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# Association between plaque characteristics and the amount of debris captured by a filter-type distal protection device in patients with acute coronary syndrome

Katsuhide Kitagawa [a], Tetsuya Amano [b], Tadayuki Uetani [c], Hideki Ishii [a, *], Takahiro Okumura [a], Susumu Suzuki [a], Hiroaki Takashima [b], Akiyoshi Kurita [b], Hirohiko Ando [b], Tatsuaki Matsubara [d], Toyoaki Murohara [a]

[a] Department of Cardiology, Nagoya Graduate School of Medicine, Nagoya, Japan
[b] Department of Cardiology, Aichi Medical School, Nagakute, Japan
[c] Department of Cardiology, Chubu Rosai Hospital, Nagoya, Japan
[d] Department of Internal Medicine, Aichi-Gakuin Graduate School of Dentist, Nagoya, Japan

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ABSTRACT

*Background and aims:* Disruption of atherosclerotic plaque and distal embolism often cause peri-procedural myocardial injury during percutaneous coronary intervention (PCI). In the present study, we evaluate the association between the characteristics of the target lesion and the amount of debris captured by the filter-type distal protection device.
*Methods:* We enrolled 120 consecutive patients with acute coronary syndrome, who underwent coronary stent implantation with a filter-type distal protection device after integrated backscatter intravascular ultrasound (IB-IVUS) analysis. The amount of debris captured by the protection filter was measured through microscopic evaluation.
*Results:* The lipid and fibrous volume evaluated with IB-IVUS was significantly correlated with the amount of the captured debris ($r = 0.657$, $p < 0.01$), ($r = 0.322$, $p < 0.01$). The lipid plaque fraction showed a positive correlation ($r = 0.335$, $p < 0.01$), while the fibrous plaque fraction was found to be inversely correlated ($r = -0.375$, $p < 0.01$) with the amount of captured debris. Multivariate regression analysis showed that lipid volume correlated independently with the amount of captured debris.
*Conclusion:* The volume of the lipid-rich plaque was associated with the amount of procedure-related debris released and captured by the filter-type distal protection device.


## 1. Introduction

Percutaneous coronary intervention (PCI) is widely performed in patients with ischemic heart disease. Peri-procedural (type IVa) myocardial infarction is observed in 5–30% of patients undergoing PCI [1,2]. The disruption of atherosclerotic plaques caused by balloon inflation or stent expansion and distal embolism are considered as a major cause of Type-II (distal type) peri-procedural myocardial injury [2].

The characteristics of the target lesion predict the development of peri-procedural distal embolism. A report has shown an association between a larger, necrotic core area in the target lesion and the release of embolic particles, detected as high-intensity signals by Doppler wire [3]. Additionally, there is a correlation between a larger, lipid-rich plaque within the target lesion, measured with integrated backscatter intravascular ultrasound (IB-IVUS), and post-procedural myocardial injury after coronary stent implantation [4]. However, the association between plaque characteristics and the amount of embolic particles released from the target site after disruption is unknown. In the present study, we evaluated the association between the characteristics of the target lesion and the amount of atherosclerotic debris captured by the filter device.

* Corresponding author. Department of Cardiology, Nagoya University Graduate School of Medicine, Postal address: 65, Tsurumai-cho, Showa-ku, Nagoya 466-8550, Japan.
*E-mail address:* hkishii@med.nagoya-u.ac.jp (H. Ishii).

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## 2. Materials and methods

### 2.1. Study population

This study is an observational study conducted from April 2010 to October 2013 in the Chubu Rosai Hospital (Nagoya, Japan) and Aichi Medical School Hospital (Nagakute Japan). We enrolled 120 consecutive patients with acute coronary syndrome (ACS), who successfully underwent coronary stent implantation with a filter-type distal protection device (Filtrap™, Nipro, Japan) after IB-IVUS analysis was performed. All enrolled patients had symptoms at rest with documented ST segment changes, elevated levels of creatine kinase-MB and/or troponin-T. All the patients provided informed consent to participate in this study. IVUS imaging for IB-IVUS analyses was recorded before first balloon dilatation. The exclusion criteria were poor quality of IB-IVUS imaging and large coronary thrombi detected on angiography or gray-scale IVUS imaging. Patients with Thrombolysis in Myocardial Infarction (TIMI) 0–2 flow after thrombus aspiration were also excluded. Thus, the study comprised a total of 81 patients.

### 2.2. Percutaneous coronary intervention procedure

Patients who did not receive anti-platelet therapy received a loading dose of aspirin 200 mg and clopidogrel 300 mg as soon as possible on admission (drug already used was not administered as loading dose). Furthermore, 10,000 IU of heparin was administered intravenously before PCI, and an additional bolus of 1000–2000 IU was administered every hour if the procedure lasted more than 1 h. No patient received glycoprotein IIb/IIIa receptor inhibitors, which are not yet approved in Japan. After diagnostic angiography, we performed thrombus aspiration in cases with TIMI 0–2 grade flow, followed by IVUS evaluation using conventional guide wire. After IVUS evaluation, the size of Filtrap™ device was determined to be larger than the distal lumen diameter of target lesion. Unless it disturbed the procedure, Filtrap™ was detained in the proximal part of main side branch. The operator decided the position and length of angioplasty and stent implantation according to angiographic and conventional IVUS findings. Successful PCI, defined as <50% residual stenosis with no occlusion of a large branch and final TIMI grade 3 flow, was achieved in all enrolled patients.

### 2.3. Angiography and conventional IVUS analysis

Angiography, IVUS, and IB-IVUS were evaluated by an independent investigator who was not involved in the procedures and was unaware of outcomes. A computerized quantitative analysis system (QCA-CMS system version 6.0.39.0, MEDIS, Leiden, the Netherlands) was used with the guiding catheter for calibration. Angiographic measurements included reference diameter, minimum lumen diameter (MLD), percent diameter stenosis and lesion length.

IVUS studies were performed after the administration of intracoronary injections of isosorbide dinitrate with a mechanical sector scanner (ViewIT, Terumo Corporation, Tokyo, Japan) and a motorized transducer pullback system (0.5 mm/s). The external elastic membrane (EEM) cross-sectional area (CSA), lumen CSA, and plaque plus media CSA (EEM CSA minus lumen CSA) of these slices were measured. The slice of the target lesion site was the image slice with the minimum lumen CSA. The target lesion EEM CSA divided by the average of the proximal and distal reference EEM CSA was defined as the remodeling index. Total plaque volume was calculated as the sum of plaque plus media in each CSA at 1-mm axial intervals for the IVUS images from the target lesion.

### 2.4. Integrated backscatter IVUS analysis

Ultrasound backscattered signals were acquired using a mechanically rotating IVUS catheter (ViewIT, Terumo Corporation, Tokyo, Japan), and were digitized and subjected to spectral analysis. A personal computer (Windows XP Professional, CPU: 3.4 GHz) equipped with commercially available custom software (VISIWAVE-IB, Terumo Corporation, Tokyo, Japan) was connected to the IVUS imaging system (VISIWAVE, Terumo Corporation, Tokyo, Japan) to obtain radio frequencies and signal trigger outputs [5]. The integrated backscatter (IB) values (in decibels) for each tissue component were calculated as the average power of the frequency component of the backscattered signal from a small volume of tissue using a fast Fourier transform. The default settings suggested by the manufacturer were applied in order to define a range of IB values for low IB (lipid plaque), moderate IB (fibrous plaque) and high IB (calcified plaque) [6]. Subsequently, we manually excluded the vessel lumen and the area outside of the intima in two-dimensional IB-IVUS images. Color-coded maps were constructed for each 1-mm slice to illustrate the tissue characteristics into the target lesions (Fig. 1). IB-IVUS images were validated with the corresponding histology to determine diagnostic accuracy. Histological classification of coronary segments was performed according to the consensus opinion of two pathologists who were unaware of the IB-IVUS images [7]. The percentage of the plaque area that was fibrous (fibrous plaque area/plaque area), calcified (calcified plaque area/plaque area), and lipid (lipid plaque area/plaque area) was automatically calculated. Three-dimensional analysis of IB-IVUS images of the target lesion was performed for each CSA at 1-mm axial intervals to determine the lipid plaque, fibrous plaque, and calcified plaque volumes from the sum of lipid, fibrous, and calcified areas, respectively. The fibrous (fibrous volume/plaque volume), lipid (lipid volume/plaque volume), and calcified (calcified volume/plaque volume) volume fractions were then calculated.

### 2.5. Filtrap™ and pathologic filter analysis

Filtrap™ is a 0.014 inch filter wire type distal protection device. There are two variations of the filter part (the maximum expanded diameter: 3.5 mm and 5 mm) for various coronary arteries. After determining the deployment position in the distal part of the target lesion, remove the delivery catheter (3.3 Fr for 3.5 mm, 3.45 Fr for 5.0 mm) and deploy the filter. The filter membrane of Filtrap™ has about 1800 holes with 100 μm diameter in its filter. After the final interventional procedure, the distal protection device was removed using a 3.45 Fr removal catheter (Fig. 1).

After removing Filtrap™, we deployed it again outside the patient body and removed large red thrombi. We cut the shaft at the base of the filter part and entirely fixed in a 4% buffered formalin solution immediately. After the PCI procedure, the filter was expanded manually in a flat fan shape and we took ×30 magnification digital picture. The pictures were analyzed with software (Canvas9, Nihon Poladigital, Japan) to trace the border of trapped debris and calculate the area automatically. During the analysis, the red thrombi observed microscopically were excluded from the debris area (Fig. 2).

### 2.6. Statistics

A comparison of continuous variables was achieved with unpaired Kruskal-Wallis test, Student's t-test, or Mann-Whitney *U* test. Categorical variables were derived by a Chi-square analysis or Fisher's exact probability test. Three subgroups of captured debris area (tertiles) were evaluated to determine the relationship to