Effects of left ventricular assist devices on outcomes in patients undergoing heart transplantation


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 left ventricular assist devices (LVADs) to help "bridge" patients who are awaiting heart transplants. Intravenous inotrope therapy (IT) was used as a comparator.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients listed as status 1 for a heart transplant operation.

Setting
The setting was a hospital. The economic study was carried out in Minnesota, USA.

Dates to which data relate
The effectiveness evidence was gathered from patients treated between January 1995 and September 1998. The costs of the resources used were stated to have been the average price at the time of use (between January 1995 and September 1998). The prices were given in US dollars, although no price year was stated.

Source of effectiveness data
The effectiveness data were derived from a single study.

Link between effectiveness and cost data
The costing was performed retrospectively using the same sample of patients as that used in the effectiveness analysis.

Study sample
The study sample consisted of 40 consecutive patients between 1995 and 1998 who were awaiting heart transplant and listed as status 1. A power calculation was not used to determine this number. All patients were initially treated with intravenous inotropes, and exactly half (20) underwent placement of a LVAD. The other 20 continued with IT and were the comparator group. P-values were reported for all significant results.

Study design
This was a cohort study carried out in a single centre. The study was conducted retrospectively, the patients having already been assigned to one of the two treatments. The assignment of the patients was not randomised. The patients were studied from the point of listing as status 1, until 6 months after the transplant. No blinding methods were used at any level. Complications, both pre and post-transplant, were reported. These included infections, strokes, device failure, renal failure, right heart failure, cardiac rejection, severe debility, and death. All 40 patients (other than those who died) were followed-up until 6 months after the transplant.

**Analysis of effectiveness**

Characteristics of the patients that were recorded, both at the point of listing as status 1 and at the time of heart transplant, included:

- heart beat rate;
- systolic pressure;
- diastolic pressure;
- haemoglobin;
- sodium;
- blood urea nitrogen;
- creatinine;
- aspartate aminotransferase;
- alkaline phosphatase; and
- bilirubin.

The survival rates, and the complications occurring in the 6 months following the transplant, were also recorded. The analysis was performed on an intention to treat basis.

The differences in the characteristics between the patient groups were generally not statistically significant at the point of status 1 listing. The exceptions were:

- heart beat rate, 103 beats/minute for LVAD and 88 beats/minute for IT, (p<0.01);
- haemoglobin, 11.4 g/dL for LVAD and 13.1g/dL for IT, (p<0.01);
- aspartate aminotransferase, 102 U/L for LVAD and 40 U/L for IT, (p<0.05); and
- bilirubin, 1.7 mg/dL for LVAD and 1.1 mg/dL for IT, (p<0.05).

It was not necessary to analyse drop-outs due to the fact that the only non-completers were those patients who died (measured as an outcome).

**Effectiveness results**

The differences in the characteristics between the two patient groups at the time of transplant were:

- for heart beat rate, not significantly different;
- for systolic pressure, 130 mmHg for LVAD and 103 mmHg for IT (p<0.001);
for diastolic pressure, 75 mmHg for LVAD and 60 mmHg for IT, (p<0.001);

for haemoglobin, not significantly different;

for sodium, 141 mmol/L for LVAD and 137 mmol/L for IT, (p<0.001);

for blood urea nitrogen, 16 mg/dL for LVAD and 24 mg/dL for IT, (p<0.01);

for creatinine, 1.0 mg/dL for LVAD and 1.3 mg/dL for IT, (p<0.01);

for aspartate aminotransferase, not significantly different;

for alkaline phosphatase, not significantly different; and

for bilirubin, not significantly different.

Two LVAD patients died pre-transplant, and one IT patient died pre-transplant.

Eight LVAD patients suffered no complications before the transplant, compared with 11 IT patients. After the transplant, 11 of the 18 surviving LVAD patients suffered no complications, compared with 3 of the 19 surviving IT patients. However, 1 LVAD and 3 IT patients suffered cardiac rejection following the transplant. There were significantly more acute renal failures and right heart failures in the IT group following the operation, (p<0.05).

Clinical conclusions
Status 1 heart patients receiving a LVAD instead of IT exhibited an improved clinical and metabolic function in the time leading up to heart transplantation. The 6-month survival rates were greater for the LVAD group, and with fewer complications.

Measure of benefits used in the economic analysis
The authors did not derive a summary health benefit measure and separate clinical outcomes were used. A cost-consequences analysis was therefore performed.

Direct costs
Discounting was unnecessary since all the costs were incurred within the first year. The average hospital charges were measured for the time between listing as status 1 and the time of discharge after the transplant, and included any stay in intensive care units. The cost of implementing the LVAD itself was measured. The charge data were obtained from the hospital. The costs were measured at the time of use (between 1995 and 1998), and were not reflated to a given price year.

Statistical analysis of costs
The difference in the costs between the two groups was reported statistically. Any significant findings were clearly stated.

Indirect Costs
Any additional costs incurred, due to complications before and after the transplant, were accounted for by way of hospital charges. No discounting was performed since all the charges occurred within one year of the status 1 listing.

Currency
US dollars ($).
Sensitivity analysis
No sensitivity analysis was performed.

Estimated benefits used in the economic analysis
See the 'Effectiveness Results' section.

Cost results
The total costs were significantly greater for the LVAD group ($342,620) than for the IT group ($213,860), (p<0.01). This was due to the costs of the LVAD itself (around $50,000), implementation ($23,000), and a longer hospital stay prior to the transplant (77 days compared with 42), (p<0.01). No discounting was performed since all the costs were incurred within a 12-month period.

Synthesis of costs and benefits
No incremental analysis was performed. The costs and the benefits were not combined in the study. It can be inferred that the incremental cost per death averted for using LVAD as opposed to IT was $64,380, although this was not shown in the study. It can also be inferred that, if LVAD were made available to outpatients (as the authors suggest will be possible with new technology), LVAD will be both cheaper and more effective than IT, and will therefore dominate it.

Authors' conclusions
For status 1 heart transplant patients, the fitting of a left ventricular assist device (LVAD) whilst the patient awaits the transplant is more effective than inotrope therapy (IT). The authors also concluded that fitting an LVAD was more expensive than IT, although they suggested that technological improvements might lead to this method being the cheaper alternative.

CRD COMMENTARY - Selection of comparators
The main comparator used was intravenous IT, which was the most common treatment for the patient population. A 'do nothing' option was not presented in the study.

Validity of estimate of measure of effectiveness
A number of clinical and metabolic characteristics of the patients were measured, both at the time of listing as status 1 and at the point of transplant. Many other factors were also measured during the 6 months after the transplant. The patients were not randomly assigned to each treatment group. In fact, it was recommended that patients with more severe symptoms were fitted with a LVAD. This resulted in a bias, and thus the effectiveness results for the LVAD group are likely to have been underestimated.

Validity of estimate of measure of benefit
For the interventions considered, it was appropriate to present the benefits as separate outcomes, in other words deaths, complications, and other characteristics. A cost-consequences approach was therefore used.

Validity of estimate of costs
There are a number of issues regarding the assessment of the costs. Firstly, the costs were not reflated to a given price year. Biases may, therefore, exist if either of the treatment groups tended to be earlier in the study period (1995 to 1998). Secondly, the total costs for each group were reported. Since some patients died during the study, this will result in lower costs (less hospital days). More patients died in the IT group, and so the cost estimates for this treatment will be underestimated. Finally, since charges were used in the costing, this did not reflect the opportunity costs. Thus, there are limitations in terms of the generalisability of the cost results.
Other issues
The findings of the study were compared with those from other studies, and appear to have been consistent. However, since the factors were specific to this setting, the lack of a sensitivity analysis makes it difficult to consider the implications of the study if applied to other settings. An alternative scenario is considered whereby the authors consider new technology allowing the patients to wear the LVAD as outpatients. The authors estimated that this might reduce the costs by as much as $173,460.

Implications of the study
The results suggest that a LVAD should be fitted in patients listed as status 1 for heart transplantation. Since new technologies will allow outpatients to wear an LVAD, the total costs for this treatment will fall significantly. Thus, the method will become even more cost-effective, if not dominant over the alternative (intravenous IT).

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