Diagnostic Tests

What Physicians Need to Know

Coronary Artery Calcium Scoring for Prevention of Cardiovascular Disease

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Test	Indication	Population	Cost
Coronary artery calcium scoring	CHD and CVD risk stratification to determine need for statin and aspirin therapy for primary prevention	Adults with intermediate 10-year atherosclerotic CVD risk (5% to 20%)	$100[11]

CHD = coronary heart disease; CVD = cardiovascular disease.

Atherosclerotic cardiovascular disease (ASCVD) risk assessment can identify high-risk patients who are likely to benefit from pharmacologic therapy for primary prevention of cardiovascular disease (CVD). Additionally, it can prevent overtreatment of low-risk patients. Clinical risk scores based on traditional cardiovascular risk factors, such as the Pooled Cohort Equations, may overestimate or underestimate ASCVD risk.[1] Optimal management is often uncertain in those at intermediate risk (5% to 20%).[2,3]

Coronary artery calcium (CAC) is a marker of overall coronary atherosclerotic burden. It is detected by noncontrast computed tomography (CT) and quantified by the Agatston score, which is the sum of the products of attenuation (Hounsfield units) and area (mm^2) of all lesions in the coronary arteries at each slice.[2,3] Because CAC is a marker of atherosclerotic disease, it may provide superior risk estimation over traditional risk factors.

Accuracy

PREDICTIVE VALUE FOR CARDIOVASCULAR EVENTS AND MORTALITY

CAC score is a strong predictor of coronary heart disease (CHD) and ASCVD. The presence of CAC indicates a 2.6- to 4.3-fold increased risk of CHD and a 2.1- to 2.6-fold increased risk of ASCVD, compared with a CAC score of 0.[4-7]

In a 12.3-year study of 7,042 participants, the risk of major CHD events was 1.9-fold higher with a CAC score of 1 to 99 and 4.2-fold higher with a score of 100 or greater.[6] In a cohort study of 3,745 participants, the 10-year rate of major CHD events was 0.6 to 2.7 per 1,000 person-years with a CAC score of 0 vs. 6.5 to 9.9 per 1,000 person-years with a score of 100 or greater.[8] In another study of 6,749 participants, the 10-year rate of ASCVD events was 3.6% with a CAC score of 0 vs. 17.5% with a score greater than 0.[7] In a 12.3-year study of 7,042 participants, the relative risk for ASCVD events was 1.6 with a CAC score of 1 to 99 and 2.3 to 3.4 with a score of 100 or greater.[6]

CAC score is also a predictor of all-cause mortality. In a 6.8-year study, patients with a CAC score of 101 to 400 or a score greater than 400 had a 5.6- or 9.7-fold greater risk of all-cause mortality, respectively, compared with a score of 0.[9] In a 15-year study, the survival rate was 95.1% in patients with a score of 0 vs. 83.7% in those with a score greater than 0.[10]

"WARRANTY PERIOD" FOR A CAC SCORE OF 0

Patients with a CAC score of 0 have very low rates of CHD, ASCVD, and all-cause mortality, even those with traditional CVD risk factors.[10] A score of 0 has been associated with event rates of 0.6 to 5.0 per 1,000 person-years for CHD, 0.2 to 5.4 for ASCVD, and 0.87 to 1.0 for all-cause mortality.[4,7-9,11,12]

Studies have investigated how long patients with a baseline CAC score of 0 remain in the low-risk category. The mean time of progression from absence to presence of CAC is 4.1 years, but

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the all-cause mortality rate remains low (less than 3%) for 15 years.[10,13,14]

Benefit

No studies have shown that using CAC scoring to help guide preventive therapies reduces ASCVD events or mortality.[3]

CAC SCORE IMPROVES RISK DISCRIMINATION AND CLASSIFICATION

For CHD and ASCVD events and all-cause mortality, CAC scoring improves discrimination provided by traditional risk factors. It is superior to other markers, including C-reactive protein, carotid intima-media thickness, ankle-brachial index, brachial flow-mediated dilation, and family history of premature CHD.[5,15] Discrimination, quantified by the C statistic, is the ability to distinguish between individuals who will or will not experience an event.[16] The Framingham CHD Risk Score and the Pooled Cohort Equations have C statistics of 0.65 to 0.75.[16] Adding CAC to traditional risk factor models improves the C statistic by 0.035 to 0.161 for CHD risk, 0.021 to 0.040 for CVD risk, and 0.04 to 0.08 for all-cause mortality.[5,6,10,12,15-20]

CAC scoring also improves the risk classification of CHD and CVD provided by traditional risk factor models. The net reclassification index is the percentage of individuals who are correctly reclassified into higher or lower risk categories with the addition of CAC.[16] A net reclassification index threshold of 7.5% has been proposed for CVD.[21] Adding CAC score to traditional risk factor models yielded net reclassification indices ranging from 8.4% to 32% for CHD risk and 11.9% to 25% for CVD risk.[6,15,17-20] Because of significant heterogeneity in the intermediate-risk group, the net reclassification index was higher for this group compared with the general population (55% to 65.9% for CHD risk and 46.6% for CVD risk).[5,19]

CAC SCORE CAN GUIDE STATIN AND ASPIRIN THERAPY

In a 9.4-year study of 13,644 participants, statins reduced CHD events for patients with a CAC score greater than 100 in all risk categories. In patients with a score of 0, statins reduced CHD events only for those with an ASCVD risk greater than 20% based on the Pooled Cohort Equations. Risk was not reduced in the low- and intermediate-risk groups.[22]

In a 10-year study of 3,745 participants with a 10-year ASCVD risk of 7.5% or greater, rates of CHD events were higher with a CAC score of 100 or greater compared with a score of 0 (9.1 vs. 2.7 events per 1,000 person-years), resulting in a 10-year number needed to treat (NNT) of 530 and 84, respectively.[8] In a 10.3-year study of 4,758 participants, those with a 10-year ASCVD risk of 7.5% to 20% had a lower rate of ASCVD events with a CAC score of 0 than with a score greater than 0 (4.6 vs. 10.4 events per 1,000 person-years). In patients with a 10-year ASCVD risk of 5% to 7.5%, a CAC score of 0 was also associated with a low rate of ASCVD events (1.5 per 1,000 person-years). To prevent CVD, statin use had a 10-year NNT of 223 for a score of 0 and 46 for a score greater than 100.[11] Therefore, in the intermediate-risk population with a 10-year ASCVD risk of 5% to 20%, avoiding treatment in patients with a CAC score of 0 and treating those with a score greater than 100 would lower the NNT.

In a 12-year study of 4,962 participants who were eligible for statin therapy based on American College of Cardiology/American Heart Association guidelines but not USPSTF guidelines, a CAC score of 0 was associated with a low rate of CVD events (4.2 per 1,000 person-years), and a CAC score greater than 100 was associated with a high rate of CVD events (12.8 per 1,000 person-years).[23] CAC scoring could aid in deciding whether to start statins in patients with discordant statin eligibility.

For aspirin therapy, a 7.6-year study of 4,229 participants weighed the benefit of CHD reduction vs. the bleeding risk. Benefits outweighed harms in patients with a 10-year CHD risk of 10% or greater if the CAC score was greater than 0 and in patients with a 10-year risk less than 10% if the CAC score was 100 or greater. There was no net benefit from aspirin therapy in patients with a 10-year risk greater than 10% and a CAC score of 0.[24]

Harms

Radiation exposure from a CAC scan is approximately 0.89 mSv, which is similar to a mammogram.[2] Another potential harm is incidental findings that require additional evaluation, which occurs in 4% to 8% of patients.[25] CAC screening results in slightly higher (7%) medication costs but does not increase medical procedure costs.[26]

Cost

A CAC scan costs approximately $100.[11] With physician review, incidental findings, and loss in productivity time, the overall cost is estimated to be about $215.[25] A CAC score may be obtained from noncontrast chest CT performed for other reasons, including low-dose chest CT for lung cancer screening, at no additional cost. The price of statin therapy is approximately $60 to $85 per year.[11,25] One analysis concluded that statin therapy guided by American College of Cardiology/American Heart Association guidelines is similarly cost-effective to statin therapy guided by CAC scoring.[25]

Bottom Line

CAC score is a strong predictor of CHD, CVD, and mortality risk and provides risk discrimination and stratification beyond that provided by traditional risk factor models. Its greatest potential is in patients with intermediate risk

(10-year ASCVD risk of 5% to 20%), in which allocation of statins and aspirin can be improved by limiting treatment to those with elevated CAC scores (100 or greater) and deferring or delaying treatment in those with a score of 0. However, no studies have demonstrated that measuring CAC score to guide primary prevention in the intermediate-risk population improves outcomes.

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