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Differential Prognostic Effect Between First- and Second-Generation Drug-Eluting Stents in Coronary Bifurcation Lesions

Patient-Level Analysis of the Korean Bifurcation Pooled Cohorts

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ABSTRACT

OBJECTIVES The purpose of this study was to investigate the differential clinical outcomes after percutaneous coronary intervention (PCI) for coronary bifurcation lesions with 1- or 2-stenting techniques using first- or second-generation drug-eluting stents (DES).

BACKGROUND The 2-stenting technique has been regarded to have worse clinical outcomes than the 1-stenting technique after bifurcation PCI with first-generation DES. However, there has been a paucity of data comparing the 1- and 2-stenting techniques with the use of second-generation DES.

METHODS Patient-level pooled analysis was performed with 3,162 patients undergoing PCI using first- or second-generation DES for bifurcation lesions from the "Korean Bifurcation Pooled Cohorts" (COBIS [Coronary Bifurcation Stenting] II, EXCELLENT [Registry to Evaluate Efficacy of Xience/Promus Versus Cypher in Reducing Late Loss After Stenting], and RESOLUTE-Korea [Registry to Evaluate the Efficacy of Zotarolimus-Eluting Stent]). The 3-year clinical outcomes were compared between 1- and 2-stenting techniques, stratified by the type of DES.

RESULTS With first-generation DES, rates of target lesion failure (TLF) or patient-oriented composite outcome (POCO) (a composite of all death, any myocardial infarction, any repeat revascularization, and cerebrovascular accidents) at 3 years were significantly higher after the 2-stenting than the 1-stenting technique (TLF 8.6% vs. 17.5%; $p < 0.001$; POCO 18.1% vs. 28.5%, $p < 0.001$). With second-generation DES, however, there was no difference between 1- and 2-stenting techniques (TLF 5.4% vs. 5.8%; $p = 0.768$; POCO 11.2% vs. 12.9%; $p = 0.995$). The differential effects of 2-stenting technique on the prognosis according to the type of DES were also corroborated with similar results by the inverse probability weighted model. The 2-stenting technique was a significant independent predictor of TLF in first-generation DES (hazard ratio: 2.046; 95% confidence interval: 1.114 to 3.759; $p < 0.001$), but not in second-generation DES (hazard ratio: 0.667; 95% confidence interval: 0.247 to 1.802; $p = 0.425$).

CONCLUSIONS Patient-level pooled analysis of 3,162 patients in Korean Bifurcation Pooled Cohorts demonstrated that the 2-stenting technique showed comparable outcomes to 1-stenting technique with second-generation DES, which is different from the results of first-generation DES favoring the 1-stenting technique. (J Am Coll Cardiol Intv 2015;8:1318–31) © 2015 by the American College of Cardiology Foundation.

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Even with improvements in techniques and technologies, the coronary bifurcation lesion is still 1 of the most challenging lesion subsets in the field of percutaneous coronary intervention (PCI). Among the several procedural steps, the most important decision might be the choice between 1- and 2-stenting strategies. Previously, the consensus has been conflicting, but modestly favored the 1-stenting technique with provisional side branch intervention over the systemic 2-stenting technique for bifurcation lesions (1). Following these results, the current guidelines recommend a provisional strategy with a 1-stenting technique only as an initial approach for bifurcation lesions (Class I, Level of

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Evidence: A from the ACCF/AHA/SCAI 2011 guideline [2]; Class IIa, Level of Evidence: A from the ESC/EACTS 2014 guideline [3]). However, these previous results were all on the basis of studies using first-generation drug-eluting stents (DES). In real-world practice, second-generation biocompatible or biodegradable-polymer coated stents have replaced first-generation DES, and these DES have proven to have better efficacy and safety in nonbifurcation lesions (4). Thus, we can expect better results from second-generation DES than the first-generation DES also in the bifurcation subset, even using complicated strategies like the 2-stenting technique. Whether the 2-stenting technique with the use of second-generation DES will show comparable results to the 1-stenting technique is still an elusive issue in the field of bifurcation PCI. Although few previous studies (5,6) have tried to evaluate this issue, none have shown a clear answer to this question, mainly due to relatively small sample sizes.

Therefore, we sought to compare the 3-year clinical outcomes following 1- or 2-stenting techniques with the use of first- or second-generation DES with a patient-level pooled data from dedicated, large-scale, real-world registries.

METHODS

Extended description of study methods are presented in the Online Appendix.

POOLED PATIENT POPULATION. The analysis population of this study was the "Korean Bifurcation Pooled Cohorts," which includes 3 different registries in Korea. First, the COBIS II (Coronary Bifurcation Stenting) registry (NCT01642992) is a dedicated bifurcation PCI registry with the use of first- or second-generation DES. From 2003 through 2009, 2,897 consecutive patients were enrolled from 18 major coronary intervention centers in Korea (7). The inclusion criteria were: 1) coronary bifurcation lesions treated with DES only; 2) main vessel (MV) diameter of ≥2.5 mm and side branch (SB) diameter of ≥2.3 mm confirmed by quantitative coronary angiography (QCA). Patients with cardiogenic shock, who received cardiopulmonary resuscitation, or who had protected left main (LM) disease were excluded.

The EXCELLENT (Registry to Evaluate Efficacy of Xience/Promus Versus Cypher in Reducing Late Loss After Stenting) (NCT00960648) and RESOLUTE-Korea (Registry to Evaluate the Efficacy of Zotarolimus-Eluting Stent) (NCT00960908) registries were dedicated second-generation DES registries for everolimus-eluting stents (Xience V [Abbott Vascular, Santa Clara, California]/Promus [Boston Scientific, Natick, Massachusetts]) or zotarolimus-eluting Resolute stents (Endeavor Resolute [Medtronic, Minneapolis, Minnesota]) that enrolled all-comers treated with ≥1 everolimus-eluting stent or zotarolimus-eluting Resolute stent (3,056 patients in 29 centers and 1,998 patients in 25 participating centers, respectively) without exclusions during the period of 2008 through 2010 (8). Among the total 5,054 patients from the EXCELLENT and RESOLUTE-Korea registries, 265 patients who met the inclusion criteria of the COBIS II registry were included in our analysis. These 265 patients met the same inclusion and exclusion criteria and were analyzed by the same bifurcation QCA system as the COBIS II registry.

Therefore, the final sample size of the Korean Bifurcation Pooled Cohorts was 3,162 patients. Among these patients, 2,475 were treated with first-generation DES and 687 were treated with second-generation DES (**Figure 1**). Every patient in the Korean Bifurcation Pooled Cohorts was followed for clinical outcomes up to 3 years (median follow-up duration 1,096.0 days, IQR: 778.8 to 1,497.0 days).

FOLLOW-UP, DATA COLLECTION, AND ANALYSIS. Coronary angiograms were reviewed and analyzed

ABBREVIATIONS AND ACRONYMS

CI = confidence interval

DES = drug-eluting stent(s)

PCI = percutaneous coronary intervention

POCO = patient-oriented composite outcome

TLF = target lesion failure

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