Economic analysis of intravenous plus oral amiodarone, atrial septal pacing, and both strategies to prevent atrial fibrillation after open heart surgery


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
Four alternative prophylactic strategies for preventing atrial fibrillation (AF) in patients undergoing open heart surgery were compared. The alternative strategies were amiodarone, pacing, amiodarone plus pacing, and placebo. Patients received a loading dose of amiodarone (1,050 mg intravenously) within 6 hours after surgery, followed by oral amiodarone (400 mg 3 times daily) or matching placebo on postoperative days 1 to 4. Atrial septic pacing consisted of the use of a single pacing wire and one pacemaker box. It was started within 6 hours after surgery and was continued for 96 hours.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients aged 50 years and older with coronary artery and/or valvular disease, who had been selected to undergo open heart surgery. The exclusion criteria were:

chronic AF or flutter,
known hypersensitivity to amiodarone,
current use of Class I or Class III anti-arrhythmic agents,
current use of implantable cardioverter defibrillators or implantable pacemakers,
cardiogenic shock or advanced heart failure (New York Heart Association Class IV),
marked sinus bradycardia (heart rate less than 50 beats/minute),
a history of sinus arrest or second- or third-degree atrioventricular block,
moderate to severe liver disease,
atrial pacemaker use before open heart surgery, and
current use of cyclosporine, cimetidine, phenytoin, or cholestyramine.

Setting
The setting was secondary care. The economic study was carried out at the Department of Cardiology of the Hartford
Hospital, Hartford (CT), USA.

**Dates to which data relate**
The study was conducted from July 2001 to June 2003. The price year was not reported.

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

**Link between effectiveness and cost data**
The costing was carried out retrospectively on the same patient sample as that used in the clinical study.

**Study sample**
The current paper provided limited information on the clinical study. Further details are provided in the original publication (White et al. 2003, see ‘Other Publications of Related Interest’ below for bibliographic details).

The authors did not report whether any power calculations were performed. One hundred and sixty patients were included and randomised to receive amiodarone (n=77) or matching placebo (n=83). Next, patients were randomised to atrial septic pacing or no pacing. There were 48 patients in the placebo group, 39 in the amiodarone group, 35 in the pacing group and 38 in the amiodarone plus pacing group. There was no information about the number of patients who refused to participate, or who were excluded for other reasons. The mean age of the study sample was 66 years (standard deviation, SD=8.7), 76% were men and 21% had valvular surgery. Beta-blockers were administered postoperatively to 81% of the placebo group, 74% of the amiodarone group, 86% of the pacing group and 87% of the amiodarone plus pacing group.

**Study design**
The study was a randomised, placebo-controlled clinical trial that was performed in an academic hospital. The patients were followed up for their entire hospital stay.

**Analysis of effectiveness**
The current paper provided no details of the method used for the analysis of the clinical study. The primary health outcome was the frequency of postoperative AF. The authors reported that the baseline characteristics of the four patient groups were similar.

**Effectiveness results**
The proportion of patients with postoperative AF was:

- 38% in the placebo group,
- 28% in the amiodarone group,
- 40% in the pacing group, and
- 16% in the amiodarone plus pacing group.

Significant differences were found between the placebo (with and without pacing) and amiodarone plus pacing groups, (p<0.050).

No significant differences were found between the four groups concerning the frequency of nausea, hypotension, bradycardia, stroke, myocardial infraction, or mortality, (p>0.05).
Clinical conclusions
The prophylactic strategy of amiodarone plus pacing was shown to be significantly more effective in preventing postoperative AF than placebo or pacing alone.

Measure of benefits used in the economic analysis
No summary measure of health benefit was used in the economic analysis. In effect, a cost-consequences analysis was performed.

Direct costs
The direct costs consisted of hospital costs accrued during the patient's hospitalisation. These included the cost of amiodarone under non-study circumstances (amiodarone was supplied free of charge to the study patients). Professional fees were not included. Hospital charges were converted to costs using the hospital derived departmental cost-to-charge ratios. The unit costs were not reported separately. The quantities seem to have been based on the hospital management database. Mean length of stay (LOS) on the intensive care unit (ICU) and mean total LOS in the hospital were reported for each patient group. The price year was not reported. Given the follow-up period, discounting was appropriately not performed.

Statistical analysis of costs
Descriptive statistics were used for the costs, and the mean cost per patient and SD were reported. An analysis of variance was used to compare the costs between the patient groups.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
A nonparametric bootstrap method was used to analyse the joint distribution of costs and effectiveness results. In addition, a multivariate analysis was performed to assess specific factors that predicted total hospital costs.

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

Cost results
The mean costs for the patients were:

$27,026 (SD=30,226) in the placebo group,

$22,275 (SD=17,661) in the amiodarone group,

$33,868 (SD=60,309) in the pacing group, and

$18,697 (SD=8174) in the amiodarone plus pacing group.

No significant differences in LOS and cost were found between the groups, although the quantities and costs in the
pacing group were numerically higher.

The LOS and costs were lower for patients receiving amiodarone, \( p=0.080 \), and comparable for patients receiving pacing and those without pacing.

In the multivariate linear regression model, preoperative beta-blockers and amiodarone were the only predictors for lower costs after open-heart surgery. However, the model explained only 7\% of the hospital costs.

**Synthesis of costs and benefits**

No incremental cost-effectiveness ratios (ICERs) were reported. The results obtained from the bootstrap analysis showed the probabilities of the ICER for amiodarone alone (67\%) and for amiodarone plus pacing (97\%) to be superior (lower costs and higher effects) to placebo.

**Authors' conclusions**

Amiodarone, administered either alone or in conjunction with atrial septic pacing, in addition to standard care with beta-blockers, is more cost-effective than standard care in the prevention of postoperative atrial fibrillation (AF). Additional studies are needed to validate these findings.

**CRD COMMENTARY - Selection of comparators**

The comparators chosen were justified on the basis of results from the literature, which suggested that all of the comparators had the potential to decrease hospital LOS. The alternatives were used in addition to standard care, the prophylactic administration of beta-blockers in patients undergoing open-heart surgery, which represented current practice in the authors' setting. You should decide if this standard care is a widely used health technology in your own setting.

**Validity of estimate of measure of effectiveness**

The analysis was based on a randomised clinical trial, which was appropriate for the study question. The study sample seems to have been representative of the study population, although no information on the number of patients who refused to participate was given in the current paper. The patient groups were shown to be comparable at analysis. There were no details of the method used for the analysis, or whether the study was powered to find significant differences in the clinical results. The internal validity is likely to be high, given the study design, but limited reporting makes a definite statement to this effect impossible.

**Validity of estimate of measure of benefit**

No summary measure of benefit was derived for use in the economic evaluation. The analysis was therefore categorised as a cost-consequences study.

**Validity of estimate of costs**

All the categories of costs relevant to the perspective adopted were included in the analysis. The mean costs and the quantities were reported separately, thus enhancing the reproducibility of the results. The prices were taken from the authors' setting using charges that were converted to costs. However, the price year used was not reported. The resource use quantities were derived retrospectively from the clinical study. An analysis of variance was used to compare both the costs and quantities (LOS) between patient groups. The authors acknowledged that the study was not powered to detect significant differences in the total costs between groups. A bootstrap analysis was also performed.

**Other issues**

The authors compared their results with those from other studies. The generalisability of the findings to daily practice was expected to be high, as patient management was left to the discretion of the cardiologist and surgeon. The authors
did not present their results selectively and their conclusions appear to have reflected the scope of the analysis. The authors did not explicitly report any further limitations of the study.

**Implications of the study**
The authors stated that amiodarone, alone or in conjunction with atrial septic pacing, in addition to standard care with beta-blockers, is more cost-effective than standard care in the prevention of postoperative AF. Additional studies are needed to validate these findings. Finally, an additional study is required to assess whether atrial septal pacing is an effective strategy to prevent postoperative AF.

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None stated.

**Bibliographic details**

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**Other publications of related interest**

**Indexing Status**
Subject indexing assigned by NLM

**MeSH**
Administration, Oral; Amiodarone /administration & dosage /economics /therapeutic use; Anti-Arrhythmia Agents /administration & dosage /economics /therapeutic use; Atrial Fibrillation /prevention & control; Cardiac Pacing, Artificial /economics; Cardiac Surgical Procedures; Cost-Benefit Analysis; Female; Hospitalization /economics; Humans; Injections, Intravenous; Length of Stay /economics; Male; Middle Aged; Postoperative Complications /prevention & control

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