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COMPARISON OF CORONARY BYPASS SURGERY WITH ANGIOPLASTY IN PATIENTS WITH MULTIVESSEL DISEASE

THE BYPASS ANGIOPLASTY REVASCULARIZATION INVESTIGATION (BARI) INVESTIGATORS*

ABSTRACT

Background Coronary-artery bypass grafting (CABG) and percutaneous transluminal coronary angioplasty (PTCA) are alternative methods of revascularization in patients with coronary artery disease. We tested the hypothesis that in selected patients with multivessel disease suitable for treatment with either procedure, an initial strategy of PTCA does not result in a poorer five-year clinical outcome than CABG.

Methods Patients with multivessel disease were randomly assigned to an initial treatment strategy of CABG (n = 914) or PTCA (n = 915) and were followed for an average of 5.4 years. Analysis of outcome events was performed according to the intention to treat.

Results The respective in-hospital event rates for CABG and PTCA were 1.3 percent and 1.1 percent for mortality, 4.6 percent and 2.1 percent for Q-wave myocardial infarction ($P<0.01$), and 0.8 percent and 0.2 percent for stroke. The five-year survival rate was 89.3 percent for those assigned to CABG and 86.3 percent for those assigned to PTCA ($P = 0.19$; 95 percent confidence interval of the difference in survival, −0.2 percent to 6.0 percent). The respective five-year survival rates free from Q-wave myocardial infarction were 80.4 percent and 78.7 percent. By five years after study entry, 8 percent of the patients assigned to CABG had undergone additional revascularization procedures, as compared with 54 percent of those assigned to PTCA; 69 percent of those assigned to PTCA did not subsequently undergo CABG. Among diabetic patients who were being treated with insulin or oral hypoglycemic agents at base line, a subgroup not specified by the protocol, five-year survival was 80.6 percent for the CABG group as compared with 65.5 percent for the PTCA group ($P = 0.003$).

Conclusions As compared with CABG, an initial strategy of PTCA did not significantly compromise five-year survival in patients with multivessel disease, although subsequent revascularization was required more often with this strategy. For treated diabetics, five-year survival was significantly better after CABG than after PTCA. (N Engl J Med 1996;335:217-25.)

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CORONARY-artery bypass grafting (CABG), introduced in 1968,[1] results in longer survival and a better quality of life in specific subgroups of patients with multivessel coronary artery disease than does an initial strategy of medical therapy.[2-6] Since the introduction of percutaneous transluminal coronary angioplasty (PTCA) in 1977,[7] the use of this less invasive procedure for coronary revascularization has rapidly expanded. Initially, PTCA was used in patients with single-vessel disease, but as experience and technology have advanced, it has been used in those with multivessel disease as well.

Because of the growing use of both CABG and PTCA and a lack of properly controlled comparative studies, in 1987 the National Heart, Lung, and Blood Institute (NHLBI) initiated the Bypass Angioplasty Revascularization Investigation (BARI). BARI tested the hypothesis that in patients with multivessel disease and severe angina or ischemia, an initial revascularization strategy involving PTCA does not result in a poorer clinical outcome than CABG during a five-year follow-up period.[8]

Previous clinical trials comparing coronary surgery with medical therapy have found that high-risk groups defined by the presence of left main coronary artery disease,[9] triple-vessel disease with impaired left

Address reprint requests to Dr. Robert L. Frye, c/o BARI Coordinating Center, University of Pittsburgh, Rm. 127, Parran Hall, 130 DeSoto St., Pittsburgh, PA 15261.

*This article was prepared by Edwin L. Alderman, M.D., Katharine Andrews, M.S., James Bost, Ph.D., Martial Bourassa, M.D., Bernard R. Chaitman, M.D., Katherine Detre, M.D., Dr.P.H., David P. Faxon, M.D., Dean Follmann, Ph.D., Robert L. Frye, M.D., Mark Hlatky, M.D., Robert H. Jones, M.D., Sheryl F. Kelsey, Ph.D., William J. Rogers, M.D., Allan D. Rosen, M.S., Hartzell Schaff, M.D., Mary Ann Sellers, B.S.N., M.S., George Sopko, M.D., M.P.H., Kim Sutton Tyrrell, Dr.P.H., and David O. Williams, M.D., on behalf of the BARI Investigators. Dr. Frye, as study chairman, assumes responsibility for the overall content and integrity of this article.

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ventricular function,[2,5,6] or other risk factors[5] benefit from CABG. Conversely, no benefit was found in lower-risk groups, such as patients with single-vessel disease. Therefore, an analysis of subgroups was included in the design of BARI.

METHODS

Patients were eligible for the study if they had angiographically documented multivessel coronary disease with clinically severe angina or objective evidence of ischemia requiring revascularization and were suitable candidates for both CABG and PTCA as an initial revascularization procedure. A detailed description of the study's aims, patient selection, exclusion criteria, procedure guidelines, definitions, and administrative structure has been published previously.[8]

Between August 1988 and August 1991, 1829 patients were randomly assigned to undergo CABG or PTCA at 18 centers, 16 in the United States and 2 in Canada, after providing written informed consent. Another 2013 eligible patients who refused to undergo randomization and 422 who were ineligible on the basis of angiographic findings consented to follow-up by means of a registry. Screening results and base-line characteristics of randomized and registry patients have been published elsewhere.[10-14] Randomization was carried out with the use of blocks of varying length, with stratification only according to clinical center. Computers provided to the clinical centers were used to decode the encrypted assignments to ensure that treatment remained blinded until randomization.

Base-line data included the clinical profile, interpretation of a 12-lead electrocardiogram (ECG), and information on coronary angiographic features, angina and functional status, medications, risk factors, and quality of life. The protocol stipulated that initial revascularization had to be performed within two weeks after randomization. Scheduled multiple stages of PTCA were counted as a single procedure. New interventional devices, such as stents, were not used during the initial revascularization. Data obtained during hospitalizations and coronary procedures included electrocardiographic information obtained before and after each procedure and in the setting of a suspected myocardial infarction. Follow-up visits were conducted at the clinics at weeks 4 through 14 after study entry and at 1, 3, and 5 years, with telephone contacts at 6 months and 2 and 4 years. The importance of risk-factor modification was emphasized throughout the study to the patients and their primary physicians.

All ECGs obtained during rest or exercise were interpreted at a central ECG and myocardial-infarction classification laboratory. All angiograms were evaluated quantitatively (measurement with electronic calipers) and qualitatively by a central radiographic laboratory. The coordinating center was responsible for the administration of the study, data management, and statistical analysis. An independent safety and data monitoring board regularly reviewed interim study results to advise the NHLBI.

Ascertainment of Outcomes

Mortality from all causes was the primary end point. Each patient was contacted to determine vital status as of June 5, 1995. A Q-wave myocardial infarction was defined as new pathologic Q waves (a worsening by two grades) according to the Minnesota code[15,16] or new left bundle-branch block with abnormal cardiac-enzyme levels (total creatine kinase twice the normal level and an abnormal MB isoenzyme level). A Q-wave myocardial infarction during the four-day period following a revascularization procedure was diagnosed solely on the basis of the Minnesota code.

Angiographic Definitions

A clinically important lesion was defined as stenosis of at least 50 percent of the diameter of a vessel with a reference diameter of more than 1.5 mm as measured by calipers. The extent of vessel disease was determined on the basis of the number of myocardial territories (anterior, lateral, and inferoposterior) affected by clinically important lesions. The extent of coronary artery disease was quantified according to the percentage of left ventricular myocardial territory jeopardized[17] by clinically important lesions. The complexity of the lesions was categorized as type A, B, or C according to the criteria of the American Heart Association–American College of Cardiology Consensus Panel.[18] The proximal left anterior descending artery was defined as the region before the first septal branch, whereas the mid–left anterior descending artery was defined as the segment between the first septal perforator and the last major diagonal branch. The left ventricular ejection fraction was assessed with the area–length method on contrast ventriculograms. Abnormal left ventricular function was defined as an ejection fraction below 50 percent, or a total of more than 10 for the sum of five regional-wall-motion scores (each scored on a 5-point scale in which a score of 1 indicates normal motion and a score of 5 dyskinesia)[19] when ejection fraction was unavailable. Dilatation of a stenotic vessel was considered successful if the degree of stenosis was reduced by at least 20 percentage points, with residual stenosis of less than 50 percent of the lumen diameter and normal flow (a grade of 3 according to the Thrombolysis in Myocardial Infarction system).[20] Detailed angiographic definitions have been published.[8,11,12,17]

Statistical Analysis

We compared the outcomes for CABG and PTCA according to the intention-to-treat principle; however, we compared the rates of in-hospital complications only among patients who actually received the assigned treatment. For the assessment of overall outcomes, we calculated 95 percent confidence intervals of the differences between treatments. We used Kaplan–Meier analysis[21] to estimate the cumulative rates of survival, Q-wave myocardial infarction, survival free from Q-wave myocardial infarction, and repeated revascularization. The time of the occurrence of an asymptomatic Q-wave myocardial infarction detected at a routine follow-up visit was estimated as the midpoint between that follow-up visit and the ECG preceding it. We compared Kaplan–Meier curves using the log-rank test,[22] with stratification according to clinical center. We used Cox regression analysis[23] to test for a departure from a common relative risk across clinical centers.

Subgroups of patients were specified a priori by the protocol and were examined by the safety and data monitoring board. These subgroups were defined by four factors: the severity of angina, the number of diseased vessels, left ventricular function, and the complexity of the lesions. In 1992 the safety and data monitoring board requested an analysis of diabetic patients on the basis of published reports of adverse outcomes of PTCA after thrombolytic therapy in a subgroup of such patients.[24] Treated diabetes was defined as diabetes involving the use of insulin or oral hypoglycemic agents at entry into the study. To detect a treatment difference, wider confidence intervals of 99 percent and 99.5 percent for the a priori and diabetes subgroups, respectively, were used to correct for multiple comparisons.

RESULTS

Vital status as of June 5, 1995, was ascertained for 1792 patients (98 percent). Data on the remaining 2 percent of patients were censored when they withdrew consent or were lost to follow-up. The mean length of follow-up was 5.4 years, with a range of 3.8 to 6.8. Of the 1229 patients (67 percent) who were followed for at least five years, 88 percent were alive at five years and 79 percent of these survivors had a five-year ECG available. The base-line characteristics[11] were not significantly different between the group assigned to PTCA and that assigned to CABG (Table 1). The patients had

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TABLE 1. CHARACTERISTICS OF 1829 PATIENTS ASSIGNED TO UNDERGO CABG OR PTCA FOR MULTIVESSEL DISEASE.

CHARACTERISTIC	CABG (N=914)	PTCA (N=915)
Demographic profile		
Mean age (yr)	61.1	61.8
Age ≥65 yr (%)	39	39
Female sex (%)	26	27
White race (%)	89	91
Black race (%)	7	5
High-school education or less (%)	71	71
Medical history (%)		
Myocardial infarction	55	54
Congestive heart failure	9	9
Family history of coronary artery disease	50	51
Hypertension	49	49
Diabetes	25	24
Medically treated	20	19
Symptoms (%)		
Angina within preceding 6 wk	98	98
Angina classification*		
Stable angina, CCS class 1 or 2	13	14
Stable angina, CCS class 3 or 4	16	18
Unstable angina	65	63
Ischemia only in association with acute myocardial infarction	6	6
Results of ECG at rest (%)†		
Major Q-wave abnormality	17	18
Any abnormality	42	43
Angiographic assessment‡		
Percentage with triple-vessel disease	41	41
Mean percentage of myocardium jeopardized by clinically important lesions	61.4	61.5
Percentage with disease of the proximal left anterior descending artery	37	36
Percentage with ≥1 vessel with proximal disease	69	68
Mean no. of clinically important lesion per patient	3.4	3.5
Percentage with ≥1 type C lesion§	41	38
Percentage with ≥1 total occlusion	38	36
Mean ejection fraction (%)	57.6	57.1
Percentage with ejection fraction <50%	21	23
Mean total wall-motion score¶	7.4	7.4

*CCS denotes Canadian Cardiovascular Society. Because of rounding, columns do not both total 100 percent.

†Assessed by the central ECG and myocardial-infarction classification laboratory.

‡Assessed by the central radiographic laboratory.

§A type C lesion was defined according to the criteria of the American Heart Association–American College of Cardiology Consensus Panel.[18]

¶A score of more than 10 was considered to indicate abnormal left ventricular function.

an average of 3.5 clinically important lesions; 41 percent had triple-vessel disease. The mean left ventricular ejection fraction was 57 percent.

Outcome during Hospitalization

Of the 914 patients assigned to undergo CABG, 892 (98 percent) received their assigned treatment, 15 underwent PTCA as the initial treatment, and 7 were being treated medically at last contact. Of the 915 patients assigned to undergo PTCA, 904 (99 percent) received the assigned treatment, 9 underwent CABG as the initial treatment, and 2 were treated medically at last contact. Initial revascularizations were performed within two weeks after treatment assignment in 90.7 percent of cases and within eight weeks in 99.6 percent. Among the 892 patients who underwent CABG as assigned, an average of 3.1 coronary arteries were bypassed with a mean of 2.8 grafts. All intended vessels were grafted in 91 percent of patients. The mean duration of cardiopulmonary bypass was 91 minutes. At least one internal-thoracic-artery graft was used in 82 percent of patients. The median hospital stay after CABG was seven days. Among the 904 patients who underwent PTCA as assigned, angioplasty was attempted for an average of 2.4 lesions. Multilesion PTCA was attempted in 78 percent of the patients, and multivessel PTCA in 70 percent. At least one lesion was successfully dilated in 88 percent of the patients, and all were successfully dilated in 57 percent. Immediate angiographic success was achieved in 78 percent of attempts, with the mean degree of stenosis reduced from 67 percent to 31 percent. Therefore, an average of 1.9 of 3.5 clinically important lesions were successfully dilated (54 percent). The initial PTCA was undertaken in stages in 158 patients (17 percent). The median hospital stay after PTCA was three days.

Table 2 summarizes events and complications that occurred in the hospital after the initial procedures among patients who received their assigned treatment. The rates of in-hospital mortality and stroke were similar in the two treatment groups. Patients assigned to CABG were more likely to have a Q-wave myocardial infarction than patients assigned to PTCA ($P=0.004$). Patients assigned to PTCA were more likely to require early reintervention: 12.8 percent had additional procedures during hospitalization, and 6.3 percent required emergency CABG. Abrupt closure of a dilated lesion occurred in the laboratory in 86 patients who underwent PTCA as assigned. In 35 patients, all stenotic vessels were reopened and considered successfully treated, although 3 patients subsequently underwent CABG during the initial hospitalization. Of the 51 patients with abrupt closure of vessels that were not reopened by PTCA, 30 (59 percent) required CABG.

Mortality and Myocardial Infarction

There was no statistically significant difference in the cumulative survival curves (Fig. 1) for the two treatment groups (111 deaths in the CABG group and 131 in the PTCA group, $P=0.19$ by the log-rank test). The cumulative survival rates at five years were 89.3 percent for patients assigned to CABG

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TABLE 2. COMPLICATIONS OF CABG AND PTCA THAT OCCURRED IN THE HOSPITAL.*

VARIABLE	CABG	PTCA	P VALUE†
	no. (%)		
No. randomly assigned to treatment	914 (100)	915 (100)	
No. receiving assigned treatment	892 (98)	904 (99)	
Hospitalization (median no. of days)			
Total stay	12	7	<0.001
After treatment	7	3	<0.001
	no. (% of those receiving assigned treatment)		
Death	12 (1.3)	10 (1.1)	
Q-wave myocardial infarction	41 (4.6)	19 (2.1)	<0.01
Death or Q-wave myocardial infarction	52 (5.8)	27 (3.0)	<0.01
Emergency CABG	1 (0.1)	57 (6.3)	<0.001
Emergency PTCA	0	19 (2.1)	<0.001
Stroke	7 (0.8)	2 (0.2)‡	
Coma	0	4 (0.4)§	
Dementia¶	4 (0.4)	4 (0.4)	
Nonemergency CABG	0	35 (3.9)	<0.001
Nonemergency PTCA	0	12 (1.3)	<0.001
Nonfatal cardiac arrest	18 (2.0)	22 (2.4)	
Congestive heart failure or pulmonary edema	35 (3.9)	21 (2.3)	
Hypotension requiring intravenous fluid or pressor support	62 (7.0)	79 (8.7)	
Cardiogenic shock	7 (0.8)	13 (1.4)	
Peripheral arterial embolus requiring therapy	3 (0.3)	11 (1.2)	
Respiratory failure‖	20 (2.2)	9 (1.0)	<0.05
Reoperation for bleeding	28 (3.1)	4 (0.4)	<0.001
Wound dehiscence or infection	37 (4.1)	4 (0.4)	<0.001
Renal failure requiring dialysis	1 (0.1)	2 (0.2)	

*For procedures undertaken in stages, complications occurring between the initial stage and the final-stage hospital discharge are included regardless of whether the patient was discharged from the hospital between stages. If PTCA was declared to be the first stage of such a procedure but the second stage was not initiated, any complications occurring within two weeks after the initial stage were included.

†Differences between groups were evaluated with Fisher's exact test in all cases except the duration of hospitalization, which was analyzed with the Mann–Whitney–Wilcoxon test.

‡Stroke in these two patients was not preceded by CABG.

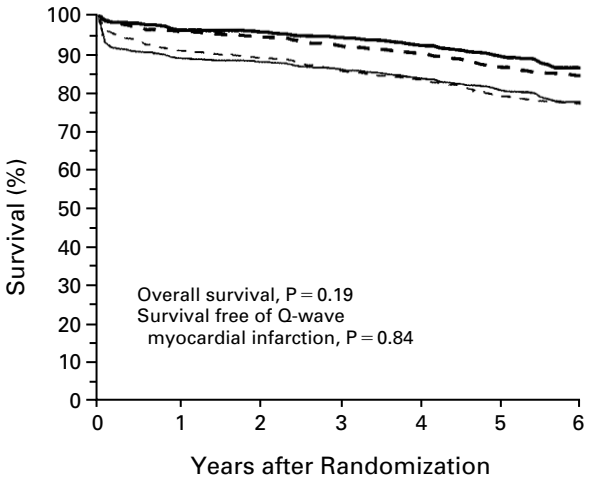
§In three of the four patients coma occurred after CABG.

¶Dementia refers to broad-based loss of higher intellectual function. In two of the four patients with dementia in the PTCA group, dementia actually occurred after CABG.

‖Respiratory failure refers to inadequate gas exchange during spontaneous ventilation with supplemental oxygen.

and 86.3 percent for those assigned to PTCA. The difference between groups rounds to 2.9 percentage points, with a 95 percent confidence interval of −0.2 percent to 6.0 percent. The results did not vary significantly among the clinical centers (P=0.76).

The rates of survival free of Q-wave myocardial infarction (Fig. 1) also did not differ significantly between assigned treatment groups (P=0.84 by the log-rank test). At five years, 80.4 percent of the patients assigned to CABG and 78.7 percent of those assigned to PTCA were alive and free from Q-wave myocardial infarction. The difference between groups rounds to 1.6 percentage points, with a 95 percent confidence interval of −2.2 percent to 5.4 percent. The cumulative rates of Q-wave myocardial infarction at five years were 11.7 percent and 10.9 percent for the CABG and PTCA groups, respectively (P=0.45 by the log-rank test) (data not shown).



OVERALL SURVIVAL			
CABG	914	857	542
PTCA	915	840	537
SURVIVAL FREE OF INFARCTION			
CABG	914	782	485
PTCA	915	780	487

Figure 1. Overall Survival (Heavy Lines) and Survival Free from Q-Wave Myocardial Infarction (Light Lines) after Study Entry.

Patients assigned to CABG are indicated by solid lines, and patients assigned to PTCA by dashed lines. The numbers of patients at risk are shown below the graph at base line, three years, and five years.

Repeated Revascularization

Eight percent of the patients assigned to CABG underwent additional revascularization procedures in the first five years: 1 percent underwent CABG and 7 percent PTCA (Fig. 2). In the PTCA group, 54 percent underwent at least one subsequent procedure, 31 percent underwent a subsequent CABG, and 34 percent underwent a second PTCA (11 percent underwent both subsequent PTCA and CABG). Unlike patients assigned to CABG, most patients assigned to PTCA who underwent a second revascularization did so in the first year of follow-up. In the PTCA group, 60 percent avoided CABG by undergoing the initial PTCA or at most one additional PTCA (Table 3). Multiple additional revascularizations, however, were required for 19 percent of the

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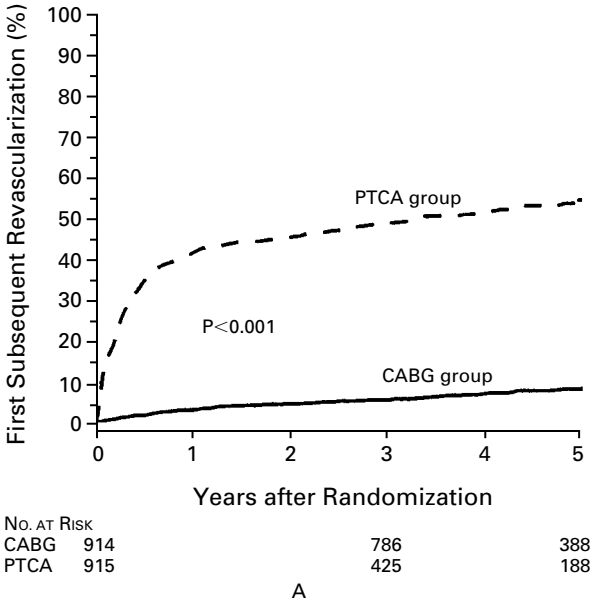

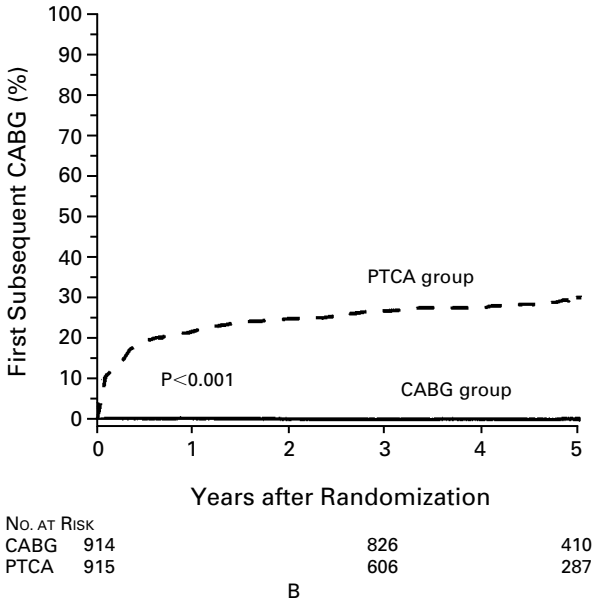

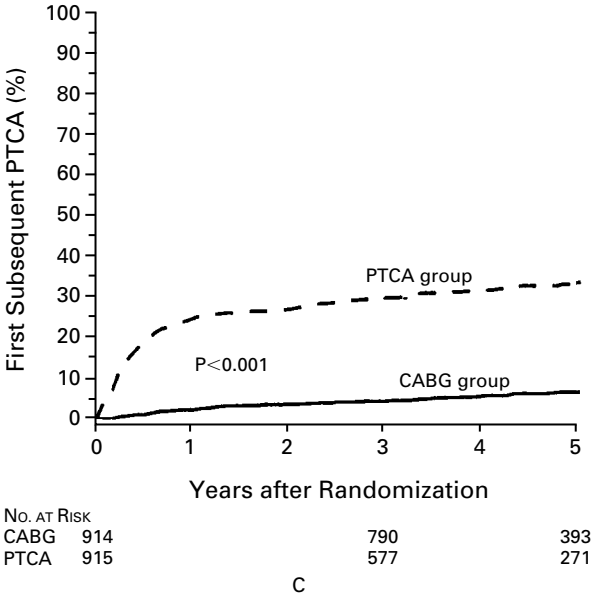

Figure 2. Percentage of Patients Who Underwent at Least One Subsequent Revascularization (Panel A), Subsequent CABG (Panel B), or Subsequent PTCA (Panel C) after Study Entry.

The numbers of patients at risk are shown below the graphs at base line, three years, and five years.

patients assigned to PTCA, as compared with 3 percent of those assigned to CABG. Reflecting this need for additional procedures, patients undergoing PTCA required more hospitalizations during follow-up, an average of 2.5 as compared with 1.9 in the CABG group ($P<0.001$ by the Mann–Whitney–Wilcoxon test).

Mortality within Subgroups

Figure 3 shows five-year survival rates for monitored subgroups, with 99 percent and 99.5 percent confidence intervals for treatment difference. The only significant difference occurred in the subgroup of patients with treated diabetes. Five-year survival was 65.5 percent among patients with treated diabetes who were assigned to PTCA, as compared with 80.6 percent among diabetics assigned to CABG (Fig. 4). The difference between groups was 15.1 percentage points, with a 99.5 percent confidence interval of 1.4 percent to 28.9 percent, corresponding to a statistically significant difference in the cumulative survival curves (37 deaths in the CABG group vs. 60 deaths in the PTCA group, $P=0.003$ by the log-rank test). The in-hospital mortality rates for the initial procedure among treated diabetics were similar: 0.6 percent for those assigned to PTCA and 1.2 percent for those assigned to CABG ($P=1.0$ by Fisher's exact test).

For the 1476 other patients (81 percent of the BARI population), survival was essentially identical in the two treatment groups (at five years, 91.4 percent for those assigned to CABG and 91.1 percent for those assigned to PTCA) (Fig. 4), with no significant differences among a priori subgroups (Fig. 3).

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TABLE 3. COMPARISON OF THE NEED FOR SUBSEQUENT REVASCULARIZATION PROCEDURES AT FIVE YEARS IN THE TWO TREATMENT GROUPS.*

SUBSEQUENT PROCEDURE	CABG (N=914)	PTCA (N=915)
	percent	
None	92.0	45.5
PTCA only	6.9	23.2
1	4.5	14.9
2	1.8	5.4
≥3	0.7	2.9
CABG only	0.7	20.5
1	0.7	20.1
≥2	0.0	0.3
Both CABG and PTCA	0.4	10.8
1 PTCA and 1 CABG	0.2	7.1
≥2 PTCA and 1 CABG	0.2	3.0
≥1 PTCA and 2 CABG	0.0	0.6

*Because of rounding not all categories add up to the total amount.

DISCUSSION

This clinical trial was designed to provide an overall comparison between coronary bypass surgery and angioplasty as initial treatment strategies in patients with multivessel coronary disease and a comparative assessment of treatment strategies in specified subgroups of patients. An analysis based on an average follow-up of 5.4 years revealed no statistically significant difference in survival between the two treatment strategies, with cumulative 5-year survival rates of 89.3 percent for patients assigned to CABG and 86.3 percent for patients assigned to PTCA. This slight difference was due to a better long-term outcome of the initial CABG strategy among patients with treated diabetes mellitus, who made up 19 percent of the entire randomized cohort. Among patients with treated diabetes, a difference of 15 percentage points in five-year survival was found in favor of CABG. Of equal importance, five-year survival and survival free of Q-wave myocardial infarction were nearly identical for the two revascularization strategies in the remaining 81 percent of the patients.

Five-year mortality in the trial was twice as high as expected at the time of study design. We attribute this difference to a more elderly and higher-risk population than the cohort with multivessel disease enrolled in the Coronary Artery Surgery Study,[19] which we used for the original estimates. One-year mortality in our trial was also higher than in a recent meta-analysis of six randomized trials comparing PTCA and CABG in patients with multivessel disease.[25] The one-year mortality rate for PTCA in our study was 4.2 percent, as compared with a combined rate of 3.1 percent in the other trials; the corresponding rates for CABG were 3.8 percent and 2.8 percent. As compared with these trials, our trial enrolled older patients, a higher proportion of women, and a higher proportion of patients with a history of myocardial infarction, hypertension, congestive heart failure, diabetes, and poor left ventricular function. In the Emory Angioplasty versus Surgery Trial (EAST), the randomized patients were similar to those in our trial, except that the prevalence of disease in the proximal left anterior descending artery was 72 percent in that trial[26] as compared with 37 percent in the current study. This difference can be attributed to differences in the definitions of anatomical boundaries. The EAST reported five-year mortality rates of 8.8 percent for CABG and 12.1 percent for PTCA,[27] values within the range observed among our centers.

Five-year survival free of Q-wave myocardial infarction was similar in both treatment groups. During the initial hospitalization, Q-wave myocardial infarction occurred more frequently in patients undergoing CABG, although this difference was offset by the occurrence of a higher rate in the PTCA group during follow-up. The total rates of myocardial infarction were underestimated in the study since non–Q-wave myocardial infarctions were not counted.

Although the mortality rates and rates of Q-wave myocardial infarction were similar for CABG and PTCA, there are clear differences in other aspects of the clinical course. An initial strategy of angioplasty was associated with a substantially greater need for additional revascularization procedures, especially during the first year of follow-up. For patients assigned to PTCA, the rate of additional procedures at one year (42 percent) was higher than the rate of 35 percent reported in the meta-analysis of other trials,[25] whereas the 3 percent rate for patients assigned to CABG was identical. Of the patients assigned to PTCA, 31 percent subsequently underwent CABG. This five-year rate was 5 percentage points higher than the rate reported in the EAST, even though the rate of subsequent CABG during the initial hospitalization was 10 percent in both studies.[26,27] In spite of the greater need for reintervention, 60 percent of the patients assigned to PTCA avoided subsequent CABG by undergoing the initial PTCA or at most one additional PTCA. Thus, for patients who prefer to avoid major surgery, angioplasty offers a reasonable alternative with an expectation of similar overall survival rates and survival rates free of Q-wave myocardial infarction.

Differences in survival between the treatment groups were not significant in any of the a priori subgroups. In 1992 the safety and data monitoring board requested that diabetic patients be monitored because of concern aroused by a previous study about the effects of PTCA in diabetics.[24] Although the difference between treatments in this subgroup exceeded a stringent level of statistical significance, this finding should be confirmed in other populations.

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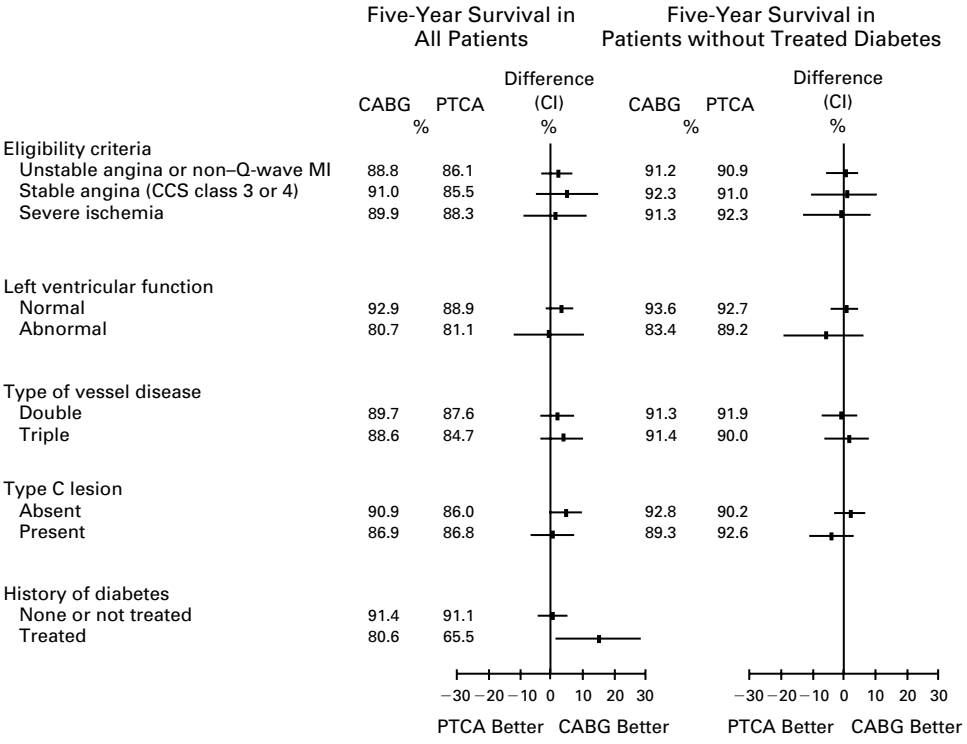

Figure 3. Five-Year Survival Rates for All Patients and Patients without Treated Diabetes at Base Line, According to Subgroups Selected on the Basis of Base-Line Characteristics.

Ninety-nine percent confidence intervals (CI) of the difference between five-year survival rates are shown for all subgroups except those with a history of diabetes, for which 99.5 percent confidence intervals are shown. CCS denotes Canadian Cardiovascular Society, and MI myocardial infarction. A type C lesion was defined according to the criteria of the American Heart Association–American College of Cardiology Consensus Panel.[18]

Two-year results for 122 diabetic patients in the Coronary Angioplasty versus Bypass Revascularization Investigation suggest that CABG improves survival to the same extent as in our trial.[28] The EAST reported no difference in five-year survival between treatment groups in 59 diabetic patients.[27] The more extensive coronary disease among diabetics and their greater tendency to have restenosis after angioplasty suggest potential mechanisms to explain the relatively better outcome after bypass surgery found in our trial. The influence of these and other factors requires further study.

Of equal importance is the finding of no difference between treatments in any other subgroup of patients examined, including those defined by clinical and angiographic characteristics for which CABG had previously been determined to be superior to medical therapy.[2-6]

The higher than expected mortality rates for both treatment strategies have implications for testing the study's original hypothesis. Overall, there was a difference between treatment groups of 2.9 percentage points, which was not statistically significant. Although a difference of this magnitude would have been significant under the original mortality assumptions, higher observed rates led to wider confidence intervals for the true difference. The power to detect relative differences between the treatment groups, however, was not compromised.

The coronary revascularization approaches used in BARI have continued to undergo refinements.[29] For instance, in the wake of reports that stents reduce the risk of early restenosis, stent implantation is now more common among patients who require coronary angioplasty.[30,31] Studies are exploring ways to avoid median sternotomy by means of "minimally invasive" surgical procedures.[32] BARI and the other clinical trials of PTCA and CABG begun in the late 1980s will provide benchmarks for the assessment of these newer approaches.

A recent survey of centers participating in the current trial and 75 other U.S. institutions performing coronary revascularization[33] confirms that our clinical sites are representative of U.S. centers in terms of patient characteristics and treatment choice based on extent of coronary disease. In combination with data on patient screening in BARI,[10] the survey suggests that approximately 12 percent of all patients

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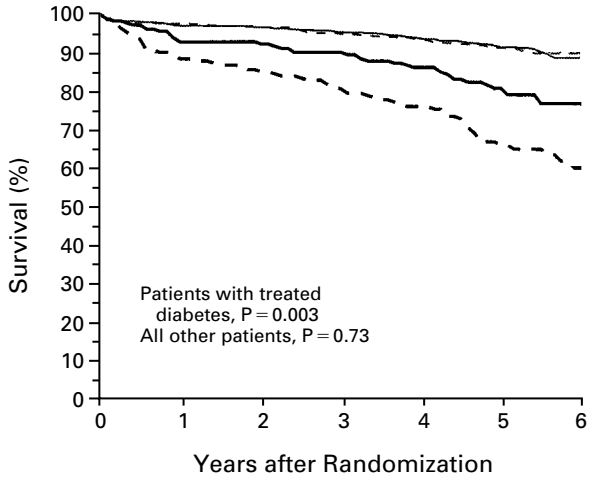

PATIENTS WITH TREATED DIABETES			
CABG	180	161	93
PTCA	173	139	69
ALL OTHER PATIENTS			
CABG	734	696	449
PTCA	742	701	468

Figure 4. Survival among Patients Who Were Being Treated for Diabetes at Base Line (Heavy Lines) and All Other Patients (Light Lines).

Patients assigned to CABG are indicated by solid lines, and those assigned to PTCA by dashed lines. The numbers of patients at risk are shown below the graph at base line, three years, and five years.

who require coronary revascularization would be eligible for the BARI trial. For the remaining majority, indicators of treatment are better established.

Continuing follow-up will further elucidate the advantages and disadvantages of PTCA and CABG, since graft failure[34] and the development of new coronary disease[2-4,35] may have substantial effects over the long term on mortality, morbidity, and the need for additional procedures.

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APPENDIX

The following institutions and persons participated in the BARI trial: **University of Alabama** — W. Rogers, W. Baxley, L. Dean, G. Roubin, J.K. Kirklin, J.W. Kirklin, A. Pacifico, G. Zorn, E. Charles, T. Paine, S. Brewer, G. Duke, L. Maske, T. Morgan, K. Doss, K. Anderson, M. Brunner-Scott, F. Harris, T. Bulle, J. Cavender, P. Garrahy; **Rhode Island Hospital** — D. Williams, T. Drew, A. Singh, G. Cooper, B. Sharaf, J. Wheeler, M. Grogan; **Bellevue Hospital** — F. Feit, M. Attubato, S. Colvin, A. Galloway, G. Ribakove, P. Pasternack, M. Rey, S. Shapiro; **Boston University** — A. Jacobs, D. Faxon, G. Garber, N. Ruocco, R. Shemin, G. Aldea, T. Ryan, D. Weiner, B. Hankin, M. Mazur; **Cleveland Clinic Foundation** — P. Whitlow, S. Ellis, I. Franco, R. Raymond, E. Topol, D. Cosgrove, F. Loop, B. Lytele, R. Stewart, P. Taylor, A. Dimas, A. Lincoff, M. Lowrie, K. Comella; **Duke University** — R. Califf, R. Bauman, V. Behar, Y. Kong, M. Krucoff, K. Morris, R. Peter, H. Phillips, R. Stack, J. Tcheng, R. Jones, H. Oldham, R. Van Tright, W. Baker, T. Bashore, D. Fortin, K. Lee, E. Ohman, L. Drew, M. Sellers, V. Bass; **Beth Israel Hospital** — D. Baim, J. Aroesty, B. Lorell, R. Johnson, R. Thurer, R. Weintraub, M. Flatley; **Maine Medical Center** — M. Kellett, Jr., W. Alpern, R. Anderson, D. Cutler, P. Sweeney, D. Donegan, S. Katz, R. Kramer, C. Lutes, J. Morton, E. Nowicki, J. Tryzelaar, R. White, C. Lambrew, S. Bosworth-Farrell, J. Kane, N. Tooker; **University of Massachusetts** — B. Weiner, J. Moran, O. Okike, A. Pezzella, T. VanderSalm, M. Borbone, K. Quist; **Mayo Clinic Foundation** — R. Frye (study chair), M. Mock, J. Bresnahan, D. Holmes, G. Reeder, C. Mullany, T. Orszulak, H. Schaff, P. Berger, R. Gibbons, S. Kopecky, R. Schwartz, H. Smith, S. Matheson, L. Kelly, L. Pierre, D. Bresnahan, B. Gersh, F. Nobrega, M. Peterson, R. Vlietstra; **Medical College of Virginia** — M. Cowley, G. Vetrovec, A. Guerraty, D. Salter, A. Wechsler, K. Kelly Hall; **University of Michigan** — B. Pitt, E. Bates, D. Muller, S. Bolling, M. Deeb, M. Kirsh, M. Stock, J. Corbett, P. Fox, T. Johnson, K. McNeely, S. Pitt, K. Burek; **Montreal Heart Institute** — M. Bourassa, R. Bonan, G. Cote, J. Crepeau, P. DeGuise, Y. Leclerc, C. Pelletier, J. Gregoire, G. Hudon, J. Lesperance, J. Trudel, C. Faille; **Toronto Hospital** — L. Schwartz, H. Aldridge, T. David, C. Feindel, B. Goldman, L. Mickleborough, R. Weisel, C. Lazzam, M. McLoughlin, L. Zelovitsky, P. Liu, L. Lazzam; **New York Medical College** — M. Weiss, R. Moggio, R. Pooley, G. Reed, M. Sarabu, R. Steinberg; **St. Louis University** — B. Chaitman, F. Aguirre, M. Kern, G. Kaiser, V. Willman, R. Wiens, C. Huffman, T. Stonner, S. Aubuchon, M. Kramer; **Jewish Hospital** — R. Krone, N. Kouchoukos, A. Salimi, T. Wareing, P. Cole, K. Fischer, R. Kleiger, J. Humphrey, D. Bowen, G. Eisenkramer, P. Rice, J. Waldschmidt; **Georgetown University (former site); Institute of Clinical and Experimental Medicine, Prague, Czech Republic (parallel study); Central Electrocardiographic and Myocardial Infarction Classification Laboratory: St. Louis University Medical Center** — B. Chaitman, P. Bjerregaard, I. Gussak, R. Wiens, L. Younis, K. Stocke, K. Russell, S. Cannon, C. Homeyer, M. Miller; **Central Radiographic Laboratory: Stanford University Medical Center** — E. Alderman, M. Stadius, B. Brown, W. Sanders, L. Wexler, B. Hollak; **Coordinating Center: University of Pittsburgh** — K. Detre, S. Kelsey, K. Sutton-Tyrrell, A. Rosen, S. Crow, K. Andrews, J. Bost, M. Brooks, R. Hardison, G. Harger, R. Holubkov, A. Siewers, J. Martin, J. Greenhouse, A. Sampson, C. Ravotti; **NHLBI** — G. Sopko, D. Follmann, M. Horan; **Safety and Data Monitoring Board** — J. Bristow, J. Childress, T. Gardner, C. Grines, J. Kennedy, G. Knatterud, J. Waldhausen, C. White; **Morbidity and Mortality Classification Committee** — R. Prineas, C. Fisch, H. Greene, R. Karp, S. King III, J. Mason, J. Titus.

REFERENCES

1. Favaloro RG. Saphenous vein autograft replacement of severe segmental coronary artery occlusion: operative technique. Ann Thorac Surg 1968;5:334-9.

2. The Veterans Administration Coronary Artery Bypass Surgery Cooperative Study Group. Eleven-year survival in the Veterans Administration randomized trial of coronary bypass surgery for stable angina. N Engl J Med 1984;311:1333-9.

3. Varnauskas E, European Coronary Surgery Study Group. Twelve-year follow-up of survival in the randomized European Coronary Surgery Study. N Engl J Med 1988;319:332-7.

4. Alderman EL, Bourassa MG, Cohen LS, et al. Ten-year follow-up of survival and myocardial infarction in the randomized Coronary Artery Surgery Study. Circulation 1990;82:1629-46.

5. Detre KM, Peduzzi P, Murphy M, et al. Effect of bypass surgery on survival of patients in low- and high-risk subgroups delineated by the use of simple clinical variables: Veterans Administration cooperative study of surgery for coronary arterial occlusive disease. Circulation 1981;63:1329-38.

6. Passamani E, Davis KB, Gillespie MJ, Killip T, CASS Principal Investi-

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gators. A randomized trial of coronary artery bypass surgery: survival in patients with a low ejection fraction. N Engl J Med 1985;312:1665-71.
7. Grüntzig AR, Senning A, Siegenthaler WE. Nonoperative dilatation of coronary-artery stenosis: percutaneous transluminal coronary angioplasty. N Engl J Med 1979;301:61-8.
8. Protocol for the Bypass Angioplasty Revascularization Investigation. Circulation 1991;84:Suppl V:V-1–V-27.
9. Takaro T, Hultgren HN, Lipton MJ, Detre KM. The VA cooperative randomized study of surgery for coronary arterial occlusive disease. II. Subgroup with significant left main lesions. Circulation 1976;54:Suppl III: III-107–III-117.
10. Bourassa MG, Roubin GS, Detre KM, et al. Bypass Angioplasty Revascularization Investigation: patient screening, selection, and recruitment. Am J Cardiol 1995;75:3C-8C.
11. Rogers WJ, Alderman EL, Chaitman BR, et al. Bypass Angioplasty Revascularization Investigation (BARI): baseline clinical and angiographic data. Am J Cardiol 1995;75:9C-17C.
12. Williams DO, Baim DS, Bates E, et al. Coronary anatomic and procedural characteristics of patients randomized to coronary angioplasty in the Bypass Angioplasty Revascularization Investigation (BARI). Am J Cardiol 1995;75:27C-33C.
13. Schaff HV, Rosen AD, Shemin RJ, et al. Clinical and operative characteristics of patients randomized to coronary artery bypass surgery in the Bypass Angioplasty Revascularization Investigation (BARI). Am J Cardiol 1995;75:18C-26C.
14. Hlatky MA, Charles ED, Nobrega F, et al. Initial functional and economic status of patients with multivessel coronary artery disease randomized in the Bypass Angioplasty Revascularization Investigation (BARI). Am J Cardiol 1995;75:34C-41C.
15. Prineas RJ, Crow RS, Blackburn H. The Minnesota Code manual of electrocardiographic findings: standards and procedures for measurement and classification. Boston: John Wright–PSG, 1982.
16. Rautaharju PM, Calhoun HP, Chaitman BR. NOVACODE serial ECG classification system for clinical trials and epidemiologic studies. J Electrocardiol 1991;24:Suppl:179-87.
17. Alderman EL, Stadius M. The angiographic definitions of the Bypass Angioplasty Revascularization Investigation. Coron Artery Dis 1992;3: 1189-207.
18. Ryan TJ, Faxon DP, Gunnar RM, et al. Guidelines for percutaneous transluminal coronary angioplasty: a report of the American College of Cardiology/American Heart Association Task Force on assessment of diagnostic and therapeutic cardiovascular procedures. J Am Coll Cardiol 1988;12:529-45.
19. Principal Investigators of CASS. National Heart, Lung, and Blood Institute Coronary Artery Surgery Study: a multicenter comparison of the effects of randomized medical and surgical treatment of mildly symptomatic patients with coronary artery disease, and a registry of consecutive patients undergoing coronary angioplasty. Circulation 1981;63:Suppl I:I-1–I-81.
20. Sheehan FH, Braunwald E, Canner P, et al. The effect of intravenous thrombolytic therapy on left ventricular function: a report on tissue-type plasminogen activator and streptokinase from the Thrombolysis in Myocardial Infarction (TIMI phase I) trial. Circulation 1987;75:817-29.
21. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. J Am Stat Assoc 1958;53:457-81.
22. Mantel N, Haenszel W. Statistical aspects of the analysis of data from retrospective studies of disease. J Natl Cancer Inst 1959;22:719-48.
23. Cox DR. Regression models and life-tables. J R Stat Soc [B] 1972;34: 187-220.
24. Mueller HS, Cohen LS, Braunwald E, et al. Predictors of early morbidity and mortality after thrombolytic therapy of acute myocardial infarction: analyses of patient subgroups in the Thrombolysis in Myocardial Infarction (TIMI) trial, phase II. Circulation 1992;85:1254-64.
25. Pocock SJ, Henderson RA, Rickards AF, et al. Meta-analysis of randomised trials comparing coronary angioplasty with bypass surgery. Lancet 1995;346:1184-9.
26. King SB III, Lembo NJ, Weintraub WS, et al. A randomized trial comparing coronary angioplasty with coronary bypass surgery. N Engl J Med 1994;331:1044-50.
27. Kosinski AS, Barnhart HX, Weintraub WS, et al. Five year outcome after coronary surgery or coronary angioplasty: results from the Emory Angioplasty vs Surgery Trial (EAST). Circulation 1995;91:Suppl I:I-543. abstract.
28. Bertrand M. Long-term follow-up of European revascularization trials. Presented at the 68th Scientific Sessions, Plenary Session XII, American Heart Association, Anaheim, Calif., November 16, 1995.
29. Ellis SG, Cowley MJ, Whitlow PL, et al. Prospective case-control comparison of percutaneous transluminal coronary revascularization in patients with multivessel disease treated in 1986-1987 versus 1991: improved in-hospital and 12-month results. J Am Coll Cardiol 1995;25:1137-42.
30. Fischman DL, Leon MB, Baim DS, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994;331:496-501.
31. Serruys PW, de Jaegere P, Kiemeneij F, et al. A comparison of balloon-expandable–stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994;331:489-95.
32. Benetti FJ, Ballester C. Use of thoracoscopy and a minimal thoracotomy, in mammary-coronary bypass to left anterior descending artery, without extracorporeal circulation: experience in 2 cases. J Cardiovasc Surg 1995;36:159-61.
33. Detre KM, Rosen AD, Bost JE, et al. Contemporary practice of coronary revascularization in U.S. hospitals and hospitals participating in the Bypass Angioplasty Revascularization Investigation (BARI). J Am Coll Cardiol (in press).
34. Campeau L, Lespérance J, Corbara F, Hermann J, Grondin CM, Bourassa MG. Aortocoronary saphenous vein bypass graft changes 5 to 7 years after surgery. Circulation 1978;58:Suppl I:I-170–I-175.
35. Bourassa MG, Enjalbert M, Campeau L, Lesperance J. Progression of atherosclerosis in coronary arteries and bypass grafts: ten years later. Am J Cardiol 1984;53:102C-107C.

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