

## JAMA Insights

## Cardiac CT Calcium Score

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**What Is Coronary Artery Calcium and the Cardiac Computed Tomography Calcium Score?**

Coronary artery plaque can consist of calcified and/or noncalcified material. Computed tomography (CT) can detect and measure coronary artery calcium (CAC) levels in calcified plaque, which increases


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with age and is more common at all ages in men than women.<sup>1,2</sup> In a study of 19 725 asymptomatic individuals aged 30 to 45 years without known coronary disease from 3 US studies, 21% had any detectable CAC (CAC score >0).<sup>3</sup> In the Multi-Ethnic Study of Atherosclerosis (MESA) of 6110 asymptomatic US individuals without known cardiovascular

disease aged 45 to 84 years (mean age, 62 years), the presence and amount of CAC was greater in older adults.<sup>2</sup> Among men and women younger than 55 years, more than half of asymptomatic individuals had no detectable CAC.<sup>2</sup> However, among those 80 years or older, more than 80% had some detectable CAC.<sup>2</sup>

The standard method to detect and quantify CAC is gated cardiac CT, which uses the patient's electrocardiogram (ECG) to time CT imaging acquisition to improve image quality. CAC can also be identified on non-ECG-gated CT chest imaging but may not be as precise as an ECG-gated CT. CAC is quantified by the Agatston score, a measure of total coronary atherosclerotic burden. The Agatston score is the sum of the attenuation (in Hounsfield units) and area of all CAC lesions in all coronary arteries. Scores range from 0 (no calcified plaque) to more than 1000 (extensive calcified atherosclerosis), with no specific maximum score. The CT-derived Agatston score represents the extent of coronary atherosclerosis and has been strongly associated with future atherosclerotic cardiovascular disease (ASCVD) in several large studies. Using data from MESA, individuals with CAC scores greater than 300 Agatston units had 10-year ASCVD event rates (defined as myocardial infarction, stroke, resuscitated cardiac arrest, and cardiac deaths) of 13.1% to 25.6% (higher rates in men and older individuals), compared with 1.3% to 5.6% in those with a CAC score of 0.<sup>3</sup> For each 2-fold higher CAC score, there was a 14% relative increase in ASCVD risk.<sup>4</sup> Conversely, a CAC score of 0 in MESA participants was associated with low ASCVD event rates (5.2 per 1000 person-years), even for individuals in whom statins were recommended based on predicted 10-year risk of 7.5% or greater in the 2019 American College of Cardiology (ACC)/American Heart Association (AHA) Primary Prevention Guidelines.<sup>5</sup>

Incidentally detected CAC on nongated CT chest scans, which is generally reported qualitatively as absent, mild, moderate, or severe, also predicts coronary heart disease (CHD) risk. In patients referred for lung cancer screening due to tobacco use in the National Lung Screening Trial, CAC was present in more than 70% of individuals on nongated thoracic CT scans. In multivariable analysis of time to CHD death, compared with a CAC score of 0, CAC

scores of 1 to 100, 101 to 1000, and greater than 1000 Agatston units were associated with hazard ratios of 1.27 (95% CI, 0.69-2.53), 3.57 (95% CI, 2.14-7.48), and 6.63 (95% CI, 3.57-14.97), respectively.<sup>6</sup>

**Coronary Heart Disease Risk Prediction Scoring**

MESA developed a CHD risk prediction score, validated in 2 external cohort studies, that uses CAC score plus traditional risk factors (age, sex, high-density lipoprotein cholesterol, total cholesterol, systolic blood pressure, antihypertensive medication use, current smoking, and diabetes).<sup>7</sup> The addition of CAC to a score using only traditional risk factors resulted in significant improvement in risk discrimination (C statistic, 0.80 vs 0.75).<sup>7</sup> A risk calculator that uses CAC plus traditional risk factors is accessible online.<sup>8</sup> However, a risk tool that integrates CAC is unlikely to be widely adopted because universal testing for CAC is not currently recommended.

**When Should CAC Testing Be Considered?**

The most common clinical scenario in which CAC testing should be considered is in an asymptomatic patient undergoing risk assessment for ASCVD. The 2019 ACC/AHA Primary Prevention Guidelines stated that the main purpose of CAC measurement is to facilitate decision-making regarding statin therapy. Therefore, CAC testing is not recommended for individuals already taking a statin, those with known ASCVD, or for individuals with certain ASCVD risk factors (eg, familial hyperlipidemia, diabetes, current smoking) in whom statin therapy is recommended regardless of CAC score.

The ACC/AHA Guidelines recommend considering CAC scoring in asymptomatic individuals aged 40 to 75 years without diabetes and low-density lipoprotein cholesterol of 70 to 189 mg/dL or greater with borderline (10-year ASCVD risk, 5.0% to <7.5%) or intermediate risk ( $\geq 7.5\%$  to 20%) if the patient or clinician is uncertain about statin therapy initiation. CAC is the preferred test in this situation due to its superior risk discrimination and risk reclassification compared with other imaging and/or serum biomarkers (such as high-sensitivity C-reactive protein, triglycerides, or lipoprotein[a]). Although the effect of CAC scoring has not been tested in a randomized clinical trial, epidemiologic data demonstrate that CAC can reclassify individuals at borderline or intermediate ASCVD risk who would benefit from additional preventive treatment, such as a statin, into a higher risk category. Conversely, a CAC score of 0 reclassifies those at borderline or intermediate risk into the low risk category. Because CAC varies by age and sex, guidelines have also suggested using age- and sex-specific CAC percentiles instead of Agatston score alone. The ACC/AHA Primary Prevention Guidelines suggest a CAC score of 100 or greater or a CAC score in the 75th percentile or above favors statin therapy. CAC scoring may also be considered when treatment decisions are uncertain for individuals with certain high-risk factors, such as a family history of ASCVD in men younger than 55 years or women younger than 65 years, chronic kidney disease, inflammatory disease (HIV, rheumatoid arthritis), or a history of preeclampsia. The clinical recommendations from the ACC/AHA Guidelines are summarized in the Table.<sup>4,9</sup>

Table. Potential Uses of Coronary Artery Calcium (CAC) Score and Estimated Risk of Atherosclerotic Cardiovascular Disease (ASCVD)<sup>a</sup>

	10-y ASCVD risk estimate according to pooled cohort equations <sup>a</sup>			
	<5%	5%-7.5%	>7.5%-20%	>20%
Using ASCVD risk estimate alone	Statin not recommended	Consider use of statin	Recommend statin	Recommend statin
Using ASCVD risk estimate + CAC score				
If CAC score = 0	Statin not recommended	Statin not recommended <sup>b</sup>	Statin not recommended <sup>b</sup>	Recommend statin
If CAC score >0	Statin not recommended	Consider use of statin <sup>b</sup>	Recommend statin <sup>b</sup>	Recommend statin

<sup>a</sup> Ten-year risk of ASCVD calculated per 2019 American College of Cardiology/American Heart Association Guidelines.<sup>4</sup>

<sup>b</sup> Groups of patients for whom CAC score can change statin recommendation.

### What Are the Direct and Indirect Costs of CAC Testing?

For asymptomatic individuals, CAC testing is not covered by the Centers for Medicare & Medicaid Services and is typically not covered by private insurance. Out-of-pocket costs range from approximately \$50 to \$400. CAC scoring can also lead to increased costs from additional cardiac testing (stress testing, invasive angiography) and from evaluation of incidental findings (lung nodules, aortic dilation). However, the discovery of a high CAC score in an asymptomatic patient should not automatically lead to additional cardiac testing, since additional testing should be based on the presence of symptoms and any other high risk factors. Recently, many health care systems have made CAC testing available by self-referral. Because of the increasing prevalence of self-referral, it will be important to evaluate characteristics of those who self-refer for CAC scoring, and the risk reclassification, downstream testing, and cost-effectiveness in this population.

### Practical Considerations

When CAC is detected, the goal is to reduce risk of future adverse cardiovascular events rather than attempt to reduce coronary cal-

cification. Lifestyle and pharmacotherapy (eg, statin and blood pressure medication) can modestly regress and stabilize atherosclerotic plaque by increasing its density, thereby reducing risk of future cardiovascular events but paradoxically increasing the CAC score. If CAC is detected and statin is prescribed per guidelines, repeat CAC scoring is not advised, as a change in CAC score would not affect management.<sup>4</sup> If the initial CAC score is 0, repeat scoring in patients older than 40 years may be considered after 5 years.<sup>10</sup>

### Summary

The CAC score improves ASCVD risk assessment, particularly in individuals at borderline or intermediate ASCVD risk who are not already taking statin medication (Table). A CAC score greater than 0 indicates the presence of calcified coronary atherosclerosis and portends higher ASCVD risk compared with those with a CAC score of 0. Statin therapy is recommended for asymptomatic individuals with a CAC score of 100 or greater Agatston units and may be considered for those with a CAC score of 1 to 99 Agatston units, especially in patients younger than 45 years.<sup>4</sup>

### ARTICLE INFORMATION

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