Effect of amiodarone +/- diltiazem +/- beta blocker on frequency of atrial fibrillation, length of hospitalization, and hospital costs after coronary artery bypass grafting


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
A clinical pathway for the secondary prevention of postoperative atrial fibrillation (AF) in patients who had undergone coronary artery bypass grafting (CABG) was examined. The pathway was based on the administration of oral amiodarone, rate and rhythm control, cardioversion, and anticoagulation. Rate control, if needed, was mainly achieved with intravenous diltiazem and less often with a beta-blocker.

Type of intervention
Secondary prevention.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients who had CABG and preoperative normal sinus rhythm. Patients were excluded in cases of contraindications to amiodarone or chronic antiarrhythmic drug therapy.

Setting
The setting was a large community hospital. The economic study was carried out in the USA.

Dates to which data relate
The data on effectiveness and resource use were gathered retrospectively from January to April 1998 for the comparison group. The corresponding data for the intervention group were gathered prospectively from September 1998 to January 1999. No price year was reported.

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

Link between effectiveness and cost data
The costing was undertaken on the same patient sample as that used in the effectiveness analysis. It was carried out retrospectively for the comparison group and prospectively for the intervention group.

Study sample
Power calculations to determine the sample size were not performed. A sample of 229 consecutive eligible patients hospitalised at the study centre were included in the analysis. Of these, 127 cases were prospectively enrolled in the intervention group, and 102 cases were retrospectively selected as the historical control group. The mean age in the
intervention group was 65.3 (+/- 105) years, and 68.4% were men. The mean age in the control group was 65.4 (+/- 11.3) years, and 63.8% were men. One patient in the control group died and was excluded from the analysis.

**Study design**
This was a controlled clinical trial with a historical control group. It was carried out in a single centre. The patients were followed for 30 days after discharge. No loss to follow-up was reported.

**Analysis of effectiveness**
All patients included in the study were accounted for in the analysis, with the exception of the patient in the control group who died. The primary health outcomes were the incidence of AF (postoperative, at discharge, and at clinical follow-up) and the postoperative length of stay (LOS). The incidences of pneumonia, postoperative myocardial infarction, stroke, death, discharge to home or intermediate care facility, and re-hospitalisation within 30 days after discharge, were also assessed. The study groups were generally comparable at baseline. However, there were significantly more patients in the age class 65 to 74 years in the control group, (p=0.04) and more patients in the intervention group suffered from prior myocardial infarction, (p=0.008).

**Effectiveness results**
The incidence of AF postoperatively was 13.4% in the intervention group and 30.7% in the control group, (p<0.001). The incidence of AD at discharge was 0.8% in the intervention group and 3% in the control group. The incidence of AF at 30-day follow-up was 3.9% in the intervention group and 4% in the control group.

The median postoperative LOS was 5 days (interquartile range: 4 - 8) in the intervention group and 5 days (interquartile range: 4 - 6) in the control group, (p=0.074).

As amiodarone was administered either pre- or post-operatively at the discretion of the attending physician, the intervention group was further divided into those patients who received amiodarone 1-week preoperatively (17 patients) and those who received the treatment postoperatively (99 patients).

The median LOS was 4 days (interquartile range: 4 - 9) for preoperative amiodarone and 5 days (interquartile range: 4 - 8) for postoperative amiodarone.

The postoperative use of beta-blocker was 70.6% with preoperative amiodarone and 80.8 with postoperative amiodarone.

The incidence of AF postoperatively was 17.6% with preoperative amiodarone and 13.1% with postoperative amiodarone. The incidence of AF at discharge was 5.9% with preoperative amiodarone and 0 with postoperative amiodarone. The incidence of AF at follow-up was 11.8% with preoperative amiodarone and 3% with postoperative amiodarone.

None of these differences in the two groups of intervention patients achieved statistical significance.

An increase in prolonged ventilator use and reintubation was observed in the intervention group, which was associated with an increased incidence of pneumonia (one case). The incidences of postoperative myocardial infarction, stroke, death, discharge to home or intermediate care facility, and re-hospitalisation within 30 days after discharge, were similar in the control and intervention groups.

**Clinical conclusions**
The effectiveness analysis showed that the amiodarone-based treatment reduced the incidence of postoperative AF, but did not result in shorter hospitalisation. Also, amiodarone administered postoperatively was as effective as preoperative dosing in the reduction of AF incidence.
Measure of benefits used in the economic analysis
The health outcomes were left disaggregated and no summary benefit measure was used in the economic analysis. A cost-consequences analysis was therefore carried out.

Direct costs
The authors stated that a 3% discount rate was used for the costs in the intervention group. This was to reflect the changes in the costs over the 8 months that separated the data collection in the two groups. A complete breakdown of the costs was not given. The unit costs were not reported separately from the quantities of resources. The authors stated that the hospital costs (from operation to discharge) were included in the analysis. The cost data were estimated from actual charges at the study centre, and these charges were multiplied by a factor of 0.52 to produce estimates close to actual costs. Consequently, the estimated costs, which were reported as a cost index with 1.0 representing the control group, were supposed to represent the true market costs of the intervention. The cost/resource boundary appears to have been that of the hospital. The resource use data were gathered retrospectively from January to April 1998 for the comparison group, and prospectively from September 1998 to January 1999 for the intervention group. No price year was reported.

Statistical analysis of costs
Statistical analyses of the total costs were conducted to test for the statistical significance of the results.

Indirect Costs
The indirect costs were not included in the analysis.

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 cost index was 1.0 in the control group and 1.08 in the intervention group. The difference reached statistical significance, (p=0.006).

In the subgroup analysis of intervention patients, the cost index was 1.0 in those patients who received amiodarone 1-week preoperatively and 0.93 in those who received the treatment postoperatively, (p=0.56).

Synthesis of costs and benefits
Irrelevant since a cost-consequences analysis was carried out.

Authors' conclusions
The clinical pathway using amiodarone for the prevention of atrial fibrillation (AF) in patients who had undergone coronary artery bypass grafting (CABG) was effective in reducing the incidence of postoperative AF. However, there was no corresponding reduction in the length of hospitalisation and overall costs, compared with standard management of these patients.
CRD COMMENTARY - Selection of comparators
The rationale for the choice of the comparator was clear. The clinical pathway was compared with no pathway, as the aim of the study was to determine the active value of the intervention. However, the separate effects of the clinical pathway (a management approach) and the use of amiodarone were unclear. The difference in cost or benefit could be attributed to either, and in different directions.

Validity of estimate of measure of effectiveness
The analysis of effectiveness used a prospective non-randomised clinical trial with an historical control group, which appeared appropriate for the study question, as practice before the introduction of the clinical pathway was compared with the new intervention. The study sample appears to have been representative of the overall study population. However, as the effectiveness was measured in different historical periods, it would be interesting to establish whether other factors could have affected the study results. In addition, the study groups were not perfectly comparable at baseline and power calculations were not performed. Also, the subgroup analysis (of intervention patients only) used a small sample only. These issues may have limited the internal validity of the analysis. As already mentioned, there is also likely confounding between the care pathway and use of amiodarone, as well as various aspects of the management approach.

Validity of estimate of measure of benefit
A cost-consequences analysis was conducted, therefore no summary benefit measure was used in the economic analysis.

Validity of estimate of costs
The details of the cost analysis were limited, thus hampering transparency. The perspective adopted in the analysis appears to have been that of the hospital. However, a complete breakdown of the costs was not given and the unit costs were not reported separately from the resource quantities. No price year was reported, thus hindering any reflation exercise. The authors used a charge-to-cost ratio to calculate the market costs of the interventions, but provided no justification for the value used. Statistical analyses were performed to test for the statistical significance of the estimated costs. Finally, discounting was conducted to reflect the changes in costs over the 8 months that separated the data collection in the two groups, although it is common practice to carry out discounting when the costs are incurred over a period longer than two years.

Other issues
The authors did not compare their findings with those from other studies, and the issue of generalisability was not addressed. In addition, sensitivity analyses were not performed and the unit costs were not reported. Consequently, the external validity of the analysis was somewhat low. The study enrolled patients after CABG and this was reflected in the conclusions of the analysis. The authors reported their findings selectively.

Implications of the study
The implication of the study was that amiodarone prophylaxis was successful in reducing the frequency of postoperative AF, but no cost-savings were observed when compared with the standard management of patients after CABG. However, these conclusions must be viewed in the light of the limitations of the analysis highlighted.

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