

Is ablation to atrial fibrillation termination of persistent atrial fibrillation the end point?

A systematic review and meta-analysis

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Abstract

Background: The ideal ablation strategy and end point for persistent atrial fibrillation (AF) have not been well founded. Defining periprocedural AF termination as the end point of catheter ablation is still controversial. This meta-analysis aimed to analyze the differences between periprocedural AF termination and non-termination in the long-term AF recurrence rate and postoperative complications.

Methods: Randomized controlled trials (RCTs) were identified by a systematic search of electronic databases including PubMed, EMBASE, and Cochrane library from January 2008 to August 2019. The primary outcome was freedom from AF or any atrial arrhythmia without antiarrhythmic drugs at the long-term (≥ 12 months) follow-up. The secondary outcome was overall postoperative complication rates. The risk ratio (RR) with 95% confidence interval (CI) was pooled for these outcomes. A forest plot, fixed-effects model or random-effect model, Q test, I^2 statistic, and Egger funnel plot were used in the statistical analysis.

Results: Fourteen RCTs were included in this meta-analysis. Overall, no significant difference was found in freedom from AF at the long-term follow-up between patients in whom AF termination was achieved and not achieved (RR=0.93, 95% CI=0.78-1.09, $P=.36$, $I^2=69\%$). Patients with AF non-termination had a lower complication occurrence rate than those with AF termination (RR=1.74, 95% CI=1.11-2.73, $P=.02$, $I^2=0\%$).

Conclusion: Our meta-analysis suggests that AF termination is not a reliable procedural end point during ablation of persistent AF.

Abbreviations: AF = atrial fibrillation, AFL = atrial flutter, AT = atrial flutter, CFAE = complex fractionated atrial electrogram, CI = confidence interval, LA = left atrium, LAA = left atrial appendage, PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses, PV = pulmonary vein, PVI = pulmonary vein isolation, PWI = posterior wall isolation, RCT = randomized controlled trial, RR = risk ratio, SR = sinus rhythm.

Keywords: persistent atrial fibrillation, radiofrequency ablation, atrial fibrillation termination, meta-analysis

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FL and XT contribute this manuscript equally.

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1. Introduction

Atrial fibrillation (AF) is the most common arrhythmia encountered in the clinical setting, and it affects 2% of the general population.^[1] It usually starts as brief periods of abnormal heart beating that become longer and persistent, but episodes often manifest with no symptoms.^[2] Elderly people are the susceptible population of AF. The mortality and risk of stroke are increased largely for patients with AF. Thus far, substantial research has been done on the mechanism of AF, but it is still unclear.^[3] Numerous studies have concluded that the occurrence of AF does not involve a single mechanism.^[4-7] In some patients with AF, especially paroxysmal AF, pulmonary veins and other ectopic excitatory lesions can cause AF.^[8] For persistent AF, the mechanism is much more complicated.

Catheter ablation is a procedure commonly used in symptomatic patients with drug-refractory AF to control symptoms. Pulmonary vein isolation is now widely used in paroxysmal AF, which is confirmed effective. Regarding persistent AF, it is much more difficult to terminate the arrhythmia during the procedure, and various strategies are used in centers. The optimal ablation strategy and end point for persistent AF have not been well established.^[9] The preferred additional ablation targets and procedural end points are diverse, usually depending on the operator's discretion.

Certain studies demonstrated that achieving AF termination is the best procedural end point during ablation for patients with persistent AF, and they claimed that it is more likely to maintain sinus rhythm (SR) in the long term.^[10,11] Nevertheless, ablation to AF termination means that the procedural duration is longer and repeat ablation rate is higher, although the perioperative risk and complications rates are unknown. In addition, some of those studies did not have consistent reproducibility.^[9] Several recent studies indicated that ablation for AF termination as a procedural end point lacks sufficient experimental, mechanistic, or clinical support and thus should not be the optimal end point.^[12]

As single studies may lack adequate evidence to provide reliable and comprehensive conclusions, a meta-analysis of all eligible studies should be performed. Therefore, in this meta-analysis, we analyzed the differences between periprocedural AF termination and non-termination in the long-term AF recurrence rate and postoperative complications and provided quantitative evidence to confirm whether AF termination is an appropriate and reliable procedural end point.

2. Material and methods

This systematic review and meta-analysis was conducted in accordance with the recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement.^[13] This is a systematic review and ethical approval was not necessary.

2.1. Data sources and search strategy

Randomized controlled trials (RCTs) were identified by a systematic search of electronic databases including MEDLINE (PubMed), EMBASE, Cochrane Central from January 2008 to August 2019. The terms “atrial fibrillation,” and “radiofrequency ablation” were used to search titles, abstracts, and key words (See Information, Supplementary Content, which shows the search strategy details). The search was conducted by two independent researchers (FL and XT). Besides, for fear of losing additional relevant studies, we conducted a manual search of additional articles using references from relevant articles and review papers.

2.2. Study selection

Criteria for inclusion were as follows:

- (1) studies about patients with persistent AF receiving radiofrequency catheter ablation;
- (2) studies that included periprocedural termination and non-termination of AF during the index procedure; and
- (3) studies that assessed long-term freedom from AF or any atrial arrhythmia without antiarrhythmic drugs at the ≥ 12 -month follow-up.

AF termination was defined as conversion to SR or atrial tachycardia (AT)/atrial flutter (AFL). Studies were excluded if the study was published as a review, case report, or an animal study and if the outcome of catheter ablation was not adjudicated as a major (primary or secondary) end point. There was no restriction for age, sex, and country of the studies. Two independent reviewers were responsible for identifying the studies (FL and DL).

2.3. Primary and secondary outcomes

The primary outcome was freedom from AF or any atrial arrhythmia without antiarrhythmic drugs at the long-term (≥ 12

months) follow-up. The secondary outcome was overall postoperative complication rates.

2.4. Data extraction

Data were extracted and quality assessments were performed independently by 2 main reviewers (XT and YJ). The following information was received from each eligible study: first author's name, sample size, country of the study, year of publication, participants' characteristics, duration of follow-up, adopted ablation strategy, left atrium (LA) diameter, AF termination rates, AF termination type, and long-term success rates for patients in whom periprocedural AF termination was achieved and those in whom the end point was not achieved.

2.5. Quality assessment

A quality assessment of each selected study was conducted by two investigators (FL and DL). We used the Cochrane Collaboration recommending tool^[14] to evaluate the risk of bias, with a focus on selection bias, detection bias, performance bias, attrition bias, and reporting bias.^[15] Any disagreements in the abstracted data were adjudicated by a third reviewer (YC).

2.6. Statistical analysis

The freedom from AF or any atrial arrhythmia without antiarrhythmic drugs at the ≥ 12 -month follow-up (primary outcomes) and overall postoperative complication rates (secondary outcomes) are dichotomous variables. Hence, the risk ratio (RR) with 95% confidence interval (CI) was calculated for these primary and secondary outcomes. A forest plot for RCTs was constructed to assess the differences between periprocedural AF termination and non-termination in the AF recurrence rate and postoperative complication rate. The summary estimates were generated using a fixed-effects model (low heterogeneity) or a random-effects model (high heterogeneity).^[16,17] Statistical heterogeneity was assessed with the Q-test and I^2 statistic. I^2 values indicated the following: 25%, low heterogeneity; 50%, moderate heterogeneity; and 75%, high heterogeneity. When $P > .1$ and $I^2 < 50\%$, the fixed-effects model was used; otherwise, the random-effects model was used. Sensitivity analysis was performed to investigate the effect of one study on the overall risk estimate by sequentially omitting a single study at a time. Potential publication bias was determined using Egger funnel plot. $P < .05$ was considered significant.

Additionally, in order to investigate whether the type of AF termination affected this study's results, we divided the RCTs into the SR subgroup and SR atrial tachycardia/atrial flutter (SR AT/AFL) subgroup. Ablation techniques were different, as some studies used the same ablation strategy in the AF termination group and non-termination group; however, some used different strategies between the 2 groups. Therefore, we categorized the RCTs into the same ablation strategy (SAS) subgroup and different ablation strategy (DAS) subgroup. AF recurrence was defined differently. If the definition of AF recurrence was any episode of documented AF, it was assigned to the AF subgroup; otherwise, it was assigned to the AF/AT/AFL subgroup. Apart from that, patients' average LA diameter of included studies varied. If the patients' average LA diameter of the study was more than 45 mm, it was assigned to the ≥ 45 mm subgroup; otherwise, it was assigned to the < 45 mm subgroup. The Cochrane

Collaboration’s Review Manager software package (RevMan 5.3) was used for this meta-analysis.

3. Results

3.1. Search results

We identified 818 articles in the systematic literature search. One hundred and 96 studies were removed due to duplicated publication and 566 articles were excluded based on the titles or abstracts. We considered 56 articles and assessed their eligibility by reviewing the full text. Ultimately, 14 RCTs met the prespecified inclusion criteria and were included in this meta-analysis.^[11,18–23,24–30] A study inclusion flow chart is shown in Figure 1.

3.2. Study characteristics

Detailed characteristics of all the included studies are presented in Table 1. All the included studies were published in the last 11 years between 2008 and 2019. Studies were conducted in centers across Europe, North America, Asia, Russia, and Australia, and they included 2212 participants. The age range of all participants was middle-aged and elderly, and the participants represented the population at high risk of having AF as well. The reported follow-up duration ranged from 10 to 42 months. All procedures were conducted using radiofrequency ablation. These studies used ablation strategies that were highly variable and included the following: only complex fractionated atrial electrogram (CFAE) ablation,^[24] a combination of pulmonary vein antrum isolation plus CFAE with or without linear ablation,^[11,18,19,22,23,24–29] and others.^[20,21] Moreover, in certain studies, different strategies were used in the AF termination and non-termination groups. In these studies, freedom from AF was defined as no AF recurrence

and no AF/AT/AFL recurrence. Table 1 shows a detailed description.

3.3. Study quality assessment

According to the Cochrane Collaboration recommending tool. The majority of studies had a low or unclear risk of bias, although 2 of those studies^[20–25] did not have blinded participants and personnel, and 1 study^[25] had a high risk of attrition bias. Results from the risk of bias assessment are shown in Figure 2.

3.4. Freedom from AF at long-term follow-up

Freedom from AF at the long-term follow-up was evaluated in 14 RCTs (n=2212). In these studies, periprocedural AF termination was achieved in 938 (42.4%) patients and not achieved in 1274 (57.6%) patients. Generally, no significant difference was found in freedom from AF at the long-term follow-up between patients in whom AF termination was achieved and not achieved. The AF recurrence rate after achieving AF termination was 0.93 times lower than after not achieving AF termination, it did not reach significance (RR = 0.93, 95% CI=0.78-1.09, P=.36, I²=69%) (Fig. 3). Sensitivity analysis was performed by sequentially omitting one study at a time. There was no substantial change in the overall combined RRs, which ranged from 0.89 (95% CI: 0.76-1.05) to 0.97 (95% CI: 0.83-1.13) after excluding studies sequentially. Additionally, we found similar heterogeneity after each exclusion, and the I² values ranged from 62% to 71%. The results indicated that no single study dominated the combined RRs and heterogeneity. Egger test suggested that there was no publication bias, as presented in Fig. 4 (P=.360).

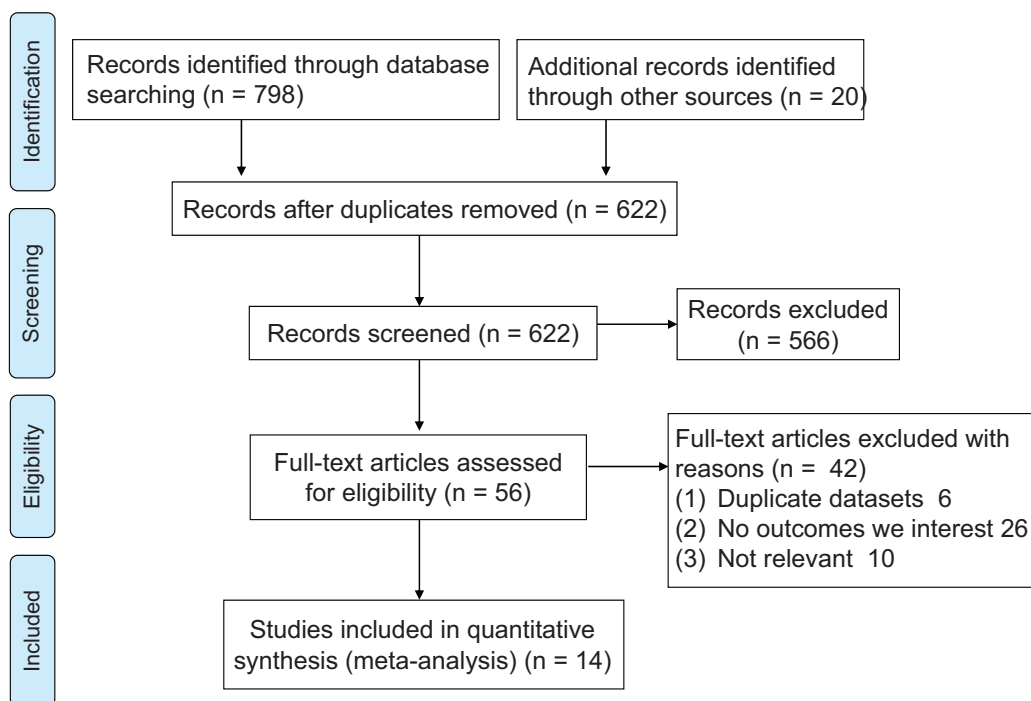


Figure 1. PRISMA (Preferred Reporting Items for Systematic reviews and Meta-Analyses) flow diagram for study identification and inclusion.

Table 1
Summary of included studies.

| Study ID (Y) | Country | sample size | Gender (M/F) | Mean age | Follow-up time (months) | Ablation technique | % of AF Termination | Type of AF Termination | Definition of AF Recurrence | LA diameter (mm) |
|------------------------------------|---------|-------------|--------------|-----------|-------------------------|---------------------------------------|---------------------|------------------------|-----------------------------|------------------|
| Ammar-Busch ^[18] (2017) | Germany | 90 | 71/19 | 64±9 | 12 | PVI+CFAE vs PVI+CFAE+Linear | 16 | SR | AEoD AF or AT/AFL>30s | 48±7 |
| Elayi ^[19] (2008) | France | 144 | 95/49 | 59.1±10.7 | 16 | PVI vs PVI+Linear vs PVI+CFAE | 44 | SR, AT/AFL | AEoD AF or AT/AFL>60s | 45.4±6.7 |
| Fink ^[20] (2017) | Germany | 118 | 84/34 | 61.5±9.7 | 12 | PVI vs PVI+Substrate Modification | 60 | SR | AEoD AF or AT/AFL>30s | 47.0±4.4 |
| Kim ^[21] (2015) | Korea | 120 | 87/33 | 57.2±10.8 | 12 | PVI+Linear vs PVI+Linear+PVI | 78 | SR | AEoD AF or AFL | 42.2±5.8 |
| Kim ^[22] (2017) | Korea | 137 | 98/39 | 61.6±10.9 | 22.3±13.2 | CPVI+Linear vs CPVI+Linear+CFAE | 21.2 | SR | AEoD AF or AT>30s | 45.0±5.46 |
| Kochhäuser ^[23] (2017) | Canada | 549 | - | - | 18 | PVI vs PVI+CFAE vs PVI+Linear | 26 | SR, AT/AFL | AEoD AF>30s | 44.2±5.2 |
| Lin ^[11] (2014) | China | 90 | 74/12 | 52±11 | 15±11 | PVI+CFAE | 25 | SR | AEoD AF or AT/AFL>60s | 44.9±6.16 |
| Oral ^[24] (2008) | USA | 85 | 74/11 | 59±10 | 17±6 | CFAE | 24 | SR, AT/AFL | AEoD AF | 46.5±6.49 |
| Oral ^[25] (2009) | USA | 119 | 96/23 | 60±9 | 12 | CFAE | 24 | SR, AT/AFL | AEoD AF | 46.5±5.99 |
| Rostock ^[26] (2013) | Germany | 110 | 88/22 | 63±9 | 20.1±13.3 | PVI vs PVI+Electrogram-based ablation | 33 | SR | AEoD AF or AT/AFL>30s | 45.5±6.50 |
| Wang ^[27] (2017) | China | 96 | 45/51 | 59±9.5 | 12 | PVI+CFAE vs PVI | 65.7 | SR | AEoD AF or AT/AFL | 45.5±4.01 |
| Wang YL ^[28] (2017) | China | 400 | 238/162 | 58±10 | 42 | PVI+Linear vs CFAE | 44.7 | SR, AT/AFL | AEoD AF>30s | 46.6±5.95 |
| Wong ^[29] (2015) | UK | 130 | 98/32 | 61±10 | 35±5 | PVI+Linear vs PVI+Linear+CFAE | 26 | SR | AEoD AF or AT/AFL | 46±6 |
| Wynn ^[30] (2016) | UK | 130 | 88/42 | 61.9±10.5 | 12 | PVI vs PVI+Linear | 72 | SR | AEoD AF or AT/AFL>30s | 43±6 |

AEoD = any episode of documented; AF = atrial fibrillation; AT/AFL = intermediate atrial tachycardia/flutter; CFAE = complex fractionated atrial electrograms; LA = left atrium; PVI = pulmonary vein isolation; PW = posterior wall isolation; SR = sinus rhythm; UK = United Kingdom; USA = the United States of America.

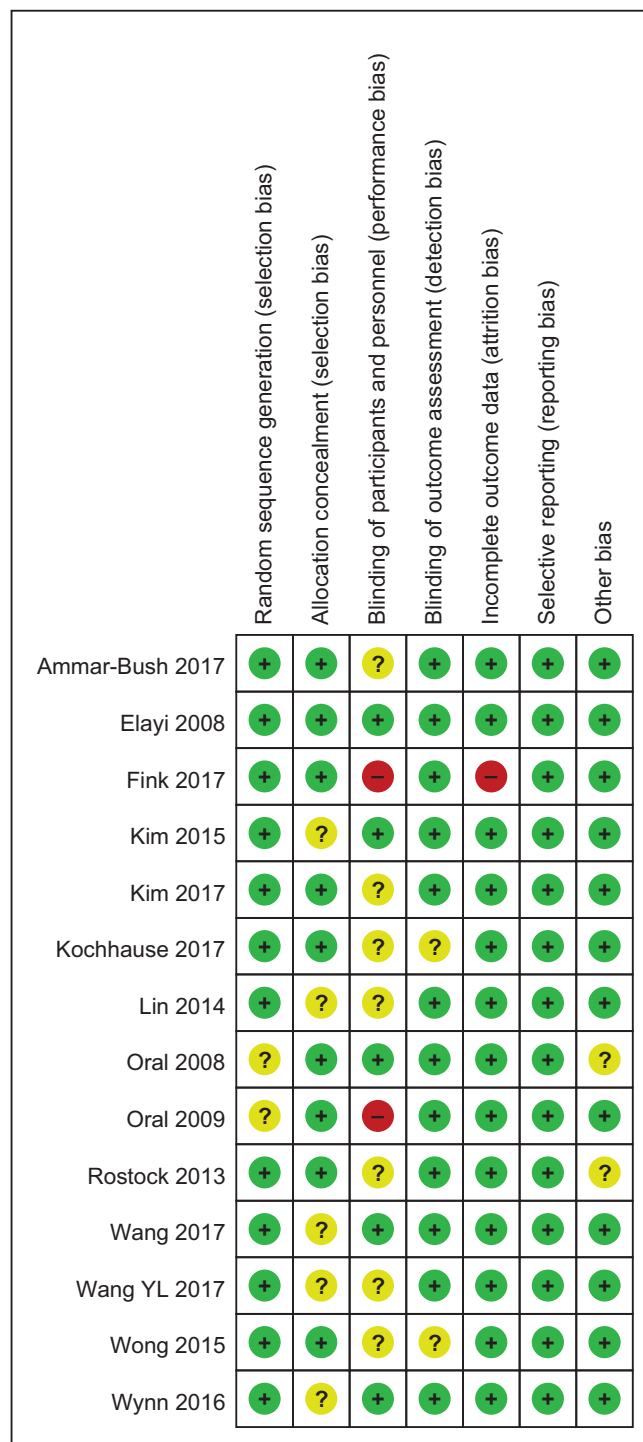


Figure 2. Forest plot demonstrating the differences of AF recurrences between periprocedural AF termination and non-termination.

3.5. Postoperative complications

In 9 studies, complications associated with periprocedural termination and non-termination of AF were reported (n = 1253).^[11,17-19,21,26-29] Table 2 shows all complications reported by the studies in this meta-analysis. Patients without AF termination had a lower complication rate than those with AF termination (RR = 1.74, CI = 1.11-2.73, P = .02, I² = 0%) (Fig. 5).

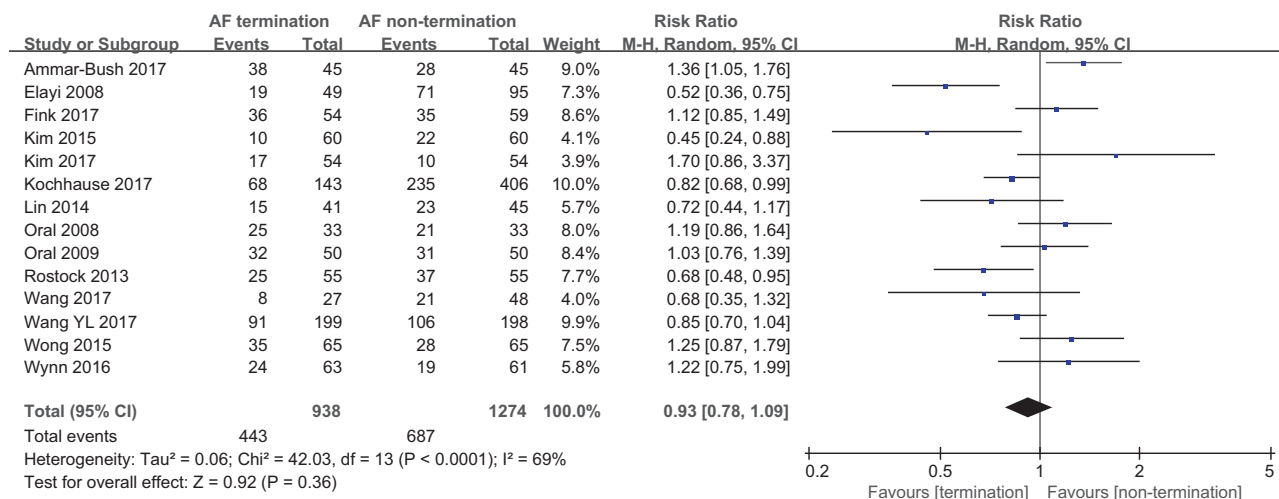


Figure 3. Forest plot demonstrating the differences of postoperative complication recurrence rates between periprocedural AF termination and non-termination.

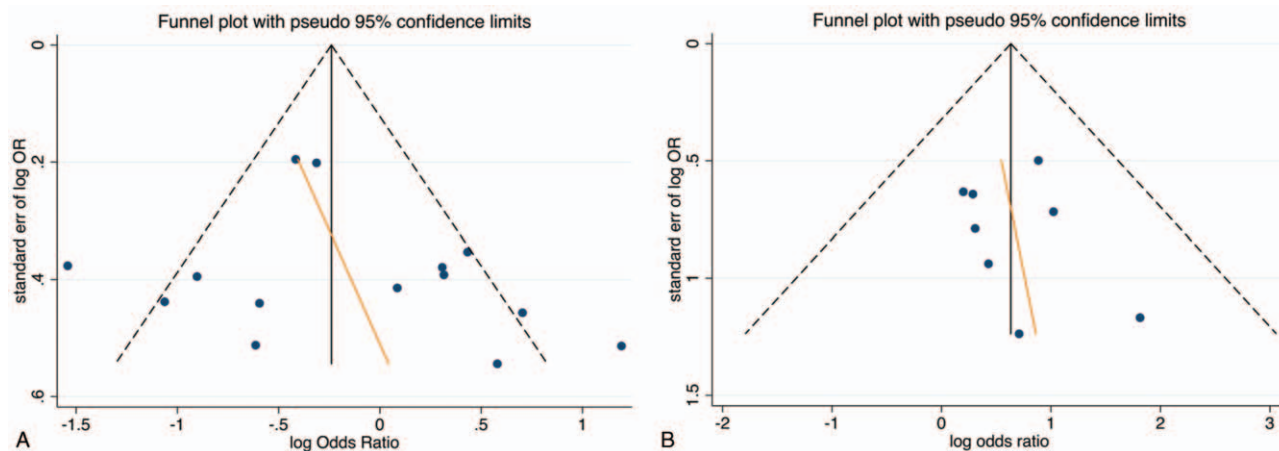


Figure 4. Risk of bias of included studies in the meta-analysis.

Table 2

Reported postoperative complications of periprocedural AF termination versus AF non-termination.

| Study | AF termination | | AF non-termination | |
|-------------------------|---|------------------------------|--------------------------------------|-------------------------------|
| | Complication | Number of patients (n = 938) | Complication | Number of patients (n = 1274) |
| Fink [20] (2017) | Cardiac tamponade | 2 | Stroke | 1 |
| | Stroke | 1 | Transient ischemic attack | 1 |
| | Groin bleeding requiring transfusion | 2 | Groin bleeding requiring transfusion | 1 |
| | Groin bleeding requiring surgical therapy | 2 | | |
| Oral [24] (2008) | - | 0 | Pericarditis | 1 |
| Wang [27] (2017) | Minor bleeding | 5 | Minor bleeding | 7 |
| Wynn [30] (2016) | Unclear | 6 | Unclear | 5 |
| Elayi [19] (2008) | Asymptomatic PV stenosis | 1 | Asymptomatic PV stenosis | 1 |
| | Pericardial effusions | 2 | | |
| Wong [29] (2015) | Cardiac tamponade/Transient ischemic attack | 11 | Atrial-esophageal fistulas | 1 |
| Wang YL [28] (2017) | Cardiac tamponade | 3 | Cardiac tamponade | 1 |
| | Femoral hematomas | 8 | Femoral hematomas | 5 |
| | Reversible right phrenic nerve injuries | 3 | | |
| | Pseudoaneurysm | 2 | LAA isolation | 1 |
| Ammar-Busch [18] (2017) | Asymptomatic PV stenosis | 1 | Pericarditis | 1 |
| | Unclear | 4 | Unclear | 3 |
| Total patients | | 44 | | 29 |

AF= atrial fibrillation; LAA=left atrial appendage; PV=pulmonary vein.

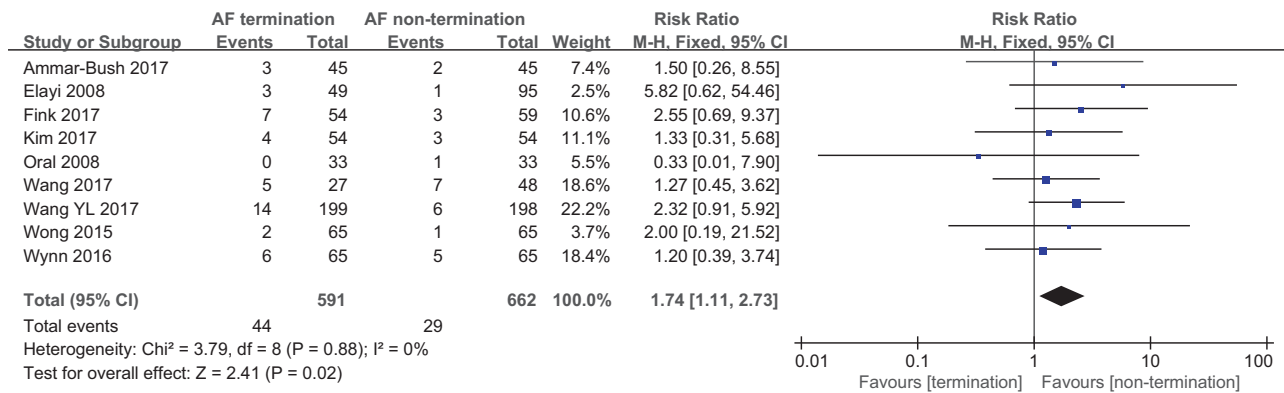


Figure 5. (A) Egger funnel plot asymmetry test for the evaluation of potential publication bias for the primary outcome (P = .360) (B) Egger funnel plot asymmetry test for the evaluation of potential publication bias for the secondary outcome (P = .408).

Otherwise, the types of complications were more variable and severe in AF termination compared with AF non-termination. We performed sensitivity analysis by sequentially omitting one study at a time. However, I² and RR were not significantly different, which indicates that our results were robust. Egger test result suggested no publication bias, as presented in Fig. 4 (P = .408). Because the study sample of patients with postoperative complications was relatively small, further analysis was not done.

3.6. Subgroup analysis

Nine RCTs defining AF termination as achieving SR were classified in the SR subgroup. The other 5 RCTs defining AF termination as achieving SR or AT/AFL were categorized as the SR AT/AFL subgroup. The SR and SR AT/AFL subgroups showed no difference in freedom from AF at the long-term follow-up between patients in whom AF termination was achieved and not achieved. (SR subgroup: RR=0.97, 95% CI=0.76-1.24, P=.83, I²=67%; SR AT/AFL subgroup: RR=0.86, 95% CI=0.70-1.06, P=.16, I²=69%) (Table 3).

Three studies used the same ablation strategy between the AF termination group and non-termination group, whereas 11 studies used different ablation strategies between the groups. The 2 subgroups showed no significant difference between patients with and without periprocedural AF termination (SAS subgroup:

RR=0.92, 95% CI=0.71-1.20, P=.54, I²=52%; DAS subgroup: RR=0.93, 95% CI=0.75-1.14, P=.47, I²=74%) (Table 3).

There were ten studies divided into the ≥45 mm subgroup and four studies divided into the <45 mm subgroup. Both of the subgroups claimed that there was no significant difference between patients with and without periprocedural AF termination (≥45 mm subgroup: RR=0.98, 95% CI=0.80-1.19, P=.81, I²=72%; <45 mm subgroup: RR=0.80, 95% CI=0.59-1.07, P=.14, I²=50%) (Table 3).

Ten studies were classified in AF/AT/AFL subgroup, and four studies were classified in AF subgroup. The 2 subgroups showed no significant difference between patients with and without periprocedural AF termination (AF/AT/AFL subgroup: RR=0.90, 95% CI=0.69-1.18, P=.44, I²=76%; AF subgroup: RR=0.93, 95% CI=0.79-1.08, P=.33, I²=40%) (Table 3).

To sum up, type of AF termination, ablation techniques used for AF patients, LA diameter and definition of AF recurrence all had no effect on the results.

4. Discussion

This meta-analysis of studies from the past 11 years on ablation for persistent AF patients clarified that there is no statistical difference between periprocedural AF termination and non-

Table 3 Subgroup analyses of differences of AF recurrences between periprocedural AF termination and non-termination.

| Factors | No. | RR (95%CI) | P | I ² | Heterogeneity, P |
|-----------------------------|-----|------------------|------|----------------|------------------|
| Type of AF termination | | | | | |
| SR | 9 | 0.97 (0.76–1.24) | .830 | 67 | .002 |
| SR AT/AFL | 5 | 0.86 (0.70–1.06) | .160 | 69 | .010 |
| Ablation strategy | | | | | |
| SAS | 3 | 0.92 (0.71–1.20) | .540 | 52 | .130 |
| DAS | 11 | 0.93 (0.75–1.14) | .470 | 74 | <.0001 |
| LA diameter | | | | | |
| ≥45mm | 10 | 0.98 (0.80–1.19) | .810 | 72 | .0002 |
| <45mm | 4 | 0.80 (0.59–1.07) | .140 | 50 | .110 |
| Definition of AF recurrence | | | | | |
| AF | 4 | 0.93 (0.79–1.08) | .330 | 40 | .17 |
| AF/AT/AFL | 10 | 0.90 (0.69–1.18) | .440 | 76 | <.0001 |

AF = atrial fibrillation; AT/AFL = intermediate atrial tachycardia/flutter; CI = confidence interval; DAS = different ablation strategy; LA = left atrium; RR = risk ratio; SAS = same ablation strategy; SR = sinus rhythm.

termination in AF recurrence. The subgroup analysis showed that type of AF termination, ablation techniques used for AF patients, LA diameter and definition of AF recurrence all had no effect on the results. Statistically, periprocedural AF termination cannot be used as an individual predictor of the long-term prognosis of patients with AF.

Recently, the choice of using AF periprocedural ablation as the end point has been a controversial discussion in the field of arrhythmia and an urgent problem to be solved. Many studies have analyzed the merits and defects of different strategies. In 2012, Shah et al.^[31] summarized acute termination, postablation arrhythmia, and extended clinical success depending on the perioperative strategies in 19 studies, and they recommended AF termination as the end point. However, in the same year, Santangelo^[12] published a systematic review article claiming that AF termination should not be the end point. Regardless of its controversy, many new research studies have been published about AF termination. We included the latest studies published over the last 10 years and performed a meta-analysis with the aim of obtaining a robust conclusion.

Once the mechanism of a disease is discovered, the disease be treated more properly using the best strategy. However, to date, the mechanisms of AF remain unclear.^[2,31] Epigenetic regulators may play a role in AF genesis and microRNAs was used as AF fibrotic and electrical alterations biomarkers.^[32] And some other comorbidities such as diabetes and chronic obstructive pulmonary disease (COPD) may be relevant triggers and aggravating factors for AF pathogenesis and recurrence.^[33,34] In persistent and long-standing AF, triggers and drivers vary remarkably among patients. The most important treatment for paroxysmal and persistent AF is catheter ablation, which can achieve procedural AF termination and conversion to SR. With regard to long-term treatment outcomes, recurrence and complications should be considered. Stroke is one of the major complications of AF. In high-risk patient populations, subclinical AF recurrence were associated with a significantly increased risk of stroke.^[35] It has been confirmed that the pathogenesis of AF is usually progressive, and the mechanisms are changeable even in the same patient.^[36-38] Therefore, even if ablation achieves procedural AF termination and conversion to SR, it cannot prevent AF from developing other new mechanisms with subsequent clinical recurrences. It is common for patients with persistent AF to be admitted to a hospital because of AF recurrence. One study showed that 0.3%/year of patients with paroxysmal AF are likely to be diagnosed with persistent AF years after catheter ablation.^[39] We can learn from these clinical facts because they highlight the fact that acute conversion to SR is not significant and essential for the long-term prognosis of patients with persistent AF.

There was no significant statistical difference between periprocedural AF termination and non-termination of persistent AF in long-term AF recurrence; however, complication rates were higher in patients with AF termination than in those without AF termination. Usually, more ablation will be performed in order to achieve procedural AF termination.^[9] When the procedural time is prolonged, it is likely to increase the risk of complications, such as cardiac tamponade, pericarditis, atrioesophageal fistula, fluid overload, and anesthetic complications.^[37] According to the present study, AF termination is not the best strategy for patients with persistent AF. In clinical practice, all prognostic factors including the procedural duration, patients' health status, and ablation strategy should be considered. Sardu's study^[32]

demonstrated that epigenetic-assisted radiofrequency ablation with microRNA target therapy may reduce recurrence of atrial fibrillation after ablation. Another study^[40] showed that an oral antioxidant treatment (α -lipoic acid) reduced ablated patients' serum levels of common markers of inflammation which may relate to AF pathogenesis and recurrence. Moreover, monitoring devices could early detect AF and avoid AF recurrences and hospital admissions for AF.^[41] It is excellent if AF terminates and converts to SR after the first ablation. However, if not, the procedure does not have to be prolonged. Drugs and other medical strategies can help with the conversion and recovery. More clinical trials are needed to support our view on the ablation end point of persistent AF.

5. Limitations

There are some limitations to this study. First, the eligible studies were limited; therefore, it is difficult to examine heterogeneity of the studies. Second, certain studies without adjustment for confounders were excluded from the meta-analysis, which may account for the introduction of bias. Third, only a few studies mentioned postoperative complications; thus, more data are needed to analyze the association between complications and perioperative strategies.

6. Conclusions

The results of this meta-analysis showed no significant difference between periprocedural AF termination and non-termination of persistent AF in the long-term AF recurrence rate. Patients with AF non-termination had a lower complication rate than those without AF termination. AF termination is not an optimal and reliable procedural end point during ablation of persistent AF. Operators should select the AF ablation strategy according to patient-specific characteristics and preferences in addition to operators' experience and preference.

Author Contribution

Rui Zeng and Dongze Li contributed to the conception of the study; Ying Jiang, Yisong Cheng, Yu Jia and Xinyu Zhang contributed significantly to analysis and manuscript preparation; Fanghui Li and Xiang Tu performed the data analyses and wrote the manuscript; Hua Fu, Hongde Hu, Jian Jiang helped perform the analysis with constructive discussions.

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