Systematic Review

Comparative Effectiveness of Cryoballoon Ablation and Laser Balloon Ablation in Atrial Fibrillation Treatment: A Meta-Analysis

Zhijing An[1],[†] , Sai Jin[2],[†], Yixuan Chang[2], Xvhua Li[1],[2], Hongxv Liu[1],[2], Guangzu Liu[1],[2], Zhili Wei[1],[2], Bing Song[1],*

[1]Department of Cardiovascular Surgery, First Hospital of Lanzhou University, 730000 Lanzhou, Gansu, China
[2]The First Clinical Medical College of Lanzhou University, 730000 Lanzhou, Gansu, China
*Correspondence: songbinldyy@163.com (Bing Song)
[†]These authors contributed equally.
Academic Editor: Curt G Tribble

Abstract

Background: Cryoballoon ablation (CBA) and laser balloon ablation (LBA) are important techniques for treating atrial fibrillation (AF). However, the differences in their effectiveness remain unclear. This study aimed to systematically evaluate and compare the efficacy of CBA and LBA in AF treatment. **Methods**: A comprehensive search of major databases, including PubMed, Cochrane Library, Embase, and Web of Science, was conducted up to July 2024 to identify clinical studies comparing CBA and LBA for treating AF. Odds ratios (ORs) were calculated using a fixed-effect model. Study differences, quality, and potential publication bias were also assessed. **Results**: A total of 16 randomized controlled trials (RCTs) involving 4437 patients were included in the meta-analysis. The meta-analysis showed that compared to LBA, CBA was associated with a higher risk of phrenic nerve paralysis (PNP) (OR: 1.81, 95% confidence interval (CI): 1.23–2.67, $p = 0.003$, $I^2 = 0.0\%$). However, CBA demonstrated a higher success rate of pulmonary vein isolation (PVI) (OR: 2.14, 95% CI: 1.18–3.88, $p = 0.013$, $I^2 = 11.2\%$) and a shorter surgery duration standardized mean difference (SMD): –0.58, 95% CI: –0.88 to –0.29, $p = 0.000$, $I^2 = 75.3\%$). No significant differences were found between CBA and LBA regarding stroke, cardiac tamponade, hematoma, or 12-month AF recurrence rates. **Conclusion**: Compared to LBA, CBA offers a higher success rate of PVI and shorter surgery durations but with an increased risk of PNP. **The INPLASY Registration**: INPLASY202480069, https://inplasy.com/inplasy-2024-8-0069/, last accessed on August 14, 2024.

Keywords: cryoballoon ablation; laser balloon ablation; atrial fibrillation; systematic review; meta-analysis

Introduction

Atrial fibrillation (AF) is the disorganization of the heart's electrical activity, characterized by irregular flutter waves that disrupt normal contraction and relaxation. AF is the most common type of rapid heart rhythm disorder observed in clinical practice, with a prevalence in the general population of 1.5–2% [1]. The incidence of AF increases with age, reaching about 2.3% in individuals over 40 and 5.9% in those over 65 [2]. According to the Framingham study [3], AF significantly elevates mortality risk by 1.5 to 1.9 times compared to individuals without AF. Additionally, AF reduces the survival advantage typically seen in women in terms of average lifespan. Patients with AF face an elevated risk of serious complications, including thromboembolism, heart failure, and stroke [4]. Among cardiovascular conditions, AF has a particularly profound impact on stroke incidence, increasing the risk by five times more than in those without AF. This risk further escalates with age [5]. The pathophysiological mechanisms of AF involve four main factors: (1) ion channel dysfunction, (2) abnormal calcium ion flow, (3) atrial structural remodeling, such as fibrosis or chamber dilation, and (4) autonomic nervous system dysregulation. These factors contribute to cardiac

muscle cell ectopic discharges and re-entry mechanisms [6]. Several risk factors, including hypertension, heart failure, obesity, smoking, and diabetes [6,7], can trigger these pathophysiological processes, leading to the development of AF.

Guidelines for managing AF [8,9] suggest considering ablation procedures based on pulmonary vein isolation (PVI) when antiarrhythmic drug therapy is insufficient. For patients with AF that is difficult to manage with medication, physicians may recommend ablation procedures based on PVI. Common methods include radiofrequency ablation, pulse field ablation, and balloon-based techniques such as cryoballoon ablation (CBA), hot balloon ablation (HBA), and laser balloon ablation (LBA). Compared to the traditional and widely used radiofrequency ablation, CBA offers several advantages, including a shorter learning curve, ease of use, enhanced safety, and more predictable patient treatment outcomes [10]. As a result, its use is becoming increasingly widespread. CBA uses liquid nitrogen to cool and destroy the heart tissue responsible for abnormal electrical activity, thereby eliminating AF [11,12]. LBA, a recent innovation, employs laser energy to deliver precise energy for more durable PVI [13] and includes an endoscope for enhanced balloon positioning and visual guidance

[14,15]. However, complications such as phrenic nerve paralysis (PNP), which may arise with these advanced balloon ablation techniques, should not be overlooked. Numerous studies have compared the overall effectiveness of CBA and LBA in treating AF, yet their conclusions are often inconsistent or supported by insufficient evidence. Therefore, this study aimed to systematically evaluate and compare these two technologies through a meta-analysis to clarify their clinical feasibility and safety. The findings will provide more comprehensive decision support for clinical management.

Methods

This study followed the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [16]. The comprehensive research protocol is officially registered with INPLASY under the number INPLASY202480069. Details are available at https://inplasy.com/inplasy-2024-8-0069/, last accessed on August 14, 2024.

Search Strategy

A literature search was conducted in PubMed, the Cochrane Library, Web of Science, and Embase databases to examine the differences in treatment effectiveness between CBA and LBA for AF. The search covered the inception of these databases until July 2024 and included additional documents from other scholarly sources. The method involved a combination of predefined keywords and free-text searches. Search terms included atrial fibrillation, fibrillation, atrial, fibrillations, atrial, auricular fibrillation, fibrillation, auricular, cryoablation, cryoballoon ablation, laser balloon ablation, and laser balloon.

Study Selection

Two researchers collaborated to select studies for inclusion. Initially, the researchers used EndNote 21 software (Clarivate, Philadelphia, PA, USA) to remove duplicates and screened titles and abstracts under the initial eligibility criteria. Subsequently, the researchers obtained and reviewed the full texts of studies that potentially met the inclusion criteria and cross-checked their findings. In disagreements between researchers, a third party determined whether to include the study. The inclusion criteria for the meta-analysis were as follows: (1) Studies must be randomized controlled trials (RCTs); (2) studies must compare CBA with LBA for the first time in patients with AF and provide clinical outcome reports; (3) study subjects must meet the diagnostic criteria outlined in the 2023 ACC/AHA/ACCP/HRS Atrial Fibrillation Diagnosis and Management Guidelines [17]. The exclusion criteria included: (1) low relevance to the topic; (2) duplicate studies; (3) studies lacking complete or valid data; (4) reviews, letters, conference abstracts, and other types of documents; (5) non-English studies.

Study Endpoints

Our primary study outcomes were PNP and surgery duration. Secondary outcomes included stroke, the 12-month AF recurrence rates, cardiac tamponade, hematoma, and the success rate of PVI.

Data Extraction

We utilized a standardized data extraction form that included the following: (1) Basic information and baseline characteristics of the study population, such as the first author and year, type of study, sample size, gender, and age. (2) Past medical history, including a history of heart failure, hypertension, diabetes, and coronary artery disease. (3) Pre-surgery tests and surgical details, including left atrial diameter and left ventricular ejection fraction. (4) Outcome measures included PNP, surgery duration, stroke, the 12-month AF recurrence rates, cardiac tamponade, hematoma, and the success rate of PVI, as well as any procedures performed to treat irregular heartbeats.

Quality Assessment

Since all the studies included in this analysis were RCTs, quality was assessed by two reviewers using Cochrane's Risk of Bias tool, version 1.0 software (Cochrane Collaboration Oxford, England, UK). The reviewers evaluated the studies based on seven key areas: the generation of random sequences, concealment of assignment, blinding of patients and trial staff to treatment allocation, blinding of outcome assessors, handling of incomplete data, reporting bias, and additional biases. Furthermore, the GRADE approach (a systematic method for grading the quality of evidence) was applied to classify the quality of evidence for each outcome. This assessment considered the risk of bias, imprecision, inconsistency, indirectness, and publication bias, ultimately resulting in an overall quality rating for the evidence.

Statistical Analysis

Traditional meta-analysis methods used Stata 18.0 software (Stata Corp LLC, College Station, TX, USA) to generate forest plots, sensitivity analysis plots, and Egger's test plots. Odds ratios (ORs) with 95% confidence intervals (95% CIs) were calculated for categorical variables, while standardized mean difference (SMD) was used for continuous variables. The study heterogeneity was primarily assessed using the I^2 statistic. An I^2 value greater than 50% or a p-value less than 0.05 indicated significant heterogeneity. In such cases, a random-effects model was employed for the meta-analysis. If no significant heterogeneity was revealed, a fixed-effects model was applied. Funnel plots were used for qualitative assessment, and Egger's test was used for the quantitative evaluation of publication bias, assessing the symmetry of the funnel plot and determining whether the p-value for Egger's test exceeded 0.05.
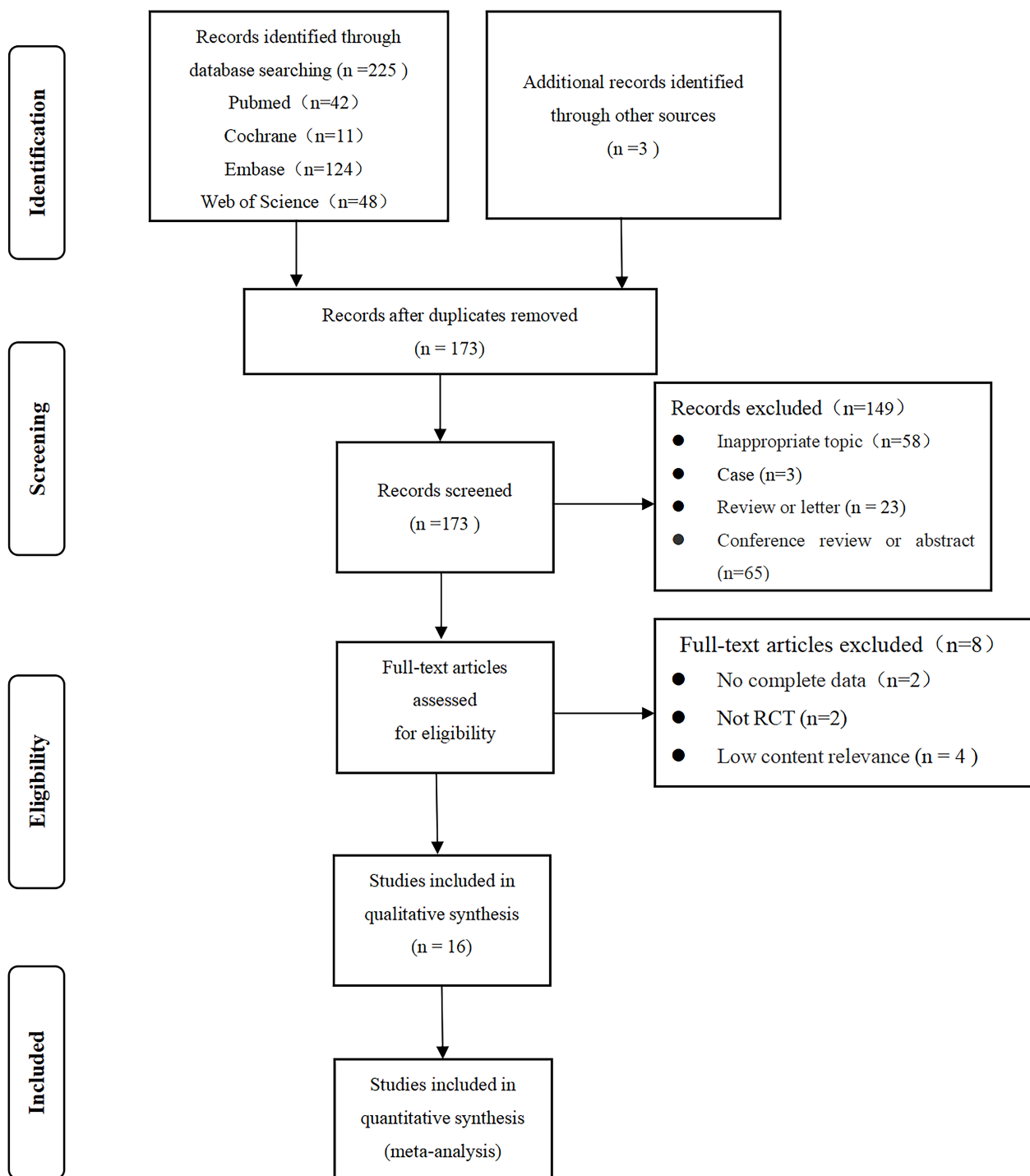
Records identified through
database searching (n =225)
Pubmed（n=42）
Cochrane（n=11）
Embase（n=124）
Web of Science（n=48）

Additional records identified
through other sources
(n =3)

Records after duplicates removed
(n = 173)

Records screened
(n =173)

Records excluded（n=149）
- Inappropriate topic（n=58）
- Case (n=3)
- Review or letter (n = 23)
- Conference review or abstract (n=65)

Full-text articles
assessed
for eligibility

Full-text articles excluded（n=8）
- No complete data（n=2）
- Not RCT (n=2)
- Low content relevance (n = 4)

Studies included in
qualitative synthesis
(n = 16)

Studies included in
quantitative synthesis
(meta-analysis)

Fig. 1. Flow diagram of the literature search and selection process. RCT, randomized controlled trial.

Table 1. Baseline features of patients.

Study	General characteristics						CHA2DS2-VASc Score	Past medical history (%)					Echocardiographic parameters		Group	
	Country	Study type	Total	Male (%)	Age (Y)	BMI		HTN (%)	Stroke (%)	HF (%)	DM (%)	CAD	LA, mm	LVEF (%)	CB	LB
Kobori et al. 2021 [21]	Japan	RCT	100	62/76	68.8/65.2	NR	NR	52.0/42.0	NR	6.0/2.0	NR	NR	36.5/35.5	62.4/62.5	CB2	LB1
Stöckigt et al. 2016 [1]	German	RCT	70	77/77	64.2/66.2	29.1/27.9	2.5/2.7	71.4/85.7	5.7/0	NR	20.0/17.1	40.0/45.7	NR	53.6 /56.8	CB2	LB1
Chun et al. 2021 [10]	US	RCT	200	58/54	65.0/66.5	28.3/28.0	2.0/2.3	65.0/68.0	2.0/4.0	1.0/2.0	12.0/9.0	12.0/21.0	39.1/39.8	61.5/61.5	CB2	LB1 and LB2
Dietrich et al. 2023 [19]	US	RCT	69	55/55	65/67	NR	NR	62.5/79.3	5.0/13.8	27.5/24.1	10.0/17.2	30.0/24.1	NR	NR	CB3	LB3
Seki et al. 2022 [25]	Japan	RCT	100	68/74	66/66	24/25	2/2	48.0/50.0	8.0/2.0	NR	6.0/12.0	12.0/16.0	40/38	58/58	CB4	LB1
Bordignon et al. 2013 [18]	German	RCT	140	70/61	63/63	NR	NR	62.9/60.0	NR	NR	10.0/14.3	5.7/12.9	39.8/39.9	63/63	CB1	LB1
Tohoku et al. 2020 [26]	German	RCT	2433	56/57	66/66	28.0/28.6	NR	NR	NR	NR	NR	NR	40.0/40.6	NR	CB3	LB2 and LB3
Tsyganov et al. 2015 [28]	Czech Republic	RCT	100	66/60	62.2/62.8	NR	NR	60.0/68.0	NR	NR	12.0/20.0	NR	42.4/43.5	NR	CB2	LB1
Khan et al. 2023 [20]	US	RCT	558	70/82	65/66	NR	NR	72.2/72.7	7.6/4.8	36.6/56.4	19.0/23.3	19.3/22.9	NR	NR	CB3	LB1
Schiavone et al. 2022 [24]	Italy	RCT	110	69/67	62.9/63.4	25.8 /26.7	2/2	67.3/70.0	10.9/14.6	7.3/1.8	7.3/9.1	12.7/9.1	NR	61.7/60.3	CB2	LB2 and LB3
Ohkura et al. 2023 [22]	Japan	RCT	65	79/72	66.5/67.9	24.0/23.9	NR	36.4/59.4	0/3.1	15.2/3.1	12.1/21.9	NR	36.7/38.9	NR	CB2	LB1
Tokuda et al. 2023 [27]	Japan	RCT	245	76/84	61.7/61.2	24.6/24.2	1/1	47.7/40.2	NR	NR	10.4/5.4	NR	38.0/37.0	64.8/65.2	CB4	LB1 and LB3
Wissner et al. 2014 [29]	German	RCT	64	70/66	61/63	NR	1.9/2.0	70.0/68.2	10.0/9.1	NR	5.0/4.6	15.0/6.8	41/43	64/64	CB1	LB1
Yano et al. 2021 [30]	Japan	RCT	111	58/57	76/70	22.7/23.7	3/2	56.4/60.7	10.9/8.9	9.1/5.4	9.1/19.6	NR	43/42	70/70	CB2	LB1
Kumar et al. 2014 [15]	Holland	RCT	60	73/75	58/58.9	28/29	NR	37.5/40.0	NR	NR	NR	17.5/20.0	NR	58/57	CB2	LB1
Reddy et al. 2008 [23]	Czech Republic	RCT	12	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR	NR
Total	/	/	4437	61.0/64.5	64.8/64.9	23.5/23.7	1.8/1.7	57.8/61.7	6.8/6.1	22.6/26.0	13.3/15.4	17.4/19.8	39.6/39.8	61.7/61.8	/	/

HTN, hypertension; HF, heart failure; BMI, body mass index; CAD, coronary artery disease; LA, left atrial diameter; LVEF, left ventricular ejection fraction; DM, diabetes mellitus; RCT, randomized controlled trial; NR, not reported.

Results

Study Selection

A total of 225 papers were initially identified, with an additional three papers obtained from other sources. After digitally removing duplicate studies, 173 papers remained for initial screening based on titles and abstracts. Subsequently, a more detailed preliminary screening was conducted. The full texts of 24 papers were thoroughly examined to assess their eligibility for inclusion in the analysis. After applying the inclusion and exclusion criteria, 16 papers [1,10,15,18–30] met the standards and were selected for the meta-analysis. The details of this selection are illustrated in Fig. 1.

Patient Characteristics

Table 1 (Ref. [1,10,15,18–30]) summarizes the basic characteristics of the study populations included in the literature. The study involved 4437 patients, averaging 61.2 years (ranging from 58 to 76 years), and 62.4% (ranging from 55% to 84%) were male. Seven reports provided CHA2DS2-VASc scores, a measure to predict stroke risk in patients with AF. The average CHA2DS2-VASc score was 2.0. Among these patients, hypertension was present in 59.7% (ranging from 37.5% to 85.7%), 12.7% (ranging from 4.6% to 23.3%) had diabetes, 12.8% (ranging from 1.8% to 56.4%) had heart failure, and 18.9% (ranging from 5.7% to 45.7%) had coronary heart disease.

Study Characteristics

This study includes research published between 2008 and 2023, encompassing 16 papers that discuss the first to fourth generations of CB and the first to third generations of LB. The second-generation CB (Arctic Front Advance, Medtronic Inc.) and the first-generation LB (HeartLight, CardioFocus) were the most commonly used in these studies.

Quality Assessment

We evaluated the studies in our review using the Cochrane quality assessment tool. As illustrated in Fig. 2a,b, all 16 studies were rated high quality. In the GRADE assessment of evidence quality, three outcomes were rated as high, three as moderate, and one as low. Table 2 presents the detailed GRADE evidence quality assessments.

Meta-analysis

PNP

Fourteen studies [1,10,15,18,20–22,24–30] investigated PNP. These studies showed no significant differences, as indicated by an I^2 of 0.0%. Therefore, a fixed-effect model, which assumes a single true effect size across studies, was used for the meta-analysis. These results indicated a significantly higher rate of PNP in the CBA group compared to the LBA group (OR: 1.81, 95% CI: 1.23–2.67, $p = 0.003$; $I^2 = 0.0\%$). See Fig. 3 for more details.

Surgery Duration

Nine studies [1,15,18,19,21,24,28–30] provided results on surgical duration. Due to significant heterogeneity among the studies ($I^2 = 75.3\%$), a random-effects model was applied for the meta-analysis. This statistical method combines the results of multiple studies while accounting for variability between them. The results showed that the CBA group had a shorter surgery duration than the LBA group (SMD: –0.58, 95% CI: –0.88 to –0.29, $p = 0.000$; $I^2 = 75.3\%$). See Table 3 for further details.

Stroke

The analysis included four studies [10,18,22,25] that reported stroke outcomes. Since there was no significant difference between the studies ($I^2 = 0.0\%$), a fixed-effects model was applied for the meta-analysis. The results indicate no significant difference in stroke incidence between the CBA and LBA groups (OR: 0.32, 95% CI: 0.05–2.08, p-value: 0.235; $I^2 = 0.0\%$), as shown in Table 3.

Cardiac Tamponade

Five studies [1,18,21,25,30] reported outcomes on cardiac tamponade. The meta-analysis used a fixed-effect model with an I^2 of 0.0%, indicating consistent study findings. The results showed no statistically significant difference in the occurrence of cardiac tamponade between the CBA and LBA groups (OR: 0.83, 95% CI: 0.25–2.76, $p = 0.765$; $I^2 = 0.0\%$). Refer to Table 3 for detailed results.

Hematoma

Five studies [15,18–20,24] reported on hematomas, which are pools of blood outside the blood vessels. Researchers used a fixed effect model due to an I^2 of 0.0% for the meta-analysis, a statistical method that combines the results of multiple studies. This analysis showed no meaningful difference between the CBA and LBA groups. The OR was 1.31 (OR:1.31, 95% CI: 0.55–3.12, $p = 0.545$; $I^2 = 0.0\%$). See Table 3 for more details.

Success Rate of PVI

Seven studies [1,10,15,18,21,28,29] reported on the success rate of PVI. Given the low heterogeneity among these studies ($I^2 = 11.2\%$), a fixed effect model was used for the combined analysis (meta-analysis). The analysis showed that the PVI success rate in the CBA group was significantly higher than in the LBA group (OR: 2.14, 95% CI: 1.18–3.88).

Twelve-month AF Recurrence Rates

Six studies [1,10,18,21,23,28] reported on the 12-month AF recurrence rates. Given the low heterogeneity among the studies ($I^2 = 30.7\%$), a fixed-effect model
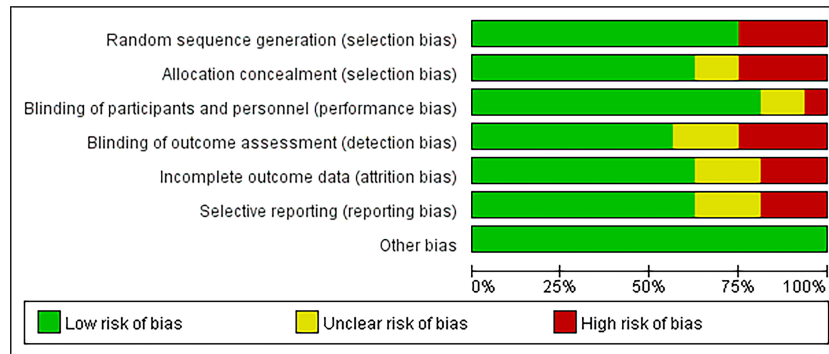
(a)
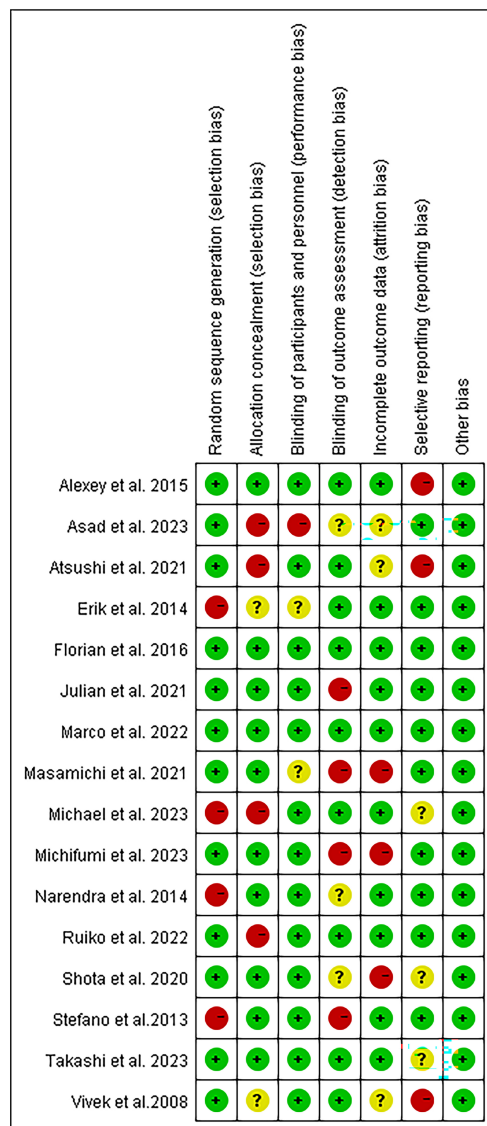
(b)

Fig. 2. Included study bias risk assessment results. (a) Bar chart of the risk of bias. (b) Risk of bias summary chart.

was employed for the meta-analysis. The results showed no statistically significant difference between the CBA and LBA groups (OR: 1.21, 95% CI: 0.83–1.76, $p = 0.312$; $I^2 = 30.7\%$). See Table 3 for further details.

Table 2. Grade evidence profile.

Certainty assessment							№ of patients	Certainty
№ of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias		
PNP								
14	RCT	Not serious	Not serious	Not serious	Not serious	Undetected	4296	High
Surgery Duration								
9	RCT	serious	Not serious	Not serious	Not serious	Undetected	824	Moderate
Stroke								
4	RCT	Not serious	Not serious	Not serious	Very serious	Undetected	505	Low
Cardiac Tamponade								
5	RCT	Not serious	Not serious	Not serious	Not serious	Undetected	521	High
Hematoma								
5	RCT	Not serious	Not serious	Not serious	serious	Undetected	937	Moderate
Success Rate of PVI								
7	RCT	Not serious	Not serious	Not serious	Not serious	Undetected	804	High
12-month AF Recurrence Rates								
6	RCT	Not serious	Not serious	serious	Not serious	Undetected	622	Moderate

PNP, phrenic nerve paralysis; PVI, pulmonary vein isolation; RCT, randomized controlled trial.
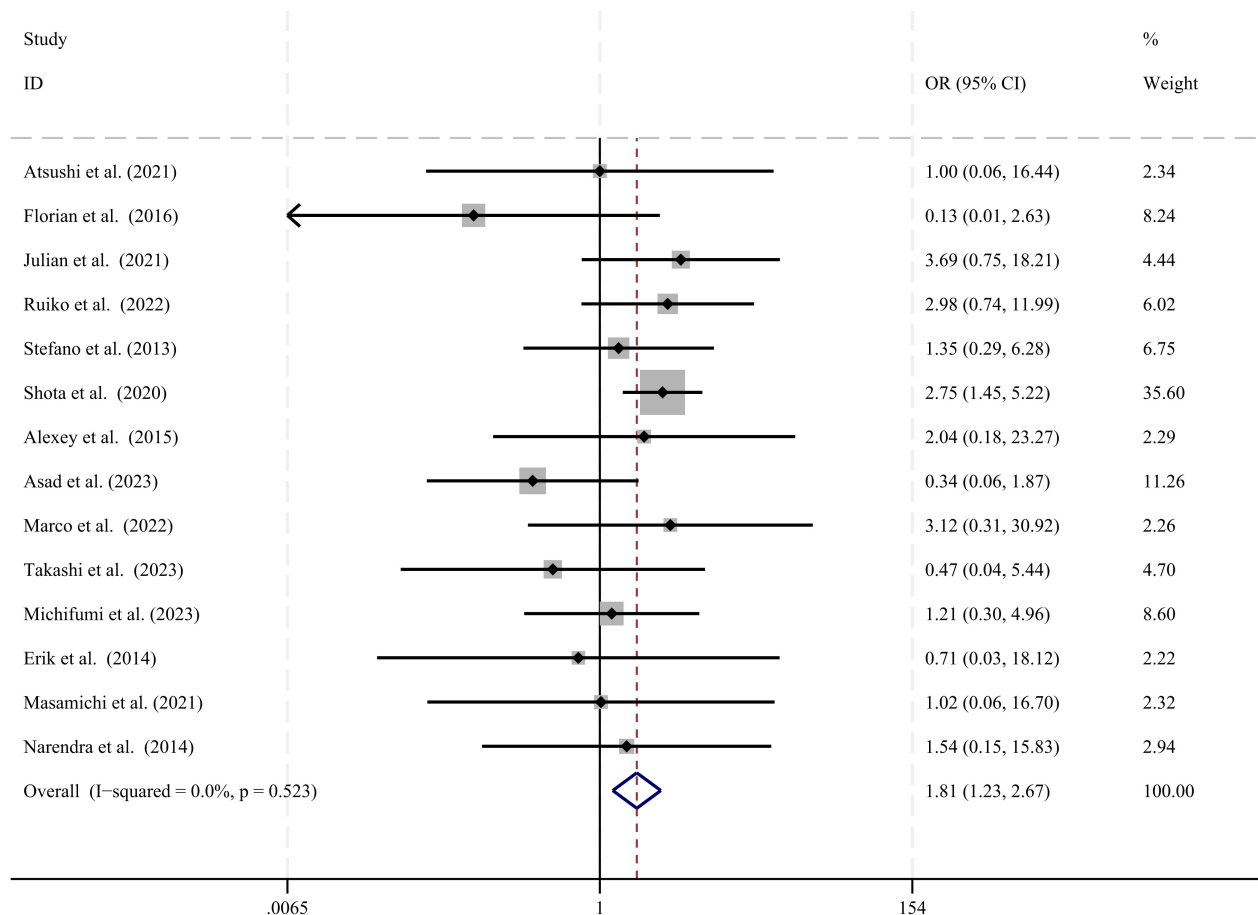
Fig. 3. Forest plots for PNP. OR, odds ratio; 95% CI, 95% confidence interval; PNP, phrenic nerve paralysis.
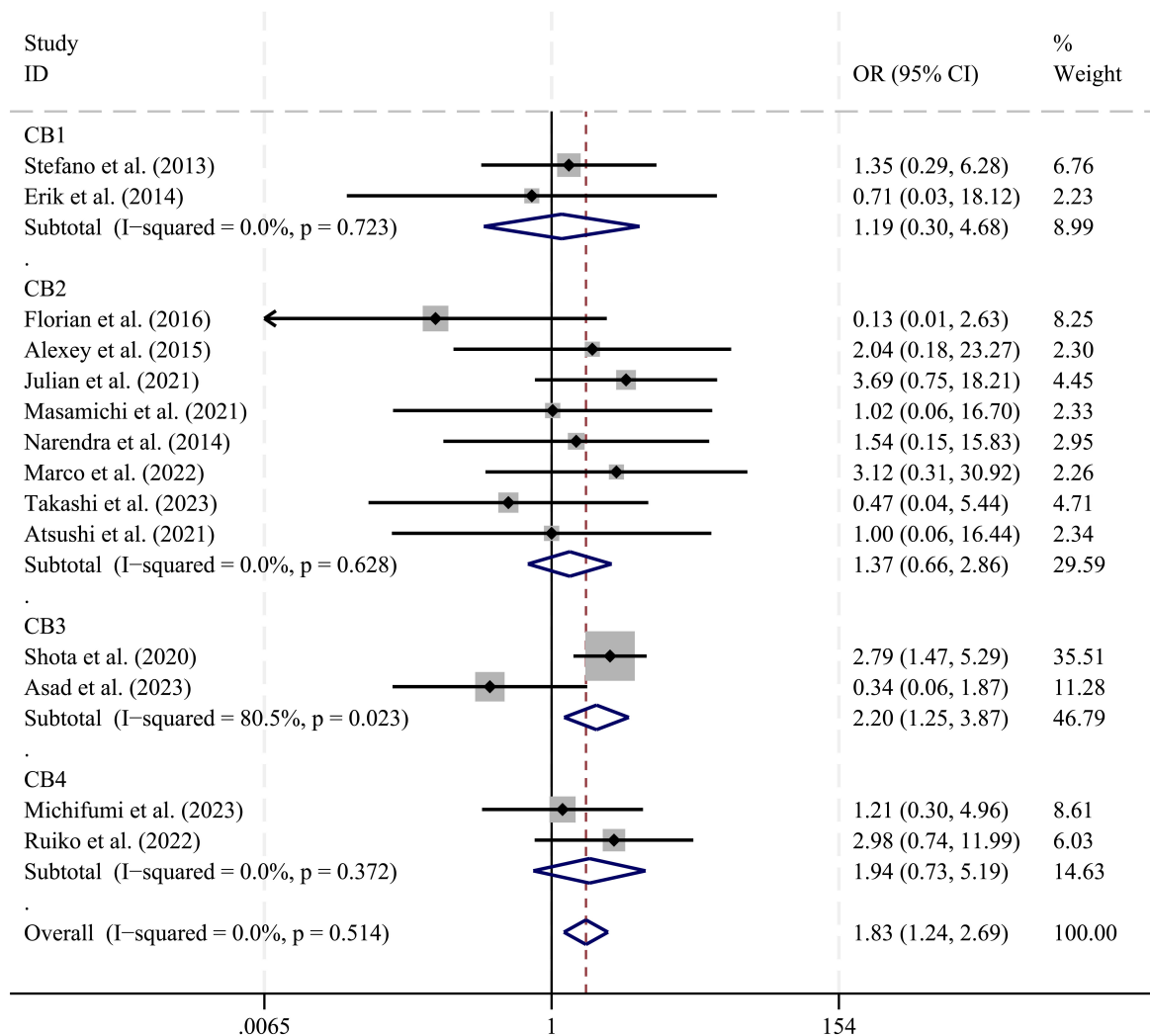
Subgroup Analysis

Due to significant heterogeneity in some of the outcome measures, we aimed to identify the sources of this variation. We used the CB and LB subgroup categories as the basis for our analysis, conducting analyses sequentially for each outcome measure. Figs. 4,5 show the main outcomes for CB1 to CB4 and LB1 to LB3, respectively. The study of the other secondary outcomes is presented in Table 3.

Table 3. Secondary outcomes.

Outcomes	Studies	Patients	OR/SMD	95% CI	p-value	I^2 (%)
Twelve-month AF recurrence rates	6	622	1.21	0.83–1.76	0.312	30.7
Success rate of PVI	7	804	2.14	1.18–3.88	0.013	11.2
Cardiac tamponade	5	521	0.83	0.25–2.76	0.765	0.0
Hematoma	5	937	1.31	0.55–3.12	0.545	0.0
LB1	2	200	0.70	0.09–5.52	0.732	0.0
LB2 or LB3	2	179	1.26	0.20–8.02	0.804	14.9
Stroke	4	505	0.32	0.05–2.08	0.235	0.0
Surgery duration	9	824	–0.58	–0.88 to –0.29	<0.001	75.3
LB1	7	645	–32.34	–50.49 to –14.19	<0.001	87.7
LB2 or LB3	2	179	–16.30	–27.42 to –5.17	0.004	0.0

OR, odds ratio; SMD, standard mean difference; 95% CI, 95% confidence interval; PNP, phrenic nerve paralysis; PVI, pulmonary vein isolation; LB, laser balloon.
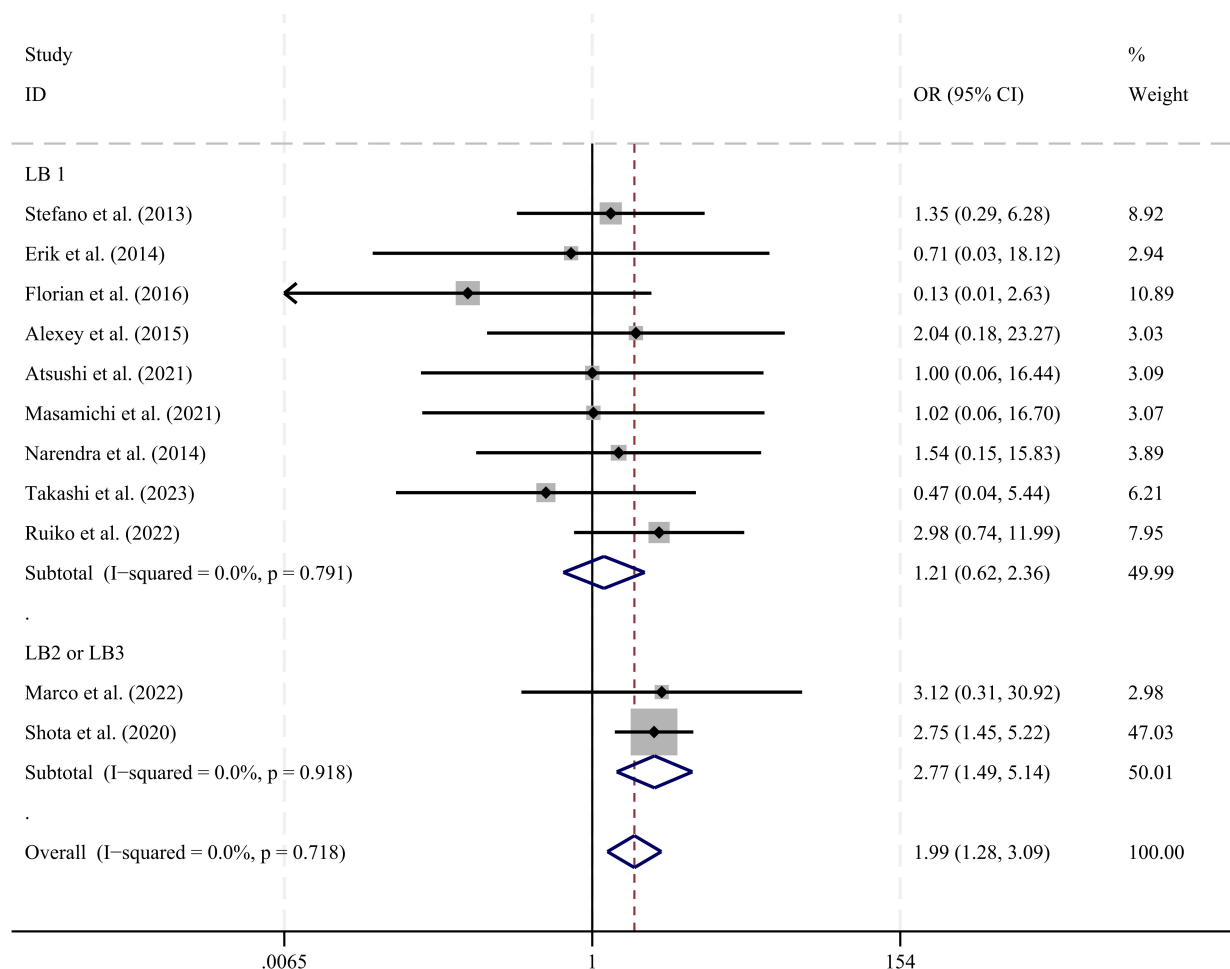

Fig. 4. Forest plot of the subgroup analysis of PNP in groups CB1–4. OR, odds ratio; 95% CI, 95% confidence interval; PNP, phrenic nerve paralysis; CB, cryoballoon.

Subgroup Analysis of PNP in Groups CB1–4

In group CB1 (Arctic Front, Medtronic Inc., Minneapolis, MN, USA), which included two studies [18,29], no significant difference was found between the CBA and LBA groups (OR: 1.19, 95% CI: 0.30–4.68, p = 0.800; I^2 = 0.0%). Similarly, Group CB2, which included eight

Fig. 5. Forest plot of the subgroup analysis of PNP in groups LB1–LB3. OR, odds ratio; 95% CI, 95% confidence interval; PNP, phrenic nerve paralysis; LB, laser balloon.

studies [1,10,15,21,22,24,28,30], found no significant difference between the CBA and LBA groups (OR: 1.37, 95% CI: 0.66–2.86, $p = 0.395$; $I^2 = 0.0\%$). Group CB3 (Arctic Front Advance-Short Tip Medtronic Inc., Minneapolis, MN, USA), which comprised two studies [20,26], found a significant difference, with a higher likelihood of developing peripheral neuropathy (PNP) (OR: 2.20, 95% CI: 1.25–3.87, $p = 0.007$; $I^2 = 80.5\%$). In Group CB4 (Arctic Front Advance Pro, Medtronic Inc., Minneapolis, MN, USA), which also included two studies [25,27], no significant difference was found between the CBA and LBA groups (OR: 1.94, 95% CI: 0.73–5.19, $p = 0.186$; $I^2 = 0.0\%$).

Subgroup Analysis of PNP in Groups LB1–3

In the LB1 group, which included nine studies [1, 15,18,21,22,25,28–30], no significant difference was found between the CBA and LBA groups (OR: 1.21, 95% CI: 0.62–2.36, $p = 0.570$; $I^2 = 0.0\%$). For the LB2 (HeartLight Excalibur Balloon; CardioFocus, Marlborough, MA, USA) and LB3 (HeartLight X3; CardioFocus, Marlborough, MA, USA) groups, which included two studies [24,26], the analysis showed a significant difference, indicating a higher probability of developing peripheral neuropathy (PNP) in the CBA group compared to the LBA group (OR: 2.77, 95% CI: 1.49–5.14, $p = 0.001$; $I^2 = 0.0\%$).

Sensitivity Analysis

We performed a sensitivity analysis specifically for outcomes with high heterogeneity. Even after removing each study one at a time, the results remained consistent, indicating a high level of stability in our findings. Fig. 6 illustrates one of these outcomes: surgery duration.

Publication Bias

We assessed publication bias using Stata18.0 software, generating funnel plots (graphs commonly used to detect bias in systematic reviews or meta-analyses) for all outcomes. The plots for the studies are mostly symmetrical, suggesting no evident reporting bias. For instance, the plot for PNP is illustrated in Fig. 7 in the appendix. To further assess publication bias, we used Egger's test and found the following results: PNP ($p = 0.064$), surgery duration
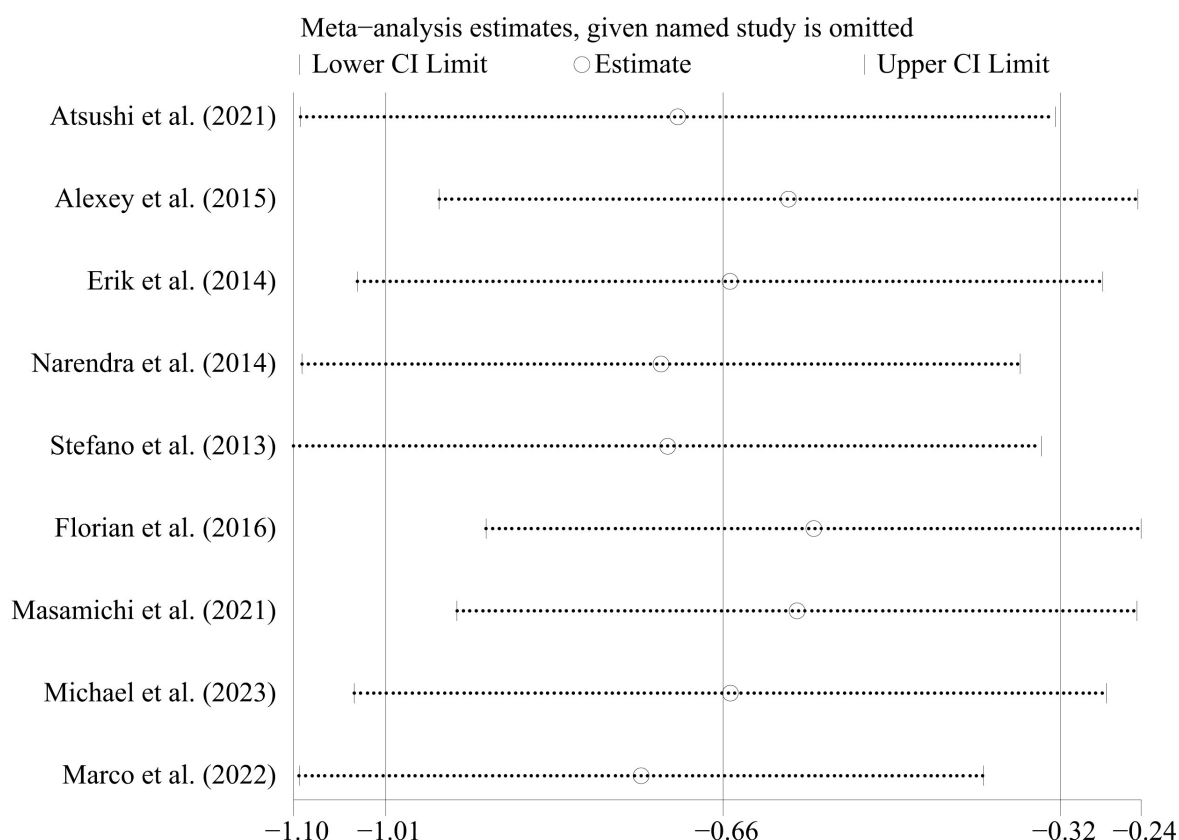
Fig. 6. Sensitivity analysis of surgery duration. CI, confidence interval.

(p = 0.173), stroke (p = 0.078), 12-month AF recurrence rates (p = 0.719), hematoma (p = 0.492), success rate of PVI (p = 0.462), and cardiac tamponade (p = 0.571). Since all p-values are above 0.05, the publications exhibited no significant bias. These results suggest that the findings are statistically reliable and unbiased. The Egger's test for PNP is shown in Fig. 8.

Discussion

This report analyzes 16 studies involving 4437 patients focused on evaluating the practicality, safety, and feasibility of CBA and LBA in clinical applications. The main findings are as follows: (1) CBA shows a higher success rate for complete PVI during surgery than LBA; (2) PNP is the most common complication, with a higher incidence in the CBA group than in the LBA group. No significant differences were found between CBA and LBA in stroke, cardiac tamponade, or hematoma; (3) CBA significantly reduces surgery duration compared to LBA; (4) according to the 12-month follow-up results, there was no significant difference in the AF recurrence rate between the two groups.

In 2015, a study by Alexey *et al*. [28] found no significant difference in the success rate of PVI with a single balloon between CBA and LBA (OR = 1.47, p = 0.83). However, in 2016, Florian *et al*. [1] found that CBA had a signif-

icantly higher success rate in achieving PVI than LBA (OR = 15.58, p = 0.003). Regarding postoperative complications, Masamichi *et al*. [30] conducted a study in 2021 that showed no significant difference in the likelihood of developing PNP between CBA and LBA (OR = 1.02, p = 0.990). Conversely, a 2022 study by Ruiko *et al*. [25] revealed a significantly higher probability of developing PNP with CBA compared to LBA (OR = 2.98, p < 0.001). Discrepancies were also found regarding surgery duration: Alexey *et al*. [28] reported in 2015 that the surgery duration required for CBA was significantly shorter compared to LBA (OR = –1.26, p = 0.003), while Marco *et al*. [24] reported in 2022 that there was no significant difference between the two (OR = –0.03, p = 0.264). Given these inconsistent findings on the efficacy of CBA and LBA, this study provides a comprehensive analysis to clarify the overall efficacy differences between these two methods.

This meta-analysis showed no significant differences in outcomes such as stroke, cardiac arrest, and hematoma, with both CBA and radiofrequency ablation (RFA) exhibiting similar and low incidence rates, indicating minimal impact on patients' coagulation functions.

Furthermore, the 12-month AF recurrence rates were comparable between the two groups, suggesting similar medium-term efficacy for CBA and RFA. However, signif-
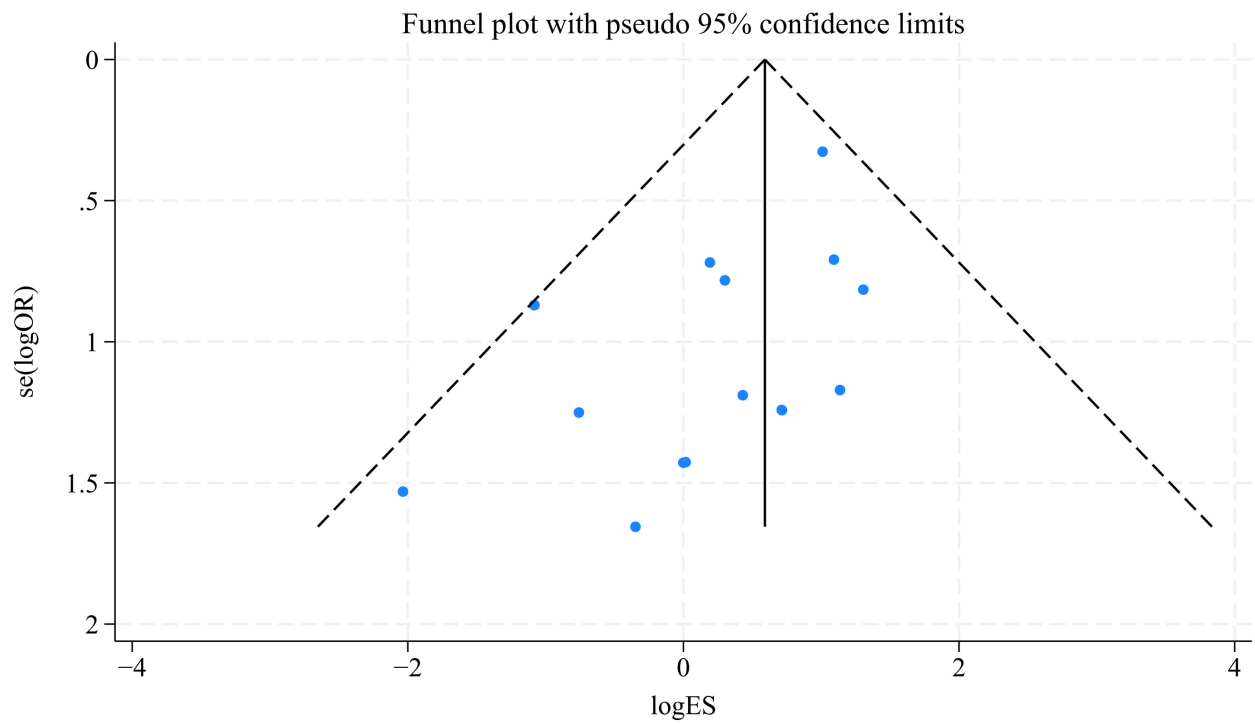
Fig. 7. Funnel plot for PNP. OR, odds ratio; ES, effect size; PNP, phrenic nerve paralysis.
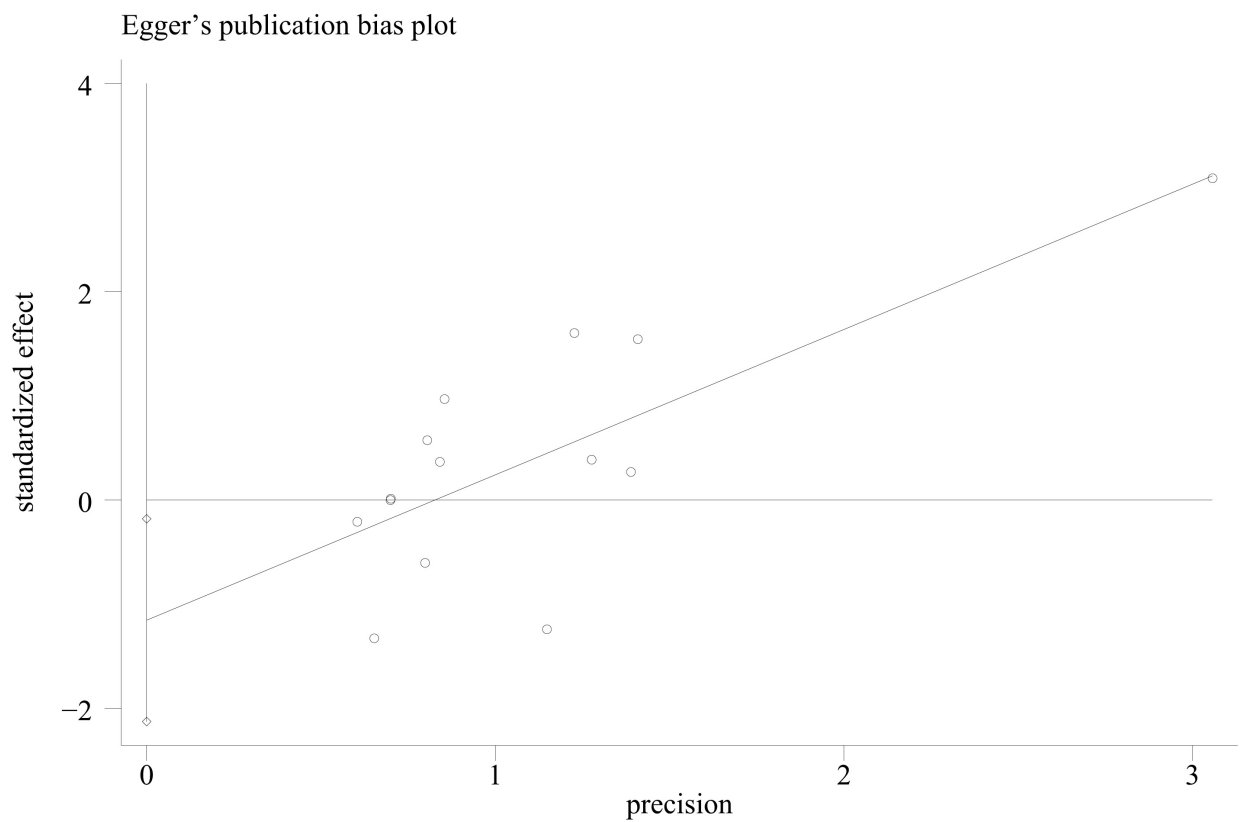
Fig. 8. Egger's test for PNP. PNP, phrenic nerve paralysis.

icant differences were observed in PNP, surgery duration, and success rate of PVI, aligning with the findings of previous studies [1,10,21,25,26,28–30].

The likelihood of PNP is significantly higher with CBA than LBA, consistent with the findings from studies [10,25,26]. Several factors contribute to this difference: (1) During the procedure, controlled energy is intentionally applied only to the target vein [28]. (2) CBA does not permit real-time monitoring of diaphragmatic movement during catheter advancement, which can cause the balloon to come dangerously close to the diaphragm [26], potentially affecting phrenic nerve (PN) conduction. In contrast, LBA facilitates diaphragmatic movement monitoring by palpation during PN pacing [31–33], enabling timely adjustments to the ablation site and preventing rapid cooling of the PN due to its concentrated energy delivery [14], thus maintaining normal function [34]. (3) Additionally, the cooling cycles utilized in CBA also play a role in influencing this phenomenon [35,36]. (4) Studies have reported the incidence of PNP to range from approximately 3.5% to 25%, but this can be substantially reduced in some institutions, likely due to operator experience and balloon size (such as 28 mm CBA) [28]. Fortunately, PNP is typically transient, with most patients experiencing a recovery of PN function within three to six months [10,25], and long-term complications are rare.

We found that the surgery duration for CBA is significantly shorter than that for LBA, consistent with the findings [1,19,28–30]. This might be attributed to the following reasons: (1) LBA requires more controlled environmental conditions, and if there is incomplete contact in areas where the esophagus temperature increases, the balloon must be repositioned to avoid blind spot ablation [10], leading to longer surgical times. (2) CBA often performs single-time pulmonary vein isolation (PVI) [37,38], while the highly compliant balloon used in LBA allows adjusting to different sizes, enabling precise, point-by-point lesion ablation, which extends surgery duration [10]. Additionally, the LB3 now includes an integrated motor unit [39], and its "RAPID" mode may expedite energy delivery, potentially reducing the surgery durations. In our study, the duration of the surgery demonstrates significant variability attributable to, as suggested by our subgroup analyses and clinical experiences, the varying generations of instruments used in LBA and CBA and variations in surgeon expertise.

In terms of the success rate of PVI, CBA demonstrates significantly higher success than LBAs, consistent with findings [1,29]. Several factors contribute to these differences: (1) Research indicates that when using lasers to transfer energy, the esophagus temperature rises too quickly and excessively, often leading to premature termination of energy delivery, particularly in LIPV [40]; (2) PVI failure is also closely related to the design of ablation tools. Studies have shown that the first-generation LB sheath offers limited controllability and steerability, affecting the balloon's

stable connection to the PV and complicating the operations [1]; (3) the occurrence of PNP can also lead to ablation interruption [18]. In addition, it is noteworthy that the current diagnostic tools for AF remain very limited and cannot enable early diagnosis of AF. Standardized perioperative management for AF patients is also an aspect that deserves attention.

Limitations

This meta-analysis includes 16 studies with 4437 research subjects but has several limitations: First, this analysis only encompasses English-language studies, which might introduce selection bias. Second, due to insufficient data, this study does not consider certain complications, such as pulmonary vein stenosis (PVS) [27,41] or silent cerebral events [42]. Additionally, most studies have a follow-up period of around 12 months, which limits our understanding of long-term health outcomes. Moreover, the recurrence of asymptomatic AF might be overlooked due to the limited use of continuous heart monitoring techniques, such as regular ECG and Holter-ECG, potentially affecting the long-term efficacy assessments of treatments, including CBA and LBA.

Conclusion

CBA and LBA are both effective and safe methods for radiofrequency ablation surgeries. Compared to LBA, CBA significantly reduces surgery durations and enhances the success rate of PVI, although it is associated with a higher risk of PNP. Therefore, we recommend CBA as the preferred treatment option for patients with AF; however, it is crucial to rigorously monitor for developing PNP complications intraoperatively or postoperatively. Fortunately, complications arising from both techniques typically resolve over time. We sincerely hope that more treatment methods for AF will emerge to improve patient prognosis.

Availability of Data and Materials

The original data has been uploaded as an attachment to the manuscript.

Author Contributions

ZA, ZW, and BS were responsible for topic selection and research design. SJ and YC conducted the literature search, paper screening, and data extraction. GL, XL, and HL performed the statistical analysis. SJ, YC, and GL wrote the manuscript. HL, ZA, and ZW proofread the manuscript. XL and BS reviewed and revised the paper. All authors contributed to editorial changes in the manuscript. All authors read and approved the final version. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the project.

Ethics Approval and Consent to Participate

Acknowledgment

Funding

Conflict of Interest

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.31083/HSF47013.

References

[1] Stöckigt F, Kohlmann AT, Linhart M, Nickenig G, Andrié RP, Beiert T, et al. Laserballoon and Cryoballoon Pulmonary Vein Isolation in Persistent and Longstanding Persistent Atrial Fibrillation. Pacing and Clinical Electrophysiology: PACE. 2016; 39: 1099–1107. https://doi.org/10.1111/pace.12929.

[2] Feinberg WM, Blackshear JL, Laupacis A, Kronmal R, Hart RG. Prevalence, age distribution, and gender of patients with atrial-fibrillation - analysis and implications. Archives of Internal Medicine. 1995; 155: 469–473. https://doi.org/10.1001/archinte.155.5.469.

[3] Benjamin EJ, Wolf PA, D'Agostino RB, Silbershatz H, Kannel WB, Levy D. Impact of atrial fibrillation on the risk of death: the Framingham Heart Study. Circulation. 1998; 98: 946–952. https://doi.org/10.1161/01.cir.98.10.946.

[4] Staerk L, Sherer JA, Ko D, Benjamin EJ, Helm RH. Atrial Fibrillation: Epidemiology, Pathophysiology, and Clinical Outcomes. Circulation Research. 2017; 120: 1501–1517. https://doi.org/10.1161/CIRCRESAHA.117.309732.

[5] Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991; 22: 983–988. https://doi.org/10.1161/01.str.22.8.983.

[6] Andrade J, Khairy P, Dobrev D, Nattel S. The clinical profile and pathophysiology of atrial fibrillation: relationships among clinical features, epidemiology, and mechanisms. Circulation Research. 2014; 114: 1453–1468. https://doi.org/10.1161/CIRCRESAHA.114.303211.

[7] Bizhanov KA, Abzaliyev KB, Baimbetov AK, Sarsenbayeva AB, Lyan E. Atrial fibrillation: Epidemiology, pathophysiology, and clinical complications (literature review). Journal of Cardiovascular Electrophysiology. 2023; 34: 153–165. https://doi.org/10.1111/jce.15759.

[8] Camm AJ, Lip GYH, De Caterina R, Savelieva I, Atar D, Hohnloser SH, et al. 2012 focused update of the ESC Guidelines for the management of atrial fibrillation: an update of the 2010 ESC Guidelines for the management of atrial fibrillation–developed with the special contribution of the European Heart Rhythm Association. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2012; 14: 1385–1413. https://doi.org/10.1093/europace/eus305.

[9] Calkins H, Kuck KH, Cappato R, Brugada J, Camm AJ, Chen SA, et al. 2012 HRS/EHRA/ECAS Expert Consensus Statement on Catheter and Surgical Ablation of Atrial Fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2012; 14: 528–606. https://doi.org/10.1093/europace/eus027.

[10] Chun JKR, Bordignon S, Last J, Mayer L, Tohoku S, Zanchi S, et al. Cryoballoon Versus Laserballoon: Insights From the First Prospective Randomized Balloon Trial in Catheter Ablation of Atrial Fibrillation. Circulation. Arrhythmia and Electrophysiology. 2021; 14: e009294. https://doi.org/10.1161/CIRCEP.120.009294.

[11] Wazni OM, Dandamudi G, Sood N, Hoyt R, Tyler J, Durrani S, et al. Cryoballoon Ablation as Initial Therapy for Atrial Fibrillation. The New England Journal of Medicine. 2021; 384: 316–324. https://doi.org/10.1056/NEJMoa2029554.

[12] Andrade JG, Khairy P, Guerra PG, Deyell MW, Rivard L, Macle L, et al. Efficacy and safety of cryoballoon ablation for atrial fibrillation: a systematic review of published studies. Heart Rhythm. 2011; 8: 1444–1451. https://doi.org/10.1016/j.hrthm.2011.03.050.

[13] Metzner A, Wissner E, Schmidt B, Chun J, Hindricks G, Piorkowski C, et al. Acute and long-term clinical outcome after endoscopic pulmonary vein isolation: results from the first prospective, multicenter study. Journal of Cardiovascular Electrophysiology. 2013; 24: 7–13. https://doi.org/10.1111/j.1540-8167.2012.02427.x.

[14] Bordignon S, Chun KRJ, Gunawardene M, Schulte-Hahn B, Nowak B, Fuernkranz A, et al. Endoscopic ablation systems. Expert Review of Medical Devices. 2013; 10: 177–183. https://doi.org/10.1586/erd.12.86.

[15] Kumar N, Blaauw Y, Timmermans C, Pison L, Vernooy K, Crijns H. Adenosine testing after second-generation balloon devices (cryothermal and laser) mediated pulmonary vein ablation for atrial fibrillation. Journal of Interventional Cardiac Electrophysiology: an International Journal of Arrhythmias and Pacing. 2014; 41: 91–97. https://doi.org/10.1007/s10840-014-9921-z.

[16] Knobloch K, Yoon U, Vogt PM. Preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement and publication bias. Journal of Cranio-maxillo-facial Surgery: Official Publication of the European Association for Cranio-Maxillo-Facial Surgery. 2011; 39: 91–92. https://doi.org/10.1016/j.jcms.2010.11.001.

[17] Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the Diagnosis and Management of Atrial Fibrillation: A Report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation. 2024; 149: e1–e156. https://doi.org/10.1161/CIR.0000000000001193.

[18] Bordignon S, Chun KRJ, Gunawardene M, Fuernkranz A, Urban V, Schulte-Hahn B, et al. Comparison of balloon catheter ablation technologies for pulmonary vein isolation: the laser versus cryo study. Journal of Cardiovascular Electrophysiology. 2013; 24: 987–994. https://doi.org/10.1111/jce.12192.

[19] Dietrich M, Dye C, du Fay de Lavallaz JM, Kenigsberg DN, Detloff LR, Park AM, et al. A comparison of third generation cryoablation versus x3 laser balloon systems for pulmonary vein isolation for treatment of atrial fibrillation. Heart Rhythm. 2023; 20: S306. https://doi.org/10.1016/j.hrthm.2023.03.1576.

[20] Khan A, Dye C, Dietrich M, du Fay de Lavallaz JM, Detloff LR, Krishnan K, et al. A comparison of clinical outcomes for three different modalities used for pulmonary vein isolation in

patients with atrial fibrillation. Heart Rhythm. 2023; 20: S184. https://doi.org/10.1016/j.hrthm.2023.03.570.

[21] Kobori A, Sasaki Y, Pak M, Okada T, Toyota T, Kim K, *et al*. Early experiences with three types of balloon-based ablation catheters in patients with paroxysmal atrial fibrillation. Heart Rhythm O2. 2021; 2: 223–230. https://doi.org/10.1016/j.hroo.2021.03.009.

[22] Ohkura T, Yamasaki T, Kakita K, Hattori T, Nishimura T, Iwakoshi H, *et al*. Comparison of maximum-sized visually guided laser balloon and cryoballoon ablation. Heart and Vessels. 2023; 38: 691–698. https://doi.org/10.1007/s00380–022–02208-7.

[23] Reddy VY, Neuzil P, d'Avila A, Laragy M, Malchano ZJ, Kralovec S, *et al*. Balloon catheter ablation to treat paroxysmal atrial fibrillation: what is the level of pulmonary venous isolation? Heart Rhythm. 2008; 5: 353–360. https://doi.org/10.1016/j.hrthm.2007.11.006.

[24] Schiavone M, Gasperetti A, Montemerlo E, Pozzi M, Sabato F, Piazzi E, *et al*. Long-term comparisons of atrial fibrillation ablation outcomes with a cryoballoon or laser-balloon: A propensity-matched analysis based on continuous rhythm monitoring. Hellenic Journal of Cardiology: HJC = Hellenike Kardiologike Epitheorese. 2022; 65: 1–7. https://doi.org/10.1016/j.hjc.2022.03.006.

[25] Seki R, Nagase T, Asano S, Fukunaga H, Inoue K, Sekiguchi Y, *et al*. Radiofrequency Current Versus Balloon-Based Ablation for Atrial Fibrillation. The American Journal of Cardiology. 2022; 178: 52–59. https://doi.org/10.1016/j.amjcard.2022.05.029.

[26] Tohoku S, Chen S, Last J, Bordignon S, Bologna F, Trolese L, *et al*. Phrenic nerve injury in atrial fibrillation ablation using balloon catheters: Incidence, characteristics, and clinical recovery course. Journal of Cardiovascular Electrophysiology. 2020; 31: 1932–1941. https://doi.org/10.1111/jce.14567.

[27] Tokuda M, Yamashita S, Shiomi S, Sakurai R, Sato H, Oseto H, *et al*. Pulmonary Vein Stenosis After Catheter Ablation of Atrial Fibrillation Using a Cryoballoon, Hot Balloon, or Laser Balloon. Circulation Journal: Official Journal of the Japanese Circulation Society. 2023; 87: 1711–1719. https://doi.org/10.1253/circj.CJ-23–0048.

[28] Tsyganov A, Petru J, Skoda J, Sediva L, Hala P, Weichet J, *et al*. Anatomical predictors for successful pulmonary vein isolation using balloon-based technologies in atrial fibrillation. Journal of Interventional Cardiac Electrophysiology: an International Journal of Arrhythmias and Pacing. 2015; 44: 265–271. https://doi.org/10.1007/s10840–015–0068–3.

[29] Wissner E, Metzner A, Neuzil P, Petru J, Skoda J, Sediva L, *et al*. Asymptomatic brain lesions following laserballoon-based pulmonary vein isolation. Europace: European Pacing, Arrhythmias, and Cardiac Electrophysiology: Journal of the Working Groups on Cardiac Pacing, Arrhythmias, and Cardiac Cellular Electrophysiology of the European Society of Cardiology. 2014; 16: 214–219. https://doi.org/10.1093/europace/eut250.

[30] Yano M, Egami Y, Ukita K, Kawamura A, Nakamura H, Matsuhiro Y, *et al*. Impact of myocardial injury and inflammation due to ablation on the short-term and mid-term outcomes: Cryoballoon versus laser balloon ablation. International Journal of Cardiology. 2021; 338: 102–108. https://doi.org/10.1016/j.ijcard.2021.06.016.

[31] Dukkipati SR, Neuzil P, Kautzner J, Petru J, Wichterle D, Skoda J, *et al*. The durability of pulmonary vein isolation using the visually guided laser balloon catheter: multicenter results of pulmonary vein remapping studies. Heart Rhythm. 2012; 9: 919–925. https://doi.org/10.1016/j.hrthm.2012.01.019.

[32] Dukkipati SR, Cuoco F, Kutinsky I, Aryana A, Bahnson TD, Lakkireddy D, *et al*. Pulmonary Vein Isolation Using the Visually Guided Laser Balloon: A Prospective, Multicenter, and Randomized Comparison to Standard Radiofrequency Ablation. Journal of the American College of Cardiology. 2015; 66: 1350–1360. https://doi.org/10.1016/j.jacc.2015.07.036.

[33] Schmidt B, Gunawardene M, Urban V, Kulikoglu M, Schulte-Hahn B, Nowak B, *et al*. Visually guided sequential pulmonary vein isolation: insights into techniques and predictors of acute success. Journal of Cardiovascular Electrophysiology. 2012; 23: 576–582. https://doi.org/10.1111/j.1540-8167.2011.02247.x.

[34] Bunch TJ, Bruce GK, Mahapatra S, Johnson SB, Miller DV, Sarabanda AV, *et al*. Mechanisms of phrenic nerve injury during radiofrequency ablation at the pulmonary vein orifice. Journal of Cardiovascular Electrophysiology. 2005; 16: 1318–1325. https://doi.org/10.1111/j.1540-8167.2005.00216.x.

[35] Chun KRJ, Stich M, Fürnkranz A, Bordignon S, Perrotta L, Dugo D, *et al*. Individualized cryoballoon energy pulmonary vein isolation guided by real-time pulmonary vein recordings, the randomized ICE-T trial. Heart Rhythm. 2017; 14: 495–500. https://doi.org/10.1016/j.hrthm.2016.12.014.

[36] Andrade JG, Champagne J, Dubuc M, Deyell MW, Verma A, Macle L, *et al*. Cryoballoon or Radiofrequency Ablation for Atrial Fibrillation Assessed by Continuous Monitoring: A Randomized Clinical Trial. Circulation. 2019; 140: 1779–1788. https://doi.org/10.1161/CIRCULATIONAHA.119.042622.

[37] Neumann T, Vogt J, Schumacher B, Dorszewski A, Kuniss M, Neuser H, *et al*. Circumferential pulmonary vein isolation with the cryoballoon technique results from a prospective 3-center study. Journal of the American College of Cardiology. 2008; 52: 273–278. https://doi.org/10.1016/j.jacc.2008.04.021.

[38] Chun KRJ, Schmidt B, Metzner A, Tilz R, Zerm T, Köster I, *et al*. The 'single big cryoballoon' technique for acute pulmonary vein isolation in patients with paroxysmal atrial fibrillation: a prospective observational single centre study. European Heart Journal. 2009; 30: 699–709. https://doi.org/10.1093/eurheartj/ehn570.

[39] Heeger CH, Tiemeyer CM, Phan HL, Meyer-Saraei R, Fink T, Sciacca V, *et al*. Rapid pulmonary vein isolation utilizing the third-generation laserballoon - The PhoeniX registry. International Journal of Cardiology. Heart & Vasculature. 2020; 29: 100576. https://doi.org/10.1016/j.ijcha.2020.100576.

[40] Metzner A, Wissner E, Schoonderwoerd B, Burchard A, Tilz R, Fürnkranz A, *et al*. The influence of varying energy settings on efficacy and safety of endoscopic pulmonary vein isolation. Heart Rhythm. 2012; 9: 1380–1385. https://doi.org/10.1016/j.hrthm.2012.03.059.

[41] Nagase T, Bordignon S, Perrotta L, Bologna F, Weise FK, Konstantinou A, *et al*. Low Risk of Pulmonary Vein Stenosis After Contemporary Atrial Fibrillation Ablation - Lessons From Repeat Procedures After Radiofrequency Current, Cryoballoon, and Laser Balloon. Circulation Journal: Official Journal of the Japanese Circulation Society. 2018; 82: 1558–1565. https://doi.org/10.1253/circj.CJ-17-1324.

[42] Koshikawa M, Harada M, Nomura Y, Nishimura A, Motoike Y, Watanabe E, *et al*. Impact of different energy sources on coagulation biomarkers and silent cerebral events in balloon-based ablation for atrial fibrillation. Heart Rhythm O2. 2024; 5: 520–528. https://doi.org/10.1016/j.hroo.2024.06.009.