Noninvasive Detection of Vulnerable Coronary Plaques

Locking the Barn Door Before the Horse Is Stolen*

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It is well established from post-mortem studies that ruptured atherosclerotic plaques in proximal coronary arteries usually have a large necrotic core with a thin overlying fibrous cap (1,2). These “thin cap fibroatheromas” usually have little calcification, and they may not cause critical narrowing of the coronary lumen because of positive remodeling (outward expansion) of the artery. Intravascular ultrasound (IVUS) has also shown that, when compared with patients with stable coronary artery disease, patients who recently had an acute coronary event showed more positive remodeling and larger plaque areas (3).

How can this important information be applied clinically? Contrast-enhanced computed tomographic angiography (CTA) has emerged as a promising approach for the noninvasive assessment of coronary anatomy. It is useful in the recognition and characterization of congenital anomalies of the coronary arteries and in determining the patency of coronary artery bypass grafts. CTA is becoming more widely employed in the detection of coronary luminal narrowing in patients with or suspected of having chronic coronary artery disease. It appears to be especially useful in ruling out obstructive disease in patients with equivocal findings on clinical examination and on stress myocardial perfusion scanning. It is likely that with continuing improvement in accuracy, CTA will grow in importance for this application.

The use of contrast-enhanced CTA for the characterization of coronary artery plaques is more challenging, and because of its potential clinical importance, it has been the focus of attention of several research groups. Building on the histologic and IVUS findings, and using multi-row detectors, it has been demonstrated that contrast-enhanced CTA can provide measurements of plaque area and volume (4), and that it can be used to quantify plaque density, which correlates well with plaque echogenicity and composition (5). These findings, using contrast-enhanced CTA, correlate with those obtained by IVUS (4,5).

Motoyama et al. (6) compared disrupted plaques in patients who had experienced an acute coronary syndrome (ACS) with plaques obtained from patients with stable angina. As was the case with disrupted plaques studied by IVUS, disrupted plaques assessed by CTA also showed positive vascular remodeling, low plaque density, and spotty calcification (6). In this issue of the Journal, Motoyama et al. (7) describe the next important step in the clinical study of coronary atheroma. These investigators employed contrast-enhanced CTA to identify vulnerable plaques that had not yet ruptured in patients who had not experienced an acute coronary event—in other words, before the horse had been stolen from the barn. They analyzed 10,037 coronary arterial segments in 1,059 patients with known or suspected coronary artery disease for 2 of the features previously identified in plaques that have already ruptured, namely, positive coronary artery remodeling and the presence of plaques exhibiting low attenuation (“soft”) plaques. Of the 1,059 patients studied, 15 (1.5%) had an ACS over a mean follow-up of 27 months. The risk for an acute coronary event was quite high, namely, 22% in subjects with both of these features. An ACS developed in 11% of subjects with either of the 2 features. Only 0.5% of the patients without either feature had an acute coronary event, providing a strong negative predictive value. The development of an acute coronary event in 2 years could, for all practical purposes, be excluded in >80% of patients with known or suspected coronary artery disease.

In addition, and in accord with previous histologic and IVUS studies, Motoyama et al. (7) also found that spotty calcification occurred more frequently and that total plaque volume and the ratio of low-attenuation plaque to total plaque area were both significantly higher in patients who subsequently had an ACS than in those who did not. The positive remodeling prevented many of these enlarged vulnerable plaques from encroaching on the coronary lumen. Thus, these plaques are often not responsible for either ischemic symptoms or impaired myocardial perfusion during stress. That explains the frequent finding of the sudden, unheralded development of ACS, and even sudden cardiac death, in previously asymptomatic patients.

Risk stratification for the development of ACS began with the well-established Framingham risk score (8), which has recently been refined by Ridker et al. (9) by adding C-reactive protein and family history—the so-called Reynolds risk score. These scores can identify patients who require intensive primary preventive mea-

*Editorials published in the Journal of the American College of Cardiology reflect the views of the authors and do not necessarily represent the views of JACC or the American College of Cardiology.

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sures. How could detection of vulnerable plaques by CTA fit into the prevention scheme? It does not appear appropriate at this time to propose the use of CTA to detect vulnerable plaques in patient populations such as those studied by Motoyama et al. (7). To be of clinical value, the procedure would probably have to be repeated every 2 or 3 years. The costs of such an approach and the burden of radiation exposure are both too high and the yield too low to make this strategy clinically useful at present. However, this field is still in its infancy, and it is safe to predict that the limitations noted in the preceding text will diminish in the next few years. Certainly, the new 320- and 256-detector row CT scanners are improving image quality and resolution (10,11), while the use of dual-source CT is enhancing temporal resolution (12). Also, a greater yield would clearly be obtained if patients at higher risk of having an ACS than those studied by Motoyama et al. (7) had been investigated.

The widespread clinical application of the approach of Motoyama et al. (7) for the detection of vulnerable plaques at risk of future rupture (namely, locking the barn door before the horse is stolen) would require the development of measures for the prevention of plaque rupture that are more potent than those currently employed, in what we currently refer to as intensive prevention. One measure could be the use of dual antiplatelet therapy (aspirin and a thienopyridine), although the risk of bleeding from the prolonged use must be considered. Perhaps stenting or surgically bypassing these plaques could be considered in some patients. Newer and more potent anti-inflammatory drugs are in the developmental stage, and if proved to be safe for long-term administration, they could be employed. Indeed, the ability to detect these vulnerable plaques noninvasively is likely to serve as a powerful stimulus for increased effort in the development of such therapies (13). When more effective therapies for these plaques do become available, the paper by Motoyama et al. (7) will be surely become a landmark in the effort to prevent acute coronary events.

References