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Review

Coronary artery calcium scoring in risk stratification: from international cohorts to local adaptation in Saudi Arabia

CAC scoring in global and Saudi populations

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Abstract

Coronary artery calcium (CAC) scoring is a non-invasive imaging technique that quantifies the burden of calcified atherosclerotic plaque, thereby aiding in cardiovascular disease (CVD) risk stratification. Its clinical utility has been validated across multiple ethnic cohorts, primarily via the Multi-Ethnic Study of Atherosclerosis (MESA). However, populations such as Saudi Arabians are not included in MESA, limiting the direct applicability of percentile-based risk estimations. This article provides an overview of CAC scoring, its clinical utility, insights from MESA, and proposed strategies to address the underrepresentation of Middle Eastern populations, especially the Saudi population, in CAC reference databases.

Keywords

coronary artery disease, risk assessment, atherosclerosis, Saudi Arabia, artificial intelligence

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Introduction

Cardiovascular disease (CVD) continues to be the predominant cause of morbidity and mortality worldwide.[1] Subclinical atherosclerosis is the underlying cause of most CVDs, often developing before any noticeable symptoms appear, making it a critical target for early prevention efforts.[2] These efforts can include coronary artery calcium (CAC) scoring. The purpose of this review is to summarize the clinical utility and limitations of CAC scoring, discuss the Multi-Ethnic Study of Atherosclerosis (MESA) and its applicability to the global population, and highlight the gaps in representation for Middle Eastern populations, particularly Saudi Arabia, while proposing strategies for local adaptation.

Clinical Utility and Limitations of CAC Scoring

CAC scoring, obtained through non-contrast cardiac computed tomography (CT) scans, is a valuable method for assessing heart disease risk by directly visualizing the accumulation of atherosclerotic plaque within the coronary arteries in asymptomatic individuals, offering a direct measure of subclinical atherosclerosis and thus helping predict risk and guide treatment.[3] Additionally, it has a low radiation dose of no more than 1.0 mSv, which is similar to that associated with a standard screening mammogram (around 0.8 mSv).[4]

The limitations of CAC scoring include its ability to detect only calcified plaques while missing non-calcified ones. It also cannot distinguish between stable and unstable plaques, nor does it provide comprehensive information on plaque morphology and the extent of coronary artery stenosis.[5, 6] Furthermore, its predictive value may be limited in specific populations, including patients with diabetes and younger individuals. In such cases, the absence of coronary calcium does not always indicate low cardiovascular risk, partly because of the possible presence of non-calcified plaques.[7]

CAC Quantification

Agatston method: CAC scoring utilizes the Agatston method to quantify the coronary artery calcification burden. The total score corresponds with the risk of future cardiovascular events. This method supplements traditional risk models like the Framingham Risk Score and the ASCVD Pooled Cohort Equations, especially in borderline and intermediate-risk patients.[8] The Society of Cardiovascular Computed Tomography introduced the Coronary Artery Calcium Data and Reporting System (CAC-DRS), which advocates for reporting both the total Agatston score and the regional distribution of CAC scores. Additionally, it offers risk stratification based on the quantified calcium score.[3]

Table 1. CAC-DRS categories determined by Agatston and visual assessment

CAC-DRS category	Agatston score	Visual score	Risk
0	0	0	Very low
1	1–99	1	Mild
2	100–299	2	Moderate
3	> 300	3	Moderate to severe

To aid clinical decision-making, CAC-DRS provides a standardized approach for reporting CAC scores from all non-contrast CT scans. It also offers guidance on patient management strategies. The CAC-DRS categories are based on the Agatston score and help assess the risk of coronary artery disease (CAD). A score of 0 indicates no detectable calcified plaque and a very low risk of CAD, often supporting the decision to delay statin therapy while emphasizing lifestyle changes. A score between 1 and 99 reflects mild plaque buildup and low risk, prompting consideration of statins and attention to modifiable risk factors. Scores ranging from 100 to 299 suggest a higher plaque burden and moderate risk, where more active preventive measures may be needed. Scores of 300 or more point to a substantial burden of coronary artery calcification and a moderate to high risk of CAD events. In such cases, intensive prevention strategies including moderate- to high-intensity statins, additional lipid-lowering drugs, and aspirin, as well as possible cardiology referral.[9-12] The CAC-DRS categories determined by Agatston and visual assessment are summarized in Table 1.

CAC percentiles and calculators: Following the results of CAC scoring, a patient's scores are compared against reference findings from MESA to determine the patient's percentile ranking. MESA is foundational to the current CAC percentile charts. This study included 6,814 participants aged between 45 and 84 years who were free of clinical evidence of CVD at baseline and who represented different ethnic groups: White (38%), African American (28%), Hispanic (22%), and Chinese-American (12%).[13, 14] MESA demonstrated that CAC predicts events across all these groups, but it also identified substantial variability in CAC scores across ethnicities, necessitating ethnicity-specific percentile charts for accurate interpretation.[15]

The Saudi Population and CAC Scoring: A Missing Link

Despite the extensive validation of CAC scoring in multi-ethnic cohorts such as MESA, the Saudi population—and, more broadly, Middle Eastern cohorts—remain underrepresented in global reference datasets.[13] This lack of inclusion raises significant concerns regarding the accuracy and generalizability of percentile-based CAC risk stratification in this region.

One key issue is risk misclassification. Without ethnicity-specific percentile charts, clinicians in Saudi Arabia may over- or under-estimate cardiovascular risk, leading to inappropriate clinical decisions. MESA data have demonstrated that CAC scores and their predictive value vary substantially across ethnic groups. Applying these percentiles to unrepresented populations risks introducing systemic bias, mainly when used for borderline or intermediate-risk patients, where treatment decisions are susceptible to risk estimates.[15,16]

Additionally, demographic and clinical differences between Saudi and MESA populations further complicate the extrapolation of findings. The Saudi population exhibits high rates of obesity, diabetes, metabolic syndrome, and consanguinity—factors that influence the pathophysiology and distribution of atherosclerosis.[16,17] These differences suggest a unique risk profile that may not align with existing percentile benchmarks derived from Western or East Asian populations.

Studies from Saudi Arabia, such as Al Helali et al., have attempted to address this gap by providing preliminary CAC percentiles for

asymptomatic Saudi patients, deriving their findings from small, referral-based cohorts rather than nationally representative samples.[16] Such designs are prone to selection bias, limiting external validity. Moreover, the small sample size restricts the ability to generate robust age- and sex-specific percentiles and precludes stratified analysis based on key risk modifiers such as diabetes status or body mass index.

In the interim, some clinicians may rely on absolute CAC thresholds (e.g., 100 or 300 Agatston units) rather than percentiles to guide management, as these have been shown to predict adverse outcomes across ethnicities.[18] However, it remains uncertain whether these thresholds have equivalent prognostic value in Saudi Arabia. This uncertainty stems from the high prevalence of metabolic disorders that may influence plaque composition—particularly a greater proportion of non-calcified plaques in younger patients or those with diabetes.[7,17,19]

Future Directions: Toward Local Adaptation and Innovation

To address the limitations of applying MESA-derived CAC percentiles to Saudi populations, several strategies have been proposed. First, establishing Saudi-specific CAC reference values through large-scale, multicenter cohort studies is needed to develop age- and sex-specific percentiles. Such data would better account for the high prevalence of metabolic risk factors, including diabetes and obesity, which differ substantially from MESA populations.[16,20] Second, given the shared demographic and epidemiologic characteristics across Middle Eastern countries, regional collaboration, such as a Gulf Corporation Council, would enhance statistical power, enable cross-country comparisons, and produce more generalizable reference values for Middle Eastern populations.[21] Third, integration of artificial intelligence and machine learning provides a promising avenue by enabling ethnicity-independent risk prediction models and automated CAC scoring from both gated and non-gated CT scans, potentially reducing reliance on reference databases while expanding accessibility.[22] Finally, hybrid approaches for risk stratification combining absolute CAC thresholds (e.g., 100 or 300 Agatston units) with AI-derived predictive models may offer an interim solution. This dual strategy could mitigate the risk of misclassification while awaiting population-based percentile charts.

Ethics Approval

Not applicable. This article is a narrative review and did not involve human participants or animals, and no new data were collected.

Limitations

This article is a narrative, not a systematic, review. Although efforts were made to include key and contemporary studies, the search strategy was not designed to comprehensively identify all eligible publications and may be susceptible to selection and publication bias.

Conclusion

CAC scoring is a well-validated tool for cardiovascular risk stratification, but current reference standards—largely derived from MESA—do not include Saudi or Middle Eastern populations. This limits accuracy and risks misclassification, especially given the region's high prevalence of diabetes, obesity, and metabolic syndrome. Local studies highlight this gap but remain methodologically limited. To address this challenge, large population-based cohorts and regional collaborations are needed to establish robust local reference values. In parallel, artificial intelligence offers opportunities for ethnicity-independent risk prediction and automated CAC scoring. Together, these approaches may ensure more precise cardiovascular risk assessment in Saudi Arabia and the broader Middle East.

Animal and Human Rights Statement

Not applicable. No procedures involving human participants or animals were performed.

Informed Consent

Not applicable.

Data Availability Statement

Not applicable. No original datasets were generated or analyzed in this narrative review.

Conflict of Interest

The authors declare that there is no conflict of interest.

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Scientific Responsibility Statement

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