Cost-effectiveness of functional cardiac testing in the diagnosis and management of coronary artery disease: a randomised controlled trial. The CECaT trial

L Sharples,1* V Hughes,2 A Crean,3 M Dyer,4 M Buxton,4 K Goldsmith1 and D Stone5

1 MRC Biostatistics Unit, Cambridge, UK
2 R&D Unit, Papworth Hospital, Cambridge, UK
3 Academic Unit of Cardiovascular Medicine, Leeds General Infirmary, UK
4 Health Economic Research Group, Brunel University, Uxbridge, UK
5 Cardiac Unit, Papworth Hospital, Cambridge, UK

* Corresponding author

Executive summary

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Objectives

The objectives of this trial were to assess the following:

- acceptability and feasibility of functional tests as a gateway to angiography for the management of coronary artery disease (CAD)
- ability of diagnostic strategies to identify patients who should undergo revascularisation
- patient outcomes in each diagnostic strategy
- the most cost-effective diagnostic strategy for patients with suspected or known CAD.

Setting

The setting was Papworth Hospital NHS Foundation Trust, a tertiary cardiothoracic referral centre.

Participants

The trial participants were patients with suspected or known CAD and an exercise test result that required non-urgent angiography.

Exclusion criteria were: recent myocardial infarction or revascularisation, admission with chest pain; urgent revascularisation; contraindication to pharmacological stress testing on magnetic resonance imaging (MRI); incapable of performing modified Bruce exercise test; not available by telephone.

Interventions

Patients were randomised to one of four initial diagnostic tests: angiography (controls); single photon emission computed tomography (SPECT); MRI; stress echocardiography.

Main outcome measurements

The main outcome measurements were as follows:

- Primary: at 18 months post-randomisation: exercise time (modified Bruce protocol); cost-effectiveness compared with angiography (diagnosis, treatment and follow-up costs). The aim was to demonstrate equivalence in exercise time between those randomised to functional tests and those randomised to angiography [defined as the confidence interval (CI) for mean difference from angiography within 1 minute].
- Secondary: exercise time at 6 months post-treatment; successful completion of initial diagnostic test; Canadian Cardiovascular Society (CCS) classification of angina; health-related quality of life (HRQoL) measured by the Seattle Angina Questionnaire, the Short Form with 36 Items and the EuroQoL; revascularisation rate; adverse events; clinician confidence in test results.

Results

Between September 2001 and September 2004, 898 patients were randomised to angiography ($n = 222$), SPECT ($n = 224$), MRI ($n = 226$) or stress echo ($n = 226$). There were no significant differences between the groups at baseline. At 18 months, compliance was 86% for the full protocol and 94% for cost-effectiveness data.

Initial diagnostic tests were completed successfully with unequivocal results for 98% of angiography, 94% of SPECT ($p = 0.05$), 78% of MRI ($p < 0.001$) and 90% of stress echocardiography patients ($p < 0.001$).

Some 22% of SPECT patients, 20% of MRI patients and 25% of stress echo patients were not subsequently referred for an angiogram. Positive functional tests were confirmed by positive angiography in 83% of SPECT patients, 89% of MRI patients and 84% of stress echo patients.

Positive functional tests were confirmed by positive angiograms in 31% of SPECT patients, 52% of MRI patients and 48% of stress echo patients tested.

The proportions who had coronary artery bypass graft (CABG) surgery were 10% (angiography), 11% (MRI) and 13% (SPECT and stress echo) and percutaneous coronary intervention (PCI) 25% (angiography), 18% (SPECT) and 23% (MRI and stress echo).
At 18 months, comparing SPECT and stress echo with angiography, a clinically significant difference in total exercise time can be ruled out. The MRI group had significantly shorter mean total exercise time of 35 seconds and the upper limit of the CI was 1.14 minutes less than in the angiography group, so a difference of at least 1 minute cannot be ruled out.

At 6 months post-treatment, SPECT and angiography had equivalent mean exercise time. Compared with angiography, the MRI and stress echo groups had significantly shorter mean total exercise time of 37 and 38 seconds, respectively, and the upper limit of both CIs was 1.16 minutes, so a difference of at least 1 minute cannot be ruled out. The differences were mainly attributable to revascularised patients.

There were significantly more non-fatal adverse events in the stress echo group [rate relative to angiography: 1.95 (95% CI: 1.23 to 3.08), \( p = 0.012 \)], mostly admissions for chest pain, but no significant difference in the number of patients reporting events [1.59 (95% CI: 0.90 to 2.79), \( p = 0.327 \)].

There was no significant difference among the groups in CCS class at either assessment. Clinically important differences in HRQoL could be ruled out.

Mean (95% CI) total additional costs over 18 months, compared with angiography, were £415 (–£310 to £1084) for SPECT, £426 (–£247 to £1088) for MRI and £821 (£10 to £1715) for stress echocardiography, with very little difference in quality-adjusted life-years (QALYs) amongst the groups (less than 0.04 QALYs over 18 months). Cost-effectiveness was mainly influenced by test costs, clinicians’ willingness to trust negative functional tests and by a small number of patients who had a particularly difficult clinical course.

**Conclusions**

Between 20 and 25% of patients can avoid invasive testing using functional testing as a gateway to angiography without substantial effects on outcomes. The SPECT strategy was as useful as angiography in identifying patients who should undergo revascularisation. The additional cost for the SPECT strategy was not significant and would be reduced further by restricting the rest test to patients who have a positive stress test.

MRI had the largest number of test failures and, in this study, had the least practical use in screening patients with suspected CAD, although it had similar outcomes to stress echo. This technology and decision rules for its interpretation are still evolving.

Stress echo patients had a 10% test failure rate, significantly shorter total exercise time and time to angina at 6 months post-treatment, and a greater number of adverse events, leading to significantly higher costs. Much of the excess costs were attributable to a small number of patients with particularly difficult clinical courses, unrelated to the diagnostic strategy. Given the level of skill required for stress echo, it may be best to reserve this test for those who have a contraindication to SPECT and are unable or unwilling to have MRI.

**Implications for the NHS**

Functional testing has a place in the diagnostic pathway for the assessment of chest pain in an outpatient population, avoiding invasive tests in a significant proportion of patients. The choice of test may be determined by local expertise and evolution of MRI. In this study, SPECT had the best outcomes, reflecting the greater experience of using this technique, although most differences between the tests were minor and there is a place for all three.

**Recommendations for future research**

Further research, using blinded reassessment of functional test results and angiograms, is required to formally assess diagnostic accuracy.

Longer-term cost-effectiveness analysis should assess whether decisions based on the functional tests have significant impact in the longer term.

Further studies of MRI and new generation computed tomography are required.

**Publication**

The Health Technology Assessment (HTA) programme, now part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the costs, effectiveness and broader impact of health technologies for those who use, manage and provide care in the NHS. ‘Health technologies’ are broadly defined to include all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care, rather than settings of care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the ‘National Knowledge Service’.

The HTA Programme is needs-led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, the public and consumer groups and professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Secondly, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Thirdly, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer-reviewed by a number of independent expert referees before publication in the widely read monograph series Health Technology Assessment.

The research reported in this monograph was commissioned by the HTA Programme as project number 99/26/04. The contractual start date was in July 2001. The draft report began editorial review in August 2006 and was accepted for publication in July 2007. As the funder, by devising a commissioning brief, the HTA Programme specified the research question and study design. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors’ report and would like to thank the referees for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

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