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Original article

Association between fractional flow reserve and coronary plaque characteristics assessed by optical coherence tomography

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ABSTRACT

Background: The assessment of fractional flow reserve (FFR) in coronary lesions determines the strategy of percutaneous coronary intervention. However, the association between FFR and characteristics of the underlying coronary plaque has not been sufficiently investigated.
Methods: A total of 110 coronary lesions in 106 patients were evaluated using both FFR and optical coherence tomography (OCT). Coronary plaques were classified into fibrous, fibrocalcific, or fibroatheroma according to OCT evaluation at the site of minimal lumen area. Plaque microstructures such as cap thickness, macrophage accumulation, intimal vasculature, or cholesterol crystals were also evaluated.
Results: Lesions with FFR $\leq$ 0.8 showed a higher frequency of fibroatheroma, macrophage accumulation, and cholesterol crystals when compared to those with FFR $>$ 0.8. The angle of lipid was wider in lesions with FFR $\leq$ 0.8 ($145.1 \pm 63.0^{\circ}$ vs. $120.7 \pm 48.9^{\circ}$, $p = 0.047$), and the longitudinal length was longer in those with FFR $\leq$ 0.8 (4.2 ± 2.8 mm vs. 2.5 ± 2.9 mm, $p = 0.007$). However, multiple linear regression analysis revealed that the morphological characteristics of plaques assessed by OCT were not independently associated with FFR. Minimal lumen area [coefficient, 0.035; 95% confidence interval (CI), 0.022–0.048; $p < 0.001$] and area stenosis (coefficient, −0.003; 95% CI, −0.005 to −0.001; $p = 0.001$) assessed by OCT significantly correlated with FFR.
Conclusion: The morphological characteristics of coronary plaque derived from OCT are not directly related to FFR.

Introduction

The assessment of fractional flow reserve (FFR) in patients with stable coronary artery disease determines whether stenotic lesions are necessary for percutaneous coronary intervention (PCI) [1–4]. Meanwhile, PCI in lesions with physiological ischemia reduced adverse cardiac events when compared with medical therapy alone [1,2], but PCI in lesions without physiologic ischemia failed to improve the event-free survival [3,4]. Accordingly, FFR examination has been recommended for selection of PCI candidates, particularly for intermediate coronary lesions. Although a previous study reported an association between FFR and plaque characteristics using intravascular ultrasound [5], this may not be sufficient because the low resolution of intravascular ultrasound limits the detailed visualization of coronary plaques, particularly in thin-cap fibroatheroma (TCFA) [6,7]. Thus, this study investigated the relationship between FFR and plaque characteristics using optical coherence tomography (OCT).

Materials and methods

Using the OCT registry of our institute, we identified 112 patients with stable angina who had coronary lesions with diameter stenosis between 40% and 80% by visual estimation at one or more major

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coronary arteries and underwent both FFR and OCT examination in the same lesions. Among these 112 patients, 6 patients were excluded for poor quality OCT images. Thus, 106 patients with 110 lesions were enrolled in our study. This study was approved by the Institutional Review Board of our institute, and written informed consent was obtained from each patient.

Coronary pressure was measured using a 0.014-inch pressure guide wire (St. Jude Medical, Minneapolis, MN, USA). After the equalizing process, the pressure guide wire was positioned distal to the target lesion, and maximal hyperemia was induced by intravenous adenosine infusion administered at 140 μg/kg/min through a central vein. FFR was calculated using the following formula: mean hyperemic distal coronary pressure/mean aortic pressure. The stenosis was considered functionally significant when the FFR was ≤0.80.

The frequency-domain C7-XR™ OCT system (LightLab Imaging, Inc., St. Jude Medical) was used in this study. The OCT cross-sectional images were generated at a rotational speed of 100 frames/s, while the fiber was withdrawn at a speed of 20 mm/s within the stationary imaging sheath. All acquired OCT images were analyzed using certified offline software (QIvus, Medis Medical Imaging System, Leiden, the Netherlands) at the core laboratory (Cardiovascular Research Center, Seoul, Korea) by analysts who were blinded to patient and procedural information [8].

Cross-sectional OCT images were analyzed at 1-mm intervals (i.e. every 15 frames). The site of the minimal lumen area was defined as the segment with the smallest lumen area and largest plaque burden. Measurements of reference lumen area were performed at the reference segment with the largest lumen area within 10 mm proximal or distal to the site of the minimal lumen area and before any side branch. Area stenosis was calculated using the following formula: (reference lumen area − minimal lumen area) × 100/reference lumen area. Stenosis length was defined as the longitudinal length of continuous frames that had more than 50% area stenosis. Plaque morphology was analyzed at the site of minimal lumen area in at least three consecutive frames and was classified into fibrous, fibrocalcific, or fibroatheroma according to the presence of calcification or lipid-pool [9]. Fibrous plaque had high backscattering and a relatively homogeneous OCT signal. Fibrocalcific plaque contained fibrous tissue with calcium that appeared as a signal-poor or heterogeneous region with a sharply delineated border. Fibroatheroma was the lesion with OCT-delineated fibrous cap and a necrotic core [9]. Among fibroatheromas, thin-cap fibroatheroma (TCFA) was defined as a lipid-pool with overlying fibrous cap in which the minimal thickness of the fibrous cap was less than 65 μm and the angle of the lipid-pool ≥180° [9]. Additional microstructures detected by OCT were defined as follows: (1) macrophage accumulation with signal-rich, distinct, or confluent punctate regions that exceeded the intensity of background speckle noise; (2) intimal vasculature with signal-poor regions that had a sharp delineation in contiguous frames; (3) cholesterol crystals with thin and linear regions of high intensity [9]. Fig. 1 shows representative images of plaque morphology and microstructures.

Quantitative coronary angiography analysis was performed using an offline computerized quantitative coronary angiographic system (CASS system, Pie Medical Imaging, Maastricht, the Netherlands) in an independent core laboratory (Cardiovascular Research Center, Seoul, Korea). The minimal lumen diameter and reference diameters of target lesions were measured in the view with the narrowest lumen and the least amount of foreshortening.

All statistical analyses were performed using PASW (version 18.0.0, SPSS Inc., Chicago, IL, USA). Categorical data were expressed as number and percentage (%), and analyzed with a chi-square test or a Fisher's exact test. Continuous variables were expressed as mean ± standard deviation or median (interquartile range), and were compared using a Student's *t*-test or a Mann–Whitney test. Multiple linear regression analysis was applied to determine the independent factors for FFR. OCT variables with a *p*-value <0.1 resulting from univariate analysis were considered for entrance into the multivariable model. A *p*-value <0.05 was considered statistically significant.

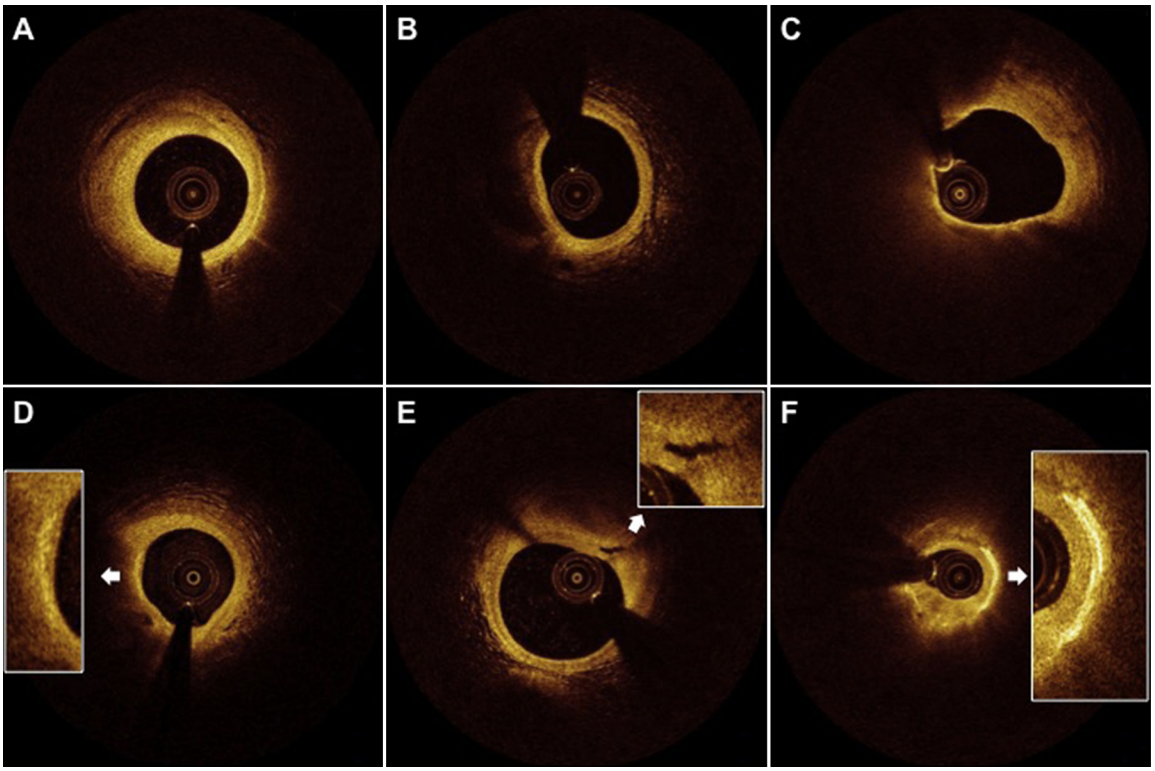

Fig. 1. Plaque morphology and microstructure assessed by optical coherence tomography. (A) Fibrous plaque, (B) fibrocalcific plaque, (C) thin-cap fibroatheroma, (D) macrophage accumulation, (E) intimal vasculature, and (F) cholesterol crystal.