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Systematic Review

Efficacy and Safety of Catheter Ablation vs Antiarrhythmic Drugs as Initial Therapy for Management of Symptomatic Paroxysmal Atrial Fibrillation: A Meta-Analysis

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Abstract

Background: Catheter ablation is an effective treatment for atrial fibrillation (AF), primarily performed in patients who fail antiarrhythmic drugs. Whether early catheter ablation, as first-line therapy, is associated with improved clinical outcomes remains unclear. **Methods**: Electronic databases (PubMed, Scopus, Embase) were searched until March 28th, 2021. Randomized controlled trials (RCTs) compared catheter ablation vs antiarrhythmic drug therapy as first-line therapy were included. The primary outcome of interest was the first documented recurrence of any atrial tachyarrhythmia (symptomatic or asymptomatic; AF, atrial flutter, and atrial tachycardia). Secondary outcomes included symptomatic atrial tachyarrhythmia (AF, atrial flutter, and atrial tachycardia) and serious adverse events. Unadjusted risk ratios (RR) were calculated from dichotomous data using Mantel Haenszel (M-H) random-effects with statistical significance considered if the confidence interval (CI) excludes one and $p < 0.05$. **Results**: A total of six RCTs with 1212 patients (Ablation n = 609; Antiarrhythmic n = 603) were included. Follow- up period ranged from 1–2 years. Patients who underwent ablation were less likely to experience any recurrent atrial tachyarrhythmia when compared to patients receiving antiarrhythmic drugs (RR 0.63; 95% CI 0.55–0.73; $p < 0.00001$). Symptomatic atrial tachyarrhythmia was also lower in the ablation arm (RR 0.53; 95% CI 0.32–0.87; $p = 0.01$). No statistically significant differences were noted for overall any type of adverse events (RR 0.93; 95% CI 0.68–1.27; $p = 0.64$) and cardiovascular adverse events (RR 0.90; 95% CI 0.56–1.44; $p = 0.65$) respectively. **Conclusions**: Catheter ablation, as first-line therapy, was associated with a significantly lower rate of tachyarrhythmia recurrence compared to conventional antiarrhythmic drugs, with a similar adverse effect risk profile. These findings support a catheter ablation strategy as first-line therapy among patients with symptomatic paroxysmal atrial fibrillation.

Keywords: catheter ablation; radiofrequency ablation; cryoballoon; first-line therapy; pulmonary vein isolation

1. What is New?

• Catheter ablation of paroxysmal AF aiming at electrical pulmonary vein isolation (PVI) as first line therapy resulted in maintenance of sinus rhythm in drug naïve patients.

• Cryoballoon Catheter Ablation was superior to antiarrhythmic drug (AAD) therapy, significantly reducing Atrial tachycardia recurrence in treatment-naive patients with symptomatic paroxysmal atrial fibrillation.

• Catheter ablation was associated with a similar adverse risk profile as compared to antiarrhythmic drug therapy.

2. Introduction

Atrial Fibrillation is the most common cardiac arrhythmia encountered in clinical practice. It is associated with increased morbidity, mortality, and impaired quality of life [1]. It is frequently recurrent and follows a progressive course over time [2]. Current guidelines recommend the use of antiarrhythmic drugs (AAD) as initial therapy for AF and before catheter ablation (CA) is considered [3]. However, antiarrhythmic drugs have limited efficacy and are associated with adverse effects [4].

Multiple randomized controlled trials (RCTs) have shown that CA is superior and safe than AAD in maintaining sinus rhythm and preventing recurrent arrhythmias [5–12]. CA has also demonstrated improvement in left ventricular ejection fraction (LVEF) and quality of life compared to AAD pharmacotherapy in patients with heart failure [13–16].

In clinical practice, patients with symptomatic refractory AF or those intolerant to AADs undergo CA. This is mainly preceded by the failure of AADs [17]. However, accumulating evidence has suggested that early ablation in AF with shorter diagnosis-to-ablation times allows better rhythm control [18–20]. Similarly, the recent Early Treatment of Atrial Fibrillation for Stroke Prevention Trial (EAST-AFNET 4) showed that early rhythm control results in better clinical outcomes than standard care management [21]. To date, only a few studies have investigated the role of CA as a first-line therapeutic modality for AF patients [22–27]. Whether early CA halts AF progression or is associated with improved clinical outcomes remains unclear. The best appropriate timing for ablation in patients with symptomatic AF, regardless of AF type, has not been determined.

Considering recent evidence regarding this matter [25–27], a systematic review and meta-analysis was performed to examine the safety and efficacy of CA vs AAD as first-line treatment for the maintenance of sinus rhythm in symptomatic AF patients.

3. Methods

3.1 Search Strategy and Selection

This meta-analysis was carried out adhering to Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines (PRISMA) was performed (Fig. 1) [28]. A systematic search was performed on online bibliographic databases including PubMed, Embase, and Scopus. ClinicalTrials.gov and Google Scholar were searched to identify grey literature. No restrictions on date, language and publication type existed wherein the search was conducted from inception until the 28th of March 2021. Using Boolean logic, the following combination of MeSH terms and keywords were used on online databases: “atrial fibrillation”, “radiofrequency ablation”, “cryoablation”, “antiarrhythmic drug”, “isolation”, and “first-line catheter ablation” “pulmonary vein isolation”. A cross-reference check of previously published meta-analysis on this topic was also performed.

3.2 Inclusion Criteria

Eligibility criteria for the analysis included studies with an adult patient population (age $\geq$18 years) who had symptomatic AF with at least one episode detected on electrocardiography and no previous maintenance antiarrhythmic drug treatment before randomization were selected for the qualitative and quantitative analysis. In an attempt to decrease the risk of bias inherent with including observational studies, only randomized controlled trials evaluating CA (Radiofrequency and Cryoballoon) vs AAD therapy as first-line treatment were included.

3.3 Exclusion Criteria

Patients younger than 18 with a history of scheduled use of class IC or class III antiarrhythmic drugs at therapeutic doses were excluded. Patients were also excluded if they had a previous ablation for AF, a left atrial diameter $>$50 mm, LVEF $<$40%, severe heart failure, moderate to severe left ventricular hypertrophy, and contraindication to oral anticoagulation therapy. Studies with insufficient data, such as systematic reviews, meta-analyses, letters, editorials, case reports, conference abstracts and case series with less than ten patients (total n = 1504) were also excluded.

3.4 Data Extraction and Quality Assessment

Two independent reviewers (A.A.R. and S.P) screened titles, abstracts and searching reference lists of included studies (backward snowballing). Extracted data was verified by the reviewers and duplicates were removed using Endnote X9 (Clavariaye Analytics, Chandler, AZ, US). The senior author arbitrated any discrepancies concerning the evaluation of the studies. The study design, demographic characteristics, and various outcomes were extracted. No language restrictions were made. For the quality assessment of included RCTs in the systematic review and meta-analysis, evaluation with the Revised Cochrane Risk of Bias

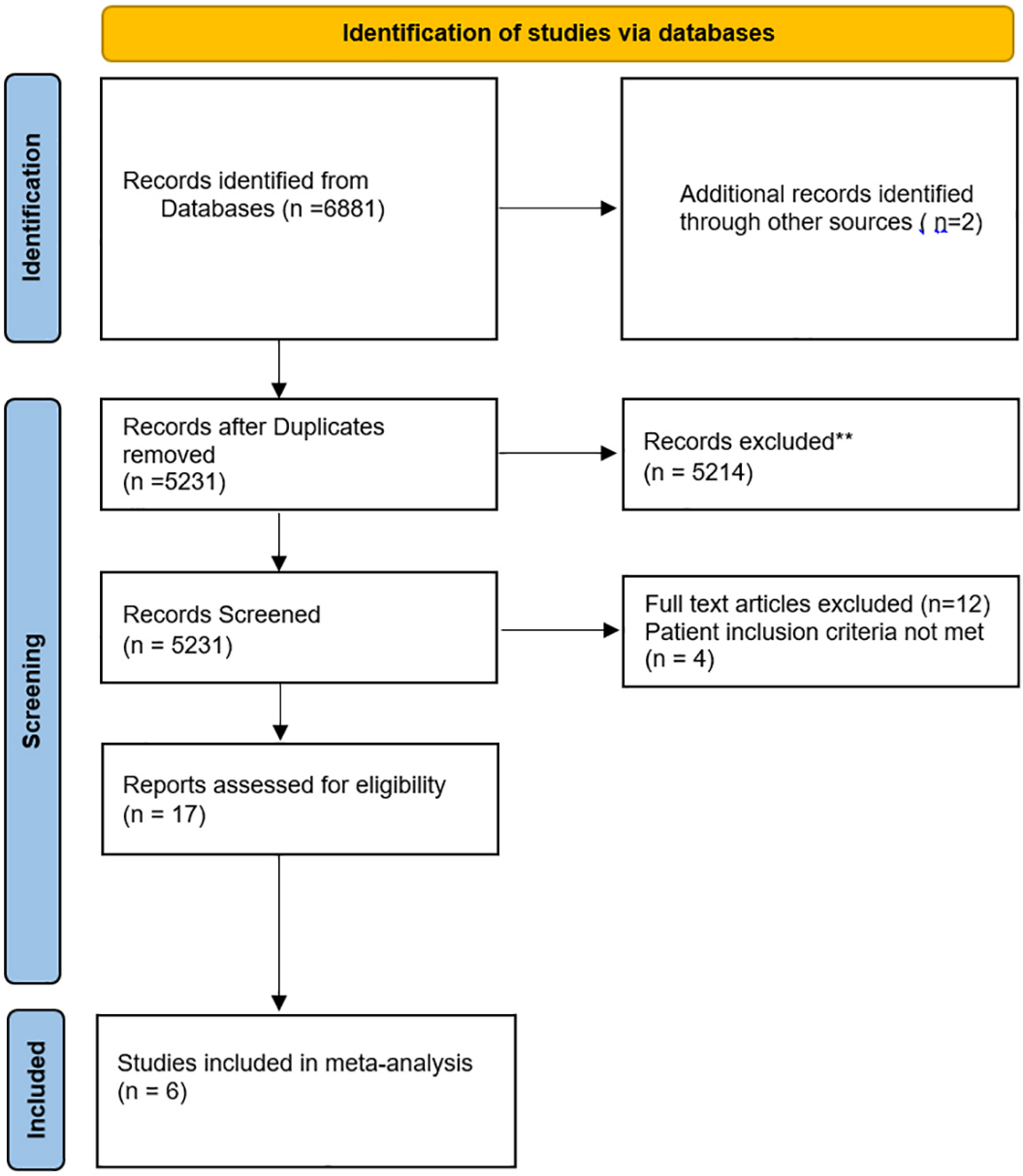

Fig. 1. PRISMA Flow of the search strategy for systematic review and meta-analysis on ablation versus antiarrhythmics as first line therapy for atrial fibrillation.

tool (ROB 2) was employed to ascertain the quality of studies by two independent reviewers (A.A.R and H.N) [29].

3.5 Interventions

Pulmonary-vein isolation (PVI) was the primary intention of the catheter ablation group. During the cryoballoon procedure, operators performed pulmonary-vein isolation by the fluoroscopic guided device placement at each pulmonary-vein antrum and advanced towards the pulmonary vein to obtain occlusion. The balloon was filled with liquid refrigerant for cooling the tissue.

In the radiofrequency group, operators performed pulmonary-vein isolation using electro anatomical navigation and created a contiguous circular lesion around each pulmonary-vein antrum with point-by-point applications of radiofrequency energy.

3.6 Study Definitions and Endpoints

The primary outcome of interest was the first documented recurrence of any type of atrial tachyarrhythmia. The follow-up period ranged from 1–2 years. Arrhythmia recurrence was defined as any symptomatic or asymptomatic; AF, atrial flutter, and atrial tachycardia that occurred outside the blanking period of 90 days. The blanking period was defined as the first 90 days after the index ablation procedure or drug initiation. The current Heart Rhythm

Society consensus statement on catheter ablation for atrial fibrillation recommends the use of a 3-month blanking period immediately post-ablation to accurately characterize the long-term clinical outcomes of catheter ablation procedures [3].

A separate analysis was performed for studies that have specifically evaluated cryoballoon CA vs AAD therapy as a first-line treatment strategy in patients with symptomatic AF.

Secondary outcomes included symptomatic atrial tachyarrhythmia (AF, atrial flutter, and atrial tachycardia) and serious adverse events. A separate analysis was performed for cardiovascular adverse events, defined as ischemic and embolic events (myocardial infarction, stroke or transient ischemic attack), hospitalizations for heart failure, major bleeding, pulmonary vein stenosis, atrio-esophageal fistula, pericardial complications (effusion, hemorrhage, tamponade, and perforation), syncope, and life-threatening arrhythmias. Quality of life (QoL) was also examined when reported by included studies.

3.7 Statistical Analysis

Statistical analyses were performed using Review Manager (RevMan) [Computer program] Version 5.4 Cochrane Collaboration (The Cochrane Community, London, UK). The Cochran-Mantel Haenszel method was used with the random-effects model to calculate unadjusted risk ratios (RR) for the primary and secondary endpoints. The estimated effect size was reported as a point estimate and 95% confidence interval (CI). An alpha criterion of p-value ≤ 0.05 was considered statistically significant. The Higgins's I-squared (I^2) statistical model was used for assessment of study heterogeneity, with values <25%, 25–50%, 50–75%, and >75% corresponding to no, low, moderate, and high degrees of heterogeneity, respectively [30]. A confidence interval (CI) of 95% and a p-value < 0.05 were used in all our analyses to assess statistical significance. The publication bias was depicted graphically and numerically as a forest plot and Egger's regression test [31].

4. Results

The initial search yielded 6881 results, of which 5231 articles were screened for title and abstract. Consequently, records were removed due to ineligibility (reviews, editorials, non RCTs, ongoing trials, and abstracts). The search strategy is shown in Fig. 1. A full-text screening of 17 articles led to the inclusion of 6 studies, with 1212 participants (609 patients in the CA group and 603 patients in the AAD group) [22–27]. Quality assessment findings of the included studies are summarized in **Supplementary Figs. 1,2.**

4.1 Study Characteristics

Baseline demographics, comorbidities and characteristics of studies included in the meta-analysis are summarized in Table 1 (Ref. [22–27]). The follow-up period ranged from 1–2 years. The average age was 56.6 years in both groups. Approximately 70% of patients were men in both groups. The type of CA was radiofrequency in three studies [22–24] and cryoablation in another three studies [25–27]. Five studies [23–27] included patients with paroxysmal AF and one study involved 35 patients with paroxysmal AF and two patients with persistent AF [22]. Holter monitor and 12-lead electrocardiography was the most frequently used method for monitoring [22–24,26,27], while one study stated the use of an implantable cardiac device [25]. The CA had a 37.2% and a 6.9% prevalence of hypertension and diabetes, while in the AAD cohort, 39.8% patient population had hypertension and 10% had diabetes, respectively. There was a prior history of stroke or transient ischemic attack in 2.4% and 2.9% of patients in the ablation and AAD groups. Out of 609 patients in the Ablation group, 248 (42.9%), 204 (44.6%), 44 (10.2%) and 64 (23.6%) were on oral anticoagulation, β-Blockers, calcium channel blockers and aspirin, respectively. Finally, out of 603 patients in the AAD group, 232 (54.4%), 216 (47.4%), 42 (9.8%) and 49 (15.2%) were on oral anticoagulation, β-Blockers, calcium channel blockers and aspirin.

4.2 Clinical Outcomes

4.2.1 Primary Efficacy Endpoint

Five out of six studies reported the recurrence of any atrial tachyarrhythmia (Symptomatic/Asymptomatic; AF, Atrial flutter, atrial tachycardia) [22–26]. Recurrence occurred in 160 of 577 (27.7%) patients who underwent CA and 223 of 457 (45%) patients on AAD. Our meta-analysis revealed a 37% reduction in the risk of recurrence of any type of atrial tachyarrhythmia (RR 0.63; 95% CI 0.55–0.73; $p < 0.00001$) with no heterogeneity among studies $I^2 = 0$ (Fig. 2).

Cryoablation as an ablation procedure was evaluated in three recent studies. There was a 40% reduction in the risk of recurrence of any types of atrial tachyarrhythmia (RR 0.60 95% CI 0.50–0.72; $p < 0.00001$) with no heterogeneity among the studies ($I^2 = 0$) (Fig. 3).

4.2.2 Secondary Efficacy Endpoint

4.2.2.1 Recurrence of Symptomatic Atrial Tachyarrhythmia

Four out of five studies reported recurrence of symptomatic Atrial Tachyarrhythmia [22–25]. A secondary outcome of symptomatic recurrence of AF, atrial flutter or atrial tachyarrhythmia was reported in 83 patients of 398 patients (20.8%) in the CA group compared with 141 (35.8%) in the ablation group. A better response was observed in the CA group with a 47% reduction in the risk of recurrence

Table 1. Baseline demographics, comorbidities and study characteristics of studies included in the meta-analysis.

Variable	RAAFT-1	MANTRA-PAF	RAAFT-2	EARLY-AF	STOP-AF First	Cryo-FIRST
	2005 [22]	2012 [23]	2014 [24]	2020 [25]	2020 [26]	2021 [27]
Sample (n) Ablation/AAD	32/35	146/148	66/61	154/149	104/99	107/111
Age	53/54	56/54	56.3/54.3	57.7/59.5	60.4/61.6	50.5/54.1
Male (n)	NA	100/106	51/45	112/102	63/57	76/72
CAD risk factors						
Hypertension	8/10	43/53	28/25	57/55	58/57	33/40
Diabetes Mellitus	NA	6/10	1/4	NA	15/17	1/4
Stroke/TIA	NA	6/5	3/4	4/5	2/3	0/1
Left atrial size mean (SD), (mm)	41 $\pm$ 8/42 $\pm$ 7	40 $\pm$ 6/40 $\pm$ 5	40 $\pm$ 5/43 $\pm$ 5	39.5 $\pm$ 5.0/38.1 $\pm$ 6.5	38.7 $\pm$ 5.7/38.2 $\pm$ 5.4	37.0 $\pm$ 5.9/38.0 $\pm$ 4.9
LV ejection fraction mean (SD), %	53 $\pm$ 5/54 $\pm$ 6	NA	61.4 $\pm$ 4.8/60.8 $\pm$ 7.0	59.6 $\pm$ 7.0/59.8 $\pm$ 7.6	60.9 $\pm$ 6.0/61.1 $\pm$ 5.9	62.8 $\pm$ 5.4/63.7 $\pm$ 5.4
CHA2DS2-VASc score	N/A		N/A			
0		92/80				49/38
1		37/49				33/40
2		13/14				13/15
3		3/4				4/10
4		1/1				3/2
Type of AF	35 patients had paroxysmal AF and 2 had persistent AF	Paroxysmal	Paroxysmal	Paroxysmal	Paroxysmal	Paroxysmal
Type of CA	Radiofrequency–Pulmonary Vein Isolation	Radiofrequency–Pulmonary Vein Isolation	Radiofrequency–Pulmonary Vein Isolation	Cryoballoon–Pulmonary Vein Isolation	Cryoballoon–Pulmonary Vein Isolation	Cryoballoon–Pulmonary Vein Isolation
Monitoring	24-hour Holter monitoring	7-day Holter-monitor recording	Holter, transtelephonic monitor, or rhythm strip	Implantable cardiac monitoring device	12-lead ECG	12-lead ECG and 7-day Holter.
Medications						
Oral anticoagulation	NA	NA	35/19	103/96	72/68	38/49
β-Blockers	19/23	NA	40/36	85/92	6/9	54/56
Calcium channel blockers	NA	NA	14/13	11/10	10/4	9/15
Aspirin	NA	NA	38/29	NA	21/13	5/7

Table 1. Continued.

Variable	RAAFT-1	MANTRA-PAF	RAAFT-2	EARLY-AF	STOP-AF First	Cryo-FIRST
	2005 [22]	2012 [23]	2014 [24]	2020 [25]	2020 [26]	2021 [27]
AAD tolerable dose	oral flecainide 100–150 mg twice daily, propafenone 225–300 mg 3 times daily, sotalol 120–160 mg twice daily	Flecainide (200 mg/day) or propafenone (600 mg/day)	Flecainide 176 mg; Propafenone 487 mg; Dronedarone 60 mg	NA	NA	NA
Study design						
Study	Prospective RCT	Prospective RCT	Prospective RCT	Prospective RCT	Prospective RCT	Prospective RCT
Year	2005	2012	2014	2020	2020	2021
Center	Multi-center	Multi-center	Multi-center	Multi-center	Multi-center	Multi-center
Study Period	2001–2002	2005–2009	2006–2010	2017–2018	2017–2019	
Sample size	67	294	127	303	203	218
Follow-up Duration	12 months	24 months	24 months	12 months	12 months	12 months
Main outcomes	Recurrence of AF, Hospitalization and QoL assessment.	Burden of AF, freedom from any AF, freedom from symptomatic AF and QoL assessment.	First documented atrial tachyarrhythmia (symptomatic or asymptomatic AF, atrial flutter, or atrial tachycardia), symptomatic recurrences of atrial tachyarrhythmia and QoL assessment.	First documented recurrence of any atrial tachyarrhythmia (AF, atrial flutter, or atrial tachycardia), freedom from symptomatic arrhythmia, the AF burden, and QoL assessment.	Freedom from initial failure of the procedure for atrial arrhythmia recurrence post 90-day blanking period, serious adverse events.	Freedom from any AA recurrence (at least one episode of AF, atrial flutter, or atrial tachycardia) lasting >30 s, rate of serious adverse events (SAEs) and recurrence of symptomatic palpitations.
Results	Ablation was superior to AAD.	No significant difference between the treatment groups.	Ablation compared with AAD resulted in a lower rate of recurrent atrial tachyarrhythmia.	Ablation compared with AAD resulted in a significantly lower rate of recurrent atrial tachyarrhythmia.	Ablation as initial therapy was superior to AAD for the prevention of atrial arrhythmia recurrence.	Ablation as initial therapy was superior to AAD therapy significantly reducing AA recurrence in treatment naive patients with paroxysmal AF.

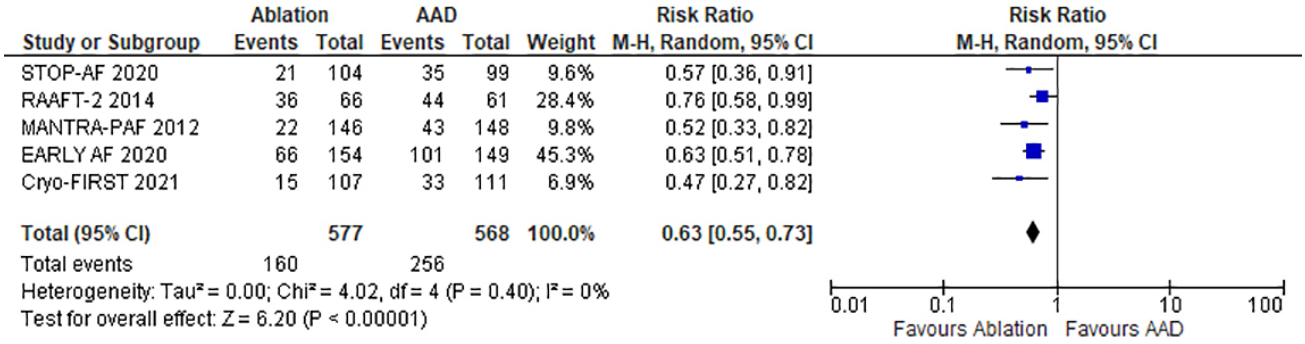

Fig. 2. Forrest plot comparing the primary efficacy endpoint of catheter ablation to antiarrhythmic drug therapy as first line treatment for atrial fibrillation.

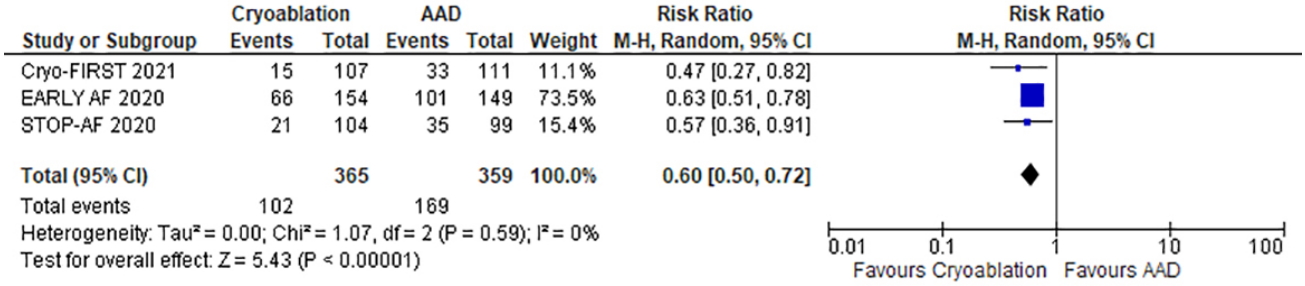

Fig. 3. Forrest plot comparing the primary efficacy endpoint of cryoablation to antiarrhythmic drug therapy as first line treatment for atrial fibrillation.

of symptomatic atrial tachyarrhythmia (RR 0.53; 95% CI 0.32–0.87; $p = 0.01$). There was moderately high heterogeneity among the studies included for the analysis ($I^2 = 71\%$) (Fig. 4).

4.2.2.2 Quality of Life (QoL)

QoL was reported only in three of the six included studies. It was measured by using the 36-item Short Form General Health Survey (SF-36) in 1 study [22] and European Quality of Life 5 Dimension (EQ-5D) in 2 studies [24,25]. The study that used SF-36 reported an improvement in QoL both in the physical and mental domains in patients who underwent CA. A significant improvement (WMD 11 95% CI 8–12; $p < 0.001$) was observed in general health at a six-month follow-up visit. Similar improvement was observed in the other two studies that used EQ-5D to assess QoL. These results could not be compared because different measurements were used to evaluate QoL parameters.

4.2.2.3 Safety-Adverse Events

All six studies reported the overall adverse effects after treatment and were included in the meta-analyses [22–27]. The details of adverse events are described in **Supplementary Table 1**. The number of adverse events were 111 of 609 (18.2%) patients who underwent CA and 124 of 603 (20.5%) patients who were on AAD. However, there was no significant difference in the incidence of major adverse events between ablation and AAD (RR 0.93; 95% CI 0.68–1.27; $p = 0.64$) with homogenous findings ($I^2 = 36\%$) (Fig. 5).

4.2.2.4 Cardiovascular Adverse Events

The cardiovascular events have been described in **Supplementary Table 2**. Out of 609 patients in the ablation arm and 603 patients in the AAD arm, 61 (10%) and 75 (7.9%) experienced cardiovascular events, respectively. Using a random-effects model, we determined that the catheter ablation group had similar odds as compared to the AAD group in experience cardiovascular adverse events (RR 0.90; 95% CI 0.56–1.44; $p = 0.65$), with no heterogeneity among studies ($I^2 = 43\%$) (Fig. 6).

5. Publication Bias

On visual assessment, the funnel plot was symmetrical with an equal number of studies on each side of the vertical axis. There was no publication bias demonstrated. Egger's test for the assessment of publication bias was non-significant (2-tailed $p > 0.05$) (**Supplementary Figs. 3,4,5,6,7**).

6. Discussion

This meta-analysis of six RCTs, including 1212 patients, compares the CA's efficacy and safety outcomes as

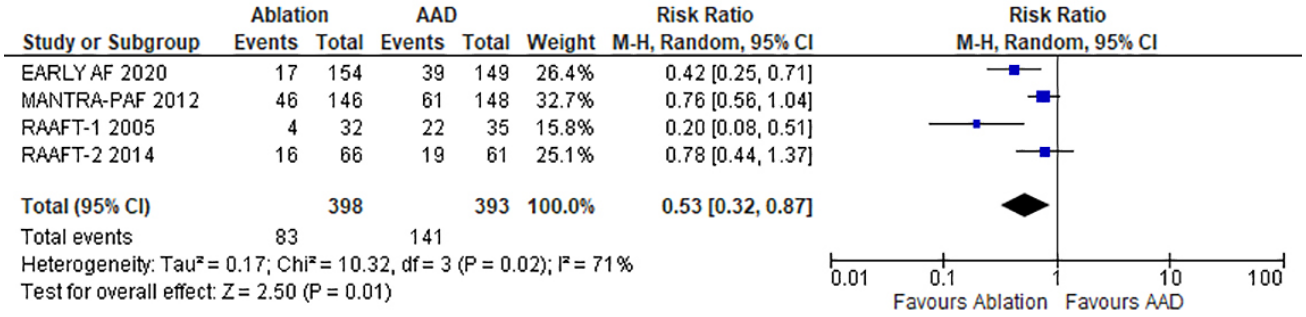

Fig. 4. Forrest plot comparing catheter ablation to antiarrhythmic drug therapy (as first line treatment for atrial fibrillation) for the recurrence of symptomatic tachyarrhythmia.

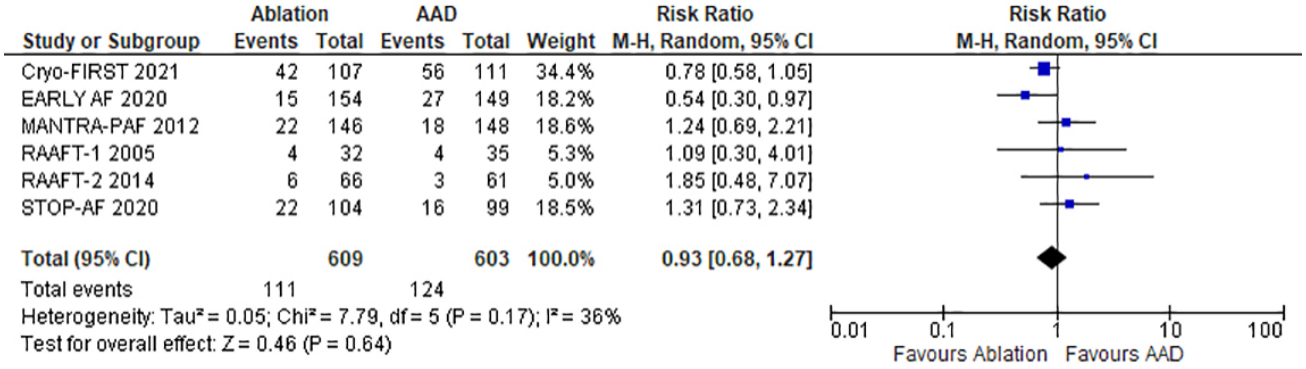

Fig. 5. Forrest plot comparing catheter ablation to antiarrhythmic drug therapy (as first line treatment for atrial fibrillation) for the incidence of adverse events.

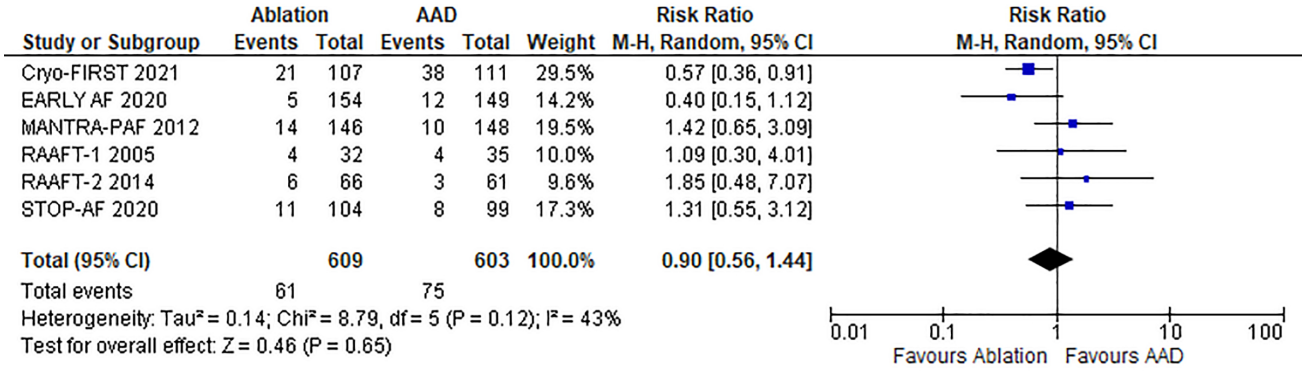

Fig. 6. Forrest plot comparing catheter ablation to antiarrhythmic drug therapy (as first line treatment for atrial fibrillation) for the incidence of cardiovascular adverse events.

first-line therapy versus AAD in symptomatic AF patients. The main findings of this meta-analysis are as follows: (i) CA (Cryoballoon or Radiofrequency- Pulmonary vein Isolation) resulted in a significantly lower rate of any recurrent atrial tachyarrhythmias when used in antiarrhythmic naïve patients. (ii) This effect was observed irrespective of follow-up duration (short versus long term), and type of catheter ablation (radiofrequency versus cryoablation). (iii) CA was not associated with an increase in the rates of overall severe adverse events and cardiovascular adverse events; while procedural adverse events included tamponade, pulmonary stenosis and pericardial effusion.

To our knowledge, this is the first comprehensive meta-analysis to compare clinical outcomes of CA versus AAD as first-line therapy for symptomatic AF and included the results of the recent EARLY-AF, STOP-AF First and Cryo-FIRST trials [25–27]. A prior meta-analysis from 2015 explored the impact of CA and AAD as initial therapy but was underpowered due to paucity of data and a limited number of included studies [32]. In addition to exploring

more endpoints, the current study is the first to include both radiofrequency and cryoballoon studies to compare CA and AAD as first-line treatments for AF.

Radiofrequency ablation (RFA) and cryoballoon ablation (CBA) are both safe and effective options for treating atrial fibrillation. In a recent meta-analysis comparing RFA and CBA, there were no statistically significant differences between the two energy sources regarding AF/atrial tachycardia-free survival and overall adverse events [33]. CBA has emerged as a promising alternative with comparable efficacy to RF ablation for the maintenance of sinus rhythm, primarily in patients with paroxysmal AF. Triggers originating from the pulmonary and thoracic veins appear to be the primary mechanism of subjects with paroxysmal AF [34]. Extending the role of CBA aiming at the electrical pulmonary vein as a novel catheter ablation strategy, the current study supports the use of CBA as initial first-line therapy, like that observed with radiofrequency ablation. These findings from the current meta-analysis are in concordance with the recent EARLY-AF, STOP-AF First and Cryo-FIRST trials [25–27].

Although more successful than AAD, most ablations in clinical practice are performed in patients who fail AAD due to either inefficacy or side effects [17]. However, this conventional "standard of care" consisting of the first attempt of rhythm control with AAD may represent a delay in an optimal treatment. Drug therapy often fails due to adverse events and arrhythmia breakthroughs, and the time that passes between AAD introduction and failure can cause a delay in time-to-ablation, during which progressive electro-anatomical remodeling may render AF more refractory. A shorter diagnosis-to-ablation time has been associated with better ablation outcomes [18–20]. Similarly, a prior study from our center showed that markers of atrial remodeling such as hemodynamic strain and inflammation progress with longer diagnosis-to-ablation times in persistent AF.

Furthermore, the longer diagnosis-to-ablation time has been associated with worse AF-related outcomes such as heart failure and death [35]. In the progressive course of AF, atrial scarring and fibrosis can occur, reducing the ability to maintain sinus rhythm as observed in the DECAAF trial [36]. Finally, the ARISTOTLE trial showed a higher risk of stroke at advanced stages in AF progression [37], which further supports earlier ablative intervention; but this requires further investigation. This data and the current findings suggest implications for the timing of early aggressive management of AF and its favorable impact on disease progression. Moreover, progression of AF is less common with CA intervention than AAD therapy [35–37]. Therefore, CA provides the most significant benefit earlier in the disease.

Many patients are given AAD first in clinical practice, owing to concerns with the invasive nature of catheter ablation. In the current study, the incidence of both overall adverse events and cardiovascular adverse events including ischemic and embolic events (myocardial infarction, stroke, or transient ischemic attack), hospitalizations for heart failure, major bleeding, pulmonary vein stenosis, pericardial complications (effusion, hemorrhage, tamponade, and perforation), syncope, and life-threatening arrhythmias were similar in both CA and AAD groups. The ability of CA procedures to obviate the need for AAD long term may inherently avoid the risks associated with long term use of antiarrhythmics.

Although AADs are not benign, invasive procedures and long-term radiation exposure are similar risks to medical therapy. Complications were reported in 9.35% patients and included pericardial tamponade/effusion (1.8%), symptomatic pulmonary vein stenosis (0.67%), bleeding complications (0.5%), and phrenic nerve injuries (0.5%). Cardiac tamponade was the most common fatal complication of AF ablation, occurring in seven of 609 patients. **Supplementary Table 2** summarizes the common complications occurring during CA of AF. The operator's experience is critical regarding safety issues of catheter ablation of AF. Moreover, most reported adverse events occurred after 30 days. However, the safety profile for procedural risks is excellent, especially at tertiary care centers with experienced operators. CA should be done carefully after weighing the benefits and risks of the procedure.

7. Limitations and Strengths

Several limitations of our study should be acknowledged. The definition of outcomes varied substantially among the included studies. This analysis included studies that differed in the use of Class I or III AADs, types of AF and method of surveillance used to monitor recurrence, with the follow-up period varying from 1–2 years. Five studies included patients with paroxysmal AF, and hence the data is only relevant to patients with paroxysmal AF and should not be extrapolated to patients with persistent AF. This meta-analysis combines the different ablation techniques (RFA and Cryoballoon) to evaluate the primary efficacy endpoints, thereby adding a new dimension to the study while presenting as a limitation.

Furthermore, ablation targets beyond the pulmonary veins are variable and mostly up to operators' preferences. However, the primary efficacy endpoint was consistent in the ablation arm across all studies. The study has the strength of compiling RCT and confirming the superiority of ablation vs AAD to prevent arrhythmia recurrences without significant risks.

8. Conclusions

In this study, comparing the efficacy and safety of catheter ablation (RFA and CBA) and antiarrhythmic drugs as first-line therapy for symptomatic AF, catheter ablation aiming at electrical pulmonary vein resulted in a significantly lower recurrence rate of atrial tachyarrhythmia and

maintenance of sinus rhythm. Catheter ablation for AF rhythm control is superior to AAD in drug naïve patients.

Author Contributions

AAR—Conception of the study, drafting, editing, reviewing, and final approval of the study to be submitted. HML—Help in the design of the study, drafting, editing, reviewing, and final approval of the study to be submitted. SP—Drafting, editing, and final approval of the study to be submitted. SR—Drafting, editing, and final approval of the study to be submitted. SAH—Drafting, editing, and final approval of the study to be submitted. NH—Drafting, editing, and final approval of the study to be submitted. HN—Drafting, editing, and final approval of the study to be submitted. KTR—Drafting, editing, and final approval of the study to be submitted. HS—Drafting, editing, and final approval of the study to be submitted. FY—Drafting, editing, and final approval of the study to be submitted. AM—Drafting, editing, and final approval of the study to be submitted. SC—Drafting, editing, and final approval of the study to be submitted. MBM—Critical revision of the manuscript, editing, reviewing, and final approval of the study to be submitted. AFB—Critical revision of the manuscript, editing, reviewing, and final approval of the study to be submitted.WS—Critical revision of the manuscript, editing, reviewing, and final approval of the study to be submitted. OW—Critical revision of the manuscript, editing, reviewing, and final approval of the study to be submitted. AAH—Critical revision of the manuscript, editing, reviewing, and final approval of the study to be submitted.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

Oussama Wazni serves a consultant speaker for Boston Scientific and Biosense Webster. The remaining authors have no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://www.imrpress.com/journal/RCM/23/3/10.31083/j.rcm2303112.

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