Effectiveness and costs of chemical versus electrical cardioversion of atrial fibrillation
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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 study compared the use of chemical versus electrical cardioversion as an initial treatment to convert atrial fibrillation (AF) to sinus rhythm in patients with persistent AF of less than 6 months. The authors not only compared the initial strategies, but they also evaluated whether a strategy that started with either method followed by the other was comparable to the opposite strategy. The drugs for chemical cardioversion or for sedation were left to the investigator's criteria, as were the energy, anticoagulation, and the number of shocks applied for electrical cardioversion. The most frequently used drug was quinidine (maximum dose 1,600 mg) administered orally, either isolated or following intravenous digitalis. Other intravenous regimens included procainamide (maximum dose 2 mg/kg of intravenous infusion) and amiodarone (maximum dose 600 mg intravenously). After restoration of sinus rhythm, most patients were treated with sotalol or quinidine.

Type of intervention
Treatment.

Economic study type
Cost-effectiveness analysis.

Study population
Patients eligible for the study were those presenting a persistent episode of AF of less than 6 months, with indication for restoration of sinus rhythm by either of two methods of cardioversion (chemical or electrical). The duration of AF was determined by the onset of symptoms or, in the case of asymptomatic or oligosymptomatic patients, it was considered as the period since the last electrocardiogram on sinus rhythm. Eligibility criteria also included haemodynamically stable patients, serum potassium greater than 3.8 mequiv./L, no anaesthetic contraindication, and absence of signs of digitalis toxicity.

The exclusion criteria included a strong belief from the physician, or the patient, that either of the therapeutic options would have better results based on acquired experience in previous episodes. Other criteria were moderate or severe heart failure, hypertension (diastolic blood pressure greater than 110 mmHg), alcohol or drug abuse, pregnancy or lactation, renal failure, myocardial infarction in the last 30 days, current therapy with anti-arrhythmic drugs, and left ventricular ejection fraction less than 0.40.

Ethical commissions of all the participating institutions approved the protocol.

Setting
The setting was tertiary care. The economic study was carried out in Brazil.

Dates to which data relate
The dates to which the effectiveness evidence and resource use data related were not reported. 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. Although it was not clearly stated, it would appear that the costing was undertaken prospectively.

Study sample
A power and sample size calculation was reported. It was estimated that 140 patients would be needed (70 per group) to detect a 15% absolute difference in the success rates between the two strategies (assuming alpha = 0.05 and beta = 0.20). The trial enrolled 139 patients, of which 72 were assigned to initial chemical cardioversion (group C) and 67 to initial electrical cardioversion (group E). Of the 72 patients in group C, 35 (49 %) were female. The mean age (+/- standard deviation, SD) was 56 (+/- 13) years and the mean duration of AF (+/- SD) was 18 (+/- 41) hours. Sixty-five patients (90%) had 5 or fewer prior episodes, and 64 (89%) were Class I according to the New York Heart Association's (NYHA) congestive heart failure classification. Of the 67 patients in group E, 30 (45%) were female. The mean age (+/- SD) was 56 (+/- 13) years and the mean duration of AF (+/- SD) was 23 (+/- 44) hours. Sixty-one patients (91%) had 5 or fewer prior episodes, and 60 (90%) were Class I according to the NYHA's congestive heart failure classification.

Study design
The study was a randomised clinical trial that was conducted in multiple centres. Each participating centre received sealed opaque envelopes sequentially numbered, with a randomised indication for starting with chemical or electrical cardioversion. In case of failure of the initial procedure (chemical or electrical), it was recommended that the investigator attempted cardioversion using the other method. The duration of follow-up was unclear, but it appears to have been until restoration of sinus rhythm or waiving new attempts.

Analysis of effectiveness
The analysis of the clinical study was conducted on an intention to treat basis. The primary health outcome corresponded to the cardioversion success rate of each strategy. The secondary health outcomes assessed were length of stay and clinical complications of cardioversion. Success of cardioversion was defined as maintenance of sinus rhythm 24 hours after the successful attempt. Early recurrences of AF (until 24 hours after cardioversion) were considered to be a failure of therapy. The primary success rates and conversion rates were also assessed by a sub-group analysis. Statistical tests were performed to analyse differences in demographic and clinical characteristics, as well as outcomes. There were no significant differences in the demographic and clinical characteristics of the groups at baseline.

Effectiveness results
The overall analysis of the initial procedure did not reveal a difference in the success rates between chemical (74%, 53 patients) and electrical (73%, 49 patients) cardioversion, (p=0.95). However, the strategy of starting with chemical cardioversion was more effective than that starting with electrical cardioversion, 96% (69 patients) versus 84% (56 patients), (p=0.016).

In patients with recent-onset AF, the primary success rate and conversion rate did not differ significantly between strategies. Similar results were obtained in patients with structural heart disease and in patients with chronic AF.

In patients with lone AF, the primary success rate did not differ significantly between strategies.

All 30 patients with lone AF who started with chemical therapy were converted to sinus rhythm, versus only 77% (20 patients) of the cases who began with the electrical procedure, (p=0.007).

The length of stay did not differ between the two groups. The mean length of stay was 1 day (SD=2) in group C versus
2 days (SD=2) in group E, (p=0.65).

Forty-three patients (50%) who underwent electrical cardioversion had mild complications versus only 10 patients (12%) undergoing chemical cardioversion, (p<0.001). There were 4 cases (5%) of severe complications associated with anti-arrhythmic drug therapy, all of them in patients with structural heart disease. No severe complication was observed with electrical procedures. There were no deaths.

Clinical conclusions
Since the primary success rates of electrical and chemical cardioversion were similar, the best result obtained by strategy C was due to the differences observed in the success rates of the subsequent procedure. In a sub-group with recent-onset and chronic AF, the success rates of both strategies did not differ significantly. The chemical cardioversion strategy was significantly superior to the electrical one in patients with lone AF, while in patients with structural heart disease this was not evident. All patients with lone AF who were not converted to sinus rhythm with drugs, were successfully converted in the subsequent electrical cardioversion. This suggested that this is the sub-group that benefits the most from that strategy.

Measure of benefits used in the economic analysis
No summary measure of benefit was used in the economic evaluation. Therefore, the authors, in effect, conducted a cost-consequences analysis.

Direct costs
The costs were calculated from admission to the hospital until restoration of sinus rhythm or waiving new attempts. The categories of costs included in the analysis were hospitalisation, diagnostic tests and cardioversion procedures. Hospital charges were used as a proxy for direct costs. These included hospital and intensive coronary unit daily expenses, hours of heart monitoring and of oxygen therapy, electrocardiograms, chest radiographies, echocardiograms, defibrillator fees and drugs used. Anaesthesiologist costs were not included since sedation for electrical cardioversion was performed by cardiologists in all procedures. The costs associated with the alternative cardioversion (costs of electrical cardioversion in the initial chemical cardioversion arm and vice versa) were also included in the analysis.

Discounting was not carried out. This was appropriate because of the short-term horizon of the study. The quantities and the costs were reported partially separately. The quantities and the costs were estimated from actual data, although the authors stated that the costs of cardiovascular care varied widely in their setting. The quantity and cost data were collected from participating centres. The dates relating to the quantity of resources measured and the price year were not reported. Also, although the currency reported was US dollars ($), the conversion rate of the original currency was not reported.

Statistical analysis of costs
The costs were treated stochastically and statistical tests were carried out. All tests were two-tailed and p<0.05 was considered significant. Mean values were also presented.

Indirect Costs
No indirect costs were reported.

Currency
US dollars ($).

Sensitivity analysis
No sensitivity analysis was carried out.
Estimated benefits used in the economic analysis
Successful cardioversion rate was used as the benefit measure for estimating cost-effectiveness ratios. See the 'Effectiveness Results' section.

Cost results
The cost analysis favoured the chemical cardioversion strategy as the initial regimen. The mean cost per patient was $1,188 (range: 185 - 6,605) for group C and $1,603 (range: 720 - 6,734) for group E, (p=0.0002).

The main factors for the increased costs of electrical cardioversion were heart monitoring, (p=0.05), the use of drugs, (p=0.00001) and oxygen, (p=0.00001). Other costs, such as diagnostic tests, were not significantly different.

Synthesis of costs and benefits
Cost-effectiveness was expressed as the cost per successful cardioversion. It was reported as $/patient converted to the sinus rhythm.

Strategy C was not only more effective, but it also incurred a lower mean cost per case reverted ($1,240 versus $1,917; p=0.002). In a sub-group analysis, cost-effectiveness varied according to the underlying heart disease. In cases of lone AF, strategy C had a lower average cost-effectiveness ratio than strategy E ($965 versus $2,021). In cases of structural heart disease, strategy C also showed a better cost-effectiveness ratio than strategy E (($1,223 versus $1,814).

Authors' conclusions
The effectiveness of chemical or electrical cardioversion as the initial method was similar, but starting with chemical cardioversion was more effective and less expensive than starting with electrical cardioversion, especially in patients without underlying heart disease. In the case of patients with structural heart disease, the risks of severe complications with chemical cardioversion must be carefully evaluated. This fact might influence the choice of the initial strategy to be used.

CRD COMMENTARY - Selection of comparators
The choice of the comparators used was justified on the grounds that there is no consensus regarding the best treatment for converting AF, and no prospective randomised study comparing the strategies for cardioversion of AF had been published until this study was carried out.

The authors mentioned that a recent meta-analysis of randomised controlled trials showed that some drugs, other than those used in this study, seem to be the most efficient drugs to convert AF (see Other Publications of Related Interest). Also, they speculated that the conversion rate with the electrical procedure was inferior to that expected based on the literature, and that it might have influenced their results. However, comparison would be difficult because of the variation in the patients' characteristics. In addition, the increased efficacy of electrical conversion might have been the result of patients undergoing prior treatment with anti-arrhythmic drugs, according to the results of recent studies demonstrating that.

You should judge whether these strategies are relevant in your setting, or whether other comparators from other drug classes or therapeutic options could also have been relevant.

Validity of estimate of measure of effectiveness
The analysis was based on a randomised trial. This is an appropriate design given the study question but, because no significant clinical differences were detected in most of the results, concerns about sample size and power calculations to detect clinically significant differences should be taken into consideration. In addition, the authors stated that it was difficult to determine how many patients would follow spontaneous conversion in the study, although because the studied groups were randomised and well matched, this variable would not influence the observed results. The study
sample appears to have been representative of the study population. An appropriate statistical analysis was undertaken to determine potential differences in outcomes between both groups.

**Validity of estimate of measure of benefit**
Effective cardioversion at 24 hours was used as the benefit measure. This is a valid measure in this population, but it limits the comparability of its cost-effectiveness to other health problems. Defining success at 24 hour follow-up could also alter the results if strategies have different longer term effects.

**Validity of estimate of costs**
The analysis of costs seems to have been performed from the perspective of a hospital. According to this perspective, all relevant costs appear to have been included, although the costs were not reported in detail. Although some costs might have been omitted, their omission is unlikely to have affected the authors’ conclusions if clinical effects and side effects were similar between groups. The costs and the quantities were reported partially separately, which would not allow the analysis to be easily extrapolated to other settings. Charges were used as a proxy for costs. The source and dates of the cost data were not reported. All these factors could affect the robustness of the cost results. A statistical analysis of the costs was performed. Discounting was not reported, but it was not relevant because of the short-term horizon of the study. The price year was not reported, which will make any future reflation exercise difficult. The authors stated that a limitation of their analysis was the fact that the costs of cardiovascular care varied widely. Therefore, the results of their economic evaluation may be of limited applicability to other countries.

**Other issues**
The authors compared their findings with those from other studies. In general, their clinical findings were similar to the findings of other studies. However, the cost findings were not similar, mainly because of variations in drug prices, hospital length of stay, and the omission of anaesthesiology costs. The authors addressed the issue of generalisability of the results to other settings, especially in the economic evaluation. The authors appear to have presented their results selectively. They stated specific study limitations. For example, the open label protocol, the purpose of which was to include a large number of cardiologic centres to reflect the current practice in their country. Also, the lack of homogeneous patient characteristics in terms of duration of AF (recent-onset and chronic AF), and the short-term follow-up to assess the efficacy of the initial challenge of anti-arrhythmic therapy.

**Implications of the study**
The authors did not state any explicit recommendations. However, according to the study, it can be inferred that chemical cardioversion should be preferred as the initial treatment for patients with AF and without underlying heart disease. Otherwise, the risks of complications with chemical cardioversion must be carefully evaluated and the choice between strategies is more difficult. The authors stated that longer term studies are needed.

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