Journal of the American College of Cardiology
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Published by Elsevier Science Inc.

Vol. 35, No. 5, 2000
ISSN 0735-1097/00/$20.00
PII S0735-1097(00)00546-5

Eight-Year Mortality in the Emory Angioplasty Versus Surgery Trial (EAST)

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OBJECTIVES To evaluate the long-term outcome of patients randomized to coronary bypass surgery or coronary angioplasty.

BACKGROUND The Emory Angioplasty versus Surgery Trial (EAST) is a single center randomized comparison of a strategy of initial coronary angioplasty (n = 198) or coronary bypass surgery (n = 194) for patients with multivessel coronary artery disease. The primary end point (death, myocardial infarction or a large ischemic defect at 3 years) was not different, and repeat revascularization was significantly greater in the angioplasty group. Subsequently, the National Heart, Lung and Blood Institute supported a five-year extension of the trial.

METHODS After the three year anniversary visit, annual questionnaires, telephone contact and examination of medical records were accomplished until death or the eight year anniversary in 100% of the patients surviving at 3 years.

RESULTS Survival at 8 years is 79.3% in the angioplasty group and 82.7% in the surgical group (p = 0.40). Patients with proximal left anterior descending stenosis and those with diabetes tended to have better late survival with surgical intervention although not reaching statistical significance. After the first 3 years, repeat interventions remained relatively equal for both treatment groups.

CONCLUSIONS Long-term survival is not significantly different between angioplasty and surgery, and late (three to eight year) revascularization procedures were infrequent. Patients without treated diabetes had similar survival in both groups. (J Am Coll Cardiol 2000;35:1116–21) © 2000 by the American College of Cardiology

The Emory Angioplasty versus Surgery Trial (EAST) was the first trial supported by the National Heart, Lung and Blood Institute (NHLBI) to compare the outcomes of the strategy of performing angioplasty (n = 198) or surgery (n = 194) in patients with multivessel coronary artery disease (CAD) (1). Enrollment began in June 1987 and ended in April 1990. Baseline characteristics reflected multivessel patients who could undergo either procedure (Table 1). The primary end point was the composite of death, Q wave myocardial infarction (MI) occurring over a three-year follow-up or a major ischemic thallium defect at the three-year follow-up visit. Secondary end points included the components of the composite end point, the requirement for repeat interventional procedures and the economic and quality of life impact. Angiographic evaluation was also performed at one year and three years to assess the degree of revascularization (2).

See page 1130

The three-year primary end point was reached by 27.3% of the surgery patients and 28.8% of the angioplasty patients (3). Death, which occurred in 6.2% of the surgery group and 7.1% of the angioplasty group, was also not different. Several other studies evaluating the outcomes of surgery or angioplasty also showed no significant differences in survival (4–8). The major difference in all these studies, including EAST, was the marked excess utilization of repeat revascularization procedures in the angioplasty groups.

Because long-term follow-up may show further differences based on treatment selection, an extended five-year follow-up was proposed and subsequently supported by the NHLBI. Although the extended observations were not designed to evaluate the original composite end point, and the power was not adequate to evaluate mortality differences, it was important to track this population carefully to understand possible trends that could strengthen larger

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Manuscript received April 22, 1999; revised manuscript received September 20, 1999, accepted December 17, 1999.

Abbreviations and Acronyms

BARI = Bypass Angioplasty Revascularization Investigation
CAD = coronary artery disease
EAST = Emory Angioplasty versus Surgery Trial
MI = myocardial infarction
NHLBI = National Heart, Lung and Blood Institute
PTCA = percutaneous transluminal coronary angioplasty

long-term randomized trials. This report constitutes the completed eight-year follow-up of all patients randomized in EAST.

METHODS

The Emory Angioplasty versus Surgery Trial, a single center study, was composed of patients referred for revascularization at Emory University Hospital, Crawford W. Long Hospital and the Atlanta VA Hospital. Eligibility requirements were patients of any age with multivessel CAD who had not undergone prior angioplasty or surgery. Excluded were those patients with left main disease, multiple chronic total occlusions, old chronic occlusions (more than eight weeks duration) of bypassable vessels serving viable myocardium and an ejection fraction of 25% or less. Additionally, patients judged to have insignificant myocardium at risk to warrant surgery, those with MI within five days, and those with other illnesses threatening survival were excluded. Finally, patients judged to be unsafe for performance of surgery by the surgical consultant or judged to be unsafe for angioplasty by the angioplasty operator were excluded.

Table 1. Baseline Demographic and Clinical Characteristics of the Randomized Patients

	CABG	PTCA
Characteristic	(n = 194)	(n = 198)
Age (yr)	61.4 ± 10.0	61.8 ± 10.1
Male gender	141 (72.7)	148 (74.7)
White	183 (94.3)	184 (92.9)
No. of diseased vessels		
Two	117 (60.3)	119 (60.1)
Three	77 (39.7)	79 (39.9)
Proximal LAD stenosis ≥50%	143 (73.7)	140 (70.7)
Number of lesions per patient	3.4 ± 1.4	3.4 ± 1.2
Ejection fraction (%)	62.0 ± 11.8	60.8 ± 11.6
Prior myocardial infarction	79 (40.7)	81 (40.9)
Congestive heart failure	8 (4.1)	5 (2.5)
Angina		
CCS class III and IV	155 (7.9)	147 (74.2)
Diabetes mellitus	41 (21.2)	49 (24.7)
Hypertension	100 (51.5)	106 (53.5)
Total cholesterol (mg/dl)	224.1 ± 46.7	218.0 ± 46.5

Plus-minus values are means ± SD; all other values are numbers of patients, with percentages given in parentheses.
CCS = Canadian Cardiovascular Society; LAD = left anterior descending artery.

Of 842 patients eligible for the trial, 392 (198 assigned to angioplasty and 194 to surgery) volunteered to be randomized. Randomization was performed separately for the patients with two-vessel disease and those with three-vessel disease. Follow-up was performed every six months for three years, and a stress thallium study and coronary arteriogram were performed at one year and three years. After three years, follow-up of vital status, subsequent hospitalizations and procedures was performed annually from year 4 through year 8 by telephone contact with the patient or family members. When hospitalizations were identified, the hospital records were requested.

The primary focus of the extended follow-up is all-cause mortality and requirement for repeat revascularization procedures. Death was also classified as to cause, and these were divided into cardiac and noncardiac according to the predefined classification scheme (1). Because routine electrocardiograms were not performed at Emory University after the three-year follow-up visit and adjudication of Q wave development was not performed after that point, no accurate analysis of Q wave MI can be made over the extended follow-up period.

Definitions. The angiographic definitions in EAST have been previously reported (1,3). Two-vessel disease refers to patients with obstruction in two of the three major coronary systems; three-vessel disease refers to involvement of all three systems. Proximal left anterior descending disease refers to lesions in the proximal one third of that vessel. Left ventricular ejection fraction was determined angiographically by the area length method. Diabetes mellitus was reported for patients who were diagnosed and were on therapy with insulin or oral hypoglycemic agents at the time of randomization.

Statistical methods. Data were analyzed according to the intention-to-treat principle. Unadjusted Kaplan-Meier survival curves are presented with p values calculated according to the log-rank test (9). All tests are two-tailed, and a p value ≤ 0.05 was considered to indicate statistical significance. The study was not powered to detect a difference in survival at three years. Taking the percutaneous transluminal coronary angioplasty (PTCA) group as the reference survival value (79.3%), one would require 7,192 patients to detect an eight-year mortality absolute difference of 3% between the groups (hazard ratio 0.84) with 90% power and alpha = 0.05, two-tailed (10). To detect a 5% difference (hazard ratio 0.74) would require 2,466 patients. With the available number of patients (n = 392), one would have 78% power to detect hazard ratio of 0.5 (absolute difference in mortality of 9.8%).

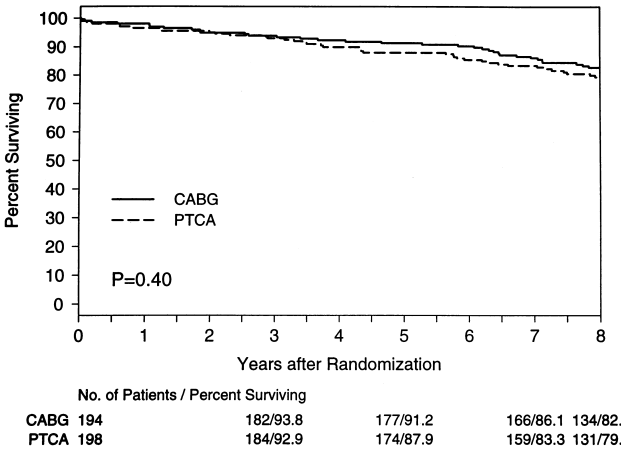

Figure 1. Survival of all EAST patients after initial treatment with CABG or PTCA. The number of patients at risk and the estimated probability of survival at 3, 5, 7 and 8 years are shown below the figure. CABG = coronary artery bypass grafting; EAST = Emory Angioplasty versus Surgery Trial; PTCA = percutaneous transluminal coronary angioplasty.

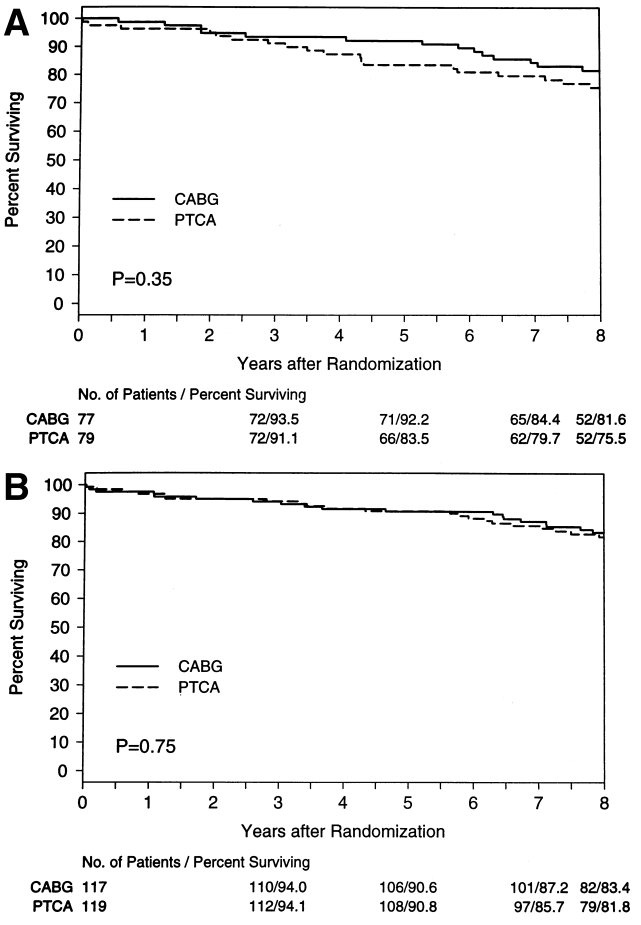

Figure 2. Survival of patients with three-vessel coronary disease **(Panel A)** and patients with two-vessel coronary disease **(Panel B)**. The number of patients at risk and the estimated probability of survival at 3, 5, 7 and 8 years are shown below the figure. CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

RESULTS

Patients were followed between eight and 10.5 years. All 392 patients were followed until the eight-year anniversary point or until death for a 100% follow-up rate. Although there was almost identical survival at the three-year end point (93.8% surgery vs. 92.9% angioplasty), there has been a slight divergence of the survival curve since that time. At eight years the surgery survival is 82.7% and the angioplasty survival is 79.3%, and this does not reach statistical significance ($p = 0.40$) (Fig. 1).

Because of the concern that patients with more diffuse disease might have better outcomes with surgery, the patients were randomized according to the presence of three-vessel disease (40% of the patients) or two-vessel disease (60% of the patients). At three years neither the three-vessel disease patients nor the two-vessel disease patients showed better survival by treatment assignment (three-vessel: surgery 93.5%, angioplasty 91.1%; two-vessel: surgery 94.0%, angioplasty 94.1%). By eight years there was slight, but not significant, separation of the curves in favor of surgery for three-vessel disease (three-vessel surgery 81.6%, angioplasty 75.5%, $p = 0.35$) but not for two-vessel disease (two-vessel surgery 83.4%, angioplasty 81.8%, $p = 0.75$) (Fig. 2).

Patients with proximal left anterior descending stenosis had little difference in survival at three years, and the curves diverged slightly, but not significantly, for this cohort over the remaining follow-up (eight-year surgical survival 85.6%, angioplasty 79.6%, $p = 0.16$) (Fig. 3).

Because diabetic patients in the Bypass Angioplasty Revascularization Investigation (BARI) showed a significant survival advantage in the surgery group, these patients were also examined in EAST. There were 59 treated diabetic patients in EAST (30 surgery, 29 angioplasty). At three years the survival was similar (surgery 90%, angioplasty 93.1%), and this was also similar to the patients without treated diabetes. In the extended follow-up this has changed. After five years the curves began to diverge, and by eight years, even though they did not reach statistical significance, they favored surgery in this group (surgical survival 75.5%, angioplasty 60.1%, $p = 0.23$) (Fig. 4A). Likewise, the angioplasty patients with diabetes had a worse survival than the nondiabetic patients by eight years (nondiabetic 82.6%, diabetic 60.1%, $p = 0.02$) (Fig. 4B). Similar to the BARI five-year follow-up of patients without treated diabetes (11), this follow-up of EAST showed no survival advantage for either treatment assignment for the 333 nondiabetic patients at eight years (surgery 84%, angioplasty 82.6%, $p = 0.71$) (Fig. 4C).

Comparisons were made for all other baseline variables including left ventricular function, age, gender, anginal status, hypertension, cigarette smoking and baseline choles-

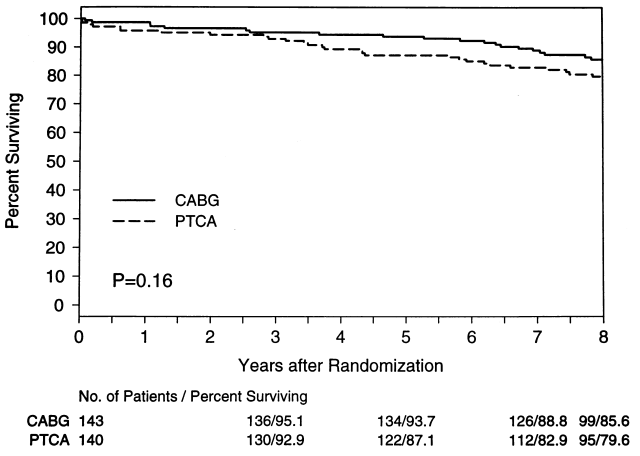

Figure 3. Survival of patients with proximal left anterior descending stenosis. The number of patients at risk and the estimated probability of survival at 3, 5, 7 and 8 years are shown below the figure. CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

terol values, and no survival differences by treatment assignment were seen. Freedom from cardiac death was not different for the entire cohort (surgery 92.3%, angioplasty 90.7%) at eight years (Fig. 5A). Cardiac survival among the patients with three-vessel disease was 94.7% in the surgery group and 87.7% in the angioplasty group ($p = 0.17$) (Fig. 5B), consistent with the all-cause mortality. Overall, approximately one half of the deaths in EAST were classified as noncardiac.

Further revascularization. After the initial procedure, additional revascularization procedures were performed much more commonly in the angioplasty randomized patients. The first additional procedure occurred primarily in the first three years. During the extended follow-up, the curves representing the percent of patients having additional angioplasty or surgery remain parallel for the treatment assignment groups. The surgery patients had very few surgical procedures in follow-up, and after three years the percent of angioplasty patients having surgery was also relatively low. At eight years 2.4% of the surgery patients had had a second operation and 29.3% of the angioplasty patients had undergone surgery ($p < 0.001$) (Fig. 6A). The use of angioplasty in the follow-up period also favored surgery patients, but this was an early effect, and after three years the curves of the percent of patients requiring angioplasty remained parallel to eight years. An additional 11.3% of the surgery patients had first angioplasty between years 3 and 8, and an additional 7.5% of the angioplasty patients had first subsequent angioplasty between years 3 and 8 (Fig. 6B). The curves of the percent of patients having either angioplasty or surgery in follow-up also remained parallel after the three-year mark. For the surgery group, the increase from year 3 to year 8 was 12.7%, while the percent of angioplasty patients having their first subsequent revascularization procedure

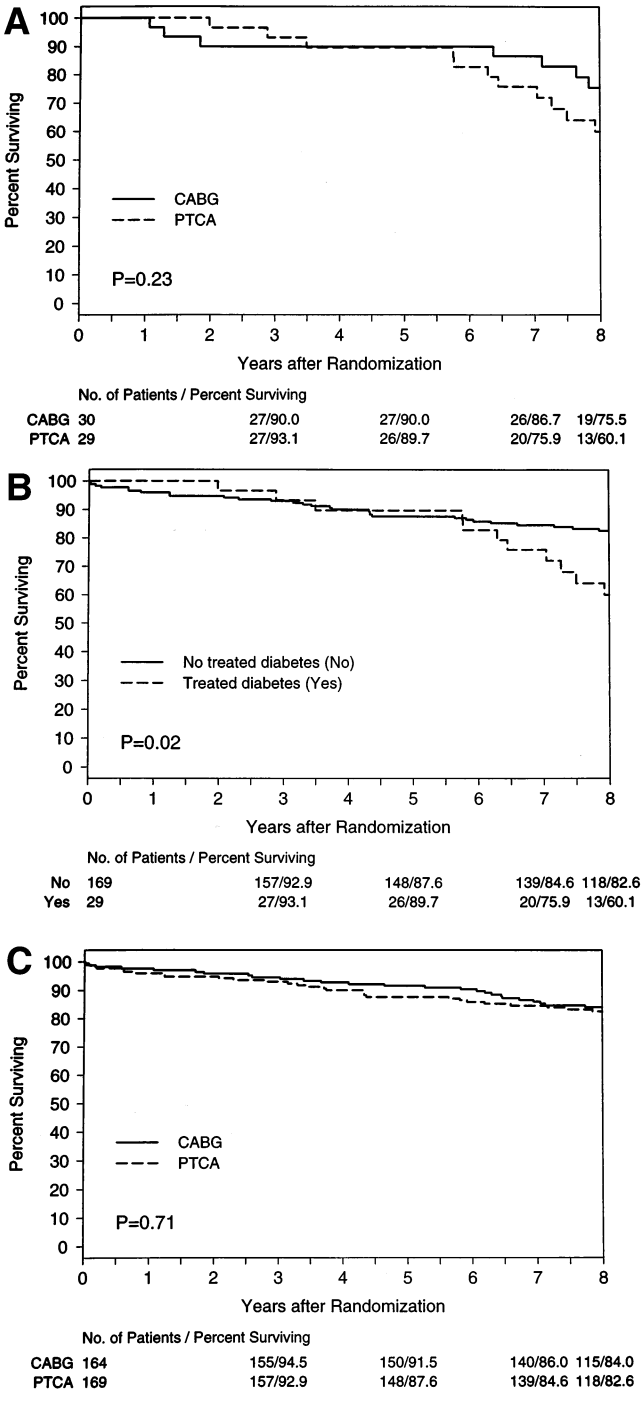

Figure 4. Survival of treated diabetic patients **(Panel A)**, patients with initial PTCA treatment **(Panel B)** and patients without treated diabetes **(Panel C)**. The number of patients at risk and the estimated probability of survival at 3, 5, 7 and 8 years are shown below the figure. CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

increased during the same period by 8.6%. However, due to the early excess of repeat revascularization in the angioplasty group, by eight years 26.5% of the surgery patients had had an additional procedure compared with 65.3% of the angio-

JACC Vol. 35, No. 5, 2000
April 2000:1116–21

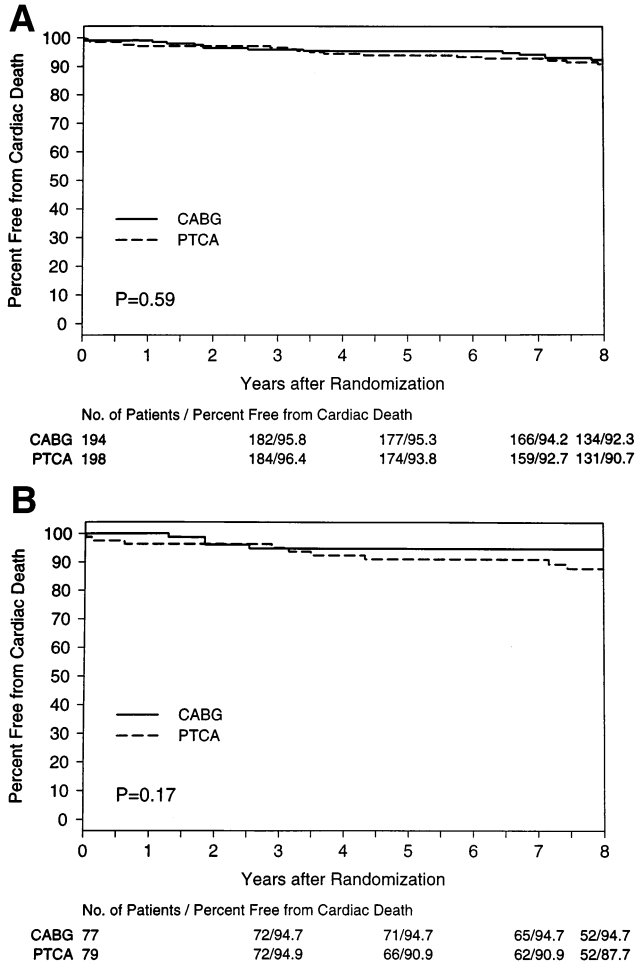

Figure 5. Percent of patients free from cardiac death for all EAST patients **(Panel A)** and for patients with three-vessel coronary disease **(Panel B)**. The number of patients at risk and the estimated probability of freedom from cardiac death at 3, 5, 7 and 8 years are shown below the figure. CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

plasty patients ($p < 0.001$) (Fig. 6C). Because of restenosis, a second procedure is frequently contemplated. Of the angioplasty randomized patients, 55.6% had either a single index procedure (36.4%) or only one additional angioplasty (19.2%).

Detailed cost analysis of EAST during the first three years has been published previously (12). Repeat procedures, however, may be a surrogate for late cost. After the initial procedure, the total number of subsequent surgeries in the surgical group was four and in the angioplasty group 59. The total number of subsequent angioplasties was 72 in the surgery group and 181 in the angioplasty group.

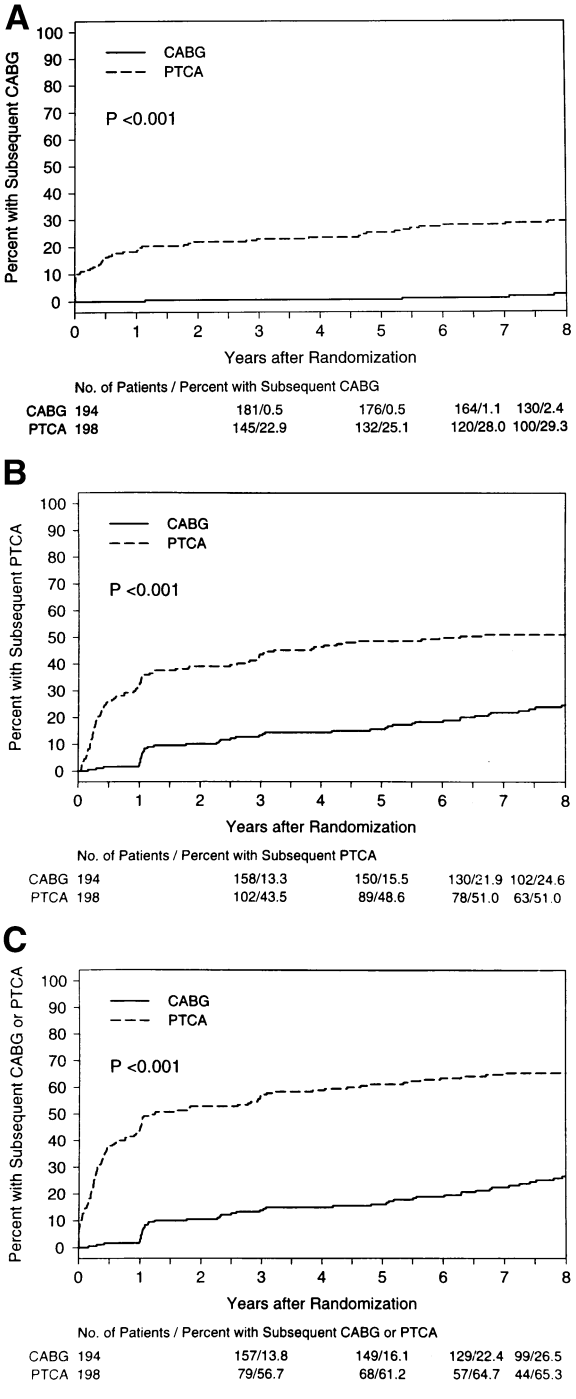

Figure 6. Percent of all EAST patients with subsequent PTCA **(Panel A)**, with subsequent CABG **(Panel B)** and with subsequent CABG or PTCA **(Panel C)** after the initial revascularization procedure. The number of patients at risk and the estimated probability of the first subsequent procedure at 3, 5, 7 and 8 years are shown below the figure. CABG = coronary artery bypass grafting; PTCA = percutaneous transluminal coronary angioplasty.

DISCUSSION

Previous reports from EAST and other studies have shown similar survival for multivessel patients treated with angioplasty or surgery. This long-term follow-up provided additional insight into survival and the percent of patients who subsequently require an additional revascularization procedure. In this single center study, almost 50% of eligible patients could be randomized, and 100% follow-up has been

completed at eight years. The modest size of the study prevented definitive conclusions regarding survival differences, but the trends may be predictive of larger observations. The survival differences at five years closely approximate those found in BARI for the entire cohort and for those without diabetes. Although no difference in the diabetic population was seen at three years, the eight-year follow-up was in the direction of the better late survival in the surgery group as seen in BARI.

In addition, the clinical impression that patients with more diffuse disease and those with proximal left anterior descending disease (almost all of whom received internal mammary artery grafts in the surgical group) may have better outcomes with surgery was not established by this study. There was a trend toward better survival with surgery for the patients with proximal left anterior descending coronary artery lesions ($p = 0.16$).

Because of the structure of this trial, which required a one- and three-year angiographic follow-up, the number of repeat procedures was probably artificially elevated compared with what it would have been without angiography. Note the bumps on the procedure curves at 1 and 3 years (Fig. 6 A–C). Comparison to the EAST registry, which did not show this clustering of repeat procedures, confirms this impression (13). These repeat procedures, influenced by angiography, were almost equally present in both groups, and it remains that repeat procedures are markedly excessive in the angioplasty group. This effect was driven primarily by restenosis after angioplasty producing the early divergence of the curves within the first year (Fig. 6 A–C). It is interesting to note that over the five years since the primary study was completed, the percent of patients requiring a first additional procedure actually favors angioplasty. This was not unexpected since more surgical patients are eligible for their first repeat procedure in the late follow-up.

The continuing occurrence of late events in both groups speaks to the need to evaluate the impact of aggressive secondary prevention measures in these revascularized patients. Such measures were not consistently applied in EAST or the other angioplasty versus surgery trials. Two studies, Clinical Outcome Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) and BARI II, which will utilize optimal risk modification, may improve on the late results in such patients. Ongoing studies comparing angioplasty using stents to coronary bypass surgery (Artery Revascularization Therapy Study and Stent or Surgery) will likely significantly reduce the number of repeat procedures in the angioplasty groups.

Study limitations. The study was not powered to detect a difference in survival. It is possible that long-term follow-up could show additional differences between the groups. Due to the aging of the population (average age 70 at the eight-year follow-up), about one half of the patients who have died have had noncardiac causes of death, further weakening the power to analyze cardiac survival differences.

Conclusions. This long-term follow-up of EAST continues to show no significant survival difference based on treatment with surgery or angioplasty. Trends toward improved survival with surgery in patients with diabetes and proximal left anterior descending coronary disease should be compared with other studies with adequate long-term follow-up. Patients without treated diabetes have almost identical survival at eight years. Whether the excess repeat revascularization procedures and late vascular events can be reduced with newer techniques such as stenting and secondary prevention awaits the outcome of subsequent trials, which are underway.

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