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Quantitative assessment of tissue prolapse on optical coherence tomography and its relation to underlying plaque morphologies and clinical outcome in patients with elective stent implantation

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ABSTRACT

Background: Tissue prolapse (TP) is sometimes observed after percutaneous coronary intervention (PCI), but its clinical significance remains unclear. We investigated the relationship between TP volume on optical coherence tomography (OCT) after PCI and underlying plaque morphologies and the impact of TP on clinical outcomes.
Methods: We investigated 178 native coronary lesions with normal pre-PCI creatine kinase-myocardial band (CK-MB) values (154 lesions with stable angina; 24 with unstable angina). TP was defined as tissue extrusion from stent struts throughout the stented segments. All lesions were divided into tertiles according to TP volume. The differences in plaque morphologies and 9-month clinical outcomes were evaluated.
Results: TP volume was correlated with lipid arc ($r = 0.374$, $p < 0.0001$) and fibrous cap thickness ($r = -0.254$, $p = 0.001$) at the culprit sites. The frequency of thin-cap fibroatheroma (TCFA) was higher in the largest TP tertile (≥1.38 mm^3) ($p = 0.015$). In multivariate analysis, right coronary artery lesion (odds ratio [OR]: 2.779; $p = 0.005$), lesion length (OR: 1.047; $p = 0.003$), and TCFA (OR: 2.430; $p = 0.022$) were related to the largest TP tertile. Lesions with post-PCI CK-MB elevation (>upper reference limit) had larger TP volume than those without (1.28 [0.48 to 3.97] vs. 0.70 [0.16 to 1.64] mm^3, $p = 0.007$). The prevalence of cardiac events during the 9-month follow-up was not significantly different according to TP volume.
Conclusions: TP volume on OCT was related to plaque morphologies and instability, and post-PCI myocardial injury, but not to worse 9-month outcomes.

1. Introduction

Stent restenosis is a major concern after percutaneous coronary intervention (PCI) in patients with coronary artery disease. Several studies have reported that intravascular ultrasound (IVUS)-guided PCI had favorable outcomes in the reduction of stent restenosis [1,2]. IVUS findings such as stent edge dissection and malapposition have been associated with the occurrence of stent complications [3,4]. Tissue prolapse (TP) after stent implantation has also been related to worse short-term outcome after PCI [3–7].

Recently, the use of optical coherence tomography (OCT), which has a 10-fold higher resolution than IVUS, has enabled more clear and frequent visualization of TP [8,9]. However, the clinical significance of TP on OCT has not been fully investigated.

In the present study, we hypothesized that TP volume was related to the underlying plaque morphologies and affected the occurrence of adverse clinical outcomes. Accordingly, we conducted a quantitative assessment of TP volume after PCI using OCT and investigated its relationship with the underlying plaque morphologies before PCI and the clinical outcomes during follow-up.

2. Methods

2.1. Patient population

Two-hundred and nineteen consecutive lesions with normal pre-PCI creatine kinase-myocardial band (CK-MB) values underwent PCI with pre- and post-procedural OCT examination from April 2010 to July 2012 in Yokosuka Kyosai Hospital. Unstable angina pectoris (UAP) was defined as angina with a progressive crescendo pattern or angina at rest without increased CK-MB values greater than the 99th percentile upper reference limit (URL). Stable angina pectoris (SAP) was defined as angina with no change in frequency, duration, or intensity of anginal symptoms within 6 weeks before PCI. We excluded 6 multiple culprit lesions, 11 chronic total

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occluded lesions, 2 left main disease, 12 lesions treated with rotational atherectomy or distal protection devices, 5 lesions with side branch occlusion after PCI, and 5 lesions with insufficient OCT image quality. Thus, 178 lesions in 178 patients (154 patients with SAP and 24 patients with UAP) who underwent 9-month follow-up coronary angiography were investigated. This study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the human research committee of our hospital, and all patients provided written informed consent.

2.2. Procedures

All patients were treated with aspirin (100 mg/day) and clopidogrel (300-mg loading dose, followed by 75 mg/day). Before PCI, all patients received intravenous unfractionated heparin (8000 to 10,000 units) and intracoronary nitroglycerin (1 mg). Target lesions were identified by a combination of coronary angiography, left ventricular wall motion abnormalities, electrocardiographic findings, angiographic lesion morphology, and scintigraphic evidence of ischemia. Conventional PCI was performed using the strategy selected by the interventionists. All patients underwent stent implantation and showed <25% residual stenosis on quantitative coronary angiography analysis.

2.3. Laboratory data analysis

Values of CK-MB were examined just before PCI, just after PCI and at 12 and 24 h after PCI. CK-MB values were measured using an immunoinhibition assay (N-assay L CK-MB Nittobo reagents, Nittobo Medical Co., Ltd., Tokyo, Japan) (lower detection limit, 4 IU/L; URL, 21 IU/L; coefficient of variation, <5% at 200 IU/L). Other laboratory data were measured before PCI according to established procedures. Post-PCI CK-MB elevation was defined as peak CK-MB values above the URL (21 IU/L) [10].

2.4. Coronary angiography analysis

Quantitative coronary angiography analysis was performed using CAAS 4.1.1 software (Pie Medical Imaging BV, Maastricht, the Netherlands). Minimal lumen diameter (MLD), reference diameter, diameter stenosis, and lesion length of the culprit lesions were measured, and acute gain was calculated by subtracting pre-intervention MLD from post-intervention MLD [11]. Coronary flow was assessed according to the Thrombolysis in Myocardial Infarction (TIMI) flow grade [12] and corrected TIMI frame counts [13]. Transient slow-reflow phenomenon was defined as transient deterioration of coronary flow to TIMI flow grade 0, 1, or 2 without any evidence of dissection, significant stenosis, or vasospasm [14]. At 9-month angiographic follow-up, MLD, reference diameter, and diameter stenosis were measured at the stented sites, and late loss was calculated by subtracting follow-up MLD from post-intervention MLD. Binary restenosis was defined as >50% diameter stenosis. Coronary angiograms were analyzed by 2 experienced observers (S.K. and K.H.) who were unaware of the OCT findings.

2.5. OCT image acquisition and analysis

Pre- and post-procedural OCT examination was performed using time-domain OCT (M3 system; LightLab Imaging Inc., Westford, MA, USA) or frequency-domain OCT (C7 ILUMIEN system; St. Jude Medical, St. Paul, MN, USA) as previously described [15]. With the M3 system, an occlusion balloon (Helios; LightLab Imaging Inc.) was advanced proximal to the lesion and inflated at 0.3 to 0.5 atm during image acquisition. The imaging wire was automatically pulled back from the distal to the proximal site at 1.5 mm/s (20 frames/s), and lactated Ringer's solution was continuously infused from the tip of the occlusion balloon. With the C7 system, an OCT imaging catheter (Dragonfly; LightLab Imaging Inc.) was advanced distal to the lesion, and automatic pull-back at 20 mm/s (100 frames/s) was initiated in concordance with blood clearance by injection of contrast media or low molecular weight dextran. OCT images were analyzed after PCI by using an offline review workstation (LightLab Imaging Inc.). Cross-sectional OCT images were analyzed at every frame. Qualitative and quantitative analyses of plaque morphologies were performed according to the previously validated criteria for OCT plaque characterization [16–20]. Before PCI, the degrees of lipid arc and the overlying fibrous cap thickness at the thinnest part were measured in lipidic plaques. Lipid-rich plaque was defined as a plaque with lipid arc >180°. Thin-cap fibroatheroma (TCFA) was defined as a plaque with lipid arc >180° and fibrous cap thickness <70 μm [19]. Calcified plaque was defined as a plaque with calcification arc >90° at the largest part [20]. Plaque rupture was defined as fibrous cap discontinuity with cavity formation [20]. Intracoronary thrombus was defined as a mass protruding into the vessel lumen [20]. Reference sites were decided at the site with the largest lumen, either proximal or distal to the target lesion and with plaque burden <50% but within the same segment, when vessel and lumen border at both reference segments could be measured, and lesion length was measured from the distal to the proximal reference site [18]. TP after PCI was defined as tissue extrusion through the stent struts [20]. In each cross-sectional area, the stent area and lumen area were measured, and TP area was calculated by subtracting lumen area from stent area. TP volume was calculated by adding the TP area in each cross-sectional area at 1-mm intervals throughout the stented segments (Fig. 1). Similarly, stent volume was calculated by adding stent area. TP ratio was calculated by dividing TP volume by stent volume. All lesions were grouped into tertiles according to TP volume. OCT images were analyzed by 2 experienced investigators (T.S. and D.A.) who were unaware of the angiographic findings. If there was discordance between the two observers, a consensus diagnosis was obtained with repeated off-line readings.

2.6. Clinical outcomes after PCI

All patients underwent 9-month follow-up coronary angiography. The incidence of adverse cardiac events including cardiac death, nonfatal myocardial infarction, target lesion revascularization, and congestive heart failure (presence of a third heart sound, Forrester subset ≥2, or evidence of pulmonary congestion on chest X-ray), was evaluated during the 9-month follow-up period. Stent thrombosis assessed by the Academic Research Consortium definitions was also evaluated [21].

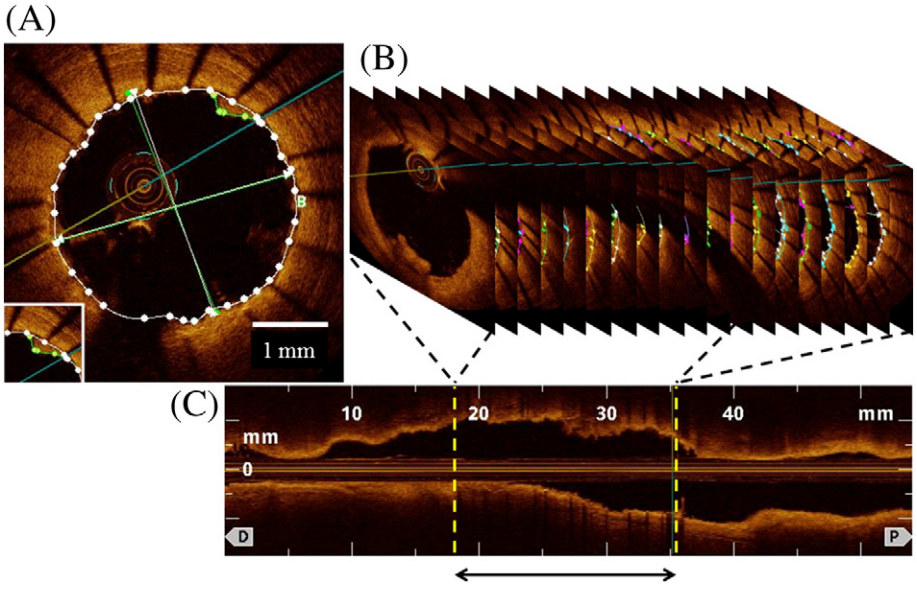

Fig. 1. Evaluation of TP volume on OCT. (A) In each cross-sectional area, the stent area (outer line) and lumen area (inner line) were measured, and tissue prolapse (TP) area was calculated by subtracting lumen area from stent area on optical coherence tomography (OCT) after percutaneous coronary intervention (PCI). (B and C) TP volume was calculated by adding the TP area in each cross-sectional area at 1-mm intervals throughout the stented segments (arrow).