Cost-effectiveness of preoperative positron emission tomography in ischemic heart disease

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 use of positron emission tomography (PET) to detect patients with hibernating myocardium among those with ischaemic heart disease (IHD) and severe left ventricular (LV) dysfunction, for subsequent operation.

Type of intervention
Diagnosis and treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with IHD and severe LV dysfunction. For the purpose of this study, patients with severe LV dysfunction were defined as those with an ejection fraction of less than 30%.

Setting
The setting was a hospital. The study was carried out in London, United Kingdom.

Dates to which data relate
The dates to which the effectiveness data and the resource quantities related were not reported. The price year was not given.

Source of effectiveness data
The effectiveness data were derived from data obtained from the hospital in which the study was carried out, from a review of studies, and from the authors’ assumptions.

Study sample
No sample data were available since the study modelled the cost-effectiveness of the proposed strategies. A total of 1,000 hypothetical patients were considered for the purposes of the decision tree.

Study design
The study was observational, using hospital data collected regularly. The period of follow-up was 1 year.

Analysis of effectiveness
The primary health outcomes assessed by the single study were obtained from hospital data for patients with IHD and ejection fractions of less than 30%. The primary health outcomes reported were:
the mean lengths of stay in the preoperative ward, overnight intensive recovery (OIR), intensive care unit (ICU) and postoperative ward;

the overall hospital survival rates of patients undergoing CABG; and

the hospital survival rates from the operating theatre, OIR, ICU and the ward.

**Effectiveness results**
The mean lengths of stay were 1.6 days in the preoperative ward, 1.0 days in the OIR, 5.6 days in the ICU, and 6.5 days in the postoperative ward.

The overall hospital survival was 91.4% for patients undergoing CABG.

Hospital survival was 96.5% from the operating theatre, 100% from the OIR, 94.3% from the ICU, 98.2% from the ward.

**Clinical conclusions**
The effectiveness data derived from hospital sources were introduced as input parameters in the decision tree.

**Modelling**
A decision analysis model was performed to estimate the costs and the outcomes for each strategy considered in the study. Three alternative strategies were considered in the model:

- to operate on all patients without first obtaining a PET scan;
- to obtain a PET scan for all the patients, then to treat those with no hibernating myocardium with MT, and those with hibernating myocardium with operation, followed by MT; and
- to treat all the patients with MT.

**Outcomes assessed in the review**
The outcomes assessed in the review were:

- the prevalence of significant hibernation myocardium;
- the sensitivity and specificity of PET to detect a mismatch pattern predictive of hibernation;
- the nondiagnostic rate of the PET scan;
- the 1-year survival rate for patients with mismatch who underwent CABG;
- the 1-year survival rate for patients with mismatch who were treated with MT;
- the 1-year survival rate for patients with match defects who underwent CABG; and
- the 1-year survival rate for patients with match defects who were treated with MT.

Mismatch was defined as the pattern associated with hibernating myocardium, as detected by a PET scan. Match was the pattern associated with myocardial necrosis in the absence of hibernating myocardium, as detected by a PET scan.

**Study designs and other criteria for inclusion in the review**
Not stated.

**Sources searched to identify primary studies**
Not stated.

**Criteria used to ensure the validity of primary studies**
Not stated.

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

**Number of primary studies included**
Four primary studies were included in the review. The authors did not state the type of studies included.

**Methods of combining primary studies**
The methods used to combine and select the estimates used at baseline were not reported.

**Investigation of differences between primary studies**
Not reported.

**Results of the review**
The prevalence of significant hibernation myocardium was 50%.

The sensitivity and specificity of PET to detect a mismatch pattern predictive of hibernation were both 80%.

The nondiagnostic rate of the PET scan was 5%.

The authors reported two different values (88 and 91.4%) for the 1-year survival rate for patients with mismatch who underwent CABG. It would seem that the default value for the model was 91%.

The 1-year survival rate for patients with mismatch who were treated with MT was 50%.

The authors also reported two different values (94 and 91.4%) for the 1-year survival rate for patients with match defects who underwent CABG. It would appear that 91% was the value used in the model.

The 1-year survival rate for patients with match defects who were treated with MT was 92%.

These values obtained from the review were included as input parameters in the decision tree.

**Methods used to derive estimates of effectiveness**
The authors made some assumptions about the effectiveness.

**Estimates of effectiveness and key assumptions**
The authors assumed that the patients referred for consideration of operation had technically operable disease, and that an appropriate risk assessment was carried out. All surgical deaths occurred in the perioperative period.
Measure of benefits used in the economic analysis
The summary measure of benefit was the number of life-years generated during the 1-year of follow-up for the 1,000 patients considered in the study. This measure was calculated from the survival rates obtained in the effectiveness analysis and in the review.

Direct costs
The resource quantities and the costs were reported separately. The direct costs considered in the analysis were those of the hospital. These were calculated specifically for patients with poor LV function. The costs of the preoperative PET scan (742) were for the radioactive tracers and the use of the PET centre (including staff, consumables, equipment and maintenance). The cost of the surgical intervention comprised the cost of CABG (4,117, including staff, consumables, equipment and maintenance), and the daily costs of the OIR (404), ICU and the ward. The cost of MT (780) included the costs of the drugs but not those for medical consultations and hospital admissions, because these data were unavailable.

The costs were estimated from actual data. The costs related to CABG were obtained from the prices charged by Guy's and St. Thomas' Hospital Trust to other parts of the UK National Health Service. The costs related to a PET scan were obtained from another study. The cost of MT was derived using the prices reported by the hospital pharmacy for drug treatment within the National Health Service. The authors reported the average and incremental costs. The price year was not given. Discounting was not carried out as the costs were incurred over less than 2 years.

Statistical analysis of costs
No statistical analysis of the costs was performed.

Indirect Costs
The indirect costs were not reported.

Currency
UK pounds sterling ( ).

Sensitivity analysis
One-way sensitivity analyses were performed to test for the effect of variability in the data. Some of the thresholds for dominance were reported. The following parameters were considered:

- the sensitivity of PET (50, 99%);
- the specificity of PET (50, 99%);
- the cost of PET (400, 3,000);
- the cost of CABG (2,500, 7,000);
- the cost of the ICU (400, 2,000);
- the cost of MT (400, 1,000);
- the percentage of patients with mismatch (5, 95%);
- the 1-year survival rate for patients with mismatch who underwent CABG (80, 91%);
- the 1-year survival rate for patients with match who underwent CABG (80, 91%);
the 1-year survival rate for patients with match who were treated with MT (80, 100%); and
the 1-year survival rate for patients with mismatch who were treated with MT (30, 70%).

Estimated benefits used in the economic analysis
The life-years gained were 855 with MT, 915.79 with preoperative PET and CABG, and 913.79 with CABG (without PET).

The incremental life-years gained with PET and CABG were 60.79 when compared with MT.

When CABG (without PET) was compared with CABG with preoperative PET, the incremental life-years gained were -2.

Cost results
The total costs were 666,900 for MT, 5,359,146 for CABG with preoperative PET, and 8,146,717 for CABG (without PET).

The incremental cost of CABG with preoperative PET was 4,692,246 when compared with MT.

The incremental cost of CABG (without PET) was 2,787,572 when compared with CABG with preoperative PET.

Synthesis of costs and benefits
The estimated benefits and costs were combined using incremental cost-effectiveness ratios, stated to be the cost per life-year obtained with one strategy in comparison with another. The incremental cost per life-year saved with CABG with preoperative PET was 77,186 when compared with MT. CABG with preoperative PET proved to be a dominant strategy in comparison with CABG without PET, as it was a cheaper and more effective alternative.

The one-way sensitivity analyses showed that MT was always the least costly strategy, while CABG without PET was always the most expensive. The cost-effectiveness results were affected by changes in the prevalence of hibernation in the referral population, and in the survival of patients with no hibernation receiving MT. The PET versus no PET strategy remained dominant if the prevalence of hibernation did not exceed 53%. Otherwise, CABG without PET generated more benefits but with higher costs. When the PET sensitivity was 77.4%, the CABG without PET strategy generated more benefits but at a cost of almost 117 million per additional life-year.

Authors' conclusions
The use of preoperative positron emission tomography (PET) to select patients for revascularisation was cost-effective, because it was a cheaper strategy than performing coronary artery bypass grafting (CABG) without PET. The money savings derived from refusing CABG to those patients with myocardial necrosis (no hibernating myocardium), who cannot benefit from revascularisation, outweighed the costs of introducing PET scans. The PET option had minimal impact on the 1-year survival rates. The net gains in survival made by patients with necrosis who do not receive operation (and therefore, avoid the risks of operation) are balanced by the net losses experienced by patients with myocardial hibernation with a false-negative PET. In comparison with medical treatment only, there was an additional cost of 77,000 per life-year gained.

CRD COMMENTARY - Selection of comparators
The comparators were justified on the grounds that CABG represented existing practice. The consideration of MT was justified because existing practice may not be cost-effective by itself, and the interpretation of the results of comparisons between PET and CABG may be misleading.

Validity of estimate of measure of effectiveness

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The analysis used an uncontrolled trial, which seems to have been appropriate for the study question. Sample data were unavailable, and therefore, the study used the results obtained from a hypothetical study sample. The authors did not state that a systematic review of the literature had been undertaken. They also did not report the method used to derive the estimates of effectiveness from the primary studies. The impact of differences between the primary studies was not considered when estimating effectiveness. The authors warned about the lack of information on some of the parameters assessed in the review, for example, the prevalence of hibernation. Therefore, one of the limitations of the study reported by the authors was a potential problem of bias. However, the authors tried to mitigate bias by being explicit about the assumptions used in the study. The sensitivity analyses showed that the uncertainty surrounding the available data might alter the cost-effectiveness conclusions.

**Validity of estimate of measure of benefit**
The estimation of benefits was modelled using a decision analysis model. The survival rates used were obtained from the single study and from the review of the literature.

**Validity of estimate of costs**
Most of the categories of cost relevant to the perspective adopted were included in the analysis. As the authors acknowledged, some relevant costs were omitted. The cost of MT included the costs of the drugs but not those for medical consultations and hospital admissions, because these data were unavailable. The authors reported that the cost of MT was therefore underestimated. This may affect the authors' conclusions in the sense that MT might become more expensive than any of the other strategies. However, MT alone might not be chosen due to the low outcomes that this strategy generated in comparison with the other strategies. The costs and the quantities were reported separately, which enhances the generalisability of the results. However, sensitivity analyses of the quantities and the costs were not conducted. This may limit the interpretation of the study findings. The price year was not reported, which hinders reflation exercises to other settings.

**Other issues**
The authors made appropriate comparisons of their findings (in terms of some of the baseline values obtained for the parameters) with those from other studies. The issue of the generalisability of the results to other settings was not addressed. The authors do not appear to have presented the results selectively, although they reported two different values for some of the parameters, and it was unclear which of these values were used in the analysis.

The authors reported that although PET is regarded as the most accurate imaging technique for hibernation, it is perceived also as the most costly. In addition, its availability in the UK is very limited and other techniques could be used, for example, stress echocardiography. A further issue posed by the authors was the uncertainty surrounding how the presence or absence of hibernating myocardium influenced perioperative complications and mortality. Therefore, no definitive conclusions about the cost-effectiveness of PET can be drawn.

**Implications of the study**
The use of PET to select patients with hibernating myocardium for operation, and to refuse those without hibernating myocardium, may be a cost-effective strategy for the baseline values presented in the study because it is less costly, although the health benefits generated are minimal. However, the sensitivity analyses have shown that the cost-effectiveness of preoperative PET depends on the prevalence of hibernating myocardium and on the survival rates. This has to be borne in mind when extrapolating the results to other settings.

The authors warn about the lack of studies informing the prevalence of hibernating myocardium. They state that the performance of a prospective trial of MT versus surgical treatment is necessary. However, they also highlight the ethical difficulties inherent in justifying the randomisation of patients with hibernating myocardium to receive MT, which is likely to be less beneficial.

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