Drug-eluting stents versus coronary artery bypass grafting for the treatment of coronary artery disease: A meta-analysis of randomized and nonrandomized studies

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Background: We performed the present systematic review and meta-analysis of randomized and nonrandomized comparative studies in an attempt to compare the safety and efficacy of drug-eluting stents with coronary artery bypass grafting for patients with coronary artery disease.

Methods: Twenty-five eligible comparative studies (1 randomized and 24 nonrandomized) were assessed. Two reviewers independently appraised each study. Meta-analysis was performed by combining the results of reported incidence of morbidity, mortality, and repeat revascularization. The relative risk was used as a summary statistic.

Results: In these 25 studies 34,278 patients were compared, of whom 18,538 received drug-eluting stents and 15,740 underwent coronary artery bypass grafting. It must be acknowledged that this comparison represented a selected group of patients who received drug-eluting stents or underwent coronary artery bypass grafting. The accumulative incidences of all-cause mortality at 12 months (4.5% vs 4.0%, $P = .92$) and 24 months (6.2% vs 8.4%, $P = .27$) and 30-day myocardial infarction (1.4% vs 2.0%, $P = .60$) were similar, respectively, between the drug-eluting stent and coronary artery bypass grafting groups. Drug-eluting stents were associated with lower rates of all-cause mortality at 30 days (0.9% vs 2.3%, $P < .001$), stroke (0.4% vs 1.7%, $P < .001$), and 30-day major adverse cardiac and cerebrovascular events (3.6% vs 5.5%, $P < .04$). However, the coronary artery bypass grafting group had a lower incidence of postprocedural myocardial infarction (5.5% vs 4.7%, $P = .03$), repeat revascularization (22.2% vs 4.1%, $P < .001$), and 12-month major adverse cardiac and cerebrovascular events (16.7% vs 10.5%, $P < .001$). Subgroup analysis of patients with multivessel coronary artery disease showed similar results.

Conclusions: Drug-eluting stents are associated with less periprocedural risks but a higher incidence of postprocedural myocardial infarction, repeat revascularization, and 12-month major adverse cardiac and cerebrovascular events compared with coronary artery bypass grafting. (J Thorac Cardiovasc Surg 2011;141:1134-44)

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Coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) are alternative revascularization techniques for symptomatic patients with coronary artery disease.¹ Increased experience with PCI and improved

technological advent have expanded its use in patients with severe coronary artery disease and complex anatomic lesions. A meta-analysis by Mercado and colleagues² comparing randomized controlled trials (RCTs) of PCI with bare metal stents (BMSs) versus CABG demonstrated similar degrees of protection against death, myocardial infarction, and stroke for patients with multivessel coronary artery disease at 1 year after the initial procedure. However, repeat revascularization procedures remained more likely after use of BMSs. A subsequent meta-analysis by Daemen and co-workers³ comparing RCTs on the long-term outcomes between PCI with BMSs and CABG (the Stent of Surgery trial, the Arterial Revascularization Therapies Study, Edstudio Randomizado Argentino de Angioplastia vs Cirugia II, and the Medicine, Angioplasty or Surgery Study II) indicated that BMSs were associated with a long-term safety profile similar to that of CABG but also reinforced higher revascularization and major adverse cardiac and cerebrovascular events (MACCEs) in the BMS group.³

Drug-eluting stents (DES) demonstrate similar rates of death and myocardial infarction but reduced rates of repeat

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Abbreviations and Acronyms

BMS	= bare metal stent
CABG	= coronary artery bypass grafting
CI	= confidence interval
DES	= drug-eluting stent
MACCE	= major adverse cardiac and cerebrovascular event
PCI	= percutaneous coronary intervention
RCT	= randomized controlled trial
RR	= relative risk
SYNTAX	= Synergy Between PCI with Taxus and Cardiac Surgery

revascularization compared with BMSs,⁴ thus increasing the percentage of patients with multivessel disease treated with PCI. However, recent data suggested a higher rate of thrombotic occlusion with DESs than BMSs.⁵ The recent Synergy Between PCI with Taxus and Cardiac Surgery (SYNTAX) trial compared DESs versus CABG in patients with triple-

vessel or left main coronary artery disease.⁶ This RCT demonstrated that at 12 months the rates of death and myocardial infarction were similar between the 2 groups, but DESs were associated with a significantly higher rate of MACCEs (17.8% vs 12.4%, $P = .002$) and lower rate of stroke (0.6% vs 2.2%, $P = .003$). As is generally true with RCTs, the study population is predefined and hence subject to trial design bias. We performed the present systematic review and meta-analysis of the randomized and nonrandomized comparative studies in an attempt to assess the safety and efficacy of DESs versus CABG with the current clinical evidence.

METHODS**Search Strategy**

Electronic searches were performed in 6 databases from their inception to September 2009: Medline, Embase, Pubmed, Cochrane Central Register of Controlled Trials, Cochrane Database of Systematic Reviews, and Database of Abstracts of Review of Effectiveness. To achieve the maximum sensitivity of the search strategy and identify all trials comparing DESs and CABG, we used appropriate free text and thesaurus terms, including “percutaneous coronary intervention,” “coronary angioplasty,” “coronary artery stenting,” “drug-eluting stent,” and “coronary artery bypass

TABLE 1. Summary of 25 comparative studies included in the present systematic review

Reference	Study design	Study population	Study period	No. of patients		Age of cohort (mean $\pm$ SD)		Ejection fraction (mean $\pm$ SD)	
				DES	CABG	DES	CABG	DES	CABG
Ben-Gal and coworkers ⁹	OC	DM	2002–2005	86	86	NA	NA	NA	NA
Ben-Gal and coworkers ¹⁰	OC	LAD	2002–2003	83	83	NA	NA	NA	NA
Briguori and coworkers ¹¹	OC	MVD, LAD, DM, OPCAB	2002–2004	69	149	63 $\pm$ 9	66 $\pm$ 9	54 $\pm$ 12	53 $\pm$ 9
Cheng and coworkers ¹²	OC	LMCAD	2000–2007	94	216	68 $\pm$ 10	67 $\pm$ 9	56 $\pm$ 17	56 $\pm$ 20
Chieffo and coworkers ¹³	OC	LMCAD	2002–2004	107	142	64 $\pm$ 10	68 $\pm$ 10	52 $\pm$ 10	52 $\pm$ 11
Domínguez-Franco and coworkers ¹⁴	OC	MVD, LAD, DM	2000–2004	128	142	68	65	52 $\pm$ 13	54 $\pm$ 14
Gioia and coworkers ¹⁵	OC	LV dysfunction	2002–2005	128	92	69 $\pm$ 10	68 $\pm$ 10	28 $\pm$ 6	27 $\pm$ 8
Hannan and coworkers ¹⁶	OC	MVD	2003–2005	9963	7437	65 $\pm$ 12	66 $\pm$ 11	NA	NA
Hong and coworkers ¹⁷	OC	LAD	2003	119	70	61 $\pm$ 10	61 $\pm$ 10	53 $\pm$ 9	52 $\pm$ 9
Javaid and coworkers ¹⁸	OC	MVD	NA	979	701	66 $\pm$ 11	65 $\pm$ 11	NA	NA
Kukreja and coworkers ¹⁹	OC	MVD, LAD	1997–2003	289	206	63 $\pm$ 10	62 $\pm$ 9	59 $\pm$ 12	61 $\pm$ 13
White and coworkers ²⁰	OC	LMCAD	2003–2005	50	123	72 $\pm$ 15	70 $\pm$ 10	51 $\pm$ 15	52 $\pm$ 10
Li and coworkers ²¹	OC	MVD	2004–2005	1834	1886	58 $\pm$ 10	61 $\pm$ 9	NA	NA
Mäkilä and coworkers ²²	OC	LMCAD	2005–2007	49	238	72 $\pm$ 10	70 $\pm$ 9	55 $\pm$ 12	54 $\pm$ 11
Moshkovitz and coworkers ²³	OC	LAD, OPCAB	2002–2003	116	116	NA	NA	NA	NA
Palmerini and coworkers ²⁴	OC	LMCAD	2003–2006	98	161	81*	78*	50*	53*
Park and coworkers ²⁵	OC	MVD	2003–2005	1547	1495	62 $\pm$ 10	62 $\pm$ 9	59 $\pm$ 9	56 $\pm$ 11
Sanmartín and coworkers ²⁶	OC	LMCAD	2000–2005	96	245	66 $\pm$ 13	66 $\pm$ 10	NA	NA
Serruys and coworkers ⁶	RCT	MVD or LMCAD	2005–2007	903	897	65 $\pm$ 10	65 $\pm$ 10	NA	NA
Tarantini and coworkers ²⁷	OC	MVD, DM	2004–2005	93	127	65 $\pm$ 9	67 $\pm$ 7	62 $\pm$ 14	62 $\pm$ 14
Toutouzas and coworkers ²⁸	OC	LAD, DM	2001–2006	39	38	59 $\pm$ 13	61 $\pm$ 10	48 $\pm$ 7	49 $\pm$ 9
van Domburg and coworkers ²⁹	OC	MVD or LMCAD	2002	798	275	62 $\pm$ 11	64 $\pm$ 11	NA	NA
Yang ³⁰	OC	MVD	2003–2004	235	231	65 $\pm$ 10	65 $\pm$ 10	51 $\pm$ 9	50 $\pm$ 11
Yang and coworkers ³¹	OC	MVD	2003–2005	441	390	63 $\pm$ 10	63 $\pm$ 8	58 $\pm$ 12	53 $\pm$ 14
Yi and coworkers ³²	OC	MVD, OPCAB	2003–2005	194	194	63 $\pm$ 10	62 $\pm$ 9	NA	NA

SD, Standard deviation; DES, drug-eluting stent; CABG, coronary artery bypass grafting; OC, observational cohort; DM, diabetes mellitus; NA, not applicable; LAD, left anterior descending coronary artery; MVD, multivessel disease; OPCAB, off-pump coronary artery bypass; LMCAD, left main coronary artery disease; LV, left ventricle; RCT, randomized controlled trial. *Median.

TABLE 2. Follow-up data of 25 comparative studies included in the present systematic review

Reference	Total patients enrolled (DES/CABG)	Total patients included in study (DES/CABG)	Follow-up periods (mo)	No. of patients at last follow-up (%)
Ben-Gal and coworkers ⁹	518 (176/342)	172 (86/86)	18	Not mentioned
Ben-Gal and coworkers ¹⁰	376 (272/104)	166 (83/83)	22	Not mentioned
Briguori and coworkers ¹¹	355	218 (69/149)	12	218 (100%)
Cheng and coworkers ¹²	Not mentioned	363 (94/216)	27	325 (90%)
Chieffo and coworkers ¹³	Not mentioned	249 (107/142)	12	249 (100%)
Domínguez-Franco and coworkers ¹⁴	Not mentioned	270 (128/142)	24	263 (97.4%)
Gioia and coworkers ¹⁵	230	220 (128/92)	15	220 (100%)
Hannan and coworkers ¹⁶	29,095	17,400 (9963/7437)	18	Not mentioned
Hong and coworkers ¹⁷	Not mentioned	189 (119/70)	6	184 (97%)
Javaid and coworkers ¹⁸	Not mentioned	1680 (979/701)	12	Not mentioned
Kukreja and coworkers ¹⁹	1812	682 (289/206)	36	682 (100%)
White and coworkers ²⁰	Not mentioned	173 (50/123)	6	Not mentioned
Li and coworkers ²¹	Not mentioned	3720 (1834/1886)	36	3679 (98.9%)
Mäkikallio and coworkers ²²	6705†	287 (49/238)	12	Not mentioned
Moshkovitz and coworkers ²³	522 (168/354)	232 (116/116)	12	Not mentioned
Palmerini and coworkers ²⁴	259	259 (98/161)	24	258 (99.6%)
Park and coworkers ²⁵	Not mentioned	3042 (1547/1495)	36	Not mentioned
Sanmartín and coworkers ²⁶	Not mentioned	341 (96/245)	12	334 (98%)
Serruys and coworkers ⁶	4337	1800 (903/897)	12	1740 (96.7%)
Tarantini and coworkers ²⁷	Not mentioned	220 (93/127)	24	220 (100%)
Toutouzas and coworkers ²⁸	314 (191/123)	77 (39/38)	20	77 (100%)
van Domburg and coworkers ²⁹	1073*	1073 (798/275)	15	1073 (100%)
Yang and coworkers ³⁰	Not mentioned	466 (235/231)	25	436 (93.6%)
Yang and coworkers ³¹	1212	831 (441/390)	12	795 (95.7%)
Yi and coworkers ³²	508 (267/241)	388 (194/194)	36	382 (98.5%)

DES, Drug-eluting stent; CABG, coronary artery bypass grafting. *Control group not included. †All patient undergoing coronary angiographic analysis.

grafting.” The reference lists of all retrieved articles were reviewed for further identification of potentially relevant studies.

Study Selection

All studies assessing DESs versus CABG for coronary artery disease published in English were included. We excluded studies that did not include a comparative group that contained CABG as a form of intervention. When centers have published duplicate trials with accumulating numbers of patients or increased lengths of follow-up, only the most recent or complete reports were included for qualitative appraisal and meta-analysis. The publication types of letters, editorials, or reviews were excluded.

Data Extraction and Critical Appraisal

Two investigators (R.P. and T.D.Y.) independently reviewed each included article. Discrepancies between the 2 investigators were resolved by means of discussion and consensus with a senior investigator. The final results were reviewed by 3 senior investigators (M.K.W., P.G.B., and M.P.V.). Time points for analysis of outcomes were 30 days, 1 year, 2 years, and greater than 2 years. Data regarding the end points were extracted and reported separately as all-cause mortality at 30 days, all-cause mortality at 12 months, all-cause mortality at 24 months, all-cause stroke at last follow-up, 30-day myocardial infarction, myocardial infarction at last follow-up, repeat revascularization, 30-day MACCEs, and 12-month MACCEs. Where data were available, the following subgroups for analysis were proposed: vessels involved (left anterior descending coronary artery disease, left main coronary artery disease, and multivessel coronary artery disease), surgical intervention (standard CABG and off-pump coronary artery bypass), and comorbidities (diabetes). Because of the lack of a large number of patients to generate robust clinical conclusions, only multivessel disease was subject to separate analysis.

Statistical Analysis

Meta-analysis was performed by combining the results of reported incidence of morbidity, all-cause mortality, and repeat revascularization. The relative risk (RR) was used as a summary statistic. In this study both fixed- and random-effects models were tested. In a fixed-effects model it was assumed that treatment effect in each study was the same, whereas in a random-effects model it was assumed that there were variations between studies, and the calculated ratios thus had more conservative value.⁷ χ^2 Tests were used to study heterogeneity between trials. The I^2 statistic was used to estimate the percentage of total variation across studies because of heterogeneity rather than chance. The I^2 statistic can be calculated as follows: $I^2 = 100\% \times (Q - df)/Q$, with Q defined as Cochran's heterogeneity statistics and df defined as degree of freedom.⁸ An I^2 value of greater than 50% was considered substantial heterogeneity. If there was substantial heterogeneity, the possible clinical and methodological reasons for this were explored qualitatively. In the present meta-analysis the results using the random-effects model were presented to take into account the possible clinical diversity and methodological variation among studies. Specific analyses considering confounding factors were not possible because raw data were not available. All P values were 2-sided. All statistical analysis was conducted with Review Manager Version 4.2 (Cochrane Collaboration, Software Update, Oxford, United Kingdom).

RESULTS

Quantity and Quality of Trials

A total of 616 references were identified through electronic database searches. After exclusion of duplicate or irrelevant references, 557 potentially relevant articles were retrieved for more detailed evaluation. An additional 3

Review: Drug-eluting Stent versus Coronary Artery Bypass Grafting
 Comparison: 01 DES versus CABG
 Outcome: 01 All-cause Mortality

FIGURE 1. Forest plot of the relative risk (RR) of all-cause mortality after drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) for coronary artery disease. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

potentially relevant reports were identified through scanning of reference lists. When inclusion and exclusion criteria were applied, 36 comparative studies remained for assessment. Four duplicate publications in which investigators reported initial accumulating numbers of participants or increased length of follow-up were excluded. Three studies were excluded because primary outcome data were not

available. Four studies were withdrawn from the analysis because the treatment outcomes contained a mixture of DESs and BMSs. The final 25 most definitive reports (1 RCT⁶ and 24 nonrandomized comparative studies⁹⁻³²) were included for appraisal and data extraction (Table 1).^{6,9-32}

In these 25 studies 34,278 patients were compared, of whom 18,538 underwent PCI with DESs and 15,740

Review: Drug-eluting Stent versus Coronary Artery Bypass Grafting
 Comparison: 01 DES versus CABG
 Outcome: 02 All-cause Stroke at Last Follow-up

FIGURE 2. Forest plot of the relative risk (RR) of all-cause stroke after drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) for coronary artery disease. The studies were analyzed according to the type of morbidity and mortality. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

underwent CABG.^{6,9-32} Seven studies focused on 1640 patients with left anterior descending coronary artery disease.^{10,11,14,17,19,23,28} Six studies compared DESs versus CABG in 1619 patients with left main coronary artery disease.^{12,13,20,22,24,26} Eleven studies assessed 28,693 patients with multivessel disease.^{11,14,16,18,19,21,25,27,30-32} Five studies focused on 950 diabetic patients with coronary artery disease.^{9,11,14,27,28} Three studies compared DESs versus off-pump coronary artery bypass surgery in 838 patients.^{11,23,32}

This comparison represented a selected group of patients, in that not all patients who were initially screened underwent treatments (Table 2).^{6,9-32} Follow-up periods varied among studies and were mostly focused on short-term or midterm outcomes. Twenty-three studies^{6,9-16,18,19,21-32} had at least 1 year of follow-up, 9 studies^{12,14,19,21,24,25,27,30,32} had at least 2 years of follow-up, and 4 studies^{19,21,25,32} provided 3-year follow-up data. Seventeen studies^{6,11-15,17,19,21,24,26-32} reported the numbers of patients available at the last follow-up, and this ranged from 90% to 100%.

Assessment of Morbidity and Mortality

All-cause mortality was lower with DESs at 30 days (0.9% vs 2.3%; RR, 0.50; 95% confidence interval [CI], 0.34–0.75; $P < .001$; $I^2 = 0\%$) and similar between DESs and CABG at 12 months (4.5% vs 4.0%; RR, 0.98; 95% CI, 0.61–1.56; $P = .92$; $I^2 = 61.6\%$) and 24 months (6.2% vs 8.4%; RR, 0.81; 95% CI, 0.55–1.18; $P = .27$; $I^2 = 0\%$; Figure 1). Seventeen studies^{6,11-14,17-22,25-27,30-32} compared the incidence of stroke and demonstrated that DESs were associated with a lower incidence of stroke at last follow-up (0.4% vs 1.7%; RR, 0.33; 95% CI, 0.22–0.50; $P < .001$; Figure 2). There was no substantial heterogeneity among the randomized and nonrandomized studies ($I^2 = 0\%$; heterogeneity $P = .77$). Composite results from 2 studies^{11,32} on DESs versus off-pump coronary artery bypass surgery showed that there was no significant difference in the accumulative stroke rate in 606 patients (0.4% vs 1.7%, respectively; RR, 0.64; 95% CI, 0.04–11.45; $P = .76$; $I^2 = 44.7\%$). Seventeen studies^{9,11-14,17,20,21,23,24,26-32} showed similar accumulative

Review: Drug-eluting Stent versus Coronary Artery Bypass Grafting
 Comparison: 01 DES versus CABG
 Outcome: 03 Myocardial Infarction

FIGURE 3. Forest plot of the relative risk (RR) of myocardial infarction after drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) for coronary artery disease. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

incidence of 30-day myocardial infarction between DESs and CABG (1.4% vs 2.0%; RR, 0.88; 95% CI, 0.54–1.43; $P = .60$), and there was no substantial heterogeneity among the studies ($I^2 = 32\%$; heterogeneity $P = .11$; Figure 3). Twenty-three studies^{6,9-11,13-19,21-32} compared the overall incidence of myocardial infarction at last follow-up and demonstrated that CABG was associated with a lower rate of post-procedural myocardial infarction (5.5% vs 4.7%; RR, 1.11;

95% CI, 1.01–1.22; $P = .03$), and there was no heterogeneity among the randomized and nonrandomized studies ($I^2 = 0\%$; heterogeneity $P = .48$; Figure 3).

Twenty-three studies^{6,9-17,19,21-32} reported the incidence of repeat revascularization and demonstrated that DESs were associated with a higher rate of repeat revascularization (22.2% vs 4.1%; RR, 3.75; 95% CI, 2.80–5.02; $P < .001$; $I^2 = 77.0\%$; Figure 4). Subgroup

Review: Drug-eluting Stent versus Coronary Artery Bypass Grafting
 Comparison: 01 DES versus CABG
 Outcome: 04 Repeat Revascularization

FIGURE 4. Forest plot of the relative risk (RR) of repeat revascularization after drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) for coronary artery disease. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

analyses of 8 studies^{11-13,17,23,26,31,32} with 1 year of follow-up (8.8% vs 2.0%; RR, 3.81; 95% CI, 2.35–6.18; $P < .001$; $I^2 = 17.3\%$), 7 studies^{9,10,15,16,22,28,29} with 2 years of follow-up (28.2% vs 5.0%; RR, 4.27; 95% CI, 2.81–6.49; $P < .001$; $I^2 = 37.5\%$), 7 studies^{14,19,21,24,25,27,30} with more than 2 years of follow-up (12% vs 2.9%; RR, 3.95; 95% CI, 2.20–7.10; $P < .001$; $I^2 = 83.4\%$), and the RCT⁶ (13.5% vs 5.6%; RR, 2.29; 95% CI, 1.67–3.14; $P < .001$) all demonstrated that the

rates of repeat revascularization were significantly higher with DESs compared with those seen after CABG (Figure 4).

Combined results showed that the accumulative incidence of MACCEs at 30 days was significantly lower with DESs (3.6% vs 5.5%; RR, 0.56; 95% CI, 0.32–0.98; $P = .04$; $I^2 = 51.3\%$) but much higher with DESs at 12 months (16.7% vs 10.5%; RR, 1.61; 95% CI, 1.23–2.12; $P < .001$; $I^2 = 68.2\%$; Figure 5).

Review: Drug-eluting Stent versus Coronary Artery Bypass Grafting
 Comparison: 01 DES versus CABG
 Outcome: 05 MACCE

FIGURE 5. Forest plot of the relative risk (RR) of major cardiac and cerebrovascular events (MACCE) after drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) for coronary artery disease. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

Assessment of Multivessel Coronary Artery Disease

In studies^{11,14,16,18,19,21,25,27,30-32} assessing patients with multivessel coronary artery disease, the accumulative rates of 30-day myocardial infarction (0.8% vs 1.1%; RR, 0.99; 95% CI, 0.51–1.51; $P = .64$; $I^2 = 0\%$) and myocardial infarction at last follow-up (5.9% vs 5.1%; RR, 1.17; 95% CI, 0.92–1.49; $P = .19$; $I^2 = 21.1\%$) were similar between the DES group and the CABG group (Figure 6). The accumulative incidence of repeat revascularization was higher in the DES group compared with that seen in the CABG group (24.4% vs 4.2%; RR, 4.03; 95% CI, 2.70–6.01; $P < .001$; $I^2 = 84.4\%$). The accumulative incidence of MACCEs was lower in the DES group compared with that in the CABG group at 30 days (2.0% vs 4.1%; RR, 0.58; 95% CI, 0.35–0.97; $P = .04$; $I^2 = 0\%$) but was higher in the DES group at 12 months (16.1% vs 8.6%; RR, 1.74; 95% CI, 1.24–2.44; $P = .001$; $I^2 = 55.1\%$).

DISCUSSION

Since 2002, DESs have been shown to reduce repeat revascularization rates without affecting the short- and long-

term safety of the treatment.^{4,33} The recently published SYNTAX trial demonstrated that in patients with triple-vessel or left main coronary artery disease at 12 months, the rates of death and myocardial infarction were similar between the DES and CABG groups, and DESs were associated with a lower rate of stroke (0.6% vs 2.2%, $P = .003$).⁶ However, for the primary end point, 12-month MACCEs, the noninferiority of use of DESs compared with CABG was not demonstrated; CABG was proved to be superior (17.8% vs 12.4%, $P = .002$).⁶ Other large-scale RCTs, such as Future Revascularization Evaluation in Patients with Diabetes: Optimal Management of Multivessel Disease and Coronary Artery Revascularization in Diabetics, are ongoing.

The present meta-analysis demonstrated the following key findings: the accumulative incidences of all-cause mortality at 12 and 24 months and 30-day myocardial infarction were similar between the 2 groups. DESs were associated with lower rates of all-cause mortality at 30 days, stroke, and 30-day MACCEs; however, the CABG group had a lower incidence of overall myocardial infarction at last follow-up, repeat revascularization, and 12-month

Review: Drug-eluting Stent versus Coronary Artery Bypass Grafting
 Comparison: 01 DES versus CABG
 Outcome: 06 Revascularization of Multi-vessel Coronary Artery Disease

FIGURE 6. Forest plot of the relative risk (RR) of 30-day myocardial infarction, myocardial infarction at last follow-up, repeat revascularization, and 30-day and 12-month major cardiac and cerebrovascular events (MACCE) after drug-eluting stents (DES) versus coronary artery bypass grafting (CABG) for multi-vessel coronary artery disease. The estimate of the RR of each trial corresponds to the middle of the squares, and the horizontal line shows the 95% confidence interval (CI). On each line, the numbers of events as a fraction of the total number randomized are shown for both treatment groups. For each subgroup, the sum of the statistics, along with the summary RR, is represented by the middle of the solid diamonds. A test of heterogeneity between the trials within a subgroup is given below the summary statistics.

MACCEs. Subgroup analysis on patients with multivessel coronary artery disease showed similar results. The present meta-analysis emphasized that in assessing use of DESs versus CABG, one must consider the relative merits of the CABG procedure with lasting benefits against less-invasive DESs with traditionally higher rates of reintervention.

Although procedural success rates are high and periprocedural complication rates are relatively low with PCI, rates of restenosis, which might require reintervention, have traditionally been a significant limitation of coronary stenting. The advent of antiproliferative DESs has dramatically reduced target-lesion and target-vessel restenosis and the incidence of repeat revascularization compared with BMSs.^{4,33,34} However, there is still a lack of high-level clinical evidence on the use of DESs for patients with multivessel disease. Because of the aging population in Western countries and a growing incidence of coronary artery disease in the developing world, multivessel revascularization is increasing. Most of these patients have significant comorbidities. Hannan and colleagues¹⁶ identified 17,400 patients with multivessel disease from a large-scale registry and demonstrated that CABG was associated with lower 18-month rates of repeat revascularization, death, and/or myocardial infarction compared with DESs. The present meta-analysis on both randomized and nonrandomized comparative studies confirmed that CABG was still more effective than DESs in reducing 12-month MACCEs and the need for target-vessel revascularization and confirmed the advantages of CABG as the standard of care for patients with multi-vessel coronary artery disease in real-world clinical practice.

It needs to be acknowledged that (1) the data included in the present meta-analysis were mostly extrapolated from nonrandomized studies, which are subject to selection bias; (2) this comparison represented a subset of patients who were initially enrolled or screened for treatments; and (3) although not clearly stated in each study, from the SYNTAX registry, we know that at least one third of patients undergoing CABG are ineligible for PCI because of complexity of lesions, and in the absence of comparison of the baseline characteristics among all the studies, it is reasonable to assume that there were confounding factors in allocating patients to undergo either CABG or PCI and patients who underwent CABG had more complex disease. In the current meta-analysis the accumulative results from the observational cohorts demonstrated concordant results to the SYNTAX trial,⁶ and this might reflect the outcomes in a more heterogeneous group of patients in clinical practice. As with any meta-analysis, the conclusions drawn from such data are subject to the limitations of the original included studies and the differences in patients and techniques among different centers. The validity of the effect estimates in the studies depends on factors such as the recruitment of inception cohorts, patient selection criteria,

and length of follow-up. Clinical follow-up to date is still limited at the short-term to midterm threshold, which might capture most of the repeat procedures needed with stent technology, but does not have sufficient follow-up to capture even half of the graft failures, which would require 10 years. It is understood that the survival benefit of CABG could not be fully demonstrated when most studies only had limited follow-up. Large-scale RCTs with long follow-up will provide complementary data comparing DESs and CABG, especially in the context of late stent thrombosis, but the rate of technological advancement is likely to make the results of such trials obsolete.

Although DESs are associated with less periprocedural risks, the current literature suggests that DESs are inferior to CABG in terms of a higher incidence of postprocedural myocardial infarction, repeat revascularization, and 12-month MACCEs.

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