Long-term (10-year) outcomes of stenting or bypass surgery for acute coronary syndromes and stable ischemic heart disease with unprotected left main coronary artery disease

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Background Acuity of clinical presentation may influence decision making of percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG) for left main coronary artery (LMCA) disease. However, it is undetermined whether clinical indication for myocardial revascularization may affect the relative long-term effect after PCI and CABG.

Methods In the MAIN-COMPARE study including 2,240 patients with LMCA disease treated with PCI (n = 1102) or CABG (n = 1138), we examined interaction between acuity of clinical presentation (acute coronary syndromes [ACS] or non-ACS) and revascularization strategy on 10-year outcomes. Primary outcome was a composite of all-cause death, Q-wave myocardial infarction, or stroke. Secondary outcomes were all-cause death or target vessel revascularization.

Results In overall patients, 1,603 patients (71.6%) presented with ACS and 637 patients (28.4%) presented with non-ACS. The 10-year adjusted risks for primary composite outcome were similar after PCI and CABG among patients who presented with non-ACS (hazard ratio [HR] 1.07; 95% CI 0.71-1.61) and those who presented with ACS (HR 1.00; 95% CI 0.81-1.24) (*P* for interaction = .29). The adjusted risks of death were also similar between 2 groups in non-ACS (HR 0.98; 95% CI 0.63-1.51) and ACS (HR 1.02; 95% CI 0.81-1.28) patients (*P* for interaction = .62). The adjusted risks of target vessel revascularization were consistently higher after PCI in non-ACS (HR 6.38; 95% CI 3.14-12.96) and ACS (HR 3.96; 95% CI 2.80-5.60) patients (*P* for interaction = .39).

Conclusions In patients with LMCA disease, we have identified no significant interaction between the acuity of clinical indication and the relative treatment effect of PCI versus CABG on 10-year clinical outcomes. (Am Heart J 2019;218:9-19.)

Percutaneous coronary intervention (PCI) for left main coronary artery (LMCA) disease has been increasingly performed in clinical practice since several landmark randomized trials reported at least comparable outcomes compared with coronary artery bypass grafting (CABG).[1-6] This practical change resulted from the widespread use of drug-eluting stents (DESs) with advanced procedural technique, adjunctive antithrombotic drugs, and growing experience of interventional cardiologists.[7,8] Although many aspects of PCI for LMCA disease have been widely investigated, there are still several clinical questions related to decision making for revascularization strategy and for addressing the comparative long-term risks on the basis of individual baseline characteristics.

Acute coronary syndrome (ACS) is an important disease entity that remains an important cause of mortality and morbidity after coronary revascularization. In daily clinical practice, the acuity of clinical presentation is an important factor for planning revascularization strategy in patients with coronary artery disease (CAD).[9] An early invasive strategy with prompt revascularization is preferred treatment strategy for high-risk patients presenting with ACS. Although CABG has been recommended as the first choice of revascularization strategy for unprotected LMCA disease,[10,11] the clinical pathway for prompt or immediate revascularization in patients with ACS is not

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equally available for PCI and CABG. In addition, it is not well established whether long-term clinical outcomes after PCI and CABG for LMCA disease are differentially affected by the acuity of clinical indication for coronary revascularization. Therefore, we sought to determine whether an interaction exists between the presence of ACS and treatment with PCI compared with CABG using the long-term (10-year) report of the Revascularization for Unprotected Left Main Coronary Artery Stenosis: Comparison of Percutaneous Coronary Angioplasty Versus Surgical Revascularization (MAIN-COMPARE) registry.[12]

Methods

Study population

MAIN-COMPARE was a prospective, multicenter, observational study that included consecutive patients with *unprotected LMCA disease* (defined as stenosis of >50% with no patent graft to the left coronary system) who underwent either CABG or PCI between January 2000 and June 2006.[13,14] Patients who had undergone prior CABG or concomitant valvular or aortic surgery and had ST-elevation myocardial infarction (STEMI) or presented with cardiogenic shock were excluded. The final 10-year report of the MAIN-COMPARE study has been published recently.[12]

The choice of revascularization strategy (CABG or PCI) was based on patient or treating physician preference after considering several clinical and anatomic factors or surgical risk associated with CABG. Clinical and anatomical conditions favoring either PCI or CABG and details of procedural and operative characteristics were described previously.[12-14] PCI was performed exclusively with bare-metal stents (BMS) between January 2000 and May 2003 and exclusively with DES between May 2003 and June 2006.

This study was approved by the local ethics committee at each hospital, and all patients provided written informed consent for use of their clinical data for this study. There was no industry involvement in the design, conduct, or analysis of the study.

Study outcomes and follow-up

The main purpose of this study was to determine whether there are differences in clinical outcomes between PCI and CABG according to the clinical presentation: ACS (unstable angina or non–ST-segment elevation myocardial infarction [NSTEMI]) versus stable CAD (stable angina or silent ischemia). The diagnosis of unstable angina was made based on clinical findings of prolonged angina at rest; new onset of severe angina; angina that is increasing in frequency, longer in duration, or lower in threshold; or angina that occurs after a recent episode of myocardial infarction (MI). The primary outcome of the study was a serious composite outcome of all-cause death, Q-wave MI, or stroke. Secondary outcomes included all-cause mortality or target vessel revascularization (TVR). *Q-wave MI* was defined as the documentation of any newly developed pathologic Q wave with clinical symptoms or signs after the index treatment. Stroke, as detected by neurologic deficits, was confirmed by a neurologist based on neurologic imaging. *TVR* was defined as any 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, 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 of at least 10 years of follow-up. The detailed methods for data acquisition and management during extended follow-up have been reported elsewhere.[12]

Statistical analysis

Continuous variables were reported as mean ± SD and compared using Student *t* test or Wilcoxon rank sum test as appropriate. Categorical variables were presented as numbers (percentages) and compared using either Pearson χ^2 test or the Fisher exact test, as appropriate. Event rates were based on Kaplan-Meier estimates in time-to-first-event analyses and were compared by the log-rank test.

Multivariate Cox regression analyses were used to adjust for differences in baseline characteristics and clinically relevant covariates. The following variables were entered into the multivariable models: age, sex, body mass index, hypertension, hyperlipidemia, diabetes mellitus, previous MI, atrial fibrillation, previous PCI, peripheral arterial disease, chronic renal failure, congestive heart failure, extent of diseased vessel, location of LMCA disease, and combined right CAD. Formal interaction testing was performed to determine whether the acuity of clinical presentation (ACS vs non-ACS) influenced the relative risk of PCI versus CABG for the occurrence of clinical outcomes at 10 years in the multivariable model. As described previously,[12-14] these analyses were performed in the overall cohort, wave 1 cohort of the BMS era (BMS vs concurrent CABG between January 2000 and May 2003), and wave 2 cohort of the DES era (DES vs concurrent CABG between May 2003 and June 2006). Because the "Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery" (SYNTAX) score was available for a subset of patients only, we performed analyses in the overall patient population and in the subgroup with the baseline SYNTAX score. All reported *P* values are 2-sided; *P* value <.05 was considered statistically significant. No adjustments were made for multiple comparisons. All statistical analyses were performed with the use of SPSS software, version 22 (SPSS Inc, Chicago, IL).

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responsible for the design and conduct of this study, all study analyses, the drafting and editing of the paper, and its final contents.

Results

Study population and baseline characteristics

Between January 2000 and June 2006, a total of 2,240 patients with unprotected LMCA disease were included. Among them, 1,102 patients underwent PCI with stent implantation (318 [29%] treated with BMS and 784 [71%] treated with DES), and 1,138 underwent CABG. Details of the baseline characteristics according to revascularization strategy have been published previously.[12]

Of 2,240 patients, 1,603 (71.6%) patients presented with ACS (1383 unstable angina and 220 NSTEMI) and 637 (28.4%) patients presented with non-ACS (58 silent ischemia and 579 chronic stable angina). Baseline demographic, clinical, and angiographic characteristics according to clinical presentation are shown in Table I. As compared with patients who presented with non-ACS, patients who presented with ACS were older and were more likely to have a higher risk of clinical and anatomic risk-factors profiles (ie, a higher incidence of hyperlipidemia, smoking, previous history of MI, peripheral artery disease or heart failure, lower ejection fraction, and higher EURO score). Regarding anatomic characteristics, ACS patients had a greater prevalence of additional CAD and distal bifurcation involvement and had higher mean SYNTAX score. Detailed baseline characteristics stratified by clinical presentation and treatment are shown in Supplementary Table I. Procedural and operative data are shown in Table II. PCI was chosen as revascularization strategy for 386 (60.6%) patients in the non-ACS group and 716 (44.7%) patients in the ACS group, respectively. Although DES was more commonly used in the non-ACS group, there were no significant differences in PCI characteristics (ie, number of stents, stent length, average stent diameter, stenting techniques, or use of intravascular ultrasound) between groups. Off-pump CABG was more frequently performed in non-ACS patients. The number of grafts was significantly higher in the ACS group because the extent of diseased vessel (ie, left main plus 3-vessel disease) was more severe in patients with ACS.

Long-term clinical outcomes

The median follow-up duration was 12.0 years (interquartile range, 10.7-13.5) for the overall study population. By multivariable analysis, the presence of ACS was an independent predictor of the primary composite outcome of all-cause death, Q-wave MI, or stroke at 10 years (adjusted hazard ratio [HR] 1.29; 95% CI 1.05-1.57; $P = .02$) (Supplementary Table II). The Kaplan-Meier event curves of clinical outcomes after PCI and CABG according to the clinical presentation in the overall cohort, wave 1 (BMS era) cohort, and wave 2 (DES era) cohort are shown in Figure 1 and Supplementary Figures 1 and 2, respectively. Observed 10-year cumulative incidence rates of the primary composite outcome of death, Q-wave MI, or stroke and all-cause mortality were not significantly different between PCI and CABG, irrespective of the acuity of presentation. The incidence of TVR was consistently higher in the PCI group independent of the presence of ACS.

After multivariable adjustment of baseline covariates, the adjusted comparative outcomes after PCI and CABG according to the clinical indication for revascularization are shown in Table III and Figure 2. Among non-ACS

Table I. Baseline clinical and anatomic characteristics of the patients, according to clinical presentation*

Variable	Non-ACS (n = 637)	ACS (n = 1603)	*P* value
Clinical characteristics			
Age (y)	61.0 ± 10.6	62.6 ± 10.6	<.001
Men, n (%)	468 (73.5)	1141 (71.2)	.30
Body mass index (kg/m^2)	24.8 ± 2.8	24.4 ± 3.0	.006
Hypertension, n (%)	300 (47.1)	808 (50.4)	.16
Diabetes mellitus, n (%)	193 (30.3)	529 (33.0)	.23
Diabetes mellitus on insulin, n (%)	45 (7.1)	123 (7.7)	.66
Hyperlipidemia, n (%)	168 (26.4)	518 (32.3)	.006
Smoking, n (%)	157 (24.6)	464 (28.9)	.04
Previous MI, n (%)	42 (6.6)	179 (11.2)	.001
Previous PCI, n (%)	103 (16.2)	222 (13.8)	.16
Previous CVA, n (%)	39 (6.1)	122 (7.6)	.24
Previous PAD, n (%)	13 (2.0)	65 (4.1)	.02
Chronic lung disease, n (%)	12 (1.9)	33 (2.1)	.87
Chronic renal failure, n (%)	13 (2.0)	51 (3.2)	.16
Congestive heart failure, n (%)	11 (1.7)	54 (3.4)	.05
Valvular heart disease, n (%)	8 (1.3)	28 (1.7)	.46
Ejection fraction (%)	60.6 ± 10.1	58.3 ± 11.9	<.001
Ejection fraction <40 (%)	17 (3.8)	119 (8.6)	.001
Atrial fibrillation, n (%)	10 (1.6)	43 (2.7)	.13
Clinical indication			<.001
Silent ischemia, n (%)	58 (9.1)	–	
Stable angina, n (%)	579 (90.9)	–	
Unstable angina, n (%)	–	1383 (86.3)	
NSTEMI, n (%)	–	220 (13.7)	
EURO score	2.7 ± 2.1	4.8 ± 2.1	<.001
EURO score ≥6	68 (10.7)	524 (32.7)	<.001
Anatomic characteristics			
Extent of diseased vessel			<.001
Left main only	119(18.7)	230(14.3)	
Left main +1-vessel disease	134(21.0)	249(15.5)	
Left main +2-vessel disease	168(26.4)	418 (26.1)	
Left main +3-vessel disease	216 (33.9)	706 (44.0)	
Left main disease location			.02
Ostium or shaft	334 (52.4)	749 (46.7)	
Distal bifurcation	303 (47.6)	854 (53.3)	
RCA disease	284 (44.6)	916 (57.1)	<.001
In-stent restenosis	14 (2.2)	32 (2.0)	.87
Moderate to severe calcification	63 (9.9)	166 (10.4)	.74
Thrombus containing	8 (1.3)	39 (2.4)	.08
Ulceration	13 (2.0)	35 (2.2)	.83
SYNTAX score†	27.9 ± 12.3	32.2 ± 14.7	<.001

CVA, cerebrovascular accident; *PAD*, peripheral arterial disease; *RCA*, right coronary artery.

*Data are mean ± SD or number (%).

†The SYNTAX score reflects a comprehensive angiographic assessment of coronary atherosclerotic burden and anatomic complexity. SYNTAX scores were only available for 1580 patients (70.5% of the overall population).

Table II. Baseline procedural characteristics of the patients, according to clinical presentation*

Variable	Non-ACS	ACS	*P* value
Revascularization treatment	n = 637	n = 1603	
PCI	386 (60.6)	716 (44.7)	<.001
CABG	251 (39.4)	887 (55.3)	<.001
Characteristics of PCI procedure	n = 386	n = 716	
BMS	92 (23.8)	226(31.6)	.008
DES	294 (76.2)	490 (68.4)	.008
SES	243 (83.2)	364 (74.9)	.007
PES	49 (16.8)	122 (25.1)	.007
Total number of stents per patient	1.96 ± 1.19	1.91 ± 1.11	.46
Total stent number at LM site	1.20 ± 0.49	1.18 ± 0.44	.54
Total stent length at LM site, mm	27.99 ± 20.78	28.04 ± 20.64	.97
Average stent diameter at LM site	3.49 ± 0.44	3.54 ± 0.45	.07
Stent technique			.48
LM stent only	164 (42.7)	289 (40.6)	
Stenting crossing LAD	19 (4.9)	24 (3.4)	
Stenting crossing LCX	132 (34.4)	260 (36.5)	
Bifurcation 2 stents	69 (18.0)	139 (19.5)	
Bifurcation technique			.51
Kissing	25 (36.2)	39 (28.1)	
T stenting	11 (15.9)	29 (20.9)	
Crush	28 (40.6)	64 (46.0)	
Others	5 (7.2)	7 (5.0)	
Final kissing	111 (30.4)	219 (31.6)	.73
IVUS guidance, n (%)	290 (77.1)	529 (75.0)	.46
Characteristics of CABG procedure	n = 251	n = 887	
Off-pump	134 (53.4)	344 (38.8)	<.001
On-pump	117 (46.6)	543 (61.2)	<.001
IMA use	248 (98.8)	861 (97.1)	.17
Anastomosis to LAD	247 (98.4)	875 (98.6)	.999
IMA to LAD	244 (97.2)	852 (96.1)	.45
Total number of grafts	2.67 ± 0.94	2.93 ± 1.02	<.001
Number of arterial grafts	2.09 ± 0.86	2.2 ± 0.94	.03
Numbers of venous grafts	0.59 ± 0.76	0.71 ± 0.85	.05

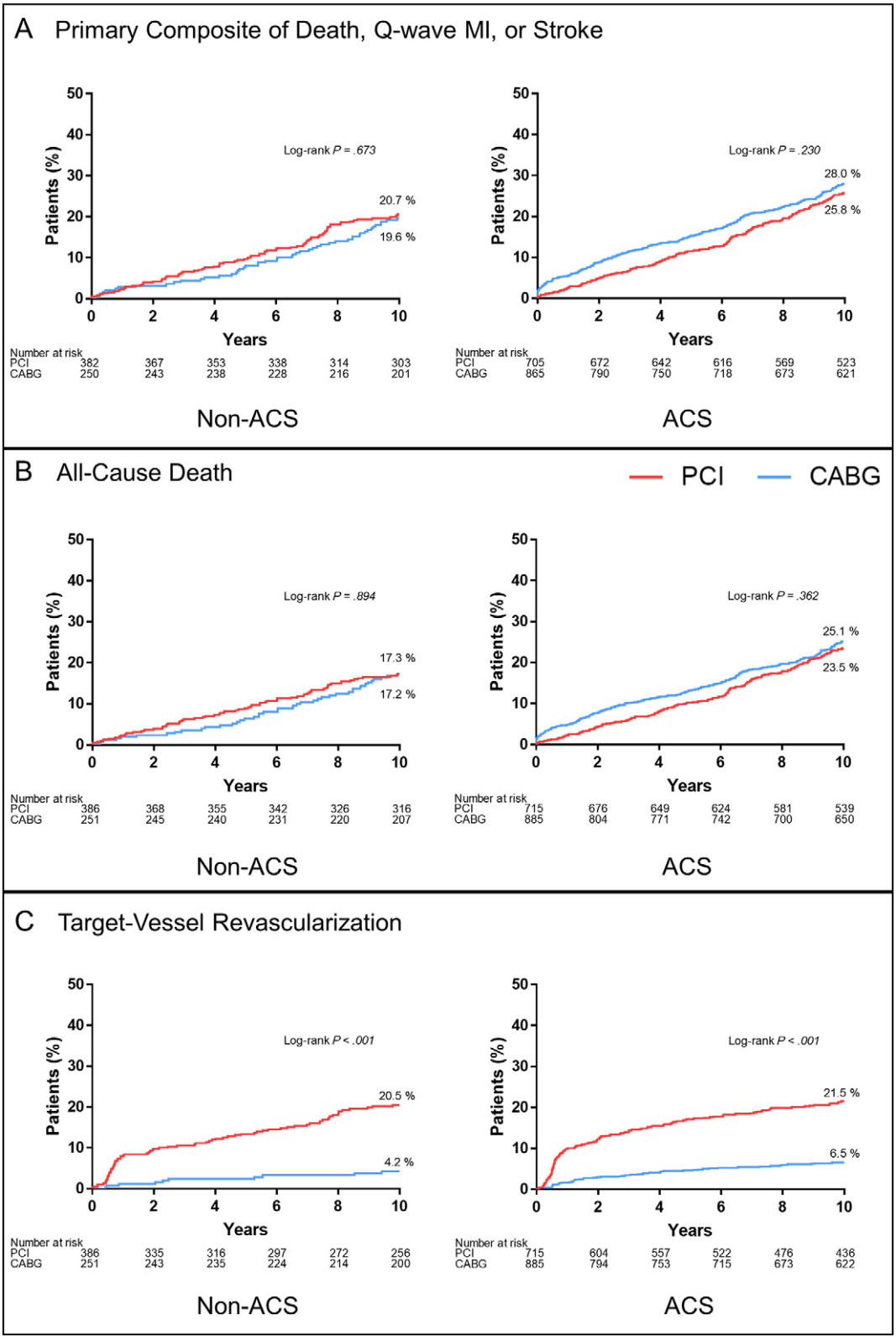
SES, sirolimus-eluting stents; *PES*, paclitaxel-eluting stents; *LM*, left main artery; *LAD*, left circumflex artery; *LCX*, left circumflex artery; *IVUS*, intravascular ultrasound; *IMA*, internal mammary artery.
*Data are mean ± SD or number (%).

patients, the adjusted risks for the primary composite outcome and all-cause death were not significantly different in patients treated with PCI versus CABG. These findings were also similar among ACS patients. Thus, there were no significant interactions between the clinical presentation and the relative long-term effect of PCI versus CABG on the primary composite outcome (*P* for interaction = .29) and death (*P* for interaction = .62). The adjusted risk of TVR was consistently higher after PCI than after CABG in the non-ACS and ACS groups (*P* for interaction = .39). When we assessed 3 clinical spectrum of stable CAD, unstable angina, or NSTEMI, uniform findings were noted (Supplementary Table III). Overall findings were also consistent in the wave 1 cohort comparing BMS and concurrent CABG and in the wave 2 cohort comparing DES and concurrent CABG (Table IV, Figure 2, Supplementary Figures 1 and 2).

Several sensitivity analyses were performed. Regardless of the diabetic status, there was no significant interaction between the acuity of clinical presentation and treatment effect on 10-year outcomes (Supplementary Table IV). When additional analyses were stratified by disease extent, similar findings were observed. There were no significant interactions between clinical presentation and revascularization strategy on outcomes in diverse spectrum of disease extent (Supplementary Table V).

Baseline SYNTAX scores were only available in 1,580 patients (70.5%), and baseline characteristics of this subgroup are shown in Supplementary Tables VI and VII. In the cohort with available SYNTAX score, the Kaplan-Meier event curves of clinical outcomes after PCI and CABG according to the clinical presentation are shown in Figure 3. After further adjustment of the SYNTAX score, the adjusted risks for primary composite outcome and death were similar between PCI and CABG in non-ACS patients (Table V). Among ACS patients, the risks for primary outcome and death tended to be higher in the PCI group than in the CABG group. However, the interaction between the acuity of presentation

Figure 1



Ten-year event rates according to acuity of presentation in the overall cohort of patients who underwent PCI or CABG.

Table III. Comparative outcomes for PCI versus CABG according to clinical presentation

Events at 10 y	PCI	CABG	Adjusted HR* (95% CI)	$P_{interaction}$†
Non-ACS (n = 637)	n = 386	n = 251		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	79 (20.7)	49 (19.6)	1.07 (0.71-1.61)	.29
All-cause death	66 (17.3)	43 (17.2)	0.98 (0.63-1.51)	.62
TVR	74 (20.5)	10 (4.2)	6.38 (3.14-12.96)	.39
ACS (n = 1603)	n = 716	n = 887		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	183 (25.8)	250 (28.0)	1.00 (0.81-1.24)	.29
All-cause death	167 (23.5)	221 (25.1)	1.02 (0.81-1.28)	.62
TVR	146 (21.5)	52 (6.5)	3.96 (2.80-5.60)	.39

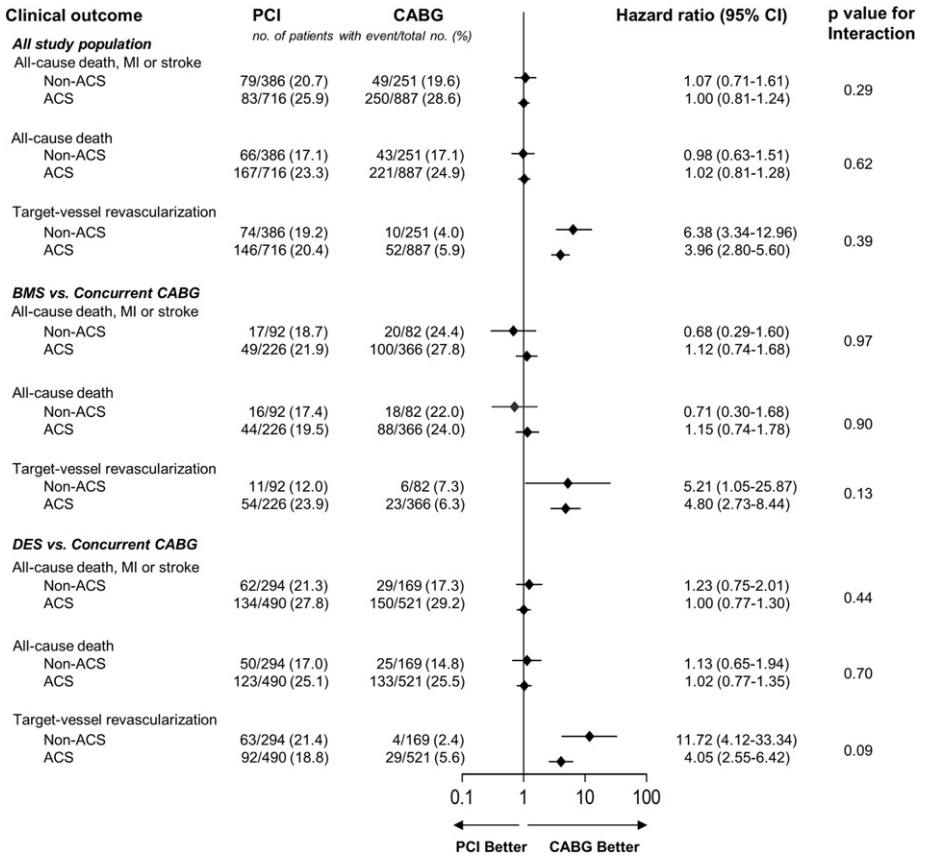
Cumulative incidences are numbers (%) as derived from the Kaplan-Meier estimates.
* HRs are for the PCI group as compared with the CABG group. HRs are adjusted for age, sex, body mass index, hypertension, hyperlipidemia, diabetes mellitus, previous MI, atrial fibrillation, previous PCI, peripheral arterial disease, chronic renal failure, congestive heart failure, extent of diseased vessel, location of LMCA disease, and combined right CAD.
† *P* interaction for clinical presentation (ACS vs. non-ACS) and revascularization strategy (PCI vs. CABG)

and effect of PCI versus CABG on outcomes was not significant (*P* for interaction = .62 for primary composite outcome and *P* for interaction = .49 for death, respectively).

Discussion

The present analyses evaluated the relative long-term treatment effect of PCI and CABG for significant LMCA disease stratified by the index clinical indication for myocardial revascularization. In this subgroup analysis from the 10-year report of the MAIN-COMPARE study, the major findings are (1) that the presence of ACS was independently associated with a higher incidence of the primary composite outcome of death, Q-wave MI, or stroke at 10 years and (2) that the adjusted risks of primary composite outcome and all-cause mortality were

Figure 2



Multivariable adjusted Cox proportional hazards estimates of the 10-year risk for clinical outcomes, according to the acuity of presentation.

Table IV. Comparative outcomes for stenting versus concurrent CABG, according to stent type and clinical presentation

Events at 10 y	Stents	CABG	Adjusted HR* (95% CI)	$P_{interaction}$ †
Wave 1: BMS vs concurrent CABG				
Non-ACS (n = 174)	n = 92	n = 82		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	17 (18.7)	20 (24.4)	0.68 (0.29-1.60)	.97
All-cause death	16 (17.6)	18 (22.0)	0.71 (0.30-1.68)	.90
TVR	11 (20.5)	6 (4.2)	5.21 (1.05-25.87)	.13
ACS (n = 592)	n = 226	n = 366		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	49 (21.9)	100 (27.4)	1.12 (0.74-1.68)	.97
All-cause death	44 (19.6)	88 (24.2)	1.15 (0.74-1.78)	.90
Target-vessel revascularization	54 (24.7)	23 (7.0)	4.80 (2.73-8.44)	.13
Wave 2: DES vs concurrent CABG				
Non-ACS (n = 463)	n = 294	n = 169		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	62 (21.3)	29 (17.3)	1.23 (0.75-2.01)	.44
All-cause death	50 (17.2)	25 (14.9)	1.13 (0.65-1.94)	.70
TVR	63 (22.9)	4 (2.6)	11.72 (4.12-33.34)	.09
ACS (n = 1011)	n = 490	n = 521		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	134 (27.7)	150 (28.4)	1.001 (0.77-1.30)	.44
All-cause death	123 (25.4)	133 (25.8)	1.02 (0.77-1.35)	.70
TVR	92 (20.0)	29 (6.2)	4.05 (2.55-6.42)	.09

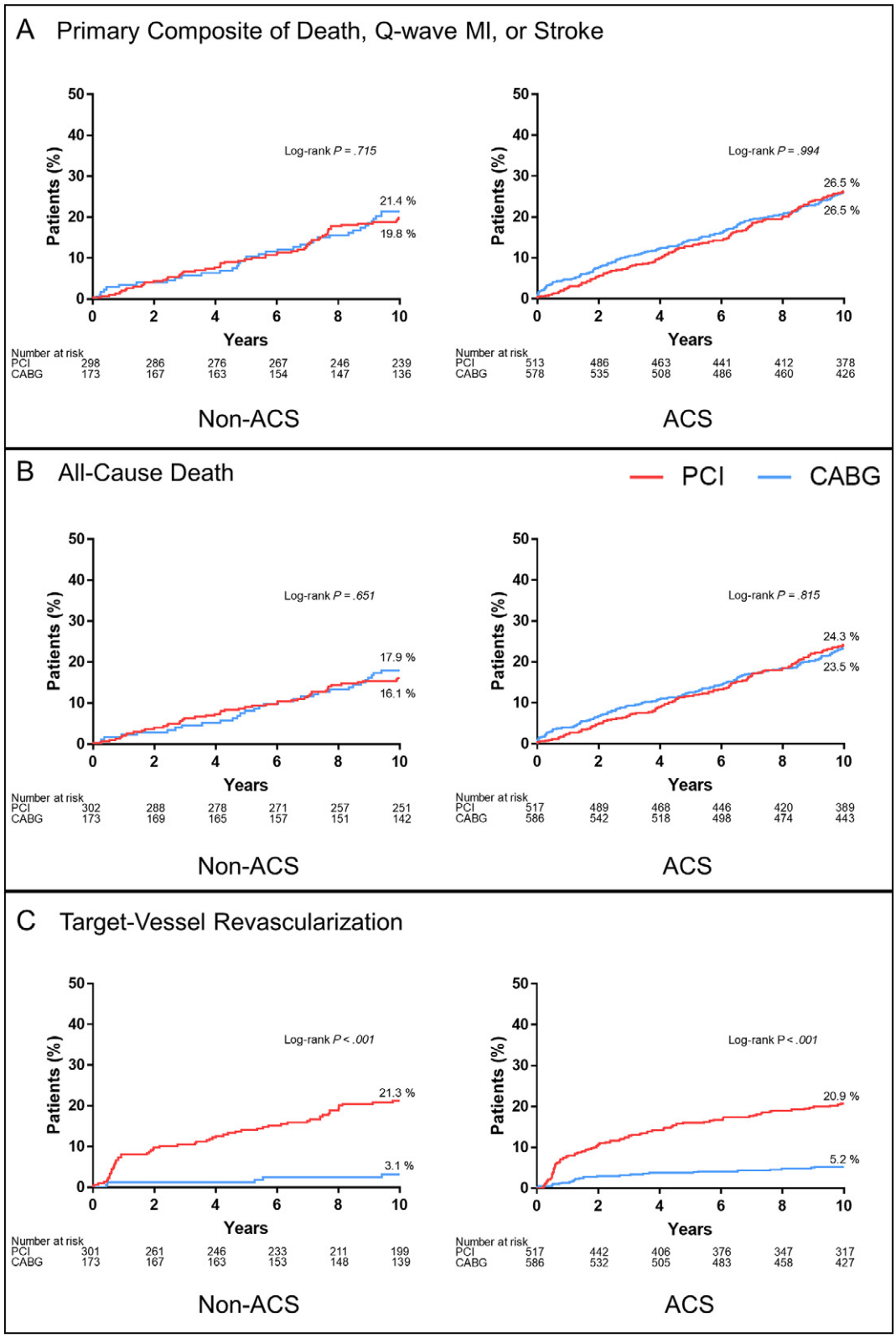
Cumulative incidences are numbers (%) as derived from the Kaplan-Meier estimates.
* HRs are for the PCI group as compared with the CABG group. HRs are adjusted for age, sex, body mass index, hypertension, hyperlipidemia, diabetes mellitus, previous MI, atrial fibrillation, previous PCI, peripheral arterial disease, chronic renal failure, congestive heart failure, extent of diseased vessel, location of LMCA disease, and combined right CAD.
† *P* interaction for clinical presentation (ACS vs non-ACS) and revascularization strategy (PCI vs CABG).

similar between PCI and CABG in patients with ACS as well as in those with non-ACS. However, the risk of TVR was consistently higher after PCI, and (3) most importantly, there was no significant interaction between the acuity of clinical presentation and treatment strategy on the relative 10-year risks of serious composite outcomes, all-cause death, and TVR.

As compared with patients with stable ischemic heart disease, patients with ACS are known to have higher risks of recurrent cardiovascular events and mortality[15]. Patients with ACS include heterogenous population with varying cardiovascular risks. According to current guidelines, early invasive strategy has become the standard of care for high-risk ACS patients.[16,17] Especially for selection of revascularization strategy, numerous factors should be considered in the decision-making process, including clinical presentation, concomitant risk factors, and high-risk features specific for a revascularization strategy such as age, frailty, cognitive function, life expectancy, and anatomical severity of CAD.[11] Because the large area of myocardium was usually affected by obstructive LMCA disease, as shown in our study, a substantial proportion of patients with significant LMCA disease presented with ACS at the index hospitalization. In the practical viewpoint, PCI for LMCA disease may offer the advantages of faster and safer revascularization, and CABG allows a complete revascularization (CR) and subsequently results in less need for repeated revascularization. In addition, long-term outcomes are required to examine whether PCI versus CABG outcomes vary meaningfully over time as a function of clinical syndrome presentation. Given the paucity of prior long-term data to guide decision making in patients with ACS and LMCA disease, the present study might provide clinically relevant information on understanding the comparative 10-year outcomes after PCI and CABG and feasible decision making of LMCA revascularization strategy according to the clinical presentation.

Until recently, there are limited data comparing the relative long-term effectiveness of CABG versus PCI with stenting in patients presenting with ACS. Also, there is no randomized comparison of PCI versus CABG in the specific setting of non–ST elevation ACS, and the currently available evidence indirectly suggests that the criteria applied to patients with stable IHD to guide the choice of revascularization modality. In our previous report of patient-level pooled analysis of the BEST, PRECOMBAT, and SYNTAX trials, which evaluated 1,246 patients with non–ST elevation ACS and multivessel or LMCA disease, the 5-year composite outcome of death, MI, or stroke was significantly lower in the CABG than with PCI.[18] This difference was mainly driven by a significant reduction of MI with CABG. In the analysis regarding non-ST in the MILESTONE registry, which includes ACS patients with multivessel disease, CABG was associated with a nonsignificantly superior rate of 3-year survival in a subgroup of 100 patients with LMCA disease.[19] By contrast, post hoc analysis of the ACUITY trial, which included propensity-matched 1,056 patients with moderate or high-risk ACS and multivessel disease

Figure 3



Ten-year event rates according to acuity of presentation in the subgroup with the SYNTAX score.

Table V. Outcomes for PCI versus CABG according to clinical presentation in the subgroup with the SYNTAX score

Events at 10 y	PCI	CABG	Adjusted HR* (95% CI)	$P_{interaction}$ †
Non-ACS (n = 474)	n = 301	n = 173		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	59 (19.8)	37 (21.4)	1.03 (0.63-1.69)	.62
All-cause death	48 (16.1)	31 (17.9)	0.94 (0.56-1.60)	.49
TVR	60 (21.3)	5 (3.1)	10.81 (4.08-28.59)	.35
ACS (n = 1106)	n = 518	n = 588		
Primary composite outcome: all-cause death, Q-wave MI, or stroke	136 (26.5)	154 (26.5)	1.38 (1.03-1.84)	.62
All-cause death	125 (24.3)	137 (23.5)	1.34 (0.98-1.82)	.49
TVR	101 (20.9)	28 (5.2)	5.08 (3.04-8.48)	.35

Cumulative incidences are number (%) derived from the Kaplan-Meier estimates.
* HRs are for the PCI group as compared with CABG group. HRs are adjusted for age, sex, body mass index, hypertension, hyperlipidemia, diabetes mellitus, previous MI, atrial fibrillation, previous PCI, peripheral arterial disease, chronic renal failure, congestive heart failure, extent of diseased vessel, location of LMCA disease, combined right CAD and SYNTAX score.
† *P* interaction for clinical presentation (ACS vs non-ACS) and revascularization strategy (PCI vs. CABG).

(including 105 LMCA disease), there were no differences in 1-year mortality between CABG and PCI.[20] In the CUSTOMIZE registry, which enrolled 583 patients with LMCA disease and ACS, PCI was associated with similar 1-year rate of death or MI compared with CABG.[21] In the study from DELTA registry, which evaluated 379 patients with LMCA disease and ACS, PCI showed similar clinical outcome (death, MI, and cerebrovascular accident) compared to CABG at a median follow-up of 1,120 days despite the use of first-generation DES.[22] However, these studies were hampered by few patients, a relatively low proportion of LMCA disease, low use of DES, or limited follow-up duration. Thus, prior studies could not guide proper decision making in patients with LMCA disease who presented with ACS. In the present analyses, the 10-year risks of serious composite outcome and mortality in patients with ACS were similar between PCI and CABG. Based on these points, the current study could have clinical implication for clinical decision making in patients with significant LMCA disease who presented with ACS.

The key finding of the present study was that there was no significant interaction between the clinical presentation and the relative effect of revascularization strategy on long-term outcomes. Comparative treatment effect of PCI and CABG in ACS patients was consistent with findings in non-ACS patients, thus supporting the concept that the principles of stable IHD should apply to stabilized patients with non–ST elevation ACS as well. The acuity of clinical presentation did not affect 10-year outcomes of PCI versus CABG in patients with LMCA disease, implying that attending physicians may not have to get rushed into a certain type of revascularization in patients with ACS and LMCA disease. These findings may influence clinical practice pattern and decision making related to optimal revascularization by decreasing the clinical impetus for immediate or urgent revascularization for ACS patients. Except in very unstable subsets such as STEMI, careful patient selection for optimal revascularization strategy and the ability to achieve CR should be much considered rather than the urgency of revascularization driven by the acuity of presentation.[11] In addition, it is noteworthy that CABG patients received a mean of 2 arterial grafts in our study. Arterial grafts are widely regarded as superior to venous grafts. This may have contributed to lower target vessel failure in the CABG group and may translate into improved benefit on major clinical events or survival in future follow-up.

This study had several limitations. First, this study was a nonrandomized, observational study. In such post hoc analysis, although a wide range of baseline covariates was adjusted in the multivariable analyses, it is impossible to fully account for unmeasured important cofounders. Therefore, overall findings should be considered as hypothesis generating only. Second, the timing of CABG and PCI after initial clinical presentation and status of urgent revascularization were not exactly evaluated in the present study. Thus, our findings might not be fully applicable in patients with ACS requiring emergent revascularization or STEMI. Furthermore, it was not possible to determine whether significant LM disease was the culprit lesion causing ACS presentation. Third, the accurate information on CR was not available in our study. The difference in CR at the index procedure could affect the clinical outcomes. Fourth, our study evaluated the first generation of DESs for LMCA disease. Thus, the present findings should be compared to those from other recent studies using contemporary DESs. Finally, our findings should be confirmed by further insights from comparative long-term follow-up of the EXCEL and NOBLE trial using contemporary DES.

Conclusions

In this longest follow-up study of patients with LMCA disease, the 10-year rates of serious composite outcome (death, Q-wave MI, or stroke) and all-cause mortality were similar between PCI and CABG in non-ACS as well as in

ACS patients. There was no significant interaction between the acuity of clinical presentation and the relative treatment effect of PCI or CABG. These findings suggest that the acuity of clinical presentation might not penalize the specific type of LMCA revascularization strategy in the heart-team discussion for optimal decision making.

Supplementary data to this article can be found online at https://doi.org/10.1016/j.ahj.2019.08.014.

Author contributions and disclosures

Author contributions: S. Park, J.-M. Ahn, and D.-W. Park had full access to all of the data in the study and take responsibility of the data and the accuracy of the data analysis. Conception and design: D.-W. Park and S.-J. Park; analysis and interpretation of data: S. Park, J.-M. Ahn, and D.-W. Park; drafting of the manuscript: S. Park, J.-M. Ahn, and D.-W. Park; critical revision of the manuscript for important intellectual content: K. Lee, O. Kwon, H. Park, Y.-H. Yoon, D.-Y. Kang, P.-H. Lee, S.-W. Lee, and S.-W. Park; statistical expertise:D.-W. Park; obtaining of public funding: D.-W. Park, and S.-J. Park; administrative, technical, or logistic support: D.-W. Park, and S.-J. Park.

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Disclosures

The authors have no conflicts of interest to declare.

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