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Relationship between quantities of tissue prolapse after percutaneous coronary intervention and neointimal hyperplasia at follow-up on serial optical coherence tomography examination☆

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ABSTRACT

Background: The clinical significance of the extent of tissue prolapse (TP) after percutaneous coronary intervention (PCI) for long-term outcomes remains undetermined. This study investigated the relationship between the quantities of TP immediately after PCI and neointimal hyperplasia (NIH) at follow-up on serial optical coherence tomography (OCT) examination.

Methods: We evaluated 145 native coronary lesions (89 lesions with stable angina pectoris [SAP] and 56 with acute coronary syndrome [ACS]). OCT was performed to examine pre-PCI plaque morphologies at the narrowest culprit sites, post-PCI TP area in each cross-sectional area (CSA) and TP volume throughout the stented segments, 9-month follow-up NIH area in each CSA and NIH volume throughout the stented segments. We investigated the relationships between the quantities of TP and NIH and their differences according to clinical presentation.

Results: ACS lesions had a larger TP area at the narrowest culprit sites (0.39 [0.14–0.85] vs. 0.11 [0.00–0.32] mm^2, $P < 0.001$) and at the most protruding sites (0.51 [0.24–1.08] vs. 0.21 [0.10–0.52] mm^2, $P < 0.001$) compared with SAP lesions. In ACS lesions, TP area was correlated with NIH area at the culprit sites ($r = 0.283$, $P = 0.042$) and at the most protruding sites ($r = 0.288$, $P = 0.038$). In SAP lesions, TP area was correlated with NIH area at the most protruding sites ($r = 0.244$, $P = 0.030$), but not at the culprit sites.

Conclusions: The extent of TP immediately after PCI was quantitatively related to the degree of NIH at 9-month follow-up on serial OCT examination. The quantities of TP might influence long-term stent outcomes.

1. Introduction

Percutaneous coronary intervention (PCI) with stent implantation is the most commonly performed procedure for patients with coronary artery disease [1]. In the era of drug-eluting stents (DES), stent restenosis is still a major concern after PCI. Stent restenosis is mainly attributed to excessive in-stent neointimal proliferation [2]. Intracoronary imaging modalities have been widely used during PCI to obtain adequate stent expansion that may lead to the reduction of stent restenosis after PCI [3]. The use of optical coherence tomography (OCT) has enabled clearer and more frequent visualization of intra-stent findings such as stent expansion, malapposition, and tissue prolapse (TP) during PCI [4]. We have previously reported that TP detected on OCT immediately after PCI was quantitatively correlated with lipid arc and fibrous cap thickness of the underlying plaques [5]. Moreover, the impact of TP after PCI on the occurrence of stent restenosis at follow-up has been reported recently [6]. However, the significance of the volume and components of TP and their impact on stent neointimal proliferation have not been fully clarified. In the present study, we hypothesized that TP after PCI was quantitatively related to neointimal hyperplasia (NIH) at follow-up. We conducted a quantitative assessment of TP after PCI and NIH at follow-up by serial OCT examination, and investigated the relationship between TP and NIH and their differences according to clinical characteristics.

2. Methods

2.1. Patient population

We retrospectively selected native coronary lesions that underwent serial OCT examination immediately after PCI and at 9-month follow-up coronary angiography from

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January 2012 to March 2015 in Yokosuka Kyosai Hospital. We excluded in-stent restenotic lesions, bypass lesions, chronic total occluded lesions, lesions with left main disease, lesions that could not be passed with an OCT catheter during the procedure, and lesions with insufficient OCT image quality. A total of 145 lesions in 145 patients (89 patients with stable angina pectoris [SAP] and 56 with acute coronary syndrome [ACS]) were enrolled in this study. SAP was defined as angina with no change in frequency, duration, or intensity of angina symptoms within 6 weeks before PCI. ST-elevation ACS was defined as continuous chest pain >30 min, new persistent ST-segment elevation, cardiac troponin-T rise and fall, and/or new regional wall motion abnormalities. Non-ST-elevation ACS was defined as at least two episodes of angina at rest or one episode lasting >30 min during the preceding 48 h and with rise and fall (non-ST-elevation myocardial infarction) or without elevation (unstable angina) of cardiac troponin-T levels [7]. All lesions of SAP and ACS were each divided into the two subgroups according to TP volume in their median value. Further, the differences were compared according to stent type: lesions treated with DES and those with bare metal stents (BMS). Informed consent was obtained from each patient, and the study protocol conformed to the ethical guidelines of the 1975 Declaration of Helsinki as reflected in a priori approval by the institution's human research committee.

2.2. Procedures

All patients were treated with aspirin (100 mg/day) and clopidogrel (75 mg/day). Target lesions were identified by using 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. 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 vessel diameter, diameter stenosis, and length of the culprit lesions were measured, and acute gain was calculated by subtracting the pre-intervention MLD from the post-intervention MLD [8]. At 9-month angiographic follow-up, MLD, reference vessel diameter, and diameter stenosis were measured at the stented sites, and late lumen loss was calculated by subtracting the follow-up MLD from the post-intervention MLD. Binary restenosis was defined as >50% diameter stenosis. Coronary angiograms were analyzed by two experienced observers (S.K. and K.H.) who were unaware of the OCT findings.

2.4. OCT image acquisition and analysis

OCT examinations were performed using frequency-domain OCT (C7 ILUMIEN system and C8 ILUMIEN Optis system; St. Jude Medical, St. Paul, MN, USA) as previously described [5]. With the C7/C8 system, an OCT imaging catheter (Dragonfly [C7]/Dragonfly JP [C8], LightLab Imaging Inc.) was advanced distal to the culprit lesion, and automatic pull-back at 20 mm/s with the C7 system or 18 mm/s with the C8 system was initiated in concordance with blood clearance by using a short 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 plaque characterization [9–11]. Lipid was defined as a signal-poor region with a poorly defined or diffuse border. Before PCI, the degree 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 a lipid arc >180 degrees. Thin-cap fibroatheroma (TCFA) was defined as a plaque with a lipid arc >180 degrees and a fibrous cap thickness < 70 μm [10]. Calcification was defined as a signal-poor or heterogeneous region with a sharply delineated border [11]. Calcified plaque was defined as a plaque with a calcification arc >90 degrees [12]. Plaque rupture was defined as fibrous cap discontinuity with cavity formation [11]. Intracoronary thrombus was defined as a mass protruding into the vessel lumen [11]. Reference sites were determined at the site with the most normal looking with largest lumen and free of lipidic plaque, either proximal or distal to the target lesion, and the lesion length was measured from the distal to the proximal reference site [5,13]. Immediately after PCI, the presence of TP, edge dissection, and malapposition were evaluated. TP was defined as tissue extrusion through the stent struts [5,11]. Edge dissection was defined as disruption of the luminal vessel surface in the stent edge segments [11]. Malapposition was defined as the distance between the surface of the strut and the vessel wall greater than the actual stent thickness [11]. For quantitative analysis, the stent area and lumen area were measured in each cross-sectional area (CSA), and TP area was calculated by subtracting lumen area from stent area [5] (Fig. 1A). TP area was assessed in each CSA at 1-mm intervals throughout the stented segments, and TP area at the narrowest culprit sites and the most protruding sites were evaluated. TP volume was calculated by adding the TP area at 1-mm intervals throughout the stented segments [5]. Similarly, stent volume was calculated by summing stent area measurements. The percentage of stent expansion was defined as minimal stent area divided by the mean of the largest proximal and distal reference lumen CSAs [14]. At 9-month follow-up, the presence of edge dissection, malapposition, and intracoronary thrombus were evaluated. NIH was defined as neointimal tissue overlying the stent struts. Homogeneous neointima was defined as restenotic tissue with uniform optical properties that showed no

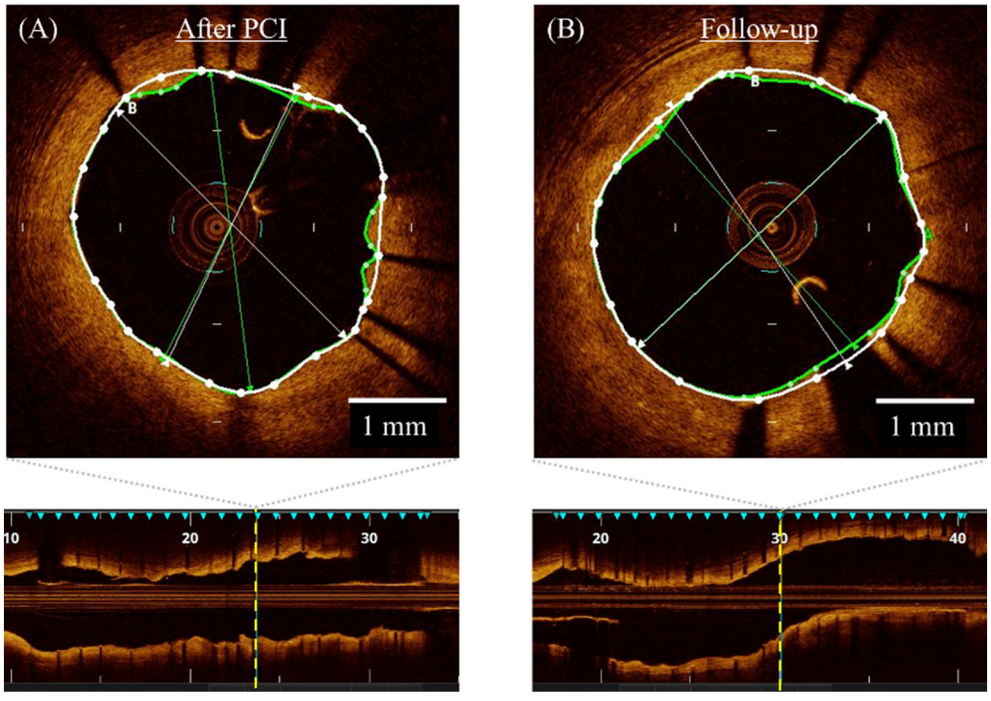

Fig. 1. Evaluation of tissue prolapse and neointimal hyperplasia on optical coherence tomography. (A) Immediately after percutaneous coronary intervention, the stent area (outer line) and lumen area (inner line) were measured in each cross-sectional area (CSA) on optical coherence tomography (OCT), and tissue prolapse (TP) area was calculated by subtracting lumen area from stent area. TP area was assessed in each CSA at 1-mm intervals throughout the stented segments, and TP area at the narrowest culprit sites and the most protruding site were evaluated. TP volume was calculated by adding the TP area in each CSA at 1-mm intervals throughout the stented segments (blue arrowhead). (B) At follow-up, the stent area (outer line) and lumen area (inner line) were measured in each CSA, and neointimal hyperplasia (NIH) area was calculated by subtracting lumen area from stent area. NIH area were evaluated at the identical sites where the TP of the narrowest culprit sites and the most protruding sites were obtained in the initial procedure. NIH volume was calculated by adding the NIH area in each CSA at 1-mm intervals throughout the stented segments (blue arrowhead). (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

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