Original research

Catheter ablation as first-line treatment for paroxysmal atrial fibrillation: a systematic review and meta-analysis

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ABSTRACT

Objective To assess the efficacy and safety of catheter ablation (CA) compared with antiarrhythmic drugs (AADs) as first-line treatment for symptomatic paroxysmal atrial fibrillation (AF).

Methods Systematic review and meta-analysis of randomised controlled trials identified using MEDLINE, Cochrane Library and Embase published between 01/01/2000 and 19/03/2021. The primary efficacy endpoint was the first documented recurrence of atrial arrhythmias following the blanking period. The primary safety endpoint was a composite of all serious adverse events (SAEs).

Results From 441 records, 6 studies met the inclusion criteria. 609 patients received CA, while 603 received AAD therapy. 212/609 patients in the CA group had a recurrence of atrial arrhythmias as compared with 318/603 in the AADs group resulting in a 36% relative risk reduction (risk ratio: 0.64, 95% CI 0.51 to 0.80, p<0.01). The risk of all SAEs was not statistically different between CA and AAD (0.87, 0.58 to 1.30, p=0.49); 107/609 SAE in the CA group vs 126/603 in the AAD group. Both recurrence of symptomatic atrial arrhythmias (109/505 vs 186/504) and healthcare utilisation (126/397 vs 185/394) were significantly lower in the CA group (0.53, 0.35 to 0.79 and 0.65, 0.48 to 0.89, respectively). There was a 79% reduction in the crossover rate during follow-up among patients randomised to CA compared with AAD (0.21, 0.13 to 0.32, p<0.01).

Conclusions First-line treatment with CA is superior to AAD therapy in patients with symptomatic paroxysmal AF, as it significantly reduces the recurrence of any atrial arrhythmias and symptomatic atrial arrhythmias, and healthcare resource utilisation with comparable safety profile.

INTRODUCTION

Atrial fibrillation (AF) is the most common sustained cardiac arrhythmia worldwide and it significantly impacts patients' morbidity, mortality and quality of life.[1 2] Current international guidelines recommend both rhythm and rate control strategies to achieve symptom control in patients with AF.[3 4] Historical studies performed at the end of the last century comparing these two approaches failed to demonstrate any prognostic advantage of one over the other.[5] However, these studies had several limitations which may have influenced the results, including high rates of anticoagulation discontinuation in patients randomised to rhythm control and treatment crossover during follow-up. Recent evidence suggests instead that early rhythm control (using any approach) may be beneficial in terms of cardiovascular outcomes over rate control.[6]

In terms of rhythm control for AF, catheter ablation (CA) has been shown to be more effective than antiarrhythmic drugs (AADs) in decreasing arrhythmia burden and recurrences, when AADs are not tolerated or have failed.[7] With increasing safety and success rates of CA in recent years, there is emerging interest in its role as first-line therapy to achieve better holistic care for patients. Indeed, several randomised clinical trials (RCTs) evaluating this have been published, both using radiofrequency ablation (RFA), as well as more recently cryoballoon ablation.

The aim of the present meta-analysis was to evaluate the efficacy and safety of CA as compared with AADs as first-line strategy in patients with AF.

METHODS

Search strategies, study selection and data extraction

We performed a systematic review and meta-analysis of RCTs following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) recommendations.[8] The study protocol was registered with PROSPERO (CRD42021228041). Multiple electronic databases (MEDLINE, Cochrane Library, Embase) were searched for publications between 01/01/2000 and 19/03/2021, with no language restrictions. The following search terms were used: 'atrial fibrillation' and 'ablation' and 'first line therapy' and 'early rhythm control', including word variations. Studies were included if all the following inclusion criteria were met: (1) original RCTs comparing CA and AAD; (2) CA performed as first-line therapy; (3) availability of follow-up data on atrial arrhythmia recurrence. Two independent reviewers (WYD and AK) screened all titles and abstracts, identified studies eligible for full-text evaluation and extracted data on a prespecified customised spreadsheet for subsequent statistical analysis. A third independent reviewer (DG) resolved potential disagreements.

Whenever available, data extracted included: study, population and treatment characteristics, outcomes, outcome assessment measures and all

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reported adverse events. The full list of the data points extracted from each study is reported in online supplemental appendix 1.

Two coauthors (JFI, JZ) independently assessed the risk of bias for each study using V.2 of the Cochrane 'Risk of Bias' tool (RoB2),[9] following guidance in the current Cochrane Handbook for Systematic Reviews of Interventions. Any discrepancies between the assessors were resolved via discussion and arbitration with a third coauthor (DG). An internet-based graphic generating platform *Robvis* was used to create the ROB plot with the results from RoB2.[10] In keeping with Cochrane guidance, publication bias was assessed if the number of included studies exceeded 10.[11]

Endpoints

The primary efficacy endpoint was the first documented recurrence of atrial arrhythmias (defined as AF/atrial flutter/atrial tachycardia) following the blanking period. The primary safety endpoint was a composite of all serious adverse events (SAEs) as defined per each individual study protocol. Secondary endpoints were recurrence of symptomatic atrial arrhythmias post-blanking, healthcare resource utilisation and treatment crossovers. Crossovers were defined as use of AADs after the blanking period in the CA group, and use of CA in the AAD group.

Statistical analysis

The meta-analysis was performed using RevMan 5.4.0. Mantel-Haenszel method to obtain the pooled effect sizes for outcomes of interest was used. The random-effects model was chosen. Dichotomous outcomes were presented as risk ratios (RRs) with 95% CIs, and continuous data as mean difference or standardised mean difference with 95% CIs. The outcomes were analysed on an intention-to-treat basis. Forest plots were used to visualise the direction and magnitude of effects and the degree of overlap between CIs. The I^2 statistic was employed to measure heterogeneity among the studies for each analysis. Possible causes for the heterogeneity were explored if it was found to be significant (I^2>75%). Sensitivity test was carried out for outcomes with heterogeneity by removing one study each time. Subgroup analysis comparing RFA and cryoballoon ablation was performed. A p value of less than 0.05 was considered statistically significant.

Patient and public involvement

In this meta-analysis of published papers, there was no patient or public involvement. No patients were involved at any stage of the study development, recruitment, data extraction and analysis, interpretation of the results or writing of the manuscript.

RESULTS

Study and population characteristics

A total of 441 records were identified through the literature search. Fifteen full text articles were assessed for eligibility, of which six matched the inclusion criteria and were included in the present analysis. Details of the study selection process are reported in figure 1. All the included studies were prospective, multicentre RCTs; main inclusion and exclusion criteria are reported in online supplemental table 1. Three of these (RAAFT, RAAFT-2 and MANTRA-PAF)[12–14] used RFA, while the remainder (EARLY-AF, STOP-AF and CRYO-FIRST)[15–17] used cryoballoon ablation. Additional ablation lesions other than pulmonary vein encircling were allowed in MANTRA-PAF,[13] RAAFT-2[14] and CRYO-FIRST.[17] AAD choice (class IC or class III) was left to investigator's discretion in all studies. The follow-up period ranged from 12 to 24 months (table 1).

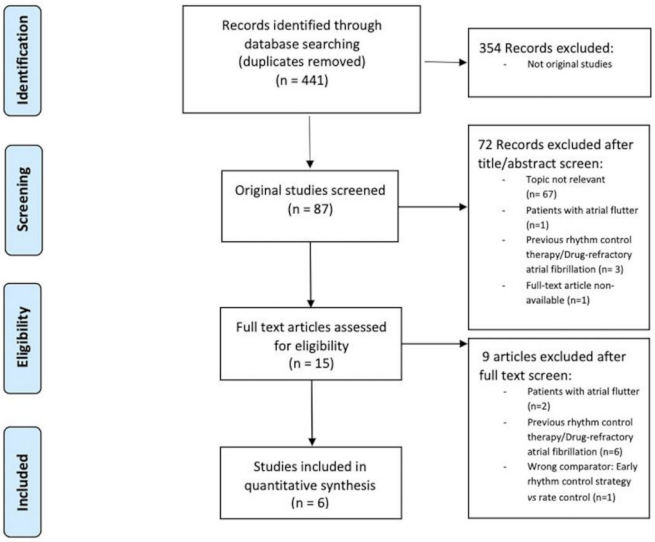

Figure 1 Flow diagram showing the study selection process.

A total of 609 patients received CA as first-line strategy, while 603 were treated with AAD across the 6 studies. Baseline population characteristics were well balanced between the study groups with virtually all patients classified as paroxysmal AF (table 2).

Primary outcomes

First documented recurrence of atrial arrhythmias postblanking

CA resulted in a 36% relative risk reduction in the recurrence of atrial arrhythmias as compared with AAD (pooled RRs: 0.64, 95% CI 0.51 to 0.80, p<0.01) (figure 2A). There was moderate heterogeneity among the studies (I^2: 63%). Subgroup analysis for RFA and cryoballoon ablation compared with AAD showed a trend for reduced (0.65, 0.42 to 1.01, p=0.05) and significantly reduced (0.61, 0.51 to 0.73, p<0.01) recurrence of atrial arrhythmias, respectively. The heterogeneity was significant in the RFA subgroup (I^2: 78%), but not in the Cryoballoon subgroup (I^2: 0%).

Composite of all serious adverse events

The pooled risk of all SAEs was not statistically different between CA and AAD (0.87, 0.58 to 1.30, p=0.49) (figure 2B). There was moderate heterogeneity among the studies (I^2: 58%). In the subgroup analysis, no significant difference was found in either of the groups (RFA subgroup: 0.82, 0.31 to 2.20, p=0.70; Cryoballoon subgroup: 0.90, 0.64 to 1.26, p=0.53). There was significant heterogeneity within the RFA subgroup (I^2: 79%), but not in the Cryoballoon subgroup (I^2: 20%). A list of the most relevant individual SAEs observed in the two study groups is provided in online supplemental table 2).

Secondary outcomes

Recurrence of symptomatic atrial arrhythmias

There was a significantly reduced risk of recurrence of symptomatic atrial arrhythmias in the CA group as compared with AAD (0.53, 0.35 to 0.79, p<0.01) (figure 2C). There was moderate heterogeneity among the studies (I^2: 71%). Subgroup analysis found a trend for reduced recurrence of symptomatic atrial arrhythmias in the RFA subgroup (0.61, 0.37 to 1.01, p=0.06), and significant reduction of symptomatic atrial arrhythmias in the Cryoballoon subgroup (0.42, 0.28 to 0.62, p<0.01), as compared with AAD. There was significant heterogeneity within

Table 1 Main characteristics of the included studies

Study	Sample size	Follow-up (months)	Ablation method	Procedural endpoint	AADs following ablation	Arrhythmia monitoring on follow-up	Primary efficacy endpoints	Secondary efficacy endpoints	Funding
RAAFT (2005)[12]	70	12	RF 8-mm tip catheter (Biosense Webster, Baldwin Park, California, USA, and EP Technologies, Sunnyvale, California, USA)	Abolition of PV potentials along the antrum or inside the vein, or electrical dissociation of the PV from the LA.	Not stated	24-hour Holter at 3, 6 and 12 months. Monthly telephone call. Loop event-recorder for 1 months at discharge and at 3 months	Any symptomatic or asymptomatic AF episode ≥15 s	Hospitalisation rate. Quality of life (SF-36)	Acuson, Siemens Medical Solutions
MANTRA-PAF (2012)[13]	294	24	RF 3.5-mm catheter with an irrigated tip or 8-mm solid tip (Biosense Webster)	Elimination of all high-frequency electrical activity with an amplitude exceeding 0.2 mV inside the encircled areas	Allowed only during 90-days blanking period	7-day Holter at 3, 6, 12, 18 and 24 months	AF burden: percentage of time in AF on each and on all Holter recordings	Freedom and time to first recurrence of symptomatic and asymptomatic AF and AFL ≥60 s. Cumulative and per-visit burden of symptomatic AF. Quality of life (SF-36)	Danish Heart Foundation. Biosense Webster
RAAFT-2 (2014)[14]	127	24	RF Ablation catheter, power and irrigation settings and use of navigation systems left to investigator's discretion	Confirmation of entrance block into each PV	Allowed only during 90-days blanking period	ECG at 1, 3, 6, 12 and 24 months. Trans-telephonic monitor (transmissions at symptoms and biweekly)	Time to first recurrence of symptomatic or asymptomatic AF, AFL or AT episode ≥30 s	First recurrence of AF, AFL and AT episodes. Repeated episodes of symptomatic or asymptomatic AF, AFL and AT. Quality of life (EQ-5D)	Biosense Webster. Population Health Research Institute at McMaster University
EARLY-AF (2020)[15]	303	12	CRYO 23-mm or 28-mm cryoballoon (Arctic Front Advance, Medtronic)	PV bidirectional conduction block	Allowed only during 90-day blanking period	ECG at 3, 6 and 12 months. Implantable loop recorder (daily transmissions)	Any atrial tachyarrhythmia (AF, AFL or AT) ≥30 s. Repeat ablation was considered to be a primary end-point event	First recurrence of symptomatic AT. Percentage of time in AF. Success of multiple ablatio procedures. Quality of life (AFEQT, EQ-5D, EQ-VAS). Healthcare utilisation	Cardiac Arrhythmia Network of Canada. Medtronic. Baylis Medical. University of British Columbia
STOP-AF (2020)[16]	203	12	CRYO Second-generation Cryoballoon (Arctic Front Advance, Medtronic)	PV entrance block and where assessable exit block	Allowed only during 90-day blanking period	ECG at 1, 3, 6 and 12 months. 24-hour Holter at 6 and 12 months. Telephone monitoring weekly and at symptoms	Any atrial tachyarrhythmia (AF, AFL or AT) ≥30 s. Initial failure of the procedure, repeat ablation/ AF surgery, cardioversion or use of AADs (ablation group only) outside the blanking period were considered to be a primary end-point event.	Quality of life in the ablation group (AFEQT, EQ-5D). Healthcare utilisation. Initial success of the procedure. Procedural characteristics	Medtronic
Cryo-FIRST (2021)[17]	218	12	CRYO Second-generation Cryoballoon (Arctic Front Advance, Medtronic)	PV entrance block and where assessable exit block	Allowed only during 90-day blanking period	ECG and 7-day Holter at 1, 3, 6, 9 and 12 months	Any atrial arrhythmia (AF, AFL or AT) >30 s	Recurrence of patient-reported symptomatic palpitations	Medtronic

AF, atrial fibrillation; AFL, atrial flutter; AT, atrial tachycardia; CRYO, cryoablation; ECG, electrocardiogram; LA, left atrium; PV, pulmonary veins; RF, radiofrequency.

Table 2 Baseline population characteristics

	Number of studies	Ablation group (n=609), n (%)*	AAD group (n=603), n (%)*
Paroxysmal AF	6	601 (98.7)	592 (98.2)
Age (years), mean±SEM	6	56.1±1.4	56.7±1.4
Males	5	402 (69.7)	382 (67.2)
Hypertension	5	219 (37.9)	230 (40.5)
Diabetes	4	23 (5.4)	35 (8.3)
CAD/MI	4	28 (5.9)	12 (2.5)
CHF	4	17 (3.9)	18 (4.3)
Stroke/TIA	5	15 (2.6)	18 (3.2)
Previous CV	3	121 (33.1)	143 (39.9)
LA diameter (mm), mean±SEM	6	40.9±1.2	41.1±1.5
LVEF (%), mean±SEM	5	60.4±1.7	60.7±1.6
Beta-blocker	6	310 (51.0)	323 (53.6)
Calcium-channel blocker	5	72 (12.5)	58 (10.2)

*Unless otherwise stated.
AAD, antiarrhythmic drug; AF, atrial fibrillation; CAD, coronary artery disease; CHF, congestive heart failure; CV, cardioversion; LA, left atrial; LVEF, left ventricular ejection fraction; MI, myocardial infarction; SEM, SE error of the mean; TIA, transient ischaemic attack.

the RFA subgroup (I^2: 75%) but not within the Cryoballoon subgroup (I^2: 0%).

Healthcare resource utilisation

Healthcare resource utilisation was reported in four studies: RAAFT, EARLY-AF, STOP-AF and Cryo-FIRST.[12 15–17] There was a 35% reduction in the utilisation of healthcare resources in the CA group as compared with AAD (0.65, 0.48 to 0.89, p<0.01) (figure 2D). Moderate heterogeneity was noted in the analysis (I^2: 57%). No subgroup analysis was performed due to limited number of studies in the RFA subgroup.

Crossover

There was a 79% reduction in the crossover rate during follow-up among patients randomised to CA compared with AAD (0.21, 0.13 to 0.32, p<0.01) (figure 3). The Cryoballoon subgroup had a lower pooled risk of crossover to AAD therapy compared with the RFA subgroup (Cryoballoon subgroup 0.09, 0.03 to 0.31, p<0.01; RFA subgroup: 0.23, 0.15 to 0.37, p<0.01). There was no significant heterogeneity between the studies or within either of the subgroups (I^2: 0%). Details of crossover are reported in online supplemental table 3).

Risk of bias, publication bias and heterogeneity among included studies

All studies included were rated as low risk in each domain in the RoB2 and the overall ROB, following the algorithm in RoB2 (figure 4). Publication bias was not assessed in this meta-analysis due to limited number of included studies. A funnel plot is provided in online supplemental figure S1). Sensitivity analysis demonstrated that the RAAFT trial[12] was the major source of heterogeneity across all the outcomes except the crossover rate (online supplemental table 4).

Discussion of results

CA targeting electrical isolation of the pulmonary veins has traditionally been reserved for symptomatic patients with AF who are either refractory and/or intolerant to AADs. In such populations, CA has been shown to be superior to AAD therapy. However, with the improving success rates and safety profile of CA, there has been emerging interest in offering this treatment earlier on in the patient pathway, including as first-line therapy.[18] The effectiveness of AF ablation in this setting and, in particular, its safety and cost efficacy, remains to be established. This meta-analysis of six prospective, multicentre RCTs comparing CA versus AAD as the first-line therapy for patients with paroxysmal AF showed that: (i) CA significantly reduced the overall

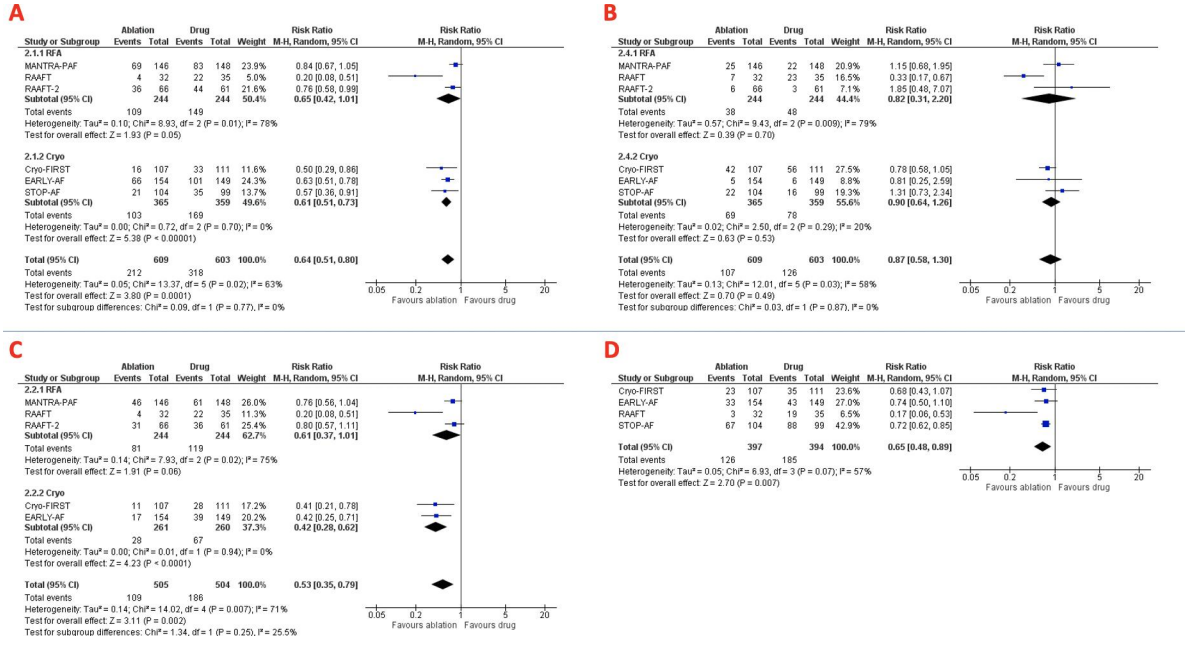

Figure 2 Forest plots showing the comparative efficacy and safety of catheter ablation versus antiarrhythmic drugs as first-line treatment of paroxysmal atrial fibrillation. (A) Risk of atrial arrhythmia recurrence. (B) Risk of serious adverse events. (C) Risk of symptomatic arrhythmia recurrence. (D) Risk of healthcare resources use. CI, confidence interval; Cryo, cryoballoon ablation; M-H, Mantel-Haenszel; RFA, radiofrequency ablation; RR, risk ratio.

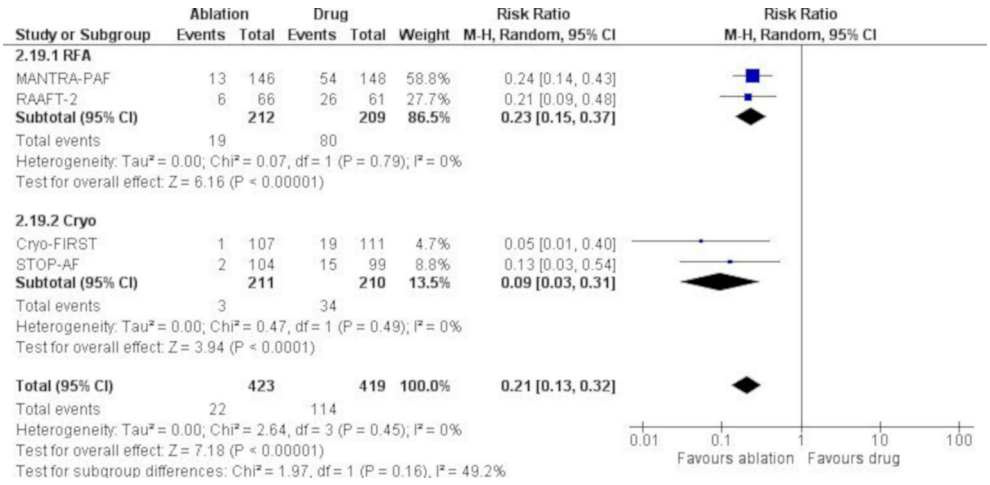

Figure 3 Risk ratios of crossing over to alternative therapy. CI, confidence interval; Cryo, cryoballoon ablation; M-H, Mantel-Haenszel; RFA, radiofrequency ablation.

recurrence of atrial arrhythmias as compared with AAD during a 2-year follow-up period; (ii) CA was more effective than AAD in reducing symptomatic atrial arrhythmia recurrences; (iii) there were no statistically significant differences in terms of SAEs between CA and AAD and (iv) CA was associated with reduced healthcare resource utilisation as compared with AADs.

Moreover, compared with AADs, the beneficial effect of cryoballoon ablation on any atrial arrhythmia recurrence and symptomatic atrial arrhythmia recurrence appeared to be more pronounced than RFA. There are a few potential explanations to this observation. Of note, studies using cryoballoon ablation were undertaken more recently compared with the historical RFA studies which do not reflect contemporary practice. In this regard, the RFA studies were performed in an earlier era before the widespread use of newer technologies such as contact force sensing catheters and ablation index when late pulmonary vein reconnection was the rule. This was demonstrated in the GAP study,[19] done during a similar period, where 70% of patients who were randomised to a complete pulmonary vein isolation strategy using RFA had at least 1 reconnection of at least one vein identified at 3 months. In comparison, late pulmonary vein reconnection rates with the currently employed second generation cryoballoon were much lower, in just 21% of patients in the SUPIR trial.[20] Furthermore, although headline results in the FIRE AND ICE trial stated that RFA and cryoballoon ablation were equal, the actual AF burden, rate of AF hospitalisations and rate of redo AF ablation were lower in the cryoballoon group as the degree of reconnection was often very limited.[21] In this meta-analysis, we also found that there was substantial heterogeneity between the RFA studies but not the cryoballoon ablation studies which may have contributed further to this discrepancy. Notably, the pooled risk of crossover to AAD therapy was lower with cryoablation, as compared with RFA. Overall, it may be surmised that the quality of pulmonary vein isolation performed with the second generation cryoballoon is superior to that of RFA using historical methods, as reflected in our findings. Nonetheless, our meta-analysis was not designed to compare the effects of RFA and cryoballoon ablation which has previously been evaluated, although not in the context of an early rhythm control approach.[22] Shorter procedure duration has been reported as a potential advantage of cryoballoon ablation over RFA at the expense of an increased fluoroscopy

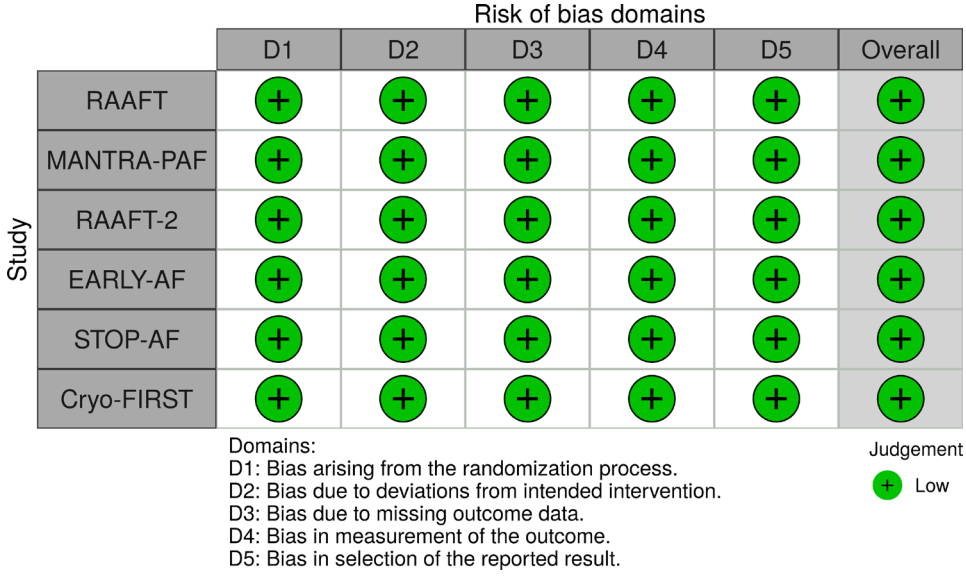

Figure 4 Risk of bias. The risk of bias for each study included in the meta-analysis was assessed following the algorithm in RoB2. ROB, risk of bias.

time. Procedure and fluoroscopy time were reported in three out of six studies[14–16] and the data were not suitable to combine for a meta-analysis. In their RFA study, Morillo *et al*[14] reported a mean procedure and fluoroscopy time of 210±72 min and 70±60 min, respectively. As regards cryoballoon studies, Wazni *et al*[16] reported a mean procedure and fluoroscopy time of 139±74 min and 18.2±11.8 min, respectively, while the median procedure and fluoroscopy time reported by Andrade *et al*[15] were 106 (IQR 89–131) min and 18.9 (IQR 12.6–27.0) min, respectively.

In terms of safety, the rate of SAEs was comparable between the CA and AAD groups (17.6% vs 20.9%). Furthermore, the rate of SAEs was similar with both cryoballoon ablation and RFA over AADs. Overall, the risk of all-cause death and stroke was low with a total of seven deaths (0.6%; three in CA group and four in AAD group) and six strokes (0.5%; four in CA group and two in AAD group). The most frequent complications were cardiac tamponade or pericardial effusion requiring drainage (1.1%) and haematoma or haemorrhage (1.0%) in CA group and bradycardia or atrioventricular block requiring pacemaker implantation (1.2%) and syncope (1.2%) in the AAD group (online supplemental table 2). The safety of CA has been established in previous studies and registries[23] with major complications occurring in 4.5%–6% of the all procedures, more frequently in older female patients, with extremes of body mass index or underlying structural heart disease.[24 25] The low rate of major complications observed with CA in the present meta-analysis is likely due to the inclusion of patients with a lower risk profile, and the fact that the procedures were performed in highly experienced centres. Our findings suggest that both rhythm control strategies have equal safety profile but carry specific risks that should be individualised in a shared-decision making approach with the patient.

For the recurrence of symptomatic atrial arrhythmias, early CA was more effective than AADs. Likewise, early CA was associated with reduced healthcare resource utilisation as compared with AADs. Moderate heterogeneity was noted in this analysis, mostly derived from the results of the RAAFT study,[12] in which only hospitalisations were recorded (3 events in the CA group vs 19 events in the AAD group). In the studies employing cryoballoon ablation,[15–17] hospitalisations, emergency department visits and unscheduled outpatient visits were analysed (123 events in the CA group vs 166 events in the AAD group). This was consistent with other studies which demonstrated that AF ablation was related to a significant decline in all-cause hospitalisations; driven mainly by a reduction in hospitalisations for AF and heart failure. The independent predictors for decreased hospitalisation were age below 55 years, obstructive sleep apnoea and heart failure. Notably, in the CABANA trial,[7] CA led to a significantly lower risk of death or cardiovascular hospitalisation (HR 0.83; 0.74 to 0.93) as compared with AADs.

Several previous clinical trials have already demonstrated the superiority of CA over AADs among patients with drug-refractory paroxysmal AF.[7 26] Here, it was found that the time interval of less than a year between AF diagnosis and CA was associated with a lower rate of AF recurrence, and a reduction in unfavourable atrial remodelling (ie, lower values of B-type natriuretic peptide, C reactive protein and size of left atrium) as compared with patients with a delay in CA.[27] Our meta-analysis confirms the beneficial role of early CA over AAD therapy in patients with paroxysmal AF with significantly better maintenance of sinus rhythm, reduced utilisation of healthcare resources and comparable safety profile over long-term follow-up.

Strengths and limitations

Our meta-analysis has the methodological strength of including only RCTs. As compared with a previous meta-analysis on this topic,[28] we included twice the number of studies. Moreover, reflecting current advancements in cardiac electrophysiology, we considered RFA studies and also studies that employed cryoballoon ablation.

There are a few limitations to our study. There were variations in terms of duration of follow-up, monitoring strategies and definitions of outcome between the included studies. The follow-up period in the RAAFT-2[14] and MANTRA-PAF[13] studies was longer (24 months) than in other studies[12 15–17] (12 months) and patients had continuous rhythm monitoring with implantable loop recorders only in EARLY-AF.[15] Nonetheless, these parameters were consistent within each trial which compared CA and AADs, and therefore, the relative differences between both treatment approaches reported in our meta-analysis were unlikely to be significantly influenced by this. Patients included in all studies were relatively young and healthy, which could potentially limit the generalisability of the results to the whole population with AF. Moreover, the role of early CA in patients with persistent AF remains undetermined though a recent multicentre registry[29] showed that cryoballoon ablation might be considered a first-line treatment even for patients with persistent AF. During 24 months of follow-up, the arrhythmia-free survival rate was 64% in such patients. The RAAFT-3 trial (ClinicalTrials.gov Identifier: NCT04037397) is an ongoing RCT which is aimed at addressing this topic. The treatment effect of AAD therapy may have been undermined by inadequate optimisation, potentially causing overestimation of the efficacy of CA in comparison. The role of early arrhythmia recurrences during the blanking period as a predictor of long-term recurrences was not assessed due to lack of available data, and ad hoc clinical trials are warranted to shed light on this issue. Although individual studies included in the present meta-analysis showed improved QoL with both treatments (with CA being superior to AADs in the RAAFT study),[12] we were unable to meta-analyse the results due to the different measures of QoL used in these studies.

Key messages

What is already known on this subject?

- Early rhythm control may be beneficial in terms of cardiovascular outcomes over rate control in patients with atrial fibrillation. Catheter ablation (CA) has been shown to be more effective than antiarrhythmic drugs (AADs) in decreasing arrhythmia burden and recurrences, but it is usually indicated when AADs are not tolerated or have failed.

What might this study add?

- This meta-analysis demonstrates that first-line treatment with CA is superior to AAD therapy in patients with symptomatic paroxysmal atrial fibrillation, as it significantly reduces the recurrence of any atrial arrhythmias and symptomatic atrial arrhythmias and healthcare resource utilisation with comparable safety profile.

How might this impact on clinical practice?

- Our results indicate that CA should be considered early in the treatment of patients with symptomatic paroxysmal atrial fibrillation as it results in better outcomes and healthcare related costs compared with AAD therapy.

CONCLUSION AND POLICY IMPLICATIONS

Our meta-analysis demonstrates that first-line treatment with CA is superior to AAD therapy in patients with symptomatic paroxysmal AF, as it significantly reduces the recurrence of any atrial arrhythmias and symptomatic atrial arrhythmias, and healthcare resource utilisation with comparable safety profile, thus benefiting both patients and healthcare systems.

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Contributors JFI and WYD contributed equally to this work. JFI contributed to the design of the study, interpreted the data and drafted the manuscript. WYD contributed to the design of the study, interpreted the data and revised the manuscript. AK contributed to the design of the study, interpreted the data and drafted the manuscript, JZ analysed and interpreted the data and drafted the manuscript. DG contributed to the conception of the study, interpreted the data and revised the manuscript and he is the guarantor. GB, JA and GL contributed to the interpretation of the data and revised the manuscript critically for important intellectual content.

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