Costs and clinical outcomes associated with low-molecular-weight heparin vs unfractionated heparin for perioperative bridging in patients receiving long-term oral anticoagulant therapy

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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) during the perioperative period, as a bridging therapy, for patients who routinely receive oral anticoagulant therapy (OAT) and who need their OAT to be interrupted so that they may undergo surgery.

Type of intervention

Secondary prevention.

Economic study type

Cost-effectiveness analysis.

Study population

The study population comprised patients who:

had all received long-term OAT with intent to treat for at least 3 months for venous or arterial thromboembolic disease, atrial fibrillation, or cardiac valvular disease;

had undergone an elective surgical procedure in which UFH or LMWH therapy was used in the perioperative period;

were at least 18 years old on the date of the procedure; and

had a goal INR (international normalised ratio measure of the risk of bleeding) of 2.5 for routine intensity warfarin therapy and 3.0 for high-intensity therapy.

Patients were excluded if they had undergone an urgent or emergent surgical procedure, had experienced major bleeding within 3 months of the elective surgical procedure, or were hospitalised for a reason other than the elective surgical procedure. They were also excluded if they had severe chronic renal insufficiency, severe liver disease, or a bodyweight greater than 330 lb (150 kg).

Setting

The study took place in an integrated primary care/secondary care setting. The economic study was carried out in New Mexico, USA.

Dates to which data relate

Data were collected from 1994 to 1996 for the comparator group and between 1998 and 2000 for the intervention group. The prices were reported for the current year (with no indexation to allow for inflation during the course of the study).

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

Link between effectiveness and cost data
The cost and health outcome data were collected retrospectively and referred to the same patient groups.

Study sample
Power calculations were not reported. Patients conforming to the inclusion and exclusion criteria were selected from a review of patients' notes. There were 66 patients in all (40 in the intervention group and 26 in the comparator group). Data from all eligible patients were included in the study.

Study design
This was a retrospective comparative study with historical controls using information from a single centre. The cost data referred to the period from 10 days prior to the procedure or operation to 30 days after the procedure or operation. Outcome data referred only to the 30 days after the procedure or operation. There was no report of losses to follow-up. The data abstractors were not blinded to the treatment.

Analysis of effectiveness
The inclusion criteria ensured that only patients having treatment conforming to clinical guidelines were included in the study. These guidelines allowed for the use of OAT post procedure, in addition to LMWH, if indicated. The health outcomes were measured by the occurrence of one or more of the following adverse events:

death from any cause;

confirmed venous thromboembolic events;

confirmed pulmonary embolism;

confirmed cardiac valvular or mural thrombus;

suspected transient ischaemic attack;

confirmed peripheral arterial thromboembolic event;

a major bleed, or any bleeding resulting in a hospital visit;

other bleeding;

significant thrombocytopenia;

a 50% drop in platelet count from baseline.

A co-morbidity score based on the Charlson index was used to test for differences between the comparator and the intervention groups. The groups were reported to be similar in terms of their age, gender, indications for long-term warfarin therapy, mean INR prior to the procedure, and their Charlson score.

Effectiveness results
Forty per cent of the intervention (LMWH) group and 34.6% of the comparator (UFH) group experienced one or more adverse event. This difference was not statistically significant.

No deaths occurred in either group.

Clinical conclusions
The authors concluded that there was no difference in the overall rate of adverse events between patients receiving UFH and those receiving LMWH.

Measure of benefits used in the economic analysis
No summary measure of benefit was derived. With no difference in clinical outcomes detected, the study was, in effect, a cost-minimisation analysis.

Direct costs
The costs were classified as inpatient, outpatient and pharmacy, with outpatient costs further subdivided between primary care, specialist care, laboratory, radiology, home health, outpatient surgery, emergency, and other. The costs were derived from the charges recorded in an administrative data set. All the costs were at current prices (there was no adjustment for inflation). With costs incurred over a relatively short period of time, and no major items of capital equipment involved, discounting was not relevant to this study. The quantities of resources used were only reported for drugs. There was no discussion of whether the costs were intended to be the marginal costs of the intervention. There was no mention of the exclusion of costs common to both procedures.

Statistical analysis of costs
The costs were reported with p-values to indicate the probability that the difference between mean values for the various cost components occurred by chance. Both parametric tests (t-tests) and non-parametric tests (Wilcoxon rank sum tests) were used.

Indirect Costs
The indirect costs were not discussed or reported.

Currency
US dollars ($).

Sensitivity analysis
While there was a stochastic examination of the estimates of mean health care costs, based on the cost estimates for individual patients, no attempt was made to consider uncertainty in the way in which these costs were derived. Nor did the authors consider the possibility of uncertainty in the effectiveness outcomes obtained.

Estimated benefits used in the economic analysis
No summary measure of benefit was derived. See the 'Effectiveness Results' section.

Cost results
The total health care cost in the intervention (LMWH) group was $18,511 per person (standard error, SE=5,021).

The total health care cost in the comparator (UFH) group was $31,625 per person (SE=4,205).

Synthesis of costs and benefits
Not relevant.

Authors' conclusions
There were substantial mean total health-care cost-savings ($13,114) in favour of the low molecular weight heparin (LMWH) group.

CRD COMMENTARY - Selection of comparators
The authors reported that UFH was conventionally used in the perioperative management of high-risk patients requiring continuous anticoagulant therapy. You should consider whether this is relevant to your own setting.

Validity of estimate of measure of effectiveness
This was a retrospective comparative study with historical controls. This design does not provide the most powerful evidence for a study of this sort. With few exceptions, the study sample comprised all patients receiving long-term warfarin therapy, with preoperative heparin used as a bridge therapy, within the authors' institution between the specified dates. Thus, the sample was representative of patients treated within the institution. The patient groups were shown to be comparable at analysis. However, this type of study design fails to eliminate bias or confounding and, consequently, the internal validity of the results obtained is likely to be low. In addition, the conclusion that there was no difference in outcomes may be questioned, especially since the patient sample may have been too small to be reasonably certain that there were no differences in fatalities. The question of the power of the study was not adequately addressed.

Validity of estimate of measure of benefit
No summary measure of benefit was derived as the authors reported that equal outcomes had been achieved. The reader is referred to the comments in the 'Validity of estimate of measure of effectiveness' field (above).

Validity of estimate of costs
All the costs relative to the purchaser's perspective were included in the analysis. The unit costs were not reported, although categories (i.e. primary care, radiology, home health, etc.) and their associated costs were. It would appear that charges were used to proxy cost. However, it was unclear if any cost-to-charge ratio was applied. Discounting was not necessary because of the short time horizon (30 days). The price year was not explicitly reported. Statistical analyses of the cost data and a multivariate regression analysis were conducted. All results were presented in full.

Other issues
The issue of generalisability to other settings was not addressed. The authors presented their results in full and their conclusions reflected the scope of the analysis. Several limitations to the study were reported. These included the retrospective nature of the study design, and the different time periods in which patients underwent perioperative bridging. In addition, the costs were not standardised across the study years, and there was a lack of power to detect statistically significant differences in the adverse events.

Implications of the study
The authors suggested that the use of LMWH for patients on OAT appears sensible. However, the conclusions reached should be considered in view of the limitations highlighted in this study.

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