Cost-Benefit Analysis of Electron Beam CT as a Life Insurance Coronary Disease Risk Assessment Tool

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Electron beam CT (EBCT) or ultrafast CT is a diagnostic imaging technique that can identify calcium deposits within coronary arteries. Intra-coronary calcium is associated with coronary artery atherosclerosis. EBCT imaging has been advocated as a “better” way to screen for coronary artery disease. By producing a measure of the amount of calcium present, it may provide a non-invasive risk assessment tool that can predict the risk of future coronary events and death. Medical literature concerning identification and assessment of coronary risk using EBCT in the clinical setting is reviewed. The primary purpose is to illustrate one approach to a simple “back of the envelope” cost-benefit analysis (protective value) comparing EBCT with exercise electrocardiography as a life insurance coronary disease risk assessment tool. The performance and results of this analysis are contingent on a number of critical assumptions that are outlined in the text. The analysis limitations, and the future research required to refine the results are reviewed. With optimum levels of EBCT test performance, favorable thresholds of test costs, and long-term mortality data useful for assessment of value preservation, EBCT might prove to be a valuable risk assessment tool from a cost-benefit perspective under certain circumstances. Answers to key clinical research questions from prospective studies in asymptomatic cohorts are essential for refinement of a cost-benefit estimate.

Since half of first cardiac events (including MI and sudden death) occur in otherwise asymptomatic people, much effort has been directed at identifying screening tests for coronary heart disease and assessment of future risk of serious coronary events. The availability of effective risk reduction strategies such as lifestyle modification, lipid lowering drugs, and anti-platelet adhesion therapies has stimulated the search for tests that can properly classify at-risk individuals. For new tests to be useful in clinical practice or in risk assessment, they must be shown to be valid disease markers, and they must be cost effective in their application. This paper will review current medical literature concerning the use and performance of EBCT testing to detect and measure coronary calcium in asymptomatic populations. Using a series of assumptions based on the literature, a simple cost-benefit analysis of 2 screening strategies for coronary risk, EBCT and treadmill exercise electrocardiography (TMT), will be presented.
BACKGROUND

EBCT detects calcium in the walls of coronary arteries. Calcium is deposited in areas affected by the atherosclerotic process and not in normal coronary arterial tissue. The histopathologic connection between intracoronary calcium and coronary artery disease was first observed in autopsy studies, and later in fluoroscopy (x-ray) examinations. As a result, the presence of coronary calcium has been viewed as a potential means for detecting and predicting prognosis of coronary artery disease.

Basic scientific research has characterized the stages of atherogenesis leading to acute coronary syndromes (unstable angina, myocardial infarction and sudden cardiac death). It is unlikely that a particular EBCT-imaged calcium deposit in a coronary artery will be the trigger for an acute coronary event. Ruptured plaques that have caused thrombosis and acute coronary syndromes often do not contain calcium upon histologic examination.

The existence of a direct causal link between coronary calcium, and active atherosclerosis would be a valid basis for use of EBCT as a coronary risk assessment tool. However, the risk of future coronary events based on EBCT is related to the overall “burden” of coronary atherosclerosis present at a given time. That is, calcium score reflects the level of disease that has developed up to the time of the scan rather than the level of atherogenesis that may be continuing at present. It is also not a direct measure of coronary lesions at-risk for causing acute events. (For the interested reader, in-depth discussion of the role of inflammation in coronary artery disease, and the relation of unstable plaque to coronary calcium appears elsewhere.)

HOW IS EBCT PERFORMED?

EBCT uses an electron beam to acquire images in very short scanning times. This permits the acquisition of 30 to 40 image “slices” that are 3–6 mm thick during 1 or 2 breath-holding sequences. The density of a coronary artery wall image is measured using “Hounsfield” units. Areas that exceed a standard image density threshold are regarded as being consistent with intra-coronary calcium. Calcium scores are calculated based on the area and density of these lesions, most commonly using the “Agatston” method. Calculation of total calcium score from a single EBCT examination has been reported as having excellent interobserver and intraobserver reliability, but reproducibility of scores between 2 scanning runs has varied from poor to fair depending on the lab and calculation method.

HOW HAS TEST BEEN USED CLINICALLY?

Currently, EBCT is not “routinely” used in clinical medical practice. The American College of Cardiology/American Heart Association (ACC/AHA) recently developed a Consensus Document concerning EBCT. They found that the published literature did not clearly define which asymptomatic people require or would benefit from EBCT. Suggested uses for EBCT include coronary risk classification in cases where other tests are equivocal or as a means of monitoring therapeutic interventions. However, these uses were not recommended because insufficient evidence has been developed.

LITERATURE REVIEW

Investigators have assessed the correlation of EBCT with a “gold standard” test, coronary angiography, in patients with symptomatic coronary disease (chest pain syndromes, unstable angina, acute myocardial infarction) and asymptomatic individuals with varying levels of coronary risk. Table 1 summarizes clinical study designs that form the basis of current evidence.

SYMPTOMATIC KNOWN CAD PATIENTS

The possible uses of EBCT for patients with typical ischemic symptoms, or known CAD, include diagnosis and assessment of risk for
Table 1. Study Designs That Appear in EBCT Assessment Evidence

1. EBCT performed in conjunction with coronary angiography at the time of an acute coronary event or clinically significant symptoms—often in patients with known CAD.
2. EBCT performed in asymptomatic individuals with elevated coronary risk: followed to occurrence of cardiac event or symptoms requiring angiography.
3. EBCT performed in individuals self-referred for CAD screening, often voluntarily self-paying to have EBCT performed.
4. EBCT included as a modality for asymptomatic screening in populations on randomized, prospective basis.

future acute coronary events. A meta-analysis conducted by the ACC/AHA Working Group including 16 studies with 3683 patients requiring diagnostic angiography, evaluated the diagnostic accuracy of EBCT. These were symptomatic patients without prior diagnosis of coronary disease.² EBCT results were compared to coronary angiography results. The summary odds of having any coronary artery lesion on angiography with an abnormal calcium score were elevated approximately 20-fold (95% CI, OR 4.6 to 87.8). The summary odds of having >70% coronary artery stenosis was elevated approximately 50-fold (95% CI, OR 24.1 to 103.0). The pooled sensitivity and specificity values were 90.5% and 49.2%, respectively. There was considerable heterogeneity among the studies pooled in the analysis with respect to diagnostic calcium score thresholds (eg, any CS, CS ≥5, ≥100 were cut-points used), patient entry criteria, and angiographic disease thresholds (percent stenosis considered diagnostic). This heterogeneity is responsible for the wide confidence intervals observed.

Direct comparisons between EBCT and other tests used for diagnosis are few. However, the results of the meta-analysis performed to assess EBCT (above) can be compared to meta-analyses of the diagnostic accuracy of the exercise ECG, exercise echocardiography and myocardial perfusion imaging. The reported mean sensitivity of EBCT is somewhat higher than for exercise ECG but is similar to the mean sensitivity for perfusion imaging and echocardiography. Mean specificity of exercise echocardiography, perfusion imaging and exercise ECG are better than EBCT for predicting the presence of obstructive CAD.

Kajinami et al³ studied 251 patients who underwent elective coronary angiography for suspected coronary disease, comparing EBCT, ECG and thallium exercise tests for prediction of the presence of obstructive CAD. Agreement between non-invasive methods measured by the kappa statistic (0 = no agreement, 1 = complete agreement) was 0.31–0.39, which can be considered “fair” agreement. Sensitivity and predictive value of each test in predicting angiographic findings was comparable. Overall sensitivity for EBCT was 77%, for exercise ECG 74%, and for thallium exercise test 83%. Overall positive predictive value for EBCT was 86%, for exercise ECG 77%, and for thallium exercise test 70%. The results for thallium testing may have been low because the thallium scan protocol applied in the study yielded many false positives. “Best” applications of EBCT appeared to be in woman over age 60 and for men age 40–50 in this study. This study did not have enough power to distinguish a clear advantage of one test over another.

Major limitations to interpreting individual studies or meta-analysis of the diagnostic accuracy of EBCT relate to measurement issues and bias. Measurement issues include the use of a wide variety of diagnostic thresholds and protocols for interpreting EBCT, angiography and other diagnostic tests. None of the studies have been randomized trials, so selection bias, workup bias, and lack of blinding of the investigators are issues.

Most clinicians who perform diagnostic testing are also looking to stratify the patient’s risk of coronary events including cardiac death. Existing modalities such as exercise testing, exercise echocardiography, and perfusion imaging are well validated with respect to prognostic implications. As pointed
out by the ACA/AHA, these tests provide prognostic information that is implicit in exercise capacity in addition to information concerning the presence of obstructive CAD. EBCT is not a dynamic test and cannot provide information on functional capacity. This is a clear disadvantage of EBCT in patients who are able to exercise.

The use of EBCT to assess future risk and prognosis in known CAD is limited. EBCT does not appreciably add to information concerning the severity of obstructive lesions already obtained via angiography in known CAD patients. It has been shown that future coronary heart disease events (MIs and death) are more frequent in patients with high CS (>400) in a study by Detrano et al.4

ASYMPTOMATIC, NON-CAD POPULATIONS

The possible uses of EBCT in the asymptomatic population include screening for the presence of obstructive coronary disease and risk stratification for future acute coronary events, including myocardial infarction and cardiac death. The threshold calcium score level for diagnosis of “high risk” is most commonly related to 75th to 90th percentile. Calcium scores related to these distribution percentiles are relatively consistent between studies. Hoff et al5 recently published calcium score distributions by age and gender for over 35,000 patients screened with EBCT who were free of known coronary disease. This provides a picture of calcium score prevalence at various levels within a voluntarily screened population, and a basis for studying relative risk of age/gender specific CS for CAD. Additional prevalence studies continue to appear and increase our knowledge of the relationship of EBCT CS and demographic factors,6 as well as with related conditions such as diabetes.7

Very high CS (≥1000) appears to portend high risk in asymptomatic patients who have undergone EBCT. In a subgroup analysis of 98 asymptomatic patients (nearly all men, age 60 ± 10 years) voluntarily screened with EBCT, 35 events (23 acute MIs and 12 cardiac deaths) occurred over an average follow-up period of 17 ± 11 months.8 Those that had a coronary event had a higher average CS than those that did not (1561 ± 270). There was a 25% annual event rate (MI or death). The authors indicated that this rate is higher than coronary event rates reported by others for patients who have had positive SPECT imaging or exercise echocardiography. This was a very small, uncontrolled study but provides reasonable evidence for caution with patients with extremely high CS.

Caution is required in interpreting very high CS in the elderly. In a subgroup analysis of participants of the Cardiovascular Health Study with a mean age of 78, groups with subclinical or clinical CAD had higher mean CS than a group without evidence of CAD (mean CS 176). However, 25% of this “non-diseased” group had CS greater than 541, with an overall range of 0–1460.9 In a subsequent expansion of this analysis to a larger cohort of older adults with average age 80 (range 67–99 years), CS ranged from 0–5459 with a mean of 622 for men and 205 for women. Thirty-four percent of men and 13% of women had CS >1000.10 In addition to wide variability of CS, attenuation of any association between CS and conventional coronary risk factors in older adults was seen. These findings suggest that a relation between coronary risk and high CS in individuals age 70 and above is tenuous.

On the other hand, absence of coronary calcium by EBCT has high negative predictive value (94%-100% for a CS of 0) for future coronary events in asymptomatic and symptomatic patients. The negative predictive value improves with advancing age. Lamont11 looked at EBCT as a way of excluding obstructive coronary disease in patients with an abnormal treadmill ECG. In a group of 153 patients with chest pain and a positive treadmill ECG, a CS of 0 was shown to have a NPV of 93%. This suggested that EBCT might be useful for evaluation of positive exercise ECG tests. Others have also concluded that patients with CS of 0 (up to CS = 5, in
Table 2. Summary of Studies That Have Assessed Risk of Hard Cardiac Events (HCE, Acute MI and Cardiac Death) With EBCT Calcium Score in Asymptomatic Individuals

<table>
<thead>
<tr>
<th>Author</th>
<th>Publication Year</th>
<th>No. of Patients</th>
<th>CS Score Level Studied</th>
<th>Odds or Risk Ratio of HCE (95% CI)</th>
<th>Patient Follow-up Duration (months)</th>
<th>Patient Age Mean (se)</th>
<th>% Males</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detrano et al4</td>
<td>1996</td>
<td>491</td>
<td>&gt;75th percentile</td>
<td>10.8 (1.4–85.6)*</td>
<td>30 ± 13</td>
<td>55 ± 12</td>
<td>57</td>
</tr>
<tr>
<td>Arad et al19,20</td>
<td>1996/2000</td>
<td>1172</td>
<td>CS &gt; 160</td>
<td>15.8 (7.4–33.9)†</td>
<td>48–47</td>
<td>53 ± 11</td>
<td>71</td>
</tr>
<tr>
<td>Secci et al21</td>
<td>1997</td>
<td>326</td>
<td>&gt;75th percentile</td>
<td>7.5 (2.1–27)‡</td>
<td>32 ± 4</td>
<td>66 ± 8</td>
<td>82</td>
</tr>
<tr>
<td>Agatston et al22</td>
<td>1996</td>
<td>367</td>
<td>CS &gt; 50</td>
<td>6.9 (1.7–28.5)</td>
<td>36–72</td>
<td>52</td>
<td>68</td>
</tr>
<tr>
<td>Detrano et al23</td>
<td>1999</td>
<td>1196</td>
<td>CS &gt; 40</td>
<td>2.3§</td>
<td>41 ± 5</td>
<td>66 ± 8</td>
<td>89</td>
</tr>
</tbody>
</table>

* Highest quartile (CS > 397) compared to lowest quartile (CS = 0–2.1).
† Odds ratio (OR) for CS above level indicated for events included MI, revascularization, and cardiac death. OR for CS > 600 was 13.8 (7.0–27.4) in same analysis.
‡ Odds ratio for sum of hard (MI, cardiac death) and soft (revascularization) events comparing highest quartile to lowest quartile. Odds ratio for hard events only was not statistically significant.
§ Analysis of same cohort as Secci et al21 the South Bay Heart Watch Cohort. Confidence interval for odds ratio of HCE was not given.

Available evidence suggests that the presence of coronary calcification is associated with risk of a defined coronary event within a period of up to 72 months. Additionally, when unadjusted data is examined a relationship between level of calcium score and risk of hard coronary events may exist. To take analysis a step further, Secci et al21 and Detrano et al (1999)23 used multivariate logistic regression to adjust for the effect of other common clinical coronary risk factors (eg, age, sex, diabetes, ECG abnormalities, cholesterol, others) in data from the same cohort. Secci et al21 found that CS was not a significant predictor of coronary death or MI in a multivariate model. In a later analysis of a larger set of patients, Detrano et al (1999)23 found that coronary risk prediction models had similar ability with or without inclusion of CS. These contrast with earlier analyses by Detrano et al (1996)4 and Agatston et al22 that adjusted for factors such as age, smoking status, diabetes and hypertension. These found that CS did remain a significant predictor with adjustment for other factors.

CONCLUSIONS FROM LITERATURE REVIEW

The EBCT literature has limitations that include repeated publication bias, workup bias and selection bias. EBCT is not covered under most health insurance plans; therefore, participation in asymptomatic EBCT screening creates potential selection bias in studies that involve series of volunteers. With dissemination of this technology, independent prospective research will improve the quality of evidence available for assessment of EBCT.

Prospective studies will address some of the controversies concerning EBCT use in risk assessment of asymptomatic patients. The Multi-Ethnic Study of Atherosclerosis (MESA) study13 is designed to study new markers (including EBCT) of preclinical coronary atherosclerosis in asymptomatic populations. Analysis and publication of results is targeted for 2008. The Prospective Army Coronary Calcium Study (PACC)14 will assess the coronary calcium prevalence, the predictive value of EBCT, and the impact of self-knowledge of CS on risk factor modification
in a cohort of Army personnel participating in mandatory over-age-40 physical assessments. Enrollment began in 1998, with plans for at least 5 years of follow-up. If successful, these and other similarly designed prospective trials should furnish evidence for the assessment of the predictive value of EBCT in the asymptomatic populations.

For those who are asymptomatic and at low risk for CAD, whether the positive predictive value of EBCT supplements Framingham coronary risk factor assessment is uncertain. EBCT does appear to add predictive value to Framingham risk for those at moderate or high CAD risk. Risk ratios vary by level of pretest CAD risk, age and gender suggesting that EBCT calcium score may not be an independent predictor of risk.

For asymptomatic individuals, especially those with low pretest probability of CAD, the negative predictive value of a zero or very low calcium score is high, reproducible and appears valid. Regardless of the study scenario, most investigators report wide confidence intervals for risk or odds ratios associated with calcium score levels. This lack of precision contributes to the challenge of using calcium score as a precise measure of risk.

ASSESSING THE PROTECTIVE VALUE OF EBCT VS EXERCISE ECG (TMT)

What if EBCT were compared head to head with standard TMT for purposes of risk classification? Would one testing method be shown to provide greater protective value than the other? Data needed to conduct such an analysis are not available with the precision or for the insured lives context desired. The following illustrates one of potentially many approaches to these questions. By using estimates for test performance, costs and value based on clinical literature and insurance practice, a “back of the envelope” cost-benefit analysis may be conducted. A number of assumptions are required to conduct the analysis and are critical in determining its outcome. The author believes that the assumptions used are reasonable and acknowledges that other reasonable assumptions will necessarily lead to different conclusions.

METHOD

Using a range of potential pre-test probabilities of coronary disease and the literature-based specificity and specificity ranges listed below, Bayesian post-test probabilities of coronary disease with a positive test result were calculated using Microsoft Excel® and Precision Tree®, a decision analysis software tool. Recall that with knowledge of pre-test probability (= prevalence) and the sensitivity and specificity of a test, one can calculate the predictive value of a positive test, the post-test probability. Then using the cost and value estimates listed below, the present/protective value of each test option (EBCT vs TMT) was calculated.

Sensitivity analysis was used to evaluate the effect of varying 1 or more key factors (in this illustration: sensitivity, specificity and prevalence = pre-test probability). Sensitivity analysis is the technique of evaluating the effect of varying a key parameter or parameters through a range of values on an analytic result. In this analysis, “net” protective value is the analytic result of interest. For example, as shown in this analysis in Figures 1 and 2, the effect of varying sensitivity through a range of possible values, while holding all else constant can be assessed (see Results). The protective value of performing each study is plotted as separate lines. The “net” protective value (Net PV) is the difference in value between the 2 tests. The protective value of each test is equal where the lines cross and favors one over the other when the Net PV exceeds $0. Sensitivity analysis can be performed by varying 1 parameter (1-way), or multiple parameters (2-way, etc.) simultaneously through ranges of reasonable expected values. In this illustration, 2-way sensitivity analyses varying EBCT and CAD pretest probability, and EBCT sensitivity and specificity were also performed (see Results).

The following assumptions were used in this illustration. To re-emphasize, several are
Figure 1. Comparison of net protective value (Net PV, assuming $5000 with a rating from a positive test) using EBCT and TMT in a population with a pretest probability of CAD = 0.2, over the range of EBCT sensitivity reported in the medical literature (0.5–0.95) and using the “unbiased” estimate of TMT sensitivity and specificity. See description of sensitivity analysis as well as assumption 3 in Methods section. EBCT is the favored option when its sensitivity is greater than approximately 0.65.

Figure 2. Comparison of net protective value (Net PV, assuming $10,000 per case with a rating from a positive test) via the use of EBCT and TMT in a population with a pretest probability of CAD = 0.2, over the range of EBCT sensitivity reported in the medical literature (0.5–0.95) and the “unbiased” estimate of TMT sensitivity and specificity. See description of sensitivity analysis as well as assumption 3 in Methods section. EBCT is the favored option when EBCT sensitivity is greater than approximately 0.5.

particularly critical in defining limitations to interpretation of the results and other reasonable alternatives exist.

1. The level of future mortality from a positive test result that indicates the presence of obstructive coronary disease, based on either EBCT or TMT, is equivalent. The risk was conceptually equated to the mortality risk attributed to stable coronary artery disease, that is, similar to the mortality risk attributed to positive angiographic findings or perfusion abnormalities on nuclear exercise imaging.

Stated another way, the mortality ratio attributed to a positive EBCT is regarded as being the same as the mortality ratio attributed to angiography or perfusion study evidence of obstructive CAD. In underwriting, we use diagnostic tests to modify the probability that an impairment is present. A diagnostic test modifies the pre-test probability of an impairment providing us with a predictive value, or the post-test probability. It is common to assess mortality risk related to the post-test probability of an impairment when true presence or absence of the impairment is not known.

2. EBCT sensitivity in asymptomatic screening populations will be similar to existing published accounts for the detection of risk for future coronary events. This is a critical point in this analysis. EBCT calcium score (CS) distributions are age and gender specific. From the medical literature, it appears that age and gender specific 75th and 90th percentile levels may be appropriate thresholds for highest risk. However, generalizable sensitivity and specificity performance of CS at these levels in asymptomatic patients are unknown.

3. Sensitivity and specificity values were obtained from medical literature reviews of each test, EBCT and exercise ECG for the detection of obstructive CAD. The base values for exercise ECG (TMT) were “unbiased means” (sensitivity = 0.5, specificity = 0.9). For EBCT, values applied were weighted averages from a meta-analysis of patients with known CAD (sensitivity = 0.8, specificity = 0.4). Ranges from these reviews were used to establish ranges for sensitivity analysis. The EBCT review surveys studies with heterogeneous definitions of calcium score cutpoint. Pretest probability of CAD in the EBCT and exercise ECG reviews may be higher than those in many insured populations. As noted above, generalizable sensitivity and
specificity performance of CS in asymptomatic individuals consistent with an insured population is unknown.

4. Current testing costs are based on direct experience of underwriting and provider sources. The costs of testing applied were $375 for EBCT and $250 for exercise ECG (TMT).

5. Protective value of future claims resulting from the assessment of higher mortality for a positive test depends on applicant age, lapse rates, interest rate assumptions and other factors that can vary widely. For this analysis, 2 levels of protective value, $5000 and $10,000, were judged to be appropriate for an “average” size policy amount of $250,000, with a 20-year term, for a 50- and 59-year-old male applicant.

6. Claims missed by false-negative tests, value of lost business or increased premium from rating applied to false-positive tests are not included.

To emphasize again, the results of this analysis depend on the ultimate sensitivity of calcium score in predicting future hard coronary events when EBCT is used for risk assessment in large asymptomatic populations, ideally those that resemble insurance applicants. The assumption that a positive exercise ECG and EBCT measures the same level of mortality risk is also important.

**RESULTS**

Sensitivity analyses varying EBCT sensitivity are illustrated in Figure 1 assuming a protective value of $5000 from a rating and Figure 2, assuming a protective value of $10,000 from a rating. Given a pre-test probability of coronary disease leading to coronary events of 20%, if EBCT sensitivity exceeds approximately 0.65 (for $5000) or 0.5 (for $10,000), EBCT becomes favored over TMT for maximizing protective value from performing a screening test for coronary artery disease.

Sensitivity analysis holding EBCT sensitivity and specificity “fixed” (0.8 and 0.4, respectively, based on weighted averages from the published meta-analysis), while varying pre-test probability is shown in Figure 3. EBCT is favored over TMT for maximizing protective value for pre-test probability of coronary artery disease of 10% and higher. Figure 3 assumes a protective value of $5000 from a rating. For higher levels of protective value attributed to CAD identification and assignment of mortality level, possibly associated with higher face amounts or different mortality assumptions, EBCT shows a more favorable result than is illustrated in this example. With higher levels of assumed protective value per case, EBCT is favored at even lower sensitivity levels (with fixed pre-test probability).

A 2-way sensitivity analysis that varied EBCT sensitivity from 0.5 to 0.95 and pre-test probability of CAD from 5% to 50% simultaneously favored EBCT for maximizing protective value across all combinations. A second 2-way sensitivity analysis that varied EBCT sensitivity from 0.5 to 0.95 and EBCT specificity from 0.4–0.95 simultaneously, also favored EBCT for maximizing protective value across all combinations (not shown).

**DISCUSSION**

Using the simplified assumptions described in this analysis, EBCT is favored over
TMT when pretest probability of CAD exceeds 10%, or when the sensitivity of EBCT exceeds a level of 0.65. For higher assumed amounts of protective value per case, possibly associated with higher face amounts or different mortality assumptions attributed to the test results, EBCT shows a more favorable result than is indicated in this example. For reference, in the United States, the prevalence of coronary heart disease in men age 55–64 is 13.1%, and for women age 65–74 prevalence is 11.1%. The favorable cost-benefit results in this analysis using a population with pretest probability of 10% or higher suggests the possible utility of EBCT screening in these age/sex groups commonly required to have coronary screening tests. If more favorable levels of EBCT sensitivity can be demonstrated, favorable cost-benefit results may carry to younger age groups of males and females with lower prevalence and pre-test probability of coronary disease (at the anticipated protective value levels used in this analysis).

The limitations of this analysis are related to the main assumptions including the performance (sensitivity, specificity) of EBCT testing in a prospectively screened, presumed asymptomatic population of insurance applicants, and that conventional exercise electrocardiography and EBCT abnormalities are identifying coronary artery disease status that translates to the same mortality risk. Evaluation of a range of EBCT test sensitivity was addressed in this analysis. A differential between the level of mortality expected when a specific level of CS score is identified and when an exercise ECG detects an abnormality could have significant impact on these conclusions. Test cost has some influence on the result as well, but if EBCT use becomes more widespread, cost differential between EBCT and exercise ECG will be less of a factor. Additionally, sensitivity analyses allowing variation of more than 2 factors could be performed; however, this is beyond the complexity and precision allowed by the methods used here.

Can EBCT replace TMT as the preferred initial screen for CAD in insurance applicants? Data to support an answer is still being developed. Many assumptions that went into this model are simplifications for purposes of illustrating this method. Whether EBCT CS is an independent predictor of cardiac risk remains in question. The purpose was to illustrate an approach to a simple “back of the envelope” analysis that could stimulate interest in more detailed analysis.

Key questions that must be addressed before a conclusive answer can be provided are:

- How does EBCT perform in asymptomatic population when performed on a blinded, prospective basis?
- What is the mortality risk associated with a defined level or levels of calcium score for age, gender and pretest coronary risk?
- Does the mortality risk associated with EBCT calcium score relate to the same or different disease process than is measured by exercise electrocardiography (TMT)?
- Can risk predictions using EBCT be enhanced by using additional markers or tests using a multivariate approach?

For now, we must look expectantly for the maturation and completion of prospective clinical studies that will assess risk in the majority of individuals whose calcium scores fall in the middle ranges for age and gender.

EDITORIAL NOTE

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