An Evidence-Based Guide for Coronary Calcium Scoring

in Asymptomatic Patients without Coronary Heart Disease

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After over half a century, the Framingham Risk Score (FRS)[1] remains the most common tool for medical practitioners to use in predicting cardiovascular risk in asymptomatic patients without established coronary heart disease (CHD) or a CHD-equivalent disease (for example, peripheral arterial atherosclerosis or diabetes mellitus). In addition, FRS-estimated 10-year risk is the primary basis for the treatment of hypercholesterolemia in the 2004 updated National Cholesterol Education Program Adult Treatment Panel III (ATP III) guidelines.[2] More recent evaluation of the FRS suggests that its discriminant accuracy, or its ability to predict who will and who will not have an event, is approximately 75%.[3] For this reason, there has been significant recent interest in cardiovascular imaging techniques that enable direct visualization of individual atherosclerotic burden and offer improved FRS discrimination. Two such techniques to detect coronary artery calcium (CAC) are non-contrast electron-beam computed tomography (EBCT) and multidetector computed tomography (MDCT). Given the potential benefits of CAC screening in cardiovascular risk assessment, patients in clinical practice are increasingly interested in such testing and are questioning their physicians about it. These practitioners should anticipate the most common questions and should be adequately educated to answer them.

Why Is Coronary Calcium Important?

The presence of CAC indicates underlying CHD, with essentially no false positive findings.[4] In addition, CAC burden correlates strongly with coronary plaque area measured at autopsy.[5] Important caveats are that for every calcified plaque, there are many noncalcified plaques capable of plaque erosion or rupture and that CAC does not predict luminal obstruction.[6]

What Tests Are Available to Measure Coronary Calcium, and Are They Effective?

Coronary artery calcium can be detected by various imaging techniques, but in the outpatient setting it is most commonly evaluated by noncontrast, electrocardiographic (ECG)-gated cardiac EBCT or MDCT. These studies are sensitive and reproducible in the detection of CAC and can be performed within 10 minutes.[7,8] Coronary artery calcium on EBCT and MDCT is defined as a hyperattenuating lesion >130 Hounsfield units with an area of ≥3 pixels. Coronary artery calcium scoring is generally performed by one of two widely used systems: the original Agatston method[9] or the "volume" method.[10] The volume method has better interscan reproducibility, due to decreased dependence on image-slice thickness.[7]

Are There Any Differences between EBCT and MDCT Coronary Calcium Scans?

The EBCT uses electronic manipulation of the x-ray source-point to achieve a rapid exposure time of 50 to 100 ms. In contrast, MDCT uses traditional mechanical manipulation of the x-ray source-point and has slightly longer exposure times of 83 to 210 ms.[7] The difference in exposure times results in a slightly higher effective radiation dose for MDCT, discussed in further detail below. In addition, MDCT provides better spa-

tial resolution and is more prevalent in clinical practice than EBCT. On the other hand, EBCT has been the primary technique used for research on CAC screening.

What Are the Costs and Risks Associated with a Coronary Calcium Scan?

A typical CAC screening costs $400[11] (MDCT is generally less expensive than EBCT), and patients might have to pay out-of-pocket because this cost is not always covered by health insurance policies. With prospective ECG gating, which is now strongly recommended for all cardiac CT studies, EBCT has an effective radiation dose of 0.7 to 1.0 mSv in men and 0.9 to 1.3 mSv in women. Because of its slightly longer exposure time, MDCT has a slightly higher effective radiation dose of 1.0 to 1.5 mSv in men and 1.1 to 1.9 mSv in women.[7] As useful comparisons, a standard chest radiograph has an effective radiation dose of 0.02 mSv,[12] and the average annual background radiation in the United States is 3.0 to 3.6 mSv.[13] Radiation from CAC screening results in a small but measurable increase in the risk of cancer.[14] Another risk of CAC screening is that it can result in an increased number of unnecessary tests and downstream procedures for individuals and in increased healthcare costs for the public.[6]

Who Should Undergo a Coronary Calcium Scan?

Although CAC screening improves the discriminant accuracy (c-index)[15] and risk classification[16] of the FRS, no prospective data currently indicate that CAC screening results in a reduction of coronary events or other clinical outcomes. Moreover, even improved outcomes would not establish value without additional consideration of the direct and indirect costs of care.[17] For these reasons, the U.S. Preventive Services Task Force now recommends against routine CAC screening by CT for either the presence of severe coronary artery stenosis or the prediction of CHD events in asymptomatic, low-risk adults (10-yr risk for hard CHD, <10%).[18] The American College of Cardiology and partner societies, in the 2010 Appropriate Use Criteria for Cardiac CT document,[19] also state that CAC screening by CT is inappropriate in asymptomatic, low-risk adults, but is appropriate in the low-risk subset with a family history of premature CHD (male first-degree relative, <55 yr; female first-degree relative, <65 yr); CAC screening by CT is also appropriate for asymptomatic, intermediate-risk adults (10-yr risk for hard CHD, 10%–20%). The rationale in intermediate-risk patients is the potential for reclassification; an absence of CAC might shift them to a low-risk category, whereas advanced CAC might shift them to a high-risk category that would call for increased intensity of risk-factor modification. Finally, CAC screening in asymptomatic, low-risk women might be appropriate because women are more likely to be classified as low-risk by the FRS and because any CAC in low-risk women is associated with an increased risk for CHD events.[20]

What Does the CAC Score Mean?

Coronary artery calcium scores increase with advancing age and are generally higher in men.[21,22] These scores are therefore commonly reported as percentiles of calcification in a reference population that is stratified by age and sex. Although the prevalence and extent of coronary calcification differ substantially among ethnic groups,[23] there are no detectable differences in the predictive value of CAC scores among ethnic groups.[15] A calcium score of zero in asymptomatic, low-risk adults makes the presence of atherosclerotic plaque or significant luminal obstructive disease highly unlikely and is associated with a very low risk (0.1% per year) of any cardiovascular event within 2 to 5 years (negative predictive value, 95%–99%).[7,24] Conversely, positive (non-zero) CAC scores confirm the presence of coronary atherosclerotic plaque, and rising scores are directly proportional to increased CHD risk. In particular, CAC scores higher than 100 or greater than the 75th percentile are associated with a high risk (>2% annual risk) of a CHD event within 2 to 5 years and provide a rationale for intensified low density lipoprotein cholesterol–lowering therapy.[7,15] However, further testing (for example, a stress test or cardiac catheterization) should be dictated by the clinical history and other conventional clinical criteria.

How Often Should the CAC Score Be Checked?

Whether knowledge of CAC score progression improves risk prediction is currently unclear. Furthermore, no randomized controlled trial data, to date, suggest that statin therapy or any other intervention slows the progression of CAC. Finally, there are concerns related to cumulative radiation exposure from repeat CT studies. For these reasons, routine serial CAC quantification is not currently recommended in clinical practice.[25]

Summary

As public awareness and clinical use of CAC screening increases, physicians should, at a minimum, know the following information:

1) The presence of CAC indicates underlying CHD but does not predict luminal obstruction.
2) Non-contrast, prospectively ECG-gated cardiac EBCT and MDCT are sensitive, reproducible, rapid, and essentially equivalent imaging techniques commonly used to screen for CAC.
3) Currently, CAC screening is appropriate for all intermediate-risk patients and low-risk patients with a family history of premature CHD, and might be appropriate for all low-risk women.
4) The risks associated with CAC screening are a small but measurable excess risk of cancer and the risk of unnecessary downstream tests and procedures.

5) A CAC score of zero has a very high negative predictive value for CHD events.
6) Increasingly positive (non-zero) CAC scores are directly proportional to increased CHD event risk, and a CAC score >100 or greater than the 75th percentile indicates high risk.
7) Repeat screening to determine CAC progression or regression is not currently recommended.

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