Long-Term Outcomes After Percutaneous Coronary Intervention With Second-Generation Drug-Eluting Stents or Coronary Artery Bypass Grafting for Multivessel Coronary Disease

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More evidence is required with respect to the comparative effectiveness of percutaneous coronary intervention (PCI) with second-generation drug-eluting stents (DESs) versus coronary artery bypass grafting (CABG) in contemporary clinical practice. This prospective observational registry−based study compared the outcomes of 6,647 patients with multivessel disease who underwent PCI with second-generation DES (n = 3,858) or CABG (n = 2,789) between January 2006 and June 2018 and for whom follow-up data were available for at least 2 to 13 years (median 4.8). The primary outcome was a composite of death, spontaneous myocardial infarction, or stroke. Baseline differences were adjusted using propensity scores and inverse probability weighting. In the overall cohort, there were no significant between-group differences in the adjusted risks for the primary composite outcome (hazard ratio [HR] for PCI vs CABG 1.03, 95% confidence interval [CI] 0.86 to 1.25, p = 0.73) and all-cause mortality (HR 0.95, 95% CI 0.76 to 1.20, p = 0.68). This relative treatment effect on the primary outcome was similar in patients with diabetes (HR 1.15, 95% CI 0.91 to 1.46, p = 0.25) and without diabetes (HR 0.95, 95% CI 0.73 to 1.22, p = 0.67) (p for interaction = 0.24). The adjusted risk of the primary outcome was significantly greater after PCI than after CABG in patients with left main involvement (HR 1.39, 95% CI 1.01 to 1.90, p = 0.044), but not in those without left main involvement (HR 0.94, 95% CI 0.76 to 1.16, p = 0.56) (p = 0.03 for interaction). In this prospective real-world long-term registry, we observed that the risk for the primary composite of death, spontaneous myocardial infarction, or stroke was similar between PCI with contemporary DES and CABG. **(Am J Cardiol 2021;160:21−30)**

Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are two complementary treatment modalities for patients with multivessel coronary artery disease (CAD).[1,2] The revascularization gap in favor of CABG over PCI for multivessel CAD has narrowed over time with incremental improvements in PCI devices, technologies, experiences, and adjunctive drug therapies.[3] To date, limited data are available regarding comparisons of PCI with contemporary second-generation drug-eluting stents (DESs) to CABG for multivessel CAD.[4] Furthermore, given the marked advances in periprocedural and postprocedural medical care for both CABG and PCI, new comparisons are required to provide updated clinical insights for optimal revascularization for multivessel CAD in the contemporary clinical setting. Therefore, we evaluated the outcomes of PCI using second-generation DES compared with those of concurrent CABG in patients with multivessel CAD, using data from a large-sized, prospective "real-world" clinical practice registry.

Methods

The study population was derived from the Asan-Multivessel (Asan Medical Center-Multivessel Revascularization) Registry. The design and enrollment characteristics of the Asan-Multivessel Registry have been published previously.[5,6] In brief, the Asan-Multivessel Registry is a single-center, prospective study designed to investigate the "real-world" outcomes of PCI, CABG, or medical therapy

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See page 27 for disclosure information.

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alone in patients with multivessel CAD (defined as stenosis of more than 70% in at least 2 of the 3 major epicardial vessels) and/or left main coronary artery (LMCA) disease (defined as stenosis of >50%). This prospective registry contains information on patient demographics, cardiovascular risk factors, clinical manifestation, hemodynamic status, left ventricular function, disease extent, procedures details, and in-hospital and follow-up outcomes, which was recorded by independent research personnel. This study was approved by the Asan Medical Center Institutional Review Board, and all patients provided written informed consent.

The study population in this analysis comprised consecutive patients with multivessel CAD and/or LMCA disease who underwent PCI with second-generation DES or isolated CABG between January 1, 2006, and June 1, 2018. Patients who underwent concomitant valvular or aortic surgery and those with an ST-segment elevation myocardial infarction within 24 hours before revascularization or who presented with cardiogenic shock were excluded. The follow-up period was extended through June 1, 2020, to ensure that all patients had an opportunity for at least 2 years and up to 13 years of follow-up. The choice of revascularization strategy was made at the discretion of the treating physicians and/or patients after consideration of several clinical and anatomic factors or surgical risk for CABG.[5,6] All PCI procedures were performed with standard interventional techniques, and the use of specific stent types and use of intravascular ultrasound were at the operator's discretion. After the intervention, aspirin administration was continued indefinitely and P2Y12 receptor inhibitors were prescribed for at least 12 months. Surgical revascularization was also performed using standard bypass techniques. The internal thoracic artery was preferentially used for revascularization of the left anterior descending artery. Complete revascularization was performed, when possible, with arterial conduits or saphenous vein grafts. On-pump or off-pump surgery was performed at the surgeon's discretion. During the follow-up, medical therapy for secondary prevention and patient management were performed in accordance with accepted guidelines and established standard of care. Clinical follow-up was recommended at 1, 6, and 12 months, and every 6 months thereafter. Clinical follow-up was performed by way of office visits or telephone contact. Monitoring and verification of registry data were periodically performed by members of the academic coordinating center (Clinical Research Center, Asan Medical Center, Seoul, Korea).

The primary outcome was a composite of death from any cause, spontaneous myocardial infarction (MI), or stroke. The major secondary outcomes included the individual components of the primary outcome and repeat revascularization. All outcomes were assessed according to the standard end point definitions.[7] In the present study, all-cause mortality was assessed, which was the most unbiased method to report deaths in a clinical trial or observational study. Spontaneous MI was defined as the appearance of newly developed ischemic symptoms or signs with an increase in cardiac enzyme level to higher than the upper reference limit requiring re-hospitalization (defined as an emergency admission with a principal diagnosis of MI). This study disregarded periprocedural MI owing to the conflicting definitions and prognostic impact of this event.[8] Stroke was defined as a sudden onset of neurologic deficit (i.e., vertigo, numbness, aphasia, or dysarthria) resulting from vascular lesions of the brain, including hemorrhage, embolism, thrombosis, or rupturing aneurysm, that persisted for >24 hours. Repeat revascularization was defined as any repeat percutaneous intervention or surgical bypass of the treated or nontreated vessel, regardless of whether the procedure was clinical or ischemia driven. All clinical events were confirmed by source documentation collected during each event and adjudicated by an independent group of clinicians unaware of the type of revascularization treatment.[5,6]

Analyses for treatment-related differences in the long-term outcomes after PCI or CABG were planned for all patients and separately for major clinical (the presence or absence of diabetes) or anatomic (the presence or absence of LMCA disease) subsets. With regard to baseline characteristics, continuous variables were compared with Student's t test or the Wilcoxon rank-sum tests, and categorical variables were compared with the chi-square test or Fisher's exact test, as appropriate. Inverse probability weighting based on the propensity scores was used as the primary tool to adjust for differences in baseline characteristics between the PCI and CABG groups. The propensity score is the conditional probability of having a particular treatment exposure (PCI vs CABG) given a set of baseline-measured covariates.[9] This score was estimated using a nonparsimonious multivariable logistic regression model,[10] with the treatment group as the dependent variable; all measured baseline characteristics are listed in Table 1. The c statistic for the propensity score model was 0.83 (Hosmer-Lemeshow goodness of fit, $p = 0.23$). The cumulative event curves of the adverse composite outcome were estimated by weighted Kaplan-Meier method.[11] The treatment effects between PCI and CABG were compared using weighted Cox regression models with robust standard errors after inverse probability weighting. In these models, the use of the drug at discharge was further adjusted. In addition, we performed sensitivity analyses using propensity score matching. We also conducted prespecified subgroup analyses according to the baseline clinical and anatomical characteristics such as gender, age, body mass index, hypertension, hypercholesterolemia, previous MI, atrial fibrillation, renal insufficiency and left ventricular systolic function, or complete revascularization. We applied tests for interaction to assess the heterogeneity of the treatment effects in these subgroups.

All p values were two sided, with those <0.05 considered statistically significant. The p values and 95% confidence intervals (CIs) for secondary outcomes and subgroups analyses were not adjusted for multiple comparisons, and therefore, inferences drawn from these intervals may not be reproducible. All statistical analyses were performed using Statistical Analysis System version 9.4 (SAS Institute, Cary, North Carolina).

Results

From June 2000 to June 2018, the data of 15,712 patients with multivessel CAD were entered into the Asan-

Table 1
Baseline characteristics of the patients before and after adjustment using inverse probability weighting

Variable	Unadjusted data				Adjusted data with inverse probability weighting		
	PCI (N = 3858)	CABG (N = 2789)	p value	Standardized difference (%)	PCI (N = 3858)	CABG (N = 2789)	Standardized difference
Age (years)	64.8 ± 10.1	64.5 ± 9.2	0.189	3.24%	64.9 ± 9.9	65.2 ± 9.2	3.34%
Men	2850 (73.9%)	2089 (74.9%)	0.343	2.36%	2868 (74.4%)	2044 (73.3%)	2.44%
Body mass index (kg/m^2)	25.0 ± 3.1	24.7 ± 3.1	0.002	10.45%	24.9 ± 3.1	24.9 ± 3.0	2.40%
Diabetes mellitus							
Any diabetes mellitus	1403 (36.5%)	1259 (45.4%)	<0.001	18.12%	1495 (38.9%)	1097 (39.7%)	1.57%
Requiring insulin	205 (5.3%)	222 (8.0%)	<0.001	10.65%	236 (6.1%)	178 (6.4%)	1.11%
Hypertension	2606 (68.2%)	1883 (67.6%)	0.660	1.10%	2621 (68.5%)	1912 (68.8%)	0.71%
Hyperlipidemia	1834 (52.8%)	870 (37.3%)	<0.001	31.64%	1699 (48.8%)	1071 (45.3%)	6.91%
Current smoker	989 (25.7%)	664 (23.8%)	0.090	4.23%	953 (24.7%)	671 (24.2%)	1.33%
Previous MI	210 (5.5%)	230 (8.3%)	<0.001	11.13%	261 (6.8%)	185 (6.7%)	0.37%
Previous CABG	63 (1.6%)	14 (0.5%)	<0.001	11.02%	49 (1.3%)	45 (1.6%)	3.02%
Previous PCI	530 (13.7%)	442 (15.9%)	0.016	5.97%	578 (15.0%)	438 (15.8%)	2.10%
Previous heart failure	157 (4.1%)	166 (6.0%)	<0.001	8.66%	181 (4.7%)	147 (5.3%)	2.75%
Previous stroke	324 (8.4%)	268 (9.6%)	0.088	4.22%	362 (9.4%)	244 (8.8%)	2.19%
Chronic kidney disease	169 (4.4%)	167 (6.0%)	0.003	7.26%	204 (5.3%)	139 (5.0%)	1.38%
Chronic lung disease	83 (2.2%)	55 (2.0%)	0.618	1.24%	82 (2.1%)	58 (2.1%)	0.30%
Atrial fibrillation	99 (2.6%)	91 (3.3%)	0.093	4.14%	113 (2.9%)	96 (3.4%)	2.83%
Mean ejection fraction (%)	58.8 ± 8.9	54.6 ± 12.1	<0.001	39.95%	57.5 ± 10.3	57.0 ± 10.9	5.78%
Normal LV function	2591 (80.0%)	1777 (64.6%)	<0.001	37.06%	2449 (75.4%)	1996 (72.6%)	6.08%
Mild LV dysfunction	370 (11.4%)	418 (15.2%)			407 (12.5%)	368 (13.4%)	
Moderate LV dysfunction	187 (5.8%)	293 (10.7%)			234 (7.2%)	219 (8.0%)	
Severe LV dysfunction	90 (2.8%)	263 (9.6%)			160 (4.9%)	167 (6.1%)	
Clinical presentation							
Atypical chest pain	674 (17.5%)	457 (16.4%)	<0.001	31.55%	679 (17.6%)	531 (19.1%)	4.78%
Stable angina pectoris	1874 (48.6%)	1080 (38.7%)			1707 (44.2%)	1200 (43.0%)	
Unstable angina pectoris	923 (23.9%)	1059 (38.0%)			1137 (29.5%)	840 (30.1%)	
Non-ST elevation MI	387 (10.0%)	193 (6.9%)			335 (8.7%)	218 (7.8%)	
No. of coronary arteries managed							
2	1953 (50.6%)	401 (14.4%)	<0.001	94.30%	1406 (36.5%)	937 (33.6%)	4.61%
3	1201 (31.1%)	1526 (54.7%)			1564 (40.5%)	1173 (42.1%)	
Left main	704 (18.3%)	862 (30.9%)	<0.001	29.73%	887 (23.0%)	679 (24.4%)	3.17%
Left main and 1 vessel	81 (2.1%)	39 (1.4%)			72 (1.9%)	57 (2.0%)	
Left main and 2 vessels	326 (8.5%)	178 (6.4%)			307 (8.0%)	225 (8.1%)	
Left main and 3 vessels	297 (7.7%)	645 (23.1%)			508 (13.2%)	398 (14.3%)	
Proximal LAD disease	3470 (89.9%)	2718 (97.5%)	<0.001	31.29%	3584 (92.9%)	2624 (94.1%)	4.75%
PCI procedure							
Number of stents, mean	2.2 ± 1.2				2.2 ± 1.2		
Length of stents, mean	59.3 ± 33.0				60 ± 33.2		
CABG procedure							
Number of grafts, mean		2.9 ± 0.9				2.9 ± 0.9	
Arterial grafts, mean		1.8 ± 1.0				1.8 ± 1.1	
Venous grafts, mean		1.1 ± 0.9				1.1 ± 1.0	
Off-pump surgery		1767 (63.4%)				1730 (62.0%)	
Complete revascularization	1239 (32.1%)	1666 (59.7%)	<0.001	57.68%	1645 (42.6%)	1266 (45.4%)	5.55%
Medication at discharge							
Aspirin,	3627 (97.2%)	14 (1.2%)	<0.001	28.03%	3624 (97.0%)	2374 (90.7%)	26.39%
Clopidogrel	3449 (92.5%)	2171 (81.9%)	<0.001	32.03%	3454 (92.5%)	2119 (81.0%)	34.33%
Dual antiplatelet therapy	3428 (91.9%)	2150 (81.1%)	<0.001	32.02%	3433 (91.9%)	2093 (80.0%)	34.75%
Beta-blocker	2365 (64.3%)	695 (24.9%)	<0.001	78.99%	2336 (60.5%)	734 (26.3%)	73.58%
Calcium channel blocker	2948 (76.4%)	1456 (52.2%)	<0.001	52.22%	2930 (75.9%)	1389 (49.8%)	56.20%
ACE inhibitor or ARB	1111 (28.8%)	513 (18.4%)	<0.001	24.69%	1118 (29.0%)	493 (17.7%)	26.94%
Statin	3482 (90.3%)	2363 (84.7%)	<0.001	16.85%	3452 (89.5%)	2373 (85.1%)	13.21%

The plus-minus values are mean ± SD. Percentages may not total 100 because of rounding. The standardized differences are reported as percentages; a difference of less than 10.0% indicates a relatively small imbalance.

CABG = coronary artery bypass grafting; LAD = left anterior descending; LV = left ventricle; MI = myocardial infarction; PCI = percutaneous coronary intervention; VD = vessel disease.

Multivessel Registry. We identified 6,647 patients with multivessel disease among the aforementioned patients who met our inclusion criteria, of whom 3,858 (58.0%) underwent PCI with second-generation DES and 2,789 (42.0%) underwent CABG between January 2006 and June 2018 (Supplementary Figure 1). Among the patients who underwent PCI, the relative proportions of different types of second-generation DES are summarized in Supplementary Table 1. Durable polymer everolimus-eluting stents (36.3%) and durable polymer zotarolimus-eluting stents (35.0%) were the most commonly used. A mean of 2.2 ± 1.2 stents was used per patient, and the median total length of the implanted stents was 59.3 ± 33.0 mm. Among the patients who underwent CABG, 1,767 (63.4%) underwent off-pump surgery, and 2,704 (97.0%) received at least 1 arterial conduit that was used in revascularization of the left anterior descending artery in 2,673 patients (95.8%). A mean of 1.8 ± 1.0 arterial and 1.1 ± 0.9 venous grafts was used per patient. Table 1 lists selected baseline characteristics of the patients. Before adjustment using inverse probability weighting, there were differences between the PCI and the CABG groups in several of the baseline variables. Overall, patients who underwent CABG had higher clinical and anatomic risk factor profiles than patients who underwent PCI. The largest difference between the groups was in the distribution of the number of diseased vessels, with patients in the PCI group more often having two-vessel disease and patients in the CABG group more often having three-vessel disease and complex LMCA. As expected, the patients in the PCI group had a lower probability of being selected for CABG than did those in the CABG group, with the median and interquartile range of the propensity scores for CABG reflecting this difference (PCI group: median 23.6%, interquartile range 11.0 to 38.3; CABG group: median 66.2%, interquartile range 39.6 to 84.5) (Figure 1). After adjustment using inverse probability weighting, all the clinical covariates were well balanced.

The follow-up duration ranged from 2 to 13 years (average: overall 5.1 years, CABG group 5.7 years, PCI group 4.7 years; median follow-up: overall 4.8 years, CABG group 5.3 years, PCI group 4.3 years). The observed (unadjusted) event rates are shown in Figure 2 and Supplementary Table 3. The unadjusted rates of the primary composite outcome and all-cause mortality were significantly lower in the PCI group than those in the CABG group. In contrast, the rates of spontaneous MI and repeat revascularization were significantly higher in the PCI group. The adjusted rates and risks for the primary and secondary outcomes using inverse probability weighting are summarized in Figure 2 and Table 2. In the overall cohort, we observed no significant differences in the risks of the primary composite of death, spontaneous MI, or stroke between the PCI and CABG groups (hazard ratio [HR] PCI vs CABG: 1.03, 95% CI 0.86 to 1.25, p = 0.73) and all-cause mortality (HR 0.95, 95% CI 0.76 to 1.20, p = 0.68). However, the risks of spontaneous MI and repeat revascularization were significantly higher in the PCI group (Supplementary Figure 2).

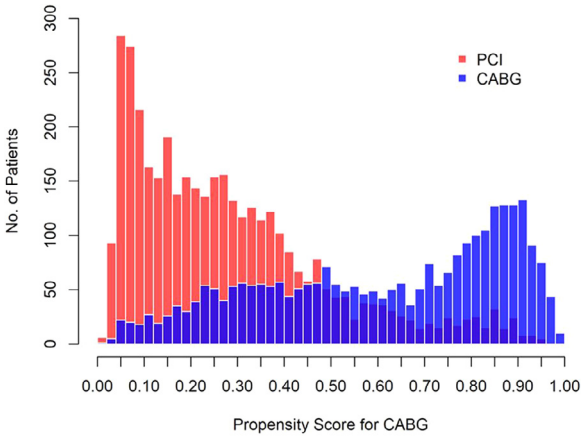

Figure 1. Propensity scores for CABG in the PCI and CABG populations. The propensity score for CABG is the probability, given the baseline variables, that any patient in either group would be selected for CABG. No. = number.

The relative treatment effects after PCI and CABG on the primary composite outcome and all-cause mortality were similar in patients without or with diabetes (Figure 3 and Table 2). The incidence of spontaneous MI and repeat revascularization was consistently higher after PCI than after CABG, regardless of diabetes status. No significant interaction was found between diabetic status and the treatment effect regarding the primary and secondary outcomes. The adjusted risks of the primary composite outcome were similar between the interventions in patients with multivessel disease not involving left main disease (HR 0.94, 95% CI 0.76 to 1.16, p = 0.56), whereas the adjusted risk of primary outcomes was higher after PCI than after CABG in patients with multivessel disease involving left main disease (HR 1.39, 95% CI 1.01 to 1.90, p = 0.04), with a significant treatment interaction (p = 0.03 for interaction) (Figure 3). We observed a similar trend for all-cause mortality (p = 0.02 for interaction).

The results of subgroup analyses using inverse probability of treatment weighting reflected the broad consistency of the relative effect of PCI and CABG on the primary composite outcome and all-cause mortality (Figure 4 and Supplementary Figure 3) except for the nominally significant interactions between treatment with PCI versus CABG and the involvement of LMCA disease.

In the sensitivity analyses using propensity score matching (a matched cohort of 1,582 pairs of patients who underwent PCI and CABG), the overall findings were similar (Supplementary Table 2). We observed no significant between-group differences in the primary composite outcome and all-cause mortality in the overall matched cohort (Supplementary Table 4).

Discussion

In this large cohort of patients with multivessel CAD, we observed no significant difference in the risks of the primary composite outcome of death, spontaneous MI, or stroke between PCI with second-generation DES and CABG for up to 10 years. The risk of all-cause mortality was also similar between the 2 groups, but the risks of spontaneous MI and repeat revascularization were higher in the PCI group than in the CABG group. The relative treatment

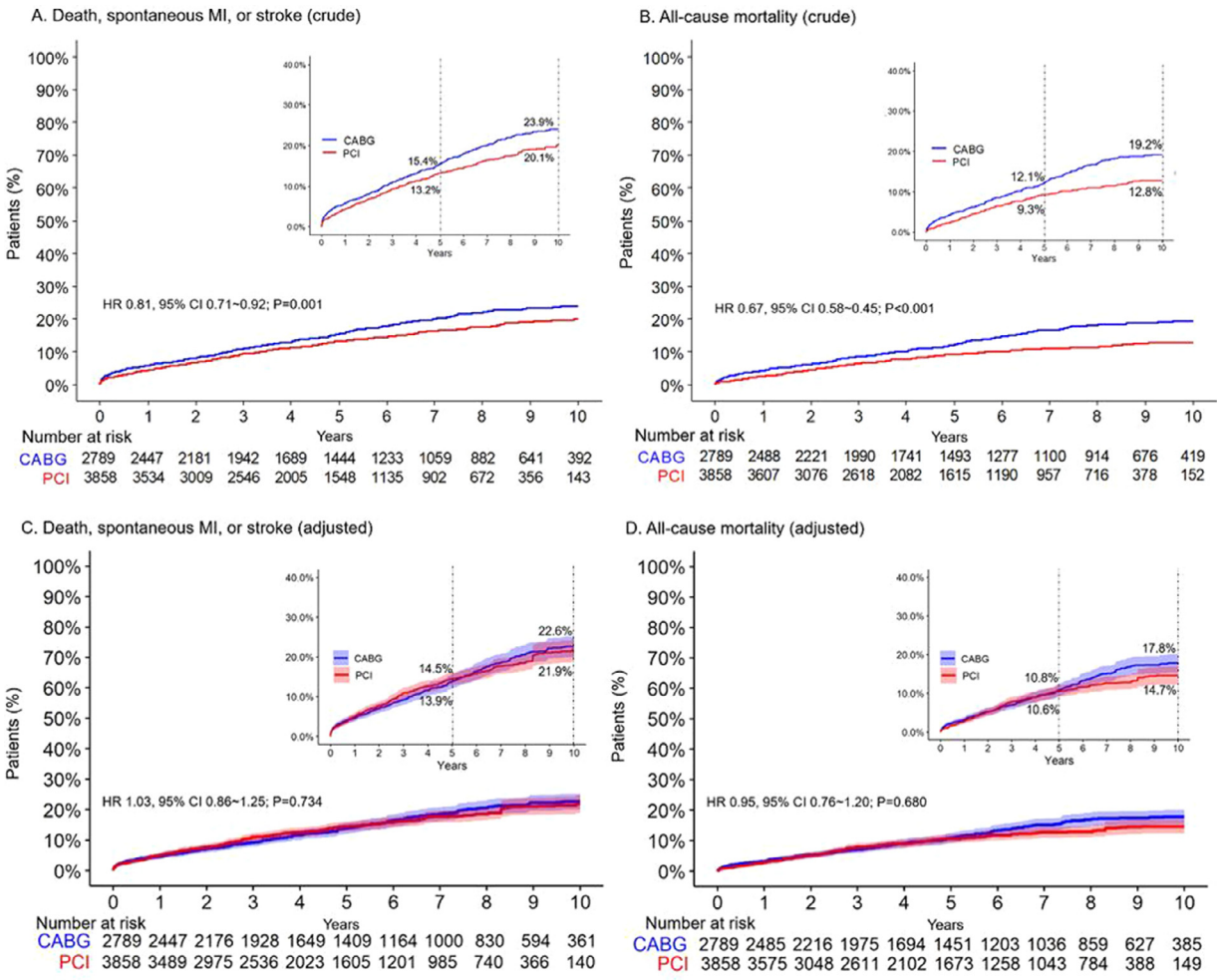

Figure 2. Unadjusted and adjusted event curves for the primary composite outcome and all-cause mortality The upper panel shows the unadjusted event curves for the primary composite outcome of death from any cause, spontaneous myocardial infarction, or stroke (*A*) and all-cause mortality (*B*). The lower panel shows the adjusted event curves for the primary composite outcome of death from any cause, stroke, or spontaneous myocardial infarction (*C*) and all-cause mortality (*D*). The hazard ratios are for the PCI group as compared with the CABG group. In each panel, the inset shows the same data on an enlarged y axis.

effect of PCI or CABG was consistent, irrespective of diabetes. By contrast, we observed a long-term benefit of CABG over PCI in patients with LMCA involvement, but not in those without LMCA involvement. Until recently, several trials and observational studies reported the long-term clinical outcomes of CABG and PCI with DES in patients with multivessel and/or LMCA disease.[4,11–16] However, because these studies assessed first-generation DES (i.e., paclitaxel- or sirolimus-eluting) or specific types of second-generation DES (i.e., everolimus- or biolimus-eluting), the direct application of these findings to contemporary daily clinical practice using several types of second-generation DES having varying characteristics. In addition, given that contemporary CABG or PCI techniques were not fully incorporated in previous studies and optimal medical therapy for secondary prevention is also rapidly evolving, the current findings of our study provide updated clinical insights on the relative performance of PCI with contemporary DES and CABG in the "real-world" clinical setting. Although the incidence of primary composite outcome and all-cause mortality was not significantly different after PCI and CABG in the present study, the incidence of spontaneous MI and repeat revascularization was consistently higher in the PCI group, which is consistent with the findings of previous studies.[4,12,17,18] Restenosis and stent thrombosis in the target vessel and de novo lesion progression in the non-target vessel are two potentially serious complications of PCI that are associated with significant increases in MI rates during follow-up. Owing to the differential revascularized nature of bypass graft compared with stenting, CABG has a stronger protective effect against late-occurring thrombotic or atherosclerotic events.[19]

Diabetes is regarded a critical determinant for predicting poor prognosis and selecting optimal revascularization strategies among several clinical risk factors.[20] Recently, an extended follow-up of a clinical trial, registry data, and meta-analysis showed that coronary revascularization with CABG leads to lower all-cause mortality or major cardiovascular events than PCI with DES in patients with diabetes.[18,21,22] By contrast, we observed no significant

Table 2
Adjusted rates and hazard ratios for the primary and secondary clinical outcomes using inverse probability weighting

Adverse outcomes	Analyses with inverse probability weighting				
	No. of events (%) at 5 years		Hazard ratio (95% CI)	p value	p interaction
Overall population	**PCI (N = 3858)**	**CABG (N = 2789)**			
Primary composite of death, spontaneous MI, or stroke	537 (14.5%)	429 (13.9%)	1.03 (0.86−1.25)	0.73	
All-cause mortality	375 (10.6%)	337 (10.8%)	0.95 (0.76−1.20)	0.68	
Spontaneous MI	146 (3.6%)	48 (1.5%)	2.16 (1.42−3.30)	<0.001	
Stroke	101 (2.6%)	89 (3.1%)	0.81 (0.53−1.26)	0.353	
Repeat revascularization	451 (11.7%)	124 (4.3%)	2.60 (1.87−3.63)	<0.001	
Without diabetes mellitus	**PCI (N = 2357)**	**CABG (N = 1686)**			
Primary composite of death, spontaneous MI, or stroke	269 (11.3%)	231 (12.1%)	0.95 (0.73−1.22)	0.67	0.24
All-cause mortality	163 (7.7%)	172 (8.7%)	0.81 (0.59−1.11)	0.18	0.09
Spontaneous MI	83 (3.0%)	32 (1.7%)	1.81 (1.04−3.14)	0.04	0.25
Stroke	68 (2.5%)	57 (3.6%)	0.85 (0.48−1.49)	0.56	0.77
Repeat revascularization	261 (10.6%)	80 (4.3%)	2.32 (1.53−3.52)	<0.001	0.28
With diabetes mellitus	**PCI (N = 1501)**	**CABG (N = 1103)**			
Primary composite of death, spontaneous MI, or stroke	269 (19.7%)	198 (16.7%)	1.15 (0.91−1.46)	0.25	
All-cause mortality	212 (15.3%)	166 (14.2%)	1.13 (0.86−1.48)	0.40	
Spontaneous MI	64 (4.7%)	16 (1.2%)	2.88 (1.58−5.26)	0.001	
Stroke	33 (2.6%)	33 (2.4%)	0.76 (0.44−1.30)	0.31	
Repeat revascularization	189 (13.5%)	44 (4.3%)	3.14 (2.03−4.85)	<0.001	
Without left main disease	**PCI (N = 2971)**	**CABG (N = 2110)**			
Primary composite of death, spontaneous MI, or stroke	378 (12.8%)	317 (13.5%)	0.94 (0.76−1.16)	0.56	0.03
All-cause mortality	254 (9.1%)	247 (10.4%)	0.84 (0.65−1.08)	0.17	0.02
Spontaneous MI	102 (3.0%)	34 (1.6%)	2.03 (1.23−3.35)	0.005	0.49
Stroke	85 (2.7%)	67 (3.2%)	0.86 (0.53−1.41)	0.56	0.43
Repeat revascularization	325 (10.7%)	97 (4.6%)	2.29 (1.56−3.37)	<0.001	0.04
With left main disease	**PCI (N = 887)**	**CABG (N = 679)**			
Primary composite of death, spontaneous MI, or stroke	160 (20.4%)	112 (14.9%)	1.39 (1.01−1.90)	0.044	
All-cause mortality	122 (16.0%)	90 (12.2%)	1.38 (0.95−2.01)	0.09	
Spontaneous MI	44 (5.7%)	14 (1.3%)	2.68 (1.36−5.28)	0.004	
Stroke	16 (2.2%)	22 (3.0%)	0.62 (0.30−1.28)	0.20	
Repeat revascularization	126 (15.3%)	27 (3.3%)	4.00 (2.61−6.15)	<0.001	

Event rates (%) shown are the incidences as estimated by Kaplan-Meier survival analysis, with p values derived from log-rank tests.

CABG = coronary artery bypass grafting; CI = confidence interval; DES = drug-eluting stents; MI = myocardial infarction; PCI = percutaneous coronary intervention.

differences in serious composite outcome and all-cause mortality between PCI with contemporary DES and CABG. These discrepant findings might be partly explained by some reasons such as (1) a gradual bridging of the gap between CABG and PCI in patients with diabetes was observed, with remarkable improvements in stent platform with newer-generation DES, technology, experience, and adjunctive drug therapies[23,24] and (2) advanced and rapidly evolving optimal medical therapy might also attenuate the treatment gap of CABG over PCI.[25]

A recent pooled analysis of 11 randomized controlled trials (RCTs) showed that CABG had a mortality benefit over PCI in patients with multivessel disease but not in patients with LMCA disease.[22] However, in this analysis, patients with LMCA disease were excluded in 9 RCTs with bare-metal stent or first-generation DES, and only 2 RCTs (i.e., EXCEL and NOBLE) included patients with LMCA disease and low or intermediate anatomical complexity. Our registry enrolled unrestricted patients with multivessel disease who underwent newer-generation DES, in whom more complex LMCA disease was included. These minimal exclusion criteria might explain the additive negative prognostic impact of LMCA involvement in patients with multivessel disease, which was not observed in a previous meta-analysis.[22] PCI of distal LMCA bifurcation lesions in addition to multivessel CAD frequently requires complex two-stent strategies that are associated with increased risks of MI and repeat revascularization during follow-up. In contrast, the status of LMCA disease did not affect the operative strategy of CABG, and there was no difference in long-term clinical outcomes with regard to LMCA involvement. Thus, the larger relative benefit of CABG over PCI was most likely because of more complex CAD.

As with the results previously mentioned, better clinical outcomes could be obtained if the revascularization strategy is established on the basis of clinical judgment considering detailed coronary anatomic characteristics and co-morbidity.[26] Our study has several limitations. First, this was a nonrandomized observational study and thus was vulnerable to a selection bias. Although we used a rigorous statistical adjustment using inverse probability−weighted propensity score methods, unmeasured confounders could have influenced the observed findings. It must be acknowledged that statistical adjustments in ensuring balance in the

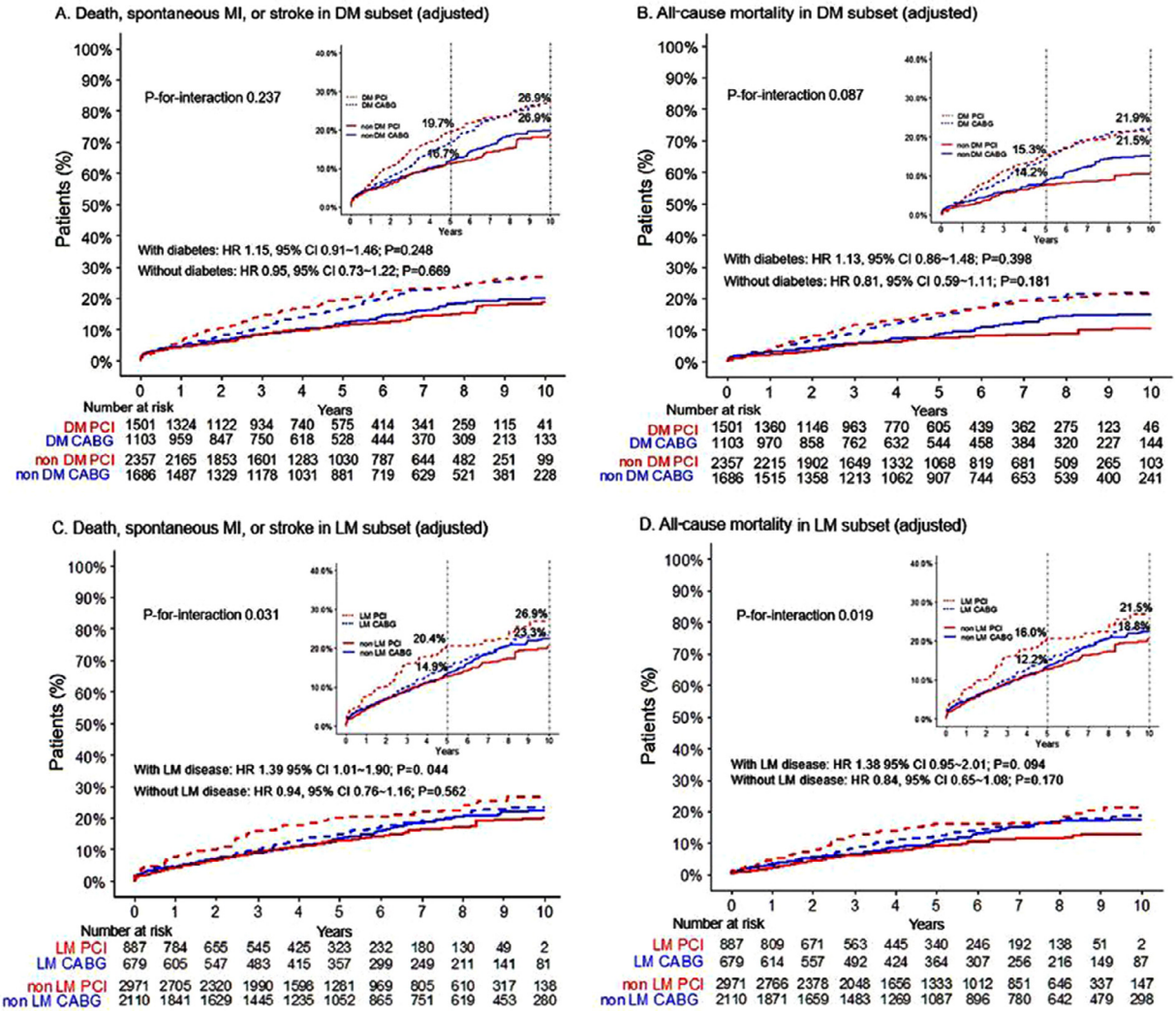

Figure 3. Adjusted event curves for the primary composite outcome and all-cause mortality stratified by the presence or absence of diabetes and left main disease The upper panel shows the adjusted event curves for the primary composite outcome of death from any cause, spontaneous MI, or stroke (*A*) and all-cause mortality (*B*) stratified by the DM status. The lower panel shows the adjusted event curves for the primary composite outcome of death from any cause, stroke, or spontaneous myocardial infarction (*C*) and all-cause mortality (*D*) stratified by LM disease status. The HRs and 95% CIs are for the PCI group as compared with the CABG group. In each panel, the inset shows the same data on an enlarged y axis. DM = diabetes mellitus; LM = left main.

treatment groups concerning measured and unmeasured confounding factors cannot replace the power of randomization. Second, we did not systematically collect detailed information on long-term medication use and compliance with guideline-directed medical management after PCI and CABG, which might have varied substantially over time. Third, our registry did not prospectively capture the SYNTAX score, and thus, this variable could not be included in the propensity scores. Finally, the number of patients and clinical events in each subgroup was relatively too small to detect clinically relevant differences in mortality and hard clinical end points.

In conclusion, in this contemporary cohort of patients with multivessel CAD, PCI with second-generation DES and CABG showed similar risks of the primary composite outcomes of death, spontaneous MI, or stroke. The risk of all-cause mortality was also similar between the 2 groups, but the risks of spontaneous MI and repeat revascularization were greater in the PCI group than in the CABG group. However, even if the potential selection bias was mitigated by rigorous adjustment, this finding should be considered hypothesis generating, highlighting the need for further research reflecting cardiologist clinical judgment.

Disclosures

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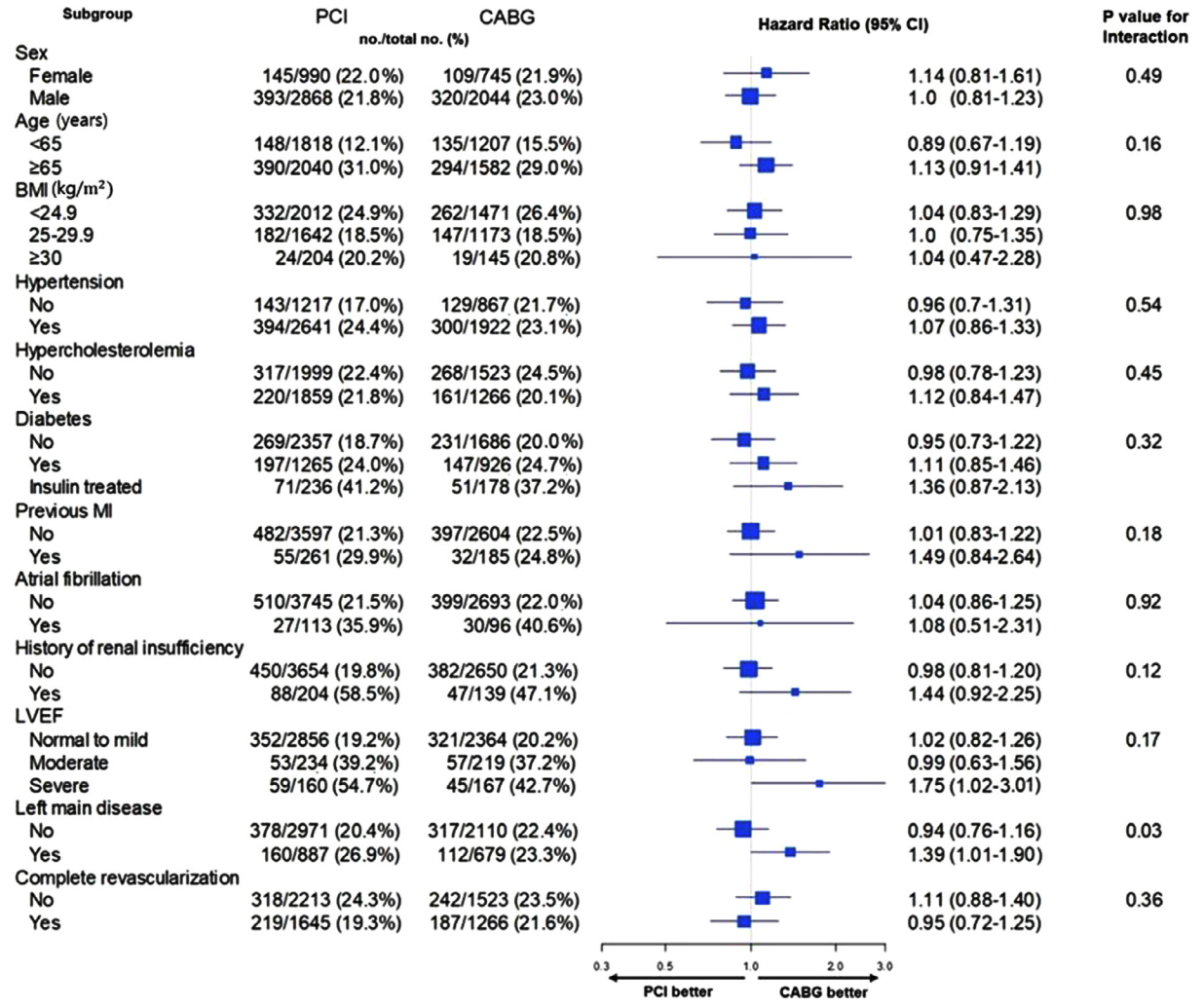

Figure 4. Adjusted risks for the primary composite outcome by clinical and anatomic subgroup Data are shown as the number of primary composite outcome (death from any cause, spontaneous myocardial infarction, or stroke) events per total number of patients in that subgroup and the event rate. The event rates were based on Kaplan-Meier estimates (thus, the rate is not the same as the ratio of the numerator and denominator). The HRs and 95% CIs are for the PCI group as compared with the CABG group. The p value for interaction represents the likelihood of interactions between the subgroups and the treatment. BMI = body mass index; LVEF = left ventricular ejection fraction; no. = number.

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Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2021.08.047.

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