

EDITORIAL COMMENT

## Coronary Plaque Characterization by Computed Tomographic Angiography

### Present Promise and Future Hope\*

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Until recently, high-resolution coronary angiograms could only be obtained by invasive techniques. Advances in computed tomographic angiography (CTA) have now made it possible to accurately image the coronary vasculature noninvasively, with excellent accuracy for the presence and severity of luminal stenoses (1,2). Whether CTA has the capability to delineate the morphological features of complex ruptured coronary plaque, let alone “vulnerable” plaque, has not been fully elucidated. In this issue of *JACC*, Kitigawa et al. (3) employed CTA to characterize

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atherosclerotic plaque in patients with acute coronary syndrome (ACS). Their findings suggest that, compared to stable cases, ACS patients more commonly exhibit plaques with vulnerable features, with such lesions more frequently multifocal in distribution.

**Ground rules for plaque characterization.** Before each baseball game, the managers and umpires gather at home plate to discuss “ground rules.” Analogously, interpretation of the present observations first requires careful consideration of plaque characterization terminology and technology. The following definition of terms is offered: 1) “unstable plaque,” the proximate cause of ACS characterized pathologically by a ruptured inflamed plaque with superimposed thrombus; 2)

“complex lesions,” the invasive angiographic hallmark of a frankly unstable plaque, characterized by haziness, fissuring, ulceration, filling defect, and impaired flow; 3) “vulnerable plaque,” rupture-prone precursor of unstable plaque, linked pathologically to thin-capped fibroatheroma; 4) “culprit lesion,” the unstable plaque responsible for ACS; and 5) “target lesion,” that plaque designated for revascularization. Although these definitions are widely accepted, unfortunately these terms are often applied imprecisely or misused interchangeably.

An appreciation of the information necessary to precisely characterize plaques and fundamental data provided by plaque imaging technologies is essential. Comprehensive plaque analysis should include the following: 1) architecture: plaque volume, length, eccentricity, remodeling, and impact on lumen area; 2) physiology: impact on coronary flow reserve; 3) content: lipid, fibrous, calcium, and so forth; and 4) pathobiology: presence of inflammation, neovascularization, fibrous cap metabolism, apoptosis, and so forth.

Invasive angiography produces an image of the vessel lumen only, but little insight regarding atherosclerotic plaque other than indirectly by its effects on luminal architecture. Invasive angiography is effective at delineating grossly disrupted complex lesions, but may miss the plaques with subtler but pathologically manifest ulceration and rupture, and clearly fails to detect the many vulnerable but not yet ruptured plaques that serve as the substrate for subsequent coronary events (4). Intravascular ultrasound (IVUS) images the vessel wall and delineates the extent and, to some extent, the character of intramural plaque. By IVUS, unstable plaques are typically bulky, ec-

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centric, and positively remodeled, with complex features including ulceration, intimal flaps, and thrombus (5). Expansive remodeling by IVUS may identify vulnerable but not yet disrupted plaque. Other novel invasive imaging devices hold promise to further plaque characterization. For example, near-infrared spectroscopy has been validated and approved for accurate delineation of lipid-core content of plaques (6), whereas optical coherence tomography provides breathtaking images of plaque architecture, including fibrous cap thickness (7). CTA noninvasively provides a high-resolution, contrast-enhanced “lumenogram” similar to invasive angiography; furthermore, by virtue of differential tissue attenuation capabilities, CTA also facilitates imaging of the vessel wall, thereby providing IVUS-like insights regarding the character and extent of intramural atherosclerosis.

**CTA delineation of vulnerable plaque.** In the present study, Kitigawa et al. (3) analyzed “noncalcific coronary atherosclerotic lesions” in 101 patients, comparing 21 ACS cases and 80 non-ACS cases. The CTA features of vulnerable plaque were analyzed according to 3 parameters: 1) low CT density; 2) positive remodeling index; and 3) patterns of adjacent spotty calcification. Major findings showed that ACS patients had comparatively more noncalcific lesions (3 vs. 2 per patient), with such lesions exhibiting more “vulnerable” characteristics. Statistical analysis revealed that in ACS cases, a high degree of positive remodeling was the only independent discriminator of culprit versus nonculprit lesions. These findings are similar to those of prior studies documenting that culprit lesions in ACS patients are characterized by lower CT density and positive remodeling (8). These results are also consistent with prior IVUS studies demonstrating similar morphological features (e.g., positive remodeling) in unstable and vulnerable lesions. Another important finding of the present study demonstrated that ACS patients manifested more lesions per patient compared with non-ACS patients. Given that such ACS lesions exhibited more vulnerable plaque features, the authors conclude that ACS patients harbor multiple vulnerable plaques. These findings support the concept that plaque instability is a pancoronary, multicentric process, a notion first demonstrated by our documentation of multiple unstable plaques in patients with acute myocardial infarction (9).

**Considerations pertinent to the methods of the present study.** Interpretation of the present results (3) requires consideration of both terminology and methodology. The fundamental premise of this study is based on the assumption that the CTA criteria employed can accurately detect vulnerable plaque. Although prior CTA-IVUS correlates have been published, true validation of CTA sensitivity and specificity utilizing “gold standard” histopathology comparators has not yet been established. Terminology in the present study also may pose challenges: the terms “culprit lesion” and “target lesion” are utilized interchangeably and employed without distinction to concepts of “unstable lesions” and “vulnerable plaques.” Furthermore, no invasive angiographic data are provided, nor is there information regarding revascularization. Neither did the present CTA analysis comment on morphological features indicating plaque disruption such as ulceration, filling defect, or intraplaque dye penetration. In aggregate, these considerations may limit firm conclusions regarding whether any given lesion is truly vulnerable, complex, culprit, or target.

**CTA documentation of complex lesion morphology.** We recently demonstrated that CTA can delineate the morphology of unstable coronary plaques (10). In patients presenting with unstable chest pain and proven complex ruptured plaques by invasive angiography, the CTA portrait of an unstable coronary plaque is strikingly similar to patterns depicted by invasive angiography, and is characterized by a bulky, hypodense, eccentric, positively remodeled lesion with angiographic evidence of plaque disruption indicated by ulceration and intraplaque contrast penetration. Importantly, in some lesions judged noncomplex and stable by invasive angiography, CTA revealed intramural plaques that were eccentric, bulky, hypodense, and positively remodeled, but that lacked features of frank rupture. One can only speculate whether such lesions represent vulnerable plaques. These observations emphasize that its IVUS-like capabilities impart to CTA the power and potential to detect subtler areas of plaque instability/vulnerability that invasive lumenography may miss.

**The future of plaque characterization: looking beyond the lumen.** The pioneers of coronary angiography were justifiably awarded a Nobel Prize in 1956. The present results (3) add momentum to the ongoing rapid transformation beyond invasive lumenography to a more sophisticated, comprehensive, and at least partially noninvasive approach to plaque de-

tection and characterization. Ultimately, CTA plaque characterization will require validation by gross histopathological correlates and correlation with direct invasive imaging modalities (e.g., IVUS, angiography, near-infrared spectroscopy, optical coherence tomography). Clearly, further research will be necessary to determine whether CTA can provide diagnostic, prognostic, and therapeutic data

that will influence the management and outcomes of coronary atherosclerosis.

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