

Saturday 17 May 2003



## Finding the age of the patient's heart

*Electron beam computed tomography detects early coronary atherosclerosis*

**A**therosclerosis is the leading cause of morbidity and mortality in industrialised nations, and its prevalence in developing countries is rising. In up to 70% of patients the initial manifestation of coronary artery disease is either myocardial infarction or sudden death.<sup>1</sup> Studies comparing coronary angiography with intravascular ultrasound, the reference standard for detection of atherosclerotic disease, have shown that vascular remodelling accompanies the early stages of the development of atherosclerotic plaque, and luminal narrowing therefore often does not occur until a clinically significant amount of intimal plaque has been formed.<sup>2</sup> About 70% of acute coronary syndromes occur from rupture of haemodynamically insignificant or non-obstructive coronary artery plaques<sup>3</sup> in previously asymptomatic individuals. The need is growing to identify accurately asymptomatic patients with a sizeable burden of coronary atherosclerotic plaque for intensive treatment.

The inflammatory response, which also contributes to atherogenesis, results in calcium being deposited in the atherosclerotic plaque. Histopathological studies confirm the close correlation between the extent of coronary artery calcification and the total burden of atherosclerotic plaque.<sup>3</sup> Electron beam computed tomography (G E Imatron, South San Francisco, California) is an evolving, non-invasive technique for the detection of calcium in the coronary atherosclerotic plaque,<sup>4</sup> which can also accurately quantify the extent of coronary calcification, commonly expressed as Agatston units or volumetric scores.

Recent publications have drawn attention to the incremental prognostic value of coronary calcium imaging by electron beam computed tomography in combination with traditional risk factors and C-reactive protein in predicting future coronary events.<sup>5</sup> In a study of 10 377 asymptomatic patients with an average follow up of five years, Callister et al evaluated the independent and additional prognostic value of coronary artery calcification scores and showed that five year survival rates worsened with increasing calcification as evidenced by coronary artery scores.<sup>6</sup> The authors also propose a concept of "heart age," whereby coronary calcium scores derived by electron beam computed tomography are used to predict an individual's risk of death or myocardial infarction. The patients are then assigned the heart age that corresponds to their level of risk. This novel concept could improve patients' understanding and effectively replace biological age as a risk factor in the

Framingham equation, which is used to assess risk of coronary heart disease.

Electron beam computed tomography uses an electronically steered electron beam to generate x rays, thus permitting rapid acquisition of gated images of a moving target such as the heart. Holding breath for 30-40 seconds produces reproducible measurements of a high quality (median inter-observer variability in coronary artery calcification scores of 5-8%),<sup>7</sup> which represents the burden of coronary artery plaque.<sup>4</sup> In addition electron beam computed tomography has a low radiation dose (twice that of a chest x ray or a fifth of the dose of conventional computed tomography of the chest). The absence of coronary calcium is associated with a very low rate of future cardiac events (0.1% per year)<sup>8</sup> and has 99% negative predictive value for the presence of obstructive coronary artery disease. Callister et al have also shown that a coronary artery calcification score of less than 10 is associated with a five year survival rate of 99%.

Exercise tolerance testing by using a treadmill is often the initial test to investigate chest pain, despite its limited sensitivity and specificity for detecting obstructive coronary artery disease in patients with low to intermediate probability of coronary artery disease. The national service framework for coronary heart disease also recommends it. This strategy has led to a notable increase in the referrals for angiography, resulting in a high rate of normal angiograms.<sup>9</sup> Rumberger et al from the Mayo clinic and subsequently Raggi et al found that a pathway based on electron beam computed tomography as the initial test to evaluate symptomatic patients with a low to intermediate probability of coronary disease provided a substantial cost benefit over that based on exercise treadmill testing.<sup>10</sup> Although the results of the ongoing multiethnic study of atherosclerosis may better define the clinical value and cost effectiveness,<sup>11</sup> we require similar studies for our health system.

The two groups of patients that may be considered for coronary calcium imaging by electron beam computed tomography are asymptomatic individuals with cardiovascular risk factors and symptomatic patients with low to intermediate probability of coronary artery disease, who would normally be referred for exercise treadmill testing. Since the detection of coronary artery calcification in such patients does not always imply a clinically significant luminal stenosis, in our view a functional stress test, such as myocardial perfusion imaging, may be used as a gatekeeper for the



Extra references  
appear on [bmj.com](http://bmj.com)

BMJ 2003;326:1045-6

referral of patients for further invasive coronary angiography or intervention.<sup>7</sup> The presence of myocardial ischaemia and its extent strongly predict the short and long term risk of coronary events<sup>11</sup> and are associated with increasing calcification of the coronary artery scores (more than 400 Agatston units).

Another remarkable development is the use of electron beam computed tomography to monitor lipid lowering treatment. Achenbach et al in a prospective study showed clinically significant progression of coronary calcification and hence atherosclerotic plaque disease in untreated patients with hyperlipidaemia within 12 months. They further showed that progression of the plaque (calcification of the coronary artery) could be reduced and even that regression of the plaque was induced by lipid lowering treatment.<sup>12</sup> The recently published heart protection study and the promising early results from the Anglo-Scandinavian cardiac outcomes trial (ASCOT) have further strengthened the role of lipid lowering treatment in the primary prevention of coronary heart disease. However, translating the results of these trials into clinical practice is extremely costly and perhaps unaffordable. To achieve cost effectiveness, treatment should be targeted at those patients at the highest risk of coronary events. In addition we also need to monitor response to treatment and improve compliance, which is a major issue. Could electron beam computed tomography bridge these gaps effectively?

D Vijay Anand *research registrar in cardiology*

Northwick Park Hospital, Harrow HA1 3UJ

David Lipkin *consultant cardiologist*

Royal Free Hospital, London NW3 2QG

Avijit Lahiri *honorary consultant cardiologist*

Cardiac Imaging and Research Centre, Wellington Hospital, London NW8 9LE

Competing interests: AL and DL are co-directors of the Wellington Cardiac Imaging Research Centre, which performs non invasive investigations including electron beam computed tomography.

- 1 Thaulow E, Erikssen J, Sandvik L, Erikssen G, Jorgensen L, Cohn PF. Initial clinical presentation of cardiac disease in asymptomatic men with silent myocardial ischemia and angiographically documented coronary artery disease (the Oslo Ischemia Study). *Am J Cardiol* 1993;72:629-33.
- 2 Mintz GS, Painter JA, Pichard AD. Atherosclerosis in angiographically "normal" coronary artery reference segments: an intravascular ultrasound study with clinical correlation. *J Am Coll Cardiol* 1995;25:1479-85.
- 3 Rumberger JA, Simons B, Fitzpatrick L, Schwartz RS. Coronary artery calcium area by electron-beam computed tomography and coronary atherosclerotic plaque area: a histopathologic correlative study. *Circulation* 1995;92:2157-62.
- 4 Agatston AS, Janowitz WR, Hildner EJ, Zusmer NR, Viamonte MJ, Detrano R. Quantification of coronary artery calcium using ultrafast computed tomography. *J Am Coll Cardiol* 1990;15:827-32.
- 5 Park R, Detrano R, Xiang M. Combined use of computed tomography calcium scores and C-reactive protein levels in predicting cardiovascular events in nondiabetic individuals. *Circulation* 2002;106:2073-7.
- 6 Callister TQ, Schisterman EF, Berman D, Raggi P, Shaw LJ. Risk-adjusted mortality by extent of coronary calcification [abstract]. *J Am Coll Cardiol* 2002;39(suppl A):447A.
- 7 Anand DV, Lipkin D, Lahiri A. Myocardial perfusion imaging is a gate-keeper for risk stratifying asymptomatic patients with increased coronary calcium scores. *J Nucl Cardiol* 2003 (in press).
- 8 Raggi P, Callister TQ, Cooil B, He Z, Lippolis NJ, Russo DJ, et al. Identification of patients at increased risk of first unheralded acute myocardial infarction by electron beam computed tomography. *Circulation* 2000;101:850-5.
- 9 Wong Y, Rodwell A, Simpson IA. Sex differences in investigation results and treatment in subjects referred for investigation of chest pain. *Heart* 2001;85:149-52.
- 10 Raggi P, Callister TQ, Cooil B, Russo DJ, Lippolis NJ, Patterson RE. Evaluation of chest pain in patients with low to intermediate pretest probability of coronary artery disease by electron beam computed tomography. *Am J Cardiol* 2000;85:283-8.
- 11 Hachamovitch R, Berman DS, Kiat H, Cohen I, Cabico JA, Friedman J, et al. Exercise myocardial perfusion SPECT in patients without known coronary artery disease: incremental prognostic value and use in risk stratification. *Circulation* 1996;93:905-14.
- 12 Achenbach S, Roper D, Pohle K, Leber A, Thilo A, Knez A, et al. Influence of lipid lowering therapy on the progression of coronary artery calcification: a prospective evaluation. *Circulation* 2002;106:1077-82.

## Chronic obstructive pulmonary disease

*The lack of a national service framework should not allow us to ignore it*

Chronic obstructive pulmonary disease causes significantly more mortality and morbidity than other causes of airflow limitation in adults<sup>1</sup> but is underdiagnosed and under-recognised. The World Health Organization estimates that chronic obstructive pulmonary disease is the fourth leading cause of death worldwide, with 2.74 million deaths in 2000, and this burden is growing rapidly.<sup>2</sup> The main cause is cigarette smoking, and the United Kingdom is now experiencing the ravages of a past high prevalence of smoking in its ageing population. Costs for 1996-7 showed that the NHS spent more than £818m (\$1.3bn; €1.2bn) on the disease.<sup>3</sup>

In the United Kingdom chronic obstructive pulmonary disease accounts for as many as one in eight medical admissions.<sup>1</sup> Emergency admissions for chronic obstructive pulmonary disease have recently risen dramatically, contributing notably to the hospital bed crisis.<sup>4</sup> Annual admissions peak in early January, due, in part, to increased respiratory illness, acute exacerbations, and reduced primary care support over the holidays.<sup>5, 6</sup>

The prevalence of chronic obstructive pulmonary disease is greatest in socioeconomically deprived people; the differential effect between higher and lower social groups is perhaps greater for chronic obstructive pulmonary disease than for any other disease.<sup>5</sup> The number of undiagnosed people with the condition in the United Kingdom is unknown, but in the United States one estimate is that only 14-46% of all cases are diagnosed.<sup>7</sup> Chronic obstructive pulmonary disease is underdiagnosed partly because many people do not consult their general practitioners or do not reveal all their symptoms unless specifically asked.<sup>8</sup> Patients often regard their symptoms as a result of age or lack of fitness and do not seek treatment, or they perceive treatment to be ineffective. Surprisingly, people with undiagnosed disease do not necessarily have less severe symptoms than those whose disease has been diagnosed.<sup>5</sup>

The main advantage of early diagnosis is that patients may be persuaded to stop smoking. One study found that respiratory function, as measured by FEV<sub>1</sub>, in people with for chronic obstructive pulmonary

BMJ 2003;326:1046-7