A contemporary role of coronary artery calcium scoring in the assessment of the risk for coronary artery disease

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Abstract: The growing prevalence of coronary artery disease, also in younger populations, stimulates constant development of methods of coronary atherogenesis risk stratification and early diagnosis. The coronary artery calcium score obtain in computed tomography is a simple parameter that requires only a relatively small radiation dose. Studies published so far have provided consistent evidence in support of its specificity to exclude coronary artery disease, along with its predictive value for future cardiac events. Our paper is a review of peerviewed journals regarding in coronary artery calcium scoring, including the most recent guidelines on its use in establishing a diagnosis of coronary artery disease.

Key words: coronary artery calcium score, coronary artery disease risk

The unstable coronary plaque rupture, followed by clot and the subsequent calcium deposit formation, is an integral and widely recognized process involved in atherogenesis. The calcium deposits are believed to be found in the atherosclerotic lesions within the arterial wall (fig. 1) and not in normal vessels. The coronary calcifications are more common in the elderly, however they have been also occasionally reported in individuals in their twenties, which may reflect the early stages of atherogenesis. The coronary artery calcium score (CACS), assessed by means of computed tomography, is an acknowledged indicator of coronary atherosclerotic plaque burden [1]. Percentile charts have been developed to represent the expected extent of coronary calcification, depending on age and sex (fig. 2). In line with previous observations on gender differences in the prevalence of atherosclerotic vascular disease, the CACS values up to the age of 60 are typically higher in males; in older subjects the difference between males and females diminishes. Some regional differences in calcification distribution have also been noted. The CACS values obtained in European population tend to be lower than those in the North Americans, particularly in individuals with no cardiologic treatment record [2].

The need for intensive prevention of cardiovascular diseases remains beyond discussion in patients with a 10-year risk of coronary artery disease (CAD) exceeding 20% - the high risk group according to Framingham Risk Score (FRS). The majority of coronary events, however, occur in CAD patients with the intermediate long-term risk (10–20% risk of coronary events within 10 years). Numerous reports indicate a particular value of CACS, along with the FRS, in the prediction, if evaluated in combination, of coronary events in that group of patients [3,4].

The probability of the presence of CAD remains strictly related to CACS. The cut-off values, which are considered to differentiate between groups with low, intermediate and high risk of hemodynamically significant CAD incidence, are 100 and 400 Agatston units (A.u.), respectively. According to the published data, the myocardial perfusion determined in single photon emission computed tomography (MP-SPECT) proves impaired in less than 1% of patients with CACS below 100 A.u. The value of CACS exceeding 400 A.u. conveys a 40–50% risk of abnormal MP-SPECT findings. The intermediate values of CACS reflect approximately 12% risk of myocardial perfusion defect [5,6]. A head-to-head study, involving 140 patients, has been performed to compare MP-SPECT and full-protocol (both CACS and coronary angiography - CA) multislice spiral computed tomography (MSCT). Strikingly, only about a half of patients with unaltered myocardial perfusion in MP-SPECT were found to have a normal MSCT result [7]. These data indicate that both diagnostic methods along with high efficacy of MSCT and CACS complement in identifying the subclinical coronary arteriosclerosis.

Detection of particularly high CACS values (>800 or >1000 A.u. – center-dependable) most likely justifies performing invasive CA without prior MSCT CA. Such a view is

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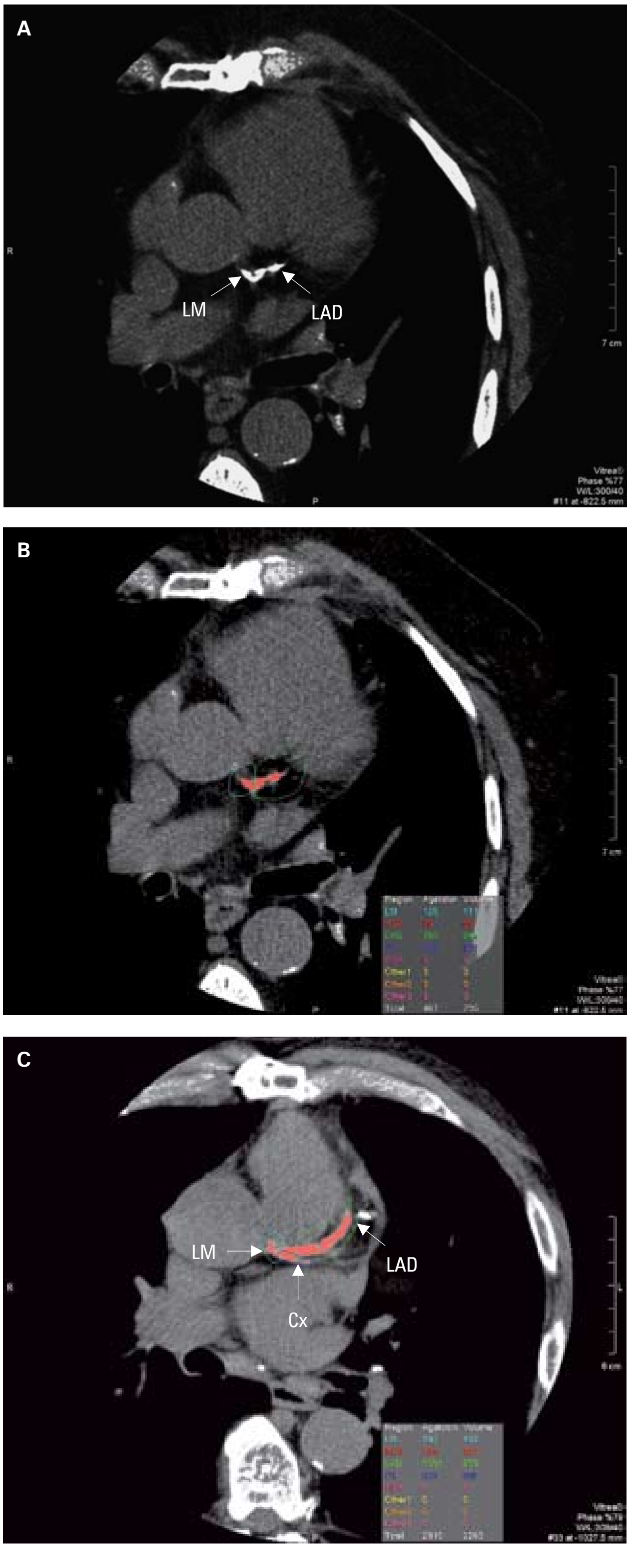
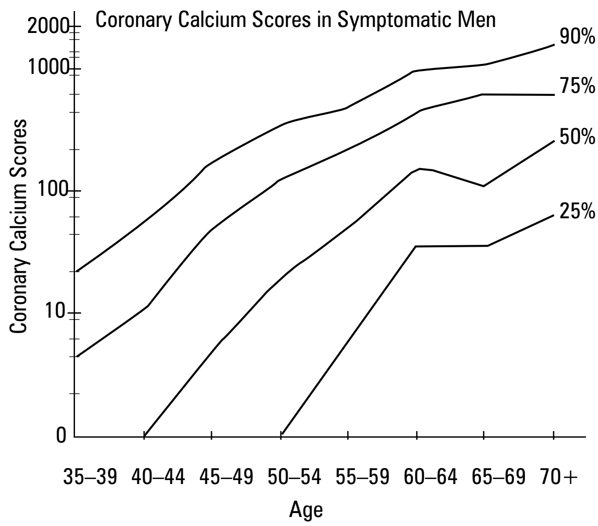


Ryc. 1. A-B. Visible calcifications in the left main (LM) coronary artery and in the proximal segment of the left anterior descending (LAD). **C.** Massive calcifications in the LM, LAD and circumflex artery (Cx) in another patient

Calcium Score

Region	Agatston	Volumen
LM	532	401
RCA	709	602
LAD	1071	842
CX	586	490
PDA	0	0
other 1	0	0
other 2	0	0
other 3	0	0
total	2898	2335

Density threshold (HU): 130
Pixel threshold: 3
Algorithm: Discrete



calcium score	implication	risk of coronary artery disease
0	no identifiable plaque	very low, generally less than 5 percent
1–10	minimal identifiable plaque	very unlikely, less than 10 percent
11–100	definite, at least mild atherosclerotic plaque	mild or minimal coronary stenosis likely
101–400	definite, at least moderate atherosclerotic plaque	mild coronary artery disease highly likely, significant narrowing possible
401	extensive atherosclerotic plaque	high likelihood of at least one significant coronary stenosis

Ryc. 2. The exemple result sheet coronary artery calcium score (CACS)

validated by a remarkably high probability of hemodynamically significant stenosis occurrence in high-CACS patients. Furthermore, extensive coronary calcifications may severely hinder the reliability of CA interpretation in MSCT. The amount of coronary calcifications correlates with the presence and severity of stenoses demonstrated using invasive CA, no direct association between calcifications and stenoses localization has been proven, though. It is worth underlining that the negative (zero) CACS has a particularly high specificity to exclude CAD [8].

There are numerous clinical reports on a significant prognostic value of CACS. In a study involving 10 000 asymptomatic individuals followed-up for 5 years, coronary calcification extent has been shown to better predict overall mortality than conventional risk factors do [9]. Further prospective trials proved the CACS efficacy in predicting the CAD presence, regardless of traditional risk factors and C-reactive protein level. Furthermore, the CACS ability to predict cardiac events was confirmed to be higher than that shown by FRS [10,11]. A positive correlation has also been demonstrated between CACS and other non-invasive, well-established CAD predictors, such as carotid artery intima-media complex thickness [12] and brachial artery stiffness [13]. In CAD patients with intermediate long-term risk the CACS values above 100 A.u. or the 75^{th} percentile substantiate upgrading an individual to high-risk group, whereas those below 10 A.u. or the 25^{th} percentile reflect the actual low long-term risk of CAD. Moreover, there is also a concept suggesting that in asymptomatic subjects CACS evaluation should always precede invasive CA or even exercise ECG testing (to be performed if CACS is above 400 A.u.) [14]. According to some investigators while estimating the FRS one should add 10 years to metrical age for the CACS values between the 75^{th} and 90^{th} percentiles, and 20 years for those above the 90^{th} percentile [15]. Thus, the CACS testing in asymptomatic patients with intermediate long-term risk of CAD may successfully discriminate those who benefit from advanced diagnostic procedures or more rigorous lipid profile target values and therefore considerably influence the diagnosis and therapy.

The CACS usefulness to predict coronary incidents in asymptomatic patients has also been confirmed in meta-analyses of randomized clinical trials [16]. In comparison to the zero CACS, its values between 1–100 A.u. increase the risk of coronary event by 2.1-fold, while those above 400 A.u. by 10-fold ($p < 0.0001$). According to the data recently published by American Heart Association (AHA) [4] any detectable coronary calcium indicates about 4-fold increase of event relative risk of coronary or myocardial infarction if compared to zero CACS ($n = 395$ incidents/27 622 pts, $p < 0.0001$). In the same analysis the zero CACS associates with a remarkably low risk (0.4%) of coronary incident or myocardial infarction during 3 to 5 years of follow-up ($n = 49$ incidents/11 815 pts).

The exclusion of coronary calcifications presence (zero CACS) may prove an efficient "sieve" preceding referral of a symptomatic patient to invasive CA [4]. CACS values below 100 A.u. correlate with low risk (<3%) of significant stenosis (>50%) detection in invasive CA [17,18]. Zero CACS reaches a 96–100% negative predictive value to exclude the presence of stenoses in invasive CA [17-19]. We need, however, to acknowledge that serial CACS testing has not yet been approved as a tool to monitor the CAD progression, regardless of the symptom presence or absence [4].

It should be emphasized that CACS maintains a highly favorable benefit to risk ratio. The effective radiation dose conveyed by a contemporary 64-slice computed tomography protocol is estimated at about 11.0 ±4.1 mSv [20]. Liminitation of the procedure to CACS testing solely reduces the effective radiation dose to approximately 1–4.1 mSv [21]. This constitutes about a half of a yearly environmental radiation dose [22]. For comparison, a chest X-ray delivers an effective radiation dose of 0.2 mSv [22], while an invasive CA – roughly 2.1–56 mSv [22,23]. The CACS testing is a non-invasive procedure carries no additional risk of vessels cannulation complications, nor does it require contrast agent administration.

Despite the above mentioned observations the American College of Cardiology (ACC) statement, published in October, 2006, remained rather conservative [24]. No indication for CACS testing in asymptomatic patients was found fully appropriate. Only in intermediate and high long-term CAD risk patients (>10% within 10 years according to FRS) was the method's level of appropriateness defined as uncertain. In asymptomatic low risk subjects CACS testing was declared inappropriate. More favorable judgment of the technique has been introduced in the 2007 ACC/AHA guidelines. They emphasize the usefulness of CACS testing in asymptomatic intermediate CAD risk patients (possibility of upgrading the high-CACS patient to the high risk group) as well as in low CAD risk patients with atypical symptoms (to reliably exclude CAD) [4].

We sincerely hope that further studies on a role of coronary calcium in estimating the total coronary risk along with the increasing accessibility of CACS testing, will increase the routine use of that valuable parameter.

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