no. (%)	103 (39.9)	95 (37.7)	0.61
Previous myocardial infarction — no. (%)	111 (43.0)	103 (40.9)	0.62
Previous congestive heart failure — no. (%)	31 (12.0)	19 (7.5)	0.09
Previous stroke or TIA — no. (%)	54 (20.9)	47 (18.7)	0.50
Diabetes — no. (%)			
Treated with oral agents	49 (19.0)	52 (20.6)	0.84
Treated with insulin	48 (18.6)	49 (19.4)	0.84
Current smoker — no. (%)	128 (49.6)	114 (45.2)	0.41
Albumin — g/dl	3.7±0.6	3.7±0.5	0.99
Hemoglobin — g/dl	14.0±2.4	13.8±1.9	0.26
Total cholesterol — mg/dl	175±45	182±51	0.13
LDL cholesterol — mg/dl	105±37	107±42	0.60
HDL cholesterol — mg/dl	37±10	37±11	0.95
Glycosylated hemoglobin — %	6.6±1.7	6.8±1.9	0.41
C-reactive protein — mg/dl			0.12
Median	0.4	0.3	
Interquartile range	0.05–1.4	0.04–1.3	
Homocysteine — mg/dl			0.63
Median	10.3	9.8	
Interquartile range	0.8–13.6	0.3–12.8	
Left ventricular ejection fraction — %	54±12	55±12	0.36
Three-vessel coronary artery disease — no. (%)	91 (35.3)	79 (31.3)	0.69
Previous CABG — no. (%)	38 (14.7)	39 (15.5)	0.83
Indication for surgery†			0.61
Abdominal aneurysm — no. (%)	88 (34.1)	81 (32.1)	—
Claudication — no. (%)	100 (38.8)	89 (35.3)	—
Pain at rest — no. (%)	30 (11.6)	35 (13.9)	—
Tissue breakdown — no. (%)	40 (15.5)	47 (18.7)	—

* Plus–minus values are means ±SD. TIA denotes transient ischemic attack, LDL low-density lipoprotein, and HDL high-density lipoprotein. To convert the values for hemoglobin to millimoles per liter, multiply by 0.6206. To convert the values for cholesterol to millimoles per liter, multiply by 0.02586.
† A single P value is provided for the entire group (two-by-four chi-square test with three degrees of freedom). A dash denotes not applicable.

ocardial perfusion was determined at each site and graded semiquantitatively as small, moderate, or large. The size of the perfusion defect was moderate or large in 226 patients. Overall, 74 percent of the study patients had three or more of the Eagle clinical criteria, two or more variables defined by the Revised Cardiac Risk Index, or a moderate or large reversible defect on stress imaging. In the majority of the remaining patients, angina or abnormal results on the stress test were the reason for preoperative coronary angiography.

CORONARY-ARTERY REVASCULARIZATION

Of the 258 study patients assigned to preoperative coronary-artery revascularization, 240 (93 percent) underwent either CABG (99 patients) or percutane-

ous coronary intervention (141 patients). Of the 18 patients who did not undergo preoperative revascularization, 8 (3 percent) required urgent vascular surgery and 9 (3 percent) chose not to undergo revascularization. In one patient, a stroke precluded proceeding with the scheduled CABG. Table 2 summarizes the results for the 240 patients who underwent CABG or percutaneous coronary intervention as part of the assigned treatment. Of four deaths associated with revascularization, two deaths in the percutaneous-coronary-intervention group and one death in the CABG group occurred after successful revascularization and shortly after vascular surgery. Those three deaths were considered complications of revascularization because they occurred during the same hospitalization period.

After randomization, 9 of the 252 patients assigned to undergo no revascularization before vascular surgery (4 percent) required preoperative revascularization because of an unstable change in cardiac status. Seven of them subsequently underwent vascular surgery after revascularization.

Table 2. Procedural Characteristics and Postprocedural Complications of CABG and Percutaneous Coronary Intervention (PCI) in 240 Patients Assigned to Undergo Coronary-Artery Revascularization before Elective Major Vascular Surgery.*

Characteristic	CABG (N=99)	PCI (N=141)
Days since randomization		
Median	18	1
Interquartile range	7–34	0–7
Urgent or emergency cardiac status — no. (%)	2 (2.0)	1 (0.7)
No. of vessels revascularized	3.0±0.8	1.3±0.8
Completeness of revascularization — %†	98.0	61.9
Death — no. (%)‡	2 (2.0)	2 (1.4)
Myocardial infarction — no. (%)	7 (7.1)	7 (5.0)
Stroke, loss of leg, or renal dialysis — no.	0	0
Reoperation — no. (%)	6 (6.1)	NA
Urgent CABG — no. (%)	NA	1 (0.7)
Days in hospital after procedure		
Median	7	1
Interquartile range	5–12	1–2

* Plus–minus values are means ±SD. NA denotes not applicable.
† Completeness of revascularization indicates the percentage of major epicardial vessels with stenosis of more than 70 percent that were revascularized.
‡ One of the deaths in the CABG group and the two in the PCI group occurred within two weeks of the revascularization and after the vascular operation. They are listed as complications of both the revascularization and the vascular procedures, because they occurred within the same hospitalization period. Myocardial infarction associated with CABG or PCI was defined by cardiac-enzyme elevations and ischemic changes on the electrocardiogram.

VASCULAR SURGERY

Of the 258 patients assigned to undergo preoperative revascularization, 225 (87 percent) underwent the planned vascular operation, as did 237 of the 252 patients (94 percent) assigned to no preoperative revascularization. Of the 33 patients randomly assigned to revascularization who did not undergo vascular surgery, 10 died after uncomplicated CABG or percutaneous coronary intervention, 18 declined the surgery (5 on the advice of the primary physician), and a severe coexisting condition developed in 5. Of the 15 patients randomly assigned to no preoperative revascularization who did not undergo vascular operation, 1 died after urgent CABG, 9 declined (3 on the advice of the primary physician), and a severe coexisting condition developed in 5. Among the patients who underwent vascular surgery, there was a significantly longer time to vascular surgery in the group assigned to revascularization than in the group assigned to no revascularization. In the group assigned to revascularization, the vascular operation occurred a median of 48 days after CABG and 41 days after percutaneous coronary intervention. There were no other intergroup differences in perioperative management (Table 3). With the exception of the use of intravenous nitroglycerin, there were no significant differences in perioperative medications.

POSTOPERATIVE OUTCOMES

Before vascular surgery, there were 10 deaths in the revascularization group and 1 death in the no-revascularization group. Within the 30-day period after the vascular surgery, there were seven deaths (3 percent) in the revascularization group and eight deaths (3 percent) in the no-revascularization group (Table 3). Two of the deaths in the revascularization group occurred in patients who had undergone successful percutaneous coronary intervention but required urgent vascular surgery seven days later. The core laboratory for measurement of cardiac enzymes received blood samples from 88 percent of the patients, and a postoperative myocardial infarction, defined by elevated troponin levels, occurred in 16 percent of those patients; this rate is consistent with the percentage of myocardial infarctions recorded for all patients at the individual sites (Table 3).

Table 3. Clinical Features and Outcomes of Vascular Surgery According to the Assigned Treatment before the Elective Major Vascular Surgery.

Characteristic	Revascularization (N=225)	No Revascularization (N=237)	P Value
Surgical management			
Abdominal surgery — no. (%)*	89 (39.9)	99 (42.1)	0.89
Urgent or emergency status — no. (%)	13 (5.8)	14 (5.9)	0.90
General anesthesia — no. (%)	180 (80.0)	199 (84.0)	0.50
Altered surgical procedure — no. (%)†	33 (14.7)	27 (11.4)	0.30
Days after randomization			<0.001
Median	54	18	
Interquartile range	28–80	7–42	
Perioperative medications — no. (%)			
Beta-adrenergic blockers	188 (83.6)	204 (86.1)	0.45
Aspirin‡	168 (76.7)	165 (70.2)	0.12
Statins§	121 (53.8)	122 (54.0)	0.93
Heparin*	209 (93.7)	219 (93.2)	0.82
Intravenous nitroglycerin	63 (28.0)	87 (36.7)	0.05
Postoperative events (within 30 days)			
Death — no. (%)	7 (3.1)	8 (3.4)	0.87
Myocardial infarction¶			
Enzymes — no. (%)	26 (11.6)	34 (14.3)	0.37
Enzymes and ECG — no. (%)	19 (8.4)	20 (8.4)	0.99
Stroke — no. (%)	1 (0.4)	2 (0.8)	0.59
Loss of leg — no. (%)	1 (0.4)	5 (2.1)	0.11
Renal dialysis — no. (%)	1 (0.4)	1 (0.4)	0.97
Reoperation — no. (%)	17 (7.6)	18 (7.6)	0.99
Total days in the intensive care unit			0.25
Median	2.0	2.0	
Interquartile range	1–3	1–4	
Total days in the hospital			0.29
Median	6.5	7.0	
Interquartile range	4–10	5–12	

* No information was available for two patients in each group.
† An altered surgical procedure refers to a surgical procedure (abdominal or infrainguinal) that differed from the projected surgical procedure that was planned before randomization.
‡ No information was available for six patients in the revascularization group and two in the no-revascularization group.
§ No information was available for 11 patients in the no-revascularization group.
¶ Myocardial infarction was defined by any elevation in cardiac enzymes after surgery, as well as by any elevation in cardiac enzymes with ischemic changes on the electrocardiogram (ECG).

LONG-TERM OUTCOME

Three months after vascular surgery, the left ventricular ejection fraction was 54±13 percent in the revascularization group and 55±12 percent in the no-revascularization group (P=0.69). The median follow-up time for mortality was 2.8 years (interquartile range, 1.7 to 3.9) in the revascularization group and 2.6 years (interquartile range, 1.6 to 3.8) in the no-revascularization group. There were 137 deaths (70 in the revascularization group and 67 in the no-revascularization group). At a median of 2.7 years after randomization, mortality was 22 percent

in the revascularization group and 23 percent in the no-revascularization group (relative risk, 0.98; 95 percent confidence interval, 0.70 to 1.37; P=0.92) (Fig. 1). Among the patients assigned to no preoperative coronary-artery revascularization, 21 (8 percent) underwent postoperative coronary-artery revascularization after vascular surgery. When the analysis was repeated according to treatment received rather than treatment assigned at randomization, the rate of death at 2.7 years was 22 percent of the patients who underwent revascularization (249 patients) and 23 percent of the patients who did not undergo revascularization (261 patients) (relative risk, 0.97; 95 percent confidence interval, 0.69 to 1.36; P=0.86).

A Cox regression model used to analyze subgroups of patients with characteristics indicating a high risk showed that coronary-artery revascularization did not impart a survival benefit in any of the high-risk subgroups (Table 4). Beta-blockers, antiplatelet agents (aspirin or inhibitors of adenosine diphosphate), angiotensin-converting–enzyme inhibitors, and statins were used by the vast majority of patients 24 months after randomization, and their use did not differ between the groups (Fig. 2).

DISCUSSION

The principal finding of this cooperative study at 18 VA medical centers is that, among patients with stable coronary artery disease, coronary-artery revascularization before elective major vascular surgery does not improve long-term survival. Although the study was not designed to test the short-term benefit of prophylactic revascularization, there was also no reduction in early postoperative outcomes, including death, myocardial infarction, and length of the hospital stay. The findings support the opinions of the task force of the American College of Cardiology and the American Heart Association and of the American College of Physicians, which have recommended that CABG or percutaneous coronary intervention be reserved for patients with unstable cardiac symptoms or advanced coronary artery disease, for whom a survival benefit with CABG has been proved.[6,7] Despite these published guidelines, there is a lack of consensus among cardiologists regarding the indications for preoperative coronary-artery revascularization,[8] which probably reflects the absence of published data.

The results reported here differ from the findings of the prospectively designed Coronary Artery

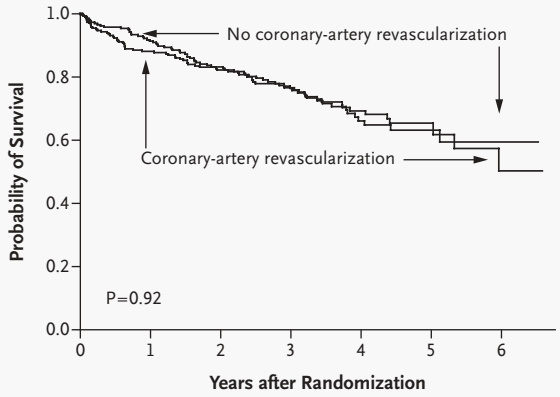

Figure 1. Long-Term Survival among Patients Assigned to Undergo Coronary-Artery Revascularization or No Coronary-Artery Revascularization before Elective Major Vascular Surgery.

Kaplan–Meier estimates were used to generate survival curves, from the time of randomization, for all study patients.

Table 4. Influence of Coronary-Artery Revascularization on Long-Term Survival among High-Risk Subgroups of Patients Scheduled for Vascular Surgery.*

High-Risk Variable	Patients (N=510)	Hazard Ratio (95% CI)	P Value
	no. (%)		
Angina	198 (38.8)	1.45 (0.79–2.64)	0.23
Positive stress imaging test†	226 (44.3)	1.26 (0.77–2.06)	0.35
Fulfillment of criteria of Eagle and colleagues[4]‡	142 (27.8)	0.90 (0.51–1.62)	0.73
With large stress-induced defect	37 (7.3)	3.96 (0.82–19.11)	0.09
Category of revised Cardiac Risk Index[13]§	248 (48.6)	1.20 (0.76–1.89)	0.44
With large stress-induced defect	50 (9.8)	1.65 (0.64–4.25)	0.30
Prior CABG	77 (15.1)	1.81 (0.81–4.05)	0.15
Three-vessel disease and left ventricular dysfunction	74 (14.5)	1.29 (0.62–2.65)	0.50
Pain at rest and tissue breakdown	152 (29.8)	0.76 (0.43–1.34)	0.34

* CI denotes confidence interval.
† The stress imaging test refers to a moderate or large reversible defect.
‡ The criteria include at least three of the following clinical risk factors: an age greater than 70 years, previous myocardial infarction, Q waves on an electrocardiogram, previous congestive heart failure, previous ventricular tachycardia, angina, or diabetes mellitus.
§ The index includes at least two of the following clinical risk factors: prior stroke or transient ischemic attack, congestive heart failure, coronary artery disease (excluding previous coronary-artery revascularization), a serum creatinine concentration greater than 2.0 mg per deciliter (177 μmol per liter), insulin-dependent diabetes mellitus, or a suprainguinal operation.

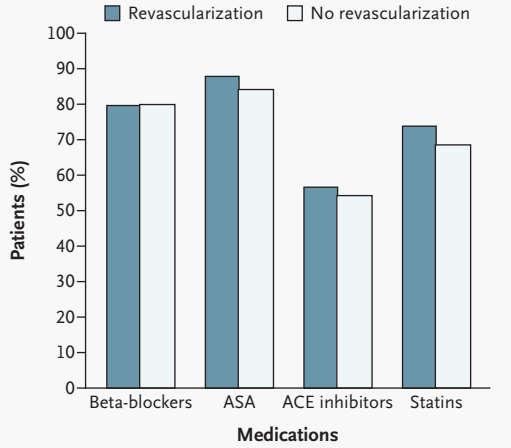

Figure 2. Long-Term Use of Medical Therapy in the Revascularization and No-Revascularization Groups at 24 Months after Randomization.

The cardiac medications used were beta-blockers, antiplatelet agents (ASA) such as aspirin or inhibitors of adenosine diphosphate, angiotensin-converting–enzyme (ACE) inhibitors, and statins.

Surgery Study, which showed a survival benefit associated with CABG among patients with severe vascular disease.[10] It is unlikely that our failure to demonstrate a long-term benefit with revascularization was a result of procedural complications. The mortality and morbidity associated with CABG and percutaneous coronary intervention in this trial were lower than that in previous reports involving prophylactic revascularization before vascular surgery[11] and are more consistent with the expected rates in a general medical population.[19] It is also unlikely that our trial failed to detect differences in treatment because of insufficient power. Although enrollment was 9 percent lower than the target sample size and the minimal follow-up was slightly reduced, the follow-up in the patients from the pilot study was longer than expected, and the actual number of deaths in the trial was higher than expected. Therefore, the power of this study, recalculated at a two-sided α level of 0.05, was 90 percent, showing no net loss of power.

We believe our findings can be generalized to a large group of male patients who are considered at increased risk for cardiac complications of elective vascular surgery. Before patients were enrolled in our study, a cardiology consultant at each site initially screened all patients and recommended coronary angiography on the basis of his or her interpretation of the cardiac risk. Analysis of the baseline data showed that at least 74 percent of the study patients would have been considered to be at least at intermediate risk because of either clinical criteria[4,13] or results from noninvasive imaging tests showing a high risk.[14] The majority of the remaining patients were considered to be at risk because of either an abnormal stress test or the presence of angina, which has been shown to be a risk factor.[20] Although the results may help guide preoperative therapy for a broad group of patients with stable cardiac symptoms, they cannot be extrapolated to all patients in need of vascular surgery, particularly those with unstable angina, aortic stenosis, or severe left ventricular dysfunction.

The potential effect of advances in medical therapy since the Coronary Artery Surgery Study cannot be overemphasized. The widespread use of beta-blockers, antiplatelet agents, angiotensin-converting–enzyme inhibitors, and statins in our study population throughout the follow-up period may have improved the outcomes in all patients and diminished the differences in long-term survival between those treated according to an initial aggressive preoperative strategy and those treated according to a conservative strategy. Moreover, in the perioperative period, beta-adrenergic–blocking agents, which have been demonstrated to improve outcomes among patients undergoing vascular surgical procedures,[21,22] were judiciously administered to most study patients. This treatment, as well as the use of statins, may have adequately protected the medical therapy group at the time of the vascular surgery.

The intense perioperative management by the study investigators may also have influenced favorably the outcome of the patients who did not undergo revascularization. This management included the perioperative care by the anesthesiologists and surveillance by the vascular surgical team in the early postoperative period. With staff available 24 hours a day in the catheterization laboratory to intervene if necessary, patients with acute coronary syndromes in the present era may have an improved postoperative prognosis. The incidence of postoperative myocardial infarctions was not reduced by coronary interventions, suggesting that the mechanism of cardiac-enzyme release after vascular surgery involves more complex mechanisms than the number of coronary arteries with critical stenoses. There is

emerging evidence that postoperative myocardial infarctions are commonly associated with disease progression in vessels with minimal stenosis.[23] Incomplete revascularization could be a factor in the lack of protection against postoperative myocardial infarctions, but the completeness of both percutaneous coronary intervention and CABG in the present study were similar to those in previous studies.[16]

In conclusion, this multicenter, randomized trial shows that coronary-artery revascularization before elective vascular surgery does not alter long-term survival. Although the study was not powered to detect a beneficial effect in the short term, there also appears to have been no reduction in the number of postoperative myocardial infarctions, deaths, or days in the hospital. On the basis of these data, coronary-artery revascularization before elective vascular surgery among patients with stable cardiac symptoms cannot be recommended.

Supported by the Cooperative Studies Program of the Department of Veterans Affairs Office of Research and Development.

This article is dedicated to the memory of William C. Krupski.

APPENDIX

Organizational members of the Coronary Artery Revascularization Prophylaxis trial were as follows: *Site Investigators* — M. Icenogle, M. Langsfeld, S. Pett (Albuquerque, N.M.); K. Mavromatis, A.A. Salam, J.D. Vega (Atlanta); J. Jean-Claude, G. Pinault, J. Ortiz (Cleveland); P. Frenkel, M. Jessen, J.G. Modrall (Dallas); W. Krupski, B. Hattler (Denver); J. Gray, K. Morris, W. Wolfe (Durham, N.C.); R. Kerensky, S. Lind, M. Staples (Gainesville, Fla.); A. Greene, S. Lalka, T. Sharp (Indianapolis); M. Moursi, Y.W. Aude, T. Antakli (Little Rock, Ark.); G. Pierpont, S. Santilli (Minneapolis); S. Muluk, F. Sonel, M. Zenati (Pittsburgh); J. Edwards, G. Larsen, P. Ravichandran (Portland, Oreg.); G. Chilton, E. Sako, M. Sykes, B. Toursarkissian (San Antonio, Tex.); J. Rapp, M. Ratcliffe, K. Shunk (San Francisco); T.R. Kohler, K. Lehmann (Seattle); M. Back, D. Novitzky, M.A. Siddique (Tampa, Fla.); S. Goldman, G. Sethi, A. Westerband (Tucson, Ariz.); D. Baker, R. Ebrahimi, F. Esmailian, B. Singh (West Los Angeles); D. DePinto, F. Littooy, H. Loeb (Hines, Ill.); T. Gavin, K.B. Ramanathan, D. Weiman (Memphis, Tenn.); S. Khuri, G. Sharma (West Roxbury, Mass.); *End-Point Committee* (confirmed end points on the basis of pertinent hospital records) — K. Weir, R. Kelly, J. Davenport; *Cooperative Studies Program Coordinating Center, Hines, Ill.* — N. Ellis, T. Moritz, W. Henderson, D. Reda, L. Thottapurathu; *Clinical Coordinator* — C. Jaenicke; *Angiography Core Laboratory* (reviewed all angiograms) — K. Weir; *Specimen Testing Core Laboratory* (validated perioperative cardiac enzymes) — F. Apple (Hennepin County Medical Center, Minneapolis); *Good Clinical Practice* — C. Haakenson; *Study Coordinators* — D. Robertson (Albuquerque, N.M.); D. House (Atlanta); G. Webbs (Cleveland); A. Swann (Dallas); W. Klenke (Denver); K. Swails (Durham, N.C.); J. Brown (Gainesville, Fla.); M. Rusomaroff (Indianapolis); R. Pacheco (Little Rock, Ark.); J. Weigenan, (Minneapolis); M. DiTommaso (Pittsburgh); S. Perez (San Francisco); A. Sorley (Seattle); A. Esquivel (San Antonio, Tex.); S. Thomas (Tampa, Fla.); A. Morgan, K. Zadina (Tucson, Ariz.); L. Cole (West Los Angeles); J. Maggio (Hines, Ill.); R. Thomas (Memphis, Tenn.); J. Bannister (West Roxbury, Mass.); *Executive Committee* — E. McFalls (Chair), H. Ward (Co-Chair), C. Jaenicke, T. Moritz, S. Goldman, W. Krupski, F. Littooy, D. Reda; *Data and Safety Monitoring Board* — N. Hertzer, B.J. Gersh, F. Grover, R. Chappell.

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