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Review Article

Methods of plaque quantification and characterization by cardiac computed tomography

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Abstract. The pathologic evolution of coronary artery atherosclerosis occurs slowly over decades, which may provide an opportunity for diagnostic imaging to identify patients before clinical events evolve. Cardiac computed tomography (CT) is an emerging noninvasive imaging tool, which can visualize the entire coronary tree with submillimeter resolution. We reviewed the current status of cardiac CT to qualitatively and quantitatively determine coronary plaque dimensions and composition, and its potential to improve our understanding of the natural history of coronary artery disease as well as prevention of cardiovascular events.

Background

Even though effective treatment strategies to lower coronary event risk are available, an estimated 1.3 million Americans will have a myocardial infarction in 2009, and approximately 37% of these Americans will die of it.[1] A main reason for these devastating statistics is that between 50% and 60% of myocardial infarctions occur in previously asymptomatic persons with no significant coronary artery stenosis. In the majority of the cases (two-thirds), the rupture of a thin cap fibroatheroma and the sudden thrombotic occlusion of a main epicardial vessel leads to the acute event.[2,3] In approximately one-third of patients, the thrombus is formed on an intact plaque after erosion of the intimal surface.[3,4]

Although invasive technologies such as intravascular ultrasound (IVUS), optical coherence tomography, infrared spectroscopy, and angioscopy were shown to identify characteristics of high-risk plaques, these tests are not feasible in asymptomatic patients.[5] In contrast, a noninvasive method with the ability to characterize and quantify features of individual plaque and overall coronary atherosclerotic burden could have a tremendous effect on prevention and treatment of coronary artery disease.[4,6,7]

By identifying patients with high-risk coronary plaques, early therapeutic interventions could be initialized, and treatment effect on plaque size and composition continuously monitored. Furthermore, a noninvasive imaging technique, which is able to quantify and characterize the coronary plaque burden, holds the promise to significantly shorten the length of clinical regression/progression trials by monitoring changes in plaque composition and dimensions.

In this article, the current status of computed tomography (CT)–based detection of coronary atherosclerosis with an emphasis on noncalcified plaque is reviewed.

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Furthermore, a perspective on the prerequisites and potential benefits of improved quantification and characterization of coronary artery disease are provided.

Current methods of plaque quantification and characterization

IVUS is a catheter-based imaging technique, which permits the assessment of atherosclerotic plaque in clinical practice and research. It is considered as the clinical "gold standard" for detection and quantification of coronary plaques.[8] IVUS with a spatial resolution of approximately 150 microns permits visualization of normal vessel wall and early atherosclerotic lesions.[9] Cross-sectional analysis of IVUS images permits the measurements of atheroma dimensions with a close correlation to histology ($r = 0.84–0.94$, $P < 0.0001$), allowing longitudinal assessment of changes in plaque dimensions with a high accuracy.[10,11] IVUS has also been used in clinical trials to assess the effect of lipid-lowering therapies on plaque progression.[12–14] IVUS assessments of patients with coronary artery disease (CAD) in the ASTEROID study documented a reduction in the total atheroma volume of -14.7 mm^3 during 24 months of follow-up in patients treated with rosuvastatin.[12] In the REVERSAL study, the mean change in total atheroma volume was 5.1 mm^3 in the pravastatin treatment group and -0.4 mm^3 in the atorvastatin group ($P = 0.02$).[13] Despite the promising results of these trials, the use of IVUS scanning as a surrogate for clinical events in coronary disease trials remains controversial, mainly because the IVUS-derived indexes of plaque size failed to predict cardiovascular events in all trials reported so far.[15] Moreover, the invasive nature of IVUS with the associated risks precludes its use in asymptomatic patients. Importantly, use of IVUS is limited in patients with severe coronary stenosis or occlusion. In addition, IVUS-based plaque measurements are typically limited to 1 or 2 coronary segments, and it remains doubtful whether this information is representative of the patient's overall plaque growth in clinical trials.

Coronary CT imaging

Multidetector-row CT (MDCT) permits imaging of calcified coronary atherosclerotic plaque using noncontrast scan and the additional detection of noncalcified plaque and luminal narrowing by using contrast-enhanced image acquisition.

Detection of coronary plaque by MDCT

The newest MDCT technology with gantry rotation times of 270–350 milliseconds, temporal resolution of 75–106 milliseconds, coverage in z-direction of 3.2–16 cm, and isotropic resolution of 0.4 mm now provides technical prerequisites for coronary atherosclerotic plaque imaging.[16–22] Thus, research targeting the qualitative and quantitative assessment of coronary plaque, including assessment of plaque size, composition, and remodeling is feasible.[20,23–25]

The normal coronary wall (intimal thickness, 0.15 ± 0.07 mm in healthy adults <50 years of age and in IVUS studies[9] labeled as <0.5 mm) cannot be assessed because of limits in spatial CT resolution. In contrast, plaques of potential clinical importance tend to be large, have a sizeable necrotic core (2–17 mm in length; median, 8 mm),[3] and are often (95%) found in the proximal coronary segments, which make them accessible for CT-based visualization. Even the typical lipid pool (1–5 mm^2) and core dimensions (often >1.0 mm^2)[3,26] are within the spatial detection limits of CT. Furthermore, 95% of high-risk plaques are confined to the proximal and mid segments of the coronary arteries, and most of these lesions are accompanied by positive remodeling. These morphologic features are promising imaging targets for MDCT-based plaque detection, quantification, and characterization.

Earlier clinical studies relied on 16-slice technology with limited temporal and spatial resolutions. These pioneer studies provided the initial data indicating a reasonable overall diagnostic accuracy per segment compared with IVUS with limitations to detect noncalcified plaque[20,27] (Table 1).

More studies were performed after 64-slice MDCT was introduced in 2005. The new 64-slice MDCT scanners provided improved spatial and temporal resolutions. However, these technologic advances were not always reflected in the results of subsequent studies (Table 1). Leber et al were able to show slightly improved sensitivity for noncalcified plaque detection with 64-slice MDCT compared to their previous findings with 16-slice MDCT (83% versus 78%).[27,29] However, the sensitivity for calcified plaque detection and, more importantly, the specificity for overall plaque detection did not change considerably (95% versus 95% and 94% versus 92%, respectively).[29] Sun et al[30] reported excellent sensitivity (97%) and specificity (90%) of 64-MDCT for the detection of coronary plaques. The results of a recent publication are in accordance with the above-mentioned 64-slice MDCT studies with sensitivity and specificity values for the detection of coronary plaque of 95% and 89%, respectively.[31] Despite the improved sensitivity values for the detection of noncalcified plaque with 64-slice CT, the specificity has not changed significantly with the advances in CT technology, probably because of the minor improvements in spatial and contrast resolutions. Furthermore, the accuracy of coronary CT angiography for plaque detection may be lower in everyday clinical practice and in a population with lower prevalence of CAD, because most published studies included only preselected, symptomatic patients with high prevalence of CAD and excellent image quality.