Upture of vulnerable plaque is the main cause of acute coronary syndrome (ACS) and myocardial infarction (MI). Identification of vulnerable plaques is therefore essential to enable the development of treatments that will stabilize such plaques.

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Because MI and its consequences are so important, options for identifying those areas that will be responsible for future events must be investigated.

Lipid and blood sugar profiles and inflammatory markers are thought to be promising predictors of ACS, and intravascular imaging modalities have progressed in the detection of the morphology of culprit lesions.

Intravascular coronary ultrasound (IVUS) provides real-time high-resolution images of the vessel wall and lumen. Depending on the distance from the catheter the axial resolution is approximately 150 microns, the lateral 300 microns. Features of the vessel can be detected based on the echogenicity and thickness of the material. Small structures can be visualized; however, only those sized over 160 microns can be estimated accurately. The normal thickness of the media is approximately 125–350 μm. IVUS provides some insight into the composition of coronary plaques. In comparative studies between histology and IVUS, plaque calcification can be detected with a sensitivity of between 86 and 97%. The sensitivity for detecting micro-calcification might be included in lipid core ranges around 60%.

Angioscopy is another intravascular modality that has been used for detecting vulnerable plaques in patients with ACS. Intracoronary angioscopy offers direct visualization of the plaque surface and intraluminal structures such as tears and thrombi. It enables assessment of the color of the plaque and thrombus, with a sensitivity for detecting such structures that is higher than angiography. Angioscopic rupture and thrombus have been shown to be associated with adverse clinical outcomes in patients with complex lesions. Furthermore, yellow plaques seem to have an increased instability in a comparison between IVUS and angioscopy. In patients with MI reported by Asakura et al., all 3 coronary arteries were widely diseased and had multiple yellow plaques. In a 12-month follow-up study of 157 patients with stable angina, ACS occurred more frequently in patients with yellow plaques than in those with white plaques. These results indicate that ACS occurs more frequently in patients with yellow plaques, which can be imaged with angioscopy, but not angiography. However, angioscopy is difficult to perform, invasive and only a limited part of the vessel tree can be investigated. Most importantly, to enable clear visualization of the vessel wall, the vessel has to be occluded and the remaining blood flushed away with saline, thereby potentially inducing ischemia. Information regarding the degree of plaque extension into the vessel wall is not provided by angioscopy.

Kawano et al. investigated angioscopic yellow plaques (vulnerable plaques) using intravascular ultrasound radiofrequency data analysis. They reported that angioscopic yellow plaque included a larger amount of necrotic core than white stable plaque, as analyzed by VH-IVUS.

Sawada et al. investigated the usefulness of imaging modalities (VH-IVUS and OCT) for detecting thin-cap fibroatheroma (TCFA) in vivo and concluded that neither modality alone is sufficient. The combined use of OCT and VH-IVUS might be a feasible approach to evaluating TCFA. Spectral analysis of IVUS radiofrequency data can provide detailed quantitative and qualitative information on coronary plaque composition in vivo. There are many imaging modalities that are able to detect some aspects of unstable plaque; however, there is not yet a modality that can detect vulnerable plaque by itself (ie, single modality) in vivo before plaque rupture in patients with ACS.

Several invasive and noninvasive imaging techniques are currently in development. MRI and CT have the advantage of noninvasive imaging. OCT has the advantage of high resolution. IVUS is easy to perform and assess morphology and mechanical instability. All techniques are still under development and, at present, none of them can identify a vulnerable plaque alone or predict its further development.

It is known that matrix metalloproteinase-2 and -9 (MMP-2, MMP-9), tissue inhibitor of metalloproteinase-1 (TIMP-1), adiponectin and macrophage migration inhibitory factor (MIF) correlate with plaque destabilization or stabilization. However, there are only a few studies that have evaluated the relationship between plasma biomarkers and plaque characteristics as determined by an imaging study.

Park et al. investigated whether biomarkers that are known to be associated with plaque vulnerability, such as MMP-2, MMP-9, TIMP-1, adiponectin and MIF, can be predictors of the presence of ruptured plaque or VH-TCCA as determined by 3-vessel VH-IVUS study. They concluded that the MMP-9...
level was significantly higher in patients with ruptured plaque; however, measurements of several biomarkers, including MMP-9, were not capable of predicting the presence of VH-TCFA. The relationship between ruptured plaques and MMP-9 was elucidated by this report and may be an important contribution to future research into vulnerable plaque in this field. MMP-9 exists in the sub-intima, and there are many cases in which ACS patients present with silent ruptured plaques. Therefore, it might be useful to detect the existence of vulnerable plaque.

The clinical testing of these new techniques will provide us with sensitivity, specificity and predictive values for morbidity and mortality. As soon as these are established, a reliable statement on surrogate endpoints for clinical trials can be made.

Investigation into using biomarkers to detect vulnerable patients as seen in this study should be continued in the future.

References