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Clinical and Angiographic Outcomes of Patients Treated With Everolimus-Eluting Stents or First-Generation Paclitaxel-Eluting Stents for Unprotected Left Main Disease

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Objectives The goal of this study was to compare the outcomes of patients treated with everolimus-eluting stents (EES) with outcomes of patients treated with first-generation paclitaxel-eluting stents (PES) for unprotected left main disease (ULMD).

Background No data exist about the comparison of these 2 types of stents in ULMD.

Methods The primary endpoint of the study was a 1-year composite of cardiac death, nonfatal myocardial infarction, target vessel revascularization, and stroke (MACE). Secondary endpoints were 1-year target vessel failure (TVF) and 9-month angiographic in-segment restenosis >50%.

Results From 2004 to 2010, a total of 390 patients underwent ULMD percutaneous coronary intervention (224 received PES and 166 EES). The 1-year MACE rate was 21.9% in the PES group and 10.2% in the EES group ($p = 0.002$). TVF rate was 20.5% in the PES group and 7.8% in the EES group ($p < 0.001$). The in-segment restenosis rate was 5.2% in the EES group and 15.6% in the PES group ($p = 0.002$). EES and EuroSCORE were the only variables related to the risk of MACE. EES (odds ratio: 0.32; $p = 0.007$) was also independently related to the risk of restenosis.

Conclusions EES implantation for ULMD is associated with a reduced incidence of 1-year MACE, TVF, and restenosis as compared with PES implantation. (J Am Coll Cardiol 2012;60:1217–22) © 2012 by the American College of Cardiology Foundation

Randomized studies have shown the superiority of the everolimus-eluting stent (EES) over first-generation paclitaxel-eluting stents (PES) in non-left main coronary artery lesions, whereas no data exist about the 2 types of stents in patients treated for unprotected left main disease (ULMD) (1–4). The SYNTAX (SYNergy Between PCI With TAXus and Cardiac Surgery) trial that compared coronary artery bypass graft surgery with PES-supported percutaneous coronary intervention (PCI) in patients with ULMD and/or 3-vessel disease did not met the primary endpoint of noninferiority of PCI as compared with surgery, mainly because of the increased rate of repeat revascularization in the PCI arm, and it has been hypothesized that the use of a more effective stent would have changed the results of the study (5–7).

The aim of this study was to compare the 2 types of stents in consecutive patients treated for ULMD.

Methods

The ULMD Florence registry started in 2004 and enrolled patients treated with drug-eluting stents for ULMD. Details on this registry have been previously published (8,9). From the registry, we identified patients who received exclusively EES (either XIENCE V, Abbott Vascular, Santa Clara, California; or PROMUS, Boston Scientific, Natick, Massachusetts) or PES (either Taxus Express or Taxus Liberté, Boston Scientific). The only exclusion criterion from the study was ST-segment elevation myocardial infarction (MI). Patients underwent PCI instead of coronary surgery because of either the patient's preference or the high risk associated with surgery. High surgical risk was defined as a logistic EuroSCORE ≥6 (10).

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Abbreviations and Acronyms

EES = everolimus-eluting stent(s)

MACE = major adverse cardiovascular event(s)

MI = myocardial infarction

PCI = percutaneous coronary intervention

PES = paclitaxel-eluting stent(s)

TVF = target vessel failure

TVR = target vessel revascularization

ULMD = unprotected left main disease

PCI was performed using standard techniques. For distal left main disease, a single-stent technique was preferred in patients with a normal or diminutive-appearing side branch, whereas a double-stent technique was considered in patients with disease of both ostia and proximal segments of the left anterior descending coronary artery and circumflex coronary artery. Whatever the stenting technique used, routine final kissing balloon post-dilation with noncompliant balloons had to be performed in all cases.

Multivessel disease was defined as stenosis >70% of ≥1 major coronary arteries at baseline angiography besides the left main lesion. Disease of the left anterior descending coronary artery and of the circumflex coronary artery included lesions beyond 10 mm from the ostia. Completeness of revascularization was defined as the successful revascularization of all vessels with a diameter stenosis >70% and a diameter >2 mm achieved either during the index hospitalization or at any time within 30 days after ULMD PCI.

Procedural antithrombotic therapy included unfractionated heparin to achieve an activated clotting time of 200 to 250 s, whereas the use of glycoprotein IIb/IIIa inhibitors was at discretion of the operator. Chronic antithrombotic treatment included aspirin (300 mg/day indefinitely) and clopidogrel (75 to 150 mg daily) for at least 1 year.

The primary endpoint of the study was the 1-year major adverse cardiovascular events (MACE) that included cardiac death, nonfatal MI, target vessel revascularization (TVR), and stroke. Secondary endpoints were 1-year target vessel failure (TVF) and in-segment left main restenosis. All deaths were considered cardiac unless an unequivocal noncardiac cause could be documented. TVF was defined as the composite of cardiac death, MI not clearly attributable to a non-left main vessel, and clinically driven ULMD revascularization within 1 year. Stent thrombosis was defined according to the Academic Research Consortium criteria (11), whereas restenosis was defined as >50% luminal narrowing at the segment site including the stent and 5 mm proximal and distal to the stent edges. Angiographic parameters were assessed using a computer analysis system (Innova 2100IQ, General Electric Healthcare Technologies, Little Chalfont, United Kingdom).

The treatment protocol included routine 6- to 9-month angiographic follow-up.

The study was approved by the institutional review committee and all patients gave informed written consent to intervention and the study.

Statistical analysis. On the basis of the results of previous studies (8,9,12,13), we assumed PES to be associated with MACE and TVF rates of 22% and 20%, respectively. We hypothesized a >50% reduction in both endpoints with EES. To achieve a statistical power >80%, a sample size of at least 160 patients per group was needed, considering an experimental type I error of 0.05.

Discrete data were summarized as frequencies, and continuous data were expressed as mean ± SD or median and interquartile range as appropriate. The chi-square test was used for comparison of categorical variables, and the unpaired 2-tailed Student *t* test or Mann-Whitney rank sum test was used to test differences among continuous variables. Survival curves were generated with the use of the Kaplan-Meier method, and the difference between groups was assessed by log-rank test. The multivariable analysis for the primary endpoint was performed by the forward stepwise Cox proportional hazards model, whereas for angiographic restenosis, analysis was by forward stepwise logistic regression. The following variables were tested: age (years), male sex, diabetes mellitus, EuroSCORE, previous MI, right coronary artery chronic total occlusion, left main stenting of both branches, minimal lumen diameter post-PCI (mm), maximum pressure inflation (atm), completeness of revascularization, year of the index procedure, and EES. Interaction between EES and year of the index procedure was tested with the Cox regression model. A propensity score–matched analysis (1:1) was also performed because of expected differences in baseline characteristics between patients receiving EES and patients receiving PES due to broader indication to PCI in the last years. An optimal data-matching technique was performed using the propensity score as calipers. Propensity score analysis was performed with the use of a logistic regression model from which the probability for the use of EES was calculated for each patient. The variables entered into the model were: age (years), male sex, serum creatinine >150 μmol/l, history of MI, left ventricular ejection fraction <40%, peripheral vascular disease, EuroSCORE, left main stenting of both branches, and left main stent length >24 mm. Model discrimination was assessed with the c-statistic and goodness of fit with the Hosmer-Lemeshow test. All tests were 2-sided, and a p value <0.05 was considered significant. Analyses were performed using the software package SPSS version 11.5 (SPSS, Chicago, Illinois).

Results

From 2004 to 2010, 470 patients underwent left main PCI with drug-eluting stents. Of these, 390 patients received exclusively PES or EES (224 received PES and 166 EES).

The majority of patients were at high surgical risk. In the PES group, there was a higher incidence of hypercholesterolemia, peripheral vascular disease, and renal insufficiency and a higher EuroSCORE, as compared with the EES