Curative catheter ablation in atrial fibrillation and typical atrial flutter

Curative catheter ablation in atrial fibrillation and typical atrial flutter: systematic review and economic evaluation

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Executive summary

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Executive summary

Background

Atrial fibrillation (AF) and typical atrial flutter are common and debilitating abnormalities of the heart rhythm (arrhythmias).

There are two broad strategies for the management of AF and atrial flutter. Rhythm control strategies attempt to control the arrhythmia by restoring and maintaining a normal heart rhythm (sinus rhythm) whereas rate control strategies aim to control heart rate without attempting to remove the underlying arrhythmia. Both strategies are normally combined with anticoagulants or antiplatelet drugs to reduce the risk of stroke. Long-term rhythm and rate control strategies typically involve treatment with antiarrhythmic drugs (AADs). Acute conversion of an arrhythmia to sinus rhythm ('cardioversion') can be achieved using AADs or by controlled application of direct electrical current.

Radio frequency catheter ablation (RFCA) for the treatment of cardiac arrhythmias involves the percutaneous insertion of catheters that are guided by fluoroscopy to the heart. Small areas of tissue responsible for the propagation of abnormal electrical activity through the heart are selectively destroyed (ablated) using radio frequency energy to restore normal sinus rhythm. In recent years, focus has been on ablating tissue around the pulmonary veins in the left atrium for the treatment of AF and in an area of the right atrium called the cavotricuspid isthmus (CTI) for typical atrial flutter.

Technical aspects of RFCA continue to evolve such that the clinical studies represent experience with many variations in equipment and technique.

Objectives

The aim of this project was to determine the safety, clinical effectiveness and cost-effectiveness of RFCA for the curative treatment of (1) AF and (2) typical atrial flutter.

Methods

This technology assessment comprises the following sections: systematic reviews of clinical studies and economic evaluations of catheter ablation for AF and typical atrial flutter. In addition we developed a de novo economic model of catheter ablation in the treatment of AF.

For the systematic reviews of clinical studies we searched 25 bibliographic databases and internet sources, and checked the references of all included studies. The database searches were originally conducted in July 2006, with subsequent update searches for controlled trials conducted in April 2007.

We included randomised (RCTs) and non-randomised controlled trials comparing RFCA with alternative treatment strategies (i.e. AAD therapy and/or cardioversion) in adults with symptomatic AF or typical atrial flutter. We also included case series of at least 100 patients as well as studies comparing two or more variations on the RFCA approach. The latter were treated as uncontrolled RFCA case series.

An 18-item checklist was used to assess the quality of the included studies. All 18 items were applicable to controlled studies and a subgroup of eight of these items was applicable to case series.

The primary outcome was the proportion of patients free of arrhythmia at 12 months' follow-up; relative risks (RR) and related 95% confidence intervals (CIs) were calculated and, when considered sufficiently homogenous, statistically pooled using a fixed-effects model. When studies failed to report freedom from arrhythmia at 12 months, mean follow-up data were shown but not included in any pooled analyses. Secondary outcomes were the occurrence of complications or adverse events and quality of life.

A broad range of studies was considered for inclusion in the review of cost-effectiveness,

including economic evaluations conducted alongside trials, modelling studies and analyses of administrative databases. Only full economic evaluations that compared two or more options and considered both costs and consequences (including cost-effectiveness, cost-utility and cost-benefit analyses) were included. The quality of studies was assessed according to a checklist updated from that developed by Drummond and Jefferson.[1]

A decision model was developed to evaluate a strategy of RFCA (without long-term AAD use) compared with long-term AAD treatment alone (amiodarone) in adults with paroxysmal AF. This was used to estimate the cost-effectiveness of RFCA in terms of cost per QALY under a range of assumptions. Decision uncertainty associated with this analysis was presented and used to inform future research priorities using the value of information analysis.

Results

Review of clinical effectiveness

A total of 4858 studies were retrieved from the searches. Of these, eight controlled studies and 53 case series of AF were included. Two controlled studies and 23 case series of typical atrial flutter were included. The majority of case series were judged to be of 'poor' quality; six of the ten included controlled studies were rated as 'satisfactory'.

Clinical effectiveness of RFCA for atrial fibrillation

Freedom from arrhythmia at 12 months in case series (when reported) ranged from 28% to 85.3% with a weighted mean of 76%.

Three RCTs (298 patients) suggested that RFCA is more effective than long-term AAD therapy in patients with drug-refractory paroxysmal AF [per-protocol RR 2.36 (95% CI 1.89–2.95)]. A large non-randomised trial had similar findings. Single RCTs also suggested superiority of RFCA over electrical cardioversion followed by long-term AAD (amiodarone) therapy and of RFCA plus AAD therapy over AAD maintenance therapy alone in drug-refractory patients.

The available RCTs provided insufficient evidence to determine the effectiveness of RFCA beyond 12 months or in patients with persistent or permanent AF.

Adverse events and complications were generally rare. Some events were specific to ablation (tamponade, pericardial effusion, groin haematoma) whereas others were specific to AADs (corneal microdeposit, thyroid dysfunction, pro-arrhythmia, sexual impairment). Mortality rates were low in both RCTs and case series. Cardiac tamponade and pulmonary vein stenosis were the most frequently recorded complications.

Clinical effectiveness of RFCA for typical atrial flutter

Freedom from arrhythmia at 12 months in case series (when reported) ranged from 85% to 92% with a weighted mean of 88%.

Neither of the atrial flutter RCTs reported freedom from arrhythmia at 12 months. One RCT found a statistically significant benefit favouring ablation over AADs in terms of freedom from arrhythmia at a mean follow-up of 22 months [RR 2.2 (95% CI 1.33–3.63)]. This study suggested a very large effect favouring ablation in terms of freedom from atrial flutter [RR 14.03 (95% CI 3.67–53.7)] and a smaller, but also significant, effect in terms of freedom from AF during follow-up [RR 1.77 (95% CI 1.08–2.90)].

A second RCT reported a more modest effect favouring ablation in terms of freedom from atrial flutter at follow-up in older patients (mean age 78 years) after their first episode of flutter [RR 1.36 (95% CI 1.13–1.64)]. No significant effect was observed for freedom from occurrence of significant AF [intention to treat RR 1.44 (95% CI 0.68–3.08)].

In the atrial flutter case series, mortality was rare and the most frequent complications were atrioventricular block and haematomas. Across case series, no single complication occurred at a rate of more than 0.5%. Complications during longer-term follow-up were rarely reported. Complications in the RCTs were similar, except for those events likely to have been caused by AAD therapy (i.e. thyroid dysfunction).

Review of cost-effectiveness and decision model

The review of cost-effectiveness evidence found one relevant study, which from a UK NHS perspective had a number of important limitations.

The base-case analysis in the decision model demonstrated that if the quality of life benefits of

RFCA are maintained over the remaining lifetime of the patient then the cost-effectiveness of RFCA appears clear. These findings were robust over a wide range of alternative assumptions, being between £7763 and £7910 per additional QALY with very little uncertainty.

If the quality of life benefits of RFCA are assumed to be maintained for no more than 5 years, cost-effectiveness of RFCA is dependent on a number of factors, including: (1) any prognostic benefits associated with normal sinus rhythm (NSR); (2) the magnitude of any quality of life differences between RFCA and AADs; and (3) the long-term reduction in risk of recurrent AF following RFCA. Estimates of cost-effectiveness that explored the influence of these factors ranged from £23,000 to £38,000 per QALY.

Conclusions

The available evidence suggests that RFCA is a relatively safe and efficacious procedure for the therapeutic treatment of AF and typical atrial flutter. There is some randomised evidence to suggest that RFCA is superior to AADs in patients with drug-refractory paroxysmal AF in terms of freedom from arrhythmia at 12 months. RFCA appears to be cost-effective if the observed quality of life benefits are assumed to continue over a patient's lifetime. However, there remain uncertainties around longer-term effects of the intervention and the extent to which published effectiveness findings can be generalised to 'typical' UK practice.

Recommendations for research

All catheter ablation procedures for the treatment of AF or atrial flutter undertaken in the UK should be recorded prospectively and centrally. A Central Cardiac Audit Database already exists, but measures to increase compliance in recording RFCA procedures may be needed. This would be of particular value in establishing the long-term benefits of RFCA and the true incidence and impact of any complications. Collection of appropriate quality of life data within any such registry would also be of value to future clinical and cost-effectiveness research in this area.

Any planned multicentre RCTs comparing RFCA against best medical therapy for the treatment of AF and/or atrial flutter should be conducted among 'non-pioneering' centres using the techniques and equipment typically employed in UK practice and should measure relevant outcomes.

Publication

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NIHR Health Technology Assessment Programme

The Health Technology Assessment (HTA) Programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The research findings from the HTA Programme directly influence decision-making bodies such as the National Institute for Health and Clinical Excellence (NICE) and the National Screening Committee (NSC). HTA findings also help to improve the quality of clinical practice in the NHS indirectly in that they form a key component of the 'National Knowledge Service'.

The HTA Programme is needs led in that it fills gaps in the evidence needed by the NHS. There are three routes to the start of projects.

First is the commissioned route. Suggestions for research are actively sought from people working in the NHS, from the public and consumer groups and from professional bodies such as royal colleges and NHS trusts. These suggestions are carefully prioritised by panels of independent experts (including NHS service users). The HTA Programme then commissions the research by competitive tender.

Second, the HTA Programme provides grants for clinical trials for researchers who identify research questions. These are assessed for importance to patients and the NHS, and scientific rigour.

Third, through its Technology Assessment Report (TAR) call-off contract, the HTA Programme commissions bespoke reports, principally for NICE, but also for other policy-makers. TARs bring together evidence on the value of specific technologies.

Some HTA research projects, including TARs, may take only months, others need several years. They can cost from as little as £40,000 to over £1 million, and may involve synthesising existing evidence, undertaking a trial, or other research collecting new data to answer a research problem.

The final reports from HTA projects are peer reviewed by a number of independent expert referees before publication in the widely read journal series *Health Technology Assessment*.

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Reports are published in the HTA journal series if (1) they have resulted from work for the HTA Programme, and (2) they are of a sufficiently high scientific quality as assessed by the referees and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search, appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

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The views expressed in this publication are those of the authors and not necessarily those of the HTA Programme or the Department of Health.

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