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Nine-year clinical outcomes of drug-eluting stents *vs.* bare metal stents for large coronary vessel lesions

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Abstract

Objectives To evaluate the very long-term safety and effectiveness of drug-eluting stents (DES) compared to bare-metal stents (BMS) for patients with large coronary vessels. **Methods** From April 2004 to October 2006, 2407 consecutive patients undergoing de novo lesion percutaneous coronary intervention with reference vessel diameter greater than or equal to 3.5 mm at Fu Wai Hospital in Beijing, China, were prospectively enrolled into this study. We obtained 9-year clinical outcomes including death, myocardial infarction (MI), thrombosis, target lesion revascularization (TLR), target vessel revascularization (TVR), and major adverse cardiac events (MACE, the composite of death, MI, and TVR). We performed Cox's proportional-hazards models to assess relative risks of all the outcome measures after propensity match. **Results** After propensity scoring, 514 DES-treated patients were matched to 514 BMS-treated patients. The patients treated with BMS were associated with higher risk of TLR (HR: 2.55, 95%CI: 1.520–4.277, P = 0.0004) and TVR (HR: 1.889, 95%CI: 1.185–3.011, P = 0.0075), but the rates of death/MI and MACE were not statistically different. All Academic Research Consortium definition stent thrombosis at 9-year were comparable in the two groups. **Conclusions** During long-term follow-up through nine years, use of DES in patients with large coronary arteries was still associated with significant reductions in the risks of TLR and TVR.

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Keywords: Bare metal stent; Drug-eluting stent; Large coronary artery; Revascularization; Target vessel

1 Introduction

Compared with bare-metal stents (BMS), randomized trials have demonstrated that drug-eluting stents (DES) can reduce the risk of target vessel revascularization (TVR).[1] This benefit is particularly large for patients with smaller coronary arteries, but smaller in larger vessels where the risk of restenosis is lower.[2] Furthermore, subgroup analyses of BASKET trial showed that there was a higher rate of late stent thrombosis-related events in patients with large coronary arteries treated with DES than BMS.[3] It is unknown whether DES is superior to BMS for larger coronary arteries in the setting of routine clinical practice. This study sought to evaluate the very long-term safety and effectiveness of DES compared to BMS for patients with large coronary vessels.

2 Methods

2.1 Study population

From April 2004 to October 2006, 2407 consecutive patients undergoing de novo lesion percutaneous coronary intervention (PCI) with reference vessel diameter greater than or equal to 3.5 mm by visual estimation on angiogram by the operator at Fu Wai Hospital (Beijing, China), were prospectively enrolled into this study. All enrolled patients were divided into DES group (n = 1620) and BMS group (n = 787).

We excluded the patients with acute ST-elevation myocardial infarction treated with primary PCI from analysis, as the patients who received both DES and BMS. The study complied with the Declaration of Helsinki and was approved by the Ethics Committee of Fu Wai Hospital.

2.2 Procedure and periprocedural practices

Decisions regarding for interventional strategy and in-

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strumentation used were made by the interventional cardiologists. Administration of periprocedural antiplatelet and antithrombotic medications was based on operator's discretion and current guidelines. Lifelong aspirin (100 mg/d) was prescribed to all patients. One year of clopidogrel (75 mg/d) was recommended to all patients treated with DES. At least three months of clorpidogrel (75 mg/d) was recommended to the patients treated with BMS.

2.3 Follow-up data collection and main outcome measures

Clinical follow-up were performed at 3, 12 and 24 months and 9 years through an outpatient clinic visit or by telephone interview. We compared the combination of all-cause mortality and myocardial infarction (MI), target lesion revascularization (TLR), TVR, and major adverse cardiovascular events (MACE, the composite of mortality, MI, and TVR) between the two groups at 9-year point, as well as the risk difference for stent thrombosis (definite, probable, possible thrombosis, early thrombosis, late thrombosis, very late thrombosis). All end points were defined according to Academic Research Consortium (ARC) definitions.[4]

2.4 Statistical analysis

Because patients in our study were not randomized to receive either DES or BMS, we utilized propensity-score matching of subjects to adjust for differences of baseline characteristics in the two groups.[5] We selected all available variables that might be of potential relevance. Thirty variables were employed in propensity-score matching, including gender, age, diabetes mellitus, hypertension, hyperlipidemia, prior MI, prior PCI, prior coronary artery bypass grafting (CABG), family history of coronary artery disease (CAD), prior cerebral vascular disease, prior peripheral vascular disease, smoking history, angina pectoris, left ventricular ejection fraction, multiple vessel disease, number of target lesions, number of stents, target lesion location, reference vessel diameter by visual estimate, lesion length by visual estimate, pre- and post-procedural percentage diameter stenosis by visual estimate, ACC/AHA lesion type, total occlusion, ostial lesion, bifurcation, total stent length, calcification, post-dilatation, and intravascular ultrasound usage. A 1: 1 matched analysis was performed without replacement on the basis of the estimated propensity score of each patient in the study. If the difference of the estimated propensity score between DES and BMS group is < 0.01, then these two patients were eligible for matching.

Continuous variables were reported as mean ± SD and compared through the use of the Student unpaired *t* test on data before propensity match or of Student paired *t* test on that after propensity match. Categorical variables were presented as counts and percentages, and were compared using the χ^2 test.

In the study cohort, the reduction in the risk of all the outcome measures at 9 years was compared with Cox's proportional-hazards models. The results are reported as hazard ratio (HR) with 95% confidence interval (CI). Cumulative incidences concerning endpoints of the cohort after propensity match were estimated by the Kaplan-Meier method and compared by use of the log-rank test. All statistical tests were two sided, and value of $P < 0.05$ was considered to indicate statistical significance. All analyses were performed with SAS 9.3 system (SAS Institute, Cary, NC, USA).

3 Results

3.1 Patient, lesion, and procedure characteristics

Between April 2004 and October 2006, 2407 consecutive patients with reference vessel diameter greater than or equal to 3.5 mm underwent successful stents implantation at Fu Wai Hospital. Of these, 1620 (67.3%) received DES stents, 787 (32.7%) received BMS stents. Patients receiving both DES and BMS were excluded.

Patient, lesion, and procedural characteristics differed significantly between DES and BMS group before propensity match (Table 1 & 2). Compared to patients in the DES group, patients in the BMS group demonstrated higher risk

Table 1. Patient characteristics before propensity match.

	DES (*n* = 1620)	BMS (*n* = 787)	*P*
Age, yrs	56.6 ± 10.6	57.7 ± 11.7	0.0124
Female	250 (15.4%)	117 (14.9%)	0.7168
Prior MI	597 (36.9%)	386 (49.0%)	< 0.0001
Prior PCI	274 (16.9%)	99 (12.6%)	0.0051
Prior CABG	35 (2.2%)	16 (2.0%)	0.8380
Diabetes mellitus	297 (18.3%)	124 (15.8%)	0.1158
Hypertension	905 (55.9%)	421 (53.5%)	0.2731
Hyperlipidemia	557 (34.4%)	229 (29.1%)	0.0091
Family History of CAD	85 (5.2%)	42 (5.3%)	0.9264
Smoking history	857 (52.9%)	444 (56.4%)	0.1042
Unstable angina	864 (53.3%)	513 (65.2%)	< 0.0001
LVEF	67.58% ± 10.93%	66.48% ± 12.16%	0.0497
Multi-target vessel/lesion	343 (21.2%)	120 (15.2%)	0.0004

Data are presented as mean ± SD or *n* (%). CABG: coronary artery bypass grafting; CAD: coronary artery disease; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Table 2. Lesion and procedure characteristics before propensity match.

	DES (*n* = 2087)	BMS (*n* = 946)	*P*
Target vessel			< 0.0001
Left anterior descending	1013 (48.5%)	315 (33.3%)	
Circumflex	218 (10.4%)	111 (11.7%)	
Right coronary	639 (30.6%)	484 (51.2%)	
Pre-RVD by visual, mm	3.53 ± 0.32	3.71 ± 0.37	< 0.0001
Pre-lesion length by visual, mm	21.63 ± 12.97	19.75 ± 11.24	0.0001
ACC/AHA lesion type B2-C	1614 (77.3%)	719 (76.0%)	0.1364
Total occlusion	189 (9.1%)	170 (18.0%)	< 0.0001
Ostial lesion	294 (14.1%)	86 (9.1%)	0.0001
Bifurcation lesion	776 (37.2%)	252 (26.6%)	< 0.0001
Lesion calcification			0.1761
None	1331 (63.8%)	636 (67.2%)	
Mild	560 (26.8%)	232 (24.5%)	
Moderate	161 (7.7%)	59 (6.2%)	
Severe	35 (1.7%)	19 (2.0%)	
Direct stenting	657 (31.5%)	311 (32.9%)	0.4459
Long lesion (> 30 mm)	288 (13.8%)	128 (13.5%)	0.8417
Stent length per lesion, mm	26.92 ±13.20	24.29 ±11.86	< 0.0001
Post-dilatation	729 (34.9%)	107 (11.3%)	< 0.0001

BMS: bare-metal stents; DES: drug-eluting stents; RVD: reference vessel diameter.

clinical profiles including older age as well as greater incidences of prior MI, unstable angina, and total occlusion lesion, but less of hyperlipidemia, prior PCI, multi- target vessel, left anterior descending artery lesions, bifurcation and ostial lesions, lesion and stent length, and post-dilatation. After propensity match, 514 DES-treated patients were matched to 514 BMS-treated patients, and the baseline profiles in the two groups became comparable (Table 3 and Table 4). The logistic model which was used to calculate the propensity score presented good predictive value (C statistic = 0.818).

3.2 Clinical outcomes after propensity match

The median follow-up for surviving patients was about nine years, and the follow-up period was similar for two groups (2795.9 ± 1181.9 *vs*. 2890.9 ± 1309.3 days, P = 0.2146). Cumulative incidences of the various adverse events in the two groups after propensity match were listed in Table 5. At 1-year and 2-year follow-up, patients with DES had significantly lower rates of TLR (1.8% *vs*. 6.4%, P = 0.0001 and 2.3% *vs*. 8.0%, P < 0.0001), TVR (3.3% *vs*. 7.8%, P = 0.016 and 4.3% *vs*. 9.7%, P = 0.0006) and MACE (4.5% *vs*. 9.3%, P = 0.0016 and 5.6% *vs*. 11.5%, P = 0.0007). At 9 years, the rates of TLR and TVR remained significantly lower in patients with DES (4.1% *vs*. 10.7%, P = 0.0001 and 5.6% *vs*. 11.3%, P = 0.0011, respectively). While concerning the rate of MACE at 9 years, the results showed a non-significant trend towards superiority of DES group (13.0% *vs*. 17.3%, P = 0.0574). Kaplan-Meier curves

Table 3. Patient characteristics after propensity match.

	DES (*n* = 514)	BMS (*n* = 514)	*P*
Age, yrs	57.50 ± 10.51	57.03 ± 11.78	0.5096
Female	83 (16.1%)	76 (14.8%)	0.5527
Prior MI	227 (44.2%)	227 (44.2%)	1.0000
Prior PCI	64 (12.5%)	62 (12.1%)	0.8474
Prior CABG	9 (1.8%)	11 (2.1%)	0.6547
Diabetes mellitus	81 (15.8%)	95 (18.5%)	0.2498
Hypertension	270 (52.5%)	275 (53.5%)	0.7464
Hyperlipidemia	152 (29.6%)	164 (31.9%)	0.4185
Family history of CAD	29 (5.6%)	27 (5.3%)	0.7893
Smoking history	290 (56.4%)	289 (56.2%)	0.9505
Unstable angina	314 (61.1%)	320 (62.3%)	0.7967
LVEF, %	67.01% ± 10.76%	66.71% ± 12.30%	0.9343
Multi-target vessel/lesion	86 (16.7%)	79 (15.4%)	0.5610

Data are presented as mean ± SD or *n* (%). BMS: bare-metal stents; CABG: coronary artery bypass grafting; CAD: coronary artery disease; DES: drug-eluting stents; LVEF: left ventricular ejection fraction; MI: myocardial infarction; PCI: percutaneous coronary intervention.

Table 4. Lesion and procedure characteristics after propensity match.

	DES (*n* = 670)	BMS (*n* = 616)	*P*
Target vessel			0.4372
Left anterior descending	250 (37.3%)	252 (40.9%)	
Circumflex	71 (10.6%)	70 (11.4%)	
Right coronary	289 (43.1%)	273 (44.3%)	
Pre-RVD by visual, mm	3.61 ± 0.37	3.64 ± 0.32	0.1356
Pre-lesion length by visual, mm	20.20 ± 11.17	20.35 ± 11.89	0.8225
ACC/AHA lesion type B2-C	498 (74.3%)	473 (76.8%)	0.0853
Total occlusion	96 (14.3%)	93 (15.1%)	0.6973
Ostial lesion	59 (8.8%)	59 (9.6%)	0.6320
Bifurcation lesion	197 (29.4%)	180 (29.2%)	0.9428
Lesion calcification			0.5413
None	440 (65.7%)	419 (68.0%)	
Mild	176 (26.3%)	151 (24.5%)	
Moderate	47 (7.0%)	36 (5.8%)	
Severe	7 (1.0%)	10 (1.6%)	
Direct stenting	221 (33.0%)	195 (31.7%)	0.6107
Long lesion (> 30 mm)	79 (11.8%)	86 (14.0%)	0.2453
Stent length per lesion, mm	25.09 ± 11.38	25.12 ± 12.78	0.9619
Post-dilatation	109 (16.3%)	93 (15.1%)	0.5640

Data are presented as *n* (%). BMS: bare-metal stents; DES: drug-eluting stents; RVD: reference vessel diameter.

Table 5. Outcomes after propensity match.

	DES (*n* = 514)	BMS (*n* = 514)	*P*
30-days			
All-cause mortality	1 (0.2%)	2 (0.4%)	0.5637
Myocardial infarction	1 (0.2%)	3 (0.6%)	0.3173
Death/MI	2 (0.4%)	4 (0.8%)	0.4142
TLR	3 (0.6%)	4 (0.8%)	0.7055
TVR	3 (0.6%)	6 (1.2%)	0.3173
MACE	5 (1.0%)	9 (1.8%)	0.2482
Stent thrombosis	1 (0.2%)	5 (1.0%)	0.1025
1-year			
All-cause mortality	5 (1.0%)	5 (1.0%)	1.0000
Myocardial infarction	1 (0.2%)	7 (1.4%)	0.0339
Death/MI	6 (1.2%)	9 (1.8%)	0.4386
TLR	9(1.8%)	33 (6.4%)	0.0001
TVR	17 (3.3%)	40 (7.8%)	0.0016
MACE	23 (4.5%)	48 (9.3%)	0.0016
Stent thrombosis	1 (0.2%)	8 (1.6%)	0.0196
2-years			
All-cause mortality	6 (1.2%)	6 (1.2%)	1.0000
MI	2 (0.4%)	7 (1.4%)	0.0956
Death/MI	7 (1.4%)	10 (1.9%)	0.4669
TLR	12 (2.3%)	41 (8.0%)	0.0000
TVR	22 (4.3%)	50 (9.7%)	0.0006
MACE	29 (5.6%)	59 (11.5%)	0.0007
Stent thrombosis	2 (0.4%)	8 (1.6%)	0.0578
9-years			
All-cause mortality	36 (7.0%)	27 (5.3%)	0.2568
MI	7 (1.4%)	10 (1.9%)	0.4669
Death/MI	41 (8.0%)	34 (6.6%)	0.4189
TLR	21 (4.1%)	55 (10.7%)	0.0001
TVR	29 (5.6%)	58 (11.3%)	0.0011
MACE	64 (13.0%)	89 (17.3%)	0.0574
Stent thrombosis	9 (1.8%)	12 (2.3%)	0.6547

Data are presented as *n* (%). BMS: bare-metal stents; DES: drug-eluting stents; MACE: major adverse cardiovascular events; MI: myocardial infarction; TLR: target lesion revascularization; TVR: target vessel revascularization.

(Figure 1) showed no differences in 9-year cumulative incidences of mortality, MI and definite/probable thrombosis, but DES implantation was associated with a lower risk of TLR (5.0% *vs*. 12.0%, $P < 0.0001$), TVR (6.0% *vs*. 12.0%, $P = 0.0012$) and MACE (15.0% *vs*. 19.0%, $P = 0.0365$).

Table 6 shows the comparisons of adjusted 9-year cumulative incidences of the various adverse events evaluated with Cox's proportional-hazards models in the two groups after propensity match. The patients treated with BMS were associated with higher risk of TLR (HR: 2.55, 95%CI: 1.520–4.277, $P = 0.0004$) and TVR (HR: 1.889, 95%CI: 1.185–3.011, $P = 0.0075$). However, death/MI rates, stent thrombosis rates and MACE were not significantly different between the groups.

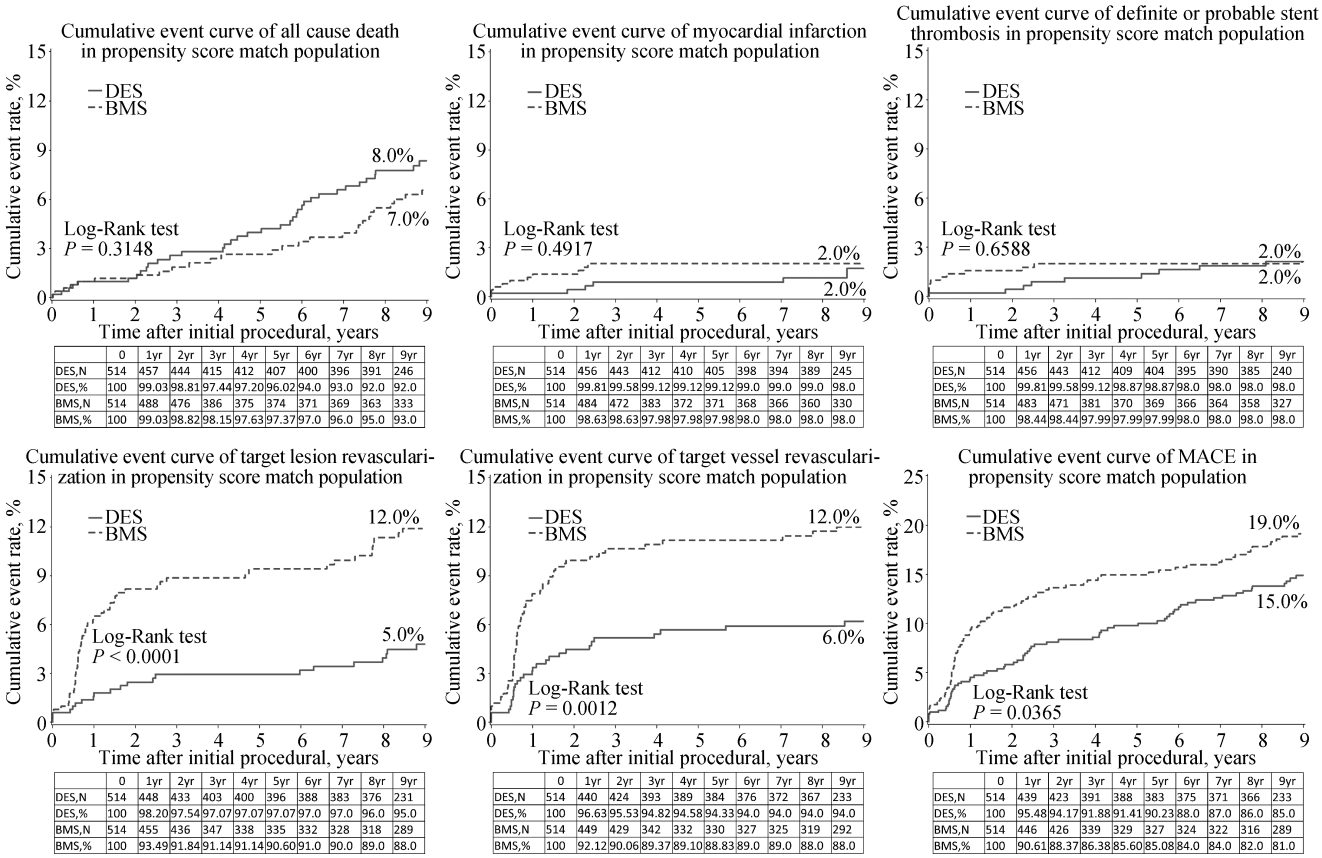
The cumulative incidences of thrombosis at 9 years were showed in Table 7. All the specifications of thrombosis rates, according to ARC definitions, were comparable between DES and BMS.

4 Discussion

The major findings in the current study were that the use of DES in large coronary arteries was associated with significantly lower rates of TLR and TVR but with similar death/MI or stent thrombosis compared with BMS during a 9-year clinical follow-up. This finding demonstrated that the important advantage of a lower restenosis rate with DES over BMS in large vessels existed till very long term.

Our findings were consistent with those of previous trials. An analysis of TAXUS IV trial showed that patients with DES had significantly lower revascularization rates than BMS (HR: 0.48, 95% CI: 0.25–0.92) in the large vessel (> 3.0 mm) subgroup.[6] The BASKET-PROVE trial, which included vessels > 3.0 mm patients, also showed that the rate of TVR was significantly reduced among patients receiving DES, as compared with BMS during a 2-year follow-up.[7] Recently, a meta-analysis of randomized controlled trials included 4399 patients and demonstrated that DES is superior to BMS in terms of clinical events in large coronary arteries.[8] In our current study, the rates of TLR and TVR showed significantly lower in patients with DES (4.1% *vs*. 10.7%, $P = 0.0001$ and 5.6% *vs*. 11.3%, $P = 0.0011$, respectively) compared with BMS for large coronary arteries (≥ 3.5 mm) during a 9-year clinical follow-up.

However, other previous studies showed that there were no significantly different about clinical outcome between DES and BMS in large coronary artery lesions.[9–13] They thought that, given a similar degree of neointimal hyperplasia around a stent of any diameter, a larger reference vessel size would be associated with a relatively lower rate of restenosis and events.[10,14] Nevertheless, it is also important to note that in-stent restenosis depended on several clinical factors, such as diabetic status, lesion complexity and stent length. A propensity-score-matched study showed that the rates of TVR were comparable between the DES group and the BMS group in patients with lower risk for restenosis (no diabetes, large vessel and short lesions),[15] while DES was associated with significant reduction of TVR in patients with high risk of restenosis. A previous study in our center,[16] which included non-diabetic patients with simple de novo lesions (stent diameter > 3.0 mm and stent length <



	0	1yr	2yr	3yr	4yr	5yr	6yr	7yr	8yr	9yr
DES,N	514	457	444	415	412	407	400	396	391	246
DES,%	100	99.03	98.81	97.44	97.20	96.02	94.0	93.0	92.0	92.0
BMS,N	514	488	476	386	375	374	371	369	363	333
BMS,%	100	99.03	98.82	98.15	97.63	97.37	97.0	96.0	95.0	93.0

	0	1yr	2yr	3yr	4yr	5yr	6yr	7yr	8yr	9yr
DES,N	514	456	443	412	410	405	398	394	389	245
DES,%	100	99.81	99.58	99.12	99.12	99.12	99.0	99.0	99.0	98.0
BMS,N	514	484	472	383	372	371	368	366	360	330
BMS,%	100	98.63	98.63	97.98	97.98	97.98	98.0	98.0	98.0	98.0

	0	1yr	2yr	3yr	4yr	5yr	6yr	7yr	8yr	9yr
DES,N	514	456	443	412	409	404	395	390	385	240
DES,%	100	99.81	99.58	99.12	98.87	98.87	98.0	98.0	98.0	98.0
BMS,N	514	483	471	381	370	369	366	364	358	327
BMS,%	100	98.44	98.44	97.99	97.99	97.99	98.0	98.0	98.0	98.0

	0	1yr	2yr	3yr	4yr	5yr	6yr	7yr	8yr	9yr
DES,N	514	448	433	403	400	396	388	383	376	231
DES,%	100	98.20	97.54	97.07	97.07	97.07	97.0	97.0	96.0	95.0
BMS,N	514	455	436	347	338	335	332	328	318	289
BMS,%	100	93.49	91.84	91.14	91.14	90.60	91.0	90.0	89.0	88.0

	0	1yr	2yr	3yr	4yr	5yr	6yr	7yr	8yr	9yr
DES,N	514	440	424	393	389	384	376	372	367	233
DES,%	100	96.63	95.53	94.82	94.58	94.33	94.0	94.0	94.0	94.0
BMS,N	514	449	429	342	332	330	327	325	319	292
BMS,%	100	92.12	90.06	89.37	89.10	88.83	89.0	89.0	88.0	88.0

	0	1yr	2yr	3yr	4yr	5yr	6yr	7yr	8yr	9yr
DES,N	514	439	423	391	388	383	375	371	366	233
DES,%	100	95.48	94.17	91.88	91.41	90.23	88.0	87.0	86.0	85.0
BMS,N	514	446	426	339	329	327	324	322	316	289
BMS,%	100	90.61	88.37	86.38	85.60	85.08	84.0	84.0	82.0	81.0

Figure 1. Comparisons of clinical outcomes after propensity match. Kaplan–Meier curves are shown for all-cause mortality, MI, stent thrombosis, TLR, TVR and MACE. BMS: bare-metal stents; DES: drug-eluting stents; MACE: major adverse cardiac events; MI: myocardial infarction; TLR: target- lesion revascularization; TVR: target-vessel revascularization.

Table 6. Hazard ratio of all events at 9 years (BMS *vs.* DES).

Events	HR	95% CI	*P*
All-cause mortality	0.839	0.498–1.412	0.5083
Myocardial infarction	1.143	0.414–3.152	0.7964
Definite + probable thrombosis	1.111	0.451–2.734	0.8188
TLR	2.550	1.520–4.277	0.0004
TVR	1.889	1.185–3.011	0.0075
MACE	1.322	0.943–1.854	0.1057

BMS: bare-metal stents; DES: drug-eluting stents; MACE: major adverse cardiovascular events; TLR: target lesion revascularization; TVR: target vessel revascularization.

Table 7. Cumulative incidence of stent thrombosis after propensity match at 9 years.

Thrombosis	DES (*n* = 514)	BMS (*n* = 514)	*P*
Definite thrombosis	7 (1.4%)	8 (1.6%)	0.7963
Definite + probable thrombosis	9 (1.8%)	12 (2.3%)	0.5127
All thrombosis	19 (3.7%)	21 (4.1%)	0.7518
Early thrombosis	1 (0.2%)	5 (1.0%)	0.1025
Late thrombosis	1 (0.2%)	3 (0.6%)	0.3173
Very late thrombosis	17 (3.3%)	13 (2.5%)	0.4652

Data are presented as *n* (%). BMS: bare-metal stents; DES: drug-eluting stents.

18 mm), showed that there was no significant difference in the risk of MACEs between BMS and DES. On the other hand, the SIRIUS trial,[17] which included 1058 patients with complex coronary lesions, revealed that the use of sirolimus-eluting stent had a reduction in the rates of restenosis and associated clinical events compared to BMS in both small-vessel (< 2.75 mm) and large-vessel (> 2.75 mm) subgroups. These studies indicated that BMS might be equivalent to DES only in simple lesions at low risk of restenosis, such as nondiabetic, diameter > 3 mm and lesion length < 15 mm. In this study, we enrolled consecutive patients undergoing PCI with larger coronary arteries in the setting of routine clinical practice, both groups including comparable complex lesions, such as diabetes and long lesion (> 30 mm). This might explain why the results of this study disagree with those of studies with regard to no additional benefit of DES implantation compared with BMS in larger coronary arteries.

Moreover, the great baseline differences of demographic and procedural characteristics between groups might have influence on angiographic and clinical outcomes. The analysis from National Heart, Lung and Blood Institute

(NHLBI)-sponsored dynamic registry showed that in large coronary arteries, defined by a vessel diameter greater than or equal to 3.5 mm, DES provided no additional effectiveness over BMS in terms of TVR.[13] In this NHLBI dynamic registry, DES patients were more likely to have history of renal disease, hypertension, hypercholesterolemia and history of prior PCI compared to BMS; the mean reference vessel size of treated lesions was smaller (3.6 *vs*. 3.7 mm, $P < 0.01$) and mean lesion length was longer (16.7 *vs*. 13.6 mm, $P < 0.01$) in DES patients, which might be the part of reason why this study failed to show superiority of DES in efficacy and safety. Our study utilized propensity-score matching of subjects to adjust for differences of baseline characteristics in the two groups. After propensity match, the baseline profiles in the two groups became almost identical.

The effect of the use of DES on long-term mortality has not previously been established.[18] Our study showed no difference in mortality between patients with DES and those with BMS during a 9-year period, either for the combined end point of death or myocardial infarction.

There were still several safety concerns with DES, such as late stent thrombosis.[19] The BASKET trial subgroup analysis showed that patients with large coronary artery lesions had an increased risk of stent thrombosis in the DES group.[3] However, the BASKET-PROVE trial demonstrated that stent thrombosis risk in large coronary intervention did not differ significantly between DES and BMS groups during two years of follow-up.[7] The duration of dual antiplatelet therapy in BASKET trial was 6 months, and which in BASKET-PROVE was 12 months. The different durations of dual antiplatelet therapy used in these two trials might explain the difference in results.[20] During the 9-year follow-up period in our study, only 12 (2.3%) BMS and 9 (1.8%) DES recipients developed definite and probable stent thrombosis ($P = 0.5127$). In this study, all DES patients received dual antiplatelet therapy for at least 12 months, same as the duration of BASKET-PROVE trial. In this study, no significant increase in the overall rate of stent thrombosis was seen with DES. However, of the 19 DES thrombosis cases, 17 (89.5%) were very late stent thrombosis (Table 7), that was significantly more frequent in patients with DES after the first year following the procedure. As an observational study showed that the extended use of clopidogrel in patients with DES might be associated with a reduced risk for death and death or MI,[21] our findings may suggest the need for a longer duration of dual antiplatelet therapy in patients receiving DES, especially for first generation DES.

4.1 Study limitations

First, although we established a well-balanced cohort of patients receiving BMS and DES matched on the basis of the propensity score, some effect from residual unmeasured confounding may contribute to our findings. Second, because of the lack of angiographic follow-up, we can't assess binary restenosis rates. Third, the second generation DES was not included in this study, and it is necessary to evaluate the efficacy of the newest-generation DES versus BMS in large coronary arteries in further study.

4.2 Conclusions

In this large, real-world population, the use of DES in large coronary arteries is associated with significant reductions in the risks of TLR and TVR at 9-year long-term follow-up compared to BMS. There is no significant difference in all-cause mortality, MI, and thrombosis between DES and BMS in patients with large coronary arteries.

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