Long-term outcomes of bypass grafting versus drug-eluting stenting for left main coronary artery disease: Results from the IRIS-MAIN registry

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Background There are limited data on comparative outcomes and its determinants following coronary artery bypass graft surgery (CABG) and percutaneous coronary intervention (PCI) with drug-eluting stents (DES) for left main coronary artery disease (LMCAD) in a real-world setting.

Methods A total of 3,504 consecutive patients with LMCAD treated with CABG (n = 1,301) or PCI with DES (n = 2,203) from the IRIS-MAIN registry were analyzed. The relative treatment effect of one strategy over another was assessed by propensity-score matching method. The primary outcome was a composite of death, myocardial infarction, or stroke.

Results Median follow-up duration was 4.7 years. In the matched cohort, both groups demonstrated a similar risk for the primary outcome (adjusted hazard ratio [HR]: 0.94; 95% CI: 0.77-1.15; $P = .54$). Compared with CABG, PCI exhibited higher risks of myocardial infarction (HR: 2.11; 95% CI: 1.16-3.83; $P = .01$) and repeated revascularization (HR: 5.95; 95% CI: 3.94-8.98; $P < .001$). In the overall population, age, presence of chronic kidney disease, and low ejection fraction (<40%) were key clinical predictors of primary outcome regardless of the treatment strategy. However, factors deemed to be associated with perioperative morbidity were determinants of primary outcome in the CABG group, whereas those generally associated with the severity of atherosclerotic coronary artery disease were strong predictors in the PCI group.

Conclusions Among patients with significant LMCAD, the long-term risk of the composite outcome of death, myocardial infarction, or stroke was similar between CABG and PCI. Clinical variables that differentially predict adverse outcomes might be useful in triaging appropriate revascularization strategy (Am Heart J 2017;193:76-83.)

Patients with significant left main coronary artery disease (LMCAD) have historically been treated with coronary artery bypass graft surgery (CABG).[1] Over time, the introduction of drug-eluting stents (DES) has remarkably changed revascularization strategies[2-4] and led to increased use of percutaneous coronary intervention (PCI) in this patient population.[5] Numerous studies have compared the clinical results of CABG and PCI with DES for the treatment of LMCAD, generally showing comparable safety outcomes between the 2 strategies but a higher rate of repeat revascularization with PCI.[6-13] However, LMCAD contains a heterogeneous spectrum of coronary heart disease exhibiting a highly variable prognosis, and the optimal revascularization strategy for each patient subset remains controversial.[8,14,15] Also, there are limited data comparing long-term outcomes of the 2 revascularization strategies in "real-world" patients with LMCAD,[11,16] and the differential predictors of serious adverse cardiovascular events after each revascularization strategy in this setting are not well known.

In the present study, we compared long-term outcomes after CABG versus those after PCI with DES in 3,504 patients with significant LMCAD and assessed predictors of serious adverse cardiovascular events using data from the large multinational "all-comers" Interventional Research Incorporation Society–Left MAIN Revascularization (IRIS-MAIN) registry.

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Methods

Study population and procedure

The IRIS-MAIN is a nonrandomized, multinational, multicenter observational registry which consists of a cohort of consecutive Asian patients with *significant unprotected LMCAD* (defined as stenosis of more than 50%).[17] The study adopted an "all-comers" design to evaluate characteristics of patients, treatments, and outcomes in real-world clinical practice. The exclusion criteria were minimal; patients who had prior CABG and those who underwent concomitant valvular or aortic surgery were excluded. Patients were further excluded from the current study if they were treated medically only (n = 527), presented with ST-segment elevation myocardial infarction (n = 165), or received bare-metal stent implantation at the time of the index procedure (n = 51). A total of 3,504 consecutive patients who underwent either CABG (n = 1,301) or PCI with DES (n = 2,203) from March 2003 to December 2013 were finally included in this study. This study was supported by a grant from the CardioVascular Research Foundation, Seoul, Korea. The local ethics committee at each hospital approved the study protocol, and written informed consent was obtained from all patients. The authors are solely responsible for the design and conduct of this study, all study analyses, and the drafting and editing of the manuscript and its final contents.

Selection of the particular type of treatment was at the discretion of the attending physician. CABG and PCI were performed using standard techniques at the operator's discretion.[18] The internal thoracic artery was preferentially used for the revascularization of the left anterior descending coronary artery. All patients undergoing PCI received a loading dose of aspirin (200 mg) and clopidogrel (300 or 600 mg) before the intervention. Following both procedures, aspirin was continued indefinitely, and 75 mg/d clopidogrel was prescribed for at least 12 months after PCI.

Study outcomes and definitions

Considering that the future probability of hard outcomes is important when making decision to opt for an appropriate revascularization strategy, the primary outcome for comparison was a composite of death from any cause, myocardial infarction, or stroke during follow-up. Secondary outcomes included death from any cause, death from cardiac causes, myocardial infarction, stroke, repeat revascularization, and a composite of death or myocardial infarction. 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 following the index treatment, an increase in the creatine kinase–myocardial band concentration >5 times the upper reference limit with any of following: new pathological Q waves or new bundle-branch block, new graft or new native coronary occlusion documented on angiography, or new regional wall motion abnormality or loss of viable myocardium on imaging studies or (2) if occurring 48 hours after the index treatment, an increase in the creatine kinase–myocardial band concentration above the upper reference limit with ischemic symptoms or signs.[19] Stroke, as indicated by neurological deficits, was confirmed by a neurologist on the basis of imaging modalities. Repeat revascularization included any type of percutaneous or surgical revascularization procedure, regardless of whether the procedure was performed on a target or nontarget lesion. All events were based on the clinical diagnoses assigned by the patient's physician and were centrally adjudicated by an independent group of clinicians. Clinical, angiographic, procedural or operative, and outcome data were recorded in the dedicated databases by independent research personnel. 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 contact.

Statistical analysis

Continuous variables are presented as mean ± SD and categorical variables as frequencies. Time-to-event outcomes were determined using Kaplan-Meier methodology and compared with the log-rank test. Given the differences in the characteristics of patients between PCI and CABG enrolled in an observational study, propensity-score matching was used to assemble patients with similar baseline features and who might be equivalently amenable to the 2 revascularization strategies. Propensity scores were estimated without regard to outcomes via multiple logistic-regression analysis using variables outlined in Supplemental Table I. Matching was performed with the use of a 1:1 matching protocol without replacement and with a caliper width equal to 0.2 of the SD of the logit of the propensity score. Standardized differences were estimated for all the baseline covariates before and after matching, and values of less than 10.0% for a given covariate indicate a relatively small imbalance (Supplemental Figure 1). Cox proportoinal hazards regression models, with robust standard errors that accounted for the clustering of pairs, were used to compare the risks of outcomes in the matched cohort.[20] Secondary analysis for primary outcome was conducted in several clinically relevant subgroups with tests for interactions. To identify the predictors of the primary outcome for each treatment modality, we performed the Cox's proportional hazards regression analysis using relevant clinical and angiographic parameters. The proportional hazards assumption was tested by examination of log (−log [survival]) curves and partial (Schoenfeld) residuals; no relevant violations were found. The final multivariable models for each modality were determined by backward stepwise elimination

procedures where the least significant variable was discarded one by one from the full model. These analyses included the entire data set, with multiple imputations of missing values.[21] Analyses were performed using R software, version 3.3.0 (R Foundation for Statistical Computing, Vienna, Austria; www.r-project.org). All reported *P* values are 2-sided, and $P < .05$ was considered significant.

Results

Patient characteristics

The study cohort comprised 2,691 (76.8%) men with a mean age of 64.0 ± 10.1 years. More than two-thirds of patients had distal left main bifurcation involvement, and 73.9% had multivessel involvement. Compared with PCI-treated patients, CABG-treated patients were found to be older and tended to have a higher prevalence of diabetes, history of myocardial infarction or heart failure, acute coronary syndrome, peripheral vascular disease, and chronic pulmonary disease (Supplemental Table II). Moreover, the CABG group had lower left ventricular ejection fraction (55.8% ± 11.5% vs 59.8% ± 9.3%, $P < .001$) accompanied by a higher degree of vascular disease extent. In the CABG group, a mean of 3.0 ± 1.0 grafts was used, and the proportion of internal thoracic artery use was high (94.7%). In the PCI group, a mean of 2.3 ± 1.3 DES was implanted, intravascular ultrasound guidance was used in 81% of patients, and a complex 2-stent approach was used in 23.7% of patients for left main bifurcation lesions (Supplemental Table III). At discharge, patients in the PCI group were more likely to receive antiplatelet agents including aspirin or P2Y12 receptor inhibitors.

Table I. Clinical and angiographic characteristics in the propensity-matched cohort

	PCI (n = 950)	CABG (n = 950)	*P* value
Age	64.7 ± 9.3	64.5 ± 10.3	.61
Male sex	740 (77.9)	731 (76.9)	.66
Body mass index (kg/m^2)	24.6 ± 3.0	24.5 ± 2.9	.15
Current smoker	248 (26.1)	224 (23.6)	.23
Diabetes	367 (38.6)	369 (38.8)	.96
Hypertension	604 (63.6)	611 (64.3)	.77
Hypercholesterolemia	482 (50.7)	483 (50.8)	>.99
Family history of CAD	103 (10.8)	106 (11.2)	.87
Prior PCI	150 (15.8)	141 (14.8)	.62
Prior cardiac surgery†	5 (0.5)	4 (0.4)	>.99
History of myocardial infarction	101 (10.6)	96 (10.1)	.76
History of heart failure	27 (2.8)	27 (2.8)	>.99
History of stroke	86 (9.1)	83 (8.7)	.87
Chronic kidney disease*	49 (5.2)	48 (5.1)	>.99
Peripheral vascular disease	54 (5.7)	57 (6.0)	.84
Chronic lung disease	31 (3.3)	34 (3.6)	.80
Clinical diagnosis			
Silent ischemia/stable angina	412 (43.3)	387 (40.7)	.25
Unstable angina	452 (47.6)	471 (49.6)	.38
NSTEMI	86 (9.1)	92 (9.7)	.69
Left ventricular ejection fraction, %	57.6 ± 10.4	57.7 ± 10.0	.99
Shock at presentation	2 (0.2)	1 (0.1)	>.99
Atrial fibrillation	19 (2.0)	19 (2.0)	>.99
Disease extent			
Isolated LMCAD	47 (4.9)	34 (3.6)	.15
LMCAD plus 1-vessel disease	83 (8.7)	83 (8.7)	>.99
LMCAD plus 2-vessel disease	241 (25.4)	250 (26.3)	.63
LMCAD plus 3-vessel disease	579 (60.9)	583 (61.4)	.86
RCA involvement	687 (72.3)	694 (73.1)	.71
Distal bifurcation involvement	687 (72.3)	693 (72.9)	.79
Antiplatelet therapy at discharge			
Aspirin	935 (98.4)	921 (96.9)	.05
ADP receptor antagonists	913 (96.1)	836 (88.0)	<.001

Data are shown as mean ± SD or number (%).
CAD, coronary artery disease; *NSTEMI*, non–ST-segment elevation myocardial infarction; *RCA*, right coronary artery; *ADP*, adenosine diphosphate.
* *Chronic kidney disease* was defined as serum creatinine ≥2.0 mg/dL.
† Surgery other than CABG.

Clinical outcomes

The median follow-up time was 4.7 years (interquartile range, 3.0-6.0 years). The primary outcome of death, myocardial infarction, or stroke occurred in 240 patients in the PCI group and 275 in the CABG group (3-year incidence, 7.5% vs 11.9%; hazard ratio [HR]: 0.66; 95% CI: 0.56-0.79; $P < .001$) (Table II). This difference favoring PCI was largely attributable to the lower incidence of death (HR: 0.60; 95% CI: 0.49-0.73; $P < .001$). Periprocedural myocardial infarction occurred in 14 patients (7 in each group, 0.32% and 0.54% after PCI and CABG, respectively), and the cumulative rate of myocardial infarction was similar between the 2 groups. Conversely, there was a strong trend toward a higher rate of stroke in the CABG group (3-year incidence, 1.4% vs 2.4%, $P = .02$) (Supplemental Figure 2).

The event rates and risks for clinical outcomes of the propensity-score matched cohort (See Table I) are shown in Table II and Figure 1. The risk for the primary outcome of death, myocardial infarction, or stroke was observed to be comparable between the 2 groups (HR: 0.94; 95% CI: 0.77-1.15; $P = .54$). There were no differences in the risks of death and stroke between the groups, whereas those for myocardial infarction (HR: 2.11; 95% CI: 1.16-3.83; $P = .01$) and repeat revascularization (HR: 5.95; 95% CI: 3.94-8.98; $P < .001$) were significantly higher in the PCI group.

Subgroup analysis and predictors of primary outcome

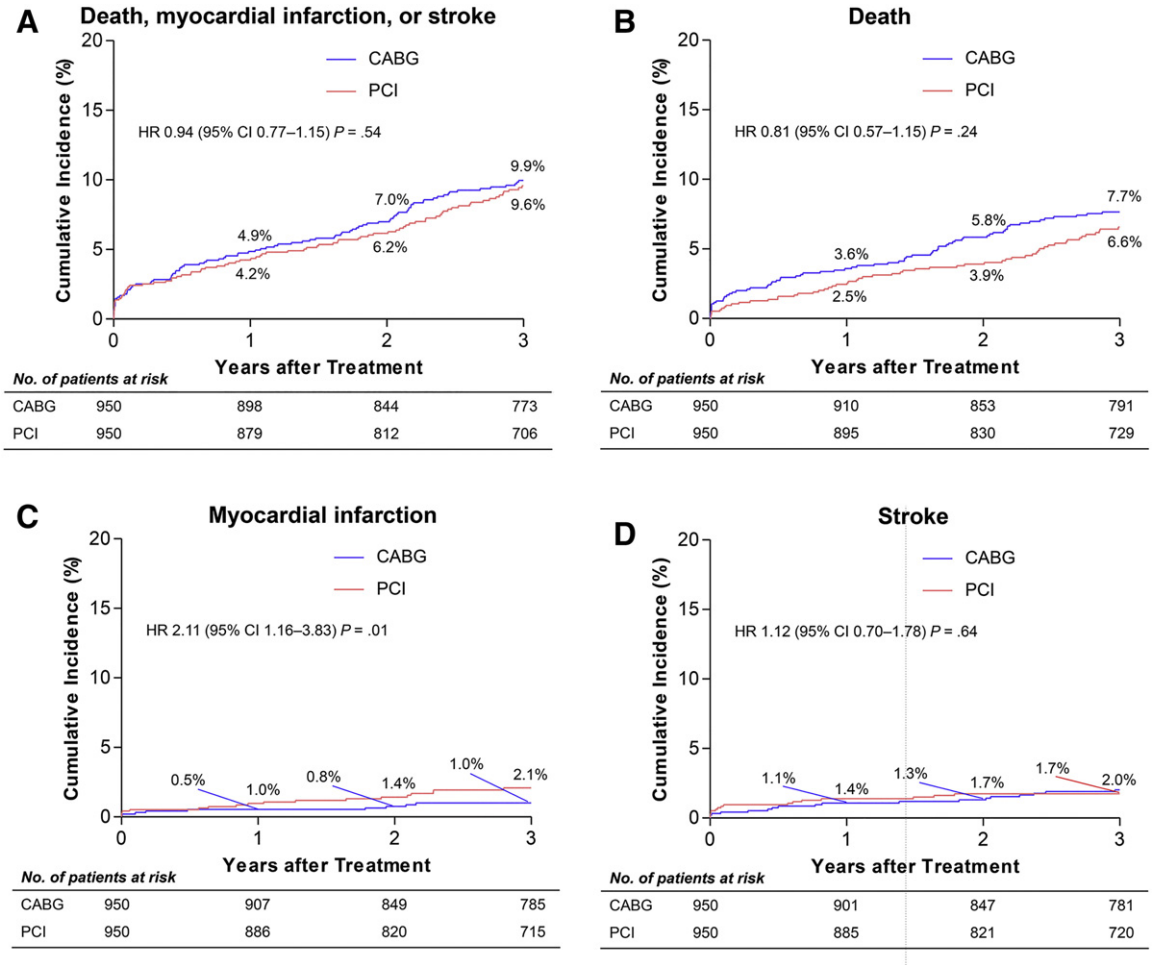
In the subgroup analysis of the matched cohort, PCI was associated with a lower risk of the primary outcome in nondiabetic patients and those younger than 65. Formal testing for interactions showed that the relative treatment effect of CABG versus PCI was consistent across multiple subgroups except for those defined according to the status of diabetes and whether age was younger than 65 or not (Figure 2).

Table II. Incidence rates and risk of clinical outcomes in the overall and propensity-matched population

	Event rate (%) at 3 y		Crude		Event rate (%) at 3 y		Propensity-matched	
Outcome	PCI (n = 2203)	CABG (n = 1301)	HR (95% CI)	*P* value	PCI (n = 950)	CABG (n = 950)	HR (95% CI)	*P* value
Death, myocardial infarction, or stroke	7.5	11.9	0.66 (0.56-0.79)	<.001	9.6	9.9	0.94 (0.77-1.15)	.54
Death or myocardial infarction	6.6	10.3	0.66 (0.55-0.80)	<.001	8.5	8.5	0.94 (0.76-1.17)	.58
Death	5.1	9.4	0.60 (0.49-0.73)	<.001	6.6	7.7	0.81 (0.57-1.15)	.24
Cardiac death	3.7	7.4	0.56 (0.44-0.70)	<.001	4.5	5.1	0.80 (0.54-0.19)	.28
Myocardial infarction	1.6	1.4	1.34 (0.83-2.18)	.23	2.1	1.0	2.11 (1.16-3.83)	.01
Stroke	1.4	2.4	0.62 (0.41-0.94)	.02	1.7	2.0	1.12 (0.70-1.78)	.64
Repeat revascularization	10.1	2.4	4.15 (3.03-5.70)	<.001	12.4	2.1	5.95 (3.94-8.98)	<.001

Hazard ratios are for patients who received PCI versus CABG.

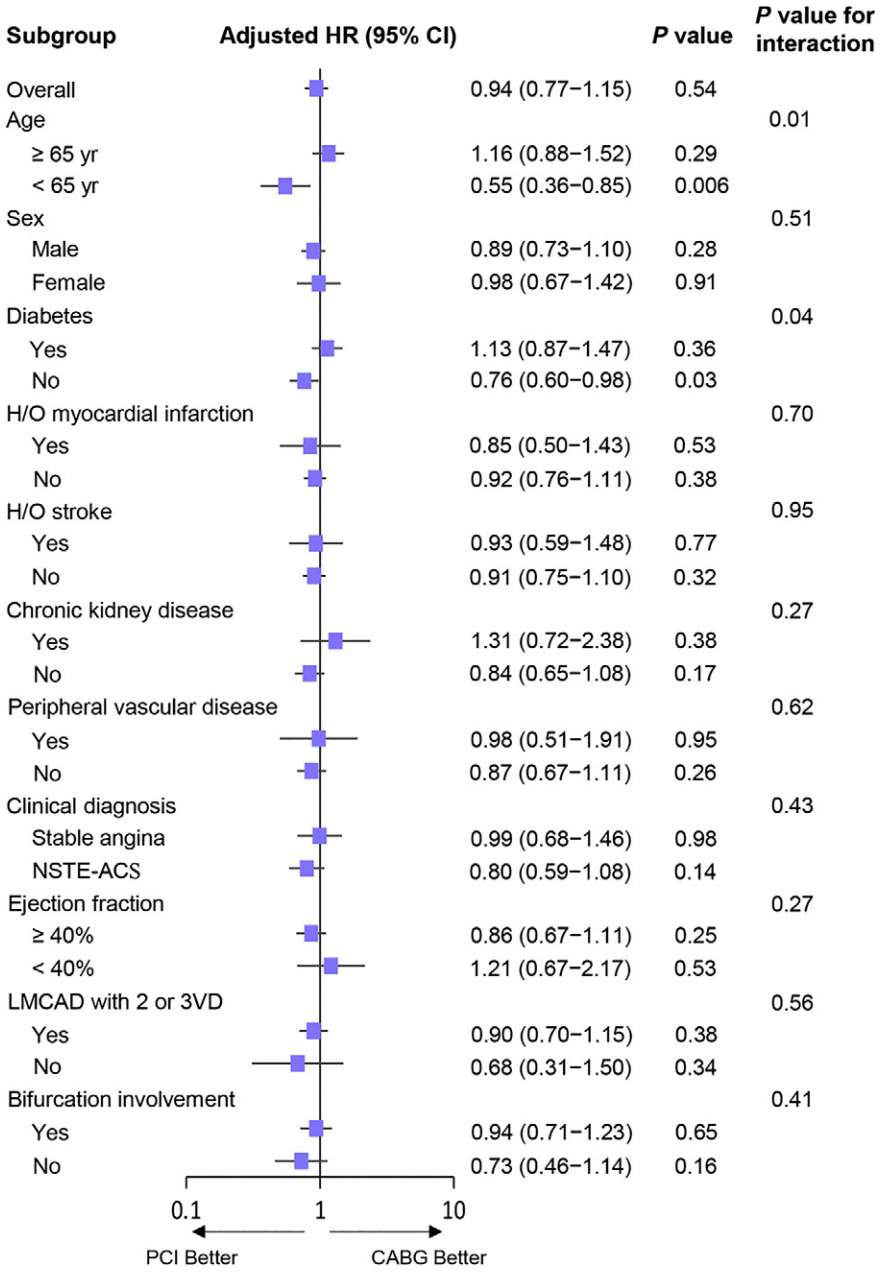
Figure 1



Kaplan-Meier curves of clinical outcomes in the matched population. The cumulative incidences of the composite of death, myocardial infarction, or stroke (**A**); death (**B**); myocardial infarction (**C**); and stroke (**D**) are shown. Percentages denote 2- and 4-year event rates.

Multivariable analysis revealed several common and disparate predictors of the composite outcome of death, myocardial infarction, or stroke after either CABG or PCI with DES (Table III and Supplemental Table IV). Age, chronic kidney disease, and low ejection fraction (<40%) were included as common predictors of primary outcome

Figure 2



Subgroup analysis of primary outcome in the matched cohort. Subgroup analyses are shown, with adjusted HRs and 95% CIs, for the composite outcome of death, myocardial infarction, or stroke. The *P* value for interaction represents the likelihood of interaction between the variable and the relative treatment effect.*H/O*, history of; *NSTE-ACS*, non–ST-segment elevation acute coronary syndrome; *VD*, vessel disease.

after both CABG and PCI with DES. Body mass index, chronic lung disease, and peripheral vascular disease revealed to be additional predictors of primary outcome after CABG, whereas diabetes, history of heart failure or stroke, and clinical diagnosis of acute myocardial infarction were distinct predictors of primary outcome after PCI.

Discussion

From this large IRIS-MAIN registry study, we found that the primary composite outcome of death, myocardial infarction, or stroke was comparable after CABG or PCI with DES for patients with significant LMCAD. However, compared with CABG, PCI with DES resulted in

Table III. Predictors of primary outcome following PCI with DES and CABG

	PCI		CABG	
Variables	Adjusted HR (95% CI)	*P* value	Adjusted HR (95% CI)	*P* value
Common predictors				
Age (per year increment)	1.07 (1.05-1.08)	<.001	1.05 (1.04-1.07)	<.001
Chronic kidney disease*	3.95 (2.72-5.72)	<.001	3.13 (2.15-4.55)	<.001
Left ventricular ejection fraction <40%	2.65 (1.76-4.00)	<.001	2.44 (1.79-3.22)	<.001
Disparate predictors				
Body mass index (per 1-kg/m^2 increment)			0.95 (0.91-0.99)	.015
Chronic lung disease			1.69 (1.06-2.71)	.028
Peripheral vascular disease			2.12 (1.53-2.94)	<.001
Diabetes	1.71 (1.32-2.22)	<.001		
History of heart failure	1.65 (1.01-2.70)	.048		
History of stroke	1.61 (1.14-2.26)	.007		
Clinical diagnosis				
Silent ischemia/stable angina	1			
Unstable angina	0.87 (0.65-1.17)	.35		
NSTEMI	1.51 (1.05-2.17)	.026		

* *Chronic kidney disease* was defined as serum creatinine ≥2.0 mg/dL.

significantly higher rates of myocardial infarction and repeated revascularization. Regardless of the treatment strategy, age, presence of chronic kidney disease, and low ejection fraction (<40%) were common clinical predictors of primary composite outcome. In addition, factors deemed to be associated with perioperative morbidity were determinants of primary outcome in the CABG group, whereas those generally associated with the severity of atherosclerotic coronary artery disease were strong predictors in the PCI group.

In the Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Drug-Eluting Stent in Patients with Left Main Coronary Artery Disease (PRECOMBAT) and Synergy between PCI with TAXUS and the Cardiac Surgery (SYNTAX) randomized controlled studies which evaluated the role of elective PCI using first-generation DES for LMCAD by directly comparing it with CABG, no between-group differences in the 5-year incidence of the composite safety end point of death, myocardial infarction, or stroke were found.[8,9] However, among recent studies using newer-generation DES, PCI and CABG were found to be comparable in the Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) trial, whereas CABG was better than PCI in the Nordic-Baltic-British Left Main Revascularization Study.[22,23] Overall, the results of the current IRIS-MAIN analysis, which reflects the real-world setting, are largely concordant with those from the PRECOMBAT, SYNTAX, and EXCEL trials. An advantage of CABG over PCI in long-term risk of myocardial infarction and repeat revascularization shown in our study is not surprising given the fundamental differences in the methodologies of CABG and PCI. In contrast with PCI, which directly relieves the culprit lesion with stents, a graft in CABG is placed beyond the culprit lesion, which may provide a protective role regarding future ischemic events arising from proximal segments and consequently leads to a reduction in myocardial infarction and revascularization rates. Because there are limited studies using a sufficient number of patients to compare the long-term outcomes of the 2 revascularization strategies in real-world patients,[11,16,24] our data may provide further solid evidence regarding the consequences of PCI with DES compared with those of CABG for LMCAD.

It has been shown that PCI, compared with CABG, displayed a greater risk of repeated revascularization.[8,9,11,24] Current guidelines recommend CABG for patients with LMCAD and a high degree of anatomical complexity (eg, SYNTAX score> 32), mainly because of the high risk of repeated revascularization following PCI.[2-4,9] However, in most clinical studies, this drawback of PCI did not translate into an increase of hard clinical outcomes.[8,9,11,16,24] LMCAD contains a broad spectrum of disease with variable prognosis, and identifying patient subgroups that affect hard clinical outcomes after each treatment may be important for risk stratification, triaging appropriate management strategy, and improving prognosis. In our study, advanced age, presence of left ventricular dysfunction, and chronic kidney disease, which are well-established determinants of mortality in patients with significant coronary artery disease,[25-27] were independently associated with primary outcome after both CABG and PCI with DES. Effect estimate was particularly high for patients who had chronic kidney disease. Renal dysfunction is associated with negative plaque characteristics, heightened states of arterial inflammation, sympathetic nervous system activation, and antiplatelet resistance, which may predispose an individual to ischemic cardiovascular events following PCI or CABG.[28,29] Regarding age as a predictor, one interesting finding from our subgroup

analysis was that patients younger than 65 were associated with a lower risk of the primary outcome after PCI rather than CABG. A plausible explanation would be that younger patients may hold less severe coronary artery characteristics including less calcification and lower atherosclerotic plaque burden, and consequently may benefit from less invasive PCI.[30]

Several disparate clinical factors, found to be associated with the risk of the serious adverse cardiovascular events after either CABG or PCI with DES, provide important insight to the differential mechanisms of treatment failure with either strategy. Lower body mass index and the presence of peripheral vascular disease or chronic lung disease generally have negative association with perioperative recovery and were predictors of the primary outcome among those who underwent CABG in our study. With the observation that the immediate mortality rate was twice after CABG than after PCI in our matched cohort (Figure 1B), careful case selection in consideration of patients' systemic condition may be important for CABG. On the contrary, factors generally associated with the severity of atherosclerotic disease were strong predictors of primary outcome among those who underwent PCI for LMCAD. Patients with diabetes or prior stroke and those under clinical situation of non–ST-elevation myocardial infarction were more likely to have diffuse form of atherosclerotic coronary artery disease in previous studies.[31-33] Because these patients may have had high-risk anatomy, optimal stenting would have been rather difficult, and a high probability of ischemic events may have persisted after PCI. In our subgroup analysis of the matched cohort, patients without diabetes had association with better outcome after PCI than after CABG, resulting in a significant interaction between diabetes and treatment effect of CABG versus PCI. It would be reasonable to assume that nondiabetic patients may present with favorable LMCAD anatomy for PCI and that using DES in this relatively large vessel may be a simpler and more effective treatment. Further understanding of the biopathologic features of the aforementioned risk factors and its connection with future serious adverse events would help guide decision making between CABG and PCI for patients with LMCAD. Considering that patients with those predictive factors were underrepresented in randomized trials, subsequent studies will be critical for the development of optimal treatment strategies for high-risk patients with LMCAD. In such perspective, our finding may also be helpful to determine patients with clinical equipoise for both CABG and PCI for future randomized trials.

This study has several limitations. First, it was observational and has inherent methodological limitations; thus, our findings should be considered hypothetical and hypothesis generating only. Second, some variables that are known in clinical practice to have a profound effect on the choice of revascularization (eg, detailed extent of coronary artery disease such as the SYNTAX score, and patient frailty) were not available for this analysis. A lack of such information could have penalized the CABG group relative to the PCI group. Finally, this study was exclusively performed in an Asian population, and it remains uncertain whether these findings can be applied to other ethnic groups with different patient and procedural characteristics.

In conclusion, PCI with DES, when compared with CABG, was associated with a comparable long-term risk of the composite outcome of death, myocardial infarction, or stroke in real-world patients with significant LMCAD. Several common and disparate clinically relevant variables were identified as the key determinants of the primary outcome after either CABG or PCI with DES. Our findings will help clinicians assess the risk of LMCAD and provide meticulous management to patients with LMCAD who would be at higher risk of future events.

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Disclosure

All authors declare that they have no conflict of interest with this study.

Appendix. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.ahj.2017.08.003.

References

1. Eagle KA, Guyton RA, Davidoff R, et al. ACC/AHA 2004 guideline update for coronary artery bypass graft surgery: summary article. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (Committee to Update the 1999 Guidelines for Coronary Artery Bypass Graft Surgery). J Am Coll Cardiol 2004;44:e213-10.
2. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. J Am Coll Cardiol 2011;58:e44-122.
3. Hillis LD, Smith PK, Anderson JL, et al. 2011 ACCF/AHA guideline for coronary artery bypass graft surgery. A report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. Developed in collaboration with the American Association for Thoracic Surgery, Society of Cardiovascular Anesthesiologists, and Society of Thoracic Surgeons. J Am Coll Cardiol 2011;58:e123-10.
4. Authors/Task Force m, Windecker S, Kolh P, et al. 2014 ESC/EACTS guidelines on myocardial revascularization: the Task Force on Myocardial Revascularization of the European Society of Cardiology (ESC) and the European Association for Cardio-Thoracic Surgery

(EACTS) developed with the special contribution of the European Association of Percutaneous Cardiovascular Interventions (EAPCI). Eur Heart J 2014;35:2541-619.
5. Park SJ, Ahn JM, Kim YH, et al. Temporal trends in revascularization strategy and outcomes in left main coronary artery stenosis: data from the ASAN Medical Center-Left MAIN Revascularization registry. Circ Cardiovasc Interv 2015;8:e001846.
6. Park SJ, Kim YH, Park DW, et al. Randomized trial of stents versus bypass surgery for left main coronary artery disease. N Engl J Med 2011;364:1718-27.
7. Serruys PW, Morice MC, Kappetein AP, et al. Percutaneous coronary intervention versus coronary-artery bypass grafting for severe coronary artery disease. N Engl J Med 2009;360:961-72.
8. 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.
9. 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.
10. Chieffo A, Park SJ, Valgimigli M, et al. Favorable long-term outcome after drug-eluting stent implantation in nonbifurcation lesions that involve unprotected left main coronary artery: a multicenter registry. Circulation 2007;116:158-62.
11. Park DW, Seung KB, Kim YH, et al. Long-term safety and efficacy of stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: 5-year results from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry. J Am Coll Cardiol 2010;56:117-24.
12. Shiomi H, Morimoto T, Furukawa Y, et al. Comparison of percutaneous coronary intervention with coronary artery bypass grafting in unprotected left main coronary artery disease—5-year outcome from CREDO-Kyoto PCI/CABG Registry Cohort-2. Circ J 2015;79:1282-9.
13. Naganuma T, Chieffo A, Meliga E, et al. Long-term clinical outcomes after percutaneous coronary intervention versus coronary artery bypass grafting for ostial/midshaft lesions in unprotected left main coronary artery from the DELTA registry: a multicenter registry evaluating percutaneous coronary intervention versus coronary artery bypass grafting for left main treatment. JACC Cardiovasc Interv 2014;7: 354-61.
14. Mehilli J, Kastrati A, Byrne RA, et al. Paclitaxel- versus sirolimus-eluting stents for unprotected left main coronary artery disease. J Am Coll Cardiol 2009;53:1760-8.
15. Morice MC, Serruys PW, Kappetein AP, et al. Outcomes in patients with de novo left main disease treated with either percutaneous coronary intervention using paclitaxel-eluting stents or coronary artery bypass graft treatment in the Synergy Between Percutaneous Coronary Intervention with TAXUS and Cardiac Surgery (SYNTAX) trial. Circulation 2010;121:2645-53.
16. Zheng Z, Xu B, Zhang H, et al. Coronary artery bypass graft surgery and percutaneous coronary interventions in patients with unprotected left main coronary artery disease. JACC Cardiovasc Interv 2016;9: 1102-11.
17. 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.
18. Park SJ, Kim YH, Lee BK, et al. Sirolimus-eluting stent implantation for unprotected left main coronary artery stenosis: comparison with bare metal stent implantation. J Am Coll Cardiol 2005;45:351-6.
19. Moussa ID, Klein LW, Shah B, et al. Consideration of a new definition of clinically relevant myocardial infarction after coronary revascularization: an expert consensus document from the Society for Cardiovascular Angiography and Interventions (SCAI). J Am Coll Cardiol 2013;62:1563-70.
20. McCaffrey DF, Griffin BA, Almirall D, et al. A tutorial on propensity score estimation for multiple treatments using generalized boosted models. Stat Med 2013;32:3388-414.
21. White IR, Royston P, Wood AM. Multiple imputation using chained equations: Issues and guidance for practice. Stat Med 2011;30:377-99.
22. 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.
23. Makikallio T, Holm NR, Lindsay M, et al. Percutaneous coronary angioplasty versus coronary artery bypass grafting in treatment of unprotected left main stenosis (NOBLE): a prospective, randomised, open-label, non-inferiority trial. Lancet 2016;388: 2743-52.
24. Chieffo A, Meliga E, Latib A, et al. Drug-eluting stent for left main coronary artery disease. The DELTA registry: a multicenter registry evaluating percutaneous coronary intervention versus coronary artery bypass grafting for left main treatment. JACC Cardiovasc Interv 2012;5:718-27.
25. Roques F, Nashef SA, Michel P, et al. Risk factors and outcome in European cardiac surgery: analysis of the EuroSCORE multinational database of 19030 patients. Eur J Cardiothorac Surg 1999;15: 816-22. discussion 22-3.
26. Weintraub WS, Grau-Sepulveda MV, Weiss JM, et al. Prediction of long-term mortality after percutaneous coronary intervention in older adults: results from the National Cardiovascular Data Registry. Circulation 2012;125:1501-10.
27. Shahian DM, O'Brien SM, Sheng S, et al. Predictors of long-term survival after coronary artery bypass grafting surgery: results from the Society of Thoracic Surgeons Adult Cardiac Surgery Database (the ASCERT study). Circulation 2012;125:1491-500.
28. Best PJ, Lennon R, Ting HH, et al. The impact of renal insufficiency on clinical outcomes in patients undergoing percutaneous coronary interventions. J Am Coll Cardiol 2002;39:1113-9.
29. Cooper WA, O'Brien SM, Thourani VH, et al. Impact of renal dysfunction on outcomes of coronary artery bypass surgery: results from the Society of Thoracic Surgeons National Adult Cardiac Database. Circulation 2006;113:1063-70.
30. Hlatky MA, Boothroyd DB, Bravata DM, et al. Coronary artery bypass surgery compared with percutaneous coronary interventions for multivessel disease: a collaborative analysis of individual patient data from ten randomised trials. Lancet 2009;373:1190-7.
31. Cho HJ, Lee JH, Kim YJ, et al. Comprehensive evaluation of coronary artery disease and aortic atherosclerosis in acute ischemic stroke patients: usefulness based on Framingham risk score and stroke subtype. Cerebrovasc Dis 2011;31:592-600.
32. Roffi M, Angiolillo DJ, Kappetein AP. Current concepts on coronary revascularization in diabetic patients. Eur Heart J 2011;32: 2748-57.
33. Song YB, Hahn JY, Kim JH, et al. Comparison of angiographic and other findings and mortality in non–ST-segment elevation versus ST-segment elevation myocardial infarction in patients undergoing early invasive intervention. Am J Cardiol 2010;106: 1397-403.