

# Systematic review and modelling of the cost-effectiveness of cardiac magnetic resonance imaging compared with current existing testing pathways in ischaemic cardiomyopathy

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Declared competing interests of authors: none

Published September 2014

DOI: 10.3310/hta18590

## Scientific summary

### Testing pathways in ischaemic cardiomyopathy

Health Technology Assessment 2014; Vol. 18: No. 59

DOI: 10.3310/hta18590

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# Scientific summary

## Background

Patients with coronary artery disease (CAD) can present with myocardial infarction (MI), while others may develop heart failure (HF), either primarily or following MI. Some patients with HF, as a result of CAD, have poor left ventricular contraction because of ischaemia, and some will have irreversibly damaged heart muscle that has been scarred by infarction, and will not benefit from revascularisation. Others will have heart muscle that is not scarred but functioning poorly because of ischaemia, which may respond to revascularisation with improved function, and are labelled as viable and potentially hibernating. The aim of viability assessment is to identify those patients in whom revascularisation is worthwhile, targeting those with viable and hibernating myocardium and avoiding intervention on those with scarred non-viable myocardium.

Assessment for viability can be done using a variety of techniques: stress echocardiography, single-photon emission computed tomography (SPECT), positron emission tomography (PET) and cardiac magnetic resonance imaging (CMR).

## Objectives

This report aimed to assess the current evidence on the clinical accuracy and cost-effectiveness of the use of CMR in viability assessment for patients being considered for revascularisation to treat ischaemic cardiomyopathy, develop an economic model to assess cost-effectiveness for different imaging strategies and to identify areas for further primary research.

## Data sources

Initial searches were conducted in March 2011 in the following databases with dates: MEDLINE including MEDLINE In-Process & Other Non-Indexed Citations via Ovid (1946 to March 2011); Bioscience Information Service (BIOSIS) Previews via Web of Science (1969 to March 2011); EMBASE via Ovid (1974 to March 2011); Cochrane Database of Systematic Reviews via The Cochrane Library (1996 to March 2011); Cochrane Central Register of Controlled Trials via The Cochrane Library 1998 to March 2011; Database of Abstracts of Reviews of Effects via The Cochrane Library (1994 to March 2011); NHS Economic Evaluation Database via The Cochrane Library (1968 to March 2011); Health Technology Assessment Database via The Cochrane Library (1989 to March 2011); and the Science Citation Index via Web of Science (1900 to March 2011). Additional searches were conducted from October to November 2011 in the following databases with dates: MEDLINE including MEDLINE In-Process & Other Non-Indexed Citations via Ovid (1946 to November 2011); BIOSIS Previews via Web of Science (1969 to October 2011); EMBASE via Ovid (1974 to November 2011); Cochrane Database of Systematic Reviews via The Cochrane Library (1996 to November 2011); Cochrane Central Register of Controlled Trials via The Cochrane Library (1998 to November 2011); Database of Abstracts of Reviews of Effects via The Cochrane Library (1994 to November 2011); NHS Economic Evaluation Database via The Cochrane Library (1968 to November 2011); Health Technology Assessment Database via The Cochrane Library (1989 to November 2011); and the Science Citation Index via Web of Science (1900 to October 2011). Relevant conference proceedings were searched via the Web of Science Conference proceedings citation index. The review team also contacted experts in the field and scrutinised the bibliographies of retrieved papers to identify relevant evidence. Searches were conducted from March to November 2011.

## Review methods

A systematic review was performed according to the recommendation of the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement. We assessed the clinical effectiveness and cost-effectiveness of CMR to establish the role of CMR in viability assessment compared with other imaging techniques (stress echocardiography, SPECT and PET).

The population considered comprised adults with CAD and left ventricular (LV) dysfunction who were potential candidates for revascularisation, to improve LV function. Studies had to have an appropriate reference standard, contain accuracy data (sensitivity, specificity, positive and negative predictive values) or sufficient details so that accuracy data could be calculated. Outcomes included accuracy data derived using different reference standards, with differing thresholds for determining viability. Criteria to define presence or absence of viable myocardium included improvement in wall motion, improvement in regional and global LV function, improvement in clinical symptoms, and reverse LV remodelling.

Data were extracted by two reviewers and discrepancies resolved by discussion. Quality of studies was assessed using the QUADAS II (quality assessment of diagnostic accuracy studies; University of Bristol, Bristol, UK) tool. The data extracted were synthesised and subjected to sensitivity analysis using STATA (2006 release 9.0; Stata Corporation, College Station, TX, USA).

A health economic model was constructed to compare diagnostic pathways for patients with ischaemic cardiomyopathy from an NHS perspective. The model was developed to estimate the costs and quality-adjusted life-years (QALYs) accrued by each potential diagnostic pathway for identifying patients with viable myocardium with a view to revascularisation. The pathways involved using stress echocardiography, late gadolinium-enhanced cardiac magnetic resonance imaging (CE CMR), stress cardiac magnetic resonance imaging (stress CMR), SPECT, PET to identify patients for revascularisation. A no-testing strategy and a revascularise everyone strategy were also included. Costs and benefits were discounted at an annual discount rate of 3.5%. The aim was to determine the optimal strategy in terms of cost-effectiveness.

The Markov model assigned each patient with a yearly probability of death, and, in each year, the patients who were alive had a risk of HF-related hospitalisations. The risks of death were estimated based on their subgroup and age using the data from different scenarios. The effect of the revascularisation on mortality was assumed to last a period of 5 years and, after this, the data from the general population were used. Each patient alive accumulated costs and QALYs every year based on his or her hospitalisation and subgroup. The model used a 40-year time horizon and the economic perspective of the model was the NHS in England and Wales. Scenario analyses were also performed using different mortality rates.

Cost-effectiveness of the different interventions was estimated using both the incremental cost-effectiveness ratio (ICER) and net monetary benefit (NMB) approach. This allows the relative value of different interventions to be compared. The ICER measures the relative value of two strategies, calculating the additional cost to accrue one additional QALY compared with the alternative. The NMB is defined as the QALYs multiplied by a value for the QALYs (e.g. £20,000) minus the costs of obtaining them. Uncertainty around the parameters used in the model (i.e. sensitivity and specificity estimates, mortality risks, hospitalisation rates, costs and utilities) were incorporated in the modelling by performing probabilistic sensitivity analysis, whereby the model is rerun (10,000 times), each time with a different value.

Another measure of uncertainty is the overall expected value of perfect information (EVPI). This estimates how often making the decision based on current evidence could be wrong and also how many QALYs (and costs) would be lost by choosing the strategy that is expected to be most cost-effective given current evidence, when in fact one of the other strategies is truly the most cost-effective. The interpretation of this number is that if one could fund research to eliminate the uncertainty in mortality risks for different patient

groups (e.g. by a large or infinitely large clinical trial) then the value of eliminating the uncertainty via such research would be expected to be the population EVPI.

## Results

Twenty-four studies met the inclusion criteria. All of the studies were conducted prospectively and 16 studies reported that patients were recruited consecutively. The included studies were small, with the number of participants ranging from 8 to 52, with a greater proportion of males included. The mean left ventricular ejection fraction ranged from 24% to 62% in the included studies reporting this outcome. CMR approaches included stress CMR and CE CMR. Recovery following revascularisation was used as the reference standard in all the included studies. Twelve studies assessed diagnostic accuracy of stress CMR with sensitivity ranging from 50% to 99%, while specificity ranged from 65% to 100%. Fourteen studies evaluated the accuracy of CE CMR to detect myocardial viability with sensitivity ranging from 86% to 99%, while specificity ranged from 24% to 94%. A bivariate regression model was used to calculate the sensitivity and specificity of both CMR approaches. Summary sensitivity and specificity for stress CMR was 82.2% [95% confidence interval (CI) 73.2% to 88.7%] and 87.1% (95% CI 80.4% to 91.7%) respectively. Summary sensitivity and specificity for CE CMR were 95.5% (95% CI 94.1% to 96.7%) and 53% (95% CI 40.4% to 65.2%) respectively. The sensitivity and specificity of PET, SPECT and echocardiography were also calculated using data from 10 studies and previous published systematic reviews. The sensitivity of PET was 94.7% (95% CI 90.3% to 97.2%), of SPECT was 85.1% (95% CI 78.1% to 90.2%) and of echocardiography was 77.6% (95% CI 70.7% to 83.3%). The specificity of PET was 68.8% (95% CI 50% to 82.9%), of SPECT was 62.1% (95% CI 52.7 to 70.7%) and of echocardiography was 69.6% (95% CI 62.4% to 75.9%). If the annual mortality rates for non-viable patients are assumed to be higher for revascularised patients than for patients on medical therapy, then testing with CE CMR, to correctly identify patients most likely to benefit from revascularisation, was the most cost-effective approach at a threshold of £20,000/QALY, but there is uncertainty involved in suggesting it as the most cost-effective strategy. The proportion of models runs in which CE CMR was the most cost-effective strategy (at £20,000 per QALY threshold) was 40%, with PET at 42% and revascularising everyone at 16.5%. The EVPI at the threshold of £20,000/QALY is £620 per patient.

If it was assumed that all patients (viable or not) gained benefit from revascularisation, then it was most cost-effective to revascularise all patients. Revascularising everyone was cost-effective in 95.2% of the proportion of models runs with CE CMR and PET cost-effective in 3.6% and 1.1% of the runs respectively. This reduction in uncertainty is also reflected in the EVPI of only £28 per patient.

## Conclusions

All the diagnostic pathways were a cost-effective use of NHS resources irrespective of the diagnostic pathway used at current National Institute for Health and Care Excellence thresholds, provided their costs and diagnostic accuracy are similar to those reported in this analysis. In terms of determining the most cost-effective strategy, diagnostic parameters and mortality rates of the different subgroups are the key drivers in the model. Two different scenarios relating the mortality rates were analysed in the model, this approach was taken to address the uncertainty in the mortality evidence. For decision-makers deciding which of these presented results are most representative of their setting, the key questions relate to the effect of revascularising non-viable patients. If one believes patients that are revascularised have lower mortality rates, even if they do not have viability, then revascularising everyone is the most cost-effective strategy. If one believes that there is no benefit for revascularising non-viable patients, then CE CMR is the most cost-effective strategy at a threshold of £20,000/QALY, but there is uncertainty involved in suggesting it as the most cost-effective strategy.

Implementation costs (such as set-up costs, staff training costs, costs for running of diagnostic services) were often missing from the studies in the review. Future studies should provide greater detail of the costs of reconfiguration and link more clearly with the financial impact (e.g. cost variation with scale and over time) on provider organisations. Wider adaptation of diagnostic imaging pathways in the NHS can be facilitated by providing financial impact data along with the cost-effectiveness information.

Consensus on reporting of diagnostic testing data in this clinical area would facilitate comparison of trial data and data synthesis in the future. Further research using universally agreed methodology of assessment of viability to answer both the question of testing viability and the impact of revascularisation or best medical therapy in this group of high-risk patients while remaining a priority, may be difficult to achieve in clinical practice.

## Funding

The National Institute for Health Research Health Technology Assessment programme.



ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Impact factor: 5.116

*Health Technology Assessment* is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index and is assessed for inclusion in the Database of Abstracts of Reviews of Effects.

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## This report

The research reported in this issue of the journal was funded by the HTA programme as project number 09/22/168. The contractual start date was in February 2011. The draft report began editorial review in October 2012 and was accepted for publication in November 2013. 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 reviewers 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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