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EXPEDITED PUBLICATION

# The Everolimus-Eluting Stent in Real-World Patients

## 6-Month Follow-Up of the X-SEARCH (Xience V Stent Evaluated at Rotterdam Cardiac Hospital) Registry

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**Objectives** The purpose of this study was to investigate the impact of everolimus-eluting stents (EES) in comparison with bare-metal stents (BMS), sirolimus-eluting stents (SES), and paclitaxel-eluting stents (PES) on the 6-month clinical outcomes in an all-comer population.

**Background** EES have been shown to be effective in the context of randomized trials with selected patients. The effect of EES implantation in more complex, unselected patients cannot be directly extrapolated from these findings.

**Methods** In total, 649 consecutive unselected patients treated exclusively with EES were enrolled. Six-month clinical end points were compared with 3 historical cohorts (BMS, n = 450; SES, n = 508; and PES, n = 576). Major adverse cardiac events (MACE) were defined as a composite of all-cause mortality, myocardial infarction, or target vessel revascularization (TVR).

**Results** The patients treated with EES were older, presented more frequently with acute myocardial infarction, and had more complicated lesions than the other groups. The EES group demonstrated a higher incidence of all-cause mortality than the SES group and a lower incidence of TVR than the BMS group. Multivariate adjustment demonstrated that BMS was associated with higher TVR and MACE risk than EES (adjusted hazard ratio [HR] for TVR: 2.02 [95% confidence interval (CI): 1.11 to 3.67]; adjusted HR for MACE: 2.15 [95% CI: 1.36 to 3.42]); that SES had a clinical outcome similar to that of EES, and that PES had a higher risk of MACE than did EES (adjusted HR: 1.57 [95% CI: 1.02 to 2.44]).

**Conclusions** This study suggests that the use of EES in an unselected population may be as safe as and more effective than BMS, may be as safe and effective as SES, may be as safe as PES, and may be more effective than PES. (J Am Coll Cardiol 2009;54:269–76) © 2009 by the American College of Cardiology Foundation

Compared with bare-metal stents (BMS), polymer-based sirolimus-eluting stents (SES) and paclitaxel-eluting stents (PES) have been shown to significantly reduce angiographic restenosis and recurrent ischemia necessitating repeat revascularization (1). Stent thrombosis and endothelial dysfunction after both PES and SES implantation, however, remains a concern with this technology. With the goal of further enhancing the safety and efficacy of drug-eluting stents (DES), an everolimus-eluting stent (EES) (Abbott Vascular, Santa Clara, California) has been designed in which the antiproliferative agent is released from a thin (7.8 $\mu$m), nonadhesive, durable, biocompatible fluoropolymer coated onto a low-profile (0.0813-mm strut thickness), flexible cobalt chromium stent. Angiographic and clinical noninferiority of the EES to the PES was proven in the SPIRIT II and III randomized studies (2,3).

The clinical trials completed so far, however, have included only elective patients with relatively noncomplex lesions and have excluded high-risk patients such as those presenting with acute myocardial infarction (MI) or those with left main stenosis or calcified lesions (2–4). The effect of EES implantation in complex, unselected patients treated in daily practice still remains unknown and cannot be extrapolated from these randomized controlled trials. We therefore sought to evaluate the impact of this second-generation DES on the clinical outcomes in consecutive patients treated in a real-life, all-comer population. The aim of this study was to report the 6-month outcomes of unrestricted universal use of EES in patients with de novo coronary artery lesions and to compare its efficacy against our historical

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**Abbreviations and Acronyms**

**BMS** = bare-metal stent(s)

**CI** = confidence interval

**EES** = everolimus-eluting stent(s)

**HR** = hazard ratio

**MACE** = major adverse cardiac event(s)

**MI** = myocardial infarction

**PES** = paclitaxel-eluting stent(s)

**SES** = sirolimus-eluting stent(s)

**TLR** = target lesion revascularization

**TVR** = target vessel revascularization

BMS, SES, and PES cohort from the RESEARCH (Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated At Rotterdam Cardiology Hospital) registries.

## Methods

**Study design and patient population.** The X-SEARCH (Xience Stent Evaluated At Rotterdam Cardiology Hospital) registry is a prospective single-center registry with the main purpose of evaluating the safety and efficacy of EES implantation in consecutive unselected patients treated in daily practice. Its conceptual design and methodology are similar to that of the RESEARCH and T-SEARCH registries (5,6) and follows the dynamic registry design described by Rothman and Greenland (7). Since EES received Conformité Européenne mark approval and became commercially available in Europe in March 2007, it has been our policy to utilize the EES as the device of choice for every percutaneous coronary intervention performed in our institution. All consecutive procedures were included, without any specific anatomical or clinical restriction.

Between March 1, 2007, and October 31, 2007, 649 consecutive patients presenting with de novo lesions were treated exclusively with EES and were included in the present report (EES group) after exclusion of patients treated with EES and other stent types in the same procedure (n = 48), those treated without stent implantation (n = 20), those treated exclusively with BMS or other DES (n = 17), and those treated with EES for in-stent restenosis (n = 44) (Fig. 1). At the initiation of the X-SEARCH registry, EES was available in lengths of 8, 12, 15 and 23 mm and diameters from 2.5 to 4.0 mm. This EES group was compared with a historical cohort from the RESEARCH and T-SEARCH registries that comprised 1) the pre-SES arm of the RESEARCH registry (BMS group, n = 450); 2) the active arm of the RESEARCH registry (SES group, n = 508); and 3) the PES group of the T-SEARCH registry (PES group, n = 576) (Fig. 2).

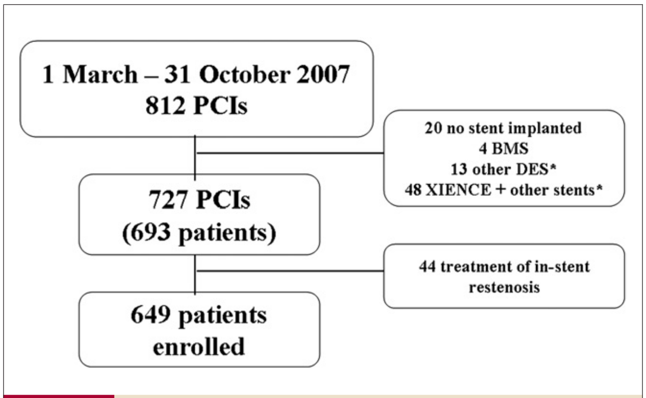


**Figure 1** **Flowchart of Patient Selection**

The flowchart represents patient inclusion and exclusion in the X-SEARCH (Xience Stent Evaluated At Rotterdam Cardiology Hospital) registry. *Occurring in the short transitional period (2 weeks) between paclitaxel-eluting stent/everolimus-eluting stent. BMS = bare-metal stent(s); DES = drug-eluting stent(s); PCI = percutaneous coronary intervention.

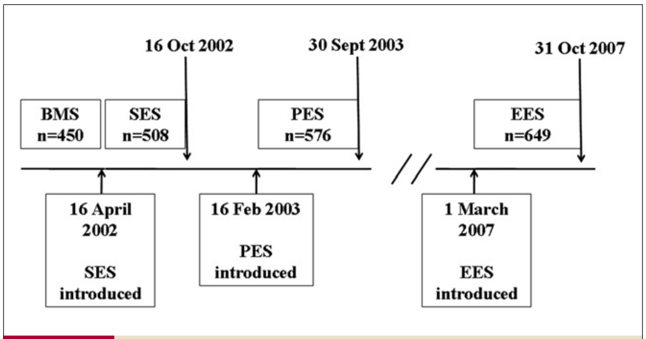


**Figure 2** **Inclusion Periods of X-SEARCH and Historical Cohorts**

Chronological order of 4 cohorts included in analysis: BMS, everolimus-eluting stent (EES), paclitaxel-eluting stent (PES), and SES. X-SEARCH = Xience Stent Evaluated At Rotterdam Cardiology Hospital; other abbreviations as in Figure 1.

Written informed consent was obtained from every patient. All procedures were performed according to standard clinical guidelines at the time of enrollment (8). All patients were pre-treated with 300 mg clopidogrel. At least 1 month of clopidogrel treatment (75 mg/day) was recommended for patients treated with BMS. Clopidogrel was prescribed for ≥3 months for patients with SES, or >6 months for patients with PES, and 12 months for patients with EES, according to the data from the pivotal DES randomized trials (9,10). Life-long aspirin therapy was recommended for all patients.

**Definitions.** Hypercholesterolemia was defined as fasting total cholesterol >5 mmol/l (193 mg/dl) or the use of lipid-lowering therapy. Hypertension was defined as blood pressure >140/90 mm Hg or the use of antihypertensive medications. Angiographic success was defined as a residual stenosis ≤30% by visual analysis in the presence of TIMI (Thrombolysis In Myocardial Infarction) flow grade 3. The primary end point was major adverse clinical events (MACE), defined as all-cause death, nonfatal MI, or target vessel revascularization (11). Secondary end points included all-cause mortality, MI, target vessel revascularization (TVR), target lesion revascularization (TLR), definite stent thrombosis, and the composites of all-cause death or nonfatal MI. MI included reinfarction (defined as recurrence of symptoms together with ST-segment elevation or new left bundle branch block and an increase in cardiac enzymes after stable or decreasing values) or spontaneous MI (diagnosed by a rise in creatine kinase-MB fraction of 3 times the upper limit of normal together with symptoms and either

**Table 1 Patient Characteristics**

| | BMS (n = 450) | SES (n = 508) | PES (n = 576) | EES (n = 649) | p Value |
|---|---|---|---|---|---|
| Age, yrs | 61 ± 11 | 61 ± 11 | 62 ± 11 | 64 ± 12 | <0.001 |
| Female | 28.6 | 32.1 | 26.4 | 28.4 | 0.22 |
| Current smoker | 34.0 | 30.7 | 29.0 | 30.0 | 0.36 |
| Diabetes mellitus | 14.9 | 17.7 | 18.4 | 20.8 | 0.1 |
| Noninsulin dependent | 10.9 | 11.8 | 13.2 | 14.4 | 0.32 |
| Insulin dependent | 4 | 5.9 | 5.2 | 6.4 | 0.37 |
| Hyperlipidemia | 55.3 | 55.5 | 62.2 | 47.6 | <0.001 |
| Hypertension | 47.6 | 41.3 | 41.8 | 49.3 | 0.01 |
| Family history of coronary artery disease | 28.2 | 32.5 | 40.6 | 45.4 | <0.001 |
| Previous MI | 39.7 | 30.2 | 34.5 | 25.9 | <0.001 |
| Previous CABG | 8.0 | 9.3 | 6.1 | 7.3 | 0.25 |
| Previous PCI | 18.0 | 188 | 18.2 | 15.3 | 0.37 |
| Clinical presentation | | | | | |
| Stable angina | 47.6 | 44.6 | 45.3 | 38.8 | 0.03 |
| Unstable angina/NSTEMI | 34.7 | 37.1 | 27.0 | 20.2 | <0.001 |
| STEMI | 17.8 | 18.1 | 28.0 | 39.3 | <0.001 |
| Cardiogenic shock | 2.0 | 1.8 | 3.8 | 6.0 | <0.001 |
| No. of vessels diseased | 1.6 ± 0.7 | 1.8 ± 0.8 | 1.8 ± 0.8 | 1.8 ± 0.9 | 0.006 |
| Multivessel disease | 47.8 | 54.1 | 56.1 | 50.2 | 0.03 |
| No. of lesions treated | 1.8 ± 0.9 | 2.0 ± 1.0 | 1.7 ± 0.9 | 1.8 ± 1.0 | <0.001 |
| ACC/AHA lesion classification* | | | | | |
| Type A | 19.6 | 21.9 | 7.3 | 6.5 | <0.001 |
| Type B1 | 31.8 | 30.7 | 25.0 | 31.1 | 0.049 |
| Type B2 | 49.6 | 48.6 | 54.3 | 51.5 | 0.25 |
| Type C | 29.8 | 42.5 | 47.2 | 38.9 | <0.001 |
| Bifurcation | 7.8 | 15.7 | 15.9 | 22.2 | <0.001 |
| Treated vessels† | | | | | |
| LMS | 2.2 | 2.9 | 4.3 | 7.6 | <0.001 |
| RCA | 34.0 | 38.5 | 37.7 | 33.9 | 0.25 |
| LAD | 59.3 | 58.5 | 55.2 | 38.7 | <0.001 |
| LCx | 33.1 | 31.6 | 33.2 | 19.1 | <0.001 |
| SVG | 2.0 | 3.3 | 3.3 | 4.0 | 0.33 |
| Number of stents | 1.9 ± 1.2 | 2.1 ± 1.4 | 2.2 ± 1.5 | 2.1 ± 1.4 | <0.001 |
| Average stent diameter, mm | 3.1 ± 0.3 | 2.8 ± 0.2 | 3.0 ± 0.3 | 3.1 ± 0.3 | <0.001 |
| Total stent length, mm | 30 ± 20 | 39 ± 24 | 43 ± 31 | 57 ± 26 | <0.001 |
| Clopidogrel duration, months | 1.0 ± 0.1 | 4.0 ± 2.0 | 6.0 ± 0 | 11.9 ± 0.7 | <0.001 |
| Procedural success | 97.3 | 97.2 | 97.4 | 98.3 | 0.4 |

Data are presented as % or mean ± SD *Expressed as percentage of patients with each lesion type, hence total >100%. †Expressed as percentage of patients with each vessel type, hence total >100%.
BMS = bare-metal stent(s); CABG = coronary artery bypass graft surgery; EES = everolimus-eluting stent(s); LAD = left anterior descending artery; LCx = left circumflex artery; LMS = left main stem; MI = myocardial infarction; NSTEMI = non–ST-segment elevation myocardial infarction; PCI = percutaneous coronary intervention; PES = paclitaxel-eluting stent(s); RCA = right coronary artery; SES = sirolimus-eluting stent(s); STEMI = ST-segment elevation myocardial infarction; SVG = saphenous vein graft.

the development of ST-segment elevation or new left bundle branch block) (12). TVR was defined as a repeat revascularization of a lesion in the same epicardial vessel treated in the index procedure (13). TLR was defined as a repeat intervention in the stent or within 5 mm proximal or distal to the stent. Stent thrombosis was defined as angiographically defined thrombosis with TIMI flow grade 0 or 1 or the presence of flow-limiting thrombus, accompanied by acute symptoms, irrespective of whether there had been an interceding reintervention (14). The timing of stent thrombosis was categorized as early (within 30 days after implantation), late (between 30 days and 1 year) or very late (>1 year) (11).

**Follow-up data.** Survival data for all patients were obtained from municipal civil registries at 1 and 6 months after the procedure. A questionnaire was subsequently sent to all living patients with specific queries on rehospitalization and MACE. As the principal regional cardiac referral center, most repeat revascularizations (either percutaneous or surgical) are usually performed at our institution and recorded prospectively in our database. For patients who suffered an adverse event at another center, medical records or discharge letters from the other institutions were systematically reviewed. General practitioners and referring physicians were contacted for additional information if necessary. Over the last 30 years, regular scientific interaction with the referring

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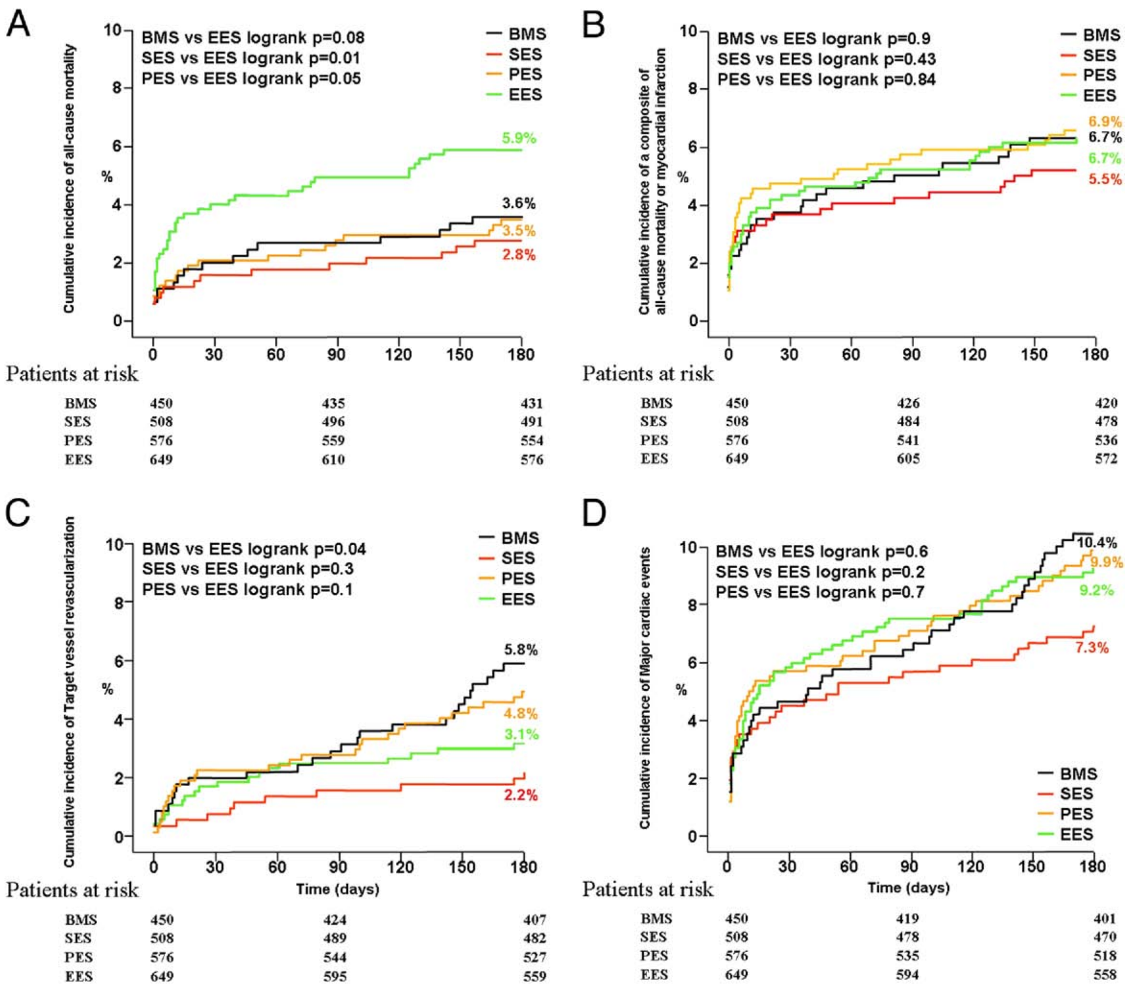


**Figure 3** **Unadjusted Survival Curves**

Kaplan-Meier survival curves stratified according to the stent types: **(A)** all-cause death; **(B)** the composite of death or myocardial infarction; **(C)** target vessel revascularization; and **(D)** the composite of major adverse cardiac events (all-cause mortality, any myocardial infarction, or target vessel revascularization). BMS **(black lines)**; EES **(green lines)**; PES **(yellow lines)**; SES **(red lines)**. Abbreviations as in Figures 1 and 2.

physicians from the local catchment area has encouraged a high level of data collection and source documentation.

**Statistical analysis.** Continuous variables are presented as mean ± SD, whereas categorical variables are expressed as percentages. Categorical variables were compared using Pearson chi-square test or Fisher exact test, and continuous variables were compared using the F test for analysis of variance. All statistical tests were 2-tailed, and a p value $<0.05$ was considered as statistically significant. The crude survival curves were constructed with the use of the Kaplan-Meier method to describe the incidence of events over time, and log-rank tests were applied to evaluate differences between the treatment groups. Patients lost to follow-up were considered at risk until the date of last contact, at

**Table 2** **Cumulative Incidence of Definite Stent Thrombosis**

| | BMS (n = 450) | SES (n = 508) | PES (n = 576) | EES (n = 649) | p Value |
|---|---|---|---|---|---|
| Early (≤30 days) | 7 (1.6%) | 2 (0.4%) | 7 (1.2%) | 4 (0.6%) | 0.19 |
| Acute (≤24 h) | 4 (0.9%) | 1 (0.2%) | 1 (0.2%) | 2 (0.3%) | 0.22 |
| Subacute (>1, ≤30 days) | 3 (0.7%) | 1 (0.2%) | 6 (1.0%) | 2 (0.3%) | 0.21 |
| Late (>30 days) | 2 (0.4%) | 1 (0.2%) | 1 (0.2%) | 0 (0%) | 0.41 |
| Overall (up to 6 months) | 9 (2.0%) | 3 (0.6%) | 8 (1.4%) | 4 (0.6%) | 0.09 |

Abbreviations as in Table 1.

which point they were censored. Adjusted survival curves were calculated using Cox regression models. These models were built to adjust for multiple potential confounders in the baseline characteristics for each paired treatment comparison. Firstly, a univariate analysis was performed to identify significant variables among the following: age, gender, hypertension, type 1 or 2 diabetes mellitus, current smoking, family history, previous coronary artery bypass graft surgery, previous MI, previous percutaneous coronary intervention, clinical presentation of acute MI or unstable angina (stable angina as a reference), presentation with shock, multivessel disease, treated vessel, American Heart Association/American College of Cardiology lesion type, bifurcation treatment, number of lesions treated, number of stents implanted, average stent diameter, and total stented length. Second, a Cox model was built forcing stent type and significant variables in the univariate analysis. The stent type was entered as a categorical variable with EES as the reference. The results are presented as adjusted hazard ratios (HRs) with 95% confidence intervals (CIs). Statistical analysis was performed with SPSS version 16 for Windows (SPSS Inc., Chicago, Illinois).

## Results

Baseline characteristics are presented in Table 1. Across the study period, patients became progressively older and were more likely to have hypertension and present with ST-segment elevation myocardial infarction (STEMI) or cardiogenic shock—likely a reflection of changes in disease presentation with time. Bifurcations, left main disease, and the use of longer stents were more common in the DES groups. Fewer EES patients had a history of previous bypass surgery.

**6-month clinical outcomes.** Clinical follow-up at 6 months was complete in 99% of patients. The cumulative incidences of 6-month clinical end points are presented in Figure 3. The crude all-cause mortality rate was significantly higher in the EES group than in the SES group: 5.9% in the EES group versus 3.6%, 3.5%, and 2.8% in the BMS, PES, and SES groups, respectively (Fig. 3A). The cumulative incidence of all-cause death or any MI was similar in the 4 groups (Fig. 3B). TVR was observed in a significantly lower percentage of EES patients than in BMS patients (3.1% vs. 5.8%, p = 0.04) (Fig. 3C). The composite end point of MACE was observed in 9.2% of the EES patients; comparable event rates were observed in the BMS, SES, and PES groups (Fig. 3D). The cumulative incidences of definite stent thrombosis at various time points are shown in Table 2. The overall rate of definite stent thrombosis was similar across the cohorts (BMS 2.0%, SES 0.6%, PES 1.4%, and EES 0.6%).

**Multivariate analyses.** Cox multivariable regression models were used to correct for differences across the 4 groups and calculate independent predictors of all-cause mortality. Cardiogenic shock (adjusted HR: 8.1, 95% CI: 4.3 to 15.5), type 1 diabetes (adjusted HR: 3.3, 95% CI: 1.5 to 7.2), presentation with STEMI (adjusted HR: 2.6, 95% CI: 1.4 to 5.0), and multivessel disease (adjusted HR: 2.0, 95% CI: 1.2 to 3.4) were identified as independent predictors of 6-month mortality; in contrast, type A lesion classification was protective (adjusted HR: 0.20, 95% CI: 0.1 to 0.8).

Adjusted hazard ratios of pair-wise comparisons of the EES group to other stent groups are shown in Table 3. The risks of TVR, MACE, and composite of MI or all-cause mortality were significantly higher in the BMS than in the EES group (adjusted HR: 2.02, 2.15, and 1.92, respectively). PES was associated with a higher risk of MACE than EES was (adjusted HR: 1.57, 95% CI: 1.02 to 2.44). SES was similar when compared with EES.

The same Cox regression models were used to draw survival curves adjusted for differences in baseline characteristics, as presented in Figure 4. After adjustment, all-cause mortality was similar among stent types, with a trend toward better survival in the EES group than in the BMS group (1.5% vs. 3.1%, p = 0.059). TVR was significantly lower in the EES group than in the BMS group (2.8% vs. 5.8%, p = 0.02) but was comparable with other DES groups (SES 2.0%, PES 4.6%). The composite end point of MACE was significantly lower in the EES group than in the BMS group (5.5% vs. 11.0%, p = 0.003) and PES group (5.5% vs. 8.6%, p = 0.04); the EES and SES groups had similar MACE rates (5.5% vs. 6.1%, p = 0.6).

**Table 3** Adjusted Hazard Ratios for Pair-Wise Comparisons Between Stents

| | Adjusted Hazard Ratio | 95% CI |
|---|---|---|
| BMS versus EES | | |
| All-cause mortality* | 1.98 | 0.97–4.01 |
| MI or all-cause mortality† | 1.92 | 1.14–3.25 |
| TVR‡ | 2.02 | 1.11–3.67 |
| MACE§ | 2.15 | 1.36–3.42 |
| SES versus EES | | |
| All-cause mortality* | 1.15 | 0.52–2.55 |
| MI or all-cause mortality† | 1.45 | 0.85–2.47 |
| TVR‡ | 0.69 | 0.33–1.45 |
| MACE§ | 1.18 | 0.71–1.94 |
| PES versus EES | | |
| All-cause mortality* | 1.01 | 0.53–1.92 |
| MI or all-cause mortality† | 1.49 | 0.89–2.32 |
| TVR‡ | 1.60 | 0.89–2.88 |
| MACE§ | 1.57 | 1.02–2.44 |

*The model for all-cause mortality was adjusted for the following variables: age, cardiogenic shock, type 1 diabetes, clinical presentation, multivessel disease, type A lesion characteristics. †The model for MI or all-cause mortality was adjusted for type 1 diabetes, age, multivessel disease, clinical presentation, cardiogenic shock, number of stent and type A lesion characteristics. ‡The Cox model for TVR is adjusted for diabetes, number of stents, number of treated lesions, and type B2 lesion characteristics. §The model for MACE is adjusted for age, cardiogenic shock, clinical presentation, multivessel disease, type 1 or 2 diabetes, smoking, and bifurcation.

MACE = major adverse cardiac events (all-cause death, MI, or TVR); TVR = target vessel revascularization; other abbreviations as in Table 1.

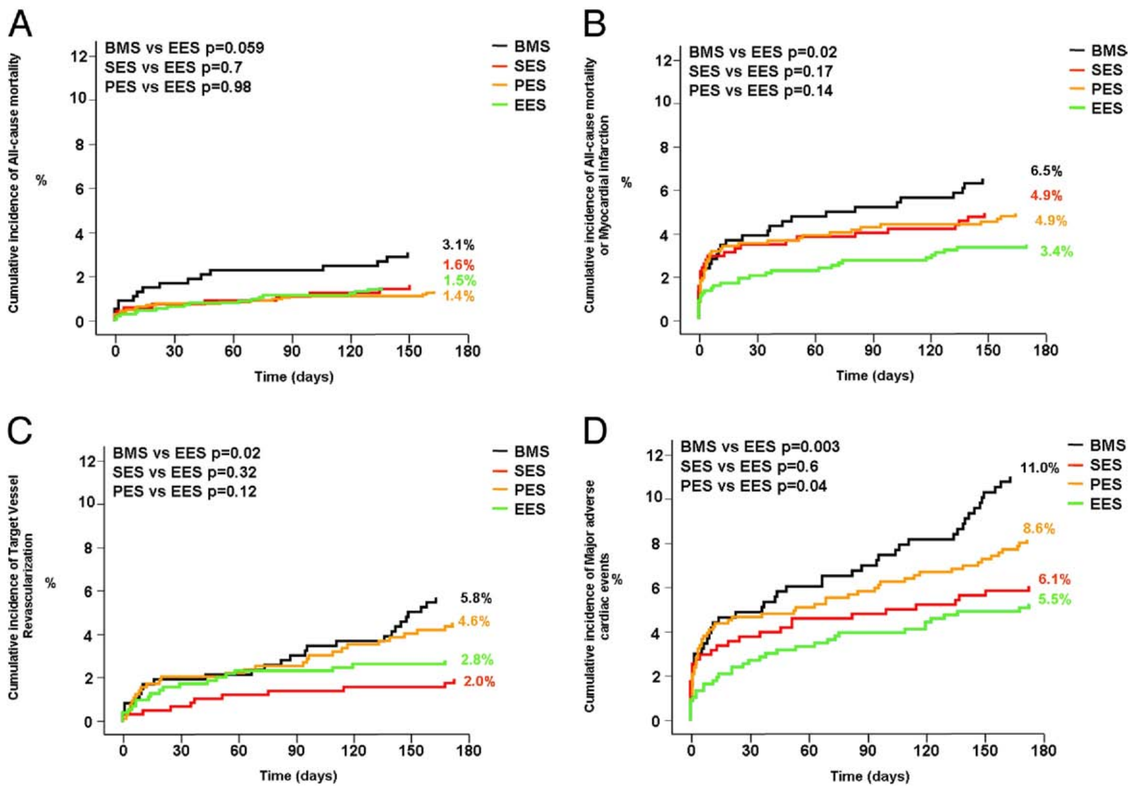


**Figure 4** **Adjusted Survival Curves**

Adjusted survival curves stratified according to the stent types using Cox proportional hazard model: **(A)** all-cause death; **(B)** the composite of death or myocardial infarction; **(C)** target vessel revascularization; and **(D)** the composite of major adverse cardiac events (all-cause mortality, any myocardial infarction, or target vessel revascularization). BMS **(black lines)**; EES **(green lines)**; PES **(yellow lines)**; SES **(red lines)**. Abbreviations as in Figures 1 and 2.

## Discussion

The X-SEARCH registry, the focus of this report, is a contemporary, all-comer, single-center registry of patients treated with EES. In this registry, patients were older, presented more frequently with STEMI, and had more complicated lesions compared with patients who were treated in the past with BMS, SES (RESEARCH registry) and PES (T-SEARCH registry). At 6-month follow-up, the EES group demonstrated a higher cumulative incidence of all-cause mortality than the SES group, and a lower incidence of TVR than BMS. Taking into account the high-risk patient profile in the X-SEARCH registry, multivariate adjustment with Cox regression model demonstrated that 1) EES was associated with lower TVR and MACE risk than BMS was; 2) EES had a lower MACE rate than PES did; and 3) EES had clinical outcomes similar to SES.

The safety and efficacy of the EES stents have been demonstrated in low-risk profile patients. The randomized SPIRIT II trial, in which 300 patients were enrolled and randomly assigned 3:1 to receive an EES (n = 223) or a PES (n = 77), was performed in Europe, New Zealand, and India. The trial met its primary end point, demonstrating not only noninferiority, but also superiority with respect to in-stent late loss at 6 months with EES (0.11 ± 0.27 mm) compared with PES (0.36 ± 0.39 mm). No significant differences were present, however, in the secondary end points of MACE (cardiac death, MI, or ischemia-driven TLR), presumably because of the small sample size (2,15,16). In the larger SPIRIT III trial performed in the U.S. (3), 1,002 patients with noncomplex coronary artery disease were randomly assigned 2:1 to treatment with EES (n = 669) or PES (n = 333). Angiographic follow-up at 8 months demonstrated a significant reduction in the primary angiographic end point of in-segment late loss with EES compared with PES. At 1 year, EES was noninferior to PES for the co-primary clinical end point of target vessel failure (cardiac death, MI, or ischemia-driven TVR) and resulted in a significant reduction in MACE. The lower MACE risk of EES compared with PES in the current study with all-comer cohorts reconfirms the superiority of EES over PES, not only in low-risk patients but also in the high-risk all-comer populations.

The first-generation DES have been associated with higher rates of late stent thrombosis and thrombosis-related events than BMS (17,18). The cause of late stent thrombosis is partly due to the antiproliferative medications retarding the growth of healthy endothelium over stent struts and partly due to chemical features of their durable polymer coating (19–21). The EES, using a novel drug as well as a different polymer, might address this issue. Pre-clinical studies have shown more rapid endothelialization and reduced expression of platelet-endothelial cell adhesion molecule-1 and increased secretion and messenger ribonucleic acid levels of vascular endothelial growth factor at 14 days with EES than with SES or PES (22). The SPIRIT III study suggested that thienopyridine discontinuation after 6 months might be associated with a lower rate of subsequent stent thrombosis with EES than with PES through 2 years of follow-up (0.4% vs. 2.6%), although given the relatively low rates of stent thrombosis, this difference did not reach statistical significance ($p = 0.10$). In the present study, the rate of overall stent thrombosis at 6 months was similar in the EES and other stent groups, although there were no incidences of late stent thromboses with EES up to 6 months. Larger studies with longer follow-up will be necessary to assess the differential effects of EES on late and very late stent thrombosis.

The low incidence of hypercholesterolemia in the EES group might result from the under-diagnosis of hypercholesterolemia in the acute MI population, in which the incidence of hypercholesterolemia was low (24%). Eighty percent of these patients did not have any history related to atherosclerosis, and their cholesterol level was not available at the time of the procedure.

**Study limitations.** This is a single-center, nonrandomized, observational study. Because we used consecutive but non-sequential patient data from past registries as historical controls, the baseline patient characteristics vary across the cohorts. We used Cox regression analysis to address these differences in baseline characteristics; however, the result can be influenced by the selection of the variables and quality of data. In the current registry, the data in Table 1, which were subsequently used in the Cox regression models, were carefully checked by 2 experienced cardiologists, with review of medical records and cine-angiograms to ensure accurate and complete data entry. In addition, there was no bias in stent selection, because only 1 stent was available in each period of the registries, unlike at other institutions where the penetration of DES has fluctuated after the ESC firestorm in 2006 (23,24). Our study had inadequate statistical power to detect significant differences in adverse outcomes associated with low event rates (e.g., late stent thrombosis). These observations, therefore, can only be used to generate hypotheses when comparing the EES results with those for the other stents.

## Conclusions

The current analysis of patients treated with EES compared with SES, PES, and BMS suggests that the use of EES in an unselected population, including high-risk patients, may be as safe as and more effective than BMS, may be as safe and effective as SES, may be as safe as PES, and may be more effective than PES.

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**Key Words:** everolimus-eluting stent ▪ all-comer registry ▪ sirolimus-eluting stent ▪ paclitaxel-eluting stent.