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Editorial

Which is better for predicting ischemic events: Physiology or morphology?

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The presence of myocardial ischemia is the most important prognostic factor in patients with coronary artery disease. Fractional flow reserve (FFR), which is determined by both lesion severity and the amount of myocardium supplied, has been accepted as an important index for decision-making in terms of revascularization of coronary artery stenosis. That is, stenosis with an ischemic FFR should be revascularized, whereas lesions with a non-ischemic FFR can be better treated medically due to a more favorable prognosis [1]. In the Flow Reserve Versus Angiography for Multivessel Evaluation (FAME) study, FFR-guided percutaneous coronary intervention (PCI) in patients with multivessel coronary artery disease who underwent PCI with drug-eluting stents reduced the rate of the composite endpoint of death, nonfatal myocardial infarction, and repeat revascularization at 1 year compared with standard angiography-guided PCI [2,3]. In line with these findings, the results of the FAME II study demonstrated that FFR-guided PCI is superior to optimum medical treatment alone for relieving angina and improving outcome [4].

The spectrum of clinical syndromes caused by coronary atherosclerosis ranges from asymptomatic disease and stable angina pectoris to acute coronary syndrome (ACS). ACS develops as a series of nonlinear events in an otherwise gradual progressive process. In fact, in 60–80% of patients with ACS, a coronary angiogram performed weeks or months before the acute event, showed diameter narrowing in the culprit site to be <70%, and often <50% [5]. The nonlinearity has been attributed to a combination of factors, of which plaque rupture and superimposed thrombosis are considered the most important. Plaques with a thick fibrous cap are considered clinically stable, whereas plaques with a high lipid content and thin fibrous cap are considered vulnerable. Plaque rupture occurs in plaque fissuring at one point, which ultimately brings platelets into contact with the lipid core content and the blood coagulation factors into contact with tissue factor. Thus, the thinner the fibrous cap, the higher the risk of rupture. The Providing Regional Observations to Study Predictors of Events in the Coronary Tree (PROSPECT) trial showed for the first time that lesion characteristics predictive of events associated with nonculprit lesions include a large plaque burden, a small luminal area, and thin-cap fibroatheroma (TCFA) [6]. TCFA is the precursor lesion associated with plaque rupture. TCFA has been defined as a lesion with a fibrous cap <65 μm thick. This thickness was chosen as a criterion of instability because it has been reported that the mean thickness of the fibrous cap near the rupture site was 23 ± 19 μm, with 95% of the cap <65 μm. Intravascular optical coherence tomography (OCT) has been proposed as a high-resolution imaging method for plaque characterization [7]. OCT may enable us to evaluate the micro-structure of coronary plaques and measure fibrous cap thickness, which is accepted as the most important assessment of plaque vulnerability [8,9].

The present case demonstrated moderate lesions in the right coronary artery, which had no evidence of ischemia, as indicated by the FFR value (0.96), and rapidly progressed to protruding red thrombi and plaque disruption of thin-cap TCFA, which was identified by OCT six months later. The authors addressed the view that FFR is an insufficient index for predicting future events related to the morphologically vulnerable plaques in mild to moderate lesions, but not severe stenosis, while OCT-derived TCFA is likely to discriminate morphologically malignant lesions from mild to moderate lesions [10]. That is, the report suggests that OCT-derived TCFA bridges the gap from physiologically benign but morphologically malignant in mild to moderate lesions. In fact, OCT has been accepted as a useful tool for identifying TCFA *in vivo*. Fujii et al. performed an OCT study with coronary vessels to evaluate the incidence and predictors of TCFA in patients with acute myocardial infarction (AMI) and stable angina pectoris (SAP) [11]. TCFAs were found more frequently at the culprit site than at the remote sites in AMI patients, and multiple TCFAs were more prevalent in AMI patients than in SAP patients. In addition, the same groups [12] demonstrated that TCFAs and ruptured plaques were common in the proximal segments of the left anterior descending artery, as previously described [13]. These results are in agreement with our reports of *in vivo* OCT studies [14,15]. However, some cases have an intracoronary plaque rupture without symptoms or a clinical ACS event. Indeed, previous OCT studies have reported plaque rupture even in patients diagnosed with SAP [11]. In addition, the factors used to determine the occurrence of sustained thrombotic vessel occlusions leading to ACS remain poorly understood. Therefore, future investigations are warranted to validate this clinically hot topic. For example, a prospective clinical assessment based on a comparative study of FFR-guided versus OCT-guided revascularization strategies or a combination study of both will provide some clues.

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