Coronary calcification score: the coronary-risk impact factor

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Context Identification of asymptomatic high-risk individuals is integral to current policies for preventing coronary heart disease, but existing methods of estimating risk lack sensitivity. To overcome this limitation increasing use is being made of non-invasive methods to detect subclinical coronary artery disease—eg, computed tomography (CT) to scan for coronary artery calcification. The location and extent of calcification correlate closely with pathological and angiographic abnormalities, but whether such calcification predicts clinical events, especially in younger individuals, is equivocal. Most data on coronary calcification have been obtained with electron-beam CT, but recently multislice CT, which is more versatile, less expensive, and available in most large hospitals, has been increasingly used.

Starting point Leslee Shaw and colleagues (Radiology 2003; 228: 826–33) showed that the coronary calcification score predicted total mortality within subsets of patients classified at low, intermediate, or high risk according to Framingham criteria. In a cohort of over 10 000 individuals, 5-year risk-adjusted survival was 95% when the score was over 1000 compared with 99% for scores of 10 or less. These results agree with other recent studies showing strong correlations between coronary calcification and coronary heart disease events.

Where next? The increasing use of multislice CT scanners should generate more data for comparison with those obtained from electron-beam CT. Radiation dose, which is higher with multislice than with electron-beam procedures, needs to be reduced, and calcification in scans needs to be quantified more accurately than with existing computer-based analyses. Further studies are needed to establish the predictive power of the coronary calcification score for clinical events and the effects of therapeutic intervention on both these outcomes. It would also be worth investigating the relation between coronary calcification and risk factors not quantified in Framingham-based estimates, including familial and racial predisposition to premature coronary heart disease.

Current guidelines for the prevention of coronary heart disease advocate the identification of individuals at high absolute risk (commonly defined as >20% over 10 years) and starting appropriate risk-reducing measures. However, lipid-lowering intervention trials show that the number needed to be treated to prevent each coronary heart disease event is 2–3-fold greater in primary than in secondary prevention. To target prevention of asymptomatic individuals better, we need a non-invasive means of identifying which of those ostensibly at high risk are most likely to develop clinical coronary heart disease.

In this context, the potential usefulness of electron-beam computed tomography (CT) scanning for detecting coronary calcification was reviewed several years ago.1 The coronary calcification score has been shown to correlate strongly with the presence and severity of coronary atherosclerosis, on histological and angiographic criteria, and has been proposed as a means of determining the need for further cardiological investigation and risk-factor modification. A score of 0–10 makes the probability of significant coronary artery disease very unlikely; 11–100 indicates that mild disease is likely; 101–400 makes non-obstructive disease highly likely; and over 400 indicates a high likelihood of at least one significantly stenosed lesion.2 However, concerns have been expressed about the low specificity of coronary calcification, lack of evidence that it provides additional information to Framingham-based estimates of risk,3 and the paucity of prospective data relating the coronary calcification score to coronary heart disease events.4

Another limitation has been the cost of the electron-beam scanners. Recently, however, multislice CT scanners have been shown to produce similar calcium scores to the electron-beam technique, and they are more widely available.

Electron-beam and multislice CT scanners Electron-beam CT scanning for coronary calcification has been used for over 10 years in the USA; most data on this topic stem from that source. For example, the profound influence on the coronary calcification score of age and sex has been documented in electron-beam scans of over 35 000 US individuals.5 In that study the 75th percentile was proposed as a cutoff for identifying high-risk individuals. A smaller study6 with multislice CT showed good correlation between the coronary calcification score in German individuals and the US electron-beam data, especially in the distribution of 75th percentile values. But further comparative studies are needed, with similar methods to acquire data and calculate calcium scores. Acquisition time and radiation exposure are less with the electron-beam method,7 but multislice CT yields greater reproducibility.8

Predictive value of coronary calcification for clinical events Initial data on the predictive power of coronary calcification were ambiguous in that almost 20% of myocardial
In the second study, by Pohle et al,14 102 patients aged under 60 years, mostly men, had an electron-beam CT scan within 2 weeks of a first myocardial infarction and before any form of intervention. The results showed that 61% had a coronary calcification score over the 90th percentile, compared with 6% in controls matched for age, sex, and risk factors. This difference was even greater in those aged under 35 years than in those aged 45–59 years. In 90% of cases, the culprit vessel was calcified.

**Coronary calcification and Framingham scores as estimates of risk**

Several studies have shown correlations between coronary calcification and conventional risk factors, notably the total cholesterol to HDL-cholesterol ratio, but most of the variation in calcification scores between individuals remains unexplained by differences in risk factors.3,5,10,14,16 Also, the correlation between the coronary calcification score and C-reactive protein, an emerging marker of coronary heart disease, remained significant even after adjustment for age and the Framingham risk score.17 Further evidence of the anomalous relation between risk factors for coronary heart disease and coronary calcification comes from three studies, each of which compared estimates of absolute risk on the basis of the coronary calcification score and Framingham criteria.

Elkeles et al11 studied asymptomatic hypercholesterolaemic men in London with electron-beam CT, dividing them according to whether their risk of coronary heart disease was high (≥20% over 10 years) or low (<10% over 10 years), estimated by the Framingham logistic function.11 Mean absolute risks over 10 years were 25-3% and 7-4%, respectively. As expected, the frequency of a coronary calcification score of 0–10 and over 400 differed significantly between the low-risk and high-risk groups, but it is noteworthy that 27% of high-risk men had a low calcification score whereas 2% of low-risk men had a high score (figure 1).

In a second study, Brown et al12 looked at the relation between angiographically determined stenosis burden in the proximal coronary artery, risk factors, and coronary calcification score by electron-beam CT. On multivariate analysis, the coronary calcification score correlated better with proximal stenosis burden, a strong determinant of clinical events, than did the Framingham-derived estimate of absolute risk.

In the third study, Greenland and Gaziano13 analysed published data to compare Framingham-derived estimates of coronary heart disease risk with estimates on the basis of the coronary calcification score. These researchers calculated that for any given pretest probability of a coronary heart disease event, on the basis of risk factors, having a calcification score of 80 or more would triple the probability whereas having a score below 80 would reduce it by a factor of 5. As shown in figure 2, if the threshold for risk-factor modification is set at 20% over 10 years, then virtually all individuals at intermediate risk (6–20% over 10 years) qualify for treatment if their calcification score is 80 or more, whereas none do if their score is under 80. Extrapolation of these conclusions to the data on hypercholesterolaemic men in figure 1 implies that the 27% of the high-risk group with a calcification score of 0–10 would not need to be treated, although low scores in younger men (<50 years old) should be interpreted cautiously, especially if they are smokers. Conversely, most of those in the low-risk group who had a coronary calcification score over 80 would be eligible for lipid-lowering therapy. Several studies have shown that statin treatment slows the rate of the annual increase in coronary
Conclusions

CT scanning for coronary calcification is rapidly establishing itself as a non-invasive means of assessing the presence and severity of coronary artery disease. Recent data showing correlations with both C-reactive protein and coronary heart disease events imply that coronary calcification reflects the extent of unstable as well as stable plaques. Correlations between the calcification score and clinical events are stronger than those between clinical events and commonly used risk-factor-based estimates of coronary risk, as shown by Leslee Shaw and colleagues.4 Their results showed that assessment of coronary calcification added prognostic information over and above that derived from traditional risk factors. One explanation for these findings is that the coronary calcification score reflects the overall impact of risk factors, both known and unknown, on the arterial wall. Discrepancies between the calcification score and Framingham-based estimates of risk presumably reflect the differing susceptibility of individuals to their prevailing risk factors. Evidence that this differing susceptibility might have a genetic basis comes from a preliminary report that calcification scores are higher in asymptomatic persons with a family history of premature coronary heart disease.5 Combining the two approaches—calcification measurement and Framingham risk estimation—should enable clinicians to assess better the management of asymptomatic individuals, as is recognised in the latest European guidelines8 on the prevention of cardiovascular disease. The limitations of conventional methods of assessing risk and the need for new strategies to detect vulnerable patients have been endorsed recently in an internationally based consensus document.9,10

We have no conflict of interest to declare.

References

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