Pulsed-field ablation versus thermal ablation for persistent atrial fibrillation: a systematic review and meta-analysis

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Received 14 November 2025. Revised 15 November 2025. Accepted 1 December 2025.

How to cite: Kashapov R.I., Guseva A.V., Khrushchev S.E., Ruzankin P.S., Romanov A.B. Pulsed-field ablation versus thermal ablation for persistent atrial fibrillation: a systematic review and meta-analysis. *Patologiya krovoobrashcheniya i kardiokhirurgiya = Circulation Pathology and Cardiac Surgery*. 2025;29(4):54-66. https://doi.org/10.21688/1681-3472-2025-4-54-66

Funding
The research was carried out within the state assignment of Ministry of Health of Russian Federation (theme No 124022000090-0).

Conflict of interests
The authors declare no conflict of interest.

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Abstract

Background: Pulsed field ablation (PFA) is a widespread safe and effective approach to treat paroxysmal atrial fibrillation (AF). However, data regarding its use in persistent AF are limited, especially in comparison with thermal energy sources.

Objective: The study aimed to assess the efficacy and safety of PFA for persistent AF treatment in comparison with radiofrequency (RFA) and cryoballoon ablations (CBA). The primary concern was to evaluate 1 year freedom from any atrial arrhythmias (AA) recurrence, including AF, atrial flutter or atrial tachycardia lasting 30 seconds or longer after the blanking period.

Methods: We performed an extensive search using MEDLINE, EMBASE, and PubMed databases for studies providing outcome data on PFA in patient with persistent AF. Additionally, several studies on RFA and CBA involvement for persistent AF treatment were selected for comparative analysis.

Results: Freedom from AA at 1 year after PFA, RFA and CBA was 68.95% [95 % CI 62.72%, 74.57%], 61.72% [95 % CI 51.74%, 70.79%], 68.23% [95 % CI 63.76%, 72.39%] respectively, with no significant differences between types of energy used. No significant differences were revealed in periprocedural and postprocedural complications between compared ablation types, as well.

Conclusion: In patients with persistent AF, PFA required a shorter total procedural time than RFA but a longer one than CBA. Fluoroscopy time for PFA was significantly shorter than for thermal energy sources. No significant differences were found in safety or freedom from atrial arrhythmias at the 1-year follow-up between the compared ablation methods. Large randomized multicenter trials are needed to further assess the benefits of PFA compared to thermal energy sources in persistent AF treatment.

Keywords: atrial fibrillation; catheter ablation; electroporation; persistent atrial fibrillation; pulsed field ablation; thermal ablation

Abbreviations
AA – atrial arrhythmia
AF – atrial fibrillation
CBA – cryoballoon ablation
IQR – interquartile range
LAPWI – left atrium posterior wall isolation
PFA – pulsed field ablation
PVI – pulmonary vein isolation
RFA – radiofrequency ablation
SD – standard deviation

Introduction

Atrial fibrillation (AF) remains the most common atrial tachyarrhythmia and is associated with increased morbidity and mortality. According to the current guidelines, catheter ablation can be considered first-line therapy for symptomatic patients with paroxysmal AF [1]. The efficacy of the catheter ablation for paroxysmal AF, particularly with pulmonary vein isolation using the most common energy types (radiofrequency and cryo-energy), is quite high. However, patients with persistent AF often required additional lesion sets to improve outcomes. Furthermore, thermal ablation carries non-negligible risks, and procedure-related complications are well-documented.

In recent years, pulsed field ablation (PFA) technology, which induces non-thermal cell apoptosis, has demonstrated a high safety profile and efficacy in patients with paroxysmal AF [2; 3]. Moreover, PFA technology is associated with improvements in procedural parameters, such as ablation time, catheter dwell time in the left atrium, and overall procedure duration. However, available data on PFA for persistent AF are insufficient to draw conclusions regarding its superiority over thermal ablation sources. We aimed to conduct a meta-analysis to compare the outcomes of PFA versus radiofrequency ablation (RFA) and cryoballoon ablation (CBA) for persistent AF.

Material and methods

A literature search was conducted using Ovid MEDLINE, EMBASE, Pubmed for full-text manuscripts from their date of inception to October 2025. All databases were searched using the following keywords: "pulsed field ablation", "electroporation", "PFA", "persistent atrial fibrillation". The PROSPERO (The international Prospective Register of Systematic Reviews) protocol was applied to register the meta-analysis (ID CRD42024551739). Studies were included if they met the following selection criteria: clinical trials and observational studies involving patients with persistent atrial fibrillation undergoing catheter ablation using PFA, RFA, or CBA. Comparative studies comparing RFA versus CBA or either of these with PFA were also included. All articles were required to be published in peer-reviewed scientific journals. A key limitation of this study is that only patients with persistent AF were included, excluding those with paroxysmal AF. Studies without full-text articles, case reports, conference presentations, meta-analyses, reviews, and non-English studies were excluded. The inclusion of studies was assessed by two independent reviewers. After a preliminary assessment, the full texts of the articles were reviewed to make the final decision on inclusion. Any differences in opinion were resolved through discussion with a third investigator.

Study objectives

The primary objective was one year freedom from any documented atrial arrhythmia (AA) recurrence (on 12-lead ECG or Holter monitoring), including AF, atrial flutter or atrial tachycardia lasting 30 seconds or longer after the blanking period. The 1-year period was chosen based on the available data from a preliminary literature analysis. The secondary objectives included:

1) Periprocedural/postprocedural complications (safety assessment);

2) Procedural data;

3) Freedom from atrial arrhythmia recurrence with regard to the type of lesion set.

Statistical analysis

In the included studies, baseline characteristics were reported as mean ± standard deviation (SD) or median with interquartile range (IQR). To ensure accurate calculations, the medians were transformed into means following the method by Wan et al [4]. For each energy type, the assessed outcomes were graphically represented using forest plots.

To compare continuous outcomes between the three energy types, we employed linear meta-regression models with random effects. For binary outcomes, logistic meta-regression models with random effects were used. In these models, PFA was considered the base category among ablation methods, meaning that each of the other energy ablation methods (RFA and CBA) was compared to PFA. The article ID (DOI) served as the only random effect; thus, if two groups from one study were considered, they were assigned the same effect value. The moderators in the meta-regression models included types of ablation set: pulmonary vein isolation (PVI) and left atrium posterior wall isolation (PVI+LAPWI). No risk of bias assessment was conducted, as this study relied on individual cohorts rather than studies directly comparing the methods. The R statistical software with "glmer" and "metaphor" packages was used for the analysis. The PRISMA guidelines were used to report the results.

Results

Study selection

In the initial phase of keyword searching, 375 abstracts were identified. After applying the selection criteria, reviewing ablation outcomes, and removing duplicates, 20 articles were selected for the meta-analysis. Ultimately,

we included 14 prospective and 6 retrospective studies, with a total sample size of 4,575 participants.

Study characteristics

The baseline characteristics of the included studies are summarized in Table 1. This review includes 11 studies investigating PFA and 9 studies using thermal energy sources (RFA or CBA) in patients with persistent AF. Detailed procedural characteristics, as well as perioperative and postoperative complications, are presented in Table 2 and Supplementary Table 1, respectively.

Study endpoints

1-year freedom from atrial arrhythmias

The overall mean freedom from AA at 1-year after PFA, RFA and CBA was 68.95% [95 % CI 62.72%, 74.57%], 61.72% [95 % CI 51.74%, 70.79%], 68.23% [95 % CI 63.76%,

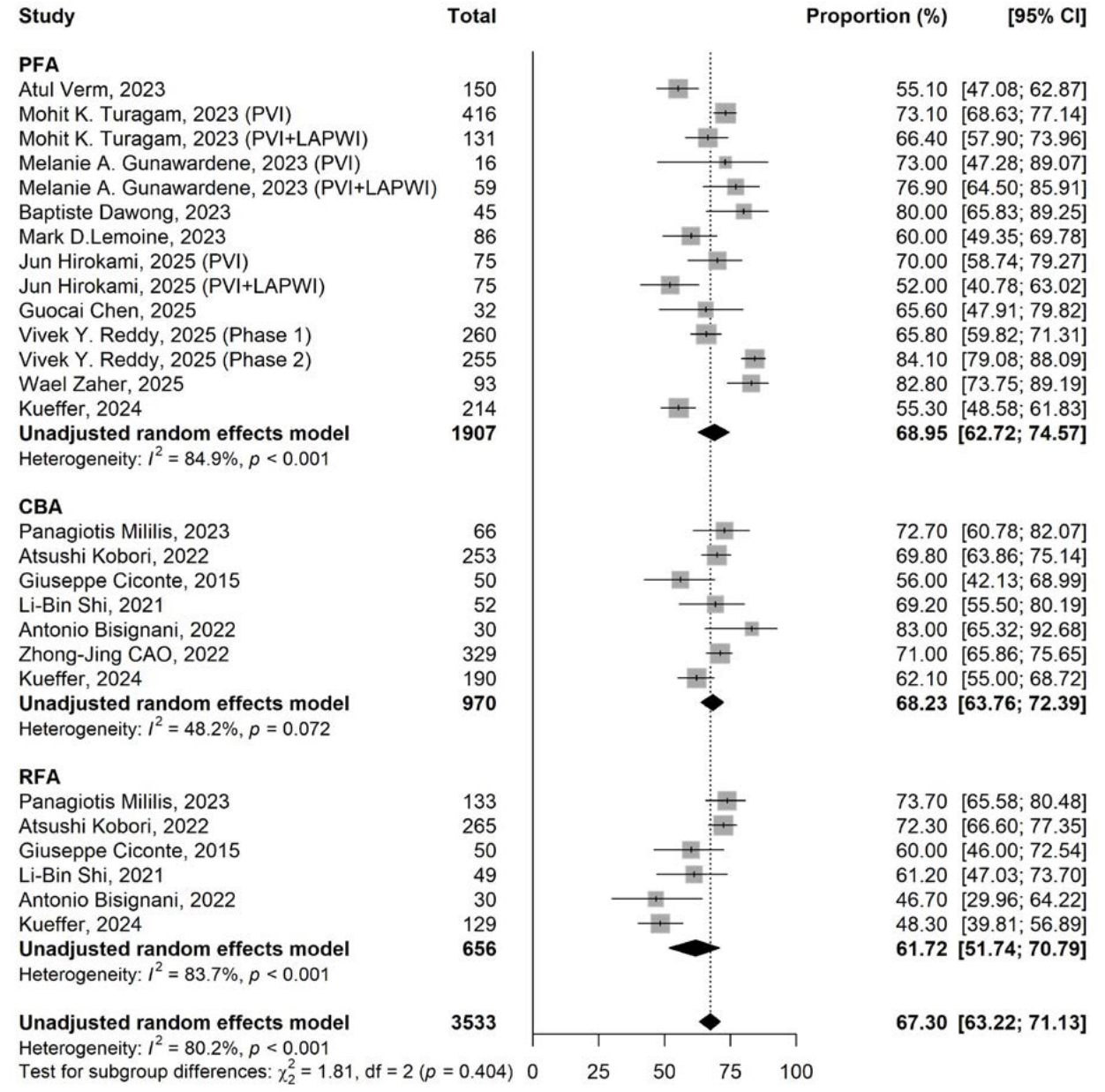

Fig. 1. Forest plot diagram of the "1-year freedom from atrial arrhythmias"

Abbreviations: CBA – cryoballon ablation, CI – confidence interval, LAPWI – left atrium posterior wall isolation, PVI – pulmonary vein isolation, PFA – pulsed field ablation, RFA – radiofrequency ablation.

72.39%], respectively (Fig. 1). There were no statistically significant differences between CBA and PFA (p = 0.87) or between RFA and PFA (p = 0.26) in the adjusted comparisons. No significant statistical dependence was observed between freedom from AA and the type of lesion set (PVI and PVI+LAPWI; p = 0.40, and p = 0.44 respectively) (Table 3).

Total procedural time

The overall mean total procedural time for PFA, RFA, and CBA was 94.58 [81.71, 107.46], 156.65 [117.11, 196.19], and 96.02 [65.13, 126.91] minutes, respectively (Supplementary Fig. 1). The results of the linear meta-regression are presented in Table 4, where PFA was used as the baseline category for energy type.

Table 1. Baseline characteristics

First author	Year	Type of Study	Study period	Numbers of patients	Age (mean/median)	Male (%)	Duration of AF (years\ months; mean/median)	LA diameter (mean/median)	LVEF (mean/median)	Antiarrhythmic drugs_before ablation (%)		
										Class I	Class II	Class III
Atul Verm [5]	2023	PRO	2021	150	66.0 ± 9.0	75.0	2.7 ± 3.7	42.0 ± 5.0	57.6 ± 6.4	17.0	45.0	35.0
Mohit K. Turagam [6]	2024	RETRO	2021– 2022	416	66.7 ± 10.8	69.0	–	44 (40–48)	55 (50–60)	12.1	0.0	25.8
				131	64.8 ± 10.4	72.5	–	45 (42–48)	60 (50–60)	24.0	0.0	22.9
Vivek Y. Reddy [7]	2020	PRO	2019–2020	25	67.0 (60–70)	80.0	–	43 (42–47)	60 (51–65)	24.0	28.0	52.0
Melanie A. Gunawardene [8]	2023	PRO	2021–2023	16	69.9 ± 9.0	63.0	2 (0.5–6)	44 (40–46)	–	0.0	0.0	19.0
	2023			59	64.0 ± 14.0	78.0	8 (3–13)	45 (42–50)	–	20.0	0.0	11.0
Baptiste Dawong [9]	2023	PRO	2021–2022	45	67.1 ± 10.0	75.6	22.0 ± 12.6	–	56.5 ± 11.2	13.3	11.1	46.7
Mark D.Lemoine [10]	2023	PRO	–	86	–	–	–	–	–	–	–	–
Jun Hirokami [11]	2025	RETRO	2021–2022	347 (75)	69 ± 8	63.0	–	–	55 ± 11	–	–	–
				101 (75)	68 ± 8	63.0	–	–	53 ± 10	–	–	–
Guocai Chen [12]	2025	PRO	–	32	57.8 ± 8.8	78.1	14.5 ± 8.9	43.1±4.3	60.4 ± 5.5	–	–	–
Vivek Y. Reddy [13]	2025	PRO	2023–2025	260	66.2 ± 9.3	69.2	3 ± 6 (years)	43±6	57.2 ± 6.9	57.7	0	58.9
Vivek Y. Reddy [14]	2025	PRO	2023–2024	255	66.7 ± 9.3	31.4	3 ± 4 (years)	43±6	56.6 ± 6.7	26.3	0	32.5
Wael Zaher [15]	2025	PRO	2022–2023	93	65 ± 10.1	65.6	20 (7–60)	–	55.5 ± 11.1	28	0	45.1
Panagiotis Mililis [16]	2023	PRO	2020–2021	133	60.2 ± 9.9	83.3	5.6 ± 3.8	44.9 ± 4.8	55.2 ± 7.1	–	67.7	55.6
				66	62.7 ± 9.1	77.3	6.1 ± 6.5	43.6 ± 4.7	55.7 ± 6.2	–	72.7	56.1
Atsushi Kobori [17]	2022	RETRO	2014–2020	265	70.7 ± 9.1	69.8	6 (4, 7)	42.9 ± 5.9	42.9 ± 5.9	–	–	–
				253	70.0 ± 9.6	78.3	5 (4, 7)	58.9 ± 7.9	41.4 ± 5.2	–	–	–
Giuseppe Ciconte [18]	2015	PRO	2012–2013	50	62.4 ± 9.5	76.0	26.7 ± 23.7	47.2 ± 6.2	56.3 ± 4.1	–	–	–
				50	62.4 ± 9.8	72.0	32.7 ± 37.6	46.0 ± 7.2	57.5 ± 3.7	–	–	–
Li-Bin Shi [19]	2021	PRO	2016–2020	49	64.0 ± 8.7	71.4	–	4.4 ± 0.7	56.8 ± 8.1	6.1	61.2	61.2
				52	62.4 ± 8.4	86.5	–	4.6 ± 0.6	56.0 ± 7.2	5.8	69.2	80.7
René Worck [20]	2022	PRO	2016–2017	24	64 (50–75)	83.0	9 (6–12)	–	60 (45–60)	–	–	–
Antonio Bisignani [21]	2022	RETRO	2018–2019	30	55.5 ± 9.8	63.3	41 ± 38	45 ± 7	56.7 ± 5.8	16.7	53.3	36.7
				30	58.1 ± 11.5	63.3	33 ± 21.9	42.7 ± 8.2	57.4 ± 6.2	16.7	46.7	13.3
Zhong-Jing CAO [22]	2022	RETRO	2016–2018	329	56.7 ± 9.8	75.5	33.2 ± 50	42,1 ± 4,5	62.2 ± 4.2	–	–	–
Vinit Sawhney [23]	2019	RETRO	2011–2017	609	63 ± 11	72.0	1.4 ± 1.67	42.0 ± 12	–	1.0	28.0	44.0
Kueffer [24]	2024	PRO	2021–2022	214	69.0 (61.0–74.0)	76.6	18.0 (6.0–50.8)	–	55.0 (45.0–60.0)	40.0	0.0	40.0
				190	68.2 (58.0–74.0)	72.6	17.5 (5.0–62.8)	–	55.0 (45.0–60.0)	26.6	0.0	26.6
				129	67.5 (59.2–73.0)	69.8	26.5 (5.8–71.2)	–	55.0 (44.5–60.0)	36.4	0.0	36.4

Abbreviations: AF – atrial fibrillation, PRO – prospective study, RETRO – retrospective study, LA – left atrium, LVEF – left ventricular ejection fraction.

Table 2. Procedural characteristics

First author	Type of energy	PVI (%) *	PVI+LAPWI (%) *	Total procedural time, min (mean/median)	Fluoroscopy time during procedure (mean/median)	Freedom from AA in 1 year (%)	Follow-up duration
Atul Verm [5]	PFA	100.0	0.0	145.0 ± 60.0	29.0 ± 21.0	55.1 (95% CI, 46.7 – 62.7)	1.0 y
Mohit K. Turagam [6]	PFA	100.0	0.0	61 (40–95)	12.4 (6.7–20.8)	73.1 (95% CI, 68.5–77.2)	367 (289–421) d
	PFA	0.0	100.0	80 (61–114)	14.9 (9.3–20.3)	66.4 (95% CI, 57.6–74.4)	367 (289–421) d
Vivek Y. Reddy [7]	PFA	4.0	96.0	125 (108–166)	16 (12–23)	–	–
Melanie A. Gunawardene [8]	PFA	100.0	0.0	76.0 ± 31	14.0 ± 7.0	73.0% (95% CI [54–100%])	354.0±197.0 d
	PFA	0.0	100.0	91.0 ± 30.0	14.0 ± 7.0	76.9% (95% CI [62–95%])	354.0±197.0 d
Baptiste Dawong [9]	PFA	0.0	100.0	84.1 ± 20.0	23.6 ± 6.8	80.0	107.8±57.5 d
Mark D.Lemoine [10]	PFA	100.0	0.0	–	–	60.0±10.0	249.0±90.0 d
Jun Hirokami [11]	PFA	0.0	0.0	63 ± 34	16±9	70.0	363 (288–381)
		0.0	89.0	100 ± 40	24±10	52.0	363 (288–381)
Guocai Chen [12]	PFA	0.0	100.0	78.6 ± 31.3	4.4±1.4	65.6	10.7±2.6 months
Vivek Y. Reddy [13]	PFA	0.0	100.0	103 ± 34.8	19.5±13.1	65.8	360 d
Vivek Y. Reddy [14]	PFA	0.0	100.0	105 ± 36	18±12	84.1	360 d
Wael Zaher [15]	PFA	0.0	100.0	–	–	82.8	12 (8–15) months
Panagiotis Mililis [16]	RFA	100.0	0.0	136.6 ± 43.33	12.5 ± 8.8	73.7	365 d
	CBA	100.0	0.0	75.2 ± 17.2	12.9 ± 10.6	72.7	365 d
Atsushi Kobori [17]	RFA	100	49.8	207.3 ± 47.6	20.1 ± 1.0	72.3	25.5±12.5 months
	CBA	100.0	39.9	163.7 ± 40.5	37.9 ± 1.0	69.8	25.5±12.5 months
Giuseppe Ciconte [18]	RFA	100.0	0	140.2 ± 46.9	19.8 ± 6.8	60.0	1.0 y
	CBA	100.0	0	90.5 ± 41.7	14.5 ± 6.6	56.0	1.0 y
Li-Bin Shi [19]	RFA	100.0	0	197.2 ± 38.4	23.4 ± 11.2	61.2	1.0 y
	CBA	100.0	0	160.4 ± 30.6	21.5 ± 7.8	69.2	1.0 y
René Worck [20]	RFA	0.0	100.0	172 (143–198)	7 (5–8)	–	0.5 y
Antonio Bisignani [21]	RFA	0.0	100.0	164.9 ± 26.8	37.8 ± 8.2	46.7	1.0 y
	CBA	0.0	100.0	93.0 ± 18.1	20.0 ± 5.6	83	1.0 y
Zhong-Jing CAO [22]	CBA	71.0	0.0	54.6 ± 11.9	–	71.0	30.0 months
Vinit Sawhney [23]	CBA	98.0	23.0	95 ± 65	13 ± 10	–	2.4 years (IQR 1.0–4.0)
Kueffer [24]	PFA	100.0	0.0	101.0 (85.0–126.0)	23.0 (16.6–29.0)	55.3 (95 CI 47.5–63.1)	9.4 months (IQR 4.8–12.6)
	CBA	100.0	0.0	84.0 (68.0–101.0)	19.7 (15.1–24.1)	62.1 (95% CI 54.8–69.4)	–
	RFA	100.0	0.0	171.0 (141.0–204.0)	6.5 (3.2–12.5)	48.3 (95 CI 38.9–57.8)	–

Abbreviations: AA – atrial arrhythmia, CI – confidence interval, PFA – pulsed field ablation, RFA – radiofrequency ablation, CBA – cryoballon ablation, PVI – pulmonary vein isolation, LAPWI – left atrium posterior wall isolation.

* % of the total group undergone the specified ablation set.

Table 3. Meta-regression results for "1 year freedom from atrial arrhythmias" and "Safety"

Moderators	Odds Ratios	95% CI	P-value
1 year freedom from atrial arrhythmias			
CBA vs PFA	1.02	0.76, 1.38	0.87
RFA vs PFA	0.83	0.61, 1.15	0.26
PVI	1.01	0.99, 1.02	0.40
PVI LAPWI	1.01	0.99, 1.02	0.44
Safety			
CBA vs PFA	1.35	0.56, 3.21	0.50
RFA vs PFA	1.17	0.46, 2.99	0.75
PVI	0.99	0.96, 1.02	0.70
PVI LAPWI	1.00	0.97, 1.03	0.89

Abbreviations: CI – confidence interval, CBA – cryoballon ablation, LAPWI – left atrium posterior wall isolation, PFA – pulsed field ablation, PVI – pulmonary vein isolation, RFA – radiofrequency ablation.

Table 4. Meta-regression results for "Total procedural time" and "Fluoroscopy time"

Moderators	Estimate	95% CI	P-value
	Total procedural time		
CBA vs PFA	–15.25	–20.49, –10.03	<0.001
RFA vs PFA	46.26	39.73, 52.78	<0.001
PVI	–1.50	–2.31, –0.69	<0.001
PVI_LAPWI	–1.27	–2.07, –0.46	0.002
	Fluoroscopy time		
CBA vs PFA	–6.41	–7.92, –4.91	<0.001
RFA vs PFA	–10.18	–11.77, –8.59	<0.001
PVI	–1.44	–1.55, –1.33	<0.001
PVI_LAPWI	–1.42	–1.53, –1.31	<0.001

Abbreviations: CI – confidence interval, CBA – cryoballon ablation, LAPWI – left atrium posterior wall isolation, PFA – pulsed field ablation, PVI – pulmonary vein isolation, RFA – radiofrequency ablation.

In the adjusted analysis, statistically significant differences between CBA and PFA ($p < 0.001$), as well as between RFA and PFA ($p < 0.001$) were observed.

Fluoroscopy time

The overall mean fluoroscopy time for PFA, RFA, and CBA was 17.67 [14.28, 21.07], 18.18 [10.21, 26.14], and 19.95 [13.48, 26.42] minutes, respectively (Supplementary Fig. 2). The results of the linear meta-regression are presented in Table 4, where PFA was used as the baseline category for energy type. In the adjusted analysis, statistically significant differences were observed between CBA and PFA ($p < 0.001$) and between RFA and PFA ($p < 0.001$). The effect sizes of these differences are presented in Table 4.

Safety

No statistically significant differences were found in safety, regardless of the type of energy source or lesion set, as measured by the comprehensive indicator of periprocedural and postprocedural complications, with a mean of 4.34% across all ablation types (Fig. 2). The results of the logistic meta-regression are presented in Table 3.

Discussion

To the best of our knowledge, this is the first systematic review and meta-analysis evaluating the results of PFA in patients with persistent AF compared with RFA and CBA.

The present meta-analysis showed that the overall procedure time was significantly shorter compared with RFA, while CBA demonstrated shorter overall procedure time compared with PFA. Additionally, the type of energy and the lesion set significantly affected the average fluoroscopy time ($p < 0.001$). Due to lack of data in the reviewed studies, an analysis of catheter dwell time in the left atrium was not feasible.

PFA technology is based on the electroporation, where the electrophysiological mechanism involves destabilizing the cell's electrical potential by creating nanoscopic pores in the cell membrane [25]. These pores lead to an intracellular ionic imbalance, resulting in functional cell death. A key feature of PFA is the focal impact on the target areas, while surrounding tissues remain intact. This contrasts with thermal sources of ablation, where adjacent tissues are also affected beyond the pathological focus. In practical terms, this should result in a lower frequency of adverse events with PFA. According to the MANIFEST17 study, which evaluated the safety of PFA in 17,642 patients, major complications were reported in approximately 1% of patients (173 out of 17,642), with no cases of esophageal complications, symptomatic pulmonary vein stenosis, or persistent phrenic nerve injury [26]. These findings further demonstrate the high safety profile of PFA compared to thermal ablation. However, our meta-analysis did not find significant differences in procedural safety between PFA and RFA or CBA in persistent AF ($p = 0.75$ and 0.50, respectively).

A comparative analysis of PFA versus thermal ablation in patients with paroxysmal AF is detailed in the landmark non-inferiority ADVENT Trial (Randomized Controlled Trial for Pulsed Field Ablation versus Standard of Care Ablation for Paroxysmal Atrial Fibrillation). The results demonstrated no statistically significant differences in freedom from atrial arrhythmias at one year (73.3% for PFA and 71.3% for thermal ablation, with a posterior probability >0.999 for non-inferiority and >0.708 for

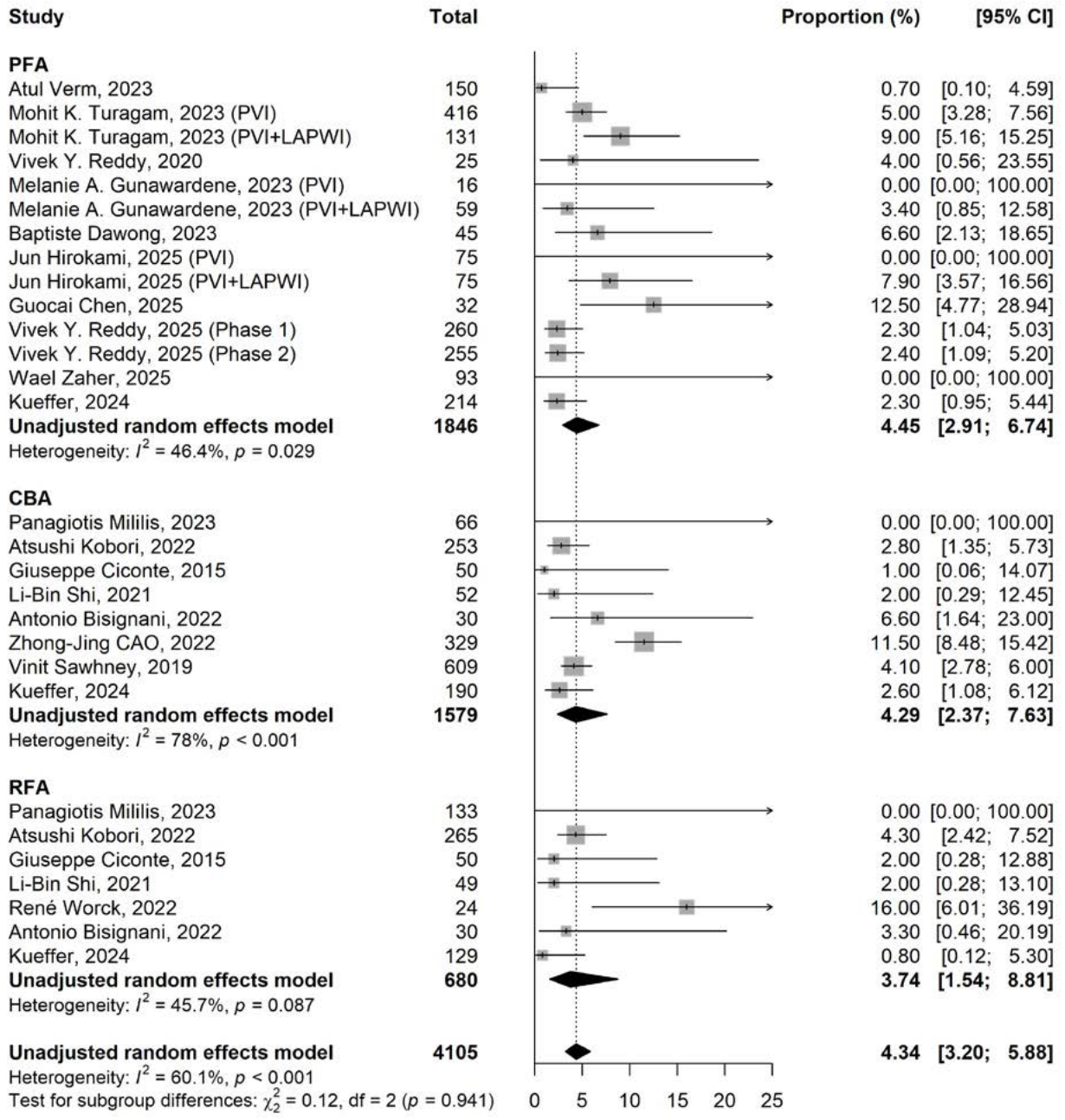

Fig. 2. Forest plot diagram of the "Safety"

superiority) [3, 27]. These data align with the results of our meta-analysis (68.95% for PFA, 61.72% for RFA, 68.23% for CBA, with no significant difference in meta-regression). However, it must be noted that this was a completely different patient population.

The question remains whether a definitive conclusion can be made that PFA technology is non-inferior to thermal energy sources in the treatment of persistent atrial fibrillation. Currently, many authors argue that the binary assessment of freedom from atrial arrhythmia, accepted as the gold standard, does not fully reflect the patient's functional state. Even with recurrences of atrial arrhythmias, patients may report improvements in overall well-being and quality of life.

Therefore, there is a need for a quantitative criterion to evaluate the effectiveness of ablation, including the consideration of major cardiovascular events. In several recent studies, atrial arrhythmias burden (AAB) has been used as an alternative criterion for assessing the effectiveness of catheter ablation, serving as a more objective indicator of procedural success [28–31]. Moreover, when AAB exceeds 0.1% at one year after ablation, it is associated with poor quality of life, an increased risk of rehospitalization, and the need for repeat ablation procedures or cardioversion [28, 30].

In a secondary analysis of the ADVENT trial, among patients who underwent ablation using PFA, the majority (n = 245, [81.9%]) had a residual AAB burden of <0.1%, equivalent to an atrial arrhythmia duration of less than 1.4 minutes per day. These results are statistically significant compared to the group that used thermal ablation sources (n = 220, [74.8%], p = 0.035) [32]. Due to the population heterogeneity of the selected studies and a lack of data, calculating AAB in this meta-analysis was not feasible. Further studies are needed to compare the clinical effectiveness of PFA and thermal ablation technologies in patients with persistent AF using AAB as a metric.

Persistent AF is classified as stage 3B of AF [1]. Some operators use additional lesions sets beyond pulmonary vein isolation to improve the results. However, the data on this approach remain controversial. In the present meta-analysis, no statistically significant differences were found between different ablation strategies using PFA in patients with persistent AF.

Limitations

Our meta-analysis has several limitations that should be considered when interpreting the results. First, the review included studies with heterogeneous populations, designs, and protocols. Due to the absence of a comparison group with thermal ablation in several studies, we had to acquire cohorts from studies evaluating the effects of RFA and/or CBA specifically for persistent AF. This necessitated the use of meta-regression models in the statistical analysis to account for potential heterogeneity in important baseline characteristics. Second, all included studies used 12-lead ECG or Holter monitoring as the primary method for assessing AA recurrences. The lack of continuous monitoring might lead to an underestimation of the primary endpoint in each study and the meta-analysis as a whole. Nevertheless, this is the first meta-analysis evaluating the effectiveness and safety of PFA in patients with persistent AF compared to thermal energy sources.

Conclusion

In conclusion, our meta-analysis and systematic review of 15 studies demonstrated that among patients with persistent AF, PFA had a shorter total procedural time compared to RFA but a longer one compared to CBA. Fluoroscopy time for PFA was significantly shorter than for thermal energy sources. No statistically significant differences were found in safety or freedom from atrial arrhythmias at the 1-year follow-up. Large randomized multicenter trials are needed to further assess the role of PFA compared to thermal energy sources in persistent AF.

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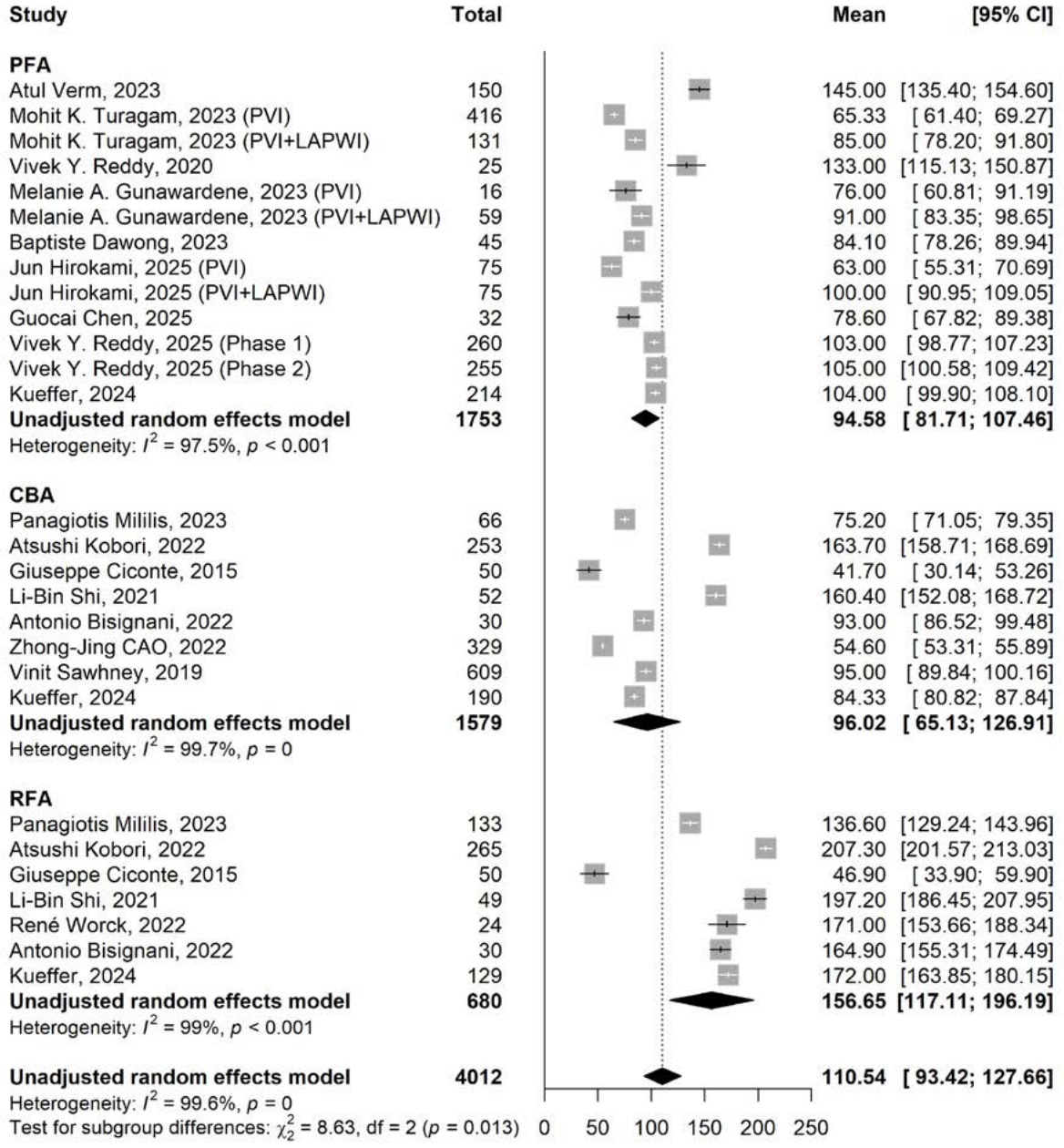
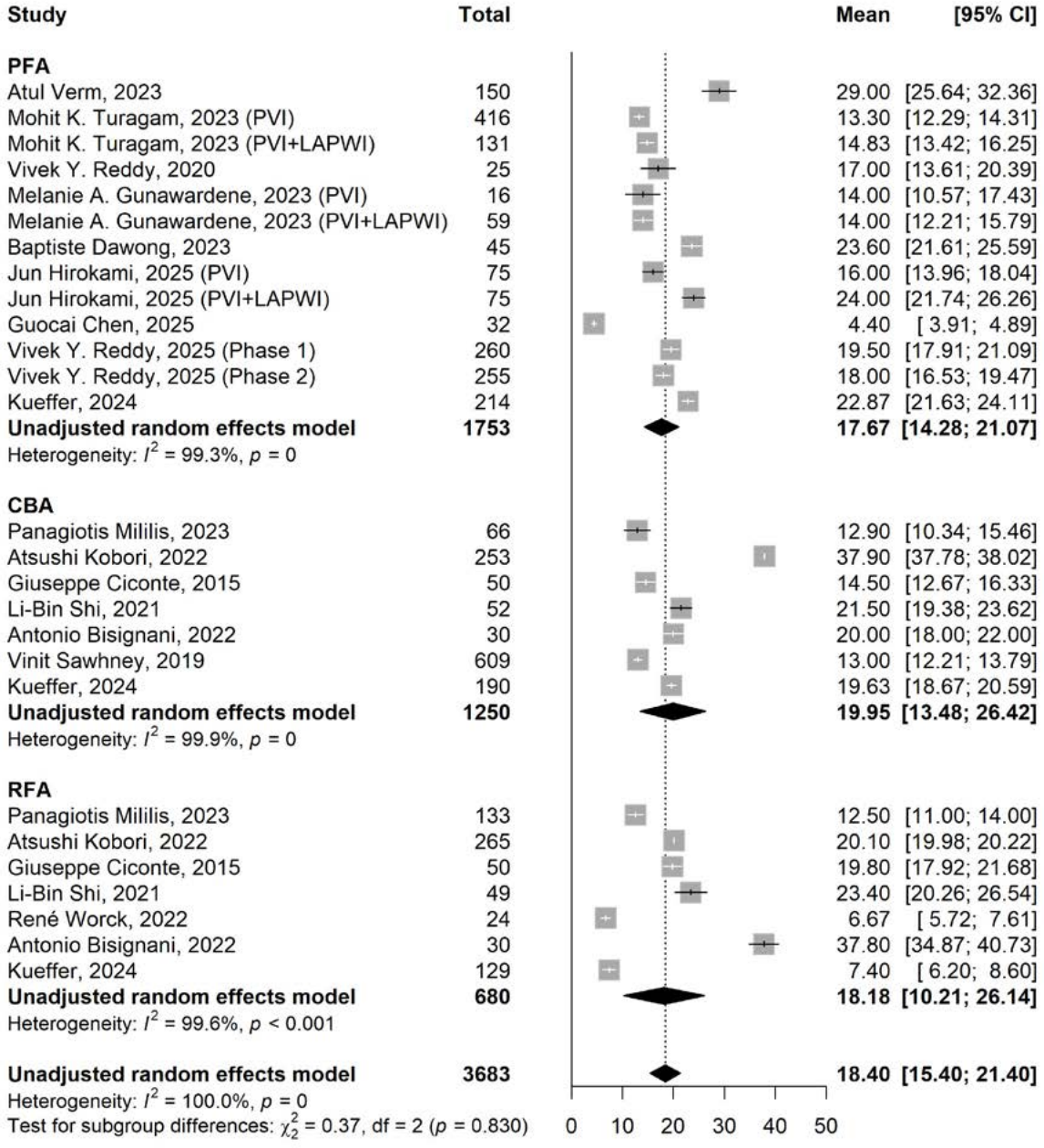
Supplementary figures:



Supplementary fig. 1. Forest plot diagram of the "Total procedural time"

Abbreviations: CBA – cryoballon ablation, CI – confidence interval, LAPWI – left atrium posterior wall isolation, PVI – pulmonary vein isolation, PFA – pulsed field ablation, RFA – radiofrequency ablation.



Supplementary fig. 2. Forest plot diagram of the "Fluoroscopy time"

Abbreviations: CBA – cryoballon ablation, CI – confidence interval, LAPWI – left atrium posterior wall isolation, PVI – pulmonary vein isolation, PFA – pulsed field ablation, RFA – radiofrequency ablation.

Supplementary Table 1. Perioperative and postoperative complications

First author	Type of energy	Safety (%) *	Pulmonary vein stenosis	Phrenic nerve injury	Atrio-esophageal fistula	Cardiac tamponade	CVA	TIA	MI	Pericarditis requiring intervention	Vagal nerve injury	Vascular access complications	Death
Atul Verm [5]	PFA	0.7	0.0	0.0	1.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Mohit K. Turagam [6]	PFA	5.0	0.0	0.2	0.0	1.2	0.2	0.5	-	0.0	-	2.1	0.0
	PFA	9.0	0.0	0.0	0.0	0.8	0.8	0.0	-	1.6	-	3.0	0.0
Vivek Y. Reddy [7]	PFA	4.0	0.0	0.0	0.0	4.0	0.0	0.0	0.0	0.0	-	0.0	0.0
Melanie A. Gunawardene [8]	PFA	0.0	-	0.0	0.0	0.0	0.0	0.0	-	-	-	-	0.0
	PFA	3.4	-	0.0	0.0	0.0	0.0	0.0	-	-	-	-	0.0
Baptiste Dawong [9]	PFA	6.6	-	-	0.0	0.0	0.0	0.0	-	-	-	0.0	0.0
Mark D.Lemoine [10]	PFA	-	-	-	-	-	-	-	-	-	-	-	-
Jun Hirokami [11]	PFA	0.0	-	0	-	0	0	0	-	0	-	0	0
		7.9	-	0	-	0	1.3	0	-	0	-	1.3	0
Guocai Chen [12]	PFA	12.5	0	0	0	0	12.5	0	0	0	0	0	0
Vivek Y. Reddy [13]	PFA	2.3	0	0	0	0	0	0	0.4	0/4	0	0	0
Vivek Y. Reddy [14]	PFA	2.4	0	0	0	0.4	1.2	0	0	0	0	0.8	0.4
Wael Zaher [15]	PFA	0.0	0	0	0	0	0	0	0	0	0	0	0
Panagiotis Mililis [16]	RFA	0	0	0	0	0	0	0	0	0	0	0	0
	CBA	0	0	0	0	0	0	0	0	0	0	0	0
Atsushi Kobori [17]	RFA	4.3	0	0.4	-	0.8	0.4	-	-	0.8	-	1.9	0
	CBA	2.8	0	1.2	-	0.4	0.0	-	-	0	-	1.2	0
Giuseppe Ciconte [18]	RFA	2.0	-	0.0	-	1.0	0.0	-	-	-	-	1.0	0
	CBA	1.0	-	0.0	-	0.0	0.0	-	-	-	-	1.0	0
Li-Bin Shi [19]	RFA	2.0	-	-	-	-	-	-	-	-	-	2.0	0
	CBA	2.0	-	2.0	-	-	-	-	-	-	-	-	0
René Worck [20]	RFA	16.0	0	-	0	0	-	-	-	-	-	2	0
Antonio Bisignani [21]	RFA	3.3	-	0	-	3.3	0	-	-	-	-	-	0
	CBA	6.6	-	6.6	-	0	0	-	-	-	-	-	0
Zhong-Jing CAO [22]	CBA	11.5	-	3.6	0.0	0.0	0.0	0.0	0.0	0.0	7.9	0.0	0.0
Vinit Sawhney [23]	CBA	4.1	-	3.1	0.0	0.6	0.0	0.2	0.0	0.0	0.0	0.2	0.0
Kueffer [24]	PFA	2.3	-	0.0	0.0	0.0	0.0	-	-	0.9	-	-	-
	CBA	2.6	-	2.6	0.0	0.0	0.0	-	-	0.0	-	-	-
	RFA	0.8	-	0.0	0.0	0.0	0.0	-	-	0.0	-	-	-

Abbreviations: CVA – cerebrovascular accident, TIA – Transient ischemic attack, MI – Myocardial infarction, PFA – pulsed field ablation, RFA – radiofrequency ablation, CBA – cryoballon ablation.

* – Safety as a sum of all perioperative and postoperative complication.