Coronary Artery Bypass Grafting Versus Drug-Eluting Stents Implantation for Previous Myocardial Infarction

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Patients with previous myocardial infarction (MI) have a high risk of recurrence. Little is known about the effectiveness of coronary artery bypass grafting (CABG) versus percutaneous coronary intervention (PCI) with drug-eluting stents (DES) in patients with a previous MI and left main or multivessel coronary artery disease (CAD). We compared long-term outcomes of these 2 strategies in 672 patients with previous MI and left main or multivessel CAD, who underwent CABG (n = 349) or PCI with DES (n = 323). A pooled database from the BEST, PRECOMBAT, and SYNTAX trials was analyzed, and the primary outcome was a composite of death from any causes, MI, or stroke. Baseline characteristics were similar between the 2 groups. The median follow-up duration was 59.8 months. The rate of the primary outcome was significantly lower with CABG than PCI (hazard ratio [HR] 0.59, 95% CI 0.42 to 0.82; p = 0.002). This difference was driven by a marked reduction in the rate of MI (HR 0.29, 95% CI 0.16 to 0.55, p <0.001). The benefit of CABG over PCI was consistent across all major subgroups. The individual risks of death from any causes or stroke were comparable between the 2 groups. Conversely, the rate of repeat revascularization was significantly lower with CABG than PCI (HR 0.34, 95% CI 0.22 to 0.51, p <0.001). In conclusion, in the patients with previous MI and left main or multivessel CAD, compared to PCI with DES, CABG significantly reduces the risk of death from any causes, MI, or stroke. **(Am J Cardiol 2016;118:17−22)**

Both coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) with drug-eluting stents (DES) have been used for revascularization of the left main or multivessel coronary artery disease (CAD).[1−5] Patients with previous myocardial infarction (MI) after the index procedure are more likely to report angina at follow-up.[6] Therefore, in current clinical practice, patients with a history of MI represent a significant portion of all patients with left main or multivessel CAD.[7,8] These patients are at much greater risk of cardiovascular events than those who did not have a previous MI. However, the optimal revascularization strategy for such patients remains unclear. In the present study, we compared the effects of CABG and PCI with DES on long-term outcomes in patients with previous MI and left main or multivessel CAD using individual patient data from the Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease (BEST), Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease (PRECOMBAT), and Synergy between PCI with Taxus and Cardiac Surgery (SYNTAX) trials.

Methods

The major aspects and differences among the 3 trials are as follows.[9−13] All the trials were conducted in multicenter, and patients eligible for both CABG and PCI were randomized to treatment with either strategy. The BEST trial included 880 patients with 2- or 3-vessel CAD, and the PRECOMBAT trial included 600 patients with left main CAD. The SYNTAX trial included 1,800 patients with 3-vessel and/or left main CAD. Everolimus-eluting stents were used in the BEST trial, sirolimus-eluting stents were used in the PRECOMBAT trial, and paclitaxel-eluting stents were used in the SYNTAX trial. Individual patient-level data were pooled from the BEST, PRECOMBAT, and SYNTAX trials, and 672 patients with previous MI were included in this study.

A protocol with prespecified outcomes and a common set of baseline variables were established by principal investigators for each trial (SJP and PWS). Individual patient

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data from each trial was sent to the coordinating institution, Asan Medical Center in Seoul, Korea, to be merged. An independent clinical event committee that was blind to the randomization adjudicated all the end points in each study. The pooled database was checked for completeness and consistency by responsible investigators from Asan Medical Center.

The merged database included demographics, clinical history, risk factors, angiographic and echocardiographic findings, revascularization strategies, medication history, and clinical outcomes during follow-up. Unless specified, previously reported definitions from each study were used as variables. The primary outcome, from available follow-up information, was a composite of death from any causes, MI, or stroke. Secondary outcomes included individual components of the primary outcome, any coronary revascularization, and a composite of death from any causes or MI. Previously reported definitions from each study were used for individual clinical outcomes.[9−13]

Data were analyzed according to the intention-to-treat principle. The databases from 3 trials were combined for an overall pooled analysis, and time-to-event outcomes were displayed using Kaplan−Meier method, compared by the log-rank test. The stratified Cox proportional hazards model was used to analyze the impact of revascularization strategy on clinical outcomes. A forward stepwise Cox regression model was used to identify independent predictors of primary outcome. Analyses were performed by an independent statistician who was unaware of the treatment assignments. All reported p values were 2-sided, and p values <0.05 were considered statistically significant. Statistical analyses were conducted with SPSS software, version 18.0 (SPSS Inc., Chicago, Illinois).

Table 1
Baseline characteristics

Variables	CABG (N=349)	PCI (N=323)
Age (years)	64.6±9.7	65.1±9.3
Men	283 (81.1%)	253 (78.3%)
Body mass index (kg/m^2)	27.4±4.5	27.7±5.1
Current smoker	85 (24.6%)	64 (19.8%)
Diabetes mellitus		
Any	96 (27.5%)	96 (27.7%)
Requiring insulin	33 (9.5%)	42 (13.0%)
Hypercholesterolemia	257 (73.9%)	243 (75.2%)
Hypertension	195 (55.9%)	191 (59.1%)
Clinical presentation		
Stable angina pectoris	202 (57.9%)	185 (57.3%)
Acute coronary syndrome	147 (42.1%)	138 (42.7%)
Previous stroke	18 (5.5%)	15 (4.8%)
Peripheral vascular disease	31 (8.9%)	25 (7.7%)
Chronic kidney disease (Cr >200μmol/L)	11 (3.2%)	9 (2.8%)
Left ventricular ejection fraction < 40%	19 (8.3%)	22 (10.2%)
No. of coronary arteries narrowed		
2	9 (2.6%)	10 (3.1%)
3	233 (66.8%)	199 (61.6%)
Proximal left anterior descending narrowed	188 (54.2%)	160 (49.5%)
Left main narrowed		
Isolated	7 (2.0%)	9 (2.8%)
Plus one vessel	18 (5.2%)	18 (5.6%)
Plus two vessel	36 (10.3%)	31 (9.6%)
Plus three vessel	46 (13.2%)	56 (17.3%)
EuroSCORE	4.6±2.8	4.6±2.7
SYNTAX score	28.6±10.4	29.1±11.4
Follow-up (years)	4.2±1.6	4.3±1.4

Percentages are based on the number of nonmissing values.
Cr = creatinine.

Results

Of the 3,280 study patients, 672 (20.5%) had previous MI, of whom 349 underwent CABG and 323 underwent PCI with DES. The baseline characteristics were well balanced across the 2 groups (Table 1). The mean age of the patients was 64.9 years; 79.8% of the patients were men, and 28.6% had diabetes mellitus. The extent of CAD was similar in the 2 groups. Most patients received optimal medical therapy at discharge, which was less frequent in the CABG group than in the PCI group; namely, aspirin (89.8% vs 95.7%, respectively, p = 0.004), statins (77.8% vs 85.4%, respectively, p = 0.013), and β blockers (74.3% vs 81.7%, respectively, p = 0.022).

The median follow-up time was 59.8 months (interquartile range: 50.7 to 60.3 months). The primary outcome of death from any causes, MI, or stroke occurred in 56 patients (16.0%) in the CABG group compared with 87 (26.9%) in the PCI group (hazard ratio [HR] 0.59, 95% CI 0.42 to 0.82; p = 0.002; Figure 1, Table 2). This difference was mainly attributed to a reduction in the rate of MI. In the subgroup analyses, there was no significant interaction between treatment effects and major baseline variables (Figure 2). By multivariate analysis, age, revascularization strategy, peripheral artery disease, SYNTAX scores, and optimal medical therapies at discharge were independently related to the primary outcome (Table 3).

Death from any causes in the CABG group was comparable to that of the PCI group, and a consistent trend was observed for death from cardiac causes. Although, the rate of MI was markedly lower in the CABG group compared with the PCI group (HR 0.29, 95% CI 0.16 to 0.55, p <0.001), the rate of stroke was comparable between the 2 groups (HR 0.38, 95% CI 0.12 to 1.21, p = 0.101). In contrast, repeat revascularization was less frequently needed among patients undergoing CABG compared with those undergoing PCI (HR 0.34, 95% CI 0.22 to 0.51, p <0.001).

Discussion

In this study involving patients with previous MI and left main or multivessel CAD compared with PCI with DES, CABG led to a significant decrease in the rate of death from any causes, MI, or stroke. The benefit of CABG was consistent across all major subgroups and was mainly driven by a reduction in MI. In contrast, there were no significant differences between the 2 groups with respect to death from any causes or stroke. These findings suggest that CABG may be the preferred approach to revascularize for patients with previous MI and left main or multivessel CAD.

In recent decades, the rates of age-adjusted CAD mortality remarkably decreased with same trends in many countries.[14,15] Evidence-based therapy has increased the

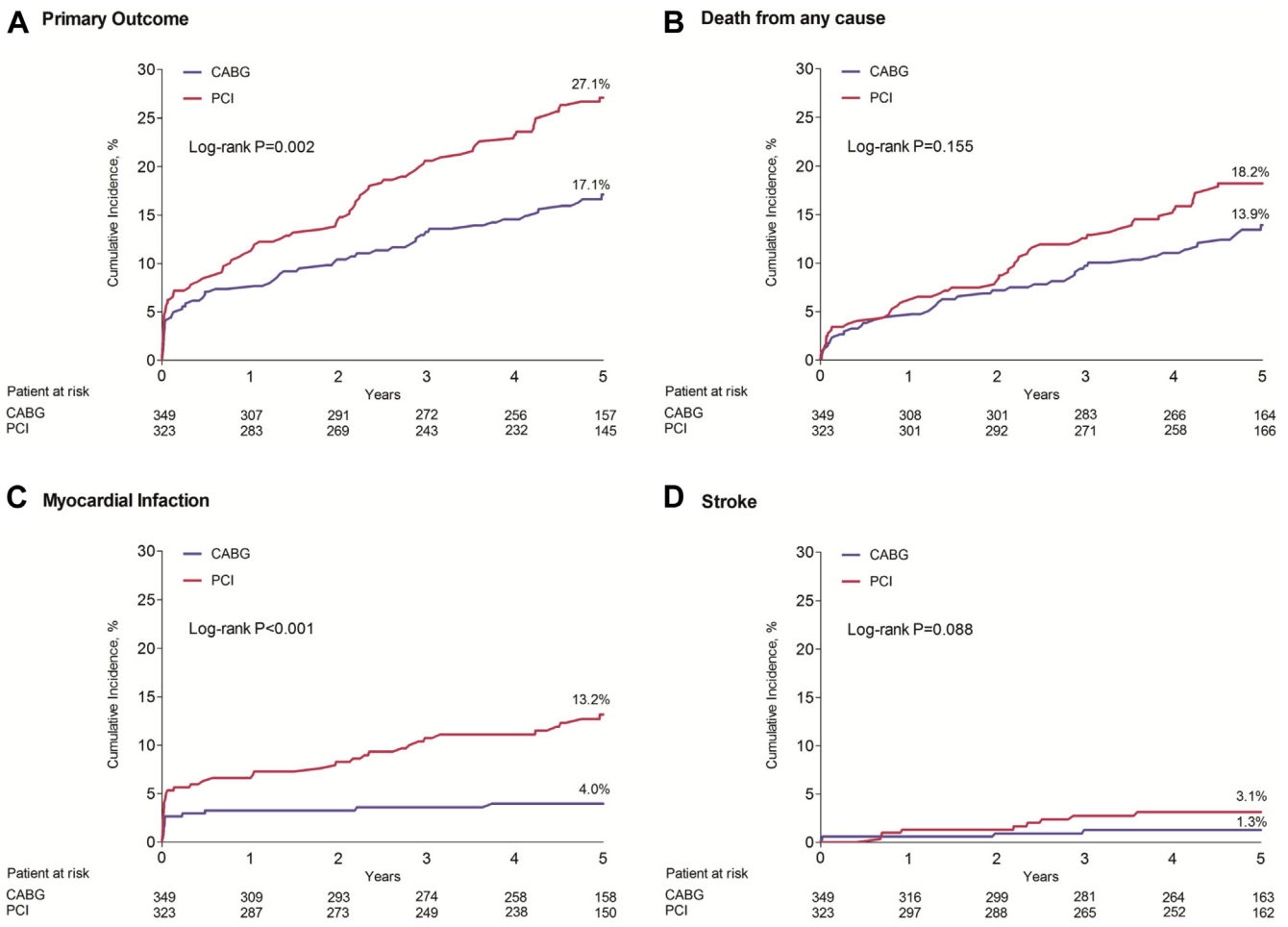

Figure 1. Time-to-event curves comparing the outcomes of CABG and PCI with DES. *(A)* Death from any causes, MI, or stroke; *(B)* death from any causes; *(C)* myocardial infraction; *(D)* stroke. The p values were calculated using the log-rank test with all available follow-up data. The percentages denote 5-year event rates.

Table 2
Clinical outcomes

Variables	CABG (N=349)	PCI (N=323)	Hazard ratio (95% CI)	p-value
	no. (%)			
Primary outcome: death, myocardial infarction, or stroke	56 (16.0%)	87 (26.9%)	0.59 (0.42-0.82)	0.002
Secondary outcomes				
Death from any causes	45 (12.9%)	57 (17.6%)	0.75 (0.51-1.12)	0.157
Death from cardiac causes	28 (8.0%)	40 (12.4%)	0.67 (0.41-1.08)	0.101
Myocardial infarction	13 (3.7%)	41 (12.7%)	0.29 (0.16-0.55)	<0.001
Stroke	4 (1.1%)	10 (3.1%)	0.38 (0.12-1.21)	0.101
Repeat revascularization	30 (8.6%)	79 (24.5%)	0.34 (0.22-0.51)	<0.001
Death or myocardial infarction	54 (15.5%)	81 (25.1%)	0.61 (0.44-0.87)	0.005

The p values were calculated with all available follow-up data.
CI = confidence interval.

chance of survival during the early phase of acute MI, which is one of the major reasons for the decrease in mortality due to CAD. However, patients with previous MI remain at risk for recurrent events and mortality.[16–19] In our pooled analysis, patients with previous MI had a twofold higher risk of mortality than those without previous MI (HR 1.97, 95% CI 1.55 to 2.49, p <0.001). An analysis from the National Cardiovascular Data Registry showed that 30% of the total PCI volume between 2009 and 2012 occurred in patients with previous MI.[7] In our pooled database, 20.5% of the

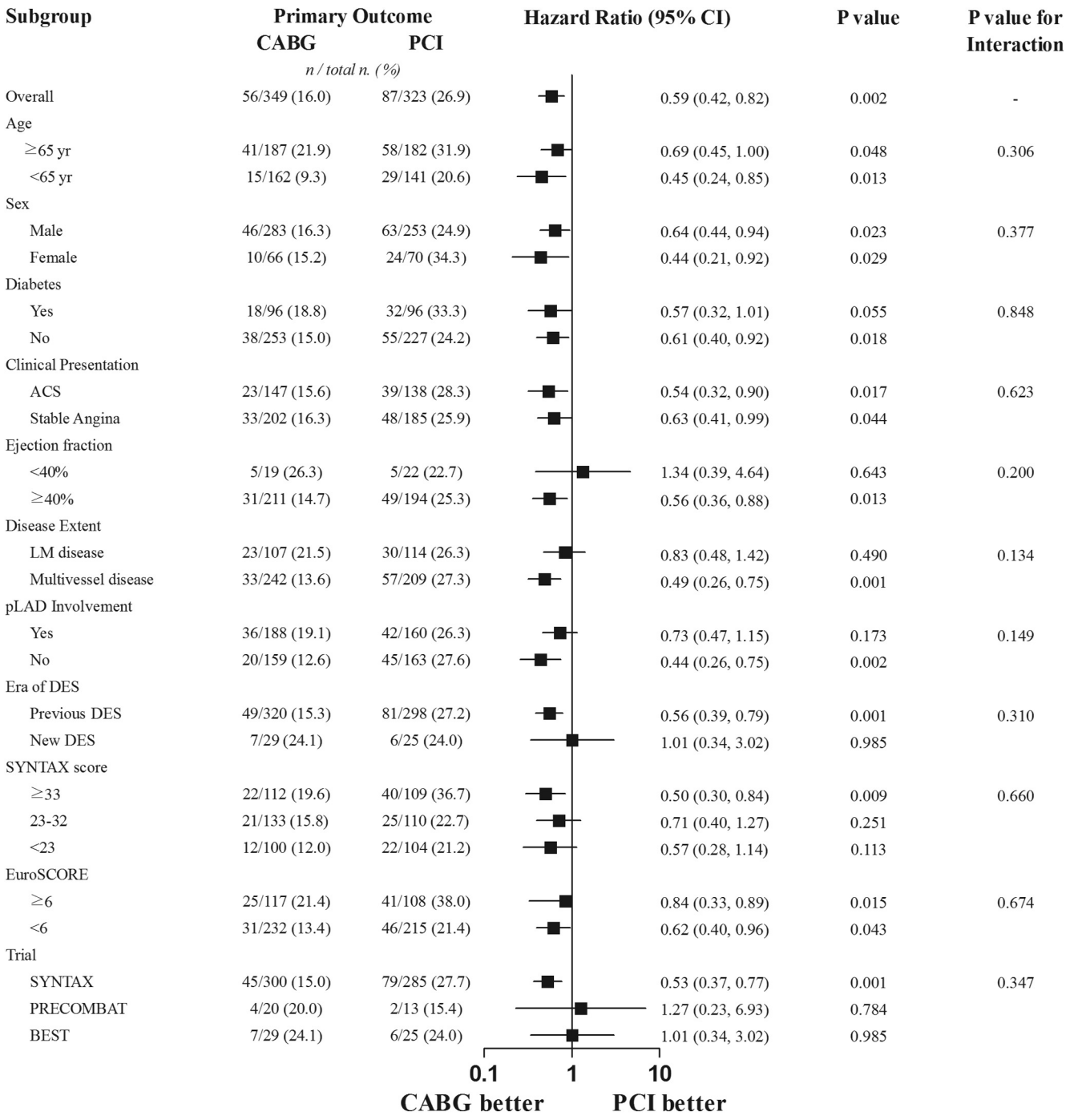

Figure 2. Primary outcome stratified by major subgroups. Subgroup analyses were performed using Cox proportional hazards regression. ACS = acute coronary syndrome; LM = left main; pLAD = proximal left anterior descending coronary artery.

total cohort had a history of MI. In contemporary practice in PCI, therefore, patients with previous MI comprise a significant proportion of those requiring revascularization for left main or multivessel CAD. Until now, there has been no specific randomized trial to compare revascularization strategies for left main or multivessel CAD in this patient population.

CABG had offered greater protection against MI compared with PCI or medical therapy.[20,21] In our study, the rate of MI was significantly lower after CABG than after PCI with DES. The relative risk reduction of ~70% in the rate of MI appears to be larger than that in previous findings, suggesting that patients with previous MI with left main or multivessel CAD may have a much greater atherosclerotic burden and derive greater benefit from CABG versus PCI with DES. Death from any causes or cardiac causes was numerically lower after CABG than after PCI with DES; otherwise, our study was not statistically powered to detect a

Table 3
Predictors of primary outcome by Cox regression analyses

Variables	Univariate analysis			Multivariate analysis		
	HR	95% CI	p-value	HR	95% CI	p-value
Age	1.06	1.04-1.08	<0.001	1.05	1.03-1.08	<0.001
CABG vs. PCI	0.59	0.42-0.82	0.002	0.41	0.28-0.59	<0.001
Peripheral artery disease	1.99	1.24-3.20	0.004	1.99	1.23-3.23	0.005
SYNTAX score	1.03	1.01-1.04	0.001	1.02	1.01-1.04	0.004
Discharge medications						
*Antiplatelet therapy	0.25	0.14-0.45	<0.001	0.20	0.10-0.38	<0.001
Statin	0.45	0.31-0.65	<0.001	0.39	0.26-0.56	<0.001
β-blocker	0.63	0.44-0.91	0.015			
EuroSCORE	1.17	1.11-1.24	<0.001			
Diabetes mellitus	1.44	1.02-2.03	0.037			

CI = confidence interval; HR = hazard ratio.
* At least one antiplatelet therapy (aspirin or clopidogrel).

small difference in mortality. For stroke, CABG is considered to be associated with an increased risk during a postoperative period.[22] In our current analyses, it was reassuring that there was no obvious increase in stroke associated with CABG. Nevertheless, the early risk of postoperative stroke needs to be balanced against the long-term benefits of CABG.

Several limitations of this study are noteworthy. First, this was a post hoc analysis of CABG compared with PCI with DES in patients with previous MI. Given this limitation, our present findings should be interpreted cautiously. Second, previous DES was used in the PRECOMBAT and SYNTAX trials, and newer-generation DES was used in the BEST trial. In addition, most patients were recruited from the SYNTAX trial. Nonetheless, there was no interaction of the primary outcome between previous and newer-generation DES. Third, the number of patients with previous MI was relatively small (20.5% of the total cohort), limiting the power of the analysis. Finally, standard medications were less frequently used in the CABG group compared with the PCI group. Antiplatelet, β blocker, and statin therapies were independent predictors of primary outcomes, suggesting that there may be room for further improvements from optimal medical therapies in patients with CABG.

Disclosures

The authors have no conflicts of interest to disclose.

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