Clinical and economic impact of exercise electrocardiography and exercise echocardiography in clinical practice

Marwick T H, Shaw L, Case C, Vasey C, Thomas J D

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 technologies studied were:

- exercise electrocardiogram (ExECG), whereby patients underwent maximum symptom-limited tests using treadmill protocols while constantly being monitored clinically and with the ECG; and

- exercise echocardiography (ExEcho), whereby echocardiography was performed at rest and immediately post-exercise, with images in the same planes being compared side by side.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with suspected or known CAD.

Setting
The practice setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The authors did not state when the clinical study was carried out. All the costs included in the study were reported in year 2000 prices.

Source of effectiveness data
The evidence for the final outcomes was derived from a single study.

Link between effectiveness and cost data
The costing was undertaken prospectively on the same patient sample as that used in the effectiveness study.

Study sample
No sample size was determined in the planning phase of the study. In addition, no power calculations were performed retrospectively. Patients referred to a large cardiology department with suspected or known CAD were subsequently referred for an evaluation of chest pain symptoms using ExEcho (n=3,860) or ExECG (n=3,796).
Study design
The study was a prospective cohort study, which was carried out in a single large cardiology department at a cardiac referral centre in the USA. All of the patients were followed for the occurrence and date of major adverse events, including all-cause and ischaemic heart disease deaths, MI and the occurrence of percutaneous coronary intervention (PCI) or coronary artery bypass surgery (CABG). The follow-up data were gathered by clinic review or telephone contact with the patient or physician after 2.5 (+/- 2.0) years (range: 0.5 - 5) in the ExECG group and after 3.2 (+/- 2) years (range: 0.5 - 5) in the ExEcho group. The authors quoted no loss to follow-up.

Analysis of effectiveness
All the patients appear to have been accounted for in the analysis. The primary health outcomes were:

the exercise test results, which included exercise time, exertional chest pain, ST depression, resting left ventricular function and ischaemia extent for the ExEcho group, and exercise time, exertional chest pain (non/limiting), ST depression and Duke treadmill score for the ExECG group; and

the management decision outcomes of patients with or without CAD based on their post-test assessment of ischaemic risk, which included catheterisation, revascularisation, PCI and CABG.

In the ExECG group, the presence and severity of angina, ST segment change and the exercise capacity were used to calculate the Duke treadmill score in all patients. In the ExEcho group, the extent of abnormal wall motion was the basis for evaluating left ventricular function as normal, mild, moderate or severely reduced.

The groups were shown to be comparable apart from a slightly lower average age in those undergoing ExEcho (61 versus 63 years, p<0.001). Approximately 40% of the study sample were women (40% in the ExEcho group and 42% in the ExECG group). Both groups showed a similar prevalence of low risk (11% versus 12%), intermediate risk (58% versus 60%) and high risk (30% versus 28%). The two groups were also shown to be comparable in terms of the presence of cardiac risk factors, and prior history of coronary disease. A propensity score, used as a summary measure of probability of referral to coronary angiography and other procedures, was used to control for referral bias in analysing the clinical outcomes for the groups.

Effectiveness results
The procedure utilisation rates were as follows.

In a risk-adjusted comparison for cardiac catheterisation rates (i.e. adjusting for pre-test clinical risk and including a propensity score), 12% of patients without exertional ischaemia on ExEcho had angiography performed during follow-up. This rate increased to 51% in those with 2 to 3 vascular territories with ischaemia, (p<0.0001).

However, this same linear increase in angiography was not observed in those undergoing ExECG.

Forty-five per cent of the patients with a low-risk treadmill score were referred to angiography during follow-up. The vast majority of them had a prior history of CAD, with catheterisation more often performed more than 90 days after testing. Consequently, coronary revascularisation occurred in 35% of the patients with established CAD who did not have inducible ischaemia during ECG.

A proportional relationship existed between the rates of revascularisation and the extent of ischaemia for both ExEcho and ExECG, (p<0.0001). However, revascularisation, PCI and CABG were more frequently performed in CAD patients without inducible ischaemia during ExECG, and in high-risk patients undergoing ExEcho. All of these differences were statistically significant.

Clinical conclusions
The angiography and revascularisation rates with ExEcho in this study showed referral rates significantly increasing with worsening scan results. In contrast, the responses to ExECG demonstrated little difference in the intervention with
increasing risk. The authors believed this reflected the preponderant use of the ST segment results and, therefore, a binary response to positive or negative studies.

Modelling
Cox proportional hazards models were used to derive the predicted probability of cardiac death or myocardial infarction (MI), in order to obtain the pre-test clinical risk with the intention of adjusting accordingly for clinical outcomes, the ExEcho extent of ischaemia, and the low/intermediate/high risk Duke treadmill score. A stratified Cox model was employed to assess the relative changes in event-free survival for intermediate to high-risk patients undergoing revascularisation. A decision analytic model was used to determine the clinical outcome and economic data of ExEcho and ExECG, using Treeage (version 2.6) and Answer Tree (version 3.1) software.

Measure of benefits used in the economic analysis
The measure of health benefit used in the economic analysis was the life-years saved (LYS).

Direct costs
The resource quantities and the costs were not reported separately. The direct costs included in the analysis were those of the health service. These were for diagnosis (including both initial testing and diagnostic angiography) and follow-up (including coronary revascularisation procedures and cardiac-related hospitalisations). Standard cost estimations were calculated using a median of charges that were adjusted by a national median cost-charge ratio, and available cost data from published articles. Discounting was necessary, as all the costs were incurred during 3 years, and was carried out at a rate of 5%. All the costs were inflation corrected to year 2000.

Statistical analysis of costs
The total costs were treated as point estimates (i.e. the data were deterministic). A multivariate linear regression analysis was carried out to determine the predicted costs of care, which were risk adjusted by the pre-test likelihood of CAD and noninvasive test results.

Indirect Costs
The societal economic cost for cardiac death was based on cost estimates derived from American Heart Association data (see [http://www.americanheart.org/statistics/economic.html](http://www.americanheart.org/statistics/economic.html) for details).

Currency
The authors reported their results in Euros (Euro). However, the original cost data were obtained in US dollars ($) and expressed in Euros at an exchange rate of 1.00.

Sensitivity analysis
No sensitivity analyses were performed.

Estimated benefits used in the economic analysis
There were 89,459 LYS in the ExEcho group versus 88,464 LYS in ExECG group.

Cost results
The discounted lifetime costs were Euro 17,419,657 for the ExEcho group and Euro 16,842,611 for the ExECG group. This resulted in an incremental cost of Euro 2,603,141.
### Synthesis of costs and benefits

The estimated costs and benefits were combined as the costs per LYS. The authors performed an incremental analysis, which resulted in an incremental cost-effectiveness ratio of Euro 2,615/LYS when ExEcho was compared with ExECG. The results of the multivariate regression analysis revealed an incremental cost-effectiveness ratio of Euro 3,903/LYS for ExEcho, compared with ExECG, in patients with established disease.

### Authors' conclusions

Exercise echocardiography (ExEcho) has been shown to be a more cost-efficient approach in the evaluation of patients with known or suspected coronary artery disease (CAD).

### CRD COMMENTARY - Selection of comparators

A justification was given for using ExECG as the comparator. AHA/ACC guidelines recommended using ExECG as the first test for the evaluation of known or suspected coronary disease. You should decide if this is a widely used health technology in your own setting.

### Validity of estimate of measure of effectiveness

Even though a randomised controlled trial would have been more appropriate, as it is the 'gold' standard study design when comparing health technologies with less potential of confounding or bias affecting the results, the prospective cohort study design was still appropriate and valid. Both study groups were large and were shown to be comparable at analysis, apart from a slightly lower average age in those undergoing ExEcho (less than two years difference between the two groups). Propensity scores were used as summary measures of the probability of referral to various procedures post-test in an attempt to control for referral bias. Further, the study sample was representative of the study population since it included patients with known or suspected CAD. The analysis of effectiveness was handled credibly. Continuous variables were compared using t-tests at analysis and analysis of variance, while categorical variables were compared by chi-squared analysis.

### Validity of estimate of measure of benefit

The estimation of health benefits, in this case the LYS, was modelled. The authors provided little information on the decision analytic model used to determine the LYS. However, the sound methodology used in the effectiveness study would suggest that the health benefits derived had high validity. The health benefits were also appropriately discounted at a rate of 5%.

### Validity of estimate of costs

All the categories of cost (both direct and indirect) that were relevant to the societal perspective adopted were included in the analysis. However, it would also have been desirable for the authors to have summarised the information on the indirect costs derived from the American Heart Foundation website. For each category of cost, all the relevant costs were included in the analysis. The costs and the quantities were not reported separately, which will hamper the generalisability of the authors' results to other settings. The cost estimations were calculated using a median of charges, with charges being used to proxy prices, as well as published cost data. Appropriate statistical analyses, in the form of linear regression techniques, were used to calculate the predicted costs controlling for pre-test clinical risk and prior history of CAD. The authors clearly stated the exchange rate used to convert from US dollars to Euros. Since the costs were incurred over the patients’ lifetime, discounting was necessary and was performed. The price year was reported, which facilitates any possible reflation exercises.

### Other issues

The authors compared the results from their study with others. In particular, they found that a similar study suggested that for patients at intermediate probability of CAD, ExEcho showed an incremental cost-effectiveness of Euro 41,900 per quality-adjusted life-year saved in comparison with ExECG. However, the authors pointed out that these studies focused on the diagnostic strength of the tests rather than greater accuracy. The authors addressed the issue of
generalisability to other settings. Even though they stated that costings varied across the world, the authors suggested that similar ratios between the two tests would hold in other environments, and the main conclusions of their study would still hold.

The authors do not appear to have presented their results selectively. However, a more detailed explanation of the decision model would have been desirable. The authors’ conclusions reflected the scope of the analysis. The authors reported a further limitation of their study, in that different treatment strategies might be associated with differences in quality of life, which could perhaps justify differences in the costs. As the authors did not use quality of life as a health benefit, these issues could not be addressed.

Implications of the study
Even though the authors did not give any explicit implication of their findings, based on their results and conclusion, it is possible to infer a recommendation of diagnosing patients with known or suggested CAD with ExEcho in preference to ExECG.

Source of funding
Supported in part by the American Society of Echocardiography and the National Heart Foundation of Australia.

Bibliographic details

PubMedID
12804930

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Coronary Artery Disease /diagnosis /economics; Cost-Benefit Analysis; Echocardiography /economics; Electrocardiography /economics; Exercise Test /economics /methods; Female; Follow-Up Studies; Humans; Male; Middle Aged; Prognosis; Risk Assessment

AccessionNumber
22003000960