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# Is there still a role for additional linear ablation in addition to pulmonary vein isolation in patients with paroxysmal atrial fibrillation? An Updated Meta-analysis of randomized controlled trials☆

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ABSTRACT

*Background:* The benefits and risks of additional left atrium (LA) linear ablation in patients with paroxysmal atrial fibrillation (AF) remain unclear.

*Methods:* Randomized controlled trials were identified in the PubMed, Web of Science, Embase and Cochrane databases, and the relevant papers were examined. Pooled relative risks (RR) and 95% confidence interval (95% CI) were estimated using random effects models. The primary endpoint was the maintenance of sinus rhythm after a single ablation.

*Results:* Nine randomized controlled trials involving 1138 patients were included in this analysis. Additional LA linear ablation did not improve the maintenance of the sinus rhythm following a single procedure (RR, 1.03; 95% CI, 0.93–1.13; $P = 0.60$). A subgroup analysis demonstrated that all methods of additional linear ablation failed to improve the outcome. Additional linear ablation significantly increased the mean procedural time ($166.53 \pm 67.7$ vs. $139.57 \pm 62.44$ min, $P < 0.001$), the mean fluoroscopy time ($54.56 \pm 38.7$ vs. $44.32 \pm 31.6$ min, $P < 0.001$) and the mean radiofrequency (RF) energy application time ($78.94 \pm 28.39$ vs. $59.74 \pm 22.38$ min, $P < 0.001$). No statistically significant differences in the rates of complications were noted (RR, 0.57; 95% CI, 0.27–1.19; $P = 0.13$).

*Conclusions:* Additional LA linear ablation did not exhibit any benefits in terms of sinus rhythm maintenance for paroxysmal AF patients following a single procedure. Additional linear ablation significantly increased the mean procedural, fluoroscopy and RF application times. This additional ablation was not associated with a statistically significant increase in complication rates. This finding must be confirmed by further large, high-quality clinical trials.



## 1. Introduction

Atrial fibrillation (AF) is one of the most common forms of cardiac arrhythmia in clinical practice [1,2]. This arrhythmia significantly increases the risk of stroke and thrombus events and is associated with higher morbidity and mortality [3,4]. Currently, catheter ablation technology is widely applied to treat paroxysmal AF. Given that the pulmonary veins (PVs) are a critical site for the initiation of AF, current ablation strategies for paroxysmal AF primarily focus on pulmonary vein isolation (PVI). However, the postablation recurrence remains high in some patients. Therefore, the focus has subsequently shifted to modify areas of abnormal atrial tissue which may act as a substrate for maintaining AF. Additional left atrium (LA) linear ablation has been widely conducted in persistent AF ablation as a means of substrate modification. However, whether additional LA linear ablation is also effective in paroxysmal AF patients remains controversial. Several clinical studies and meta-analyses have evaluated the efficacy of additional LA linear ablation for paroxysmal AF patients, but the conclusions were inconsistent [5–7]. Moreover, additional LA linear ablation has been reported in some studies to be associated with increased procedural, fluoroscopy and radiofrequency (RF) energy durations. Therefore, we performed this meta-analysis to evaluate the benefits and risks of additional LA linear ablation for paroxysmal AF patients.

## 2. Methods

### 2.1. Search strategy

We searched PubMed, Web of Science, Cochrane Database and Embase (until August 2015) to identify clinical trials only published in English. The search terms included “atrial fibrillation,” “pulmonary

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vein isolation," "radiofrequency catheter ablation," "left atrium," and "linear ablation". We also manually searched the previously published meta-analyses and bibliographies of the selected publications. Additionally, gray literature was identified by searching the related agencies and clinical trial registers. Only randomized controlled trials (RCTs) were included, cohort studies, case–control studies and case reports were excluded.

### 2.2. Eligibility criteria

Only RCTs that compared PVI to the same procedure with additional LA linear ablation in paroxysmal AF patients were included. Additional inclusion criteria included a follow-up of ≥3 months and a study population > 18 years old. The ablation could be performed as a first-line therapy or after failure of antiarrhythmic drugs (AADs) regardless of the AF burden or the severity of the symptoms. Any methods of PVI (segmental PVI or circumferential PVI) were accepted as long as PVI was confirmed. Additional LA linear ablation could be performed in any manner that caused continuous linear lesions anywhere within the left atrium. Two reviewers (X.L.H. and J.Z.J.) independently screened the studies to determine whether they satisfied the eligibility criteria. Discrepancies between reviewers were resolved by consensus, and a third reviewer was consulted when necessary.

### 2.3. Data extraction

Two independent reviewers screened the data from the included studies using a predefined checklist for each study. Disagreements between reviewers were resolved by discussion until a consensus was reached. Data extraction and presentation for this article followed the recommendations of the PRISMA group [8]. The following data were extracted for each selected study whenever available: demographics and sample characteristics, AF duration, presence of concomitant disease, left atrial size, ablation technique, criteria and location for additional linear ablation, complications, follow-up duration, procedural times, monitoring strategy of AF recurrence and AADs use. The primary outcome was the maintenance of sinus rhythm following a single ablation procedure with or without the use of AADs. The secondary outcomes included total procedural times, fluoroscopy times, RF energy application times and ablation-related complications.

### 2.4. Quality assessment

Two reviewers independently assessed the included studies for systematic bias according to the Cochrane Handbook for Systematic Reviews of Interventions. We fully evaluated the sequence generation for randomization, allocation concealment, the masking of outcome assessors, incomplete outcome data, selective outcome and other potential risks reporting in all of the studies. Disagreements between reviewers were resolved by consensus and consultation with a third reviewer when necessary.

### 2.5. Data analysis

The continuous variables are expressed as the mean ± standard deviation. The categorical data are presented as frequencies and percentages. We computed the pooled RR and 95% CI as well as the heterogeneity of the included studies. Heterogeneity was quantified using the $I^2$ statistic. Low, moderate and high levels of heterogeneity were defined as $I^2$ value of 40, 70 and 100%, respectively. $I^2$ value ≤40% indicate no evidence of heterogeneity. Heterogeneity was considered significant when the P-value was less than 0.1. If between-study heterogeneity was observed, we performed sensitivity analyses by excluding each study individually to explore the possible sources of heterogeneity. Subgroup analyses were also conducted to test the effects of different linear ablation strategies. All statistical analyses were performed with the REVMAN software (version 5.2; Cochrane Collaboration, Oxford, United Kingdom). Two-tailed P-values less than 0.05 were considered statistically significant. Publication bias was visually evaluated by examining the funnel plots.

## 3. Results

### 3.1. Search results

The search strategy revealed 132 potentially eligible references, and 20 additional records were identified by other means. After the duplicates were removed, 92 studies remained. When the abstracts were reviewed in terms of the inclusion and exclusion criteria, 19 studies warranting further review were identified. Among these, 10 studies were excluded for the reasons listed in Fig. 1. The remaining 9 studies were all included in this meta-analysis. Among these 9 studies [9–17], 8 RCTs were from journal articles (full manuscripts acquired) [9–14,16,17], and 1 RCT was from a meeting abstract [15].

### 3.2. Study characteristics

The characteristics of the trials included in this meta-analysis are presented in Table 1. Of the 9 randomized controlled trials, 7 studies [10,11,13–17] included only paroxysmal AF patients, and 2 studies [9,12] included both paroxysmal and nonparoxysmal AF patients. The effects of additional linear ablation on the patients with paroxysmal and nonparoxysmal AF were reported separately. The follow-up durations ranged from 9 to 36 months, and postablation AADs use also varied widely. Four studies [13,14,16,17] used blanking periods of 3 months, 1 study [12] used a blanking period of 2 months, and 4 studies [9–11,15] did not report the blanking period. The results of the quality assessments of the included studies are presented in Table 2.

### 3.3. Baseline patient characteristics

Table 3 summarizes the baseline characteristics of the patients in the included studies. These 9 studies included 1138 paroxysmal AF patients. The mean age of the patients was 56 years, and 73.6% were male. The mean LA dimension was 39.6 mm, and the mean ejection fraction was 62.2%. The mean follow-up duration was >1 year in the majority of the studies. The baseline characteristics were balanced between the PVI and PVI + additional linear ablation groups in 6 studies. Three studies [9,12,15] did not report the baseline patient characteristics of the paroxysmal AF group.

### 3.4. Details of catheter ablation

The catheter ablation techniques and ablation endpoints are listed in Table 4. All of the studies defined the electrical isolation of PV potentials as the endpoint of PVI. Among these studies, 5 studies [10,14–17] conducted circumferential PVI (CPVI) strategy, 3 studies [9,11,12] conducted segmental PVI (SPVI) strategy, and 1 study [13] applied both the SPVI and CPVI methods to achieve pulmonary vein isolation. Regarding the additional LA linear ablation, 1 study [9] conducted mitral isthmus linear (MIL) ablation, 4 studies [10,14–16] conducted roofline ablation, 3 studies [11–13] conducted both MIL and roofline ablation, 2 studies [14,15] conducted roofline and posterior inferior wall (PostBox) linear ablation, and 2 studies [15,17] conducted PostBox linear ablation together with LA anterior wall ablation. Four studies [10,12,14,17] performed cavotricuspid isthmus ablation in all patients. One study [10] also ablated fragmented potentials and non-PV triggers in all patients. Eight studies [9,10,12–17] confirmed bidirectional block following additional linear ablation, and 1 study [11] didn't test the bidirectional conduction block.