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Long-Term Outcomes After Stenting Versus Coronary Artery Bypass Grafting for Unprotected Left Main Coronary Artery Disease

10-Year Results of Bare-Metal Stents and 5-Year Results of Drug-Eluting Stents From the ASAN–MAIN (ASAN Medical Center–Left MAIN Revascularization) Registry

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Objectives This study sought to evaluate the long-term safety and effectiveness of percutaneous coronary intervention (PCI), as compared with coronary artery bypass grafting (CABG), for unprotected left main coronary artery (LMCA) disease.

Background Data on the long-term (beyond 5-year) comparative results of treatment of unprotected LMCA disease with stent implantation or CABG are limited.

Methods We performed a 10-year clinical follow-up of 350 patients with unprotected LMCA disease who underwent PCI with bare-metal stents (BMS) (n = 100) or CABG (n = 250) from January 1995 to April 1999, and 5-year clinical follow-up of 395 patients with unprotected LMCA disease who underwent PCI with drug-eluting stents (DES) (n = 176) or CABG (n = 219) from January 2003 to May 2004. The primary safety end points were all-cause mortality and the composite of death, Q-wave myocardial infarction (MI), or stroke, and the primary efficacy end point was target vessel revascularization (TVR).

Results In the 10-year follow-up cohort of BMS and concurrent CABG, the adjusted risks of death (hazard ratio [HR]: 0.81; 95% confidence interval [CI]: 0.44 to 1.50; p = 0.50) and the composite of death, Q-wave MI, or stroke (HR: 0.92; 95% CI: 0.55 to 1.53; p = 0.74) were similar between the 2 groups. The rate of TVR was significantly higher in the group that received BMS (HR: 10.34; 95% CI: 4.61 to 23.18; p < 0.001). In the 5-year follow-up cohort of DES and concurrent CABG, there was no significant difference in the adjusted risk of death (HR: 0.83; 95% CI: 0.34 to 2.07; p = 0.70) or the risk of the composite outcome (HR: 0.91; 95% CI: 0.45 to 1.83; p = 0.79). The rates of TVR were also higher in the DES group than the CABG group (HR: 6.22; 95% CI: 2.26 to 17.14; p < 0.001).

Conclusions For the treatment of unprotected LMCA disease, PCI with stent implantation showed similar long-term mortality and rates of death, Q-wave MI, or stroke. However, stenting, even with DES, was associated with higher rates of repeat revascularization than was CABG. (J Am Coll Cardiol 2010;56:1366–75) © 2010 by the American College of Cardiology Foundation

Percutaneous coronary intervention (PCI) for patients with unprotected left main coronary artery (LMCA) disease represents a considerable challenge because of technical limitations and the risk of acute or late closure attributable to thrombosis or restenosis. Current guidelines and appropriateness criteria for coronary revascularization recommend coronary artery bypass grafting (CABG) as the standard treatment for patients with LMCA disease (1–3). However,

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improvements in interventional techniques and adjunctive pharmacologic therapy have led to a re-evaluation of the role of PCI as an optional treatment for LMCA disease, and several studies have shown the feasibility and the favorable midterm outcomes of PCI with stenting (4–6). In addition, the availability of drug-eluting stents (DES), which significantly reduce the rates of restenosis and repeat revascularization, has widened the application of PCI to such patients (7–10).

Recently, several reports have shown the successful use of coronary stenting compared with CABG in patients with unprotected LMCA disease (11–13). However, there are currently no data available on the comparative outcomes after PCI or CABG for LMCA disease with follow-up durations of 5 to 10 years (14). We therefore compared the long-term (beyond 5 years) safety and effectiveness of coronary stenting and CABG among patients with unprotected LMCA disease.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CABG = coronary artery bypass grafting
CI = confidence interval
DES = drug-eluting stent(s)
HR = hazard ratio
IVUS = intravascular ultrasound
LMCA = left main coronary artery
MI = myocardial infarction
PCI = percutaneous coronary intervention
TLR = target lesion revascularization
TVR = target vessel revascularization

Methods

Study population and revascularization procedures. The study population consisted of 2 follow-up cohorts: 1) a 10-year follow-up cohort of patients with bare-metal stents (BMS) and concurrent CABG; and 2) a 5-year follow-up cohort of patients with DES and concurrent CABG, as a part of the ASAN-MAIN (ASAN medical center–left MAIN revascularization) registry; a single-center, retrospective study designed to evaluate the treatment effects of stenting and CABG for LMCA disease in the "real world."

For the 10-year follow-up cohort, consecutive patients with unprotected LMCA disease (defined as stenosis of more than 50%) who underwent PCI with BMS or isolated CABG at the Asan Medical Center (Seoul, Korea) between January 1, 1995, and April 30, 1999, were included, and the follow-up period was extended through May 31, 2009, to ensure that all patients had an opportunity to provide at least 10 years of follow-up information. For the 5-year follow-up cohort, consecutive patients with unprotected LMCA disease who underwent DES implantation or isolated CABG between January 1, 2003, and May 31, 2004, were included, and the follow-up period was extended through June 30, 2009, to ensure that all patients had an opportunity for at least 5 years of follow-up information if they were alive. Patients who had prior CABG, those who underwent concomitant valvular or aortic surgery, and those who had myocardial infarction (MI) with ST-segment elevation or presented with cardiogenic shock were excluded.

Patients underwent PCI, instead of CABG, because of either the patient's or physician's preference or the high risk associated with CABG. Methods of stent implantation for patients with LMCA disease have been described previously (9,15). The choice of the specific type of DES (i.e., sirolimus-eluting stent [Cypher, Cordis, Johnson & Johnson, Miami Lakes, Florida] or paclitaxel-eluting stent [Taxus, Boston Scientific, Natick, Massachusetts]) was left to the operator's discretion. All patients undergoing PCI were prescribed aspirin plus ticlopidine (loading dose, 500 mg) or clopidogrel (loading dose, 300 or 600 mg) before or during the coronary intervention. After the procedure, aspirin was continued indefinitely. Patients treated with BMS were prescribed ticlopidine (250 mg twice a day) for at least 1 month, and patients treated with DES were prescribed clopidogrel (75 mg once a day) for at least 6 months, regardless of DES type (16). Treatment beyond this duration was at the discretion of the physician. Surgical revascularization was performed with the use of standard bypass techniques (1). Whenever possible, the internal thoracic artery was used preferentially for revascularization of the left anterior descending artery. Complete revascularization was performed when possible using arterial conduits or saphenous vein grafts.

This study was approved by the local institutional review board.

Outcome variables and definitions. The primary safety outcomes were death and the composite of death, Q-wave MI, or stroke. The primary efficacy outcome was target vessel revascularization (TVR).

All deaths were considered cardiac unless an unequivocal noncardiac cause could be established. The diagnosis of MI was assessed by the universal definition of MI (17). Q-wave MI was defined as the documentation of a new pathologic Q-wave after index treatment. Stroke, as indicated by neurologic deficits, was confirmed by a neurologist on the basis of imaging studies. TVR was defined as repeat revascularization of the treated vessel, including any segments of the left anterior descending or left circumflex coronary artery; TLR was defined as any revascularization performed on the treated segment. The occurrence of stent thrombosis in the DES group was assessed by the Academic Research Consortium definitions (18).

All events were carefully verified and adjudicated by independent clinicians.

Data collection and follow-up. Clinical, angiographic, procedural or operative, and outcome data were recorded in the dedicated PCI and surgical databases by independent research personnel (16). Clinical follow-up after PCI and after CABG was recommended at 1 month, 6 months, and 1 year and then annually thereafter. Routine angiographic follow-up for all patients treated with PCI was recommended 6 to 10 months after the procedure. However, patients who were at high risk for procedural complications of angiography and had no symptoms or signs of ischemia, as well as patients who declined the recommendation, did

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not undergo routine follow-up angiography. For patients who underwent CABG, angiographic follow-up was recommended only if there were ischemic symptoms or signs during follow-up.

For validation of complete follow-up data, information about vital status was obtained through May 31, 2009, for the 10-year follow-up cohort or through June 30, 2009, for the 5-year follow-up cohort, from the National Population Registry of the Korea National Statistical Office with the use of a unique personal identification number. To ensure accurate assessment of clinical end points, additional information was obtained from visits or telephone contacts with living patients or family members and from medical records obtained from other hospitals, as necessary.

Statistical analysis. Continuous variables were compared with the *t* test or Wilcoxon rank sum tests, and categorical variables were compared with the chi-square statistics or Fisher exact test, as appropriate. Survival curves were constructed using Kaplan-Meier estimates and compared with the log-rank test.

To compensate for the nonrandomized design of our observational study and to test for selection bias, we used propensity-score methods (19). The propensity scores were estimated without regard to outcomes, using multiple logis-

Table 1 Baseline Characteristics of the Overall Patient Population

	10-Yr Follow-Up Cohort				5-Yr Follow-Up Cohort			
			p Value				p Value	
Variable	BMS (n = 100)	CABG (n = 250)	Unadjusted	Adjusted*	DES (n = 176)	CABG (n = 219)	Unadjusted	Adjusted*
Demographic characteristics								
Age, yrs	55.1 ± 10.4	60.7 ± 9.1	<0.001	0.47	61.1 ± 11.5	62.4 ± 8.1	0.20	0.84
Male sex	60 (60.0)	186 (74.4)	0.008	0.86	125 (71.0)	162 (74.0)	0.51	0.83
Body mass index, kg/m^2	24.6 ± 3.1	24.6 ± 2.7	0.86	0.82	24.5 ± 2.6	24.6 ± 2.9	0.58	0.99
Cardiac or coexisting conditions								
Diabetes mellitus								
Any diabetes	21 (21.0)	82 (32.8)	0.03	0.57	52 (29.5)	81 (37.0)	0.12	0.61
Insulin-requiring	4 (4.0)	18 (7.2)	0.27	0.88	8 (4.5)	12 (5.5)	0.67	0.25
Hypertension	23 (23.0)	125 (50.0)	<0.001	0.95	83 (47.2)	121 (55.3)	0.11	0.66
Hyperlipidemia	34 (34.0)	115 (46.0)	0.04	0.63	62 (35.2)	121 (55.3)	<0.001	0.98
Current smoker	36 (36.0)	68 (27.2)	0.10	0.79	31 (17.6)	43 (19.6)	0.61	0.92
Previous MI	14 (14.0)	40 (16.0)	0.64	0.81	15 (8.5)	24 (11.0)	0.42	0.81
Previous coronary angioplasty	12 (12.0)	26 (10.4)	0.66	0.98	41 (23.3)	31 (14.2)	0.02	0.90
Previous congestive heart failure	0	8 (3.2)	0.11	—†	1 (0.6)	11 (5.0)	0.01	0.72
Chronic lung disease	0	5 (2.0)	0.33	—†	4 (2.3)	8 (3.7)	0.43	0.79
Cerebrovascular disease	4 (4.0)	40 (16.0)	0.002	0.99	15 (8.5)	26 (11.9)	0.28	0.80
Peripheral vascular disease	4 (4.0)	22 (8.8)	0.12	0.63	3 (1.7)	26 (11.9)	<0.001	0.91
Renal failure	4 (4.0)	13 (5.2)	0.79	0.99	10 (5.7)	15 (6.8)	0.64	0.86
Ejection fraction (%)	60.3 ± 9.1	56.8 ± 11.9	0.004	0.46	59.9 ± 7.7	56.5 ± 11.2	<0.001	0.62
EuroSCORE value	3.3 ± 2.1	4.4 ± 2.2	<0.001	0.90	3.3 ± 2.7	4.5 ± 2.6	<0.001	0.92
Parsonnet score	3.0 ± 4.0	5.0 ± 4.8	<0.001	0.75	5.4 ± 4.7	5.8 ± 6.6	<0.001	0.93
Clinical indication			<0.001	0.98			<0.001	0.96
Stable angina	29 (29.0)	27 (10.8)			97 (55.1)	36 (16.4)		
Unstable angina	68 (68.0)	216 (86.4)			61 (34.7)	171 (78.1)		
NSTEMI	3 (3.0)	7 (2.8)			18 (10.2)	12 (5.5)		
Angiographic characteristics								
Involved location			<0.001	0.40			0.78	0.96
Ostium, midshaft, or both	70 (70.0)	102 (40.8)			57 (32.4)	68 (31.1)		
Distal bifurcation	30 (30.0)	148 (59.2)			119 (67.6)	151 (68.9)		
Extent of diseased vessel			<0.001	0.99			<0.001	0.98
Left main only	55 (55.0)	26 (10.4)			40 (22.7)	10 (4.6)		
Left main plus single-vessel disease	21 (21.0)	36 (14.4)			46 (26.1)	13 (5.9)		
Left main plus double-vessel disease	16 (16.0)	56 (22.4)			47 (26.7)	56 (25.6)		
Left main plus triple-vessel disease	8 (8.0)	132 (52.8)			43 (24.4)	140 (63.9)		
Right coronary artery disease	18 (18.0)	167 (66.8)	<0.001	0.86	74 (42.0)	176 (80.4)	<0.001	0.91
Total occlusion ≥1	13 (13.0)	81 (32.4)	<0.001	0.59	NA	NA	NA	NA
Restenotic lesion	NA	NA	NA	NA	9 (5.1)	5 (2.3)	0.13	0.94

Data are shown as mean ± SD for continuous variables and absolute numbers (percentages) for dichotomous variables. *Propensity score-adjusted p value. Comparisons were performed with the use of a logistic regression model with patient risk factors and propensity score as independent control variables. †Could not be estimated.

BMS = bare-metal stent(s); CABG = coronary-artery bypass grafting; DES = drug-eluting stent(s); MI = myocardial infarction; NA = not available; NSTEMI = non–ST-segment elevation myocardial infarction.

tic regression analysis. A full nonparsimonious model was developed that included all variables shown in Table 1. Model discrimination was assessed with *c*-statistics, and model calibration was assessed with Hosmer-Lemeshow statistics. The individual propensity score, as well as the type of revascularization, was incorporated into the Cox regression model as a covariate to calculate the propensity-adjusted hazard ratio (HR). The propensity score was also subdivided into quartiles (20). Treatment effect was separately estimated within each quartile, and quartile estimates were combined to measure an overall estimate of the treatment effect. All statistical analyses were performed using SAS version 9.1 (SAS Institute, Cary, North Carolina). A 2-tailed p value of <0.05 was considered statistically significant.

Results

Baseline characteristics and revascularization procedures. Between January 1995 and April 1999, a total of 350 patients with unprotected LMCA disease met the criteria for inclusion. Of these, 100 were treated with PCI with BMS and 250 with CABG, and were eligible for the 10-year follow-up cohort. Between January 2003 and May 2004, a total of 395 patients with unprotected LMCA disease met the study inclusion criteria and met none of the criteria for exclusion. Of these, 176 who were treated with PCI with DES and 219 with CABG were eligible for the 5-year follow-up cohort.

The baseline characteristics of study patients according to revascularization procedure are shown in Table 1. CABG patients had a significantly higher-risk clinical and angiographic profile than PCI patients. Procedural characteristics are presented in Table 2. For the 10-year follow-up cohort, complete revascularization was achieved in 67 BMS patients (67.0%) and in 209 CABG patients (83.6%; p = 0.001). For the 5-year follow-up cohort, complete revascularization was achieved in 126 DES patients (71.6%) and in 176 CABG patients (80.4%; p = 0.04). In the DES group, sirolimus-eluting stents were used exclusively, and intravascular ultrasound (IVUS)-guided stenting was performed in almost 90% of patients.

Observed in-hospital and long-term event rates. The observed (unadjusted) in-hospital clinical events are shown in Table 3. Individual rates of in-hospital death, MI, stroke, and TVR were not different between the 2 groups. However, the rate of the composite of death, Q-wave MI, or stroke in the CABG group was significantly higher than in the stenting group, irrespective of stent type.

For the 10-year follow-up cohort, complete follow-up data for major clinical events at 10 years were obtained in 96.9% of the overall cohort (96.0% for the BMS group and 97.2% for the CABG cohort). For the 5-year follow-up cohort, complete follow-up data for major clinical events at 5 years after index treatment were obtained in 97.2% of the overall cohort (97.7% for the DES group and 96.8% for the CABG group). Crude event rates and unadjusted long-term event-free survival curves according to treatment approach are presented in Table 3 and Figure 1. The observed (unadjusted) long-term rates of death and the composite of death, Q-wave MI, or stroke were significantly lower in the PCI group than in the CABG group, whereas the rate of TVR was higher in the PCI group.

In the DES group, 3 patients had definite thrombosis, none had probable thrombosis, and 2 had possible thrombosis. At 5-year follow-up, the cumulative incidence of definite or probable stent thrombosis was 1.8%. Among patients with definite or probable stent thrombosis, 1 patient had acute, 1 had subacute, and 1 had very late (4.3 years after the procedure) thrombosis. Acute and subacute cases were on dual antiplatelet therapy at the time of thrombotic events, and a very late case arose 2 months later, after all antiplatelet therapy was interrupted.

Adjusted primary safety and efficacy outcomes. Table 4 and Figure 2 represent the adjusted primary safety and efficacy outcomes based on revascularization procedure. The *c*-statistic for the propensity score model was 0.87 (Hosmer-Lemeshow goodness-of-fit p = 0.56) in the 10-year cohort and 0.88 (Hosmer-Lemeshow goodness-of-fit p = 0.97) in the 5-year cohort. All covariates differed nonsignificantly after propensity score adjustment (Table 1). In the propensity score– and propensity score quartile–adjusted analyses,

Table 2 Procedural Characteristics of Patients Treated With CABG and Stenting

	10-Yr Follow-Up Cohort	5-Yr Follow-Up Cohort
CABG patients, n	250	219
On-pump surgery	243 (97.2)	178 (81.3)
Grafts per patients	4.3 ± 1.2	3.3 ± 1.0
Arterial grafts per patient	1.1 ± 0.7	2.5 ± 0.9
Venous grafts per patient	3.2 ± 1.4	0.9 ± 0.7
Use of at least 1 arterial conduit	226 (90.4)	215 (98.2)
Use of IMA-to-LAD graft	225 (90.0)	209 (95.4)
PCI patients, n	100 with BMS	176 with DES
Stent type		
Sirolimus-eluting stents	—	168 (95.5)
Paclitaxel-eluting stents	—	8 (4.5)
Total number of stents in LMCA lesions	1.3 ± 0.6	1.3 ± 0.6
Total length of stents in LMCA lesions	16.2 ± 9.2	35.2 ± 27.0
Total number of stents in a patient	1.6 ± 0.9	2.5 ± 1.4
Maximal balloon size	4.4 ± 0.6	3.9 ± 0.5
Maximal pressure, atm	15.8 ± 2.4	18.7 ± 2.4
Support of intra-aortic balloon pump	5 (5.0)	12 (6.8)
Guidance of intravascular ultrasound	67 (67.0)	157 (89.2)
Use of glycoprotein IIb/IIIa inhibitor	5 (5.0)	11 (6.3)
Distal bifurcation treatment, n	30	119
Single stenting	15 (50.0)	71 (59.7)
Complex bifurcation stenting	15 (50.0)	48 (40.3)

Data are shown as mean ± SD for continuous variables and absolute numbers (%) for dichotomous variables.

IMA = internal mammary artery; LAD = left anterior descending coronary artery; LMCA = left main coronary artery; PCI = percutaneous coronary intervention; other abbreviations as in Table 1.

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Table 3 In-Hospital and Long-Term Clinical Events According to Study Group*

	10-Yr Follow-Up Cohort			5-Yr Follow-Up Cohort		
	BMS (n = 100)	CABG (n = 250)	p Value†	DES (n = 176)	CABG (n = 219)	p Value†
Clinical events, n (%)						
In-hospital outcomes						
Death	0	6 (2.4)	0.19	0	5 (2.3)	0.07
Cardiac	0	4 (1.6)	0.58	0	5 (2.3)	0.07
Noncardiac	0	2 (0.8)	>0.99	0	0	—
MI	8 (8.0)	21 (8.4)	0.90	19 (10.8)	17 (7.8)	0.30
Q-wave	2 (2.0)	14 (5.6)	0.26	3 (1.7)	8 (3.7)	0.36
Non–Q-wave	6 (6.0)	7 (2.8)	0.21	16 (9.1)	9 (4.1)	0.04
Stroke	0	2 (0.8)	>0.99	1 (0.6)	6 (2.7)	0.14
Death, Q-wave MI, or stroke	2 (2.0)	19 (7.6)	0.046	4 (2.3)	18 (8.2)	0.01
Any revascularization	2 (2.0)	1 (0.4)	0.20	1 (0.6)	1 (0.5)	>0.99
Percutaneous	1 (1.0)	1 (0.4)	0.49	1 (0.6)	1 (0.5)	>0.99
Surgical	1 (1.0)	0	0.29	0	0	—
TLR	2 (2.0)	1 (0.4)	0.20	1 (0.6)	1 (0.5)	>0.99
TVR	2 (2.0)	1 (0.4)	0.20	1 (0.6)	1 (0.5)	>0.99
Cumulative long-term outcomes						
Death	15 (15.9)	59 (24.1)	0.02	10 (5.9)	24 (11.2)	0.03
Cardiac	6 (6.9)	25 (11.0)	0.10	6 (3.7)	13 (6.1)	0.22
Noncardiac	9 (9.6)	34 (14.8)	0.08	4 (2.3)	11 (5.4)	0.06
MI	15 (16.0)	29 (12.1)	0.43	27 (15.7)	21 (9.7)	0.12
Q-wave	7 (7.8)	20 (8.5)	0.72	9 (5.5)	12 (5.6)	0.67
Non–Q-wave	8 (8.3)	9 (3.6)	0.09	18 (10.2)	9 (4.1)	0.02
Stroke	5 (5.5)	18 (8.8)	0.22	3 (1.7)	12 (5.9)	0.04
Death, Q-wave MI, or stroke	24 (25.2)	78 (32.1)	0.04	17 (10.0)	41 (19.1)	0.004
Any revascularization	41 (43.1)	15 (6.7)	<0.001	32 (19.7)	10 (5.0)	<0.001
Percutaneous	31 (34.2)	14 (6.2)	<0.001	27 (16.6)	9 (4.5)	0.002
Surgical	10 (10.2)	1 (0.5)	<0.001	5 (3.1)	1 (0.5)	0.11
TLR	24 (24.9)	11 (4.9)	<0.001	21 (13.2)	6 (2.9)	0.001
TVR	35 (36.7)	11 (4.9)	<0.001	26 (16.2)	6 (2.9)	<0.001

Values are n (%). *Outcome rates were derived from Kaplan-Meier curves. †The p values were calculated with the use of the chi-square test or Fisher exact test for in-hospital outcomes, as appropriate, and the log-rank test for cumulative long-term outcomes.

TLR = target lesion revascularization; TVR = target vessel revascularization; other abbreviations as in Table 1.

long-term risks of death and the composite of death, Q-wave MI, or stroke in the 10-year follow-up cohort of BMS and concurrent CABG were similar in the 2 groups. However, the adjusted risk of TVR was significantly higher in the PCI group. These findings were consistent with those of the 5-year follow-up cohort of DES and concurrent CABG.

Discussion

In a long-term (10-year for BMS and 5-year for DES) observational study of consecutive patients with unprotected LMCA disease, we found that the adjusted long-term risks of death and a composite of serious outcomes (death, Q-wave MI, or stroke) were similar in the PCI group and the CABG group. In contrast, the rate of TVR was significantly lower in the CABG group than in the PCI group.

Several small observational studies comparing DES and CABG in LMCA disease showed that the early clinical events of left main stenting were similar or superior to those of bypass surgery, because of a significant increase in periprocedural MI or stroke in CABG patients, and that mid-term mortality within 1 year was similar in the PCI and CABG groups (11,12,21,22). However, the risk of TVR was consistently higher with PCI than with CABG. Recent results from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry with median 3-year follow-up and the LMCA subgroup analysis of the SYNTAX (Synergy Between Percutaneous Coronary Intervention With TAXUS and Cardiac Surgery) trial also showed similar findings (13,23). On the basis of these results, recent practice guidelines have updated the class of recommendation of PCI for patients with unprotected LMCA disease from class III to IIb (2). However, several clinical trials comparing PCI to CABG for multivessel disease, in which LMCA disease was mostly excluded, frequently include patients with follow-up durations of 5 to 10 years (24,25). Whether or not the results achieved with coronary stents will be stable for 5 to 10 years remains to be

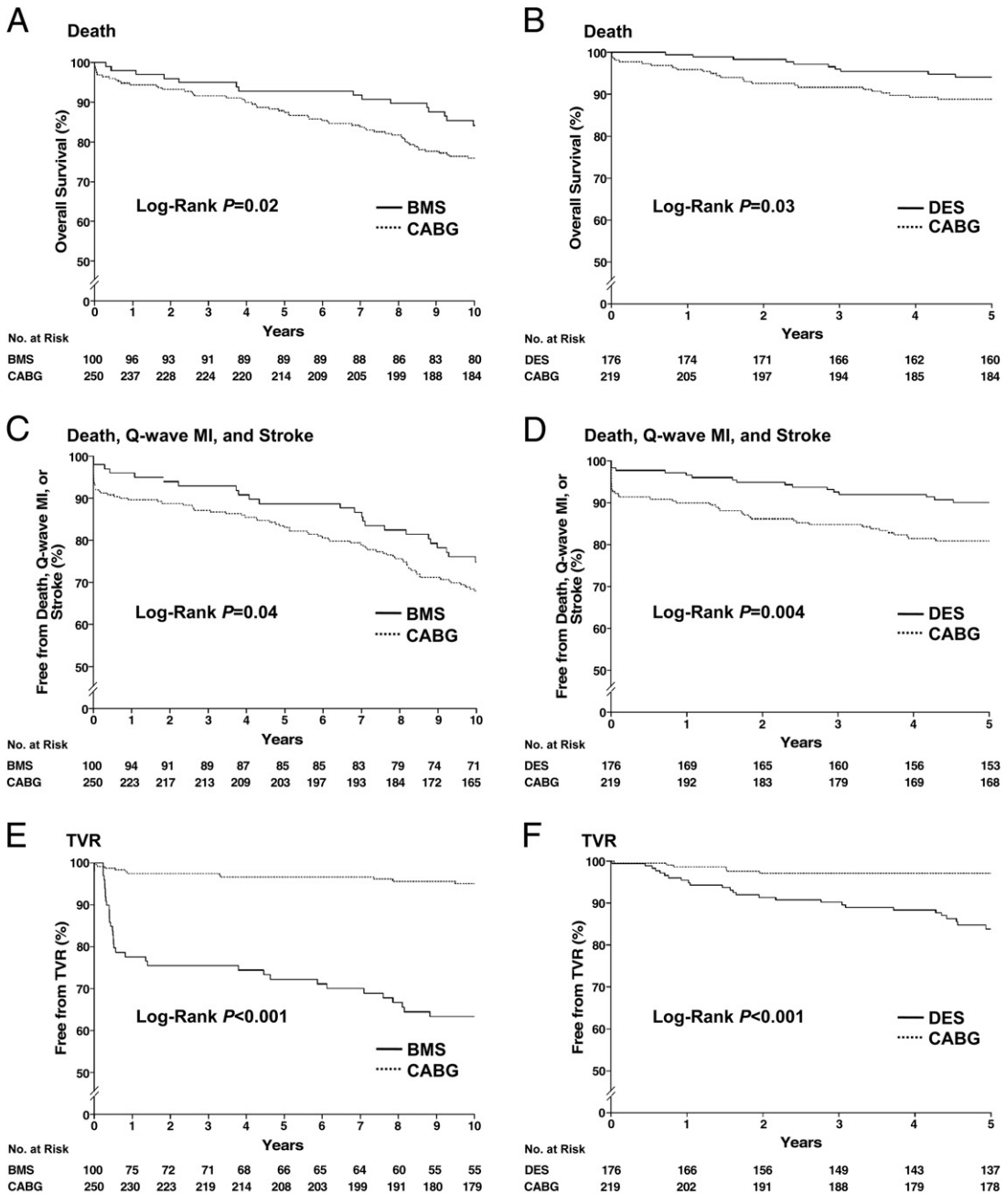

Figure 1 **Unadjusted Survival Curves**

(A and B) show long-term survival, **(C and D)** show survival free from Q-wave myocardial infarction or stroke, and **(E and F)** show survival free from target vessel revascularization. **A, C, and D** show 10-year unadjusted survival curves between bare-metal stents (BMS) and concurrent coronary artery bypass grafting (CABG), and **B, D, and F** show 5-year unadjusted survival curves between drug-eluting stents (DES) and concurrent CABG.

determined in unprotected LMCA disease. To the best of our knowledge, this study is the longest follow-up study to compare coronary stenting, even with BMS or DES, with bypass surgery for treatment of unprotected LMCA stenosis. Therefore, our study provides important information about a sufficient long-term effect of stenting as compared with CABG, and it is probably best viewed as an indication to proceed with larger, randomized trials with long-term follow-up.

The current study extends the previous findings of several observational studies and clinical trials up to 5 to 10 years. Although adjusted risks of safety outcomes were similar between the 2 groups, the benefits of surgery over PCI have been evident for fewer repeat revasculariza-

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Table 4 Hazard Ratios for Primary Safety and Efficacy Clinical Outcomes After Stenting as Compared With After CABG*

Model	Death		Composite of Death, Q-Wave MI, or Stroke		TVR	
	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value	Hazard Ratio (95% CI)	p Value
10-yr follow-up cohort (BMS vs. concurrent CABG)						
Crude	0.53 (0.31–0.90)	0.02	0.64 (0.42–0.99)	0.04	8.80 (4.57–16.91)	<0.001
Propensity score adjusted	0.81 (0.44–1.50)	0.50	0.92 (0.55–1.53)	0.74	10.34 (4.61–23.18)	<0.001
Stratified analyses based on propensity scores						
Quartile 1	2.35 (0.32–17.46)	0.40	1.78 (0.24–13.09)	0.57	—†	—†
Quartile 2	0.67 (0.20–2.20)	0.51	0.73 (0.26–2.04)	0.54	5.07 (1.21–21.25)	0.03
Quartile 3	0.49 (0.14–1.71)	0.26	0.78 (0.33–1.86)	0.58	18.80 (4.23–83.46)	<0.001
Quartile 4	2.41 (0.52–11.03)	0.26	2.27 (0.65–7.91)	0.20	9.71 (1.30–72.37)	0.03
Summary‡	0.91 (0.49–1.69)	0.76	1.02 (0.61–1.71)	0.93	9.25 (4.17–20.50)	<0.001
5-yr follow-up cohort (DES vs. concurrent CABG)						
Crude	0.46 (0.22–0.94)	0.04	0.45 (0.26–0.78)	0.005	4.64 (2.01–10.68)	<0.001
Propensity score adjusted	0.83 (0.34–2.07)	0.70	0.91 (0.45–1.83)	0.79	6.22 (2.26–17.14)	<0.001
Stratified analyses based on propensity scores						
Quartile 1	—†	—†	0.55 (0.07–4.04)	0.55	15.44 (2.17–110.09)	0.006
Quartile 2	0.63 (0.07–5.41)	0.68	0.78 (0.22–2.75)	0.69	2.35 (0.53–10.52)	0.26
Quartile 3	0.56 (0.16–1.94)	0.36	0.69 (0.23–2.04)	0.50	6.00 (0.77–46.89)	0.09
Quartile 4	—†	—†	—†	—†	—†	—†
Summary‡	0.58 (0.23–1.46)	0.25	0.79 (0.39–1.59)	0.50	5.31 (1.91–14.71)	0.001

*Hazard ratios are for the stent group as compared with the CABG group. †Could not be estimated. ‡Likelihood ratio test for homogeneity: in the 10-year follow-up cohort ($p = 0.30$ for death; $p = 0.45$ for composite of death, Q-wave MI, or stroke; $p = 0.67$ for TVR) and in the 5-year follow-up cohort ($p = 0.99$ for death; $p = 0.99$ for composite of death, Q-wave MI, or stroke; $p = 0.52$ for TVR).
CI = confidence interval; other abbreviations as in Tables 1 and 3.

tions. However, there was the possibility that a significantly higher rate of follow-up angiography in the PCI group than in the CABG group (94.0% in BMS vs. 19.6% in concurrent CABG, $p < 0.001$, and 76.1% in DES vs. 11.9% in concurrent CABG, $p < 0.001$) could have penalized the PCI group, and the rate of asymptomatic graft occlusion might have been underestimated in the CABG group. In addition, higher rates of incomplete revascularization in PCI patients might have influenced the rate of subsequent late revascularization, particularly if those were scheduled for surveillance angiography. The increase in the rate of repeat revascularization with PCI did not appear to translate into significant overall increases of mortality or serious safety outcomes. The risk of repeat revascularization after PCI needs to be balanced against the greater invasiveness and the higher procedural risk associated with CABG, without significant differences in long-term safety outcomes.

In our multicenter, observational study (MAIN-COMPARE registry), there was a trend toward higher rates of death and the composite end point (death, Q-wave MI, or stroke) in the DES group compared with CABG (13). However, a nonsignificant trend toward higher event rates with DES was not seen in this longer-term follow-up study. Because current available studies were underpowered to detect significant differences in mortality or hard end points, these findings should be confirmed or refuted through a larger cohort of patients with longer-term follow-up.

Recently, long-term safety concerns about DES use have been raised, due to increased risks of late stent thrombosis and late mortality (26,27). Considering the catastrophic consequences of stent thrombosis in LMCA stenting, a lack of long-term clinical data have hampered the widespread use of PCI with DES as an alternative to CABG for such patients. Overall ST rates (definite or probable) in patients with unprotected LMCA stents have been reported to range between 1% and 2% within 1 to 3 years (13,28–30). Although our number of patients was too small to accurately assess the long-term risk of stent thrombosis, we observed a similar incidence of definite or probable stent thrombosis (1.8%), providing further evidence that LMCA stenting with DES results in lower or, at worst, similar rates of stent thrombosis and long-term mortality than are observed in patients with other coronary lesions (31).

In our study, the adjunctive use of IVUS is generally recommended while performing left main stenting. Although the clinical impact of IVUS in DES placement is not yet clear, routine use of IVUS can be very helpful in optimally expanding the stent, with or without post-stent balloon dilation, to avoid under- or overstretch of the stent diameter in complex settings such as left main disease, and might partly contribute to better long-term outcomes as compared with conventional angiography guidance (32).

Study limitations. First, our study is an observational study, and therefore, the choice of treatment was at the discretion of the physician or the patient. Although we used propensity analysis to enable a rigorous adjustment for selection bias and confounding, there is no way to eliminate bias caused by the influence of unmeasured confounders, or the presence of patients deemed to be

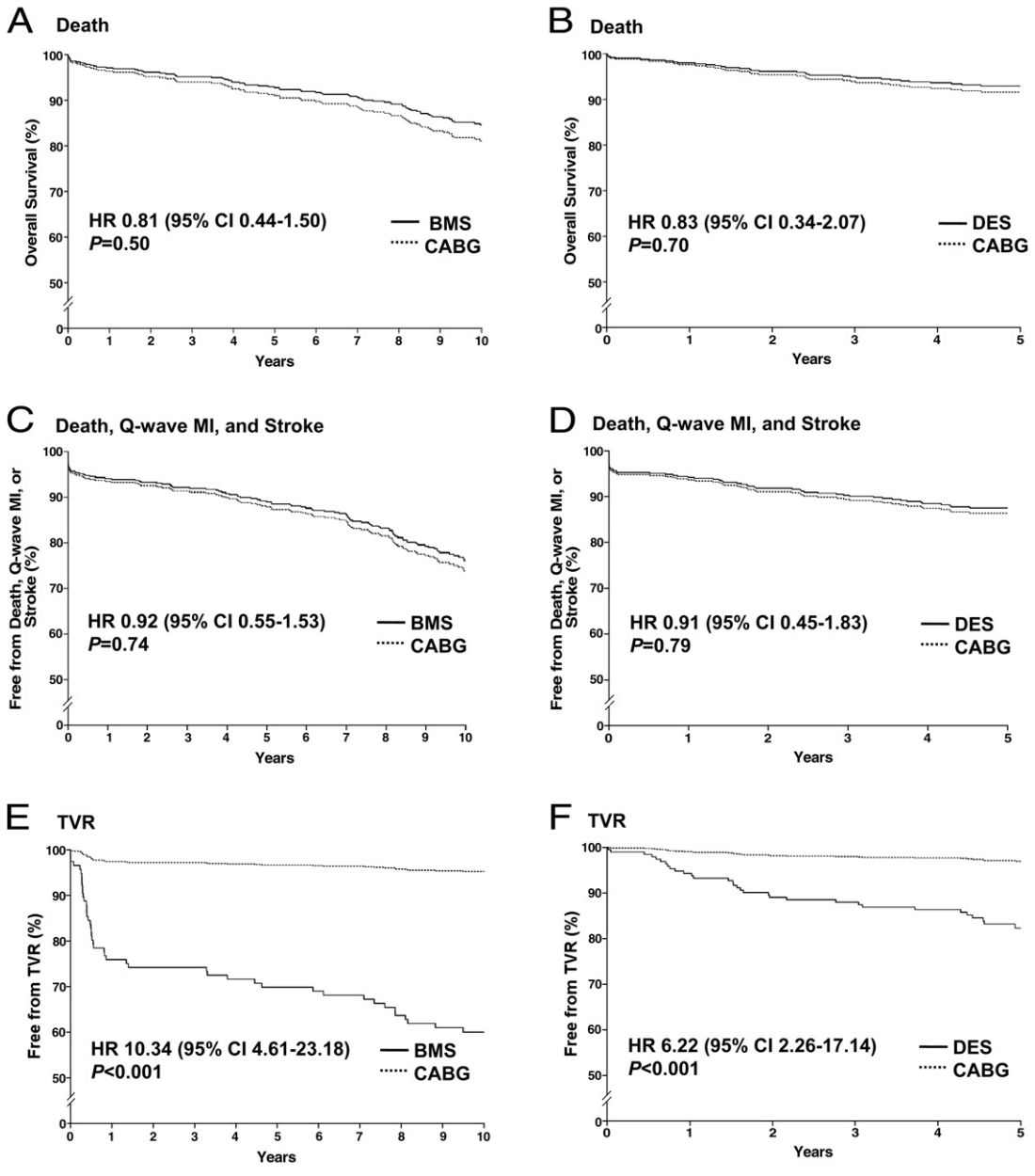

Figure 2 **Adjusted Survival Curves**

(A and B) show long-term survival, **(C and D)** show survival free from Q-wave myocardial infarction (MI) or stroke, and **(E and F)** show survival free from target vessel revascularization (TVR). **A, C, and D** show 10-year adjusted survival curves between bare-metal stents (BMS) and concurrent coronary artery bypass grafting (CABG), and **B, D, and F** show 5-year adjusted survival curves between drug-eluting stents (DES) and concurrent CABG. The curves represent estimations from the Cox regression model at the mean level of the propensity score.

ineligible for 1 of the procedures. Thus, rather than subgroup analysis, LMCA-specific randomized trials with a larger number of patients and longer follow-up, such as the PRE-COMBAT (Randomized Comparison of Bypass Surgery Versus Angioplasty Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease) or EXCEL (Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) clinical trial, are needed to confirm whether PCI treatment for LMCA disease is equivalent to CABG (14). Second, our analysis was underpowered to detect significant differences in mortality and serious composite outcomes among the treatment groups and to assess the long-term risk of stent thrombosis, due to the limited number of events. Third, we did not use a detailed scoring system (i.e., the SYNTAX

score) to more accurately reflect atherosclerotic disease burden and anatomic complexity. Fourth, the average surgical risk of our study population, as measured by EuroSCORE and Parsonnet score, was relatively low. Finally, the particulars of clinical practice as well as the specific expertise of the interventional cardiologists and cardiac surgeons in our institution may differ from those of other institutions and practitioners, potentially limiting the reproducibility of these results in other settings.

Conclusions

During 10-year follow-up with BMS and 5-year follow-up with DES, PCI with coronary stenting and CABG were associated with similar long-term rates of death and the composite end point of death, Q-wave MI, or stroke for patients with unprotected LMCA disease. Rates of TVR were higher among patients who underwent PCI than among those who underwent CABG. These findings should be confirmed or refuted through larger clinical trials with long-term follow-up.

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Key Words: coronary disease ■ revascularization ■ stents ■ surgery.