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Systematic Review

Effect of Post-Ablational Antiarrhythmic Drugs on Atrial Fibrillation Recurrence: A Systematic Review and Meta-Analysis

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Abstract

Background: The efficacy of antiarrhythmic drugs in reducing the risk of recurrence of atrial fibrillation (AF) after ablation is still uncertain. Therefore, we conducted a systematic evaluation on post ablation antiarrhythmic drugs (AADs) to reduce the risk of recurrent atrial fibrillation. **Methods**: The databases of PubMed, Embase, Web of Science (WOS), China Science and Technology Journal (CSTJ) Database, Wanfang Database, China National Knowledge Infrastructure (CNKI), and China Biology Medicine (CBM) were searched from inception to 31 December 2023. Randomized controlled trials (RCTs) investigating the efficacy of AADs in preventing AF recurrence were included. Statistical analysis was performed using Review Manager 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane collaboration, 2014) and Stata18.0 (Stata, College Station, TX, USA). **Results**: A total of 16 studies, with 3834 patients were included in the final analysis. The use of AADs was found to reduce early risk of recurrence ($\leq$3 months) by 28% (risk ratio (RR) = 0.72, 95% confidence interval (CI): 0.53–0.99, p = 0.04), intermediate risk of recurrence (3–12 months) by 22% (RR = 0.78, 95% CI: 0.67–0.91, p = 0.001), and late risk of recurrence ($\geq$12 months) by 29% (RR = 0.71, 95% CI: 0.47–1.07, p = 0.1). No published bias was detected. In sensitivity analyses, the result is consistent and stable after removal of either study. **Conclusions**: The use of AADs after ablation can reduce the recurrence of AF, and the effect can last for at least 6 months in the overall population. In subgroup analysis, this protective effect can even last for 12 months in the Asian region. In addition, AADs should be used for at least 3 months after ablation to achieve this protective effect.

Keywords

antiarrhythmic drugs; atrial fibrillation; catheter ablation; recurrence; meta-analysis

Introduction

Atrial fibrillation (AF) is a serious public health issue [1]. It not only has a high fatality rate, but also results in brings significant morbidity such as heart failure and cerebral infarction, which impact the quality of life [2]. According to 2020 epidemiological data, the current global prevalence of AF in adults is approximately 2–4%, with a total number of 33.5 million, resulting in a 2-fold increase in mortality and a 5-fold increase in stroke [3]. Rhythm control is the first-line therapy for AF patients. Catheter ablation (CA) has been shown to be the most effective regimen for restoring sinus rhythm, especially in patients with drug-refractory symptomatic AF, and is increasingly used in routine clinical practice [4]. However, post-ablation recurrence of AF limits its effectiveness and is a great concern for electrophysiologists [4]. It has been reported that the recurrence rate of AF within 4 years after radiofrequency catheter ablation (RFCA) is as high as 49.9% [5]. Recurrence and subsequent repeat ablation is associated with increased morbidity and financial burden on patients and society.

A Study [6] shows that the atrial electrical remodeling after AF resulting from alternations in refractory period and action potential duration, takes some time to return to normal. Antiarrhythmic drugs (AADs), especially class I and class III AADs [6], can prolong the action potential and refractory period of the atria by blocking the sodium and potassium channels. Therefore, AADs may help in the process of atrial recovery and promote the more rapid return of normal atrial activity, and reduce the risk of recurrent AF. Several studies have tried to confirm this hypothesis, however, no consensus has been reached [7]. Different regions (races), dosages used, and duration of use may lead to different outcomes [8–10]. Therefore, the current study aims to conduct a meta-analysis based on the existing studies on this issue, to provide guidance for future clinical practice and scientific research.

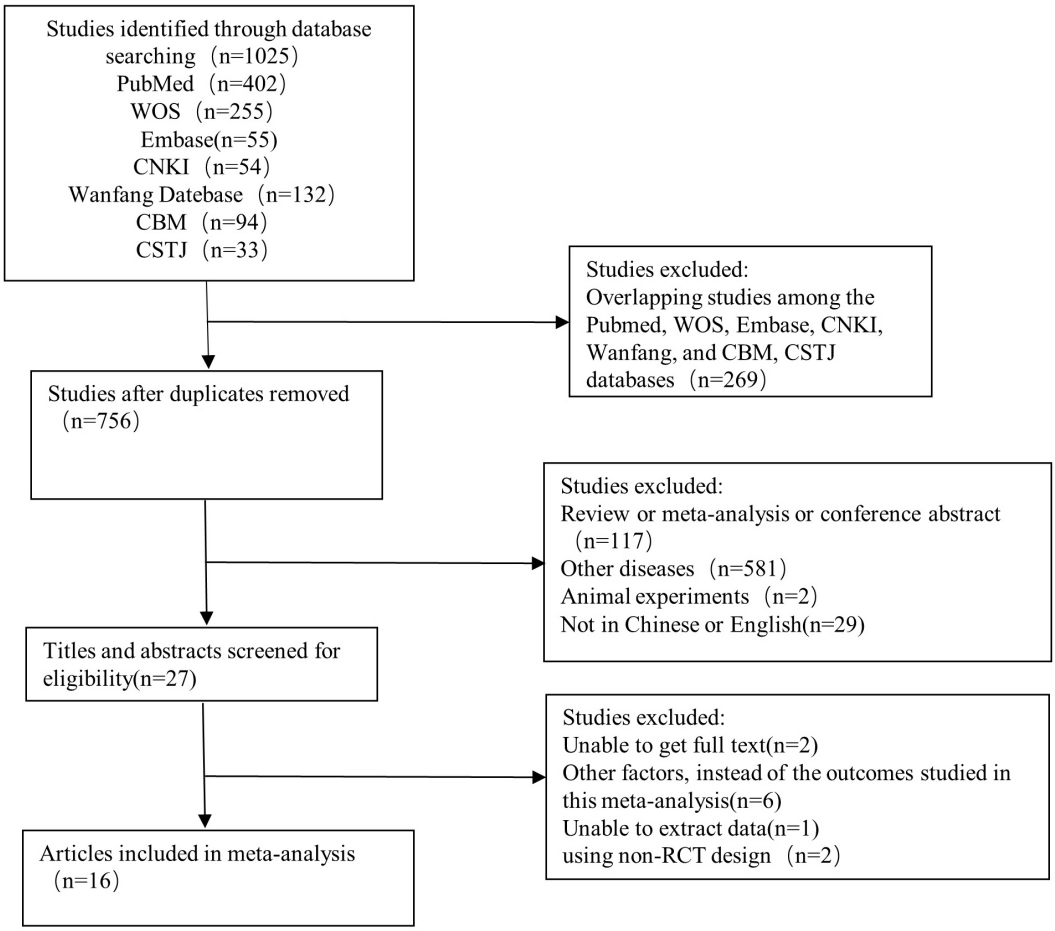


Fig. 1. Flow diagram of studies included in this meta-analysis. WOS, Web of Science; CKNI, China National Knowledge Infrastructure; CBM, China Biology Medicine; CSTJ, China Scientific Journal Database; RCT, randomized controlled trial; ADDs, antiarrhythmic drugs; AF, atrial fibrillation.

Methods

Data Source and Study Identification.

All studies exploring the effects of post-ablation use of AADs in reducing the risk of AF recurrence published before 31 December 2023 were included. Adhering to PRISMA guidelines (see **Supplementary Table 1**), studies were identified by searching the PubMed, Embase, Web of science (WOS), China Science and Technology Journal (CSTJ) Database, Wanfang Database, China National Knowledge Infrastructure (CNKI), and China Biology Medicine (CBM) using different combinations of terms (see **Supplementary Table 2**), including "atrial fibrillation", "anti-arrhythmic drugs", "catheter ablation" and "randomized controlled trial". Studies retrieved were reviewed by two experienced researchers (YYW and WJZ) independently and in parallel to minimize subjective selection bias. Divergences were adjudicated by discussion with a third investigator (HW). Studies were excluded if they fulfilled the following criteria: (i) review, meta-analysis, conference abstract; (ii) clinical studies but using non-RCT design; (iii) studies not in Chinese or English; (iv) data was repetitive or unavailable; (v) animal experiments and mechanism studies; (vi) patients were not in AF or not using ADDs.

Date Extraction

Data extraction was conducted by YYW, and independently confirmed by other authors (YFG and YS). For every study, the following information was extracted: first author, year of publication, country, AF type, AF duration, sample size, demographics of patients, echocardiographic parameters (left ventricular ejection fraction, anterior and posterior diameters of the left atrium), comorbidities of patients and outcomes data (recurrence number, follow-up duration, study endpoints), AADs type and duration in the AADs group, therapeutic strategy in the control group. If the data was only reported as a survival curve, the raw date was extracted using Engauge Digitizer 12.1 (Markum Mitchell, Toowoomba in Queensland, Australia) [11]. The Engauge

Table 1. Characteristics of the 16 included RCTs in this meta-analysis.

First author/year	Country	AF type	NO. Patients		Male		Mean follow-up (months)	Ablation type	AADs	Control group prescription	AADs period (months)
			On	Off	On	Off					
Chen 2022 [15]	China	Paroxysmal and Persistent AF	38	38	21	20	12	catheter ablation	amiodarone	No-ADDs	3
Chen 2019 [16]	China	Paroxysmal and Persistent AF	62	62	38	37	6	Radiofrequency ablation	amiodarone	No-ADDs	6
Wang 2022 [17]	China	Paroxysmal AF	32	28	18	16	18.5	Radiofrequency ablation	dronedarone	No-ADDs	3
Zhang 2016 [18]	China	Paroxysmal AF	24	24	30		>12	Radiofrequency ablation	amiodarone	No-ADDs	3
Zhao 2016 [19]	China	Paroxysmal AF	42	42	28	27	12	Radiofrequency ablation	amiodarone	No-ADDs	3
Darkner 2014 [20]	Danish	Paroxysmal and Persistent AF	108	104	87	89	6	AF ablation	amiodarone	No-ADDs	6
Hayashi 2014 [21]	Japan	Paroxysmal and Persistent AF	62	63	48	49	17	Radiofrequency ablation	Flecainide	No-ADDs	3
Kettering 2018 [22]	Germany	Persistent AF	115	115	67	70	24	Radiofrequency ablation	amiodarone	No-ADDs	3
Lodziński 2014 [23]	Poland	AF	114	57	77	41	2	PVI	class III or class IC antiarrhythmic drug	No-ADDs	2
Roux 2009 [24]	USA	AF	53	57	70	72	3	Radiofrequency ablation	class III or class I antiarrhythmic drug	No-ADDs	1.5
Turco 2007 [25]	Italy	drug refractory AF	54	53	69		12	catheter ablation	class III or class IC antiarrhythmic drug	No-ADDs	NA
Mohanty 2015 [26]	USA	long-standing persistent AF	56	56	42	38	32	catheter ablation	amiodarone	No-ADDs	1.5
Leong-Sit 2011 [27]	USA	paroxysmal AF	53	57	37	41	6	PVI	class III or class IC antiarrhythmic drug	No-ADDs	1.25
Wu 2008 [28]	China	Paroxysmal and Persistent AF	37	37	28	29	12	circumferential ablation of pulmonary vein	amiodarone	No-ADDs	3
Kaitani 2016 [29]	Japan	Paroxysmal, Persistent, or long-lasting AF	1016	1022	741	789	15	ATP-guided PVI	class III or class I antiarrhythmic drug	No-ADDs	3
Duytschaever 2018 [30]	Belgium	paroxysmal AF	77	76	57	55	12	PVI	class III or class I antiarrhythmic drug	No-ADDs	3

ADDs, antiarrhythmic drugs; AF, atrial fibrillation; PVI, pulmonary vein isolation.

Table 2. Detailed patient information of the 16 included RCTs in this meta-analysis.

First author/year	AF duration (mean months)		Mean age		Hypertension		Coronary heart disease		Mean LVEF (%)		LAD (mm)		Jadad scale
	On	Off	On	Off	On	Off	On	Off	On	Off	On	Off	
Chen 2022 [15]	26.16 ± 11.64	26.40 ± 11.28	62.42 ± 5.74	61.95 ± 5.81	20	22	5	6	-	-	40.71 ± 3.34	41.83 ± 3.28	5
Chen 2019 [16]	25.80 ± 3.84	27.12 ± 4.68	57.73 ± 5.51	57.81 ± 5.18	-	-	-	-	55.3 ± 4.7	47.7 ± 4.2	-	-	4
Wang 2022 [17]	48.00 ± 13.32	42.32 ± 14.64	63.97 ± 7.36	63.00 ± 7.64	11	8	2	1	50.36 ± 5.11	44.45 ± 4.86	-	-	5
Zhang 2016 [18]	-	-	-	-	-	-	-	-	-	-	-	-	3
Zhao 2016 [19]	18.00 ± 4.80	15.60 ± 6.00	54.70 ± 3.53	55.80 ± 3.30	3	3	1	1	55.1 ± 7.9	52.6 ± 8.0	32.6 ± 3.1	34.2 ± 3.3	5
Darkner 2014 [20]	78 ± 78	76 ± 65	62	61	40	44	6	8	51 ± 9	50 ± 8	44 ± 7	44 ± 7	6
Hayashi 2014 [21]	62.4 ± 69.6	52.8 ± 42.0	62 ± 11	64 ± 10	40	39	-	-	69 ± 8	68 ± 9	38 ± 5	38 ± 6	4
Kettering 2018 [22]	69.6 ± 14.4	70.8 ± 8.4	61.9 ± 11.1	60.4 ± 11.3	-	-	21	22	46.5 ± 10.4	48.4 ± 10.4	45.7 ± 5.5	45.1 ± 5.6	4
Lodziński 2014 [23]	-	76	-	47.6 ± 13.0	56	22	13	5	-	-	-	41 ± 4	5
Roux 2009 [24]	71 ± 68	81 ± 65	56 ± 8	55 ± 9	47	53	13	12	61 ± 8	62 ± 7	43 ± 7	41 ± 6	4
Turco 2007 [25]	54.0 ± 50.4		57 ± 10		61		-	-	57 ± 7		48 ± 6		4
Mohanty 2015 [26]	78.5 ± 38.8	73.8 ± 36.5	60 ± 11	62 ± 10	27	26	12	14	55 ± 10	54 ± 12	48 ± 5	47 ± 5	4
Leong-Sit 2011 [27]	71 ± 68	81 ± 65	56 ± 8	55 ± 9	47	53	13	12	61 ± 8	62 ± 7	4.3 ± 0.7	4.1 ± 0.6	5
Wu 2008 [28]	14.7 ± 7.9	13.8 ± 6.2	51.2 ± 17.7	53.6 ± 19.1	10	13	2	2	59 ± 8	61 ± 7	29.4 ± 6.7	28.1 ± 7.5	4
Kaitani 2016 [29]	24.7 [8.8–62.3]	26.1 [9.3–62.9]	65.9 ± 9.6	60.7 ± 9.6	561	526	-	-	64.5 ± 7.5	64.2 ± 7.8	38.9 ± 6.2	39.0 ± 6.2	5
Duytschaever 2018 [30]	26 (7–84)	26 (12–81)	63 (56–63)	62 (54–70)	23	33	-	-	-	-	41 ± 5	41 ± 5	4

AF, atrial fibrillation; LVEF, left ventricular ejection fraction; LAD, left atrial diameter.

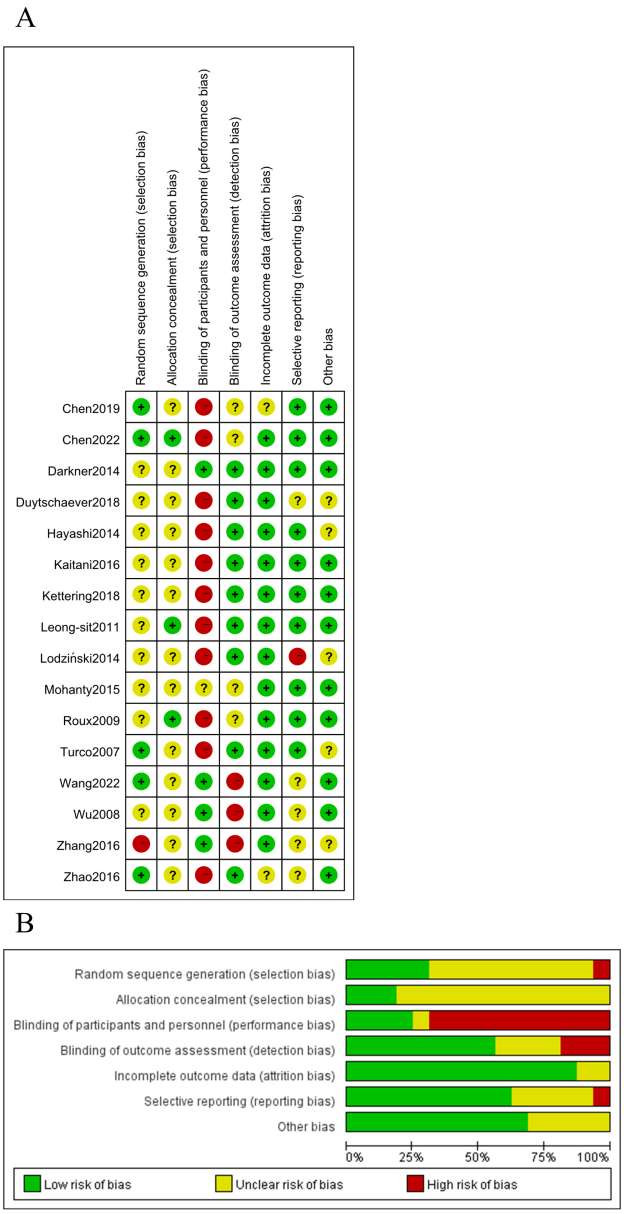


Fig. 2. Risk of bias assessment for the included trials. (A) Summary of the risk of bias for each individual trial. (B) Overall risk of bias.

Digitizer 12.1 (Markum Mitchell, Toowoomba in Queensland, Australia) can extract accurate data from various literature charts, and generate accurate data points by adding pivot points and other points along the curve.

Quality Assessment

A modified Jadad scale was used to evaluate the quality of included studies, which referred to four aspects: randomization, concealment of allocation, double blinding, and withdrawals and dropouts. The scores were 2 points, 2 points, 2 points, and 1 point, respectively. The quality of the RCT receiving 1–3 points was evaluated as low, while 4–7 points was high [12]. In addition, the methodological quality of each included study was assessed at the outcome level independently by two reviewers (YFG and YS) using the risk-of-bias assessment tool developed by the Cochrane Bias Methods Group [13], which includes 7 domains: random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias. We judged trials with 2 or more high-risk domains as having a high risk of bias and trials with 1 high-risk domain as having a moderate risk of bias. Quality assessment was also independently carried out by 2 authors. All disagreements between the 2 authors were resolved by discussion. The results of the two evaluation methods were reviewed by a third researcher (HW).

Data Analyses

Statistical analysis was performed using Review Manager 5.3 (Copenhagen, Denmark: The Nordic Cochrane Centre, The Cochrane collaboration, 2014) and Stata18.0 (Stata, College Station, TX, USA). Data were pooled from all trials and calculated relative risks (RRs) at 95% confidence interval (CI) to compare dichotomous results. The inconsistency index (I^2) was used to assess the heterogeneity across each study. A random-effects model was used to analyze the data if a value of $I^2 > 50\%$, which was considered to have significant heterogeneity. Otherwise, a fixed-effects model was used. I^2 less than 25% indicates low heterogeneity, 25% to 50% indicates moderate heterogeneity, or greater than 50% indicates high heterogeneity [14]. Sources of heterogeneity were further explored by performing subgroup analysis and sensitivity analysis. We conducted subgroup analysis by region (Asia, Europe, and the Americas) and medication duration (less than or equal to 2 weeks, 3 weeks, and 6 weeks), and stratified the follow-up time (short-, mid-, and long-term). Postoperative follow-up periods of $\leq$3 months, 3–12 months and $\geq$12 months were defined as short-term, mid-term and long-term, respectively. Publication bias was detected according to the Begg's rank correlation test and the Egger's linear regression test using the Stata18.0 (Stata, College Station, TX, USA). A two tailed value of $p < 0.05$ was considered statistically significant.

Results

Characteristics of the Included Studies

A total of 1025 potential studies were retrieved by the initial search. Among them, 982 were discarded by screening titles, abstracts, or full-length texts, as summarized in Fig. 1. Ultimately, a total of 16 studies were included, with 3834 patients. The detailed characteristics of

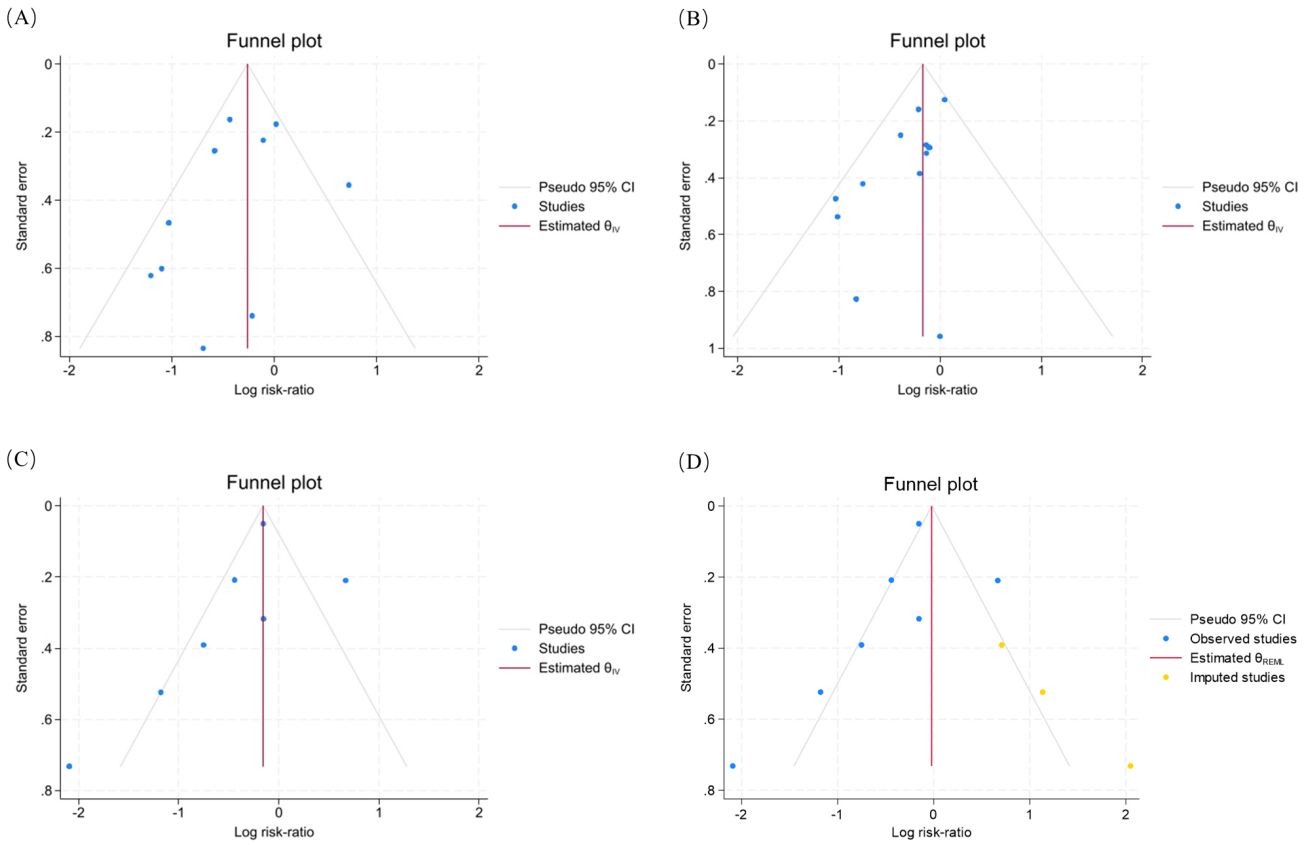


Fig. 3. Funnel plots for short-term, mid-term, and long-term follow-up. (A) Funnel plot of short-term follow-up using ADDs in patients with atrial fibrillation after radiofrequency ablation. (B) Funnel plot of mid-term follow-up using ADDs in patients with atrial fibrillation after radiofrequency ablation. (C) Funnel plot of long-term follow-up using ADDs in patients with atrial fibrillation after radiofrequency ablation. (D) Funnel plot of long-term follow-up of atrial fibrillation patients using ADDs after radiofrequency ablation using trim-and-fill method. CI, confidence interval.

the 16 studies are summarized in Tables 1,2 (Ref. [15–30]). The AADs used in these studies are different, with 1 study [17] used dronedarone, 1 study [21] used flecainide, 8 studies [15,16,18–20,23,26,28] used amiodarone, 6 studies [23–25,27,29,30] used different kinds of class III or class IC antiarrhythmic drugs according to the presence of structural heart disease of each patient. Regarding prognosis, 10 [15,18–25,28], 13 [15–22,24–28], and 7 [15,17,22,26,28–30] studies reported short-term, mid-term, and long-term postoperative follow-up times, respectively.

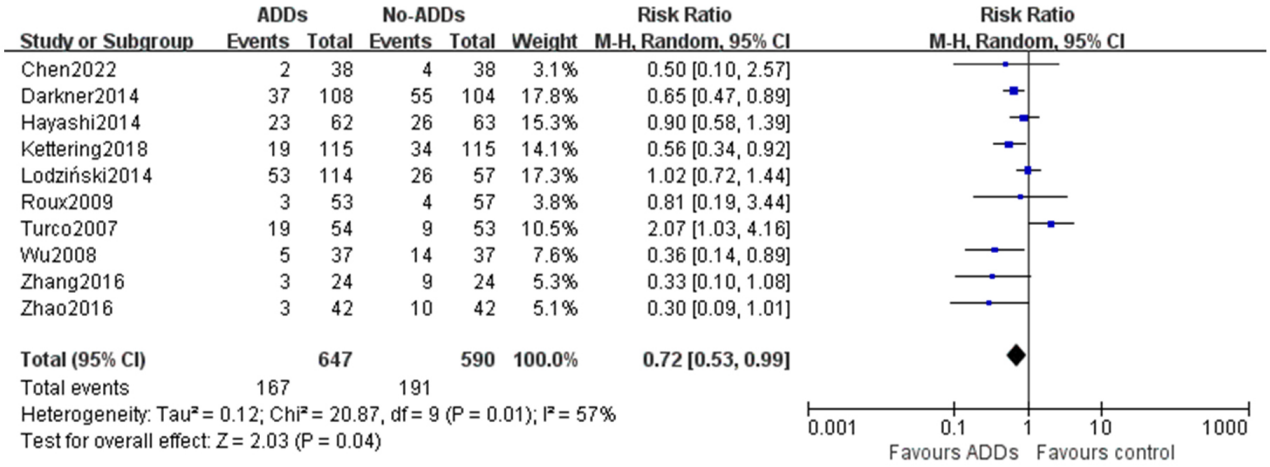
Literature Quality Assessment

Except for Zhang *et al*. 2016 [18], the remaining 15 [15–17,19–30] studies were defined as high quality by the modified Jadad scale (score ≥4). Using the Cochrane Collaboration's tool, it was found that in the study by Lodziński 2014 [23], selective reporting was a high risk. The risk of other bias was low in 11 studies [15–17,19,20,22,25–29] and was unclear in the other studies. In 11 studies [15,16,19,21–25,27,29,30] high-risk performance bias was identified. Overall, 2 studies [20,26] had a low risk of bias, 2 studies [18,23] had a high risk of bias; and the remaining studies [15–17,19,21,22,24,25,27–30] had a moderate risk of bias. The results are summarized in Fig. 2.

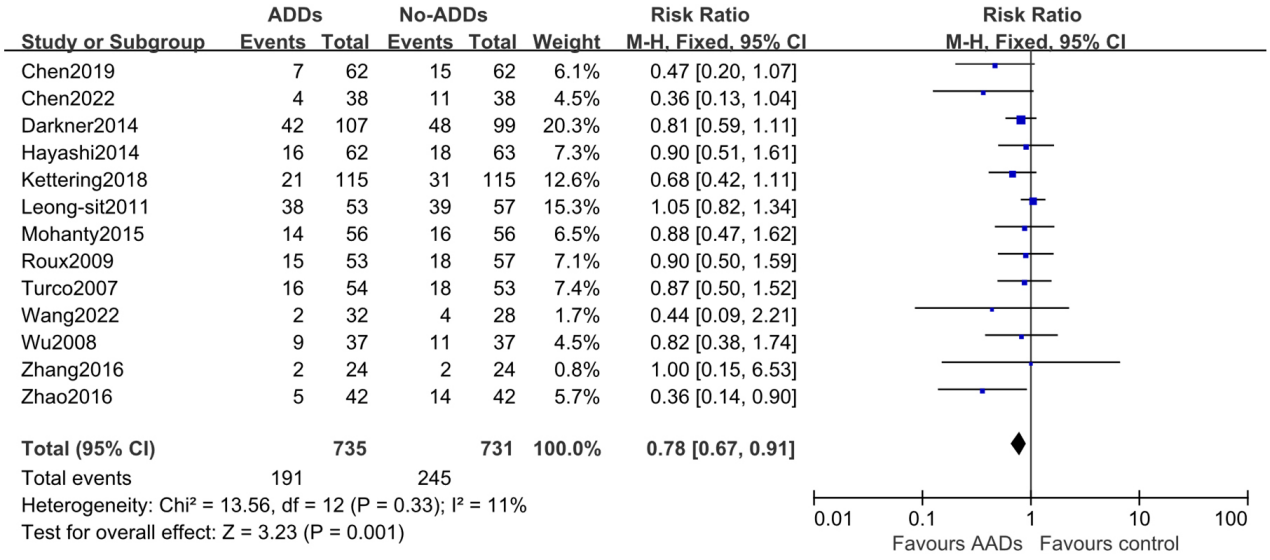
Publication Bias

A visual examination of the funnel plots for short-term, mid-term, and long-term follow-up (Fig. 3A–C) revealed asymmetry. Therefore, both Begg's test and Egger's test provided evidence for publication bias. Specific data were as follows: (1) short-term recurrence: Begg test $z = 0.89$, $p > 0.371$, Egger test $p = 0.693$; (2) medium-term recurrence: Begg test $z = 1.77$, $p > 0.077$, Egger test $p = 0.105$; (3) long-term recurrence: Begg test $z = 0.60$, $p > 0.548$, Egger test $p = 0.005$. No significant publication bias was found among short- and medium-term follow-up outcomes, given that the total number of studies was fewer than 20, and previous statistical analyses have demonstrated greater sensitivity of Egger's test compared to Begg's. Therefore, based on Egger's test, there is significant publication bias in the long-term recurrence group. Therefore, we use the trim-and-fill method to recalculate the merging effect of long-term groups. A total of 3 studies were added to the funnel plot, and the combined effect size

(A)



(B)



(C)

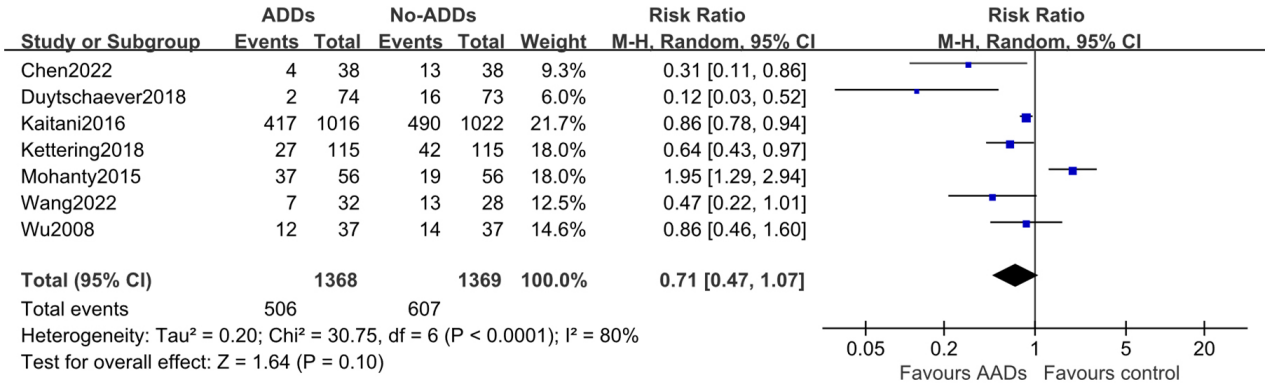


Fig. 4. Efficacy of post-ablation AADs application in reducing AF recurrence. (A) Short term follow-up analysis of using ADDs in patients with atrial fibrillation after radiofrequency ablation. (B) Analysis of mid-term follow-up of using ADDs in patients with atrial fibrillation after radiofrequency ablation. (C) Analysis of long-term follow-up of patients with atrial fibrillation using ADDs after radiofrequency ablation.

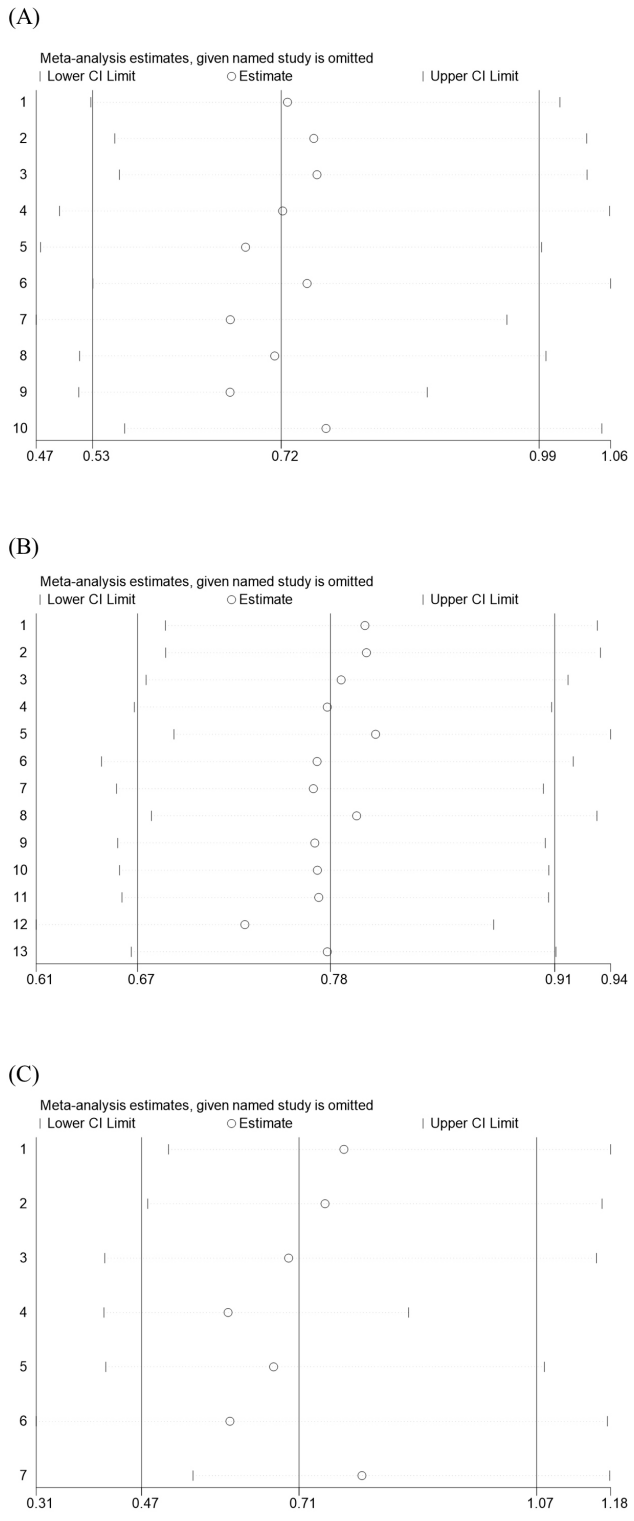


Fig. 5. Sensitivity analysis for three subgroups. (A) Sensitivity analysis of short-term follow-up using ADDs in patients with atrial fibrillation after radiofrequency ablation. (B) Sensitivity analysis of mid-term follow-up using ADDs in patients with atrial fibrillation after radiofrequency ablation. (C) Sensitivity analysis of long-term follow-up using ADDs in patients with atrial fibrillation after radiofrequency ablation.

remained stable (Log risk-ratio = –0.022, 95% confidence interval (CI): –0.642–0.599) (Fig. 3D).

Efficacy of Post-Ablation AADs Application in Reducing AF Recurrence

Because many included studies have reported recurrence information at multiple stages, the current study directly divided the different levels according to the follow-up time. The short-term recurrence rate of AF was 25.8% (167 of 647) in the AADs group and 32.4% (191 of 590) in the control group (RR = 0.72, 95% CI: 0.53–0.99; $p = 0.04$; $I^2 = 57\%$). For mid-term comparison, the AF recurrence rate was 26.0% (191 of 735) and 33.5% (245 of 731) in AADs group and control group, correspondingly (RR = 0.78, 95% CI: 0.67–0.91; $p = 0.001$; $I^2 = 11\%$). For long-term recurrence, the recurrence rate was 37.0% (506 of 1368) and 44.3% (607 of 1369) with and without AADs usage (RR = 0.71, 95% CI: 0.47–1.07; $p = 0.1$; $I^2 = 80\%$), as shown in Fig. 4.

Sensitivity Analysis

Sensitivity analyses (Fig. 5) were performed using a single study-by-study exclusion in Stata18.0 (Stata, College Station, TX, USA). In sensitivity analyses, removing each individualized trial did not have any relevant influence on the results. This is consistent with the results of previous meta-analyses in the same direction [31,32]. The results showed no significant change in the results of the Meta-analyses, indicating a more stable and reliable result for the combined effect.

Subgroup Analysis

Performing subgroup analysis by region and stratifying according to follow-up time (as mentioned above): 8 studies [15–19,21,28,29] were from Asia, 5 studies [20,22,23,25,30] were from Europe, and 3 studies were from the Americas (Figs. 6,7,8). Due to limited data on the Americas, long-term results were not included. All three groups showed significant effects (short-term follow-up in Asia: RR = 0.58, 95% CI: 0.41–0.82; mid-term follow-up in Asia: RR = 0.60, 95% CI: 0.43–0.83; long-term follow-up in Asia: RR = 0.83, 95% CI: 0.76–0.92; short-term follow-up in Europe: RR = 0.88, 95% CI: 0.57–1.38; mid-term follow-up in Europe: RR = 0.79, 95% CI: 0.62–1.00; long-term follow-up in Europe: RR = 0.32, 95% CI: 0.06–1.71; mid-term follow-up in the Americas: RR = 0.97, 95% CI: 0.77–1.22).

Subgroup analysis was conducted based on medication duration and stratified according to follow-up time (as mentioned above): 4 studies [23,24,26,27] only used AADs of 2 weeks or less, 9 studies [15,17–19,21,22,28–30] used AADs of 3 weeks, 2 studies [16,20] used AADs of 6 weeks, 1 study [25] has no relevant data (excluded)

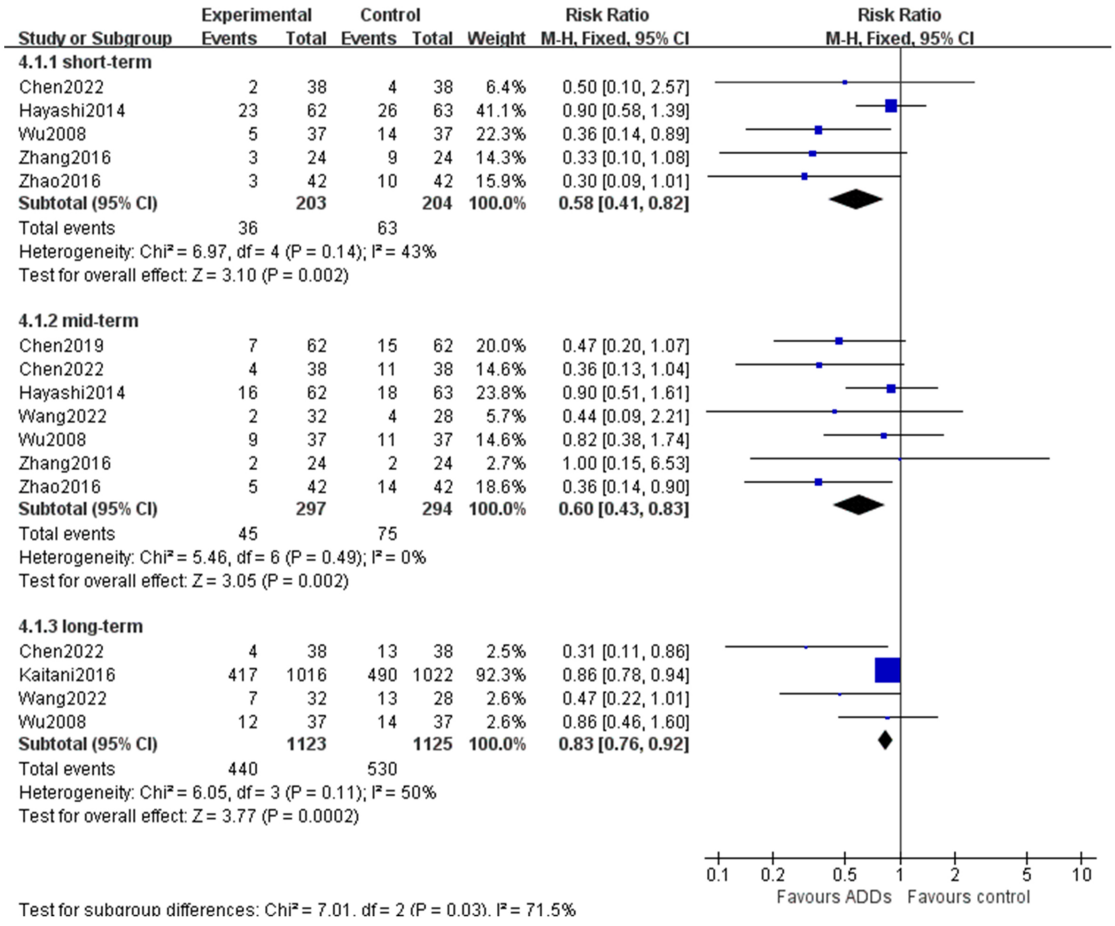


Fig. 6. Subgroup analysis of AADs used after ablation in AF patients in the Asian population.

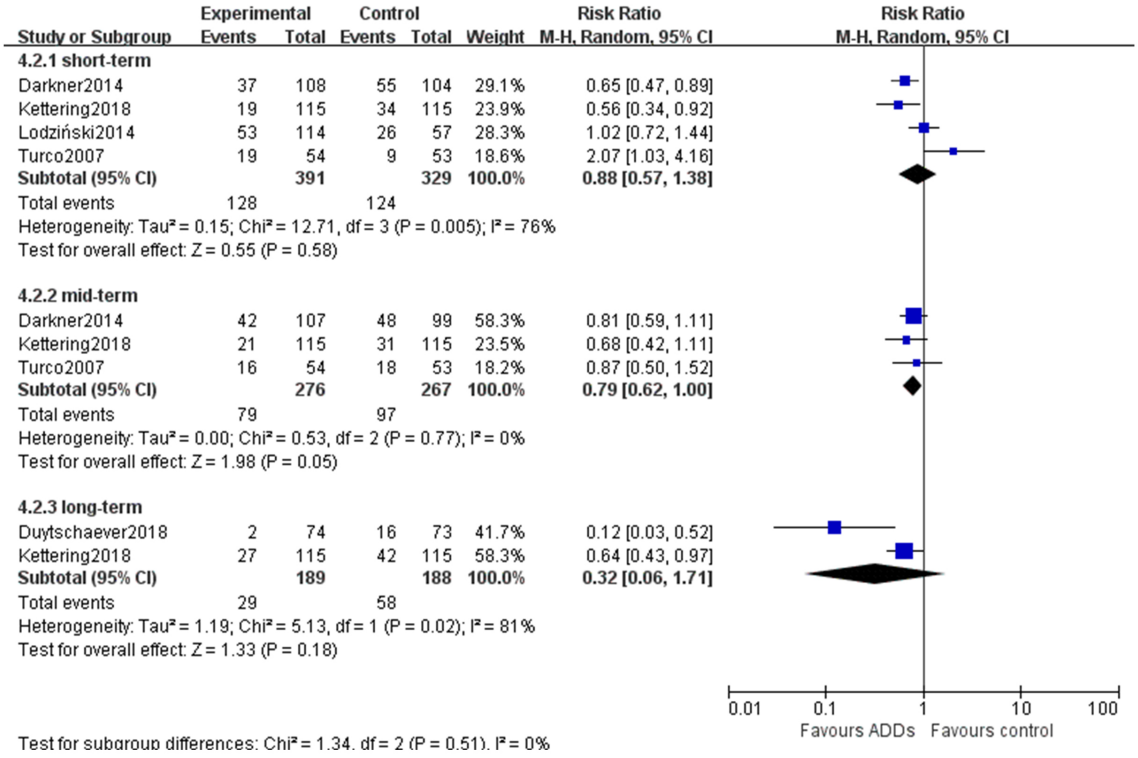


Fig. 7. Subgroup analysis of AADs used after ablation in AF patients in the European population.

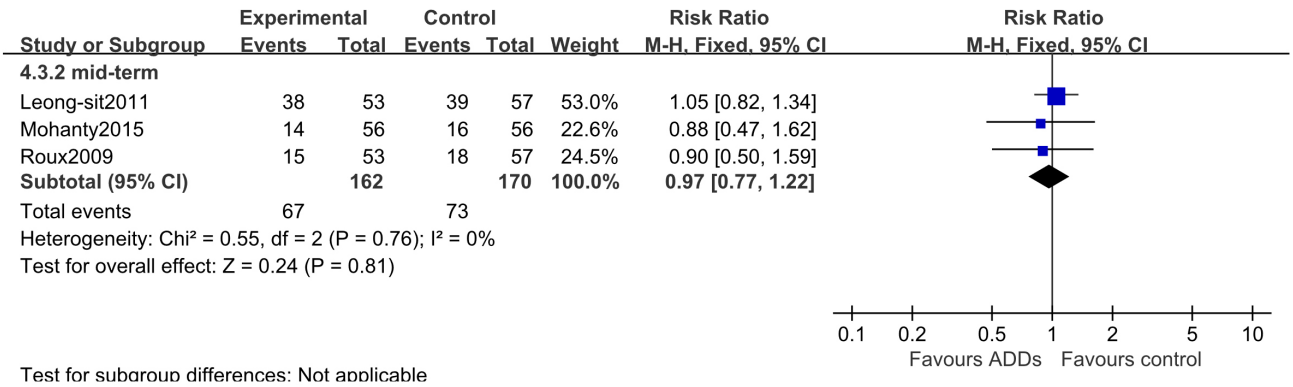


Fig. 8. Subgroup analysis of AADs used after ablation in AF patients in the America population.

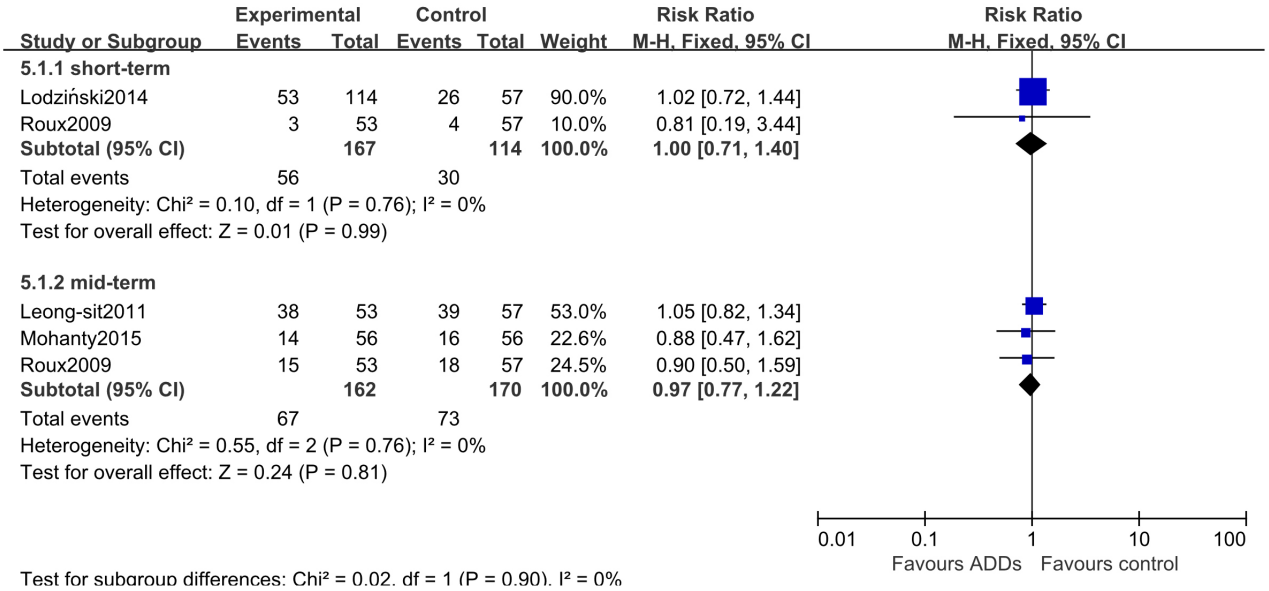


Fig. 9. Subgroup analysis of AF patients who underwent ablation using ADDs for no more than 2 weeks.

(Figs. 9,10,11). Due to limited data, long-term follow-up results using ADDs for less than two weeks were not included, and only mid-term follow-up results using ADDs for 6 weeks were included. All three groups showed significant effects (short-term follow-up with AADs of less than 2 weeks: RR = 1.00, 95% CI: 0.71–1.40; mid-term follow-up with AADs of less than 2 weeks: RR = 0.97, 95% CI: 0.77–1.22; short-term follow-up with 3-week AADs: RR = 0.56, 95% CI: 0.38–0.82; mid-term follow-up with 3-week AADs: RR = 0.67, 95% CI: 0.50–0.90; long-term follow-up with 3-week AADs: RR = 0.60, 95% CI: 0.41–0.88; mid-term follow-up with 6-week AADs: RR = 0.73, 95% CI: 0.454–0.98).

Discussion

Our meta-analysis comprehensively and systematically reviewed the existing literature, including 3834 patients from 16 RCTs, and found that use of AADs after ablation could significantly reduce the risk of AF recurrence, and this protective effect can last for more than one year.

The early occurrence of AF was shown to be related to changes in the electrophysiology and ion channel characteristics of the atrium, associated with atrial electrical remodeling [33]. The mechanism for these observations is that the expression of L-type calcium channels is down-regulated, and the action potential duration and refractory period are shortened, thus forming a positive feedback loop that is easier to generate AF [34]. With the further development of AF, the content and configuration of atrial muscle collagen fibers are altered, which leads to atrial structural remodeling, aggravates local tissue conduction block and reentry, and forms the abnormal substrate for maintaining AF. The combination of electrical reconstruction, energy reconstruction and structural reconstruction of atrial tissue is the core link for AF generation and maintenance [30]. Therefore, the formation of atrial fibrosis associated with atrial remodeling and the abnormal atrial matrix that maintains its pathological state is the pathophysiological basis

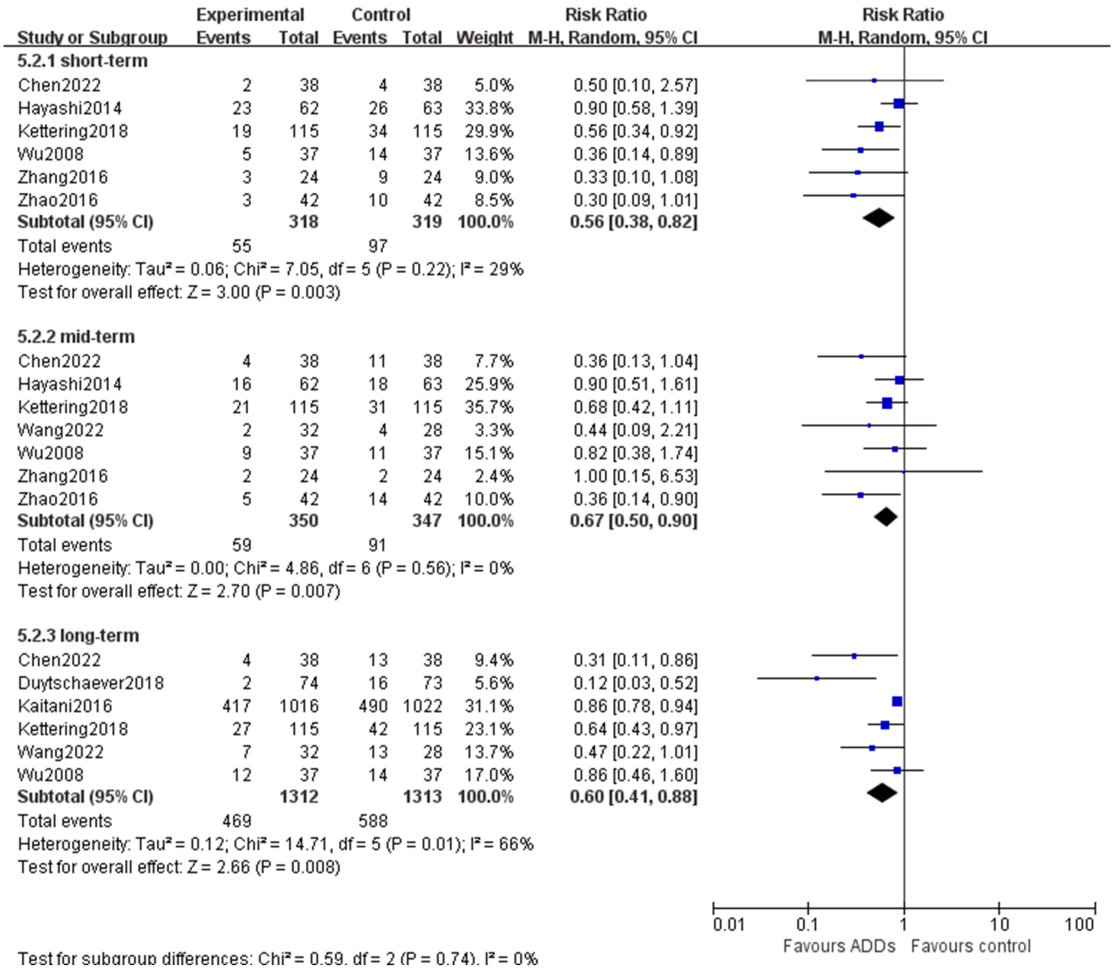


Fig. 10. Subgroup analysis of AF patients who underwent ablation using ADDs for 3 weeks.

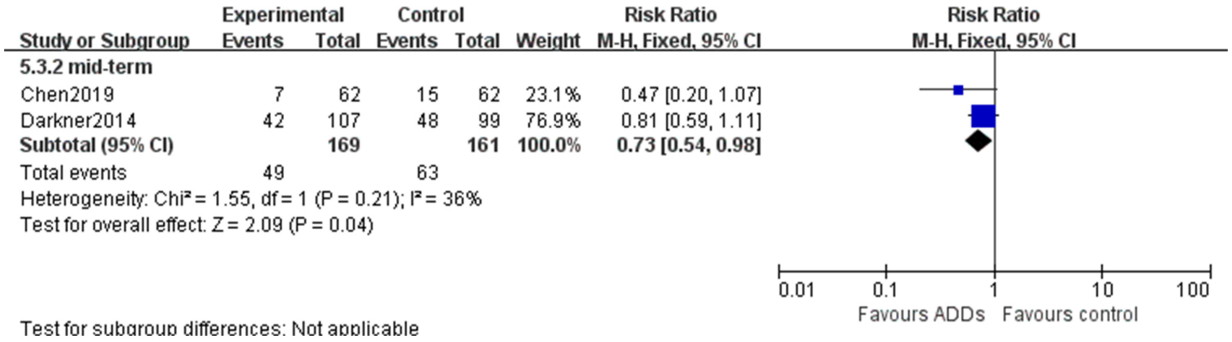


Fig. 11. Subgroup analysis of AF patients who underwent ablation using ADDs for 6 weeks.

for AF recurrence after RFCA. The mechanism of action of AADs [33] is to inhibit myocardial conduction fiber sodium ion flow, prolong the effective refractory period of myocardial tissue cells, reduce the autoregulation of the sinoatrial node, and prevent the recurrence of AF.

In this systematic review and meta-analysis of the effectiveness of AADS on the recurrence rate of AF after ablation, we demonstrated the beneficial effect of AADS treatment on reducing the postoperative recurrence rate in patients with AF. This is partially consistent with the previous meta-analysis conducted by Xu *et al*. [31] and Chen *et al*. [32] in 2016. We have all found that AADs can be maintained for at least 6 months after surgery, but our study has also found that AADs can be maintained for at least 12 months after RFCA. This difference in results may be due to the fact that we included a larger sample size and avoided false negatives due to small sample sizes. In the studies by Xu *et al*. [31] and Chen *et al*. [32], there were only 2442 and 2345 patients over 12 months, respectively, while ours had 2737, so the statistical power and credibility are im-

proved. Our results were not biased in publication. In the sensitivity analysis, the results were stable when any of the studies were removed, further confirming the robustness of the results.

These findings may have important clinical significance. In recent years, it is no longer hoped that RFCA will replace conventional drug therapy for AF, but that the benefits of combining AADs and RFCA may outweigh the benefits of ablation alone or AADs alone [35]. The mechanism may be due to the rapid restoration of sinus rhythm in a short period of time by catheter ablation (which addresses the triggering mechanism) and then the electrical modification of the mechanism with drugs, and perhaps the combination of the two will become a new treatment in the future. Considering the high cost of repeated ablation and the potential for postoperative complications, it becomes very important to promote sinus rhythm after ablation by using AADs. According to our study, the continuous use of AADs after AF RFCA to maintain sinus rhythm seems to be necessary for the prevention of recurrent AF. However, this evidence is based on a limited number of studies and patients. More data are needed to consolidate our study conclusions.

There are some limitations in this meta-analysis. First, it is based on studies instead of on individually personal data, so further detailed analyses could not be performed. For example, the included studies used different types of AADs, even in different patients in the same study, and the duration of AADs varied. Future research needs to explore the types, treatment courses, and even individualized medication regimens of AADs in more detail. Second, most trials included were not blinded, which is also important for AF recurrence as psychological factors have been found to play an essential role in AF. It is inevitable for patients to be anxious when knowing their medication. It might lead to certain bias that affects the level of evidence for the results.

Conclusions

The use of AADs after ablation can reduce the recurrence of AF, and the effect can last for at least 6 months in the overall population. In subgroup analysis, this protective effect can even last for 12 months in the Asian region. In addition, AADs should be used for at least 3 months after ablation to achieve this protective effect.

Availability of Data and Materials

All data used in this study have been listed in Tables 1,2.

Author Contributions

YYW and WJZ are responsible for the framework design of the entire meta-analysis, the development of literature retrieval strategies, the determination of inclusion and exclusion criteria, and the quality evaluation of screened studies, data extraction and integration, statistical analysis, as well as writing the initial and revised drafts of the paper. YS, QMD and YFG are responsible for guiding the use of statistical software for data processing, conducting statistical tests for meta-analysis, including heterogeneity testing, sensitivity analysis, and publication bias assessment. HW and SSL is responsible for reviewing the literature ultimately included in the analysis to ensure that it meets the quality requirements of the meta-analysis, and has accurately controlled the scientific content of the paper. Each author actively participated in every stage of the research, and through regular meetings and discussions, jointly resolved the problems that arose during the analysis process and ensured the quality of the research. All authors participated in the review and revision of the draft paper and agreed to the final submitted version. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7591.

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