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CARDIOLOGY // IMAGING

Computed Tomography Biomarkers of Vulnerable Coronary Plaques

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ABSTRACT

An unstable plaque has a high risk of thrombosis and at the same time for a fast progression of the stenosis degree. Also, "high-risk plaque" and "thrombosis-prone plaque" are used as synonym terms for characterization of a vulnerable plaque. The imaging biomarkers for vulnerable coronary plaques are considered to be spotty calcifications, active remodeling, low-density atheroma and the presence of a ring-like attenuation pattern, also known as the napkin-ring sign. Computed cardiac tomography can determine the plaque composition by assessing the plaque density, which is measured in Hounsfield units (HU). The aim of this manuscript was to provide an update about the most frequently used biomarkers of vulnerability in a vulnerable plaque with the help of computed cardiac tomography.

Keywords: unstable plaque, vulnerability biomarkers, CTA, VH-IVUS, OCT

INTRODUCTION

A coronary atherosclerotic plaque, which is considered vulnerable, has a high risk of thrombosis and fast progression of the stenosis degree. Also, "high-risk plaque" and "thrombosis-prone plaque" are used as synonyms for the characterization of unstable plaques.[1] The most frequent form of vulnerable plaque is the thin-cap fibroatheroma, which is associated with a local inflammatory response, leading to 60–70% of acute coronary syndromes. The remaining 30–40% of coronary syndromes occur at proteoglycan-rich erosion sites, appearing more frequently in young women. The unstable plaques are supplied with blood by an abundant vasa vasorum, which penetrates the plaque from intima to adventitia.[2]

The aim of this manuscript is to perform an update on the most current knowledge regarding the noninvasive imaging biomarkers of vulnerability in an unstable coronary plaque, as demonstrated by computed tomography angiography (CTA).

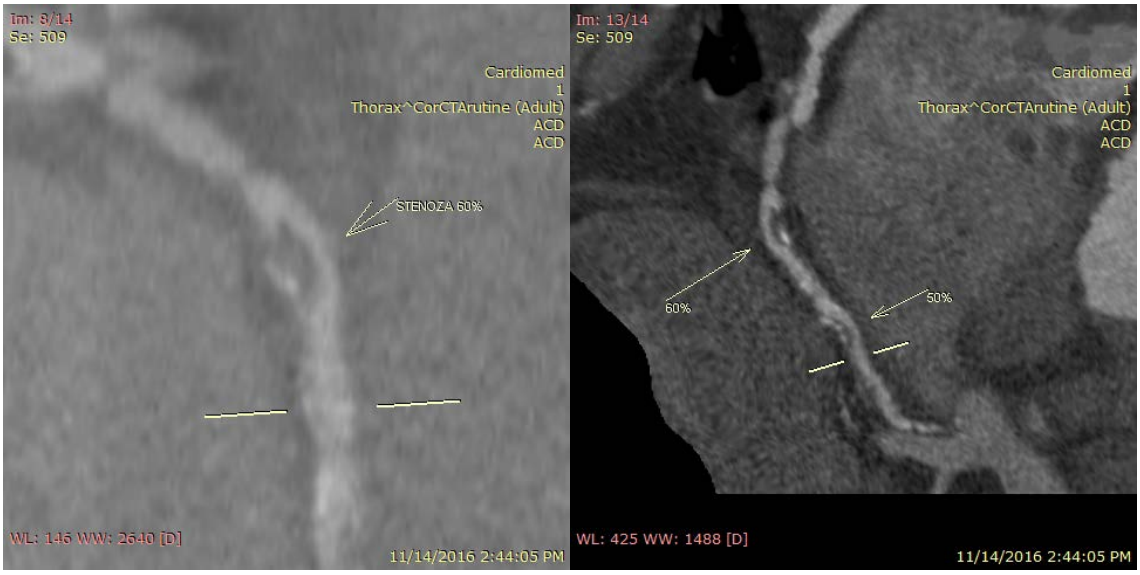

FIGURE 1. Positive vascular remodeling – CTA imaging

MARKERS OF PLAQUE INSTABILITY

The noninvasive imaging biomarkers of vulnerable coronary plaques, shown to be strong predictors for the occurrence of acute coronary events, are represented by spotty calcifications, active positive vascular remodeling (Figure 1), low-density atheroma, and the presence of a ring-like attenuation pattern, also known as the napkin-ring sign.[3,4] The spotty calcifications are valuable markers in predicting the rupture of coronary plaques. It has been demonstrated that the smaller the spotty calcifications are within the plaque, the higher the risk for the presence of a necrotic core or a thin fibrous cap.[5] Also, it was demonstrated, in retrospective and prospective studies, that plaques with spotty calcifications and positive remodeling determined with the help of CTA, have an increased risk of rupture and evolution towards an acute coronary event.[6,7] Benedek *et al*. showed in a previous study that vulnerable plaques have larger volumes of low-density lipid cores and a low CT density plaque. A plaque density of <30 Hounsfield units (HU) is linked to the development of an acute coronary event.[8]

IMAGING EVALUATION TECHNIQUES FOR THE CORONARY VULNERABLE PLAQUE

It has been demonstrated that the presence of spotty calcifications, active remodeling and low density atheroma in a plaque, assessed with the help of CTA, is strongly associated with the rupture of the plaque, resulting in a higher rate of acute coronary syndromes during the 2-year follow-up.[1] Optical coherence tomography (OCT) is another imaging technique for the assessment of vulnerable coronary plaques. OCT has the ability to make accurate measurements of the fibrous cap, in the detriment of a limited penetration through the arterial wall. Near-infrared Spectroscopy (NIR) is a newly introduced technique, which can precisely describe lipid cores, but has a limited usability in describing plaque morphology and provides limited information about the coronary lumen.

Near-infrared diffuse reflectance spectroscopy (NIRS) is used frequently in fields such as chemistry, in identifying the chemical composition of substances. NIRS can easily penetrate through blood and surrounding tissues, and can describe precisely the details of cholesterol-rich plaques. VH-IVUS is an imaging technology that can precisely characterize the architecture of the vulnerable plague, in the detriment of spatial resolution.[9] This technique is extensively used in detecting and describing vulnerable plaques with a high risk of rupture. Studies demonstrated that combining one IVUS catheter and one NIRS probe in a single catheter, allowing both imaging techniques to be acquired simultaneously, is more efficient in detecting and describing plaques, than the techniques being used separately.[10] Hybrid approaches are already used and described in several clinical studies and can diminish the limitations that these methods have when used alone.[9]

OCT is currently the gold standard method for measuring the thickness of the fibrous cap and for the visualization of intimal rupture or intracoronary thrombus. The size of the fibrous cap is the most frequently assessed biomarker with the help of OCT. Studies found that a thin fibrous cap

(<65 microns) is an indicator of vulnerable plaque, with a high risk of rupture and evolving into an acute coronary syndrome.[11]

THE IMPORTANCE OF CTA IN THE ASSESSMENT OF VULNERABLE PLAQUES

CTA can determine plaque composition by assessing its density, which is measured in Hounsfield units. Intraluminal contrast has a density of 300 HU. If a calcified plaque is detected, the density will be greater than 400 HU.[12] Nace *et al.* assessed the role of CTA in the evaluation of 458 patients with acute chest pain but without acute coronary syndrome. Their results revealed that a non-calcified plaque (<130 HU) and a strictly calcified plaque (>130 HU) have a lower risk of developing major adverse cardiac events (MACE) at 13 months compared to subjects that presented mixed density plaques.[13] Studies suggested a cut-off value of 60 HU for identifying lipid-rich plaques, thus others have found that the optimal cut-off value can be different according to the computed tomography systems used, acquisition parameters and the vessel of approach.[14–16]

PROSPECTIVE FOLLOW-UP OF PATIENTS WITH VULNERABLE PLAQUES

CTA evaluation is effective in detecting plaques with a higher risk of tear among patients without atherosclerotic coronary artery disease. A high positive remodeling index (cut-off >1.4), low-attenuation plaque (cut-off <30 HU), plaque burden (cut-off >0.7) and napkin-ring sign (NRS) are plaque characteristics found in patients with an increased risk of suffering an acute coronary event during the long-term follow-up.[4,17,18] Nadijiri *et al.* demonstrated in a study with a 5-year follow-up period that included 1,168 subjects with coronary artery disease, that the presence of all four plaque characteristics of instability (low-attenuation plaque, napkin-ring sign, positive vascular remodeling and total non-calcified plaque volume) are predictors of major acute cardiac events, independent of the clinical risk at presentation.[19]

CONCLUSIONS

The developments made in the last years in computed tomography and related software have significantly improved the assessment and treatment of vulnerable coronary plaques. Spotty calcifications, active remodeling and low-density atheroma are considered CT imaging biomarkers of vulnerability if found in the same plaque. However, further upgrades should be achieved in CTA for a better and detailed characterization of the vulnerable plaque.

CONFLICT OF INTEREST

Nothing to declare.

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