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Clinical Impact of Second-Generation Everolimus-Eluting Stent Compared With First-Generation Drug-Eluting Stents in Diabetes Mellitus Patients

Insights From a Nationwide Coronary Intervention Register

Elvin Kedhi, MD, PhD,* Marc E. Gomes, MD, PhD,*† Bo Lagerqvist, MD, PhD,‡ J. Gustav Smith, MD, PhD,§ Elmir Omerovic, MD, PhD,‖ Stefan James, MD, PhD,‡ Jan Harnek, MD, PhD,§ Göran K. Olivecrona, MD, PhD§

Rotterdam, the Netherlands; and Uppsala, Lund, and Göteborg, Sweden

Objectives This study sought to study the second-generation everolimus-eluting stent (EES) as compared with first-generation sirolimus-eluting (SES) and paclitaxel-eluting stents (PES) in diabetes mellitus (DM) patients.

Background There are limited data available comparing clinical outcomes in this setting with EES and SES, whereas studies comparing EES with PES are not powered for low-frequency endpoints.

Methods All DM patients treated with EES, PES, or SES from January 18, 2007, to July 29, 2011, from the SCAAR (Swedish Coronary Angiography and Angioplasty Registery) were included. The EES was compared with SES or PES for the primary composite endpoint of clinically driven detected restenosis, definite stent thrombosis (ST), and all-cause mortality.

Results In 4,751 percutaneous coronary intervention-treated DM patients, 8,134 stents were implanted (EES = 3,928, PES = 2,836, SES = 1,370). The EES was associated with significantly lower event rates compared with SES (SES vs. EES hazard ratio [HR]: 1.99; 95% confidence interval (CI): 1.19 to 3.08). The same was observed when compared with PES (PES vs. EES HR: 1.33; 95% CI: 0.93 to 1.91) but did not reach statistical significance. These results were mainly driven by lower incidence of ST (SES vs. EES HR: 2.87; 95% CI: 1.08 to 7.61; PES vs. EES HR: 1.74, 95% CI: 0.82 to 3.71) and mortality (SES vs. EES HR: 2.02; 95% CI: 1.03 to 3.98; PES vs. EES HR: 1.69; 95% CI: 1.06 to 2.72). No significant differences in restenosis rates were observed between EES and SES or PES (SES vs. EES HR: 1.26; 95% CI: 0.77 to 2.08; PES vs. EES HR: 1.05; 95% CI: 0.71 to 1.55).

Conclusions In all-comer DM patients the use of EES was associated with improved outcomes compared with SES and PES mainly driven by lower rates of ST and mortality. These results suggest better safety rather than efficacy with EES when compared with SES or PES. (J Am Coll Cardiol Intv 2012;5:1141–9) © 2012 by the American College of DM

From the *Department of Cardiology, Maasstad Hospital, Rotterdam, the Netherlands; †Cardiology Department, Heart and Lung Institute Sahlgrenska University Hospital, Göteborg, Sweden; ‡Department of Medical Sciences and Uppsala Clinical Research Center, Uppsala University, Uppsala, Sweden; §Department of Cardiology, Lund University, Lund, Sweden; and the ‖Cardiology Department, Heart and Lung Institute Sahlgrenska University Hospital, Göteborg, Sweden. Dr. Kedhi has received lecture fees from Abbott Vascular, St. Jude Medical, and Terumo, Europe. Dr. Omerovic has received institutional research grants from Medtronic, Inc., AstraZeneca, and St. Jude; and has served on the advisory board and received honoraria from AstraZeneca. Dr. James has received institutional research grants from Medtronic, Inc., Vascular Solutions, Terumo, Inc., AstraZeneca, and Eli Lilly; and has served on the advisory board and received honoraria from AstraZeneca, Eli Lilly, Abbott Vascular, Boston Scientific, and Medtronic. Dr. Harnek has received institutional research grants from Medtronic, Inc., and Boston Scientific; and has served on the advisory board and received honoraria from Abbott Vascular. All other authors have reported that they have no relationships relevant to the contents of this paper to disclose. Drs. Kedhi and Gomes contributed equally to this work.

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The introduction of the first-generation sirolimus-eluting (SES) and paclitaxel-eluting stents (PES) has led to markedly reduced restenosis rates and reduced need for target lesion revascularization, compared with bare-metal stents, in DM patients as well as non-DM patients (1–5). However, DM remains associated with increased risk of in-stent restenosis, target lesion revascularization, and target vessel revascularization in patients undergoing percutaneous coronary interventions (PCI) (6). The second-generation everolimus-eluting stent (EES) has recently been found to be superior to the first-generation PES for reduction of target lesion revascularization, target vessel revascularization, and stent thrombosis (ST) in 2 large randomized trials; however, these significant improvements in safety and efficacy endpoints were limited to the nondiabetic subgroup of patients, because no differences in treatment effect between these 2 stents were observed in DM patients in both trials (7,8). These findings were further confirmed by a large patient-level pooled analysis from 4 randomized clinical trials comparing EES with PES (9). Whether these results hold true in larger all-comer populations is unknown. There is a paucity of data on differences in clinical outcomes between EES and SES for treatment of DM patients, because the only data available derive from a relatively small series of patients and therefore are not adequately powered to detect low-frequency endpoints (10). Different issues with regard to the impact of metal alloy, strut thickness, polymer biocompatibility, and especially the effect of eluted active principle in patients with DM still remain unanswered. Therefore, we compared the safety and efficacy of the second-generation EES with the most-studied first-generation drug-eluting stent (DES), represented by the SES and PES in diabetic patients, with the data from the SCAAR registry (Swedish Coronary Angiography and Angioplasty Register) (11).

Abbreviations and Acronyms

CI = confidence interval
CTO = chronic total occlusion
DES = drug-eluting stent(s)
DM = diabetes mellitus
EES = everolimus-eluting stent(s)
HR = hazard ratio
PCI = percutaneous coronary intervention
PES = paclitaxel-eluting stent
SES = sirolimus-eluting stent(s)
ST = stent thrombosis

Methods

Study sample. For the present analysis we studied all PCI-treated DM patients from the SCAAR database. During the period from January 18, 2007, to July 27, 2011, 71,639 PCIs with stent implantations were performed in Sweden, of which 13,830 (19.3%) were in DM patients. A total of 110,610 stents were implanted. Of these, 21,962 (19.8%) stents were used in DM patients, 87,789 in non-DM patients, and 859 in patients without information about DM status. Of the 21,962 stents implanted in DM patients, 11,493 were BMS, and 47 were not classified as BMS or DES. Of the remaining 10,422 DES, 30 were excluded in the analysis due to missing data. Of these 10,422 DES, 2,836 were PES, 1,370 were SES, and 3,929 were EES, whereas the remaining 2,258 stents represent Biolimus-eluting and Zotarolimus-eluting stents (not included in these analyses).

The SCAAR registry has been previously described (11,12). Briefly, this registry holds data on consecutive patients from all 29 centers that perform coronary angiography and PCI in Sweden. The registry is sponsored by the Swedish Health Authorities and is independent of commercial funding. The technology is developed and administered by the Uppsala Clinical Research Centre. Since 2001, the SCAAR registry has been web-based, with recording of data online through a Web-interface in the catheterization laboratory; data are transferred in an encrypted format to a central server at the Uppsala Clinical Research Centre. All patients undergoing a coronary angiography or a PCI procedure nationwide are included. Since May 2005, all information with respect to restenosis and ST of previously treated patients that return in the catheterization laboratory for subsequent coronary angiography or PCI is entered in the SCAAR registry as well as the indication of such procedures. The web-based system provides each center with immediate and continuous feedback on processes and quality-of-care measures. Monitoring and verification of registry data are periodically performed in all hospitals since 2001 by comparing 50 entered variables in 20 randomly selected interventions/hospital and year with patient hospital records.

Study design and endpoints. The SCAAR registry includes follow-up data for every implanted stent device, permitting device-oriented as well as patient-oriented endpoint analysis. For the current analysis the EES was compared individually with PES and SES in DM patients. Diabetes mellitus was defined either by patient-reported diagnoses on clinical files at baseline or use of antidiabetic medication before procedure. The primary endpoint of the study was a composite safety and efficacy endpoint of all-cause mortality, ST, and restenosis at 1 year.

The restenosis and ST are performed at device level, whereas mortality is analyzed at patient level. The same definition for restenosis, as defined by the SCAAR steering committee, was used. The SCAAR definition of restenosis is defined as a stenosis assessed by angiographic visual estimation (>50%) or by fractional flow reserve value of <0.80 in a previously stented segment identified by coronary angiography for any clinical indication in any of the 29 centers in Sweden (11,12). The clinical relevance of restenotic lesions was detected by symptoms, routine noninvasive functional testing (exercise test, nuclear scan) and/or invasive functional evaluation by fractional flow reserve. The