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CORRESPONDENCE

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Frequency and Predictor of Coronary Thin-Cap Fibroatheroma in Patients With Acute Myocardial Infarction and Stable Angina Pectoris

A 3-Vessel Optical Coherence Tomography Study

To the Editor: Autopsy studies suggest that the main mechanisms of acute myocardial infarction (AMI) are plaque ruptures followed by thrombus formation (1). Post-mortem studies have shown that rupture-prone plaques, known as thin-cap fibroatheromas (TCFAs), have certain characteristics: a thin, fibrous cap (<65 μm); a large, lipid-rich pool; and increased macrophage activity (1). The identification of the thin fibrous cap is important because plaque is prone to rupture when the fibrous cap becomes <65 μm (1,2). Optical coherence tomography (OCT) has been introduced as a high-resolution imaging modality (3). We conducted a prospective OCT analysis of all 3 major epicardial arteries to evaluate the incidence and predictors of TCFAs in patients with AMI and stable angina pectoris (SAP).

A prospective but nonconsecutive series of 20 SAP and 35 AMI patients who were scheduled for coronary intervention underwent 3-vessel OCT examinations. The ethics committee at Hyogo College of Medicine approved the protocols, and written informed consent was obtained from all patients. The OCT examinations of all 3 major epicardial arteries were performed with a 0.016-inch wire-type imaging wire (ImagingWire, LightLab Imaging Inc., Westford, Massachusetts) with the use of an automated pullback at 1.0 mm/s. At least two-thirds of the lengths of the arteries were imaged continuously over a 20- to 50-mm length from the distal segment to the ostium. Only the most proximal 3-mm segments of the arteries under the occlusion balloon were not imaged. For all plaques with an OCT-determined lipid pool, the fibrous cap thickness was measured at its thinnest part. The fibrous cap thicknesses were measured 5 times, and the average of 3 middle values was computed. For OCT analysis, we defined a TCFA as a plaque with lipid content (≥1 quadrant within a plaque) and the thinnest part of a fibrous cap measuring ≤65 μm (3). A typical plaque rupture and thrombus is shown in Figure 1.

Continuous variables were reported as mean ± 1 SD. The unpaired Student *t* test was used to test the differences between 2 sets of data. Categorical variables were reported as frequencies and compared using chi-square statistics.

Intramural thrombus was observed in 34 (97%) AMI and 5 (25%) SAP patients at the infarct-related/target lesion ($p < 0.001$), and in 16 (45%) AMI and 3 (15%) SAP patients at the noninfarct-related/nontarget lesion ($p = 0.04$), respectively. Infarct-related/target lesion plaque rupture was found in 16 (46%) AMI and 2 (10%) SAP patients ($p = 0.008$). There was at least 1 noninfarct-related/nontarget plaque rupture in 11 (31%) AMI and 3 (15%) SAP patients ($p = 0.2$). The difference in incidence of multiple plaque ruptures between AMI and SAP patients (24% vs. 10%, $p = 0.2$) was not statistically significant. Infarct-related/target lesion TCFA was found in 27 (77%) AMI and 5 (25%) SAP patients ($p < 0.001$). There were at least 1 noninfarct-related/nontarget TCFA in 27 (77%) AMI and 6 (30%) SAP patients ($p < 0.001$). The incidence of TCFAs was significantly greater in the right as compared with the left circumflex or left anterior descending arteries (0.87 ± 1.67 TCFAs/artery vs. 0.31 ± 0.47 TCFAs/artery or 0.53 ± 1.04 TCFAs/artery, $p = 0.006$). Multiple TCFAs were observed more frequently in AMI patients than in SAP patients (69% vs. 10%, $p < 0.001$).

In the entire cohort, multivariate analysis revealed that the only independent predictor of TCFA was AMI ($p = 0.02$, risk ratio [RR]: 4.12; 95% confidence interval [CI]: 2.35 to 9.87). In AMI patients, the independent predictors of multiple TCFAs were male gender ($p = 0.04$, RR: 2.01; 95% CI: 1.12 to 6.09) and high-sensitivity C-reactive protein (hs-CRP) level ($p = 0.01$, RR: 2.49; 95% CI: 1.39 to 8.64).

The present study found a lower incidence of infarct-related lesion plaque rupture (46%) than that observed in previous pathological studies (≈70%) (1,3) and greater than that of studies in which intravascular ultrasound (IVUS) was used. A large intramural thrombus covering and effectively masking the underlying ulcerations may disturb the accurate diagnosis of plaque rupture at the infarct-related lesion of patients with AMI. The detection of plaques with complex morphology, such as ruptured plaques, may be more precise with OCT than detection with IVUS, because the higher resolution of OCT permits better differentiation of heterogeneous plaque constituents.

Vulnerable plaques that are prone to rupture possess a TCFA, a large lipid pool, and activated macrophages near the fibrous cap (1). The identification of the fibrous cap is especially important because the thickness of the fibrous cap is a major determinant of plaque vulnerability in lipid-rich plaque (1). In accordance with a previous pathological study (4), our results support the observation that TCFAs are associated not only with infarct-related lesions but also with noninfarct-related segments in patients with AMI. Our data indicate that TCFAs exist extensively throughout the major coronary arteries of patients with AMI, providing further evidence of the multifocal nature of inflammation in noninfarct-related atherosclerosis and supporting the hypothesis that this inflammation is manifested in vivo by thinning of the fibrous caps of both culprit and nonculprit lesions.

A previous post-mortem study found that number of macrophages in TCFA was significantly greater in patients with high plasma CRP levels than those with low plasma CRP levels, and an increase in hs-CRP was associated with immunohistochemical deposition of CRP within the plaque, supporting the

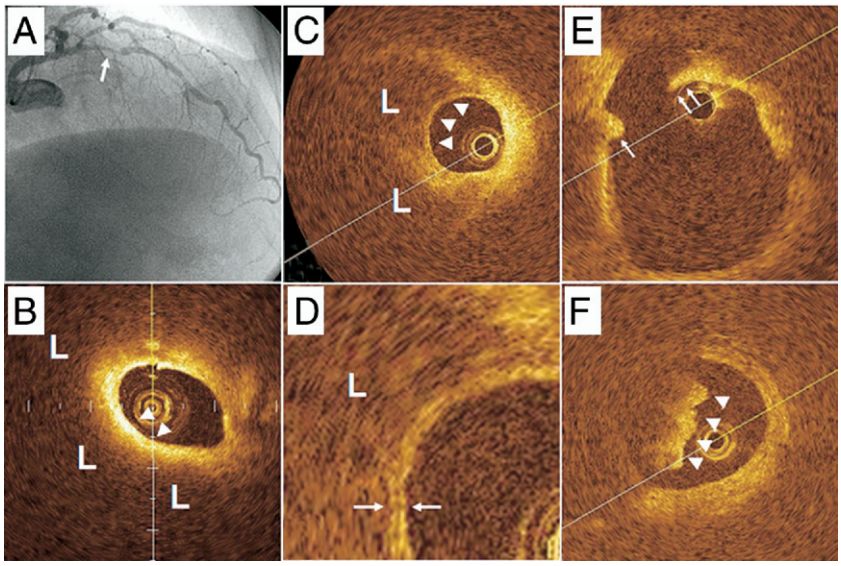

Figure 1 **Optical Coherence Tomography Images of Vulnerable Plaques**

(A) A 90% stenosis observed in the middle left anterior descending artery in patients with stable angina pectoris **(arrow)**. **(B)** Lipid-rich plaque (L) covered by thin fibrous cap (63.3 μm) **(arrowheads)** observed in the target lesion of a patient with stable angina pectoris. **(C)** Lipid-rich plaque (L) covered by thin fibrous cap **(arrowheads)** detected in the noninfarct-related lesion of an acute myocardial infarction patient. **(D)** Magnification of **(C)**. The thickness of the fibrous cap that existed between the lumen and plaque **(arrows)** measured 46.7 μm. **(E)** A plaque rupture was defined as a plaque containing a cavity that communicated with the lumen with an overlying residual fibrous cap fragment **(arrows)**. **(F)** A thrombus was defined as an irregular mass protruding into the lumen with a measured dimension ≥250 μm **(arrowheads)**.

hypothesis that inflammation is an important component of plaque instability (5). In accordance with the present study, a previous IVUS study reported that hs-CRP levels had a positive correlation with the number of plaque ruptures evaluated by IVUS in AMI patients who underwent IVUS examination within 6 h from the onset of symptoms (6). This is a small observational study. Because the proximal segments of the target arteries had to be occluded by the occlusion balloon to remove blood for OCT examinations, ostial segments were not imaged in each coronary artery.

The 3-vessel OCT imaging showed that culprit lesion TCFAs, secondary remote TCFAs, and multiple TCFAs were more common in AMI patients than in SAP patients. In AMI patients, male gender and hs-CRP level are associated with the presence of multiple TCFAs.

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