ORIGINAL RESEARCH

Comparison of Different Types of Drug-Eluting Stents for De Novo Long Coronary Artery Lesions

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ABSTRACT

BACKGROUND Outcomes of percutaneous coronary intervention for diffuse long lesions remain relatively unfavorable. Prior clinical trials investigated the relative efficacy and safety of different types of drug-eluting stents (DES) in long lesions.

OBJECTIVES This study sought to compare the relative performance of different types of DES for de novo long (≥25 mm) coronary artery lesions.

METHODS Using a pooled analysis of individual data of 1,450 patients from 3 randomized clinical trials, we compared angiographic and clinical outcomes of 5 different types of DES: 224 patients with cobalt-chromium everolimus-eluting stents (EES), 255 with platinum-chromium EES, 250 with Resolute zotarolimus-eluting stents, 245 with biodegradable polymer biolimus-eluting stents, and 476 with first-generation sirolimus-eluting stents (SES). The primary endpoint was in-segment late lumen loss at 9 months.

RESULTS The primary endpoint was not significantly different between 4 second-generation DES and 1 first-generation SES (0.17 ± 0.41 mm in cobalt-chromium EES; 0.11 ± 0.37 in platinum-chromium EES: 0.14 ± 0.38 in Resolute zotarolimus-eluting stents; 0.14 ± 0.38 in biodegradable polymer biolimus-eluting stents; or 0.10 ± 0.37 in SES, respectively, overall $P = 0.38$). Also, there were no significant between-group differences with respect to death, myocardial infarction, target-vessel revascularization, or stent thrombosis at 12 months. In the multiple treatment propensity-score analysis, the risk of angiographic and clinical outcomes was also similar among several types of DES.

CONCLUSIONS In this patient-level pooled analysis, several second-generation DES showed similar angiographic and clinical outcomes in patients with de novo long coronary lesions. (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-III [LONG-DES-III]; NCT01078038; Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent-IV [LONG-DES-IV]; NCT01186094; and Everolimus-eluting [PROMUS-ELEMENT] vs. Biolimus A9-Eluting [NOBORI] Stents for Long-Coronary Lesions [LONG-DES-V]; NCT01186120)
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Diffuse long lesions comprise more than 20% of contemporary clinical practice of percutaneous coronary intervention (PCI) and are a major determinant of unfavorable clinical outcomes.[1,2] Although the use of drug-eluting stents (DES) has dramatically reduced the rate of angiographic and clinical restenosis compared with bare-metal stents (BMS),[3] the occurrence of in-stent restenosis and ischemic events still remains problematic for patients with diffuse long coronary lesions.[4-8] The technology and engineering of DES have continuously advanced over time, and second-generation DES adopted more active antiproliferative drugs with enhanced release kinetics, biocompatible or biodegradable polymers, and novel stent technology with thinner struts.[9] Cumulative clinical evidence of comparative clinical trials showed that second-generation DES demonstrated better efficacy and safety compared with first-generation DES and BMS.[10-15] However, there are limited data on the relative efficacy and safety of different types of contemporary DES for diffuse long lesions. Such information may have important clinical implications to help treating physicians to select the optimal type of DES for treating high-risk, long coronary lesions. To resolve this issue, we did a pooled analysis of individual-patient data from randomized trials comparing different DES to examine the comparative effects of these devices in patients with de novo long coronary artery disease.

METHODS

STUDY POPULATION AND DATA COLLECTION.
For the current analysis, we merged individual patient data from the 3 randomized clinical trials of the LONG-DES (Percutaneous Treatment of LONG Native Coronary Lesions With Drug-Eluting Stent) III, IV, and V trials for targeting long coronary lesions. Each trial's designs, detailed entry criteria, and outcomes have been described previously,[16-18] and the key features are summarized in Supplemental Table 1. In brief, LONG-DES III compared cobalt-chromium everolimus-eluting stents (EES) (PROMUS, Boston Scientific, or XIENCE V, Abbott Vascular) and first-generation sirolimus-eluting stents (SES) (Cypher, Cordis, Johnson & Johnson) in

450 patients,[16] LONG-DES IV compared Resolute zotarolimus-eluting stents (Endeavor Resolute, Medtronic) and SES in 500 patients,[17] and the LONG-DES V compared platinum chromium (PtCr)-EES (Promus Element, Boston Scientific) and Nobori biolimus A9-eluting stents (BES) (Nobori, Terumo Corporation) in 500 patients.[18] Key features of DES used in the study are described in Supplemental Table 2. Uniformly, patients with long (visual lesion length ≥25 mm) native coronary lesions were eligible for randomization, and exclusion criteria included ST-segment elevation myocardial infarction (MI); severe left ventricular dysfunction (ejection fraction <30%) or cardiogenic shock; left main coronary artery disease (defined as >50% stenosis); renal dysfunction (serum creatinine level ≥2.0 mg/dL) or dependence on dialysis; allergy to antiplatelet drugs, heparin, stent material or stent drugs; and a life expectancy <1 year. Each trial was approved by the ethics committee at each participating center, and all patients provided written informed consent for participation in these trials.

Individual patient data from each trial were merged for analysis with a common set of variables. The pooled database was checked for completeness and consistency by investigators in Asan Medical Center. The merged database included demographics, clinical history, risk factors, procedural characteristics, baseline and follow-up angiographic findings, and clinical outcomes during follow-up. Unless specified, previously reported definitions from each trial were used for variables.
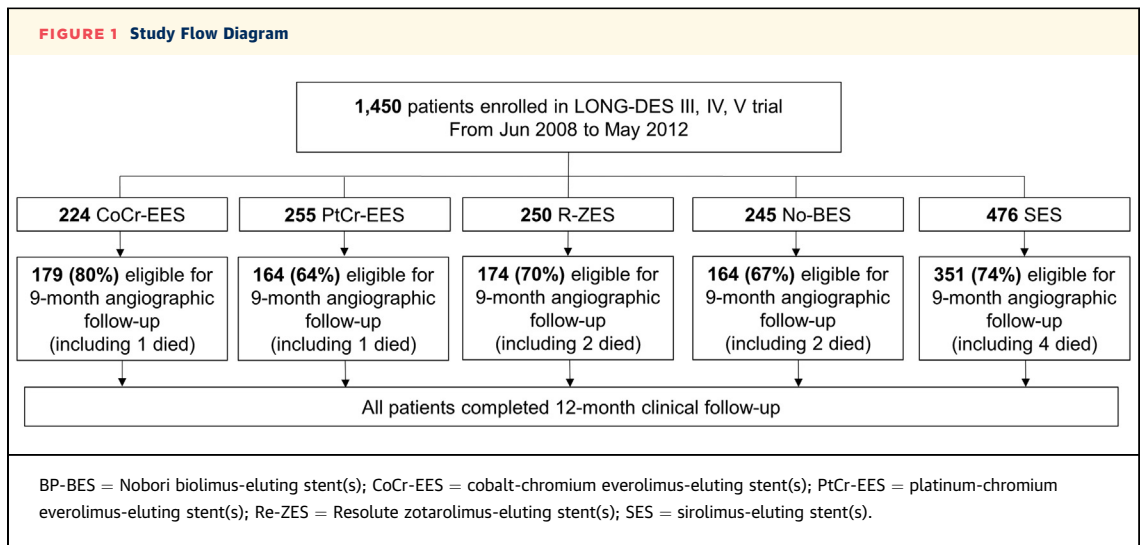
PCI PROCEDURE AND QUANTITATIVE CORONARY ANGIOGRAPHY DATA.
Enrolled patients were randomly assigned to either stent after diagnostic angiography. Stent implantation was performed according to standard PCI techniques. Full lesion coverage was attempted by implanting 1 or several stents without limitations. Before or during the procedure, all patients received ≥200 mg of aspirin and a 300- to 600-mg loading dose of clopidogrel. After the procedure, all patients received 100 mg/d of aspirin indefinitely, as well as 75 mg/d clopidogrel for ≥12 months.

FIGURE 1 Study Flow Diagram

1,450 patients enrolled in LONG-DES III, IV, V trial
From Jun 2008 to May 2012

| 224 CoCr-EES | 255 PtCr-EES | 250 R-ZES | 245 No-BES | 476 SES |

179 (80%) eligible for 9-month angiographic follow-up (including 1 died)

164 (64%) eligible for 9-month angiographic follow-up (including 1 died)

174 (70%) eligible for 9-month angiographic follow-up (including 2 died)

164 (67%) eligible for 9-month angiographic follow-up (including 2 died)

351 (74%) eligible for 9-month angiographic follow-up (including 4 died)

All patients completed 12-month clinical follow-up

BP-BES = Nobori biolimus-eluting stent(s); CoCr-EES = cobalt-chromium everolimus-eluting stent(s); PtCr-EES = platinum-chromium everolimus-eluting stent(s); Re-ZES = Resolute zotarolimus-eluting stent(s); SES = sirolimus-eluting stent(s).

All patients were mandatorily recommended to have angiographic follow-up at 9 months after the procedure, or earlier, if anginal symptoms occurred. Coronary angiograms were digitally recorded at baseline, immediately after the procedure, and at follow-up and were assessed off-line in the angiographic core laboratory (Asan Medical Center) using CAAS V automated edge-detection system (Pie Medical Imaging). Standard qualitative and quantitative analyses and definitions were used for angiographic analysis.[19] All quantitative angiographic measurements were obtained within the stented segment (in-stent) and over the entire segment, including the stent and its 5-mm proximal and distal margins (in-segment).

STUDY ENDPOINTS. The primary endpoint of this study was in-segment late luminal loss at 9 months after the index procedure (defined as the difference in the minimal luminal diameter assessed immediately after the procedure and at angiographic follow-up, measured within the margins, 5 mm proximal and 5 mm distal to the stent). Secondary angiographic outcomes were in-segment binary restenosis and in-segment minimal lumen diameter at 9 months. Secondary clinical outcomes included death, MI, target-lesion revascularization (TLR), target-vessel revascularization (TVR), stent thrombosis, and major adverse cardiac events (MACE) (a composite of death, MI, and TVR) within 12 months. Periprocedural MI was defined as an elevation of creatine kinase-MB fraction >3 times the normal upper limit in at least 2 blood samples within 48 hours of the procedure. Detailed information of definition for clinical endpoints are described in detail previously.[16-18]

STATISTICAL ANALYSIS. Baseline characteristics, including patient demographics, risk factors or comorbidities, clinical presentation, cardiac status, and anatomic and procedural features, were described according to each type of DES. Categorical variables were presented as counts (proportions) and continuous variables were presented as mean ± SD. Differences between treatment groups were evaluated by analysis of variance for continuous variables and by the chi-square or Fisher exact test for categorical variables.

Cumulative events of clinical outcomes were assessed using Kaplan-Meier estimates and compared with the log-rank test. To reduce the impact of selection bias and potential confounding factors among patients enrolled in different trials, we performed an adjustment for differences in baseline characteristics of patients using a weighted Cox proportional hazards regression model with an inverse probability of treatment weighting. When that technique was used, weights for patients receiving each treatment were the inverse of each propensity score. The propensity scores for multiple treatments were estimated by multiple generalized logistic regression model.[20] A full nonparsimonious model was developed with clinical and angiographic variables. Using the estimated weights, we examined the balance between treatment groups and the pooled sample across all treatments by calculating "population" standardized differences for each of the baseline variables (Supplemental Table 3). Standardized differences for most baseline covariates were <0.1.[21]

All reported *P* values are 2-sided and have not been adjusted for multiple testing. All the analyses were performed with the use of SAS software, version 9.3

TABLE 1 Baseline Demographic and Clinical Characteristics of Patients, According to Different Types of Drug-Eluting Stents						
	CoCr-EES (n = 224)	PtCr-EES (n = 255)	Re-ZES (n = 250)	BP-BES (n = 245)	SES (n = 476)	P Value
Age, y	62.9 ± 9.9	63.5 ± 10.6	62.8 ± 9.7	63.1 ± 10.5	62.8 ± 9.7	0.93
Men	165 (73.7)	184 (72.2)	184 (73.6)	167 (68.2)	330 (69.3)	0.50
Body mass index, kg/m²	24.8 ± 3.0	24.7 ± 2.9	25.1 ± 3.1	25.3 ± 2.9	25.2 ± 2.9	0.09
Diabetes mellitus	71 (31.7)	89 (34.9)	68 (27.2)	79 (32.2)	138 (29.0)	0.33
Hypertension	137 (61.2)	154 (60.4)	150 (60.0)	161 (65.7)	263 (55.3)	0.10
Hyperlipidemia	127 (56.7)	145 (56.9)	141 (56.4)	131 (53.5)	264 (55.5)	0.94
Current smoker	52 (23.2)	74 (29.0)	68 (27.2)	63 (25.7)	119 (25.0)	0.63
Previous MI	10 (4.5)	11 (4.3)	3 (1.2)	6 (2.4)	12 (2.5)	0.15
Previous CHF	3 (1.3)	6 (2.4)	3 (1.2)	3 (1.2)	3 (0.6)	0.40
Previous PCI	15 (6.7)	26 (10.2)	17 (6.8)	16 (6.5)	33 (6.9)	0.46
Previous CABG	5 (2.2)	0 (0)	4 (1.6)	1 (0.4)	8 (1.7)	0.12
Renal failure	1 (0.4)	5 (2.0)	1 (0.4)	1 (0.4)	3 (0.6)	0.19
Cerebrovascular disease	15 (6.7)	13 (5.1)	11 (4.4)	15 (6.1)	29 (6.1)	0.81
Peripheral vascular disease	1 (0.4)	1 (0.5)	3 (1.2)	1 (0.4)	7 (1.5)	0.42
Chronic lung disease	2 (0.9)	5 (2.0)	7 (2.8)	7 (2.9)	6 (1.3)	0.33
Multi-vessel disease	132 (58.9)	140 (54.9)	124 (49.6)	123 (50.2)	240 (50.4)	0.17
Ejection fraction, %	60.3 ± 7.4	60.1 ± 7.7	59.1 ± 7.9	60.3 ± 7.6	60.1 ± 6.4	0.73
Clinical indication for PCI						0.03
Stable angina	137 (61.2)	145 (56.9)	160 (64.0)	142 (58.0)	283 (59.5)	
Unstable angina	69 (30.8)	74 (29.0)	71 (28.4)	68 (27.8)	156 (32.8)	
NSTEMI	18 (8.0)	36 (14.1)	19 (7.6)	35 (14.3)	37 (7.8)	

Values are mean ± SD or n (%).

BP-BES = Nobori biolimus-eluting stent(s); CABG = coronary-artery bypass grafting; CAD = coronary artery disease; CHF = congestive heart failure; CoCr-EES = cobalt-chromium everolimus-eluting stents; MI = myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; PtCr-EES = Promus platinum-chromium everolimus-eluting stent(s); Re-ZES = Resolute zotarolimus-eluting stent(s); SES = sirolimus-eluting stent(s).

(SAS Institute), and SPSS version 21.0 (IBM Corporation).

RESULTS

STUDY POPULATION AND BASELINE CHARACTERISTICS.
The study flow diagram for the current analyses is shown in **Figure 1**. A total of 1,450 patients from 3 LONG-DES III, IV, and V trials between June 2008 and May 2012 were available for the current analysis (n = 224 with cobalt-chromium EES, 255 with PtCr-EES, 250 with Resolute zotarolimus-eluting stents, 245 with biodegradable-polymer BES, and 476 with SES). Baseline demographics and clinical characteristics of the study population according to different types of DES are shown in **Table 1**. Overall, there were no significant differences in baseline clinical covariates across the multiple cohorts of different DES except for the clinical indications for PCI. **Table 2** showed baseline lesion and procedural characteristics of the study population according to different DES types. There were significant differences across the stent groups with respect to anatomic and procedural characteristics such as bifurcation lesions, number of stents, average stent diameter, or direct stenting.

ANGIOGRAPHIC OUTCOMES. Quantitative coronary angiography results at baseline, immediately after the procedure, and 9-month follow-up according to different DES types are shown in **Table 3**. There were significant differences across the stent groups with respect to angiographic measurements. Follow-up angiography was performed in 71% of patients. In-segment late luminal loss (the primary outcome) was not different among groups at the 9-month angiographic follow-up (*P* = 0.38) (**Table 3, Figure 2A**). In addition, the rates of in-segment and in-stent binary restenosis were similar between stent groups. The results were consistent after adjustment by Cox proportional hazards regression with an inverse probability of treatment weighting (*P* = 0.73 for in-segment late luminal loss and *P* = 0.49 for in-segment binary restenosis).

CLINICAL OUTCOMES. During 12-month of follow-up period, there were 10 deaths (0.7%), 176 MIs (12.1%) (167 [11.5%] periprocedural MI and 9 [0.6%] spontaneous MI), 67 repeat revascularizations (4.6%) (33 [0.2%] TLR and 38 [0.3%] TVR), and 6 definite or probable stent thrombosis (0.4%). In total, 212 had at least 1 MACE event (14.6%). There were no significant between-group differences with respect to death, MI,

TABLE 2 Baseline Lesion and Procedural Characteristics, According to Different Types of Drug-eluting Stents

	CoCr-EES (n = 224)	PtCr-EES (n = 255)	Re-ZES (n = 250)	BP-BES (n = 245)	SES (n = 476)	*P* Value
Lesion characteristics						
Target vessel						0.20
Left anterior descending	146 (65.2)	171 (67.1)	156 (62.4)	159 (64.9)	281 (59.3)	
Left circumflex	27 (12.1)	32 (12.5)	31 (12.4)	33 (13.5)	69 (14.6)	
Right coronary	50 (22.3)	52 (20.4)	62 (24.8)	53 (21.6)	124 (26.2)	
Ramus intermedius	1 (0.4)	0 (0)	1 (0.4)	0 (0)	0 (0)	
TIMI flow grade 0 or 1	14 (6.3)	25 (9.8)	27 (10.8)	21 (8.6)	36 (7.6)	0.37
Bifurcation lesions	94 (42.0)	68 (26.7)	91 (36.4)	74 (30.2)	175 (36.8)	0.003
Thrombus	4 (1.8)	10 (3.9)	2 (0.8)	11 (4.5)	15 (3.2)	0.09
Severe tortuosity	4 (1.8)	3 (1.2)	1 (0.4)	5 (2.0)	4 (0.8)	0.41
Severe calcification	34 (15.4)	39 (15.3)	37 (14.8)	23 (9.4)	66 (13.9)	0.28
Procedural characteristics						
No. of stents used at the target lesion	1.84 ± 0.69	1.66 ± 0.69	1.71 ± 0.68	1.59 ± 0.61	1.62 ± 0.66	<0.001
Length of stents used at the target lesion, mm	46.5 ± 16.9	44.5 ± 16.8	45.9 ± 17.1	40.2 ± 13.4	45.6 ± 17.1	<0.001
Average stent diameter at the target lesion, mm	3.2 ± 0.4	3.2 ± 0.4	3.3 ± 0.4	3.2 ± 0.3	3.20 ± 0.30	0.002
Maximal pressure at stent deployment, atm	13.8 ± 3.8	13.5 ± 3.5	13.1 ± 3.9	12.0 ± 4.0	15.2 ± 4.1	<0.001
Direct stenting	38 (17.0)	12 (4.7)	23 (9.2)	16 (6.5)	65 (13.7)	<0.001
Postadditional balloon inflation	184 (82.1)	178 (69.8)	172 (68.8)	190 (77.6)	378 (79.4)	0.001
Intravascular ultrasound guidance	182 (81.3)	188 (73.7)	201 (80.4)	189 (77.1)	389 (81.7)	0.10
Glycoprotein IIb/IIIa antagonists	5 (2.2)	6 (2.4)	3 (1.2)	5 (2.0)	14 (2.9)	0.68

Values are n (%) or mean ± SD.
TIMI = Thrombolysis In Myocardial Infarction; other abbreviations as in Table 1.

TVR, or stent thrombosis at 12 months (Table 4). The Kaplan-Meier estimates of MACE at 12 months are shown in Figure 2B, showing no significant difference among groups (*P* = 0.60). By multivariable Cox proportional hazards regression model, increased length of stent used at the target lesion, together with age, hypertension, and acute coronary syndrome presentation, were independent predictors of MACE (Supplemental Table 4).

The unadjusted and adjusted HRs for multiple DES comparisons after application of multiple treatment propensity score weighting are shown in Table 5. With the SES as the reference group, the HRs for the other types of second-generation DES were similar with respect to risk of death, MI, TLR, and MACE (Figure 3).

DISCUSSION

In this patient-level pooled analysis of 3 randomized clinical trials, the primary endpoint of angiographic in-segment late lumen loss was similar between 5 different types of DES for de novo long coronary lesions. In addition, clinical outcomes of various stents were comparable, suggesting that contemporary DES and first-generation SES are equally effective for the treatment of long coronary artery lesions (Central Illustration).

Our collective analysis may be clinically important and relevant for several reasons. The first is the seemingly growing prevalence of stable, diffuse plaques in many patients that require longer length of stents. The lesion length is still a major determinant of unfavorable outcomes after coronary stent implantation.[3-7] However, this is a difficult clinical scenario that warrants investigation, and until recently, there was no systematic comparative analysis of the contemporary DES for long coronary lesions. The threshold of stent length with regard to the risk of stent thrombosis was 31.5 mm after first-generation DES implantation.[4] The recent analysis with the IRIS-DES (Interventional Cardiology Research In-Cooperation Society-Drug-Eluting Stents) registry showed that the stent length of 43.0 mm was the differential cutoff for predicting the risk of target-vessel failure with second-generation DES.[22] Similar to the previous findings, longer length of stents, which are a proxy for longer lesion length, was an important risk factor of the occurrence of MACE in our study. Second, this work is important because if shows equipoise between differing types of modern era stents from different companies. Although various kinds of contemporary DES have different profiles regarding stent platform, polymer coating, and antiproliferative drugs, the current pooled analyses suggest that several second-generation DES could be effectively and safely used for the treatment of long coronary lesions. It is reassuring to know that the lack of availability of specific

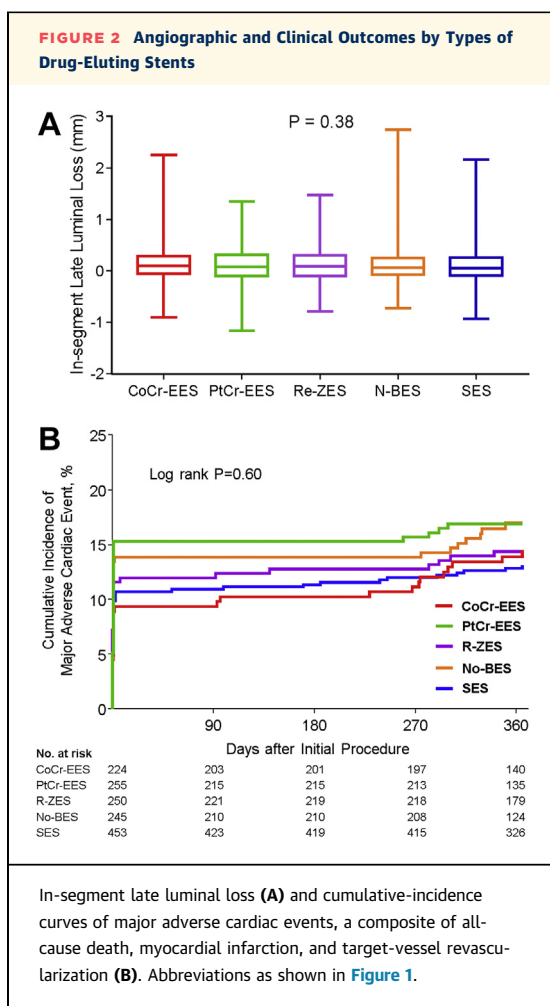| TABLE 3 Quantitative Angiographic Analysis						
	CoCr-EES (n = 224)	PtCr-EES (n = 255)	Re-ZES (n = 250)	BP-BES (n = 245)	SES (n = 476)	*P* Value
Before procedure						
Lesion length, mm	34.0 ± 15.4	32.27 ± 13.84	32.4 ± 13.5	29.24 ± 12.17	32.3 ± 13.4	0.001
Reference vessel diameter, mm	3.18 ± 0.47	3.03 ± 0.45	3.25 ± 0.47	3.02 ±0.46	3.18 ± 0.46	<0.001
Minimal luminal diameter, mm	1.07 ± 0.45	0.83 ± 0.42	0.92 ± 0.46	0.85 ± 0.42	1.00 ± 0.47	0.12
Diameter stenosis, %	66.3 ± 13.5	72.61 ± 13.95	71.4 ± 14.3	71.7 ± 13.4	68.3 ± 13.9	<0.001
Immediately after procedure						
Minimal luminal diameter, mm						
In segment	2.33 ± 0.46	2.21 ± 0.40	2.36 ± 0.49	2.23 ± 0.43	2.32 ± 0.49	<0.001
In stent	2.64 ± 0.42	2.52 ± 0.36	2.67 ± 0.47	2.52 ± 0.40	2.64 ± 0.45	<0.001
Diameter stenosis, %						
In segment	17.4 ± 9.3	17.1 ± 10.0	18.8 ± 9.4	17.8 ± 10.0	18.3 ± 10.1	0.30
In stent	9.7 ± 6.8	10.0 ± 8.3	10.4 ± 7.2	10.6 ± 8.8	10.3 ± 7.5	0.67
Acute gain, mm						
In segment	1.27 ± 0.57	1.38 ± 0.61	1.44 ± 0.64	1.33 ± 0.53	1.32 ± 0.60	0.034
In stent	1.57 ± 0.53	1.68 ±0.57	1.76 ± 0.64	1.67 ± 0.51	1.64 ± 0.58	0.013
Follow-up at 9 months	179 (80)	164 (64)	174 (70)	164 (67)	351 (74)	<0.001
Minimal luminal diameter, mm						
In segment	2.17 ± 0.49	2.11 ± 0.46	2.24 ± 0.49	2.08 ± 0.51	2.26 ± 0.52	0.001
In stent	2.42 ± 0.52	2.27 ± 0.50	2.45 ± 0.52	2.35 ± 0.52	2.47 ± 0.53	<0.001
Proximal margin	3.02 ± 0.66	2.88 ± 0.60	3.12 ± 0.65	2.91 ± 0.64	3.13 ±0.56	<0.001
Distal margin	2.25 ± 0.51	2.25 ± 0.43	2.34 ± 0.45	2.17 ± 0.48	2.35 ± 0.48	0.001
Diameter stenosis, %						
In segment	23.7 ± 15.3	23.6 ± 13.1	23.4 ± 13.3	22.6 ± 17.1	23.0 ± 13.7	0.33
In stent	17.8 ± 14.6	20.5 ± 13.9	19.5 ± 13.0	17.1 ± 15.6	18.5 ± 14.3	0.005
Proximal margin	16.5 ± 15.1	15.9 ± 11.3	14.7 ± 13.3	15.3 ± 12.8	14.0 ± 11.3	0.23
Distal margin	18.8 ± 12.3	14.4 ± 9.3	17.7 ± 9.5	17.4 ± 13.6	17.7 ± 10.4	0.022
Late luminal loss, mm						
In segment (primary outcome)	0.17 ± 0.41	0.11 ±0.38	0.13 ± 0.36	0.14 ±0.38	0.10 ± 0.37	0.38
In stent	0.22 ± 0.42	0.24 ± 0.38	0.26 ± 0.36	0.20 ± 0.41	0.21 ± 0.36	0.08
Angiographic restenosis						
In segment	13 (7.3)	8 (4.9)	9 (5.2)	10 (6.1)	17 (4.8)	0.39
In stent	7 (3.9)	8 (4.9)	7 (4.0)	6 (3.7)	15 (4.3)	0.23

Values are mean ± SD or n (%).

Abbreviations as in **Table 1**.

stents in local catheterization laboratories may not affect patient outcomes.

Although angiographic lumen loss has been considered a key measure for comparison of stent performance, it is a surrogate marker of clinical outcomes.[23] There was a strong correlation between long-term TLR and angiographic lumen loss higher than 0.50 mm in a recent meta-analysis of 7 clinical studies, whereas a minor lumen loss was not related with an increased incidence of TLR.[24] The minimal lumen loss difference among stents in our study ensures that the long-term clinical outcomes would be equivalent. However, considering the contemporary PCI practice without routine angiographic surveillance, additional large comparative-effectiveness studies are required to provide more solid scientific and clinically important insights on the optimal PCI treatment of diffuse coronary long lesions.

In the current analyses, there were trends toward higher rates of MI with newer PtCr-EES and No-BES stents, mainly because of the occurrence of periprocedural MI. Because those 2 stents were compared in the LONG-DES V trial,[18] which was conducted most recently, the characteristics of the study population differed from the other groups. The minimal lumen diameter of the 2 groups was significantly smaller than other stent groups, and the rate of IVUS guidance was lowest in those groups, which could affect the procedural results.

In our study, the low incidence of hard endpoints, including cardiac death, spontaneous MI, or stent thrombosis, might be explained in part by the difference in the details of PCI procedures (ie, more frequent use of IVUS [79.2%] and higher rates of post-dilation [76.0%]).[25] Several previous studies demonstrated that the use of intravascular imaging for stent

FIGURE 2 Angiographic and Clinical Outcomes by Types of Drug-Eluting Stents

In-segment late luminal loss **(A)** and cumulative-incidence curves of major adverse cardiac events, a composite of all-cause death, myocardial infarction, and target-vessel revascularization **(B)**. Abbreviations as shown in **Figure 1**.

optimization was significantly associated with better clinical outcomes,[26-28] especially for the long coronary lesions.[29,30] The IVUS-guided PCI had achieved larger minimal lumen area immediately after procedure and 9-month angiographic follow-up with larger and longer stents (Supplemental Table 5), and the lower rate of repeat revascularization after 12 months (4.0% vs 7.0%; $P = 0.029$). Such findings suggest that IVUS-guided PCI using contemporary DES would be associated with improved procedural and clinical outcomes in treatment of diffuse long coronary lesions.

Treatment strategies for treatment of diffuse long coronary lesions have been evolving. The introduction of the 48-mm-length stents enabled optimal treatment of diffuse long lesions with fewer implanted stents, showing favorable procedural and excellent clinical outcomes.[31] Also, given that there was a significant mismatch in determining lesion severity and length among angiography, fractional flow reserve (FFR), and IVUS evaluations,[32] the widespread adoption of intravascular imaging and physiology have further developed the understanding of diffuse long lesions. Furthermore, patients with long lesions with diffuse atherosclerosis who had lower post-PCI FFR showed worse clinical outcomes compared with those with a normal range of post-PCI FFR.[33] This warrants future studies to determine the optimal PCI strategy for diffuse long coronary lesions with integration of intravascular imaging and physiology concept.

STUDY LIMITATIONS. First, there were significant differences in lesion and procedural characteristics

TABLE 4 Clinical Events at 12 Months According to Different Types of Drug-eluting Stents

|	CoCr-EES (n = 224)	PtCr-EES (n = 255)	Re-ZES (n = 250)	BP-BES (n = 245)	SES (n = 476)	P Value
Death	1 (0.4)	1 (0.4)	2 (0.8)	2 (0.8)	4 (0.8)	0.94
Cardiac	0	1 (0.4)	1 (0.4)	2 (0.8)	2 (0.4)	0.75
Noncardiac	1 (0.4)	0	1 (0.4)	0	2 (0.4)	0.71
Myocardial infarction	22 (9.8)	40 (15.7)	29 (11.6)	34 (13.9)	51 (10.7)	0.64
Periprocedural	20 (8.9)	39 (15.3)	29 (11.6)	32 (13.1)	47 (9.9)	0.14
Spontaneous	2 (0.9)	1 (0.4)	0	2 (0.8)	4 (0.8)	0.46
Death or MI	23 (10.3)	35 (13.7)	31 (12.4)	30 (12.2)	52 (10.9)	0.72
Death or spontaneous MI	3 (1.3)	2 (0.8)	2 (0.8)	3 (1.2)	8 (1.7)	0.81
Stent thrombosis, definite or probable	1 (0.4)	0	0	3 (1.2)	2 (0.4)	0.71
Repeat revascularization						
All type	15 (6.7)	10 (3.9)	7 (2.8)	16 (6.5)	19 (4.0)	0.15
Target-lesion	7 (3.1)	5 (2.0)	4 (1.6)	8 (3.3)	9 (1.9)	0.30
Target-vessel	9 (4.0)	5 (2.0)	5 (2.0)	9 (3.7)	10 (2.1)	0.20
Composite of death, MI, or TLR	30 (13.4)	42 (16.5)	36 (14.4)	40 (16.3)	61 (12.8)	0.53
MACE[a]	32 (14.3)	42 (16.5)	35 (14.0)	41 (16.7)	62 (13.0)	0.58

Values are n (%). [a]Prespecified major adverse cardiac events (MACE) were defined as a composite of all-cause death, myocardial infarction (MI), and ischemia-driven target-vessel revascularization (TVR).
NA = not available; TLR = target lesion revascularization; other abbreviations as in **Table 1**.

TABLE 5 Unadjusted and Adjusted HRs for Clinical Outcomes Between Pairs of Drug-eluting Stents

Stent Comparison	Death	MI	Death or MI	TLR	MACE[a]
Crude population					
CoCr-EES vs SES	0.53 (0.06-4.74)	0.90 (0.55-1.48)	0.88 (0.54-1.45)	1.69 (0.63-4.53)	1.10 (0.72-1.68)
	$P = 0.57$	$P = 0.67$	$P = 0.61$	$P = 0.30$	$P = 0.67$
PtCr-EES vs SES	0.47 (0.05-4.18)	1.47 (0.97-2.22)	1.25 (0.82-1.92)	1.08 (0.36-3.22)	1.34 (0.91-1.97)
	$P = 0.50$	$P = 0.07$	$P = 0.30$	$P = 0.89$	$P = 0.14$
Re-ZES vs SES	0.95 (0.17-5.19)	1.08 (0.69-1.70)	1.13 (0.73-1.77)	0.84 (0.26-2.72)	1.12 (0.74-1.69)
	$P = 0.90$	$P = 0.74$	$P = 0.58$	$P = 0.77$	$P = 0.58$
N-BES vs SES	0.98 (0.18-5.33)	1.25 (0.81-1.93)	1.10(0.7-1.73)	2.27 (0.92-5.59)	1.32 (0.89-1.95)
	$P = 0.98$	$P = 0.32$	$P = 0.67$	$P = 0.07$	$P = 0.17$
IPTW population					
CoCr-EES vs SES	0.32 (0.03-2.97)	0.67 (0.39-1.16)	0.66 (0.38-1.14)	1.46 (0.49-4.35)	0.84 (0.52-1.34)
	$P = 0.32$	$P = 0.16$	$P = 0.13$	$P = 0.50$	$P = 0.46$
PtCr-EES vs SES	0.29 (0.03-2.70)	1.22 (0.77-1.93)	1.07 (0.66-1.72)	0.62 (0.19-2.01)	1.10 (0.71-1.71)
	$P = 0.28$	$P = 0.40$	$P = 0.79$	$P = 0.42$	$P = 0.66$
Re-ZES vs SES	0.77 (0.13-4.52)	1.02 (0.61-1.73)	1.06 (0.64-1.77)	0.74 (0.21-2.63)	1.06 (0.66-1.69)
	$P = 0.77$	$P = 0.93$	$P = 0.81$	$P = 0.65$	$P = 0.82$
N-BES vs SES	0.82 (0.12-5.54)	0.94 (0.59-1.5)	0.83 (0.51-1.34)	1.77 (0.64-4.84)	1.06 (0.69-1.62)
	$P = 0.84$	$P = 0.80$	$P = 0.44$	$P = 0.27$	$P = 0.79$

Values are adjusted HR (95% CI). [a]Prespecified MACE were defined as a composite of all-cause death, MI, and ischemia-driven TVR.
IPTW = inverse probability of treatment weighting; other abbreviations as in **Tables 1 and 4**.

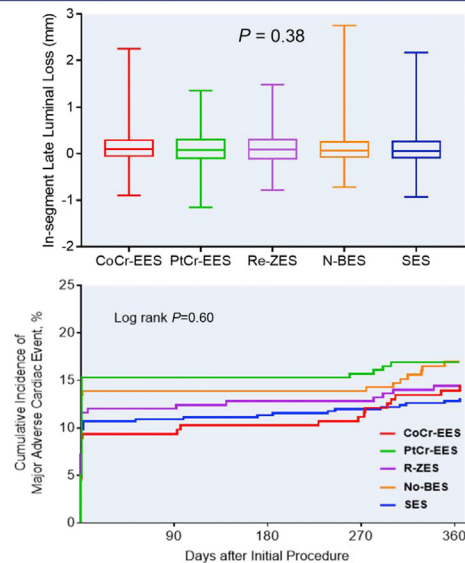**FIGURE 3 Adjusted HRs of Clinical Outcomes Between Different Drug-Eluting Stents**
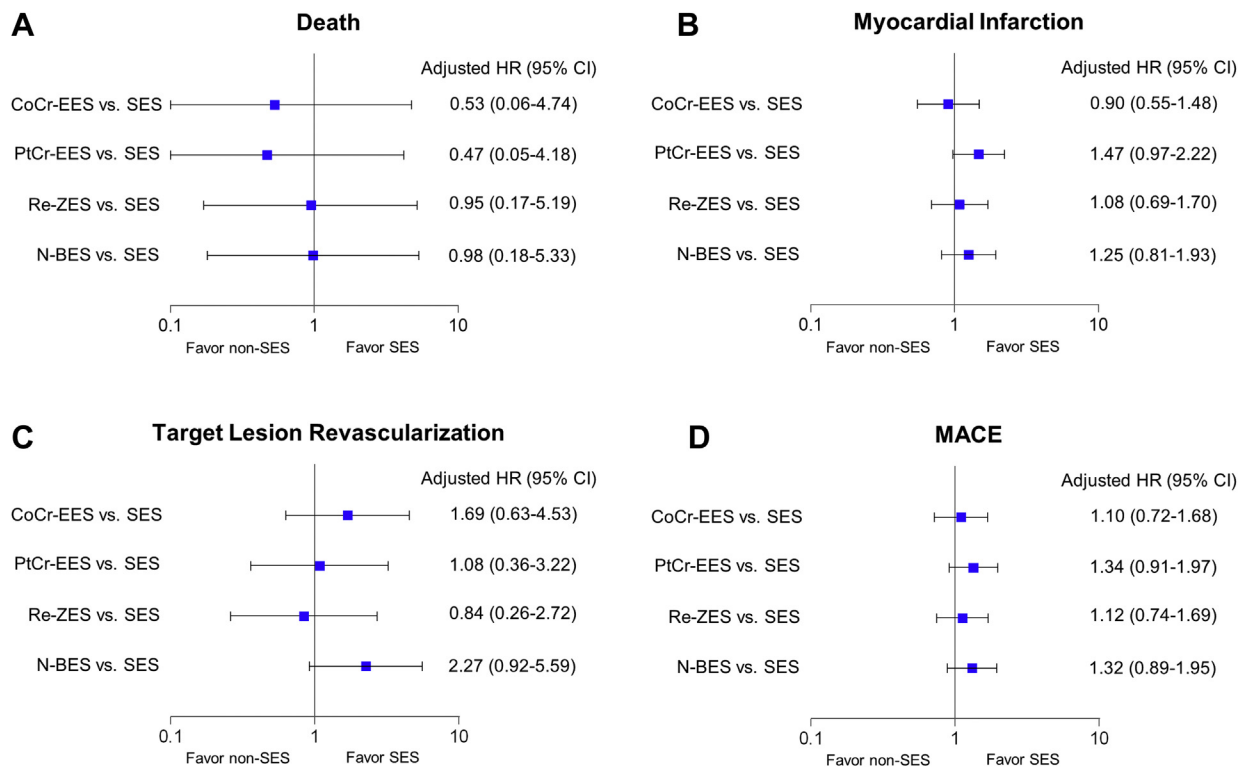
Adjusted HRs are given for difference stent types compared with the SES: **(A)** death, **(B)** myocardial infarction, **(C)** target lesion revascularization, and **(D)** major adverse cardiac events (MACE). Abbreviations as in **Figure 1**.

CENTRAL ILLUSTRATION Primary Angiographic Endpoint and Secondary Clinical Endpoint by Different Drug-Eluting Stents

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Abbreviations as in **Figure 1**.

among stent groups. Although we used propensity-score analysis to enable more extensive adjustment, the unmeasured confounding variables could remain. Second, although merged analyses were performed, the current analyses were underpowered to detect any meaningful difference in clinical endpoints such as death, MI, or stent thrombosis. Third, 3 clinical trials included in these analyses were conducted in different time periods; therefore, unmeasured secular trends could have influenced study results. Fourth, the LONG-DES trials used angiographic endpoints, which may be less precise than intracoronary imaging-measured stent area. Fifth, given that certain current PCI practice patterns in South Korea such as the rates of direct stenting (higher), imaging guidance (higher), and post-dilation (lower) may be different than other parts of the world, the possible limitation of generalizability might exist. Sixth, because this study included relatively older stent platforms, the observed findings of this study may have limited applicability to contemporary PCI practice with a widespread use of thin-strut stents. Finally, an additional limitation of our study was the relatively short follow-up period of 12 months. A longer follow-up

period is essential to confirm the continuing durability of these DES.

CONCLUSIONS

This patient-level pooled analysis of 3 randomized controlled trials comparing different types of DES for long coronary lesions showed no significant differences with regard to angiographic efficacy outcome and clinical efficacy and safety outcomes among several second-generation DES and also first-generation SES.

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PERSPECTIVES

COMPETENCY IN PATIENT CARE AND PROCEDURAL SKILLS: There is limited data regarding the relative efficacy and safety of different types of contemporary DES for diffuse long lesions. In this pooled analysis of individual-patient data from 3 randomized clinical trials, we did not detect significant differences in angiographic efficacy outcome and clinical efficacy and safety outcomes between several DES. The results may have important clinical implication to help treating physicians to select the optimal type of DES for treating high-risk, long diffuse coronary lesions.

TRANSLATIONAL OUTLOOK: Even in the era of second-generation DES, it should be noted that diffuse long lesions showed a relatively unfavorable risk of major adverse cardiac events after PCI. It is needed to reduce the risk of adverse events after stenting for diffuse long lesions through the development of newer techniques, newer devices, and adjunctive medications.

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KEY WORDS coronary artery disease, drug-eluting stents, percutaneous coronary intervention

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APPENDIX For supplemental tables, please see the online version of this paper.