Computed Tomographic Angiography for Localizing the Site of Plaque Disruption/Thrombus: Is Detection So Complex?

John A. Ambrose, MD; Sundararajan Srikanth, MD

In the 1980s, our group published a series of articles using invasive angiography (ICA) to investigate the pathogenesis of unstable angina and acute myocardial infarction.1-5 In individuals in whom an angina-producing lesion could be assessed angiographically and the vessel was <100% occluded at the time of angiography, the qualitative morphology of these lesions was different from that of lesions associated with stable angina.1 Unstable angina was precisely defined as either the acute onset of rest pain or crescendo angina with an abrupt increase in duration and/or frequency in angina pectoris. Myocardial infarction was defined according to the terminology of the day as either subendocardial or transmural myocardial infarction.

Unstable angina or infarct lesions were severe (>70% diameter stenosis) and were usually eccentric with irregular borders, overhanging edges, ulcerations, and/or intra luminal filling defects. These lesions were found in more than two-thirds of the culprit vessels and were initially called type II eccentric lesions; later, they were called complex lesions.6 We proposed that these lesions represented plaque disruption and/or intracoronary thrombus formation, based on the postmortem angiographic/histological correlations of Levin and Fallon.7 These authors found that eccentric and irregular lesions on postmortem angiography in patients dying after myocardial infarction represented plaque disruption and or intracoronary thrombus formation in 79% on pathological examination. Other angiographic studies and other modalities including angioscopy and intravascular ultrasound have corroborated our initial observations in acute coronary syndromes (ACS).8,9 In patients with stable angina and a complex culprit lesion, it has also been shown that their outcome on follow-up was worse than outcomes for those without a complex lesion.10

Can the complex lesion representing plaque disruption/intracoronary thrombus formation be detected noninvasively? Computed tomographic angiography (CTA) is an established tool for plaque characterization that can not only evaluate luminal narrowing but also characterize the arterial wall of the coronary arteries.11 Initial studies with CTA in patients presenting with an ACS showed that the culprit plaque was positively remodeled and the plaque had a low Hounsfield density, with spotty calcification.12 A subsequent study suggested that plaques with these same characteristics determined by CTA predicted subsequent ACS on follow-up. However, it was unclear whether the lesion responsible for the ACS always developed at the same plaque site as on the initial study.13

In this issue of Circulation: Cardiovascular Imaging, Madder et al14 expand on the utility of CTA by adding a qualitative assessment to the quantitative evaluation of lesions. In their study, CTA was retrospectively compared with ICA for the presence or absence of plaque disruption. In patients with a diagnosis of unstable angina undergoing CTA before ICA, all plaques with >25% stenosis by CTA were evaluated for CTA features of disruption and compared with the ICA definition of a complex lesion using “Ambrose” criteria, which was considered their gold standard. Plaques with either plaque ulceration or intraplaque dye penetration (the 2 characteristics used to define plaque disruption by CTA) were more voluminous; nearly all (94.5%) were positively remodeled, and these had lower plaque attenuation than nondisrupted plaques by CTA. CTA features of disruption correlated with the ICA complex lesions with moderate sensitivity and good specificity. The presence of either plaque ulceration and/or intraplaque dye penetration on CTA was 81% sensitive and 79% specific for the detection of a complex lesion by ICA. The positive predictive value was 58% and the negative predictive value was 92%. These authors concluded that CTA could delineate features of plaque disruption including ulceration and intraplaque dye penetration, which were specific markers of invasively identified complex lesions. They also suggested that this methodology might be clinically useful in identifying high-risk patients presenting with acute chest pain or in identifying patients with multiple plaque ruptures, some of which may be clinically silent but “vulnerable.”

Before accepting CTA as a reliable maker of plaque disruption, certain potential limitations of this study must be considered beyond those discussed in their report. (1) First and foremost, this was a retrospective analysis, and the patients studied represented a low-risk group of patients. The retrospective design resulted in a hiatus between the 2 imaging modalities (in some instances by as much as a month). This temporal separation complicates the comparisons between lesions using the 2 modalities and probably is responsible for the fact that CTA did not demonstrate intracoronary thrombus in any case. In addition, the inclusion characteristics of unstable angina used in this article excluded most patients with rest pain. Other patients in the study carried a diagnosis of new-onset angina as the definition of unstable angina. It is unknown if these patients fall...
under the true umbrella of unstable angina because only new-onset angina and severe angina (class ≥III) constitute an appropriate definition for unstable angina. An angina-producing or infarct-related stenosis was identified, and its morphology was characterized (simple versus complex). In the study by Maddler et al, CT lesions with >25% stenosis were compared with invasive angiography. The significance of taking these less-than-severe lesions and comparing their morphology with ICA is of unclear significance because there has not been adequate validation of ICA in qualitatively complex but mild lesions. Ideally, as a more valid proof of concept, future studies should assess sensitivity, specificity, and positive and negative predictive values for culprit lesions in a more acute setting with little temporal separation between the 2 techniques. (3) There was ambiguity in the comparisons of culprit plaques between the 2 methodologies. Although both techniques indicated an incidence of complex/disrupted plaques in about 60% of culprit lesions, whether there was concordance between the 2 techniques for a given culprit lesion is not clear. (4) The authors of the present study suggest that coronary calcification might be an explanation for why CTA missed up to 19% of complex lesions identified by ICA. However, the presence of coronary calcification also interferes with the qualitative assessment of coronary morphology by ICA, particularly in overdiagnosing intra coronary thrombus when calcium is present. (5) Is invasive angiography the best gold standard for diagnosing plaque disruption? It has been shown that this definition of a complex lesion is very specific for plaque disruption/intracoronary thrombus as long as angiography is properly performed with adequate, orthogonal views that minimize vessel overlap and vessel foreshortening. However, its sensitivity is only moderate. Future CTA comparisons might consider other invasive methods including intravascular ultrasound or ocular coherence tomography in appropriate patients.

Nevertheless, this article represents a first step in developing a proven noninvasive detector of plaque disruption. Additional studies will be necessary. Although a prospective study in an acute population with ACS in which the CTA and ICA studies are performed in close proximity will address the question of how well CTA mimics ICA in diagnosing plaque disruption/intracoronary thrombus, the ethics of such a study also must be considered. If prospective evaluations show excellent sensitivity and specificity of the technique, the clinical utility of CTA for this purpose could be significant. Furthermore, the recently published PROSPECT (Providing Regional Observations to Study Predictors of Events in the Coronary Tree) trial suggests that the identification of the so-called “vulnerable plaque” responsible for subsequent acute coronary events remains difficult if not presently impossible. A noninvasive detector of plaque disruption might hold promise for identifying some such lesion, thus demystifying the progression from an asymptomatic plaque to the thrombosed plaque responsible for unstable angina, acute myocardial infarction, and a majority of sudden coronary death.

Disclosures

None.

References

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