Long-Term Outcome of Stents Versus Bypass Surgery in Diabetic and Nondiabetic Patients With Multivessel or Left Main Coronary Artery Disease

A Pooled Analysis of 5775 Individual Patient Data

Duk-Woo Park, MD; Young-Hak Kim, MD; Hae Geun Song, MD; Jung-Min Ahn, MD; Won-Jang Kim, MD; Jong-Young Lee, MD; Soo-Jin Kang, MD; Seung-Whan Lee, MD; Cheol Whan Lee, MD; Seong-Wook Park, MD; Sung-Cheol Yun, PhD; Sung-Ho Chung, MD; Suk Jung Choo, MD; Cheol Hyun Chung, MD; Jae-Won Lee, MD; Seung-Jung Park, MD

***Background*—**Coronary artery bypass grafting and percutaneous coronary intervention (PCI) are alternative treatments for complex multivessel or left main disease. However, the relative treatment effects in diabetic and nondiabetic patients remain uncertain.

***Methods and Results*—**We performed a pooled analysis of 5775 patients from 3 clinical studies comparing PCI and coronary artery bypass grafting for multivessel or left main disease and compared adverse outcomes (death; a composite outcome of death, Q-wave myocardial infarction, or stroke; and repeat revascularization) according to the diabetic status. Over a median follow-up of 5.5 years, risk-adjusted mortality after PCI relative to coronary artery bypass grafting was not different in diabetic (hazard ratio [HR], 1.15; 95% CI, 0.88–1.51) and nondiabetic (HR, 1.15; 95% CI, 0.88–1.50) patients. The adjusted risks of the composite outcome of death, Q-wave myocardial infarction, or stroke were also not different in diabetic (HR, 1.00; 95% CI, 0.79–1.26) and nondiabetic (HR, 0.99; 95% CI, 0.78–1.26) patients. However, PCI was significantly associated with higher risk of repeat revascularization both in diabetic (HR, 3.56; 95% CI, 2.62–4.83) and in nondiabetic (HR, 3.55; 95% CI, 2.61–4.83) patients. Significant interactions were absent between diabetic status and revascularization strategies for death (P=0.27), composite outcome of death, Q-wave myocardial infarction, or stroke (P=0.97), and repeat revascularization (P=0.08).

***Conclusions*—**For multivessel or left main disease, the long-term risks of mortality and composite serious outcomes were not different between PCI and coronary artery bypass grafting in diabetic and nondiabetic patients, but PCI was associated with higher risk of repeat revascularization. These relative treatment effects were not modified by diabetic status. These results are hypothesis generating and should be addressed in a randomized trial. **(*Circ Cardiovasc Interv*. 2012;5:467-475.)**

Key Words: coronary disease ■ revascularization ■ stents ■ surgery

Patients with diabetes mellitus are at increased risk for aggressive form of coronary artery disease (CAD) and have a higher risk of cardiovascular events and death than those without diabetes mellitus.[1,2] Coronary artery bypass graft (CABG) and percutaneous coronary intervention (PCI) are alternative revascularization procedures for patients with complex CAD, such as multivessel or left main disease. However, the relative effects of these 2 procedures on patient outcomes (mortality, myocardial infarction [MI], stroke, and repeat procedures) may vary according to the presence of diabetes mellitus and remain under considerable debate.[3] Several previous studies provide conflicting data on outcome according to diabetic status, but these studies had limited numbers of patients, restricted inclusion of study population, and lacked long-term data for drug-eluting stents (DES).[4–7]

Pooling individual patient data from observational studies substantially increases the number of patients and provides a more precise assessment of the relative treatment effects according to major clinical subset of diabetes mellitus in routine clinical practice. We, therefore, performed a pooled analysis of patient-level data from 3 observational cohorts of multivessel or left main CAD to compare outcomes after PCI and CABG in diabetic and nondiabetic patients and to

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From the Division of Cardiology (D.-W.P., Y.-H.K., H.G.S., J.-M.A., W.-J.K., J.-Y.L., S.-J.K., S.-W.L., C.W.L., S.-W.P., S.-J.P.) and Cardiac Surgery (S.-H.C., S.J.C., C.H.C., J.W.L.), and Division of Biostatistics, Center for Medical Research and Information (S.-C.Y.), University of Ulsan College of Medicine, Seoul, Korea.

Correspondence to Seung-Jung Park, MD, Division of Cardiology, University of Ulsan College of Medicine, Asan Medical Center, 388-1 Poongnap-dong, Songpa-gu, Seoul, 138-736, Korea. E-mail sjpark@amc.seoul.kr

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determine whether outcome was modified by the presence or absence of medically treated diabetes mellitus.

WHAT IS KNOWN

- Coronary artery bypass graft and percutaneous coronary intervention are alternative revascularization procedures for patients with multivessel or left main coronary artery disease.
- The relative benefits of coronary artery bypass graft and percutaneous coronary intervention on patient outcomes (mortality, myocardial infarction, stroke, and repeat procedures) vary according to the presence or absence of diabetes mellitus, but previous studies provide conflicting data on long-term outcome.

WHAT THE STUDY ADDS

- In this study, risk-adjusted long-term rates of mortality and serious composite outcomes are not different after percutaneous coronary intervention and coronary artery bypass graft both in diabetic and in nondiabetic patients with multivessel or left main coronary artery disease. However, the rate of repeat revascularization was higher in the percutaneous coronary intervention group.
- Due to the nonrandomized nature of data, these results are hypothesis generating and should be confirmed through large, randomized clinical trials.

Methods

Study Population and Procedures

For the present analysis, databases from 3 clinical registries were pooled to provide a patient-level analysis. The features of the merged 3 study cohort (the Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization [MAIN-COMPARE] registry,[8] the Asan-Multivessel registry,[9] and the ASAN Medical Center–Left MAIN Revascularization [ASAN–MAIN] registry)[10] are shown in Table 1. Briefly, all enrolled registries are observational cohort studies comparing the relative treatment effects of PCI and CABG for multivessel (defined as stenosis of ≥70% in at least 2 of the 3 major epicardial vessel) or left main (defined as stenosis of ≥50%) CAD in routine clinical practice. These registries contain information on patient demographics, cardiac risk factors, clinical manifestations, hemodynamic status, left ventricular function, extent of disease, details of the procedures, and outcomes during follow-up, which are recorded in a uniform format database. The local ethics committee at each hospital approved the use of clinical data for this study, and all patients provided written informed consent.

The choice of revascularization was at the discretion of the treating physician and the patient. For these decisions, several clinical (age, comorbidity, hemodynamic status, clinical presentations, left ventricular function, prior history of PCI or CABG, and patient's refusal) and angiographic (coronary anatomy, angiographic disease extents, and procedural complexities) factors were considered as possible factors that were likely to have influenced the selection of a procedure for individual. All interventions were performed according to current standard guidelines, and the type of stent implanted was at the discretion of the operator. Antiplatelet therapy and periprocedural anticoagulation were administered according to standard regimens. All patients undergoing PCI were prescribed aspirin (loading dose, 200 mg) plus clopidogrel (loading dose, 300 mg or 600 mg) or ticlopidine (loading dose, 500 mg) before or during the coronary intervention. After the procedure, aspirin was continued indefinitely. Patients treated with bare-metal stents (BMS) were prescribed clopidogrel or ticlopidine for at least 1 month, and patients treated with DES were prescribed clopidogrel for at least 6 months. Surgical revascularization was performed using standard bypass techniques, and whenever possible, the internal thoracic artery was used preferentially for revascularization of the left anterior descending artery.

End Points, Definitions, and Follow-Up

The primary safety outcomes were death and a composite of death, Q-wave MI, or stroke. The primary efficacy outcome was repeat revascularization. All events were based on clinical diagnoses made by the patient's physician and were centrally adjudicated by an independent group of clinicians. Death was defined as death from any cause. Q-wave MI was defined as documentation of a new, pathological Q wave in 2 contiguous leads after the index treatment. Stroke, as indicated by neurological deficits, was confirmed by a neurologist on the basis of imaging studies. Repeat revascularization included any type of subsequent target vessel and nontarget vessel revascularization, regardless of whether the procedure was clinically or angiographically driven. For the primary analysis, medically treated diabetes mellitus was defined as treatment with oral hypoglycemic agents or insulin at the time of enrollment in accordance with prior studies.[11,12]

Clinical, angiographic, procedural or operative, and outcome data were recorded in the dedicated PCI and surgical databases by independent research personnel. Clinical follow-up was performed at 1 month, 6 months, and 1 year and then annually thereafter, via office visit or telephone contact. For validation of complete follow-up data regarding mortality, information about vital status was obtained from the National Population Registry of the Korea National Statistical Office using a unique personal identification number.

Statistical Analysis

Differences between treatment groups were evaluated by the Student *t* test for continuous variables and by the χ^2 or Fisher exact test for categorical variables. For descriptive analyses, we pooled individual patient data from all 3 studies and created unadjusted Kaplan-Meier survival curves. For statistical analyses, we used Cox proportional-hazards models to compare clinical end points of PCI and CABG in diabetic and nondiabetic patients.[13] We tested for interactions of treatment methods with the presence of diabetes mellitus by use of multivariable, stratified Cox models that included treatment group (PCI or CABG), diabetic status, and their interaction. The assumptions of the proportional hazards statistically were assessed on the basis of Schoenfeld residuals and graphically using log-log plots.

To compensate for the nonrandomized design of observational studies and to reduce the impact of selection bias between the 2 revascularization procedures, we performed rigorous adjustment for differences in baseline characteristics of patients using weighted Cox proportional-hazards regression models with inverse-probability-of-treatment weighting.[14] For this technique, the weights for patients undergoing CABG were the inverse of (1–propensity score), and weights for patients receiving PCI were the inverse of the propensity score. The propensity scores were estimated without regard to outcomes, using multiple logistic-regression analysis. All prespecified variables were included in the respective models (Table 1). Model discrimination was assessed with *c*-statistics, and model calibration was assessed with Hosmer-Lemeshow statistics. Interaction terms in the weighted Cox model using the inverse-probability-of-treatment weighting method were used to test for the statistical significance of 2 treatment effects (PCI versus CABG) by diabetic status on clinical outcomes. We also assessed whether the presence or absence of left main disease or the types of stent (ie, BMS or DES) had an effect on treatment outcome.

All reported *P* values are 2-sided, and $P<0.05$ was considered statistically significant. SAS software version 9.1 (SAS Institute, Inc, Cary, NC) was used for statistical analyses.

Table 1. Study Characteristics

	MAIN-COMPARE Registry	ASAN-Multivessel Registry	ASAN-MAIN Registry
Study type	Multicenter (12 hospitals), prospective, observational	Single-center, prospective, observational	Single-center, retrospective, observational
Study criteria	Left main disease Isolated CABG or PCI; Exclude previous CABG, STEMI or cardiogenic shock, and concomitant valvular or aortic surgery	Multivessel±left main disease Isolated CABG or PCI; Exclude previous CABG, Acute MI or cardiogenic shock, and concomitant valvular or aortic surgery	Left main disease Isolated CABG or PCI; Exclude previous CABG, STEMI or cardiogenic shock, and concomitant valvular or aortic surgery
Total number of CABG patients	1138	1495	469
Total number of PCI patients	1102 (784 DES, 318 BMS)	1547 (all DES)	276 (176 DES, 100 BMS)
Recruitment period of the study patients	January 2000 to June 2006	January 2003 to December 2005	Pre-DES cohort: January 1995 to April 1999 DES cohort: January 2003 to May 2004
Age (mean)	62	63	61
Male, %	72	71	72
Diabetes mellitus, %	32	29	32
Noninsulin treated, %	24	24	26
Insulin treated, %	8	5	6
Previous MI, %	10	10	13
Acute coronary syndrome, %	72	53	75
Ejection fraction, % (mean)	59	58	58
IMA use in CABG, %	98	96	93
Follow-up, y (median)	5.3	5.6	5.8
Follow-up completeness	98.1% in the PCI and 97.6% in the CABG	97.7% in the PCI and 97.0% in the CABG	97.2% in the PCI and 97.0% in the CABG

ASAN–MAIN indicates ASAN Medical Center–Left MAIN Revascularization; BMS, bare-metal stents; CABG, coronary artery bypass grafting; DES, drug-eluting stents; IMA, internal mammary artery; MAIN-COMPARE, Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization; MI, myocardial infarction; PCI, percutaneous coronary intervention; STEMI, ST-Segment–Elevation Myocardial Infarction. Data are mean±SD or number (%).

Results

Patient Characteristics

The 3 studies used in this analysis provided data on 6027 patients. After exclusion of patients concurrently enrolled in different studies, the main analysis cohort included 5775 patients with multivessel or left main CAD, in which 2789 subjects were treated with PCI and 2986 subjects were treated with CABG. In the overall population, 1761 (31%) patients had medically treated diabetes mellitus. Among patients treated with PCI, 15% received BMS and 85% received DES.

The baseline characteristics of study patients according to diabetic status and revascularization strategies are presented in Table 2. Overall, diabetic patients had higher-risk profiles of baseline characteristics than nondiabetic patients, and the CABG group had higher clinical and angiographic risk profiles than the PCI group both in diabetic and in nondiabetic patients.

Clinical Outcomes

The median overall follow-up time was 5.5 years (interquartile range, 4.4–6.5 years). During follow-up, 740 patients (12.8%) died, of whom 446 (7.7%) died of a cardiovascular cause. A total of 117 (2.0%) patients suffered an acute Q-wave MI, and 157 (2.7%) suffered a stroke. Repeat revascularization was performed in 660 patients (11.4%).

Unadjusted (observed) 5-year clinical outcomes of PCI versus CABG according to diabetic status are shown in Figure 1 and Table 3. Among patients with and without diabetes mellitus, the 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 repeat revascularization was significantly higher in the PCI group. No significant interactions were noted between treatment strategies and diabetic status for the 5-year unadjusted risks of death (P=0.34), composite outcome (P=0.77), and repeat revascularization (P=0.16).

Adjusted outcomes using the weighted Cox model with inverse-probability-of-treatment weighting are shown in Table 4. In the diabetic population, the risks of death and the composite of death, Q-wave MI, or stroke were not significantly different between the 2 treatment groups. However, the adjusted risk of revascularization remained consistently higher in the PCI group. Among patients with diabetes mellitus, these findings were consistent, regardless of treatment with insulin. Similarly, in the nondiabetic population, there were no significant differences in the 5-year, adjusted rates of death and the composite of death, Q-wave MI, or stroke

Table 2. Baseline Characteristics of the Patients

	Diabetic Patients (n=1761)			Nondiabetic Patients (n=4014)		
Variable	PCI (n=846)	CABG (n=915)	*P* Value	PCI (n=1943)	CABG (n=2071)	*P* Value
Demographic and clinical characteristic						
Age, y	63.4±9.6	63.2±8.3	0.72	60.6±11.3	61.8±9.2	<0.001
Male sex	554 (65.5)	662 (72.3)	0.002	1392 (71.6)	1524 (73.6)	0.17
Body mass index	25.1±3.1	24.6±3.0	0.001	24.7±2.9	24.6±2.9	0.84
Hypertension	519 (61.3)	552 (60.3)	0.66	949 (48.8)	762 (36.8)	<0.001
Current smoker	190 (22.5)	199 (21.7)	0.72	594 (30.6)	428 (20.7)	<0.001
Hyperlipidemia	227 (26.8)	407 (44.5)	<0.001	509 (26.2)	613 (29.6)	0.02
Previous MI	75 (8.9)	180 (19.7)	<0.001	187 (9.6)	299 (14.4)	<0.001
Previous coronary angioplasty	175 (20.7)	119 (13.0)	<0.001	316 (16.3)	196 (9.5)	<0.001
Congestive heart failure	25 (3.0)	60 (6.6)	<0.001	25 (1.3)	59 (2.8)	0.001
Chronic obstructive pulmonary disease	13 (1.5)	15 (1.6)	0.86	28 (1.4)	47 (2.3)	0.05
Cerebrovascular disease	70 (8.3)	111 (12.1)	0.008	97 (5.0)	161 (7.8)	<0.001
Peripheral vascular disease	22 (2.6)	86 (9.4)	<0.001	32 (1.6)	123 (5.9)	<0.001
Renal failure*	45 (5.3)	78 (8.5)	0.008	34 (1.7)	61 (2.9)	0.01
Electrocardiographic findings			0.40			0.09
Sinus rhythm	804 (95.0)	877 (95.8)		1870 (96.2)	2018 (97.4)	
Atrial fibrillation	25 (3.0)	27 (3.0)		46 (2.4)	33 (1.6)	
Others	17 (2.0)	11 (1.2)		27 (1.4)	20 (1.0)	
Clinical indication			<0.001			<0.001
Stable angina	369 (43.6)	239 (26.1)		832 (42.8)	574 (27.7)	
Acute coronary syndrome	477 (56.4)	676 (73.9)		1111 (57.2)	1497 (72.3)	
Ejection fraction, %	58.6±9.9	55.6±12.1	<0.001	59.8±8.7	57.4±10.4	<0.001
euroSCORE value	3.8±2.5	4.6±2.4	<0.001	3.4±2.3	4.0±2.3	<0.001
Anatomic characteristic						
Extent of diseased vessel, % of patients						
Multivessel CAD without left main disease	442 (52.2)	299 (32.7)	<0.001	926 (47.7)	822 (39.7)	<0.001
2-vessel disease†	240 (54.3)	52 (17.4)		566 (61.1)	218 (26.5)	
3-vessel disease†	202 (45.7)	247 (82.6)		360 (38.9)	604 (73.5)	
Mutivessel CAD with left main disease	404 (47.8)	616 (67.3)	<0.001	1017 (52.3)	1249 (60.3)	<0.001
Left main only†	83 (20.5)	15 (2.4)		323 (31.8)	93 (7.4)	
Left main plus single-vessel disease†	112 (27.7)	46 (7.5)		306 (30.1)	141 (11.3)	
Left main plus double-vessel disease†	108 (26.7)	139 (22.6)		203 (20.0)	341 (27.3)	
Left main plus triple vessel disease†	101 (25.0)	416 (67.5)		185 (18.2)	674 (54.0)	
Involved location of left main disease			0.02			0.01
Ostium and mid-shaft†	183 (45.3)	235 (38.1)		506 (49.8)	554 (44.4)	
Distal bifurcation†	221 (54.7)	381 (61.9)		511 (50.2)	695 (55.6)	
Proximal LAD disease	377 (44.6)	561 (61.3)	<0.001	827 (42.6)	1073 (51.8)	<0.001
Right coronary artery disease	265 (31.3)	764 (83.5)	<0.001	576 (29.6)	1560 (75.3)	<0.001
Bifurcation lesion	279 (33.0)	381 (41.6)	<0.001	652 (33.6)	695 (33.6)	0.99
Restenotic lesion	36 (4.3)	63 (6.9)	0.02	87 (4.5)	102 (4.9)	0.50
Total occlusion ≥1	41 (4.8)	267 (29.2)	<0.001	102 (5.2)	602 (29.1)	<0.001

CABG indicates coronary artery bypass grafting; euroSCORE, The European System for Cardiac Operative Risk Evaluation; MI, myocardial infarction; LAD, left anterior descending artery; PCI, percutaneous coronary intervention; CAD, coronary artery disease.

Data are mean±SD or number (%).

*Renal failure was defined as a creatinine ≥2.0 mg/dL or chronic hemodialysis.

†Percentage denotes a relative proportion in each category.

among the 2 treatment methods, but the rate of repeat revascularization was consistently higher in the PCI group. As a result, there were no statistically significant interactions between diabetes mellitus and revascularization strategies for covariate-adjusted risks of death (P=0.27), composite of death, Q-wave MI, or stroke (P=0.97), and repeat

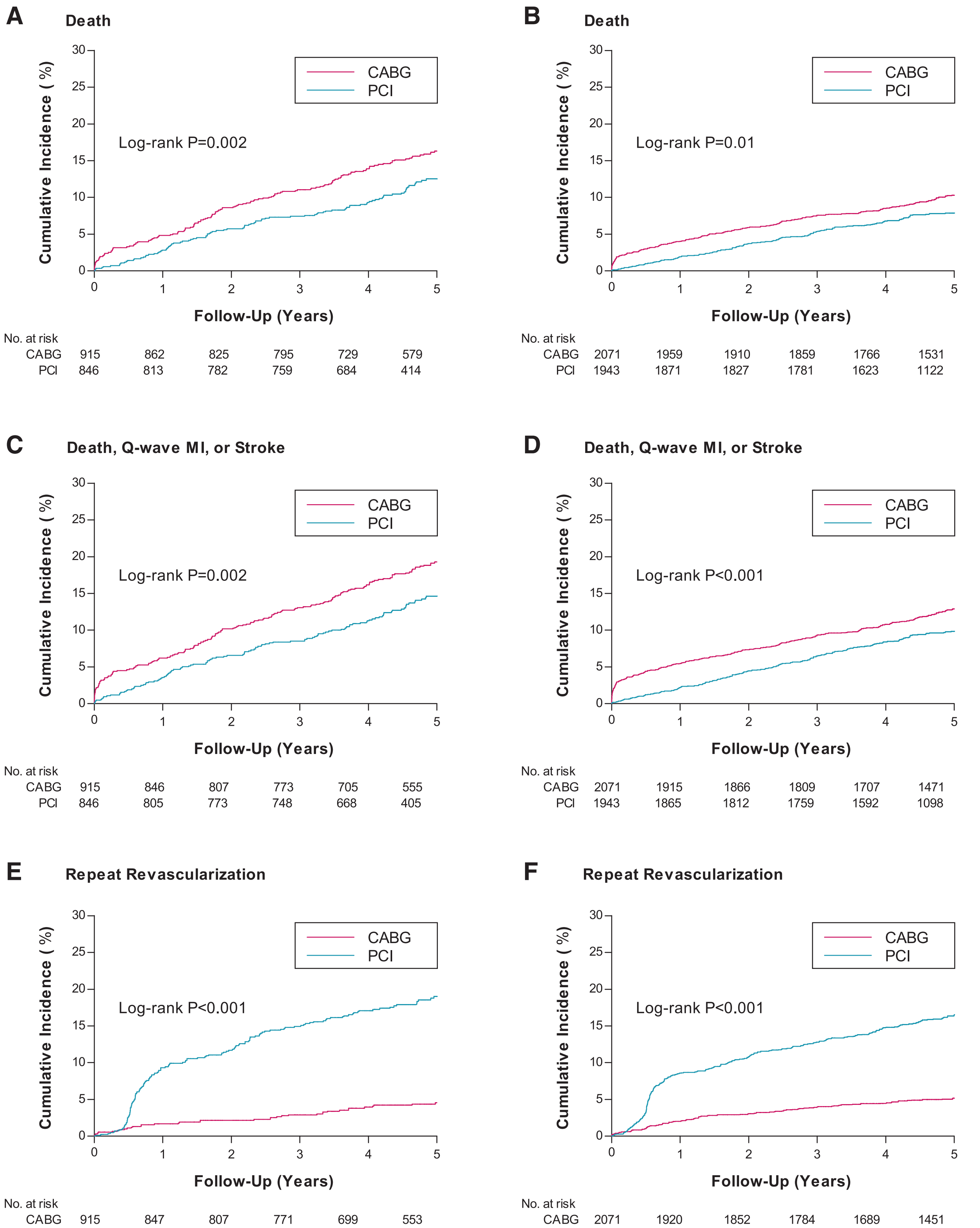

Figure 1. Outcomes of treatment with percutaneous coronary intervention (PCI) or coronary artery bypass graft (CABG) by diabetic status. **Left** and **right**, Outcomes of diabetic and nondiabetic patients, respectively. Data show overall unadjusted all-cause mortality (**A** and **B**), a composite of death, Q-wave myocardial infarction (MI), and stroke (**C** and **D**), and repeat revascularization (**E** and **F**).

revascularization (P=0.08). For cardiovascular death, the overall finding was also consistent (see the footnote in Table 4).

In each stratum of the study population based on the presence or absence of left main disease and stent types (BMS or DES), the relative treatment benefits of PCI and CABG according to

Table 3. Five-Year Outcomes According to Revascularization Treatments in Diabetic and Nondiabetic Patients*

	Diabetic Patients (n=1761)				Nondiabetic Patients (n=4014)				
	5-Year Event Rate, %				5-Year Event Rate, %				Interaction
Outcome	PCI	CABG	Hazard Ratio (95% CI)	*P* Value	PCI	CABG	Hazard Ratio (95% CI)	*P* Value	*P* Value
Death	12.6	16.5	0.70 (0.55–0.88)	0.003	8.1	10.4	0.78 (0.65–0.95)	0.01	0.34
Composite outcome (death, QMI, or stroke)	14.9	19.9	0.71 (0.57–0.89)	0.002	10.1	13.6	0.73 (0.61–0.86)	<0.001	0.77
Repeat revascularization	19.0	4.6	4.55 (3.27–6.32)	<0.001	16.6	5.4	3.27 (2.65–4.03)	<0.001	0.16

CABG indicates coronary-artery bypass grafting; QMI, Q-wave myocardial infarction; PCI, percutaneous coronary intervention.

*Event rates are unadjusted, 5-y Kaplan-Meier estimates. Hazard ratios for PCI vs CABG are based on the full duration of follow-up from all studies.

diabetic status were also assessed (Figure 2). After adjustment of other covariates using inverse-probability-of-treatment weighting, the risks of death and serious composite outcomes were not significantly different between the 2 treatment groups, but the rate of repeat revascularization was consistently higher after PCI in each subpopulation. Diabetic status also did not significantly modify the relative treatment effects in these subgroups, with multivessel CAD combined with or without left main disease and treated with BMS or DES.

Discussion

In this large-sized, pooled analysis of patients with multivessel and left main CAD who underwent PCI or CABG, we assessed whether the relative treatment effect of revascularization strategies on long-term outcomes was modified by diabetic status. Because patients receiving CABG had higher-risk clinical and angiographic features, which were related to outcomes, unadjusted risks of mortality and serious composite outcomes have always penalized the CABG group, irrespective of the diabetic status. After a propensity score adjustment to reduce the disadvantage caused by the higher-risk profile of CABG population, the risks of death and composite outcome of death, Q-wave MI, or stroke were not different between PCI and CABG both in diabetic and in nondiabetic population, but the risk of repeat revascularization was significantly higher in the PCI group. There was no significant heterogeneity of treatment effect on clinical outcomes with respect to the diabetic status of patients. As a secondary analysis, we found that these findings were consistent, regardless of the presence or absence of left main disease and stent type.

Although randomized trials provide the reference standard for comparing the efficacy of treatments for a given clinical condition, they do not always provide a conclusive claim to treatment effectiveness, as there are many restrictions that limit the generalizability of the data obtained. Therefore, observational studies such as ours have a role to quantify effectiveness and other real-world experiences.[15] Several observational studies comparing PCI and CABG for

Table 4. Adjusted Outcomes According to Revascularization Treatments in Diabetic and Nondiabetic Patients

Outcomes	Diabetic Status	Hazard Ratio*	95% CI	*P* Value	Interaction *P* Value†
Death‡	All patients	1.05	0.85–1.29	0.65	
	No diabetes mellitus	1.15	0.88–1.50	0.31	0.27
	Diabetes mellitus	1.15	0.88–1.51	0.30	
	Noninsulin treated	0.89	0.58–1.39	0.61	
	Insulin treated	0.88	0.48–1.62	0.68	
Composite outcome (death, QMI, or stroke)	All patients	1.01	0.83–1.23	0.90	
	No diabetes mellitus	0.99	0.78–1.26	0.96	0.97
	Diabetes mellitus	1.00	0.79–1.26	0.97	
	Noninsulin-treated	1.05	0.70–1.58	0.81	
	Insulin-treated	0.89	0.51–1.56	0.68	
Repeat revascularization	All patients	4.24	3.30–5.44	<0.001	
	No diabetes mellitus	3.55	2.61–4.83	<0.001	0.08
	Diabetes mellitus	3.56	2.62–4.83	<0.001	
	Noninsulin treated	5.71	3.50–9.31	<0.001	
	Insulin treated	6.42	2.83–14.53	<0.001	

QMI indicates Q-wave myocardial infarction; PCI, percutaneous coronary intervention; CABG, coronary-artery bypass grafting.

*Adjusted hazard ratios are for patients with PCI, compared with those with CABG, using weighted Cox model with inverse probability weights.

†*P* value for the treatment by diabetic status (nondiabetes mellitus vs diabetes mellitus) interaction.

‡For cardiovascular death, adjusted hazard ratio (95% CI) was 1.09 (0.84–1.41) in all patients, 1.11 (0.80–1.54) in nondiabetic patients, 1.11 (0.81–1.54) in diabetic patients, 0.77 (0.38–1.55) in noninsulin-treated diabetic patients, and 1.02 (0.60–1.75) in insulin-treated diabetic patients. *P* value for the treatment by diabetic status interaction was 0.60.

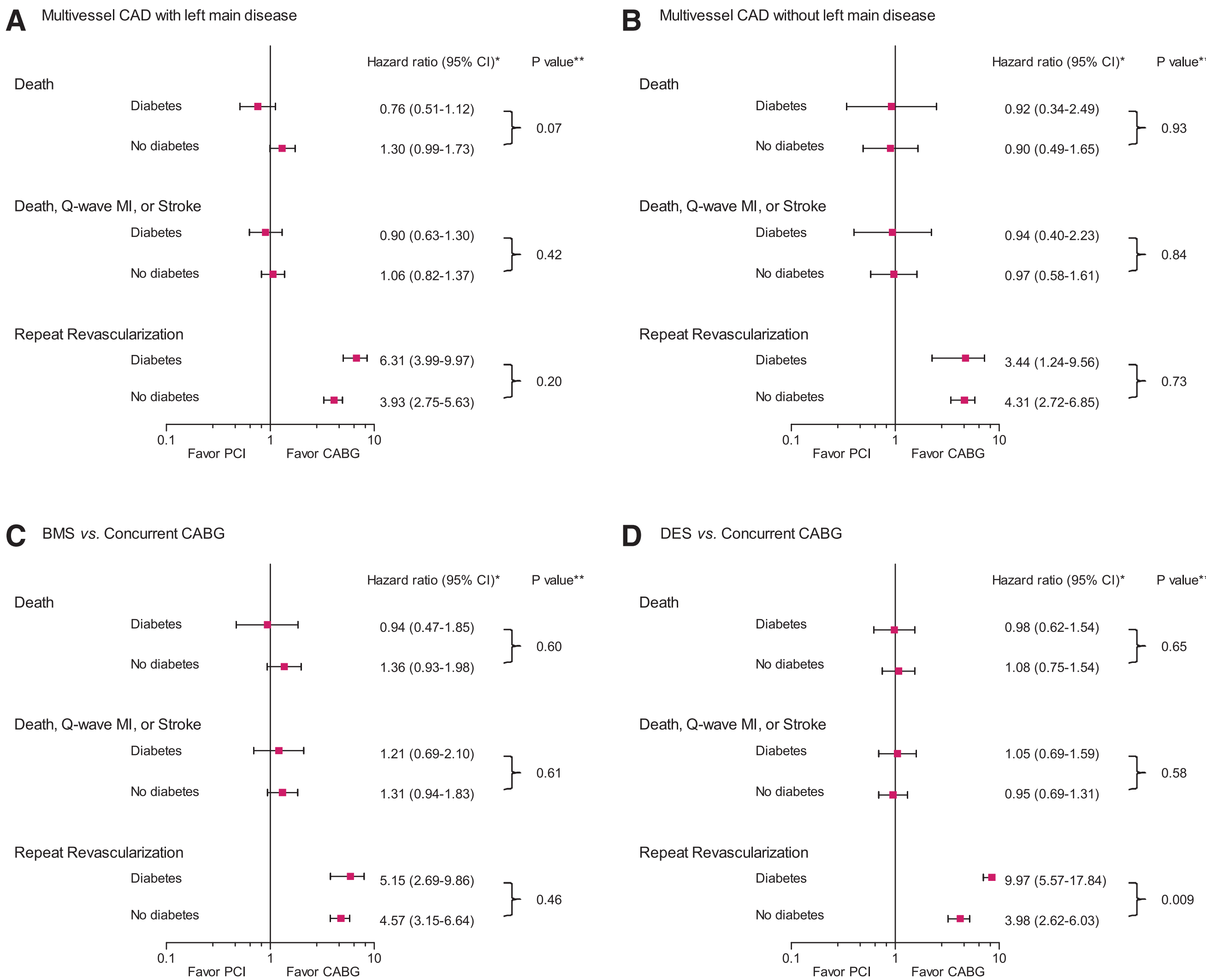

Figure 2. Adjusted hazard ratio for outcomes in diabetic and nondiabetic patients, according to the presence of left main disease and stent type. **A** and **B**, Adjusted outcomes in diabetic and nondiabetic patients according to the presence or absence of left main disease. **C** and **D**, Adjusted outcomes in diabetic and nondiabetic patients according the stent type; for concurrent comparisons, patients who received bare-metal stents (BMS) were compared with those who underwent coronary-artery bypass grafting (CABG) before May 2003, and patients who received drug-eluting stents (DES) were compared with those who underwent CABG after May 2003, according to previous Wave criteria.[19] *Adjusted hazard ratios were derived from the weighted Cox proportional-hazards regression models with inverse-probability-of-treatment weighting in each subgroup. ***P* value for the treatment by diabetic status (nondiabetes mellitus vs diabetes mellitus) interaction. MI indicates myocardial infarction; PCI, percutaneous coronary intervention.

multivessel or left main revascularization have shown inconsistent findings.[16–19] The effectiveness of treatments may vary among major clinical subsets, and this variance cannot be tested adequately in a single study because of limited statistical power. Combining individual patient data from several observational studies helps to overcome this limitation by increasing the number of patients available for analysis in important clinical subgroups, thus enhancing statistical power and providing valuable information for decision making in comparative effectiveness research. Furthermore, with continued advancements in devices, techniques, and adjunctive pharmacological therapy, reassessment of treatment effects of CABG and PCI according to diabetic status is needed in current situations. Therefore, our data provide more precise estimates of the relative effect of revascularization strategies, according to diabetic status; as a result, diabetes mellitus does not modify the treatment effect of PCI or CABG on the long-term outcomes of patients with multivessel or left main CAD.

There are several reports evaluating the interaction between diabetes mellitus and revascularization methods on clinical outcomes in such patients. Initially, the Bypass Angioplasty Revascularization Investigation (BARI) trial, in which balloon angioplasty was the default strategy of PCI, reported that patients with diabetes mellitus had substantially better survival rates after CABG than after PCI.[20] However, other large clinical registries and several subsequent randomized controlled trial did not confirm this effect and were unable to replicate these findings.[21–24] A recent meta-analysis of 10 randomized trials suggested that mortality was substantially lower in the CABG group than in the PCI group among patients with diabetes mellitus; in contrast, mortality was similar between groups in patients without diabetes mellitus.[7] However, none of the 10 trials included in that study used

DES for PCI. Accordingly, further evidence in this long-running debate should, therefore, be provided by the results of more current trials. In the diabetic subgroup of the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) and ARTS II (Arterial Revascularization Therapies Study–Part II) study and the CARDia (Coronary Artery Revascularization in Diabetes) trial, in which DES was used for the default devices of PCI, the mortality and safety composite were similar between the 2 treatment groups, whereas revascularization was significantly higher in the DES arm.[11,25,26] Treatment-related effect was also not modified by the diabetic status.[11] These findings were consistent with our study. In addition, the future results of ongoing, large-sized, randomized FREEDOM (Comparison of Two Treatments for Multivessel Coronary Artery Disease in Individuals With Diabetes) trial will provide more definite answers regarding the relative long-term benefits of PCI and CABG for diabetic patients.

We cannot fully explain the discrepancy regarding the interaction of diabetic status with revascularization strategies over the change in the PCI field from balloon angioplasty PCI, BMS, to DES. One potential interpretation of this finding is that marked advances in PCI devices and adjunctive pharmacology may lessen the relative benefits of CABG over PCI in diabetic patients with more complex CAD. Another potential interpretation is that background medical treatments have markedly improved, and, therefore, clinical equipoise among CABG and PCI for mortality and hard clinical end points over the long-term period has been ensured on the background of intensive medical therapy.

Study Limitations

The present study has the limitations inherent to nonrandomized, observational studies. First, although we performed appropriate statistical analysis using propensity scores 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 ineligible for one of the procedures. Second, for interpretation of specific clinical subgroup analysis, these exploratory results are to be considered hypothetical and hypotheses generating only. Third, in our study, we did not systematically perform a detailed angiographic scoring system (ie, the SYNTAX score) to more accurately reflect anatomic complexity. Because the SYNTAX score was developed in the DES era as an integral part of the SYNTAX trial design, this scoring system was not available at the study period of ours. Fourth, we have no data on concomitant drug treatment or on control of coronary risk factors during follow-up. Finally, because this study evaluated BMS and the first-generation of DES, the direct application of our findings to real-life practice predominantly using second-generation DES may be limited.

Conclusions

With appropriate clinical judgment based on the individual characteristics of patients and angiographic factors influencing the selection of a revascularization procedure, risk-adjusted long-term rates of mortality and serious composite outcomes are not different after PCI and CABG both in diabetic and in nondiabetic patients with multivessel or left main CAD, in which no significant interaction exists between diabetes mellitus and treatment strategies. However, the rate of repeat revascularization was consistently higher in the PCI group. Due to the nonrandomized nature of data and unmeasured confounders, these results are hypothesis generating and should be confirmed or refuted through large, randomized clinical trials with long-term follow-up.

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Disclosures

None.

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