JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY VOL. 71, NO. 8, 2018

PUBLISHED BY ELSEVIER

Safety and Effectiveness of Second-Generation Drug-Eluting Stents in Patients With Left Main Coronary Artery Disease

Pil Hyung Lee, MD,[a] Osung Kwon, MD,[a] Jung-Min Ahn, MD,[a] Cheol Hyun Lee, MD,[a] Do-Yoon Kang, MD,[a] Jung-Bok Lee, PhD,[b] Soo-Jin Kang, MD, PhD,[a] Seung-Whan Lee, MD, PhD,[a] Young-Hak Kim, MD, PhD,[a] Cheol Whan Lee, MD, PhD,[a] Seong-Wook Park, MD, PhD,[a] Duk-Woo Park, MD, PhD,[a] Seung-Jung Park, MD, PhD[a]

ABSTRACT

BACKGROUND Limited data are available on the relative performances between different types of drug-eluting stents (DES) for obstructive left main coronary artery disease (LMCAD).

OBJECTIVES This study sought to compare effectiveness and safety profiles of various second-generation DES for LMCAD in real-world clinical practice.

METHODS Among 4,470 patients in 3, multicenter, prospective registries (IRIS-DES [Interventional Cardiology Research Incorporation Society-Drug-Eluting Stents] registry, the IRIS-MAIN [Interventional Cardiology Research Incorporation Society-Left MAIN Revascularization] registry, and the PRECOMBAT [PREmier of Randomized COMparison of Bypass Surgery versus AngioplasTy Using Drug-Eluting Stent in Patients with Left Main Coronary Artery Disease] study) treated between July 2007 and July 2015, the authors identified 2,692 patients with significant LMCAD who received second-generation DES; 1,254 with cobalt-chromium everolimus-eluting stents (CoCr-EES), 232 with biodegradable polymer biolimus-eluting stents (BP-BES), 616 with platinum-chromium EES (PtCr-EES), and 590 with Resolute zotarolimus-eluting stent (Re-ZES). The primary outcome was target-vessel failure.

RESULTS The observed 3-year rates of target-vessel failure were not significantly different for the different types of DES (16.7% for the CoCr-EES, 13.2% for the BP-BES, 18.7% for the PtCr-EES, and 14.7% for the Re-ZES; $p = 0.15$). In multiple treatment propensity score analysis, the adjusted hazard ratios (HRs) for target-vessel failure were similar in between-group comparisons of the different DES, except for the PtCr-EES versus the BP-BES (reference; HR: 1.60; 95% confidence interval: 1.01 to 2.54; $p = 0.046$). There were no significant differences in risk of composite of all-cause death, any myocardial infarction, or any revascularization and its individual components according to the different types of DES. Although the 3-year incidence of stent thrombosis was considerably low (≤1.0%) for all types of DES, between-group differences were observed, generally favoring the EES platforms.

CONCLUSIONS In this pooled analysis of 3 prospective registries involving unrestricted use of various second-generation DES for LMCAD, we found no significant between-group differences in 3-year risk of target-vessel failure, except for a higher risk of primary outcome with PtCr-EES compared to BP-BES. (Evaluation of the First, Second, and New Drug-Eluting Stents in Routine Clinical Practice [IRIS-DES]; NCT01186133) (J Am Coll Cardiol 2018;71:832–41)

Listen to this manuscript's audio summary by *JACC* Editor-in-Chief Dr. Valentin Fuster.

From the [a]Department of Cardiology, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea; and the [b]Division of Biostatistics, Center for Medical Research and Information, Asan Medical Center, University of Ulsan College of Medicine, Seoul, Korea. This work was partly supported by the Cardiovascular Research Foundation, Seoul, Korea. The sponsors played no role in this study. There was no industry involvement in the design or conduct of the study, collection, management, analysis, or interpretation of the data; the preparation, review, and approval of the manuscript; or the decision to submit the manuscript for publication. All authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. P.H. Lee and Kwon contributed equally to this work.

Manuscript received September 13, 2017; revised manuscript received December 11, 2017, accepted December 11, 2017.

ISSN 0735-1097/$36.00 https://doi.org/10.1016/j.jacc.2017.12.032

The technology and engineering of drug-eluting stents (DES) have continuously advanced (1). Compared with the previous versions, newer-generation DES have been developed that use different antiproliferative drugs with improved drug release kinetics, novel stent materials, thin strut platforms, and biocompatible or biodegradable polymers. In several studies, the newer-generation DES were associated with better safety and efficacy profiles than the first-generation DES and have thus become the default percutaneous coronary intervention (PCI) devices for broad clinical and anatomical subsets including left main coronary artery (LMCA) disease (2,3).

SEE PAGE 842

The cumulative evidence from clinical trials and registries has suggested that PCI using a DES is an acceptable alternative to coronary artery bypass grafting (CABG) in selected patients with LMCA disease (4–8). Recently, the primary results of 2 large randomized trials using second-generation DES have been reported; 1 study found PCI to be noninferior to CABG, whereas another study showed CABG to be superior to PCI (9,10). Although the disparate findings of the 2 trials lead to some uncertainty concerning the optimal revascularization strategy, both studies demonstrate how much PCI with a DES for LMCA revascularization has improved. However, until recently, data for the relative performance of the second-generation DES for the treatment of significant LMCA disease were limited. We therefore evaluated the comparative effectiveness and safety profiles of several second-generation DES for LMCA disease by using a pooled database from 3 large prospective clinical practice registries.

METHODS

STUDY POPULATION, PROCEDURES, AND DATA COLLECTION. The study population that underwent DES implantation for significant LMCA disease between July 15, 2007, and July 29, 2015 was pooled from 3 independent, multicenter observational studies; the IRIS-DES (Interventional Cardiology Research Incorporation Society-Drug-Eluting Stents) registry, the IRIS-MAIN (Interventional Cardiology Research Incorporation Society-Left MAIN Revascularization) registry, and the PRECOMBAT (PREmier of Randomized COMparison of Bypass Surgery versus AngioplasTy Using Drug-Eluting Stent in Patients with Left Main Coronary Artery Disease) registry. The study design and detailed entry criteria of each registry have been described previously (8,11,12), and the key features are summarized in Online Table 1. Briefly, the IRIS-DES study involved prospective, multicenter recruitment of unrestricted patients undergoing PCI with DES in Korea and consisted of several arms of first- and second-generation DES in a real-world setting (11). The IRIS-MAIN study was a prospective, multinational registry consisting of a cohort of consecutive Asian patients with significant, unprotected LMCA disease who were treated with PCI, bypass surgery, or medical therapy alone (8). The PRECOMBAT registry involved Korean patients with significant LMCA disease treated with second-generation DES for historical comparison with a patient cohort from the PRECOMBAT randomized trial (12). The current analysis included patients treated with 4 different types of DES: the cobalt-chromium everolimus-eluting stent (CoCr-EES; Xience V, Prime, Xpedition, or Alpine model; Abbott Vascular, Santa Clara, California), the biodegradable polymer-biolimus-eluting stent (BP-BES; BioMatrix model; Biosensors, Newport Beach, California, and Nobori, Terumo Clinical Supply, Kakamigahara, Japan), the platinum chromium-EES (PtCr-EES) (Promus Element or Premier model; Boston Scientific, Natick, Massachusetts), and the Resolute-zotarolimus-eluting stent (Re-ZES; Resolute Integrity model; Medtronic Inc., Santa Rosa, California). 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 findings. The ethics committee of each participating center approved the study protocol, and all patients provided written, informed consent.

In each registry, PCI was performed according to standard techniques at the discretion of each operator. The registries did not specify stent types according to clinical or anatomical features; therefore each operator was responsible for the choice of a DES. By protocol, the same type of stent implanted for LMCA was used in other non-left main lesions whenever necessary. The maximal available stent diameter was 4.0 mm for all kinds of DES involved in the current study. Periprocedurally, anticoagulant agent was administered according to standard regimens. Administration of 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

ABBREVIATIONS AND ACRONYMS

BP-BES = biodegradable polymer-biolimus eluting stent

CABG = coronary artery bypass grafting

CoCr-EES = cobalt-chromium everolimus-eluting stent

DES = drug-eluting stent

LMCA = left main coronary artery

MI = myocardial infarction

PCI = percutaneous coronary intervention

PtCr-EES = platinum chromium everolimus-eluting stent

Re-ZES = resolute zotarolimus-eluting stent

TVR = target-vessel revascularization