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Comparison of Coronary Artery Bypass Surgery and Percutaneous Drug-Eluting Stent Implantation for Treatment of Left Main Coronary Artery Stenosis

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Objectives The purpose of this study was to compare outcomes for drug-eluting stents (DES) and coronary artery bypass graft (CABG) surgery in patients with unprotected left main coronary artery (ULMCA) stenosis.

Background Expert guidelines recommend coronary artery bypass graft (CABG) surgery for the treatment of significant stenosis of the unprotected left main coronary artery (ULMCA) if the patient is eligible for CABG; however, treatment by percutaneous coronary intervention (PCI) is common.

Methods Details of patients (n = 343, ages 69.9 ± 11.9 years) undergoing coronary revascularization for ULMCA stenosis (April 2003 to January 2007) were recorded. A total of 223 patients were treated with CABG (mean [interquartile range]: follow-up 600 [226 to 977) days) and 120 by PCI (follow-up 362 [192 to 586) days). The hazard ratios (HRs) for death and major adverse cardiovascular and cerebrovascular events (MACCE) were calculated incorporating propensity score adjustment. Survival comparisons were conducted in propensity-matched subjects (n = 134), and in low- and high-risk subjects for CABG.

Results Patients treated by PCI were more likely to be ≥75 years of age (49% vs. 33%; p = 0.005), and of greater surgical risk (Parsonnet score 17.2 ± 11.2 vs. 13.0 ± 9.3; p < 0.001) than patients treated by CABG. Overall, the propensity-adjusted HR for death was not statistically different (HR 1.93, 95% confidence interval [CI] 0.89 to 4.19, p = 0.10), but MACCE was greater in the PCI group (HR 1.83, 95% CI 1.01 to 3.32, p = 0.05). In propensity-matched individuals, neither survival nor MACCE-free survival were different. Survival was equivalent among low-risk candidates, but PCI had a tendency to inferior survival in high-risk candidates (Ellis category IV, log-rank p = 0.05). Interaction testing, however, failed to demonstrate a difference in outcomes of the 2 revascularization techniques as a function of baseline risk assessment.

Conclusions Overall, the propensity-adjusted risk of mortality for treatment of ULMCA disease does not differ between PCI- and CABG-treated groups. There appears to be sufficient equipoise that a randomized clinical trial to compare the techniques would not be ethically contraindicated. (J Am Coll Cardiol Intv 2008;1:236–45) © 2008 by the American College of Cardiology Foundation

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Hemodynamically significant left main coronary artery stenosis is found in approximately 4% of diagnostic coronary angiograms (1) and is known as unprotected left main coronary artery (ULMCA) stenosis if the left coronary artery has no previous grafts. Such anatomical pathology compromises perfusion to approximately two-thirds of the myocardium and is thus an intuitively dangerous lesion. Studies by Veteran's Affairs (2,3), CASS (Coronary Artery Surgery Study) (4,5), and European (6) groups in the 1970s

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and 1980s confirmed very high mortality rates among such individuals and also demonstrated substantial reductions in mortality when revascularization by coronary artery bypass graft (CABG) surgery was undertaken (7,8). Subsequently, the mortality benefit of CABG compared with medical management for ULMCA disease was also confirmed in a meta-analysis (9).

The beneficial treatment effect of surgery is probably even greater in the current era because of routine use of a mammary graft to the left anterior descending (LAD) coronary artery wherever possible. Current practice guidelines do not recommend percutaneous coronary intervention (PCI) for revascularization for ULMCA stenosis if the patient is a candidate for CABG (10,11) because of the proven benefit of surgery, high rates of restenosis with use of bare-metal stents in the LMCA position (12–14), and concern that restenosis may present with sudden death rather than angina in this anatomic location (13). If a patient with ULMCA stenosis is a candidate for revascularization, but not for CABG, the guidelines consider PCI of the lesion reasonable (Class IIa indication) (10).

Approximately 20% of ULMCA revascularizations in the U.S. are currently performed by PCI (15). Treatment of ULMCA stenosis with PCI is often undertaken in the best interests of individuals, where the risk of CABG would be unacceptably high, or in patients who refuse to undergo a sternotomy. The advent of drug-eluting stents (DES), and nonrandomized data that suggest the long-term outcomes of DES to treat ULMCA stenoses are acceptable (16–19) have led some cardiologists to consider the possibility of a broader role for PCI as a treatment option for ULMCA stenosis.

Randomized procedural and outcomes data that compare CABG and PCI using DES for treatment of ULMCA stenosis would be a great advance in our clinical knowledge but no such dataset exists. With the advent of DES and with increasing appreciation of neuropsychiatric deficits after cardiac surgery (20), such a trial is now considered by many to be not only ethical but in fact highly warranted (21). When completed and published, the SYNTAX trial (Synergy between PCI and Taxus and Cardiac Surgery) of CABG versus DES will have a subset of individuals with ULMCA stenosis available for analysis to shed some light on this question.

In this context, we analyzed the results of ULMCA stenosis revascularization procedures and outcomes from Cedars-Sinai Medical Center, Los Angeles, California, since the introduction of DES. We used propensity scoring, which is a statistical technique that models an individual's propensity (or probability) of belonging to a certain group (for example, treatment by CABG or PCI). The effect of incorporation of the propensity score is to balance subject characteristics in the 2 groups (22,23). In the absence of randomized data, this technique may be the closest we can get to a fair comparison of the 2 revascularization techniques for ULMCA stenosis.

Methods

Study population. Three hundred forty-three patients with ULMCA diameter stenosis who were revascularized at our institution during the time period of April 2003 to January 2007 were included in this observational study. The definition of ULMCA stenosis used for inclusion in this prospective registry was angiographic diameter stenosis of greater than 50% relative to a reference segment of the left main coronary artery. Individuals who had valve replacement surgery concomitantly with revascularization surgery, and individuals who had a bare-metal stent placed in the left main position were excluded from this prospective registry. Choice of revascularization technique was a nonrandomized process that involved evaluation and advice from treating doctors, and discussions with patient and family. Two hundred twenty-three patients underwent CABG, and 120 underwent PCI with DES (Fig. 1). In keeping with published guidelines (10), individuals generally underwent CABG unless their cardiac surgeon or cardiologist advised against CABG on the basis of high surgical risk, or the patient, with their family, had a strong preference not to undergo cardiac surgery.

The primary end points were the hazard ratio (HR) for death and the HR for major adverse cardiovascular and cerebrovascular events (MACCE) using a Cox proportional hazards model that incorporated propensity score as a covariate. This study was approved by the Institutional Review Board of Cedars-Sinai Medical Center.

Abbreviations and Acronyms

CABG = coronary artery bypass graft (surgery)
CI = confidence interval
DES = drug-eluting stent(s)
HR = hazard ratio
IABP = intra-aortic balloon pump
LAD = left anterior descending (coronary artery)
MACCE = major adverse cardiovascular and cerebrovascular event
PCI = percutaneous coronary intervention
ULMCA = unprotected left main coronary artery

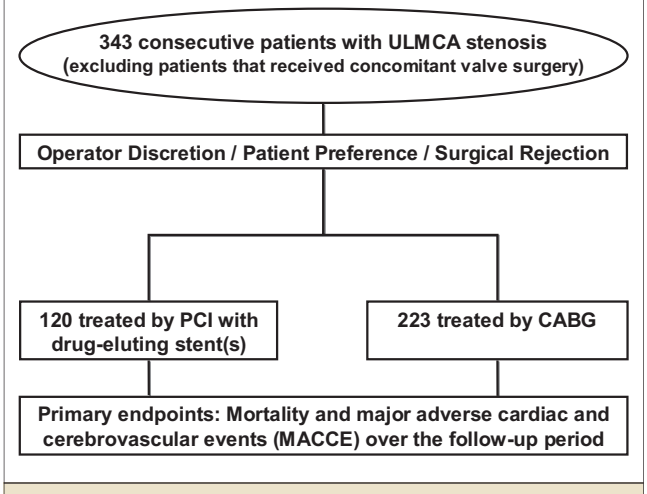

Figure 1. Participant Flow Through the Study

CABG = coronary artery bypass grafting; MACCE = major adverse cardiovascular and cerebrovascular event; PCI = percutaneous coronary intervention; ULMCA = unprotected left main coronary artery.

Calculation of surgical risk estimates. Subgroup analysis was conducted by the use of 2 multivariate models of cardiac operative risk estimation, the Parsonnet (24) and Ellis (25) scores, to divide patients into high and low estimated risk categories. The Parsonnet score is a points-based additive model that uses 15 variables with various assigned weights (24): female gender (1 point); pre-operative intra-aortic balloon pump (IABP; 2 points); obesity, diabetes, and hypertension (3 points each); left ventricular aneurysm (5 points); emergency surgery after catheterization lab complications or dialysis dependency (10 points each); ejection fraction (>50%, 0 points; 30% to 49%, 2 points; <30%, 4 points); age (<70 years, 0 points; 70 to 74 years, 7 points; 75 to 79 years, 12 points; ≥80 years, 20 points); and reoperation (first, 5 points; second, 10 points). Another 3 components of the model relate to concomitant valve surgery, which was not relevant to the current study population. A patient with a Parsonnet score ≤ 15 was considered to have low surgical risk, and a patient with a Parsonnet score >15 was considered to be at high surgical risk.

The Ellis score is another validated points-based cardiac surgical risk estimation model (25). Points are allocated for chronic obstructive pulmonary disease (2 points), renal insufficiency (3 points), age 60 to 69 years (3 points), age 70 to 79 years (6 points), or age older than 80 years (9 points). Individuals are then allocated to an Ellis score category, based on their score as follows: category I (0 points), category II (1 to 3 points), category III (5 to 6 points) and category IV (≥7 points), with a higher category implying a higher surgical risk.

PCI. Percutaneous coronary intervention was performed with the use of standard vascular access, guiding catheter, and coronary wiring techniques. Lesions at the ostium or in the shaft of the ULMCA were generally treated with a single DES. Where there was involvement of the distal bifurcation of the ULMCA, the judgment of the primary operator was used to decide upon an appropriate stenting strategy. Techniques used included a single stent deployed across the ostium of one branch (usually the circumflex), or use of 2 stents using a "T", crush, or kissing stent technique. The choice of sirolimus- or paclitaxel-eluting stent was at the operator's discretion and not mandated by the study protocol. Intra-vascular ultrasound was routinely used to check for adequate stent apposition to the vessel wall, unless an adverse hemodynamic situation made this imaging modality dangerous. Aspirin and clopidogrel were commenced before the procedure. Aspirin was continued indefinitely and clopidogrel recommended for a minimum of 6 months. Cardiac enzymes were measured post-procedure if there was clinical suspicion of ischemia, but were not measured routinely. Periprocedural IABP and glycoprotein IIb/IIIa antagonist infusions were used at the operator's discretion.

CABG. Standard techniques for sternotomy, cardioplegia, arterial harvest, and anastamoses and wound closure were used. Arterial conduits were preferred to saphenous vein grafts, and in particular an internal mammary artery was anastamosed to the LAD whenever possible.

MACCE. Major adverse cardiovascular and cerebrovascular events was a composite of death, myocardial infarction, repeat revascularization, and stroke. The intense focus currently on the incidence of late acute stent thrombosis following implantation of DES is noted (26,27), but because full importance of this issue was not appreciated at the commencement of this registry, data on occurrence of acute stent thrombosis was not specifically prospectively collected in this study. Such events would however have been likely to be detected as one of the MACCE component events.

Statistical methods. Data are presented as mean ± SD or as percentages, except where indicated. Comparison of categorical variables was performed with the use of chi-square or Fishers exact tests as appropriate, and normally distributed continuous variables were compared with the use of *t* tests. Comparisons of Kaplan-Meier survival curves were made by applying the log-rank test.

A multivariate logistic regression analysis that uses 18 variables was used to develop a model of propensity score, to estimate the probability that a given individual in this study was treated with CABG. This was done in an effort to take into the account the different characteristics of the groups that were inevitably present by virtue of the clinical decision-making process. The power of the model to predict group membership for a given individual was assessed by the c-statistic (similar to area under the curve of a receiver-operator characteristic of a test). The 18 variables used to construct the propensity score consisted of 15 categorical (yes/no) and 3 continuous pre-treatment variables. The

categorical variables were the presence/absence of age >75 years, male gender, diabetes (defined by use of insulin or oral hypoglycemic agents), hypertension, chronic renal impairment (defined by a serum creatinine of ≥1.5 mg/dl in the absence of an identified reversible cause), chronic obstructive pulmonary disease, hypercholesterolemia, history of myocardial infarction, history of coronary artery disease (defined as previous electrocardiogram, enzyme, perfusion or angiographic evidence of coronary artery disease), presentation with unstable angina, presentation with stable angina, presentation with myocardial infarction, involvement of distal left main coronary artery, right coronary artery stenosis, and Ellis score category III or IV (vs. I or II). The continuous variables were age, serum creatinine, and Parsonnet score.

This propensity score was used in 2 ways. First, the propensity score was used as a covariate in a Cox proportional hazards model for death and for MACCE to derive HRs for the primary end points. Second, the propensity score was used to construct Kaplan-Meier curves for freedom from death and freedom from MACCE using the subset of patients that could be matched for propensity score within 0.03 (n = 67 PCI, n = 67 CABG). Comparisons between these propensity-matched treatment groups were made by the log-rank test. Interaction tests were performed to investigate whether treatment effects differed as a function of initial surgical risk as assessed by Parsonnet score or Ellis category. All statistical tests were 2-tailed. A value of $p < 0.05$ was used to determine statistical significance.

Table 1. Baseline Characteristics of the Study Population

	CABG	PCI	p Value
n	223	120	
Age, yrs, mean ± SD	69.4 ± 10.7	70.9 ± 13.9	0.31
Age ≥75 yrs	74 (33)	59 (49)	0.005
Gender, male	171 (77)	70 (58)	<0.001
Diabetes mellitus	60 (27)	42 (35)	0.11
Hypertension	170 (76)	90 (76)	0.90
Hypercholesterolemia	171 (77)	89 (75)	0.69
Current smoker	37 (17)	21 (18)	0.76
Chronic renal insufficiency ≥1.5 mg/dl	22 (10)	21 (18)	0.06
Previous stroke	19 (9)	8 (7)	0.68
Left ventricular ejection fraction, %	54 ± 11	54 ± 14	0.94
Clinical presentation			<0.001
Stable angina	101 (45)	32 (27)	
UA/MI/other	122 (55)	88 (73)	
Parsonnet score, mean ± SD	13.0 ± 9.3	17.3 ± 11.3	<0.001
Patients with Parsonnet score >15	82 (37)	65 (54)	0.002
Ellis score			
Category I	27 (12)	25 (21)	<0.001
Category II	68 (30)	19 (16)	
Category III	75 (34)	30 (25)	
Category IV	53 (24)	46 (38)	

Data are presented as number (%) unless otherwise specified.
CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention; UA = unstable angina.

Results

Baseline characteristics. Three hundred forty-three patients with ULMCA stenosis were treated (age 69.9 ± 11.9 years, 70.3% male gender): 223 with CABG and 120 with PCI using a DES (Table 1). As compared with those treated with CABG, a greater proportion of patients treated with PCI were ages 75 years or older (49% vs. 33%; $p = 0.005$) and a lower proportion were men (58% vs. 77%; $p < 0.001$). Patients treated with PCI were also less likely to have presented with stable angina (27% vs. 45%; $p < 0.001$) and had a greater Parsonnet score (17.3 ± 11.3 vs. 13.0 ± 9.3; $p < 0.001$) than those treated with CABG. A greater proportion of patients treated with CABG had additional disease of the right coronary artery (71% vs. 28%; $p < 0.0001$) and/or presence of stenosis involving the bifurcation of the left main coronary artery (77% vs. 64%; $p = 0.01$) than those treated with PCI.

Within the PCI group, 50 patients (41.7%) had been turned down for CABG after cardiac surgical consultation, 25 patients (20.8%) had not been referred for surgical consultation because they were considered to be poor surgical candidates by their physician, and 45 patients (37.5%) preferred PCI over surgery.

Procedural characteristics. Ninety-one patients (75.8%) had sirolimus-eluting stents (Cypher, Cordis Corporation, Miami Lakes, Florida) and 29 (24.2%) had paclitaxel-eluting stents (Taxus, Boston Scientific, Natick, Massachusetts) used in the left main position. An average of 2.6 ± 1.4 stents per patient, with an average total length of 49.9 ± 33.7 mm were implanted in these procedures (not just in the left main position). A total of 77 of 120 PCI patients (64%) had disease involving the bifurcation of the left main coronary artery. When bifurcation disease was present, the following stenting techniques were used to deal with the bifurcation lesion: One stent placed across the ostium of the circumflex into the proximal LAD, 33 (43%); 2 stents placed by the kissing stent technique, 22 (29%); 2 stents placed using the crush technique, 17 (22%); and 2 stents placed using T-stenting technique, 5 (6%). Intravascular ultrasound was used in 103 (85.8%) and glycoprotein IIb/IIIa antagonists in 17 (14.2%) cases. Hemodynamic support included IABP in 58 (48.3%) cases and tandem heart percutaneous left ventricular assist device in 3 (2.5%) cases. Eighty-six (72%) PCI-treated patients received a stent to a coronary lesion other than the one in the left main coronary artery.

Within the CABG group, the average number of grafts was 3.0 ± 0.8, and 215 (96.4%) of patients received a LIMA graft to the LAD. Length of stay in hospital was longer in the CABG group than the PCI group (7.5 ± 4.6 days vs. 4.3 ± 5.1 days; $p < 0.0001$).

Follow-up. Longer follow-up was available for the CABG-treated group compared with the PCI-treated group (median [interquartile range]: 600 [226 to 977] days vs. 362 [192 to 586] days). Of the 10 target vessel revascularization procedures in the group initially treated with PCI, 7 were clinically driven; 9 were performed for recurrent narrowings, and 1 for a previously untreated coronary lesion.

Propensity analysis. Propensity analysis was performed because the treatment group characteristics were so different (Table 1) as to render comparison of raw outcome data unreliable. The C-statistic of the propensity model was 0.81. The average propensity score (where a hypothetical score of 1 would be a certainty to be treated with CABG) was 0.25 ± 0.19 in the PCI group and 0.52 ± 0.24 in the CABG group ($p < 0.0001$).

Propensity-matched subjects (individuals from each group with propensity scores within 0.03 of each other, n = 134) were found to have similar characteristics (Table 2), providing good evidence that propensity score was an effective method to account for differences between the treatment groups. When the propensity score was entered as a covariate into a Cox proportional hazards regression model for death, there was no statistically significant evidence for a different risk of death in the PCI versus the CABG group (HR 1.93, 95% confidence interval [CI] 0.89 to 4.19, $p = 0.10$). With a similar Cox proportional hazards model for MACCE, there was evidence of a greater risk of MACCE in the PCI group versus the CABG group (HR 1.83; 95% CI 1.01 to 3.32, $p = 0.05$).

Propensity-matched subjects were used to construct Kaplan-Meier survival curves for comparison of death-free (Fig. 2A) and MACCE-free (Fig. 2B) survival. This method of analysis showed no evidence for a difference in absolute survival (log-rank $p = 0.40$), and no evidence for a difference in MACCE-free survival (log-rank $p = 0.32$).

Outcomes according to baseline estimation of risk. Next, raw outcome data were used to examine the influence of baseline operative risk assessment upon survival, with the inclusion of both the Parsonnet (24) and Ellis (25) scoring estimates of operative risk to divide the database. Survival was not different between CABG and PCI among individuals with a Parsonnet score ≤15 (Fig. 3A) (log-rank $p = 0.81$), but in individuals with a Parsonnet score >15, there was a trend toward worse survival in the PCI group than the CABG group (Fig. 3B) (log-rank $p = 0.09$). MACCE-free survival also showed a differential depending on Parsonnet score. MACCE-free survival was not different between CABG and PCI among individuals with a Parsonnet score ≤15 (Fig. 3C) (log-rank $p = 0.44$) but in those with a Parsonnet score >15, MACCE-free survival was worse in the PCI group (Fig. 3D) (log-rank $p = 0.04$). Despite this apparent divergence of clinical outcome between the 2 techniques as a function of baseline Parsonnet score, the interaction test for death ($p = 0.61$) or MACCE ($p = 0.70$) is not significant. Thus, treatment effects did not differ as a function of baseline risk.

Survival was not different between CABG and PCI among individuals with an Ellis category of I, II, or III (Fig. 4A) (log-rank $p = 0.60$), but in individuals in Ellis category IV the PCI group had worse survival than the CABG group (Fig. 4B) ($p = 0.05$). In neither those individuals within Ellis category I, II or III (Fig. 4C) (log-rank $p = 0.07$), nor those in Ellis category IV (Fig. 4D) (log-rank $p = 0.14$) was there a statistically significant difference in MACCE-free survival between the CABG and PCI groups. Interaction testing was again performed and, similarly, there was no statistical evidence that PCI differentially affected the HR of death (interaction test, $p = 0.72$) or MACCE (interaction test, $p = 0.80$) in the Ellis IV group versus the Ellis category I, II, or III group.

There was no significant difference in the HR for death (HR 1.09, 95% CI 0.40 to 2.97, log rank $p = 0.86$) according to the baseline presence of bifurcation disease of

Table 2. Characteristics of 134 Subjects Who Were Able to Be Matched for Propensity Score Within 0.03

	CABG	PCI	p Value
N	67	67	
Age, yrs, mean ± SD	72.2 ± 11.9	68.6 ± 13.2	0.11
Age ≥ 75 yrs	32 (48)	25 (37)	0.21
Gender, male	42 (63)	44 (66)	0.72
Diabetes mellitus	21 (31)	23 (34)	0.72
Hypertension	52 (78)	49 (73)	0.56
Hypercholesterolemia	50 (75)	52 (78)	0.68
Current smoker	8 (12)	14 (21)	0.18
Chronic renal insufficiency ≥1.5 mg/dl	9 (13)	8 (12)	0.80
Previous stroke	5 (8)	4 (6)	0.74
Left ventricular ejection fraction, %	52.9 ± 12.9	55.0 ± 11.9	0.30
Clinical presentation			0.10
Stable angina	26 (39)	18 (27)	
UA/MI/other	41 (61)	49 (73)	
Parsonnet score, mean ± SD	17.0 ± 11.3	14.4 ± 11.0	0.22
Patients with Parsonnet score >15	34 (51)	26 (39)	0.16
Ellis score			0.56
Category I	9 (13)	15 (22)	
Category II	14 (21)	15 (22)	
Category III	20 (30)	19 (28)	
Category IV	24 (36)	18 (27)	

Data are presented as number (%) unless otherwise specified.
Abbreviations as in Table 1.

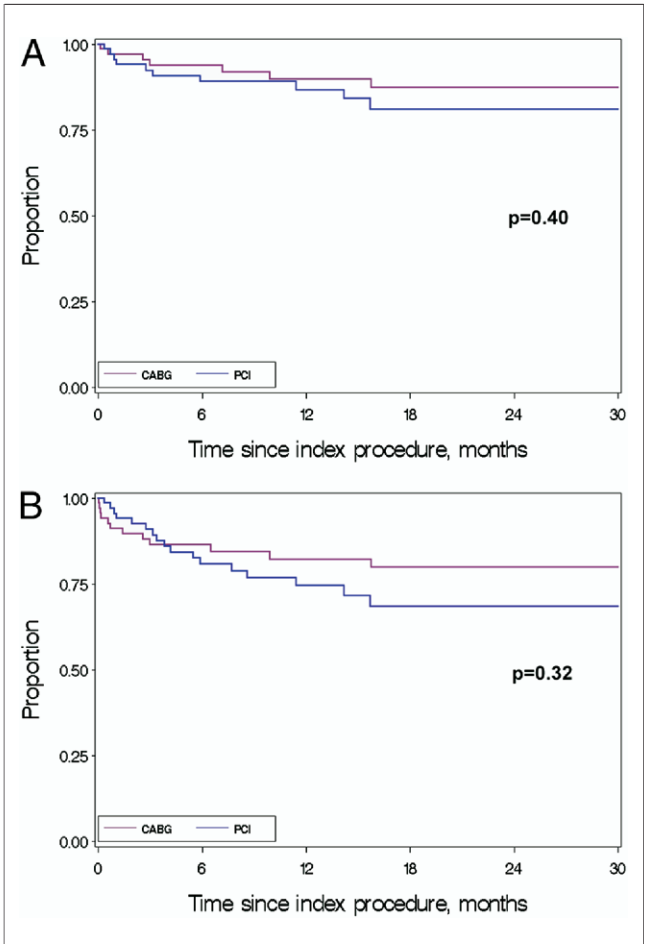

Figure 2. Survival Curves in Propensity-Matched Individuals

There were 67 patients in the PCI group and 67 patients in the CABG group (n = 134). **(A)** Survival in 134 propensity-matched individuals. **(B)** Major adverse cardiovascular and cerebrovascular event-free survival in 134 propensity-matched individuals. Abbreviations as in Figure 1.

the left main coronary artery in the PCI treated group. There was a trend toward an increased HR for MACCE (HR 1.80, 95% CI 0.80 to 4.03, log rank p = 0.15) if bifurcation disease was present, though this was statistically not significant.

Discussion

The main finding of this study is that after accounting for pre-treatment group differences, the risk for death after revascularization for ULMCA was not different between PCI and CABG during the follow-up period. This finding is noted, in the context of current guidelines for management of ULMCA by revascularization, which state that use of PCI to treat significant ULMCA stenosis is a class III indication ("not effective. . .may be harmful. . .") if the patient is a candidate for CABG (10). In patients who are candidates for revascularization but are not eligible for CABG (a description that applies to a majority of the PCI group in this study), PCI of ULMCA stenosis is considered reasonable (class IIa indication) (10).

In contrast to similar mortality rates with either procedure, MACCE-free survival calculated by the Cox proportional hazards model was lower in the PCI-treated group, mostly because of an excess of repeat revascularization procedures. We note that the use of the propensity score in 2 ways yielded different results with respect to MACCE outcomes. The differences in the results between the 2 adjustment tools may relate to the difference in sample size—the Cox proportional hazard method used all of the individuals in the registry (n = 343), whereas the propensity matching method could use less than one-half this number (n = 134). Among the methodological tools that have been developed to minimize bias (confounding) in observational studies, propensity score-matched comparison is generally considered to be the most robust.

In contrast to similar mortality rates with either procedure, MACCE-free survival was lower in the PCI-treated group, mostly because of an excess of repeat revascularization procedures. Of note, many physicians at our institution scheduled follow-up angiography after PCI to the ULMCA, even in the absence of symptoms. This inevitably led to treatment of newly discovered stenoses. Such nonclinically driven repeat procedures have the potential to contribute systematically to MACCE events in the PCI but not the CABG group. Nonetheless, the excess of repeat procedures in the PCI group represents one of its principal limitations, which in an individual patient must be balanced against the recovery period following CABG.

Our higher rate of repeat revascularization procedures after PCI treatment is consistent with previous randomized comparisons of PCI and CABG using bare metal stents (28–30), although not specifically in ULMCA stenosis. Restenosis appears to be an inherent trade-off for the reduced invasiveness of PCI. Our study, the first report from a U.S. medical center, is also broadly comparable with 2 Italian studies that both concluded that the mortality rates for revascularization of ULMCA are similar with either technique (31,32).

The clinical cardiology community has come to accept higher rates of target vessel revascularization associated with treatment of multivessel disease by PCI because survival rates are similar to CABG. However, extrapolation of these results to ULMCA is inappropriate because at this anatomic location, restenosis could present as sudden death (13). Our data, therefore, provide a rational basis for use of DES in selected patients with ULMCA because DES have substantially reduced the incidence of restenosis after PCI.

Patients who were treated with PCI in this study had higher risk characteristics than those treated with CABG (Table 1). A larger proportion of subjects ages 75 years and older were treated with PCI, and the Parsonnet score, a

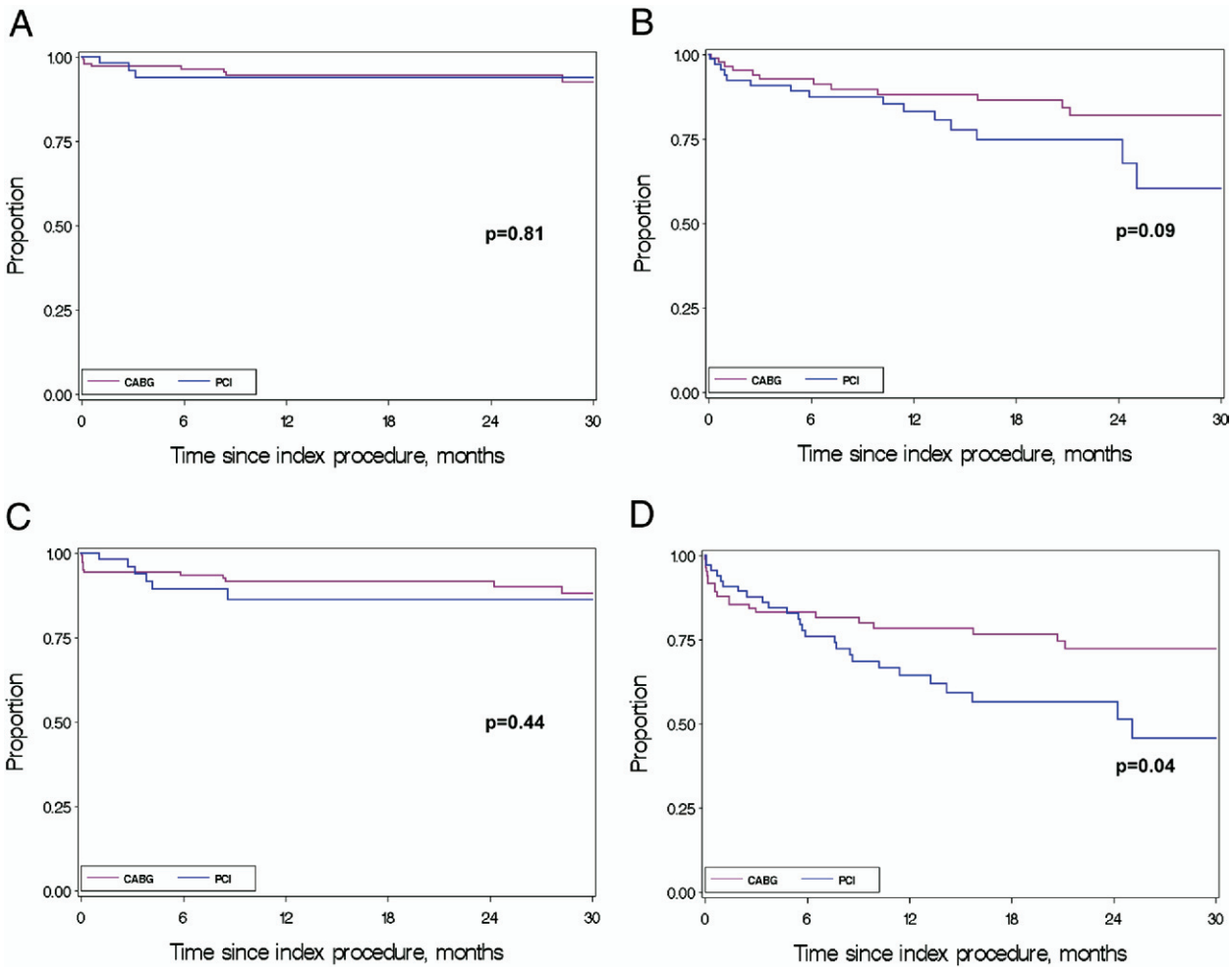

Figure 3. Survival Curves According to Pre-Procedural Estimation of Risk by Determination of Parsonnet Score

(A) Overall survival in individuals with a Parsonnet score ≤15. **(B)** Overall survival for individuals with a Parsonnet score >15. **(C)** MACCE-free survival in individuals with a Parsonnet score ≤15. **(D)** MACCE-free survival for individuals with a Parsonnet score >15. Abbreviations as in Figure 1.

multivariable validated surgical risk predictor, was greater in the PCI group. On the other hand, other institutions may have different criteria for selecting PCI or CABG. In a Milanese group of patients revascularized for ULMCA stenosis (31), it was the CABG-treated group with higher risk characteristics (older, with a greater proportion with renal failure). In our institution PCI was usually reserved for patients felt to be at high surgical risk, in keeping with the guidelines (10), and this clinical practice pattern is reflected in the characteristics of the groups.

There are no published comparative long-term data between PCI with DES and CABG for ULMCA stenosis from any center in the U.S. Preliminary outcome data from our registry were first reported approximately 2 years ago (33). These data showed no increase in immediate complications for PCI compared with CABG. Our current report studies a larger population, and most critically, a longer follow-up, and uses propensity analysis to minimize the limitations of pre-treatment group differences that characterized the earlier report.

The second main finding of this paper was a suggestion that subgrouping patients by surgical risk may have clinical value. We used 2 different scoring systems. Independent of the method used, in individuals with lower "surgical risk" the 2 revascularization techniques had raw survival outcomes that were not different. Among those with baseline high surgical risk, however, there was a greater rate of mortality in the PCI group than the CABG group. This difference reached statistical significance when the Ellis method of risk assessment was used. It must be emphasized, however, that statistical interaction testing failed to demonstrate a difference in outcomes of the 2 revascularization techniques as a function of initial risk assessment. Given the limited power of subgroup analyses, however, we cannot

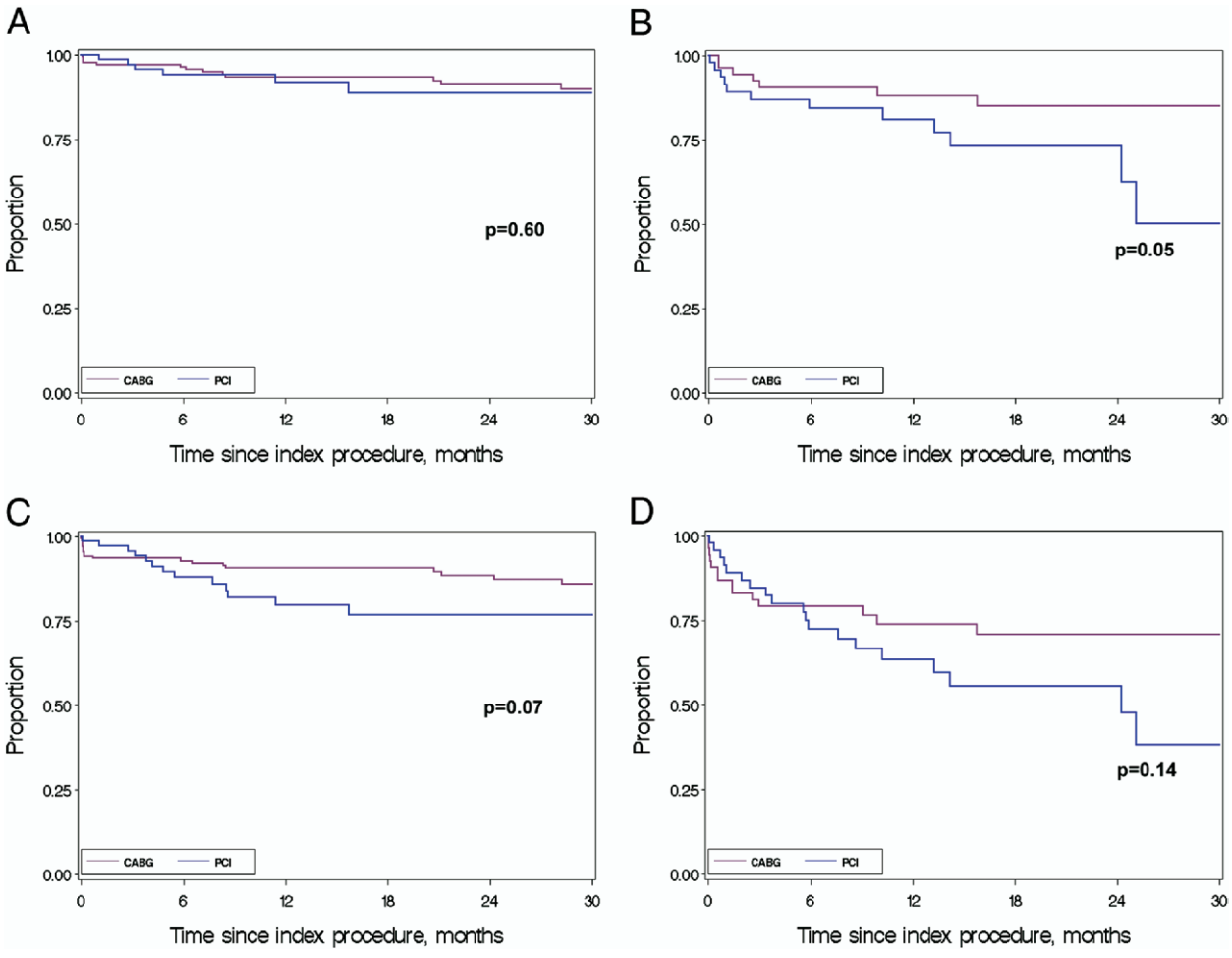

Figure 4. Survival Curves According to Estimation of Surgical Risk by Determination of Ellis Category

(A) Overall survival in individuals in Ellis category I, II, or III. **(B)** Overall survival for individuals in Ellis category IV. **(C)** Freedom from MACCE for individuals in Ellis category I, II, or III. **(D)** Freedom from MACCE for individuals in Ellis category IV. Abbreviations as in Figure 1.

completely exclude the possibility that the 2 revascularization techniques may provide different treatment effects in low- versus high-risk groups.

It is highly likely that there are selection biases for PCI patients to be sicker and have worse outcomes and that these biases are not fully accounted for by stratification according to Parsonnet or Ellis risk scoring. Examples of factors that are not captured by either of the risk scoring systems, yet clearly have the potential to influence choice of treatment modality and/or subsequent outcome include presence of bifurcation left main disease, presence of concomitant other coronary lesions and an impression of patient "frailty" by the treating physician.

Although the current guideline recommendations are based predominantly on experience with bare-metal stents, even in that era ULMCA stenting in low-risk patients had good clinical outcomes. For example, in 187 patients (age 56.2 ± 11.2 years, 68% male) with normal ejection fraction (62.4 ± 8.3%) there was a 97.7% cumulative probability of cardiac death-free survival over 5 years of follow-up (34) (although there was a 21% target lesion revascularization rate over that time). Similarly, in the ULTIMA registry (12), low-risk patients (<65 years, left ventricular ejection fraction >30%, and not in cardiogenic shock) had good outcomes (1-year actuarial outcomes; 3.4% death, 16.9% death/MI/CABG).

The outcome differences we observed between PCI and CABG in the high-risk category become apparent at about 6 months. Because interaction testing ruled out an effect of baseline Parsonnet or Ellis score upon the CABG/PCI differential outcomes, an alternative and equally plausible explanation is that the curves validate physicians' intuitive and experiential judgment in predicting survival, and that the results reflect the appropriate allocation of sicker pa-

tients to the less invasive treatment (PCI) despite the guidelines.

Although propensity scoring is a recognized technique that can be used to correct for baseline differences, it is not a substitute for a large prospective trial with extended follow-up that randomizes individuals to CABG or DES for ULMCA stenosis. Such a trial could answer the question of whether DES PCI is noninferior to CABG for ULMCA stenosis within a particular patient population but might not predict outcomes in clinical practice. Thus, each type of data analysis, registry, and randomized trial is valuable to fully analyze the relative merits of the 2 procedures. Although we failed to detect an influence of bifurcation left main disease on clinical outcome, we are aware that others have demonstrated that this variable is a predictor of outcome (35), and we also noted a trend in this direction.

Conclusions

Our data suggest that the propensity-adjusted risk of intermediate-term mortality is similar for the treatment of ULMCA stenosis by PCI with DES or CABG, although we certainly cannot recommend widespread adoption of this practice on the basis of the current data. A randomized clinical trial to compare the techniques, adequately powered to detect a mortality difference, would have considerable logistical and financial barriers, but appears not to be ethically contraindicated.

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