Biatrial versus Isolated Left Atrial Ablation in Atrial Fibrillation: A Systematic Review and Meta-Analysis

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Received 3 October 2017; Revised 10 March 2018; Accepted 14 March 2018; Published 29 April 2018

Objective. The outcomes of biatrial ablation (BA) and isolated left atrial ablation (LA) in atrial fibrillation remain inconclusive. In this meta-analysis, we assess the currently available evidence to compare outcomes between BA and LA.

Methods. Electronic searches were performed from database inception to December 2016, and relevant studies were accessed. Odds ratios and weight mean differences with 95% confidence intervals are reported. Twenty-one studies comprising 3609 patients were included in the present meta-analysis.

Results. The prevalence of sinus rhythm in the BA cohort was similar to that in the LA cohort at discharge, at 12 months, and after more than 1 year of follow-up. However, at 6 months, the prevalence of sinus rhythm was higher in the BA cohort than in the LA cohort. The rate of permanent pacemaker implantation was higher in the BA cohort than in the LA cohort. However, 30-day and late mortality and neurological events were similar between the BA and LA groups. Conclusion. There was no significant difference in the rate of restored sinus rhythm, the risk of death, and cerebrovascular events between BA and LA, but BA had a higher rate of permanent pacemaker implantation.

1. Introduction

Atrial fibrillation (AF) is a major healthcare problem worldwide which has enormous economic and public health implications. AF is associated with an increased risk of stroke, heart failure, and all-cause mortality [1–3].

Surgical ablation was introduced as a treatment option by Cox et al. [4] in 1991, and it is currently an effective curative strategy for AF. Haïssaguerre et al. [5] suggested that ectopic beats from pulmonary veins may cause AF, and the field of pulmonary vein isolation (PVI) was consequently established and is now performed via catheter or surgical ablation [6]. Left ablation (LA) has historically been the main method used to treat AF, and it has a fairly good clinical effect [7, 8]. However, some studies have suggested that LA is less efficacious than biatrial ablation (BA), especially when a right-side AF trigger is present [9]. Hence, because outcomes have been inconclusive, Phan et al. [10] and Zheng et al. [11] reported relevant meta-analyses in 2014, but they arrived at a different conclusion. The authors showed that BA was more effective than LA and that the rate of permanent pacemaker implantation was also higher in the BA cohort than in the LA cohort. However, Zheng et al. [11] suggested that the effects of BA and LA are the same.

In the past two years, several other studies [8, 12–15] have compared BA and LA in AF, with controversial outcomes. Hence, in this meta-analysis, we sought to assess the current evidence available on this issue.
2. Methods

2.1. Literature Search Strategy. Electronic searches were performed in August 2016 without search restrictions. The primary sources were the electronic Medline, PubMed, Cochrane Library, and EMBASE databases, which were searched from their date of inception to August 2016. The following search terms were used: “maze,” “biantial,” “biantial,” “uniatrial,” “left atrial,” and “ablation.” When duplicate published trials with accumulating numbers of patients or increased lengths of follow-up were encountered, the most recent or most complete report was considered. All titles and abstracts identified in the electronic search were uploaded into an EndNote (version X7; Thomson Corporation, Stanford, USA) database (Figure 1).

2.2. Inclusion and Exclusion Criteria. All available randomized, controlled trials (RCTs) and retrospective comparative studies that compared BA with LA in all age groups were included. Abstracts, case reports, conference presentations, editorials, reviews, and expert opinions were excluded. When institutions published duplicate studies with accumulating numbers of patients or increased lengths of follow-up, only the most complete report was included. Reference lists were also manually searched for further relevant studies.

2.3. Data Extraction and Critical Appraisal. Two reviewers (Hongmu Li and Xifeng Lin) conducted data extraction independent of the included studies. Data on authorship, year of publication, study design, study population, baseline characteristics, characteristics related to outcomes, and duration of follow-up were extracted from each study. Reported percentages were approximated to numbers. The risk of bias was assessed using the Downs and Black checklist [16] for randomized and observational studies. Discrepancies between the reviewers were resolved by discussion until consensus was reached. The final results were reviewed by the senior investigator (Ping Hua).

2.4. Quality Assessment and Statistical Analysis. The included studies were rated to determine the level of quality of the provided evidence according to the criteria of the Centre for Evidence-Based Medicine in Oxford, UK [17]. The methodological quality of the RCTs was assessed with the
Cochrane risk of bias tool [18]. The methodological quality of retrospective studies was assessed with the modified Newcastle-Ottawa scale [19, 20].

This meta-analysis was performed using Review Manager Version 5.3 (Cochrane Collaboration, Oxford, UK). Dichotomous variables from individual studies were analyzed using odds ratios (ORs) with 95% confidence intervals (CIs). Q-statistics ($P < 0.10$) or $I^2$ statistics were performed to test for heterogeneity between included studies, and values of 50% or higher were considered to be indicative of substantial heterogeneity. If there was substantial heterogeneity, the possible clinical and methodological reasons for this were explored qualitatively. Publication bias was examined through a visual inspection of funnel plots and assessed by applying Egger’s weighted regression statistic and considering a $P$ value less than 0.05 as indicating significant publication bias. A $P$ value of less than 0.05 was considered statistically significant for all analyses.

2.5. Synthesis of Evidence. Our electronic literature search resulted in the retrieval of 398 citations. Of these, 372 were excluded after duplicate and irrelevant references were excluded, and 49 potentially relevant articles were retrieved. Finally, following a manual search of reference lists and a critical appraisal, 21 studies comprising 3609 patients were included in this meta-analysis. Two articles had redundant publications but covered different characteristics [21, 22].

2.6. Quality Assessment and Baseline Characteristics of Eligible Studies. In all, 21 studies were included in this meta-analysis, including three prospective randomized trials [23–25], five prospective observational studies [26–29], and 13 retrospective observational studies [8, 12–15, 21, 22, 30–36]. The risk of bias in each study is shown in Figure 2 and Table 1. Among the 3609 patients, 1901 received BA, and 1708 received LA. Patients in the BA group underwent a classical or modified maze procedure, including both left-sided and right-sided maze procedures. However, patients in the LA group underwent a left-sided maze procedure that included PVI, left atrial posterior wall isolation, mitral isthmus ablation, and left atrial appendage excision.

Three studies used cryoablation energy [15, 27, 31], eleven studies used radiofrequency energy [12–14, 21, 23, 25, 26, 29, 32–34], and the remaining studies used a combination of different energy sources, including radiofrequency, cryoablation, and microwave and “cut-and-sew” [8, 22, 24, 28, 30, 35, 36]. Concomitant coronary artery bypass grafting surgery was reported in 10 studies [8, 13, 21, 22, 25, 27–31, 36], while a concomitant valvular operation was performed in other included studies. The baseline characteristics of the patients in the included studies are shown in Tables 2 and 3.

3. Outcomes

3.1. Assessment of Efficacy. The data were pooled from 16 studies [12–15, 21–26, 28, 29, 31–33, 36] that assessed the efficacy of restoring sinus rhythm (SR), and the results showed that there was no significant difference between the BA and LA groups at discharge (78.3% versus 73.8%; OR: 1.02; 95% CI: 0.69–1.51; $P = 0.92$; $I^2 = 66$%). However, the overall prevalence of SR was higher in the BA group than in the LA group at a 6-month follow-up (78.82% versus
| Study                  | Assignment for treatment | Selection | Comparability          | Outcome | Quality score |
|-----------------------|--------------------------|-----------|------------------------|---------|---------------|
| Gualis et al., 2016   | No                       | Yes       | Yes 1, 2, 3, 4         | Yes     | No            |
| Liu et al., 2015      | No                       | Yes       | Yes 1, 2, 3, 4         | No      | Yes           |
| Henn et al., 2015     | No                       | Yes       | Yes NR 5, 6            | Yes     | No            |
| Pecha et al., 2014    | No                       | Yes       | Yes 1, 2, 3, 4         | Yes     | NR            |
| Jiang, 2014           | No                       | Yes       | Yes 1, 2, 3, 4         | Yes     | No            |
| Soni et al., 2013     | No                       | Yes       | Yes 1, 2, 3, 4         | Yes     | No            |
| Pecha et al., 2014    | No                       | Yes       | Yes 1, 2, 3, 4         | Yes     | Yes           |
| Onorati et al., 2011  | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | Yes           |
| Kim et al., 2011      | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | No            |
| Breda et al., 2011    | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| No      | No            |
| Albage et al., 2011   | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| No      | No            |
| McCarthy et al., 2010 | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | Yes           |
| Deneke et al., 2009   | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | Yes           |
| Geuzebroek et al., 2008| No                     | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| No      | Yes           |
| Deneke et al., 2007   | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | Yes           |
| Ryan et al., 2004     | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | No            |
| Guden et al., 2003    | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | Yes           |
| Takami et al., 1999   | No                       | Yes       | Yes 1, 2, 3, 4, 5, 6, 8| Yes     | Yes           |

NR: no report; comparability variables: 1 = age; 2 = gender; 3 = body mass index; 4 = type of AF; 5 = Euro score; 6 = preoperative antiarrhythmic drugs; 7 = anatomic complexity (more than one artery and/or vein); 8 = single surgeon.
## Table 2: Characteristics of the studies that were initially included in the meta-analysis.

| First author | Year | Country | Study period | Type of study | Follow-up (MO) | \( n \) (BA) | \( n \) (LA) | Type of ablation | Lesion set | Cardiac operation |
|--------------|------|---------|--------------|---------------|---------------|------------|------------|----------------|-----------|------------------|
| Gualis       | 2016 | Spain   | 2006–2011    | R             | 36            | 67         | 83         | CY             | PVI, LAA, RAA, TC, CS, WG | AVR, AVP, MVR, MVP, TVP |
| Liu          | 2015 | China   | 2012–2012    | R             | 3–12R         | 86         | 111        | RF             | PVI, LAA, RAA     | MVR, DVR, TVP      |
| Henn         | 2015 | USA     | 2002–2014    | P, non-RCT    | 5 years       | 532        | 44         | RF             | PVI, LAA, RAA, TC, CS, WG | AVR, CABG, MVR, MVP, TVP |
| Pecha        | 2014 | Germany | 2008–2011    | R             | 12            | 66         | 66         | RF, CY         | PVI, MV, LA, RAA, TC, CS | AVR, MVR, TVP     |
| Jiang        | 2014 | China   | 2008–2012    | R             | NR            | 61         | 48         | RF             | PVI, MV, LA, RAA, TC, CS, WG | MVR, MVP, TVP   |
| Soni         | 2013 | USA     | 2007–2011    | R             | 12            | 91         | 214        | RF, CY, MW     | PVI, PW, MI, LAA MM | AVR, MVR, CABG, MVP, TVP |
| Pecha        | 2014 | Germany | 2003–2012    | R             | 30 days       | 131        | 463        | CY, RF         | PVI, MV, LA, RAA, TC, CS, WG | AVR, AVP, MVR, MVP, TVP, CABG ASD, VSD |
| Onorati      | 2011 | Italy   | 2003–2008    | P, non-RCT    | 15            | 109        | 32         | RF             | PVI MV LA, RAA, TC, CS, WG | AVR, AVP, MVR, MVP, TVP |
| Kim          | 2011 | South Korea | 2006–2009 | R             | 26 ± 13.3     | 199        | 82         | CY             | PVI, PW, MI, LAA MM, CS | AVR, AVP, MVR, MVP, TVP, CABG ASD, VSD |
| Breda        | 2011 | Brazil  | 2003–2009    | R             | 12.16 ± 10.89 | 15         | 15         | RF             | PVI, PW, MI, LAA MM | MVR, MVP |
| Albage       | 2011 | Sweden  | 2005–2010    | P, non-RCT    | 1–12R         | 44         | 71         | CY             | PVI, PW, MI, LAA, Maze III | AVR, CABG, MVP, TVP, MVR, ASD, MVP |
| McCarthy     | 2010 | USA     | 2004–2008    | P, non-RCT    | 5–24R         | 91         | 75         | RF, CY, cut-and-sew | PVI LAA RAA, TC | AVR, MVR, TVP, CABG |
| Deneke       | 2009 | Germany | NR           | R             | 55 ± 17       | 64         | 66         | RF             | PVI, PW, MI, LAA, Maze III | MVR, AVR, CABG |
Table 2: Continued.

| First author | Year | Country | Study period | Type of study | Follow-up (MO) | n (BA) | n (LA) | Type of ablation | Lesion set | Cardiac operation |
|--------------|------|---------|--------------|---------------|----------------|--------|--------|------------------|------------|-------------------|
| Wang         | 2009 | China   | 2004–2007    | P, RCT        | 28 ± 5         | 150    | 149    | RF               | PVI, PW, MI, LAA, CTI, MM | MVR AVR MVP TVR TVP AVP |
| Srivastava   | 2008 | India   | NR           | P, RCT        | 44             | 40     | 40     | RF, CY           | PVI, PW, MI, LAA, Maze III | MVR AVR MVP TVR TVP AVP |
| Geuzebroek   | 2008 | Netherlands | 1999–2005  | R             | NR             | 26     | 40     | RF               | PVI, PW, MI, LAA, Maze III | MVR AVR MVP TVR TVP AVP |
| Deneke       | 2007 | Germany | 1997–2005    | R             | 21             | 106    | 116    | RF               | PVI MV LAA RAA, MM | MVR MV P C A B G A V R |
| Calo         | 2006 | Italy   | NR           | P, RCT        | 15 ± 5 (BA)/13 ± 6 (LA) | 39 | 41 | RF | PVI MV LAA RAA TC CS WG | NR |
| Ryan         | 2004 | USA     | 1996–2003    | R             | 595 ± 750 days | 36 | 7 | RF, CY, cut-and-sew | PVI, PW, MI, LAA, Maze III | NR |
| Guden        | 2003 | Turkey  | 2001         | P, non-RCT    | 10.9 ± 5.58    | 48     | 57     | RF               | PVI, PW, MI, LAA, Maze III | AVR CABG MVP TVR MVP ASD MVP |
| Takami       | 1999 | Japan   | NR           | R             | 34.1 ± 11.3 (BA)/178 ± 3.8 (LA) | 30 | 20 | CY, cut-and-sew | PVI, PW, MI, LAA, CTI, Maze III | MVR, CABG, AVR, TVR |

MO: month; R: range; P: p retrospective observational; RCT: randomized, controlled trial; BA: biatrial ablation; LA: left atrial ablation; CY: cryoablation; RF: radiofrequency ablation; MW: microwave ablation; PVI: pulmonary vein isolation; LAA: left atrial appendage; RAA: right atrial appendage; TC: terminal crest; CS: coronary sinus; WG: Waterston's groove; MI: mitral isthmus; MM: modified maze; CI: cavotricuspid isthmus; PW: posterior wall; AVR: aortic valve replacement; AVP: aortic valvuloplasty; MVR: mitral valve replacement; MVP: mitral valvuloplasty; TVP: tricuspid valvuloplasty; CABG: coronary artery bypass grafting; ASD: atrial septal defect repair; VSD: ventricular septal defect repair; NR: no report.
Table 3: Baseline characteristics of the included studies.

| First author | Age (BA/LA, years) | Male (BA/LA) | Diabetes (BA/LA) | Heart failure (BA/LA) | Cerebrovascular events (BA/LA) | Hypertension (BA/LA) | Type of AF |
|--------------|--------------------|--------------|------------------|----------------------|-------------------------------|---------------------|------------|
| Gualis       | 65.1 ± 10.2/71.6 ± 6.8 | 29/39        | 15/17            | 32/31                | 7/12                          | NR                  | Permanent persistent |
| Liu          | 49.87 ± 8.96/47.98 ± 8.64 | 21/23        | NR               | NR                   | NR                            | NR                  | Permanent persistent |
| Henn         | 64 ± 12             | NR           | NR               | NR                   | NR                            | NR                  | Permanent persistent |
| Pecha        | 70.5 ± 73/70.1 ± 7.5 | 45/40        | 16/13            | NR                   | NR                            | NR                  | Paroxysmal persistent permanent |
| Jiang        | 52.7 ± 4.9/50.7 ± 5.9 | 22/21        | 7/8              | 36/29                | 2/2                           | 11/8                | Paroxysmal persistent permanent |
| Soni         | NR                 | NR           | NR               | NR                   | NR                            | NR                  | Paroxysmal persistent permanent |
| Pecha        | 59 ± 28/68 ± 12     | 54/116       | 16/40            | NR                   | NR                            | 67/118              | Paroxysmal persistent permanent |
| Onorati      | 64 ± 9/65 ± 8       | 79/18        | 40/10            | NR                   | NR                            | 37/15               | Paroxysmal persistent permanent |
| Kim          | 56.3 ± 12.0/52.1 ± 11.9 | 75/47       | 19/5             | NR                   | NR                            | 32/21               | Permanent persistent |
| Breda        | 60.0 ± 8.07/46.3 ± 9.54 | 9/5         | NR               | 10/6.                | NR                            | NR                  | Paroxysmal persistent permanent |
| Albage       | 64.9 ± 10.4/66.9 ± 6.7 | 34/54        | 4/11             | 17/28                | 2/7                           | 10/27               | Paroxysmal persistent permanent |
| McCarthy     | 68.7 ± 10.3/66.8 ± 12.1 | 42/88        | 13/22            | NR                   | NR                            | NR                  | Paroxysmal persistent permanent |
Table 3: Continued.

| First author | Age (BA/LA, years) | Male (BA/LA) | Diabetes (BA/LA) | Heart failure (BA/LA) | Cerebrovascular events (BA/LA) | Hypertension (BA/LA) | Type of AF                          |
|--------------|--------------------|--------------|------------------|-----------------------|-----------------------------|----------------------|-----------------------------------|
| Wang         | 67 ± 8/69 ± 9      | NR           | NR               | NR                    | NR                          | NR                   | Permanent persistent              |
| Deneke       | 53.4 ± 10.8/54.2 ± 10.1 | 54/62       | NR               | NR                    | NR                          | NR                   | Permanent persistent              |
| Srivastava   | 37.11 ± 11.2/36.03 ± 7.99 | 19/22       | NR               | NR                    | NR                          | NR                   | Permanent persistent              |
| Geuzebroek   | 63.3 ± 7.9/61.1 ± 10.3 | 21/17       | NR               | NR                    | NR                          | NR                   | Paroxysmal persistent permanent  |
| Deneke       | 68 ± 9             | NR           | NR               | NR                    | NN                          | NR                   | Paroxysmal persistent permanent  |
| Calo         | 579 ± 8.9/59.2 ± 9.1 | 26/26       | NR               | NR                    | NR                          | 16/18                | Paroxysmal persistent permanent  |
| Ryan         | NR                 | NR           | NR               | NR                    | NR                          | NR                   | Paroxysmal persistent permanent  |
| Guden        | 52 ± 11/54 ± 9     | 14/23       | NR               | NR                    | N                           | NR                   | Permanent persistent              |
| Takami       | 54.7 ± 8.8/58.3 ± 8.7 | 11/9        | NR               | NR                    | NR                          | NR                   | Paroxysmal persistent permanent  |

BA: biatrial ablation; LA: left atrial ablation; NR: no report.
69.67%; OR: 1.54; 95% CI: 1.17–2.03; \( P = 0.002; I^2 = 0\% \) [14, 15, 22, 24–26, 30–32, 36]. For patients with a follow-up at 12 months [8, 14, 15, 26, 27, 30, 31, 34] and after more than 1 year [12, 15, 23–25, 31], the prevalence of SR in the BA group was similar to that in the LA group (63.01% versus 65.47%; OR: 1.31; 95% CI: 0.70–2.48; \( P = 0.40; I^2 = 77\% \)). The weighted average mean follow-up for studies reporting SR after more than 1 year was 23.3 months. These results are shown in Figure 3.

### 3.2. Mortality and Major Complications

Eight studies with 1185 patients investigated mortality after the BA or LA procedure. When effects were pooled, there was no significant difference in either early mortality [8, 14, 23, 27–29, 33] (<30 days, OR: 1.02; 95% CI: 0.36–2.90; \( P = 0.97; I^2 = 31\% \), Figure 4) or late mortality [23, 27, 29, 31, 35] (OR: 2.31; 95% CI: 0.86–6.22; \( P = 0.10; I^2 = 0\% \), Figure 5) between the BA and LA groups.

There was no significant increase in the risk of cerebrovascular events [8, 27, 28, 31] between the two groups (OR: 0.61; 95% CI: 0.16–2.40; \( P = 0.48; I^2 = 0\% \), Figure 6). In eight studies that compared LA with BA, BA increased the risk of permanent pacemaker implantation [22, 23, 30, 31, 33, 36] (OR: 2.46; 95% CI: 1.55–3.91; \( P = 0.0001; I^2 = 0\% \), Figure 7). No heterogeneity was observed.

### 3.3. Sensitivity Analysis and Publication Bias

The risk of bias was comprehensively assessed according to the guidelines of the Cochrane Collaboration, and neither visual inspection of funnel plots nor Egger's test detected significant publication bias for the major outcomes explored in this meta-analysis, including the prevalence of SR at discharge (\( t = 0.04; P = 0.972 \), SR at a 6-month follow-up (\( t = 0.27; P = 0.791 \)), SR at a 12-month follow-up (\( t = 0.90; P = 0.401 \)), SR after more than 1 year (\( t = 0.52; P = 0.626 \)), early mortality (\( t = 1.03; P = 0.363 \)), late mortality (\( t = -1.07; P = 0.397 \)), neurological events (\( t = 51.13; P = 0.012 \)), and permanent pacemaker implantation (\( t = 2.42; P = 0.060 \)). To evaluate the effect of heterogeneity on the pooled effect, we carried out a sensitivity analysis. Sensitivity and subgroup analyses found no significant heterogeneity (Table 4).

### 4. Discussion

Two recent meta-analyses [10, 11] that compared BA, LA, and surgical ablation in AF arrived at conflicting conclusions. However, these meta-analyses excluded several studies that compared BA with LA [8, 12–15, 25]. Therefore, we performed a new meta-analysis to compare BA with LA. This meta-analysis included three RCTs and 18 retrospective studies that collectively contained 3609 patients and compared the efficacy and safety of BA and LA. There was no significant difference between BA and LA in the rate of restored SR, but BA groups had a higher probability of SR after 6 months of follow-up. We also found that while BA and LA had similar rates of death and cerebrovascular events, the BA groups had a higher rate of permanent pacemaker implantation.

A pooled analysis of restored postoperative SR showed that there was no difference between the BA and LA groups. However, several recent studies [21, 23, 36] have shown that BA is inferior to the more complete LA when used alone. Patients in the LA group had shorter aortic cross-clamping times and cardiopulmonary bypass times than were observed in the BA group. Furthermore, the techniques used in AF ablation vary widely, even within the same procedure group, and if the different lesion sets used for ablation were included, the results may have indicated that this procedure has greater efficacy.

In contrast, some studies have reported that BA is superior to LA for restoring SR [8, 12, 15, 25–28, 30–33]. This finding rests mainly on the finding that BA groups have much more tissue damage and a higher rate of cardiac conduction system injury. However, all of these studies have common limitations. First, some patients took antiarrhythmic drugs (including amiodarone) perioperatively and continued the use of these drugs until the operation, and few researchers sufficiently addressed this variable. Second, the sample size in most of the articles was small (less than 150 individuals), weakening the power of the studies. Third, long rhythm registration during follow-up was not available in all of the patients. Furthermore, only a few of the studies were RCTs. Unlike previous reviews, we included the largest studies in our meta-analysis, and our inclusion criteria did not limit our search to articles published in English. We also conducted...
**Figure 3:** Restored SR at discharge, 6 months, and 12 months and beyond 1 year.

### 1.1.3 SR at 12 months

| Study or Subgroup | BA Events Total | LA Events Total | Weight | Odds Ratio M-H, Random, 95% CI | Odds Ratio M-H, Random, 95% CI |
|-------------------|----------------|----------------|--------|-----------------------------|-----------------------------|
| **Total events**  | 905            | 844            |        |                             |                             |
| Heterogeneity: $\chi^2 = 105.12, df = 15 (P < 0.0001);$ $I^2 = 66%$ |                             |                             |

Test for overall effect: $Z = 0.10 (P = 0.92)$

### 1.1.3 SR at 12 months

| Study or Subgroup | BA Events Total | LA Events Total | Weight | Odds Ratio M-H, Random, 95% CI | Odds Ratio M-H, Random, 95% CI |
|-------------------|----------------|----------------|--------|-----------------------------|-----------------------------|
| **Total events**  | 611            | 555            |        |                             |                             |
| Heterogeneity: $\chi^2 = 21.65, df = 7 (P = 0.003);$ $I^2 = 68%$ |                             |                             |

Test for overall effect: $Z = 1.27 (P = 0.20)$

### 1.1.4 SR beyond 1 year

| Study or Subgroup | BA Events Total | LA Events Total | Weight | Odds Ratio M-H, Random, 95% CI | Odds Ratio M-H, Random, 95% CI |
|-------------------|----------------|----------------|--------|-----------------------------|-----------------------------|
| **Total events**  | 419            | 311            |        |                             |                             |
| Heterogeneity: $\chi^2 = 26.60, df = 6 (P = 0.0002);$ $I^2 = 77%$ |                             |                             |

Test for overall effect: $Z = 0.84 (P = 0.40)$

| Total (95% CI)   | 3367           | 3093           | 100.0% | 1.25 [1.00, 1.55]            |                             |
| Total events     | 2519           | 2197           |        |                             |                             |
| Heterogeneity: $\chi^2 = 105.12, df = 40 (P < 0.00001);$ $I^2 = 62%$ |                             |                             |

Test for overall effect: $Z = 1.97 (P = 0.05)$

Test for subgroup difference: $\chi^2 = 2.81, df = 3 (P = 0.42),$ $I^2 = 0%$
a subgroup analysis of RCT and non-RCT studies and of small-sample and large-sample studies to assess the effect of heterogeneity on the pooled effect estimate.

The findings of the present meta-analysis confirm that BA increases the risk of permanent pacemaker implantation. This finding may be attributed to the fact that LA has shorter aortic cross-clamping and cardiopulmonary bypass times and promotes more extensive lesions. There was no significant increase in the risk of cerebrovascular events or early and late mortality between the two groups. We hypothesize that report selection resulted in fewer such events, and these results remain to be discussed.

The most important findings of our meta-analysis include the following: (1) LA and BA were equally effective in restoring SR, (2) BA resulted in higher prevalence of SR at the 6-month follow-up, and (3) unlike previous analyses, this
meta-analysis included the largest studies, and its inclusion criteria did not limit the search to articles published in the English language.

The results of our study show that there was no difference in the rate of restored SR between LA and BA. While some previous studies have proposed that BA alone is inferior to a more complete LA, this significance disappeared in a multivariate analysis. The difference in these results may have been caused by differences in inclusion criteria between previous studies and our study. The other studies limited inclusion to articles reported in the English language. Additionally, the techniques used for AF ablation varied widely, including, for example, the use of different lesion sets, even within same procedure group.

One of the most important reasons that researchers have suggested for why BA is better than LA at restoring SR is that there is a significant difference in electrical activity between patients with chronic and paroxysmal AF [37, 38]. Lazar et al. [37] demonstrated that a left-to-right atrial frequency gradient exists in paroxysmal but not persistent AF. This prompted them to propose that the maintenance of persistent or chronic AF may be less dependent on the posterior left atrium. Additionally, Sanders et al. [39] proposed that, in patients with paroxysmal AF, the dominant sources of activity are often localized in the pulmonary veins. In contrast, in patients with persistent AF, the dominant sites are more often localized in the atria, including right atrial sites. Unsurprisingly, patients with persistent or long-standing persistent AF are more likely to receive BA, and this may affect clinical outcomes [25].

The present meta-analysis has the following limitations. Its main limitation is that only small-sample RCTs were included. Inadequate random sequence generation and blinding tend to increase the risk of bias. Hence, larger RCTs are needed to determine the best treatment. Another limitation is that the original meta-analysis was based on the assumption that the surgical subgroups (BA and LA) were sufficiently similar to be assessed together, but the operation methods and ablation technologies used in these procedures are continually developing. Additionally, there was extreme heterogeneity among the studies in study design, data, and energy source, and a subgroup analysis yielded results that differed from those obtained in the original analysis. Future systematic reviews should, when sufficient literature is available, evaluate different indications separately. Finally, follow-up periods were generally short. Therefore, the long-term outcomes of BA and LA remain to be explored.

5. Conclusion

In this comparative meta-analysis, we show that BA is not more efficacious than LA in restoring SR. Additionally, the risks of death and cerebrovascular events are significantly different between BA and LA, but BA results in a higher rate of permanent pacemaker implantation.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors’ Contributions

Hongmu Li and Xifeng Lin contributed equally to this article.

Acknowledgments

This work was supported by the National Natural Science Foundation of China (NSFC) (no. 81771165), the Natural Science Foundation Project in Guangdong province, China (Grant no. 2016A030313295), the Major Project Development and Emerging, Interdisciplinary Funding Projects of Sun Yat-sen University (Grant no. Iykjcl7b), Guangzhou Science and Technology Project of Major Special Research Topics on International Collaborative Innovation (Grant no. 201704030032), and the grants from the Health System Training Project in Fujian Province (2015ZQNJC38).
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