Economic evaluation of a randomized clinical trial of haemodilution with cell salvage in aortic surgery


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
Two blood transfusion techniques were evaluated, homologous (allogenic) versus autologous transfusion. Homologous transfusion was performed using a combination of acute normovolaemic haemodilution and intraoperative cell salvage.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing elective infrarenal aortic reconstruction, who were aged between 30 and 85 years, and had a haemoglobin concentration of greater than 11 g/dL and a platelet count of more than 150,000/L. The exclusion criteria were myocardial infarction in the last 6 months, severe angina (according to the American Heart Society), myocardial ischaemia on resting electrocardiography, and aortic stenosis. Also, a left ventricular ejection fraction of less than 40%, a preoperative creatinine level of greater than 200 mmol/L, or an aspartate aminotransferase level of greater than 100 units/L. Further exclusion criteria were patient refusal of homologous blood, haematological disorders excluding either transfusion technique, or severe pulmonary disease.

Setting
The setting was secondary care. The economic study was conducted in eight hospitals in Northwest England, UK.

Dates to which data relate
The effectiveness and resource use data were gathered between July 1997 and December 1999. The costs were estimated in the financial year 1999 - 2000.

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

Link between effectiveness and cost data
The costing was performed prospectively on the same patients as those used in the effectiveness study.

Study sample
Power calculations were performed on the basis of an audit of transfusion practice in South Manchester University Hospital. These suggested that 70 patients in each group were required to show a statistical significant difference in
exposure to allogenic blood (80% power; 5% level of significance). During 30 months, 197 patients were screened for inclusion in the study. Of these, 52 were excluded, mainly due to their ineligibility (only 4 out of 52 refused to participate). The final sample comprised 145 patients, 71 in the homologous group and 74 in the autologous group. The median age was 69 years (interquartile range, IQR: 62 - 74) in the homologous group and 72 years (IQR: 62 - 77) in the autologous group. There were 60 men in the homologous group and 56 in the autologous group.

Study design
This was a prospective, multicentre, single-blind randomised trial, which was conducted in eight hospitals in the UK. A central computer randomised and allocated the patients to the study groups. The allocation was stratified using minimisation for hospital, occlusive or aneurismal aortic disease, antiplatelet or anticoagulant drugs, and estimated blood volume. The patients were followed from operation until hospital discharge. The loss to follow-up was not reported. The patients were blinded to the transfusion approach, but it was impossible to blind the clinicians and researchers. To avoid assessment bias, a physician independent of the research team decided whether to give homologous transfusion, based on a rigid protocol.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary outcomes used in the analysis were blood loss during the operation, the units of blood received, theatre time, mortality, complications, length of hospital stay, and the need for intensive care. The study groups were comparable at baseline, although those in the autologous group were significantly older and those in the homologous group had slightly higher mean preoperative haemoglobin concentrations. Multiple regression tests were conducted to assess the impact of baseline prognostic factors.

Effectiveness results
The median blood loss during operation was 1,000 mL (IQR: 688 - 1,734) in the homologous group and 921 mL (IQR: 661 - 1,374) in the autologous group, (p=0.37).

The median number of units of blood received was 2 (IQR: 0 - 4) in the homologous group and 0 (IQR: 0 - 2) in the autologous group, (p=0.008).

The median theatre time was 205 minutes (IQR: 170 - 231) in the homologous group versus 195 minutes (IQR: 162 - 238) in the autologous group, (p=0.86).

The median length of hospital stay was 9 days (IQR: 7 - 12) in the homologous group versus 10 days (IQR: 8 - 13) in the autologous group, (p=0.17).

There were no statistically significant differences in the need for intensive care, mortality (11 versus 13 deaths), or complications (46% versus 43%).

Multiple linear regressions confirmed the influence of the transfusion strategy, hospitals with median blood loss more than 1,000 mL, low blood volume, and low preoperative haemoglobin on volume transfused.

Clinical conclusions
The results of the effectiveness study revealed that the two transfusion approaches were equivalent.

Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic analysis because the two interventions were shown to be comparable in terms of the health outcomes. Therefore, a cost-minimisation analysis was conducted.
**Direct costs**
Discounting was not performed, which was appropriate since the costing was carried out in a short time horizon. The unit costs were not reported separately from the quantities of resources used. The costs considered in the analysis were grouped into the categories of theatre, transfusion, intensive care, ward stay, and complications. The perspective of the study was that of the NHS. Resource use was estimated from the data for the patients in the ATIS trial from July 1997 to December 1999. The theatre costs were estimated on the basis of the duration of each procedure. The hospital costs were derived from the finance departments of each participating hospital. The costs of complications were estimated from SMUTH finance department, while drug costs were obtained from the British National Formulary. Other costs came from suppliers’ list prices. Cell salvage devices were assumed to have a capital lifespan of 8 years, thus an annual discount rate of 6% was applied. The costs were estimated in the financial year 1999 - 2000. It was assumed that small vascular units would perform approximately 20 annual operations, average sized units would perform about 50 annual operations, and large units would perform 150 operations per annum.

**Statistical analysis of costs**
A bias-corrected bootstrap analysis was used since the cost data were not distributed normally. The costs were presented as mean values with 95% confidence intervals (95% CIs). The total costs estimated in the analysis were compared statistically.

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

**Currency**
UK pounds sterling (£).

**Sensitivity analysis**
Sensitivity analyses were carried out to ensure the generalisability of the results. The impact of different levels of activity and different cell salvage devices was assessed. The type of analysis was not reported.

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

**Cost results**
The mean cost of treatment was 5,859 in the homologous group and 5,384 in the autologous group. The difference of -745 (95% CI: -2,247 - 1,052) did not reach statistical significance. The main cost drivers were intensive care and ward stay. The variations explored in the sensitivity analysis did not affect the estimated cost difference.

**Synthesis of costs and benefits**
Not relevant as a cost-minimisation analysis was conducted.

**Authors' conclusions**
Autologous and homologous transfusions were similarly effective and costly from the perspective of the NHS.

**CRD COMMENTARY - Selection of comparators**
The authors stated that homologous transfusion was a standard approach, but the NHS Executive in the UK recommended the implementation of autologous transfusion, in particular by cell salvage. Intraoperative cell salvage is widely used in the USA and its combination with acute normovolaemic haemodilution may offer several advantages.
Validity of estimate of measure of effectiveness
The study design was appropriate for the study question. The randomisation and sample selection methods were described. Power calculations were conducted to determine the appropriate sample size. Regression analyses were conducted to identify potential confounding factors because the study groups were not perfectly balanced at baseline. These issues tend to enhance the internal validity of the analysis. Double-blinding was not feasible, thus only the patients were unaware of their allocation to the transfusion technique.

Validity of estimate of measure of benefit
No summary benefit measure was used in the economic analysis and the health outcomes were equivalent. The analysis was therefore categorised as a cost-minimisation study.

Validity of estimate of costs
The authors explicitly stated the perspective of the study. It appears that all the relevant categories of costs have been included in the analysis. However, the unit costs and the quantities of resources used were not analysed separately. A detailed breakdown of the costs was not provided since the costs were grouped into five main categories. The source of the cost data was reported. The authors adopted a stochastic approach to deal with the non-normal distribution of the costs. The dates during which the cost data were gathered were reported. The authors stated that more than 1,000 patients should have been recruited to find statistically significant differences in the total costs.

Other issues
The authors compared their findings with those from other studies. Sensitivity analyses were conducted to address the issue of the generalisability of their results to other settings. Three types of medical centres, classified according to the number of operations performed, were considered. The authors noted that the low recruitment rate observed in the ATIS trial could limit the validity of the analysis. The study referred to patients undergoing elective infrarenal aortic reconstruction and this was reflected in the conclusions of the analysis.

Implications of the study
The main implication of the analysis was that, due to the economic and clinical equivalence of the two transfusion techniques, the "choice of transfusion strategy should be made exclusively on the basis of optimal clinical care".

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