Stenting versus coronary artery bypass grafting for unprotected left main coronary artery disease: A meta-analysis of comparative studies

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Although coronary artery bypass grafting (CABG) is currently recommended to treat unprotected left main coronary artery (LMCA) disease, the treatment of this disorder by percutaneous coronary intervention represents a considerable challenge for interventional cardiologists.¹ Several studies have analyzed the treatment of unprotected LMCA disease with CABG versus percutaneous coronary intervention with stents (PCI-S), but no meta-analyses of these studies have been conducted to date. To compare the treatment of unprotected LMCA disease with PCI-S versus CABG, we performed a meta-analysis of comparative studies for prevention of death, repeated revascularization, and major adverse cardiac and cerebrovascular events (MACCEs) at follow-up.

MATERIALS AND METHODS

All comparative studies of PCI-S (with bare metal or drug-eluting stents) versus CABG (conventional or off-pump CABG) enrolling patients with unprotected LMCA disease were identified by means of a 2-level search strategy. First, a public domain database (MEDLINE) was searched with a web-based search engine (PubMed). Second, relevant studies were identified through a manual search of secondary sources, including references of initially identified articles and a search of reviews and commentaries. The MEDLINE database was searched from January 1966 to March 2008. MeSH keywords included *coronary artery bypass*; *angioplasty*; *transluminal, percutaneous coronary*; and *stents*. Studies considered for inclusion met the following criteria: the study design was comparative (randomized controlled or nonrandomized observational); the study population consisted of patients with unprotected LMCA disease; patients were assigned to undergo PCI-S versus CABG; and main outcomes included death, repeated revascularization, or MACCEs (death, myocardial infarction, stroke, or repeated revascularization) at follow-up. Data regarding detailed inclusion criteria, stent type, duration of follow-up, and negative outcomes (death, repeated revascularization, and MACCEs) at follow-up were abstracted as available from each individual study. Adjusted risk estimates for nonrandomized controlled comparisons and crude risk ratios for randomized controlled comparisons were pooled after logarithmic transformation according to a random-effects model with generic inverse variance weighting. Interstudy heterogeneity was analyzed by means of standard χ^2 tests.

RESULTS

Our search identified 6 comparative studies¹⁻⁶ of PCI-S versus CABG that had enrolled patients with unprotected LMCA disease. These included 1 randomized controlled trial² and 5 nonrandomized observational studies.^{1,3-6} We excluded 2 nonrandomized observational studies, by Brener and colleagues (2008) and Sanmartín and associates (2007), because adjusted risk estimates could not be abstracted. In total, our meta-analysis included data on 2181 patients with unprotected LMCA disease assigned to undergo PCI-S (n = 1006) or CABG (n = 1175). The baseline patient and procedural characteristics are summarized in Table 1. For death at follow-up, 3 studies^{1,2,4} demonstrated a statistically nonsignificant benefit of PCI-S relative to CABG, whereas 2 studies^{3,6} demonstrated a statistically nonsignificant benefit of CABG relative to PCI-S. Pooled analysis of the 5 studies reporting this outcome demonstrated no significant difference in death rate between PCI-S and CABG ($P = .97$; Figure 1, A). There was no significant interstudy heterogeneity of results ($P = .36$). For repeated revascularization at follow-up, all 4 studies reporting this outcome^{1-3,6} demonstrated a statistically significant benefit of CABG relative to PCI-S. Pooled analysis of these 4 studies demonstrated a statistically significant increase in repeated revascularization with PCI-S relative to CABG ($P < .00001$; Figure 1, B). There was no significant interstudy heterogeneity of results ($P = .25$). For MACCEs at follow-up, 2 studies^{1,5} demonstrated a statistically nonsignificant benefit of PCI-S relative to CABG, whereas 1 study² demonstrated a statistically nonsignificant benefit of CABG relative to PCI-S. Pooled analysis of the 3 studies that reported MACCEs as an outcome demonstrated a statistically nonsignificant reduction in MACCEs with PCI-S relative to CABG ($P = .32$; Figure 1, C). There was no significant interstudy heterogeneity of results ($P = .07$). When data were pooled with a fixed-effects model, the overall results of our analysis were not substantively altered.

DISCUSSION

On the basis of this meta-analysis, CABG is likely to provide better results than PCI-S not in terms of death and MACCEs but in terms of repeated revascularization at 6 months to 3 years of follow-up. Main limitations of our analysis are the following: only a single randomized, controlled trial was included, and it was small; both bare metal and drug-eluting stents were used in the PCI-S group; both conventional and off-pump CABG were performed in the

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Received for publication March 7, 2008; accepted for publication June 15, 2008.

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J Thorac Cardiovasc Surg 2009;137:e54-7

0022-5223/\$36.00

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doi:10.1016/j.jtcvs.2008.06.006

TABLE 1. Baseline patient and procedural characteristics

	Seung et al, 2008 ³	Buszman et al, 2008 ²	Palmerini et al, 2007 ⁴	Chieffo et al, 2006 ¹	Lee et al, 2006 ⁵	Palmerini et al, 2006 ⁶
Design	Observational	Randomized	Observational	Observational	Observational	Observational
Follow-up	1017 d* (IQR 688–1451 d), 1152 d* (IQR 681–1590 d)	1 y	2 y	1 y	5.6 ± 3.9 mo, 6.7 ± 6.2 mo	417 d* (2–830 d), 430 d* (105–730 d)
<i>P</i> value†					.26	.439
Patients (No.)	542,‡ 542‡	52, 53	98, 161	107, 142	50, 123	157, 154
Age (y)	64* (IQR 56–71), 64* (IQR 56–70)	60.6 ± 10.5, 61.3 ± 8.4	81* (75–88), 78* (75–88)	63.6 ± 10.3, 67.5 ± 9.7	72 ± 15, 70 ± 10	73.0 ± 10.9, 69.3 ± 9.5
<i>P</i> value†	.41	.69	<.001	.002	.33	.002
Male (%)	71.6%, 71.2%	60%, 73%	54%, 66%	NR	50%, 76%	70.1%, 76.0%
<i>P</i> value†	.95	.13	.06		<.01	.296
Ejection fraction (%)	61%* (IQR 54%–66%), 61%* (IQR 55%–66%)	53.5% ± 10.7%, 53.7% ± 6.7%	50%* (20%–70%), 53%* (25%–78%)	52.0% ± 10.4%, 52.2% ± 11.4%	51% ± 15%, 52 ± 10%	51.8 ± 13.8%, 54.6 ± 12%
<i>P</i> value†	.62	.86	.68	.91	.64	.069
Clinical presentation						
Stable angina (%)	29.2%, 28.4%§	CCS class 3.1 ± 1.0, 2.8 ± 1.0	NR	NR	34%, 55%	26.8%, 27.9%
<i>P</i> value†		.17			NR	.917
Unstable angina (%)	57.4%, 57.9%§		Acute coronary syndrome 77%, 52%	31.8%, 21.8%	46%, 25%	Braunwald class IB + IIB 13.4%, 20.1% (<i>P</i> = .149); IIB 13.4%, 7.8% (<i>P</i> = .157)
<i>P</i> value†			<.001	.08	NR	
Myocardial infarction (%)	10.7%, 11.1% §			NR	20%, 20%	39.5%,¶ 31.2%¶
<i>P</i> value†					NR	.157
Surgical risk						
EuroSCORE	NR	3.3 ± 2.3, 3.5 ± 2.3	8* (4–18), 7* (3–14)	4.4 ± 3.6, 4.3 ± 3.4	NR	6* (0–18), 5* (0–14)
<i>P</i> value†		.65	<.001	.85		.032
Parsonnet score		NR	22.5* (12.5–38.5), 14* (5–36)	NR	18.3 ± 10.9, 13.7 ± 9.7	16.5* (2.5–37), 12.5* (2–36)
<i>P</i> value†			<.001		<.01	.004
Coexisting conditions						
Diabetes mellitus (%)	32.7%, 33.0%	19%, 17%	31%, 26%	18.7%, 23.2%	36%, 31%	26.1%, 25.3%
<i>P</i> value†	.95	.80	.72	.44	.48	.976
Hypertension (%)	49.4%, 50.0%	75%, 70%	77%, 73%	58.8%, 76.0%	88%, 81%	69.4%, 72.7%
<i>P</i> value†	.9	.78	.67	.006	.37	.605
Hyperlipidemia (%)	29.3%, 30.1%	65%, 60%	53%, 47%	70.0%, 69.0%	74%, 72%	62.4%, 72.1%
<i>P</i> value†	.84	.78	.43	.89	.85	.09
Procedural characteristics						
DES (%)	71.1%	35%	100%	100%	100%	59.9%
Distal LMCA disease (%)	51.7%, 52.2%	56%, 60%	89%, 70%	81.3%, NR	60%, NR	80.3%, 82.5%
<i>P</i> value†	.9	.63	<.001	NR	NR	.742

TABLE 1. Continued

	Seung et al, 2008 ³	Buszman et al, 2008 ²	Palmerini et al, 2007 ⁴	Chieffo et al, 2006 ¹	Lee et al, 2006 ⁵	Palmerini et al, 2006 ⁶
Off-pump CABG (%)	42%	2%	21%	39.5%	0%	0%
Arterial conduit (%)	98.4%	72%#	93%**	NR	96%††	94.2%**
Pharmacologic treatment						
Percutaneous coronary intervention with stents	Aspirin indefinitely + clopidogrel or ticlopidine ≥1 mo (BMS) or clopidogrel ≥6 mo (DES)	Double antiplatelet treatment ≥1 y	Aspirin indefinitely + ticlopidine or clopidogrel 3–12 mo	NR	Aspirin indefinitely + clopidogrel ≥6 mo	NR
CABG	NR				NR	

When two values are given, the first represents percutaneous coronary intervention with stenting and the second represents coronary artery bypass grafting. *IQR*, Interquartile range; *NR*, not reported; *CCS*, Canadian Cardiovascular Society; *DES*, drug-eluting stents; *LMCA*, left main coronary artery; *CABG*, coronary artery bypass grafting; *BMS*, bare metal stent. *Median. †Reported in each individual study. ‡Propensity-matched patients from 1102 in the percutaneous coronary intervention with stenting group and 1138 in the coronary artery bypass grafting group. §P = .97. ||Non-ST elevation. ¶Non-Q wave. #Left internal thoracic artery. **Internal thoracic artery. ††Internal thoracic artery to left anterior descending coronary artery.

CABG group; and the durations of follow-up of the included studies were relatively short. In an attempt to correct for and minimize selection bias in nonrandomized observational studies, we pooled adjusted risk estimates. Nevertheless, these findings should be viewed in light of the need to wait for the results of ongoing large randomized, controlled trials (eg, COMBAT, SYNTAX, and REVASCULARIZE studies) before drawing any definitive conclusion.

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Review: PCI-S vs CABG for unprotected LMCA
 Comparison: 01 PCI-S vs CABG
 Outcome: 01 Death

Review: PCI-S vs CABG for unprotected LMCA
 Comparison: 01 PCI-S vs CABG
 Outcome: 02 Repeat revascularization

Review: PCI-S vs CABG for unprotected LMCA
 Comparison: 01 PCI-S vs CABG
 Outcome: 03 MACCE

FIGURE 1. Outcomes and meta-analyses at follow-up for death (A), repeated revascularization (B), and major adverse cardiac and cerebrovascular events (MACCE; C). *PCI-S*, Percutaneous coronary intervention with stents; *CABG*, coronary artery bypass grafting; *LMCA*, left main coronary artery; *CI*, confidence interval.