Computed Tomography to Detect Coronary Artery Calcification

**Description**

Electron beam computed tomography (CT; also known as ultrafast CT) uses an electron gun rather than a standard x-ray tube to generate x-rays, thus permitting very rapid scanning. Spiral CT scanning (also referred to as helical CT scanning) also creates images at greater speeds by rotating a standard x-ray tube around the patient such that data are gathered in a continuous spiral or helix rather than in individual slices.

**Background**

While both electron beam CT (EBCT) and spiral computed tomography (CT) scanning may be valued as an alternative to conventional CT scanning due to their faster throughput, their speed of image acquisition also permits unique imaging of the moving heart. For example, the rapid image acquisition time virtually eliminates motion artifact related to cardiac contraction, permitting visualization of the calcium in the epicardial coronary arteries. EBCT software permits quantification of calcium area and density, which are translated into calcium scores. Calcium scores have been investigated as a technique for detecting coronary artery calcification, both as a diagnostic technique in symptomatic patients to rule out an atherosclerotic etiology of symptoms or, in asymptomatic patients, as an adjunctive method for risk stratification for coronary artery disease.

EBCT and multi-detector computed tomography (MDCT) were initially the primary fast CT methods for measurement of coronary artery calcification. A fast CT study for coronary artery calcium measurement generally takes 10 to 15 minutes and requires only a few seconds of scanning time. More recently, CT angiography (CTA) has been used to assess coronary calcium. Because of the basic similarity between EBCT and CTA in measuring coronary calcium, it is expected that CTA provides similar information on coronary calcium as does EBCT.

**Regulatory Status**

The EBT Ultrafast CT Scanner System (Imatron, South San Francisco); C-100, C-150, C-150xp Or C-150xp Scanner Systems; Electron Beam Scanner System have 510 (k) clearance from the Food and Drug Administration. Aquilion Prime (Toshiba America Medical Systems, Inc., Tustin, CA) received 510(k) approval in April 2012. (1)
The use of computed tomography (CT) to detect coronary artery calcification is considered **not medically necessary**.

**Rationale**

The rationale for measuring calcium in coronary arteries is that it measures coronary atherosclerosis. Coronary calcium is present in coronary atherosclerosis, but the atherosclerosis detected may or may not be causing ischemia or symptoms. Such a measure may be correlated with the presence of critical coronary stenoses or serve as a measure of the patient's proclivity toward atherosclerosis and future coronary disease. Thus, it could serve as a variable to be used in a risk assessment calculation for the purposes of determining appropriate preventive treatment in asymptomatic patients. Alternatively, in other clinical scenarios, it might help determine whether there is atherosclerotic etiology or component to the presenting clinical problem in symptomatic patients, thus helping to direct further workup for the clinical problem. In this second scenario, a calcium score of zero usually indicates that the patient’s clinical problem is unlikely to be due to atherosclerosis and that other etiologies should be more strongly considered. In neither case does the test actually determine a specific diagnosis. Most clinical studies have examined the use of coronary calcium for its potential use in estimating the risk of future coronary heart disease events.

Coronary calcium levels can be expressed in many ways. The most common method is the Agatston score, which is a weighted summed total of calcified coronary artery area observed on CT. This value can be expressed as an absolute number, commonly ranging from 0 to 400. These values can be translated into age and sex-specific percentile values. Different imaging methods and protocols will produce different values based on the specific algorithm used to create the score, but the correlation between any 2 methods appears to be high, and scores from 1 method can be translated into scores from a different method.

This policy is based, in part on a 1998 Technology Evaluation Center (TEC) Assessment. (2)

**Coronary calcium for coronary disease risk stratification**

Many prospective studies have shown evidence for predictive capacity of calcium scores in addition to assessment of traditional risk factors for CHD among asymptomatic subjects. In a study of 1,029 asymptomatic adults with at least 1 coronary risk factor, Greenland et al. (3) showed that a calcium score of greater than 300 predicted increased risk of cardiac events within Framingham risk categories. A study by Arad et al. (4) showed similar findings in a population-based sample of 1,293 subjects who
had both traditional risk factors and calcium scores evaluated at baseline. A study by Taylor et al. (5) studied the association of the Framingham risk score and calcium scores in a young military population (mean age 43 years). Although only 9 acute coronary events occurred, calcium scores were associated with risk of events while controlling for the risk score. LaMonte et al. (6) also analyzed the association of calcium scores and coronary heart disease (CHD) events in 10,746 adults. In this study, coronary risk factors were self-reported. During a mean follow-up of 3.5 years, 81 CHD events occurred. Similar to the other studies, the relationship between calcium scores and CHD events remained after adjustment for other risk factors. Budoff et al evaluated the association of coronary calcium scores and CHD events during 5 years of follow up in an analysis of 2232 adults from the Multiethnic Study of Atherosclerosis (MESA), a prospective cohort study to evaluate cardiac risk factors, and 3119 subjects from the Heinz Nixdorf RECALL (HNR; Risk factors, Evaluation of Coronary Calcium and Lifestyle Factors) study. (7) Increasing Agastson score was associated with increased risk of CHD; in the MESA study, compared with a coronary artery calcification (CAC) score of 0, having a score >400 was associated with a hazard ratio (HR) for CHD of 3.31 (95% confidence interval [CI] 1.12 to 9.8) after adjusting for CHD risk factors; a score of 100-399 was associated with a HR of 3.27 (95% CI 1.19 to 8.95). In the HNR study, the HR for CHD was 2.96 (95% CI 1.22 to 7.19). Lower CAC scores were not significantly associated with CHD after adjustment for other risk factors. Other studies (8-11) show similar findings.

Additional studies have defined how the incorporation of calcium scores into risk scores changes risk prediction. In a study by Polonsky et al., (12) incorporation of calcium score into a risk model resulted in more subjects (77% vs. 66%) being classified in either high-risk or low-risk categories. The subjects who were reclassified to high risk had similar risk of CHD events as those who were originally classified as high risk. A study by Elias-Smale et al. (13) showed similar findings; reclassification of subjects occurred most substantially in the intermediate risk group (5-10% 5-year risk) where 56% of persons were reclassified.

Numerous studies have also evaluated the predictive ability of coronary calcium using CT angiography (CTA). (14-17) These studies have included different population, such as patients with or without risk factors or patients with an intermediate risk of CAD. Similar to studies that use EBCT, these studies have demonstrated that calcium scores derived from CTA provide incremental predictive information for the overall risk of CAD as compared to coronary angiography and for the future occurrence of major cardiac events.

Section Summary: Multiple prospective studies have found that CAC scoring is associated with future risk of coronary heart disease events. CAC scores likely add to the predictive ability of clinical risk prediction models. However, studies enrolled different populations, assessed different traditional risk factors, and assessed different coronary disease outcomes. Different calcium score cutoffs were analyzed in the studies. Given the variation in the studies, the magnitude of increased risk conferred by a given calcium score is still uncertain.

Impact on cardiac risk factor profiles in practice

While epidemiologic studies suggest that CAC scoring may be associated with future CHD risk, this does not, by itself, demonstrate that the use of CAC scoring improves clinical outcomes.
There have been a small number of randomized controlled trials (RCTs) of the impact of electron-beam computed tomography (EBCT) on cardiac risk factors. In 2012, Whelton et al published a meta-analysis of RCTs that evaluated the impact of coronary calcium scores on cardiac risk profiles and cardiac procedures. There were 4 trials identified with a total of 2490 participants; the individual trials ranged in size from 50 to 1934 patients. The authors pooled data from 4 trials on the impact of calcium scores on blood pressure, 3 on the impact on low-density lipoprotein, and 2 on the impact on high-density lipoprotein. Pooled analysis did not show a significant change in any of these parameters as a result of calcium scores. Similarly, in 4 studies that looked at the rates of smoking cessation following calcium scores, there was not significant change found. There were 2 studies that included rates of coronary angiography and 2 studies that included rates of revascularization. Pooled analysis of these studies did not show a significant change following measurement of coronary calcium.

Two RCTs representative of this evidence are discussed further here. O’Malley et al (19) randomized 450 subjects to receive EBCT or not and assessed outcomes 1 year later for change in Framingham Risk Score. Thus, EBCT was to be used as a guide to refine risk in patients and possibly provide motivation for behavioral change. The study was not powered for clinical end points. EBCT did not produce any benefits in terms of a difference in Framingham risk score at 1 year.

An RCT was published in 2011 evaluating the impact of computed tomography (CT) scanning for coronary artery calcium on cardiac risk factors. A total of 2137 healthy individuals were randomized to CT scanning or no CT scanning and followed for 4 years. At baseline, both groups received 1 session of risk factor counseling by a nurse practitioner. The primary outcome was change in 12 different cardiac risk profile measures, including blood pressure, lipid and glucose levels, weight, exercise, and the Framingham risk score. At the 4-year follow-up, there was differential dropout among the groups, with 88.2% of follow-up in the scan group versus 81.9% in the no-scan group. Results demonstrated differences in 4 of the 12 risk factor measurements between groups: systolic blood pressure, low-density lipoprotein, waist circumference, and mean Framingham risk score.

This trial highlights the potential benefit of coronary artery calcium screening in modifying cardiac risk profile but is not definitive in demonstrating improved outcomes. Limitations of this study include different intensity of interventions between groups and differential dropout. It is possible that the small differences reported in the trial were the result of bias from these methodologic limitations. In addition, this trial does not compare the impact of other types of risk factor intervention, most notably more intensive risk factor counseling. Finally, the generalizability of the findings is uncertain given that this was a volunteer population that may have been highly motivated for change.

Johnson et al reported results from a descriptive prospective study to assess the association between CAC score and subsequent health behavior change. The study included a convenience sample of 174 adults with CHD risk factors who underwent CAC scoring. The authors found no significant change in risk perception measured by the Perception of Risk of Heart Disease Scale (PRHDS) scores between groups (CAC score 0, 1-10, 11-100, 101-400, >400), with the exception of a small increase in the moderate-risk group (CAC score 101-400) from 55.5 to 58.7 (P=0.004). All groups demonstrated increases in health-promoting behavior over time.
Section Summary: Studies that use CAC scoring in asymptomatic patients have reported mixed findings about whether CAC testing leads to improved cardiovascular risk profiles or improvements in other meaningful clinical outcomes. The largest meta-analysis did not find significant improvements in cardiac risk profiles or use of cardiac procedures with the use of CAC scoring.

Coronary calcium for ruling out atherosclerotic etiology of disease in symptomatic patients

In certain clinical situations such as patients presenting with chest pain or other symptoms, it is uncertain whether the symptoms are potentially due to CHD. Coronary calcium measurement has been proposed as a method that can rule out CHD in certain patients if the coronary calcium value is zero. Since coronary disease can only very rarely occur in the absence of coronary calcium, the presence of any coronary calcium can be a sensitive but not specific test for coronary disease. False positives occur because the calcium may not be causing ischemia or symptoms. The absence of any coronary calcium can be a specific test for the absence of coronary disease and direct the diagnostic workup toward other causes of the patient's symptoms. In this context, coronary calcium measurement is not used to make a positive diagnosis of any kind but as a diagnostic “filter” used to rule out an atherosclerotic cause for the patient's symptoms.

For example, Yerramasu et al reported results of a prospective study to evaluate an evaluation algorithm including CAC scoring for patients presenting to a rapid access chest pain clinic with stable chest pain possibly consistent with CHD.(22) Three hundred patients presenting with acute chest pain to 1 of 3 chest pain clinics underwent CAC scoring. If the CAC score was greater than or equal to 1000 Agatston units invasive coronary angiography was performed and if the CAC score was less than 1000 coronary CT angiography (CCTA) was performed. All patients with a CAC of zero and low pre-test likelihood of CHD had no obstructive CHS on CCTA and were event-free during follow up. Of the 18 patients with CAC score from 400 to 1000, 17 (94%) had greater than 50% obstruction on subsequent CCTA and were referred for further evaluation, of whom 14 (78%) had obstructive CHD. Of 15 patients with CAC score greater than or equal to 1000 and who were referred for coronary angiography, obstructive CHD was present in 13 (87%). This study suggests that CAC can be used in the acute chest pain setting to stratify decision-making for further testing.

In a study by Laudon et al in the emergency department setting, 51% (133/263) patients with chest pain and low-to-moderate probability of CAD had calcium scores of zero.(23) One of these patients was found to actually have coronary disease. The others were presumed to not have coronary disease, and it is claimed that these patients could have been safely discharged from the emergency department. However, the study is not rigorous in its methods regarding the alternative workup of potential coronary artery disease in the emergency department or in the long-term follow-up of patients.

In addition to studies that use coronary calcium scores to rule out CHD among patients presenting with symptoms potentially consistent with CHD, coronary calcium scoring has also been evaluated to rule in or out potential CHD in symptomatic patients before invasive coronary angiography or stress nuclear imaging. 2007 expert consensus guidelines from the American College of Cardiology and the American Heart association states that CAC may serve “as a filter prior to invasive coronary angiography or stress nuclear imaging” but that “prognostic studies of CAC in symptomatic patients have generally
been limited by biased samples (e.g., patients referred for invasive coronary angiography) and small numbers of hard outcome events.”

Since the 2007 consensus statement, several studies have addressed the use of CAC scoring as part of a management strategy for patients presenting with symptoms possibly consistent with CHD. In 2014, Hulten et al published results from a retrospective cohort study among symptomatic patients without a history of CHD to evaluate the accuracy of CAC for excluding coronary stenosis among symptomatic patients, using coronary CT angiography (CCTA) as the gold standard. The study included 1,145 patients who had symptoms possibly consistent with CHD who underwent a non-contrast CAC score and a contrast enhanced CCTA from 2004-2011. For detection of greater than 50% stenosis, CAC had a sensitivity of 98% and specificity of 55%, corresponding to a negative predictive value of 99%. For prediction of cardiovascular death or myocardial infarction, the addition of either or both CAC or CCTA to a clinical prediction score did not significantly increase prognostic value.

Van't Kate et al conducted a prospective study to evaluate the accuracy of cardiac CT, including CAC scoring with or without CCTA, in distinguishing heart failure due to coronary artery disease (CAD) from heart failure due to non-CAD causes. Data on the predictive ability of a negative CAC in ruling out CAD was also included. The study included 93 symptomatic patients with newly diagnosed heart failure of unknown etiology, all of whom underwent CAC scoring. Those with a CAC score of greater than 0 underwent CCTA, and if the CCTA was positive for CAD (>20% luminal diameter narrowing), invasive coronary angiography was recommended. Forty-six percent of patients had a CAC score of zero. At follow up of (mean duration 20 months), no patient with a CAC score of zero had a myocardial infarction, underwent percutaneous coronary intervention, had a coronary artery bypass graft, or had signs of coronary artery disease.

Dharampal et al retrospectively evaluated a cohort of 1,975 symptomatic patients who underwent clinical evaluation and CAC scoring and CCTA or invasive coronary angiography (ICA). The primary outcome was obstructive CAD (≥50% stenosis) on ICA or CCTA (if ICA was not done). The authors evaluated the net reclassification improvement with the addition of CAC score to a clinical prediction model for patients who had an intermediate probability of CHD (10-90%) after clinical evaluation based on chest pain characteristic, age, gender, risk factors, and EKG. Discrimination of CAD was significantly improved by adding CAC score to the clinical evaluation (area under the curve: 0.80 vs 0.89, P<0.001).

Section Summary: A number of studies suggest that CAC scoring could be used to rule in or rule out CHD, particularly regarding decision about further invasive imaging. However, relatively few studies have employed a prospective design. Further studies need to be conducted to address some of the potential barriers to such an approach, including whether performing CAC scoring in symptomatic patients’ delays diagnosis or intervention and whether the net effect of CAC scoring is to increase or decrease invasive testing.

Future research needs

The current research mainly establishes that coronary artery calcium screening improves risk prediction for coronary artery disease. The 2011 Rozanski et al (20) randomized controlled trial (RCT) suggests...
that scanning may favorably impact cardiac risk profiles but is not sufficient in itself to demonstrate improved outcomes. In order to demonstrate that use of calcium scores improves the efficiency or accuracy of the diagnostic workup of symptomatic patients, rigorous studies that define exactly how coronary calcium scores are used in combination with other tests in the triage of patients would be necessary. Study designs need to explicitly evaluate diagnostic strategies that compare one strategy which uses calcium scores, to an alternative, which does not use calcium scores. Ideally, patient outcomes and resource utilization would need to be prospectively evaluated.

Ongoing Clinical Trials

A search of the database ClinicalTrials.gov identified the following studies that are evaluating outcomes after interventions using CAC measurements:

- **Individualized Comprehensive Atherosclerosis Risk-reduction Evaluation Program (iCARE) (NCT00969865)** – This study will prospectively evaluate differences in heart disease related risk factors between patients receiving usual care and those receiving blood tests for markers of heart disease, DNA and RNA analysis, and CAC scanning, in addition to usual care. Enrollment is planned for 670 patients; the planned study completion date is July 2014.

Practice Guidelines and Position Statements

In 2006, the American Heart Association (AHA) issued a scientific statement (27) on the use of cardiac computed tomography (CT). Most of the document reviewed the utility of calcium scoring for the use of determining prognosis and diagnosis. In addition to reviewing a large body of evidence regarding calcium scoring, clinical recommendations were also offered. No indications received a class I recommendation, i.e., evidence and/or agreement that the procedure is useful and effective. Several indications received a class IIb recommendation, which means that there is conflicting evidence and/or a divergence of opinion regarding usefulness or efficacy. The “b” qualifier indicates usefulness/efficacy is less well established. The indications that received an IIb recommendation were:

- **Class IIb recommendations:**
  - Patients with chest pain with equivocal or normal ECGs [electrocardiograms] and negative cardiac enzymes
  - Determining the etiology of cardiomyopathy
  - Symptomatic patients, in the setting of equivocal treadmill or functional tests
  - Asymptomatic patients with intermediate (e.g., 10–20% 10-year risk) risk of CAD [coronary artery disease]

- **Class III recommendation** (evidence that the procedure or treatment is not useful or possibly harmful).
  - Low-risk (<10% 10-year risk) and high-risk (>20% 10-year risk) asymptomatic patients
  - Establishing the presence of obstructive disease for revascularization in asymptomatic persons
  - Serial imaging for assessment of progression of coronary calcification
A 2007 clinical consensus document co-authored by the American College of Cardiology Foundation (ACCF) and the AHA (28) reviewed much of the same evidence as the 2006 AHA scientific statement. It should be noted that this type of consensus document represents the best attempt of the ACCF and AHA to inform clinical practice where rigorous evidence is not yet available. Thus formal grading of evidence and classification of clinical recommendations are not reported in this type of document. This document essentially concludes that the indications receiving an IIb recommendation in the 2006 scientific statement “may be reasonable….“ Recommendations from the 2010 ACCF/AHA Guidelines are noted below.

In 2009, the U.S. Preventive Services Task Force (USPSTF) issued recommendations regarding the use of nontraditional or novel risk factors in assessing CHD risk in asymptomatic persons. (29, 30) Calcium score was 1 of 9 risk factors considered in the report. They concluded that the current evidence is insufficient to assess the balance of benefits and harms of using any of the nontraditional risk factors studied to assess risk of coronary disease in asymptomatic persons. In their focused review of 5 studies, which they judged to have valid study designs, they found wide variation in the estimates of the risk ratio for higher calcium scores. Higher quality studies had lower relative risks for a given difference in calcium score. This review disagrees with the ACCF/AHA 2007 clinical consensus document (28) regarding the effect of calcium scores on reclassifying risk of coronary disease. Rather than the 4 studies that the ACCF/AHA document claims provides information about reclassification, the USPSTF report only finds one such study.

In 2010, the ACC/AHA released recommendations on calcium scoring as part of their guidelines on the management of cardiovascular risk in asymptomatic patients. (31) These recommendations include the following:

- Class IIa: Measurement of CAC [coronary artery calcification] is reasonable for cardiovascular risk assessment in asymptomatic adults at intermediate risk (10% to 20% 10-year risk). (Level of Evidence: B)
- Class IIb: Measurement of CAC may be reasonable for cardiovascular risk assessment in persons at low to intermediate risk (6% to 10% 10-year risk). (Level of Evidence: B)
- Class III: No Benefit. Persons at low risk (<6% 10-year risk) should not undergo CAC measurement for cardiovascular risk assessment. (Level of Evidence: B)

In 2012, the ACC/AHA released guidelines for the diagnosis and management of patients with stable ischemic heart disease that include some recommendations related to CAC scoring. (32)

- Class IIb: For patients with a low to intermediate pretest probability of obstructive IHD [ischemic heart disease], noncontrast cardiac computed tomography to determine the coronary artery calcium score may be considered. (Level of Evidence: C)

A systematic review by Ferket et al. (33) identified 14 guidelines that evaluated diagnostic imaging for asymptomatic coronary artery disease, which included those reviewed above and additional guidelines from New Zealand and Canada. Ten of the guidelines addressed use of calcium score as a method to
improve coronary risk assessment. Four guidelines concluded that there was sufficient evidence for consideration of its use, and 1 guideline recommended for its use. The only group of patients for whom its use was recommended was that of intermediate-risk patients. For subjects at low risk or high risk, guidelines were unanimous in not advocating calcium scoring.

Summary

There is extensive evidence on the predictive value of coronary artery calcium (CAC) score screening for cardiovascular disease among asymptomatic patients, and this evidence demonstrates that scanning has incremental predictive accuracy above traditional risk factor measurement. However, evidence from high-quality studies that demonstrate that the use of CAC score measurement in clinical practice leads to changes in patient management or in individual risk behaviors that improve cardiac outcomes is lacking.

CAC scoring has a potential role as a diagnostic test to rule out coronary artery disease in patients presenting with symptoms or as a “gatekeeper” test before invasive imaging is performed. Evidence from retrospective studies suggests that negative results on CAC scoring rules out coronary artery disease with good reliability. However, further prospective trials would be needed to demonstrate that such a strategy is effective in practice and is at least as effective as alternate strategies for ruling out CAD.

Because of the lack of high-quality evidence demonstrating improved outcomes from either the use of CAC score as a screening test to risk stratify patients or as a diagnostic test to in symptomatic patients, the use of coronary artery calcium scoring is considered not medically necessary.

References

2. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Diagnosis and screening for coronary artery disease with electron beam computed tomography. TEC Assessments 1998; Volume 13, Tab 27.


American College of Radiology, the American Heart Association, the American Society of Echocardiography, the American Society of Nuclear Cardiology, the North American Society for Cardiovascular Imaging, the Society for Cardiovascular Angiography and Interventions, and the Society for Cardiovascular Magnetic Resonance. J Am Coll Cardiol 2010; 56(22):1864-94.


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<td>New Policy</td>
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<td>Update Policy</td>
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**Keywords**

Cine Computed X-ray Tomography (See Electron Beam CT)
Computed X-ray Tomography (See Electron Beam CT)
Electron Beam Computed Tomography (CT) for Imaging of Coronary Artery Disease
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on September 12, 2014 and is effective October 15, 2014.

Signature on File
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