JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 76, NO. 12, 2020

PUBLISHED BY ELSEVIER

ORIGINAL INVESTIGATIONS

Revascularization in Patients With Left Main Coronary Artery Disease and Left Ventricular Dysfunction

Sangwoo Park, MD,[a] Jung-Min Ahn, MD,[b] Tae Oh Kim, MD,[b] Hanbit Park, MD,[b] Do-Yoon Kang, MD,[b] Pil Hyung Lee, MD,[b] Yeong Jin Jeong, MD,[b] Junho Hyun, MD,[b] Junghoon Lee, MD,[b] Ju Hyeon Kim, MD,[b] Yujin Yang, MD,[b] Kyungjin Choe, MD,[b] Seung-Jung Park, MD,[b] Duk-Woo Park, MD,[b] for the IRIS-MAIN Registry Investigators

ABSTRACT

BACKGROUND Left main coronary artery (LMCA) disease is associated with high mortality and morbidity due to a large area of jeopardized myocardium. However, the optimal revascularization strategy for patients with LMCA disease and left ventricular dysfunction is still unclear.

OBJECTIVES This study sought to examine long-term comparative outcomes after percutaneous coronary intervention (PCI) or a coronary artery bypass grafting (CABG) according to the severity of left ventricular dysfunction.

METHODS The authors evaluated a total of 3,488 patients with LMCA disease who underwent CABG (n = 1,355) or PCI (n = 2,133) from the IRIS-MAIN (Interventional Research Incorporation Society-Left MAIN Revascularization) registry. Left ventricular function was categorized according to left ventricular ejection fraction (LVEF) as normal function (LVEF ≥55%), mild dysfunction (LVEF ≥45% to <55%), moderate dysfunction (LVEF ≥35% to <45%), or severe dysfunction (LVEF <35%). The primary outcome was a composite of death, myocardial infarction, or stroke.

RESULTS Among the overall patient population, 2,641 (75.7%) patients had normal LVEF and 403 (11.6%), 260 (7.5%), and 184 (5.3%) had mild, moderate, and severe left ventricular dysfunction at baseline, respectively. Compared with CABG, PCI was associated with a higher adjusted risk of primary outcomes in patients with moderate (hazard ratio [HR]: 2.23; 95% confidence interval [CI]: 1.17 to 4.28) or severe (HR: 2.45; 95% CI: 1.27 to 4.73) dysfunction. In contrast, PCI and CABG had similar risks of the primary outcomes in patients with normal (HR: 0.80; 95% CI: 0.59 to 1.07) or mild (HR: 1.17; 95% CI: 0.63 to 2.17) dysfunction (p for interaction = 0.004).

CONCLUSIONS In the revascularization of LMCA disease, PCI was associated with an inferior primary composite outcome of death, MI, or stroke compared with CABG in patients with moderate or severe left ventricular dysfunction. However, the risk for the primary outcome was comparable between PCI and CABG in those with normal or mild left ventricular dysfunction. (Observational Study for Left Main Disease Treatment; NCT01341327)
(J Am Coll Cardiol 2020;76:1395-406) © 2020 by the American College of Cardiology Foundation.

Listen to this manuscript's audio summary by Editor-in-Chief Dr. Valentin Fuster on JACC.org.

From the [a]Department of Cardiology, Ulsan University Hospital, University of Ulsan College of Medicine, Ulsan, Korea; and the [b]Department of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea. This work was partly supported by a grant from the Cardiovascular Research Foundation of South Korea. The sponsors played no role in this study. There was no industry involvement in the design or conduct of the study; the collection, management, analysis, and interpretation of the data; the preparation, review, and approval of the manuscript; or the decision to submit the manuscript for publication. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.
The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the *JACC* author instructions page.

Manuscript received March 18, 2020; revised manuscript received July 6, 2020, accepted July 20, 2020.

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2020.07.047

ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting

CAD = coronary artery disease

IPTW = inverse probability of treatment weighting

IVUS = intravenous ultrasound

LMCA = left main coronary artery

LV = left ventricular

LVEF = left ventricular ejection fraction

MI = myocardial infarction

OMT = optimal medical therapy

PCI = percutaneous coronary intervention

Coronary artery disease (CAD) is the leading cause of left ventricular (LV) dysfunction. Although prior studies have shown better clinical outcomes after a coronary artery bypass grafting (CABG) than after optimal medical therapy (OMT) or percutaneous coronary intervention (PCI) in patients with CAD and LV dysfunction (1–4), there is still no robust evidence regarding the proper revascularization strategy in patients with reduced LV function. Furthermore, few reports have directly compared the long-term outcomes of CABG and PCI in patients with LV dysfunction and more complex or extensive CAD, such as 3-vessel or left main coronary artery (LMCA) disease.

SEE PAGE 1407

Historically, CABG has been regarded as the first choice for patients with significant LMCA diseases. With major advances in PCI, several studies have shown that CABG and PCI have comparable efficacies for LMCA disease in the medium term (3 to 5 years) (5–8). However, further longer-term reports showed conflicting results (9–14), with some reporting a trend of late catchup or crossover in the incidences of primary composite outcomes or mortality in favor of CABG over PCI (11,13,14). Therefore, the optimal choice between CABG and PCI is still under considerable debate, and a specific subset of patients with LMCA disease with high-risk clinical and anatomic characteristics (e.g., diabetes, concomitant multivessel disease, low left ventricular ejection fraction [LVEF], and a high SYNTAX score) may benefit more from CABG despite the remarkable improvements in the procedural techniques and stent profiles (10,15).

Because a large area of myocardium is jeopardized by LMCA disease, the major long-term manifestations of significant LMCA disease could be associated with LV dysfunction and heart failure, which are subsequently related to increased mortality (16,17). However, it is not yet established whether long-term outcomes after CABG and PCI for LMCA disease are differentially affected by the degree of LV dysfunction. Therefore, we sought to evaluate the treatment effect of the revascularization strategy according to the severity of LV dysfunction in patients with LMCA disease using the large-sized IRIS-MAIN (Interventional Research Incorporation Society-Left MAIN Revascularization) registry.

METHODS

STUDY POPULATION. The study population was composed of a part of the prospective, ongoing IRIS-MAIN registry. Details on the study design have been published previously (7). Briefly, the IRIS-MAIN is a nonrandomized, multinational, observational registry wherein consecutive patients with unprotected LMCA disease who were treated with PCI, CABG, or medication alone are enrolled. The study patients were recruited from 50 academic and community hospitals in Asia (China, India, Indonesia, Japan, Malaysia, South Korea, Taiwan, and Thailand). This study had an "all-comers" design to evaluate characteristics, treatments, and clinical outcomes of patients with LMCA disease in the real-world setting. The exclusion criteria were minimal; patients who had prior CABG, those who underwent concomitant valvular or aortic surgery, and those who had terminal malignancy with expected life expectancy <1 year were excluded. For the current analyses, patients who received medical treatment alone and those for whom information on baseline LVEF or coronary anatomy was not available were also excluded. The research protocol was approved by the research ethics committee of each participating center, and written informed consent was obtained by all participants.

Study patients were categorized according to the severity of LV dysfunction at the index hospitalization. Global LV systolic function was qualitatively measured from the 2-dimensional echocardiogram as LVEF. LV dysfunction was defined as LVEF <55%, and patients with LV dysfunction were further stratified into mild (LVEF ≥45% to <55%), moderate (LVEF ≥35% to <45%), and severe LV dysfunction (LVEF <35%).

STUDY OUTCOMES AND FOLLOW-UP. The primary outcome of the study was a composite of death, myocardial infarction (MI), and stroke. Secondary outcomes included all-cause mortality or repeat revascularization. Death from any cause was primarily considered. MI was defined as follows: 1) if occurring within 48 h after the index treatment, an increase in the creatine kinase-myocardial band values >5 times the upper limit of normal with any of the following: the development of new pathological Q waves or a new bundle branch block, a documented new graft or new coronary occlusion on angiography, and a new or worsening regional wall motion abnormality or loss of viable myocardium on imaging studies; and 2) if

occurring after 48 h after the index revascularization, any increase in the creatine kinase-myocardial band above the upper limit of normal with symptoms or signs suggestive of ischemia (7). Stroke was defined as a sudden onset of neurological deficit confirmed by a neurologist using imaging studies. The index hospitalization was defined as the hospitalization in which an LMCA intervention was performed for the first time. Repeat revascularization included any type of percutaneous or surgical revascularization procedure after the index revascularization regardless of whether the procedure was performed on a target or nontarget lesion. All clinical events were confirmed by source documentation collected from each hospital and were centrally adjudicated by an independent group of clinicians who were blinded to the index revascularization treatment.

Clinical follow-up was performed at 1 month, 6 months, and 1 year after the index treatment and then annually thereafter via an office visit or telephone follow-up. Information on baseline demographic and clinical characteristics, including LV function, coronary angiographic findings, procedural or operative data, and in-hospital and follow-up outcome data, was collected from each participating center using a pre-specified electronic case report form and periodically monitored by independent study personnel.

STATISTICAL ANALYSIS. The main purpose of this study was to evaluate whether there are differences in long-term clinical outcomes between CABG and PCI according to the severity of LV dysfunction. Baseline characteristics of the study population, including demographics and clinical characteristics, coronary angiographic findings, and procedural or operative data, were compared according to the severity of LV dysfunction and revascularization strategy. Categoric variables were reported as frequencies with percentages and were compared using either the Pearson chi-square test or the Fisher exact test as appropriate. Continuous variables were presented as mean ± SD and were compared using the Student's *t*-test or 1-way analysis of variance. Restricted cubic splines were fitted with 4 degrees of freedom with regard to LVEF as the continuous variable to investigate the association of LVEF with clinical outcomes, and a test for linearity was performed in these models. To identify independent predictors and potential confounders for the primary composite outcome and all-cause mortality, univariate and multivariate analyses using the Cox regression model were performed. Cumulative event rates and incidence curves for clinical outcomes after CABG and PCI were generated using the Kaplan-Meier method and compared with log-rank tests.

Considering the differences in baseline characteristics between 2 revascularization strategies and model overfitting due to the relatively small number of patients with severe LV dysfunction, stabilized inverse probability of treatment weighting (IPTW) using the propensity score was used to reduce the effects of observed confounding (18,19). Propensity scores were estimated via multiple logistic regression analysis using the pretreatment variables listed in **Table 1** and time periods based on the generation of stents used in PCI (7). For each group of LV dysfunction, a separate propensity score was calculated. We examined the similarities in baseline characteristics between the treatment groups before and after IPTW. Weighted standardized mean differences were estimated for all of the baseline covariates, and values <0.10 for a given covariate indicated a relatively small imbalance (20). Weighted Cox proportional hazards regression models with stabilized IPTW were used to compare the effect of the revascularization strategy according to the severity of LV dysfunction. Further adjustment was performed for estimating the adjusted treatment effect, including post-treatment variables such as cardiovascular medications at discharge. Finally, the doubly robust method was applied by including independent predictors for each clinical outcome in the weighted model (21). To assess the interaction between the severity of LV dysfunction and the relative treatment effect, formal tests for interactions were conducted in the weighted Cox regression models. For sensitivity analysis, repeated analyses on hard clinical endpoints were conducted with different LVEF cutoffs (i.e., preserved LVEF [LVEF ≥55%], midrange LVEF [LVEF ≥40% to <55%], and reduced LVEF [LVEF <40%]).

All reported p values were 2-sided, and $p < 0.05$ was considered significant for all tests. No adjustment for multiple testing was undertaken. Because of the potential for type I error due to multiple comparisons, all findings of this study should be interpreted as exploratory. Statistical analyses were performed using SPSS version 22.0 (IBM Corporation, Armonk, New York) and R software version 3.6.2. (R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS. Between January 2003 and December 2016, a total of 5,349 patients were included in the IRIS-MAIN registry. Among them, we identified 3,488 patients with

TABLE 1 Baseline Clinical and Anatomic Characteristics of the Patients According to Severity of Left Ventricular Dysfunction and Revascularization Methods

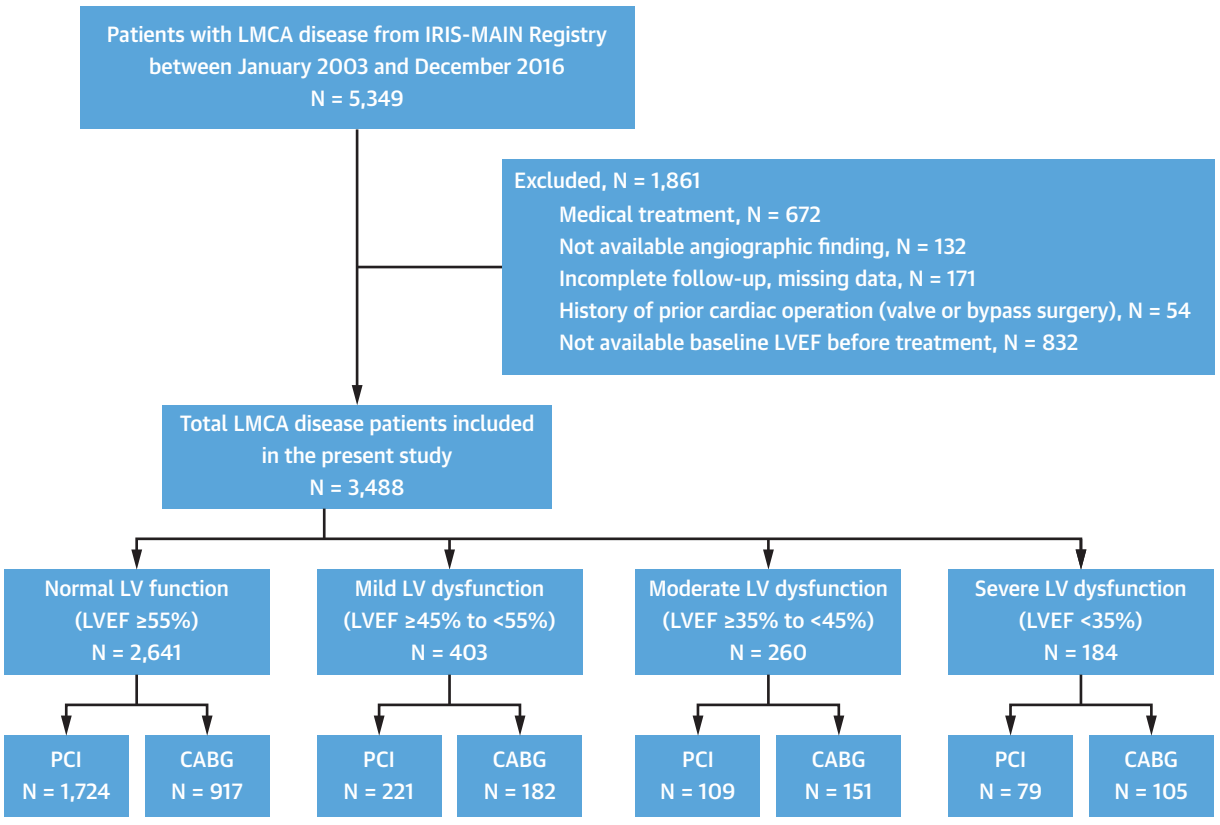
	Normal LV Function (LVEF ≥55%)			Mild LV Dysfunction (LVEF ≥45% to <55%)			Moderate LV Dysfunction (LVEF ≥35% to <45%)			Severe LV Dysfunction (LVEF <35%)		
	PCI (n = 1,724)	CABG (n = 917)	p Value	PCI (n = 221)	CABG (n = 182)	p Value	PCI (n = 109)	CABG (n = 151)	p Value	PCI (n = 79)	CABG (n = 105)	p Value
Year of revascularization*												
2003–2006	260 (15.1)	337 (36.8)	<0.001	25 (11.3)	70 (38.5)	<0.001	10 (9.2)	50 (33.1)	<0.001	8 (10.1)	38 (36.2)	<0.001
2007–2016	1464 (84.9)	580 (63.2)	<0.001	196 (88.7)	112 (61.5)	<0.001	99 (90.8)	101 (66.9)	<0.001	71 (89.9)	67 (63.8)	<0.001
Clinical characteristics												
Age, yrs	63.6 ± 10.5	64.4 ± 8.9	0.02	66.1 ± 11.4	65.8 ± 8.7	0.73	65.8 ± 11.8	65.2 ± 8.3	0.64	67.7 ± 9.9	65.3 ± 9.9	0.11
Men	1319 (76.5)	708 (77.2)	0.72	184 (83.3)	151 (83.0)	>0.99	80 (73.4)	125 (82.8)	0.09	66 (83.5)	81 (77.1)	0.38
BMI, kg/m^2	24.7 ± 3.0	24.8 ± 2.9	0.32	24.2 ± 2.9	24.9 ± 3.4	0.02	23.6 ± 3.2	23.8 ± 3.1	0.54	23.1 ± 3.1	23.6 ± 3.1	0.27
Hypertension	1114 (64.6)	604 (65.9)	0.55	134 (60.6)	120 (65.9)	0.32	66 (60.6)	88 (58.3)	0.81	50 (63.3)	63 (60.0)	0.76
Diabetes mellitus	555 (32.2)	359 (39.1)	<0.001	84 (38.0)	80 (44.0)	0.27	48 (44.0)	80 (53.0)	0.19	36 (45.6)	52 (49.5)	0.70
Insulin requiring	71 (4.1)	52 (5.7)	0.09	9 (4.1)	15 (8.2)	0.12	11 (10.1)	19 (12.6)	0.67	6 (7.6)	14 (13.3)	0.32
Hyperlipidemia	1188 (68.9)	519 (56.6)	<0.001	135 (61.1)	87 (47.8)	0.01	66 (60.6)	75 (49.7)	0.11	38 (48.1)	54 (51.4)	0.77
Smoking	380 (22.0)	222 (24.2)	0.22	69 (31.2)	54 (29.7)	0.82	33 (30.3)	47 (31.1)	0.99	19 (24.1)	38 (36.2)	0.11
Previous MI	83 (4.8)	75 (8.2)	0.001	38 (17.2)	37 (20.3)	0.50	20 (18.3)	37 (24.5)	0.30	10 (12.7)	26 (24.8)	0.06
Previous PCI	268 (15.5)	109 (11.9)	0.01	54 (24.4)	35 (19.2)	0.26	22 (20.2)	21 (13.9)	0.24	10 (12.7)	9 (8.6)	0.51
Previous CVA	135 (7.8)	76 (8.3)	0.74	26 (11.8)	16 (8.8)	0.42	11 (10.1)	10 (6.6)	0.43	7 (8.9)	17 (16.2)	0.22
Previous PAD	76 (4.4)	67 (7.3)	0.002	6 (2.7)	22 (12.1)	<0.001	5 (4.6)	12 (7.9)	0.41	5 (6.3)	7 (6.7)	>0.99
Chronic lung disease	31 (1.8)	35 (3.8)	0.002	14 (6.3)	6 (3.3)	0.24	3 (2.8)	4 (2.6)	>0.99	3 (3.8)	4 (3.8)	>0.99
Chronic renal failure	49 (2.8)	29 (3.2)	0.73	20 (9.0)	7 (3.8)	0.06	20 (18.3)	18 (11.9)	0.20	13 (16.5)	11 (10.5)	0.33
Dialysis	20 (1.2)	16 (1.7)	0.29	12 (5.4)	4 (2.2)	0.16	13 (11.9)	11 (7.3)	0.29	10 (12.7)	5 (4.8)	0.10
CHF	14 (0.8)	6 (0.7)	0.83	10 (4.5)	4 (2.2)	0.32	12 (11.0)	15 (9.9)	0.94	13 (16.5)	23 (21.9)	0.46
Ejection fraction, %	63.1 ± 4.8	62.1 ± 4.3	<0.001	49.7 ± 2.9	49.7 ± 3.1	0.96	39.8 ± 2.9	39.7 ± 2.8	0.91	27.2 ± 5.0	27.6 ± 4.6	0.62
Atrial fibrillation	25 (1.5)	7 (0.8)	0.18	13 (5.9)	6 (3.3)	0.33	5 (4.6)	7 (4.6)	>0.99	5 (6.3)	2 (1.9)	0.25
ACS	901 (52.3)	571 (62.3)	<0.001	144 (65.2)	125 (68.7)	0.52	69 (63.3)	105 (69.5)	0.36	53 (67.1)	90 (85.7)	0.005
Clinical indication			<0.001			0.001			0.01			<0.001
Silent ischemia	98 (5.7)	58 (6.3)		13 (5.9)	15 (8.2)		12 (11.0)	13 (8.6)		11 (13.9)	10 (9.5)	
Stable angina	725 (42.1)	288 (31.4)		64 (29.0)	42 (23.1)		28 (25.7)	33 (21.9)		15 (19.0)	5 (4.8)	
Unstable angina	752 (43.6)	522 (56.9)		75 (33.9)	95 (52.2)		29 (26.6)	72 (47.7)		9 (11.4)	51 (48.6)	
NSTEMI	124 (7.2)	39 (4.3)		53 (24.0)	24 (13.2)		26 (23.9)	20 (13.2)		25 (31.6)	24 (22.9)	
STEMI	25 (1.5)	10 (1.1)		16 (7.2)	6 (3.3)		14 (12.8)	13 (8.6)		19 (24.1)	15 (14.3)	
Anatomic characteristics												
Extent of CAD			<0.001			<0.001			<0.001			<0.001
Left main only	202 (11.7)	25 (2.7)		16 (7.2)	0 (0.0)		7 (6.4)	2 (1.3)		9 (11.4)	2 (1.9)	
Left main + 1VD	437 (25.3)	52 (5.7)		43 (19.5)	8 (4.4)		19 (17.4)	10 (6.6)		18 (22.8)	4 (3.8)	
Left main + 2VD	619 (35.9)	188 (20.5)		89 (40.3)	38 (20.9)		42 (38.5)	21 (13.9)		22 (27.8)	13 (12.4)	
Left main + 3VD	466 (27.0)	652 (71.1)		73 (33.0)	136 (74.7)		41 (37.6)	118 (78.1)		30 (38.0)	86 (81.9)	
Left main disease location												
Ostium or shaft	850 (49.3)	356 (38.8)	<0.001	102 (46.2)	77 (42.3)	0.50	55 (50.5)	80 (53.0)	0.78	36 (45.6)	47 (44.8)	>0.99
Distal bifurcation	1024 (59.4)	608 (66.3)	0.001	131 (59.3)	118 (64.8)	0.30	67 (61.5)	84 (55.6)	0.42	48 (60.8)	69 (65.7)	0.59
Proximal LAD disease	1233 (71.5)	716 (78.9)	<0.001	164 (74.2)	144 (80.0)	0.21	89 (81.7)	110 (73.8)	0.18	57 (72.2)	81 (77.1)	0.47
RCA disease	707 (41.0)	722 (78.7)	<0.001	111 (50.2)	153 (84.1)	<0.001	59 (54.1)	129 (85.4)	<0.001	38 (48.1)	91 (86.7)	<0.001
No. of total lesions	2.3 ± 1.3	3.9 ± 1.6	<0.001	2.7 ± 1.4	4.1 ± 1.7	<0.001	2.7 ± 1.2	4.2 ± 1.5	<0.001	2.7 ± 1.5	4.1 ± 1.5	<0.001

Values are n (%) or mean ± SD. *Historic time periods were chosen based on the generation of stent used in PCI: first-generation drug-eluting stent era for 2003 to 2006 and second-generation drug-eluting stent era for 2007 to 2016.

ACS = acute coronary syndrome; BMI = body mass index; CAD = coronary artery disease; CHF = congestive heart failure; CVA = cerebrovascular accident; LAD = left anterior descending artery; MI = myocardial infarction; PAD = peripheral artery disease; NSTEMI, non-ST-segment elevation myocardial infarction; RCA = right coronary artery; STEMI = ST-segment elevation myocardial infarction; VD = vessel disease; other abbreviations as in Figure 1.

significant LMCA disease who met our inclusion and exclusion criteria (Figure 1), of whom 1,355 (38.8%) underwent CABG and 2,133 (61.2%) underwent PCI with stenting. In this overall population, 2,641 (75.7%) patients had normal LV function, but 403 (11.6%), 260 (7.5%), and 184 (5.3%) had mild, moderate, and severe LV dysfunction at index admission, respectively. Baseline clinical and anatomic characteristics according to the severity of LV dysfunction and treatment strategy are summarized in Table 1 and Supplemental Tables 1 and 2. Overall and in each group of LV dysfunction, patients receiving CABG had a higher risk factor profile with respect to clinical and comorbid conditions as well as angiographic

FIGURE 1 Study Flowchart



Patient selection and grouping. The numbers of patients excluded and enrolled in the present study are shown. CABG = coronary artery bypass grafting; IRIS-MAIN = Interventional Research Incorporation Society-Left MAIN Revascularization; LMCA = left main coronary artery; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention.

complexity compared with those receiving PCI. In addition, patients with a severe degree of LV dysfunction tended to be older and had a higher proportion of clinical and anatomic risk factors than those with relatively less severe dysfunction.

Detailed information on procedural or operative characteristics according to the severity of LV dysfunction is summarized in Table 2. In the PCI arm, patients with a more severe form of LV dysfunction underwent the complex bifurcation 2-stent technique less frequently but had more use of mechanical circulatory support compared with those with relatively less severe dysfunction. In the CABG arm, patients with a severe form of LV dysfunction had less use of off-pump CABG, less use of a left internal mammary artery graft, and a lower number of arterial grafts compared with those with relatively less severe dysfunction. Complete revascularization in the PCI arm was achieved in 63.4% of the patients overall (64.7% in normal, 59.3% in mild, 51.4% in moderate, and 62.0% in severe LV dysfunction). Medical management at discharge differed between the CABG and PCI groups; patients who underwent CABG received less pharmacological treatment, whereas those who underwent PCI were consistently treated with antiplatelet medications (Table 3).

LONG-TERM CLINICAL OUTCOMES. In the overall population, the median follow-up duration was 3.8 years (interquartile range: 2.1 to 5.5 years). The relationships between LVEF and the primary and secondary clinical outcomes in each arm of CABG or PCI and the relative risk of CABG versus PCI according to LVEF change are shown in Supplemental Figures 1 to 3. The risks for primary outcome and all-cause mortality increased with decreasing values of LVEF; nonlinearity was not identified for the effect of LVEF on clinical outcomes. In addition, LVEF was an independent predictor for the primary composite

TABLE 2 Procedural or Operative Characteristics of the Patients According to the Severity of Left Ventricular Dysfunction and Revascularization Methods

	Normal (n = 2,641)	Mild (n = 403)	Moderate (n = 260)	Severe (n = 184)	p Value
Revascularization					<0.001
PCI	1,724 (65.3)	221 (54.8)	109 (41.9)	79 (42.9)	
CABG	917 (34.7)	182 (45.2)	151 (58.1)	105 (57.1)	
Characteristics of PCI procedure	1,724	221	109	79	
BMS	24 (1.4)	5 (2.3)	3 (2.8)	1 (1.3)	0.047
DES					0.047
First-generation DES	383 (22.5)	33 (15.2)	17 (15.9)	10 (13.3)	
Second-generation DES	1293 (76.1)	179 (82.5)	87 (81.3)	64 (85.3)	
Total number of stents per patient	2.2 ± 1.2	2.5 ± 1.4	2.4 ± 1.2	2.3 ± 1.5	0.04
Total stent number at LM site	1.7 ± 0.9	1.8 ± 1.0	1.8 ± 0.9	1.6 ± 0.9	0.52
Total stent length, mm	52.4 ± 34.4	59.6 ± 37.2	54.8 ± 32.9	53.1 ± 39.5	0.16
Stent technique					0.20
LM stent only	315 (18.3)	33 (14.9)	21 (19.3)	20 (25.3)	
Stenting crossing LAD	62 (3.6)	10 (4.5)	9 (8.3)	4 (5.1)	
Stenting crossing LCX	934 (54.2)	121 (54.8)	57 (52.3)	39 (49.4)	
Bifurcation 2 stents	401 (23.3)	56 (25.3)	21 (19.3)	14 (17.7)	
Others	12 (0.7)	1 (0.5)	1 (0.9)	2 (2.5)	
Final kissing	582 (33.8)	84 (38.5)	25 (23.6)	22 (28.6)	<0.001
IVUS guidance	1428 (83.0)	166 (75.1)	74 (67.9)	39 (50.0)	<0.001
Use of MCS	46 (2.7)	12 (5.4)	18 (16.5)	21 (26.6)	<0.001
Complete revascularization	1116 (64.7)	131 (59.3)	56 (51.4)	49 (62.0)	0.02
Characteristics of CABG procedure	917	182	151	105	
Off-pump	552 (60.3)	95 (52.8)	77 (51.0)	51 (48.6)	0.02
On-pump	364 (39.7)	85 (47.2)	74 (49.0)	54 (51.4)	0.02
LIMA graft use	884 (96.4)	167 (91.8)	142 (94.0)	91 (86.7)	<0.001
Radial artery graft use	500 (54.5)	89 (48.9)	68 (45.0)	44 (41.9)	0.02
Total number of grafts	3.0 ± 1.0	3.0 ± 0.9	3.0 ± 0.9	3.0 ± 1.0	0.61
Number of arterial grafts	2.0 ± 0.9	1.8 ± 0.9	1.8 ± 1.0	1.7 ± 1.0	<0.001

Values are n (%), n, or mean ± SD. Left ventricular dysfunction was defined as LVEF <55%, and patients with left ventricular dysfunction were further stratified into mild (LVEF ≥45% to <55%), moderate (LVEF ≥35% to <45%), or severe dysfunction (LVEF <35%).

BMS = bare-metal stent; DES, drug-eluting stent; IVUS = intravascular ultrasound; LAD = left anterior descending artery; LCX = left circumflex artery; LM = left main; LIMA = left internal mammary artery; MCS = mechanical circulatory support; other abbreviations as in Figure 1.

outcome and all-cause mortality (Supplemental Tables 3 and 4).

The observed (unadjusted) rates of primary and secondary outcomes after PCI versus CABG stratified by the severity of LV dysfunction are shown in **Table 4**. The incidences of the primary composite outcome of death, MI, or stroke and all-cause mortality proportionally increased according to the increasing severity of LV dysfunction, and the relative outcomes after revascularization favored CABG over PCI in patients with a more severe form of LV dysfunction (**Figure 2**). A higher incidence of mortality after PCI than after CABG was also noted in patients with severe LV dysfunction (Supplemental Figure 4). However, the incidences of repeat revascularization were consistently higher after PCI than after CABG (Supplemental Figure 5).

Variables included in the propensity score model and the corresponding odds ratios for being treated with PCI are shown in Supplemental Table 5. The distribution of propensity scores in the treatment groups are illustrated in Supplemental Figure 6; the overlap between the propensity score for the treatment groups became poorer as the severity of LV dysfunction worsened. After adjustment with the use of IPTW, all pretreatment covariates were well balanced between the 2 groups (Supplemental Table 6). The unadjusted and principal adjusted risks for the primary composite outcome and secondary outcomes are shown in **Table 5** and the **Central Illustration**. In the final adjusted model (stabilized IPTW with the doubly robust method and further adjustment for the important post-treatment variables of cardioactive medications), PCI was associated with a higher risk of the primary composite outcome compared with CABG in patients with moderate or severe LV dysfunction, whereas the adjusted risk for the primary outcome was comparable between PCI and CABG in those with normal or mild LV dysfunction. Thus, there was a significant interaction between the severity of LV dysfunction and the treatment effect of PCI versus CABG on the primary outcome. These findings were consistent in the different analytic techniques (Supplemental Tables 7 and 8, Supplemental Figure 7). A similar nonsignificant trend was observed for the adjusted risks of all-cause mortality. The adjusted risk of repeat revascularization was consistently higher after PCI than after CABG; however, this trend was less prominent in patients with severe LV dysfunction.

When we assessed the relative treatment effect according to the complete revascularization status of PCI, the trend favoring CABG over PCI in patients with moderate to severe LV dysfunction was only significant in comparison with PCI with incomplete revascularization versus CABG (Supplemental Table 9, Supplemental Figure 8). In the sensitivity analysis using different LVEF cutoffs, the overall findings were similar (Supplemental Table 10).

DISCUSSION

In this large-sized contemporary cohort of patients with significant LMCA disease who underwent PCI or CABG, we evaluated the effectiveness of the revascularization strategy according to the severity of LV dysfunction. The major findings of this study are that: 1) lower LVEF was an independent predictor for hard clinical endpoints and all-cause mortality; 2) a significant interaction was present between the severity of LV dysfunction and treatment with PCI compared

TABLE 3 Cardiac-Related Medications at Discharge According to the Severity of Left Ventricular Dysfunction and Revascularization Methods

	Normal			Mild			Moderate			Severe		
	PCI (n = 1,724)	CABG (n = 917)	p Value	PCI (n = 221)	CABG (n = 182)	p Value	PCI (n = 109)	CABG (n = 151)	p Value	PCI (n = 79)	CABG (n = 105)	p Value
Aspirin	1,713 (99.4)	893 (97.4)	<0.001	215 (97.3)	178 (97.8)	0.99	103 (94.5)	142 (94.0)	0.999	69 (87.3)	93 (88.6)	0.98
$P2Y_{12}$ inhibitor	1,690 (98.0)	791 (86.3)	<0.001	213 (96.4)	159 (87.4)	0.001	102 (93.6)	126 (83.4)	0.02	69 (87.3)	80 (76.2)	0.09
Clopidogrel	1,632 (94.7)	791 (86.3)	<0.001	190 (86.0)	159 (87.4)	0.79	90 (82.6)	126 (83.4)	0.99	63 (79.7)	80 (76.2)	0.69
Ticagrelor	40 (2.3)	0 (0.0)	<0.001	19 (8.6)	0 (0.0)	<0.001	10 (9.2)	0 (0.0)	0.001	5 (6.3)	0 (0.0)	0.03
Prasugrel	21 (1.2)	0 (0.0)	0.002	6 (2.7)	0 (0.0)	0.07	2 (1.8)	0 (0.0)	0.34	1 (1.3)	0 (0.0)	0.89
Beta-blocker	1,148 (66.6)	466 (50.8)	<0.001	139 (62.9)	93 (51.1)	0.02	81 (74.3)	69 (45.7)	<0.001	37 (46.8)	42 (40.0)	0.44
CCB	1,042 (60.4)	620 (67.6)	<0.001	89 (40.3)	109 (59.9)	<0.001	36 (33.0)	79 (52.3)	0.003	14 (17.7)	43 (41.0)	0.001
ACE inhibitor	174 (10.1)	52 (5.7)	<0.001	51 (23.1)	18 (9.9)	0.001	29 (26.6)	12 (7.9)	<0.001	15 (19.0)	22 (21.0)	0.89
ARB	432 (25.1)	123 (13.4)	<0.001	57 (25.8)	29 (15.9)	0.02	40 (36.7)	40 (26.5)	0.10	24 (30.4)	37 (35.2)	0.59
Statin	1,626 (94.3)	886 (96.6)	0.01	195 (88.2)	176 (96.7)	0.003	101 (92.7)	141 (93.4)	>0.99	66 (83.5)	93 (88.6)	0.44

Values are n (%). Left ventricular dysfunction was defined as LVEF <55%, and patients with left ventricular dysfunction were further stratified into mild (LVEF ≥45% to <55%), moderate (LVEF ≥35% to <45%), or severe dysfunction (LVEF <35%).

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blocker; CCB = calcium-channel blocker; other abbreviations as in Figure 1.

with CABG on the relative risk of the 5-year primary composite outcome of death, MI, or stroke; 3) in patients with moderate or severe LV dysfunction, PCI was associated with a higher risk of primary composite outcome compared with CABG (however, the risk for the primary outcome was comparable between PCI and CABG in those with normal or mild LV dysfunction); and 4) a similar trend without statistical significance was noted for all-cause mortality, whereas PCI was consistently associated with an increased risk of repeat revascularization.

The optimal revascularization strategy in patients with significant CAD and severe LV systolic dysfunction still remains unclear (22). For optimal revascularization in patients with chronic heart failure and severe LV dysfunction (LVEF ≤35%), the recent European guidelines recommend CABG as a Class I indication in patients with multivessel disease and acceptable surgical risk, whereas they recommend PCI as a Class IIa indication in patients with 1- or 2-vessel disease or consider PCI as a Class IIa indication in patients with 3-vessel disease on the evaluation of the patient's coronary anatomy, the expected completeness of revascularization, diabetes status, and comorbidities by the Heart Team (23). By contrast, the U.S. appropriate use criteria propose that CABG is a reasonable option (Class IIa) in patients with moderate LV dysfunction (LVEF 35% to 50%) and may be considered (Class IIb) for patients with severe LV dysfunction (LVEF <35%); however, they confer no recommendations for PCI (24). In the 10-year reports from the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) trial and the PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trial, the long-term risk of all-cause death was not different between CABG and PCI

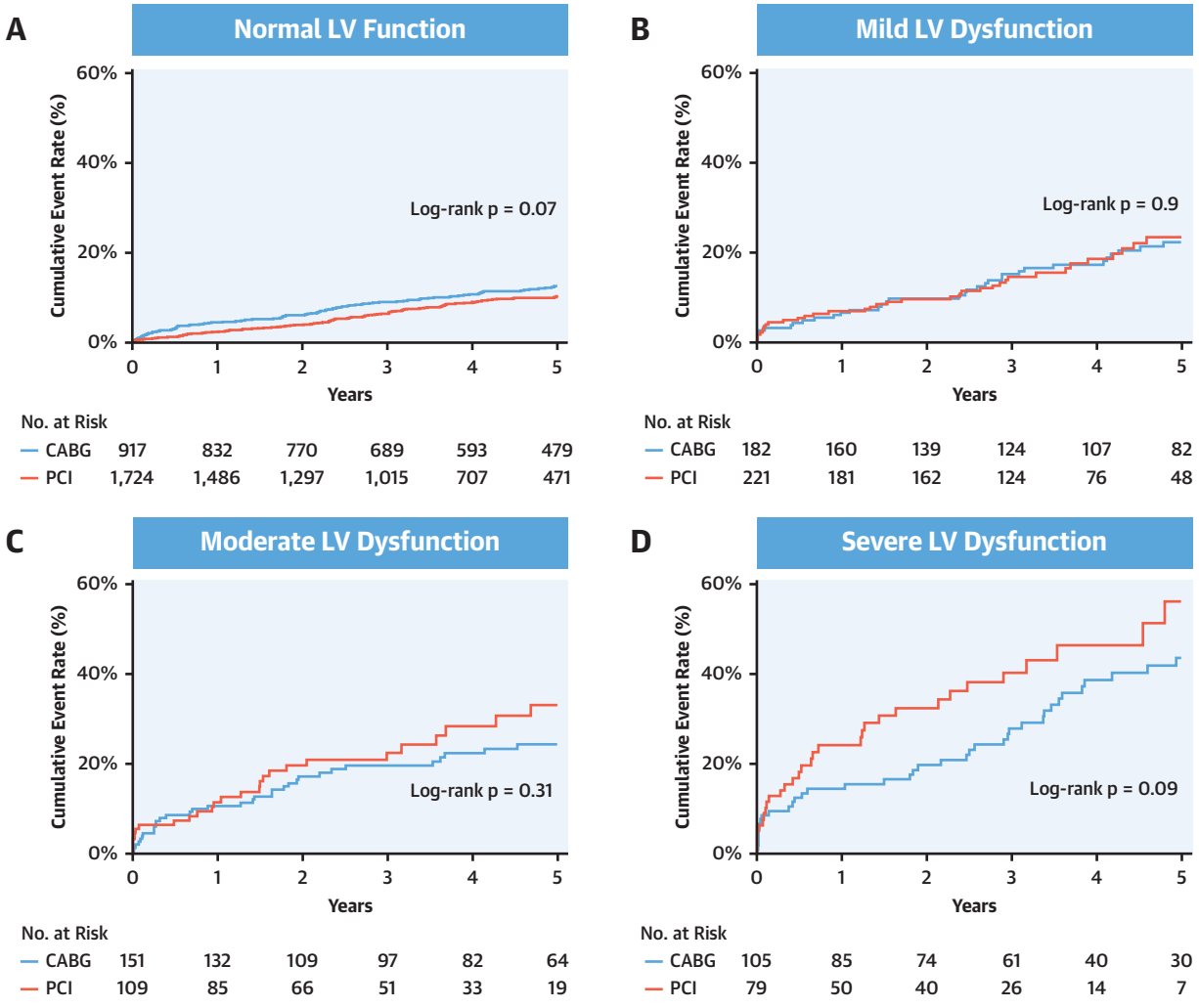
TABLE 4 Unadjusted (Observed) 5-Year Clinical Outcomes After PCI and CABG Stratified by the Severity of LV Dysfunction

	Normal LV Function (LVEF ≥55%)			Mild LV Dysfunction (LVEF ≥45% to <55%)			Moderate LV Dysfunction (LVEF ≥35% to <45%)			Severe LV dysfunction (LVEF <35%)		
	PCI (n = 1,724)	CABG (n = 917)	p Value	PCI (n = 221)	CABG (n = 182)	p Value	PCI (n = 109)	CABG (n = 151)	p Value	PCI (n = 79)	CABG (n = 105)	p Value
Primary composite outcome: death, MI, or stroke at 5 yrs	127 (10.6)	101 (12.6)	0.07	36 (23.5)	34 (22.2)	0.90	26 (33.1)	33 (24.4)	0.31	31 (56.2)	38 (43.6)	0.09
Secondary outcomes												
All-cause mortality	98 (8.4)	78 (9.8)	0.12	30 (19.5)	30 (20.2)	0.99	22 (28.7)	27 (20.2)	0.30	27 (44.2)	34 (38.9)	0.23
MI	20 (1.6)	10 (1.4)	0.56	5 (4.4)	0 (0)	0.02	2 (4.3)	1 (0.9)	0.25	3 (11.3)	2 (2.9)	0.23
Stroke	22 (1.7)	22 (2.8)	0.08	3 (1.4)	7 (4.1)	0.12	4 (4.9)	6 (2.7)	0.97	4 (11.2)	6 (9.9)	0.60
Repeat revascularization	163 (12.2)	30 (3.9)	<0.001	21 (15.2)	4 (2.7)	0.001	8 (12.3)	3 (2.7)	0.01	7 (12.8)	6 (7.6)	0.26

Values are n (%). Event rates were based on Kaplan-Meier estimates in time to first event analyses, and p values are derived using the log-rank test.

EF = ejection fraction; other abbreviations as in Figure 1.

FIGURE 2 Unadjusted 5-Year Event Rates for the Primary Composite Outcome According to the Severity of LV Dysfunction in Patients Who Underwent PCI or CABG for LMCA Disease



Crude event curves after CABG and PCI are shown in **(A)** the normal LV function group (EF ≥55%), **(B)** mild LV dysfunction group (EF ≥45% to <55%), **(C)** moderate LV dysfunction group (EF ≥35% to <45%), and **(D)** severe LV dysfunction group (EF <35%). The primary composite outcome was defined as the composite of death from any cause, myocardial infarction, or stroke. EF = ejection fraction; LV = left ventricular; other abbreviations as in Figure 1.

(12,25). Updated meta-analysis showed that PCI with drug-eluting stents showed similar long-term mortality compared with CABG for LMCA disease (26). Among SYNTAX score II variables, LVEF was an independent predictor of 4-year mortality and showed a moderate interaction effect in affecting long-term mortality predictions with CABG and PCI (27). However, given the fact that prior clinical trials mostly excluded patients with severe LV dysfunction, there is still limited evidence with regard to the optimal revascularization strategy in such high-risk patients. Therefore, our study provides important insights on the comparative effectiveness of CABG and PCI for patients with LMCA disease and LV dysfunction, which could aid in decision making for the optimal revascularization strategy in contemporary practice.

There are currently no dedicated randomized trials comparing PCI versus CABG in patients with significant LMCA disease and with reduced ejection fraction. In the STICH (Surgical Treatment for Ischemic Heart Failure) trials in which patients with LMCA disease were excluded, there was no survival benefit of CABG over OMT up to 5 years in patients with ischemic severe LV dysfunction (28); however, CABG was associated with a better survival rate than OMT over a 10-year extended follow-up (4). A meta-

TABLE 5 Adjusted Hazard Ratios for 5-Year Clinical Outcomes After PCI and CABG Stratified by the Severity of Left Ventricular Dysfunction With the Use of Inverse Probability Weighting*

	Normal LV Function (LVEF ≥55%)		Mild LV Dysfunction (LVEF ≥45% to <55%)		Moderate LV Dysfunction (LVEF ≥35% to <45%)		Severe LV Dysfunction (LVEF <35%)		
	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value	HR (95% CI)	p Value	$p_{interaction}$ Value†
Unadjusted									
Primary composite outcome: death, MI, or stroke at 5 yrs	0.78 (0.60–1.02)	0.07	1.03 (0.64–1.65)	0.90	1.31 (0.78–2.19)	0.31	1.51 (0.93–2.43)	0.10	0.06
Secondary outcomes									
All-cause mortality	0.79 (0.59–1.07)	0.12	1.00 (0.60–1.66)	0.99	1.35 (0.77–2.38)	0.30	1.36 (0.82–2.27)	0.23	0.13
MI‡	1.26 (0.59–2.69)	0.56	NA	NA	3.78 (0.34–42.1)	0.28	2.92 (0.48–17.8)	0.25	0.78
Stroke‡	0.59 (0.33–1.07)	0.08	0.36 (0.09–1.40)	0.14	1.02 (0.29–3.63)	0.97	1.41 (0.39–5.12)	0.60	0.58
Repeat revascularization	3.38 (2.29–4.99)	<0.001	5.44 (1.86–15.93)	0.002	4.84 (1.28–18.32)	0.02	1.86 (0.62–5.62)	0.27	0.70
Stabilized IPTW with the doubly robust method§ and medication¶									
Primary composite outcome: death, MI, or stroke at 5 yrs	0.80 (0.59–1.07)	0.13	1.17 (0.63–2.17)	0.61	2.23 (1.17–4.28)	0.02	2.45 (1.27–4.73)	0.008	0.004
Secondary outcomes									
All-cause mortality	0.92 (0.65–1.30)	0.63	1.21 (0.62–2.36)	0.58	1.70 (0.80–3.61)	0.17	2.10 (1.01–4.38)	0.047	0.58
Repeat revascularization	5.35 (3.44–8.32)	<0.001	5.30 (1.51–18.58)	0.009	2.02 (0.40–10.09)	0.39	1.60 (0.44–5.91)	0.48	0.69

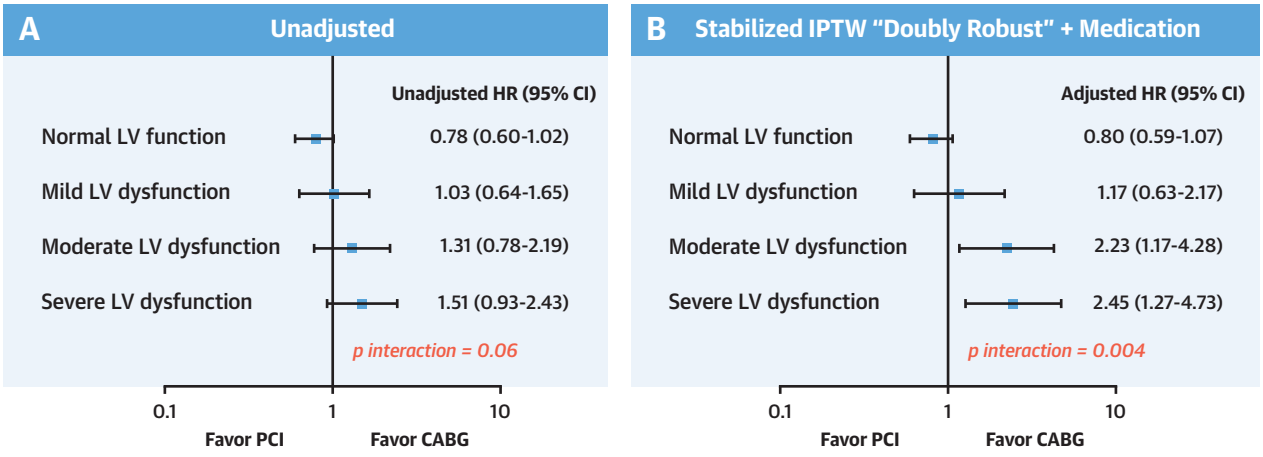
*Hazard ratios are for the PCI group as compared with the CABG group. †p interaction for severity of LV dysfunction and revascularization strategy (PCI vs. CABG). ‡Due to limited number of events, only unadjusted hazard ratios are presented for MI and stroke events. §Independent predictors of each clinical outcome were included in analysis after stabilized IPTW. ¶Post-treatment medication variables in Table 3 were included.

CI = confidence interval; EF = ejection fraction; HR = hazard ratio; IPTW = inverse probability treatment weighting; MI = myocardial infarction; NA = not available; other abbreviations as in Figure 1.

analysis comparing different methods of revascularization (PCI or CABG) against each other or against OMT in patients with CAD and LVEF ≤40% showed that there was a significant reduction in mortality with revascularization strategies compared with OMT alone; furthermore, CABG seems more favorable compared with PCI (22). In a recent observational study (29), CABG showed a significantly lower incidence of major cardiovascular events and mortality compared with PCI in diabetic patients with moderate (ejection fraction 35% to 49%) and severe (ejection fraction <35%) LV dysfunction. By contrast, data from the New York State registries suggested that PCI with everolimus-eluting stents compared with CABG showed similar long-term survival in patients with multivessel CAD and severe LV dysfunction (ejection fraction ≤35%); however, PCI was associated with a higher risk of MI and repeat revascularization, and CABG was associated with a higher risk of stroke (30). A recent extended follow-up of the EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial showed that the 5-year rate of the primary composite of death, MI, or stroke was similar for PCI and CABG, and the relative treatment effect was not different in the subgroup of LVEF <50% or LVEF ≥50% (13).

The key findings of our study were that PCI was associated with a higher risk for the primary composite of death, MI, or stroke compared with CABG in patients with moderate or severe LV dysfunction and that there was a significant interaction between the severity of LV dysfunction and the relative treatment effect of the revascularization strategy. These findings imply that the severity of LV dysfunction should be essentially considered in the decision making related to the optimal revascularization strategy for LMCA disease; for patients with moderate or severe LV dysfunction, CABG should be considered as the first choice of revascularization strategy if the surgical risk is acceptable. These findings were more pronounced after further adjustment for post-treatment cardioactive medications, which were underused in patients who underwent CABG. The exploratory finding regarding complete revascularization in this study was that when complete revascularization could possibly be achieved by PCI, the interaction between the treatment effect and the severity of LV dysfunction on hard endpoints became weaker. This result was similar to a previous study (31) in that incomplete revascularization after PCI was associated with adverse outcomes. However, there is limited evidence regarding complete revascularization in patients with reduced LVEF. In 1 study (32), patients with LVEF <35% were identified as those who benefit most from complete revascularization by CABG. Meanwhile, a controversial finding from the myocardial viability substudy of the STICH trial was that viable myocardium does not influence the long-term survival benefit from CABG in patients with ischemic cardiomyopathy and CAD (p for

CENTRAL ILLUSTRATION **Unadjusted and Adjusted Hazard Ratios for the Primary Composite Outcome According to the Severity of Left Ventricular Dysfunction in Patients Who Underwent Percutaneous Coronary Intervention or Coronary Artery Bypass Grafting for Left Main Coronary Artery Disease**



Park, S. et al. J Am Coll Cardiol. 2020;76(12):1395–406.

(A) Unadjusted hazard ratios and **(B)** adjusted hazard ratios according to the severity of left ventricular (LV) dysfunction are shown. In the final adjusted model, stabilized inverse probability of treatment weighting with the "doubly robust" method and further adjustment for the important post-treatment variables of cardioactive medications were used. The primary composite outcome was defined as the composite of death from any cause, myocardial infarction, or stroke. Hazard ratios (HRs) are for the percutaneous (PCI) group compared with the coronary artery bypass grafting (CABG) group; p interaction for the severity of LV dysfunction and revascularization strategy (PCI vs. CABG).

interaction = 0.34) (33–35). Further studies are needed to understand the impact of complete revascularization and myocardial viability on the clinical outcomes of patients with LMCA disease and LV dysfunction.

In our data, the use of IVUS guidance proportionally decreased with the severity of LV dysfunction. When hemodynamic instability might be expected from a prolonged procedure or is present in patients with severe LV dysfunction, the use of IVUS could be limited by the urgency of revascularization. Thus, the observed findings could be affected by differences in the use of IVUS guidance. The use of IVUS guidance should be encouraged in left main PCI if hemodynamically stable because it was associated with better outcomes (36). Further clinical trials are needed to prove the prognostic impact of IVUS-guided PCI for LMCA disease. Otherwise, the use of mechanical circulatory support proportionally increased with the severity of LV dysfunction. The selective or routine use and its protective role of mechanical circulatory support (i.e., intra-aortic balloon pump or Impella heart pump [Abiomed, Danvers, Massachusetts]) for high-risk PCI for patients with LMCA disease and severe LV dysfunction should be addressed through further clinical research.

STUDY LIMITATIONS. This was a nonrandomized, observational study; therefore, the present study was subject to potential selection and ascertainment biases due to inherent methodologic limitations. Although a wide range of baseline covariates were included to create the IPTW model and additional post-treatment variables were further adjusted, unmeasured confounders could have influenced the observed findings. Also, we could not accurately quantify and adjust the center effect and operators' experience, which might have affected the comparative outcomes. Because of a lack of LVEF data and medication alone, a significant proportion of patients were excluded from the IRIS-MAIN registry, which may have underestimated or overestimated the relative treatment effect. In addition, the small proportion of patients with moderate or severe LV dysfunction could potentially limit the precision of the treatment effect. Thus, our findings should be confirmed or refuted through further larger, clinical studies with long-term follow-ups. There are recent advances in the treatment of heart failure. Recently, new medications (e.g., angiotensin receptor-neprilysin inhibitors or sodium glucose cotransporter 2 inhibitors) have shown survival benefit for heart failure, but these medications were

not recognized in our registry. Because of the lack of an independent echocardiography core laboratory, the variability in LVEF could result in the misclassification of patients. Also, serial echocardiographic follow-up data (e.g., LVEF or wall motion score index) were limited. Lastly, exact information on myocardial ischemia and viability or the severity of LV remodeling was not available for the current study. Further studies are required to address the prognostic value of these factors on long-term outcomes.

CONCLUSIONS

In this real-world registry involving patients with significant LMCA disease compared with CABG, PCI was associated with a higher risk of the primary composite outcome of death, MI, or stroke at 5 years in patients with moderate or severe LV dysfunction. However, the risk for primary outcome was comparable between PCI and CABG in patients with normal or mild LV dysfunction. These findings suggest that the severity of LV dysfunction should be considered as the key factor for the decision making of the optimal revascularization choice for patients with LMCA disease.

ADDRESS FOR CORRESPONDENCE: Dr. Duk-Woo Park, Department of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, Korea. E-mail: dwpark@amc.seoul.kr. Twitter: @dukwoo_park.

PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: In patients with left main coronary artery disease and moderate or severe left ventricular dysfunction, percutaneous coronary intervention was associated with a higher risk of the composite outcome of death, myocardial infarction, or stroke within 5 years compared with coronary artery bypass grafting surgery. The relative benefit of surgical revascularization is related to the severity of ventricular dysfunction.

TRANSLATIONAL OUTLOOK: Further research is needed to identify other variables that distinguish patients with left main coronary artery disease and impaired left ventricular function who exhibit better outcomes with one type of revascularization compared with the other.

REFERENCES

1. Appoo J, Norris C, Merali S, et al. Long-term outcome of isolated coronary artery bypass surgery in patients with severe left ventricular dysfunction. Circulation 2004;110 Suppl 1:II13–7.

2. Nardi P, Pellegrino A, Scafuri A, et al. Long-term outcome of coronary artery bypass grafting in patients with left ventricular dysfunction. Ann Thorac Surg 2009;87:1401–7.

3. Deb S, Wijeysundera HC, Ko DT, Tsubota H, Hill S, Fremes SE. Coronary artery bypass graft surgery vs percutaneous interventions in coronary revascularization: a systematic review. Jama 2013;310:2086–95.

4. Velazquez EJ, Lee KL, Jones RH, et al. Coronary-artery bypass surgery in patients with ischemic cardiomyopathy. N Engl J Med 2016;374:1511–20.

5. Morice MC, Serruys PW, Kappetein AP, et al. Five-year outcomes in patients with left main disease treated with either percutaneous coronary intervention or coronary artery bypass grafting in the synergy between percutaneous coronary intervention with taxus and cardiac surgery trial. Circulation 2014;129:2388–94.

6. Ahn JM, Roh JH, Kim YH, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease: 5-year outcomes of the PRECOMBAT study. J Am Coll Cardiol 2015;65:2198–206.

7. Lee PH, Ahn JM, Chang M, et al. Left main coronary artery disease: secular trends in patient characteristics, treatments, and outcomes. J Am Coll Cardiol 2016;68:1233–46.

8. Stone GW, Sabik JF, Serruys PW, et al. Everolimus-eluting stents or bypass surgery for left main coronary artery disease. N Engl J Med 2016;375:2223–35.

9. Buszman PE, Buszman PP, Banasiewicz-Szkrobka I, et al. Left main stenting in comparison with surgical revascularization: 10-year outcomes of the (Left Main Coronary Artery Stenting) LE MANS Trial. J Am Coll Cardiol Intv 2016;9:318–27.

10. Head SJ, Milojevic M, Daemen J, et al. Mortality after coronary artery bypass grafting versus percutaneous coronary intervention with stenting for coronary artery disease: a pooled analysis of individual patient data. Lancet 2018;391:939–48.

11. Park DW, Ahn JM, Yun SC, et al. 10-year outcomes of stents versus coronary artery bypass grafting for left main coronary artery disease. J Am Coll Cardiol 2018;72:2813–22.

12. Thuijs D, Kappetein AP, Serruys PW, et al. Percutaneous coronary intervention versus coronary artery bypass grafting in patients with three-vessel or left main coronary artery disease: 10-year follow-up of the multicentre randomised controlled SYNTAX trial. Lancet 2019;394:1325–34.

13. Stone GW, Kappetein AP, Sabik JF, et al. Five-year outcomes after PCI or CABG for left main coronary disease. N Engl J Med 2019;381:1820–30.

14. Holm NR, Makikallio T, Lindsay MM, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in the treatment of unprotected left main stenosis: updated 5-year outcomes from the randomised, non-inferiority NOBLE trial. Lancet 2020;395:191–9.

15. Mohr FW, Morice MC, Kappetein AP, et al. Coronary artery bypass graft surgery versus percutaneous coronary intervention in patients with three-vessel disease and left main coronary disease: 5-year follow-up of the randomised, clinical SYNTAX trial. Lancet 2013;381:629–38.

16. Conley MJ, Ely RL, Kisslo J, Lee KL, McNeer JF, Rosati RA. The prognostic spectrum of left main stenosis. Circulation 1978;57:947–52.

17. Takaro T, Peduzzi P, Detre KM, et al. Survival in subgroups of patients with left main coronary artery disease. Veterans Administration Cooperative Study of Surgery for Coronary Arterial Occlusive Disease. Circulation 1982;66:14–22.

18. Robins JM, Hernan MA, Brumback B. Marginal structural models and causal inference in epidemiology. Epidemiology 2000;11:550–60.

19. Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Comparative effectiveness of revascularization strategies. N Engl J Med 2012;366:1467–76.

20. Rosenbaum PR. Model-based direct adjustment. J Am Stat Assoc 1987;82:387–94.

21. Funk MJ, Westreich D, Wiesen C, Sturmer T, Brookhart MA, Davidian M. Doubly robust estimation of causal effects. Am J Epidemiol 2011;173:761–7.

22. Wolff G, Dimitroulis D, Andreotti F, et al. Survival benefits of invasive versus conservative strategies in heart failure in patients with reduced ejection fraction and coronary artery disease: a meta-analysis. Circ Heart Fail 2017;10:e003255.

23. Neumann FJ, Sousa-Uva M, Ahlsson A, et al. 2018 ESC/EACTS guidelines on myocardial revascularization. Eur Heart J 2019;40:87–165.

24. Patel MR, Calhoon JH, Dehmer GJ, et al. ACC/AATS/AHA/ASE/ASNC/SCAI/SCCT/STS 2017 appropriate use criteria for coronary revascularization in patients with stable ischemic heart disease: a report of the American College of Cardiology Appropriate Use Criteria Task Force, American Association for Thoracic Surgery, American Heart Association, American Society of Echocardiography, American Society of Nuclear Cardiology, Society for Cardiovascular Angiography and Interventions, Society of Cardiovascular Computed Tomography, and Society of Thoracic Surgeons. J Am Coll Cardiol 2017;69:2212–41.

25. Park DW, Ahn JM, Park H, et al. Ten-year outcomes after drug-eluting stents versus coronary artery bypass grafting for left main coronary disease: extended follow-up of the PRECOMBAT trial. Circulation 2020;141:1437–46.

26. Ahmad Y, Howard JP, Arnold AD, et al. Mortality after drug-eluting stents vs. coronary artery bypass grafting for left main coronary artery disease: a meta-analysis of randomized controlled trials. Eur Heart J 2020 Mar 2 [E-pub ahead of print].

27. Farooq V, van Klaveren D, Steyerberg EW, et al. Anatomical and clinical characteristics to guide decision making between coronary artery bypass surgery and percutaneous coronary intervention for individual patients: development and validation of SYNTAX score II. Lancet 2013;381:639–50.

28. Velazquez EJ, Lee KL, Deja MA, et al. Coronary-artery bypass surgery in patients with left ventricular dysfunction. N Engl J Med 2011;364:1607–16.

29. Nagendran J, Bozso SJ, Norris CM, et al. Coronary artery bypass surgery improves outcomes in patients with diabetes and left ventricular dysfunction. J Am Coll Cardiol 2018;71:819–27.

30. Bangalore S, Guo Y, Samadashvili Z, Blecker S, Hannan EL. Revascularization in patients with multivessel coronary artery disease and severe left ventricular systolic dysfunction: everolimus-eluting stents versus coronary artery bypass graft surgery. Circulation 2016;133:2132–40.

31. Head SJ, Mack MJ, Holmes DR Jr., et al. Incidence, predictors and outcomes of incomplete revascularization after percutaneous coronary intervention and coronary artery bypass grafting: a subgroup analysis of 3-year SYNTAX data. Eur J Cardiothorac Surg 2012;41:535–41.

32. Bell MR, Gersh BJ, Schaff HV, et al. Effect of completeness of revascularization on long-term outcome of patients with three-vessel disease undergoing coronary artery bypass surgery. A report from the Coronary Artery Surgery Study (CASS) Registry. Circulation 1992;86:446–57.

33. Panza JA, Ellis AM, Al-Khalidi HR, et al. Myocardial viability and long-term outcomes in ischemic cardiomyopathy. N Engl J Med 2019;381:739–48.

34. Bonow RO, Maurer G, Lee KL, et al. Myocardial viability and survival in ischemic left ventricular dysfunction. N Engl J Med 2011;364:1617–25.

35. Anavekar NS, Chareonthaitawee P, Narula J, Gersh BJ. Revascularization in patients with severe left ventricular dysfunction: is the assessment of viability still viable? J Am Coll Cardiol 2016;67:2874–87.

36. de la Torre Hernandez JM, Baz Alonso JA, Gómez Hospital JA, et al. Clinical impact of intravascular ultrasound guidance in drug-eluting stent implantation for unprotected left main coronary disease: pooled analysis at the patient-level of 4 registries. J Am Coll Cardiol Intv 2014;7:244–54.

KEY WORDS coronary artery bypass grafting, left main coronary artery disease, percutaneous coronary intervention, ventricular dysfunction

APPENDIX For supplemental tables and figures, please see the online version of this paper.