Risk assessment with coronary artery calcium scoring: effects of smoking at young age

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Online publish-ahead-of-print 21 March 2006

This editorial refers to 'Prognostic value of coronary artery calcium screening in asymptomatic smokers and non-smokers'† by L.J. Shaw et al., on page 968.

In clinical cardiology, risk assessment has been focused on patients with suspected or known coronary artery disease. The available non-invasive imaging techniques have allowed differentiation between high- and low-risk patient groups. These imaging techniques mainly included nuclear imaging using SPECT and stress echocardiography. Nuclear imaging with SPECT is based on the detection of resting or stress-induced perfusion abnormalities, whereas stress echocardiography permits assessment of resting or stress-induced systolic wall motion abnormalities. Moreover, with the introduction of gated SPECT imaging and contrast-enhanced echocardiography, simultaneous evaluation of function and perfusion is now possible. Both imaging techniques rely on identification of obstructive coronary artery lesions that cause ischaemia, as reflected by stress-induced perfusion and/or systolic wall motion abnormalities. Indeed, a normal SPECT study or stress echocardiogram has been demonstrated to predict an excellent prognosis with a low event rate. Recently, a meta-analysis of 31 studies (n = 69 655 patients) on the prognostic value of SPECT demonstrated that a normal SPECT study was associated with an annual hard event rate (cardiac death or myocardial infarction) of 0.85%, comparable with the event rate in the general population without evidence of coronary artery disease. Conversely, the annual hard event rate was 5.9% in patients with moderate to severely abnormal SPECT studies. Similarly, pooled analysis of 13 stress echocardiography studies (n = 32 739 patients) demonstrated an annual hard event rate of 1.2% for a normal stress echocardiogram when compared with 7.0% for an abnormal study.

Initially, these non-invasive imaging studies were applied to high-risk individuals, but more recently, the techniques have become popular for risk stratification in patients with an intermediate likelihood of coronary artery disease, particularly in the presence of multiple risk factors without known coronary artery disease. Consequently, recent studies have confirmed the prognostic value of SPECT imaging or stress echocardiography in patients with hypertension and diabetes mellitus. In these patient groups, discrimination between high- and low-risk groups was also possible on the basis of normal and abnormal SPECT or stress echocardiographic studies.

The next step in risk assessment is to evaluate high-risk asymptomatic individuals with an elevated risk of coronary artery disease or screening for coronary artery disease. Recently, simplified imaging techniques have been introduced that do not visualize ischaemia, but rather identify coronary artery atherosclerosis. These techniques include electron beam- or multi-slice-computed tomography (EBCT or MSCT) that allows assessment of coronary artery calcium or even non-invasive coronary angiography. In particular, coronary artery calcium scoring has been used extensively for risk assessment. Indeed, coronary artery calcification is synonymous with atherosclerosis, and the coronary artery calcium score correlates well with the total plaque burden of the coronary arteries. Moreover, measurement of coronary artery calcium with CT techniques has been demonstrated to have a high accuracy and reproducibility. However, it should be emphasized that the presence of coronary artery calcium is not predictive of significant coronary stenoses and it is not site-specific.

Still, extensive data are available on risk stratification based on coronary artery calcium assessment, and large studies have demonstrated that elevated coronary artery calcium scores are associated with increased risk of cardiovascular events. Moreover, a meta-analysis including four studies (n = 3970 patients) demonstrated the incremental value of coronary artery calcium scoring over traditional risk factors. Moreover, the absence of coronary artery calcium had a high negative predictive value for future cardiovascular events. In the landmark study by Shaw et al., 7 10 377 asymptomatic individuals who underwent coronary artery calcium scoring with EBCT were followed-up for 5 years. These patients were referred by their primary care physician. Coronary artery calcium was quantified using the Agatston score, which is the most widely applied technique for the quantification of coronary artery calcium. According to this quantification, patients are frequently divided into a score ≤10, 11–100, 101–400, 400–1000, and >1000. Patients with minimal or no calcium had an excellent survival, whereas mortality increased significantly for patients with a score >1000. In a risk-adjusted model of mortality, it was shown

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†doi:10.1093/eurheartj/ehi784
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that the coronary artery calcium score was a strong and independent predictor of all-cause mortality. In addition, when patients were divided according to the Framingham risk score, 1302 patients were classified as low risk and 5876 as high risk, and in both categories, the coronary artery calcium score provided incremental prognostic value.

Thus, the available data demonstrate that the coronary artery calcium scoring permits identification of high-risk asymptomatic individuals and provides incremental information over traditional risk factors. In particular, the incremental value of the coronary artery calcium score has been evaluated in relation to two traditional risk factors, namely, diabetes and smoking.

Recently, the prognostic value of the coronary artery calcium score was explored in asymptomatic individuals with diabetes when compared with non-diabetics. The aforementioned 10 377 asymptomatic individuals were accordingly divided into 903 asymptomatic diabetics and 9474 non-diabetics. Patients with diabetes were older, and hypertension and smoking were more prevalent, whereas a family history of coronary artery disease was less prevalent. At 5-year follow-up, the mortality was 15.8% in the asymptomatic diabetics when compared with 7.8% in non-diabetics. In a risk-adjusted model, there was a significant interaction of the coronary artery calcium score and diabetes, indicating that for every increase in the coronary artery calcium score, there was a greater increase in mortality for diabetics when compared with non-diabetics. In particular, there was a 44% increased risk of death in diabetics for every increase in the coronary artery calcium score group (from 11–100 to 101–400, 401–1000, and >1000, \( P < 0.001 \)). Moreover, diabetics without coronary artery calcium exhibited a similar survival to non-diabetic subjects without coronary calcium (98.8% vs. 99.4%, ns).

Of note, the Framingham risk score could not identify the low- and high-risk subsets, as all diabetics were considered high risk according to the Framingham risk score. Shaw et al. report on the prognostic value of coronary artery calcium score in asymptomatic smokers when compared with non-smokers. Recent evidence from the World Health Organization estimates that nearly half of the world’s smokers will die as a result of health consequences of smoking. Although substantial anti-smoking efforts have been put forth in the health policy arena, evidence of coronary calcium may be a powerful message for some patients to make healthy life-style changes. The authors have used the aforementioned patient registry of 10 377 asymptomatic individuals undergoing EBCT, with a follow-up of 5 years. Of note, the prevalence of current smokers was high, with 40% (n = 4113) of the cohort currently smoking. The smokers were younger, more often male, and had a greater prevalence of cardiac risk factors. On EBCT, smokers had a coronary calcium score that was on average 72 points higher than that of non-smokers (\( P < 0.001 \)). In particular, a score \( >1000 \) was detected in 2.4% of non-smokers when compared with 4.4% of smokers. At 5-year follow-up, the survival was 98.4% in non-smokers when compared with 96.9% in smokers. Moreover, smokers who died had a significantly higher coronary artery calcium score than smokers who survived (505 ± 722 vs. 164 ± 393, \( P < 0.001 \)). Smoking was estimated to decrease a subject’s life expectancy by almost 1 year when the coronary artery calcium score exceeded 400. The reduction in life expectancy was highest in younger smokers (<50 years) with scores >400, being 4.8 years. In summary, young smokers with a high-risk calcium score were four to nine times more likely to die during 5-year follow-up when compared with non-smokers.

This study clearly confirms the incremental value of coronary artery calcium scoring for risk assessment of asymptomatic individuals with risk factors for coronary artery disease. However, it should be pointed out that this cohort comprises subjects who were referred by their primary care physician and thus not represent the general population. Moreover, this cohort was used in the previous reports. Still, the current cohort is probably the largest on the use of coronary artery calcium scoring in asymptomatic subjects.

The main question that remains is whether coronary artery calcium scoring should be used for screening of coronary artery disease in asymptomatic individuals. For screening to be justified in asymptomatic populations, different criteria need to be met, including a high prevalence of disease, the screening technique should be adequate, and therapy for the high-risk individuals should alter outcome. It is clear that the first two conditions are met, but evidence supporting the third criterion is not available yet. Accordingly, it is clear that randomized trials should be undertaken in that direction before screening for coronary artery disease with coronary artery calcium scoring should be considered. Still, the available evidence and also highlighted in the current study demonstrate the prognostic value of coronary artery calcium scoring, with incremental value of traditional risk factors for coronary artery disease.

Conflict of interest: none declared.

References