Rates and Independent Correlates of 10-Year Major Adverse Events and Mortality in Patients Undergoing Left Main Coronary Arterial Revascularization

Tae Oh Kim, MD[a,#], Jung-Min Ahn, MD[a,#], Do-Yoon Kang, MD[a], Seon Ok Kim, MSc[b], Sangwoo Park, MD[a], Hanbit Park, MD[a], Pil Hyung Lee, MD[a], Seung-Whan Lee, MD[a], Seong-Wook Park, MD[a], Duk-Woo Park, MD[a,*], and Seung-Jung Park, MD[a]

Patients who underwent myocardial revascularization for significant left main coronary artery disease (LMCA) are at high risks of ischemic events and death during follow-up. We sought to determine the independent correlates for very long-term outcomes after LMCA revascularization, which would be clinical value for risk stratification in such high-risk patients. The 10-year rates of clinical outcomes and independent correlates of adverse events were evaluated in 2,240 patients with LMCA disease in the MAIN-COMPARE registry, including 1,102 patients who underwent stenting and 1,138 who underwent coronary artery bypass grafting. The primary outcome was the composite of all-cause death, Q-wave myocardial infarction, or stroke. Secondary outcomes were all-cause mortality and target-vessel revascularization (TVR). The 10-year rates of the primary composite outcome, all-cause mortality, and TVR were 24.7%, 22.2%, and 13.6%, respectively. Age >65 years, diabetes, previous heart failure, cerebrovascular disease, peripheral arterial disease, chronic renal failure, atrial fibrillation, ejection fraction <40%, and distal LMCA bifurcation disease were independent correlates of the primary outcome in the overall population. Several clinical and anatomic parameters were also identified as independent correlates of all-cause death and TVR. Interaction analysis showed no heterogeneities of the effects of variables depending on revascularization type. These clinical descriptors can assist clinicians in identifying high-risk patients within the broad range of risk for patients who underwent LMCA revascularization. **(Am J Cardiol 2020;125:1148−1153)**

Over the last decade, several randomized controlled trials and observational registries have evaluated whether percutaneous coronary intervention (PCI) is as an alternative revascularization strategy as coronary artery bypass grafting (CABG) for significant left main coronary artery (LMCA) disease.[1−3] After myocardial revascularization, depending on individual specific clinical and/or anatomic circumstances, these patients may vary in the degree of future risks of adverse clinical events during follow-up. Accurate knowledge of the major determinants of long-term major cardiovascular events and mortality would be useful, both for clinical and investigational purposes. Until recently, the long-term follow-up study is still limited in patients who underwent LMCA revascularization. We therefore evaluated the incidence and multivariable correlates of 10-year long-term outcomes using extended 10-year follow-up data from the MAIN-COMPARE (Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization) registry.[4]

Methods

The study cohort consisted of 2,240 patients enrolled in the MAIN-COMPARE study, a prospective, multicenter, observational registry of consecutive patients with unprotected LMCA disease (defined as >50% stenosis with no patent graft to the left coronary system) who underwent either CABG or PCI between January 2000 and June 2006.[4,5] Patients who had undergone previous CABG or concomitant valvular or aortic surgery and had ST elevation myocardial infarction or presented with cardiogenic shock were excluded. The final 10-year report of the MAIN-COMPARE study has been published recently.[6]

The choice of revascularization strategy (CABG or PCI) was at the discretion of the treating physicians and/or patients after consideration of several clinical and anatomic factors or surgical risk for CABG. Clinical and anatomic

[a]Division of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea; and [b]Division of Biostatics, Center for Medical Research and Information, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Republic of Korea. Manuscript received November 24, 2019; revised manuscript received and accepted January 17, 2020.

Funding: This work was partly supported by grants 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, and approval of the manuscript; or the decision to submit the manuscript for publication.

Clinical Trial Registration: http://ClinicalTrials.gov (Identifier: NCT02791412).

[#]These two authors contributed equally to this article.

See page 1153 for disclosure information.

*Corresponding author: Tel.: (822) 3010-3995; fax: (822) 487-5918

E-mail address: dwpark@amc.seoul.kr (D.-W. Park).

0002-9149/
https://doi.org/10.1016/j.amjcard.2020.01.023

conditions favoring either PCI or CABG and details of procedural and operative characteristics were described previously.[4,5] PCI was performed exclusively with bare-metal stents (BMS) between January 2000 and May 2003 (wave 1: BMS era) and exclusively with DES between May 2003 and June 2006 (wave 2: DES era). The local ethics committee at each hospital approved the use of clinical data for this study, and all patients provided written informed consent.

The primary outcome of the study was a composite of all-cause death, Q-wave myocardial infarction (MI), or stroke. Secondary outcomes included all-cause mortality and target-vessel revascularization (TVR). Q-wave MI was defined as the documentation of any newly developed pathologic Q-wave after the index treatment. Stroke, as detected by neurologic deficits, was confirmed by a neurologist based on neurologic imaging. TVR was defined as repeat revascularization of the treated vessels, including any segments of the left anterior descending artery and/or left circumflex artery. All clinical events were confirmed by source documentation collected at each hospital and centrally adjudicated by an independent group of clinicians unaware of index revascularization methods.

Clinical follow-up was recommended at 1 month, 6 months, and 1 year, and annually thereafter. In the 10-year MAIN-COMPARE study, the follow-up period was extended through December 31, 2016, to ensure that all patients had the opportunity to be followed up for at least 10 years. Complete information on vital status and date of death were obtained through December 31, 2016, from the National Population Registry of the Korea National Statistical Office, based on the unique 13-digit personal identification number provided to each Korean citizen. The detailed methods for data acquisition and management during extended follow-up have been reported elsewhere.[6]

Categorical variables were expressed as frequencies (percentages) and compared using either Pearson's chi-square test or the Fisher's exact test, as appropriate. Continuous variables were presented as mean ± SD or median (interquartile range), depending on their distribution, which was assessed using the Kolmogorov-Smirnov test, and compared using Student's *t* test or the Wilcoxon rank sum test, as appropriate. Event rates were determined by the Kaplan-Meier method and compared by log-rank tests. Univariate and multivariable Cox regression analyses were used to investigate correlates of the primary composite outcome of all-cause mortality, Q-wave MI, or stroke, and of the secondary outcomes all-cause mortality and TVR. Of the previously published baseline clinical and anatomic covariates listed in Table 1, those with p values <0.20 on univariate analyses were included in multivariable Cox proportional hazards models. The multivariable models were determined by stepwise backward elimination methods (retention threshold: p <0.05). In addition, interaction tests were performed to compare the heterogeneity of effects of risk variables found to be independent correlates in the PCI and CABG groups. These interactions were evaluated by stratified Cox models and likelihood ratio tests. As described previously,[4–6] these analyses were performed in the overall cohort, the wave 1 cohort (ie, BMS vs concurrent CABG between January 2000 and May 2003), and the wave 2 cohort (ie, DES vs concurrent CABG between May 2003 and June 2006). Last, as sensitivity analyses, independent correlates of 10-year clinical outcomes were assessed in each treatment stratum of the CABG and PCI groups. Overall, left ventricular ejection fraction (LVEF) variables were missing for 18.5% of patients. For multivariable analyses, these missing data were handled by multiple imputations using the MCMC (Markov chain Monte Carlo) method. All reported p values are 2-sided, with p values <0.05 considered statistically significant. All statistical analyses were performed using SAS version 9.4 software (SAS Institute, Cary, NC).

Results

Between January 2000 and June 2006, 2,240 patients with unprotected LMCA disease were in included in the MAIN-COMPARE registry. Of these, 1,102 patients underwent PCI with stent implantation, including 318 (29%) who underwent BMS implantation and 784 (71%) who underwent DES implantation, and 1,138 underwent CABG. The baseline clinical and anatomic characteristics of patients who underwent PCI and CABG during the overall period and during each time period of wave 1 and wave 2 are shown in Table 1. In general, patients who underwent CABG were older and were more likely to have higher prevalence of clinical and anatomic risk factors, including higher rates of diabetes, hyperlipidemia, smoking, previous history of MI, peripheral arterial disease, and acute coronary syndrome, as well as lower LVEF, and a higher anatomic complexity. This pattern was consistent during both the wave 1 and wave 2 periods.

The median follow-up period for the overall population was 12.0 years (interquartile range 10.7 to 13.5 years), with a maximum follow-up of 17.6 years. During the entire follow-up period, 658 patients died, 55 experienced Q-wave MI, 84 experienced a stroke, 313 underwent TVR, and 738 had at least 1 primary composite outcome of death, Q-wave MI, or stroke. The observed 10-year rates of primary and secondary outcomes in the overall population are shown in Figure 1 and Table 2. Kaplan-Meier analysis during each time (waves 1 and 2) is shown in Online Figures 1 and 2, respectively.

By multivariable Cox regression analyses, independent correlates of primary composite and secondary outcomes in the overall population are shown in Table 3. Old age (>65 years), diabetes, previous heart failure, cerebrovascular disease, peripheral arterial disease, chronic renal failure, atrial fibrillation, lower LVEF <40%, and distal LMCA bifurcation disease were independent correlates of 10-year primary composite outcome in the overall population. The independent correlates of all-cause mortality were old age (>65 years), diabetes, previous heart failure, chronic lung disease, cerebrovascular disease, chronic renal failure, atrial fibrillation, lower ejection fraction <40%, and distal LMCA bifurcation disease. PCI treatment, younger age (≤65 years), previous PCI, distal LMCA bifurcation, and more severe extent of CAD were independent correlates of TVR.

To determine key predictors and assess heterogeneities in the effects of these variables in each treatment stratum of PCI and CABG, we used univariate and multivariate Cox regression models with interaction analyses for primary

Table 1
Baseline demographic, clinical, and angiographic characteristics

Variable	Overall patients (n = 2,240)		p	Wave 1 (BMS era) (n = 766)		p	Wave 2 (DES era) (n = 1,474)		p
	Stents (n = 1,102)	CABG (n = 1,138)		BMS (n = 318)	CABG (n = 448)		DES (n = 784)	CABG (n = 690)	
Age, (years)	61.3 ± 11.7	62.9 ± 9.4	<0.001	58.6 ± 12.6	61.3 ± 9.6	0.001	62.5 ± 11.1	64.0 ± 9.1	0.004
Men	779 (70.7%)	830 (72.9%)	0.25	223 (70.1%)	331 (73.9%)	0.28	556 (70.9%)	499 (72.3%)	0.59
Diabetes mellitus									
Any diabetes	327 (29.7%)	395 (34.7%)	0.01	76 (23.9%)	139 (31.0%)	0.03	251 (32.0%)	256 (37.1%)	0.04
Requiring insulin	75 (6.8%)	93 (8.2%)	0.25	11 (3.5%)	25 (5.6%)	0.23	64 (8.2%)	68 (9.9%)	0.29
Hypertension	546 (49.5%)	562 (49.4%)	0.97	128 (40.3%)	219 (48.9%)	0.02	418 (53.3%)	343 (49.7%)	0.18
Hyperlipidemia	315 (28.6%)	371 (32.6%)	0.04	74 (23.3%)	118 (26.3%)	0.37	241 (30.7%)	253 (36.7%)	0.01
Current smoker	282 (25.6%)	339 (29.8%)	0.03	89 (28.0%)	161 (35.9%)	0.02	193 (24.6%)	178 (25.8%)	0.64
Previous PCI	200 (18.1%)	125 (11.0%)	<0.001	40 (12.6%)	46 (10.3%)	0.37	160 (20.4%)	79 (11.4%)	<0.001
Previous MI	89 (8.1%)	132 (11.6%)	0.006	26 (8.2%)	57 (12.7%)	0.06	63 (8.0%)	75 (10.9%)	0.07
Previous HF	27 (2.5%)	38 (3.3%)	0.26	7 (2.2%)	16 (3.6%)	0.37	20 (2.6%)	22 (3.2%)	0.56
Chronic lung disease	22 (2.0%)	23 (2.0%)	1.00	2 (0.6%)	5 (1.1%)	0.70	20 (2.6%)	18 (2.6%)	1.00
Cerebrovascular disease	78 (7.1%)	83 (7.3%)	0.90	12 (3.8%)	35 (7.8%)	0.03	66 (8.4%)	48 (7.0%)	0.34
Peripheral arterial disease	16 (1.5%)	62 (5.4%)	<0.001	2 (0.6%)	31 (6.9%)	<0.001	14 (1.8%)	31 (4.5%)	0.004
Chronic renal failure	30 (2.7%)	34 (3.0%)	0.80	4 (1.3%)	10 (2.2%)	0.47	26 (3.3%)	24 (3.5%)	0.97
Ejection fraction (%)									
Median	62.0	60.0	<0.001	64.0	61.0	0.02	61.0	59.0	<0.001
Interquartile range	57–67	52–65		58–67	54–67		56–67	50–64	
AF	22 (2.0%)	31 (2.7%)	0.32	4 (1.3%)	10 (2.2%)	0.47	18 (2.3%)	21 (3.0%)	0.47
ACS presentation	716 (65.0%)	887 (77.9%)	<0.001	226 (71.1%)	366 (81.7%)	0.001	490 (62.5%)	521 (75.5%)	<0.001
LM bifurcation lesions	545 (49.5%)	612 (53.8%)	0.05	100 (31.4%)	246 (54.9%)	<0.001	445 (56.8%)	366 (53.0%)	0.16
Extent of coronary disease			<0.001			<0.001			<0.001
LM mainly	278 (25.2%)	71 (6.2%)		133 (41.8%)	45 (10.0%)		145 (18.5%)	26 (3.8%)	
LM and 1 VD	264 (24.0%)	119 (10.5%)		82 (25.8%)	65 (14.5%)		182 (23.2%)	54 (7.8%)	
LM and 2 VD	287 (26.0%)	299 (26.3%)		70 (22.0%)	139 (31.0%)		217 (27.7%)	160 (23.2%)	
LM and 3 VD	273 (24.8%)	649 (57.0%)		33 (10.4%)	199 (44.4%)		240 (30.6%)	450 (65.2%)	
RCA disease	396 (35.9%)	804 (70.7%)	<0.001	63 (19.8%)	266 (59.4%)	<0.001	333 (42.5%)	538 (78.0%)	<0.001
Restenotic lesion	32 (2.9%)	14 (1.2%)	0.008	5 (1.6%)	8 (1.8%)	1.00	27 (3.4%)	6 (0.9%)	0.002

Values are mean ± SD or n (%). Hyperlipidemia defined as total cholesterol greater than 200 mg/dl; or LDL greater than 130 mg/dl; or if treatment was initiated because the LDL was >100 mg/dl in patients with known coronary artery disease.

AF = atrial fibrillation; BMI = body mass index; CABG = coronary artery bypass grafting; CAD = coronary artery disease; LM = left main; NSTEMI = non-ST elevation myocardial infarction; PCI = percutaneous coronary intervention; STEMI = ST elevation myocardial infarction; VD = vessel disease.

composite outcome (Online Tables 1 and 2), all-cause mortality (Online Tables 3 and 4), and TVR (Online Tables 5 and 6). In the PCI group, old age (>65 years), diabetes, previous heart failure, cerebrovascular disease, peripheral arterial disease, chronic renal failure, atrial fibrillation, and distal LMCA bifurcation disease were independent correlates of the primary composite outcome. In the CABG group, old age (>65 years), previous heart failure, cerebrovascular disease, peripheral arterial disease, chronic renal failure, atrial fibrillation, and lower LVEF were independent correlates of the primary composite outcome. Although the magnitudes of hazard ratios and the corresponding p values were slightly different, most major correlates of 10-year clinical outcomes in the overall population remained significant correlates in each PCI and CABG treatment stratum. Interaction analyses showed no heterogeneities in the effects of type of revascularization method on predictive variables.

Discussion

The present study is the longest follow-up to date to analyze rates and independent correlates of major adverse events and mortality and to provide effect estimates of clinically relevant risk factors in patients with LMCA disease who underwent myocardial revascularization. A major finding of this study was that (1) there was no significant difference between PCI and CABG with respect to the primary composite rate of the composite outcome of death, Q-wave MI or stroke at 10 years; (2) old age (>65 years), diabetes, previous heart failure, concomitant cerebrovascular or peripheral arterial disease, renal failure, atrial fibrillation, reduced LVEF (<40%), and distal bifurcation involvement were independent correlates of the primary composite outcome; and (3) the key correlates of clinical outcomes were generally uniform in each treatment stratum without significant heterogeneities in the effect of independent correlates.

Recent updated 5-year reports of the Evaluation of XIENCE Everolimus Eluting Stent Versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization (EXCEL) and the NordicBaltic-British Left Main Revascularization Study (NOBLE) showed conflicting findings with regard to the primary and secondary trial end points.[7,8] Although we did not detect statistically significant differences in the 10-year rates of major adverse events and all-cause mortality between CABG and PCI, the rates of serious composite outcome and death tended to be higher after DES than after CABG beyond 5 years of follow-up.[6] Despite of such discordant findings, given that highly

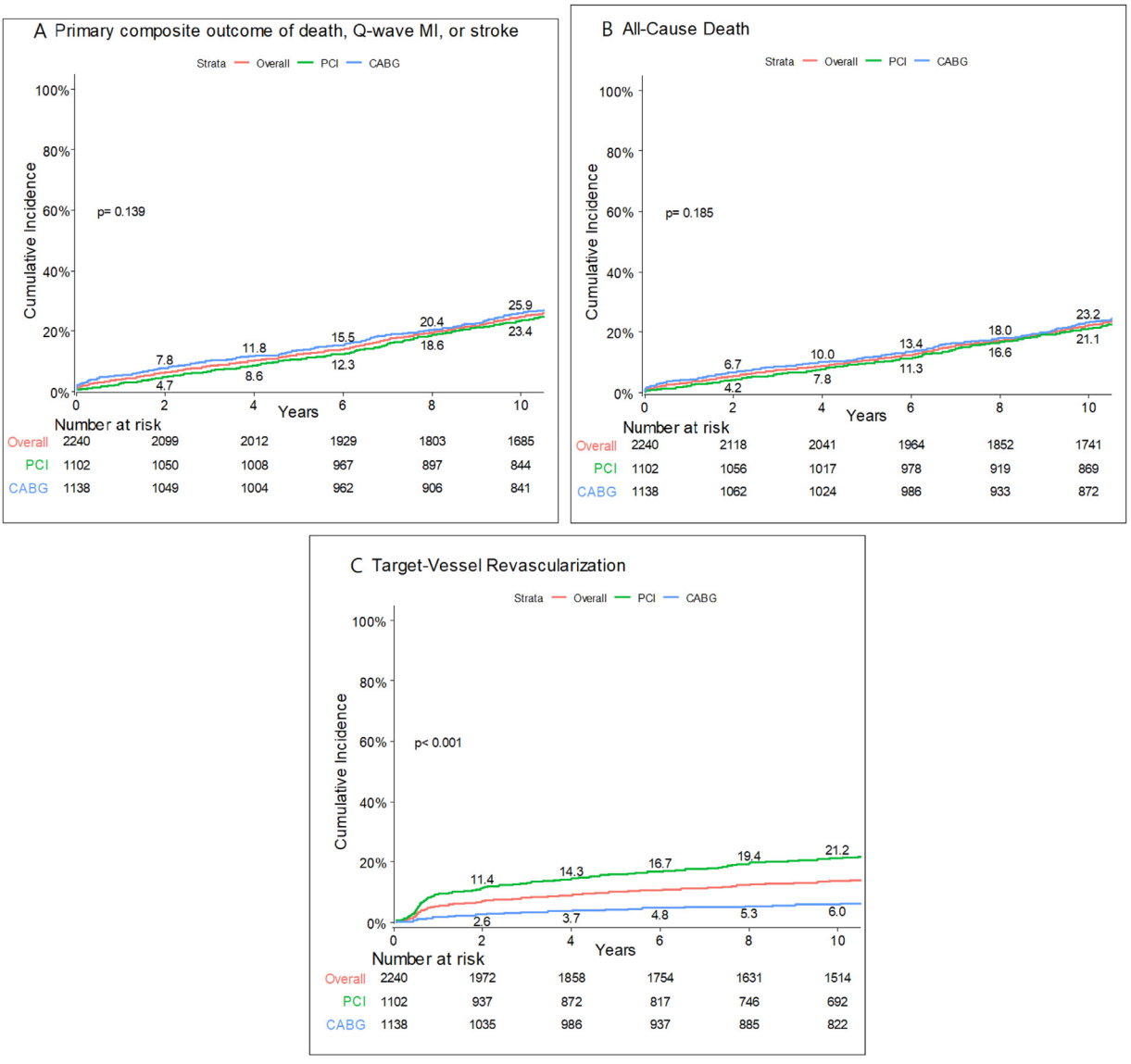

Figure 1. Kaplan-Meier analysis of 10-year rates of primary and secondary outcomes. (*A*) Cumulative incidence of the primary composite outcome of all-cause death, Q-wave myocardial infarction, or stroke; (*B*) incidence of all-cause mortality; (*C*) incidence of target-vessel revascularization. The cumulative incidence at each time point was derived from the Kaplan-Meier estimates.
CABG = coronary artery bypass grafting; MI = myocardial infarction; PCI = percutaneous coronary intervention.

selected trial cohorts may not be fully applicable to a diversity of patients or clinical circumstances encountered in daily practice, determining risk factors, predictors, and risk stratification using the "real-world" data may be clinically relevant and thus our finding would be helpful to guide optimal decision-making and future risk prediction according to important clinical and anatomic characteristics in the daily clinical practice.

Table 2
Observed 10-year rates of primary and secondary outcomes*

Adverse outcome	Overall			p	Wave 1 (BMS era)			p	Wave 2 (DES era)			p
	All (n = 2,240)	Stent (n = 1,102)	CABG (n = 1,138)		All (n = 766)	BMS (n = 318)	CABG (n = 448)		All (n = 1474)	DES (n = 784)	CABG (n = 690)	
Primary composite of death, Q-wave MI, or stroke	553 (24.7%)	258 (23.4%)	295 (25.9%)	0.139	182 (23.8%)	66 (20.8%)	116 (25.9%)	0.004	371 (25.2%)	192 (24.5%)	179 (25.9%)	0.905
All-cause mortality	497 (22.2%)	233 (21.1%)	264 (23.2%)	0.185	166 (21.7%)	60 (18.9%)	106 (23.7%)	0.012	331 (22.5%)	173 (22.1%)	158 (22.9%)	0.972
TVR	282 (13.6%)	220 (21.2%)	62 (6.0%)	<0.001	94 (13.1%)	65 (21.3%)	29 (7.1%)	<0.001	188 (13.9%)	155 (21.2%)	33 (5.3%)	<0.001

BMS = bare-metal stents; CABG = coronary artery bypass grafting; DES = drug-eluting stents; PCI = percutaneous coronary intervention; TVR = target-vessel revascularization.
* Event rates were estimated by Kaplan-Meier analysis, with p values derived from log-rank test. The estimates were unadjusted (crude).

Table 3
Independent predictors of primary composite outcome, all-cause death, and target-vessel revascularization

Variables	Overall population		Wave 1		Wave 2	
	HR (95% CI)	p	HR (95% CI)	p	HR (95% CI)	p
Primary composite outcome of death, Q-wave MI, or stroke						
Percutaneous coronary intervention treatment	1.15 (0.98 to 1.34)	0.092	0.90 (0.68 to 1.20)	0.479	1.15 (0.95 to 1.39)	0.144
Age >65 years	2.09 (1.79 to 2.43)	<0.001	2.57 (2.01 to 3.28)	<0.001	1.98 (1.64 to 2.40)	<0.001
Diabetes mellitus	1.30 (1.12 to 1.52)	0.001			1.35 (1.12 to 1.64)	0.002
Previous heart failure	2.22 (1.60 to 3.09)	<0.001	2.22 (1.32 to 3.72)	0.003	2.14 (1.38 to 3.31)	0.001
Cerebrovascular disease	1.46 (1.16 to 1.84)	0.001	1.71 (1.15 to 2.53)	0.008	1.45 (1.09 to 1.93)	0.011
Peripheral arterial disease	1.60 (1.18 to 2.18)	0.003			1.86 (1.24 to 2.79)	0.003
Chronic renal failure	2.95 (2.18 to 4.00)	<0.001	2.11 (1.07 to 4.15)	0.030	3.29 (2.33 to 4.64)	<0.001
Atrial fibrillation	1.91 (1.33 to 2.74)	0.001			2.20 (1.46 to 3.30)	<0.001
LV ejection fraction <40%	1.60 (1.23 to 2.07)	<0.001	1.71 (1.12 to 2.62)	0.013	0.98 (0.97 to 0.99)	<0.0001
LM distal bifurcation	1.20 (1.04 to 1.40)	0.016			1.39 (1.15 to 1.68)	0.001
All-cause mortality						
Percutaneous coronary intervention treatment	1.03 (0.89 to 1.21)	0.671	0.84 (0.64 to 1.09)	0.190	1.16 (0.95 to 1.42)	0.134
Age >65 years	2.46 (2.10 to 2.89)	<0.001	2.83 (2.18 to 3.66)	<0.001	2.26 (1.84 to 2.78)	<0.001
Diabetes mellitus	1.38 (1.18 to 1.62)	<0.001			1.49 (1.22 to 1.83)	<0.001
Previous heart failure	2.16 (1.53 to 3.03)	<0.001	2.27 (1.33 to 3.86)	0.034	2.02 (1.28 to 3.19)	0.003
Chronic lung disease	1.78 (1.17 to 2.70)	0.007			1.81 (1.15 to 2.87)	0.011
Cerebrovascular disease	1.54 (1.21 to 1.95)	<0.001	1.79 (1.20 to 2.68)	0.005	1.45 (1.08 to 1.95)	0.014
Chronic renal failure	3.30 (2.43 to 4.50)	<0.001	2.50 (1.27 to 4.95)	0.008	3.47 (2.44 to 4.93)	<0.001
Atrial fibrillation	1.65 (1.13 to 2.41)	0.010			1.83 (1.17 to 2.88)	0.008
LV ejection fraction <40%	1.83 (1.40 to 2.38)	<0.001	2.12 (1.38 to 3.26)	0.001	1.72 (1.21 to 2.45)	0.003
LM distal bifurcation	1.31 (1.12 to 1.53)	0.001			1.40 (1.14 to 1.72)	0.001
Target-vessel revascularization						
Percutaneous coronary intervention treatment	4.36 (3.29 to 5.77)	<0.001	3.38 (2.25 to 5.07)	<0.001	4.42 (3.08 to 6.34)	<0.001
Age >65 years	0.75 (0.59 to 0.95)	0.016				
Diabetes mellitus					1.37 (1.03 to 1.82)	0.03
Previous percutaneous coronary intervention	1.32 (1.00 to 1.74)	0.047	2.04 (1.26 to 3.29)	0.004		
LM distal bifurcation	1.27 (1.00 to 1.61)	0.046			1.41 (1.06 to 1.87)	0.018
Extent of coronary disease						
LM mainly	1.00					
LM+1VD	0.94 (0.64 to 1.40)	0.774				
LM+2VD	1.62 (1.14 to 2.31)	0.008				
LM+3VD	1.53 (1.06 to 2.20)	0.023				

CI = confidence interval; HR = hazard ratio; LM = left main; LV = left ventricular; PCI = percutaneous coronary intervention; VD = vessel disease.

Current US and European guidelines indicate that CABG is a class I recommendation for LMCA disease, whereas PCI is a class I, IIa, or III recommendation depending on anatomic complexities.[9,10] These guidelines emphasize that important clinical variables should be taken into account in the multidisciplinary heart-team discussion. Previous studies suggested several clinical variables (age, creatinine or creatinine clearance, LVEF) for predicting mortality after myocardial revascularization (ie, ACEF score or logistic clinical SYNTAX score) that similar to those in present study.[11–13] However, previous scoring tools have not been tested in prediction for very long-term outcomes. Since we mainly focused on improving longer term (>10 year) clinical prediction in patients with LMCA disease who underwent PCI or CABG, key findings may provide more objective, valuable clinical information on very long-term correlates of hard clinical end points and mortality.

One of the most important aspects of the current analyses was the interaction effects of the clinical correlates after myocardial revascularization, as they differentially influenced the relative outcomes after CABG or PCI. These interaction effects may aid in deciding whether to perform CABG or PCI; it is more predictive of clinical outcomes in patients who underwent PCI than in those who underwent CABG and vice versa. In the present study, interaction analysis showed no heterogeneities in the effect of independent variables depending on the revascularization method. These findings might suggest that, despite the distinct biological pathways of each risk factor, the prognostic impact of clinically relevant correlates was relatively uniform and carried a worse prognosis irrespective of the final revascularization strategy.

This study had several limitations. First, it was an observational study and thus has inherent methodological limitations. Because the allocation of treatment was not randomized and was at the discretion of the physician and/or patient, our findings may be subject to selection bias. Although multivariable adjustments were performed for significant confounders, unmeasured confounders could affect the study findings. Second, our study did not evaluate the detailed information on operative and procedural factors, which may also influence long-term clinical outcomes. Also, changes in risk factors during long-term follow-up (ie, blood pressure control, adequate lipid-lowering, and newly developed diabetes) were not assessed in the current analysis. Third, because the MAIN-COMPARE registry

included patients enrolled before the development of the SYNTAX score, systematic evaluation of SYNTAX score was not feasible and were only available in limited number of patients. Last, we did not exactly assess the presence or absence of complete revascularization and functional assessment (ie, fractional flow reserve) for obstructive LMCA disease, which might be a key factor for clinical events after myocardial revascularization.

In conclusion, this longest follow-up (>10 years) to date of a cohort of patients with LMCA disease found that several clinically relevant variables (old age, diabetes, previous heart failure, concomitant cerebrovascular or peripheral arterial disease, renal failure, atrial fibrillation, reduced LVEF, and distal bifurcation involvement) were independent correlates of the serious composite outcome of death, Q-wave MI, or stroke. These findings may help clinicians assess the risk stratification after LMCA revascularization and provide more aggressive preventive or therapeutic management for patients at higher risk of future events during long-term follow-up.

Disclosures

The authors have no conflicts of interest to disclose.

Author Contribution

Tae Oh Kim, MD: Data curation, Writing-Original draft preparation; Jung-Min Ahn, MD: Data curation, Visualization, Investigation; Do-Yoon Kang, MD: Software, Validation; Seon Ok Kim, MSc: Methodology, Formal analysis, Software; Sangwoo Park, MD: Validation; Hanbit Park, MD: Validation; Pil Hyung Lee, MD: Validation; Seung-Whan Lee, MD: Validation; Seong-Wook Park, MD: Validation; Duk-Woo Park, MD: Resources, Conceptualization, Writing- Review & Editing; Seung-Jung Park, MD: Supervision, Project administration.

Supplementary materials

Supplementary material associated with this article can be found in the online version at https://doi.org/10.1016/j.amjcard.2020.01.023.

1. Palmerini T, Serruys P, Kappetein AP, Genereux P, Riva DD, Reggiani LB, Christiansen EH, Holm NR, Thuesen L, Makikallio T, Morice MC, Ahn JM, Park SJ, Thiele H, Boudriot E, Sabatino M, Romanello M, Biondi-Zoccai G, Cavalcante R, Sabik JF, Stone GW. Clinical outcomes with percutaneous coronary revascularization vs coronary artery bypass grafting surgery in patients with unprotected left main coronary artery disease: a meta-analysis of 6 randomized trials and 4,686 patients. *Am Heart J* 2017;190:54–63.
2. Park DW, Ahn JM, Park SJ, Taggart DP. Percutaneous coronary intervention in left main disease: SYNTAX, PRECOMBAT, EXCEL and NOBLE-combined cardiology and cardiac surgery perspective. *Ann Cardiothorac Surg* 2018;7:521–526.
3. Boudriot E, Thiele H, Walther T, Liebetrau C, Boeckstegers P, Pohl T, Reichart B, Mudra H, Beier F, Gansera B, Neumann FJ, Gick M, Zietak T, Desch S, Schuler G, Mohr FW. Randomized comparison of percutaneous coronary intervention with sirolimus-eluting stents versus coronary artery bypass grafting in unprotected left main stem stenosis. *J Am Coll Cardiol* 2011;57:538–545.
4. Seung KB, Park DW, Kim YH, Lee SW, Lee CW, Hong MK, Park SW, Yun SC, Gwon HC, Jeong MH, Jang Y, Kim HS, Kim PJ, Seong IW, Park HS, Ahn T, Chae IH, Tahk SJ, Chung WS, Park SJ. Stents versus coronary-artery bypass grafting for left main coronary artery disease. *N Engl J Med* 2008;358:1781–1792.
5. Park DW, Seung KB, Kim YH, Lee JY, Kim WJ, Kang SJ, Lee SW, Lee CW, Park SW, Yun SC, Gwon HC, Jeong MH, Jang YS, Kim HS, Kim PJ, Seong IW, Park HS, Ahn T, Chae IH, Tahk SJ, Chung WS, Park SJ. 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;56:117–124.
6. Park DW, Ahn JM, Yun SC, Yoon YH, Kang DY, Lee PH, Lee SW, Park SW, Seung KB, Gwon HC, Jeong MH, Jang Y, Kim HS, Seong IW, Park HS, Ahn T, Chae IH, Tahk SJ, Park SJ. 10-year outcomes of stents versus coronary artery bypass grafting for left main coronary artery disease. *J Am Coll Cardiol* 2018;72:2813–2822.
7. Stone GW, Kappetein AP, Sabik JF, Pocock SJ, Morice MC, Puskas J, Kandzari DE, Karmpaliotis D, Brown WM 3rd, Lembo NJ, Banning A, Merkely B, Horkay F, Boonstra PW, van Boven AJ, Ungi I, Bogats G, Mansour S, Noiseux N, Sabate M, Pomar J, Hickey M, Gershlick A, Buszman PE, Bochenek A, Schampaert E, Page P, Modolo R, Gregson J, Simonton CA, Mehran R, Kosmidou I, Genereux P, Crowley A, Dressler O, Serruys PW. Five-year outcomes after PCI or CABG for left main coronary disease. *N Engl J Med* 2019;381:1820–1830.
8. Holm NR, Makikallio T, Lindsay MM, Spence MS, Erglis A, Menown IBA, Trovik T, Kellerth T, Kalinauskas G, Mogensen LJH, Nielsen PH, Niemela M, Lassen JF, Oldroyd K, Berg G, Stradins P, Walsh SJ, Graham ANJ, Endresen PC, Frobert O, Trivedi U, Anttila V, Hildick-Smith D, Thuesen L, Christiansen EH. 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;395:191–199.
9. Fihn SD, Blankenship JC, Alexander KP, Bittl JA, Byrne JG, Fletcher BJ, Fonarow GC, Lange RA, Levine GN, Maddox TM, Naidu SS, Ohman EM, Smith PK. 2014 ACC/AHA/AATS/PCNA/SCAI/STS focused update of the guideline for the diagnosis and management of patients with stable ischemic heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and the American Association for Thoracic Surgery, Preventive Cardiovascular Nurses Association, Society for Cardiovascular Angiography and Interventions, and Society of Thoracic Surgeons. *J Am Coll Cardiol* 2014;64:1929–1949.
10. Neumann FJ, Sousa-Uva M, Ahlsson A, Alfonso F, Banning AP, Benedetto U, Byrne RA, Collet JP, Falk V, Head SJ, Juni P, Kastrati A, Koller A, Kristensen SD, Niebauer J, Richter DJ, Seferovic PM, Sibbing D, Stefanini GG, Windecker S, Yadav R, Zembala MO. 2018 ESC/EACTS Guidelines on myocardial revascularization. *Eur Heart J* 2019;40:87–165.
11. Farooq V, Vergouwe Y, Raber L, Vranckx P, Garcia-Garcia H, Diletti R, Kappetein AP, Morel MA, de Vries T, Swart M, Valgimigli M, Dawkins KD, Windecker S, Steyerberg EW, Serruys PW. Combined anatomical and clinical factors for the long-term risk stratification of patients undergoing percutaneous coronary intervention: the logistic clinical SYNTAX score. *Eur Heart J* 2012;33:3098–3104.
12. Ranucci M, Castelvecchio S, Menicanti L, Frigiola A, Pelissero G. Risk of assessing mortality risk in elective cardiac operations: age, creatinine, ejection fraction, and the law of parsimony. *Circulation* 2009;119:3053–3061.
13. Farooq V, Serruys PW, Bourantas C, Vranckx P, Diletti R, Garcia Garcia HM, Holmes DR, Kappetein AP, Mack M, Feldman T, Morice MC, Colombo A, Morel MA, de Vries T, van Es GA, Steyerberg EW, Dawkins KD, Mohr FW, James S, Stahle E. Incidence and multivariable correlates of long-term mortality in patients treated with surgical or percutaneous revascularization in the synergy between percutaneous coronary intervention with taxus and cardiac surgery (SYNTAX) trial. *Eur Heart J* 2012;33:3105–3113.