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ORIGINAL STUDIES

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Ten-year outcomes of early generation sirolimus- versus paclitaxel-eluting stents in patients with left main coronary artery disease

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Abstract

To compare 10-year outcomes after implantation of sirolimus-eluting stents (SES) versus paclitaxel-eluting stents (PES) for left main coronary artery (LMCA) stenosis. Very long-term outcome data of patients with LMCA disease treated with drug-eluting stents (DES) have not been well described. In 10-year extended follow-up of the MAINCOMPARE registry, we evaluated 778 patients with unprotected LMCA stenosis who were treated with SES ($n = 607$) or PES ($n = 171$) between January 2000 and June 2006. The primary composite outcome (a composite of death, myocardial infarction [MI] or target-vessel revascularization [TVR]) was compared with an inverse-probability-of-treatment-weighting (IPTW) adjustment. Clinical events have linearly accumulated over 10 years. At 10 years, there were no significant differences between SES and PES in the observed rates of the primary composite outcome (42.0% vs. 47.4%; hazard ratio [HR] 0.85; 95% confidence interval [CI] 0.66–1.10), and definite stent thrombosis (ST) (1.9% vs. 1.8%; HR 1.02, 95% CI 0.28–3.64). In the IPTW-adjusted analyses, there were no significant differences between SES and PES in the risks for the primary composite outcome (HR 0.89, 95% CI 0.65–1.14) or definite ST (adjusted HR 1.05, 95% CI 0.29–3.90). In patients who underwent DES implantation, high overall adverse clinical event rates (with a linearly increasing event rate over time) were observed during extended follow-up. At 10 years, there were no measurable differences in outcomes between patients treated with SES vs. PES for LMCA disease. The incidence of stent thrombosis was quite low and comparable between the groups.

KEYWORDS
drug-eluting stents, left main coronary artery disease, mortality, percutaneous coronary intervention

Abbreviations: CABG, coronary artery bypass grafting; CI, confidence interval; HR, hazard ratio; IPTW, inverse-probability-of-treatment weighting; LMCA, left main coronary artery; MI, myocardial infarction; MAINCOMPARE, revascularization for unprotected left main coronary artery Stenosis: comparison of percutaneous coronary angioplasty versus surgical revascularization; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stent(s); SES, sirolimus-eluting stent(s); TVR, target vessel revascularization.

1 | INTRODUCTION

Percutaneous coronary intervention (PCI) with implantation of drug-eluting stents (DES) has become one of the most frequently performed therapeutic procedures in medicine and has been widely indicated for high-risk patients and lesion subsets.[1] Among the diverse clinical and anatomic indications for PCI, left main coronary artery (LMCA) disease is the highest risk lesion subset and thus coronary-artery bypass grafting (CABG) has been the standard of revascularization for this subset for many years. Despite this, PCI with DES has become a good alternative option for revascularization in patients with LMCA disease based on multiple randomized clinical trials (RCTs),[2–5] and recently extended follow-up of these studies showed comparable long-term outcomes of PCI and CABG for patients with LMCA disease who have a low-to-intermediate anatomic complexity.[6–9]

Until recently, the time horizon of follow-up in clinical studies of patients with LMCA disease treated with DES implantation has been limited, despite the fact that a significant proportion of patients enrolled in the various trials were middle-aged and many patients will live for many years with permanently implanted coronary devices. Also, few data are available on the very long-term (> 10 years) comparative effectiveness of different types of DES applied in treatment for unprotected LMCA disease. We previously reported that sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) demonstrated similar rates of death, myocardial infarction (MI), repeat revascularization, and stent thrombosis (ST) at 3 years.[10] Against this background, to evaluate the very long-term durability of DES implantation and to compare the risks and benefits of the use of SES versus PES for unprotected LMCA disease, we thus report extended 10-year follow-up of patients enrolled in the MAIN-COMPARE (revascularization for unprotected left main coronary artery stenosis: comparison of percutaneous coronary angioplasty versus surgical revascularization) registry.[11]

2 | METHODS

2.1 | Study population, procedures, and follow-up

The study design, characteristics, primary results, and final 10-year outcomes of the MAIN-COMPARE study (NCT02791412) have been reported previously.[11–13] In brief, the MAIN-COMPARE study included consecutive patients with significant LMCA disease who underwent PCI or CABG as the index procedure at 12 major cardiac centers in Korea between January 2000 and June 2006. Patients with previous CABG, concomitant valve or aortic surgery, or ST-segment elevation MI or cardiogenic shock at presentation were excluded. The use of clinical data for this study was approved by local ethics committees at each hospital, and all patients provided written informed consent.

In the MAIN-COMPARE registry, bare-metal stents and DES were exclusively used from January 2000 to May 2003 and from May 2003 to June 2006, respectively, due to the availability of these devices. The study population of the current analysis comprised 778 consecutive patients with LMCA stenosis who underwent DES implantation between May 2003 and June 2006 and who had complete 10-year follow-up information. All PCI procedures were performed with standard interventional techniques and the use of intravascular ultrasound (IVUS) and the choice of SES (Cypher and Cypher Select, Cordis, Johnson & Johnson) or PES (Taxus Express and Liberté, Boston Scientific) were at the discretion of the treating physicians. Antiplatelet therapy and periprocedural anticoagulation followed standard regimens.

The methods for data acquisition and management during the extended follow-up have been described previously.[11] Follow-up was performed in accordance with local laws and the regulations of each participating institution and was extended through December 31, 2016 to ensure availability of 10-year follow-up for all of the study subjects. Complete information on vital status were also reconfirmed from the National Population Registry of the Korea National Statistical Office.

2.2 | Study outcomes and definitions

The primary outcome of the study was the composite of death from any causes, MI, or target-vessel revascularization (TVR) at 10 years. Secondary outcomes included individual components of the composite outcome and definite ST. In the current study, all-cause mortality was assessed, which is the most unbiased method to report deaths in a clinical trial or observational study.[14] On the basis of the protocol definition of MI, MI was defined as the documentation of a new pathologic Q wave during the index hospitalization or an increase in the creatine kinase MB level to one greater than the upper limit of the normal range, plus ischemic symptoms or signs, during the follow-up. TVR was defined as any repeat revascularization (either PCI or CABG) of the treated vessel, including any segments of the left anterior descending and/or left circumflex artery. Definite ST was assessed according to the Academic Research Consortium definition.[15] All clinical outcomes were confirmed by source documentation collected at each hospital and central adjudication was performed for all clinical events by an independent group of clinicians unaware of the DES type.

2.3 | Statistical analysis

Continuous variables were compared with Student's *t*-test or the Wilcoxon rank-sum test, and categorical variables were compared with the chi-square test or the Fisher exact test as appropriate. Observed (unadjusted) cumulative event rates were estimated by the Kaplan–Meier method and compared with the log-rank test.

Crude and adjusted risk for adverse outcomes were compared by univariate and multivariable Cox proportional hazards regression analysis. Variables reported in Tables 1 and 2 with a p value <0.2 in univariate Cox regression were candidates for multivariable Cox proportional hazards models. The final models were determined by a backward elimination procedure. The proportional hazards assumption was confirmed by examination of the log (−log [survival]) curves

TABLE 1 Baseline clinical characteristics of the patients

Variable	SES ($N = 607$)	PES ($N = 171$)	p value	Standardized difference (%)[a]
Age (years)	61.9 ± 11.1	64.3 ± 10.8	0.01	21.6
Male	433 (71.3)	120 (70.2)	0.77	2.5
Body mass index (kg/m^2)	24.6 ± 2.9	24.1 ± 3.0	0.03	19.5
Diabetes mellitus				
Any type	192 (31.6)	56 (32.8)	0.78	2.4
Insulin treated	47 (7.7)	16 (9.4)	0.49	5.8
Hypertension	320 (52.7)	93 (54.4)	0.70	3.3
Hyperlipidemia	188 (31.0)	51 (29.8)	0.77	2.5
Current smoker	151 (24.9)	41 (24.0)	0.81	2.1
Family history of CAD	41 (6.8)	12 (7.0)	0.90	1.0
Previous MI	46 (7.6)	17 (9.9)	0.32	8.4
Previous PCI	125 (20.6)	34 (19.9)	0.84	1.8
Previous CHF	17 (2.8)	3 (1.8)	0.59	7.0
Peripheral vascular disease	10 (1.7)	4 (2.3)	0.52	5.0
Chronic lung disease	18 (3.0)	2 (1.2)	0.28	12.6
Chronic kidney disease	21 (3.5)	5 (2.9)	0.73	3.0
Atrial fibrillation	16 (2.6)	2 (1.2)	0.39	10.7
Left ventricular ejection fraction (%)	60 ± 11	60 ± 12	>0.99	2.5
Clinical presentation			0.06	24.2
Silent ischemia	22 (3.6)	4 (2.3)		
Stable angina	221 (36.4)	45 (26.3)		
Unstable angina	301 (49.6)	101 (59.1)		
NSTEMI	63 (10.4)	21 (12.3)		

Note: Values are mean ± SD or *n* (%).

Abbreviations: CAD, coronary artery disease; CHF, congestive heart failure; MI, myocardial infarction; NSTEMI, non-ST-elevation myocardial infarction; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stents; SES, sirolimus-eluting stents.

[a]The standardized differences are reported as percentages; a difference of less than 10.0% indicates a relatively small imbalance.

and by testing of partial (Schoenfeld) residuals,[16] and no relevant violations were found.

To reduce the impact of treatment selection bias and potential confounding and compensate for the nonrandomized design of this study, primary analysis was performed using inverse-probability-treatment-weighting (IPTW) based on propensity scores.[17] With that technique, weights for patients receiving PES were the inverse of (1-propensity score), and weights for patients receiving SES were the inverse of the propensity score. The propensity scores were estimated by multiple logistic-regression analysis.[18] To create the propensity score, multiple imputation with Markov Chain Monte Carlo methods were used to fill out incomplete baseline variables with the assumption that data were missing at random.[19] All prespecified covariates were included in the full nonparsimonious models for treatment with SES versus PES (Table 1). We also assessed the consistency of treatment effects in the several key clinical or anatomical subgroups using IPTW-adjusted Cox regression models with tests for interactions. Adjusted cumulative event rates were estimated by the weighted Kaplan–Meier method. To assess the time stratified effect of the treatment, the landmark analysis using the Cox model with time-varying coefficients for early and late (≤ 3 years or > 3 years) periods was performed.

All reported p values are two-sided, and those smaller than 0.05 were considered significant in all tests. No adjustment for multiple testing was undertaken. Because of the potential for type I error due to multiple comparisons, all findings of this study should be interpreted as exploratory. All statistical analyses were performed with the use of SAS software, version 9.4 (SAS Institute) and R version 3.6.3 (R Foundation for Statistical Computing, Vienna, Austria).

3 | RESULTS

3.1 | Baseline characteristics

A total of 778 patients who underwent DES implantation and had valid information on 10-year outcomes were included in the current

TABLE 2 Angiographic and procedural characteristics of the patients

Variable	SES ($N = 607$)	PES ($N = 171$)	p value	Standardized difference[a] (%)
Lesion location			0.20	11.1
Ostium and Shaft	254 (41.9)	81 (47.4)		
Bifurcation	353 (58.2)	90 (52.6)		
Extent of diseased vessel			0.10	22.1
Left main only	118 (19.4)	26 (15.2)		
Left main plus 1-vessel disease	149 (24.6)	31 (18.1)		
Left main plus 2-vessel disease	160 (26.4)	54 (31.6)		
Left main plus 3-vessel disease	180 (29.7)	60 (35.1)		
Right coronary artery disease	249 (41.0)	79 (46.2)	0.23	10.5
Restenotic lesion	18 (3.0)	8 (4.7)	0.27	8.9
Use of glycoprotein IIb/IIIa inhibitor	40 (6.6)	5 (2.9)	0.07	17.3
Use of intraaortic balloon pump	23 (3.8)	3 (1.8)	0.19	12.4
Guidance of intravascular ultrasound	483 (79.6)	115 (67.3)	0.001	28.2
Direct stenting	139 (22.9)	22 (12.9)	0.004	8.3
Lesion preparation				
Cutting balloon	25 (4.1)	4 (2.3)	0.28	10.1
Directional atherectomy	16 (2.6)	1 (0.6)	0.14	16.3
Rotational atherectomy	2 (0.3)	0 (0)	>0.99	8.1
No. of stents implanted in LMCA lesion	1.2 ± 0.5	1.2 ± 0.5	0.47	1.8
Total stent length in LMCA lesion	33 ± 22	32 ± 21	0.15	6.9
No. of stents per patient	2.1 ± 1.2	2.1 ± 1.2	0.74	0.6
Average stent diameter	3.3 ± 0.2	3.4 ± 0.2	0.05	18.3
Bifurcation treatment			0.93	8.3
Single stenting (cross over)	462 (76.1)	132 (77.2)		
Complex stenting (≥2 stents)	145 (23.9)	39 (22.8)		
Kissing stenting	47 (7.7)	10 (5.8)		
T-stenting	24 (4.0)	8 (4.7)		
Crush stenting	71 (11.7)	20 (11.7)		
Others	3 (0.5)	1 (0.6)		

Note: Values are mean ± SD or *n* (%).

Abbreviations: LMCA, left main coronary artery; PCI, percutaneous coronary intervention; PES, paclitaxel-eluting stents; SES, sirolimus-eluting stents.

[a]The standardized differences are reported as percentages; a difference of less than 10.0% indicates a relatively small imbalance.

analysis: 607 patients (78%) were treated with SES, 171 patients (22%) were treated with PES. Baseline clinical characteristics according to the DES type are summarized in Table 1. There were no significant differences in baseline demographics, risk factors, or comorbidities between the SES and PES groups, except that patients treated with SES were younger and had higher mean values of their body mass index. Baseline anatomic and procedural characteristics between the two stent groups are shown in Table 2. Most of these characteristics were not significantly different, except that patients with SES had a higher proportion of IVUS-guided PCI and direct stenting without predilation.

After adjustment with the use of IPTW method, all of the clinical covariates were well balanced (Table S1 and Table S2 in the supplementary appendix); the standardized differences were less than 10.0% for all variables, indicating only small differences between the two groups.

3.2 | 10-Year clinical outcomes

The median duration of follow-up among all patients was 11.5 years (interquartile range, 10.3–12.4). Complete follow-up data for major clinical events were obtained in 98.7% of the overall cohort. During the entire follow-up period, 171 patients (22.2%) died, 79 (10.4%) had an MI, and 153 (21.3%) had a TVR.

The cumulative incidences and long-term relative risks of clinical outcomes at 10 years are summarized in Table 3. Over time, we observed linearly increasing event rates with all stent types with no plateau evident over 10 years (Figure 1). The observed 10-year rates of the primary composite outcome of death, MI, or TVR were similar between the SES and PES groups (42.0% vs. 47.4%, respectively; log-rank $p = 0.22$). In addition, there were no significant differences between SES and PES in the observed 10-year rates of death

TABLE 3 Crude and adjusted hazard ratios for 10-year clinical outcomes according to the stent group[a]

	Outcome rates (%) at 10 years		Unadjusted		Multivariable		Adjusted by IPTW	
Outcome	SES	PES	Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p	Hazard Ratio (95% CI)	p
Primary composite outcome								
Death, MI, or TVR	42.0	47.4	0.85 (0.66–1.10)	0.22	0.84 (0.65–1.09)	0.18	0.86 (0.65–1.14)	0.29
Secondary outcome								
Death from any cause	21.9	23.4	0.93 (0.65–1.33)	0.69	1.06 (0.74–1.53)	0.74	1.04 (0.68–1.58)	0.87
MI	9.6	14.1	0.67 (0.41–1.09)	0.11	0.62 (0.38–1.02)	0.06	0.66 (0.39–1.12)	0.13
TVR	20.9	22.6	0.92 (0.63–1.35)	0.68	0.88 (0.60–1.29)	0.52	0.83 (0.54–1.29)	0.41
Definite ST	1.9	1.8	1.02 (0.28–3.64)	0.98	NA	NA	1.05 (0.28–3.90)	0.94

Abbreviations: MI, myocardial infarction; NA, not available; PES, paclitaxel-eluting stents; SES, sirolimus-eluting stents, stent; ST, stent thrombosis; TVR, target vessel revascularization.

[a]Hazard ratios are for the SES group, as compared with PES group.

(21.9% vs. 23.4%, respectively; long-rank $p = 0.69$), MI (9.6% vs. 14.1%, respectively; long-rank $p = 0.10$), or TVR (20.9% vs. 22.6%, respectively; long-rank $p = 0.68$). The 10-year rates of definite ST were quite low and comparable in both groups (11 patients [1.9%] vs. 3 patients [1.8%], respectively; log-rank $p = 0.98$). After multivariable adjustment, there were no significant differences between SES and PES in the adjusted risks of the primary composite outcome, death, MI, TVR, or definite ST (Table 3).

In the final adjusted models with the use of the IPTW methods, the adjusted risk for the primary composite outcome was similar between the SES and PES groups (hazard ratio [HR] 0.89, 95% confidence interval [CI] 0.65–1.14) (Table 3 and Figure 2). The adjusted risks for death, MI, TVR, or definite ST were also similar between the 2 DES groups. The IPTW-adjusted HRs for the key clinical and anatomic subgroups are illustrated in Figure 3. The 10-year adjusted risks of the primary composite outcome between SES and PES were consistent across multiple subgroups, except for subgroups according to diabetes, in which treatment effect favored PES in the diabetic subgroup, whereas it favored SES in the nondiabetic subgroup.

3.3 | Landmark analysis at 3 years

During the first 3 years, the adjusted risk for the primary composite outcome was similar between the SES and PES groups (HR 0.90, 95% CI 0.47–1.71, $p = 0.74$) (Table S3 in the supplemental appendix). There were the similar risks for the secondary outcomes prior to 3 years in patient with treated with SES versus PES (Death: HR 0.44, 95% CI 0.03–7.09, $p = 0.57$, MI: HR 0.90, 95% CI 0.46–1.74, $p = 0.75$, TVR: HR 0.42, 95% CI 0.04–4.57, $p = 0.47$, definite ST: HR 0.19, 95% CI 0.01–2.94, $p = 0.23$).

After 3 years, the adjusted risk for the primary composite outcome was persistently similar between the SES and PES groups (HR 0.85, 95% CI 0.62–1.17, $p = 0.32$) (Table S3 in the supplemental appendix). After 3 years, there were the similar risks for the secondary outcomes between two groups (Death: HR 1.05, 95% CI 0.68–1.60, $p = 0.83$, MI: HR 0.45, 95% CI 0.20–1.03, $p = 0.06$, TVR: HR 0.85, 95% CI 0.55–1.32, $p = 0.47$, definite ST: HR 1.71, 95% CI 0.37–7.88, $p = 0.49$).

4 | DISCUSSION

The results of the current report provide valuable information on the very long-term (beyond 10 years) efficacy and safety of DES for patients with unprotected LMCA disease in a real-world setting. The principal findings of this analysis are: (1) PCI with DES implantation showed durable efficacy and safety in patients with LMCA disease; (2) the unadjusted and principal adjusted risks for the primary composite outcome and secondary outcomes over 10 years were comparable between SES and PES; and (3) the incidence of documented ST was quite low and comparable in both groups. These findings may have important implications for secondary prevention after PCI with first-generation DES in patients undergoing left main PCI.

Given that PCI with DES has been widely used for patients with LMCA disease in daily clinical practice and information about the long-term durability of stenting relative to CABG is still lacking,[20] our findings are clinically relevant owing to the broad spectrum of age profiles and life expectancies of patients undergoing LMCA stenting and the relatively high proportion of patients affected in middle age. In this context, clinical studies with extended follow-up might better determine the full lifecycle risk of device- and patient-oriented clinical events in high-risk patients receiving coronary stents. In addition, our report represents the first with a very long-term follow-up (over 10 years) of patients treated with first-generation, durable polymer sirolimus- or paclitaxel-eluting stents, which were most frequently used in routine clinical practice during the initial period of PCI with DES, with respect to various clinical outcomes. The present report also demonstrates that an ongoing risk of very late events is common after DES implantation without a plateau in this ongoing risk, for which novel device-based and pharmacological approaches are needed to mitigate the long-term occurrence of device- and patient-

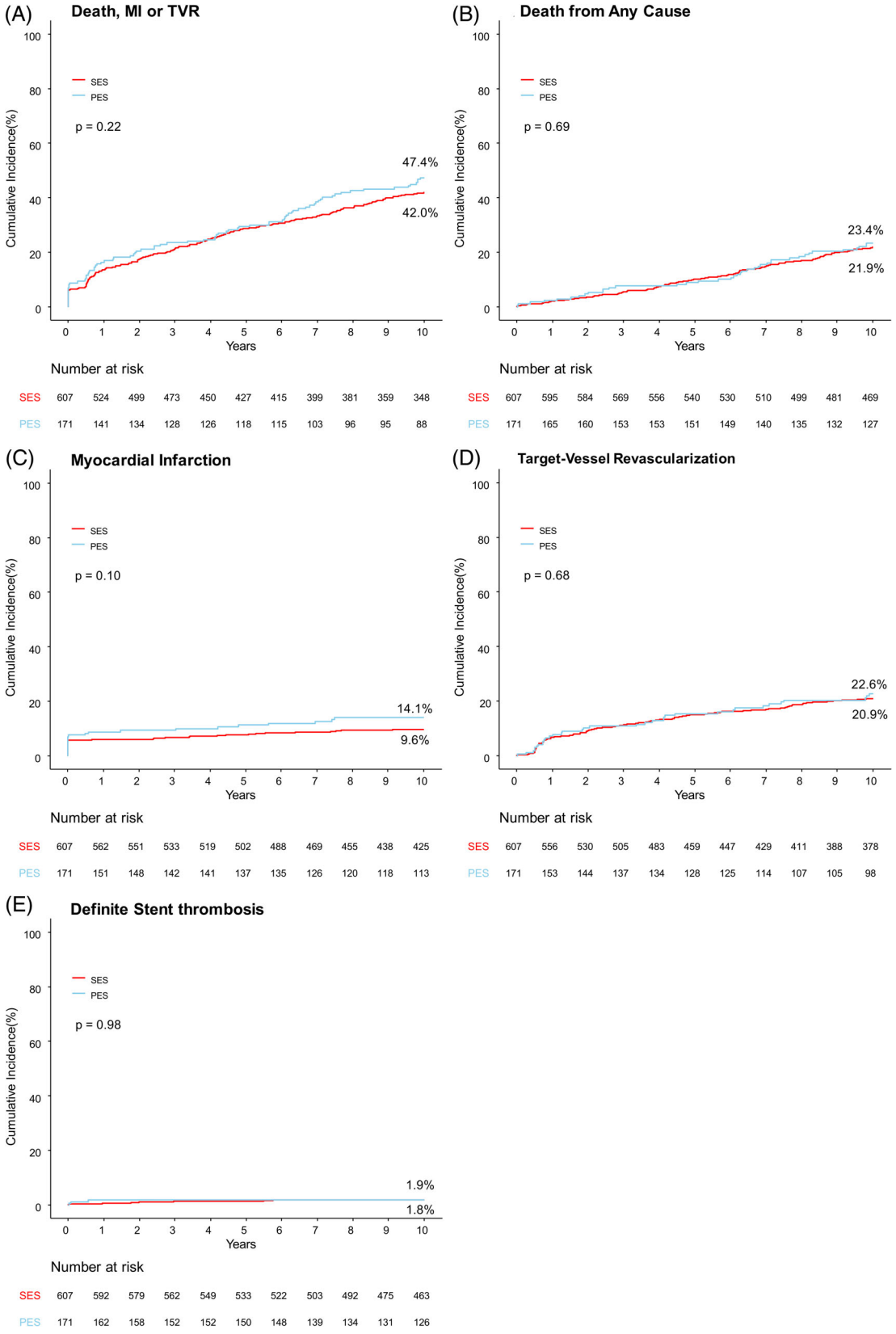

FIGURE 1 Unadjusted 10-year cumulative event rates in patients who received sirolimus stents and paclitaxel stents. (A) Results of the unadjusted analysis of the primary composite outcome of death from any cause, MI, or TVR at 10 years. The results of the analyses for key secondary outcomes are shown: (B) death from any cause; (C) MI; (D) TVR; and (E) definite ST. The event rates were based on Kaplan–Meier estimates. MI, myocardial infarction; PES, paclitaxel-eluting stents; SES, sirolimus-eluting stents; ST, stent thrombosis; TVR, target-vessel revascularization

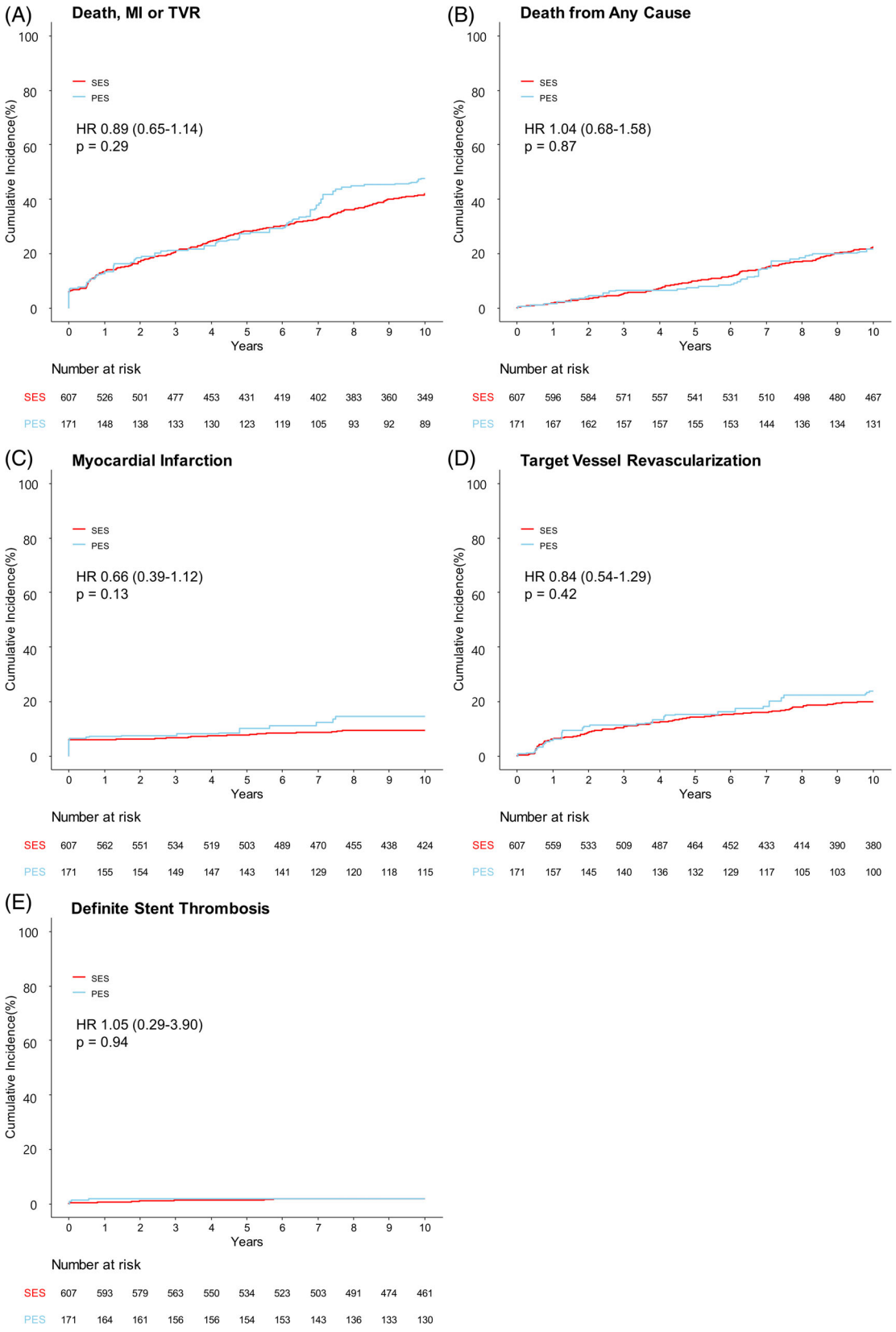

FIGURE 2 Adjusted 10-year cumulative event rates with the use of inverse probability weighting in patients who received sirolimus stents and paclitaxel stents. (A) Results of the adjusted analysis of the primary composite outcome of death from any cause, MI, or TVR at 10 years. The results of the adjusted analyses for the key secondary outcomes are shown: (B) death from any cause; (C) MI; (D) TVR; and (E) definite ST. The hazard ratios are for the SES group as compared with the PES group. HR, hazard ratio; MI, myocardial infarction; PES, paclitaxel-eluting stents; SES, sirolimus-eluting stents; ST, stent thrombosis; TVR, target-vessel revascularization

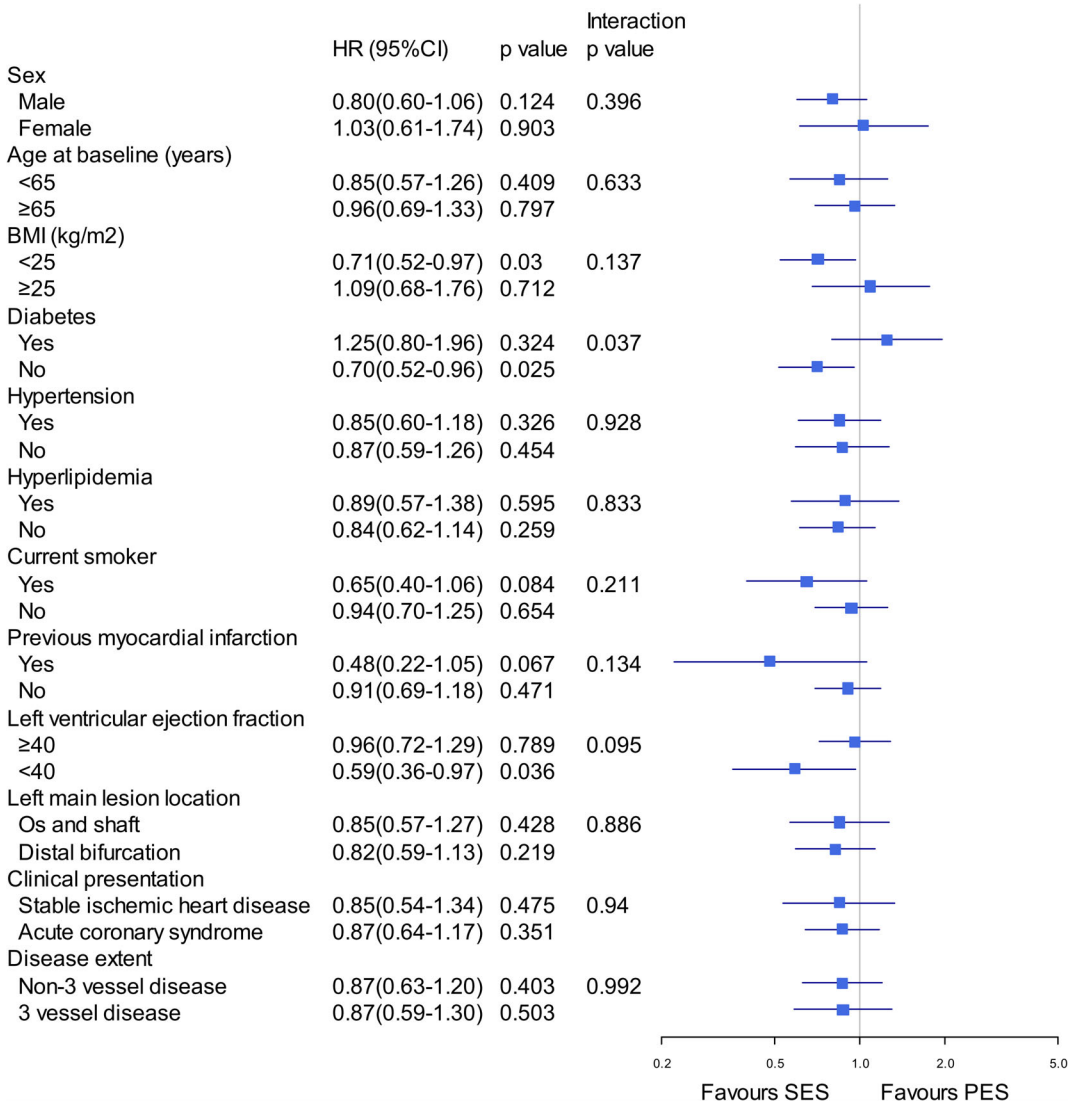

FIGURE 3 Adjusted hazard ratio for primary composite outcomes in key subgroups in patients who received sirolimus stents and paclitaxel stents. Data are shown as the hazard ratio for the primary composite outcome (i.e., a composite of death from any cause, MI, or TVR) in that subgroup and the event rate. The hazard ratios are for the SES group as compared with the PES group. Adjustment in each subgroup was performed with the use of inverse-probability-treatment-weighting. The confidence intervals that are reported in this figure have not been adjusted for multiple testing and therefore should not be used to infer definitive treatment effects. The *p* value for interaction represents the likelihood of interaction between the subgroups and the treatment. BMI, body mass index; CI, confidence interval; HR, hazard ratio; MI, myocardial infarction; PES, paclitaxel-eluting stents; SES, sirolimus-eluting stents; ST, stent thrombosis; TVR, target-vessel revascularization

related events to further improve the prognosis of patients undergoing PCI for LMCA disease.

Recently, some studies reported 10-year outcomes of DES implantation in patients who underwent PCI. The SIRTAX (Sirolimus-Eluting vs. Paclitaxel-Eluting Stents for Coronary revascularization) VERY LATE trial, which was a randomized comparison of SES and PES in all-comers, reported the 10-year rate of the primary endpoint of major adverse cardiac events (MACE; a composite of cardiac death, MI, or target-lesion revascularization [TLR]) of 34%.[21] A 10-year report of the ISAR-TEST-4 (intracoronary stenting and angiographic results: the efficacy of 3 limus-eluting stents) trial comparing durable or biodegradable polymer-based SES or durable polymer-based everolimus-eluting stents (EES) showed that the 10-year incidence of primary MACE (a composite of death, MI, or TLR) ranged from 46% to 55% according to DES type.[22] Also, the 10-year outcomes of patients enrolled in the ISAR-TEST-5 trial comparing sirolimus- and probucol- and zotarolimus-eluting stents reported the 10-year incidence of primary MACE (a composite of cardiac death, target-vessel MI, or TLR) was approximately 44% and a patient-oriented outcome of any death, MI, or revascularization of approximately 66%.[23] In the current study, we observed the 10-year rate of a primary composite outcome of all-cause death, MI, or TVR of approximately 43%. Given that our study

population involved "all-comers" patients with LMCA disease, our findings might provide a durable efficacy and safety of DES implantation for such complex lesions as compared with other long-term follow-up studies on this issue.

A prior report comparing SES and PES demonstrated that the incidence of angiographic restenosis was much lower with SES than with PES, owing to a higher suppression of neointimal hyperplasia.[24] However, these better angiographic results favoring SES over PES have not been reflected in substantial differences in long-term clinical outcomes. The 10-year report of the SIRTAX VERY LATE trial showed no significant differences of the primary endpoint MACE and several key secondary endpoints, including ST, between SES and PES.[21] Also, the 10-year follow-up of the SORT OUT II (Danish Organization on Randomized Trials With Clinical Outcome II) study comparing SES and PES in unselected all-comer patients demonstrated that the long-term annual MACE rate and the ST rate appeared constant for both stent types without between-group differences. As such, we did not observe any remarkable differences in primary and secondary outcomes between SES and PES over 10 years in patients undergoing PCI for LMCA disease. Interestingly, there has been a trend favoring SES over PES beyond 5 years with respect to MI and TVR, but unfortunately the exact reason for such late changes is still unknown; this finding might be partly explained by more IVUS-guided PCI in the SES group.

Since ST is associated with acute MI and sudden cardiac death, the occurrence of ST after LMCA stenting might be clinically more catastrophic. In our extended follow-up of the MAIN-COMPARE study, ST occurrence was quite low and did not significantly differ between SES and PES. Such a finding is consistent with a previous report showing the low incidence of ST in very long-term follow-up.[7,21,22,25] This observation might provide further clinical evidence on the long-term safety of DES implantation in LMCA disease. In addition, recent merged analyses reported that the occurrences of very late clinical MACE and ST were significantly lower in patients treated with second-generation DES as compared to those treated with first-generation DES.[26] Thus, late catastrophic ST events in patients undergoing contemporary DES might be clinically not of concern based on these observations.

There are several limitations in our study. First, because this was a nonrandomized observational study, there must be inherent limitations and bias in treatment selection. Although IPTW analysis was used to adjust for potential selection bias, unmeasured confounders that could have affected the results cannot be excluded. Second, owing to the relatively limited number of patients, this study is not sufficiently powered to detect a clinically relevant difference in ST or MI. Third, our study evaluated the efficacy and safety of first-generation DES, not contemporary DES. Since second-generation DES showed better clinical outcomes as compared with first-generation DES,[27] this might limit the generalizability of our findings to contemporary clinical practice. However, our findings should be interpreted in the context of very long-term evaluations of the relative treatment effect of DES implantation for LMCA disease. Our findings should be confirmed or refuted by further studies using contemporary DES in patients receiving LMCA-PCI.

5 | CONCLUSIONS

In this 10-year very long-term follow-up of patients who underwent PCI with DES for unprotected LMCA disease, there were no measurable differences in outcomes between patients treated with SES versus PES for LMCA disease. The incidence of ST was quite low and comparable in both groups. High overall adverse clinical event rates were observed during extended follow-up, and thus new approaches are required to improve long-term outcomes after PCI.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interest..

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are openly available in [repository name e.g "figshare"] at [doi], reference number [reference number].

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

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