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ORIGINAL RESEARCH

Impact of Complete or Incomplete Revascularization for Left Main Coronary Disease

The Extended PRECOMBAT Study

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ABSTRACT

BACKGROUND Whether complete revascularization (CR) or incomplete revascularization (IR) may affect long-term outcomes after PCI) and coronary artery bypass grafting (CABG) for left main coronary artery (LMCA) disease is unclear.

OBJECTIVES The authors sought to assess the impact of CR or IR on 10-year outcomes after PCI or CABG for LMCA disease.

METHODS In the PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) 10-year extended study, the authors evaluated the effect of PCI and CABG on long-term outcomes according to completeness of revascularization. The primary outcome was the incidence of major adverse cardiac or cerebrovascular events (MACCE) (composite of mortality from any cause, myocardial infarction, stroke, or ischemia-driven target vessel revascularization).

RESULTS Among 600 randomized patients (PCI, n = 300 and CABG, n = 300), 416 patients (69.3%) had CR and 184 (30.7%) had IR; 68.3% of PCI patients and 70.3% of CABG patients underwent CR, respectively. The 10-year MACCE rates were not significantly different between PCI and CABG among patients with CR (27.8% vs 25.1%, respectively; adjusted HR: 1.19; 95% CI: 0.81-1.73) and among those with IR (31.6% vs 21.3%, respectively; adjusted HR: 1.64; 95% CI: 0.92-2.92) (*P* for interaction = 0.35). There was also no significant interaction between the status of CR and the relative effect of PCI and CABG on all-cause mortality, serious composite of death, myocardial infarction, or stroke, and repeat revascularization.

CONCLUSIONS In this 10-year follow-up of PRECOMBAT, the authors found no significant difference between PCI and CABG in the rates of MACCE and all-cause mortality according to CR or IR status. (Ten-Year Outcomes of PRE-COMBAT Trial [PRECOMBAT], NCT03871127; PREmier of Randomized COMparison of Bypass Surgery Versus AngioplasTy Using Sirolimus-Eluting Stent in Patients With Left Main Coronary Artery Disease [PRECOMBAT], NCT00422968) (JACC: Asia 2023;3:65–74) © 2023 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass grafting surgery

CR = complete revascularization

IR = incomplete revascularization

LMCA = left main coronary artery

MACCE = major adverse cardiac or cerebrovascular event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

RCT = randomized controlled trial

TVR = target vessel revascularization

Although coronary artery bypass grafting (CABG) is still a major part of the treatment of unprotected left main coronary artery (LMCA) disease, percutaneous coronary intervention (PCI) has been a good alternative for the revascularization strategy based on favorable results from several randomized clinical trials (RCTs) and observational studies.[1-3] Current guidelines recommend either CABG or PCI with drug-eluting stents for patients with LMCA disease and low-to-intermediate anatomical complexity.[4-6] These guidelines mainly rely on the principal findings from 4 landmark RCTs of the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) trial left main subgroup,[7] the PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trial,[8] the NOBLE (Nordic-Baltic-British Left Main Revascularization Study),[9] and the EXCEL (Evaluation of XIENCE versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization) trial.[10] All of these RCTs recently completed long-term (at least 5 and up to 10 years) clinical follow-up.[11-14]

LMCA disease involves frequent concomitant multivessel disease, but debate still exists over whether complete revascularization (CR) of all obstructive lesions substantially improves clinical outcomes compared with some degree of incomplete revascularization (IR). Furthermore, achieving CR with PCI and CABG may not be always feasible owing to patient comorbidities, anatomical factors, and technical or procedural considerations, in which a CR attempt could result in more aggressive revascularization techniques with multiple stents or more grafts than IR.[15] Although several studies have suggested a potential benefit of CR in patients with complex coronary disease who were treated either by PCI or CABG,[16-22] scarce data were noted on the long-term (>5 or 10 years) prognostic effect of CR or IR in patients who underwent LMCA revascularization. We therefore evaluated the impact of CR or IR status on 10-year outcomes after PCI or CABG for LMCA disease and determined whether an interaction exists between the CR status and the relative effect of revascularization strategies using data from the extended 10-year follow-up of the PRECOMBAT trial.[14]

METHODS

STUDY POPULATION AND PROCEDURES. The PRECOMBAT trial was a prospective, open-label, randomized trial comparing PCI with sirolimus-eluting stents with CABG in patients with unprotected LMCA disease from 13 hospitals in Korea from April 2004 to August 2009 and had extended 10-year follow-up. The protocol, trial design, patient eligibility criteria, and methods of the PRECOMBAT trial have been previously described,[8,23] and the primary and key secondary results of the 10-year extended follow-up have been reported.[14,24] The trial was approved by the investigational review board or ethics committee at each participating center. Written informed consent was obtained from all patients.

In this trial, interventional cardiologists and cardiac surgeons at each participating site assessed the patients for clinical and anatomical eligibility for myocardial revascularization, which was considered to be equally suitable for both PCI and CABG. Details of the PCI and CABG procedures have been previously described.[8,14,23] First-generation sirolimus-eluting stents (Cypher stent, Cordis/Johnson & Johnson) were used in the PRECOMBAT trial, in which interventional cardiologists were encouraged to treat all stenotic lesions that were likely to contribute to ischemia or with >50% diameter stenosis at the time of the enrollment period. During CABG, complete anatomical revascularization of all diseased vessels of anatomical significance with an angiographic diameter stenosis of >50% was attempted; the use of arterial grafts was strongly recommended.

In the current study, CR status of patients who underwent PCI was assessed by comparing the diagnostic and postprocedural angiograms, and CR status of patient who underwent CABG was assessed by comparing the diagnostic angiographic analysis with the surgical procedure reports on the number and locations of their bypass grafts. In the trial protocol, angiographic CR was predefined as the successful treatment of all coronary artery lesions or segments ≥50% of the major epicardial coronary arteries with a diameter ≥2.5 mm, regardless of their

The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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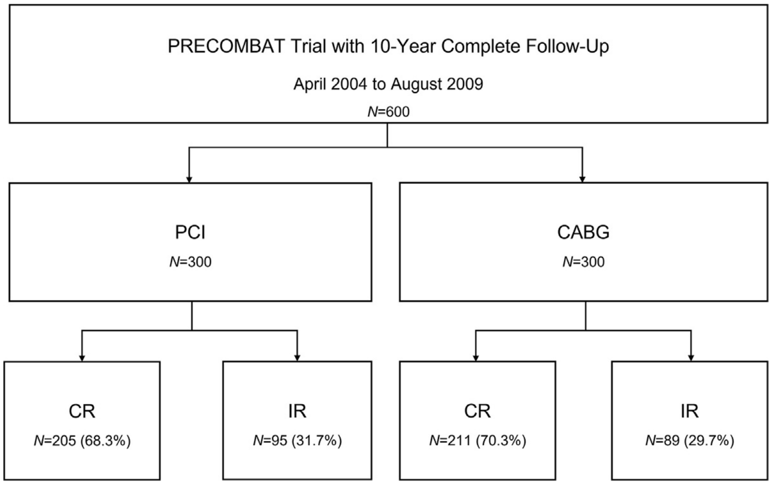
FIGURE 1 Flow Diagram of the Study



In the PRECOMBAT (Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease) trial, patients with unprotected left main coronary artery disease were randomly assigned in a 1:1 ratio to either percutaneous coronary intervention (PCI) with sirolimus-stents (n = 300) or coronary artery bypass grafting (CABG). CR = complete revascularization; IR = incomplete revascularization.

functional significance, which was done by quantitative coronary angiography analysis in the central core laboratory.[16,20] Patients not meeting these criteria were considered IR patients. Concomitant optimal medical therapy has been emphasized following related guidelines during the follow-up.

STUDY ENDPOINTS AND DEFINITIONS. The primary endpoint was the 10-year rate of major adverse cardiac and cerebrovascular events (MACCE), which was defined as a composite of death from any cause, nonfatal myocardial infarct (MI), nonfatal stroke, or ischemia-driven target vessel revascularization (TVR). Secondary outcomes included all-cause mortality; composite of death, MI, or stroke; ischemia-driven TVR or any repeat revascularization.

The definitions of all outcome measures were predefined and previously described in detail,[8,14,23] and all outcome events were centrally adjudicated by an independent clinical events committee with source documents at each hospital. We used all-cause mortality as the survival outcome because it is the most unbiased method for reporting deaths in clinical trials or observational studies. Protocol definition of MI was the appearance of both new Q waves and creatine kinase-myocardial band (CK-MB) to >5× the upper reference limit within 48 hours after PCI/CABG or a rise in CK-MB >1× the upper reference limit plus new ischemic symptoms or signs >48 hours after PCI/CABG. Stroke was defined as a focal neurological deficit resulting from vascular lesions of the brain lasting >24 h, confirmed by a neurologist and imaging. TVR was repeat revascularization with either PCI or CABG in the treated vessel, which was considered to be driven by ischemia if the stenosis was at least 50% with the presence of ischemic signs or symptoms or if the stenosis was at least 70% irrespective of ischemic signs or symptoms.

STATISTICAL ANALYSIS. A descriptive analysis was performed, and data were presented as mean ± SD or n (%). Continuous variables were compared with a 2-sample *t*-test or Kruskal-Wallis test, and categorical variables were compared with the chi-square test or Fisher's exact test. Cumulative event rates were based on Kaplan-Meier estimates and were compared using the log-rank test. A Cox proportional hazards model was used to compare the rates of primary and secondary endpoints between groups, and HRs were presented with 95% CIs. All available follow-up data for these models were used for long-term outcome analyses without censoring clinical events beyond 10 years; thus, patients lost to follow-up were included in the analyses for all outcomes by censoring at the date of the last follow-up. The assumptions of the Cox model were statistically assessed based on Schoenfeld residuals and graphically by log-log plots, and were found to be approximately satisfied for all variables.

TABLE 1 Baseline Characteristics Stratified by Revascularization Assignment and the Status of Revascularization

	PCI (n = 300)		CABG (n = 300)		
	CR (n = 205)	IR (n = 95)	CR (n = 211)	IR (n = 89)	Overall *P* Value
Age, y	60.6 ± 10.1	64.3 ± 9.3	62.6 ± 9.6	63.1 ± 9.3	0.01
Male	156 (76.1)	72 (75.8)	164 (77.7)	67 (75.3)	0.96
Body mass index, kg/m^2	24.7 ± 2.8	24.5 ± 2.5	24.1 ± 2.8	25.4 ± 3.4	0.007
Diabetes mellitus					
Any diabetes mellitus	67 (32.7)	35 (36.8)	61 (28.9)	29 (32.6)	0.57
Requiring insulin	8 (3.9)	2 (2.1)	5 (2.4)	4 (3.3)	0.65
Hypertension	102 (49.8)	61 (64.2)	104 (49.3)	50 (56.2)	0.07
Hyperlipidemia	85 (41.5)	42 (44.2)	83 (39.3)	37 (41.6)	0.88
Current smoker	67 (32.7)	22 (23.2)	57 (27.0)	26 (29.2)	0.35
Previous PCI	21 (10.2)	17 (17.9)	26 (12.3)	12 (13.5)	0.32
Previous MI	7 (3.4)	6 (6.3)	13 (6.2)	7 (7.9)	0.34
Previous heart failure	0 (0)	0 (0)	1 (0.5)	1 (1.1)	0.30
Chronic renal failure	1 (0.5)	3 (3.2)	1 (0.5)	0 (0)	0.09
Peripheral arterial disease	9 (4.4)	6 (6.3)	6 (2.8)	1 (1.1)	0.25
Chronic lung disease	5 (2.4)	1 (1.1)	8 (3.8)	2 (2.2)	0.63
Family history of coronary artery disease	22 (10.7)	9 (9.5)	12 (5.7)	7 (7.9)	0.30
Clinical presentation					0.47
Stable angina or silent ischemia	112 (54.6)	48 (50.5)	95 (45.0)	42 (47.2)	
Unstable angina	85 (41.5)	43 (45.3)	101 (47.9)	43 (48.3)	
Recent MI	8 (3.9)	4 (4.2)	15 (7.1)	4 (4.5)	
Ejection fraction, %	58.7 ± 15.8	59.8 ± 11.9	60.2 ± 9.9	60.0 ± 9.6	0.69
Electrocardiographic findings					0.98
Sinus rhythm	197/205 (96.1)	89/91 (97.8)	203/208 (97.6)	86/89 (96.6)	
Atrial fibrillation	4/205 (2.0)	1/91 (1.1)	3/208 (1.4)	2/89 (2.2)	
Other	4/205 (2.0)	1/91 (1.1)	2/208 (1.0)	1/89 (1.1)	
EuroSCORE	2.5 ± 1.7	2.9 ± 1.9	2.8 ± 1.9	2.9 ± 1.9	0.18
Left main disease location					0.38
Ostium or shaft	65/204 (31.9)	34/95 (35.8)	82/206 (39.8)	29/88 (33)	
Distal bifurcation	139/204 (68.1)	61/95 (64.2)	124/206 (60.2)	59/88 (67)	
Extent of diseased vessel					<0.001
LMCA only	27 (13.2)	0 (0)	34 (16.1)	0 (0)	
LMCA plus 1-vessel disease	45 (22.0)	5 (5.3)	51 (24.2)	2 (2.2)	
LMCA plus 2-vessel disease	76 (37.1)	25 (26.3)	68 (32.2)	22 (24.7)	
LMCA plus 3-vessel disease	57 (27.8)	65 (68.4)	58 (27.5)	65 (73.0)	
SYNTAX score by core laboratory assessment					
Mean	23.2 ± 9.6	26.3 ± 9.3	23.8 ± 11.4	29.0 ± 8.9	<0.001
Category					<0.001
<23, low risk	97/197 (49.2)	34/93 (36.6)	92/194 (47.4)	17/80 (21.3)	
23-32, intermediate risk	68/197 (34.5)	34/93 (36.6)	60/194 (30.9)	37/80 (46.3)	
>32, high risk	32/197 (16.2)	25/93 (26.9)	42/194 (21.6)	26/80 (32.5)	

Values are mean ± SD, n (%), or n/N (%). For categorical variables, chi-square test or Fisher's exact test was used. For continuous variables, 2-sample *t*-test or Kruskal-Wallis test was used.

CABG = coronary artery bypass grafting; CR = complete revascularization; IR = incomplete revascularization; LMCA = left main coronary artery; MI = myocardial infarction; PCI = percutaneous coronary intervention; SYNTAX = Synergy Between Percutaneous Coronary Intervention With Taxus and Cardiac Surgery.

Multivariate Cox regression models were finally used to assess the risk-adjusted relative effect according to the CR status and the revascularization strategies, and to determine an independent statistical interaction between the revascularization methods and the CR status. Adjusted HRs were estimated from the Cox regression models with revascularization modality (PCI or CABG), the status of CR or IR, and the interaction between revascularization modality and CR status, age, sex, diabetes, clinical presentation, left main disease location, the extent of the diseased vessel, and SYNTAX score.

All reported *P* values were 2-sided, and $P < 0.05$ was considered significant for all tests. No adjustment for multiple testing was undertaken, and thus, all findings of this study should be interpreted as

TABLE 2 Procedural or Operative Characteristics Stratified by Revascularization Assignment and the Status of Revascularization

	PCI Patients (n = 300)			CABG Patients (n = 300)		
	CR (n = 205)	IR (n = 95)	*P* Value	CR (n = 211)	IR (n = 89)	*P* Value
PCI procedures						
Median total stent number in LMCA	3.0 (1.0-3.0)	2.0 (2.0-3.0)	0.70			
Total stent length in LMCA	39.2 ± 22.2	35.7 ± 21.0	0.20			
Median total stent number per patient	1.0 (1.0-2.0)	2.0 (1.0-2.0)	0.72			
Total stent length per patient, mm	74.0 ± 42.2	60.2 ± 38.1	0.01			
Intravascular ultrasound-guided PCI	77 (77.0)	155 (77.5)	0.99			
Distal LMCA bifurcation treatment			0.77			
Single-stent technique	74 (72.5)	139 (70.2)				
Two-stent technique	28 (27.5)	59 (29.8)				
CABG procedures						
Median number of grafts per patient				3.0 (2.0-3.0)	2.0 (2.0-3.0)	0.08
Median number of arterial grafts				2.0 (1.0-3.0)	2.0 (2.0-3.0)	0.76
Median number of vein grafts				0.0 (0.0-1.0)	0.0 (0.0-1.0)	0.12
Use of left internal mammary artery				70 (93.3)	163 (94.2)	0.99
Off-pump surgery				52 (57.8)	103 (49.0)	0.21

Values are median (IQR), mean ± SD, or n (%).
Abbreviations as in Table 1.

exploratory because of the potential for type I error due to multiple comparisons. All statistical analyses were performed using R version 3.6.3. (R Foundation for Statistical Computing).

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS. From April 2004 to August 2009, a total of 600 patients with unprotected LMCA disease were randomly assigned to PCI with sirolimus-eluting stents (n = 300) or to CABG (n = 300) in the PRECOMBAT trial. Of the 600 randomized patients, 416 (69.3%) and 184 (30.7%) patients had CR and IR, respectively; 205 (68.3%) of PCI patients and 211 (70.3%) of CABG patients achieved CR, respectively (**Figure 1**).

The baseline characteristics of the patients according to revascularization assignment and CR status are summarized in **Table 1**. Patients with CR were younger and were likely to have less extent of the concomitant diseased vessel and have lower mean SYNTAX score compared with those with IR in each stratum of PCI or CABG. Baseline characteristics of patients after PCI and CABG in each stratum of CR or IR are shown in Supplemental Table 1; most of the baseline variables were not significantly different between PCI and CABG. The procedural or operative data according to CR status are provided in **Table 2**. As expected, mean stent number and length per patient were significantly higher in patients with CR than in those with IR. However, the number and length of stents implanted in the LMCA and the bifurcation treatment were not significantly different between the CR and IR groups. The number of grafts and the use of off-pump CABG were not statistically different between the CR and IR groups.

10-YEAR OUTCOMES ACCORDING TO CR OR IR STATUS. The median follow-up period for the patients was 11.3 years (IQR: 10.2-13.0 years). The 10-year follow-up for all clinical endpoint events was achieved in 288 (96.0%) and 288 (96.0%) patients randomized to PCI and CABG, respectively.

The 10-year clinical outcomes according to treatment assignment and CR status are summarized in **Table 3** and Supplemental Table 2. The overall incidence of primary composite of MACCE did not significantly differ according to revascularization strategy and CR status (log-rank *P* = 0.37) (**Figure 2**). In each stratum of PCI or CABG, the CR or IR status was not associated with differential adjusted risks of primary MACCE events. The 10-year MACCE rates were not significantly different after PCI and CABG in patients achieving CR (28.3% vs 25.7%, respectively; adjusted HR: 1.19; 95% CI: 0.81-1.73). However, there was a trend favoring CABG over PCI in patients not achieving CR (33.2% vs 22.2%, respectively; adjusted HR: 1.64; 95% CI: 0.92-2.92). There was no significant interaction between the CR status and revascularization strategy with respect to primary outcome (*P* for interaction = 0.35). The 10-year incidences of the composite of death, MI, or stroke or all-cause mortality were not different between the PCI and CABG groups, irrespective of the CR status (**Figures 3A**

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TABLE 3 Observed 10-Year Incidence and Adjusted HRs for Clinical Outcomes

	Cumulative Incidence Rate at 10 y				Each Revascularization Stratum: HR (95% CI) for CR vs IR (Referent) Stratified by		Each CR or IR Stratum: HR (95% CI) for PCI vs CABG (Referent) Stratified by		
	PCI With CR (n = 205)	PCI With IR (n = 95)	CABG With CR (n = 211)	CABG With IR (n = 89)	PCI Arm	CABG Arm	CR Group	IR Group	*P* Value for Interaction[a]
Primary outcome									
MACCE[b]	57 (28.3)	30 (33.2)	53 (25.7)	19 (22.2)	1.00 (0.63-1.59)	1.38 (0.80-2.38)	1.19 (0.81-1.73)	1.64 (0.92-2.92)	0.35
Secondary outcomes									
Death from any cause	27 (13.5)	15 (16.7)	29 (14.2)	11 (12.8)	1.01 (0.52-1.97)	1.23 (0.59-2.55)	1.07 (0.63-1.83)	1.30 (0.60-2.84)	0.69
Death, MI, or stroke	34 (16.9)	19 (21.1)	37 (18.1)	14 (16.3)	1.02 (0.57-1.85)	1.26 (0.66-2.41)	1.06 (0.66-1.71)	1.31 (0.66-2.62)	0.62
Ischemia-driven TVR	32 (16.5)	13 (15.1)	17 (8.6)	5 (6.4)	1.33 (0.67-2.65)	1.90 (0.69-5.26)	1.90 (1.05-3.44)	2.71 (0.97-7.62)	0.56
Any revascularization	43 (22.2)	16 (19.2)	20 (10.2)	9 (11.4)	1.61 (0.88-2.97)	1.34 (0.60-3.01)	2.25 (1.32-3.85)	1.87 (0.83-4.24)	0.71

Event rates (in percentage) shown are the incidences as estimated with the use of a Kaplan-Meier survival analysis. HRs were estimated from the Cox regression model with revascularization modality (PCI or CABG), status of complete revascularization (CR or IR), interaction between revascularization modality and status of complete revascularization, age, sex, diabetes, clinical presentation, left main disease location, extent of diseased vessel, and SYNTAX score. [a]Statistical interaction between the revascularization methods and the CR status. [b]The primary endpoint of major adverse cardiac or cerebrovascular events (MACCE) was a composite of death from any cause, myocardial infarction, stroke, or ischemia-driven target vessel revascularization (TVR).

Abbreviations as in Table 1.

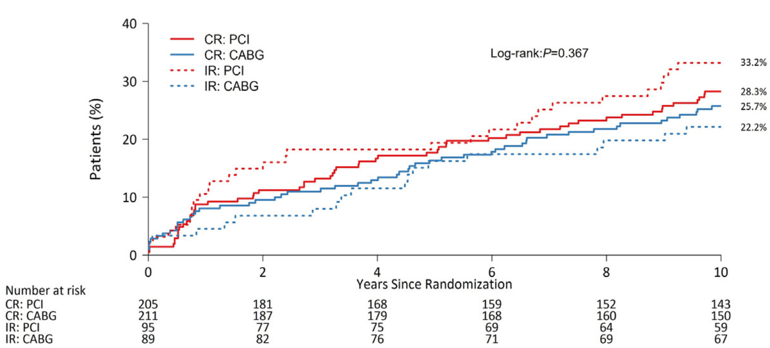
and 3B); thus, the adjusted risks for all-cause mortality after PCI and CABG were similar in the CR (HR: 1.07; 95% CI: 0.63-1.83) and IR (HR: 1.30; 95% CI: 0.60-2.84) groups (*P* for interaction = 0.69), and this trend was consistent for the composite of death, MI, or stroke in the CR (HR: 1.06; 95% CI: 0.66-1.71) and IR (HR: 1.31; 95% CI: 0.66-2.62) groups (*P* for interaction = 0.62).

Although the 10-year incidences of TVR and any repeat revascularization were significantly higher after PCI than after CABG, these events were not significant different between the CR vs the IR groups (**Figures 3C and 3D**). The adjusted risk for TVR was significantly higher after PCI than after CABG in the CR group (HR: 1.90; 95% CI: 1.05-3.44) and tended to be higher after PCI in the IR group (HR: 2.71; 95% CI: 0.97-7.62; *P* for interaction = 0.56) (**Table 3**). Similarly, the adjusted risk for any revascularization was significantly higher after PCI than after CABG in the CR group (HR: 2.25; 95% CI: 1.32-3.85) and tended to be higher after PCI in the IR group (HR: 1.87; 95% CI: 0.83-4.24; *P* for interaction = 0.71).

DISCUSSION

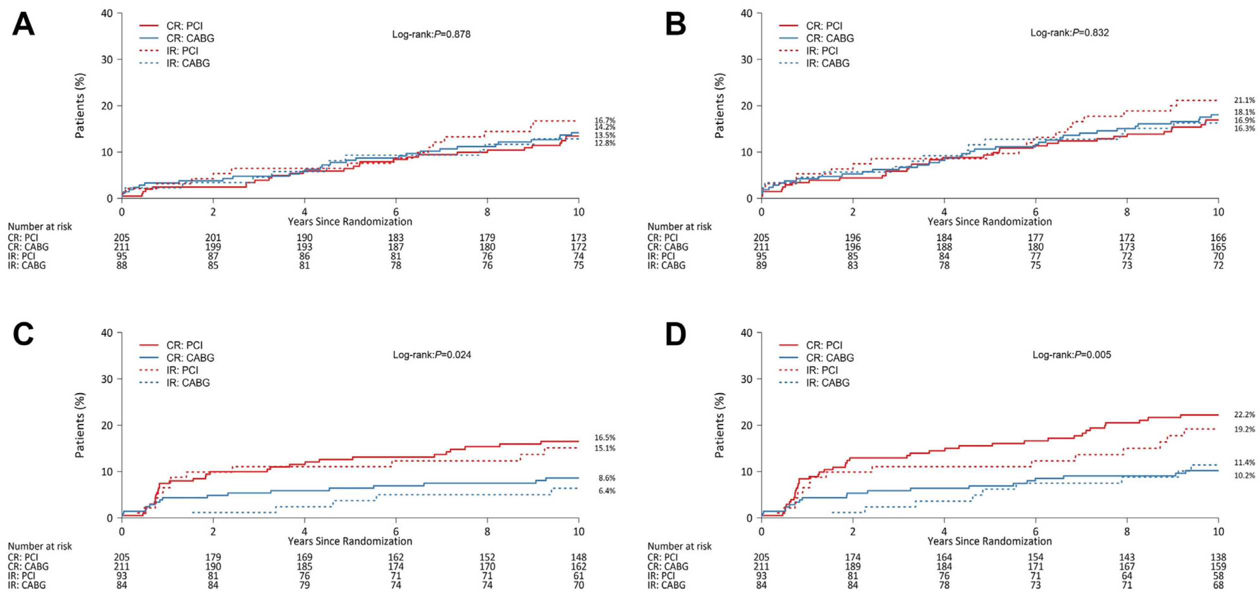
This is a prespecified subgroup analysis of the PRE-COMBAT 10-year extended study investigating the impact of CR vs IR on the relative treatment effect of PCI and CABG in patients with significant LMCA disease. The key findings are as follows: 1) approximately two-thirds of PCI and CABG patients underwent CR; 2) CR compared with IR was not associated with improved primary and secondary outcomes either in the PCI and CABG arms

FIGURE 2 10-Year Event Curves for the Primary Endpoint



The primary endpoint of major adverse cardiac or cerebrovascular events was a composite of death from any cause, myocardial infarction, stroke, or ischemia-driven target vessel revascularization. Event rates were based on Kaplan-Meier estimates and were compared with overall log-rank test. Abbreviations as in Figure 1.

FIGURE 3 **10-Year Event Curves for Key Secondary Outcomes**



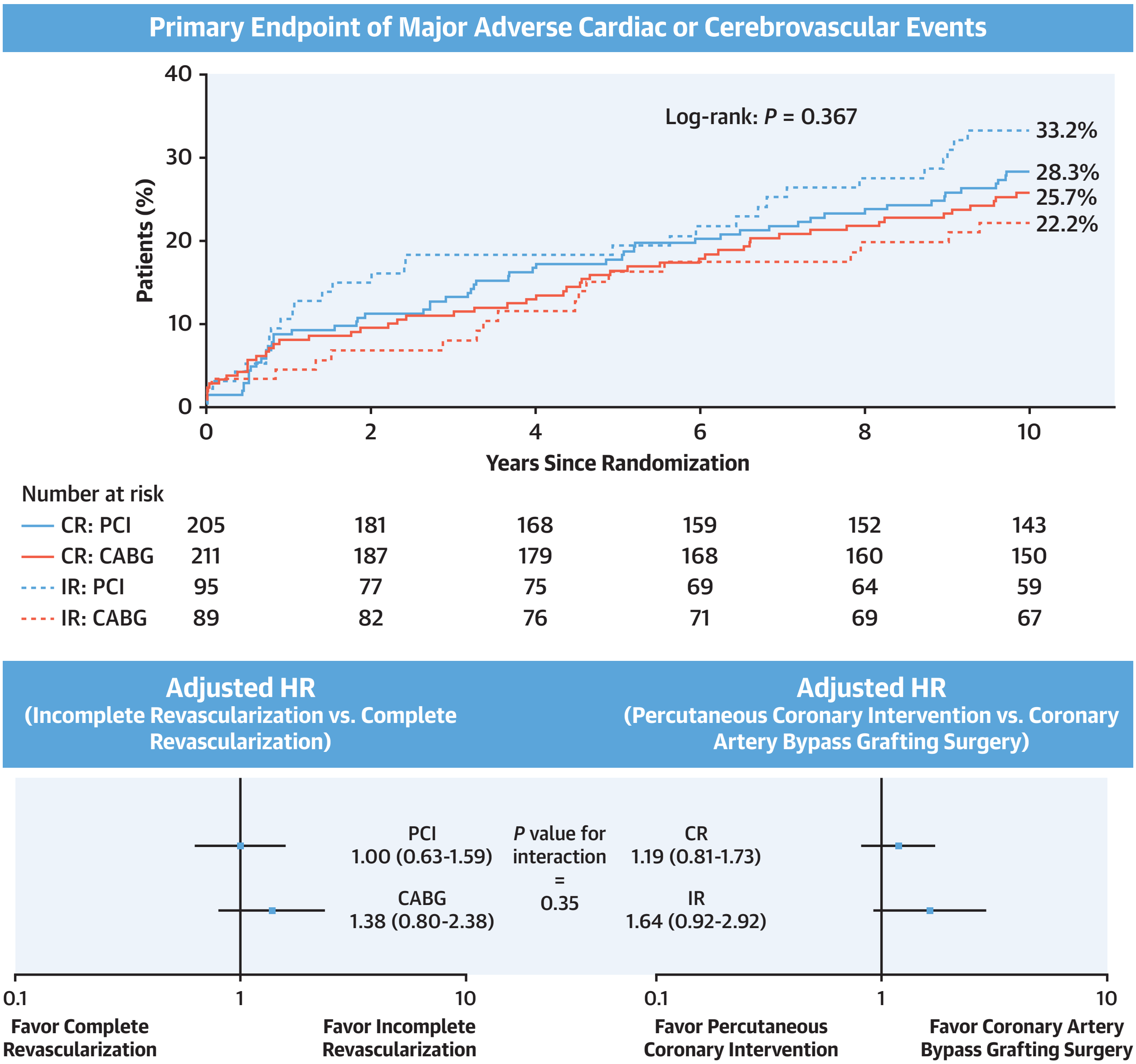
(A) All-cause mortality; **(B)** composite of death, myocardial infarction, or stroke; **(C)** ischemia-driven target-vessel revascularization; and **(D)** any revascularization. Event rates were based on Kaplan-Meier estimates and were compared with overall log-rank test. Abbreviations as in **Figure 1**.

(**Central Illustration**); 3) the 10-year MACCE rates were not significantly different between PCI and CABG, irrespective of CR or IR status; and 4) the 10-year incidences of all-cause mortality and composite of death, MI, or stroke were also not different after PCI and CABG regardless of the CR status.

A recent clinical guideline has emphasized that the expected revascularization completeness (Class IIa, Level of Evidence: B) is an important parameter for decision-making between CABG and PCI.[25] Several CR advantages may theoretically exist for treatment of multivessel or complex disease.[26] The nuclear substudy of the COURAGE (Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation) trial showed that a significant ischemic myocardium reduction resulted in a lower risk of mortality or MI.[27] Another study also showed that CR was associated with less deterioration in ejection fraction and lower mortality compared with IR in patients with heart failure with preserved ejection fraction.[28] Although CR in multivessel or complex coronary disease has such clinical benefits, achieving CR could be difficult owing to multiple factors.[26] Although anatomical CR can be more often achieved in 1 procedural stage of CABG, achieving CR with PCI is more challenging, and reasonable IR is frequent in the clinical practice.[15] Especially, PCI for chronic total occlusion lesions usually has a higher technical complexity and a higher risk of radiation exposure and contrast use. In addition, PCI for small coronary vessels (<2.5 to 3.0 mm) could be more prone to an increased risk of restenosis without an evident clinical benefit. Like this, in the real-world clinical setting, the interventional cardiologists may have a suitable reason for leaving angiographic stenotic lesions to be not treated (so-called *reasonable IR*; ie, nonviable myocardium, a relatively small vessel or of minor clinical importance, anatomically not-suitable for technical reasons, functionally not significant lesions, chronic total occlusion, or other clinical comorbidities).[20] However, whether CR can substantially improve clinical outcomes compared with some reasonable degree of IR combined with optimal guideline-directed medical therapy is still questioned.

Several clinical studies have been conducted to evaluate comparative outcomes of PCI or CABG according to the CR degree for multivessel or complex coronary disease,[15] and the observed results are still conflicting. The available evidence demonstrates that the presence and extent of both anatomical coronary artery disease and myocardial ischemia are strongly associated with adverse outcomes in patients who were conservatively treated. Nonetheless, a conclusion that CR after either PCI or CABG surgery improves prognosis (compared with some IR degree) cannot be reached from these data. In addition,

CENTRAL ILLUSTRATION **10-Year Outcomes Stratified by Revascularization Modality and Completeness of Revascularization**



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Complete revascularization (CR) was not related with improving the 10-year major adverse cardiac or cerebrovascular events rates in both percutaneous coronary intervention (PCI) and coronary artery bypass grafting (CABG). IR = incomplete revascularization.

although many (but not all) studies showed improved survival and greater freedom from adverse events after CR than after IR for multivessel disease, limited data exist on the CR impact for LMCA disease during long-term follow-up. Herein, the current study may provide the important clinical insights on the very long-term impact of CR or IR status in patients with LMCA revascularization.

In the current study, we found no significant interaction between the CR status and 10-year outcomes after PCI and CABG with respect to primary MACCE events and key secondary outcomes. However, although statistical significance was absent, PCI patients with IR had numerically higher event rates than those with CR, but this is not evident in CABG patients. Similarly, the recent 10-year report of the

SYNTAXES (SYNTAX Extended Survival study) showed that patients undergoing PCI with CR had no significant difference in all-cause mortality at 10 years compared with those undergoing CABG (with CR or IR), whereas patients undergoing PCI with IR had a significantly higher risk of all-cause mortality[22]; however, similar to our findings, a statistical significance was not achieved in the subgroup of LMCA disease (PCI with IR relative to CABG with CR; adjusted HR: 1.25; 95% CI: 0.85-1.83). Compared with prior studies showing that CR was associated with reduced mortality and major cardiovascular events, the lack of clear association of CR or IR with differential effect of PCI and CABG in our study might be explained by several reasons: a different definition of angiographic CR, a different angiographic and clinical risk profiles at baseline, a limited number of patients or low event rates attenuating the CR impact, a limitation in the angiographic evaluation of functional ischemia, and unmeasured confounders. In addition, adherence to guideline-directed medical therapy during long-term follow-up might attenuate the impact of IR status on outcomes; thus, IR was not worse than CR in LMCA revascularization. However, although a statistical significance was not evident owing to the limited number of patients, there were numerically large differences between PCI and CABG in patients with IR (absolute difference 10.3%), but only minor differences in patients with CR (absolute difference 2.7%). In the clinical viewpoint, such some of the larger nonstatistically significant trends should be clinically considered. Therefore, such findings should be confirmed or refuted through larger-sized clinical studies with long-term follow-up evaluations.

STUDY LIMITATIONS. First, owing to the relatively small number of patients, this study did not have sufficient statistical power to detect clinically significant differences in clinical endpoints in each subgroup according to CR status. In addition, analyses for outcome measures were not adjusted for multiple comparisons. Thus, the present findings should be interpreted as hypothesis-generating only, and further investigation is warranted. Second, the definition of CR in the current study was determined by anatomical criteria. Given that various anatomic or functional CR was present,[15,22,29] and the functional capacity of CR was not confirmed by stress test, the findings of our study may be different with different definitions of ischemic or functional CR. Further studies are needed to determine the revascularization completeness based on functional criteria beyond anatomic criteria affecting the long-term outcomes. Third, the exact reasons for CR or IR during PCI or CABG were not systematically captured, which might be subject to multiple confounders. Fourth, we did not have a direct angiography assessment in CABG patients owing to the absence of a routine angiographic follow-up after surgical procedures (thus, postprocedural surgical reports were used to classify CR or IR). Finally, PRECOMBAT was conducted from 2004 to 2009 with a default use of the first-generation drug-eluting stent, for which long-term safety and effectiveness were already issued,[3] and also a paradigm shift of optimal medical therapy was less concerted. These limitations may hamper the generalizability of the current findings to the contemporary clinical practice.

CONCLUSIONS

In this 10-year report of the PRECOMBAT trial, we found no significant difference between PCI and CABG in the rates of primary MACCE events, all-cause mortality, and a composite endpoint of death, MI, or stroke according to CR or IR status. However, the study had insufficient statistical power to allow for a firm conclusion, hence further research is needed in this area.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: With the extended 10-year follow-up of the PRECOMBAT trial, we found no significant difference between PCI and CABG in the rates of primary MACCE events, all-cause mortality, and a composite endpoint of death, myocardial infarction, or stroke according to completeness of revascularization status.

TRANSLATIONAL OUTLOOK: Further additional evidence from large, randomized trials may provide more compelling evidence on the long-term clinical impact of CR or IR in patients with contemporary PCI and CABG treatment.

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KEY WORDS coronary artery bypass grafting, drug-eluting stent(s), left main coronary artery disease, percutaneous coronary intervention

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