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Impact of attenuated-signal plaque observed by intravascular ultrasound on vessel response after drug-eluting stent implantation

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ABSTRACT

Background and aims: The aim of this study was to investigate the impact of attenuated-signal plaque (ASP) observed by intravascular ultrasound (IVUS) on vessel response after drug-eluting stent implantation.

Methods: Data were derived from the IVUS cohort of the J-DESsERT trial comparing paclitaxel- and sirolimus-eluting stents. Serial IVUS analysis (pre- and post-intervention, and 8-month follow-up) was performed in 136 non-AMI lesions. ASP was defined as hypoechoic plaque with ultrasound attenuation without calcification. Calcified plaque (CP) was defined as brightly echoreflective plaque with acoustic shadowing. ASP and CP scores were calculated by grading their measured angle as 0 to 4 for 0°, <90°, 90−180°, 180−270° and >270°, respectively. The entire stented segment was analyzed at 1-mm intervals.

Results: At pre-intervention, ASP was observed in 40.4% of lesions, and this group had greater % neointimal volume (%NIV) at follow-up than the no-ASP group ($p = 0.011$). ASP score at pre-intervention positively correlated with %NIV ($p = 0.023$). During the follow-up, ASP score significantly decreased ($p < 0.001$), and CP score significantly increased ($p < 0.001$), with a negative correlation between them ($p < 0.001$). A decrease in the ASP score was associated with less %NIV in PES ($p = 0.031$), but not in SES ($p = 0.229$).

Conclusions: The greater extent of plaque with IVUS-signal attenuation at pre-intervention and its persistence during follow-up were associated with neointimal proliferation, possibly representing sustained inflammatory status, depending on the type of DES used.

1. Introduction

Non-calcified coronary plaque with ultrasound signal attenuation (attenuated-signal plaque: ASP) observed by grey-scale intravascular ultrasound (IVUS) is considered vulnerable plaque containing lipid-rich tissue or necrotic core with microcalcification, as previously assessed by pathological studies [1–4], and is often seen not only in patients with acute coronary syndrome [4–13], but also in those with stable angina [4,11]. It has been reported that ASP is associated with impaired coronary blood flow mainly due to distal embolization after percutaneous coronary intervention (PCI) [4–9]. On the other hand, there are few reports investigating the long-term effect of ASP after PCI, except for one study demonstrating association of ASP with less neointimal hyperplasia after paclitaxel-eluting stent (PES) implantation in patients with acute myocardial infarction (AMI) [13]. The aim of the present study was to investigate the impact of ASP on vessel response in non-AMI

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patients treated with elective drug-eluting stent implantation.

2. Materials and methods

2.1. Study population

Data were derived from J-DESsERT (The Japan Drug Eluting Stents Evaluation: a Randomized Trial), which was a prospective, multicenter randomized study comparing PES and sirolimus-eluting stents (SES) for the treatment of *de novo* coronary lesions. The rationale and design of J-DESsERT have been previously reported [14]. Patients with AMI (including non-ST segment elevation myocardial infarction), which developed within 7 days before the procedure, were excluded from this trial. In the present IVUS study, patients meeting the following criteria were selected from the IVUS cohort of J-DESsERT: (1) patients with stable or unstable angina, or silent ischemia who had successfully undergone elective PCI using standard stent implantation techniques; (2) high-quality, automated pullback IVUS images within stented segments at pre- and post-intervention, and 8-month follow-up; and (3) complete volumetric IVUS studies at 8-month follow-up. The study protocol was approved by the institutional review board at each participating site, and eligible patients signed written informed consent prior to the interventional procedure.

2.2. IVUS analysis

IVUS was performed in a standard fashion using automated, motorized 0.5 mm/s pullback with a commercially available imaging system (40-MHz IVUS catheter, Boston Scientific Corp., Natick, MA) at pre- and post-intervention, and 8-month follow-up. IVUS analysis was conducted in an independent core laboratory at Stanford University Medical Center (Cardiovascular Core Analysis Laboratory), and investigators were blinded to patient characteristics and randomization assignments. The positions of corresponding stent edges in the pre-intervention IVUS image were carefully identified by correlating anatomical features (such as side branch, calcification, vein running around the artery, etc.) between the pre- and post-intervention IVUS images. Volumetric measurements were performed using software (echoPlaque; Indec Systems, Inc., Santa Clara, CA). Volume index (VI, volume/length, mm^3/mm) was calculated for the vessel, plaque, lumen, stent, and neointima. Percent neointimal volume (%NIV) was then calculated as neointimal volume divided by stent volume (percent). Cross-sectional narrowing (CSN; percent) was calculated as neointimal area divided by stent area in every frame within analyzed stented segment, and maximum value was selected as max %CSN. Remodeling index was obtained by dividing the target-lesion vessel area at the MLA site by the average of the proximal and distal reference-segment vessel areas. Incomplete stent apposition (ISA) was defined as $\geq$1 stent strut clearly separated from the vessel wall with evidence of blood speckles behind the strut in a vessel segment not associated with any side branches.

2.3. Evaluation of attenuated-signal plaque (ASP) and calcified plaque (CP)

ASP on IVUS was defined as a hypo- or isoechoic plaque, in contrast to the reference adventitia, with deep ultrasound attenuation without very hyperechoic reflectors. In the binary analysis, the ASP group included lesions/patients with any ASP, regardless of the arc or length. CP was defined as a brightly echoreflective (hyperechoic) region with a dense shadow more peripherally behind the region, a phenomenon known as “acoustic shadowing”. In semi-quantitative analysis, the degrees of ASP and CP were scored by grading their measured angles as 0 to 4 for 0°, <90°, 90–180°, 180–270° and >270°, respectively (Fig. 1). The entire treatment segment was analyzed at 1-mm intervals. The ASP and CP scores were calculated as total scores along the entire treatment segment divided by the number of analyzed cross-sections. These scores were calculated at pre- and post-intervention, and 8-month follow-up. Changes (Δ) in the scores from pre-to post-intervention and from post-intervention to 8-month follow-up were also calculated. Calculations of ASP score in 10 randomly selected ASP by 2 observers and by 1 observer at 2 separate sessions showed that the intraclass correlation coefficient for interobserver variability was 0.976 and that for intraobserver variability was 0.940.

2.4. Statistical analysis

Statistical analysis was performed using JMP® 13.0 (SAS Institute, Cary, NC). Categorical variables are presented as numbers and/or percentages, and compared using Chi-square test. For continuous variables without repeated measures on multiple lesions, comparisons between the ASP and no-ASP groups were performed with a 2-tailed unpaired *t*-test, and comparisons of the ASP or CP score between different time points were performed using a paired *t*-test. For continuous variables with repeated measures on

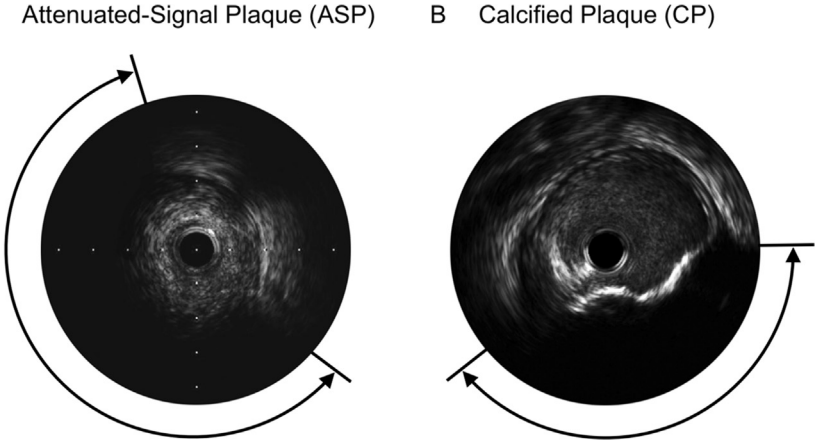

Fig. 1. Representative images of attenuated-signal plaque (ASP) and calcified plaque (CP). ASP and CP scores were calculated by grading their measured angles as 0 to 4 for 0°, <90°, 90–180°, 180–270° and >270°, respectively. (A) ASP score was calculated as 3 (measured angle was 180–270°). (B) CP score was calculated as 2 (measured angle was 90–180°).