Cost-effectiveness and accuracy of exercise stress echocardiography in the non-invasive diagnosis of coronary heart disease
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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 health technology intervention studied was exercise stress echocardiography (ESE) (which is a more recent form of totally non-invasive stress testing) in a cohort of patients referred for exercise thallium SPECT scintigraphy (ETS) imaging for the assessment of existing or suspected coronary artery disease (CAD).

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised of patients referred for exercise thallium SPECT scintigraphy (ETS) imaging for the assessment of existing or suspected coronary artery disease (CAD). Patients not achieving 85% of maximum predicted heart rate in the absence of chest pain, severe dyspnoea or significant exercise induced ECG change, were excluded from the study.

Setting
The study setting was hospital. The economic analysis was carried out in Australia.

Dates to which data relate
No dates were reported.

Source of effectiveness data
The evidence for the final outcomes was based on a single study.

Link between effectiveness and cost data
Costing appears to have been conducted retrospectively on the same patient sample as that used in the effectiveness analysis.

Study sample
Power calculations were not used to determine the sample size. The study sample was derived from 115 patients referred for ETS for the assessment of existing or suspected CAD, who consented to simultaneous ESE. Of this sample, a group of 59 patients (50 males and nine females with a mean (SD) age of 61.0 (10.4) years), underwent coronary angiography on the basis of the results of the ETS or the referring physician's clinical assessment independent of the
ESE findings.

Study design
This was a non-randomised study with self-controls, carried out in a single centre. The duration of the follow-up appears to have been until the establishment of the diagnosis. No information was given regarding loss to follow-up; except for 56 patients who did not undergo coronary angiography. All patients underwent symptom limited maximal treadmill exercise using the Bruce protocol with continuous 12-lead ECG monitoring. Two-Dimensional echocardiography was performed in the left lateral recumbent position with the use of a phased array sector scanner. Patients were imaged just prior to exercise and again immediately post-exercise with the post-exercise imaging always being completed within two minutes. The analysis was performed blinded to the clinical, EGG, ETS and coronary angiographic findings. Images were interpreted in accordance with the standard 16 segment model of the left ventricle. Coronary angiography was performed using the Judkins technique. All films were analysed by experienced cardiac radiologists, independent of clinical history and the stress test findings (EGG, ESE or ETS). Perfusion scintigraphy was interpreted 'blinded' of the clinical, EGG and ESE findings of the patient. A qualitative comparison between stress and rest images was made using segmentation parallel to that employed for ESE with grouping of the left ventricular (LV) walls into vascular regions.

Analysis of effectiveness
The principle (intention to treat or treatment completers only) used in the analysis of effectiveness was not explicitly specified. The clinical outcome measures were sensitivity, specificity and accuracy of ESE and ETS for the diagnosis of CAD (greater than 50% luminal diameter stenosis) using coronary angiography as the gold standard. Feasibility rate (defined as the echocardiographic images being of suitable quality) and prevalence and distribution of CAD were also reported. Agreement between modalities was assessed using inter-rater agreement and expressed as kappa (k).

Effectiveness results
The effectiveness results were as follows:

The feasibility of ESE was 97% (112 out of 115 patients of the total study population and 57 of the 59 patients who underwent coronary angiography).

Of the 59 patients undergoing coronary angiography, the sensitivity of ESE and ETS were not significantly different (84.1% compared to 91.3% respectively).

However, despite the apparent marked difference in specificity (92.3% compared to 61.5% respectively), the p value was non-significant, as there were only 13 normals in the group who underwent coronary angiography.

Overall accuracy was also similar (86.0% compared to 84.7% respectively) and therefore not significantly different.

By contrast, agreement with coronary angiography as measured by the kappa statistic (k +/- SEk) was good for ESE (0.66 +/- 0.11) but only moderate for ETS (0.54 +/- 0.13).

The distribution pattern of disease at coronary angiography revealed 24 patients (40.6%) with single vessel disease (SVD), 16 patients (27.1%) with double vessel disease, six patients (10.2%) with triple vessel disease and 13 normals (22.0%).

Therefore, 46 of the 59 patients had significant CAD resulting in a disease prevalence of 78.0%.

Clinical conclusions
The study findings of an overall sensitivity of 84.1% and specificity of 92.3% pertaining to ESE are in keeping with and mirror the average sensitivity and specificity of most of the previous internationally published studies. This same patient comparative study of ESE and ETS has not revealed any statistically significant differences in sensitivity or specificity, although there was a trend to lower specificity by ETS.
Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only separate clinical outcomes were reported. It appears that the economic study was reduced in scope to a cost-minimisation analysis, as there were no statistically significant differences between the two imaging modalities in terms of sensitivity, specificity, and accuracy.

Direct costs
Costs were not discounted due to the short time horizon of the cost analysis. Some resource use quantities were reported separately from the costs and cost items were reported separately. The cost analysis covered the costs of ESE (the combined cost of a stress ECG and an exercise stress echocardiogram), ETS (the sum of ECG and a exercise thallium SPECT scintigraphy), and induced costs due to the feasibility of stress echocardiography not being 100% and a specificity difference. The major components of induced costs were the cost of coronary angiography, theatre fee, and a one-day bed fee. The perspective adopted in the cost analysis was not specified. The price year was not given.

Indirect Costs
Indirect costs were not included.

Currency
The currency appears to have been Australian dollars (Aus$). The conversion rate to any other widely used currency was not reported.

Sensitivity analysis
No sensitivity analysis was carried out.

Estimated benefits used in the economic analysis
See the effectiveness results reported above.

Cost results
The total cost for the study cohort was Aus$63,103 for ETS and Aus$28,025 for ESE. There was a cost saving of at least Aus$594.00 per patient in favour of ESE.

Synthesis of costs and benefits
Costs and benefits were not combined since the economic study appears to have proceeded on a cost-minimisation basis.

Authors' conclusions
ESE is a totally non-invasive, sensitive, specific and cost-effective imaging modality for the detection and localisation of CAD.

CRD COMMENTARY - Selection of comparators
No justification appears to have been given for the choice of the comparator. It was only reported that both ESE and ETS were developed to overcome the known limitations of ECG stress testing, namely the limited diagnostic accuracy and the inability of ECG stress testing to site the region of CAD induced ischaemia. You, as a database user, should consider whether this is a widely used health technology in your own setting.
Validity of estimate of measure of effectiveness
The use of patients as their own controls enhances the validity of the results. However, the internal validity of the effectiveness results is hindered by the relatively small sample size, and the possibility of some degree of selection bias in the study cohort, given that patients analysed were those referred for ETS who consented to simultaneous ESE, as acknowledged by the authors. Furthermore, using coronary angiography with its own limitations as the gold standard may further undermine the internal validity of the effectiveness results.

Validity of estimate of measure of benefit
The analysis of benefits appears to have been based upon the therapeutic equivalence of treatment alternatives. The economic analysis therefore included only costs. The authors claimed that they did not consider quality adjusted life years as the benefit measure as this criterion, according to the authors, is imperfect and involves many assumptions.

Validity of estimate of costs
Some details of the methods of cost estimation were given. However, the price year and the perspective adopted in the cost analysis were not specified; the resource use profile was not fully reported; the effects of alternative procedures on indirect costs were not addressed but may be relevant over the longer term; statistical analyses were not performed on resource use or cost data; and cost results may not be generalisable outside the study setting.

Other issues
Given the limitations of the study design, and the lack of sensitivity analysis and statistical analysis of the costs, some degree of caution may need to be exercised in interpreting the study results. The issue of generalisability to other settings or countries was not addressed, although appropriate comparisons were made with other studies. The degree to which the study sample was representative of the study population was discussed in the authors’ comments. They do mention that one of the inevitable consequences of the design adopted in this study was that the prevalence of CAD was high and considerably higher than the prevalence of CAD in populations referred for basic evaluation with a routine treadmill or bicycle ECG stress test. It was also mentioned that the echocardiographic ultrasound scanners used in the present study were devoid of harmonic imaging; therefore, it is possible that the sensitivity of ESE may be improved further with this facility.

Implications of the study
The authors suggested that the advent of harmonic imaging to ESE, like the advent of SPECT to planar nuclear imaging, demonstrate how both modalities continue to undergo evolution and improvement. Therefore, direct comparisons of accuracy of the two modalities at any point in time may, to some extent, be arbitrary.

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