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Drug-Eluting Versus Bare-Metal Stents in Unprotected Left Main Coronary Artery Stenosis

A Meta-Analysis

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Objectives We undertook a meta-analysis to assess outcomes for drug-eluting stents (DES) and bare-metal stents (BMS) in percutaneous coronary intervention for unprotected left main coronary artery (ULMCA) stenosis.

Background Uncertainty exists regarding the relative performance of DES versus BMS in percutaneous coronary intervention for unprotected left main coronary stenosis.

Methods Of a total of 838 studies, 44 met inclusion criteria (n = 10,342). The co-primary end points were mortality, myocardial infarction (MI), target vessel/lesion revascularization (TVR/TLR), and major adverse cardiac events (MACE: mortality, MI, TVR/TLR).

Results Event rates for DES and BMS were calculated at 6 to 12 months, at 2 years, and at 3 years. Crude event rates at 3 years were mortality (8.8% and 12.7%), MI (4.0% and 3.4%), TVR/TLR (8.0% and 16.4%), and MACE (21.4% and 31.6%). Nine studies were included in a comparative analysis (n = 5,081). At 6 to 12 months the adjusted odds ratio (OR) for DES versus BMS were: mortality 0.94 (95% confidence interval [CI]: 0.06 to 15.48; p = 0.97), MI 0.64 (95% CI: 0.19 to 2.17; p = 0.47), TVR/TLR 0.10 (95% CI: 0.01 to 0.84; p = 0.01), and MACE 0.34 (95% CI: 0.15 to 0.78; p = 0.01). At 2 years, the OR for DES versus BMS were: mortality 0.42 (95% CI: 0.28 to 0.62; p < 0.01), MI 0.16 (95% CI: 0.01 to 3.53; p = 0.13), and MACE 0.31 (95% CI: 0.15 to 0.66; p < 0.01). At 3 years, the OR for DES versus BMS were: mortality 0.70 (95% CI: 0.53 to 0.92; p = 0.01), MI 0.49 (95% CI: 0.26 to 0.92; p = 0.03), TVR/TLR 0.46 (95% CI: 0.30 to 0.69; p < 0.01), and MACE 0.78 (95% CI: 0.57 to 1.07; p = 0.12).

Conclusions Our meta-analysis suggests that DES is associated with favorable outcomes for mortality, MI, TVR/TLR, and MACE as compared to BMS in percutaneous coronary intervention for unprotected left main coronary artery stenosis. (J Am Coll Cardiol Intv 2010;3:602–11) © 2010 by the American College of Cardiology Foundation

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Unprotected left main coronary artery stenosis (LMCA) is associated with poor clinical outcomes. Studies have shown improved long-term outcomes in those who undergo surgical revascularization as compared to optimal medical therapy alone (1,2). This is the basis for the American College of Cardiology/American Heart Association class I recommendation for coronary artery bypass graft surgery (CABG) in patients with ≥50% left main stenosis (3).

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Early percutaneous attempts at revascularization with balloon-only angioplasty were associated with suboptimal clinical outcomes (4). This led to an American College of Cardiology/American Heart Association Class III (contraindicated) guidelines recommendation for percutaneous coronary intervention (PCI) in CABG-eligible patients (5). The subsequent advent of coronary stents, which reduced periprocedural risks and improved clinical outcomes, renewed interest in unprotected LMCA PCI. This interest was further fueled by the subsequent introduction of drug-eluting stents (DES), which led to substantially lower rates of restenosis in coronary lesions (6,7). Based on improved clinical outcomes, the most recent American College of Cardiology/American Heart Association guidelines have given unprotected LMCA PCI a class IIb recommendation (8).

However, there remains some clinical uncertainty over the ideal stent type for unprotected LMCA PCI. The use of DES in the left main position is considered an off-label application; previous studies have identified increased adverse events for such off-label applications (9). Additionally, although the reduction in restenosis seen with DES use is particularly attractive for unprotected LMCA PCI, the large caliber of most left main arteries could attenuate this benefit. Finally, concern exists over potentially increased rates of late stent thrombosis with DES, which has serious implications in unprotected LMCA PCI (10).

We performed a meta-analysis of the current literature to assess outcomes of PCI in unprotected LMCA and to compare the relative performance of DES and bare-metal stents (BMS) in this application.

Methods

Search strategy. PubMed, clinicaltrials.gov, and BioMed Central databases were searched from January 2000 to September 2009; there were no language restrictions. Search terms included "left main," "coronary," "intervention," and "stenting." Citations were screened and evaluated using the established inclusion/exclusion criteria at the abstract level by 2 operators (S.P. and N.B.), and relevant studies were retrieved as full manuscripts. Inclusion criteria were: 1) involving unprotected left main disease; 2) involving BMS or DES; and 3) involving at least 20 patients in the overall study cohort. Exclusion criteria were defined as: 1) unpublished studies; 2) abstract only; 3) angioplasty without stenting; 4) ST-segment elevation myocardial infarction; 5) cardiogenic shock; 6) experimental devices; 7) non-English studies; and 8) studies not reporting relevant clinical outcomes. Data regarding patient demographics and clinical outcomes were then entered into a database.

End points. The co-primary end points were mortality, myocardial infarction (MI), target vessel/target lesion revascularization (TVR/TLR), and major adverse cardiac events (MACE), which were defined as mortality, MI, and TVR/TLR. These end points were reported for the following time periods post-PCI: 6 to 12 months, 2 years, and 3 years. Data for all end points at each time period were not available for every study.

Statistical analysis. Crude event rates were reported for mortality, MI, and TVR/TLR for both DES and BMS. Because these estimates were based, in part, on studies for which a causal link between stent type and outcome was not established, direct comparison of rates is not appropriate, and rates can only be seen as descriptive in nature. Subsequent comparative analysis was performed evaluating studies that provided adjusted outcomes on relevant end points or were randomized according to stent types; odds ratios (OR) were reported for this analysis. When both hazard ratios (HR) and OR were reported as end points across trials, they were combined, assuming that the follow-up was fairly complete (and thus the HR would be similar to the expected OR). Similarly, Kaplan-Meier rates and percentages were combined when 1 of the 2 was not available for an end point. Several end points did not meet the assumption of homogeneity of rates across studies, and thus random effects modeling techniques were used to combine rates and calculate confidence intervals. Comprehensive Meta Analysis software, version 2.2.048 (Biostat Inc., Englewood, New Jersey), was used for all analyses (11).

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CABG = coronary artery bypass graft surgery
CI = confidence interval
DES = drug-eluting stent(s)
HR = hazard ratio
LMCA = left main coronary artery stenosis
MACE = major adverse cardiac events
MI = myocardial infarction
OR = odds ratio
PCI = percutaneous coronary intervention
TLR = target lesion revascularization
TVR = target vessel revascularization

Results

Database searches retrieved an initial 838 studies, of which 75 were deemed relevant; 31 of these studies were eventually excluded (12–42). A final 44 studies meeting inclusion/exclusion criteria were included in the analysis (43–86),

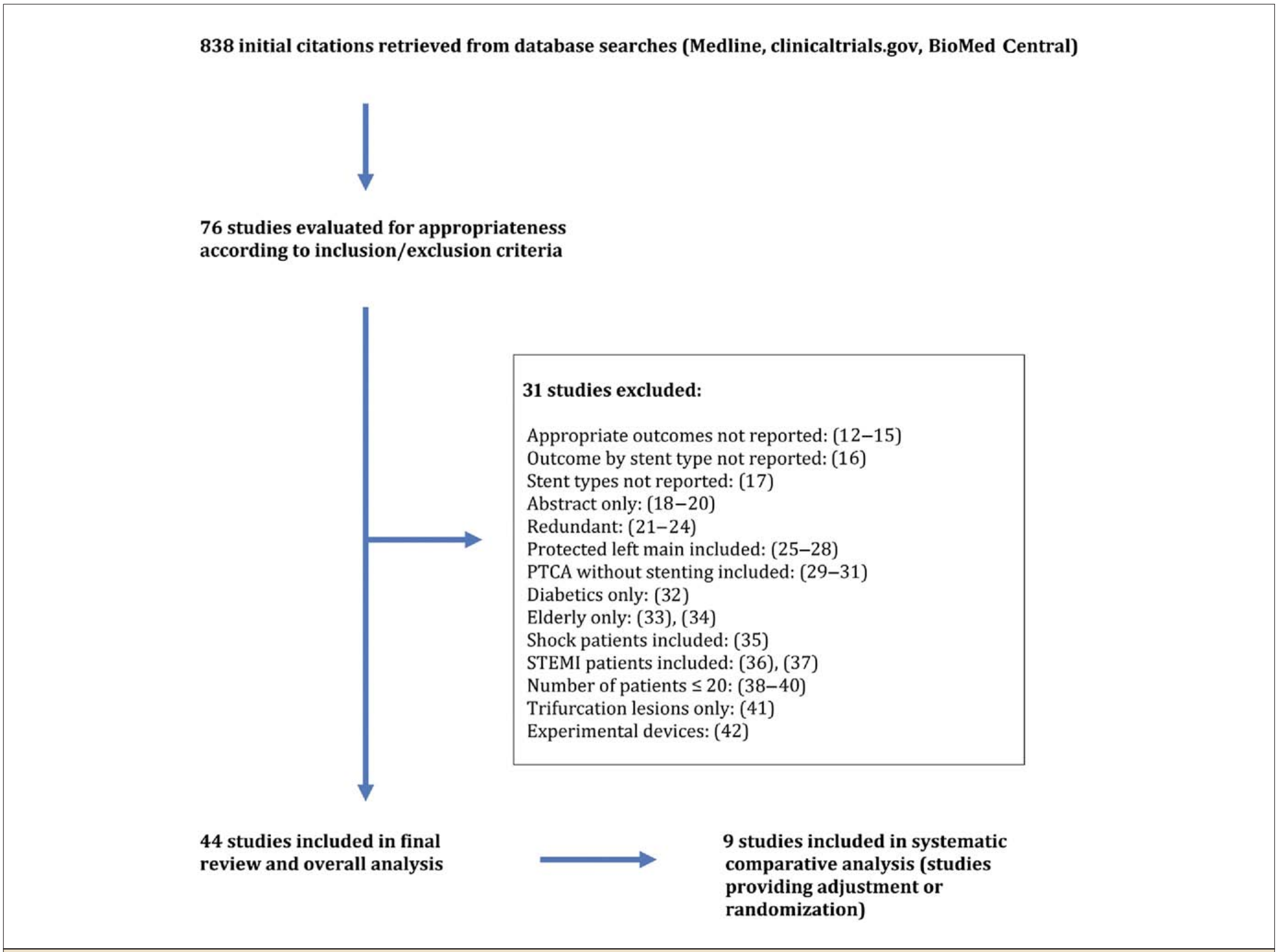

Figure 1. **Methods**

Diagram outlining inclusion/exclusion process for studies incorporated into the final overall and comparative analyses. PTCA = percutaneous transluminal coronary angioplasty; STEMI = ST-segment elevation myocardial infarction.

consisting of 10,342 patients (Fig. 1). Studies fell into general categories involving: 1) use of only BMS (43–47); 2) use of only DES (48–68); 3) comparative studies of BMS versus DES (56,69–80); or 4) comparison studies of PCI versus CABG (81–86) (Table 1).

Patient demographics in the group undergoing BMS placement were generally similar to those undergoing DES placement (Table 2). There was incomplete reporting of baseline demographics across studies. Medication profiles, including duration of antiplatelet drug therapy, were inconsistently reported.

Estimates of rates for mortality, MI, and TVR/TLR at each of the 3 recorded time points are displayed in Table 3. The rates of events are numerically higher for patients treated with BMS for most end points, at most time points. However, without adjustment, the significance and/or relevance of the differences noted cannot be fully determined. As expected, the overall rates of events are higher in patients undergoing unprotected LMCA PCI than in conventional PCI patients.

Subsequent analysis was performed on those studies comparing DES and BMS and providing either adjusted event rates, or randomization according to stent type. Of the 12 comparative studies, 9 studies (33,69–72,74,77–79) reported relevant end points, consisting of 5,081 patients (Table 4). Most utilized propensity scoring for adjustment. Comparative event estimates for DES versus BMS were calculated (Table 5). At 6 to 12 months, the OR for mortality was 0.94 (95% confidence interval [CI]: 0.06 to 15.48; $p = 0.97$) and for MI was 0.64 (95% CI: 0.19 to 2.17; $p = 0.47$). The OR clearly favored DES for TVR/TLR (0.10; 95% CI: 0.01 to 0.84; $p = 0.01$) and MACE (0.34; 95% CI: 0.15 to 0.78; $p = 0.01$) at 6 to 12 months. At 2 years, the OR favored DES for mortality (0.42; 95% CI: 0.28 to 0.62; $p < 0.01$) and MACE (0.31; 95% CI: 0.15 to 0.66; $p < 0.01$); the OR for MI did not reach statistical

Table 1. Included Studies

First Author (Ref. #)	Year	Design	Stent Type	n	DES (n)	BMS (n)	Location	Follow-Up (Months)
BMS-only studies: 5								
Black et al. (43)	2001	Retrospective cohort study	BMS	92	0	92	Europe	7 ± 5
Kelley et al. (44)	2003	Retrospective cohort study	BMS	43	0	43	U.S./Europe	12
Lee et al. (45)	2007	Prospective cohort study	BMS	187	0	187	Asia	71 ± 26
Silvestri et al. (46)	2000	Prospective cohort study	BMS	140	0	140	Europe	12
Takagi et al. (47)	2002	Prospective cohort study	BMS	64	0	64	Europe	31 ± 23
DES-only studies: 21								
Agostoni et al. (48)	2005	Retrospective cohort study	DES	58	58	0	Europe	15
Arampatzis et al. (49)	2003	Retrospective cohort study	DES	31	31	0	Europe	5.1 ± 1.8
Chieffo et al. (50)	2007	Retrospective cohort study	DES	147	147	0	U.S./Asia/ Europe	30 ± 10
Chieffo et al. (51)	2008	Retrospective cohort study	DES	731	731	0	U.S./Asia/ Europe	29 ± 13
Cherradi et al. (52)	2008	Prospective cohort study	DES	101	101	0	Europe	12 ± 3
de Lezo et al. (53)	2004	Prospective cohort study	DES	52	52	0	Europe	12
Ge et al. (54)	2007	Retrospective cohort study	DES	70	70	0	Asia/Europe	12
Khattab et al. (55)	2007	Prospective cohort study	DES	82	82	0	Europe	36
Kim et al. (56)	2006	Retrospective cohort study	DES	116	116	0	Asia	18
Kim et al. (57)	2008	Retrospective cohort study	DES	63	63	0	U.S.	12 ± 8
Lee et al. (58)	2005	Nonrandomized study (SES vs. PES)	DES	54	54	0	Asia	6
Lozano et al. (59)	2004	Prospective cohort study	DES	42	42	0	Europe	11
Mehilli et al. (60)	2009	Randomized controlled trial (SES vs. PES)	DES	607	607	0	Europe	24
Meliga et al. (61)	2008	Retrospective cohort study	DES	358	358	0	U.S./Europe	36
Migliorini et al. (62)	2006	Prospective cohort study	DES	101	101	0	Europe	10 ± 6
Price et al. (63)	2006	Prospective cohort study	DES	50	50	0	U.S.	9
Sanmartin et al. (64)	2007	Prospective cohort study	DES	100	100	0	Europe	12
Sheiban et al. (65)	2007	Prospective cohort study	DES	85	85	0	Europe	20 ± 7
Vaquerizo et al. (66)	2009	Prospective cohort study	DES	291	291	0	Europe	24
Vecchio et al. (67)	2007	Prospective cohort study	DES	114	114	0	Europe	17 ± 9
Wood et al. (68)	2008	Retrospective cohort study	DES	100	100	0	U.S.	28
BMS and DES studies: 12								
Cheiffo et al. (69)	2005	Nonrandomized study	DES vs. BMS	149	85	64	Europe	6
Erglis et al. (70)	2007	Randomized controlled trial	DES vs. BMS	103	53	50	Australia	6
Gao et al. (71)	2008	Nonrandomized study	DES vs. BMS	424	220	224	Asia	15
Han et al. (72)	2009	Nonrandomized study	DES vs. BMS	287	178	109	Asia	35 ± 14
Hertting et al. (73)	2008	Nonrandomized study	DES vs. BMS	54	16	38	Europe	24
Kim et al. (74)	2009	Nonrandomized study	DES vs. BMS	1,217	864	353	Asia	36
Palmerini et al. (75)	2008	Nonrandomized study	DES vs. BMS	1,453	1,111	342	Europe	24
Park et al. (76)	2005	Nonrandomized study	DES vs. BMS	123	102	121	Asia	12
Schrale et al. (77)	2008	Retrospective cohort study	DES and BMS	100	55	45	Europe	21 ± 14
Tamburino et al. (78)	2009	Nonrandomized study	DES vs. BMS	849	611	238	Europe	36
Tamburino et al. (79)	2009	Nonrandomized study	DES vs. BMS	479	334	145	Europe	36
Wood et al. (80)	2005	Nonrandomized study	DES vs. BMS	161	61	100	U.S.	12
PCI/CABG studies: 6								
Buszman et al. (81)	2008	Randomized controlled trial	CABG vs. PCI	52	18	34	Europe	28 ± 10
Chieffo et al. (82)	2006	Nonrandomized study	CABG vs. DES	107	107	0	Europe	12
Makikallio et al. (83)	2008	Nonrandomized study	CABG vs. DES	49	49	0	Europe	12 ± 6
Palmerini et al. (84)	2006	Nonrandomized study	CABG vs. PCI	157	94	63	Europe	14
Sanmartin et al. (85)	2007	Nonrandomized study	CABG vs. DES	96	96	0	Europe	13 ± 8
Seung et al. (86)	2008	Randomized controlled trial	CABG vs. PCI	603	396	207	Asia	34

BMS = bare-metal stent(s); CABG = coronary artery bypass graft; DES = drug-eluting stent(s); PCI = percutaneous coronary intervention.

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Table 2. Baseline Patient Demographics for Studies Included in the Overall Analysis

	DES		BMS	
	n	Percent (95% CI)	n	Percent (95% CI)
Age, yrs*	4,768	67.5 (65.8–69.3)	1,621	67.9 (66.0–69.7)
Men	6,464	74 (73–75)	2,091	71 (69–73)
DM	6,691	28 (27–29)	2,170	22 (20–23)
Insulin-dependent DM	85	11.0 (4.2–17.8)	63	8.9 (1.9–15.9)
Hypertension	6,297	65 (64–67)	2,032	53 (51–55)
Hypercholesterolemia	6,111	58 (57–59)	1,892	39 (36–41)
History of prior MI	3,036	23 (21–24)	1,165	12 (10–14)
History of PCI	1,912	19 (18–21)	794	13 (10–15)
COPD	1,962	9.4 (7.9–10.9)	996	1.6 (0.8–2.4)
Renal insufficiency	3,570	7.7 (6.8–8.6)	1,241	4.5 (3.4–5.6)
Peripheral arterial disease	1,168	6.8 (5.5–8.2)	560	0.9 (0.03–1.9)

*Age is represented as mean (95% CI). n refers to the number of patients within the studies who contributed to the estimate of interest. Rates are the estimated percent of patients with the characteristic and associated 95% confidence intervals (CIs).

COPD = chronic obstructive pulmonary disease; DM = diabetes mellitus; MI = myocardial infarction; other abbreviations as in Table 1.

significance (0.16; 95% CI: 0.01 to 3.53; p = 0.13). The OR for TVR/TLR at 2 years could not be estimated due to a lack of reported data. Findings at 3 years favored DES for mortality (0.70; 95% CI: 0.53 to 0.92; p = 0.01), MI (0.49; 95% CI: 0.26 to 0.92; p = 0.03), and TVR/TLR (0.46; 95% CI: 0.30 to 0.69; p < 0.01); the OR for MACE did not reach statistical significance (0.78; 95% CI: 0.57 to 1.07; p = 0.12).

Discussion

Percutaneous coronary intervention is increasingly being performed for lesions previously considered contraindicated, such as unprotected LMCA. Given the lower rates of restenosis reported with DES in PCI of standard coronary lesions, there has been a trend toward their use in unprotected LMCA PCI. However, the superiority of DES over BMS for unprotected LMCA has not been clearly established.

We reviewed the literature on unprotected LMCA PCI to compare outcomes between DES and BMS. We identified 44 studies involving PCI for unprotected LMCA as a source for crude event rates. Crude event rates were lower for DES than BMS for mortality, TVR/TLR, and MACE at 6 to 12 months, 2 years, and 3 years, but appeared equivalent for MI at these same time points. However, these rates are unadjusted, rendering them prone to selection bias and confounding.

To address this, we performed a subsequent analysis involving studies that provided adjusted event rates or randomized patients according to stent type (DES vs.

Table 3. Estimated Cumulative Event Rates by Stent Type in the Overall Analysis

	Stent Type	6–12 Months	2 Years	3 Years
Mortality	DES	5.94% (4.73%–7.44%) n = 2,691	7.89% (6.07%–10.20%) n = 4,430	8.80% (6.20%–12.34%) n = 2,912
	BMS	7.24% (3.51%–14.33%) n = 763	14.14% (8.96%–21.62%) n = 1,266	12.71% (6.94%–22.15%) n = 959
MI	DES	6.26% (4.71%–8.27%) n = 2,356	3.90% (1.98%–7.55%) n = 2,182	4.04% (2.33%–6.91%) n = 2,516
	BMS	9.97% (6.09%–15.90%) n = 157	3.06% (1.18%–7.69%) n = 607	3.43% (1.87%–6.21%) n = 752
TVR/TLR	DES	7.83% (5.95%–10.24%) n = 2,257	10.20% (8.55%–12.13%) n = 4,772	8.03% (5.62%–11.37%) n = 2,912
	BMS	16.95% (12.92%–21.92%) n = 985	16.15% (13.93%–18.66%) n = 1241	16.40% (12.23%–21.64%) n = 959
MACE	DES	15.87% (12.93%–19.32%) n = 2,593	18.99% (14.92%–23.86%) n = 2,623	21.43% (14.85%–29.91%) n = 1,652
	BMS	39.31% (31.68%–47.50%) n = 554	32.69% (17.72%–52.26%) n = 441	31.60% (23.15%–41.47%) n = 399

n refers to the number of patients within the studies who contributed to the estimate of interest. Rates are the estimated percent of patients with the event and associated 95% CIs.

MACE = major adverse cardiac events; TLR = target lesion revascularization; TVR = target vessel revascularization; other abbreviations as in Tables 1 and 2.

Table 4. Comparative Studies of DES Versus BMS

First Author (Ref. #)	Design	Method of Adjustment	DES (n)	BMS (n)	Follow-Up (Months)	Adjusted Point Estimate at Follow-Up			
						Mortality	MI	TVR/TLR	MACE
Chieffo et al. (69)	Nonrandomized study	Propensity score matching	85	64	6	N/A	N/A	OR: 0.28 (0.09–0.81) p = 0.01	OR: 0.27 (0.09–0.73) p = 0.007
Erglis et al. (70)	Randomized controlled trial	Randomization	53	50	6	OR: 0.94 (0.06–15.48) p = 1.00	OR: 0.64 (0.19–2.17) p = 0.47	OR: 0.10 (0.01–0.84) p = 0.01	OR: 0.36 (0.13–0.96) p = 0.04
Gao et al. (71)	Prospective cohort study (DES compared with historical BMS cohort)	Propensity score matching	220	224	15	N/A	N/A	N/A	OR: 0.49 (0.26–0.94) p = 0.032
Han et al. (72)	Prospective cohort study	Propensity score matching	178	109	35 ± 14	OR: 0.25 (0.08–0.81) p < 0.01	OR: 0.16 (0.01–3.53) p = 0.13	OR: 0.26 (0.08–0.83) p < 0.001	OR: 0.23 (0.09–0.56) p < 0.001
Kim et al. (74)	Prospective cohort study	Weighting with propensity score	864	353	36	HR: 0.86 (0.50–1.47) p = 0.569	N/A	HR: 0.32 (0.17–0.61) p < 0.001	HR: 0.81 (0.54–1.21) p = 0.31
Palmerini et al. (33)	Nonrandomized study	Propensity score as a covariate	1,111	342	24	HR: 0.48 (0.32–0.74) p = 0.002	N/A	N/A	N/A
Schrale et al. (77)	Retrospective cohort study	Multivariate Cox regression	55	45	21 ± 14	HR: 0.23 (0.06–0.91) p = 0.034	N/A	N/A	N/A
Tamburino et al. (78)	Nonrandomized study	Propensity score matching	611	238	36	HR: 0.75 (0.52–1.12) p = 0.17	HR: 0.49 (0.26–0.92) p = 0.03	HR: 0.46 (0.29–0.74) p = 0.001	N/A
Tamburino et al. (79)	Nonrandomized study	Propensity score matching	334	145	36	HR: 0.51 (0.30–0.86) p = 0.01	N/A	HR: 0.79 (0.33–1.90) p = 0.39	HR: 0.73 (0.44–1.21) p = 0.22

n refers to the number of patients within the studies who contributed to the estimate of interest. Odds ratios and hazard ratios are reported with 95% CIs.

HR = hazard ratio; OR = odds ratio; other abbreviations as in Tables 1 to 3.

Table 5. Cumulative OR for Comparative Studies (DES Versus BMS)

	Time	Contributing Studies First Author (Ref. #)	DES (n)	BMS (n)	OR (95% CI)	p Value
Mortality	6–12 months	Erglis et al. (70)	53	50	0.94 (0.06–15.48)	0.97
	2 yrs	Han et al. (72) Palmerini et al. (33) Schrale et al. (77)	1,344	496	0.42 (0.28–0.62)	<0.01
	3 yrs	Kim et al. (74) Tamburino et al. (78) Tamburino et al. (79)	1,809	736	0.70 (0.53–0.92)	0.01
MI	6–12 months	Erglis et al. (70)	53	50	0.64 (0.19–2.17)	0.47
	2 yrs	Han et al. (72)	178	109	0.16 (0.01–3.53)	0.13
	3 yrs	Tamburino et al. (78)	611	238	0.49 (0.26–0.92)	0.03
TVR/TLR	6–12 months	Erglis et al. (70)	53	50	0.10 (0.01–0.84)	0.01
	2 yrs	No studies	—	—	—	—
	3 yrs	Kim et al. (74) Tamburino et al. (78) Tamburino et al. (79)	1,809	736	0.46 (0.30–0.69)	<0.01
MACE	6–12 months	Chieffo et al. (69) Erglis et al. (70)	138	114	0.34 (0.15–0.78)	0.01
	2 yrs	Gao et al. (71) Han et al. (72)	398	333	0.31 (0.15–0.66)	<0.01
	3 yrs	Kim et al. (74) Tamburino et al. (79)	1,198	498	0.78 (0.57–1.07)	0.12

n refers to the number of patients within the studies who contributed to the estimate of interest. Odds ratios (ORs) are reported with 95% CIs.
Abbreviations as in Tables 1 to 4.

BMS). Although event rates at 6 to 12 months favored DES, the sample size was small, involving predominantly 1 study (70). At 2 and 3 years post-PCI, the sample size was larger, and improved outcomes with DES over BMS were observed for mortality, MI, TVR/TLR, and MACE. Statistically significant differences were observed in most cases.

Although the finding of lower TVR/TLR rates is consistent with the known performance of DES, no study to date has shown a consistent mortality benefit with DES over BMS in unprotected LMCA PCI. The reason for the lower mortality rate in the DES group seen in our meta-analysis is unclear. It may be that DES, with known lower rates of restenosis, provides a true advantage over BMS. In the critical left main position, a small or moderate degree of restenosis could theoretically precipitate critical ischemia. Alternatively, this finding could be due to methodological issues. Selection bias may have favored DES: patients with fewer medical comorbidities may have preferentially undergone DES placement. A review of overall patient demographics in our analysis does not support this, as similar rates of cardiac risk factors were found between both groups (Table 2). An alternative explanation may relate to a procedural learning curve, as operators may have become more technically proficient at unprotected LMCA PCI by the time DES were favored. Finally, as medication profiles at baseline and follow-up were not consistently reported, it is possible that the benefit seen with DES could be due, in part, to a longer duration of dual antiplatelet drug therapy as compared with BMS. Similarly, patients deemed to be poor candidates for long-term dual or triple antiplatelet therapy may have been denied treatment with DES.

A recent meta-analysis of patients undergoing DES for unprotected LMCA by Biondi-Zoccai et al. (87) noted similar findings, reporting an adjusted OR of 0.34 for both MACE and TVR, favoring DES over BMS. This meta-analysis was performed through 2006 and included far fewer patients than our analysis (206 DES patients, 190 BMS patients). Since our analysis was performed, Buszman et al. (88) have reported on the long-term follow-up of a group of 252 patients from the LE MANS (Left Main Coronary Artery Stenting) registry. Their results mirror ours. Unmatched analysis showed a significantly lower rate of major adverse cardiovascular or cerebral events with DES as compared with BMS at 4-year follow-up (14.9% vs. 25.9%, $p = 0.039$); subsequent propensity matched analysis showed similar results. Buszman et al. (88) noted that mortality rates favored DES, although this did not reach statistical significance (9.6% vs. 13.3%, p = NS). In a subgroup of patients with distal unprotected LMCA, however, DES, when compared with BMS, was associated with a statistically significant lower mortality rate ($p = 0.03$). Results from the left main subset of the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial (89) were presented at Transcatheter Cardiovascular Therapeutics 2008 conference. Reported 12-month DES event rates were similar to our cumulative crude estimates, with a rate of 4.2% for mortality, 4.3% for MI, and 15.8% for major cardiac or cerebrovascular adverse events (90). As these results have yet to be published, they were not included in our analysis. The SYNTAX study did not include a BMS arm and thus would not influence our comparative analysis.

Currently, there are no large, randomized controlled clinical trials comparing DES to BMS in unprotected LMCA. Two ongoing studies comparing PCI with DES to CABG for unprotected LMCA (PRECOMBAT [Premier of Randomized Comparison of Bypass Surgery versus Angioplasty Using Sirolimus-Eluting Stent in Patients with Left Main Coronary Artery Disease] and the recently announced EXCEL trial [Evaluation of Xience Prime versus Coronary Artery Bypass Surgery for Effectiveness of Left Main Revascularization]) do not include a comparison with BMS. Therefore, our meta-analysis may offer evidence to guide clinical practice.

Study limitations. Our study has clear limitations. The limitations of the meta-analytical approach are well known and documented (91); the meta-analytical approach with observational data is even more fraught with limitations (92). The inclusion of only published studies makes our analysis prone to publication bias. Our results, particularly the crude event rates, are prone to confounding and selection bias and thus direct comparison of these overall rates was not performed. We did not have data for all studies at each time period; therefore, this limits comparison of rates across time within a specific end point. Finally, we were unable to control for the specific type of DES or BMS used, as some studies suggest heterogeneous outcomes within the stent types.

Conclusions

The results of this meta-analysis suggest that DES is associated with favorable outcomes as compared with BMS in unprotected LMCA PCI. The improved outcomes observed when DES is compared with BMS support a continued re-evaluation of the role of PCI for the treatment of unprotected LMCA.

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