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Original article

Favorable early vessel healing after everolimus-eluting stent implantation: 3-, 6-, and 12-month follow-up of optical coherence tomography

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ABSTRACT

Background: Although a prospective randomized control study revealed that 3-month dual anti-platelet therapy (DAPT) is safe and does not compromise the efficacy of everolimus-eluting stent (EES) in selected patients, detailed vessel healing at early phase after EES implantation has yet to be investigated in Japanese patients.

Methods and results: A total of 27 lesions in 19 patients treated with EES were serially evaluated by using optical coherence tomography (OCT) at 3, 6, and 12 months after stent implantation. In addition to standard quantitative OCT parameters, the percentage of stents with peri-strut low-intensity area (PLIA, a region around stent struts homogenously showing lesser intensity than the surrounding tissue, suggesting fibrin deposition or impaired neointima maturation) and that with in-stent thrombi were evaluated.

There was a significant, but small increase in neointimal thickness (63 ± 17 μm; 83 ± 30 μm; and 111 ± 44 μm, respectively; $p = 0.006$) and small decrease in average lumen area (6.80 ± 2.57 mm^2, 6.62 ± 2.58 mm^2, 6.33 ± 2.58 mm^2, $p = 0.038$) from the 3- to the 12-month follow-up. The incidences of uncovered and malapposed struts were low at 3 months and did not significantly change at 6 months and 12 months (3.01 ± 4.43; 2.45 ± 3.75; and 1.47 ± 3.16, $p = 0.143$, and 0.75 ± 0.65; 0.63 ± 0.73; and 0.58 ± 1.42, $p = 0.162$, respectively). Also, frequency of struts with PLIA was already low at three months and significantly decreased during the follow-up (6.4 ± 6.5; 4.6 ± 5.4; and 2.3 ± 3.3, respectively; $p = 0.001$).

Conclusion: Favorable vessel healing was achieved at 3 months after EES implantation without neointimal hyperplasia which was persistently suppressed up to 12 months.

Introduction

Everolimus-eluting stents (EES; Boston Scientific Corporation, Natick, MA, USA) showed favorable healing profile at mid-term follow-up due to thinner stent struts and high biocompatibility of durable polymer [1,2], which has been associated with a lower incidence of late stent thrombosis as compared with first-generation drug-eluting stents (DES).

Optical coherence tomography (OCT) provides high resolution cross-sectional images to evaluate detailed vessel healing after stent deployment [3]. A previous study revealed the association between late stent thrombosis and the frequency of uncovered struts assessed by OCT [4]. This study suggests that uncovered struts measured by OCT could be a potential surrogate for the risk assessment of future stent thrombosis.

Although American Heart Association/American College of Cardiology/European Society of Cardiology guidelines recommend at least 6 months of dual anti-platelet therapy (DAPT) after DES

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implantation [5,6], the ShortT and OPtimal duration of DualAnti-Platelet Therapy after everolimus-eluting cobalt-chromium stent (STOPDAPT) trial and another report revealed that 3-month DAPT is safe and does not compromise the efficacy of EES in selected patients [7,8]. However, there has been limited notion of vessel healing at this time point and 3-month OCT parameters after EES implantation have yet to be investigated in Japanese patients.

In this study, the primary endpoint was to evaluate the percentage of uncovered strut at 3-month follow-up and to show that this parameter was not significantly different to that of 6 months and 12 months after EES implantation. Therefore, this present study aimed to clarify the time course of arterial healing after EES implantation using matched, serial OCT at 3, 6, and 12 months in patients with coronary artery disease who agree with serial OCT evaluation.

Methods

Study population

In this prospective observational cohort study, a total of 25 patients treated with EES who agreed to participate in this study were consecutively enrolled during the enrollment period from March 2012 to August 2013. Patients aged over 18 years and eligible for percutaneous coronary intervention (PCI) were included. The index PCI procedure was performed with intravascular ultrasound (IVUS) guidance using a mechanical ultrasound transducer (Boston Scientific Corporation) or a dynamic-aperture ultrasound transducer (Volcano Corporation, Rancho Cordova, CA, USA). All patients were recommended to take DAPT with aspirin 100 mg/day and clopidogrel 75 mg/day for at least from 6 months to 12 months after EES implantation. The exclusion criteria were: serious hepatic or renal dysfunction, a target lesion in saphenous vein graft and in-stent restenosis, target lesion revascularization during follow-up, and patients unsuitable for repeat coronary angiogram due to renal dysfunction. Finally, 36 EES-treated lesions from 25 patients were enrolled in the study (Fig. 1).

This study was approved by the ethical committee of Kobe University, and all enrolled study patients gave their written informed consent.

OCT examination

OCT examination was serially performed 3, 6, and 12 months after stenting. Frequency-domain OCT was used as previously reported [9]. Briefly, a 0.014-in. standard guide wire was positioned distally in the target vessel, and the frequency-domain OCT catheter (C7 Dragonfly^{TM}, St. Jude Medical, St. Paul, MN, USA) 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 20 mm/s. For image acquisition, blood in the coronary artery was replaced with iodine contrast media continuously flushed using a power injector, in order to create a virtually blood-free environment. The volume and infusion flow rate was decided by the operator and ranged from 8 to 20 cm^3 at 3–7 cm^3/s and 400 pounds per square inch.

OCT analysis

Off-line OCT analysis was performed using the dedicated software (LightLab Imaging Inc., Westford, MA, USA). All images were analyzed by independent observers masked to the clinical presentation, lesion characteristics, and stent assignment. For quantitative analysis, cross-sectional OCT images were analyzed at 1-mm intervals. For the image matching, we used the distance from the stent edge and landmarks such as side branch to match the location of the cross-sections between 3-, 6-, and 12-month examinations. Struts were classified as uncovered if any part of the strut was visibly exposed to the lumen, or as covered if a layer of tissue was visible over all the reflecting surfaces. Neointimal thickness was assessed from the center reflection of the stent strut to the vessel-lumen border (neointimal surface or strut surface if uncovered) for each stent strut. An uncovered strut was defined as a strut with a neointimal thickness equal to 0 μm. The frequency of covered and uncovered struts was calculated as the number of

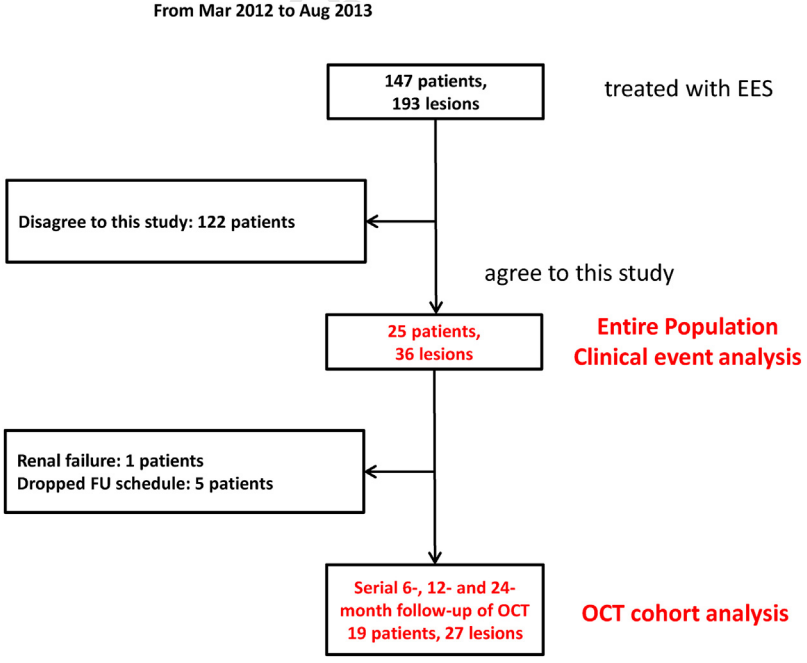

Fig. 1. Flowchart of patients included in the study.
EES, everolimus-eluting stent; FU, follow up; OCT, optical coherence tomography.

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