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Systematic Review

Effectiveness and Safety of Hybrid Ablation versus Endocardial Catheter Ablation Alone in Patients with Persistent Atrial Fibrillation: A Systematic Review and Meta-Analysis

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Abstract

Background: This systematic review and meta-analysis aimed to compare the efficacy and safety of hybrid ablation versus endocardial catheter ablation in patients with persistent atrial fibrillation. The study focused on observational research, encompassing both case-control and cohort studies, where the terms 'prospective' and 'retrospective' refer solely to the cohort study timeframes. **Methods**: A comprehensive search of the PubMed, Embase, Web of Science, and Cochrane Library databases was conducted without any time restrictions. Primary outcomes measured were the long-term success and complication rates. Secondary outcomes included rates of postoperative electrical cardioversion, repeat ablation, procedural duration, and fluoroscopy time. The Newcastle-Ottawa Scale was utilized to assess the quality of the studies included. **Results**: The analysis revealed that hybrid ablation significantly increased the long-term success rate of atrial fibrillation ablation compared to catheter ablation alone (OR 1.42; 95% CI: 1.05–1.92; $p = 0.031$). However, hybrid ablation was associated with a greater risk of overall procedural complications (OR 3.51; 95% CI: 2.18–5.64; $p < 0.001$) and major procedural complications (OR 3.28; 95% CI: 1.43–7.51; $p = 0.003$). Conversely, hybrid ablation reduced the likelihood of requiring repeat procedures (OR 0.54; 95% CI: 0.33–0.88; $p = 0.002$) and showed a trend toward lowering the need for postoperative electrical cardioversion (OR 0.71; 95% CI: 0.46–1.09; $p = 0.086$). No significant publication bias was detected. **Conclusions**: Hybrid ablation has demonstrated superior long-term efficacy compared to endocardial catheter ablation alone for treating atrial fibrillation but is linked to an elevated risk of complications. Further research is essential to evaluate the safety profile of hybrid ablation and identify the ideal patient population for this approach.

Keywords

hybrid ablation; endocardial catheter ablation; persistent atrial fibrillation; meta-analysis

Introduction

Atrial Fibrillation (AF), one of the most common arrhythmias among the elderly, significantly impacts patients' quality of life and heightens the risk of stroke and mortality [1]. While pulmonary vein isolation (PVI) has become the cornerstone treatment for drug-refractory paroxysmal atrial fibrillation, offering high success rates and a relatively low risk of complications, traditional catheter ablation techniques face limitations when addressing persistent atrial fibrillation. These limitations are primarily due to pronounced left atrial enlargement and extensive electrical and structural remodeling, which complicate the achievement of complete lesion ablation without risking damage to adjacent structures, such as the esophagus [2,3].

In response to these challenges, a hybrid ablation approach, which combines epicardial and endocardial catheter ablation, has been introduced in clinical practice. This method aims to enhance the efficacy and safety of treatment for persistent atrial fibrillation [4,5].

This systematic review and meta-analysis evaluated the efficacy and safety of hybrid ablation compared to endocardial catheter ablation alone for persistent atrial fibrillation. Our analysis revealed that hybrid ablation significantly improves the long-term success rate of atrial fibrillation ablation (OR 1.42; 95% CI: 1.05–1.92; $p = 0.031$) compared to the catheter ablation group. However, this benefit comes with a trade-off: hybrid ablation is associated with a higher risk of overall surgical complications (OR 3.51; 95% CI: 2.18–5.64; $p < 0.001$) and major surgical complications (OR 3.28; 95% CI: 1.43–7.51; $p = 0.003$). Notably, hybrid ablation also reduces the proportion of patients requiring repeat procedures and shows a trend toward decreasing the use of postoperative electrical cardioversion.

Although prior research has indicated a potentially higher success rate with hybrid ablation, these studies were largely based on single-arm data without direct comparative analysis [6–9]. Our study offers a direct comparison between hybrid and catheter ablation, providing more consistent and robust evidence [10]. Clinical trials have demonstrated that hybrid ablation is more effective in maintain-

ing sinus rhythm but comes with an increased risk of severe complications and mortality [11]. These results, which present a higher level of evidence compared to existing studies, underscore the importance of carefully weighing the potential benefits against the risks when considering hybrid ablation [12].

Materials and Methods

We conducted the systematic literature search and reported the findings in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. Since the data used in this study were sourced from publicly available materials, no informed consent or ethical review was necessary. The search and evaluation process was carried out independently by two investigators, who screened for relevant studies, determined eligibility, extracted information, and assessed study quality. Discrepancies between the investigators were resolved through discussion and consensus to ensure accuracy and consistency.

Search Strategy

On January 6, 2023, we conducted a comprehensive search of four online databases: PubMed, Embase, Web of Science, and the Cochrane Library. No time restrictions were imposed for the search. Each database was queried using syntax and terminology tailored to its unique requirements. In PubMed, for instance, search terms included: ('convergent' OR 'hybrid' OR 'surgical') AND ('atrial fibrillation' OR 'AF' OR 'atrial flutter' OR 'arrhythmia') AND (ablation OR 'catheter ablation' OR 'pulmonary vein isolation' OR 'PVI' OR 'labyrinth procedure' OR "Cox's labyrinth" OR "minilabyrinth" OR "epicardial ablation" OR "endocardial ablation" OR "radiofrequency ablation" OR "cryoablation" OR "laser ablation") AND ("treatment" OR "management" OR "efficacy" OR "safety" OR "success" OR "outcome" OR "long-term follow-up" OR "quality of life" OR "procedural complications" OR "risk of stroke" OR "risk of death" OR "recurrence rate" OR "absence of atrial fibrillation" OR "maintenance of sinus rhythm"). No language restrictions were applied. Additionally, we manually screened the reference lists of relevant articles to identify any additional studies for inclusion.

Inclusion Criteria

The primary objective of this study is to compare the long-term success and complication rates of hybrid ablation versus catheter-based ablation. Complications assessed include all surgical complications, with severe complications specifically defined as cardiac tamponade, stroke, and death. Secondary outcomes involve comparing rates of postoperative echocardiography and repeat ablation between the two groups.

The inclusion criteria are as follows: (1) The follow-up period after ablation must exceed three months to avoid short-term bias; (2) The study sample size must be greater than 20 cases; (3) The study must provide reliable data on the long-term success rates and incidence of complications for both hybrid and catheter ablation procedures.

The exclusion criteria are: (1) Repeatedly published studies; (2) Studies lacking detailed information on primary endpoints; (3) Case reports, commentaries, expert opinions, and narrative reviews.

Data Extraction

The literature and data collection process should be independently conducted by two reviewers. The reviewers will then compare their findings, and any discrepancies will be discussed and resolved to ensure consistency. During the literature review, titles and abstracts should be screened first, followed by a full-text review of potentially relevant studies. Irrelevant information should be excluded at each stage.

Essential data to be extracted and recorded in a standardized Excel file include: the name of the first author, year of publication, country, study design, participant demographics, long-term success rates, and complication rates. If crucial information is missing from a published report, we will reach out to the original study authors via email to request any unpublished data.

Quality Assessment

The quality of the included studies was evaluated using the Newcastle-Ottawa Scale (NOS) [14]. This scale is divided into three categories: selection, comparability, and outcome/exposure. Two independent raters assessed nine components of the NOS, which cover selection bias, comparability bias, and outcome bias. Based on their assessments, studies were classified as low quality (scores 0–3), medium quality (scores 4–6), or high quality (scores 7–9).

Statistical Analyses

The chi-square and I^2 statistics were employed to assess heterogeneity between trials, with I^2 values indicating the extent of variability among the included studies: an I^2 value of 0% denotes no heterogeneity, whereas a value greater than 50% indicates significant variability. We standardized the relative risks for each study and combined them using a random-effects model. Funnel plot asymmetry was analyzed to detect publication bias in the meta-analysis. If asymmetry was observed, we categorized hypothetical negative unpublished studies to evaluate whether publication bias affected the outcome estimates. For all statistical analyses, a two-sided p-value of less than 0.05 was

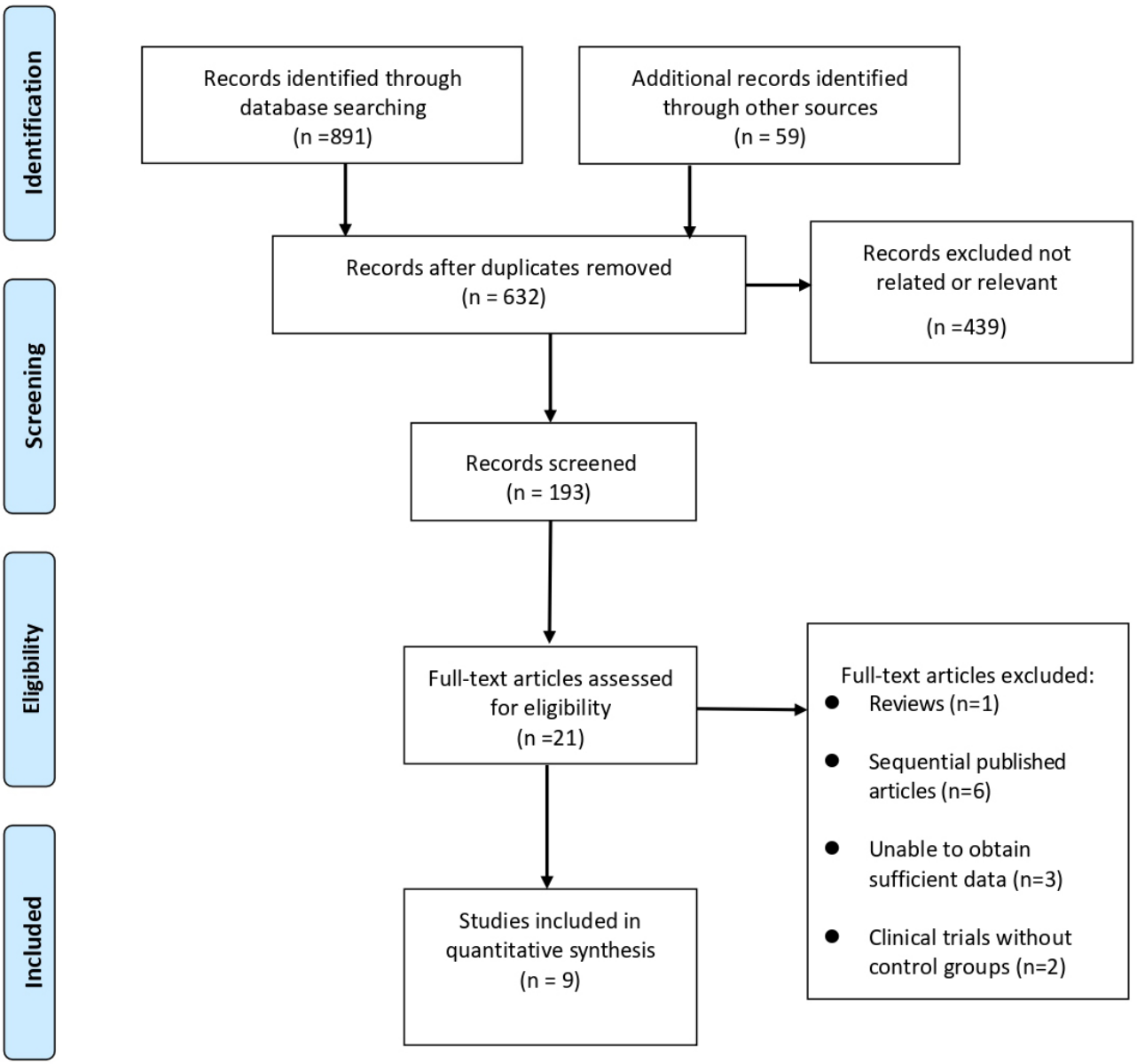

Fig. 1. Selection process of included studies.

considered statistically significant. Data from randomized controlled trials (RCTs) that met the inclusion criteria were analyzed using Stata v17 (StataCorp, College Station, TX, USA).

Results

Search Results and Study Selection

The initial search of the electronic databases yielded 950 relevant titles. After removing duplicates and thoroughly reviewing the titles and abstracts based on the inclusion and exclusion criteria, 21 articles were deemed relevant. Of these, 12 articles were excluded following a detailed assessment, resulting in a final selection of 9 articles for inclusion. The filtering process and outcomes of the literature search are illustrated in Fig. 1.

Study Characteristics

The characteristics of the studies included in this systematic review are summarized in Table 1 (Ref. [15–23]). A total of 9 clinical control studies [15–23] were analyzed, comprising 834 patients in total (380 in the hybrid ablation group and 454 in the catheter-based ablation group). Four patients were lost to follow-up, with 3 from the hybrid ablation group and 1 from the catheter-based group. The mean age of the study population was 60.9 years, and 641 of the patients (77.2%) were male.

Table 1. Characteristics of studies included in the meta-analysis.

Author	Year	Study design	Type of atrial fibrillation	Sample size	Age (years)	Atrial fibrillation duration	Left atrial diameter (mm)	Follow-up period (months)
				hybrid/catheter	hybrid/catheter	hybrid/catheter	hybrid/catheter	
DeLurgio *et al*. [23]	2020	RCT	58%P-AF 42%LSP-AF	102/51	63.7/65.1	4.4/4.5	44/43	12.0
Maclean *et al*. [22]	2020	R	LSP-AF	43/43	68.6/65.5	3.0/3.0	47.4/47.5	12.0
Nordsieck *et al*. [21]	2019	R	21%P-AF 79%LSP-AF	14/23	70.0/63.0	1.3/1.3	42/43	10.0
Jan *et al*. [19]	2018	R	P-AF	24/26	58.8/59.5	4.1/5.2	NA	30.5
Hwang *et al*. [20]	2018	RCT	55%P-AF 45%LSP-AF	72/105	53.6/52.0	NA	NA	25.2
Genev *et al*. [17]	2017	R	LSP-AF	22/72	68.1/61.4	NA	NA	24.0
Kress *et al*. [18]	2017	R	P-AF LSP-AF	64/69	60.7/ 62.3	1.0/0.6	48/47	16.0
Edgerton *et al*. [16]	2016	P	LSP-AF	24/35	63.8/63.0	6.8/5.6	51.5/52.4	24.0
Mahapatra *et al*. [15]	2011	R	73%P-AF 27%LSP-AF	15/30	59.5/59.2	5.4/4.9	52.3/45.3	20.7

R, Retrospective; P, Prospective; RCT, Randomized controlled trial; NA, Not available; P-AF, Persistent atrial fibrillation; LSP-AF, Long-standing persistent atrial fibrillation; RF, Radiofrequency ablation.

Table 2. The quality assessment according to NOS of each cohort study.

Study	Selection			Comparability	Outcome			Total score
	Representativeness of the exposed cohort	Selection of the non-exposed cohort	Ascertainment of exposure	Demonstration that outcome	Comparability of cohorts	Assessment of outcome	Was follow-up long enough	Adequacy of follow up of cohorts	
DeLurgio *et al*. [23]	★	★	★	★	★★	★	★	★	9
Maclean *et al*. [22]		★	★	★	★★	★	★	★	8
Nordsieck *et al*. [21]	★	★	★	★	★★	★	★	★	9
Jan *et al*. [19]	★	★	★	★	★★	★		★	8
Hwang *et al*. [20]	★	★		★	★	★	★	★	7
Genev *et al*. [17]	★	★	★	★	★	★	★	★	8
Kress *et al*. [18]	★	★	★	★	★★	★	★	★	9
Edgerton *et al*. [16]	★	★	★	★	★★	★	★	★	9
Mahapatra *et al*. [15]	★	★	★	★	★	★	★	★	8

NOS, New Castle-Ottawa Scale. ★ means one point. ★★ means two points.

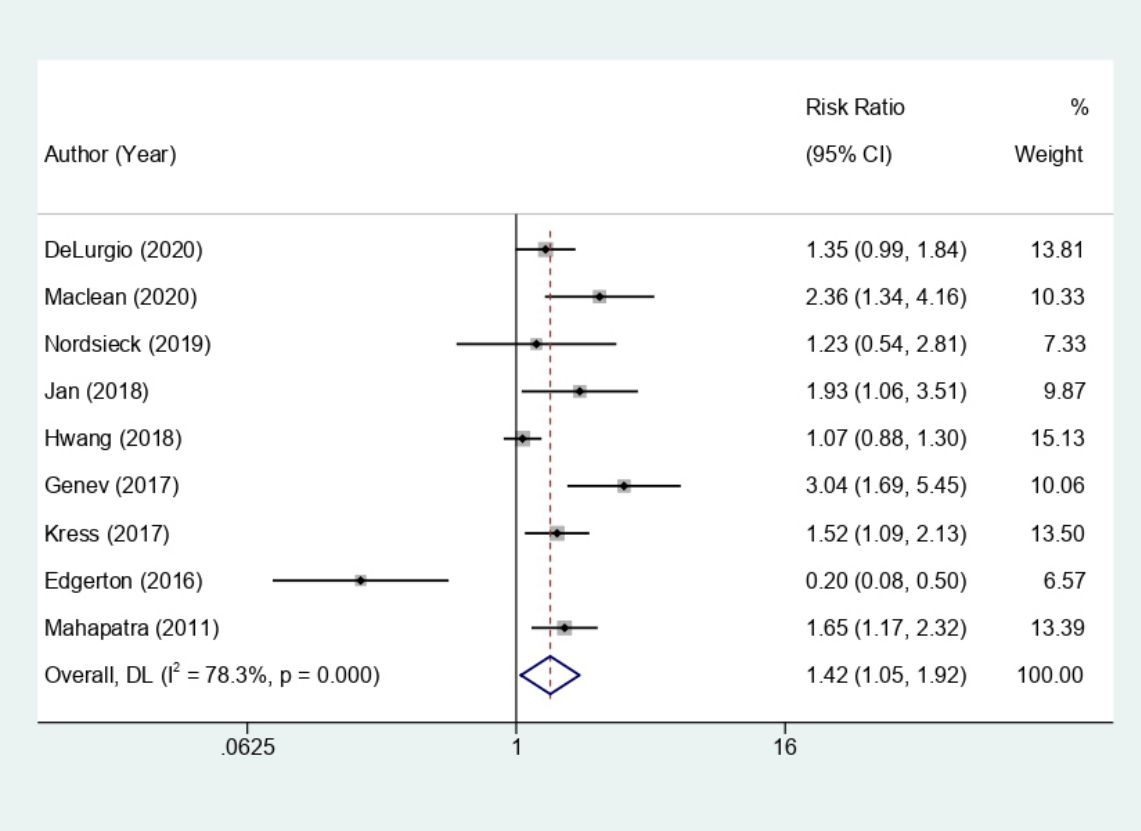

Fig. 2. Forest plots of the long-term success rate of hybrid compared to catheter ablation.

Results of Quality Assessment

The methodological quality of each randomized controlled trial (RCT) was evaluated using the Newcastle-Ottawa Scale (NOS). One study received an overall score of 7, four studies scored 8, and four studies scored 9. None of the studies exhibited evidence of funding bias. Additionally, there were no instances of unstable baseline values, premature study termination, or incomplete outcome data. Table 2 (Ref. [15–23]) provides a summary of the risk of bias and the corresponding scores.

Meta-Analysis Results for Long-Term Success Rate

All the included studies provided comprehensive data on long-term success rates, with an average follow-up duration of 19.1 months. Only one study reported a higher success rate in the catheter ablation group compared to the hybrid ablation group [16]. The meta-analysis demonstrated that hybrid ablation generally improved the long-term success rate for atrial fibrillation (OR 1.42; 95% CI: 1.05–1.92; $p = 0.031$, Fig. 2), with statistically significant differences between studies and notable heterogeneity ($I^2 = 78.3\%$, $p < 0.001$). Sensitivity analysis identified the study by Boersma *et al*. [12] as the primary source of heterogeneity ($p = 0.001$). When this study was excluded, hybrid ablation significantly increased the long-term success rate for atrial fibrillation resolution (OR 2.56; 95% CI: 1.89–3.47; $p < 0.001$), with statistically significant differences between studies and reduced heterogeneity ($I^2 = 42\%$, $p = 0.110$).

Meta-Analysis Results for Surgical Complications

The meta-analysis showed that the hybrid ablation group faced a significantly higher risk of overall surgical complications compared to the catheter ablation group (OR 3.51; 95% CI: 2.18–5.64; $p < 0.001$; $I^2 = 0$, $p = 0.760$; Fig. 3). Additionally, there was a marked increase in the risk of major surgical complications, including cardiac tamponade, stroke, and death (OR 3.28; 95% CI: 1.43–7.51; $p = 0.003$; $I^2 = 10.4\%$, $p = 0.349$; Fig. 4).

Meta-Analysis Results for Secondary Endpoints

The proportion of patients requiring repeat ablation was significantly lower in the hybrid ablation group compared to the catheter ablation group (OR 0.54; 95% CI: 0.33–0.88; $p = 0.002$; $I^2 = 0\%$, $p = 0.430$; Fig. 5). Additionally, there was a trend indicating a reduction in the number of postoperative echocardiographic examinations (OR 0.71; 95% CI: 0.46–1.09; $p = 0.086$; $I^2 = 25.1\%$, $p = 0.254$; Fig. 5).

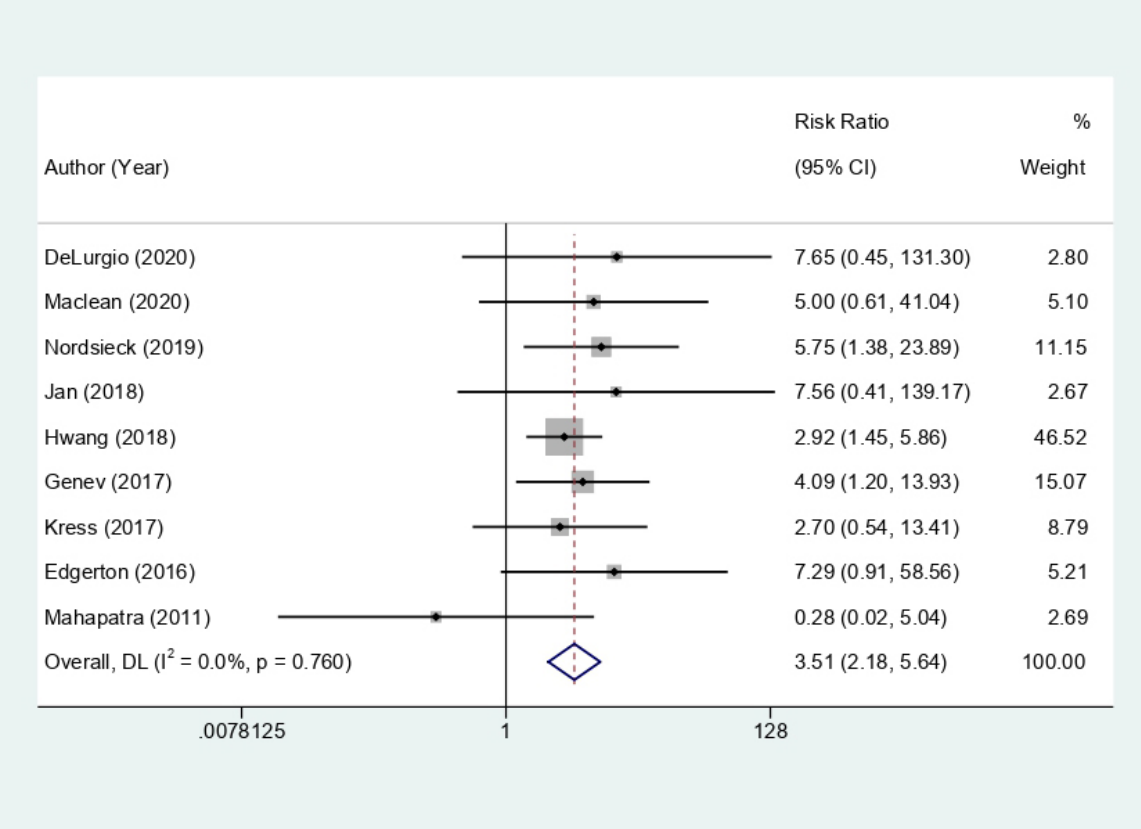

Fig. 3. Forest plots of all complications.

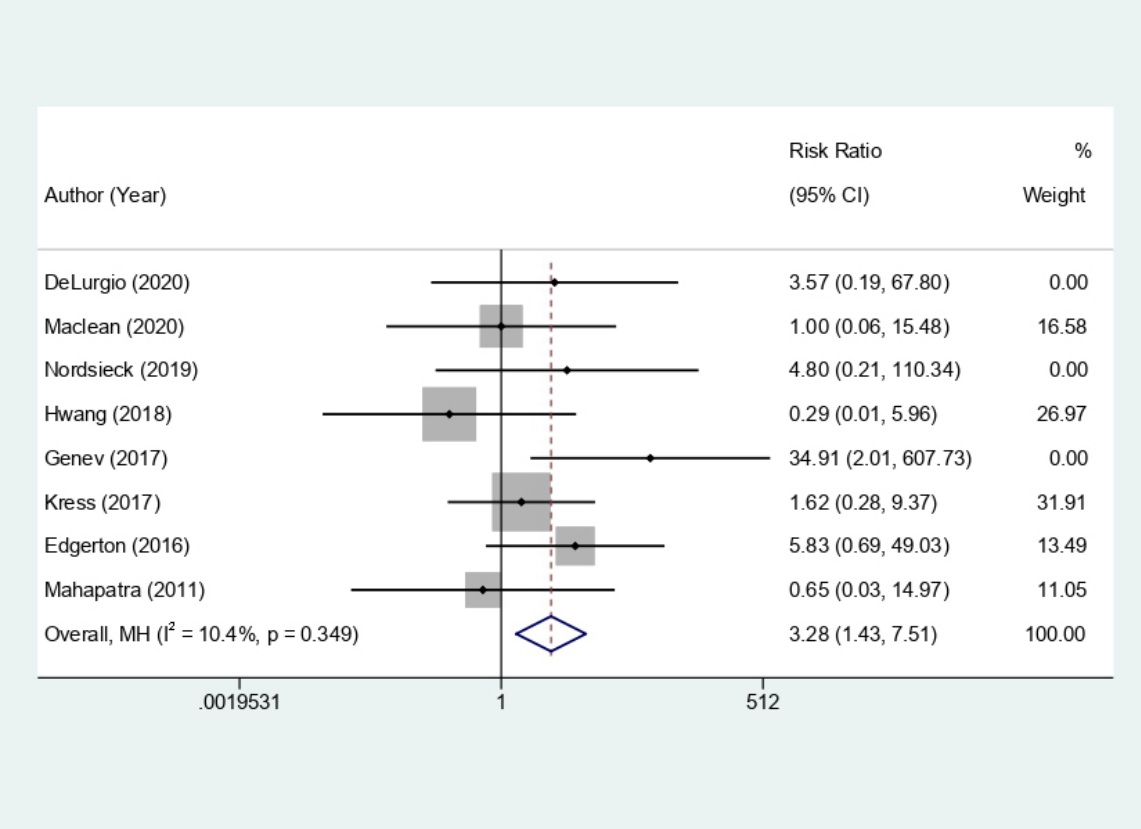

Fig. 4. Forest plots of serious complications.

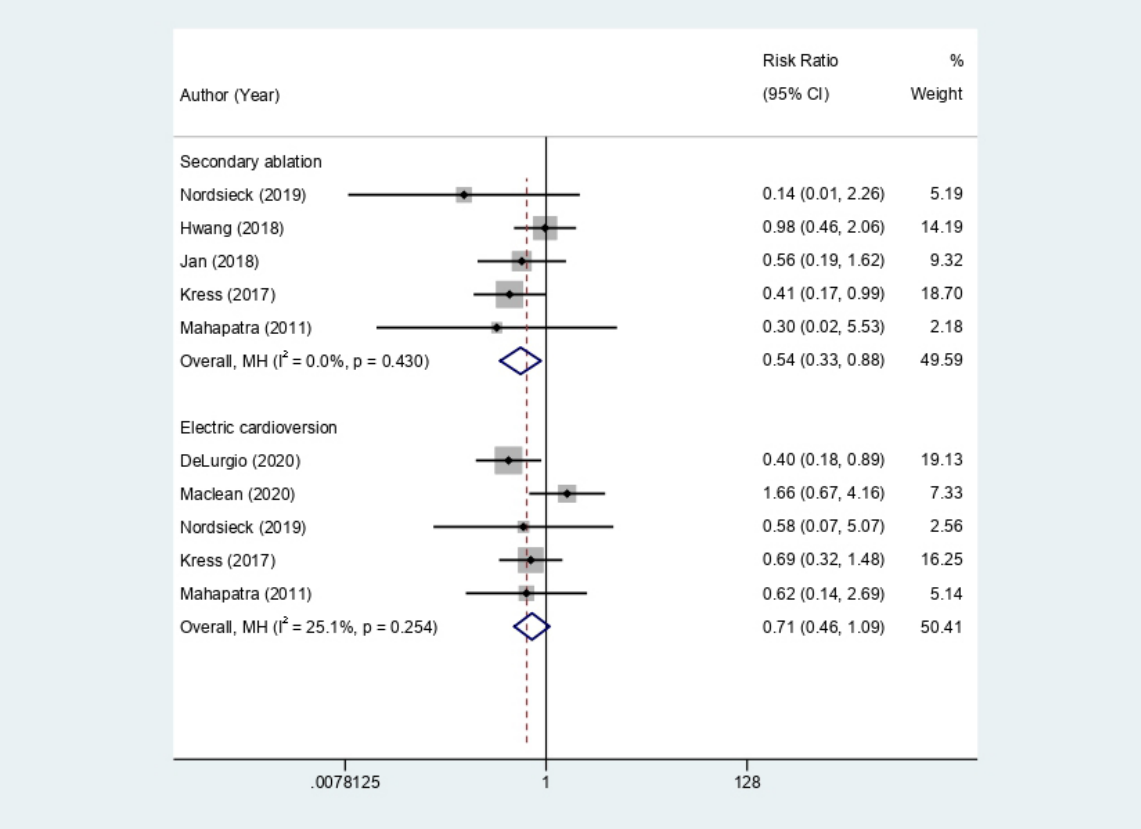

Fig. 5. Forest plots of secondary end point (secondary ablation and electric cardioversion).

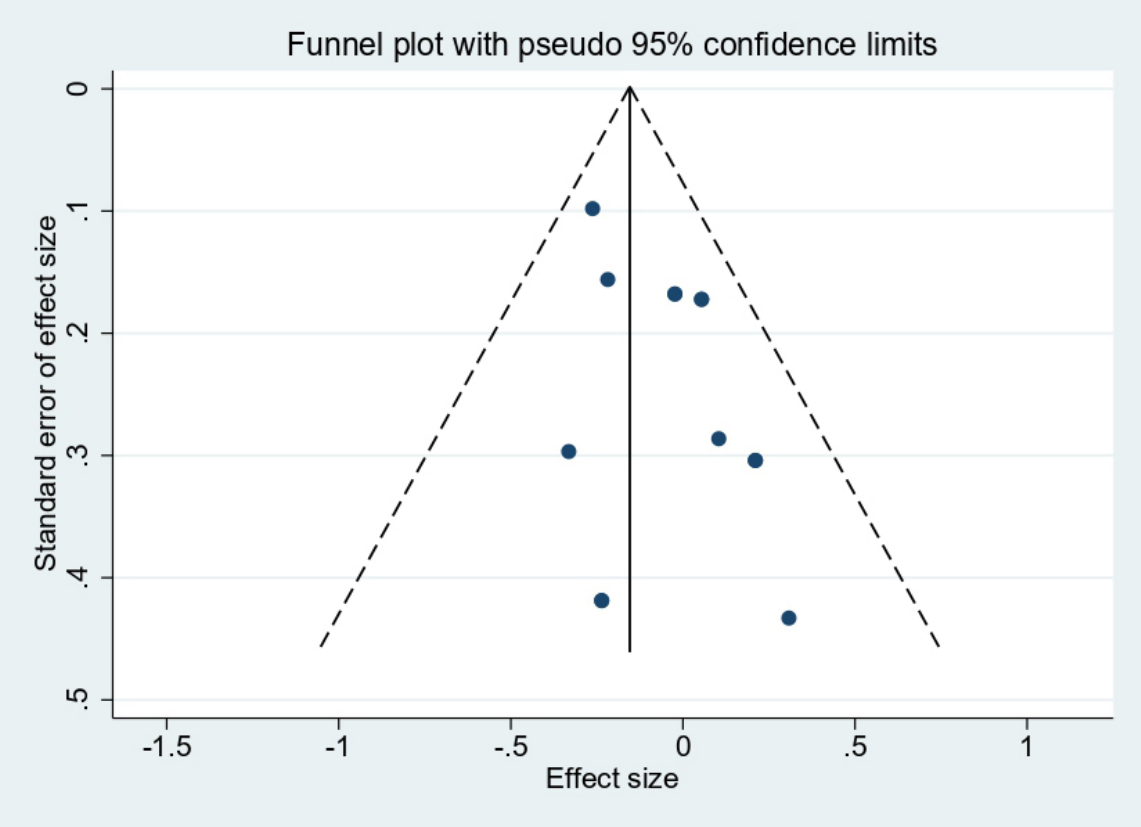

Fig. 6. Funnel plot for publication bias in all included studies.

Publication Bias

Funnel plots generated from the observational studies displayed symmetry, indicating no significant publication bias (Fig. 6).

Discussion

The findings of this study indicate that hybrid ablation is more effective in achieving long-term success for persistent atrial fibrillation compared to endocardial catheter ablation alone. This advantage is likely due to the combined benefits of epicardial and endocardial ablation, offering more comprehensive lesion coverage and thereby enhancing treatment efficacy. However, despite the improved success rates, hybrid ablation is associated with a higher incidence of complications, both general and severe, underscoring the need for a balanced consideration of both efficacy and risk in treatment planning.

The existing literature suggests that the success rate for standalone endocardial catheter ablation in persistent atrial fibrillation ranges between 20% and 60% over a two-year period [24,25]. Consistent with these reports, our study observed a 47% success rate for endocardial catheter ablation after an average follow-up of 19.1 months. Verma *et al*. [24] reported that linear or segmental catheter ablation, aside from PVI, did not significantly decrease recurrence rates in patients with persistent atrial fibrillation, likely due to factors such as left atrial enlargement and extensive structural remodeling characteristic of this condition.

Hybrid ablation, which combines surgical epicardial and intracardiac catheter ablation, has emerged as a promising approach to improve treatment outcomes for persistent and long-standing atrial fibrillation [26]. This method enables effective epicardial ablation and isolates the posterior left atrial wall, enhancing success rates. Current data suggest a two-year success rate for hybrid ablation ranging from 50% to 80% [27,28], with lower risks of postoperative electrical cardioversion and reconnection. Although some studies have reported a potentially higher success rate with hybrid ablation, their conclusions were based on pooled single-arm studies without direct comparisons, thus providing lower evidence quality [29,30].

Our study included nine direct comparisons between hybrid ablation and catheter ablation, revealing that 63.4% of patients in the hybrid group maintained sinus rhythm, compared to 47.0% in the catheter-only group. While catheter ablation remains a well-established first-line treatment for atrial fibrillation, many studies suggest that complex hybrid procedures carry a greater risk of complications [29–31]. However, evidence on the frequency of severe surgical complications remains limited. Our research showed that 572 patients undergoing hybrid ablation experienced significant complications, such as stress-induced heart failure and death [29]. Osmancik *et al*. [31] highlighted that efforts to enhance success rates might increase the risk of adverse events. A recent meta-analysis confirmed a higher complication risk with hybrid procedures, but it did not separately analyze severe outcomes like major surgical complications and fatalities [30].

Patient safety remains a critical concern for any new surgical approach. Our analysis revealed a severe complication rate of only 1.6% in the catheter ablation group, compared to 4.8% in the hybrid ablation group—a statistically significant difference ($p < 0.001$). All six recorded deaths occurred in the hybrid ablation group, a trend consistent across both randomized and observational studies. The requirement for general anesthesia, thoracoscopy, and lung ventilation in hybrid procedures may contribute to this elevated risk.

This study has several limitations: (1) It included only nine studies with a total of 834 patients, resulting in a relatively small sample size. (2) Among the included studies, only two were RCTs, while the others were observational, necessitating further confirmation through additional RCTs. (3) Variability in ablation techniques and catheter strategies may have influenced the results. Nevertheless, our systematic review and meta-analysis provide valuable insights into the relative efficacy and safety of hybrid ablation versus catheter ablation for maintaining sinus rhythm in patients with persistent atrial fibrillation. Although hybrid ablation offers improved sinus rhythm outcomes, it is associated with a higher rate of severe complications and deaths. This highlights the necessity of carefully considering the benefits and risks, particularly for high-risk patients.

Despite using a random-effects model to address heterogeneity and performing sensitivity analyses to identify its sources, our study lacked subgroup analyses to explore heterogeneity causes further. Future research should incorporate detailed patient characteristics, ablation techniques, and postoperative management in subgroup analyses to better evaluate the effects and safety of hybrid ablation across different patient populations.

In conclusion, while hybrid ablation demonstrates higher success rates in treating persistent atrial fibrillation, it also poses a greater risk of complications. Further research is required to optimize hybrid ablation techniques, minimize complications, and develop personalized treatment strategies through well-designed RCTs and long-term follow-up studies, ultimately ensuring patient safety and optimal outcomes.

Conclusions

Research indicates that hybrid ablation techniques may increase the risk of long-term fibrosis in heart tissue compared to endocardial catheter ablation alone. Treating

atrial fibrillation carries inherent risks, with serious complications such as cardiac tamponade, stroke, and death being primary concerns. To improve treatment efficacy and reduce the recurrence of persistent atrial fibrillation, hybrid ablation—combining both epicardial and endocardial approaches—has been introduced. This technique aims to optimize outcomes while carefully managing the associated risks.

Availability of Data and Materials

The original data can be provided from corresponding author under reasonable request.

Author Contributions

HD and ZD contributed to the conception of the study. XG and ZZ contributed significantly to literature search, data extraction, quality assessment, data analyses and manuscript preparation. HD contributed improving the article for language and style and protocol preparation. HD and ZD revised the manuscript and approved the final version. All authors have participated sufficiently in the work. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Ethics Approval and Consent to Participate

Not applicable.

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Conflict of Interest

The authors declare no conflict of interest.

Supplementary Material

Supplementary material associated with this article can be found, in the online version, at https://doi.org/10.59958/hsf.7767.

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