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Computed Tomography for Coronary Artery Calcification Scoring: Mammogram for the Heart

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ABSTRACT

Coronary artery calcium (CAC), identified via low-radiation, non-contrast computed tomography of the heart, quantifies the burden of calcified coronary atherosclerosis. This modality is highly useful for cardiovascular (CV) risk stratification among individuals without known coronary heart disease (CHD), especially for those at intermediate risk. The presence of CAC is associated with up to a 10-fold higher risk of adverse CV events, even after fully adjusting for the standard CV risk factors. In fact, the CAC score is among the strongest clinically available predictors of future risk of adverse CV events among primary prevention patients. Additionally, the absence of CAC in asymptomatic individuals confers a very low risk of CV events. Even in the presence of a benign CV risk factor profile and normal cardiac stress test, a very high CAC score portends a high risk of adverse CV events. On the other hand, a CAC score of zero is associated with a low CHD risk despite significant CV risk factor profiles. CAC scoring is a quick, low-cost screening tool to help risk-stratify patients and identify those likely to benefit from aggressive preventive treatments (such as high-intensity statin therapy, ezetimibe, PCSK9 inhibitors, and aspirin) and to identify those likely who warrant close monitoring. Moreover, individuals with a zero CAC score may be at low enough risk to avoid or defer daily aspirin therapy and pharmacological therapy for cholesterol management, and instead work on therapeutic lifestyle changes. An abnormal CAC score may also lead to better adherence to pharmacological regimens and suggested lifestyle changes.

Coronary artery calcium (CAC) screening is based upon x-ray computed tomography (CT) scan of the heart, either electron beam CT or multi-detector CT (MDCT). This test identifies the presence of coronary atherosclerosis by documenting the presence and extent of calcium hydroxyapatite in the arterial wall. CAC testing is among the strongest clinically available predictors of major adverse cardiovascular (CV) events (MACE) among patients with no known coronary heart disease (CHD).[1,2] This test does not require x-ray contrast, is low cost (total charge of $50–$150 in many United States [US] centers), and utilizes a modest radiation dose (typically 0.7–1.0 millisieverts).[3]

Although arterial calcium can be quantified with the calcium mass or the calcium volume score, in clinical practice and in the vast majority of medical studies, the CAC score (CACS) is calculated using the Agatston methodology, a

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Abbreviations and Acronyms

ABI = ankle-brachial index

ACC = American College of Cardiology

AHA = American Heart Association

ASCVD = atherosclerotic cardiovascular disease

ATP = Adult Treatment Program

CAC = coronary artery calcium

CACS = coronary artery calcium score

CHD = coronary heart disease

CT = computed tomography

CV = cardiovascular

FRS = Framingham Risk Score

HR = hazard ratio

LDL-C = low density lipoprotein cholesterol

MACE = major adverse cardiovascular events

NRI = net reclassification improvement

US = United States

method that gives weight to the density of calcifications.[1–3] CACS correlates closely with calcified atherosclerotic plaque burden, and the presence of CAC is virtually diagnostic of coronary atherosclerosis.[1–3]

CAC screening for predicting CHD risk

The CACS is directly and linearly associated with increased CHD risk in asymptomatic patients (Fig 1).[4] The large cumulative experience with CT for detecting preclinical coronary atherosclerosis shows that CAC screening provides powerful prognostic information that is much more accurate than algorithms for predicting CV events based upon standard CV risk factors.[1] In the Multi-Ethnic Study of Atherosclerosis (MESA), 6722 men and women from various ancestral backgrounds were followed for a median of 3.8 years. In comparison to participants with a zero CACS, the adjusted risk for CHD events was increased by a factor of 7.7 for those with CACS between 100 and 300, and 9.7 for those with scores above 300 (Fig 2). A doubling of the CACS was associated with an increase in the risk of major CHD events by 15–35%. This powerful prognostic capability for CACS was seen among all of the racial and ethnic groups.[5,6] LaMonte et al. followed nearly 11,000 adults for a median of 3.5 years after CACS. Among participants with CACS of 400 or more, they reported hazard ratios (HR) for major CHD events of 8.7 among men and 6.3 among women (Fig 3).[7] A very high CACS appears to confer a particularly high risk of CV events in the intermediate term. For example, in a report by Wayhs et al., the annualized event rate of patients with a CACS >1000 was about 25%.[8] CAC scoring also improves long term risk stratification beyond exercise tolerance testing and myocardial perfusion imaging.[9,10]

A total of 6698 individuals with no CV disease at baseline from the MESA were followed for CHD events over a mean period of 7.1 ± 1 year. This study showed that individuals with no CAC were at low risk for events, even if they had several risk factors for CV events. In contrast, individuals with no CV risk factors but with high CACS had elevated future risk for MACE.[11]

Blankstein et al. studied asymptomatic participants from MESA with LDL-C <130 mg/dl, which included 3714 individuals. The CACS added prognostic value and improved CHD risk assessment compared to traditional models during a median follow up of 5.4 years in patients with or without known CV risk factors, such as diabetes, hypertension and low high-density lipoprotein cholesterol (Fig 4). Indeed, simply the presence of a CACS >0 was associated with 4-fold increased risk of CHD events, while that risk increased to 9-fold higher in individuals with CACS >400.[12]

The utility of CAC screening as a risk-stratification tool is helpful even in both young and elderly individuals. In the 45 through 54-year-old group, increased CACS was shown to be associated with increased risk of CHD events. On the other end of the age spectrum, the cohort of 75 through 84-year-olds with CACS = 0, were at low risk for future CHD events despite their advanced ages.[5]

CAC screening for reclassification of intermediate risk individuals

Yeboah et al. compared several novel risk factors for improvement in CV risk assessment in intermediate risk individuals.[13] Using data from the MESA Study, they compared six CV risk markers including: CAC screening, carotid intima-media thickness, brachial flow-mediated dilation, ankle-brachial index, C-reactive protein, and family history of CHD. Using net reclassification improvement (NRI), which is a measure of relative improvement in classification of risk with addition of other variables, CAC screening was found to be the single best variable to be added to Framingham Risk Score (FRS).[13] CAC screening yielded superior disease identification and CHD risk reclassification compared with other modalities to assess CHD event risk. Although each of these risk factors was associated with incident CHD, the CAC screening was found to have the strongest independent predictive value for CHD events (Fig 5).[13]

In the Heinz Nixdorf Recall study (HNRS), 4129 subjects were initially categorized by standard clinical CV risk factors into low, intermediate and high risk groups according to Adult Treatment Program (ATP) III guidelines and FRS.[14] The study participants then underwent CT to obtain a CACS, which resulted in a large improvement in prediction of future risk of CHD events, especially among the intermediate-risk cohort. Usage of CAC screening among patients with intermediate score showed NRI of 66% in HNRS, which was quite similar to the 55% NRI with CAC screening in the MESA study. Adding CAC screening to other risk factors in the MESA study improved the NRI area under the receiver operator characteristic curve from 0.77 to 0.82 ($P < 0.001$).[14,15]

To summarize, both MESA and HNRS studies found that the addition of CAC screening information resulted in marked improvement in area under the curve and NRI above and beyond the prognostic information provided by standard risk factor algorithms.[14,15] Reclassifying intermediate risk patients based on CAC screening can help to identify those at high risk or low risk for future CHD events, which can allow physicians and patients to focus intensive risk factor treatment efforts on those at higher risk and allow lower risk individuals to focus