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Original article

Impact of stent diameter on vascular response after self-expanding paclitaxel-eluting stent implantation in the superficial femoral artery☆

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ABSTRACT

Background: The optimal sizing of self-expanding paclitaxel-eluting stents (PES) in the treatment for superficial femoral artery (SFA) lesions is unclear. This study sought to investigate the influence of PES diameter on stent patency in SFA lesions using optical frequency domain imaging (OFDI).
Methods: A total of 20 de novo SFA lesions were randomized 1:1 to receive either self-expanding PES with a nominal diameter of 6 mm or 8 mm. Follow-up angiography and OFDI was scheduled six months after stent implantation, and volumetric OFDI analysis was performed to evaluate vascular response to the stents. Volume index (VI) was defined as the volume divided by the stent length. The primary end point was lumen VI at the 6-month follow-up. Secondary end point was minimum lumen diameter (MLD) by quantitative vascular angiography (QVA) at the follow-up.
Results: Stent length was 78.0 ± 23.9 mm in the 6-mm group and 70.0 ± 23.6 mm in the 8-mm group ($p = 0.46$). Baseline QVA data were also similar between the two groups. MLD immediately after stent implantation was similar between the two groups (4.2 ± 0.5 mm in the 6-mm group and 3.9 ± 0.5 mm in the 8-mm group, p = NS). At the 6-month follow-up, MLD was greater in the 8-mm group compared to the 6-mm group (4.0 ± 1.0 mm vs. 3.2 ± 0.4 mm, $p < 0.05$). Stent VI was larger in the 8-mm group (28.4 ± 6.7 mm^3/mm vs. 22.2 ± 1.2 mm^3/mm, $p = 0.01$). Neointimal VI was similar between the two groups (5.8 ± 2.9 mm^3/mm vs. 5.2 ± 2.6 mm^3/mm, $p = 0.68$). Lumen VI was greater in the 8-mm group (23.2 ± 7.6 mm^3/mm vs. 17.3 ± 2.6 mm^3/mm, $p = 0.04$).
Conclusions: Chronic stent enlargement resulted in greater lumen area after implantation of self-expanding PES with a large diameter at the mid-term follow-up. Stent diameter might be important for stent patency in procedure with PES for SFA lesions.

Introduction

Similar to coronary artery disease, drug-eluting stents (DES) have successfully shown superior outcomes for peripheral artery disease (PAD) compared to self-expanding bare-metal nitinol stents (BMS) [1,2]. Primary patency rate after self-expanding paclitaxel-eluting nitinol stent (PES) implantation for superficial femoral artery (SFA) lesions was reported to be 90% at 1 year [1] and 83% at 2 years [2]. Nevertheless, the phenomenon of in-stent restenosis (ISR) due to neointimal hyperplasia remains even after DES implantation. Iida et al. [3] recently reported that 1-year real-world ISR rate after Zilver PTX (Cook Medical, Bloomington, IN, USA) implantation was 37%, which was apparently worse than that reported in previous Zilver PTX trials. So far, ISR continues to be a major clinical limitation of DES implantation in SFA lesions.

☆ Clinical Trial Registration Information: UMIN000015485.

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The mechanism of ISR is related to neointimal hyperplasia, which is an exaggerated healing response to the vessel wall injury that occurs as a result of mechanical dilatation [4,5]. An experimental study has reported that chronic outward force from self-expanding nitinol stents was stronger in vessels treated with a larger stent diameter [6]. Also, there are several animal reports describing the influence of stent diameter on neointimal proliferation after self-expanding BMS implantation [7,8]. In these reports, a higher ratio of nominal stent diameter to vessel size at target arteries resulted in an exuberant neointimal proliferation and luminal stenosis. However, no data on the influence of stent diameter on neointimal proliferation following self-expanding DES implantation has been established. Therefore, the purpose of the present study was to evaluate the impact of stent diameter on stent patency after self-expanding PES implantation in the human peripheral artery with optical frequency domain imaging (OFDI).

Materials and methods

Study design

This was a prospective, randomized, open-label study designed to investigate the influence of PES diameter on vascular response in SFA lesions, using OFDI. From December 2014 to December 2015, a total of 20 de novo SFA lesions were randomized 1:1 to receive either PES with a nominal diameter of 6 mm or 8 mm, and follow-up angiography and OFDI were scheduled to evaluate chronic vascular response 6 months after stent implantation (Fig. 1). Duplex ultrasound (DUS) evaluation for stent patency was also performed at 6 months. Patients with symptomatic PAD due to de novo SFA lesions who were classified as greater than Rutherford 1 were screened by noninvasive tests to detect limb ischemia and presence of SFA lesions. Study enrollment proceeded after satisfying the angiographic inclusion/exclusion criteria, which included lesion length $\leq$15 cm, >50% diameter stenosis (DS), and at least one patent infrapopliteal run-off vessel to the foot. Exclusion criteria were (1) acute or sub-acute limb ischemia, (2) previous bypass surgery in the lower limb or previous stenting in the SFA, (3) residual >50% DS in the inflow aorto-iliac artery, (4) lesions requiring multiple stent implantation, and (5) known intolerance to dual antiplatelet therapy (DAPT) or contrast agents. The study was conducted in accordance with the Declaration of Helsinki. The protocol was approved by the institutional review board of Hyogo College of Medicine, and written informed consent was obtained from all patients before participation. This study was registered on the UMIN clinical trial registry (UMIN000015485).

Endovascular therapy procedure

After initial diagnostic angiography of the lower limb, indications for endovascular therapy (EVT) were decided by more than two physicians. EVT procedure was performed with primary stenting strategy via a contralateral femoral approach through 6-Fr sheaths. Following the sheath insertion, unfractionated heparin (5000 units) was administered into the artery. After a 0.014-inch guidewire was passed through the lesion, pre-dilation was performed using a balloon with diameter equal to the reference vessel diameter according to visual estimation. Balloon inflation was maintained at a pressure of 6–10 atmospheres for 30–60 s and repeated routinely two to four times at the target segment. Following pre-dilation of the lesion, self-expanding PES (Zilver PTX) with a diameter of 6 mm or 8 mm was deployed. Post-dilation was performed routinely in all lesions using a balloon with 5 mm diameter at a pressure of 14 atmospheres. DAPT (aspirin 100 mg/day and clopidogrel 75 mg/day) was started at least one week prior to EVT and was continued during the follow-up period.

Quantitative vascular angiography analysis and stent fracture

Angiography was obtained before EVT, immediately after EVT, and at the 6-month follow-up. All quantitative vascular angiography (QVA) analyses, completed using commercially available software (QAngio XA 7.3, Medis Medical Imaging Systems BV, Leiden, The Netherlands), were performed by an independent core laboratory (Cardiovascular Core Analysis Laboratory, Stanford, CA, USA) in a blinded fashion. The tip of 6-Fr guiding catheter was used for calibration in QVA analysis. Minimum lumen diameter (MLD), reference lumen diameter (RLD), and stent length were obtained. DS was calculated as follows: MLD divided by average [(proximal + distal) $\times$ ½] RLD. Stent fracture was assessed on X-ray at 6 months after stent implantation. Stent fracture was defined as clear interruption of stent struts identified on X-ray from multiple projections [9].

OFDI acquisition

Follow-up OFDI procedure was performed at an image acquisition rate of 160 frames/s with a TERUMO OFDI system

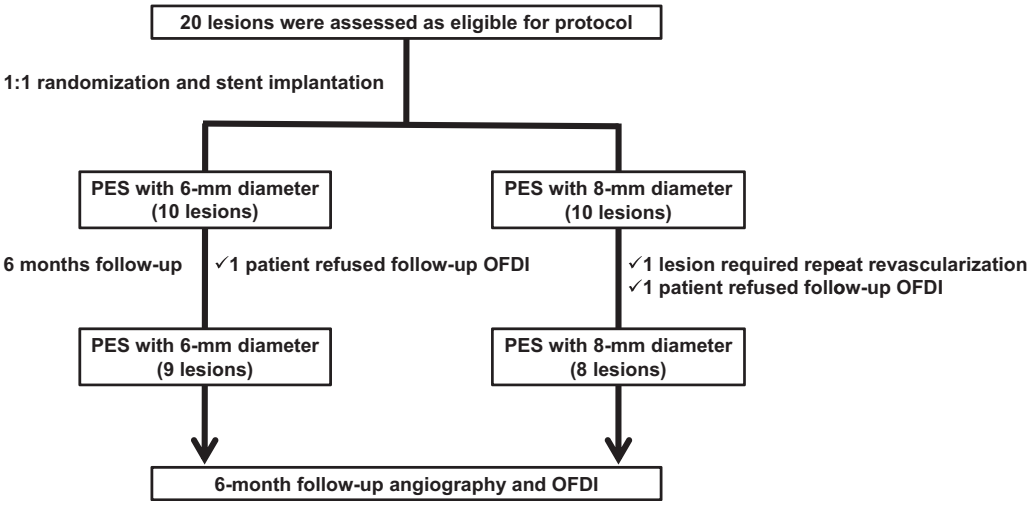

Fig. 1. Study flow chart. A total of 20 lesions from 20 patients were eligible for the study protocol. Three patients were lost to the follow-up, and the remaining 17 lesions completed the follow-up examination. OFDI, optical frequency domain imaging; PES, self-expanding paclitaxel-eluting stent.

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