

ORIGINAL ARTICLE

# Long-Term Outcomes of Coronary-Artery Bypass Grafting versus Stent Implantation

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## ABSTRACT

### BACKGROUND

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Several studies have compared outcomes for coronary-artery bypass grafting (CABG) and percutaneous coronary intervention (PCI), but most were done before the availability of stenting, which has revolutionized the latter approach.

### METHODS

We used New York's cardiac registries to identify 37,212 patients with multivessel disease who underwent CABG and 22,102 patients with multivessel disease who underwent PCI from January 1, 1997, to December 31, 2000. We determined the rates of death and subsequent revascularization within three years after the procedure in various groups of patients according to the number of diseased vessels and the presence or absence of involvement of the left anterior descending coronary artery. The rates of adverse outcomes were adjusted by means of proportional-hazards methods to account for differences in patients' severity of illness before revascularization.

### RESULTS

Risk-adjusted survival rates were significantly higher among patients who underwent CABG than among those who received a stent in all of the anatomical subgroups studied. For example, the adjusted hazard ratio for the long-term risk of death after CABG relative to stent implantation was 0.64 (95 percent confidence interval, 0.56 to 0.74) for patients with three-vessel disease with involvement of the proximal left anterior descending coronary artery and 0.76 (95 percent confidence interval, 0.60 to 0.96) for patients with two-vessel disease with involvement of the nonproximal left anterior descending coronary artery. Also, the three-year rates of revascularization were considerably higher in the stenting group than in the CABG group (7.8 percent vs. 0.3 percent for subsequent CABG and 27.3 percent vs. 4.6 percent for subsequent PCI).

### CONCLUSIONS

For patients with two or more diseased coronary arteries, CABG is associated with higher adjusted rates of long-term survival than stenting.

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**C**ORONARY-ARTERY BYPASS GRAFTING (CABG) and percutaneous coronary intervention (PCI) have long been the definitive aggressive options for treating patients with coronary artery disease. In the past few years, several randomized clinical trials<sup>1-15</sup> and observational studies<sup>16-20</sup> have examined the relative long-term benefits of these interventions. However, with few exceptions, these studies were conducted before the availability of stenting.<sup>8,11,13,15</sup> We used observational data from a very large registry to compare short-term and long-term outcomes among patients with multivessel disease who underwent CABG or stenting in New York State hospitals.

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## METHODS

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### DATABASES

The two main databases used in the study were New York's two cardiac registries, the Cardiac Surgery Reporting System (CSRS) and the Percutaneous Coronary Intervention Reporting System (PCIRS). These databases include information about numerous risk factors; admission, surgery, and discharge dates; and discharge status for all patients undergoing CABG and PCI in nonfederal hospitals in New York State.

To ensure that these registries are complete, data are matched to New York State's acute care hospital-discharge data set, the Statewide Planning and Research Cooperative System (SPARCS), which is used for reimbursement. Also, reporting of in-hospital deaths is matched against SPARCS data, and hospitals are asked to resolve discrepancies. Accuracy of risk-factor reporting is ascertained by having the Department of Health's utilization-review agent audit hospitals' medical records. To identify deaths that did not occur in hospitals, we used patients' Social Security numbers to link New York's Vital Statistics Death File to the two registries. The institutional review board of the University of Albany approved the use of these data for this study.

### STUDY GROUP AND END POINTS

The study included New York residents with multivessel coronary artery disease (defined as stenosis of at least 70 percent in at least two of the three main coronary arteries) who underwent isolated CABG or stent implantation for at least one lesion between January 1, 1997, and December 31, 2000, in New York. Patients who had previously undergone revascularization, those with disease of the left main cor-

onary artery (defined as stenosis of more than 50 percent), and those who had an acute myocardial infarction within 24 hours before revascularization were excluded. The study was limited to New York residents because the New York Vital Statistics Death File applies only to residents of the state. The study group comprised 37,212 patients who underwent CABG at the 34 hospitals in the state in which CABG was performed and 22,102 patients who underwent stenting at the 35 hospitals in the state in which PCI was performed.

End points included death and death or revascularization (CABG or PCI) at any time before December 31, 2000. Subsequent revascularizations were identified by matching patients' Social Security numbers with CABG and PCI procedures listed in CSRS and PCIRS.

### STATISTICAL ANALYSIS

The primary purpose of the data analyses was to determine whether long-term mortality differed significantly between patients undergoing CABG and those undergoing PCI, after controlling for differences in patients' preprocedural risk. A secondary purpose was to determine whether there were treatment-related differences in long-term mortality among patients with diabetes, patients with compromised ventricular function (defined by a left ventricular ejection fraction of less than 40 percent), and patients without compromised ventricular function. We planned to accomplish this by first identifying factors that were associated with a risk of death in univariate analyses and then using a multivariate (Cox proportional-hazards) model that controlled for significant risk factors while testing for significant differences in long-term mortality between patients undergoing CABG and those undergoing PCI. Because the number of diseased vessels, the presence or absence of involvement of the left anterior descending coronary (LAD) artery, and the presence or absence of disease in the proximal portion of the LAD artery are major factors in the determination of which procedure to perform, the analyses were performed separately for each of five anatomical groups among patients with two- or three-vessel disease (patients with single-vessel disease were omitted because the vast majority who undergo revascularization do so by means of PCI).

We compared the prevalences of potential risk factors for each procedure using chi-square and Fisher's exact (for binary risk factors) tests. Factors included the number of diseased vessels, the pa-

Characteristic	Stenting (N=22,102)	CABG (N=37,212)	P Value
<b>Demographic characteristics</b>			
Age (% of patients)			<0.001
<50 yr	11.7	7.3	
50–59 yr	22.3	19.7	
60–69 yr	28.0	30.7	
70–79 yr	27.3	33.9	
≥80 yr	10.8	8.5	
Median age (yr)	65	67	<0.001
Sex (% of patients)			<0.001
Male	68.6	70.9	
Female	31.4	29.1	
Hispanic ethnicity (% of patients)	6.3	5.6	0.001
Race (% of patients)			<0.001
White	87.0	89.2	
Black	6.4	5.5	
Other	6.7	5.3	
<b>Coexisting conditions or other risk factors</b>			
Ejection fraction (% of patients)			<0.001
<20%	0.7	1.8	
20–29%	3.1	7.3	
30–39%	8.0	14.9	
≥40%	81.5	74.1	
Data missing	6.8	2.0	

tient's age and sex, the presence or absence of a variety of coexisting conditions, and measures of the patient's hemodynamic state and ventricular function. Kaplan–Meier estimates were used to plot the percentage of patients in each group who underwent subsequent revascularization; data on patients who died before subsequent revascularization were censored.

Each patient was placed in one of five anatomical groups according to whether two or three vessels were diseased, whether there was clinically significant disease in the LAD artery, and if there was, whether it was in the proximal region. A backward stepwise Cox model was used to identify risk factors in each subgroup that were significantly related to long-term mortality. A P value of less than 0.05 was used to indicate statistical significance. The type of revascularization (CABG vs. PCI) was then added as an independent binary variable, with “1” denoting CABG.

For each of the five groups of patients, point estimates and confidence intervals were calculated for

hazard ratios.<sup>21</sup> Also, unadjusted survival curves were generated for each intervention for each anatomical group with the use of Kaplan–Meier estimates, and adjusted survival curves were generated with the use of the Cox model in conjunction with methods described by Ghali et al.<sup>22</sup> The log-rank test was used to identify significant differences in unadjusted survival rates. As prespecified in the protocol, survival rates in all anatomical subgroups were evaluated to identify differences in the subgroups of patients with diabetes, patients with compromised ventricular function, and those without such compromise.

Selection bias was examined with the use of a propensity model.<sup>23,24</sup> Covariates that were considered for inclusion in the models included all variables presented in Table 1. Variables that were significant predictors of the type of revascularization were identified by fitting a logistic-regression model with a binary dependent variable representing CABG. For each anatomical group, the propensity score was subdivided into quintiles and hazard ra-

Table 1. (Continued.)			
Characteristic	Stenting (N=22,102)	CABG (N=37,212)	P Value
Median ejection fraction (%)	53	50	<0.001
Previous myocardial infarction	27.4	25.0	<0.001
1–7 days	22.8	16.3	<0.001
≥8 days	4.6	8.7	
Stroke	4.4	6.9	<0.001
Carotid or cerebrovascular disease	3.5	14.0	<0.001
Aortoiliac disease	2.9	4.6	<0.001
Femoral or popliteal disease	3.6	8.7	<0.001
Hemodynamic instability	0.5	0.7	0.001
Shock	0.1	0.2	0.16
Cardiopulmonary resuscitation	0.1	0	0.01
Electrocardiographic evidence of left ventricular hypertrophy	7.4	11.5	<0.001
Congestive heart failure	11.4	19.5	<0.001
Current admission	7.0	12.3	
Before this admission	4.4	7.2	
Malignant ventricular arrhythmia	1.3	1.8	<0.001
Chronic obstructive pulmonary disease	5.9	16.4	<0.001
Diabetes	25.3	33.2	<0.001
Renal failure	2.2	3.4	<0.001
Requiring dialysis	1.0	1.4	
Creatinine >2.5 mg/dl	1.2	2.0	
No. of diseased vessels (% of patients)†			<0.001
2	80.4	30.7	
3	19.6	69.3	

\* Because of rounding, percentages may not total 100. To convert values for creatinine to micromoles per liter, multiply by 88.4.

† Diseased vessels were defined by the presence of stenosis of at least 70 percent.

tios were compared across quintiles. All analyses were conducted with the use of SAS software (version 8.2), and all reported P values are two-sided.

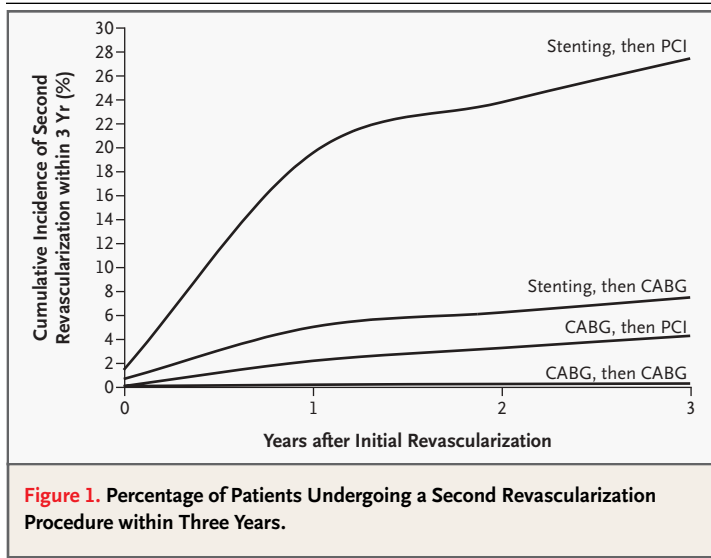
## RESULTS

The median follow-up was 706.0 days in the CABG group (interquartile range, 328 to 1089) and 585.0 days in the stenting group (interquartile range, 265 to 948). Patients who underwent CABG were significantly older than patients who received stents, although more patients in the latter group were 80 years of age or older. Also, patients who underwent CABG were more likely to be white men and less likely to be Hispanic. Patients who underwent CABG had significantly lower median ejection fractions and were less likely than patients who received stents

to have had a myocardial infarction in the week before the procedure. Patients who underwent CABG also had a significantly higher prevalence of numerous coexisting conditions and were significantly more likely to have three-vessel disease (Table 1).

In the stenting group, 7.8 percent underwent subsequent CABG and 27.3 percent underwent repeated PCI in the three years after the initial procedure. Also, 0.3 percent of the CABG group underwent CABG and 4.6 percent underwent PCI in the ensuing three-year period (Fig. 1). The overall rates of revascularization were significantly lower in the CABG group than in the stenting group ( $P<0.001$ ).

The observed (unadjusted) in-hospital mortality rate among the patients in the CABG group was significantly higher than the rate among patients who received a stent (1.75 percent [650 deaths] vs.



0.68 percent [150 deaths],  $P < 0.001$ ). The respective adjusted hazard ratios ranged from 0.76 ( $P = 0.02$ ) for patients with two-vessel disease and involvement of the nonproximal LAD artery to 0.64 ( $P < 0.001$ ) for patients with three-vessel disease and involvement of the proximal LAD artery (Table 2). Significant risk factors in the statistical models included a lower ejection fraction; the presence of diabetes, congestive heart failure, chronic obstructive pulmonary disease, carotid-artery disease, aortoiliac disease, shock, renal failure, femoral or popliteal disease, and stroke; advanced age; and male sex. Figure 2 presents unadjusted survival curves and Figure 3 presents adjusted survival curves for three of the anatomical groups. For the unadjusted curves, the survival rate was significantly higher after stent placement than after CABG among patients who had two-vessel disease without involvement of the LAD artery ( $P = 0.03$ ), whereas the opposite was true among patients who had three-vessel disease with involvement of the proximal LAD artery ( $P < 0.001$ ); there were no significant treatment-related differences in survival in the other anatomical groups.

After adjustment for the severity of illness before revascularization, CABG was associated with a significantly higher likelihood of survival in all anatomical groups, as indicated in Table 2. The finding that unadjusted survival estimates favored PCI and adjusted survival estimates favored CABG for patients with two-vessel disease without LAD-artery involvement can be explained by the fact that the prevalences of several important risk factors were much higher in the CABG group than in the stent-

ing group (e.g., 3.4 percent vs. 2.2 percent for renal failure, 16.4 percent vs. 5.9 percent for chronic obstructive pulmonary disease, and 12.3 percent vs. 7.0 percent for congestive heart failure).

When the subgroup of patients with diabetes was analyzed, the adjusted hazard ratios were lower after CABG than after stenting in all anatomical subgroups except patients who had three-vessel disease with involvement of the proximal LAD artery (0.69; 95 percent confidence interval, 0.55 to 0.86). For patients with a left ventricular ejection fraction below 40 percent, the hazard ratios were significantly in favor of CABG, as compared with stenting, for patients with three-vessel disease and patients with two-vessel disease with involvement of the proximal LAD artery, but the hazard ratios were not significant for the other patients with two-vessel disease. For patients with no left ventricular dysfunction (as defined by an ejection fraction of at least 40 percent), CABG was associated with significantly lower adjusted hazard ratios in all anatomical groups (Table 2).

The majority of patients with two-vessel disease underwent stenting, whereas the majority of patients with three-vessel disease underwent CABG. For example, 90.6 percent of patients who had three-vessel disease with involvement of the proximal LAD artery underwent CABG, and patients in this group who underwent stent implantation were more likely than patients who underwent CABG to be in shock (0.4 percent vs. 0.2 percent) or to have received cardiopulmonary resuscitation (0.2 percent vs. 0.04 percent).

In the propensity analyses, significant covariates included age, sex, race, left ventricular ejection fraction, and presence or absence of a previous myocardial infarction and a variety of coexisting conditions, including diabetes, chronic obstructive pulmonary disease, carotid disease, femoral or popliteal disease, and renal failure with a need for dialysis. Distributions of patients who underwent CABG ranged from about 10 percent to 40 percent across quintiles for the anatomical groups with two-vessel disease and no disease of the proximal LAD artery, from 82 percent to 97 percent for patients who had three-vessel disease with disease of the proximal LAD artery, and from about 45 percent to 85 percent for the other two groups of patients with multivessel disease. Hazard ratios consistently favored CABG surgery over stent implantation, with 22 of the 25 anatomical-subgroup quintiles having hazard ratios between 0.44 and 0.84.

## DISCUSSION

Our observational study, which included 37,212 patients who underwent CABG and 22,102 patients who underwent stenting, found that the adjusted hazard ratios for the long-term risk of death after CABG relative to stent implantation ranged

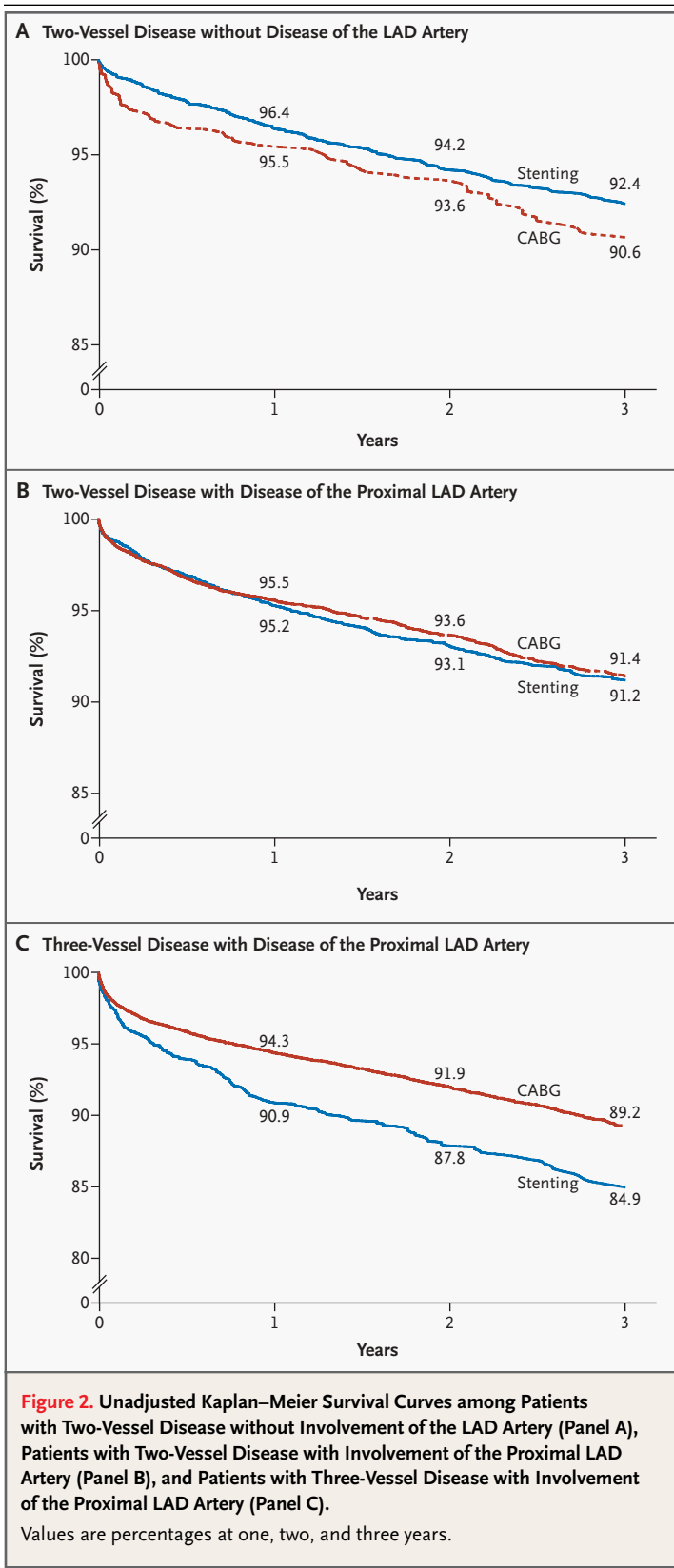
from 0.76 (95 percent confidence interval, 0.60 to 0.96) for patients with two-vessel disease with involvement of the nonproximal LAD artery to 0.64 (95 percent confidence interval, 0.56 to 0.74) for three-vessel disease with involvement of the proximal LAD artery. Also, revascularization rates were considerably higher after stenting than after CABG

**Table 2. Hazard Ratios for Death after CABG as Compared with after Stenting in Various Subgroups.\***

Subgroup	All Patients	Patients with Diabetes	Patients with Ejection Fraction <40%	Patients with Ejection Fraction ≥40%†
<b>Two-vessel disease</b>				
No disease of LAD artery				
No. of patients				
Stenting group	5,847	1352	451	5,396
CABG group	1,309	423	212	1,097
Unadjusted hazard ratio (95% CI)	1.29 (1.02–1.62)	0.95 (0.65–1.37)	1.09 (0.70–1.72)	1.18 (0.90–1.56)
Adjusted hazard ratio (95% CI)	0.75 (0.58–0.98)	0.69 (0.46–1.03)	0.95 (0.59–1.52)	0.69 (0.51–0.93)
Disease of nonproximal LAD artery				
No. of patients				
Stenting group	5,891	1485	610	5,281
CABG group	1,690	513	278	1,412
Unadjusted hazard ratio (95% CI)	1.05 (0.84–1.31)	0.70 (0.48–1.02)	1.15 (0.78–1.69)	0.89 (0.68–1.18)
Adjusted hazard ratio (95% CI)	0.76 (0.60–0.96)	0.59 (0.40–0.87)	1.01 (0.67–1.55)	0.67 (0.50–0.89)
Disease of proximal LAD artery				
No. of patients				
Stenting group	6,033	1438	803	5,230
CABG group	8,410	2472	1615	6,795
Unadjusted hazard ratio (95% CI)	0.97 (0.85–1.10)	0.87 (0.71–1.07)	0.70 (0.56–0.87)	1.00 (0.86–1.18)
Adjusted hazard ratio (95% CI)	0.75 (0.66–0.86)	0.71 (0.57–0.88)	0.64 (0.51–0.81)	0.82 (0.69–0.97)
<b>Three-vessel disease</b>				
Disease of nonproximal LAD artery				
No. of patients				
Stenting group	2,166	666	342	1,824
CABG group	4,946	1824	1196	3,750
Unadjusted hazard ratio (95% CI)	0.89 (0.74–1.06)	0.77 (0.59–0.99)	0.61 (0.46–0.81)	0.94 (0.75–1.17)
Adjusted hazard ratio (95% CI)	0.74 (0.62–0.90)	0.65 (0.49–0.85)	0.64 (0.48–0.87)	0.76 (0.60–0.96)
Disease of proximal LAD artery				
No. of patients				
Stenting group	2,165	644	399	1,766
CABG group	20,857	7115	5597	15,260
Unadjusted hazard ratio (95% CI)	0.67 (0.59–0.77)	0.66 (0.53–0.81)	0.55 (0.44–0.69)	0.64 (0.53–0.76)
Adjusted hazard ratio (95% CI)	0.64 (0.56–0.74)	0.69 (0.55–0.86)	0.68 (0.54–0.85)	0.60 (0.50–0.72)

\* CI denotes confidence interval. Adjusted hazard ratios were adjusted for the ejection fraction; the presence or absence of diabetes, congestive heart failure, chronic obstructive pulmonary disease, carotid-artery disease, aortoiliac disease, shock, renal failure, femoral or popliteal disease, and stroke; age; and sex.

† This category also included patients for whom data on the ejection fraction were missing.



(7.8 percent vs. 0.3 percent for subsequent CABG surgery and 27.3 percent vs. 4.6 percent for subsequent PCI).

Most randomized, controlled trials predating the stenting era that compared CABG with PCI did not find significant differences in long-term mortality between the two interventions. This finding may have been due in part to insufficient statistical power. For example, in the Bypass Angioplasty Revascularization Investigation study, the five-year mortality rate was 10.7 percent after CABG, as compared with 13.7 percent after PCI, but this difference was not significant ( $P=0.19$ ), at least partially because of the relatively small numbers of patients in the study (914 and 915, respectively).<sup>5</sup> A meta-analysis of randomized, controlled trials that compared CABG with PCI found that for patients with multivessel disease, CABG provided survival advantages of 2.3 percent ( $P=0.03$ ) at five years and 3.4 percent ( $P=0.03$ ) at eight years.<sup>19</sup>

Prior information on relative long-term outcomes for CABG and stent implantation has been limited to four randomized, controlled trials with relatively small numbers of patients (123 to 1205 patients in each study).<sup>8,11,13,15</sup> During follow-up periods ranging from one to three years, one of these studies found significantly lower mortality rates after CABG,<sup>8</sup> one found significantly higher mortality rates after CABG,<sup>13</sup> and the other two, one of which included patients with single-vessel disease, found no significant difference in mortality rates between the two interventions.<sup>11,15</sup> A meta-analysis of these studies found no significant differences in one-year or three-year mortality rates between the two interventions<sup>19</sup> but did find that patients who underwent CABG had significantly fewer subsequent revascularizations (15 percent fewer at one year and 15 percent fewer at three years) than patients who underwent stenting.<sup>19</sup> As evidenced by the small numbers of patients in the studies of long-term survival after stenting, as compared with CABG, very little information is currently available from randomized, controlled trials.

A caveat of our study is that it is observational, and not a randomized, controlled trial. As such, the choice of treatment was left to the physician, and one of the treatment options may have been contraindicated in some patients. Also, the analysis of survival does not include patients who died before they could undergo one of the scheduled revascularization procedures. Consequently, if there is a longer wait for one of the procedures and this re-

**Figure 3.** Adjusted Survival Curves among Patients with Two-Vessel Disease without Involvement of the LAD Artery (Panel A), Patients with Two-Vessel Disease with Involvement of the Proximal LAD Artery (Panel B), and Patients with Three-Vessel Disease with Involvement of the Proximal LAD Artery (Panel C).

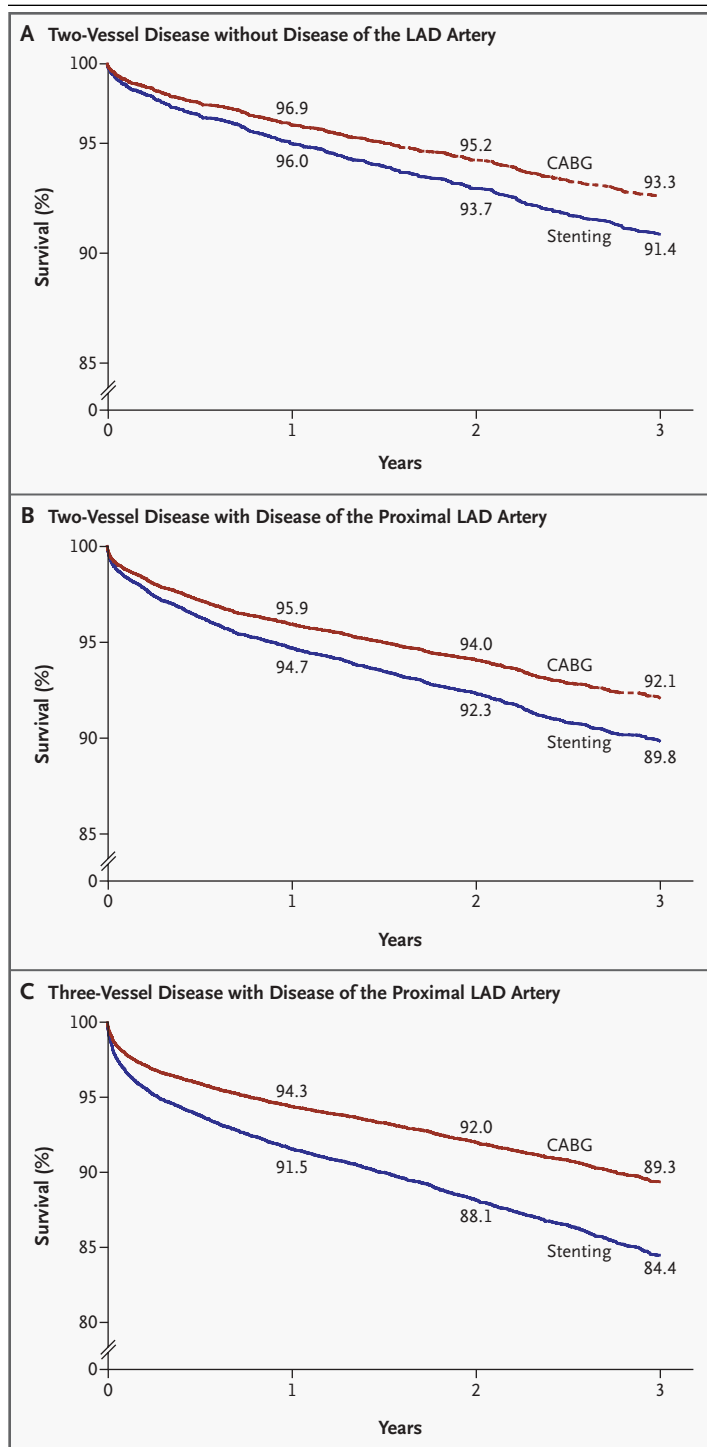
Values are percentages at one, two, and three years; they were adjusted for the ejection fraction; the presence or absence of diabetes, congestive heart failure, chronic obstructive pulmonary disease, carotid-artery disease, aortoiliac disease, shock, renal failure, femoral or popliteal disease, and stroke; age; and sex.

sults in additional adverse outcomes, this fact would not have been reflected by our findings.

We attempted to minimize the selection bias by adjusting for differences among patients in demographic characteristics, coexisting conditions, ventricular function, and hemodynamic state. Furthermore, propensity analyses demonstrated that the survival advantage for CABG persisted regardless of the chance of patients' being referred for stent implantation rather than CABG. In addition, comprehensive studies that have compared the results of randomized, controlled trials and observational studies in assessing two competing interventions have concluded that the treatment effects are not qualitatively different and that the observational studies do not overestimate the magnitude of the treatment effects.<sup>25,26</sup> Nevertheless, there remains the possibility that observational studies may fail to identify all confounders, and it is also true that propensity analyses cannot account for selection bias related to unmeasured characteristics.

Another important caveat is that although this study is based on data as recent as those used by any other study comparing these two interventions, the state of the art for both treatments is rapidly changing. The most notable of these changes is probably the availability of drug-eluting stents, but the use of CABG without cardiopulmonary bypass and cardiac arrest ("off pump") has also become much more common in the past few years and is underrepresented in our study. In particular, future studies will be needed to compare long-term outcomes for drug-eluting stents with those for CABG in patients with various types of risk factors before the procedure.<sup>27-29</sup>

There are many considerations when one is choosing an intervention for patients with ischemic heart disease. Stenting is far less invasive than CABG, and many patients may prefer to have one or



more stents implanted in the hope of avoiding CABG. As noted earlier, stent implantation has a much lower in-hospital mortality rate than CABG. Depending on the patient's life expectancy and attitude about the relative merits of short-term and



long-term risk, stent implantation may be preferred even for a patient in an anatomical group for which CABG has significantly higher risk-adjusted long-term survival. Howard et al. provide an excellent comprehensive discussion of these trade-offs.<sup>30</sup>

As with our earlier comparison of CABG with PCI in the infancy of stent implantation,<sup>16</sup> we restricted ourselves to the study of New York State residents because we were unable to determine when patients who lived in other states died after discharge. However, we had no way of knowing whether our patients moved to another state and died there

or underwent revascularization there, since we used only the New York State death file. Nevertheless, we do not believe that any bias was introduced by this limitation, because we would expect roughly the same percentage of patients in each intervention group to be lost to follow-up.<sup>16</sup>

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#### CLINICAL TRIAL REGISTRATION

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