Myocardial perfusion scintigraphy for angina and myocardial infarction

Systematic review of the effectiveness and cost-effectiveness, and economic evaluation, of myocardial perfusion scintigraphy for the diagnosis and management of angina and myocardial infarction

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Executive summary

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Executive summary

Epidemiology and background

Coronary heart disease (CHD), secondary to coronary artery disease (CAD), is the most common cause of death in the UK, resulting in over 120,000 deaths in 2001. Prevalence, which varies across the UK, increases with age; it is estimated that around 2.65 million people in the UK have CHD. Over 378,000 people received inpatient treatment for CHD in NHS hospitals in 2000–01, representing 5% of all inpatient cases in men and 2% in women.

Methods of detecting the presence and assessing the extent of CAD have become increasingly important in informing therapies aimed at reducing mortality and morbidity. Coronary angiography (CA) is considered to be the 'gold standard' for defining the site and severity of coronary artery lesions. CA carries a small (<0.1%) risk of mortality and routine use is inadvisable. Stress (usually treadmill or bicycle exercise) electrocardiography (ECG) is widely used for non-invasive detection of CAD owing to its availability and low cost.

Myocardial perfusion scintigraphy (MPS) may be added to the diagnostic pathway to improve detection of CAD. MPS involves the injection of a radioactive tracer followed by the imaging of its distribution within the myocardium using a gamma camera. Single photon emission computed tomography (SPECT) MPS allows the creation of tomographic images. The images following stress and at rest are compared to assess whether defects are reversible (ischaemia) or fixed (infarction) and to allow the site, extent and depth of abnormalities to be determined. This review assesses the effectiveness and cost-effectiveness of SPECT MPS for the diagnosis and management of angina and myocardial infarction (MI).

Methods

Electronic searches were conducted to identify published and unpublished studies. The following databases were searched: MEDLINE (1966 to October 2002), EMBASE (1980 to week 44, 2002), PREMEDLINE (5 November 2002), BIOSIS (1985 to December 2002), Science Citation Index (1981 to December 2002), The Cochrane Library (Issue 3, 2002), Health Management Information Consortium (1979 to 2002), Health Technology Assessment Database (October 2002) and NHS Economic Evaluation Database (October 2002). Two reviewers independently extracted data and assessed study quality.

A decision tree model (DTM) was used to model the diagnosis decision and a simple Markov model was developed for the management of patients with suspected CAD. The strategies considered in the models were (a) stress ECG, followed by SPECT if stress ECG positive, followed by CA if SPECT positive; (b) stress ECG, followed by CA if stress ECG positive; (c) SPECT, followed by CA if SPECT positive; and (d) CA (invasive test as first option).

Costs for the treatments and interventions within strategies were derived from the literature and expressed in 2001–02 pounds sterling. Quality-adjusted life-year (QALY) weights for the different Markov model states were also obtained from the literature.

Number and quality of studies and direction of evidence

Twenty-one diagnostic and 46 prognostic studies were included plus two studies comparing SPECT with ECG-gated SPECT and one study comparing SPECT with attenuation-corrected SPECT. The quality of the diagnostic studies was assessed using the quality assessment of diagnostic accuracy studies (QUADAS) tool developed by the NHS Centre for Reviews and Dissemination. Most studies gave clearly described selection criteria. In 13 studies the spectrum of patients was not considered to be representative of those who would receive the test in practice. Eight studies described the index test (SPECT) and 12 described the reference standard (CA) sufficiently to permit its replication. In 14 studies the index test was interpreted without knowledge of the reference standard, whereas in nine studies the reference standard was interpreted without knowledge of the index test. It was unclear from 16 studies whether the same clinical

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data were available when test results were interpreted as would be available were the test to be used in practice. The diagnostic values of SPECT were generally higher than those of stress ECG, indicating that SPECT provided a better diagnostic performance.

The prognostic studies were all observational studies and were assessed using a checklist designed to assess the methodological quality of both randomised and non-randomised studies. The overall mean score for the prognostic studies was 18.1 (out of a possible 27). The external validity of the studies was low. The evidence from the prognostic studies suggested that SPECT provided valuable independent and incremental information to that provided by stress ECG and/or CA.

Summary of benefits

Of 21 diagnostic studies, 16 included patients referred for suspected or known CAD, three evaluated patients following percutaneous transluminal coronary angioplasty (PTCA), one focused on patients suspected of asymptomatic coronary disease and one evaluated patients with left bundle branch block (LBBB). Among the largest subset of studies (those assessing patients with a suspicion or a history of CAD), sensitivity values tended to be higher for SPECT than for stress ECG whereas specificity values were similar. SPECT also provided higher positive and lower negative likelihood ratios than stress ECG but heterogeneity was evident amongst studies. The subgroup of studies including patients with previous MI tended to report a better diagnostic performance for SPECT than stress ECG, but there were too few studies to assess this reliably.

Twenty-one of the 46 prognostic studies provided general prognostic information. Important factors for predicting cardiac events included the extent and size of the perfusion defect and whether it was fixed or reversible. Normal SPECT scans were associated with a benign prognosis and the option of medical rather than invasive management. Two studies comparing different testing strategies found that a strategy incorporating SPECT with selective referral to CA resulted in lower rates of normal angiograms compared with a strategy of direct referral to CA, suggesting that SPECT was better able to identify lower risk patients for whom CA might be avoided.

The remaining prognostic studies examined the use of SPECT in different patient populations. Studies in relation to gender reported that SPECT provided important, independent prediction of survival in both men and women. Studies performed in patients following MI, and after PTCA and CABG, found that SPECT imaging provided important information for predicting future cardiac events.

Two studies, one diagnostic and the other prognostic, comparing SPECT with ECG-gated SPECT, found in favour of gated SPECT. One study comparing SPECT with attenuation-corrected SPECT reported the latter to be more accurate. Although these findings seem promising it is difficult to draw conclusions from so few studies.

Costs

For the base-case analysis, the results for costs and QALYs for the different strategies were: strategy (a) cost of £5190 and yielding 12.473 QALYs; strategy (b) £5395, 12.481 QALYs; strategy (c) £5529, 12.497 QALYs; and strategy (d) £5929, 12.506 QALYs.

Cost/QALY

The systematic review of economic evaluations indicated that strategies involving SPECT were likely either to be dominant or to produce more QALYs at an acceptable cost. There was less agreement, however, about which of the strategies involving SPECT was optimal.

At the baseline prevalence of 10.5%, SPECT–CA was cost-effective whereas CA, although generating more QALYs, did so at a relatively high incremental cost per QALY (£42,225). At 30% prevalence rates, whereas SPECT–CA was cost-effective, the CA strategy produced more QALYs at a relatively low incremental cost-effectiveness ratio (£7331). At higher prevalence rates (50 and 85%), the SPECT–CA strategy was extendedly dominated by the stress ECG–CA and CA strategies. In other words, over a defined range, if some patients received stress ECG–CA with the rest receiving CA, the costs would be lower and the QALYs higher than if SPECT–CA alone was used.

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Sensitivity analyses

The model suggested that, for low prevalence, the incremental cost per unit of output (true positives diagnosed, accurate diagnosis, QALY) for the move from stress ECG–SPECT–CA and from stress ECG–CA to SPECT–CA might be considered worthwhile. Even after allowing for different values for sensitivity or specificity, the least costly and least effective strategy was stress ECG–SPECT–CA. The sensitivity analysis suggested that the cost-effectiveness of SPECT–CA improved if it was assumed that SPECT results allowed for the adoption of a management strategy without recourse to CA. This would be the case if the assumption of perfect information from CA (sensitivity and specificity equal to 1) were relaxed.

Limitations of the calculations (assumptions made)

Linking diagnostic performance to long-term outcomes required a number of assumptions to be made about both the structure of the model and its parameters. Some assumptions were based on non-UK study data; it is unclear whether such data are applicable to a UK setting. Another assumption concerned the length of time over which the benefits from a diagnostic strategy might accrue. In the base-case analysis, a time period of 25 years was used, although the impact of shorter time horizons was explored in sensitivity analysis. As the time horizon reduced, the incremental cost per QALY increased (as the cost of initial diagnosis and treatment were not offset by survival and quality of life gains).

Other important issues regarding implications

Relatively poor data were available with which to consider longer term costs and consequences. The non-UK data used may not apply to a UK setting.

Notes on the generalisability of the findings

There was a considerable variability in terms of measurement of outcomes, management, setting and patient characteristics. Despite these differences the direction of evidence tended to favour SPECT in terms of test sensitivity, although these conclusions are based on a relatively small number of included studies.

All of the prognostic studies were observational studies and may be biased by unknown confounding factors. Thirty-four of the prognostic studies took place in North America and 12 were set in Europe. SPECT, in a variety of settings and patient populations, provided valuable independent and incremental information to that provided by stress ECG and/or CA. These results may not be generalisable to the UK as many studies were undertaken in countries with different healthcare systems to that of the UK.

Need for further research

Further research is needed on the effectiveness and cost-effectiveness, diagnostically and prognostically, of (a) gated and attenuation-corrected SPECT compared with standard SPECT, (b) standard SPECT compared with stress echocardiography and (c) the uncertainty surrounding the results presented in the cost-effectiveness analysis.

Publication

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