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Original article

Optical coherence tomography study of chronic-phase vessel healing after implantation of bare metal and paclitaxel-eluting self-expanding nitinol stents in the superficial femoral artery

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ABSTRACT

Background: This study aimed to assess chronic-phase suppression of neointimal proliferation and arterial healing following paclitaxel-coated (PTX) and bare metal stent (BMS) implantation in the superficial femoral artery using optical coherence tomography (OCT).
Methods: Twenty-five patients with 68 stents underwent an 8-month OCT follow-up. Besides standard OCT variables, neointimal characterization and frequencies of peri-strut low-intensity area (PLIA), macrophage accumulation, and in-stent thrombi were evaluated.
Results: The mean neointimal thickness was significantly less with PTX stents (544.9 ± 202.2 μm vs. 865.0 ± 230.6 μm, $p < 0.0001$). The covered and uncovered strut frequencies were significantly smaller and larger, respectively, in the PTX stent group vs. the BMS group (93.7% vs. 99.4%; $p < 0.0001$, 4.0% vs. 0.4%; $p < 0.0001$, respectively). Heterogeneous neointima was only observed in the PTX stent group (12.5% vs. 0%, $p = 0.017$). The frequencies of PLIA and macrophage accumulation were significantly greater in the PTX stent group (87.2% vs. 67.6%, $p = 0.001$ and 46% vs. 9.1%, $p = 0.003$, respectively).
Conclusion: After 8 months, reduced neointimal proliferation was observed with PTX stent implantation. On the other hand, delayed arterial healing was observed compared with BMS.

Introduction

The Zilver PTX Stent (Cook Medical, Bloomington, IN, USA), a polymer-free 3-μg/mm^2 paclitaxel-coated self-expanding nitinol stent, is the first drug-eluting stent (DES) available for the treatment of femoro-popliteal artery disease. Although the results were less dramatic than those achieved with coronary artery DES, PTX stent was shown to increase primary patency and reduce in-stent restenosis when compared with conventional balloon angioplasty and bare metal stent (BMS) [1,2]. An intravascular ultrasound (IVUS) study revealed that PTX stent achieved less neointimal proliferation relative to BMS, leading to reduced in-stent restenosis after femoro-popliteal artery intervention [3].

In coronary artery disease management, DES dramatically reduced the incidence of in-stent restenosis; however, concerns about late stent thrombosis have emerged, and the adequate duration of dual anti-platelet therapy after DES implantation in coronary arteries remains controversial [4,5]. Late stent thrombosis has also been reported to occur after PTX stent implantation for femoro-popliteal artery disease [6], and poor arterial healing with a high incidence of uncovered struts, and thrombus attachment was considered a possible substrate for stent thrombosis in an angioscopic evaluation [7].

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Optical coherence tomography (OCT) is an imaging modality that visualizes intra-vascular features with high axial resolution (10–20 mm), approximately 10 times greater than that of intravascular ultrasound (100–150 mm) [8]. OCT evaluation of vessel healing after stent implantation is considered a gold standard in the field of coronary artery evaluation because of its excellent correlation with histological findings [9–12]. Additionally, OCT can characterize the neointima and tissues around the stent strut.

The aim of this study is to assess the chronic phase arterial healing following DES and BMS implantation to superficial femoral artery.

Materials and methods

Study population

This was a multi-center retrospective study. Patients who underwent implantation of self-expanding nitinol stents into de novo superficial femoral arteries at Osaka Saiseikai Nakatsu Hospital and Kobe University Hospital between November 2012 and October 2013 were recruited for chronic-phase angiography and OCT. Patients who exhibited target vessel revascularization before 8 months post-implantation were excluded. Finally, 25 patients (32 lesions, 68 stents) were enrolled in this study.

Dual anti-platelet therapy with aspirin (100 mg/day) and clopidogrel (75 mg/day) was continued for at least 6 months in patients implanted with PTX stents and 1 month for patients implanted with BMS.

This study was approved by the ethics committees of Osaka Saiseikai Nakatsu Hospital and Kobe University and performed according to the guidelines of the Declaration of Helsinki. All enrolled study patients provided written informed consent to participate in the study.

OCT examination

OCT imaging was performed using a frequency-domain OCT system (C8 OCT-system, St. Jude Medical, St. Paul, MN, USA). A 0.014-inch guide wire was inserted distally into the target vessel, and the OCT catheter (C8 Dragonfly JP TM, St. Jude Medical) was advanced to the distal end of the target lesion. The entire length of the region of interest was scanned using the integrated automated pullback device at a speed of 40 mm/s. For image acquisition, arterial blood clearance was obtained with a combination of low-molecular-weight dextran L injection and manual compression of the common femoral artery from body surface. Low-molecular-weight dextran L flushing was done using 50 ml syringe with manual injection. For stents longer than 8 mm, lens marker of OCT was used to confirm the scanning location all through the stent.

Quantitative vascular angiography analysis

Quantitative vascular angiography (QVA) was done before endovascular therapy (EVT) and at 8-month follow-up with anteroposterior view. Reference vessel diameter, minimal lumen diameter, and minimal stent diameter were measured. Measurements were made using a quantitative coronary angiography cardiovascular measurement system (CMS-Medis Medical Imaging System, Leiden, Netherlands). In most cases, the entire lesion could not fit in one view and catheterization table needed to move. The absolute values are inaccurate, therefore, we only calculated percent diameter stenosis before EVT (pre %DS), post EVT (post %DS), and at follow-up (fu %DS). We defined %DS a ratio of the minimum lumen diameter or the stent minimum lumen diameter to the average reference vessel diameter.

OCT analysis

Off-line OCT analysis was performed using dedicated software (LightLab Imaging Inc. LightLab Imaging, Westford, MA, USA). For quantitative analysis, cross-sectional OCT images were analyzed at 5-mm intervals. Stent overlap was excluded from the analysis. Extra-stent or vessel calcification or side branches were used as a landmark to incorporate multiple pull-back images for analysis when single OCT pull-back could not cover whole stented segment mainly due to long overlap stenting. The neointimal thickness inside each stent strut was manually measured. The stent area, lumen area, and maximum and minimum stent diameters were measured manually. Stent struts with measurable neointima were defined as covered. Stent struts with a neointimal thickness equal to 0 μm were defined as uncovered. A maximum distance >200 μm between the center strut reflection and adjacent vessel surface was defined as incomplete strut apposition (Fig. 1). Neointimal area was calculated as the stent area minus the lumen area. To assess asymmetric stent expansion, a stent eccentricity index (SEI) was determined as the minimum stent diameter divided by the maximum stent diameter in each cross-section. The average SEI was calculated for each stent. To assess uneven neointimal thickness, a neointimal unevenness score was calculated for each cross-section as the maximum neointimal thickness in 1 cross-section divided by the average neointimal thickness of the cross-section.

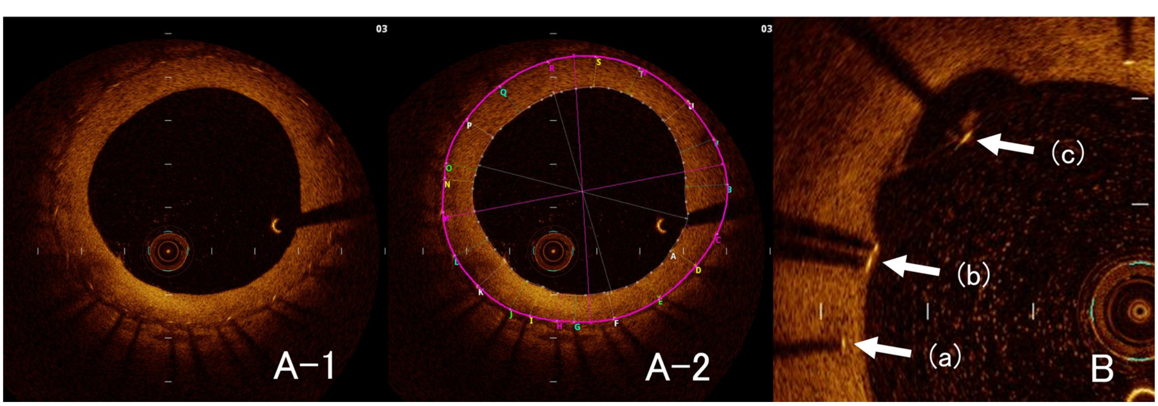

Fig. 1. Optical coherence tomography measurements and strut classifications. (A-1, A-2) First, lumen and stent contours were manually traced on the cross-sectional images at 5-mm intervals. Second, maximum and minimum lumen/stent diameters were measured manually. The neointimal thickness inside each paclitaxel-eluting stent strut was measured in each cross-section. (B) Representative image of strut classifications. (a) Covered strut, (b) uncovered strut, and (c) malapposed strut.