



Long-Term Mortality After Coronary Revascularization in Nondiabetic Patients With Multivessel Disease

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ABSTRACT

BACKGROUND In diabetic patients with multivessel coronary artery disease (CAD), the survival difference between coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention (PCI) favors CABG. However, there are few data on the mortality difference between the 2 strategies in nondiabetic patients.

OBJECTIVES This study performed a patient-level meta-analysis to compare the effect of CABG versus PCI with drug-eluting stents on long-term mortality in 1,275 nondiabetic patients with multivessel CAD.

METHODS Individual patient data from the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) and the BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary Artery Disease) trials were pooled. The primary outcome was death from any cause.

RESULTS The median follow-up time was 61 months (interquartile range: 50 months to 62 months). The risk of death from any cause was significantly lower in the CABG group than in the PCI group (hazard ratio [HR]: 0.65; 95% confidence interval [CI]: 0.43 to 0.98; $p = 0.039$). A similar finding was observed for the risk of death from cardiac causes. The superiority of CABG over PCI was consistent across the major clinical subgroups. Likewise, the rate of myocardial infarction was remarkably lower after CABG than after PCI (HR: 0.40; 95% CI: 0.24 to 0.65; $p < 0.001$). However, the rate of stroke was not different between the 2 groups (HR: 1.13; 95% CI: 0.59 to 2.17; $p = 0.714$). The need for repeat revascularization was significantly lower in the CABG group than in the PCI group (HR: 0.55; 95% CI: 0.40 to 0.75; $p < 0.001$).

CONCLUSIONS CABG, as compared with PCI with drug-eluting stents, significantly reduced the long-term risk of mortality in nondiabetic patients with multivessel CAD. (J Am Coll Cardiol 2016;68:29-36)

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Both coronary artery bypass graft (CABG) surgery and percutaneous coronary intervention (PCI) play a major role in the management of multivessel coronary artery disease (CAD) (1-5). Since the introduction of drug-eluting stents (DES), PCI has

become a widely used option for the treatment of multivessel CAD.

Several randomized trials comparing the relative outcomes of CABG versus PCI in patients with multivessel CAD have been published (6-11). In



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**ABBREVIATIONS
AND ACRONYMS**

CABG = coronary artery bypass graft
CAD = coronary artery disease
DES = drug-eluting stent(s)
PCI = percutaneous coronary intervention

general, diabetic patients have poorer clinical outcomes than nondiabetic patients and better survival with CABG than PCI (6,7,9). However, controversy still exists as to the optimal revascularization strategy in nondiabetic patients with multivessel CAD. Death from any cause is undoubtedly the most unbiased endpoint to determine treatment strategy, but each randomized trial has shown limited power to assess the clinical equipoise between CABG and PCI regarding mortality. Pooling of patient-level data from these randomized trials might be suggested to increase the statistical power and allow time-to-event analysis of this issue (12).

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Therefore, in the present study, we combined the databases from the SYNTAX (Synergy between PCI with Taxus and Cardiac Surgery) and the BEST (Randomized Comparison of Coronary Artery Bypass Surgery and Everolimus-Eluting Stent Implantation in the Treatment of Patients with Multivessel Coronary

Artery Disease) trials, and performed a patient-level analysis. The effects of CABG versus PCI with DES on long-term mortality in nondiabetic patients with multivessel CAD and the differences among major clinical subgroups were analyzed.

METHODS

STUDY PATIENTS. Each trial’s designs, detailed entry criteria, and outcomes were described previously (8,11). In brief, both trials were multicenter and multinational: SYNTAX recruited patients from Europe and the United States, and BEST recruited from Asia. The SYNTAX trial included 1,800 patients with 3 vessels or left main CAD. The BEST trial included 880 patients with 2- or 3-vessel CAD. In both studies, patients eligible for both CABG and PCI were randomized to treatment with either strategy. PCI was performed using either paclitaxel-eluting stents in the SYNTAX trial or everolimus-eluting stents in the BEST trial. Patients with concomitant left main CAD (n = 705) or diabetes mellitus (n = 700) were excluded from this study.

DATA COLLECTION. The principal investigators of each trial (S.J.P., P.W.S.) programmed a protocol with the pre-specified outcomes and a common set of baseline variables. Individual patient data from each

TABLE 1 Patient Characteristics

	CABG (n = 638)	PCI (n = 637)
Age, yrs	64.3 ± 9.8	64.8 ± 9.9
Male	512 (80.3)	499 (78.3)
Body mass index, kg/m ²	26.4 ± 3.7	26.4 ± 4.1
Current smoker	142 (22.3)	126 (19.8)
Hypercholesterolemia	411 (64.8)	424 (66.8)
Hypertension	405 (63.5)	430 (67.5)
Clinical presentation		
Stable angina	393 (61.6)	400 (62.8)
ACS	245 (38.4)	237 (37.2)
Previous myocardial infarction	172 (27.1)	144 (22.7)
Previous stroke	32 (5.0)	39 (6.1)
Peripheral vascular disease	37 (5.8)	31 (4.9)
CKD (creatinine >200 μmol/l)	5 (0.8)	5 (0.8)
Left ventricular dysfunction*	24 (4.9)	19 (3.9)
Diseased vessels		
Proximal LAD disease	365 (57.5)	375 (59.1)
2 vessels	65 (10.2)	81 (12.7)
3 vessels	573 (89.8)	556 (87.3)
SYNTAX score	26.7 ± 9.4	25.9 ± 9.1
EuroSCORE†	3.3 ± 2.4	3.3 ± 2.4
Follow-up, yrs	4.4 ± 1.4	4.4 ± 1.3

Values are mean ± SD or n (%). *Left ventricular dysfunction was defined as LVEF <40% or moderate to severe left ventricular dysfunction. †The EuroSCORE is a clinical model for calculating the risk of death after cardiac surgery on the basis of patient, cardiac, and operative factors. Possible scores range from 0 to 39, with higher scores indicating greater risk. Percentages are on the basis of the number of nonmissing values.

ACS = acute coronary syndrome; CABG = coronary artery bypass graft; CKD = chronic kidney disease; LAD = left anterior descending coronary artery; LVEF = left ventricular ejection fraction; PCI = percutaneous coronary intervention; SYNTAX = Synergy between PCI with Taxus and Cardiac Surgery.

TABLE 2 Medications at Discharge and Follow-Up

	CABG (n = 638)	PCI (n = 637)	p Value
Aspirin			
At discharge	577 (91.6)	613 (96.5)	<0.001
1 yr after randomization	541 (88.7)	570 (92.5)	0.021
5 yrs after randomization	373 (81.3)	382 (82.5)	0.624
P2Y ₁₂ inhibitors			
At discharge	310 (49.2)	611 (96.2)	<0.001
1 yr after randomization	218 (35.7)	464 (75.3)	<0.001
5 yrs after randomization	86 (18.8)	165 (35.6)	<0.001
Statins			
At discharge	494 (78.4)	544 (85.7)	0.001
1 yr after randomization	508 (83.3)	548 (89.0)	0.004
5 yrs after randomization	374 (81.5)	387 (83.6)	0.400
Beta-blockers			
At discharge	412 (65.4)	481 (75.7)	<0.001
1 yr after randomization	497 (81.5)	514 (83.4)	0.365
5 yrs after randomization	307 (66.9)	320 (69.1)	0.468
ACE inhibitors or ARBs			
At discharge	247 (39.2)	352 (55.4)	<0.001
1 yr after randomization	318 (52.1)	340 (55.2)	0.282
5 yrs after randomization	255 (55.6)	267 (57.7)	0.518

Values are n (%). Percentages are on the basis of the number of nonmissing values.

ACE = angiotensin-converting enzyme; ARB = angiotensin II receptor blockers; other abbreviations as in Table 1.

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