Efficacy and safety of catheter ablation versus antiarrhythmic drugs for atrial fibrillation: a meta-analysis of randomized trials

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CRD summary
The authors concluded that radiofrequency catheter ablation was a relatively effective and well-tolerated procedure to cure atrial fibrillation in selected patients, but that further research is required to confirm the review findings. This was a well-conducted review and the authors’ cautious conclusions are likely to be reliable.

Authors’ objectives
To evaluate the efficacy and safety of radiofrequency catheter ablation in patients with atrial fibrillation.

Searching
MEDLINE, CINAHL, the Cochrane Central Register of Controlled Trials Register (CENTRAL), the Cochrane Database of Systematic Reviews, DARE, EJS E-Journals and Health Business Full-text Elite were searched without any language restrictions. Search terms were reported but search dates were not. Reference lists of identified articles and reviews were also screened.

Study selection
Randomised controlled trials (RCTs) that compared any type of percutaneous radiofrequency catheter ablation with anti-arrhythmic drugs for the treatment of paroxysmal, persistent or long-standing persistent atrial fibrillation were eligible for inclusion. Percutaneous radiofrequency catheter ablation was described as for substrate modification or electrical isolation of pulmonary veins. Eligible trials had to follow up patients for at least six months and report any of the outcomes, which were recurrence of atrial tachycardia, time to recurrence of atrial tachyarrhythmia, treatment-related complications and/or adverse events. Trials were only included if they used adequate, unclear or inadequate allocation concealment and scored at least 3 out of 5 points on the Jadad quality scale.

Most of the included trials used segmental ostial ablation of the pulmonary vein as the main ablation technique; some trials used circumferential pulmonary vein ablation. In all but one trial, the protocol included adjunctive ablation lines in the right and left atria and/or ablation of complex fractionated electrograms in the left atrium. In most trials, concomitant anti-arrhythmic drugs were given for four and 12 weeks after the ablation treatment. Where specified, anti-arrhythmic drugs included amiodarone, flecainide and sotalol.

All but one trial considered a blanking period from 1.5 to three months after ablation when reporting arrhythmias. Most trials monitored heart rhythm using daily brief event monitoring; other trials used periodic Holter monitoring, weekly brief event monitoring or patient-assessed pulse monitoring.

Approximately two-thirds of patients had symptomatic paroxysmal atrial fibrillation; the other third had persistent or long-standing persistent atrial fibrillation. Most patients had an absence of structural heart disease or heart disease with normal left ventricular function. Most trials were of patients with atrial fibrillation who had failed to respond to at least one or two anti-arrhythmic drugs or were intolerant of anti-arrhythmic drugs. The mean age of patients ranged from 49 to 65 years across treatment groups. Most patients were male.

One reviewer identified eligible studies from titles and abstracts. Decisions on studies to completely review were made by consensus. Two reviewers then selected studies for inclusion. Disagreements were resolved by discussion with a third reviewer.

Assessment of study quality
Trial quality was assessed using allocation concealment and scored using the 5-point Jadad scale, which assessed the reporting of randomisation, blinding and withdrawals.
Two reviewers independently assessed validity. Disagreements were resolved by consensus.

**Data extraction**
Dichotomous data were extracted as relative risks (RRs) with 95% confidence intervals (CI). Hazard ratios and 95% confidence intervals were used for time to survival data; this analysis used an individual patient dataset derived from a summary of monthly mortality tables. The reviewers accepted blanking periods in which data about atrial tachyarrhythmia recurrence were not censored.

Two reviewers independently extracted data. Disagreements were resolved by consensus.

**Methods of synthesis**
Pooled relative risks and 95% confidence intervals were calculated using a random-effects model. Pooled log hazard ratios were calculated for survival data. Heterogeneity was assessed using the $\chi^2$ and the $I^2$ statistic.

Sensitivity analysis was conducted using a fixed-effect model and to examine the influence of methods of statistical analysis, each trial in turn, and missing data. Meta-regression was used to explore causes of heterogeneity.

**Results of the review**
Eight parallel RCTs were included in the review (n=844 patients). The duration of follow-up ranged from six months to one year. Four RCTs reported adequate allocation generation methods. Six RCTs reported use of intention-to-treat analysis. None of the RCTs reported methods used for allocation concealment or blinding.

Radiofrequency catheter ablation was associated with a statistically significant reduction in recurrence of atrial tachyarrhythmia compared with anti-arrhythmic drugs (23.2% versus 76.6%; RR 0.29, 95% CI 0.20 to 0.41; eight RCTs). Substantial heterogeneity was found ($I^2=69\%$). Meta-regression showed significant evidence of heterogeneity for mean age and the presence of paroxysmal atrial fibrillation. Results were similar using a fixed-effect meta-analysis and after excluding each trial in turn.

Radiofrequency catheter ablation was associated with a statistically significant lower rate of recurrence of atrial tachyarrhythmia compared with anti-arrhythmic drugs using the log-rank test (78% were event free versus 25%; HR 5.08, 95% CI 3.85 to 6.07; six RCTs; n=610 patients).

There was no significant difference between intervention groups in complications and adverse events (9% versus 13%; eight studies; no significant heterogeneity). The weighted rate of complications and adverse events in radiofrequency catheter ablation groups was 6.2% (95% CI 3.6 to 10.5).

**Authors' conclusions**
In selected patients with atrial fibrillation, radiofrequency catheter ablation was a relatively effective and well-tolerated procedure to cure atrial fibrillation. Although review results favoured ablation therapy, further research is required to confirm the efficacy and safety of radiofrequency catheter ablation for atrial fibrillation.

**CRD commentary**
The review question was clearly stated and inclusion criteria were appropriately defined. Several relevant sources were searched. No language restrictions were applied, but no specific attempts were made to minimise publication bias. Methods were used to minimise reviewer errors and bias throughout the review process.

Only higher quality trials were included in the review. Relevant information was provided about the included trials. Appropriate methods were used for the meta-analyses, heterogeneity was assessed and various sources of heterogeneity were explored. The reviewers discussed the differences between trials and the observation that participants were not representative of patients seen in clinical practice.

This was a well-conducted review and the authors' cautious conclusions regarding efficacy are likely to be reliable and
their recommendations for further research seem reasonable.

**Implications of the review for practice and research**

**Practice:** The authors did not state any implications for practice.

**Research:** The authors stated that large well-designed RCTs are required to confirm the efficacy and safety of radiofrequency catheter ablation for atrial fibrillation.

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