A prospective, randomized, controlled trial of an emergency department-based atrial fibrillation treatment strategy with low-molecular-weight heparin

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 approaches for the management of low-risk patients with newly diagnosed or new-onset atrial fibrillation (AF) were examined. The approaches were standard admission versus an accelerated emergency department (ED)-based strategy with low molecular weight heparin (dalteparin) and early cardioversion to sinus rhythm. The standard strategy consisted of patient admission for rate control, anticoagulation, exclusion of myocardial infarction (MI) and other causes, and possible cardioversion to sinus rhythm. The accelerated ED strategy was to implement rate control and anticoagulation with subsequent outpatient cardioversion, after therapeutic warfarin anticoagulation for 3 consecutive weeks according to a clinical pathway. This approach was accurately described in the article and was defined as a combined ED-outpatient-based treatment strategy.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged between 18 and 75 years, who presented to the ED with uncomplicated newly diagnosed or new-onset AF, and who had no clear indication for hospital admission other than AF and who were candidates for anticoagulation. Patients with uncontrolled hypertension, hypotension, known severe congestive heart failure with New York Heart Association class III or IV symptoms or a left ventricular ejection fraction of 35% or less, hyperthyroidism, Wolf-Parkinson-White syndrome, or hypertrophic cardiomyopathy were excluded. Also excluded were those with known moderate-to-severe valve disease, prior stroke or thromboembolism in the past year, cardiac surgery within 60 days, pregnancy, and those currently receiving therapeutic anticoagulation.

Setting
The setting was secondary care. The economic study was carried out in the USA.

Dates to which data relate
The dates when the evidence was collected were not reported. The price year was not provided.

Source of effectiveness data
The effectiveness evidence was derived from a single study.

Link between effectiveness and cost data
The costing was carried out prospectively on the same sample of patients as that used in the effectiveness study.
Study sample
Power calculations to determine the sample size were not performed. Of the 100 individuals initially identified as potentially eligible within 2 hours of presenting to the ED, 21 were found to be actually eligible and 18 were finally included in the study sample. The 3 eligible patients who were excluded from the final group refused to participate (the reasons were not reported). There were 9 patients in each group. There were 14 men and 4 women and the mean age was 48 years.

Study design
This was a prospective, randomised pilot study, which was carried out in a university hospital. Randomisation codes were assigned to 100 patients before the study. After enrolment, the patients were randomised to one of the two groups on the basis of the assigned codes. After randomisation, the pathway group received dalteparin (200 IU/kg, 18,000-unit maximum) subcutaneously, while the standard group was admitted to the hospital. Clinical follow-up was obtained through telephone contacts with both the referring physician and the patient. A chart review was also carried out. The mean follow-up was 27 days. Only one patient was lost to the follow-up assessment. The outcome evaluation was not conducted blind.

Analysis of effectiveness
It was unclear whether the analysis of the clinical study was conducted on an intention to treat basis. The health outcomes used in the study were:

- the length of stay (LOS),
- the median times to chemical or electrical cardioversion and normal sinus rhythm,
- sinus rhythm at discharge,
- AF-related complications, and
- deaths.

The study groups were comparable at baseline in terms of their clinical and demographic characteristics.

Effectiveness results
The mean LOS was 2.1 (+/- 2.3) days (range: 1 - 8) in the standard group and less than 1 day in the pathway group.

The median times to chemical or electrical cardioversion were 29.8 hours (interquartile range, IQR: 15.5 - 81.5) in the standard group and 4.8 hours (IQR: 3.8 - 8) in the pathway group, (p=0.01).

The median time to normal sinus rhythm was 15.5 hours (IQR: 5.1 - 30) in the standard group and 4.5 hours (IQR: 3.8 - 5.2) in the pathway group, (p=0.04).

The rate of patients with sinus rhythm at discharge was 88.9% in the standard group and 100% in the pathway group.

There were no AF-related complications in any of the groups. Only two hospitalisations were observed in the pathway group and these were unrelated to AF.

There were no deaths.

Clinical conclusions
The effectiveness study showed that the clinical pathway represented not only a safe alternative to standard hospitalisation for low-risk patients with AF, but also an effective strategy in terms of reduced hospital stay.
Measure of benefits used in the economic analysis
No summary benefit measure was used in the economic study. The study was therefore classified as a cost-consequences analysis.

Direct costs
Discounting was not relevant since the costs per patient were incurred during a short time. The unit costs and the quantities of resources used were not reported separately. A detailed breakdown of the cost categories was not provided, but the authors stated that the costs were a combination of inpatient stay (professional fees excluded), additional outpatient testing, and drugs. Both fixed and variable costs were included. The cost/resource boundary adopted in the study was likely to have been that of the hospital. The resource use data were estimated using actual data prospectively gathered and related to the sample of patients who were included in the effectiveness study. The costs were estimated using a cost-allocation program (Transition System Inc.). The price year was not reported.

Statistical analysis of costs
Statistical tests were carried out to test the statistical significance of the difference in costs. The mean costs were compared using Student's t test, while the median costs were compared using the Mann-Whitney Wilcoxon rank sum test.

Indirect Costs
The indirect costs were not included in the economic evaluation.

Currency
US dollars ($).

Sensitivity analysis
Sensitivity analyses were not performed.

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

Cost results
The mean costs were $1,706 (+/- 1,512) in the standard group and $879 (+/- 394) in the pathway group, (p=0.15).

The median costs were $1,112 (IQR: 948 - 1,886) in the standard group and $984 (IQR: 663 - 1,024) in the pathway group, (p=0.18).

Dalteparin accounted for 39.5% of the total costs in the pathway group.

Synthesis of costs and benefits
The costs and benefits were not combined because a cost-consequences analysis was carried out.

Authors’ conclusions
Compared with the standard care provided to low-risk patients with newly diagnosed or new-onset atrial fibrillation (AF), the clinical pathway was effective in reducing hospital stay and it showed a trend towards a reduction in the costs.
CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. Hospital care was selected as it represented the traditional approach for patients with AT presenting to the ED. You should decide whether this represents a valid comparator in your own setting.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a prospective randomised study, which was appropriate for the study question. The methods of randomisation and sample selection were reported. The study sample was likely to have been representative of the study population. As this represented a pilot study, the authors admitted that the main limitation to the internal validity of the study was the very small sample size. In fact, power calculations were not performed and there was no evidence to justify the number of patients included in the final sample. Three patients declined to participate in the trial, but their reasons for refusal were not reported. One patient was lost to follow-up. The basis of the data analysis (intention to treat versus treatment completers only) was not stated. The evidence came from a single centre. The outcome assessment was not blinded, therefore observer bias might have occurred. These issues limit the internal validity of the analysis. The study groups were comparable at baseline and this reduced the impact of confounding factors.

Validity of estimate of measure of benefit
No summary benefit measure was used in the analysis because a cost-consequences analysis was conducted.

Validity of estimate of costs
The perspective was not explicitly stated, but it appears to have been that of the hospital. Few details on the cost analysis (e.g. unit costs and price year) were provided, which makes replication of the study and refiation exercises in other settings difficult. The source of the data was reported, as was the method used to derive the costs. However, a detailed breakdown of the cost items was not given. Statistical tests were appropriately performed to compare the data estimated in the two groups. The costs were presented as mean values with standard deviations and as median values with IQRs. The authors acknowledged that the small sample size limits the power of the study to detect statistically significant differences in costs between the two groups. The cost estimates were specific to the study setting.

Other issues
The authors compared some of their findings with those from published studies. However, the issue of the generalisability of the study results to other settings was not addressed and sensitivity analyses were not performed. This reduces the external validity of the analysis. The study referred to low-risk patients with uncomplicated AF and this was reflected in the conclusions of the analysis. The authors noted some limitations of their analysis, such as the small sample size or the lack of recommendations on the safety of low molecular weight heparin in their setting.

Implications of the study
The authors suggested that further research is required to confirm the results of this pilot study, which suggests that the use of a clinical pathway for the outpatient management of uncomplicated AF in low-risk patients leads to reductions in hospital stay at potentially lower costs than the standard approach.

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