Role of Electron Beam Computed Tomography in Detecting and Assessing Coronary Artery Disease

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Coronary artery disease (CAD) is the leading cause of death worldwide and in the United States, where it accounts for more than 494,000 deaths per year.[1,2] Approximately 18% of patients with CAD present with sudden cardiac death as their first sign of disease.[3] Disruption of plaque commonly causes acute coronary syndromes (ACS) and may result in death due to myocardial infarction in CAD patients.[4] Timely risk reduction with lifestyle changes,[5] aspirin use,[6] β-blockade,[7] angiotensin-converting enzyme inhibition,[8] and cholesterol control[5,9] has been shown to effectively reduce cardiac events in patients with CAD. Thus, early detection of subclinical atherosclerosis is important as it allows initiation of risk-reduction interventions that could hamper disease progression and prevent acute myocardial infarction. The challenge, however, lies in developing effective testing that reliably detects subclinical CAD. The predictive value of traditional risk factors and current imaging/testing strategies is suboptimal, especially in patients at low to intermediate risk for CAD who are asymptomatic[10] or have experienced atypical chest pain symptoms.

Calcium deposition in the coronary arteries is part of the atherosclerotic process and does not occur in normal arteries. Detecting coronary artery calcification by electron beam computed tomography (EBCT) has recently emerged as a promising method of evaluating patients for the presence of CAD. This article discusses the role of EBCT as a noninvasive tool among other tests currently available for detecting and assessing CAD. Other potential uses of EBCT, many of which are currently investigational, will not be discussed. These include: intravenous EBCT coronary angiography for detection of obstructive CAD[11,12]; differentiating ischemic from nonischemic cardiomyopathy by calcium scoring[13]; determining the functional capacity of right and left ventricles[14]; determining myocardial perfusion (employing EBCT, injecting contrast)[15]; and detecting pulmonary embolism (employing EBCT, injecting contrast)[16–18] and aortic lesions.[19]

TAKE HOME POINTS

- Electron beam computed tomography (EBCT) can be used to detect coronary calcification as a means to assess atherosclerosis.
- The accuracy of EBCT in detecting coronary artery disease (CAD) is comparable to that of traditional tests.
- EBCT can be employed in selected individuals at intermediate risk of CAD in whom standard cardiac risk assessment tools are insufficient.
- EBCT does not provide information regarding the physiologic significance or vulnerability of the plaque.
- The availability of EBCT is currently limited because specific indications for EBCT have not yet been generally accepted, and insurance companies do not readily reimburse for the test.
- If further studies continue to affirm the value of EBCT, this test is likely to become more widely accepted as a tool for CAD evaluation.

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Figure 1. Electron beam computed tomography image of a patient with coronary artery disease, with calcium within the coronary vessels appearing bright white. From left to right, the image reveals calcium in the left main artery, calcium at the site of bifurcation of the left main into the left anterior descending and left circumflex arteries, and calcium in the left anterior descending artery. This patient's calcium score was 1074.

CORONARY CALCIUM AS A CAD SURROGATE

Calcification of coronary arteries indicates the presence of atherosclerotic CAD.[20] Autopsy and pathology studies have demonstrated excellent correlation between coronary calcification and total atherosclerotic plaque burden within the coronary tree.[20–22] Over the past few years, interest in using coronary calcification as a marker for CAD has led to the development of various methods for detecting and quantifying coronary calcium. Cardiac fluoroscopy,[23] helical (or spiral) computed tomography (CT), and EBCT have been employed clinically for measurement of calcification. The sensitivity of fluoroscopy as a tool for detecting coronary calcification is very low (40%),[24] while the accuracy of helical CT in detecting CAD is also limited[25] because its slower image acquisition speed results in blurring of calcium deposits due to cardiac motion artifact.[26] EBCT is the most studied method of detecting coronary calcification as a means to assess atherosclerosis.

TECHNIQUE OF EBCT

Using an electron gun and stationary tungsten target, EBCT images are obtained within 25 to 100 ms, and this short acquisition time minimizes motion artifact.[27] Between 30 and 40 adjacent axial scans with a slice thickness of 3 to 6 mm are obtained during 1 or 2 breath-holding sequences.[28] In order to further minimize cardiac motion effect, scans are triggered by electrocardiogram (ECG) signal at 60% to 80% of the R-R interval near end diastole, before at rial contraction.[28] Computerized scoring algorithms are used to quantify the area and density of calcium within the coronary tree, and a calcium score is obtained by multiplying the x-ray attenuation coefficient (CT number in Hounsfield units) by the area of calcium deposition and summing the products (**Figure 1**).[29] An alternative method for quantifying coronary calcium, calcium volume scoring, measures the total volume of calcified plaque and has demonstrated better reproducibility than the traditional method.[30]

ACCURACY OF EBCT IN DETECTING CAD

Because the calcium score is measured as a continuous variable, the accuracy (sensitivity and specificity) of EBCT in detecting CAD depends upon the calcium score threshold that is chosen. Rising calcium scores indicate increasing likelihood of coronary artery stenosis, and a calcium score exceeding 400 suggests a high probability of the presence of significant vessel obstruction.[31] The results of studies that evaluated the accuracy of EBCT in detecting CAD are summarized in **Table 1**.[32–39] The specificity of EBCT was shown to be superior to that of myocardial perfusion imaging (MPI) in one study[40] but inferior to MPI in another[39]; in general, the specificity of EBCT is considered to be relatively low.[28] EBCT does not identify specific lesions, and patients with a noncalcified soft lesion at risk for ACS can have a low calcium score on EBCT, which thereby lowers the sensitivity of EBCT. However, the sensitivity of EBCT compares favorably with other routinely performed noninvasive studies (**Table 2**).[41,42]

To determine whether EBCT could identify patients with scintigraphic ischemia on the basis of calcium score, a group of investigators sought to correlate the severity of artery calcification detected by EBCT with findings of myocardial ischemia detected by MPI.[31] In a cohort of asymptomatic patients who had risk factors for CAD, the occurrence of inducible ischemia on exercise increased with the calcium score, from 0% in patients with a calcium score below 10 to 46% in those with a score of 400 or higher.[31] In another study, ischemia on MPI was strongly associated with an elevated calcium score.[43] Thus, inducible ischemia is associated with elevated calcium score, whereas it is unlikely with low calcium score.

APPLICABILITY OF EBCT IN CAD ASSESSMENT

According to the American College of Cardiology/American Heart Association (ACC/AHA) guidelines, patients with a positive EBCT test result are more likely to have coronary stenosis and an increased risk for ACS in the 2 to 5 years following the test compared with

Table 1. Sensitivity and Specificity of Electron Beam Computed Tomography

Study	Gold Standard		Sensitivity of EBCT (%)	Specificity of EBCT (%)
Mautner et al[32]	Histologic CAD		94	76
Baumgart et al[33]	Coronary angiography		66	78
	Intravascular ultrasound		66	88
Budoff et al[34]	Coronary angiography		95	44
Nallamothu et al[35] (meta-analysis)	Coronary angiography		92.3	51.2
Breen et al[36]	Coronary angiography		94	72
Budoff et al[37]	Coronary angiography	Cut-off: CS > 20	90	58
		CS > 80	79	72
		CS > 100	76	75
Arad et al[38]	Occurrence of cardiovascular events during 19-month follow-up	Cut-off: CS > 100	89	77
		CS > 160	89	82
		CS > 680	50	95
Yao et al[39]	Coronary angiography		65	77

CAD = coronary artery disease; CS = calcium score; EBCT = electron beam computed tomography.

patients with a negative EBCT test.[28] Recent data suggest that calcium score can modify risk predicted on the basis of the Framingham risk assessment score, especially in individuals at intermediate risk of disease.[44] Increasing amount of calcium is directly associated with increasing likelihood of obstruction and plaque burden.[28]

Screening and Prognosis

EBCT has been studied as a screening tool for CAD in asymptomatic individuals. High calcium score has been shown to indicate silent ischemia[31] and predict risk of future cardiac events in an asymptomatic population.[38,45–50] In predicting patient prognosis in asymptomatic patients with CAD, EBCT provides incremental value beyond that provided by traditional risk factors for CAD.[47,51,52] When adjusted for CAD risk factors, the relative risk of a cardiovascular event in asymptomatic individuals with a calcium score between 81 and 270 was 4.5, and in those with a calcium score of 271 or higher, it was 8.8.[49] Clinically, patients with a calcium score of 10 or less are considered to be at very low to low cardiovascular risk.[53] Patients with a score between 10 and 100 are considered at moderate risk, and those with a score exceeding 100 are at moderately high risk.[53] Patients with a calcium score exceeding 400 are considered to be at very high risk. However, it is generally advisable to consider the calcium score in conjunction with risk factors for disease for purposes of screening or risk stratification.

Because the specificity of EBCT for CAD detection is relatively low, the ACC/AHA consensus statement recommends that the test should not be made available to the general public without physician's request.[28] According to the ACC/AHA guidelines, EBCT can be employed in selected asymptomatic patients after the standard cardiac risk estimation does not provide adequate information to direct subsequent management. In asymptomatic patients at intermediate risk of disease, a high calcium score would push them toward the high-risk category,[28] thus mandating aggressive risk reduction. Alternatively, individuals with a score of zero or a low calcium score (1–10) would enter a low-risk category,[28] and these patients could possibly be observed. The test would thus clarify the need for aggressive disease management in this population.

Table 2. Sensitivity and Specificity of Stress Testing Modalities for Detecting Coronary Artery Disease

Test	Sensitivity (%)	Specificity (%)
Exercise stress testing[41]	66	80
Myocardial perfusion imaging[42]	87	70
Exercise echocardiography[42]	80	81
Dobutamine echocardiography[41]	78	88

EBCT also may be of value for predicting risk in asymptomatic elderly patients.[54,55] In the elderly, EBCT has been shown to be superior to exercise ECG in CAD detection.[56] The ACC/AHA guidelines therefore commented that EBCT may be particularly useful in elderly asymptomatic individuals since the results could alter management of risk factors of CAD in these patients.[28]

Risk Stratification

In symptomatic patients, the EBCT calcium score was shown to be independently and significantly associated with angiographically detected stenoses.[57] Irrespective of risk factors, calcium score greater than 80 increased the likelihood of any coronary disease, and calcium score greater than 170 increased the likelihood of obstructive coronary disease in persons undergoing angiography.[58] In patients with symptoms suggestive of CAD, the relative risk of angiographically detected obstructive CAD was higher in those with an abnormal EBCT than in those with an abnormal a treadmill test or technetium stress test.[59] In this study, the limited specificity of EBCT improved with the addition of treadmill test.[59] Symptomatic patients with low calcium scores have a lower probability of having angiographically detected stenosis[60] or future cardiac event(s),[61,62] and the probability increases with increasing calcium score. An algorithm that uses conventional cardiac risk assessment in conjunction with EBCT to measure a "noninvasive index" has been developed to rule in or rule out angiographic triple-vessel or left main CAD in symptomatic patients.[63]

According to practice guidelines from the Society of Atherosclerosis Imaging (SAI),[64] EBCT should be used as the initial test for diagnosis in patients with no known CAD if they are ambulatory, aged younger than 65 years, and have atypical chest pain (ACC/AHA class I recommendation, which signifies that there is evidence and/or general agreement that a given procedure or treatment is useful and effective). Furthermore, Schmermund et al[65] recommended that patients with equivocal stress test or intermediate probability of CAD after stress test should undergo EBCT for risk stratification before angiography is considered.

EBCT has also been shown to be a quick and efficient modality for detecting CAD in patients who present to the emergency department with chest pain,[66] with one study reporting a negative predictive value of 98% in this setting.[67] Increasing calcium score is indicative of an increased probability of future cardiac events in this patient population.[68] According to the SAI practice guidelines,[64] EBCT should be used as the initial test for diagnosis in men younger than 50 years and women younger than 60 years who present to the emergency department with chest pain and have a normal or nondiagnostic ECG (ACC/AHA class I recommendation).

Assessment of the Natural Course of CAD and Influence of Therapy on Disease

EBCT has been shown to be helpful in studying the natural progression of CAD[69] and in monitoring the influence of medications on the regression of disease.[70,71] Although EBCT shows promise in these areas, current evidence does not support its use for these purposes,[72] and further research is needed to more fully define its role in this important area.[28]

General Recommendations for Use of EBCT

Based on review of current evidence and recommendations from current guidelines, EBCT may be considered for screening/risk stratification in the following situations:

- In selected asymptomatic individuals at intermediate risk of disease as determined by traditional risk factors in whom standard cardiac risk assessment tools are found insufficient by the clinician, especially when there is doubt about need of initiating or encouraging compliance with risk reduction therapy such as statins
- As the initial test for risk stratification in patients with no known CAD who present with less typical chest pain, do not have acute myocardial infarction or unstable angina, and are clinically at intermediate risk of disease
- After indeterminate results of stress testing in patients with or without chest pain before considering angiography

These recommendations are summarized in a proposed algorithm for the application of EBCT in selected patients with CAD (**Figure 2**). Clinicians should refer to the ACC/AHA guidelines[28] for application of EBCT for patient care.

LIMITATIONS OF EBCT

There are several limitations of EBCT. As a surrogate measure of disease, EBCT does not provide information regarding the physiologic significance or vulnerability of the plaque (ie, obstructive or nonobstructive, stable or unstable), and the relation between arterial calcification and probability of plaque rupture is unknown.[28] In addition, racial differences have been noted in calcium scores, with African-American patients having a lower calcium score than white patients; this difference persisted even after adjusting for risk factors for CAD.[73] In another study, the CAD event rate was higher in African-American patients than in white patients, despite African-American patients having a lower prevalence of coronary calcification.[74] Therefore, it is believed that ethnic-specific data on the presence and severity of calcification must be used when employing a calcium score to predict CAD in African-American patients.[75]

Questions regarding the cost-effectiveness of EBCT have been raised. Charges for EBCT range from $300 to $400 in most centers.[76] EBCT is less expensive than stress echocardiography and MPI but more expensive than exercise stress testing. EBCT was recently shown to be cost-effective when used to predict CAD in asymptomatic men.[52] In patients not at high risk, EBCT has been shown to be more cost-efficient than traditionally employed strategies for CAD evaluation.[77,78] However, most third-party payers currently do not reimburse for this technology, which significantly curtails its use in routine practice. In addition, because specific indications for EBCT have not yet been generally accepted, cost-to-benefit calculations are problematic. Until such information is available and insurers more readily reimburse EBCT, availability is likely to remain limited.

OTHER NEW MODALITIES FOR CAD EVALUATION

The temporal resolution of multi-detector row CT (MDCT) scanners has improved recently, making it possible to use them to scan the beating heart. Whether calcium scores obtained from MDCT are comparable with those from EBCT remains controversial.[79,80] Also, radiation doses with MDCT are higher than those with EBCT.[81] However, compared with EBCT, MDCT scanners are much more widely available and are becoming popular for determining coronary artery calcification for CAD evaluation. Noninvasive angiography techniques using EBCT, MDCT, or cardiac magnetic resonance imaging to visualize the coronary arteries have also been recently developed[11,12,82] and are quickly becoming popular.

CONCLUSION

Early detection and evaluation of CAD are extremely important for efficient disease management. Detection of coronary artery calcification with EBCT has been shown to be reasonably accurate and effective for these purposes. EBCT has particular promise in screening asymptomatic intermediate-risk patients and intermediate-risk patients presenting with atypical chest pain syndromes. An algorithm for its use has been proposed in this article. Further studies are needed to confirm the value of EBCT relative to its cost. If these studies agree with initial reports, we anticipate that insurers and centers for cardiac care will embrace EBCT for detecting and evaluating CAD. **HP**

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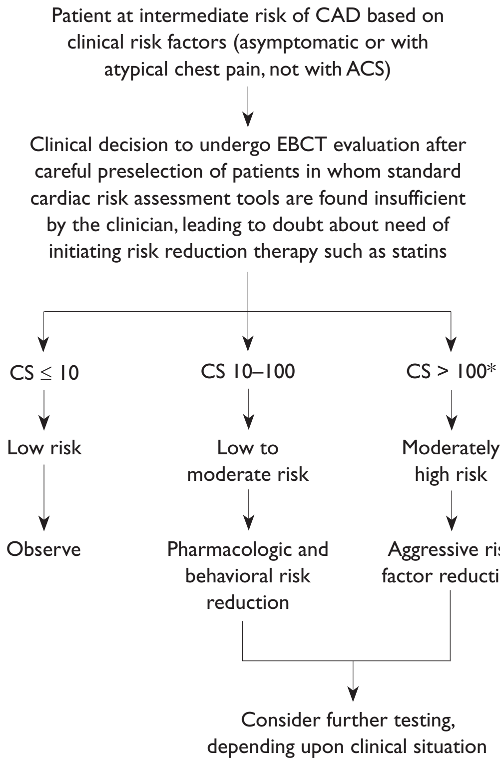

Figure 2. Algorithm for application of electron beam computed tomography (EBCT) for detection and assessment of coronary artery disease (CAD). NOTE: EBCT calcium score should be considered in conjunction with the entire clinical picture, including risk factors and symptoms. ACS = acute coronary syndrome; CS = calcium score. *Patients with CS > 400 are considered to be very high risk.

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