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Lessons from the trials

RAAFT-2: Radiofrequency ablation vs antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation

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ABSTRACT

Radiofrequency ablation (RFA) for the treatment of paroxysmal Atrial Fibrillation (pAF) has a class 1 indication in patients who have not tolerated or responded to antiarrhythmic medications. Antiarrhythmic medications (AAM) are, however, limited not only by modest efficacy, but also by significant side effects. Discontinuation rates for AAM range from 11-40% in trials. The RAAFT-2 trial evaluates the use of RFA as a first line treatment for pAF compared to optimal pharmacological management (1).

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RAAFT-2 TRIAL

The RAAFT-2 trial was a multicentre randomised clinical trial that was sponsored and co-ordinated by the Population Health Research Institute at McMaster University and an unrestricted research grant from Biosense Webster. It randomised 127 drug- & ablation-naive patients aged 18–75 with pAF to either first line catheter ablation ($n = 66$), or medical therapy ($n = 61$). Subjects were randomised in a 1:1 ratio to either treatment if they were symptomatic with recurrent pAF, and had ≤ 4 episodes within the previous 6 months, one of which had to be documented by surface electrocardiography (ECG). All patients had normal systolic function and no history of heart failure or hypertension.

At baseline there were two significant differences between the study group characteristics; previous electrical cardioversion (33.3% RFA group vs 52.5% AAM group, $p = 0.03$) and use of oral anticoagulation (53% RFA group vs 31.1% AAM, $p = 0.01$).

After randomisation patients entered a 90-day blanking period during which medications were titrated or ablation was performed. After this period, primary outcome events were recorded. Patients were followed up at 1, 3, 6, 12 and 24 months. The study also utilised transtelephonic monitoring (TTM) to assess the cardiac rhythm of patients biweekly and whenever subjects experienced symptoms of possible AF.

RFA involved circumferential isolation of the pulmonary veins with confirmation of entrance block. Additional lesions were left to investigator discretion. AAM's and cardioversions were allowed during the 90-day blanking period only.

Patients randomised to the AAM group had their medications selected according to investigator discretion, with doses being based on guidelines.¹ Patients in this group were able to undergo RFA after the 90-day treatment period if AAM had failed. This was demonstrated by either drug discontinuation due to intolerance, adverse events or inefficacy (recurrence of pAF or atrial tachyarrhythmia lasting > 30 seconds).

The primary efficacy outcome was time to first recurrence of symptomatic or asymptomatic atrial arrhythmia lasting more than 30 seconds, as documented by ECG or TTM. Secondary outcomes included first documented recurrence of AF-related atrial arrhythmia, repeated episodes of AF-related atrial arrhythmia, and quality of life at the 1-year follow-up. The study was powered to test the superiority of RFA over AAD using cox regression analysis, stratified by clinical site.

The Primary Safety Outcome was defined as the comparison of the proportion of patients with an occurrence of a cluster of serious complications in the RFA or AAM arms.

RESULTS

Primary outcome analysis demonstrated significantly lower recurrence of atrial tachyarrhythmia in the ablation group (54.5%) than in the medically treated group (72.1%) in the 2 years of follow-up (HR, 0.56; 95% CI 0.35-0.90, $P = 0.02$). Recurrence of symptomatic atrial tachyarrhythmia was also lower in the ablation group (40.9% vs. 57.4%; HR 0.52 95% CI 0.30–0.89 $P = 0.02$).

Quality of life, as assessed by the EQ5D score, was significantly improved at 12 months in the RFA group ($P = 0.03$) but not in the AAM group ($P = 0.22$), although there was no statistically significant difference between the groups at 12 months ($P = 0.25$). There were no deaths or strokes in either group.

In the AAM group, flecainide was prescribed to 69% of patients at a mean dose of 175.8 mg/d and 25% received propafenone at a mean dose of 487.7 mg/d. More than one type of drug was received by 16.4% of patients during the 90-day blanking period. Fifty-nine per cent of the AAM group had to discontinue at least one AAM, and 47.5% of patients underwent RFA during the 2-year follow up period.

In the ablation group, complete pulmonary vein isolation (PVI; defined as entrance block) was achieved in 87% of the cases. In addition to PVI, sets of ablation in other regions of the left atrium were performed in at least 21.3%. During the 2-year follow up period, 13.6% required an additional ablation and 9.09% received AAM therapy. Adverse events occurred in 9% of those in the RFA group; 6% experiencing pericardial effusion with tamponade.

DISCUSSION

The results in the RAAFT-2 trial add to an increasing body of evidence showing potential benefits of ablation therapy as a primary treatment for paroxysmal atrial fibrillation in certain patients.^{2,3}

The study demonstrated a significantly decreased rate of recurrent atrial tachyarrhythmias in patients treated with radiofrequency ablation. Freedom from symptomatic AF was also lower in the RFA arm. However, the complication rate was unexpectedly high in the RFA group, given that the operators in the trial were highly skilled and the patient population was relatively healthy. Furthermore, although all patients were reported to have pAF, a large proportion (more than 21%) of patients underwent sets of ablation beyond pulmonary vein isolation; such ablation-sets are likely to have played a role, at least in part, in development of recurrent atrial tachyarrhythmias, and thereby potentially diluted the results of outcomes following ablation therapy.

The study's strengths include the frequent assessments by TTM and the multi-institutional, international patient cohort. Limitations include the small sample size and its bias towards young, healthy patients. The baseline characteristics of the study groups were not identical; there was a statistically significantly increased rate of electrical cardioversions in the AAM group.

When removing TTM, the significance of ablation over AAM disappeared, highlighting the importance of frequent ECG monitoring. The authors highlighted the difficulty in estimating the burden of AF, even with TTM. Studies such as RAAFT-2 remain limited without the use of implantable cardiac monitors to identify the incidence of asymptomatic AF more accurately.³

In conclusion, according to this study, RFA appears to be modestly superior to AAM, reducing recurrence of symptomatic and asymptomatic atrial tachyarrhythmia in patients with pAF; ablation therapy does however carry risks and patients require careful counselling before embarking on ablation as first-line therapy for pAF.

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