The epidemic of coronary artery disease continues to affect a large number of individuals who often experience sudden and unexpected events. This underscores the need to develop more effective programs to detect silent atherosclerosis, with the ultimate goal of preventing coronary events. The use of conventional risk factors is helpful in assessing the median risk of a population, but it is often unsatisfactory in estimating the actual risk of an individual patient. As a consequence, newer imaging modalities are being developed to detect atherosclerosis in its early developmental phases. Technologies such as electron-beam computed tomography (EBCT) may render risk stratification more accurate if used in the appropriate patient populations and with the right diagnostic approach. Several studies have already demonstrated the power of coronary calcification as a strong predictor of future cardiovascular events. Nonetheless, the medical literature is currently pervaded by an animated debate, as some investigators still have concerns about the effectiveness of a preventive approach driven by technology. The use of Bayesian models to interpret data acquired with EBCT screening may provide practitioners with valuable evidence to aid in their decision making. ©2001 by Excerpta Medica, Inc.

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The Bayesian approach can be helpful in such situations and appears particularly useful when applied to hard-event prediction by EBCT. This perspective allows the application of sequential, individualized decision making using conditional probabilities.

One of the most common criticisms of the Bayesian approach is the subjectivity of the estimation of the pretest probability of disease. Nonetheless, the Framingham data provide us with commonly accepted estimates of risk based on risk factors. Pretest probabilities reflect the distribution of uncertainty before the test observation. The uncertainty changes once an observation in an individual is made, and the results of the test performed provide evidence that permits correcting the prior probability.

To obtain accurate true-positive rates, a sample of patients, who had a myocardial infarction and also underwent an EBCT study large enough to obtain narrow confidence intervals, would be required. Further, if cutoffs were used based on age- and sex-specific calcium-score percentiles as marker of risk, then the percentile chosen would, of course, determine the false-positive rate. For example, placing a cutpoint at the 75th percentile would guarantee that 25% of the population had a score higher than this level and would therefore be “false positive.”

The Bayes’ equation allows us to state that for any individual, the probability of having an event (myocardial infarction or death), given an abnormal EBCT result, can be calculated if we know 3 parameters: (1) the individual’s pretest probability of disease, (2) the probability of an abnormal EBCT test result in a patient who has had an event (true positive), and (3) the probability of an abnormal EBCT test result in a patient without events (false positive).

Evidence-based medicine supports the Bayesian approach, but it also requires the establishment of a treatment threshold. Such a threshold is necessary to help the physician understand whether the results of a test have moved a patient across a line that constitutes an indication for treatment. Thresholds have been established, for example, for the institution of statin therapy. In the more cost-conscious United Kingdom, the treatment threshold is a risk of cardiovascular events of 30% over 10 years. In the United States, a more liberal risk of 20% over 10 years has been suggested as an acceptable limit.

For the purpose of this analysis, we applied Bayesian statistics to 363 patients who underwent EBCT scanning within 2 weeks of having a first, unheralded myocardial infarction. The patients were 202 men (aged 40 to 60) and 161 women (aged 50 to 70). The age ranges were chosen because they represent the optimal ages for coronary calcium screening. To validate this model (ie, use of retrospectively acquired data), we compared the odds ratios of having a hard event predicted through EBCT and sex-specific calcium-score percentiles in this retrospective group, with our published prospective cohort. Because the results were identical, we assumed that using a cohort of patients submitted to EBCT imaging postfactum (ie, myocardial infarction) was an acceptable approach. Table 1 displays the true-positive rates with 95% confidence intervals and the false-positive rates dictated by calcium scores being >50th, 75th, and 90th age- and sex-specific percentiles. The actual false-positive rates would be slightly smaller than noted after the true-positives for each group were subtracted, but the difference would be small, and we will assume the worst-case scenario. Far more important is that the number of patients is large enough to provide narrow confidence intervals for the true-positive rates.

Figure 1 shows an example of the application of Bayes’ equation to the data presented in Table 1. Pretest probabilities are reported on the x-axis, and the y-axis shows the posttest change. As an example, consider a 53-year-old male smoker with a family history of premature CAD. His serum level of low-density lipoprotein cholesterol is 180 mg/dL. This patient asks his primary care physician whether or not he should be receiving statin therapy. His Framingham score predicts a 10-year risk of 15%, insufficient for treatment. After EBCT screening, even a low calcium score of 20 (>50th age- and sex-specific percentile) will “lift” our patient’s 10-year risk to nearly 25%, whereas a score of 0 will “decrease” the risk to a very low 0.8% over 10 years. In both cases, we have moved the patient across the treat or no-treat threshold. This example demonstrates the ability of EBCT to help the physician identify high-risk patients among individuals at intermediate risk, and the ability of the test to reclassify as “very low risk” a subject with a calcium score of 0.

This is an important, and therefore potentially controversial, finding. For the average practitioner, the intermediate-risk population represents a large, divergent group among whom most CAD events will occur. It is exactly the group where individualized risk prediction is needed. Recently, Knickelbine et al presented EBCT and risk-profile data on 2,002 patients. They concluded that “age and sex percentile scoring would have the most value and would most likely change management approach in patients with intermediate conventional NCEP risk profiles.”

There is a natural sequence to a physician’s first using standard, recognized risk factors to identify patients at high, low, and intermediate risk of cardiovascular events. The decision to further adjust risk assessment in those patients who are in the intermediate category is the next logical step. This sequential, individualized process of risk analysis is, in fact, a Bayesian approach. For each individual patient, EBCT results will provide the robust evidence necessary to change the pretest probability. The key point is that the Bayes’ formula guarantees that the effect of this evidence is always the same. For patients at intermediate risk, according to the Framingham equations, EBCT results can produce posttest probabilities that will reposition their risk into accepted high- or low-risk categories.


| Table 1 | True- and False-Positive Rates for Calcium Score Percentile* Cutpoints in Patients Submitted to Electron-Beam Tomography Imaging Within 2 Weeks After Myocardial Infarction† |
|---|---|---|---|---|
| Calcium Score (by percentile) | n/Total | True Positive | 95% CI | False Positive |
| >90th % | 168/363 | 0.46 | 0.41–0.52 | 0.10 |
| >75th % | 271/363 | 0.75 | 0.70–0.79 | 0.25 |
| >50th % | 343/363 | 0.95 | 0.92–0.97 | 0.50 |
| 0 | 10/363 | 0.03 | 0.01–0.05 | 0.48 |

CI = confidence interval.
*Age- and sex-specific percentile.
†Myocardial infarction not preceded by symptoms or signs of coronary artery disease.