Comparative effectiveness of different contemporary drug-eluting stents in routine clinical practice: a multigroup propensity score analysis using data from the stent-specific, multicenter, prospective registries

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Objective **Data on the comparative effectiveness of contemporary drug-eluting stents (DES) in the unrestricted, real-world setting are limited. We investigated the long-term effectiveness and safety of contemporary different drug-eluting stents by means of multiple treatment propensity score weighting.**

Patients and methods **From seven stent-specific, prospective DES registries conducted between July 2007 and July 2015, we evaluated 17 196 patients who received several contemporary DES and first-generation DES: 3053 treated with cobalt–chromium everolimus-eluting stents (CoCr-EES), 2985 with platinum–chromium EES (PtCr-EES), 2922 with Resolute zotarolimus-eluting stents (Re-ZES), 789 with Biomatrix biolimus-eluting stents (Bi-BES), 1907 with Nobori biolimus-eluting stents (No-BES), 1970 with Xience Prime cobalt–chromium everolimus-eluting stents (Pr-CoCr-EES), and 3570 with sirolimus-eluting stents (SES). The primary outcome was target-vessel failure (a composite of cardiac death, target-vessel myocardial infarction, or target-vessel revascularization) at 3 years of follow-up and major cardiovascular adverse events (a composite of all-cause death, any myocardial infarction, or any revascularization) was also evaluated.**

Results **The observed 3-year rates of target-vessel failure were not significantly different among different second-generation DES and SES (CoCr-EES 9.8%, PtCr-EES 9.5%, Re-ZES 9.3%, Bi-BES 9.8%, No-BES 7.7%, Pr-CoCr-EES 10.4%, SES 10.2%; overall $P = 0.07$). In multiple treatment propensity score analysis, adjusted hazard ratios for target-vessel failure were similar in between-group comparisons of several contemporary DES. In addition, no significant differences were observed with respect of the adjusted risk of major adverse cardiac events.**

Conclusion **In this comparative effectiveness research using stent-specific, clinical practice registries involving unrestricted use of several contemporary DES, there were no significant between-group differences in the 3-year rates of target-vessel failure.** ***Coron Artery Dis*** **30:255–262**

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Introduction

For the treatment of significant coronary artery disease, the use of drug-eluting stents (DES) has been shown to be more effective in the prevention of restenosis and reduction of repeat revascularization than the use of bare-metal stents (BMS) [1]. Since the introduction of first-generation DES older than 10 years ago, the technology and engineering of DES have continuously advanced [2]. Several types of newer-generation DES have been developed that use different antiproliferative drugs with improved drug release kinetics, novel stent materials, thinner strut platforms, easier delivery system, and more biocompatible or biodegradable polymers than their predecessors. These newer-generation DES were associated with better safety outcomes not only compared with first-generation DES but also even compared with BMS [3–8], and led to the rapid replacement of first-generation DES in routine clinical practice.

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Although randomized clinical trials (RCTs) and meta-analyses have reported the relative efficacy and safety profiles of second-generation DES [5,9–14], limited data are available on the comparative effectiveness of several contemporary DES in the unrestricted, daily percutaneous coronary intervention (PCI) setting, which includes more complicated clinical and anatomic characteristics. Given that RCTs have had limited generalizability and insufficient statistical power owing to strict patient-selection criteria and limited sample sizes, and that meta-analyses have used indirect evidence from trials that did not directly compare current-generation DES, evidence from well-conducted, large-sized, prospective cohort studies might provide additional valuable clinical information applicable in contemporary practice. We therefore performed a comparative effectiveness research (CER) to examine the long-term effectiveness and safety of different contemporary DES by using stent-specific, prospective, contemporary clinical practice registries.

Patients and methods

Study population

The study population, consisting of patients who underwent daily PCI procedures with DES implantation for significant coronary artery disease, was pooled from the Interventional Cardiology Research Incorporation Society – Drug-Eluting Stents (IRIS-DES) registry between 15 July 2007 and 29 July 2015. The IRIS-DES registry has been described previously [15], and the key features are summarized in Supplementary Online Table 1 (Supplemental digital content 1, *http://links.lww.com/MCA/A238*). Briefly, the IRIS-DES involves a prospective, multicenter recruitment of unrestricted patients undergoing PCI with DES in Korea and consists of several different arms of first-generation and second-generation DES in contemporary PCI situations. The exclusion criteria are minimal. Patients with cardiogenic shock, malignant disease, or other comorbid conditions with a life expectancy of less than 12 months; those treated with a mixture of different types of DES; and those with planned surgery necessitating interruption of antiplatelet drugs within 6 months after the procedure were excluded.

The current analysis included patients treated with seven types of DES: cobalt–chromium everolimus-eluting stents (CoCr-EES, Xience V; Abbott Vascular, Santa Clara, California, USA), platinum–chromium EES (PtCr-EES, Promus Element; Boston Scientific, Natik, Massachusetts, USA), Resolute zotarolimus-eluting stent (Re-ZES, Resolute Integrity; Medtronic, Meerbusch, Germany), Biomatrix biodegradable-polymer biolimus-eluting stents (Bi-BES, BioMatrix; Biosensors International, Singapore), Nobori biodegradable-polymer biolimus-eluting stents (No-BES, Nobori; Terumo Clinical Supply, Kakamigahara, Japan), Xience Prime cobalt–chromium EES (Pr-CoCr-EES, Xience Prime; Abbott Vascular), and sirolimus-eluting stent (SES, Cypher Select; Cordis Corp., Milpitas, California, USA). These registries were supported by the CardioVascular Research Foundation (Seoul, Korea), and there was no industry involvement in the design, conduct, or analysis of the study. The study protocol was approved by the ethics committee at each participating center, and all patients provided written, informed consent.

Percutaneous coronary intervention procedures and clinical follow-up

In the IRIS-DES registry, PCI was performed according to standard techniques at the discretion of each operator. This registry did not specify the stent types according to clinical or anatomic features; therefore, each operator was responsible for the decision on the choice of a specific DES. Periprocedural anticoagulants were administered according to standard regimens. Glycoprotein IIb/IIIa inhibitors were administered at the discretion of the operator. All patients undergoing PCI received a loading dose of aspirin and $P2Y_{12}$ receptor inhibitor (clopidogrel, prasugrel, or ticagrelor) before or during the intervention. After the procedure, aspirin was continued indefinitely and $P2Y_{12}$ receptor inhibitors were prescribed for at least 12 months regardless of the DES type. Drugs for secondary prevention were prescribed according to current guidelines.

Clinical follow-up was conducted during hospitalization and at 30 days, 6 months, 12 months, and every 6 months thereafter. At these visits, data pertaining to patients' clinical status, all interventions, and outcome events were recorded. All baseline characteristics and outcome data were collected by specialized personnel at each participating center, by using a dedicated, electronic case report form. The Internet-based system provides each center with immediate and continuous feedback on the processes and quality-of-care measures. Monitoring and verification of registry data are periodically performed in the participating hospitals by members of the academic coordinating center (Clinical Research Center, Asan Medical Center, Seoul, Korea) [15]. Clinical trial registration: *http://www.clinicaltrials.gov* (unique identifier: NCT01186133).

Study outcomes and definitions

The primary outcome was target-vessel failure [a composite of cardiac death, target-vessel myocardial infarction (MI), or target-vessel revascularization (TVR)]. The secondary clinical outcomes were death (any cause, cardiac cause, or noncardiac cause), MI (periprocedural or spontaneous), any revascularization (target-lesion revascularization or TVR), stent thrombosis, and major adverse cardiac events (MACE) (a composite of all-cause death, any MI, or any revascularization) as a patient-related outcome.

Death was considered as having cardiac causes unless an unequivocal noncardiac causes could be established. The diagnosis of MI was based on clinically relevant MI

according to the Society for Cardiovascular Angiography and Interventions definition [16]. Repeat revascularization included any type of percutaneous or surgical revascularization procedure and was categorized as revascularization of any lesion, target lesion, and target vessel. Stent thrombosis (definite) was defined according to the Academic Research Consortium definition and categorized as early, late, or very late [17]. All outcomes of interest were confirmed by source documentation collected at each hospital and were centrally adjudicated by an independent clinical events committee, whose members were blinded to the study devices.

Statistical analysis

Baseline characteristics, including patient demographics, risk factors or comorbidities, clinical presentation, cardiac status, and anatomic and procedural features, were described according to specific types of DES. Categorical variables were presented as counts (proportions) and continuous variables were presented as mean (SDs). Differences between treatment groups were evaluated through analysis of variance for continuous variables and the χ^2 or Fisher's exact test for categorical variables.

Cumulative events of clinical outcomes were assessed using Kaplan–Meier estimates and compared with the log-rank test. All analyses were truncated at 3 years of follow-up owing to different follow-up duration according to DES types and the small number of patients with data thereafter. To compensate for the nonrandomized design of this study and to minimize confounding and residual selection bias in observational treatment comparisons, a propensity score weighting method was applied to control for imbalances in various baseline characteristics across the treatment groups [18]. In this study, multiple treatment propensity scores were applied by using the TWANG (Toolkit for Weighting and Analysis of Nonequivalent Groups) method and corresponding inverse probabilities of treatment weight (the reciprocal of the propensity scores) were estimated with generalized boosted models through an iterative estimation procedure ($n = 3000$), by using all the related baseline characteristics [19]. (Supplementary Online Appendix II, Supplemental digital content 1, *http://links.lww.com/MCA/A238*) The balance of the pretreatment covariates was assessed, and significant improvement in baseline was achieved after weighting. (Supplementary Online Table 2 and Supplementary Online Figs 1 and 2, Supplemental digital content 1, *http://links.lww.com/MCA/A238*) For the evaluation of treatment effects, the PROC SURVEYPHREG procedure of SAS was used to correctly interpret weights as probability weights.

For the sake of missing data, albeit less than 5% once it was identified, we performed multiple imputations using Markov chain Monte Carlo in the SAS procedure. To correct multiplicity, a Bonferroni's correction was performed in all multiple outcome comparisons with a test-specific significance level of 0.05/21 equal to 0.002. All analyses were performed with SAS software, version 9.4 (SAS Institute, Cary, North Carolina, USA) and the R software version 3.2.2 (R Foundation for Statistical Computing, Vienna, Austria; *www.r-project.org*).

Results

Study population and baseline characteristics

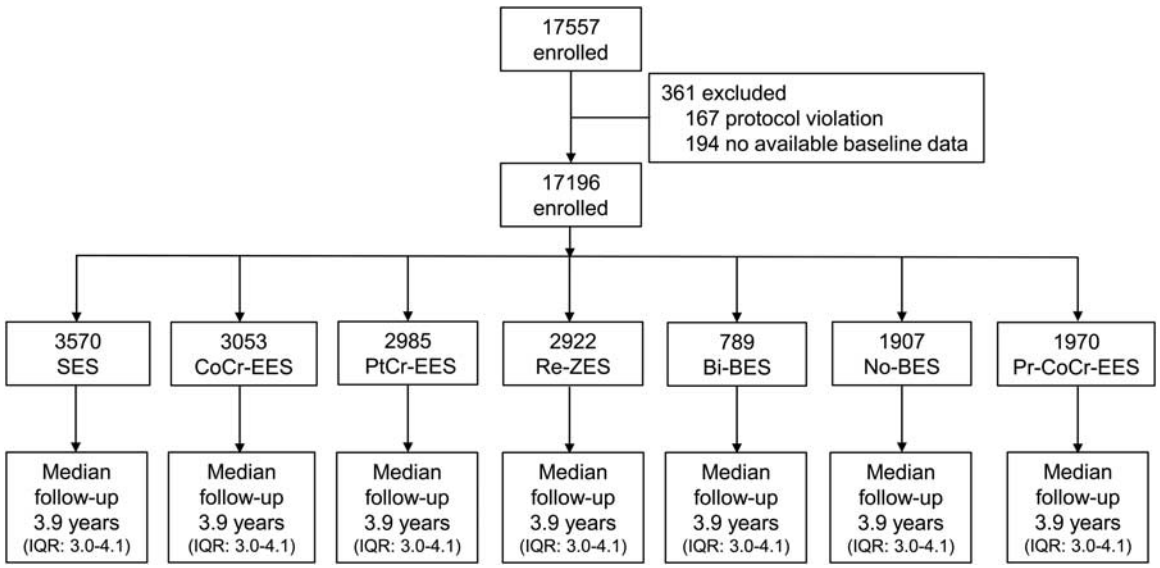
The flow diagram of the study analysis is shown in Fig. 1. Among 17 557 patients from seven stent-specific, prospective IRIS-DES registries between July 2007 and July 2015, a total of 17 196 patients were available for the current analysis (3053 with CoCr-EES, 2985 with PtCr-EES, 2922 with Re-ZES, 789 with Bi-BES, 1907 with No-BES, 1970 with Pr-CoCr-EES, and 3570 with SES). The baseline demographics and clinical characteristics of the study population according to different types of DES are shown in Supplementary Online Table 3 (Supplemental digital content 1, *http://links.lww.com/MCA/A238*). The mean age of the enrolled patients was 63 years and was similar across the multiple cohorts of different DES. However, there were significant between-group differences with regard to sex and several clinical covariates (diabetes, hyperlipidemia, smoking, history of MI, heart failure, PCI or coronary artery bypass grafting, renal failure, ejection fraction, clinical presentation, and number of treated lesions). Supplementary Online Table 4 (Supplemental digital content 1, *http://links.lww.com/MCA/A238*) shows the lesion and procedural characteristics of the study population according to different DES types at baseline. Similar to the pattern of clinical characteristics, there were significant differences across the stent groups with respect to anatomic, lesion, and procedural characteristics.

Clinical outcomes

The median duration of clinical follow-up in the overall population was 3.9 years (interquartile range: 2.6–4.1). Owing to different follow-up durations according to DES types, analyses were truncated at 3 years' follow-up. Within the 3-year follow-up period, there were 802 (4.7%) deaths [cardiac death 514 (3.0%) and noncardiac death 288 (1.7%)], 608 (3.5%) MI [periprocedural MI 370 (2.2%) and spontaneous MI 238 (1.4%)], 1366 (7.9%) repeat revascularizations [target-lesion revascularization 624 (3.6%) and TVR 829 (4.8%)], and 52 (0.3%) definite stent thrombosis. In total, 1648 (9.6%) patients had at least one target-vessel failure event and 2492 (14.5%) had at least one MACE event.

The Kaplan–Meier estimates of primary and secondary outcomes at 3 years are shown in Table 1. There were no statistically significant between-group differences in the 3-year rates of target-vessel failure (Fig. 2a). There were also no significant between-group differences with respect to death, repeat revascularization, or stent thrombosis. However, there was a significant difference in the rate of MI, mainly driven by periprocedural MI; the lowest rate (2.4%) was observed for No-BES and the highest rate (5.1%) was observed for Pr-CoCr-EES. At 3 years, as a patient-related outcome, the rates of MACE

Fig. 1



Study flow diagram. Bi-BES, Biomatrix biolimus-eluting stent(s); CoCr-EES, cobalt–chromium everolimus-eluting stent(s); IQR, interquartile range; No-BES, Nobori biolimus-eluting stent(s); Pr-CoCr-EES, Xience Prime 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).

Table 1 Observed 3-year event rates of primary and secondary clinical outcomes according to different types of drug-eluting stents[a]

Characteristics	CoCr-EES ($n=3053$) [n (%)]	PtCr-EES ($n=2985$) [n (%)]	Re-ZES ($n=2922$) [n (%)]	Bi-BES ($n=789$) [n (%)]	No-BES ($n=1907$) [n (%)]	Pr-CoCr-EES ($n=1970$) [n (%)]	SES ($n=3570$) [n (%)]	P
Primary outcome								
Target-vessel failure[b]	9.8 (300)	9.5 (285)	9.3 (271)	9.8 (77)	7.7 (146)	10.4 (204)	10.2 (365)	0.07
Secondary outcomes								
Death from any cause	4.8 (148)	5.4 (160)	3.4 (100)	4.8 (38)	3.9 (75)	4.7 (93)	5.3 (188)	0.34
Cardiac	3.0 (91)	3.6 (107)	2.3 (67)	2.8 (22)	2.8 (54)	2.8 (56)	3.3 (117)	0.84
Noncardiac	1.9 (57)	1.8 (53)	1.1 (33)	2.0 (16)	1.1 (21)	1.9 (37)	2.0 (71)	0.18
MI	3.3 (101)	2.6 (78)	4.4 (130)	3.0 (24)	2.4 (46)	5.1 (100)	3.6 (129)	<0.001
Periprocedural	2.0 (60)	1.4 (42)	3.1 (92)	1.3 (10)	1.4 (26)	3.6 (71)	1.9 (69)	<0.001
Spontaneous	1.3 (41)	1.2 (36)	1.3 (38)	1.8 (14)	1.0 (20)	1.5 (29)	1.7 (60)	0.40
Any revascularization	8.0 (244)	8.2 (244)	7.1 (208)	8.2 (65)	7.6 (144)	8.3 (163)	8.3 (298)	0.32
TLR	4.2 (127)	3.4 (101)	3.1 (91)	4.4 (35)	2.6 (50)	3.1 (61)	4.5 (159)	0.06
TVR	5.3 (163)	4.9 (147)	4.1 (120)	5.8 (46)	3.7 (71)	4.5 (88)	5.4 (194)	0.26
Definite stent thrombosis	0.4 (13)	0.2 (6)	0.2 (6)	0.4 (3)	0.3 (6)	0.2 (4)	0.4 (14)	0.87
Early (0–30 days)	0.3 (9)	0.1 (3)	0.1 (3)	0.3 (2)	0.2 (3)	0.1 (2)	0.2 (6)	0.48
Late (30 days–1 year)	0.1 (2)	0.03 (1)	0.03 (1)	–	–	–	–	0.62
Very late (1–3 years)	0.1 (2)	0.1 (2)	0.1 (2)	0.1 (1)	0.2 (3)	0.1 (2)	0.2 (8)	0.53
MACE[c]	14.6 (445)	14.6 (435)	13.6 (396)	14.2 (112)	12.8 (244)	16.1 (318)	15.2 (542)	0.11

Bi-BES, Biomatrix biolimus-eluting stent(s); CoCr-EES, cobalt–chromium everolimus-eluting stent(s); MACE, major adverse cardiovascular events; MI, myocardial infarction; No-BES, Nobori biolimus-eluting stent(s); Pr-CoCr-EES, Xience Prime 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); TLR, target-lesion revascularization; TVR, target-vessel revascularization.
[a]Cumulative 3-year rates (numbers) of events based on Kaplan–Meier estimates and compared with the long-rank test.
[b]Target-vessel failure was defined as a composite of death from cardiac causes, target-vessel MI, or TVR.
[c]MACE was defined as a composite of all-cause death, any MI, or any revascularization.

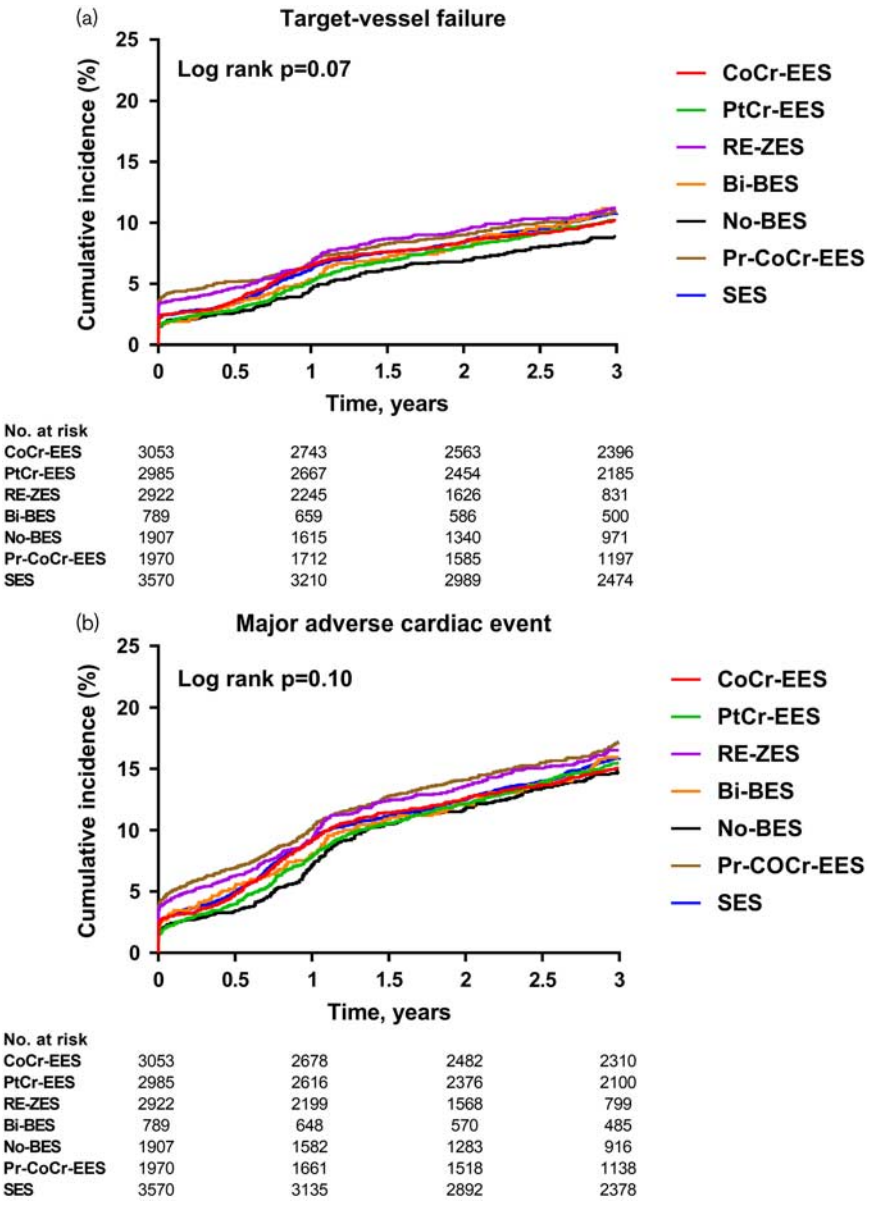
were not significantly different between several stent groups (Fig. 2b).

The adjusted hazard ratios for multiple DES comparisons from the multiple treatment propensity score weighting method are shown in Table 2. With CoCr-EES as the reference group, the hazard ratios for the other second-generation DES and first-generation SES were similar with respect to the risk of target-vessel failure as a device-related outcome (Fig. 3a). This pattern was also consistent with the risk of MACE as a patient-related outcome (Fig. 3b).

Discussion

This study is the largest, most comprehensive report to date providing a pairwise comparison of the long-term

Fig. 2



Cumulative 3-year incidence of clinical outcomes according to different types of drug-eluting stents. Cumulative incidence curves are shown for target-vessel failure (a) and major adverse cardiac events (b). *P* values were calculated by using the log-rank test. Target-vessel failure was defined as a composite of death from cardiac causes, target-vessel myocardial infarction, or target-vessel revascularization. Major adverse cardiac events was defined as a composite of all-cause death, any myocardial infarction, or any revascularization. Bi-BES, Biomatrix biolimus-eluting stent(s); CoCr-EES, cobalt–chromium everolimus-eluting stent(s); No-BES, Nobori biolimus-eluting stent(s); Pr-CoCr-EES, Xience Prime 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).

effectiveness and safety of different types of current-generation DES in daily clinical practice. In this pooled analysis of several stent-specific, multicenter, prospective registries, the rate of target-vessel failure at 3 years was similar among different types of contemporary DES. There were between-group differences in the rate of MI, mainly driven by periprocedural MI. However, there were no significant differences in the rates of stent thrombosis and a patient-related outcome of MACE according to different types of contemporary DES.

Although RCT is the best study design to control for treatment-selection bias, RCTs often involve highly selected patients and atypical practice settings, which can limit the generalizability of the trial results. Thus, non-randomized, observational data from clinical databases

Table 2 Adjusted hazard ratios for primary and key secondary clinical outcomes according to different types of drug-eluting stents in the multigroup propensity score analyses[a]

	Target-vessel failure[b]	Death	MI	TVR	Definite stent thrombosis	MACE[c]
Individual DES comparison						
PtCr-EES vs. CoCr-EES	1.09 (0.84–1.41)	1.18 (0.83–1.69)	0.91 (0.57–1.47)	0.99 (0.69–1.41)	0.39 (0.09–1.77)	1.06 (0.86–1.32)
Re-ZES vs. CoCr-EES	1.26 (0.96–1.64)	0.89 (0.59–1.34)	**1.72 (1.13–2.62)**	1.06 (0.72–1.55)	0.51 (0.11–2.34)	1.18 (0.95–1.47)
Bi-BES vs. CoCr-EES	1.15 (0.76–1.74)	1.08 (0.60–1.98)	1.06 (0.51–2.21)	1.28 (0.74–2.20)	1.13 (0.15–8.42)	1.10 (0.78–1.55)
No-BES vs. CoCr-EES	0.96 (0.69–1.33)	0.95 (0.60–1.51)	0.89 (0.50–1.61)	0.88 (0.56–1.40)	0.66 (0.14–3.10)	1.03 (0.80–1.34)
Pr-CoCr-EES vs. CoCr-EES	1.13 (0.85–1.50)	0.91 (0.60–1.39)	**1.69 (1.08–2.65)**	0.89 (0.59–1.35)	0.33 (0.06–1.91)	1.16 (0.92–1.46)
SES vs. CoCr-EES	1.09 (0.85–1.40)	1.12 (0.79–1.59)	1.18 (0.77–1.81)	1.03 (0.73–1.44)	0.82 (0.25–2.68)	1.07 (0.87–1.31)
Re-ZES vs. PtCr-EES	1.16 (0.89–1.50)	0.75 (0.50–1.12)	**1.88 (1.21–2.91)**	1.07 (0.73–1.57)	1.30 (0.22–7.74)	1.11 (0.90–1.38)
Bi-BES vs. PtCr-EES	1.05 (0.70–1.60)	0.92 (0.51–1.66)	1.16 (0.55–2.44)	1.29 (0.75–2.23)	2.90 (0.32–26.51)	1.03 (0.73–1.45)
No-BES vs. PtCr-EES	0.88 (0.63–1.22)	0.81 (0.51–1.27)	0.98 (0.54–1.78)	0.89 (0.56–1.42)	1.69 (0.28–10.25)	0.97 (0.75–1.25)
Pr-CoCr-EES vs. PtCr-EES	1.04 (0.78–1.38)	0.77 (0.52–1.16)	**1.85 (1.16–2.95)**	0.90 (0.60–1.37)	0.84 (0.12–6.16)	1.09 (0.76–1.37)
SES vs. PtCr-EES	1.01 (0.79–1.29)	0.95 (0.68–1.33)	1.29 (0.83–2.01)	1.04 (0.74–1.46)	2.10 (0.47–9.50)	1.00 (0.82–1.22)
Bi-BES vs. Re-ZES	0.91 (0.60–1.38)	1.22 (0.65–2.29)	0.62 (0.30–1.26)	1.21 (0.69–2.11)	2.23 (0.24–20.77)	0.93 (0.66–1.31)
No-BES vs. Re-ZES	0.76 (0.55–1.06)	1.07 (0.62–1.76)	**0.52 (0.30–0.81)**	0.84 (0.52–1.35)	1.30 (0.22–7.82)	0.87 (0.67–1.34)
Pr-CoCr-EES vs. Re-ZES	0.90 (0.67–1.20)	1.03 (0.62–1.62)	0.99 (0.65–1.49)	0.85 (0.55–1.31)	0.65 (0.09–4.74)	0.98 (0.77–1.24)
SES vs. Re-ZES	0.87 (0.68–1.12)	1.26 (0.85–1.87)	0.69 (0.47–1.01)	0.97 (0.68–1.40)	1.62 (0.36–7.28)	0.90 (0.73–1.11)
No-BES vs. Bi-BES	0.83 (0.53–1.32)	0.88 (0.45–1.70)	0.84 (0.37–1.92)	0.69 (0.37–1.28)	0.58 (0.06–5.46)	0.94 (0.65–1.37)
Pr-CoCr-EES vs. Bi-BES	0.98 (0.64–1.52)	0.84 (0.45–1.58)	1.60 (0.77–3.32)	0.70 (0.39–1.25)	0.29 (0.03–3.16)	1.06 (0.74–1.51)
SES vs. Bi-BES	0.95 (0.64–1.43)	1.03 (0.57–1.86)	1.12 (0.55–2.28)	0.80 (0.47–1.37)	0.73 (0.10–5.36)	0.97 (0.70–1.37)
Pr-CoCr-EES vs. No-BES	1.18 (0.83–1.67)	0.96 (0.58–1.59)	**1.89 (1.06–3.38)**	1.01 (0.61–1.68)	0.50 (0.07–3.73)	1.12 (0.85–1.47)
SES vs. No-BES	1.15 (0.83–1.57)	1.18 (0.75–1.84)	1.32 (0.76–2.32)	1.16 (0.75–1.82)	1.25 (0.27–5.78)	1.03 (0.82–1.22)
SES vs. Pr-CoCr-EES	0.97 (0.74–1.28)	1.23 (0.82–1.83)	0.70 (0.46–1.06)	1.15 (0.77–1.72)	2.50 (0.43–14.43)	0.92 (0.74–1.15)

Bi-BES, Biomatrix biolimus-eluting stent(s); CoCr-EES, cobalt–chromium everolimus-eluting stent(s); MACE, major adverse cardiovascular events; MI, myocardial infarction; No-BES, Nobori biolimus-eluting stent(s); Pr-CoCr-EES, Xience Prime 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); TVR, target-vessel revascularization.
Statistically significant values are highlighted in bold.
[a]Values are hazard ratio (95% confidence interval).
[b]Target-vessel failure was defined as a composite of death from cardiac causes, target-vessel MI, or TVR.
[c]MACE was defined as a composite of all-cause death, any MI, or any revascularization.

can complement data from RCT and may better reflect more typical practice settings. In addition, given that several types of second-generation DES are currently available in the real-world PCI practice and with the predominant use of newer-generation DES, a CER of these contemporary DES needs to be conducted [20]. Our CER using stent-specific, clinical registries determined the long-term relative effectiveness and safety of diverse types of current-generation DES in a broadly representative population, and such observational treatment comparisons might contribute substantially to the understanding of real-life clinical situations and may facilitate medical decision making in the contemporary practice setting.

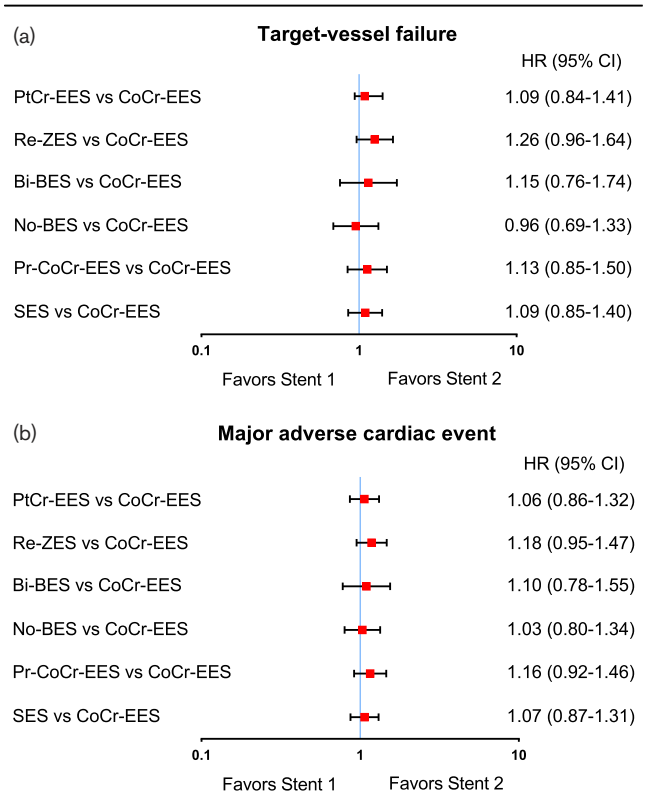
In this contemporary clinical practice registry study involving unrestricted use of several contemporary DES, in the overall population, there were no significant between-group differences with respect to the adjusted risk of target-vessel failure. In addition, no significant differences were observed with respect of the adjusted risk of MACE. Similarly, in the network meta-analysis, no significant between-group differences in clinical outcomes were observed for the pairwise comparisons of the different types of DES [4,5]. In this study, to reduce the impact of treatment-selection bias or potential confounding in our observational study, propensity score methods were used. Our propensity score estimation for multiple treatments by using generalized boosted models may provide advantages allowing a fair examination of the causal treatment effects of multiple treatment conditions [19]. Nonetheless, at best, the methods only remove confounding by observed variables. Thus, unknown or unmeasured confounders or exchangeability must hold for an unbiased estimation of the causal estimates.

In our study, the incidence of stent thrombosis was extremely low. The relatively low rate of stent thrombosis in our population, as compared with that in the Western population, might be explained in part by differences in clinical or lesion characteristics, the particulars of PCI procedures (i.e. more frequent use of intravascular ultrasound), or ethnic disparity, as previously noted [21–23]. Owing to the few number of thrombotic events, our study cannot provide reliable 'real-world' clinical evidence with regard to the relative long-term safety of contemporary DES, as reported in a previous network meta-analysis [5]. The authors found that CoCr-EES were associated with lower rates of definite stent thrombosis, MI, and even lower rates of mortality than BMS and first-generation DES (SES and paclitaxel-eluted stent), and with less stent thrombosis than BES. Also, contrary to previous studies [5,7], our study did not demonstrate reduced mortality with second-generation DES compared with first-generation DES.

Study limitations

Potential limitations of this study warrant discussion. First, as this study is observational in nature, the overall

Fig. 3



Adjusted HR for clinical outcomes according to different types of drug-eluting stents in the propensity score analyses. Adjusted HRs are shown for comparison of different types of drug-eluting stents with CoCr-EES as the reference device (a, target-vessel failure; b, major adverse cardiac events). Target-vessel failure was defined as a composite of death from cardiac causes, target-vessel myocardial infarction, or target-vessel revascularization. Major adverse cardiac events was defined as a composite of all-cause death, any myocardial infarction, or any revascularization. Bi-BES, Biomatrix biolimus-eluting stent(s); CI, confidence interval; CoCr-EES, cobalt–chromium everolimus-eluting stent(s); HR, hazard ratio; No-BES, Nobori biolimus-eluting stent(s); Pr-CoCr-EES, Xience Prime 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).

findings should be considered hypothetical and hypotheses generating only. Second, a weakness of all observational CER studies is the absence of a randomized assignment of treatments. Although we used propensity analysis to enable an even more rigorous adjustment for differences in baseline characteristics, the estimates of relative treatment effects can be biased due to residual confounding or selection bias. In addition, it must be acknowledged that unmeasured variables (i.e., distribution of DES across centers, secular trends, and impact of pharmacological therapies) can influence the results. Third, as first-generation DES comparator, there are no patients with paclitaxel-eluting stents (TAXUS) as no registry on the TAXUS stent was performed by the group of the IRIS-DES registry. Fourth, owing to the limited number of hard clinical endpoints, our study was underpowered to detect significant differences in serious safety outcomes such as stent thrombosis or mortality. Finally, longer-term follow-up is required to examine whether additional differences in late-occurring events among contemporary DES emerge over time. A final 5-year follow-up in each stent registry is currently being undertaken.

Conclusion

In this contemporary clinical practice registry study, there were no significant differences in stent-related and patient-related outcomes at 3-year follow-up in pairwise comparisons of several contemporary DES in daily PCI practice. However, the small absolute difference in outcomes in our study warrants further investigation and should be confirmed or refuted through large, clinical trials with longer-term follow-up.

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Conflicts of interest

There are no conflicts of interest.

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