Economics of myocardial perfusion imaging in Europe: the EMPIRE study
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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
Myocardial perfusion imaging (MPI) (scintigraphy) in patients newly presenting with possible coronary artery disease.

Type of intervention
Diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study investigated patients newly presenting with symptoms suggestive of coronary artery disease. Those presenting with acute coronary syndromes (myocardial infarction or unstable angina) were excluded, as were patients in whom coronary disease had been previously confirmed or excluded.

Setting
The setting was hospital. The economic analysis was carried out in the UK.

Dates to which data relate
Effectiveness and resource use data corresponded to patients presenting after 1 July 1993. The data related to sensitivities and specificities were obtained from two studies published in 1989 and 1996. The price year was 1996.

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

Link between effectiveness and cost data
Costing was 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. A total of 396 patients were included in the study, 189 from MPI user centres (Nancy 42, Hamburg 50, Naples 50, Aberdeen 47) and 207 from MPI non-users (Metz 55, Salerno 50, Heidelberg 49, Leicester 53).

When divided according to investigative strategy, the distribution of patients was as follows: strategy 1, 146 patients (mean age 55 years); strategy 2, 131 patients (mean age 53 years); strategy 3, 48 patients (mean age 61 years); and strategy 4, 76 patients (mean age 61 years).
In the user centres, the distribution of patients by strategy was as follows: strategy 1, 16; strategy 2, 121; strategy 3, 33; and strategy 4, 22. In the non-user centres the distribution was as follows: strategy 1, 130; strategy 2, 10; strategy 3, 15; and strategy 4, 54.

**Study design**

This was a multicentre, retrospective cohort study carried out in 8 centres; the aim of the study was to review 50 patients from each centre. Two hospitals (one MPI user and one non-user) were selected in each of four countries: France, Germany, Italy, and the UK. The duration of follow-up was 2 years. Loss to follow-up appears not to have been relevant to this study; except for 10% of patients who did not complete a questionnaire concerning symptoms, investigations, therapy, and clinical events in the 2 years after initial presentation. Data were abstracted from hospital records using a dedicated form which recorded relevant items of history, examination, investigations, management, therapy (drugs and interventions), clinical events, and complications. All study hospitals had access to MPI but its use was at the discretion of individual cardiologists. Thus MPI user hospitals did not always use MPI and non-users used it occasionally.

**Analysis of effectiveness**

The principle (intention to treat and treatment completers only) used in the analysis of effectiveness was not reported. The clinical outcome was the quality of diagnosis as assessed by the probability of coronary artery disease on presentation, as computed using the algorithm of Pryor and colleagues (taking account of age, sex, chest pain, resting ECG, diabetes, cholesterol, and smoking). Secondary outcomes were prognostic power at the point of diagnosis, rate of normal coronary arteriography, and rate of coronary arteriography not proceeding to revascularisation. Cardiac events were defined as soft or hard. The MPI user and non-user hospitals were comparable in terms of the mean usage of the other investigations, although Hamburg and Heidelberg had the highest rate of investigation and intervention in almost all categories. Patients assigned to different strategies were not comparable in terms of age.

**Effectiveness results**

The effectiveness results were as follows:

Mean probability of the presence of coronary artery disease when the final clinical diagnosis was that coronary artery disease was present were: strategy 1: 0.85; strategy 2: 0.82; strategy 3: 0.97, strategy 4: 1.0, (p<0.0001); users: 0.93; non-users: 0.88, (p=0.02).

When coronary artery disease was absent the mean probabilities were: strategy 1: 0.26; strategy 2: 0.22; strategy 3: 0.16; strategy 4: 0.0, (p<0.0001); users: 0.21; non-users 0.20, (non significant).

Prognostic power at diagnosis was higher (p<0.0001) and normal coronary angiography rate lower (p=0.07) in the scintigraphic centres and strategies.

Numbers of soft and hard cardiac events over 2 years and final symptomatic status did not differ between strategy and centre.

MPI users had significantly greater freedom from symptoms (63%) than non-users (37%) (p<0.001).

**Clinical conclusions**

Strategies and hospitals that used MPI in the diagnosis of patients newly presenting with suspected coronary artery disease were equally accurate as the strategies and hospitals that did not routinely use MPI. It was noteworthy that despite similar rates of revascularisation in the users and non-users of MPI, better long-term freedom from symptoms was obtained in the users, possibly because revascularisation was more appropriately targeted at patients with reversible ischaemia.
Outcomes assessed in the review
Sensitivities and specificities were the outcomes assessed.

Study designs and other criteria for inclusion in the review
Previously published meta-analyses.

Sources searched to identify primary studies
Not reported.

Criteria used to ensure the validity of primary studies
Not reported.

Methods used to judge relevance and validity, and for extracting data
Not reported.

Number of primary studies included
Two studies were included in the review.

Methods of combining primary studies
The authors did not undertake their own meta analyses, but used previously published studies to derive the required values.

Investigation of differences between primary studies
Not reported.

Results of the review
The values adopted for the sensitivity and specificity of the diagnostic modalities were as follows: exercise ECG 68% and 77%, tomographic MPI 91% and 89%, coronary angiography 100% and 100%, respectively.

Measure of benefits used in the economic analysis
No summary benefit measure was identified in the economic analysis, and only individual clinical outcomes were reported. The economic study appears to have been reduced to a cost-minimisation analysis based on the assumption of equal efficacy of the alternative diagnostic modalities.

Direct costs
Costs were not discounted despite the 2-year time frame of the cost analysis. Resource use quantities were not reported separately from the costs. Cost breakdown was reported separately. The cost analysis covered the costs of diagnosis (consumables, labour, fixed costs (including equipment maintenance) apportioned according to average throughput, and capital charges) and management over 2 years from the point of diagnosis (including outpatient attendance, inpatient admissions, and further investigations). The perspective adopted in the cost analysis was that of the health care provider. Cost calculations were performed using a single table of costs applied to all centres (to avoid discrepant results obtained from the reports supplied on costs and charges by each study centre and to simplify amalgamation of patients between centres). The cost data were based on averaging figures for both UK centres and a hospital in London, which were judged to be the most consistent. The intent of the study was to assess true costs rather than charges. The price year was 1996. The cost analysis did not include the nominal figures for rental and maintenance of space nor the cost of...
travel to hospital. The cost of inpatient days up to the point of diagnosis was not included because of the discrepancies in practice between centres.

**Statistical analysis of costs**
Statistical analysis was performed on the cost outcomes (using analysis of variance or the Kruskal-Wallis H test for multiple comparisons and Student's t-test or the Mann-Whitney U test for comparison between two independent samples), but the type of statistic used was not explicitly specified.

**Indirect Costs**
Indirect costs were not included.

**Currency**
UK pounds sterling (€).

**Sensitivity analysis**
No sensitivity analysis was conducted.

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

**Cost results**
Total 2-year costs (coronary artery disease present/absent) were: strategy 1: 4,453/710; strategy 2: 3,842/478; strategy 3: 3,768/574; strategy 4: 5,599/1,475, (p 0.05/0.0001); users: 5,563/623; non-users: 5,428/916, (non significant/0.001).

**Synthesis of costs and benefits**
costs and benefits were not combined since the economic study appears to have been conducted on the basis of cost-minimisation.

**Authors’ conclusions**
Investigative strategies using myocardial perfusion are cheaper and equally effective when compared with strategies that do not use myocardial perfusion imaging, both for cost of diagnosis and for overall 2 year management costs. Two year patient outcome is the same.

**CRD COMMENTARY - Selection of comparators**
A justification was provided for the choice of the comparator. MPI has been widely used since the 1970s and its role in diagnosis is to detect myocardial damage and reduced perfusion reverse. However, it is expensive and involves a dissociation with respect to the cardiologist and the provider of nuclear medical studies. There is therefore wide variation in its use. 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**
This multinational study addressed an important question given that no previous randomised controlled trials had examined MPI. However, the internal validity of the effectiveness results is hampered by the retrospective nature of the study design (the authors acknowledge that this makes the study prone to a number of important biases), lack of power calculations to justify the sample size, and the apparent lack of a systematic literature review. Additionally, the study
hospitals and patients were not always comparable in terms of a number of baseline characteristics (although these
differences tended to even themselves out in the larger groups). It was reported that actual sensitivity and specificity
achieved in this single study were very similar to the values reported in the literature, but it was considered more
appropriate to use published values because of the relatively small numbers of patients studied and the lack of
confirmatory angiography in some cases. The study sample appears to have been representative of the study population.
The authors provided a comprehensive and fair assessment of the limitations introduced by the study design adopted.

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 only included costs.

Validity of estimate of costs
Some features of the cost analysis, likely to enhance its validity, were: some details of the methods of cost estimation
(including cost items) were given, the price year and perspective adopted in the cost analysis were specified, the cost
analysis was intended to be based on true costs rather than charges, and statistical analysis was performed on cost
outcomes. However, a resource use profile was not provided (although this may not have been feasible within the
study's constraints), costing was conducted on a retrospective basis, the direct cost analysis was not comprehensive as
some cost components were omitted, the effects of alternative procedures on indirect costs were not addressed, and
sensitivity analysis was not performed to assess the robustness of the cost results. These latter elements tend to restrict
the generalisability of the results.

Other issues
The authors' conclusion may need to be treated with some caution due to the limitations inherent in the study design and
the lack of sensitivity analysis to address uncertainties in the data. The issue of generalisability to other settings or
countries was not fully addressed in the authors' comments; but it was acknowledged that individual purchasers of
health care are likely to make judgements on the most 'charge-effective' strategies based on local idiosyncrasies. The
multi-national approach, however, tends to enhance the generalisability of the results to other settings. The degree to
which the study sample was representative of the study population was not discussed in the authors' comments.

Implications of the study
The results suggest that diagnostic strategies that include MPI may lead to improved outcomes if patients are more
appropriately selected for intervention. No difference in prognostic power was observed in this study but a much larger
and longer study would have been required in order to do so.

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