Comparison of Outcomes of Coronary Artery Bypass Grafting Versus Drug-Eluting Stent Implantation in Patients With Severe Left Ventricular Dysfunction

Se Hun Kang, MD[a], Cheol Whan Lee, MD[b,*], Seunghee Baek, PhD[c], Pil Hyung Lee, MD[b], Jung-Min Ahn, MD[b], Duk-Woo Park, MD[b], Soo-Jin Kang, MD[b], Seung-Whan Lee, MD[b], Young-Hak Kim, MD[b], Seong-Wook Park, MD, PhD[b], and Seung-Jung Park, MD, PhD[b]

The optimal revascularization strategy for patients with significant coronary artery disease (CAD) and severe left ventricular (LV) dysfunction (ejection fraction ≤35%) remains unclear. We compared the effects of coronary artery bypass surgery (CABG, n = 442) versus percutaneous coronary intervention (PCI) with drug-eluting stents (n = 469) on long-term mortality in 911 patients with significant CAD and severe LV dysfunction using large real-world registry data. Databases of 3 real-world registries were merged for a patient-level meta-analysis. Primary outcome was death from any cause; secondary outcomes were death from cardiac causes, myocardial infarction, stroke, or repeat revascularization. At a median follow-up of 37.3 months, the risk of all-cause death (adjusted hazard ratio [HR] 0.43; 95% confidence interval [CI] 0.31 to 0.61; p <0.001) was significantly lower in the CABG group than in the PCI group after adjustment. Similar findings were observed with regard to the risks of death from cardiac cause (adjusted HR 0.49; 95% CI 0.33 to 0.73; p <0.001) and repeat revascularization (adjusted HR 0.08; 95% CI 0.03 to 0.20; p <0.001). However, there were no significant differences in the risks of myocardial infarction and stroke between the 2 groups. The superiority of CABG over PCI was particularly pronounced in patients receiving β blockers and angiotensin-converting enzyme inhibitor or angiotensin receptor blockers than those who are not. In conclusion, among patients with significant CAD and severe LV dysfunction, CABG showed a lower risk of all-cause death, cardiac-cause death, and repeat revascularization compared with PCI with drug-eluting stents. **(Am J Cardiol 2017;■:■−■)**

The prognosis of patients with ischemic left ventricular (LV) dysfunction has significantly improved with the widespread use of evidence-based therapies.[1,2] Coronary artery bypass graft (CABG) surgery might be preferred over medical therapy for patients with significant coronary artery disease (CAD) and severe LV systolic dysfunction because of the long-term survival benefit of CABG over medical therapy.[3,4] In general, percutaneous coronary intervention (PCI) with drug-eluting stents (DESs) is not recommended because of the lack of evidence demonstrating its efficacy.[5,6] In real-world practice, however, PCI with DESs are often used for the treatment of patients with ischemic LV dysfunction. Unfortunately, data comparing CABG with PCI using DESs are limited. Although some observational studies showed that survival was longer with CABG than with PCI,[7,8] other studies suggested that survival rates were comparable between CABG and PCI.[9,10] Thus, the optimal revascularization strategy in this patient population remains unclear. In the present study, we compared the long-term mortality rates of CABG and PCI with DESs in patients with significant CAD and severe LV dysfunction using large real-world registry data.

Methods

Patients in this study were identified from the merged database that included the Interventional Research Incorporation Society-Left MAIN Revascularization (IRIS-MAIN), Interventional Research Incorporation Society-drug-eluting stents (IRIS-DES), and Asan Multivessel registries. The design and methodology of these registries are described in detail elsewhere.[11−13] Patients were eligible for this study if they had significant CAD (diameter stenosis for epicardial coronary artery, ≥70% or 50% to 70% with objective evidence of myocardial ischemia; diameter stenosis for left main coronary artery, ≥50%) in at least 1 major epicardial coronary artery, exhibited severe LV dysfunction (LV ejection fraction ≤35%), and underwent either CABG or PCI with DESs. Exclusion criteria included acute ST-elevation myocardial infarction, cardiogenic shock at the time of the index procedure, malignancy, and a history of previous CABG or concomitant valvular or aortic surgery. A total of 911 patients with severe LV dysfunction

[a]Department of Cardiology, CHA Bundang Medical Center, CHA University, Seongnam, Korea; and [b]Division of Cardiology and [c]Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea. Manuscript received December 29, 2016; revised manuscript received and accepted March 24, 2017.

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*Corresponding author: Tel: (+82) 2-3010-3150; fax: (+82) 2-486-5918.

E-mail address: cheolwlee@amc.seoul.k (C.W. Lee).

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who underwent either CABG (n = 442) or PCI with DESs (n = 469) were identified from the merged database and comprised the study population. CABG or PCI with DESs were performed according to the standard guideline. All databases had a common set of variables, including patient demographics, cardiovascular risk factors, clinical manifestations, hemodynamic status, LV function, extent of CAD, chronic renal failure, details of the procedures/operations, and outcomes during in-hospital and follow-up periods (1, 6, and 12 months and annually thereafter). Data were recorded in a pre-specified, Web-based, standardized case report form and were periodically monitored by independent research personnels.

The primary outcome of the present study was death from any cause. The secondary outcomes were death from cardiac cause, myocardial infarction, stroke, or repeat revascularization. Death was considered as cardiac unless an unequivocal noncardiac cause could be established. Myocardial infarction was defined as follows: (1) if occurring within 48 hours after the index treatment, an increase in the creatine kinase−myocardial band (CK-MB) values >5 times the upper reference limit with any of following: new pathologic Q waves or new bundle branch block, new graft or new native coronary occlusion documented on angiography, and new regional wall motion abnormality or loss of viable myocardium on imaging studies; and (2) if occurring 48 hours after the index treatment, an increase in the CK-MB values above the upper reference limit with ischemic symptoms or signs.[14–16] Stroke was confirmed by a neurologist on the basis of imaging techniques. Repeat revascularization included any percutaneous or surgical revascularization procedures.

Continuous variables were presented as means ± SD, and categorical variables were presented as numbers or percentages. Cumulative event rates and incidence curves for clinical outcomes were generated using the Kaplan-Meier method and compared using the log-rank test. To identify independent predictors of death from any cause among the entire study cohort, the Cox proportional hazards model with stepwise backward elimination methods (retention threshold, p <0.05) was used to adjust potential confounders identified by the investigators using literature search and based on clinical knowledge. These clinically relevant covariates, including demographics, coexisting clinical conditions, risk factors, cardiovascular history, extent of disease, and medication history, were introduced into a multivariable model. No method was used to impute missing values or adjust the model for the presence of missing data. The proportional hazards assumption was confirmed by the examination of log curves (−log [survival]) and by testing of partial residuals (Schoenfeld),[17] and no relevant violations were found in any of the groups. Statistical analyses were performed using the SPSS software, version 21.0 (SPSS, Inc., Chicago, Illinois). All p values were 2 sided, and p values <0.05 were considered to be statistically significant.

Results

Baseline characteristics are summarized in Table 1. Patients in the CABG group were younger, and there were more men in the CABG group than in the PCI group. The frequencies of risk factors, co-morbidities, and severe CAD were higher, and the percentage of patients on medications was lower in the CABG group than in the PCI group. Conversely, the number of patients with a history of smoking and those with atrial fibrillation or chronic lung disease were higher in the PCI group than in the CABG group. In the CABG group, the mean number of grafts was 3.0 ± 1.0, and arterial conduits were used in 96.8% of the patients. In the PCI group, previous DESs (paclitaxel- or sirolimus-eluting stents) were implanted in 27.5% of the patients, whereas the remaining patients received newer generation DESs.

The median follow-up time was 37.3 months (interquartile range 13.6 to 59.6 months). The cumulative incidences of clinical events up to 5 years are listed in Table 2. The unadjusted risk ratios for all-cause death, cardiac death,

Table 1
Baseline characteristics

Variables	CABG (n = 442)	PCI (n = 469)	P value
Age, (years)	63.6 ± 10.2	66.9 ± 11.1	<0.001
BMI, (kg/m^2)	23.6 ± 3.6	23.5 ± 3.4	0.820
Diabetes mellitus	238 (53.8%)	235 (50.1%)	0.288
Dyslipidemia	163 (46.9%)	145 (30.9%)	0.057
Hypertension	246 (55.7%)	285 (60.8%)	0.135
Smoker	120 (27.1%)	243 (51.8%)	<0.001
Family history of CAD	29 (6.6%)	13 (2.8%)	0.010
Acute coronary syndrome	292 (66.1%)	251 (53.5%)	<0.001
Atrial fibrillation	2 (0.5%)	52 (12.9%)	<0.001
Chronic renal failure	52 (11.8%)	64 (13.6%)	0.452
Chronic lung disease	12 (2.7%)	28 (6.0%)	0.025
Left ventricular ejection fraction	28.4 ± 5.1	28.6 ± 5.7	0.538
Previous myocardial infarction	91 (20.6%)	78 (16.6%)	0.147
Previous heart failure	80 (18.1%)	103 (22.0%)	0.170
Previous stroke	57 (12.9%)	63 (13.4%)	0.887
Peripheral vascular disease	31 (7.0%)	17 (3.6%)	0.032
No. of coronary arteries narrowed			<0.001
1	0 (0.0%)	130 (27.7%)	
2	71 (16.1%)	167 (35.6%)	
3	371 (83.9%)	172 (36.7%)	
3 and left main	166 (37.6%)	25 (5.3%)	
Left main	224 (50.7%)	46 (9.8%)	<0.001
Type of DES			-
Previous DES	-	129 (27.5%)	
Newer-generation DES	-	340 (72.5%)	
Number of DES	-	1.9 ± 1.1	
On-pump coronary bypass	211 (47.7%)	-	-
Number of total conduit	3.0 ± 1.0	-	-
Number of artery conduit	1.9 ± 1.0	-	-
Number of venous conduit	1.1 ± 0.9	-	-
Medication at discharge			
Aspirin	391 (88.5%)	455 (97.0%)	<0.001
Clopidogrel	328 (74.2%)	446 (95.1%)	<0.001
Beta-blocker	98 (22.2%)	272 (60.6%)	<0.001
Calcium channel blocker	59 (13.3%)	83 (18.8%)	<0.001
ACEi or ARB	110 (25.1%)	277 (62.4%)	<0.001
Statin	112 (25.3%)	295 (62.9%)	<0.001

ACEi = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blockers; BMI = body mass index; CAD = coronary artery disease; DES = drug-eluting stents.