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Safety and Efficacy of Second-Generation Everolimus-Eluting Xience V Stents Versus Zotarolimus-Eluting Resolute Stents in Real-World Practice

Patient-Related and Stent-Related Outcomes From the Multicenter Prospective EXCELLENT and RESOLUTE-Korea Registries

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Objectives This study sought to compare the safety and efficacy of the Xience V/Promus everolimus-eluting stent (EES) (Abbott Vascular, Temecula, California) with the Endeavor Resolute zotarolimus-eluting stent (ZES-R) (Medtronic Cardiovascular, Santa Rosa, California) in "all-comer" cohorts.

Background Only 2 randomized controlled trials have compared these stents.

Methods The EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) and RESOLUTE-Korea registries prospectively enrolled 3,056 patients treated with the EES and 1,998 patients treated with the ZES-R, respectively, without exclusions. Stent-related composite outcomes (target lesion failure [TLF]) and patient-related composite outcomes were compared in crude and propensity score-matched analyses.

Results Of 5,054 patients, 3,830 (75.8%) had off-label indication (2,217 treated with EES and 1,613 treated with ZES-R). The stent-related outcome (82 [2.7%] vs. 58 [2.9%], p = 0.662) and the patient-related outcome (225 [7.4%] vs. 153 [7.7%], p = 0.702) did not differ between EES and ZES-R, respectively, at 1 year, which was corroborated by similar results from the propensity score-matched cohort. The rate of definite or probable stent thrombosis (18 [0.6%] vs. 7 [0.4%], p = 0.306) also was similar. In multivariate analysis, off-label indication was the strongest predictor of TLF (adjusted hazard ratio: 2.882; 95% confidence interval: 1.226 to 6.779; p = 0.015).

Conclusions In this robust real-world registry with unrestricted use of EES and ZES-R, both stents showed comparable safety and efficacy at 1-year follow-up. Overall incidences of TLF and definite stent thrombosis were low, even in the patients with off-label indication, suggesting excellent safety and efficacy of both types of second-generation drug-eluting stents. (J Am Coll Cardiol 2013;61:536–44) © 2013 by the American College of Cardiology Foundation

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First-generation drug-eluting stents (DESs) substantially reduced angiographic and clinical measures of restenosis; however, safety issues remained (1). The most widely used second-generation DESs, the Xience V/Promus everolimus-eluting stent (EES) (Abbott Vascular, Temecula, California) and the Endeavor Resolute zotarolimus-eluting stent (ZES-R) (Medtronic Cardiovascular, Santa Rosa, California), both made of cobalt-chromium with biocompatible polymers, were compared in only 2 randomized controlled trials (RCTs) (2–4). Thus, more data about their everyday use are needed. The purpose of this study was to evaluate the safety and efficacy of the EES and ZES-R in everyday real-world use with a wide range of patient and lesion complexity.

Methods

An extended description of the study methods is presented in the Online Appendix.

Study design and patient population. This study evaluated the clinical outcomes of the EES and ZES-R from 2 prospective, multicenter registries—EXCELLENT (Efficacy of Xience/Promus Versus Cypher to Reduce Late Loss After Stenting) and RESOLUTE-Korea—that enrolled all-comers treated with ≥1 EES or ZES-R (3,056/29 and 1,998/25 patients/participating centers, respectively) without exclusions (Online Fig. 1). The patients enrolled in the EXCELLENT registry were different from those enrolled in the previously reported EXCELLENT RCT, which had strict inclusion and exclusion criteria, the main results of which have been published (5).

Follow-up. After index percutaneous coronary intervention (PCI), follow-ups were performed at 1, 3, 9, and 12 months; angiography was optional at 9 months. For any clinical events, all relevant medical records were reviewed and adjudicated by an external clinical event committee. With the use of the Korean health system's unique identification numbers, the vital status of 100% of patients was crosschecked. The study protocol was approved by the ethics committee at each participating center and conducted according to the principals of the Declaration of Helsinki. All patients provided written informed consent.

Definition and outcome analysis. The primary outcome was target lesion failure (TLF), a composite of cardiac death, myocardial infarction (MI) (not clearly attributed to a nontarget vessel), or a clinically indicated target lesion revascularization (TLR). The key secondary outcome, the patient-oriented composite outcome (POCO), included all-cause mortality, any MI (including nontarget vessel territory), and any revascularization. Other secondary outcomes included individual components of TLF and POCO, and stent thrombosis (ST) defined as definite, probable, or possible, according to the Academic Research Consortium (6).

Statistical analysis. First, analysis of primary and secondary clinical outcomes was performed in the crude population. Second, a propensity score-matched population was selected to adjust for uneven distribution of baseline characteristics. Multivariable-adjusted Cox proportional hazard regression and subgroup analysis were performed in propensity score-matched cohorts. Probability values were 2-sided; $p < 0.05$ was considered statistically significant.

Abbreviations and Acronyms

- **CI** = confidence interval
- **CoCr-EES** = cobalt-chromium everolimus-eluting stent(s)
- **DES** = drug-eluting stent(s)
- **EES** = everolimus-eluting stent(s)
- **MI** = myocardial infarction
- **PCI** = percutaneous coronary intervention
- **POCO** = patient-oriented composite outcome
- **RCT** = randomized controlled trial
- **ST** = stent thrombosis
- **TLF** = target lesion failure
- **TLR** = target lesion revascularization
- **ZES-R** = Resolute zotarolimus-eluting stent(s)

Results

Baseline characteristics. The number of patients and lesions were 5,054 of 7,084 for the total cohort, 3,056 of 4,248 for the EES group, and 1,998 of 2,836 for the ZES-R group, respectively. Fifty-five (1.8%) and 32 (1.6%) patients were lost to follow-up in the EES and ZES-R groups, respectively; however, all were confirmed alive. The distribution of cardiac risk factors was similar, except for dyslipidemia, lesion complexity, and left main disease (Tables 1 and 2). High-risk patients and lesions were frequent, implying that our registries were an enriched population with PCI, reflecting real-world practice in Korea. The device, lesion, and procedure success rates were excellent and similar for both stents (Table 2).

Clinical outcomes of the crude population. At 1 year, the incidence of TLF and its individual components did not differ between the EES and ZES-R groups (2.7% vs. 2.9%, $p = 0.662$) (Table 3). POCO also was similar (7.4% vs. 7.7%, respectively, $p = 0.702$), as were its individual components. The cumulative incidence of TLF, POCO (Fig. 1), and their individual components (Online Fig. 2) did not differ between the 2 stents.

Stent thrombosis. Definite or probable ST occurred in 25 patients (25 of 5,054, 0.5%) without between-group difference (Table 4, Fig. 2). When ST occurred, only 2 patients in the EES group were not taking dual antiplatelet therapy. In the pooled analysis regarding definite or probable ST with the RESOLUTE All Comers trial and the TWENTE trial (3,4), the incidence of definite or probable ST was 0.76% (37 of 4,876 patients) in the EES group and 0.89% (34 of 3,814 patients) in the ZES-R group, and did not differ between the 2 groups (odds ratio [OR]: 1.00; 95% confidence interval [CI]: 0.46 to 2.19; $p = 0.99$) (Online Fig. 3).