
Comparison of efficacy, safety, and cost of low-molecular-weight heparin with continuous-infusion unfractionated heparin for initiation of anticoagulation after mechanical prosthetic valve implantation

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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 use of low molecular weight heparin (LMWH) as anticoagulant treatment in patients undergoing mechanical prosthetic heart valve implantation. Anticoagulation consisted of enoxaparin 1 mg/kg, rounded down to 49, 60, 80 or 100 mg, and administered subcutaneously at 12-hour intervals.

Type of intervention

Treatment.

Economic study type

Cost-effectiveness analysis.

Study population

The study population comprised patients who were undergoing mechanical prosthetic heart valve implantation. Further inclusion or exclusion criteria were not reported.

Setting

The setting was a hospital. The economic study was conducted in the USA.

Dates to which data relate

The effectiveness and resource use data were gathered from June 1999 to November 2000. The price year was not reported.

Source of effectiveness data

The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data

The costing was conducted prospectively on the same sample of patients as that used in the effectiveness analysis.

Study sample

Power calculations were not reported. A sample of 63 patients was considered in the study. First, 29 patients receiving LMWH at the authors' hospital was identified. Second, 34 control patients receiving UFH were matched to LMWH patients through the hospital's computer system. The mean age was 52.9 (+/- 14.6) years in the LMWH group and 58.7 (+/- 12.6) years in the UFH group. The LMWH group comprised 21 men and 8 women, while the UFH group comprised 14 men and 20 women. It was not stated whether some patients refused to participate or were excluded for

any reason from the initial study sample.

Study design

This was a prospective cohort study that was carried out at a single centre, the Brigham and Women's Hospital in Boston (MA). Both treatments were discontinued after two consecutive therapeutic INRs were achieved. The patients were followed for potential complications at 1-, 2- and 3-month intervals, either by telephone or through scheduled office visits. The length of follow-up was unclear but it could have been 90 days post-discharge. No patient was lost to the follow-up assessment.

Analysis of effectiveness

All the patients included in the initial study sample were accounted for in the analysis of effectiveness. The primary outcome measures used were:

the rates of death within 90 days of discharge,

thromboembolic events,

bleeding events, and

all readmissions within 30 days.

Other outcomes related to postoperative anticoagulation were also assessed:

the time from surgery to initiation of parenteral anticoagulation,

the duration of parenteral anticoagulation,

the outpatient days,

the total daily dose,

the time from surgery to first warfarin dose,

initial warfarin dose,

daily warfarin dose,

the number of warfarin doses before hospital discharge,

the discharge INR value,

the length of stay, and

the postoperative length of stay.

The study groups were generally comparable at baseline in terms of their demographics and clinical characteristics. The exception was gender distribution, for which there were significantly more women in the UFH group.

Effectiveness results

The rate of death within 90 days of discharge was 4% in the LMWH group and 12% in the UFH group.

The rates of thromboembolic events were 0% (LMWH) and 6% (UFH), respectively.

The rates of bleeding events were 10% (LMWH) and 9% (UFH), respectively.

The rates of all readmissions within 30 days were 17% (LMWH) and 12% (UFH), respectively.

The differences in the outcome measures did not reach the statistical significance.

The postoperative anticoagulation outcomes were quite similar.

However, differences in the following outcomes were observed:

the mean total daily dose was 120 (+/- 37) mg in the LMWH group versus 17,112 (+/- 5,688) U in the UFH group;

the time from surgery to first warfarin dose was 1.5 (+/- 1) days in the LMWH group versus 2.6 (+/- 2.4) days in the UFH group, (p=0.03);

the number of warfarin doses before hospital discharge was 5.3 (+/- 2.5) in the LMWH group versus 10.2 (+/- 6.8) in the UFH group, (p<0.0001);

the mean discharge INR value was 1.5 (+/- 0.2) in the LMWH group versus 2.4 (+/- 0.61) in the UFH group, (p<0.0001);

the mean length of stay was 7.8 (+/- 4) days in the LMWH group versus 18.1 (+/- 11.6) days in the UFH group, (p<0.0001); and

the mean postoperative length of stay was 6.6 (+/- 2.4) days in the LMWH group versus 15.9 (+/- 10.7) days in the UFH group, (p<0.0001).

Clinical conclusions

The effectiveness study showed that the efficacy and safety outcomes were comparable between the groups. The length of postoperative stay was significantly longer for the UFH patients.

Measure of benefits used in the economic analysis

No summary benefit measure was used in the economic analysis because the two interventions were equivalent in terms of safety and efficacy. In effect, a cost-minimisation analysis was conducted.

Direct costs

Discounting was not relevant since the costs were incurred during a timeframe shorter than 2 years. The unit costs were not presented separately from the quantities of resources used. Only hospitalisation costs were included in the economic evaluation. The health services considered were emergency department care, operating room use, hospital room and board, hospital-based physicians' fees, nursing labour, dialysis, clinical laboratory studies, radiology, ancillary services, medications, diagnostic procedures and diagnostic testing. Clinical laboratory studies covered haematology, microbiology, cytology, urinalysis, INR and activated partial thromboplastin time. Radiology covered magnetic resonance imaging, computer axial tomography and ultrasound imaging. Ancillary services were nutrition support and respiratory, occupational and physical therapy services. The diagnostic procedures were cardiac catheterisation, electrophysiological testing, endoscopy, vascular ultrasound and pathology. Diagnostic testing covered the electrocardiogram, electroencephalogram and electromyography.

The cost/resource boundary of the study was that of the hospital. Resource use was estimated using actual patient-level data, which were derived from the sample of patients included in the effectiveness study. The authors separated preoperative and operating room costs from postoperative costs in order to calculate the mean cost per postoperative hospital day. The costs presumably came from the hospital finance department, although this was not explicitly stated. The price year was not reported.

Statistical analysis of costs

The unpaired Student's t-test was used to test the statistical significance of differences in the estimated costs.

Indirect Costs

The indirect costs were not considered.

Currency

US dollars (\$).

Sensitivity analysis

Sensitivity analyses were not conducted.

Estimated benefits used in the economic analysis

See the 'Effectiveness Results' section.

Cost results

The postoperative cost per patient was lower in the LMWH group (\$10,691 +/- 7,300) than in the UFH group (\$30,214 +/- 26,617), (p=0.0003). However, the mean postoperative cost per day was not significantly different between the groups (\$1,526 +/- 737 versus \$1,825 +/- 1,266; p=0.27).

Since 112 inpatient days were saved with LMWH, the cost-savings over UFH were \$170,912, or \$5,894 per patient.

Synthesis of costs and benefits

A synthesis of the costs and benefits was not relevant since, in effect, a cost-minimisation analysis was conducted.

Authors' conclusions

The use of low molecular weight heparin (LMWH) as anticoagulation therapy in concomitance with warfarin was as effective and safe as unfractionated heparin (UFH) in the management of patients undergoing mechanical prosthetic heart valve implantation. However, the postoperative costs were far lower, mainly due to the shorter hospital stay.

CRD COMMENTARY - Selection of comparators

The rationale for the choice of the comparator was clear. UFH represented the traditional anticoagulation therapy, while LMWH was an alternative treatment. You should decide whether this is a valid comparator in your own setting.

Validity of estimate of measure of effectiveness

The analysis of effectiveness used data coming from a prospective cohort study. The use of a clinical trial would have been more appropriate for the study question, as randomisation would have reduced the potential impact of confounding factors. The study groups were quite balanced at baseline, but the gender distribution was different. Similarly, the control patients had a higher rate of concomitant surgical procedures. This could have affected the results of the analysis. The patients were identified at a single centre, which reduces the transferability of the results to other settings. It was not stated whether some patients refused to participate or were excluded from the sample of eligible patients. Therefore, it was unclear whether the study sample was representative of the study population.

The major drawback of the study was the small sample size and the lack of power calculations. In fact, none of the differences in the main outcome measures reached statistical significance. This could have been attributed to the study being underpowered. The overall length of follow-up was unclear. These issues tend to limit the internal validity of the analysis.

Validity of estimate of measure of benefit

No summary benefit measure was used in the analysis because a cost-minimisation analysis was conducted.

Validity of estimate of costs

The perspective of the study was not explicitly stated, but it appears that only costs relevant to the hospital have been included in the analysis. A detailed breakdown of the cost items was provided, but the unit costs were not presented separately from the quantities of resources used. This limits the possibility of replicating the study. Similarly, the price year was not reported, which makes reflation exercises in other settings difficult. Limited information on the source of data was provided. Statistical tests were conducted when the costs were compared. However, all the economic estimates were specific to the study setting and no sensitivity analyses were conducted.

Other issues

The authors compared their findings with those from other studies and found similar conclusions. The issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not conducted. This reduced the external validity of the analysis. The authors highlighted the advantages of LMWH over UFH (such as ease of use, better bioavailability and longer half-life), but some contraindications to the use of LMWH were also noted. Some limitations of the analysis were also stressed.

Implications of the study

The study results supported the use of LMWH in patients undergoing mechanical prosthetic heart valve implantation.

Source of funding

None stated.

Bibliographic details

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Other publications of related interest

Topol EJ, Bosker G, Casele H, et al. Anticoagulation and enoxaparin use in patients with prosthetic heart valves and/or pregnancy. *Clinical Cardiology Consensus Reports* 2002;3:1-19.

Gould MK, Dembitzer AD, Sanders GD, et al. Low-molecular-weight heparins compared with unfractionated heparin for treatment of acute deep venous thrombosis: a cost-effectiveness analysis. *Annals of Internal Medicine* 1999;130:789-99.

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