Cost utility evaluation of extracorporeal membrane oxygenation as a bridge to transplant for children with end-stage heart failure due to dilated cardiomyopathy

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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.

CRD summary
The objective was to estimate the cost-utility of extracorporeal membrane oxygenation (ECMO) as a bridge to transplant for children with end-stage heart failure, due to dilated cardiomyopathy, compared with previous standard intensive care unit treatment. ECMO bridging was highly effective, but expensive and not within the conventional criteria for cost-effectiveness. The study quality was generally good. Despite some minor limitations, the authors presented a reasonably transparent analysis and it is likely that the results reflected the available evidence.

Type of economic evaluation
Cost-effectiveness analysis, cost-utility analysis

Study objective
The objective was to estimate the cost-utility of extracorporeal membrane oxygenation (ECMO) as a bridge to transplant, for children with end-stage heart failure (ESHF) due to dilated cardiomyopathy, compared with previous standard intensive care unit (ICU) treatment.

Interventions
ECMO was started if conventional ICU treatment had failed with cardiovascular instability, with or without end-organ hypoperfusion, and there was no contraindication for ECMO. This was compared with standard intensive care unit (ICU) treatment.

Location/setting
UK/tertiary care.

Methods
Analytical approach:
A Markov model was developed and populated with efficacy and cost data from one centre. The model had an initial rapid phase, with a one-month cycle length, for two months, followed by a long-term phase, with a one-year cycle length, for over 30 years. The health states included ESHF, transplant, convalescence, and death. The non-parametric transition probabilities were based on patient-level data until the last point that these data were available, which was six years for the pre-ECMO group and two years for the post-ECMO group, and then they were extrapolated for another 30 years. The authors reported that the analysis was carried out from a health service perspective.

Effectiveness data:
The authors stated that the effectiveness of ECMO bridging was based on a comparison of a cohort of children with ESHF treated in the era before ECMO (between 1994 and January 2001; n=34), who were offered conventional intensive care, and a cohort of children with ESHF treated after ECMO was introduced (after January 2001 until 2004; n=41). The study included children aged between 1 and 18 years with severe ESHF due to dilated cardiomyopathy, who were referred from throughout the United Kingdom to a tertiary paediatric cardiac transplant centre, between 1994 and 2004. Severe ESHF was defined as poor cardiac function, with a shortening fraction of less than 20%, New York Heart Association function class IV, and receipt of intravenous inotropic agents. Children were included even if they became unsuitable for transplant due to an evolving contraindication or recovery. They were excluded if they had less severe heart failure, if they had ESHF due to congenital heart disease (including postoperative patients), if they were younger than one year old, or if they had a known contraindication for transplant before admission. Their demographics (age,
weight, highest inotrope score, mechanical ventilation, cardiac arrhythmias, and cardiac arrest) were compared, and the authors concluded that there was no evidence that the case-mix changed between the two eras. The mean follow-up was 4.39 years, with an interquartile range of 1.83 to 5.74 years.

Monetary benefit and utility valuations:
An expert panel consisting of two child psychologists and one specialist doctor estimated the utility values based on the Health Utilities Index 2.

Measure of benefit:
The primary measures of benefit were the quality-adjusted life-year (QALY) and the life-year gained (LYG). The discount rate was 3.5%.

Cost data:
The cost categories included ECMO support, ECMO assessment, assessment only, ICU stay, ward stay, and transport. The costs were based on a review of patients treated between 2004 and 2006. They were reported in UK pounds sterling (£) and discounted at a rate of 3.5%.

Analysis of uncertainty:
One-way sensitivity analyses were performed on QALY weights, costs, and the long-term survival rate for transplant recipients.

Results
The five-year survival for ESHF patients was 47.06% pre-ECMO and 87.42% post-ECMO (hazard ratio 0.181, 95% CI 0.067 to 0.489). Pre-ECMO the average life expectancy was 6.78 years and it was 9.79 years post-ECMO. Patients had an average of 5.01 QALYs pre-ECMO and 7.50 QALYs post-ECMO. The average treatment cost was £146,398 per patient pre-ECMO and £309,599 per patient post-ECMO.

The incremental cost-effectiveness ratio (ICER) was £65,645 per QALY and £54,284 per LYG.

The sensitivity analysis indicated that the ICER was sensitive to ECMO cost; at £6,000 for ECMO support per day (baseline estimate £10,539) the ICER was £48,407 per QALY and at £12,000 for ECMO support per day, the ICER was £71,191 per QALY. It was sensitive to the annual probability of death after transplant; at 2% (baseline 5%) the ICER was £46,457 per QALY and at 8% the ICER was £94,805 per QALY. It was also sensitive to the quality of life in transplant recipients; at a utility value of 0.65 (baseline 0.76) the ICER was £83,197 per QALY and at 0.87, the ICER was £54,208 per QALY.

Authors’ conclusions
The authors concluded that ECMO bridging was highly effective, but expensive and did not fall within the conventionally applied criteria for cost-effectiveness. Cost-effectiveness could be optimised by increasing the availability of organ donors, reducing the mechanical support costs possibly using alternate devices, and including those patients most likely to benefit.

CRD commentary
Interventions:
The interventions were well described and were relevant to the secondary care setting.

Effectiveness/benefits:
The effectiveness of ECMO was well reported and the methodology used to estimate the effectiveness was clearly described. The authors acknowledged that the effectiveness data were based on a small, non-randomised study, and that some conventional treatment changes occurred during the study. The estimation of the utility valuations was well reported, but it was based on expert opinion rather than a questionnaire designed for the purpose. Both the survival rate for transplant recipients and the utility valuations were explored in the analysis of uncertainty.

Costs:
The costs were relevant to the perspective taken. The unit costs and resource use data were well reported.

**Analysis and results:**
The use of a Markov model was appropriate for the disease. The methodology was well reported, except the methods used to extrapolate the survival after the last point where real patient data were available, which were not reported. The model structure was presented in a diagram along with all the relevant details and modelling assumptions. The authors conducted an incremental analysis and the results were adequately presented. The sensitivity analysis appears to have been limited to one-way, while a multi-way or a probabilistic sensitivity analysis would have been more appropriate to account for uncertainty.

**Concluding remarks:**
The quality of the study was generally good. Despite some minor limitations, the authors presented a reasonably transparent analysis and it is likely that the results reflected the available evidence.

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