

The New England Journal of Medicine

© Copyright, 2000, by the Massachusetts Medical Society

VOLUME 342

APRIL 6, 2000

NUMBER 14



THE EFFECT OF PREVIOUS CORONARY-ARTERY BYPASS SURGERY ON THE PROGNOSIS OF PATIENTS WITH DIABETES WHO HAVE ACUTE MYOCARDIAL INFARCTION

KATHERINE M. DETRE, M.D., DR.P.H., MANUEL S. LOMBARDEO, M.S., MARIA MORI BROOKS, PH.D.,
REGINA M. HARDISON, M.S., RICHARD HOLUBKOV, PH.D., GEORGE SOPKO, M.D., M.P.H., ROBERT L. FRYE, M.D.,
AND BERNARD R. CHAITMAN, M.D., FOR THE BYPASS ANGIOPLASTY REVASCLARIZATION INVESTIGATION INVESTIGATORS*

ABSTRACT

Background Acute myocardial infarction in patients with diabetes is associated with high mortality. We studied whether previous revascularization by coronary-artery bypass grafting (CABG), as compared with percutaneous transluminal coronary angioplasty (PTCA), influences the prognosis in such patients.

Methods We classified all patients eligible for the Bypass Angioplasty Revascularization Investigation who underwent coronary revascularization within three months after entry into the study according to whether they had diabetes and whether they had undergone CABG, either initially or after PTCA. The protective effect of CABG with regard to mortality in the presence and in the absence of subsequent spontaneous Q-wave myocardial infarction was estimated with the use of Cox regression models.

Results Among the 641 patients with diabetes and the 2962 without diabetes, the cumulative five-year rates of death were 20 percent and 8 percent, respectively ($P < 0.001$), and the five-year rates of spontaneous Q-wave myocardial infarction were 8 percent and 4 percent ($P < 0.001$). CABG greatly reduced the risk of death after spontaneous Q-wave myocardial infarction in the patients with diabetes (relative risk, 0.09; 95 percent confidence interval, 0.03 to 0.29). Among patients with diabetes who had undergone CABG but did not have spontaneous Q-wave myocardial infarction, the corresponding relative risk of death was 0.65 (95 percent confidence interval, 0.45 to 0.94). Among the patients without diabetes, no protective effect of CABG was evident.

Conclusions Among patients with diabetes, previous coronary bypass surgery, as compared with coronary angioplasty, has a highly favorable influence on prognosis after acute myocardial infarction and a smaller beneficial effect among patients who do not have infarction. These findings should influence the type of coronary revascularization procedure selected for patients with diabetes who have multivessel coronary artery disease. (N Engl J Med 2000;342:989-97.)

©2000, Massachusetts Medical Society.

IN 1996, the Bypass Angioplasty Revascularization Investigation (BARI), a randomized trial, found that an initial strategy of coronary-artery bypass grafting (CABG), as compared with percutaneous transluminal coronary angioplasty (PTCA), significantly improved five-year survival among patients with medically treated diabetes.^{1,2} This benefit was not observed in the periprocedural period; rather, it was a sustained, long-term effect, with the risk of death consistently reduced by about 50 percent throughout the five years of follow-up. No difference in survival was observed in this study among the patients who did not have diabetes. After eight years of follow-up, the Emory Angioplasty versus Surgery Trial, with a design similar to that of BARI, found a similar trend in the subgroup of patients with diabetes.³

The purpose of the current investigation was to elucidate the mechanism leading to different clinical courses among patients with diabetes according to the type of revascularization they underwent (i.e., CABG or PTCA). In this regard, two findings from previous studies have particular relevance. First, in previous randomized, controlled trials^{4,5} CABG was associated with better outcomes in patients who had myocardial infarction than was medical therapy. Second, it is widely reported⁶⁻¹¹ that the mortality rate after myocardial infarction is considerably higher among patients with diabetes than among those without diabetes. We evaluated whether there is a protective effect

From the Bypass Angioplasty Revascularization Investigation Coordinating Center, University of Pittsburgh, Pittsburgh (K.M.D., M.S.L., M.M.B., R.M.H., R.H.); the National Institutes of Health, Bethesda, Md. (G.S.); the Mayo Clinic Foundation, Rochester, Minn. (R.L.F.); and St. Louis University Health Sciences Center, St. Louis (B.R.C.). Address reprint requests to Dr. Detre at the BARI Coordinating Center, Graduate School of Public Health, University of Pittsburgh, 130 DeSoto St., 127 Parran Hall, Pittsburgh, PA 15261, or at detre@edc.gsph.pitt.edu.

*A complete list of the Bypass Angioplasty Revascularization Investigation investigators has been published (Circulation 1997;96:1761-9).

of previous CABG at the time of myocardial infarction in patients with diabetes, and if so, the degree to which this mechanism could explain the observed survival benefit associated with CABG (as compared with coronary angioplasty) in such patients in BARI.

METHODS

Study Design

The design of BARI has been described previously.^{12,13} Briefly, patients were eligible for the study if they had severely symptomatic and angiographically confirmed multivessel coronary artery disease requiring revascularization and were suitable candidates for either PTCA or CABG as the initial revascularization procedure. Of 4107 eligible patients recruited at 18 clinical centers in the United States and Canada, 1829 agreed to undergo random assignment to either CABG or PTCA; 2010 underwent revascularization on the basis of a recommendation by their physician, and data on these patients were entered into a registry; and 268 declined all follow-up. Both the patients in the randomized group and those in the registry group were followed according to the protocol. At the end of an average of 5.5 years of follow-up, vital status was known for 98 percent of patients.

Annual electrocardiograms were required for all patients who were followed, and an additional electrocardiogram 4 to 14 weeks after entry into the study was also required for the patients who underwent randomization. In addition, electrocardiograms were obtained in patients in whom myocardial infarction was suspected. Reading, interpretation, and coding of the electrocardiograms were conducted by the core electrocardiography laboratory at St. Louis University.

The analysis reported here is restricted to data on 3603 patients, from both the randomized trial and the registry, who underwent revascularization by either CABG or PTCA within three months after entry into the study. Patients were classified as either having diabetes or not having diabetes, according to whether or not they were receiving insulin or oral hypoglycemic medication for the treatment of diabetes at the time of entry into the study.

End Points

Death from all causes was the primary end point. The diagnosis of Q-wave myocardial infarction either was established according to the criteria of Chaitman et al.¹⁴ or was based on the classification of death as determined by an independent mortality and morbidity classification committee. Only myocardial infarctions that occurred during follow-up were considered. Q-wave myocardial infarctions were defined as "spontaneous" if the patient had not undergone a revascularization procedure within the previous seven days, and as "procedural" otherwise. This report focuses on spontaneous Q-wave myocardial infarctions, which were considered "silent" (asymptomatic) if diagnosed by a routine electrocardiogram obtained as part of the protocol and not accompanied by chest pain or elevated enzyme levels.

All initial and repeated revascularization procedures (CABG and PTCA) were documented for each patient over the course of the entire follow-up period. All patients who underwent CABG, whether as an initial or a repeated revascularization procedure, were regarded as subject to the protective effect of CABG. For analytic purposes, this status was conferred at the completion of the surgery. Thus, patients who initially underwent PTCA and later had bypass surgery were regarded as being subject to the protective effect of CABG only after the CABG procedure.

Statistical Analysis

We used chi-square tests and Student's t-test to compare base-line characteristics and Kaplan-Meier analysis¹⁵ to estimate the cumulative rates of CABG and spontaneous Q-wave myocardial infarction. For comparisons between the patients who underwent CABG and those who did not (i.e., those who underwent only

PTCA), the estimates used were based on transient-state life tables¹⁶ to accommodate changes in status with respect to CABG over time. For patients who did not have a Q-wave myocardial infarction, mortality rates were estimated from the time of the initial revascularization procedure; otherwise, they were estimated from the time of the Q-wave myocardial infarction. Results regarding mortality were evaluated with the use of Cox models,¹⁷ which included CABG and myocardial infarction as time-dependent covariates¹⁸ and other base-line variables as fixed covariates. These models were used to estimate and assess the significance of the relative risks of death that describe the protective effect of CABG both in the patients who had spontaneous Q-wave myocardial infarction and in those who did not and to compare the protective effect of CABG formally in these two groups by testing for an interaction between CABG and Q-wave myocardial infarction. Separate estimates were obtained for patients with diabetes and those without diabetes.

Base-line covariates included in the Cox models were either factors known to be important predictors of death or factors that were disproportionately more common among the patients in this study with diabetes who underwent CABG and had a subsequent spontaneous Q-wave myocardial infarction. All P values are two-tailed.

RESULTS

Table 1 shows the base-line characteristics according to CABG status at last contact for the 641 patients with diabetes and the 2962 without diabetes. Among the patients who underwent CABG, 71 percent had the surgery as their initial revascularization procedure. As described previously,² the patients with diabetes, regardless of whether they underwent CABG, were more likely to be female and black and were more likely to have a history of congestive heart failure, hypertension, renal dysfunction, and peripheral vascular disease than the patients without diabetes. However, a comparison of those who underwent CABG and those who did not undergo CABG during the study revealed some differences: those who eventually underwent CABG were more likely than those who did not to have undergone randomization, to be male (in the case of patients without diabetes), to have a fair or poor quality of life (a trend among patients with diabetes), to have unstable angina (a trend among patients with diabetes), and to present with more extensive and diffuse coronary artery disease.

Overall, 1512 of the 3603 patients underwent CABG as their initial revascularization procedure (42 percent), and an additional 442 of the remaining 2091 patients (i.e., those who underwent PTCA first) underwent CABG sometime during the first year of follow-up. Thereafter, the rate of crossover to CABG decreased to an average annual incidence of 2.8 percent. A somewhat larger proportion of the patients with diabetes than of the patients without diabetes initially underwent revascularization by CABG (45 percent vs. 41 percent, $P=0.08$), and among the patients who initially underwent revascularization by PTCA, 34 percent of those with diabetes as compared with 29 percent of those without diabetes underwent CABG within five years (relative risk of crossover to CABG among patients with diabetes, 1.25; $P=0.04$). At five years, 64 percent of the patients

TABLE 1. BASE-LINE CHARACTERISTICS OF THE PATIENTS ACCORDING TO FINAL STATUS WITH RESPECT TO CORONARY-ARTERY BYPASS GRAFTING.*

CHARACTERISTIC	PATIENTS WITH DIABETES			PATIENTS WITHOUT DIABETES		
	CABG (N=407)	NO CABG (N=234)	P VALUE	CABG (N=1727)	NO CABG (N=1235)	P VALUE
BARI-related data						
Patient was enrolled in the randomized study (%)	57.2	48.7	0.04	54.8	41.9	<0.001
Patient received CABG as the first treatment (%)	71.0	—		70.8	—	
Demographic profile						
Age (yr)						
Mean	62.1	62.2	0.89	61.3	61.2	0.71
Median	63	63		62	62	
≥65 yr (%)	41.5	42.3	0.85	39.1	37.8	0.46
Female sex (%)	44.0	42.7	0.76	20.5	25.3	0.002
White race (%)	86.0	83.8	0.44	93.4	94.3	0.35
Black race (%)	8.4	10.7	0.33	4.7	3.6	0.16
High-school education or less (%)	74.0	72.6	0.72	63.3	62.1	0.51
Sedentary or low activity level (%)	61.3	61.0	0.95	46.0	46.3	0.85
Fair or poor quality of life (%)	42.9	40.7	0.60	26.1	22.0	0.01
Body-mass index†						
Mean	29.6	30.2	0.21	27.6	27.6	0.86
Median	29	29		27	27	
Category (%)			0.84			0.47
<25	16.2	15.0		27.0	28.8	
25–29.9	38.1	40.2		47.8	47.4	
≥30	45.7	44.9		25.2	23.7	
Medical history (%)						
Myocardial infarction	56.7	52.6	0.32	51.9	51.0	0.65
Congestive heart failure	16.7	16.0	0.83	5.1	4.8	0.73
Family member with coronary disease	48.9	42.2	0.11	51.0	49.1	0.31
Smoking	57.2	63.2	0.14	70.2	72.8	0.12
Peripheral vascular disease	13.4	11.2	0.42	6.4	6.3	0.90
Chronic obstructive pulmonary disease	4.1	7.0	0.14	5.7	5.0	0.46
Cancer	4.7	5.6	0.62	5.4	4.8	0.46
Renal dysfunction	4.9	4.3	0.72	1.7	1.3	0.34
Hypertension	64.6	66.7	0.60	45.8	44.2	0.39
Hypertension, with high blood pressure at base line	32.4	37.2	0.22	21.4	18.8	0.09
Angina classification (%)			0.64			0.003
No angina or ischemia associated with acute myocardial infarction	5.8	4.8		5.3	8.2	
Stable angina	26.8	30.0		30.2	31.7	
Unstable angina	67.4	65.2		64.5	60.1	
Results of ECG at rest (%)‡						
Major Q-wave abnormality	19.9	20.5	0.86	17.7	16.8	0.51
Any abnormality	47.0	46.6	0.91	41.0	41.3	0.89
Angiographic assessment (%)						
Triple-vessel disease	49.3	37.1	0.003	41.2	30.6	<0.001
≥4 Clinically significant lesions	45.3	36.6	0.03	35.1	25.5	<0.001
Any diffuse lesion	32.7	28.4	0.27	30.7	24.4	<0.001
Clinically significant disease of the proximal left anterior descending artery	38.4	29.3	0.02	41.7	35.1	<0.001
Any class C lesion§	38.1	35.8	0.56	37.2	32.8	0.01
Any total occlusion	30.2	30.6	0.92	32.2	28.0	0.02
Left-sided or mixed dominance	14.6	13.4	0.67	14.6	15.5	0.54
Abnormal left ventricular function	20.4	27.5	0.06	17.8	15.0	0.06
Ejection fraction						
Mean percent	60.5	58.4	0.08	61.5	61.8	0.49
Median percent	61	59		61	62	

*The patients underwent either coronary-artery bypass grafting (CABG) or percutaneous transluminal coronary angioplasty (PTCA) as their initial revascularization procedure; some patients who initially underwent PTCA had CABG later. The numbers of patients in each group refer to the numbers at the end of follow-up. With the exception of ejection fraction, percentages are percentages of patients. BARI denotes Bypass Angioplasty Revascularization Investigation, and ECG electrocardiogram.

†The body-mass index is the weight in kilograms divided by the square of the height in meters.

‡ECGs were assessed by the central ECG laboratory.

§A lesion is considered to be class C if there is excessive vessel tortuosity near the lesion or excessive vessel angulation at the site of the lesion, if there is total occlusion of the vessel for more than three months or total occlusion for an unknown period, if there is critical narrowing more than 20 mm in length, or if attempts to dilate the lesion pose a risk to major side branches.

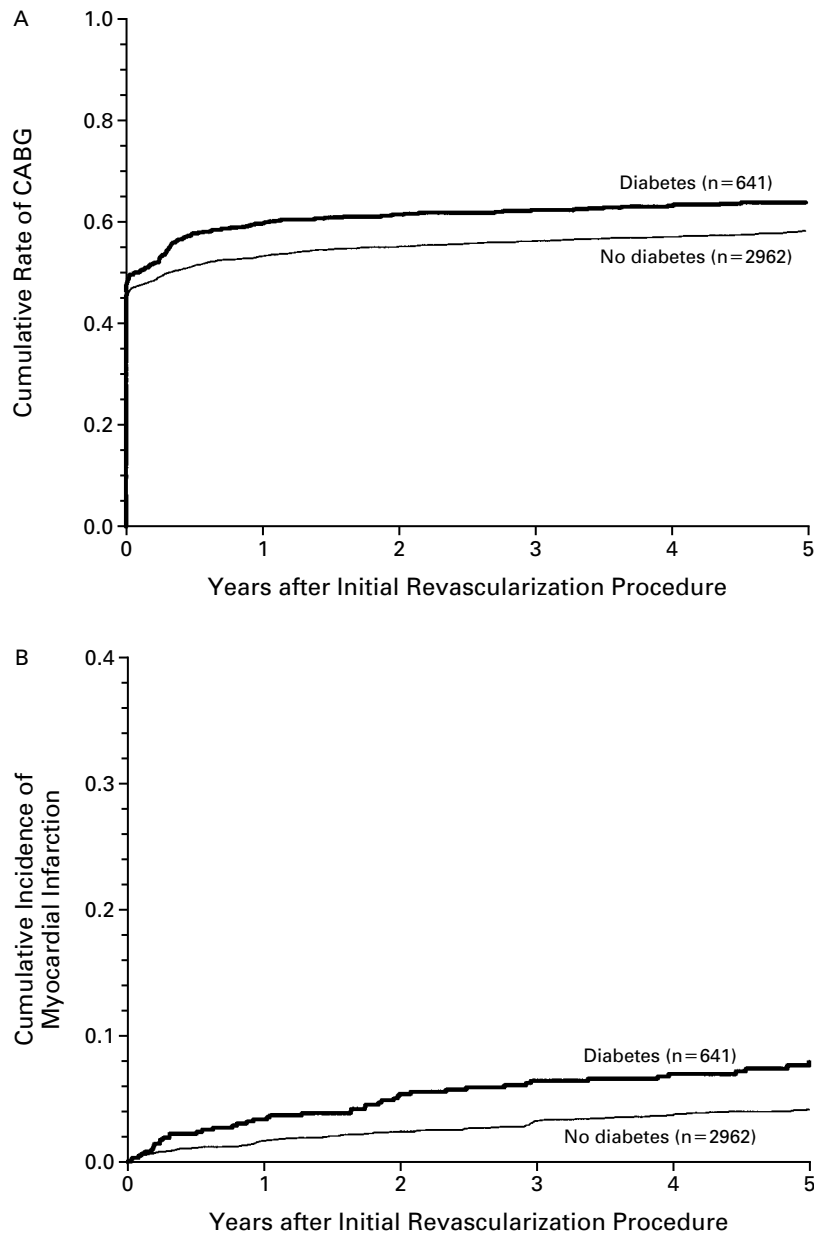


Figure 1. Rate of Coronary-Artery Bypass Grafting (CABG) and Incidence of Spontaneous Q-Wave Myocardial Infarction.

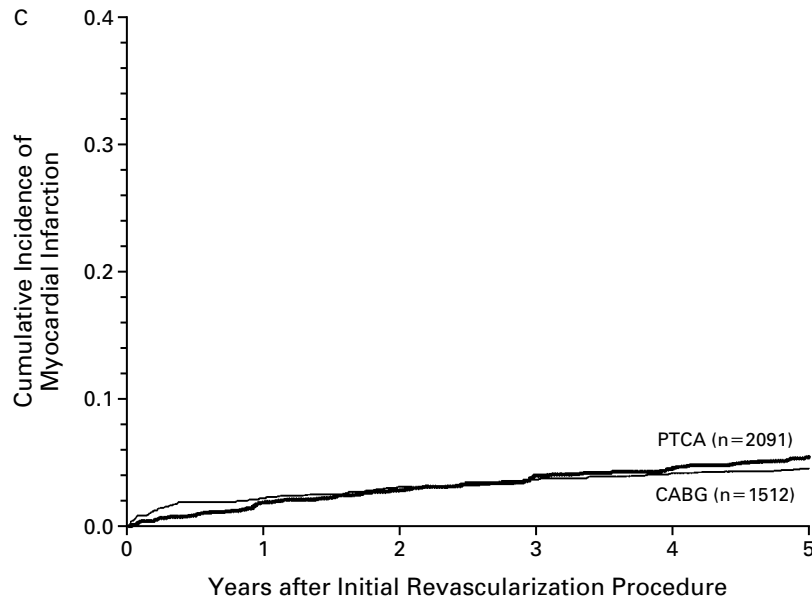
Panel A shows Kaplan–Meier estimates of the cumulative rate of CABG, and Panel B shows the cumulative incidence of spontaneous Q-wave myocardial infarction, both according to diabetes status. Panel C (facing page) shows transient-state life-table estimates of the cumulative incidence of spontaneous Q-wave myocardial infarction according to whether patients had undergone CABG at the time of the myocardial infarction. Patients who did not undergo CABG were treated only with percutaneous transluminal coronary angioplasty (PTCA).

with diabetes and 58 percent of those without diabetes had undergone CABG (Fig. 1A).

The incidence of a first spontaneous Q-wave myocardial infarction during follow-up was 4.8 percent at five years, and such infarctions occurred at a constant rate throughout this period. Patients with dia-

betes were 1.9 times as likely as those without diabetes to have a spontaneous Q-wave myocardial infarction ($P < 0.001$) (Fig. 1B).

The incidence of spontaneous Q-wave myocardial infarction was nearly identical among the patients who underwent CABG and those who did not (Fig.



IC). This was also true when the comparison was restricted to the patients with diabetes (data not shown). One hundred seventy-six patients had a total of 186 spontaneous Q-wave myocardial infarctions, 94 of which occurred in those who had undergone CABG (in 73 cases the procedure had been performed less than three years earlier, and in 46 cases less than one year earlier). Among the spontaneous Q-wave myocardial infarctions, 86 (46 percent) were silent.

Mortality at five years was 8 percent for the 2962 patients without diabetes and 20 percent for the 641 patients with diabetes ($P < 0.001$). The corresponding rates for the patients who underwent CABG were 7 percent and 18 percent, respectively; they were 8 and 25 percent for those who did not undergo CABG (Fig. 2A). The mortality rate for the 3263 patients who did not have a Q-wave myocardial infarction (91 percent of the total) was slightly lower than the overall rate (Fig. 2B). The estimated five-year mortality rate after spontaneous Q-wave myocardial infarction (Fig. 2C) varied little according to CABG status among the patients without diabetes (27 percent for those who underwent CABG and 30 percent for those who did not); however, the protection conferred by CABG was dramatic among the patients with diabetes: mortality was 17 percent among the patients who had a spontaneous Q-wave myocardial infarction and had undergone CABG, as compared with 80 percent among those who had a spontaneous Q-wave myocardial infarction but had not undergone CABG. For the patients with a spontaneous Q-wave myocardial infarction, the 17 percent mortality rate among those with diabetes who underwent CABG was not significantly different from the rates among those without diabetes.

To quantify the protection conferred by CABG in patients with spontaneous Q-wave myocardial infarction, as compared with the more moderate protection seen in patients who did not have spontaneous Q-wave myocardial infarction, we estimated the effect of CABG in terms of relative risks of death (Table 2) by means of a Cox regression model. These relative risks were used to compare mortality between specific groups of patients who underwent CABG and similar groups who did not. Adjustments were made for age (>65 years vs. ≤ 65 years), history with respect to congestive heart failure, history with respect to renal dysfunction, BARI study group (randomized group vs. registry group), and the presence or absence of significant disease of the proximal left anterior descending artery, all at base line.

Among the patients with diabetes, CABG conferred a considerable degree of protection in those with a spontaneous Q-wave myocardial infarction (relative risk of death, 0.09; $P < 0.001$) and a moderate degree of protection in those without a spontaneous Q-wave myocardial infarction (relative risk, 0.65; $P = 0.02$) (Table 2). Thus, among the patients with diabetes, the protective role of CABG was approximately seven times as great after spontaneous Q-wave myocardial infarction as in the absence of spontaneous Q-wave myocardial infarction.

Among the patients without diabetes, the estimated protective effect of CABG was smaller and was not significant (Table 2). Moreover, the reduction in mortality among the patients with diabetes who had a spontaneous Q-wave myocardial infarction, as compared with those who did not, was significantly different from the corresponding reduction among the patients without diabetes ($P = 0.04$) (Table 2).

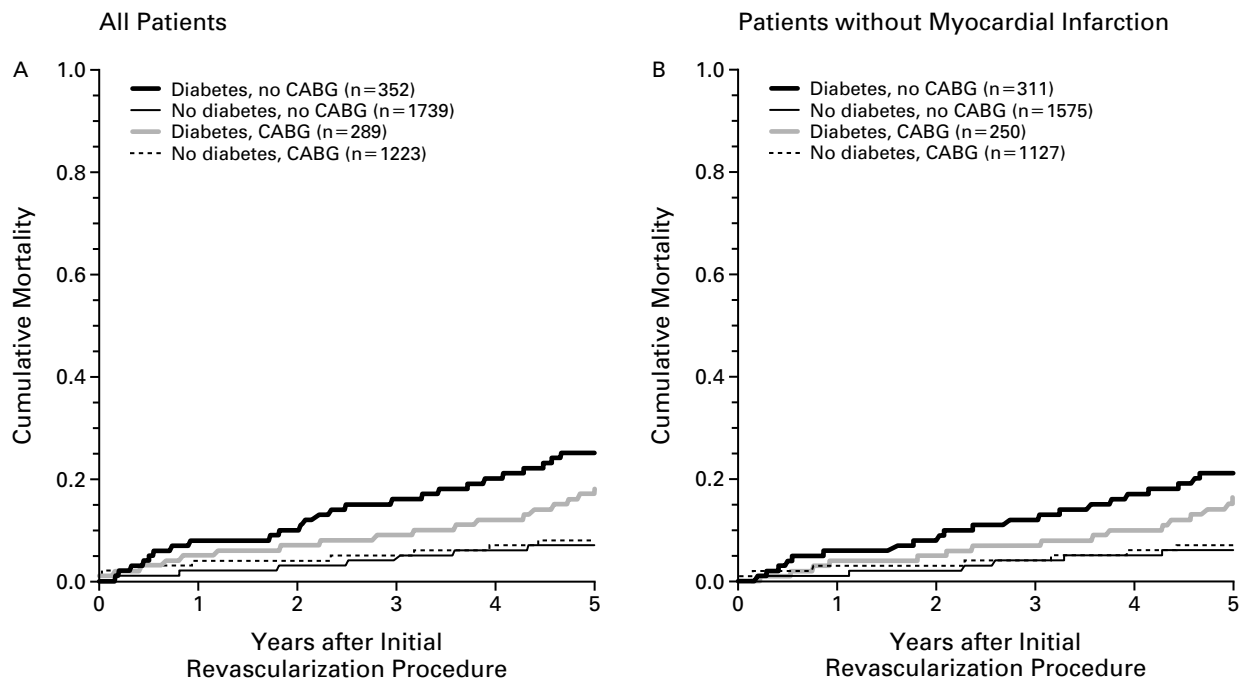
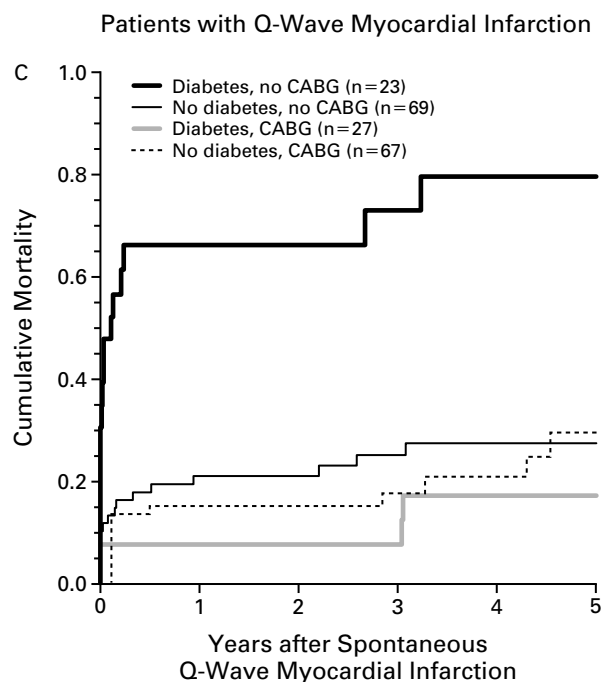


Figure 2. Mortality after the Initial Revascularization Procedure. Panel A shows transient-state life-table estimates of the cumulative mortality in all patients, and Panel B shows the cumulative mortality in patients without Q-wave myocardial infarction, both according to diabetes status and with respect to coronary-artery bypass grafting (CABG) at the time of death. Panel C shows Kaplan–Meier estimates of the cumulative mortality in patients with spontaneous Q-wave myocardial infarction according to diabetes status and CABG status (the numbers in parentheses refer to the 186 spontaneous Q-wave myocardial infarctions that occurred in 176 patients). Patients who did not undergo CABG were treated only with percutaneous transluminal coronary angioplasty.

Similar interactions were found when at least one internal-thoracic-artery graft was used, which occurred in 81 percent of the bypass procedures (single graft in 70 percent plus double graft in 11 percent). The protective effect of CABG involving this type of graft was consistently stronger than that of all types of CABG combined (i.e., the relative risk of death was lower), both among the patients with diabetes (relative risk of death after a spontaneous Q-wave myocardial infarction, 0.07; relative risk of death in the absence of a spontaneous Q-wave myocardial infarction, 0.54) and among those without diabetes (relative risk of death after a spontaneous Q-wave myocardial infarction, 0.49; relative risk of death in the absence of a spontaneous Q-wave myocardial infarction, 0.90). The long-term benefit associated with the use of internal-thoracic-artery grafts was not counteracted by higher rates of short-term complications, such as sternal-wound infections (data not shown). The relative survival advantage conferred by CABG



among the patients with diabetes was very similar regardless of whether the spontaneous Q-wave myocardial infarction was silent or symptomatic.

DISCUSSION

Our analysis identified two major ways in which CABG protected patients with diabetes. First, there

TABLE 2. PROTECTIVE EFFECT OF CABG, AS DETERMINED BY ADJUSTED RELATIVE RISKS OF DEATH.*

GROUP	RELATIVE RISK (95% CI) WITH CABG†	P VALUE	RATIO OF THE RELATIVE RISKS (95% CI)	P VALUE	RATIO OF THE RELATIVE RISKS (95% CI)	P VALUE
Diabetes						
Patients with spontaneous Q-wave myocardial infarction	0.09 (0.03–0.29)	<0.001	0.14 (0.04–0.48)	0.002	0.21 (0.05–0.89)	0.04
Patients without spontaneous Q-wave myocardial infarction	0.65 (0.45–0.94)	0.02				
No diabetes						
Patients with spontaneous Q-wave myocardial infarction	0.67 (0.34–1.34)	0.26	0.65 (0.32–1.32)	0.23		
Patients without spontaneous Q-wave myocardial infarction	1.04 (0.80–1.35)	0.77				

*Adjustments were made for the following base-line factors: age >65 years, history of renal dysfunction, history of congestive heart failure, Bypass Angioplasty Revascularization Investigation study group (randomized group vs. registry group), and presence of clinically significant proximal disease of the left anterior descending artery. CABG denotes coronary-artery bypass grafting, and CI confidence interval.

†The patients underwent either CABG or percutaneous transluminal coronary angioplasty (PTCA) as their initial revascularization procedure; some patients who initially underwent PTCA had CABG later.

was a strong protective effect of CABG with respect to survival for the relatively few patients with diabetes who had a spontaneous Q-wave myocardial infarction during follow-up. Second, CABG moderately reduced mortality among the majority of patients with diabetes who remained free of myocardial infarction during follow-up. Thus, the type of revascularization (CABG) and the presence of spontaneous Q-wave myocardial infarction interacted with one another in a manner that resulted in greater protection in patients with diabetes. Among the patients without diabetes the protective effect of CABG was substantially less (and was not significant), regardless of whether the patients had a myocardial infarction. In this study, we limited the definition of what constituted clinically diagnosed infarction to infarctions characterized by major Q waves, events that have previously been shown to be associated with particularly poor prognosis in patients with diabetes.¹⁹

In contrast to its protective effect with respect to survival, the type of revascularization had no influence on the incidence of Q-wave myocardial infarction during follow-up. This is similar to the results of earlier comparisons of CABG and medical treatment.^{4,20}

The use of single or double internal-thoracic-artery grafts enhanced the protective effects of CABG without increasing the incidence of sternal-wound infections, an adverse effect others have reported.²¹ Since internal-thoracic-artery grafts are more likely to remain patent than venous grafts,²² the increased protection conferred by internal-thoracic-artery grafts provides indirect evidence that the efficacy of CABG is due to improved perfusion supplied by the graft, which mitigates the potentially fatal effect of ischemia due to obstructed or reduced blood flow in patients with

diabetes. Also, this improved patency is particularly characteristic of the first few years after CABG, precisely the period during which most of the spontaneous myocardial infarctions in this study occurred.

The unequal protection afforded by the two types of coronary revascularization among the patients with diabetes, particularly during an acute ischemic episode, may be due in part to the different degree of myocardial jeopardy (defined as the proportion of the myocardium jeopardized by stenosis of 50 percent or more) after PTCA as compared with CABG. In the subgroup of 270 patients who were randomly assigned to treatment and who underwent angiography one year after initial revascularization,²³ the amount of jeopardized myocardium decreased substantially in both treatment groups; however, the patients who underwent PTCA had considerably more jeopardized myocardium at one year than the patients who underwent CABG (mean degree of myocardial jeopardy at base line and one year: 59.4 percent and 25.5 percent, respectively, for the patients who underwent PTCA, and 60.8 percent and 14.1 percent for the patients who underwent CABG).

Since patients with diabetes typically have more extensive and progressive disease than patients without diabetes, including disease in distal vessels, focal dilation with PTCA leaves a greater proportion of the myocardium ischemic than does CABG. Indeed, among the subgroup of randomized patients in our study, the difference in the proportion of jeopardized myocardium at one year between the patients with diabetes who underwent CABG and those who did not was larger than that between the patients without diabetes who underwent CABG and those who did not ($P=0.04$). Other studies have shown that coronary

collaterals are also less likely to form in patients with diabetes than in patients without diabetes.²⁴

Although a higher degree of myocardial jeopardy and reduced collateral formation would not affect the incidence of plaque rupture leading to the occurrence of coronary occlusion, they would affect the magnitude of ischemia after occlusion and hence contribute to the increased mortality rate among the patients with diabetes who did not undergo CABG, as compared with those who did, in our study. We cannot speculate about whether PTCA offers more protection than no revascularization in the event of spontaneous myocardial infarction but, rather, simply observe that PTCA offers less protection than does bypass surgery in patients with diabetes.

With the introduction of lytic and platelet-based therapy, outcomes in general after myocardial infarction have greatly improved in both patients with diabetes and those without.²⁵ However, since myocardial infarctions in our study were identified from routine electrocardiograms obtained at the time of clinical presentation or from death records, not all patients had the opportunity to be treated with these therapies. Specific data on the use of such treatments were not collected.

In the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction study, an infusion of insulin and glucose, followed by daily subcutaneous treatment with insulin, resulted in a 52 percent reduction in mortality within one year after myocardial infarction among patients with diabetes.^{26,27} This beneficial effect was attributed to improved metabolic control in the presence of an extreme increase in the level of catecholamines in blood and ischemic myocardium that is associated with sudden ischemic episodes. In the absence of insulin, such a rise stimulates rapid turnover of free fatty acids.

Although spontaneous Q-wave myocardial infarctions were more frequent in our study among the patients with diabetes than in those without diabetes, such infarctions were relatively rare. Thus, the protective effect of CABG for a patient with a myocardial infarction explained only about 50 percent of the overall reduction in mortality attributable to the procedure. The remaining benefit of CABG among the patients with diabetes was demonstrated by a constant reduction in mortality throughout follow-up, perhaps a result of the reduction in the degree of chronic ischemia.

Our report lacks information about factors specific to diabetes. We know very little about the duration and the severity of diabetes in the patients in this study, and we do not know how well the disease was controlled and with what measures. The glycometabolic state at the time of infarction is an important predictor of long-term outcome in patients with diabetes who have had an acute myocardial infarction.²⁸ Future studies of ischemic heart disease in patients

with diabetes should collect additional data that would allow assessment of pathophysiologic abnormalities and the methods by which they are corrected.

REFERENCES

1. The Bypass Angioplasty Revascularization Investigation (BARI) Investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. *N Engl J Med* 1996;335:217-25. [Erratum, *N Engl J Med* 1997;336:147.]
2. Influence of diabetes on 5-year mortality and morbidity in a randomized trial comparing CABG and PTCA in patients with multivessel disease: the Bypass Angioplasty Revascularization Investigation. *Circulation* 1997;96:1761-9.
3. King SB III, Kosinski AS, Guyton RA, Lembo NJ, Weintraub WS. Eight year mortality in the Emory Angioplasty vs. Surgery Trial (EAST). *J Am Coll Cardiol* (in press).
4. Peduzzi P, Detre K, Murphy ML, et al. Ten-year incidence of myocardial infarction and prognosis after infarction: Department of Veterans Affairs Cooperative Study of Coronary Artery Bypass Surgery. *Circulation* 1991;83:747-55.
5. Alderman EL. Late benefit of coronary surgery on mortality from myocardial infarction. *Circulation* 1991;83:1087-9.
6. Soler N, Burnett M, Pentecost BL, Fitzgerald M, Malins JM. Myocardial infarction in diabetics. *QJM* 1975;44:125-32.
7. Czyzk A, Krolewski AS, Szablowska S, Alot A, Kopczynski J. Clinical course of myocardial infarction among diabetic patients. *Diabetes Care* 1980;3:526-9.
8. Malmberg K, Rydén L. Myocardial infarction in patients with diabetes mellitus. *Eur Heart J* 1988;9:259-64.
9. Herlitz J, Malmberg K, Karlson BW, Rydén L, Hjalmarson Å. Mortality and morbidity during a five-year follow-up of diabetics with myocardial infarction. *Acta Med Scand* 1988;224:31-8.
10. Karlson BW, Herlitz J, Hjalmarson A. Prognosis of acute myocardial infarction in diabetic and non-diabetic patients. *Diabet Med* 1993;10:449-54.
11. Jacoby RM, Nesto RW. Acute myocardial infarction in the diabetic patient: pathophysiology, clinical course and prognosis. *J Am Coll Cardiol* 1992;20:736-44.
12. Protocol for the Bypass Angioplasty Revascularization Investigation. *Circulation* 1991;84:Suppl V:V-1-V-27.
13. Bourassa MG, Roubin GS, Detre KM, et al. Bypass Angioplasty Revascularization Investigation: patient screening, selection, and recruitment. *Am J Cardiol* 1995;75:3C-8C.
14. Chaitman BR, Zhou SH, Tamesis B, et al. Methodology of serial ECG classification using an adaptation of the NOVACODE for Q wave myocardial infarction in the Bypass Angioplasty Revascularization Investigation (BARI). *J Electrocardiol* 1996;29:265-77.
15. Kaplan EL, Meier P. Nonparametric estimation from incomplete observations. *J Am Stat Assoc* 1958;53:457-81.
16. Mantel N, Byar DP. Evaluation of response-time data involving transient states: an illustration using heart-transplant data. *J Am Stat Assoc* 1974;69:81-6.
17. Cox DR. Regression models and life-tables. *J R Stat Soc [B]* 1972;34:187-220.
18. Cox DR, Oakes D. Analysis of survival data. London: Chapman & Hall, 1984:112-39.
19. Singer DE, Moulton AW, Nathan DM. Diabetic myocardial infarction: interaction of diabetes with other preinfarction risk factors. *Diabetes* 1989;38:350-7.
20. Davis KB, Alderman EL, Kosinski AS, Passamani E, Kennedy JW. Early mortality of acute myocardial infarction in patients with and without prior coronary revascularization surgery: a Coronary Artery Surgery Study Registry study. *Circulation* 1992;85:2100-9.
21. Loop FD, Lytle BW, Cosgrove DM, et al. J. Maxwell Chamberlain Memorial Paper: sternal wound complications after isolated coronary artery bypass grafting: early and late mortality, morbidity, and cost of care. *Ann Thorac Surg* 1990;49:179-87.
22. Loop FD, Lytle BW, Cosgrove DM, et al. Influence of the internal-mammary-artery graft on 10-year survival and other cardiac events. *N Engl J Med* 1986;314:1-6.
23. Whitlow PL, Dimas AP, Bashore TM, et al. Relationship of extent of revascularization with angina at one year in the Bypass Angioplasty Revascularization Investigation (BARI). *J Am Coll Cardiol* 1999;34:1750-9.
24. Abaci A, Oguzhan A, Kahraman S, et al. Effect of diabetes mellitus on formation of coronary collateral vessels. *Circulation* 1999;99:2239-42.
25. Mak KH, Moliterno DJ, Granger CB, et al. Influence of diabetes mel-

litus on clinical outcome in the thrombolytic era of acute myocardial infarction. *J Am Coll Cardiol* 1997;30:171-9.

26. Malmberg K, Rydén L, Efendic S, et al. Randomized trial of insulin-glucose infusion followed by subcutaneous insulin treatment in diabetic patients with acute myocardial infarction (DIGAMI study): effects on mortality at 1 year. *J Am Coll Cardiol* 1995;26:57-65.

27. Malmberg K. Prospective randomised study of intensive insulin treat-

ment on long term survival after acute myocardial infarction in patients with diabetes mellitus. *BMJ* 1997;314:1512-5.

28. Malmberg K, Norhammar A, Wedel H, Rydén L. Glycometabolic state at admission: important risk marker of mortality in conventionally treated patients with diabetes mellitus and acute myocardial infarction: long-term results from the Diabetes and Insulin-Glucose Infusion in Acute Myocardial Infarction (DIGAMI) study. *Circulation* 1999;99:2626-32.

CORRECTION

The Effect of Previous Coronary-Artery Bypass Surgery on the Prognosis of Patients with Diabetes Who Have Acute Myocardial Infarction

The Effect of Previous Coronary-Artery Bypass Surgery on the Prognosis of Patients with Diabetes Who Have Acute Myocardial Infarction . On page 993, the sentence that begins on line 12 of the left-hand column should have read, "The corresponding rates for the patients who underwent CABG were 8 percent and 18 percent, respectively; they were 7 and 25 percent for those who did not undergo CABG (Figure 2A)," not "The corresponding rates for the patients who underwent CABG were 7 percent and 18 percent, respectively; they were 8 and 25 percent for those who did not undergo CABG (Figure 2A)," as printed.