

## High-risk Plaque Imaging

*Ilan Gottlieb, Maria Eduarda Derenne*

*Fonte Imagem Medicina Diagnóstica, Rio de Janeiro, RJ – Brasil; Casa de Saúde São José, Rio de Janeiro, RJ – Brazil.*

Few pathologies are more complex than coronary artery disease (CAD). More than 200 risk factors for CAD published to date and more than 400 genetic loci implicated,<sup>1</sup> associated with the long clinical course between the onset of atherosclerotic plaque and the clinical event,<sup>2</sup> are evidence of how hard it is to manage and prevent CAD. This tremendous heterogeneity makes it difficult to create clinical scores that are valid in different populations. One way to overcome the difficulty in predicting who will develop coronary artery disease is the phenotypic diagnosis of the disease, which allows to see on the other side of the mirror, that is, it makes it possible to identify organisms whose combination of risk factors — whatever they are — have developed the disease, even without symptoms, rather than determining who would be predisposed to developing the disease.<sup>3</sup> In pathologies as prevalent and as lethal as CAD, the strategy of early phenotypic diagnosis makes sense. Population studies have demonstrated and confirmed the excellent cardiovascular prognosis of patients with normal coronary computed tomography angiography or calcium score (in whom preventive drug therapies would not be beneficial), as well as progressive worsening of cardiovascular prognosis in patients with progressive CAD, irrespective of the clinical risk factors involved.<sup>4</sup>

The noninvasive test that does the phenotypic evaluation of CAD more accurately and completely is coronary computed tomography angiography (CCTA).<sup>5</sup> This does not mean that all patients should have a CCTA without distinction, but it is relevant to better understand how to direct therapy based on the results of this test. There is ample scientific evidence supporting major coronary obstruction as an important prognostic factor in CAD.<sup>6</sup> CCTA is the most accurate noninvasive method in the diagnosis of major coronary obstruction, but there are many other aspects of CAD besides luminal obstruction that can also be assessed by the method. It is known that half of the infarctions and deaths occur in patients previously not diagnosed with CAD

(no symptoms and, therefore, no obstructive disease?) and that two thirds of acute coronary syndromes originate from plaques with stenosis smaller than 50% and five sixths from plaques smaller than 70%.<sup>7,8</sup>

The histopathological pattern of atherosclerotic plaques associated with instability and acute myocardial infarction is well known.<sup>9</sup> Vulnerable plaque is thin-walled, with high content of inflammatory cells and high concentration of fat-laden macrophages (foam cells), which is not always associated with significant luminal stenosis. CCTA can reproducibly identify plaque characteristics that are related to the histopathological findings of vulnerability,<sup>7,10</sup> namely: 1) Positive remodeling: this is the expansion of the plaque exiting the adventitia, defined as the distance between the adventitia greater than or equal to 10% of the reference value in the remote segment. Positive remodeling occurs on plaques with high inflammatory activity (inflammatory cells are believed to “digest” the outer vessel layers, allowing the plaque under the endothelium to grow in the opposite direction of the lumen). 2) Hypodensity within the plaque: defined as an area greater than 1 mm<sup>2</sup> with density smaller than 30 HU. This finding is related to the high content of foam cells and lower thickness of the fibrous cap. These CCTA findings are correlated with worse prognosis, regardless of the degree of fibrosis or clinical risk factors. There are two more CCTA findings that have been shown to have a prognostic impact, namely: 3) Punctiform calcification on the plaque (as opposed to gross calcifications). 4) Napkin-ring sign, defined as a hyperdense halo around a hypodense plate. Several studies confirm these findings, defined as high-risk characteristics, as an independent prognostic variable. For example, the Romicat II study demonstrated that even after adjustment for luminal stenosis and clinical variables, the presence of at least one high-risk characteristic was associated with an impressive 8.9-fold increase in the risk of cardiovascular events.<sup>7</sup> In view of these findings, the Society of Cardiovascular Computed Tomography (SCCT) attributed a “V” modifier of vulnerability to the CAD-RADS coronary lesion classification system.<sup>11</sup>

With the non-invasive diagnostic possibility of plaque vulnerability, the vulnerable plaque theory gains new impetus. However, it should be noted that prognostic marker is not necessarily a therapeutic goal. Although it is reasonable to increase the intensity and vigilance of clinical treatment in patients with high-risk plaques, it is still necessary to demonstrate that these findings should guide coronary artery bypass grafting strategies.

### Keywords

Coronary Artery Disease; Diagnosis; CT Angiography.

**Mailing Address:** Ilan Gottlieb •

Casa de Saúde São José. Rua Macedo Sobrinho, 21 Radiologia.

Rio de Janeiro, RJ, Brazil.

E-mail.: ilangottlieb@gmail.com

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