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
Left-ventricular assist devices (LVADs) used as destination therapy for patients with end-stage heart failure (ESHF), and who were not transplant candidates, were examined. The device considered in the study was the Thoratec Heartmate VE (vented electric) Left Ventricular Assisted System. This comprised a fully implantable pump served by a percutaneous driveline, which provides for power and venting. The patient could achieve high degree of mobility with a wearable battery pack and system controller. An apical anastomosis links the left ventricle with the pump via an inflow cannula. An outflow cannula is anastomosed to the aorta.

Type of intervention
Treatment.

Economic study type
Cost-utility analysis.

Study population
The study population comprised patients belonging to New York Heart Association (NYHA) Class IV for at least 90 days, despite the use of ACE inhibitors, diuretics and digoxin. The patients also had a left-ventricular ejection fraction of 25% or less and a peak oxygen concentration of 12 mL/kg or less, or continued need for intravenous (IV) inotropic therapy for symptomatic hypotension, decreasing renal function, or worsening pulmonary congestion. Cardiac transplantation contraindications included age older than 65 years, insulin-dependent diabetes mellitus with end-organ damage, chronic renal failure, and other major physical or mental co-morbidities.

Setting
The setting was experienced cardiac transplantation centres. The economic study was carried out in the USA.

Dates to which data relate
The effectiveness, resource use and cost data were derived from studies published between 1997 and 2003. The price year was 2002.

Source of effectiveness data
The effectiveness evidence was derived from a synthesis of published studies.

Modelling
A decision model (based on a decision tree) and a Markov model were constructed to estimate the costs and benefits of LVADs and OMM in patients with ESHF not eligible for heart transplant. The time horizon of the model was the patient's lifetime, to a maximum of 3 years (owing to the poor survival of patients with ESHF). Monthly cycles were
considered. A simplified structure of the models was provided. Each branch of the model included "alive" and "dead" as health states. Time-dependent probabilities were used for Markov cohort simulations.

**Outcomes assessed in the review**
The outcomes derived from the literature were:

- cycle-specific probabilities of survival (derived directly from a clinical source for the period month 1 to month 26, and extrapolated thereafter);
- expected survival;
- the hazard ratio for survival between LVADs and OMM;
- the probability of being in NYHA Classes I/II or III/IV;
- the utility values associated with NYHA classes; and
- the probability of re-hospitalisation.

**Study designs and other criteria for inclusion in the review**
It would appear that the primary studies have been identified selectively and a systematic review of the literature has not been undertaken to identify the primary sources. Some data were derived from the REMATCH trial. The utility values came from a sample of 29 bridge-to-transplant LVAD recipients using the standard gamble approach. The method used to extrapolate survival data was described and commented upon.

**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**
Six primary studies were used to derive the model inputs.

**Methods of combining primary studies**
When relevant, the primary studies appear to have been combined using a narrative approach.

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

**Results of the review**
The probabilities of survival with an LVAD were 0.810 at one month, 0.590 at 6 months, 0.510 at 12 months, 0.360 at 18 months, 0.240 at 24 months, 0.060 at 30 months, and 0 at 36 months. The corresponding probabilities of survival with OMM were 0.800 (1 month), 0.460 (6 months), 0.280 (12 months), 0.110 (18 months), 0.080 (24 months), 0.006
(30 months) and 0 (36 months), respectively.

The overall median (mean) survival was 13.30 (12.87) months with an LVAD and 5.90 (7.26) months with OMM (difference in median survival 7.40 months; difference in mean survival 5.61 months).

The hazard ratio for survival between an LVAD and OMM was 0.52 (95% confidence interval: 0.34 - 0.78).

With LVAD, the proportions of patients in NYHA Classes I/II and III/IV were 0% and 100% at baseline, 54% and 46% at one month, 68% and 32% at 3 months, 80% and 20% at 6 months, 82% and 18% at 9 months, 71% and 29% at 12 months, 44% and 56% at 18 months, and 71% and 29% at 24 months.

The corresponding values in patients receiving OMM were 0% and 100% (baseline), 0% and 100% (1 month), 3% and 97% (3 months), 9% and 91% (6 months), 0% and 100% (9, 12 and 18 months), and 33% and 67% (24 months), respectively.

The utility values were 0.81 with NYHA Class I/II and 0.55 with NYHA Class III/IV.

The probability of re-hospitalisation was 0.22 with an LVAD and 0.15 with OMM.

Measure of benefits used in the economic analysis

The summary benefit measure used was the expected number of quality-adjusted life-years (QALYs). This was obtained by combining utility data and survival using the decision model. The assumptions made in the calculation of QALYs were explicitly reported. An annual discount rate of 3% was applied.

Direct costs

Discounting was relevant since the costs were incurred during 3 years (the maximum survival) and an annual rate of 3% was used. The costs of the individual items were not provided, but costs associated with groups of services were. The economic evaluation considered three main categories of costs (implantation costs, re-hospitalisation costs and outpatient costs). Sub-categories of hospitalisation costs were LVAD, professional payment, length of stay, special care days, regular floor, operating room, diagnostics, laboratory, blood products, drugs, miscellaneous costs and rehabilitation. Sub-categories of outpatient costs included professional payments, laboratory tests and drugs. Costs that could have increased the monthly re-hospitalisation due to device malfunction, removal or implementation were not included in the economic evaluation, nor were any additional costs associated with specific types of adverse events that were more common among LVAD recipients in the REMATCH trial.

The author stated that the cost/resource boundary of society was adopted, but the costs of the services could have been borne only by the health care system. Both the costs and quantities of resources used were derived from published studies, which included an economic evaluation of the REMATCH trial. A cost-to-charge ratio had been applied to estimate the true costs of the services. Monthly hospitalisation costs were assumed to have been the same for patients receiving LVADs and OMM. The costs were expressed in 2002 values using the Gross Domestic Product Deflator.

Statistical analysis of costs

The costs were treated deterministically.

Indirect Costs

The indirect costs were not included in the economic evaluation because it was unlikely that the patients would return to work, owing to their complicated overall condition.

Currency

US dollars ($).
Sensitivity analysis
Univariate sensitivity analyses were carried out to test the robustness of the cost-utility ratios to variations in the following model inputs:

- relative survival of LVAD and OMM groups;
- methods for extrapolating survival past the point of last follow-up;
- the utilities for NYHA categories I/II and III/IV;
- the utility discount rate;
- the cost of LVAD implantation;
- the cost of re-hospitalisation;
- the cost of outpatient care;
- the probability of re-hospitalisation for LVAD and OMM; and
- the cost discount rate.

Two-way sensitivity analyses were also carried out for pairwise combinations of several variables. More specifically, the utilities for NYHA categories I/II and III/IV, the cost of LVAD implantation, the cost of re-hospitalisation, the cost of outpatient care, and the probability of re-hospitalisation for LVAD and OMM. A best-case scenario for LVAD was also considered. Alternative values used in the sensitivity analysis were derived from the literature, or were based on the author's assumptions.

Estimated benefits used in the economic analysis
The expected number of discounted QALYs was 0.332 with OMM and 0.755 with an LVAD (difference 0.422 QALYs).

Cost results
The discounted costs were $53,025 with OMM and $391,906 with an LVAD (difference $338,881).

Synthesis of costs and benefits
An incremental cost-utility ratio was calculated to combine the costs and QALYs of the alternative strategies. The incremental cost per QALY gained with an LVAD over OMM was $802,674.

The sensitivity analysis showed that, in general, implausible variations in model inputs were required for the incremental cost per QALY to approach more reasonable values. The model inputs with the greatest impact on the results of the analysis were:

- the utility values for NYHA categories (range of the cost per QALY: $1,588,900 - $615,900);
- the cost of LVAD implantation (range of the cost per QALY: $442,600 - $1,153,200); and
- the probability of re-hospitalisation for LVAD (range of the cost per QALY: $679,400 - $936,200).

The two-way sensitivity analysis showed that when paired with other variables, the cost of LVAD implantation had the greatest influence on the results. However, unreasonably low values for the cost of LVAD were required for the cost per QALY to be below $500,000. In the best-case scenario for LVAD, the incremental cost per QALY was $214,700.
Authors' conclusions
The incremental cost per quality-adjusted life-year (QALY) with a left-ventricular assist device (LVAD) over optimal medical management (OMM) was $802,700. Reductions in the estimated cost per QALY could be achieved only under implausible variations in the model inputs.

CRD COMMENTARY - Selection of comparators
The selection of the comparator was appropriate because it covered a number of possible medical treatment options for patients with ESHF who were not eligible for heart transplantation. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The effectiveness evidence came mainly from published studies. It appears that a review of the literature has not been undertaken and the primary studies were identified selectively. The author provided several details of the design of the primary studies, and justified his choice of the values used in the base-case analysis. The methods used to extrapolate survival data were described and compared. The issue of variability in the data was addressed in the sensitivity analysis, where all relevant inputs were varied.

Validity of estimate of measure of benefit
The use of QALYs as the summary benefit measure was appropriate as they captured the impact of the intervention on life expectancy and quality of life, which are relevant aspects of care for patients with ESHF. The source of the utility values was reported, although the author noted that the use of utilities derived from the general population would have been more appropriate. Discounting was applied, as recommended in US guidelines. QALYs are comparable with the benefits of other health care interventions.

Validity of estimate of costs
A societal perspective was adopted in the study, although the author noted that some categories of costs (i.e. productivity losses) were not included because the impact of such costs was considered negligible on account of the poor expected survival of patients included in the study. All the economic data were derived from published studies, including the primary clinical trial used as the source of clinical evidence. All assumptions made in the cost analysis were explicitly stated and discussed. The costs were presented as macro-categories. The costs were treated deterministically, but relevant categories of costs or resources used were varied in the sensitivity analysis. The price year was reported, which will facilitate reflation exercises in other settings. The author reported some of the assumptions made in the cost analysis.

Other issues
The author did not make extensive comparisons of their findings with those from other studies. He also did not explicitly address the issue of the generalisability of the study results. However, extensive sensitivity analyses were carried out, which enhances the external validity of the study. The author noted some limitations of the study, including the simplicity of the Markov model.

Implications of the study
The study results showed the unfavourable cost-effectiveness of LVADs as destination therapy for the treatment of patients with ESHF in comparison with OMM.

Source of funding
None stated.
Bibliographic details

Other publications of related interest


Indexing Status
Subject indexing assigned by NLM

MeSH
Blue Cross Blue Shield Insurance Plans; Cost-Benefit Analysis; Device Approval; Evidence-Based Medicine; Heart Failure /surgery; Heart Transplantation; Heart-Assist Devices /economics; Humans; Insurance Coverage; Outcome Assessment (Health Care); Quality-Adjusted Life Years; Technology Assessment, Biomedical; United States; United States Food and Drug Administration

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