



## REVIEW

# Coronary artery calcium scoring. What clinicians need to know

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## Abstract

Coronary artery calcium (CAC) scoring, measured by computed tomography (CT), quantifies calcified coronary plaque and reflects the burden of coronary atherosclerosis. The Agatston score, calculated based on lesion density and area, stratifies patients into risk categories: a score of 0 indicates no detectable calcification, 1-99 suggests mild plaque, 100-399 indicates moderate burden, and scores of 400 or more reflect high to extensive calcification, with scores above 1000 indicate extremely high atherosclerotic burden. CAC scoring is most beneficial in asymptomatic adults aged 40 to 75 years with borderline (5-7.5%) or intermediate (7.5-20%) 10-year ASCVD risk when uncertainty exists regarding statin initiation. The Multi-Ethnic Study of Atherosclerosis (MESA) found that a CAC score of 0 significantly reduces estimated ASCVD risk compared to pooled cohort equation (PCE) predictions, with observed event rates of approximately 1.5% for borderline-risk and 4.5% for intermediate-risk individuals, supporting reclassification into a lower-risk category. Scores of 1-99 represent modestly elevated risk and may guide prevention based on clinical judgment and patient preference. Scores from 100 to 400 reflect moderate plaque burden and support statin therapy, while high scores above 400 reflect substantial atherosclerotic burden, mandating aggressive preventive interventions. CAC testing is generally not indicated in younger, low-risk adults, as they may develop ASCVD later in life, and a score of 0 could lead to false reassurance that discourages appropriate prevention. Similarly, testing is typically unnecessary in elderly individuals with established atherosclerotic disease, as results rarely change management. It is also not recommended in those with clear statin indications, including patients with diabetes, familial hyperlipidemia, existing ASCVD, or those already on lipid-lowering treatment. Frequent CAC retesting is discouraged due to limited clinical benefit, unnecessary costs, potential downstream testing, patient anxiety, and exposure to radiation, though repeating CAC after five years may be reasonable for those initially scoring zero. The recent CAUGHT-CAD trial showed that CAC-informed strategies reduced LDL cholesterol and slowed plaque progression in intermediate-risk individuals with familial coronary artery disease, highlighting its importance. Future research should focus on optimizing CAC use to enhance patient outcomes while balancing clinical utility, cost, and risk.

**Key words:** imaging; computer tomography; coronary artery disease.

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## Introduction

Cardiovascular disease (CVD) remains the leading cause of death globally, with a marked increase in both prevalence and mortality over the past two decades. The number of deaths due to CVD surged from 12.1 million in 1990 to 18.6 million in 2019.<sup>1</sup> Among the various forms of CVD, coronary heart disease (CHD) accounts for a substantial portion, necessitating

a broad array of diagnostic measures, hospital admissions, and pharmacological interventions.<sup>2</sup> Patients with CHD often present with stable angina, or chest pain, which if left untreated, can progress to fatal events. Effective management begins with a comprehensive history, followed by non-invasive diagnostic techniques like electrocardiography (ECG) and coronary computed tomography angiography (CTA) to assess coronary artery calcium (CAC) scores.<sup>2</sup>

## Coronary artery calcification

CAC scoring is a highly specific indicator of coronary atherosclerosis and has emerged as an invaluable tool for assessing the risk of major cardiovascular events, including myocardial infarction or death. This technique is especially useful in asymptomatic individuals, helping guide primary prevention strategies such as statin and aspirin therapy.<sup>3</sup> Previously thought to be a passive consequence of aging, the development of calcium-containing atherosclerotic plaques is now understood as an active process involving ectopic bone formation. Factors such as oxidative stress also play a significant role in this calcification process, with lipid oxidation generating pro-osteogenic minimally modified low-density lipoproteins and phospholipids.<sup>3</sup> Oxidative stress, a known contributor to coronary artery disease (CAD), is also central to all the other cardiovascular conditions, including heart failure.<sup>4,5</sup>

The most common method for visualizing calcified plaques in the coronary arteries is ECG-gated computed tomography (CT). Multidetector CT (MDCT), which offers higher precision, can produce results in 10 to 15 min, using only 1 mSv of radiation.<sup>3</sup> The Agatston scale, measured in Hounsfield units, is the standard grading technique for quantifying the extent of atherosclerotic plaques. This score is calculated as the product of the total calcified plaque area (in square millimeters) and a weighted peak calcium density.<sup>6,7</sup>

Interestingly, while men tend to have higher CAC scores, women are more likely to present with non-calcified, lipid-rich plaques that evade detection on CT scans. These plaques often result in diffuse multi-vessel involvement in women, likely due to smaller vascular lumen, increased arterial stiffness, and lower flow reserves. Moreover, women experience higher CVD mortality rates than men, primarily due to atypical symptoms that may be misinterpreted, late presentations and less effective risk stratification with traditional predictive models, such as the Framingham Risk Score (FRS).<sup>8</sup> Consequently, lower CAC scores in women are strongly indicative of subclinical coronary atherosclerosis and serve as independent predictors of major cardiovascular events.<sup>8</sup> However, gender-specific guidelines for CAC stratification are still lacking, despite the growing evidence of the tool's accuracy in assessing cardiovascular risk in women.<sup>1</sup>

## Clinical evidence

Numerous studies, both short- and long-term, have demonstrated the utility of CAC scoring in reducing the future risk of atherosclerotic cardiovascular diseases (ASCVD). By further stratifying individuals at intermediate risk, CAC scoring provides a more nuanced approach to preventive measures. One prominent study, the Multi-Ethnic Study of Atherosclerosis (MESA), examined age and sex-related CAC scores, identifying racial disparities in CAC prevalence. Specifically, White patients exhibited higher CAC scores than expected based on traditional risk factor models (70.4% of men and 44.6% of women showed

calcification).<sup>3</sup> MESA introduced estimated curves for the 50<sup>th</sup>, 75<sup>th</sup>, and 90<sup>th</sup> percentiles of calcium across age, providing useful reference values for clinicians to assess individual patient risk.<sup>9</sup> Similarly, the Heinz Nixdorf Recall (HNR) study, a German cohort, found a high CAC prevalence (82% in men and 55% in women), reinforcing the importance of CAC scoring across different populations.<sup>3</sup>

The Rotterdam Study, using older cohorts, also found a strong association between CAC scores and future CHD events, with a CAC score <100 showing a 3% incidence of CHD over four years, while a score >1000 had an incidence of 12%.<sup>10</sup> The Framingham Heart Study (FHS) incorporated MDCT measurements of CAC in its Offspring and Third Generation cohorts and demonstrated that each additional coronary artery with calcification increased the risk of major CHD events by nearly 70%.<sup>11</sup> The CARDIA (Coronary Artery Risk Development in Young Adults) study, focusing on a younger cohort, showed that any degree of calcification in these patients was associated with a 5-fold increased risk of CHD and a 3-fold increased risk of CVD events.<sup>12</sup> Furthermore, the Jackson Heart Study, which included African American participants, found that adding CAC scores improved the diagnostic accuracy of the Framingham Risk Score by 4% in those with a known CVD event and by 28.5% in those without prior CVD events.<sup>13</sup>

Another study identified heterogeneity in the relationship between CAC >0 and incident CVD events, noting that while a CAC score above zero led to a 2.5% increased risk of CVD, certain demographic groups (older men of White descent, less educated individuals, and former smokers) showed more pronounced associations. These patients also exhibited risk factors such as higher systolic and diastolic blood pressure, lower estimated glomerular filtration rate (eGFR), and higher diabetes prevalence.<sup>14</sup>

Importantly, while a CAC score of 0 is often interpreted as low risk, the Progression of Early Subclinical Atherosclerosis (PESA) study demonstrated that this may not indicate the absence of atherosclerotic disease.<sup>15</sup> Approximately 60% of participants with a CAC score of 0 had non-coronary plaques at other vascular sites, underscoring the need for careful interpretation of CAC results in the broader context of systemic atherosclerosis. In the Aragon Workers' Health Study, subclinical atherosclerosis was most prevalent in the femoral arteries, and the presence of femoral plaques showed a stronger association with traditional cardiovascular risk factors and positive CAC scores than carotid plaques, indicating that femoral ultrasound may improve risk stratification when assessing early coronary atherosclerosis.<sup>16</sup>

## Current guidelines

Current international guidelines recommend using CAC scores to refine risk classification in intermediate-risk patients, helping determine whether statin therapy or other interventions are appropriate. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend re-classifying intermediate-risk patients (10-year

ASCVD risk 7.5-20%) or borderline-risk patients (5-7.5% risk) based on CAC scoring and additional risk-enhancing factors. Asymptomatic patients with no history of diabetes and LDL levels between 70-189 mg/dL should be considered for CAC scoring.<sup>17</sup> Similarly, the Canadian Cardiovascular Society (CCS) integrates both CAC scores and the Framingham Risk Score (FRS),<sup>18</sup> while the Cardiac Society of Australia and New Zealand (CSANZ) and the UK's National Institute for Health and Care Excellence (NICE) guidelines recommend CAC scoring for asymptomatic individuals aged 45–75 without known CVD.<sup>19,20</sup> Most guidelines suggest withholding therapy in patients with a CAC score of 0, re-evaluating their risk after 5 years follow-up period.<sup>1</sup>

Some national guidelines, such as those from China and Japan, caution against using CAC scores in routine assessments due to lower ASCVD incidence in their regions. Other reasons could include cost-effectiveness concerns in healthcare systems with different resource allocation priorities, as well as different thresholds for initiating preventive therapies based on population-specific risk-benefit analyses (Table 1).<sup>21,22</sup> Additionally, predictive models like MESA's modified Pooled Cohort Equations (PCE) and the European Systematic COronary Risk Evaluation 2 (SCORE 2) models have been developed, combining CAC scoring with traditional risk factors for more personalized risk assessment. Other models, such as the ADVANCE (Action in Diabetes and Vascular Disease-

PreterAx and DiamicroN Controlled Evaluation) risk score, SMART (Secondary Manifestations of Arterial Disease) risk score, and MAGGIC (Meta-Analysis Global Group in Chronic Heart Failure) risk calculator, aim to further refine risk prediction in specific populations, such as diabetic patients and those with heart failure.<sup>1</sup>

## Primary and secondary prevention with CAC scores

Statin therapy remains the cornerstone for preventing ASCVD events. Statins are typically not initiated if the CAC score is 0. However, the CCS guidelines recommend considering statins in such patients if other risk factors are present.<sup>18</sup> For patients with CAC scores between 1 and 99, personalized statin therapy is advised, depending on additional risk factors. For individuals with CAC scores >100, intensive statin therapy should be considered,<sup>17,18</sup> although the CSANZ guidelines regard CAC scores between 101 and 400 in the <75<sup>th</sup> percentile as an intermediate risk.<sup>19</sup> The European Society of Cardiology (ESC) suggests reclassifying patients with CAC scores >100 and LDL-C levels <70 mg/dL into the high-risk category, though statin therapy guidance is not explicitly addressed in this context.<sup>23</sup>

The National Lipid Association (NLA) offers more in-depth

**Table 1.** International guidelines for statin and aspirin therapy in light of CAC scoring.<sup>1</sup>

International guidelines	CAC=0	CAC>0 or 1-99	CAC>100
ACC/AHA (2019)	Classified low risk, no therapy required	Consider statin therapy if risk factors present, age >55years	<ul style="list-style-type: none"> <li>Initiate statins therapy, low dose aspirin (75-100 mg daily) recommended if no bleeding risk for age 40-70 years</li> </ul>
CCS (2021)	Classified low risk, no statin therapy required No aspirin therapy	Classified low risk, no therapy required No aspirin therapy	<ul style="list-style-type: none"> <li>Initiate therapy</li> </ul>
NICE (2016)	Classified low risk, no statin therapy required No aspirin therapy	–	<ul style="list-style-type: none"> <li>Initiate statin therapy</li> <li>If chest pain diagnosed as angina/MI, start low dose aspirin</li> </ul>
CSANZ (2017)	Classified low risk, o statin therapy required No aspirin therapy	Classified low risk, no therapy required No aspirin therapy	<ul style="list-style-type: none"> <li>CAC101-400 &lt;75th percentile = consider statin therapy</li> <li>CAC score101-404 and &gt;75th percentile = initiate statin therapy</li> <li>Low dose aspirin (75-100 mg daily) recommended</li> </ul>
ESC (2019)	–	–	<ul style="list-style-type: none"> <li>Classify as risk and consider statin therapy</li> <li>If diabetes, 10-year risk &lt;20%, no bleeding risk, use aspirin 81mg daily</li> </ul>
CSC (2016)	–	–	<ul style="list-style-type: none"> <li>No information on statin use</li> <li>Consider low dose aspirin</li> </ul>
JAS (2017)	–	–	–

ACC/AHA, American College of Cardiology/American Heart Association; CCS, Canadian Cardiovascular Society; NICE, National Institute for Health and Care Excellence; CSANZ, Cardiac Society of Australia and New Zealand; ESC, European Society for Cardiology; CSC, Chinese Society of Cardiology; JAS, Japanese Atherosclerotic Society.

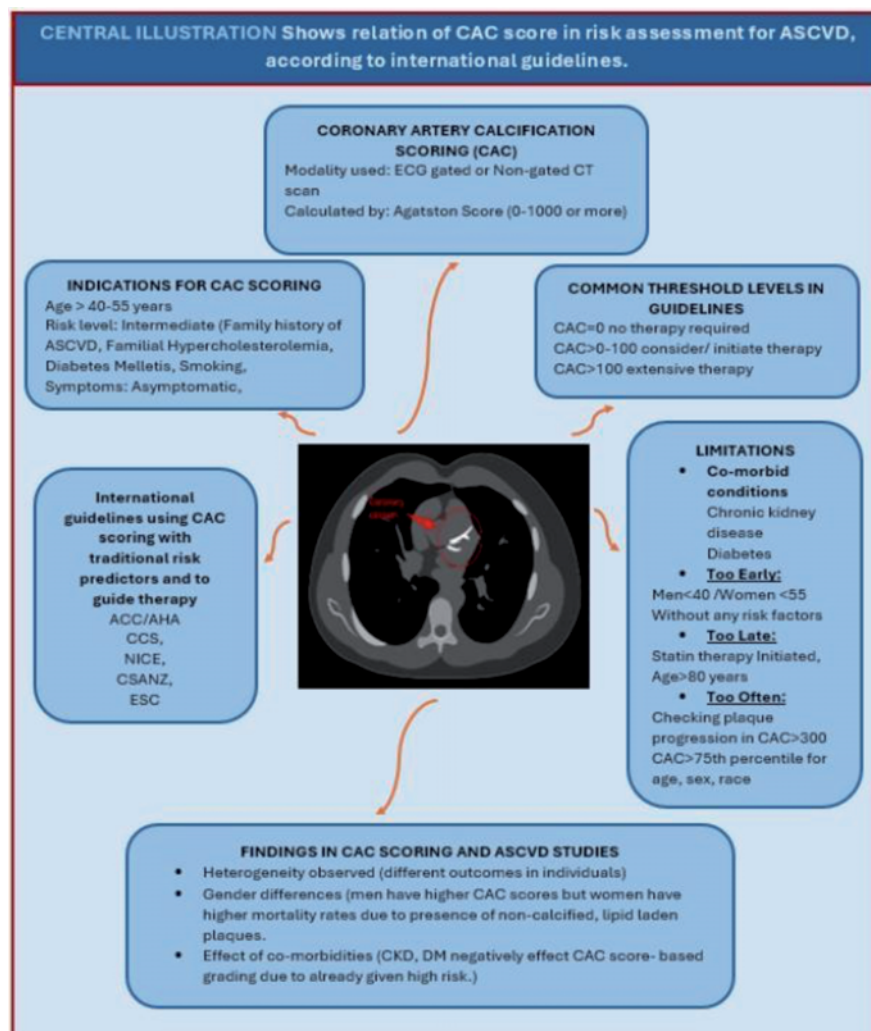
recommendations for reclassifying high-risk patients based on CAC scoring, particularly in individuals with a CAC score >400, where the benefits of aspirin outweigh the potential bleeding risks. In such cases, daily aspirin (81 mg) is recommended, assuming no contraindications.<sup>24</sup> Despite these guidelines, most international recommendations do not consider CAC scoring essential for further stratification in patients with hypertension, except in estimating blood pressure goals for intermediate-risk individuals.<sup>1</sup>

## Limitations of CAC scoring

While CAC scoring offers considerable value, its interpretation requires consideration of disease-specific factors, particularly in individuals with high-risk comorbidities such as chronic kidney disease (CKD) and diabetes. In CKD, calcified plaques tend to occur earlier, progress more rapidly, and result from

both traditional atherosclerotic mechanisms and CKD-specific pathways. Additionally, increased inflammation, impaired calcium-phosphorus homeostasis, and a higher prevalence of non-calcified plaques that are not detectable on CT may limit the utility of CAC scoring in these populations.<sup>1</sup>

CAC scoring is generally not recommended in individuals younger than 40 years in men or 55 years in women, particularly in the absence of risk factors, as the likelihood of detecting calcification is low. In this group, a CAC score of 0 may provide false reassurance, despite the potential for developing ASCVD later in life. In older adults, particularly those over 80 years of age, the prevalence of coronary calcification is high and most individuals are already receiving appropriate preventive therapies. In such cases, CAC scoring rarely alters clinical decision-making and provides limited additional value. Lastly, frequent use of CAC scoring in patients already on statin therapy with CAC scores >300 is discouraged, as there is no known benefit in monitoring



**Figure 1.** Coronary artery calcium (CAC) score in risk assessment for atherosclerotic cardiovascular diseases (ASCVD).

plaque progression in these cases.<sup>25</sup> As a result, CAC testing is most useful in asymptomatic adults aged 40 to 75 years with borderline or intermediate 10-year ASCVD risk, where it can meaningfully guide decisions regarding preventive therapy. Figure 1 summarises the review highlighting the modalities and scoring system used for Coronary Artery Calcium (CAC) scoring, the names of guidelines that promote using CAC scores for re-classification for risk prediction in intermediate-risk individuals, common threshold levels used for stratification of risk prediction, indications and limitations for CAC scoring in patients, and specific findings in different studies with respect to individual differences, age, gender, and comorbidities..

## Conclusions

CAC scoring is a valuable, non-invasive tool that enhances cardiovascular risk prediction beyond traditional models, particularly in asymptomatic, intermediate-risk individuals. It informs preventive strategies such as statin and aspirin therapy, contributing to more personalized care. As evidence grows, further refinement of its use across diverse populations and clearer guideline integration will help optimize its clinical utility and ensure equitable cardiovascular risk assessment.

## Contributions

All authors made a substantive intellectual contribution, read and approved the final version of the manuscript and agreed to be accountable for all aspects of the work.

## Conflict of interest

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