Cost analysis of different volume replacement strategies in anesthesia

Boldt J, Suttner S, Kamle B, Huttner I

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
Three volume replacement strategies were compared in patients undergoing major abdominal surgery:

- 6% low-molecular weight hydroxyethyl starch (HES 70);
- 6% medium-molecular weight hydroxyethyl starch (HES 200); and
- 3% modified fluid gelatin.

Volume replacement was administered peri-operatively until the first post-operative morning if mean arterial blood pressure (MAP) was less than 60 mm Hg and to maintain central venous pressure (CVP) at 10 to 14 mm Hg. In addition, Ringer's solution was administered to compensate for fluid loss via perspiration, gastric tubes, extensive urinary output, or as solvent for drugs such as antibiotics. For each hour of surgery, 500-800 ml of crystalloids were infused. Packed red blood cells (PRBC) were administered when haemoglobin was less than 9g/dl, and fresh frozen plasma (FFP) was given to maintain adequate haemostasis (when activated partial thromboplastin time longer than 70 seconds, fibrinogen less than 2g/L, antithrombin III less than 50%). Platelet concentrates were infused when platelet count was less than 30x10^9/L. Induction and maintenance of anaesthesia were standardised in all patients. Following surgery, patients were transferred to either an intensive care unit (ICU) or to an intermediate care unit and treated with standardised protocols. When patients in ICU required ventilation, propofol and/or sufentanil were given until extubation. Dopamine was given when MAP was less than 60 mm Hg even if CVP was greater than 10 mm Hg. Epinephrine was used when MAP remained low (less than 60 mm Hg) despite dopamine administration and volume replacement.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients undergoing major abdominal surgery.

Setting
The setting was hospital. The economic study was carried out in Germany.

Dates to which data relate
The dates relating to derivation of effectiveness, resource use and cost data were not stated.

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

**Link between effectiveness and cost data**
The cost analysis appears to have been undertaken prospectively, based on the same sample of patients used for the effectiveness analysis.

**Study sample**
Calculation of sample size was not described. Fifty patients were recruited per group. The percentages of participants who refused to participate or who were excluded were not reported.

The mean +/- sd age in years for each group was as follows:

- HES70, 63 +/-10 (range: 39 - 80);
- HES200, 59 +/-13 (range: 35 - 77);
- gelatin, 61 +/-11 (range: 31 - 77).

The mean +/- sd weight in kg for each group was as follows:

- HES70, 76.5 +/-14.7;
- HES200, 72.2 +/-12.3;
- gelatin, 74.6 +/-13.3.

The respective numbers of male/female patients in each group were as follows:

- HES70, 22/28;
- HES200, 26/24;
- gelatin, 24/26.

The types of surgery undertaken included the following: resection of sigmoid colon; resection of rectum; gastrectomy; Whipple's procedure; oesophageal surgery; resection of pancreas; resection of liver. The rates for each type of procedure were similar across the three treatment groups.

Haemodynamic data (mean arterial blood pressure and central venous pressure) and laboratory data (haemoglobin, activated partial thromboplastin time, fibrinogen, plasma creatinine, cholinesterase, and arterial blood gases) were similar across the groups.

The initial sample recruited appeared to be appropriate to the study question.

**Study design**
The study was a single-centre randomised controlled trial with three arms. The unit of randomisation was the patient; the exact method of randomisation was not stated. Volume replacement was prescribed by physicians who were not blinded to the type of infusion, but who were not aware of the aim of the study. The duration of follow-up and loss to follow-up were not reported.

**Analysis of effectiveness**
The following outcomes were assessed: duration of surgery, duration of anaesthesia, number of patients admitted to...
ICU, duration of stay on ICU, number of ventilated patients, duration of ventilation, numbers of patients requiring dopamine or epinephrine, and survival during and after the study period.

In addition, the following were assessed at the end of surgery, four hours after surgery, and during the first post-operative day: haemodynamic data (mean arterial blood pressure, central venous pressure), degree of haemodilution (haemoglobin), coagulation (activated partial thromboplastin time, fibrinogen), renal function (plasma creatinine), liver function (cholinesterase), pulmonary function (arterial blood gases), intravenous intake (colloids, crystalloids, PRBC, FFP), blood loss, and urinary output.

Student’s t-test and chi-square test were used where appropriate to compare differences in patient characteristics and peri-operative data. Two-factorial analyses of variance (ANOVA) for repeated measurements including Scheffe’s test were used to compare courses of haemodynamic and laboratory data. Differences were considered as statistically significant when p<0.05. It was not stated whether the analysis was based on intention to treat. The treatment groups appeared to be comparable at baseline.

**Effectiveness results**

The effectiveness results were as follows:

The mean +/-sd duration in minutes of surgery for each group was as follows: HES70, 190 +/-77; HES200, 200 +/-89; gelatin70, 194 +/-78.

The mean +/-sd duration in minutes of anaesthesia was: HES70, 256 +/-84; HES200, 258 +/-92; gelatin70, 248 +/- 79.

The numbers of patients admitted to ICU were: HES70, 45; HES200, 43; gelatin 42.

The duration of stay on ICU in days was: HES70, 3 +/-1; HES200, 3 +/-2; gelatin70, 4 +/-2.

The number of ventilated patients was: HES70, 22; HES200, 24; gelatin, 23.

The duration of ventilation whilst on ICU in minutes was: HES70, 656 +/-223; HES200, 602 +/-267; gelatin70, 670 +/-301.

The respective numbers of patients requiring dopamine/epinephrine were: HES70, 4/2; HES200, 3/1; gelatin, 6/3.

All patients survived the study period. The number of patients surviving after the study period were: HES70, 49; HES200, 48; gelatin, 49.

Outcomes relating to haemodynamic data (mean arterial blood pressure and central venous pressure) and laboratory data (haemoglobin, activated partial thromboplastin time, fibrinogen, plasma creatinine, cholinesterase, and arterial blood gases), were similar across the groups at all time points.

Blood loss, urinary output, amount of infused crystalloids, PRBC, and FFP were similar across the groups.

The mean +/- sd cumulative quantity of HES70 infused by the first post-operative day was 2,130mls +/-460; for HES200, 1,680mls +/-430; and for gelatin, 2,590mls +/-500, (p<0.05 for HES70 versus gelatin, HES200 versus gelatin, and HES70 versus HES 200).

There were no statistically significant differences between groups for any outcome.

**Clinical conclusions**

Clinical outcomes were similar for all three volume replacement strategies.

**Measure of benefits used in the economic analysis**
A cost-minimisation analysis was performed. The clinical outcomes were not aggregated to generate a measure of health benefit.

**Direct costs**
Drug acquisition costs were obtained from the hospital’s pharmacy list. Costs and quantities were reported separately. Discounting was not mentioned, but is unlikely to have been relevant due to the short study duration. Average costs were reported. The dates to which the price data refer were not specified.

**Statistical analysis of costs**
The Mann-Whitney U test was used for comparison of costs. Differences were considered as statistically significant when p<0.05. Costs were reported as average point estimates per patient and per treatment arm.

**Indirect Costs**
Indirect costs were not included in the analysis.

**Currency**
The cost results were reported in EUROS and US dollars only.

**Sensitivity analysis**
No sensitivity analysis was carried out.

**Estimated benefits used in the economic analysis**
See effectiveness results above.

**Cost results**
The cost of colloids per patient were as follows:

- HES70, EUR32.71, $37.20;
- HES200, EUR 18.52, $21.07; and
- gelatin, EUR17.01, $19.36,

(p<0.05 HES 70 versus HES 200 and HES 70 versus gelatin).

There were no statistically significant differences between treatment groups for costs of crystalloids, FFP, PRBC, or disposables (infusion lines and blood filters).

The total costs per patient, taking into account costs of colloids, crystalloids, FFP, PRBC, and disposables, were as follows:

- HES70, EUR118.25, $134.45;
- HES200, EUR99.66, $113.35;
- gelatin, EUR98.57, $112.06,

(p<0.05 HES 70 versus HES 200 and HES 70 versus gelatin).
Costs for each item were also presented per treatment group.

**Synthesis of costs and benefits**
A synthesis of costs and benefits was not presented.

**Authors' conclusions**
The type of fluid used for volume replacement continues to be debated. From the economic point of view, the use of gelatin offers no advantage compared to the use of HES 200/0.5. Using HES 70/0.5 for volume therapy may result in increased costs.

**CRD COMMENTARY - Selection of comparators**
The authors did not explain or justify the choice of comparators in the study.

**Validity of estimate of measure of effectiveness**
The analysis was based on a randomised controlled trial, an appropriate design for the study question. The study sample appears to have been representative of the study population, and the three groups appeared to be comparable at baseline. More details relating to the method of randomisation used, blinding, and follow-up of patients would have been useful.

**Validity of estimate of measure of benefit**
Analysis of the effectiveness data showed that the three volume replacement strategies were equivalent. Therefore the economic analysis included costs only (cost-minimisation analysis).

**Validity of estimate of costs**
Costs such as nursing care were not taken into account. Costs and quantities were reported separately and a statistical analysis of quantities was performed, but no sensitivity analysis of quantities was conducted. Prices were derived from the authors' setting. A statistical analysis of prices was undertaken, per patient and per treatment group, for each volume replacement strategy. The authors converted the original currency, German marks, into Euros and US dollars. Since all costs were incurred within a one-year period, discounting was not necessary. The date to which prices relate was not reported.

**Other issues**
The authors compared their study with others, but only in terms of the possible alterations in coagulation associated with use of HES solutions. The issue of generalisability to other settings was not addressed. The authors did not present their results selectively, and their conclusions reflected the scope of the analysis. The cost analysis was based on comparison of the acquisition costs of substances. The study authors acknowledged that this approach may be too simplistic.

**Implications of the study**
Implications for clinical practice/policy (paraphrase of authors’ remarks):

Since the adverse effect profiles of the substances studied appear to be similar, the choice of colloid in patients undergoing major abdominal surgery may be based on cost. Volume replacement using HES 70 resulted in the highest costs. Although acquisition costs for HES 200 were higher than for gelatin, total costs for volume replacement between these two groups were similar. Greater amounts of gelatin than HES 200 were necessary due to the limited volume-supporting capacity and intravascular persistence of gelatin, subsequently compensating for the advantage of lower acquisition costs of gelatin. Conflicting data on economics arise because acquisition costs of fluids for volume
replacement vary widely between countries, areas, and even hospitals. Thus, it appears to be important to take other aspects into consideration when comparing different volume replacement regimens, e.g., use of other fluids, need for repeated doses, and use of allogeneic blood.

Implications for further research:

The authors state that comparison of the acquisition costs of volume replacement solutions is too simplistic. This would appear to imply that further, more rigorous cost-effectiveness analyses would be welcome.

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