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CLINICAL RESEARCH

CORONARY

Comparative Effectiveness and Safety of New-Generation Versus Early-Generation Drug-Eluting Stents According to Complexity of Coronary Artery Disease

A Patient-Level Pooled Analysis of 6,081 Patients

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ABSTRACT

OBJECTIVES The purpose of this study was to compare the 2-year safety and effectiveness of new- versus early-generation drug-eluting stents (DES) according to the severity of coronary artery disease (CAD) as assessed by the SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score.

BACKGROUND New-generation DES are considered the standard-of-care in patients with CAD undergoing percutaneous coronary intervention. However, there are few data investigating the effects of new- over early-generation DES according to the anatomic complexity of CAD.

METHODS Patient-level data from 4 contemporary, all-comers trials were pooled. The primary device-oriented clinical endpoint was the composite of cardiac death, myocardial infarction, or ischemia-driven target-lesion revascularization (TLR). The principal effectiveness and safety endpoints were TLR and definite stent thrombosis (ST), respectively. Adjusted hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated at 2 years for overall comparisons, as well as stratified for patients with lower (SYNTAX score ≤11) and higher complexity (SYNTAX score >11).

RESULTS A total of 6,081 patients were included in the study. New-generation DES (n = 4,554) compared with early-generation DES (n = 1,527) reduced the primary endpoint (HR: 0.75 [95% CI: 0.63 to 0.89]; p = 0.001) without interaction (p = 0.219) between patients with lower (HR: 0.86 [95% CI: 0.64 to 1.16]; p = 0.322) versus higher CAD complexity (HR: 0.68 [95% CI: 0.54 to 0.85]; p = 0.001). In patients with SYNTAX score >11, new-generation DES significantly reduced TLR (HR: 0.36 [95% CI: 0.26 to 0.51]; p < 0.001) and definite ST (HR: 0.28 [95% CI: 0.15 to 0.55]; p < 0.001) to a greater extent than in the low-complexity group (TLR p_{int} = 0.059; ST p_{int} = 0.013). New-generation DES decreased the risk of cardiac mortality in patients with SYNTAX score >11 (HR: 0.45 [95% CI: 0.27 to 0.76]; p = 0.003) but not in patients with SYNTAX score ≤11 (p_{int} = 0.042).

CONCLUSIONS New-generation DES improve clinical outcomes compared with early-generation DES, with a greater safety and effectiveness in patients with SYNTAX score >11. (J Am Coll Cardiol Intv 2015;8:1657–66) © 2015 by the American College of Cardiology Foundation.

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ABBREVIATIONS AND ACRONYMS

CABG = coronary artery bypass surgery

CAD = coronary artery disease

DES = drug-eluting stent(s)

PCI = percutaneous coronary intervention

Drug-eluting stents (DES) have improved outcomes compared with bare-metal stents among patients undergoing percutaneous coronary intervention (PCI) owing to potent reduction of neointimal hyperplasia and the need for repeat revascularization (1). Early-generation DES delayed arterial healing of the stented segment and, as a result, were associated with an increased risk of stent-related thrombotic events and late restenosis (2,3). New-generation DES were introduced featuring thinner stent struts, more biocompatible durable or biodegradable polymer coatings, different antiproliferative agents, and lower drug loads (4). These refinements translated into improved clinical outcomes, and new-generation DES are the current standard of care (5–9).

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The likelihood of treatment failure directly correlates with the complexity of underlying coronary artery disease (CAD). In the large-scale SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) trial comparing early-generation paclitaxel-eluting stents with coronary artery bypass surgery (CABG) among patients with multivessel disease, PCI was inferior in terms of the composite of cardiovascular death, myocardial infarction, and repeat revascularization in the overall cohort, and differences were particularly pronounced among patients with increased SYNTAX score (10). Similarly, PCI with the use of early-generation sirolimus- or paclitaxel-eluting stents was inferior compared with CABG among diabetic patients with multivessel disease in the randomized FREEDOM (Future Revascularization Evaluation in Patients with Diabetes Mellitus: Optimal Management of Multivessel Disease) trial (11). Currently, it is not well established whether the clinical benefits of new- over early-generation DES are influenced by the anatomic complexity of CAD. We, therefore, sought to investigate the safety and effectiveness of new- compared with early-generation DES in relation to anatomic CAD complexity—defined by the SYNTAX score—in a large, broadly inclusive population of PCI patients enrolled in 4 all-comers randomized clinical trials.

METHODS

STUDY POPULATION. We pooled individual patient-level data from 4 randomized clinical studies: the SIRTAX (Sirolimus-Eluting and Paclitaxel-Eluting Stent for Coronary Revascularization) trial (NCT00297661) (12), the LEADERS (Limus Eluted from A Durable versus ERodable Stent coating) trial (NCT00389220) (13), the RESOLUTE All Comers (Randomized Comparison of a Zotarolimus-Eluting Stent with an Everolimus-Eluting Stent for Percutaneous Coronary Intervention) trial (NCT00617084) (14), and the BIOSCIENCE (Ultrathin Strut Biodegradable Polymer Sirolimus-Eluting Stent Versus Durable Polymer Everolimus-Eluting Stent for Percutaneous Coronary Revascularization) trial (NCT01443104) (15). All trials had an all-comers design and were conducted between 2004 and 2013 at European institutions, with the exclusive use of DES. Early-generation DES including sirolimus-eluting (Cypher or Cypher Select, Cordis, Miami Lakes, Florida) and paclitaxel-eluting stents (Taxus, Boston Scientific, Natick, Massachusetts) were investigated in the SIRTAX and LEADERS trials (12,13). New-generation DES encompassing everolimus-eluting (Xience V or Prime or Xpedition, Abbott Vascular, Santa Clara, California), zotarolimus-eluting (Resolute, Medtronic Inc., Santa Rosa, California), biodegradable polymer biolimus-eluting (BioMatrix Flex, Biosensors Inc., Newport Beach, California), and biodegradable polymer sirolimus-eluting stents (Orsiro, Biotronik AG, Bülach, Switzerland) were evaluated in the LEADERS, RESOLUTE All Comers, and BIOSCIENCE trials (13–15). Details on study designs and trial results were reported elsewhere (12–16). Briefly, patients with either stable CAD or acute coronary syndrome were eligible if they had at least 1 lesion with a diameter stenosis ≥50% in a vessel with reference diameter of 2.25 to 4.0 mm (SIRTAX, RESOLUTE All Comers, and BIOSCIENCE trials) or 2.25 to 3.5 mm (LEADERS trial). Inclusion

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