Review Article

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Coronary Artery Calcium Data and Reporting System (CAC-DRS): A Primer

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ABSTRACT

The Coronary Artery Calcium Data and Reporting System (CAC-DRS) is a standardized reporting method for calcium scoring on computed tomography. CAC-DRS is applied on a per-patient basis and represents the total calcium score with the number of vessels involved. There are 4 risk categories ranging from CAC-DRS 0 to CAC-DRS 3. CAC-DRS also provides risk prediction and treatment recommendations for each category. The main strengths of CAC-DRS include a detailed and meaningful representation of CAC, improved communication between physicians, risk stratification, appropriate treatment recommendations, and uniform data collection, which provides a framework for education and research. The major limitations of CAC-DRS include a few missing components, an overly simple visual approach without any standard reference, and treatment recommendations lacking a basis in clinical trials. This consistent yet straightforward method has the potential to systemize CAC scoring in both gated and non-gated scans.

Keywords: Coronary artery disease; CACDRS; Coronary artery calcium; Atherosclerosis

INTRODUCTION

Quantification of coronary artery calcium (CAC) is a reliable, reproducible, and strong predictor of cardiovascular risk. Studies have demonstrated that CAC is a reliable estimator of the risk of myocardial infarction, death due to coronary artery diseases (CADs) and all-cause mortality.[1][2] Multiple guidelines have endorsed the use of non-contrast computed tomography (CT) for CAC scoring in asymptomatic patients with intermediate-risk.[3-5] The first formal CAC score was introduced in 1990, and the subsequent CAC scores show varying strengths, weaknesses, and limitations. The traditional scoring methods include the Agatston score (AS), volume score (VS), mass score (MS), calcium coverage score (CCS), and visual score.[6] For the last 30 years, the AS has enhanced our ability to assess cardiovascular risk beyond the traditional risk factors. However, research over the last decade has identified several strategies for potential improvements.[7] One such concept is to standardize the reporting of CAC to facilitate clinical communication, prepare structured databases, implement appropriate patient management, and promote quality improvement. A new standardized reporting system, the coronary artery calcium and data and reporting system (CAC-DRS), was introduced recently

in 2018 by the Society of Cardiovascular Computed Tomography (SCCT).[8] In this review, we describe the traditional CAC scoring methods, noting their strengths, weaknesses, and limitations. We then discuss the features of CAC-DRS with illustrative examples, followed by its advantages, pitfalls, and future prospects.

CAC SCORING TECHNIQUES

AS

The AS is the most widely used scoring system in clinical practice. It was first proposed by Arthur Agatston and Warren Janowitz in 1990. The AS is derived from electron beam (EB) CT using 130-KVp tube voltage, 630-mAs tube current, 3-mm slice thickness, and a 512 × 512 reconstruction matrix. The score has been adapted to multidetector CT (MDCT) using 120 KVp, variable mA according to patient body weight, and 3-mm slice thickness. The score is a summed total score of all the calcified lesions and accounts for both the maximum coronary calcific density and the total area (**Figures 1** and **2**). Lesions with a CT attenuation value > 130 Hounsfield units (HU) and area ≥ 1 mm^2 are taken into consideration to avoid image noise (**Figure 3**). The individual lesion score is calculated by multiplying the lesion area with a density weighting factor (DWF). The DWF is derived from the maximum value of CT attenuation present within a given calcified plaque (DWF: 130 to 199 HU = 1; 200 to 299 HU = 2; 300 to 399 HU = 3; and ≥ 400 HU = 4).[9]

$$AS\ (lesion) = Area \times DWF$$

The individual scores are then added irrespective of the distribution and location to determine the total AS.

$$AS\ (total) = \sum AS\ (lesion)$$

Strengths and limitations

The greatest strength of AS is the vast large volume of available clinical data across age, gender and race and the multiple clinical risk stratification studies based on AS.[10][11] Although AS is the most commonly used score in clinical and research settings, it has many limitations. First, small variations due to noise or motion can have a significant impact on total AS, particularly if the maximum HU of the plaque is around the margins of the weighting factor strata. For example, a lesion with a maximum attenuation of 299 HU would translate into a 2-fold difference in the score in comparison with the same sized lesion with a maximum attenuation of 301 HU. Second, the AS increases nonlinearly with an increase in the amount of calcium. In addition, the AS is affected by the partial volume effect, which can lead to overestimation of the calcium score and assignment of high-risk categories. The combined effect of noise, motion, type of scanner, reconstruction window and partial volume averaging leads to substantial interscan variability, ranging from 15% to 22%.[12-15] AS calculation is based on fixed scanning parameters, and there is no mathematical correction or appropriate scaling method available if the parameters are changed.

VS

The VS was developed by Callister and colleagues in 1998.[15] The scanning parameters for VS are similar to those of the AS. A CT attenuation threshold of > 130 HU is applied. Only lesions with an area of more than 1 mm^2 are counted to avoid image noise. To calculate the VS, the area of calcification is multiplied by slice thickness rather than DWF (**Figures 1** and **2**).

$$VS\ (lesion) = Area \times Slice\ Thickness$$

The individual scores are then added irrespective of the location and distribution to determine the total VS.

Agatston score = area × density factor
Agatston score = 3 × 1 = 3

Density factor	
Max HU	Factor
130–199	1
200–299	2
300–399	3
≥ 400	4

Volume score = area × slice thickness
Volume score = 3 × 3 = 9 mm^3

Calcified area = 3 mm^2
Density (max) = 175 HU
Slice thickness = 3 mm
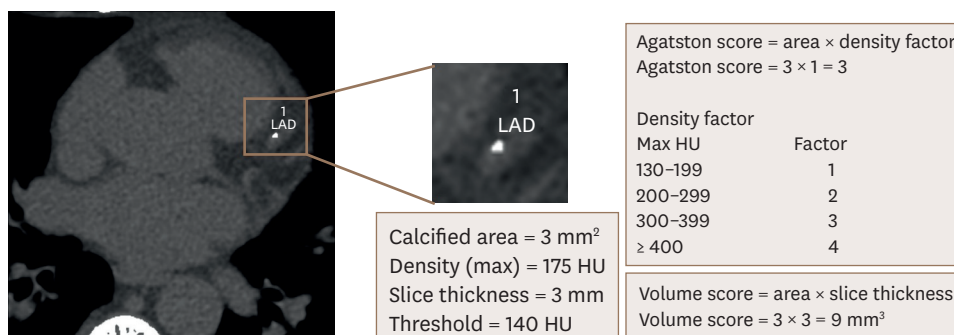Threshold = 140 HU

Figure 1. Examples for calculation of Agatston and volume score. The example shows a single calcified plaque with an area of 3 mm^2 and a maximum CT number of 175 HU. Agatston score is calculated by multiplying the area of the lesion with density factor. The density factor is determined using predefined cut off values. The volume score is determined by multiplying calcified area with slice thickness. The individual lesion scores are then added to generate the final result. CT: computed tomography, HU: Hounsfield units, LAD: left anterior descending.

Artery	Lesions	Volume / mm³	Equiv. Mass / mg	Score
LM	0	0.0	0.00	0.0
LAD	3	45.5	9.88	54.1
CX	7	184.0	41.64	216.6
RCA	3	27.0	4.73	24.1
Total	13	256.5	56.25	294.8
U1	0	0.0	0.00	0.0
U2	0	0.0	0.00	0.0

Settings
Score Type: User defined, Threshold: 130 HU (105.3 mg/cm³ CaHA)
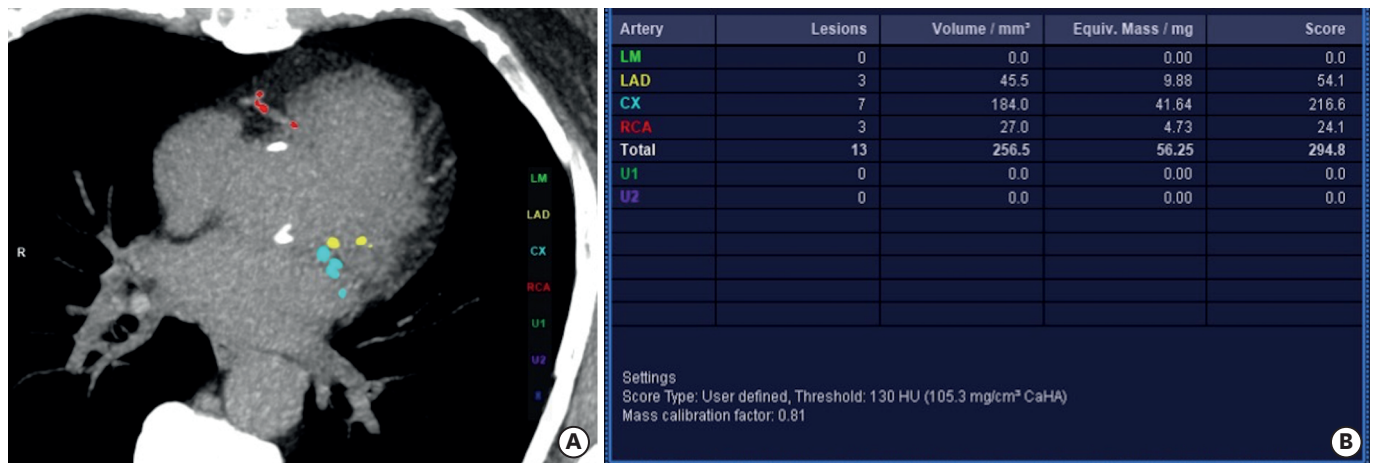Mass calibration factor: 0.81

Figure 2. Coronary calcium score. (A) Non-contrast ECG-gated axial CT image of coronary arteries demonstrate presence of multiple calcified plaques in the anatomic territory of proximal segments of LAD (yellow), left circumflex (blue) coronary arteries, and proximal segment of RCA (red) and its branch. The white dots represent the calcifications of the aortic root. (B) The measurement table provided by the CT workstation demonstrates the Agatston, volume and mass calcium score of each coronary artery and the total score. The threshold for calculating Agatston score is 130 HU. The mass calibration factor is 0.81.
ECG: electrocardiogram, CT: computed tomography, HU: Hounsfield units, LM: left main, LAD: left anterior descending, Cx: circumflex artery, RCA: right coronary artery.
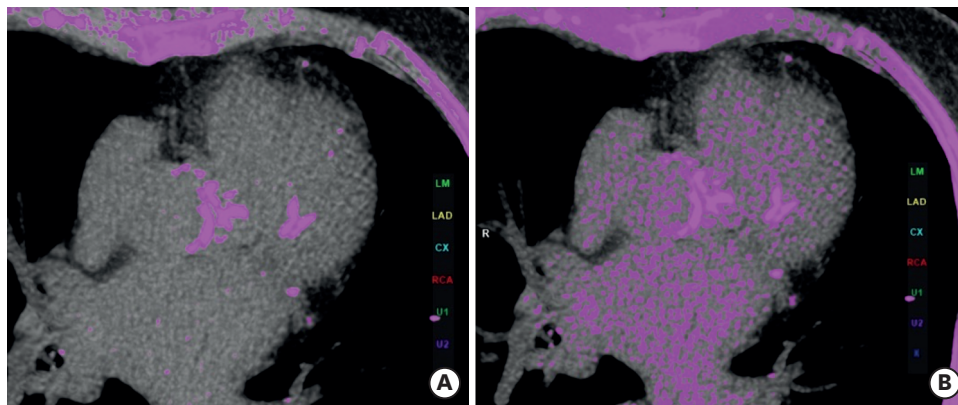

Figure 3. Effect of CT threshold on CAC score calculation. The threshold in (A) is set at 130 HU and in (B) at 110 HU. Lowering the threshold by 20 HU leads to a significant increase in image noise, which can alter the final score.
CT: computed tomography, HU: Hounsfield units, CAC: coronary artery calcium, LM: left main, LAD: left anterior descending, Cx: circumflex artery, RCA: right coronary artery.

$$VS\ (total)=\textstyle\sum VS\ (lesion)$$

Strengths and limitations
There are several advantages of the VS. First, it does not involve a DWF; therefore, it shows a linear increase with an increase in CAC. In addition, the absence of a DWF eliminates the assumption that high-density calcified plaques are more significantly associated with CADs than low-density plaques. Second, VS is less sensitive to noise, leading to better interscan reproducibility. The interscan variability of VS is 9% to 16%, which is less than that of AS (15–22%).[12-15] The limitations of VS are quite similar to those of AS. Since VS also depends upon the CT threshold, any low-density calcified plaque below the set threshold may be missed. VS is also affected by the partial volume effect. For example, if there is a small but high-density

calcified lesion and the section thickness is greater than the dimension of calcification, the highly attenuating calcification would be partial volume averaged to fill the entire voxel with a CT number above the calcification threshold. This would result in overestimations of the coronary calcium content. Finally, the extensive use of VS is limited in clinical practice due to a lack of standard reference criteria from large research studies.

MS

The MS represents the total mineral mass of coronary calcium expressed in milligrams. While AS and VS are indirect indicators of coronary calcium burden, MS provides an accurate quantitative representation of CAC. MS is measured in milligrams. It is more accurate and reproducible compared with AS and VS.[13)16)] The calculation of MS is slightly complicated. A

calibration factor is first calculated using calibration phantoms that contain calcium hydroxyapatite (CaHA) in different concentrations. This calibration phantom is placed beneath the thorax of a subject. Based on the CT attenuation value and density (ρCaHA) of a calcified phantom, the calibration factor (cHA) is determined according to the following equation:

$$cHA = \rho CaHACT\ cylinder-CT\ water$$

CT cylinder is the mean HU of the known calibration phantom, and CT water is the mean HU of water.

The MS of an individual calcified coronary artery lesion is calculated as a product of the cHA, lesion volume (V), and its mean density in HU (CTn).

$$MS\ (lesion) = cHA \times V \times CTn$$

The total MS is then calculated by adding the score of all individual lesions without considering the location and distribution (**Figures 1** and **2**).

$$MS\ (total) = \sum MS\ (lesion)$$

The final score is expressed in milligrams and it represents the absolute value of mineral mass in a calcified coronary artery lesion.

Strengths and limitations
There are several strengths of the MS. It is more accurate and reproducible compared with AS and VS. The study by Hong et al.[13] showed that the mean interscan variability of MS was 9.3%, while it was 20.4% and 13.9% for AS and VS, respectively (13). MS also allows better adaptation across and between the scanners. A study showed an excellent correlation between the calcium mass measurements at 1.25-mm and 3-mm slice thickness.[17] Ferencik et al.[18] evaluated the difference in the various CAC scores at 2 different thresholds (90 HU and 130 HU). A lower mean relative difference was seen with MS (59%) compared with the AS (94%) and VS (109%). The only limitation of MS is the restricted use in clinical practice due to a lack of established standard reference criteria from large research studies.

CCS
The CCS was proposed by Brown et al.[19] in 2008 using data from the Multi-Ethnic Study of Atherosclerosis (MESA). CCS represents the percentage of coronary arteries affected by calcific plaques. According to this method, coronary arteries are divided into absolute subdivisions of 5-mm-length segments. CCS is calculated by dividing the number of segments containing calcific plaques (A) by the total number of segments in the coronary arteries (Y) and then multiplying by 100.

$$CCS = A/Y \times 100$$

Strengths and limitations
CCS is based on the spatial distribution of calcified plaque that is an important component of coronary atherosclerosis above and beyond the overall amount of calcium and the calcium density. Brown et al.[19] showed that among different kinds of calcium scores, CCS showed the strongest association with coronary heart disease (CHD) events compared with AS and MS. CCS is also associated with diabetes, hypertension, and dyslipidemia, even with adjustments for AS and MS, which suggests that CCS reflects information on calcific plaques that is not captured by the AS and MS. Therefore, the CCS can provide better risk stratification, aiding physicians in determining appropriate individual treatment strategies. CCS can improve the communication between physicians and patients, i.e., the involvement of 10% coronary arteries (CCS score) conveys more information than a score of 1,000 (AS). The limitations of CCS include time-consuming tracing of the entire coronary tree and a lack of standard reference criteria from large studies.

Visual score
Visual score is a simple, quick, and subjective method of CAC assessment. It is commonly used for non-gated scans. There are no specific objective criteria, and it is based on a simple visual analysis of the entire coronary tree. The CAC is graded into none, mild, moderate, and severe types (**Figure 4**). There is no universal consensus on the grading of the visual score; authors have used different methods in various studies. The commonly used method, proposed by Chiles et al.,[20] grades the visual score on the basis of the distribution of CAC. CAC is classified as mild if there are only isolated flecks of calcium within a coronary artery segment. CAC is classified as severe if there are continuous deposits of calcium within a coronary segment. CAC is classified as moderate if there is more calcium than with mild grade, but less than that of the severe grade.[20]

Strengths and limitations
Since visual score does not require electrocardiogram (ECG) gating, the scoring can be done in any routine chest CT. visual score is a feasible method and correlates well with AS. Sonavane et al.[21] showed a good correlation between visual score and AS with a good inter-reader correlation. Einstein et al.[22] reported

Figure 4. Visual score. The coronary artery calcium is graded into none (A), mild (B), moderate (C), and severe type (D) by simple visual scoring.
LAD: left anterior descending, LCx: left circumflex artery.

a high degree of association between visual score and AS on ungated low-dose CT scans used for attenuation correction on positron emission tomography/CT and single-photon emission CT/CT. The national lung screening trial showed a strong association between the simple visual scoring method and cardiovascular outcomes and demonstrated an increased risk of events with an increased level of calcification, even after the adjustment for potential confounders.[20] In another lung screening trial, Huang et al.[23] demonstrated the reliability of the visual scoring method. Visual score was found to be highly concordant with AS. There are a few limitations of visual score. First, few studies in the literature have indicated its accuracy. Even in the available studies, the authors used different methods for categorizing visual score into mild, moderate and severe categories. Additionally, the results obtained from the non-gated visual method are comparable to those obtained from ECG-gated calcium scoring, but not sufficient to replace them later.

PROTOCOL

The referral for CAC scanning should be based on clinical guidelines and current consensus documents.[24] Patients without appropriate indications for CAC scanning may be offered an optional screening test. Breath-hold practicing may be helpful. Oral b-blockers may be given if the heart rate is elevated (> 75 beats/min).[25] It is advised to select an ECG-gated acquisition mode requiring the least radiation exposure. For most scanners, the mode would be a prospective, ECG-triggered axial (also known as sequential, step-and-shoot, or volumetric) mode. For dual-source (DS) systems using high-pitch acquisition mode, a prospectively ECG triggered helical (also known as a spiral) mode may be appropriate. Retrospectively acquisition modes should be avoided, except in patients with extremely high or irregular heart rates. Data acquisition or reconstruction should be done during mid-diastole (70% of the cardiac cycle); however, for patients with

higher heart rates (> 75 beats/min), systolic phase acquisition may be more appropriate.[5)26)] According to the American Heart Association (AHA) Writing Group regarding ionizing radiation dose in cardiac imaging, the estimated average effective dose is approximately 1.0–1.5 mSv for prospectively triggered scans and approximately 3.0 mSv for retrospectively gated scans.[27)]

According to the SCCT guidelines, the acquisition for CAC scoring is performed at a standard fixed tube voltage of 120 kVp, and tube current varying with patient body habitus.[24)] Studies have shown that MDCT imaging at a peak tube voltage of 120 kVp is equivalent to electron-beam CT for quantification of CAC, and this voltage allows the standard 130 HU threshold for quantifying AS and VS.[28-31)] In the last few years, multiple studies have been conducted to reduce the radiation dose by applying tube current reduction, tube voltage reduction, and spectral shaping with tin-filter techniques. Gräni et al.[32)] investigated the feasibility and accuracy of CAC scoring with reduced peak tube voltages of 80 kVp and 70 kVp using kVp-adapted thresholds. Compared with standard 120-kVp CAC scanning, lower peak tube voltages of 80 kVp and 70 kVp led to a mean radiation dose of 0.19 mSv and 0.12 mSv, respectively, representing a reduction of 68% and 80% compared with the standard 120-kVp protocol, which resulted in a radiation dose exposure of 0.60 mSv. CAC scores derived from 80-kVp and 70-kVp scans showed an excellent correlation with standard 120-kVp scans. In the study of Jakobs et al.,[33)] a 20 radiation dose was reduced by 65% by applying an 80-kVp protocol compared with the standard 120-kVp protocol. The general recommendation at this time is to use standard 120 kVp for CAC scoring with MDCT. The use of 100 kVp scans may be acceptable if a laboratory uses a new threshold for calcium based on phantom measurements with each scanner used.

Filtered back projection is the standard of care reconstruction technique proposed by SCCT. Some recent studies have applied iterative reconstruction to reduce image noise at lower tube currents,[34-36)] while other studies have suggested that the application of iterative reconstruction algorithms on 120-kVp scans has an impact on CAC measurements, generally leading to an underestimation of CAC scores.[37-39)] It is reasonable to continue to employ filtered back-projection except in centers that have validated iterative or model-based reconstruction algorithms. The other proposed dose reduction techniques include tin filter technology and ultra-high pitch (UHP) mode using DSCT. Tin filter technology modifies the X-ray spectra by eliminating low-voltage electrons, which facilitates a significant dose reduction.[39-41)] However, like voltage reduction, this method changes the CT value of the images and requires a shift in the threshold for CAC scoring.[40)] The UHP mode using DSCT

reduces the radiation dose as well as the respiratory motion artifacts. However, due to the speed of the table movement, derived measurements could result in different ASs.[39)42)43)] Another important parameter in CAC scoring is the thickness of slice reconstruction. The commonly used protocol involves a slice thickness of 3.0 mm; this thickness might lower sensitivity for detecting small, low-attenuating calcifications. Studies have shown that thinner-slice protocols may substantially improve the accuracy of calcium scoring as a result of decreased partial volume effects.[44-46)] Various studies have found different results on the effect of slice thickness on CAC score. Vliegenthart et al.[47)] demonstrated higher calcium volume in 1.5-mm slices compared with 3-mm slices in EBCT in a phantom and a patient study. In a different EBCT study, no significant changes in calcium scoring results comparing 1.5-mm and 3-mm slices were found.[48)] Hong et al.[17)] found no relevant changes in calcium mass comparing a 3-mm nonenhanced scan protocol with a 1.25-mm contrast-enhanced scan protocol in MDCT.[49)] Mühlenbruch et al.[50)] found a significant increase in the calcium score when comparing 3-mm and 1-mm slices in MDCT. To date, most centers use 2.5-mm or 3-mm slice thickness to provide scores comparable to the CAC database.

CAC scoring is strongly influenced by cardiac motion, calcification density, and slice thickness. CAC scores decrease for low-density calcifications and increase for high-density calcifications at increasing heart rates. Heart rate should be reduced, preferably below 70 bpm (64 slices MDCT) to obtain a lower degree of variability of CAC scoring.[25)] Guidelines from the Society for Atherosclerosis Imaging and Prevention Tomographic Imaging recommend the use of beta-blockers for heart rates > 75 bpm.[51)] A thinner slice reconstruction further enhances reproducibility. Although the reduction of the variability seems to be an advantage of thinner slices, the increased noise levels associated with thinner slices are a disadvantage.[50)52)53)]

VALIDATION OF THE CAC SCORE

CAC score is currently used as a sensitive marker for CAD screening and risk stratification. Several studies have shown a strong association between various types of calcium scores and cardiovascular risk. Guerci et al.[54)] showed a significant correlation between AS and coronary narrowing, suggesting that the CAC score could represent the extent of CAD. Mendoza-Rodríguez and colleagues[55)] showed a significant correlation between VS and flow-limiting CAD. In the study by Detrano et al.[56)] in the MESA population, a doubling of the CAC scores

increased the probability of a coronary event by 25% in a 3.8-year follow-up period, which was relatively stable across the different ethnic groups included in the study.

Various studies have suggested different cut-off values of CAC score for predicting severe luminal narrowing. Rumberger and colleagues[57] proposed that AS of 327 is a predictor of more than 70% narrowing in at least one of the coronary arteries. Shabestari et al.[58] showed moderate-to-good agreement between CAC of more than 100 AS and significant coronary stenosis. A study by Cheng et al.[59] on 17,967 asymptomatic individuals revealed an increased risk of CAD at all levels with AS higher than 95. In another study, Guerci and colleagues[60] suggested 80 as the cut-off value of AS in forecasting the increased likelihood of CAD. CAC scoring is especially advantageous in the diabetic population. Studies have also shown that the presence of any degree of CAC in patients with diabetes mellitus translates to a higher risk of all-cause mortality compared with patients without diabetes.[61] Kramer et al.[62] reviewed 8 studies involving 6,521 patients and found that diabetic individuals with a CAC score of < 10 were 6.8 times less susceptible to all-cause mortality and cardiovascular events as well as to cardiovascular events alone than those with diabetes and a CAC score > 10. Several international guidelines recommend that screening for silent ischemia in diabetic patients should be done in patients with a CAC score > 400. However, screening is not warranted in patients with diabetes with a CAC score < 100.[63]

An interesting property of the calcium score is its high negative predictive value. The prognostic significance of CAC = 0 was analyzed in a comprehensive meta-analysis. In a study population of 29,312 with CAC = 0, an event rate of 0.47% was seen during a mean follow-up of 50 months. The relative risk ratio of CAC = 0 compared with CAC > 0 was 0.15, indicating an 85% lower risk for individuals with zero calcium score.[64] In another large review of 44,052 patients referred for calcium scoring, individuals with CAC ≥ 400 and without any clinical risk factors experienced a significantly higher event rate than subjects with CAC = 0 and ≥ 3 risk factors.[65] This study suggests that the absence of coronary calcium can overpower clinical risk factors regarding mortality prediction. The strong association between zero calcium and a very low cardiovascular event rate does not apply to symptomatic individuals. CAC scoring cannot detect noncalcified plaque and thrombotic occlusions. Therefore, a negative CAC scan cannot be used to rule out relevant obstruction, especially in symptomatic patients. In a study of 133 symptomatic high-risk patients, 19% of patients had a negative CAC scan and 32% of them showed significant stenosis on invasive angiography.[66]

Newer studies emphasize that patients with a CAC greater than or equal to 1,000 should be considered a distinct patient group; a CAC of 0 has emerged to be a reliable negative risk factor, identifying patients at low risk of both cardiovascular disease (CVD) and non-CVD mortality.[67] Coronary Artery Risk Development in Young Adults collected data on CAC among 2,831 patients aged 32 to 46 and assessed CAC throughout a follow-up. The results showed that CAC > 0 is not rare in this age group, especially when a risk factor is present. Additionally, the CAC highly predicted risk beyond established risk variables in these young people over a 10-year follow-up (**Table 1**).[68]

Table 1. Summary of studies of different designs showing the relationship between CAC score and CAD in asymptomatic individuals

References	Study year	Design	Sample population	Conclusion
Rumberger et al.[57]	1997	Prospective	213	The optimal CAC score cut points values range from 15 for > 20% stenosis to 327 for 100% stenosis
Shabestari et al.[58]	2006	Prospective	65	Significant coronary stenosis (> 50% diameter reduction) shows moderate-to-good agreement with a Ca-Score of 100 or higher
Cheng et al.[59]	2003	Cross-sectional	17,967	There is an increased risk for prevalent CHD at all levels of CAC > 0, with the greatest increase in risk occurring in patients with CAC scores > 95
Guerci et al.[60]	1998	Prospective	290	A CAC score > 80 is associated with an increased likelihood of any CAD regardless of the number of risk factors, and a coronary calcium score ≥ 170 is associated with an increased likelihood of obstructive CAD regardless of the number of risk factors
Kramer et al.[62]	2013	Meta-analysis	6,521	In people with type 2 diabetes, a CAC score of ≥ 10 predicts all-cause mortality or cardiovascular events, or both, and cardiovascular events alone, with high sensitivity
Sarwar et al.[64]	2009	Systematic review	85,000	Absence of CAC is associated with a very low risk of future cardiovascular events
Nasir et al.[65]	2012	Prospective	44,052	Patients with CAC have a substantially higher event rates than those who have multiple risk factors but no CAC
Haberl et al.[66]	2005	Observational study	153	Multislice CT angiography, but not calcium scoring alone, offers promise to reduce the number of invasive angiography in symptomatic patients with suspected CAD by up to one third with minimal risk for the patient
Ferencik et al.[68]	2017	Prospective community-based	5,115	After surveillance for 30 years, it concluded that a CAC score of 100 or above was linked to a higher risk of mortality. Adults under the age of 50 who have any CAC found on a computed tomographic scan, even with extremely low scores, are at an increased risk of clinical CHD, CVD, and mortality

CAC: coronary artery calcium, CAD: coronary artery disease, CHD: coronary heart disease, CT: computed tomography.

Another prospective study was conducted by Carr et al.[69] on 263 patients (women aged 30–65 years and men aged 30–62 years) with chest pain and low-to-moderate risk of CAD. The researchers performed a traditional emergency department chest pain evaluation as well as a CT CAC scan. Approximately 97% of the patients with cardiac chest discomfort revealed evidence of CAC on CT. The study concluded that CT CAC assessment is an effective supplement in evaluating people at low-to-intermediate risk.

Besides the screening tool and risk stratification, the CAC score has also been proven to be a management decision tool. In a large retrospective study, Mitchell et al.[70] showed that CAC scoring could be used to identify patients who are more likely to benefit from statin therapy. CAC also predicts non-cardiac outcomes, such as dementia, hip fracture, pneumonia, and chronic renal failure, and is a generalized marker of health.[71][72]

The morphology (spotty vs. diffuse) and distribution of CAC (single vessel or multiple vessels) are also important. Different patterns in the distribution of CAC have been reported to convey different effects on plaque stability. Spotty and superficial calcium deposits have been implicated in plaque vulnerability based on previous intravascular ultrasound (IVUS) and optical coherence tomographic studies.[73][74] Biomechanical models suggest that microcalcifications can intensify stress in the fibrous cap, promoting plaque rupture. In contrast, large calcium deposits are hypothesized to promote local biomechanical plaque stability, and statin therapy has been shown to accelerate the calcification of atherosclerotic lesions.[75][76] The Framingham Offspring Study has raised awareness of CAC distribution–dependent outcomes.[68] Earlier studies have linked the involvement of the left main (LM) coronary artery to poor prognosis.[77] Lahti et al.[78] found that the patients with a LM CAC had a significantly higher mean CAC score compared with patients without LM CAC. This was also reflected in the greater proportions of very high CAC in patients with LM involvement; 43% of the LM CAC patient group, compared with only 13% of patients without LM CAC, had CAC greater than or equal to 400. Patients with LM CAC were also much more likely to present with a higher number of vessels with CAC. More than half of patients with LM CAC showed 4-vessel CAC whereas none in the group without LM CAC presented with this pathobiological feature.

CAC SCORE AND CLINICAL DECISION MAKING

An essential tenet of patient-centered imaging is that patients have a clear understanding of the benefits and risks of an imaging test, particularly focusing on safety, in the setting of a shared decision-making (SDM) discussion. SDM is a broad mandate of the Affordable Care Act that establishes a collaborative process between patients and health care professionals to incorporate the best available scientific evidence and the patient's values and preferences into medical decisions. The 2017 SCCT CAC expert consensus recommends CAC testing in asymptomatic individuals aged 40–75 years with a 5–20% 10-year ASCVD risk and in the group of individuals with less than 5% ASCVD risk with a family history of premature CAD.[79] CAC scoring is used to guide the initiation and intensity of statin therapy. According to the American College of Cardiology (ACC)/AHA guidelines, high-intensity statin therapy is recommended in any patient with a CAC > 300 or above the 75th percentile for age/gender/race. Patients with a CAC score of 100–299 require moderate-to high-intensity statin treatment. In patients with CAC 1–99, moderate-intensity statin therapy is recommended for those with a CAC percentile ≥ 75%. Patients with CAC = 0 are considered to be at the lowest risk and statins are not uniformly recommended, except for patients with familial hypercholesterolemia or diabetes.[80] Some evidence suggests that the individuals with CAC ≥ 100 had an estimated net benefit with aspirin regardless of the traditional risk status; however, there are no guidelines on it.[81]

Recent studies have emphasized the ability of CAC to identify cases of high cardiovascular risk as well as low-risk populations who may not always need statin therapy.[82] CAC = 0 appears to be the strongest negative predictor of a cardiovascular event in comparison to other subclinical cardiovascular risk factors such as ankle-brachial index or carotid intima-media thickness.[83] The so-called "Power of Zero" may allow downward reclassification (i.e., "de-risking") of patients who are considered sufficiently high risk by other risk factors. There is strong evidence that CAC = 0 can downwardly classify risk when the 10-year ASCVD risk is between 5–15% and modest evidence that CAC = 0 can downwardly reclassify risk in patients between 15–20% to a level that statin therapy would not be recommended. Patients remain at high risk regardless of the CAC score when the 10-year ASCVD risk is > 20%.[84]

There is limited data on serial CAC scanning. The evidence suggests no significant effect of statin therapy compared with placebo or varying intensity statin therapy for attenuating CAC progression.[85] A recent *post hoc* analysis of 8 prospective randomized serial coronary IVUS trials suggests that statins promote coronary calcification, hypothesized as a means of stabilizing atherosclerotic plaque. However, these findings have not been fully corroborated by several studies.[86]

There are several situations where clinical considerations and patient preferences prompt the consideration of repeat scanning. According to the consensus statement of SCCT, in patients for whom the development or progression of CAC would support intensification or alteration in preventive management, it may be appropriate to consider repeat CAC scanning at an interval of 5 years for patients with CAC = 0 and a 3–5-year interval for patients with CAC > 0.[79]

CAC SCORE AND OTHER CLINICAL SCORES

There are clinical scores for risk stratification and primary prevention of CAD. The most used clinical score is the Framingham Risk Score (FRS), which is a simple, low-cost method of cardiovascular risk stratification that can establish the 10-year risk of CAD. The method takes into consideration age, gender, a ratio of total cholesterol to high-density lipoprotein fraction, systolic blood pressure, smoking status, and the presence or absence of diabetes.[87][88] The risk of CHD at 10 years can be calculated with FRS and is divided into 3 categories: low risk (10% or less CHD risk at 10 years), intermediate risk (10–20%), and high risk (20% or more). While the low-risk individuals are reassured and tested after 5 years, individuals with high risk need active intervention. The intermediate-risk category could benefit from further investigation. The incorporation of the CAC score to FRS adds independent value in predicting all-cause mortality and mortality due to CAD in asymptomatic individuals and reclassifies the intermediate-risk category.[89] There are studies demonstrating the superiority of the CAC score over the FRS, C-reactive protein level, and carotid intima-media thickness in predicting the risk of cardiovascular events.[11][90-93]

Another commonly used clinical score is the MESA. MESA is a new risk prediction score that incorporates the CAC score in addition to the traditional risk factors like demographics, serum cholesterol level, diabetes, systolic blood pressure, family history of CHD, smoking, and the use of antihypertensive or cholesterol-lowering medications. The incorporation of the CAC score into MESA leads to superior risk prediction. The MESA CHD Risk Score was published in the Journal of the ACC in 2016. In this paper, McClelland et al.[94] used the traditional risk factors as well as family history of CHD for predicting the 10-year risk of CHD. Subjects were divided into 2 models: one model without CAC and one with CAC added to the model. The C-statistics was 0.75 using just the traditional risk factors plus family history and it increased to 0.80 after adding CAC. This proved the added benefit for CAC score with traditional MESA risk factors.

ASSUMPTIONS ABOUT CAC SCORING METHODS

There are different assumptions about the traditional CAC scores. First, in AS and MS, denser calcifications have been weighted heavily compared with less dense calcifications. However, denser plaques may be stable and relatively protective due to the absence of an active lipid core. Studies have shown that acute coronary events are significantly associated with spotty calcifications and low plaque density.[95-97] In addition, the assumed threshold value for identifying calcium (> 130 HU) is the same in AS, VS, and MS, which may miss the sub-threshold microcalcifications. The second assumption is about the location (proximal or distal) of calcific plaque in the coronary tree. Studies have shown that proximal plaques are more prone to rupture, which can cause thrombotic occlusion of involved vessels. However, these traditional scores do not provide information about the location of calcifications. Similarly, the involvement of a particular artery is not taken into account. The vessel-specific scoring or risk assessment based on the individual vessel is more informative than the total calcium score. Additionally, none of the methods provides information about the distribution of calcium in coronaries, whether the total calcium is distributed as single focal plaque or diffuse disease (**Figure 5**). This may be misleading for selecting an appropriate treatment strategy. For example, a single calcific plaque of score 100 and diffusely distribute disease with a total score of 100 carry different treatment strategies and prognostic values. Finally, none of the scores considers calcification in other cardiovascular structures (aortic valve, mitral valve, mitral annulus, aortic, and pulmonary), which may sometimes be a significant finding. These assumptions have fostered the development of a new standardized system for the interpretation of CAC. SCCT proposed an expert consensus document in 2018 for this purpose in the same line of breast imaging-reporting and data system (RADS) liver imaging-RADS, prostate imaging-RADS, and CAD-RADS.[8]

CAC-DRS

CAC-DRS stands for coronary artery calcium data and reporting system. It is defined and described in the expert consensus document of SCCT published in 2018. The purpose of this classification is to standardize the reporting of CAC.
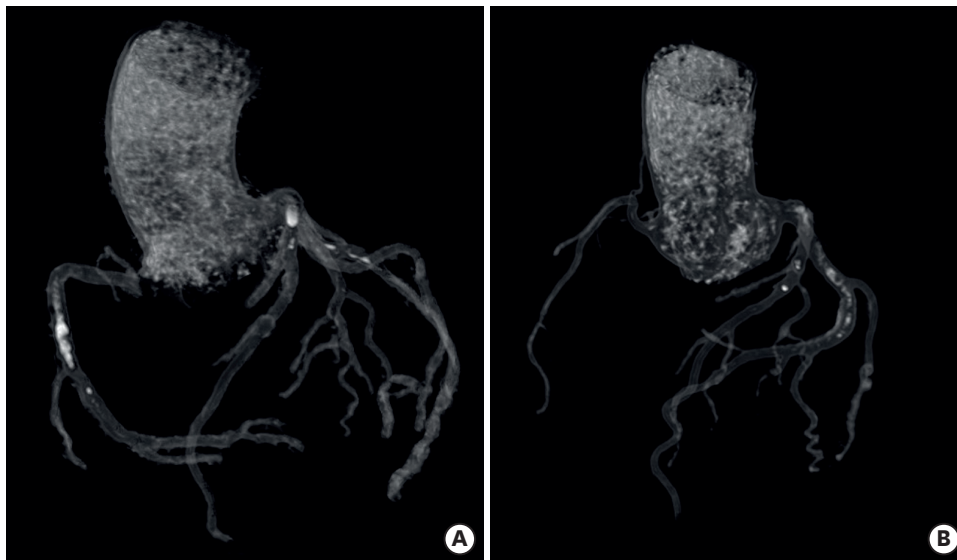
Figure 5. All 4 CAC scores fail to provide information on the distribution of calcium in vessels. (A, B) Two images have a similar Agatston score (180), but the distribution is different. Calcium is mainly distributed in RCA and LAD in (A), while (B) shows distribution in LAD and LCx.
CAC: coronary artery calcium, RCA: right coronary artery, LAD: left anterior descending, LCx: left circumflex artery.

It is applicable in both gated and non-gated chest CT scans. According to SCCT and the Society of Thoracic Radiology, CAC scoring should be done in all routine non-contrast, gated or non-gated chest CTs, irrespective of the scan indication. Of the various traditional CAC scoring methods mentioned above, CAC-DRS recommends using AS or VS. There are 4 categories in this classification, ranging from CAC-DRS 0 to CAC-DRS 3. The risk

of ASCVD increases from category 0 to category 3. Although the scoring methodology of AS and VS are entirely different, the final category and risk predictions are the same (**Figures 6-8**).[8]

In cases in which the Agatston method is used, the total AS is assigned to one of the 4 CAC-DRS risk categories: CAC-DRS 0 = AS 0, CAC-DRS 1 = AS 1–99, CAC-DRS 2 = AS 100–299, and
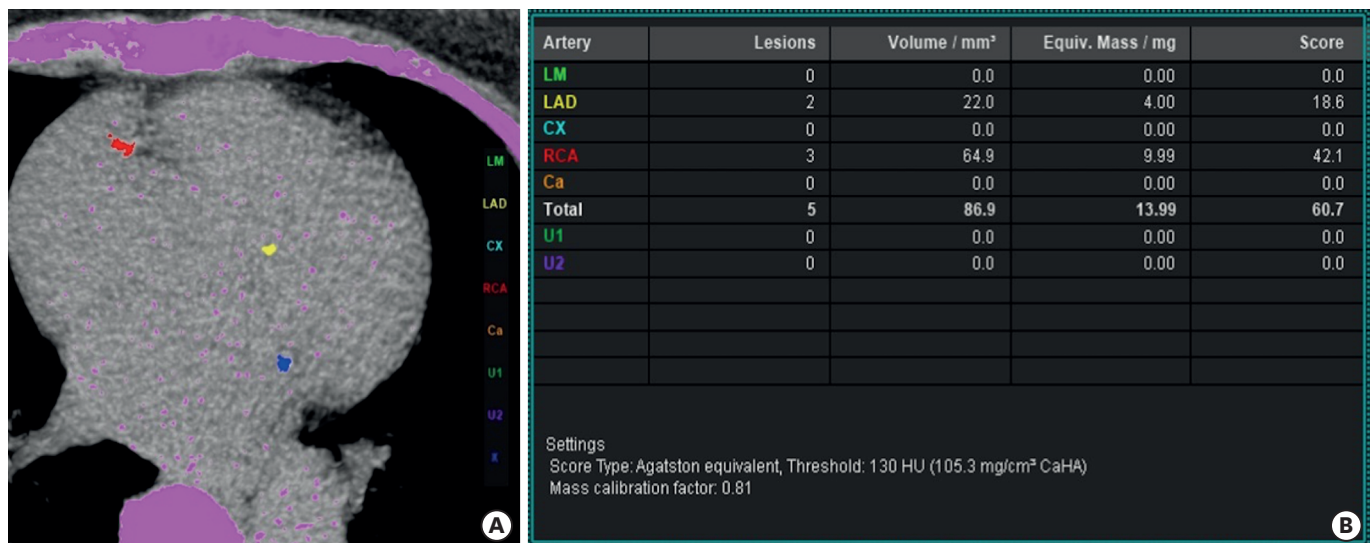

Artery	Lesions	Volume / mm²	Equiv. Mass / mg	Score
LM	0	0.0	0.00	0.0
LAD	2	22.0	4.00	18.6
CX	0	0.0	0.00	0.0
RCA	3	64.9	9.99	42.1
Ca	0	0.0	0.00	0.0
Total	5	86.9	13.99	60.7
U1	0	0.0	0.00	0.0
U2	0	0.0	0.00	0.0

Settings
Score Type: Agatston equivalent, Threshold: 130 HU (105.3 mg/cm³ CaHA)
Mass calibration factor: 0.81

Figure 6. CAC-DRS A1/N2 and V1/N2 category. (A) Coronary calcium score non-contrast ECG-gated computed tomographic views of coronary arteries demonstrate the presence of multiple calcified plaques through the anatomic territory of proximal segments of LAD (yellow) and RCA (red). The blue dots represent the calcification of mitral annulus. (B) The measurement table provided by CT workstation demonstrates the Agatston score of each coronary artery and the total score (60.7). CAC is mild (< 100) on Agatston (A1) and visual (V1) analyses with 2 vessel involvement (N2) suggesting A1N2 category.
CAC-DRS: Coronary Artery Calcium Data and Reporting System, ECG: electrocardiogram, CAC: coronary artery calcium, CT: computed tomography, LM: left main, LAD: left anterior descending, Cx: circumflex artery, RCA: right coronary artery, HU: Hounsfield units.
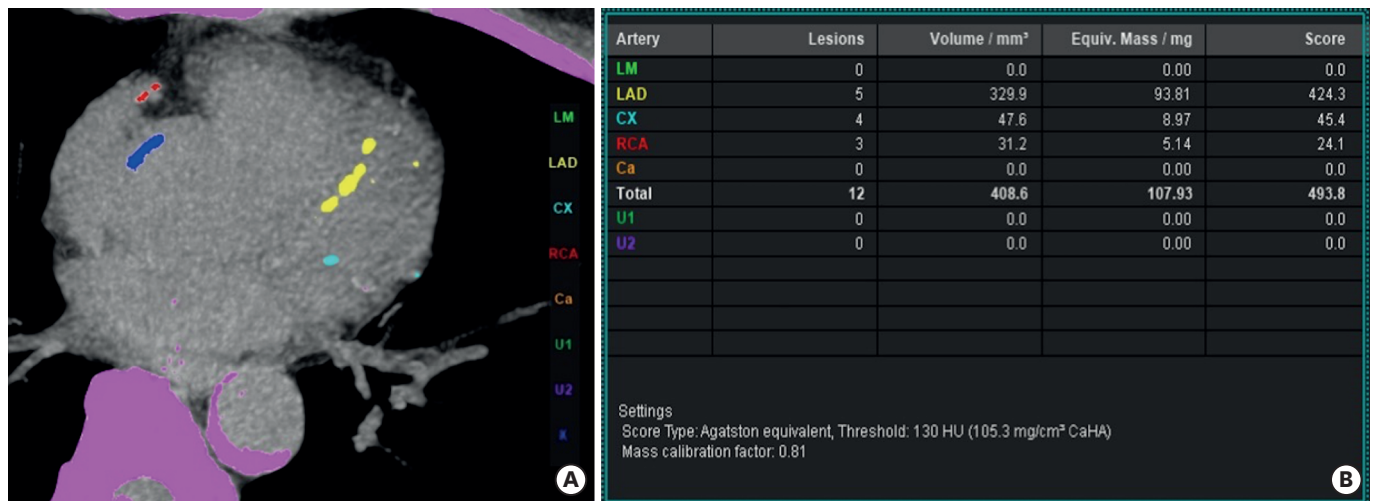
Figure 7. CAC-DRS A1/N2 and V1/N2 category. (A) Coronary calcium score non-contrast ECG-gated computed tomographic views of coronary arteries demonstrate the presence of multiple calcified plaques through the anatomic territory of proximal segments of LAD (yellow) and RCA (red). The blue dots represent the calcification of mitral annulus. (B) The measurement table provided by the CT workstation demonstrates the Agatston score of each coronary artery and the total score (60.7). CAC is mild (< 100) on Agatston (A1) and visual (V1) analyses with 2 vessel involvement (N2) suggesting A1N2 category. CAC-DRS: Coronary Artery Calcium Data and Reporting System, ECG: electrocardiogram, CAC: coronary artery calcium, CT: computed tomography, LM: left main, LAD: left anterior descending, Cx: circumflex artery, RCA: right coronary artery, HU: Hounsfield units.
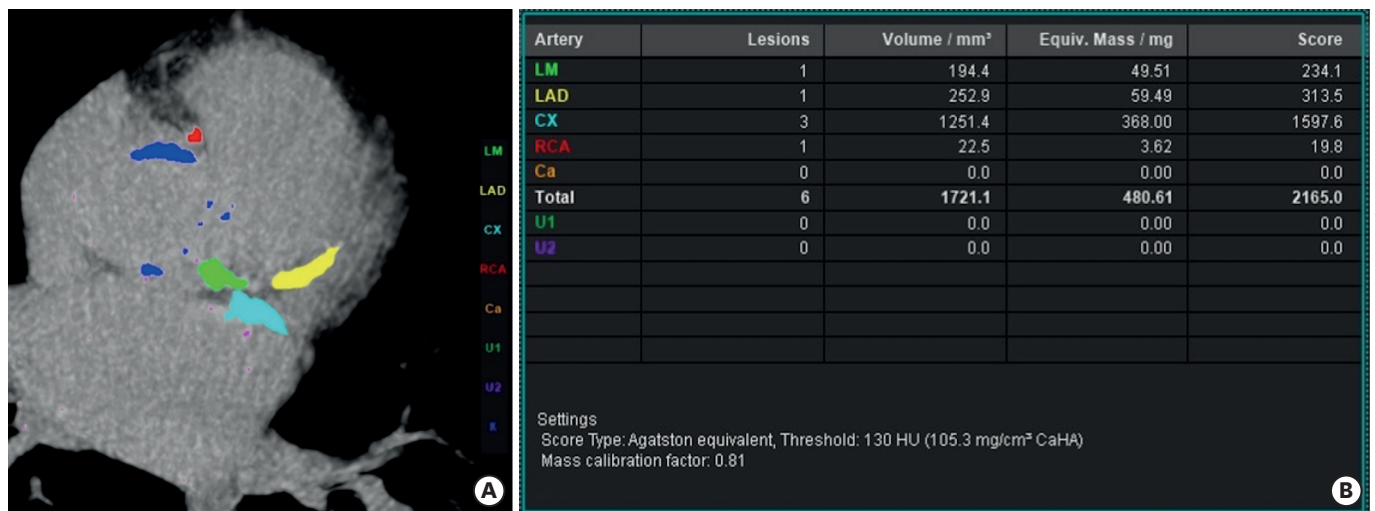

Figure 8. CAC-DRS A3/N4 and V3/N4 category. (A) Coronary calcium score non-contrast ECG-gated computed tomographic views of coronary arteries demonstrate the presence of multiple calcified plaques through the anatomic territory of proximal segments of LAD (yellow), RCA (red), LCx (light blue) and LM artery (green). The dark blue dots represent the calcification of aortic root. (B) The measurement table provided by the CT workstation demonstrates the Agatston score of each coronary artery and the total score (2,165). CAC is severe (> 300) on Agatston (A3) and visual (V3) analyses with 4 vessel involvement (N4) suggesting A3/N4 category. CAC-DRS: Coronary Artery Calcium Data and Reporting System, ECG: electrocardiogram, CAC: coronary artery calcium, CT: computed tomography, LM: left main, LAD: left anterior descending, Cx: circumflex artery, RCA: right coronary artery, HU: Hounsfield units, LCx: left circumflex artery.

CAC-DRS 3 = AS >300. With the visual method, the none, mild, moderate, and severe grades correspond to CAC-DRS 0, 1, 2, and 3 categories, respectively (**Table 2**).

Modifiers
There are 2 modifiers in the CAC-DRS classification. The first modifier denotes the type of scoring system, which could be either Agatston or visual estimation. These are represented by A for Agatston and V for visual methods, respectively. The second modifier denotes the total number of vessels involved and is represented by the N. It varies from N1 to N4 depending upon the number of coronary arteries involved, namely LM, left circumflex, left anterior descending (LAD), and right coronary artery. The 2 multipliers are separated by the slash symbol ("/").

Table 2. CAC-DRS categories based on the Agatston and visual scoring

CAC-DRS category	Agatston score	Visual score	Risk	Treatment recommendations
0	0	0	Very low	Statin generally not recommended
1	1–99	1	Mild	Moderate intensity statin
2	100–299	2	Moderate	Moderate to high intensity statin + ASA 81 mg
3	> 300	3	Moderate to severe	High intensity statin + ASA 81 mg

CAC-DRS: Coronary Artery Calcium Data and Reporting System, ASA: acetylsalicylic acid.

Other cardiac and non-cardiac findings

It is recommended to report the calcification of the thoracic aorta, aortic valve, mitral annulus, and pericardium. These should be subjectively categorized under none, mild, moderate, and severe categories. No CAC-DRS category is assigned to them, and these are not included in CAC-DRS scoring. The incidentally detected non-cardiac findings should also be reported with follow-up recommendations.

Strengths

CAC-DRS provides an effective means of communication between radiologists and referring physicians. It provides information about the number of vessels involved. Various studies have shown that multivessel atherosclerosis adds incremental prediction of cardiovascular events to the traditional CAC score.[98-100] The number of vessels involved can help in planning the appropriate management. For example, CAC-DRS A1/N4 needs aggressive management compared with CAC-DRS A1/N1, even if the total AS is the same in both conditions. Two large retrospective studies have been done on CAC-DRS that validate the new SCCT CAC-DRS scoring system for predicting cause-specific and total mortality. Dzaye et al.[101] included 54,678 patients from the CAC Consortium who had a mean CAC score of 1, a median of 2 vessels with CAC, and a mean ASCVD risk score of 7.3%. Out of these patients, 2,469 patients died over a mean follow-up of 12 years. The all-cause mortality rate of patients with an A0 score was 1.2 per 1,000 person-years, and the rate of patients with an A3/N4 score was 15.4 per 1,000 person-years. On multivariate analysis, A3/N4 patients were at significantly higher risk of CVD mortality (hazard ratio [HR], 4.0; 95% confidence interval [CI], 2.8–5.7), CHD mortality (HR, 5.9; 95% CI, 3.6–9.9), and all-cause mortality (HR, 2.5; 95% CI, 2.1–3.0) compared with A0 patients. Another retrospective study was done by Osawa and colleagues[102] on 309 patients without a history of CVD (mean age 67.4 ± 8.2 years, 61% male). Time to the incidence of major adverse cardiac events (MACEs) (non-fatal myocardial infarction, non-fatal stroke, and cardiovascular death) and all-cause death was analyzed using regression models. Forty-three patients died over a mean follow-up of 52 months. After multivariable adjustment for the ASCVD risk score, the CAC score was significantly associated with the incidence of MACEs (HR, 1.95; 95% CI, 1.11–3.44) and MACEs or all-cause

death (HR, 1.91; 95% CI, 1.46–2.51). When CAC-DRS category was included in the model instead of CAC score, the results showed that CAC-DRS is also independently associated with the incidence of MACEs and MACEs or all-cause death (HR, 1.15; 95% CI, 1.02–1.29; p = 0.02, and HR, 1.18; 95% CI, 1.10–1.25; p < 0.01, respectively). Both studies validate and strongly support the new SCCT guidelines. Another attractive feature of CAC-DRS is management recommendations. The negative predictive value of the CAC-DRS score 0 is very high. Preventive pharmacotherapy is recommended using statins or aspirin in patients with CAC > 0. The proposed recommendations are moderate-intensity statins with CAC 1–99, moderate to high-intensity statins with CAC 100–299, and high-intensity statins with CAC > 300.[103] Structured reporting can bridge the knowledge gap and can help in uniform data collection over the globe. This provides a framework for research, education, and quality assurance. Standardization in the reports will improve communications between human and computer-based systems, paving pathways for the development of artificial intelligence algorithms in the future.

Limitations

First, the proposed visual method of CAC classification is overly simple and lacks standardization. There is minimal literature available on its accuracy. Few studies have shown a good agreement between Agatston and the visual analysis method, but more studies are needed before recommending it as an alternative to the Agatston method.[20)23)] Similarly, the grading of aortic, pericardial, valvular, and mitral annulus calcification also lacks standardization. Second, CAC-DRS provides risk stratification based on total calcium score. The distribution or severity of calcification in a particular vessel is not taken into account. For example, a single dense calcific plaque with a CAC score of 97 in proximal LM is more significant than multiple plaques distributed in LAD with a total score of 97, although both will be categorized as CAC-DRS A1/N1. Lesions in the osteoproximal part of LM are more significant clinically; therefore, there is a need for vessel-based risk categorization. Finally, the proposed treatment recommendations are based on the 2013 ACC/AHA Prevention Guidelines and 2017 SCCT recommendations.[104] These recommendations are applicable for the individuals in the 40–75 years of age group with 5–20% of 10 years ASCVD risk, and < 5% ASCVD group with a family

history of CAD. Therefore the treatment recommendations cannot be generalized to all age groups.

Future perspectives

As described above, there is a need for standardization of the visual method. The current visual approach is very much subjective, with no reference standards. The distribution and severity of calcium in a particular vessel is another important aspect that should be addressed. Finally, the widespread use of the scoring system should be encouraged with the involvement of more societies and practicing physicians to understand their requirements and limitations. This could help with further refinements and the development of an ideal scoring methodology.

CONCLUSION

The standardization of a reporting system enables uniform and reproducible conclusions. It can help highlight the key imaging parameters associated with risk stratification and patient management. Moreover, it allows efficient data collection and provides a framework for research and education. The use of CAC scoring is increasing in clinical practice due to its strong predictive value in asymptomatic patients with low to intermediate cardiovascular risk. The standardization of CAC scoring allows a more meaningful and relevant representation of CAC scores along with appropriate treatment guidelines. It has both advantages and limitations. We believe that CAC-DRS is a major step forward in the development of an effective reporting system.

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