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VIEWPOINT

Coronary Artery Calcium Staging to Guide Preventive Interventions

A Proposal and Call to Action

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Coronary artery calcium (CAC) as measured by the Agatston score is a strong predictor of atherosclerotic cardiovascular disease (ASCVD) events.[1] In the 2019 American College of Cardiology (ACC) and American Heart Association (AHA) clinical practice guideline for the primary prevention of cardiovascular disease, it is a Class IIa recommendation to use the CAC score to inform shared decision-making for individuals at intermediate risk if the decision to start statins is uncertain after global risk assessment and the consideration of risk enhancing factors.[2] The 2022 ACC Expert Consensus Decision Pathway on the role of nonstatin therapies for low-density lipoprotein cholesterol (LDL-C) lowering in the management of ASCVD risk recommended that CAC measurement be considered to inform treatment decisions for adults without clinical ASCVD when there is either clinician uncertainty or patient hesitancy about starting statin therapy.[3] That document recommended LDL-C threshold levels for the consideration of different intensities of statin and nonstatin therapy depending on the CAC score among borderline and intermediate risk individuals. Budoff and colleagues reported subsequently that the risk for major adverse cardiovascular events of individuals without clinical ASCVD with a CAC score >300 is equivalent to the risk of individuals with a documented history of myocardial infarction, stroke, or peripheral arterial disease (ie, ASCVD),[4] suggesting that such patients could be treated similarly to those with clinical ASCVD.

Despite overwhelming evidence that CAC is a powerful predictor of ASCVD events and the aforementioned recommendations of medical societies, clinicians remain uncertain how to manage patients once they document the presence and quantity of CAC. A widely practiced, personalized approach to managing disease throughout medicine is to stage the disease. The rationale for staging is to determine the extent, severity, location, and prognosis of disease, and use this to tailor the type and intensity of therapy. Staging also provides a common language with which clinicians can communicate with each other and with patients. This approach has been adopted by the American Cancer Society. The AHA and ACC have developed a staging system to inform the management of heart failure.[5] More recently, the AHA developed a staging system for cardiovascular-kidney-metabolic syndrome. One of the criteria defining Stage 3 in that construct is presence of

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The authors attest they are in compliance with human studies committees and animal welfare regulations of the authors' institutions and Food and Drug Administration guidelines, including patient consent where appropriate. For more information, visit the Author Center.

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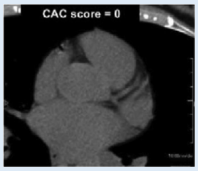
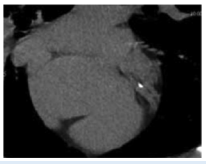
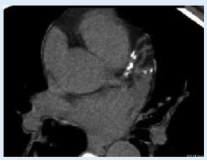
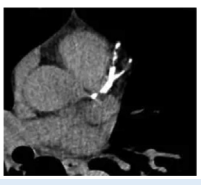
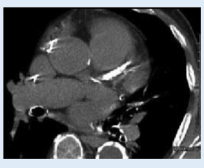
TABLE Proposed Coronary Artery Calcium Staging Guide to Therapy

Stage	CAC Score and Disease Level	Representative Scan Image (White = CAC)	Therapeutic Recommendations Based on ACC/AHA Expert Consensus and Guidelines[2,3]
0	• CAC Score: 0 • No calcified plaque • Visual score: CAC absent		• Promote American Heart Association Life's Essential 8 Optimal Risk Factor Goals[7] • Consider no statin *unless* diabetes, LDL-C ≥190 mg/dL, smoker, family history of premature ASCVD, 10-y ASCVD risk ≥20%, or high Lp(a) • Consider repeat CT for CAC or analysis of nongated chest CT at: ○ 3 y for diabetes or high 10-y risk for ASCVD ○ 3-5 y for intermediate 10-y risk for ASCVD ○ 5-7 y for low 10-y risk for ASCVD
1	• CAC Score: 1-99 and <75th percentile for age and sex • Mild atherosclerotic burden		• Promote American Heart Association Life's Essential 8 Optimal Risk Factor Goals[7] • Statin (+nonstatin) therapy as needed to achieve LDL-C goal <100 mg/dL • Serial monitoring of all risk factors (eg, LDL-C, systolic blood pressure) to achieve critical biometric targets
2	• CAC Score: 100-299 or ≥75th percentile for age and sex • Moderate atherosclerotic burden		• All of the above plus: • Statin (+nonstatin) therapy as needed to achieve LDL-C goal <70 mg/dL • Consider low-dose aspirin therapy
3	• CAC Score: 300-999 • Severe atherosclerotic burden • Very high risk; risk associated with CAC ≥300 is similar to having had a myocardial infarction		• All of the above plus: • High-intensity statin (+nonstatin) therapy as needed to achieve LDL goal <55 mg/dL[3] • Low-dose aspirin
4	• CAC Score: ≥1,000 • Extensive atherosclerotic burden • Extreme risk; risk associated with CAC ≥1,000 similar to having had multiple ASCVD events		• All of the above plus: • Statin (+nonstatin) therapy as needed to achieve LDL-C goal <55 mg/dL[3] • Consider emerging therapies[a]

[a]For example, low-dose anticoagulant in combination with low-dose aspirin, anti-inflammatory therapy (eg, low-dose colchicine).

ASCVD = atherosclerotic cardiovascular disease; CAC = coronary artery calcium; LDL-C = low-density lipoprotein cholesterol; Lp(a) = lipoprotein(a).

subclinical atherosclerosis as defined by coronary calcium.[6]

Since 2008, The Right Care Initiative has been convening medical experts, health systems administrators, and government and public health leaders with the goal of implementing the best practices to prevent myocardial infarctions and strokes (https://rightcare.berkeley.edu). The Right Care Initiative convened a CAC working group of clinical cardiologists, health services researchers, epidemiologists, clinical trialists, and cardiovascular imagers to promote implementation of best available evidence to prevent morbidity and mortality from ASCVD. The working group developed a staging system based on coronary calcium, existing primary prevention guidelines,[2] and the 2022 ACC Expert Consensus Decision Pathway[3] to guide clinicians and patients in the management of individuals who have CAC without clinical ASCVD (**Table**).

While the absence of CAC invokes a lower risk state, and the 2019 ACC/AHA primary prevention guidelines allow for no statin treatment (with the exception of high-risk states, such as diabetes, family history of premature heart disease, or active smoking),[2] it is important to still promote healthy lifestyles in this population, and control of other cardiovascular risk factors (such as hypertension and obesity) that have consequences beyond atherosclerotic heart disease.

When mild calcified atherosclerosis is present (CAC 1-99), it is important to identify whether the patient has a low score when adjusted for age, race/ethnicity and sex, or a high (≥75th percentile) relative score. While absolute scores predict events better than age-sex-race percentiles for short-term events, lifetime risk is high in those who have more CAC than expected. This construct is widely used, and 10-year risk for coronary heart disease can be calculated for most

patients with the MESA risk calculator, http://www.mesa-nhlbi.org/CACReference.aspx, or using tables with age-sex-race categories from population based assessments. For patients with mild atherosclerosis (CAC 1-99) and <75th percentile for age-sex-race, it is prudent to treat with statin (+nonstatin) therapy as needed to achieve the LDL-C goal <100 mg/dL.

When the CAC score indicates moderate atherosclerosis (CAC 100-299) or the score is >75th percentile, lifetime risk and short-term risk are elevated, and more aggressive risk factor modification and statin (+nonstatin) therapy as needed to achieve an LDL-C goal <70 mg/dL should be considered. Aspirin is recommended by numerous guidelines and expert consensus documents when CAC is >100, as the risk-benefit ratio becomes favorable at that cutpoint. Further, serial monitoring of all risk factors to ensure targets are met is advised, as these patients have a 10-fold increased risk of ASCVD events as compared with those without CAC present (score of zero).

Once the CAC score is 300 or greater, the risk of a myocardial infarction is similar to that of a myocardial infarction survivor,[4] thus high-intensity statin and aspirin therapy should be considered, and other therapies that have been mostly reserved for secondary prevention (eg, GLP1 RA, icosapent ethyl, colchicine) should also be considered as appropriate for the individual. Such patients are considered very high risk and should be targeted with statin and nonstatin therapy as needed to achieve an LDL-C <55 mg/dL. Scores >1,000 carry even higher risk,[8] and warrant even greater risk reduction (ie, LDL-C <55 mg/dL).

The Working Group recognizes that, while evidence for the association of risk of events with CAC is overwhelming, the benefit of preventive therapy based upon CAC severity is not yet fully established. Our goal is to improve implementation of existing guidelines and expert consensus with the proposed staging system and serve as a call to action. Yet CAC staging will only be useful if CAC testing is performed. Most health insurance plans do not cover CAC testing. Importantly, the lack of access to this test exacerbates health disparities in ASCVD risk assessment. Compared with municipalities where CAC testing is available, those without CAC testing have lower socioeconomic status, more non-White residents, and lower life expectancies.[9] A study in Cleveland found that when all costs for CAC scans were eliminated, testing increased among women, Black individuals, and lower income patients with a concomitant improvement in reclassification of statin eligibility, preventive interventions, and risk factor control.[10] We call upon payers and health systems to recognize the utility of CAC testing and reduce barriers to its use so that subclinical coronary disease can be detected and preventive interventions implemented in patients at risk before they suffer irreversible consequences.

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