Identifying patterns of atherosclerotic disease manifestation with coronary computed tomography. Impact on clinical management and outcome?

Paul Schoenhagen* and E. Murat Tuzcu
The Cleveland Clinic, Imaging Institute and Heart & Vascular Institute, 9500 Euclid Ave., Cleveland, OH 44195, USA

Online publish-ahead-of-print 27 August 2008

This editorial refers to ‘Evaluation of plaque characteristics in acute coronary syndromes: non-invasive assessment with multi-slice computed tomography and invasive evaluation with intravascular ultrasound radiofrequency data analysis’† by G. Pundziute et al., on page 2373

Since its introduction as a tool for non-invasive coronary imaging, computed tomographic angiography (CTA) has undergone significant clinical validation. Its feasibility and diagnostic performance for the assessment of luminal stenosis have been evaluated against conventional angiography.1,2 In multiple comparative studies, it has been demonstrated that significant luminal stenosis can be excluded with high negative predictive value. The positive predictive value for the detection of stenotic lesions is reduced by stenosis overestimation due to artefact associated with advanced, calcified atherosclerotic lesions. At the same time, CTA has been validated for assessment of plaque burden and plaque characteristics. Several studies have demonstrated reliable identification and differentiation of calcified and non-calcified plaque in comparison with intravascular ultrasound (IVUS), but further characterisation of non-calcified components based on the CT Hounsfield unit value is limited.3

The ultimate goal of atherosclerosis imaging is the identification of ‘the vulnerable plaque’, prior to their causing acute cardiovascular events. In post-mortem studies, these high-risk lesions, the so-called thin cap fibroatheromata (TCFA), are characterized by a necrotic core, separated from the lumen by a thin fibrous cap (<65 μm), which consists of smooth muscle cells and inflammatory cells in a proteoglycan-rich collagen matrix.4 While reliable in vivo identification is still not possible, invasive imaging modalities including IVUS and optical coherence tomography (OCT) allow identification of individual high-risk features.

Grey-scale IVUS studies comparing lesion morphology in stable and unstable patients found low echodensity, positive remodelling, and small ‘spotty’ calcium deposits to be more prevalent in unstable patients.5,6 Advanced analysis of the IVUS backscatter information (IVUS radiofrequency analysis (RFA)) allows further plaque differentiation.7 Based on emerging data, the IVUS-derived fibroatheroma (ID TCFA) is defined as a plaque with significant plaque burden, a confluent necrotic core >10–20% of the total plaque volume, and no imaging evidence of a fibrous cap (i.e. minimal thickness of the cap below the resolution of IVUS). The amount of calcium is variable, >10%, with a speckled appearance.8

Pundziute et al. describe data comparing IVUS RFA plaque analysis with CTA in 50 patients presenting with acute coronary syndromes (ACS) or stable CAD.9 By CTA, plaques were classified as non-calcified, calcified, and mixed (non-calcified and calcified components within the same plaque). In ACS patients, 32% of plaques were non-calcified and 59% were mixed. In patients with stable CAD, predominantly calcified lesions were most prevalent (61%). The percentage of necrotic core was higher in the plaques of ACS patients (P = 0.02), and ID TCFA were more prevalent than in stable patients (32% vs 3%, P <0.001). Importantly, ID TCFA were most frequently observed in mixed plaques. Similar to previous IVUS and CTA studies, these results suggest that mixed calcified lesions with spotty calcification are related to plaque vulnerability.6,10

The overall risk of developing an acute cardiovascular event is probably related to the number of plaques and their individual level of vulnerability. This has diagnostic and therapeutic implications. On the one hand, focal identification of the most vulnerable lesions would allow evaluation of novel, plaque-stabilizing interventions, including prophylactic stenting or local drug delivery. It has been suggested that CTA could be used as a roadmap to identify hot spots for subsequent further evaluation with IVUS in
In the context of local invasive treatment, however, a major limitation is that the fact imaging criteria of vulnerability are typically not limited to unstable lesions. In the study by Pundziute et al., mixed calcified plaques were common in both stable and unstable patients, and plaque composition by CTA and IVUS RFA was identical between culprit and non-culprit vessels of ACS patients. It is likely that additional features of individual plaques including inflammatory activity need to be evaluated, using emerging molecular imaging approaches.\(^{11}\)

In contrast to focal identification of plaque vulnerability, a systemic assessment of risk relies on the identification of the total number of plaques (plaque burden), their location, and limited morphological features in order to describe disease patterns of the entire coronary tree. CTA has already demonstrated the ability to describe patterns of atherosclerotic disease involvement. In a recent study of patients evaluated for suspected CAD, approximately one-third had no evidence of any disease (absence of plaque and stenosis).\(^{12}\) In 30%, non-calcified coronary plaques were found, which were predominantly associated with coronary calcifications (i.e. mixed plaques) and luminal narrowing of <50%. Exclusively non-calcified plaques were found in 6% of the overall group. About 40% of patients presented with predominantly calcified plaque. Patients with non-calcified and mixed plaques were characterized by significantly higher low-density lipoprotein (LDL) cholesterol and C-reactive protein levels. The prognostic value of these patterns for all-cause mortality has been examined in a cohort of 1127 patients.\(^{13}\) The presence and severity of luminal stenosis and plaque burden were assessed in each coronary segment. An overall CTA score combining stenosis and plaque was constructed similar to the angiographic Duke Coronary Artery Score.\(^{14}\) All-cause mortality over a follow-up period of ~15 months was assessed by the Social Security Death Index. In multi-variable analysis, CTA scores measuring plaque/stenosis severity, global plaque extent, plaque distribution, presence of left main or left anterior descending artery plaque, and three-vessel plaque were all independently predictive of death. However, while the presence and distribution of plaque were examined, plaque composition was not part of this analysis.

The current study by Pundziute et al., providing insights into the relationship between plaque characterization with CTA and clinical presentation, suggests that plaque composition could have incremental value and should be included in scoring systems assessing overall risk. In symptomatic intermediate risk populations, where CTA is considered clinically indicated by current consensus guidelines,\(^{15}\) comprehensive assessment of the presence, location, and number of stenoses, but also the location, presence, and characteristics of plaque allow patterns of disease manifestation to be described. These include absence of any disease (absence of plaque and stenosis), non-obstructive disease (presence of plaque/mixed plaque in the absence of significant stenosis), and suspected stenotic disease (presence of plaque and luminal stenosis). These clinical patterns can guide further management, including the need for functional stress testing, cardiac catheterization, and aggressiveness of risk factor modification, but their incremental value needs to be evaluated further in the context of extensive data available from nuclear and echocardiography stress testing, but also CT calcium scoring.\(^{16}\)

Conflict of interest: none declared.

References