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Optical coherence tomography assessment of in-stent restenosis after percutaneous coronary intervention with two-stent technique in unprotected left main

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ABSTRACT

Background: Optical coherence tomography (OCT) has contributed to a better understanding of in-stent restenosis (ISR); however, studies evaluating ISR pattern after two-stent technique in unprotected left main (ULM) are lacking. We aim to evaluate the ISR pattern of proximal LAD and LCX after two-stent technique in ULM.
Methods: We performed OCT in 26 patients with isolated or combined ISR (identified by angiography as >50%) after two stent implantation in the proximal LCX and LAD. Finally, 13 LAD and 22 LCX ISR lesions underwent OCT assessments. OCT analyses were undertaken in the proximal segments of the LAD and LCX. In addition, we compared OCT findings in the flow divider (FD) and lateral wall (LW).
Results: In both the LAD and LCX, the distance from the ostium to the minimum lumen area (MLA; LAD, 2.00 mm [1.00, 3.00]; LCX, 1.00 mm [0.00, 1.80] distal to ostium) was short. Uncovered struts were more common on the FD side compared with the LW in the LAD (6.25% [0.00, 20.00] vs 0.00% [0.00, 0.00], respectively, $p = 0.016$) and LCX (11.32% [0.00, 19.44] vs 0.00% [0.00, 4.55], respectively, $p < 0.001$). Conversely, neointimal hyperplasia (NIH) was significantly thicker on the FD side compared with the LW in the LCX (0.31 mm [0.19, 0.47] vs 0.15 mm [0.09, 0.31], $p < 0.001$).
Conclusions: While uncovered struts were more commonly found on the FD side of both arteries, NIH was significantly thicker on the FD side compared with the LW in the LCX. These unique findings might indicate inferior outcomes after two-stent techniques in ULM bifurcation lesions.

1. Introduction

Percutaneous coronary intervention (PCI) with drug-eluting stents (DESs) in unprotected left main coronary artery (ULM) has been increasingly incorporated into routine clinical practice [1–3]. While favorable clinical and angiographic results have been demonstrated in PCI of ostial and mid-shaft lesions [4,5], treatment of ULM distal bifurcation is a predictor of repeated revascularization and major adverse cardiac events (MACE) [6], markedly in patients intervened upon with two-stent techniques [7,8]. In-stent restenosis (ISR) is usually focal and most often involves the ostial left circumflex artery (LCX) ostium, either isolated or combined with the ostial left anterior descending artery (LAD) ISR [9].

Intravascular optical coherence tomography (OCT) delivers unprecedentedly detailed assessments of vascular reactions to DES implantation in vivo [9]. The feasibility of ULM assessment by OCT has been recently demonstrated [10]. In the present study, we aimed to comprehensively characterize stent–vessel interactions in the proximal LAD and LCX in patients that developed ISR in ULM bifurcation after undergoing two-stent techniques with OCT.

Abbreviations: DES, drug-eluting stents; EF, ejection fraction; FD, flow divider; GEE, generalized estimating equations; ISR, in-stent restenosis; LW, lateral wall; LAD, left anterior descending artery; LCX, left circumflex artery; MACE, major adverse cardiac events; MLA, minimum lumen area; MSA, minimum stent area; NIH, neointimal hyperplasia; OCT, optical coherence tomography; PCI, percutaneous coronary intervention; QCA, quantitative coronary angiography; ROI, region of interest; SIT, strut-level intimal thickness; ULM, unprotected left main coronary artery.

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2. Methods

2.1. Study population

We retrospectively evaluated patients who underwent OCT from April 2009 to December 2012 and presented with ISR (>50%) by angiogram in ostium-proximal LAD, LCX or both coronary arteries after two-stent technique PCI (V stent, mini-crush, crush and culotte) (Fig. 1-I). Twenty-six patients were enrolled in this single center study (New Tokyo Hospital, Chiba, Japan). Exclusion criteria included congestive heart failure with left ventricle ejection fraction (EF) <30%, acute myocardial infarction with ST-segment elevation, chronic kidney disease (serum creatinine >1.5 mg/dl), not on dialysis and known allergy to antiplatelet agents or contrast dye. The study protocol was approved by the institutional review board and informed consent was obtained for every patient before any intervention was performed.

2.2. Quantitative coronary angiography analysis

Quantitative coronary angiography (QCA) was performed at follow-up. Angiographic measurements were made in two matched orthogonal projections. Offline analyses of digital coronary angiograms (CASSII, Pie-Medical, Maastricht, The Netherlands) were performed by an independent core laboratory (Cardiovascular Imaging Core Laboratory, University Hospitals Case Medical Center, Cleveland, Ohio) using validated quantitative methods [11].

2.3. OCT image acquisition and analysis

A conventional angioplasty guide wire (0.014-in.) was advanced distal to the region of interest (ROI), then the 2.7 French OCT catheter (Dragonfly™, St Jude Medical, St Paul, Minnesota, USA) was advanced over the guide wire at least 5-mm beyond the distal edge of the stents implanted in the LAD and LCX which presented with ISR lesions. The images were calibrated by automated adjustment of the Z-offset and automated pullback was set at 20 mm/s. Data were acquired using a commercially available OCT system (C7-XR™, OCT Imaging System, St Jude Medical, St. Paul, Minnesota, USA) after intracoronary administration of 50–200 μm of nitroglycerin through conventional guiding catheters and digitally stored. During imaging acquisition, blood was displaced by injection of isosmolar contrast dye (100%) via a power injector. OCT pullbacks were performed from at least 5-mm distal to the stents implanted in the LAD and LCX to the ostial-body part of the ULM. An independent core laboratory (Cardiovascular Imaging Core Laboratory, Harrington Heart and Vascular Institute, University Hospitals, Case Medical Center, Cleveland, OH) reviewed all OCT images. The images were analyzed by 2 independent investigators blinded to the clinical data. OCT analyses were performed using dedicated software with an automated contour-detection algorithm (Off-line Review Workstation, version C.0; St Jude Medical, St Paul, Minnesota, USA). Proximal LAD and LCX segments (defined as the 5 mm-segment frame immediately distal to the take-off of the ULM carina) (Fig. 1-III) were analyzed at follow-up. All cross-sectional images were initially screened for quality assessment and excluded from analysis if any portion of the stent beyond the image field of view, if a side branch occupied >45° of the cross-section, or if the image had poor quality caused by residual blood, artifacts, or reverberation [10]. Qualitative image assessment was performed in every frame, while quantitative measurements were performed every 5 frames (i.e., every 1.0-mm). Strut-level intimal thickness (SIT) was determined based on automated measurements performed from the center of the luminal surface of each strut's high-intensity bloom to the lumen contour [12]. Struts covered by tissue had positive SIT values, whereas uncovered or malapposed struts had negative SIT values. Strut malapposition was defined when the negative value of SIT was higher than the sum of strut thickness plus abluminal polymer thickness, according to stent manufacturer specifications, plus a compensation factor of 20 μm to correct for strut blooming [13,14]. Tissue protrusion was defined as a tissue prolapse between stent struts that directly correlates with the underlying plaque, without abrupt transition and different optical properties [15]. OCT derived malapposition values were obtained by means of 360° chords, distributed between the lumen and stent contours. The pattern of neointima inside the implanted stent was classified as follows: homogeneous, heterogeneous intima and layered intima [16] (Fig. 2A–C). Atherosclerosis within

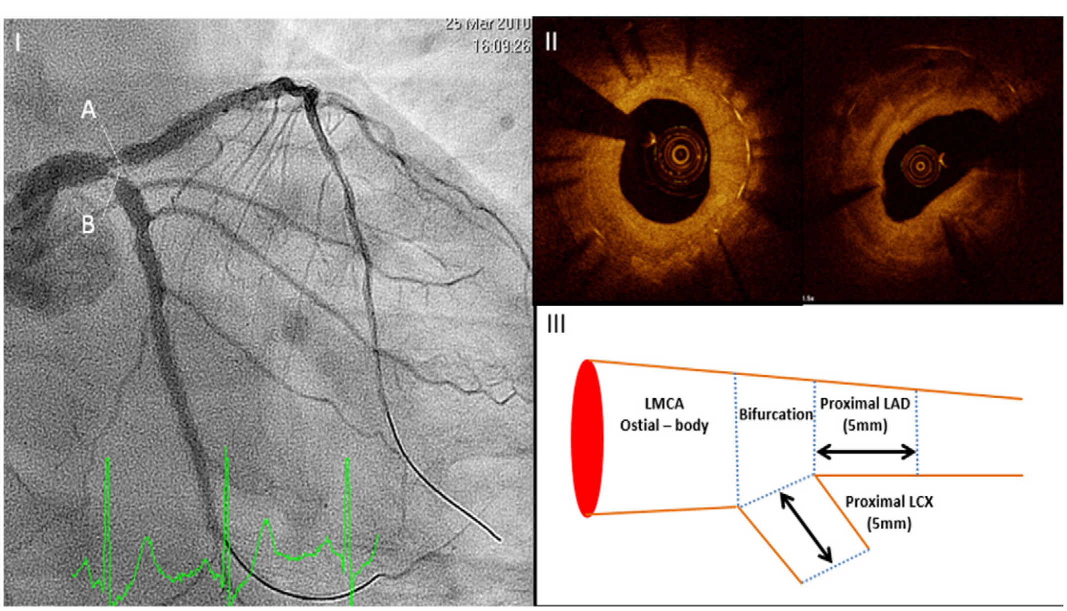

Fig. 1. Coronary angiogram and optical coherence tomography (OCT) findings of in-stent restenosis (ISR) after two-stent implantation. Panel I shows the ISR of the LAD and LCX ostium after two-stent implantation. The corresponding images in OCT are shown in II-A and B. Panel III shows the OCT analysis regions (two directional arrows) of the LAD and LCX.