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Late Restenosis After Paclitaxel-Coated Balloon Angioplasty Occurs in Patients With Drug-Eluting Stent Restenosis

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ABSTRACT

BACKGROUND There are currently inadequate data on whether "late restenosis" occurs after paclitaxel-coated balloon (PCB) angioplasty for in-stent restenosis (ISR) lesions.

OBJECTIVES To evaluate the long-term safety and efficacy of PCB angioplasty, we investigated serial clinical and angiographic outcomes after PCB angioplasty for ISR lesions.

METHODS Between September 2008 and December 2012, PCB angioplasty was performed in 468 patients with 550 ISR lesions (bare-metal stent restenosis [BMS-ISR]: 114 lesions, drug-eluting stent restenosis [DES-ISR]: 436 lesions). Two serial angiographic follow-ups were routinely planned for the patients (at 6 and 18 months after the procedure).

RESULTS Early follow-up (6 months) angiography was performed for 488 lesions (89%), and recurrent restenosis occurred in 13 lesions (13.0%) in the BMS-ISR group and in 82 lesions (21.1%) in the DES-ISR group. Target lesion revascularization was performed for 7 lesions (7.0%) in the BMS-ISR group and 54 lesions (13.9%) in the DES-ISR group. Late follow-up (18 months) angiography was performed for 377 (88%) of the remaining 427 lesions (excluding target lesion revascularization lesions), and late restenosis was found in 2 lesions (2.5%) in the BMS-ISR group and 50 lesions (16.8%) in the DES-ISR group. Delayed late lumen loss was significantly larger in the DES-ISR group. Previous stent size ≤2.5 mm, percentage diameter stenosis after the procedure, and in-stent occlusion lesion were independent predictors of early restenosis. DES-ISR, percentage diameter stenosis at early follow-up, and hemodialysis were independent predictors of late restenosis.

CONCLUSIONS Late restenosis occurs after PCB angioplasty for DES-ISR lesions. (J Am Coll Cardiol 2015;66:14–22)

Recently, paclitaxel-coated balloon (PCB) angioplasty has emerged as a potential alternative to the current treatment for in-stent restenosis (ISR). However, there are concerns about the long-term efficacy and safety of PCB angioplasty. There are currently inadequate data on whether "late restenosis" occurs after PCB angioplasty for bare-metal stent restenosis (BMS-ISR) and drug-eluting stent restenosis (DES-ISR). Treatment of BMS-ISR with a PCB persistently has been shown to reduce repeat revascularization during long-term follow-up (1,2). A recent study has shown that DES-ISR was associated with poorer outcomes than those of BMS-ISR after treatment with a PCB (3). To evaluate the safety and efficacy of PCB angioplasty, we investigated serial clinical and angiographic outcomes after PCB angioplasty for ISR lesions (BMS-ISR and DES-ISR).

METHODS

PATIENT POPULATION. This study was a retrospective analysis of a prospective protocol including serial

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angiographic follow-up. Between September 2008 and December 2012, 1,123 ISR lesions were treated with percutaneous coronary intervention (PCB or DES), and PCB angioplasty was performed in 550 ISR lesions in 468 patients (BMS-ISR: 114 lesions, DES-ISR: 436 lesions). SeQuent Please paclitaxel-coated balloon catheter (B. Braun Melsungen AG, Vascular Systems, Berlin, Germany) was used in this study. The exclusion criteria were recurrent lesions after PCB angioplasty for ISR, lesions located in bypass conduits, and bailout stenting after PCB angioplasty due to major dissection. The study was done in accordance with the provisions of the Declaration of Helsinki and local regulations. All patients provided informed consent for both the procedure and subsequent data collection and analysis for research purposes, and the study was approved by the institutional ethics committee.

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INTERVENTIONAL PROCEDURE. All patients were pre-treated with aspirin (100 mg daily) and ticlopidine (200 mg daily)/clopidogrel (75 mg daily). Aspirin and ticlopidine/clopidogrel treatment was recommended for at least 6 months. The procedures were performed according to standard clinical guidelines. In all cases, the interventional strategy and the use of adjunctive devices and pharmacotherapy were at the discretion of the operator. Pre-dilation was performed for all ISR lesions. The length of the PCB was chosen to overlap the lesion by at least 2 mm at the proximal and distal margins. The recommended inflation time for the PCB was 60 s.

FOLLOW-UP AND DEFINITIONS. Two serial angiographic follow-ups were routinely planned for the patients. Early follow-up was planned at 6 months after the procedure, and late follow-up was planned at 18 months after the procedure. The follow-up angiogram was obtained earlier if clinically indicated. Follow-up angiography performed at 5 to 12 months was considered early follow-up. Follow-up angiography performed at 12 to 24 months was considered late follow-up. When recurrent restenosis occurred within 5 months, it was included in early follow-up results. Clinical follow-up was performed by telephone contact or office visit. Binary restenosis at follow-ups was defined as stenosis occupying >50% of the diameter. Late restenosis was defined as diameter stenosis ≥50% at late follow-up in lesions of <50% diameter stenosis at early follow-up. Target lesion revascularization (TLR) was defined as any repeat percutaneous coronary intervention or aortocoronary bypass surgery because of restenosis (diameter stenosis ≥50%) associated with symptoms or objective signs of ischemia (stress electrocardiogram, myocardial perfusion imaging, or fractional flow reserve). We applied Academic Research Consortium criteria for definite stent thrombosis for adjudication of target lesion thrombosis.

ANGIOGRAPHIC ANALYSIS. Quantitative coronary angiographic analysis was performed using QCA-CMS (Medis Medical Imaging Systems, Leiden, the Netherlands). All angiograms were analyzed in a random sequence by 2 experienced observers who were blinded to the clinical characteristics of patients. Coronary angiograms were obtained in multiple views after intracoronary nitrate administration. Reference diameter, minimal lumen diameter, percentage diameter stenosis, and lesion length were measured before and after intervention and at follow-up. Acute gain was defined as minimal lumen diameter immediately after the procedure minus that at baseline. Late lumen loss was defined as minimal lumen diameter immediately after the procedure minus that at angiographic follow-up. Delayed late lumen loss was defined as minimal lumen diameter at early follow-up minus that at late follow-up. Progression case was defined as a case of delayed late lumen loss >0 mm. Measurements were done at the target lesion treated by a PCB within 5 mm proximal and distal to the treated area. ISR was classified according to the Mehran classification (4). A multifocal lesion was classified as non-focal-type restenosis lesion. Stent fracture was angiographically defined at the use of a PCB.

STUDY ENDPOINTS. The efficacy endpoint included late lumen loss, rate of binary restenosis, and rate of TLR at follow-up. The safety endpoint included major adverse cardiac events and a composite of cardiac death, myocardial infarction, or target lesion thrombosis at follow-up. The efficacy endpoints were evaluated on a per-lesion basis. The safety endpoints were evaluated on a per-patient basis.

STATISTICAL ANALYSIS. Continuous variables are expressed as mean ± SD. Values are shown as numbers with relative percentage or SD. For continuous data, the groups were compared with the Student *t* test or Wilcoxon rank-sum test on the basis of the distribution. Categorical variables were compared using the chi-square test. Risk factors of early restenosis and late restenosis after PCB angioplasty were analyzed separately. A multivariable logistic regression model instead of a Cox proportional hazard model was used to identify independent risk factors

ABBREVIATIONS AND ACRONYMS

BMS = bare-metal stent(s)

BMS-ISR = bare-metal stent restenosis

CI = confidence interval(s)

DES = drug-eluting stent(s)

DES-ISR = drug-eluting stent restenosis

ISR = in-stent restenosis

OR = odds ratio

PCB = paclitaxel-coated balloon

TLR = target lesion revascularization