Reduction in costs, blood products, and operating time in patients undergoing open-heart surgery

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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.

Health technology
The health technology studied was the use of serine protease inhibitor (aprotinin) at half dose during open-heart surgery compared to use at full dose and no use.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population consisted of patients undergoing open-heart surgery (89 men, 44 women, mean age 67.4 years).

Setting
The setting was secondary care. The economic evaluation was carried out at the St Charles Medical Center, Bend, OR, USA.

Dates to which data relate
The effectiveness evidence and resource use dates related to the period between April 1994 and January 1995. The price year was not specified.

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

Link between effectiveness and cost data
The costing was carried out on the same patient sample as that used in the effectiveness analysis and was based on patient or third party payer charges.

Study sample
A total of 133 patients (89 men, 44 women, mean age 67.4 years) undergoing open-heart surgery were included in the study. Power calculations around sample size were not reported. 52 patients (31 coronary artery bypass, 9 single-valve replacements, 4 combined coronary bypass-valve replacements, and 8 repeated open heart operations) received no aprotinin. 50 patients (15 coronary artery bypass, 10 single-valve replacements, 10 combined coronary bypass-valve replacements, and 15 repeated open heart operations) received a full-dose regimen of aprotinin. 31 patients (10 coronary artery bypass, 6 single-valve replacements, 5 combined coronary bypass-valve replacements, and 10 repeated
open heart operations) received a half-dose regimen of aprotinin. No subjects were reported to have refused to participate or to have been excluded from the study.

**Study design**
This was a single-centre prospective unmasked study in which patients in 3 consecutive groups undergoing open heart surgery were allocated to receive no aprotinin, full-dose aprotinin, or half-dose aprotinin. The duration of follow-up seems to have been the length of the operation.

Cardiopulmonary bypass was initiated through ascending aortic cannulation and 2-stage right atrial cannulation. Core temperature was reduced to 28-30 degrees C. All first time and repeated coronary bypass operations were performed by using intermittent aortic cross-clamping combined with intermittent fibrillatory arrest for performance of distal anastomosis, and by placement of partial aortic clamp on a beating heart for performance of proximal anastomosis. All valve and combined coronary bypass valve replacement operations were performed with either cold antegrade cardioplegia or a combination of combined antegrade and retrograde cardioplegia. Heparin sodium loading dose prior to cannulation was 300 USP U/kg, and heparin was administered to maintain an activated clotting time of greater than 480 seconds. If aprotinin was used an additional 5000 U of heparin sodium was administered every hour. Activated clotting time was measured with an automated coagulation timer (Medtronic Hemotec INC, Minneapolis, Minn). Indications for administration of blood products were an intraoperative haematocrit of less than 0.21. Administration of platelets, fresh frozen plasma, and cryoprecipitate were based on clinical scenario, coagulation studies and the judgement of the attending surgeon. Intraoperative salvage of shed mediastinal blood (Cell Salver-5, Haemonetics Corp, Braintree, MA) was performed for all cases with the exception of primary coronary artery bypass grafting.

**Analysis of effectiveness**
The main outcomes of the analysis were the total blood products administered during hospitalisation and closure time required in the operating room. Operating room closure time was defined as the time (in minutes) between final discontinuation from cardiopulmonary bypass to complete skin closure.

There was a significant difference (p<0.05) in age distribution between the 3 groups, with the no-dose group being younger (63.0 +/-5.3 years) than the full-dose (68.5 +/-3.2 years) and half-dose (70.7 +/-4.5 years) groups. The patients in the three studied groups varied in respect to the type of surgery.

**Effectiveness results**
The effectiveness results were as follows:

Operating room closure time was significantly reduced in the full-dose (59.2 +/-10.9 minutes) and half-dose (57.1 +/-13.0 minutes) groups compared with the no-dose (74.1 +/-12.2 minutes) aprotinin group (p<0.05).

The mean +/-SD quantities of blood products administered for full-dose, half-dose and no-dose aprotinin were as follows:

For red blood cells (U)

full dose aprotinin: 1.4 +/-0.03;

half-dose aprotinin: 1.0 +/-1.9; and

no-dose aprotinin: 3.1 +/-3.7, (p<0.05).

For platelets (U)

full dose aprotinin: 0.51 +/-1.20;

half-dose aprotinin: 0.19 +/-0.40; and
no-dose aprotinin: 5.00+/-6.10, (p<0.05).

For fresh frozen plasma (U)

full dose aprotinin: 0.44+/-1.20;

half-dose aprotinin: 0.13+/-0.50; and

no-dose aprotinin: 1.77+/-2.70, (p<0.05).

For cryoprecipitate (U)

full dose aprotinin: 0.0+/-0.0;

half-dose aprotinin: 0.0+/-0.0; and

no-dose aprotinin: 1.92+/-5.60, (p<0.05).

There were no deaths in any of the groups. Two patients in the no-aprotinin group required temporary postoperative dialysis, whereas one patient in the full-dose group and none in the half-dose group required dialysis (not significant). There were 4 strokes in the group receiving no aprotinin compared with none in the full-dose and half-dose aprotinin groups (p<0.05).

Clinical conclusions
Treatment with full-dose and half-dose aprotinin significantly reduced the administration of all types of blood products.

Measure of benefits used in the economic analysis
No measure of benefits was employed. The cost consequences of the different alternatives were analysed.

Direct costs
Direct costs included the cost of aprotinin and the cost of blood products received. The cost of operating room time was not included in the calculations. The perspective of the analysis was patient and third-party payer. Some quantities were reported separately from costs. The source of unit prices was not specified. Discounting was appropriately not conducted due to the time horizon of the study. The price year was not specified.

Statistical analysis of costs
Statistical analysis between groups was performed using 1-way analysis of variance, and p<0.05 was considered significant.

Indirect Costs
No indirect costs were included in the analysis.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analyses were carried out.
Estimated benefits used in the economic analysis
Not relevant.

Cost results
Mean total costs +/- SD were as follows: full-dose group, $1,193 +/- $303; half-dose group, $668 +/- $372; and no-dose group $949 +/- $303 respectively. Total costs were significantly reduced only in the half-dose aprotinin group, (p<0.05).

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
Use of aprotinin at half dose resulted in a significant reduction in costs, blood product use, and operating room closure time in patients undergoing open-heart surgery.

CRD COMMENTARY - Selection of comparators
A justification was given for the interventions studied as possible interventions during open-heart surgery.

Validity of estimate of measure of effectiveness
The effectiveness data was based on a single centre prospective study. As the authors acknowledged, the validity of the results could have been variable due to the non-randomised character of the study, the small number of patients, the variability of patients in their distribution of types and numbers of operative procedures, and the fact that, while the procedures in the full-dose and half-dose aprotinin groups were performed by a single surgeon, the procedures in the no-dose group were performed by different surgeons.

Validity of estimate of measure of benefit
The authors did not derive a measure of health benefit. The analysis was therefore categorised as a cost-consequences study.

Validity of estimate of costs
The costs were analysed from the perspective of third party payer and the patient. Costs and quantities were not reported separately. Sensitivity analyses on resource use and prices were not conducted. Charges were used to proxy costs and this could have introduced an error in the analysis. Some possibly relevant costs have been excluded from the analysis (i.e. the cost of operating room time, postoperative dialysis and stroke treatments).

Other issues
The authors did not present their results selectively. The authors compared their findings with those from other studies. The generalisability to other settings was addressed and the variability of costs between regions was acknowledged as a possible limitation to the generalisability of study results. The authors reported a number of limitations of the study design and acknowledged the small number of patients analysed.

Implications of the study
The authors suggested that the use of half-dose aprotinin in a community-based open heart surgery centre was more cost-effective and as efficacious as a full-dose regimen and was more cost-effective than avoidance of aprotinin use given the comparative costs of blood products.
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None stated.

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Other publications of related interest

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