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PERIPHERAL

The Characteristics of In-Stent Restenosis After Drug-Eluting Stent Implantation in Femoropopliteal Lesions and 1-Year Prognosis After Repeat Endovascular Therapy for These Lesions

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ABSTRACT

OBJECTIVES This study sought to investigate the characteristics of in-stent restenosis (ISR) after drug-eluting stent (DES) implantation for femoropopliteal (FP) lesions, and to examine 1-year prognosis after repeat endovascular therapy (re-EVT) for these DES-ISR.

BACKGROUND The morphology of DES-ISR and its association with clinical outcomes after re-EVT have not been well examined.

METHODS This was a subanalysis of the ZEPHYR (Zilver PTX for the femoral artery and proximal popliteal artery) study. The current study included 210 cases with loss of patency confirmed 1 year after DES implantation. Morphology of DES-ISR was classified into the following subgroups: class I, focal lesions (≤50 mm in length), class II, diffuse lesions (>50 mm in length), and class III, totally occluded ISR. One-year prognosis after re-EVT for DES-ISR was assessed by restenosis and major adverse limb events (MALE).

RESULTS Classes I, II, and III accounted for 50%, 25%, and 25% of DES-ISR, respectively. Factors associated with the morphology of DES-ISR were the presence of chronic total occlusion and the size of the external elastic membrane area before DES implantation ($p = 0.009$ and 0.017). Compared with the class I restenotic lesion, the class II and III lesions had a significantly higher risk of restenosis (74% and 78% vs. 53%: $p = 0.048$ and 0.019, respectively) and MALE (56% and 56% versus 32%: $p = 0.025$ and 0.022, respectively) 1 year after re-EVT.

CONCLUSIONS We evaluated the characteristics of ISR after DES implantation for FP lesions and 1-year prognosis of re-EVT for DES-ISR. The morphology of DES-ISR had a significant association with 1-year prognosis after re-EVT. (J Am Coll Cardiol Intv 2016;9:828–34) © 2016 by the American College of Cardiology Foundation.

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Clinical outcomes of endovascular therapy (EVT) for femoropopliteal (FP) lesions have improved recently thanks to the development of current devices including new-generation bare-metal nitinol stents (BNS) and drug-eluting stents (DES). However, a substantial incidence of in-stent restenosis (ISR), which is continuously increasing during the chronic phase, is reluctantly found in clinical setting (1–6).

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The morphology of post-BNS restenosis is a clinically important determinant in predicting the future occurrence of recurrent ISR after balloon angioplasty and was classified into the following 3 subgroups: class I, focal lesions (≤50 mm in length), class II, diffuse lesions (>50 mm in length), and class III, totally occluded ISR (7,8). Particularly, the prognosis of balloon angioplasty after post-BNS class III restenosis is direly poor, and the rates of repeat reintervention and conversion to bypass surgery are consequently high. However, there are no reports on the morphology of ISR after DES implantation. The aim of the current study was to investigate the characteristics of ISR after DES implantation for FP lesions, and to examine 1-year prognosis after repeated endovascular therapy (re-EVT) for these DES-ISR lesions.

METHODS

STUDY POPULATION AND DEFINITIONS. This was a subanalysis of the ZEPHYR (Zilver PTX for the Femoral Artery and Proximal Popliteal Artery) study. The ZEPHYR study was a prospective multicenter study enrolling patients with femoropopliteal lesions undergoing Zilver PTX implantation between July 2012 and April 2013. The details of the study protocol and the 1-year results were described elsewhere (9). The study was in accordance with the Declaration of Helsinki and was approved by the ethics committee of each participating hospital. Written informed consent was obtained from every participant. Antiplatelet regimens during the follow-up period were used at the physician's discretion on the basis of patient's condition.

In the ZEPHYR study, external elastic membrane (EEM) area, defined as the area enclosed by the media to adventitia interface, and minimal stent area (MSA), defined as the smallest stent area within the implanted stent, were evaluated by intravascular ultrasound (IVUS).

The current study analyzed a total of 210 cases, whose ISR was confirmed at 1 year after DES implantation. The distribution of the subsample among the centers in the ZEPHYR study are shown in Online Figure A. DES-ISR was evaluated using follow-up angiography or duplex ultrasonography (DUS), and was categorized into class I, II, and III, similarly to BNS-ISR in **Figure 1** (7,8). In brief, focal nonocclusive lesions (≤50 mm in length) were categorized as class I, whereas diffuse nonocclusive ones (>50 mm in length) were categorized as class II. Class III was defined as totally occluded lesions. Cases with stent thrombosis were excluded.

Of the 210 cases with DES-ISR, 134 cases (64%) underwent re-EVT to re-recanalize the restenotic lesions. One-year prognosis after the re-EVT was evaluated with restenosis (i.e., recurrence of in-stent stenosis) and major adverse limb events (MALE). One-year restenosis after re-EVT was again assessed by follow-up angiography or DUS, with a tolerance of ±2 months. Restenosis was defined as recurrence of ≥50% diameter stenosis determined by angiography or a peak systolic velocity ratio >2.4 by DUS (10). Requirement of any reintervention (either endovascular or surgical) or major amputation (defined as surgical limb excision above the ankle) within 1 year was automatically included in the outcome. MALE was defined as any reintervention or major amputation.

STATISTICAL ANALYSIS. Data are shown as the mean ± SD for continuous variables or as percentages for dichotomous variables, unless otherwise noted. A p value <0.05 was considered as statistically significant. p Values for trend regarding baseline characteristics at DES implantation were obtained from the 1-way analysis of variance for continuous variables, and from the linear-by-linear association test for discrete variables. The difference in treatment strategy among subgroups was tested by the chi-square test. One-year incidence rate of restenosis (i.e., recurrence of in-stent

ABBREVIATIONS AND ACRONYMS

BNS = bare-metal nitinol stent(s)
CI = confidence interval
CTO = chronic total occlusion
DES = drug-eluting stent(s)
DM = diabetes mellitus
DUS = duplex ultrasonography
EEM = external elastic membrane
EVT = endovascular therapy
FP = femoropopliteal
ISR = in-stent restenosis
IVUS = intravascular ultrasonography
MALE = major adverse limb event(s)
MSA = minimal stent area
re-EVT = repeat endovascular therapy

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