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The use of coronary artery calcium scanning in detection and risk stratification of coronary artery disease

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ABSTRACT

Coronary artery calcium (CAC) scan can be obtained using chest computed tomography, with no use of contrast agents, and with a relatively low radiation exposure. The mere absence of calcium is associated with a good prognosis in asymptomatic subjects and in patients at low to medium risk of coronary artery disease. CAC can be quantified in different ways, with higher scores being associated with a higher cardiovascular risk. CAC carries both diagnostic and prognostic information over and above that determined by classical risk factors. This paper presents the overview of the current use of CAC scanning, its advantages and limitations, as well as potential future applications.

Contents

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Introduction

Coronary artery calcium (CAC) deposits are almost entirely due to atherosclerosis. It is, therefore, logical to expect that CAC measurement may be a useful tool in excluding or confirming the presence of coronary artery disease (CAD) in subjects with or without symptoms, but with no proven cardiovascular disease (CVD).

CAC can be reliably assessed by means of computed tomography (CT).

By the widely accepted definition, coronary calcium is present when the threshold of 130 Hounsfeld units is exceeded in at least 3 adjacent pixels [1].

Although multiple quantification criteria can be applied, the Agatston score, reflected in Agatston units (AU), and determined by the product of the calcified plaque area and maximal calcium lesion density is most commonly used [2].

The lack of coronary calcium deposits does not exclude the presence of obstructive changes in the coronary tree, especially in patients aged <45 years. For example, in one study including a group of 166 subjects with intermediate CAD probability and CAC score (CACS) = 0 AU, a non-significant stenosis was present in 10%, and a significant one in 2% of patients [3]. In another study [4] no coronary lesions were found in asymptomatic subjects, while 0.8% of those with symptoms had soft obstructive changes. When it comes to high-risk groups, like patients with symptoms suggestive of ischemia who have clinical indications to invasive coronary angiography, the prevalence of obstructive stenoses in those with CACS = 0 may be as high as 19% [5].

In the MESA study, a positive CAC was a better predictor of incident coronary events than carotid plaque presence and increased carotid intima-media thickness [6].

In general, patients with no detectable CAC are at very low risk of CV events. The presence of CAC increases the risk in an incremental mode. In long-term, the relative risk of death or MI is about threefold higher in patients with CACS 1–10 as compared to those with negative CAC. A similar difference is seen between individuals with CACS > 100 and those with CACS values between 1 and 99 (RR 3.20; 95% CI 1.17–8.71) [7].

Traditionally, people with positive CAC, with the score values 1–100, 100–400 and >400 AU, are considered to be at low, intermediate and high risk of both ischemia and CV events. CACS values >400 AU can be regarded as a CAD equivalent, with a 10-year event rate of over 20%, even in asymptomatic patients [1].

However, CACS interpretation should always take into account the clinical context, including at least the symptoms and age.

Measurement of CAC volume and density may have an added value to the CACS measured in the Agatston units. In a large cohort of patients in the MESA study, followed for the median of 7.6 years, CAC volume showed an independent positive association with CAD events, while CAC density was associated with an independent inverse association at any level of CAC volume [8]. Therefore, CAC density should probably be taken into consideration in risk evaluation.

The American appropriateness use criteria for CT scanning [9] give a limited mention to the non-contrast coronary CT as a stand-alone diagnostic method. CACS assessment is deemed appropriate in patients with positive family history of premature CAD, and in asymptomatic subjects with no known CAD being in the intermediate risk group, as assessed by age, sex and symptoms.

The ESC guidelines on the management of patients with stable CAD [10] underscore that the amount of calcium correlates with the extent of atherosclerotic changes, but the correlation with the presence of hemodynamically significant stenosis is rather poor. In practice, this means that high CACS is not always associated with a significant coronary stenosis, and – on the other hand – the CACS = 0 cannot exclude CAD, especially in young patients presenting with an acute coronary syndrome.

A comprehensive overview of the pathogenesis and prognostic implications of coronary artery calcification can be found in the paper by Madhavan et al. [11].

CAC in asymptomatic subjects

In a systematic review including more than 85,000 asymptomatic subjects with CAC score = 0, only 0.56% experienced a cardiovascular event during a mean follow-up of 51 months [12]. Therefore, the absence of CAC was associated with a very low risk of cardiovascular events (0.13% per year. The absence of CAC had a 93–99% negative predictive value for detection of significant coronary lesions on invasive angiography.

Even low but positive CACS seem to be associated with an increased risk as compared to those with no CAC in asymptomatic subjects. In a subpopulation of patients from the MESA study with CACS 0–10 AU, in the analysis adjusted for age, gender, race and CAD risk factors, the subjects with CACS 1–10 AU showed a threefold increase in risk of hard CAD events (CAD death or non-fatal myocardial infarction) compared to those with CACS = 0 [13].

Higher CACS value tend to bear an incremental risk of CAD events.

Al Rifai et al. [14] followed-up a group of 4234 asymptomatic subjects with CAC score ≥400 AU. Their mean age was 64 years, males constituted 65% of the group, and the median CAC score was 809. In multivariable analysis age, diabetes, smoking, increasing CAC score and dyslipidemia were associated with 1-year all-cause mortality (HR for CAC 1.33; 95% CI 1.11–1.56). Diabetes and smoking showed the strongest association (respective HR 2.62 and 2.42), suggesting that in the presence