A randomized trial of exercise treadmill ECG versus stress SPECT myocardial perfusion imaging as an initial diagnostic strategy in stable patients with chest pain and suspected CAD: cost analysis

Sabharwal N K, Stoykova B, Taneja A K, Lahiri A

Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The authors compared exercise electrocardiography (ETT) and single-photon emission computed tomography (SPECT) myocardial perfusion imaging (MPI). ETT comprised a symptom-limited Bruce or modified Bruce protocol exercise treadmill test undertaken using a Marquette CASE 8000 system (Marquette, Milwaukee, WI). MPI patients underwent stress testing with exercise and/or dipyridamole infusion (Boehringer Ingelheim, Barcelona), followed by electrocardiography-gated technetium 99m SPECT imaging.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients referred to a chest pain clinic with stable chest pain and suspected CAD. Patients were included if they were older than 25 years and had chest pain suspicious of CAD. Patients were excluded if they had coronary syndromes or known CAD, or were pregnant or lactating women.

Setting
The setting was an outpatient clinic. The economic study was carried out in London, UK.

Dates to which data relate
The effectiveness and resource use data were collected between February 2001 and July 2002. The price year was 2002/03.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.

Study sample
The study sample was selected by including patients referred to the chest pain clinic. It comprised 457 patients who provided consent. The mean age of these patients was 59.3 years and 56% were men. Of the 457 consenting patients 207 (57.5% male) were diagnosed using ETT and 250 (55.6% male) were diagnosed using MPI. Those diagnosed using ETT had a mean age of 58.9 years, whilst those diagnosed using MPI had a mean age of 59.7 years.
Study design
This was a prospective randomised controlled trial based at a single clinic. Patients were allocated to the two study groups using computer-generated randomisation. It was not possible to blind the patients given the nature of the diagnosis. The patients were followed for 2 years, with postal questionnaires every 6 months and telephone follow-up in the event that the postal questionnaire was not returned. Where no data were available, hospital records were checked and the patient’s primary care physician was contacted. Three patients in the ETT groups did not undergo a treadmill test for varying reasons.

Analysis of effectiveness
Members of the two groups were compared extensively at analysis in terms of the demographical and clinical variables. The authors did not note any significant differences, except in the exercise characteristics of the patients when separated according to treadmill results. The patients were analysed on an intention to test basis. The primary outcomes of the study were the post-test likelihoods of CAD, the proportion of patients referred for further imaging (specifically coronary angiography), and the proportion of patients subsequently referred for revascularisation as a function of the number of angiograms obtained (i.e. the sensitivity of the two diagnostic tests).

Effectiveness results
Both ETT and MPI created a statistically significant difference in the pre- and post-test likelihoods of CAD, (p=0.0002 for ETT and p<0.0001 for MPI).

The proportion of patients referred for further imaging was 71% in the ETT arm and 16% in the MPI arm. The difference was statistically significant, (p<0.0001).

The proportion of patients referred for coronary angiography was 47% in the ETT arm and 16% in the MPI arm. The difference was statistically significant, (p<0.0001).

The proportion of patients subsequently referred for revascularisation as a function of the number of angiograms obtained was 38% (37 out of 98) in the ETT arm and 66% (27 out of 41) in the MPI arm. The difference was statistically significant, (p<0.0001).

Clinical conclusions
The authors concluded that MPI was a better discriminatory test for the diagnosis of CAD compared with ETT, although ETT would be equally good for patients with a low pre-test likelihood.

Measure of benefits used in the economic analysis
The authors did not estimate a summary measure of health benefit. The study was, in effect, a cost-consequences analysis.

Direct costs
The costing analysis was carried out from the perspective of the NHS. It therefore included staff, diagnostic test and capital-related costs. The authors considered costs to the point of diagnosis. The costs of the diagnostic test covered staff (medical and clerical), equipment (charge per person) and overhead charges (room rental and utility costs). The resource use data were collected prospectively for all patients, while the unit costs were obtained from the finance department of the relevant institution. The price year was 2002/03. Study-based costs were compared with a published technology assessment report by NICE.

Statistical analysis of costs
Continuous data were reported as means with standard deviations. Comparative testing was performed used the Mann-Whitney U test. The test results were considered to be statistically significant if the p-value was less than 0.05.
Indirect Costs
Productivity costs were not relevant to the perspective adopted. The authors explicitly noted that for this reason they were not included in the study.

Currency
UK pounds sterling ( ).

Sensitivity analysis
The authors did not explore the impact of uncertainty on the results.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The mean cost per patient was 459.83 in the ETT group and 507.36 in the MPI group, (p=0.062).

When the patients were analysed according to the pre-test likelihood of CAD, ETT was significantly less expensive for patients assessed as low risk, (p<0.001), although there was no significant difference in cost for medium- and high-risk patients.

Synthesis of costs and benefits
Not relevant as the study was, in effect, a cost-consequences analysis.

Authors' conclusions
Exercise electrocardiography (ETT) was "the preferred investigation from a diagnostic and cost point of view in patients with a low pre-test likelihood of coronary artery disease (CAD)". Myocardial perfusion imaging (MPI) was no different in cost for intermediate and high pre-test likelihood of CAD patients, and was a better discriminatory test.

CRD COMMENTARY - Selection of comparators
The authors compared ETT and MPI as alternative methods for the diagnosis of CAD. ETT was justified as being the most commonly used investigative technique, while the potential benefits of MPI were discussed. Although coronary angiography was implicitly used as the 'gold' standard comparator, the authors could have made the status of this comparator clearer from the outset. Readers should assess the most commonly used investigations in their own setting.

Validity of estimate of measure of effectiveness
The authors designed a randomised controlled trial. Such a design, if conducted well, provides good internal validity by removing the possibility of systematic differences between patients in the two study groups. This was shown by the lack of statistically significant differences at baseline. The authors stated that blinding was not possible. The study sample was a true reflection of the study population. The duration of the study was adequate in terms of establishing diagnostic accuracy, although the authors may wish to follow this up with a longer time horizon study that explores the broader costs and benefits of improved diagnosis. The authors acknowledged that they could have tested all patients with coronary angiography and estimated the rate of true-negative diagnoses, and discussed the reasons why they did not pursue this course.

Validity of estimate of measure of benefit
The authors did not estimate a summary measure of health benefit and the study was, in effect, a cost-consequences analysis. However, the authors could have estimated the number of tests required to obtain a correct (true-positive) diagnosis.

Validity of estimate of costs
The costing analysis, which was carried out from the perspective of the NHS, focused on the costs of diagnosis. Given the diagnostic nature of the study and the time horizon considered, this perspective and focus was appropriate. However, further analysis should explore whether fewer angiograms are required because of other, more accurate testing procedures and the longer term costs and benefits of such an implication. The authors considered these costs difficult to obtain. The costs included were relevant to the perspective, although changes in perspective might have affected the principal results and conclusions given the overall lack of statistical significance. The analysis was well reported and easy to understand, and provided details of the price year and the sources of the unit costs and resource use data. However, as the analysis extended over one year, the costs should have been discounted to reflect time preferences.

Other issues
Comparisons were made, particularly with the unit cost results of an analysis commissioned by NICE, and similarities and differences were discussed. The broader results of the study were also compared and found to "concur" or be "consistent" with existing published results. The issue of generalisability was not discussed and will be limited by the use of setting specific resource use and unit costs. Sensitivity analyses around the cost inputs would have improved generalisability. The authors presented the results clearly and in full. The results related well to the objectives of the study and the conclusions were an accurate reflection of the results presented.

The authors discussed several limitations to their study. These included the low cardiac event rate, the difference in patient numbers allocated to each arm, and the inability to blind and the potential investigation bias that this created. A further limitation was the fact that not all patients underwent coronary angiography, which might have been considered the 'gold' standard diagnostic test.

Implications of the study
The authors did not make any recommendations for policy or practice following on from their study. Studies with larger populations or longer follow-up are suggested as ways to overcome the low cardiac event rate that might be used in future.

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Other publications of related interest
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