Amiodarone versus implantable cardioverter-defibrillator: randomized nonischemic dilated cardiomyopathy and asymptomatic nonsustained ventricular tachycardia - AMIOVIRT


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 study compared the use of amiodarone with an implantable cardioverter-defibrillator (ICD) in patients with nonischaemic dilated cardiomyopathy (NIDCM) and nonsustained ventricular tachycardia (NSVT). Amiodarone therapy was initiated at a dose of 800 mg/day. The amiodarone dosage was decreased to 400 mg/day after 7 days and to 300 mg/day after one year. Implantable defibrillators were inserted using conventional non-thoracotomy techniques.

Type of intervention

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised patients with NIDCM and asymptomatic NSVT. The inclusion criteria were:

NIDCM, defined as left ventricular dysfunction in the absence of coronary artery disease (CAD) or disproportionate to the severity of CAD;

an ejection fraction of 0.35;

asymptomatic NSVT, defined as at least three consecutive ventricular premature depolarisations with a rate of more than 100 beats/minute, lasting less than 30 seconds and not associated with symptoms of cerebral hypoperfusion;

New York Heart Association functional class I to III; and

age 18 years.

Optimal medical therapy with angiotensin-converting enzyme inhibitors, beta-blockers, and potassium-sparing diuretics was strongly encouraged and attempted throughout the duration of the study. The exclusion criteria included syncope, pregnancy, a contraindication to amiodarone or defibrillator therapy, or concomitant therapy with a Class I anti-arrhythmic drug.

Setting
The setting was tertiary care. The economic study was carried out in Arkansas, Ohio and Michigan.

Dates to which data relate
The effectiveness evidence and resource use data were collected from 1996 to 2001. 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 undertaken on the same patient sample as that used in the effectiveness study.

Study sample
Patients were enrolled between August 1996 and September 2000. Follow-up ended on 30 June 2001. One hundred and three patients were randomly assigned to receive either amiodarone or an ICD. There were 52 patients in the amiodarone group and 51 in the ICD group. The patients in the amiodarone group had a mean age (+/- standard deviation) of 60 (+/- 12) years and 26% were female. The patients in the ICD group had a mean age of 58 (+/- 11) years and 33% were female. Power calculations showed that 219 patients in each group would be required to identify an important reduction in total mortality with 80% power. (p<0.05, two-sided t-test). However, the study was stopped early when the prospective stopping rule for futility was reached. Patients who refused to participate in the study were followed in a voluntary registry but the number was not reported.

Study design
This was a multi-centre randomised clinical trial. Randomisation was stratified among the ten participating centres. No patient was lost to follow-up. An events committee determined the causes of death by consensus. To assure a blinded review, all references to amiodarone or ICD therapy were removed from the reviewed documents.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary health outcomes used were total mortality, arrhythmia-free survival, and quality of life. A data safety monitoring board evaluated the results every 10 deaths, and prospectively determined stopping rules. Survival curves were constructed using Kaplan-Meier methods. Quality of life was measured using the Quality of Well Being Schedule and the State Trait Anxiety Inventory. Primary and secondary end points between the two groups were compared using appropriate statistical tests.

Effectiveness results
When the study enrolment was discontinued because of the stopping rule, the 1- and 3-year survival rates among patients treated with amiodarone were 90% and 87%, respectively, compared with 96% and 88% among ICD-treated patients, (p=0.8). The distribution of sudden cardiac deaths between amiodarone-treated patients (n=2, 40%) and ICD-treated patients (n=1, 25%) was similar in both groups, as were the non sudden cardiac deaths (n=3, 60% for amiodarone versus n=3, 75% for ICD), (p=0.7).

Arrhythmia-free survival rates at one and three years were 82% and 73%, respectively, among amiodarone-treated patients, and 78% and 63% among ICD-treated patients, (p=0.1).

The average values for the quality of life assessment at baseline and at one year were similar among patients in both groups. None of the differences in clinical outcomes or complications were significant between the two groups. There were no significant differences in demographic and clinical characteristics between the groups at baseline.

Clinical conclusions
No significant difference was found in the 3-year survival rate and quality of life among patients with NIDCM and NSVT who were treated with amiodarone or an ICD. There was a trend towards improved arrhythmia-free survival with amiodarone therapy.

Measure of benefits used in the economic analysis

A cost-consequences analysis was performed. Therefore, no summary measure of benefit was used in the economic evaluation. The authors found no significant difference between the two strategies within either group and, consequently, considered only the costs in the economic analysis. The economic analysis can also be categorised as a cost-minimisation analysis.

Direct costs
The categories of direct costs used were inpatient and outpatient costs, including non-cardiac care. Data were obtained from 24 patients who received care within one of the ten participating centres (University of Michigan Health System). The data were gathered for a 1-year interval, starting at the time at which the patients entered the trial. Drug costs were calculated only for those drugs for which information on the dosage was collected (e.g. amiodarone, beta-blockers, angiotensin converting enzyme inhibitors, digoxin, diuretics, warfarin, and aspirin).

The quantities and the costs were estimated using actual data (University of Michigan Health System cost accounting system). Wholesale prices were used for the drug costs. The quantities and the costs were not reported separately. Although some patients were followed for more than two years, a 1-year time horizon was used for the costs and discounting was not carried out. The price year was not reported.

Statistical analysis of costs
The costs were treated stochastically. They were compared using Student’s t-test and expressed as the mean value +/- one SD. A p-value of less than 0.05 was considered statistically significant.

Indirect Costs
The indirect costs were not included.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was reported.

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

Cost results
The total cost of medical care in the first year after entry into the study was $8,879 (+/- 27,614) in the amiodarone group and $22,079 (+/- 22,039) in the ICD group, (p=0.1). The costs associated with amiodarone therapy during that period were approximately 60% less than the costs associated with ICD therapy. The authors reported that this observation tended towards statistical significance.

Synthesis of costs and benefits
Not relevant.

Authors’ conclusions
The 3-year survival rate and the effect on quality of life were not statistically different among patients with nonischaemic dilated cardiomyopathy (NIDCM) and nonsustained ventricular tachycardia (NSVT) who were treated with amiodarone or an implantable cardioverter-defibrillator (ICD). However, amiodarone therapy was associated with
a trend towards improved arrhythmia-free survival.

According to the authors, the study provided strong evidence that amiodarone and the ICD had an equally beneficial effect on survival. However, arrhythmia-free survival is biased against the ICD, because asymptomatic tachycardias were not recognised in the patients treated with amiodarone.

During the first year of treatment, amiodarone therapy was associated with lower costs than ICD therapy. This observation tended towards statistical significance. These results have also been found in other studies.

CRD COMMENTARY - Selection of comparators
The comparator used was justified on the grounds that the optimal therapy for prevention of sudden death in patients with NIDCM and NSVT has not been determined. Studies suggested that amiodarone therapy in patients with an NIDCM may have a beneficial or neutral effect on survival. In addition, an ICD effectively prevents sudden cardiac death and improves total mortality, compared with anti-arrhythmic drug therapy, in some patient groups. However, whether ICDs also reduce mortality in patients with NIDCM and asymptomatic NSVT is unknown. The authors acknowledged that the lack of a control group was a limitation of their study. This raised the possibility that the addition of either therapy to standard medical practice might not have an incremental value. You should decide if the comparator represents a widely used technology in your own setting.

Validity of estimate of measure of effectiveness
The analysis was based on a randomised trial, which was an appropriate design given the study question. The authors stated that, because no significant clinical differences were detected, concerns about power calculations and the sample size necessary to detect clinically significant differences should be taken into consideration. The fact that the study was stopped could have contributed to this issue.

Validity of estimate of measure of benefit
No summary measure of benefit was derived. As the authors stated that the two therapies were equally effective, only the costs were assessed further. The limitations (mentioned already) of sample size and power to assure reasonably equal effectiveness also apply to this section.

Validity of estimate of costs
The analysis of costs was performed from the perspective of a single provider. Although not stated, some relevant costs could have been omitted from the analysis. Such costs were not reported in detail, although their omission is unlikely to have affected the authors’ conclusions if the clinical effects and side effects were similar between the groups. The costs and the quantities were not reported separately, thus the analysis could not be easily extrapolated to other settings. The cost data were taken from a sub-sample of patients (24 out of 103) in only one of the ten participating centres, and for a shorter time horizon than the clinical study. All these factors that could affect the robustness of the cost results. A statistical analysis of the costs was performed. Discounting was unnecessary since all the costs were incurred during one year, although the follow-up period was longer. The price year was not reported, which will make any future reflation exercises difficult.

Other issues
The authors compared their findings with those from other studies. In general, they showed their clinical findings were a departure from the findings of other studies, although the cost findings were similar. The issue of the generalisability of the results to other settings was not directly addressed. The authors do not appear to have presented their results selectively.

Implications of the study
According to the authors, the present study seems to represent a departure from the usual interpretation of superiority.
of the ICD over amiodarone, as demonstrated in other studies.

The authors recommended a change in clinical practice considering amiodarone as the initial therapy to prevent death among patients with NIDCM and NSVT. This was because of the lack of statistically different survival rates, the trend towards being more effective than the ICD in preventing symptomatic ventricular tachycardia, and substantial cost-savings. Nevertheless, the results of this study should be interpreted with caution given the limitation of sample size, and that with the observed mortality rates, approximately 12,000 patients would have been required to achieve a power of 80%.

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Other publications of related interest


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