

Meta-Analysis of Pulmonary Vein Isolation Plus Spatial/Temporal Dispersion Activation Pattern Guiding Catheter Ablation for Non-Paroxysmal Atrial Fibrillation: 10 Years of Studies Update

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ABSTRACT

Background: Pulmonary Vein Isolation (PVI) is an effective treatment for Paroxysmal Atrial Fibrillation (PAF) but has limited efficacy in Non-Paroxysmal Atrial Fibrillation (NPAF). Spatial/Temporal Dispersion (STD)-guided Catheter Ablation (CA) could offer potential additional benefits. This meta-analysis assessed the advantages and safety of the PVI+STDCA over PVI+Conventional Catheter Ablation (CCA) approaches in NPAF patients, with subgroup analyses highlighting the strategy's potential and challenges.

Methods and results: Clinical trials focusing on the PVI+STDCA approach in patients with NPAF were searched in PubMed, MEDLINE, etc. followed by quality checks. Heterogeneity among the pooled data was assessed by the I^2 test in a suitable effect model. In this analysis, 17 studies ($n=2,203$, 82.9% NPAF) were reviewed. The 12-month follow-up revealed that PVI+STDCA significantly increased Freedom from Atrial Tachyarrhythmias (FFATAs) in the non-FIRM sub-group (OR 2.44, 95% CI 1.93-3.08, $P<0.00001$, $I^2=0\%$), supported by RCTs (OR 2.43, 95% CI 1.81-3.26, $P<0.00001$, $I^2=0\%$), which was attributed to force-sensing catheters (OR 2.08, 95% CI 1.41-3.07, $P=0.0002$, $I^2=61\%$). PVI+STDCA also improved Freedom from Atrial Fibrillation (FFAF) across mapping techniques (OR 3.53, 95% CI 2.75-4.53, $P<0.00001$, $I^2=43\%$), without significant differences in post-procedural Atrial Tachycardia (AT), Radiofrequency (RF) time, or Serious Adverse Events (SAEs).

Conclusions: The PVI+STDCA strategy enhances sinus rhythm maintenance during mid to long-term follow-up in patients with NPAF, while ensuring comparable safety.

Keywords: Atrial fibrillation; Catheter ablation; Driver; Rotor mapping; Pulmonary vein isolation

INTRODUCTION

Circumferential Pulmonary Vein Isolation (CPVI) is the cornerstone of Catheter Ablation (CA) for Atrial Fibrillation (AF) and has shown its effectiveness in sustaining Sinus Rhythm (SR) in patients with Paroxysmal AF (PAF), with success rates between 70% and 75% after multiple procedures. This strategy was inspired by foundational studies by Haïssaguerre et al. and Chen et al., which recognized pulmonary vein triggers as a principal mechanism in AF arrhythmogenesis. In 2000, Pappone et al., introduced Wide Area Circumferential Ablation (WACA) of the pulmonary veins, guided by the CARTO 3-D system,

streamlining the procedure and reducing complications such as pulmonary vein stenosis [1].

However, the efficacy of PVI alone in treating Non-Paroxysmal Atrial Fibrillation (NPAF) is limited. Various additional ablation strategies have been proposed, including Posterior Wall Isolation (PWI), Left Atrial Appendage Isolation (LAAI), ethanol infusion of the vein of marshall (VOA) and ablation of Complex Fragmented Atrial Electrograms (CFAEs). Yet, the effectiveness and safety of these strategies remain subjects of ongoing debate [2].

The electrophysiological phenomenon of Spatial/Temporal Dispersion (STD) activation pattern has been observed in several

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studies. STD-guided catheter ablation, a novel strategy that diverges from purely anatomical ablation, has shown promising results in multiple studies. However, this approach is still controversial due to limited evidence, particularly when it focuses solely on ablating "driver" regions.

What are the clinical outcomes of combining PVI with STDCA in NPAF? In this meta-analysis (PROSPERO registration number: CRD42023447663), we conducted a systematic evaluation of the effectiveness and safety of this integrated approach, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [3].

MATERIALS AND METHODS

Studies search and eligibility

The studies of Randomized Controlled Trials (RCTs), propensity score matching controlled trials, and observational controlled trials published between January 2013 and June 2024 were comprehensively searched across multiple databases, including PubMed, MEDLINE, Embase, Google Scholar, the Cochrane Central Register of Controlled Trials, and the website of Connected Papers as an additional supplementary resource. Case reports and conference abstracts were excluded from this analysis.

The search strategy included various combinations of keywords such as "rotor", "rotational driver", "drivers", "spatial and temporal dispersion", "atrial fibrillation source", "atrial fibrillation", and "catheter ablation" without any language restrictions [4].

The inclusion criteria for clinical studies were as follows: publication in peer-reviewed journals, a minimum enrollment of 40 participants with a follow-up period exceeding 6 months, and investigation of the combined approach of PVI and Spatial/Temporal Dispersion-Guided Catheter Ablation (STDCA) in patients with NPAF. Linear lesions were accepted as an additional ablation strategy to eliminate interprocedural Atrial Tachycardia (AT) including Atrial Flutter (AFL) and focal atrial tachycardia. When assessing relevant studies on Complex Fractionated Electrogram (CFAE) mapping, those emphasizing rotational activation were deemed eligible.

To avoid duplication of data and prevent inappropriate power inflation, similar duplicate studies were excluded while sequential studies with distinct matched controls were included for analysis. The search strategy is outlined in Figure 1 [5].

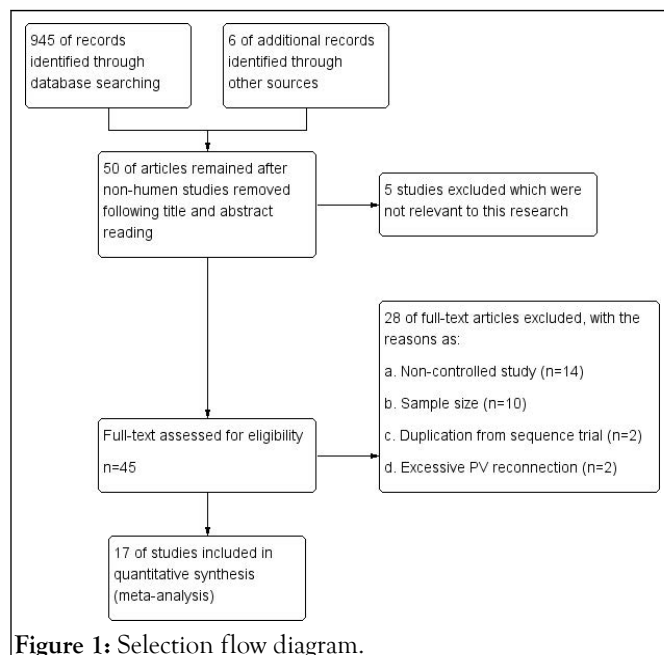


Figure 1: Selection flow diagram.

Definitions of STD mapping

The definition of STD in this study refers to the presence of visually stable (>2.5 seconds) atrial activation with spatial dispersion characteristics (atrial activation dispersion $>50\%$ of AFCL) observed between electrodes during manual mapping using a multi-electrode catheter, such as PentaRay, or a circumferential catheter, such as Lasso. Meanwhile, the exclusion of excessively rapid atrial activation (cycle length <120 ms), commonly regarded as CFAEs, was implemented.

The computer signal processing algorithm was based on the aforementioned approach, which adhered to a repetitive and spatially stable Rotational Activity Profile (RAP) or focal source. This scheme was applicable to both the mentioned catheters as well as invasive basket catheters and non-invasive arrays of surface electrodes [6].

Assessment of study quality

After an initial screening of titles and abstracts, three reviewers conducted a comprehensive cross-evaluation of full-text in potential studies. We applied the Cochrane Risk of Bias 2 (RoB 2) tool to assess the risk of bias in Randomized Controlled Trials (RCTs), classifying as high risk of bias, some concerns, or low risk of bias, according to the instruction. For non-RCTs, the Newcastle-Ottawa Scale (NOS) was performed to evaluate quality levels and categorized them as high quality (6-9 points), satisfactory quality (3-5 points), or unsatisfactory quality (0-2 points). The assessment process incorporated the principles of randomized assignment and avoidance to previous literature retrieval researchers in order to enhance its academic rigor, followed by a final cross-check.

Any discrepancies were resolved through discussion and majority vote until reaching a final consensus. In instances where agreement could not be attained, Dayong Zhang held ultimate decision-making authority [7].

Statistical analysis

The clinical data pertaining to NPAF were extracted. Dichotomous and continuous variables were presented as n (%) and mean $\pm$ Standard Deviation (SD), respectively. Data described in interquartile ranges were converted using an appropriate transformation method, such as the Tukey method. Pooled statistical analysis was conducted using Review Manager in accordance with PRISMA recommendations. Pooled Odds Ratios (ORs) and their corresponding 95% Confidence Intervals (CIs) were calculated for the outcomes, with statistical significance defined as a P value of <0.05.

The choice of effect model was based on the assessment of heterogeneity using I^2 statistics; specifically, the Fixed-Effect Model (FEM) was used for low heterogeneity ($I^2 < 25\%$), and the Random-Effect Model (REM) was used for moderate to high heterogeneity ($I^2 \geq 50\%$). In cases of significant heterogeneity, potential reasons were explored rather than defaulting to the REM.

Sensitivity analysis was performed by sequentially excluding individual studies to assess the robustness of the findings. Heterogeneity was assessed using the I^2 statistic, with stepwise exclusion of studies and pre-specified subgroup analyses conducted to identify potential sources of inconsistency. Funnel plots were employed to visually assess the presence of publication bias, complemented by statistical tests for publication bias when appropriate [8].

RESULTS

Characteristics of included studies

A total of seventeen studies were included in this analysis, consisting of nine RCTs and eight historical matched cohort trials. Among these, eight were multicenter studies and nine were single-center studies, involving a sample population of 2,203 AF patients, with NPAF accounting for 82.9% (n=1,825) of the sample.

The mean age of the study population was approximately 56.1 years, with a follow-up period of 14.3 months. A total of 23.3% of the enrolled patients had a prior ablation procedure history. The study sample was predominantly male, comprising 73.8% of the sample. The mean Left Atrial Diameter (LAD) and Left Ventricular Ejection Fraction (LVEF) for the sample were 45.7 ± 6.1 mm and $57.3 \pm 10.2\%$, respectively.

The STD mapping study employed eight approaches, including computerized automatic systems such as RhythmView/Focal Impulse and Rotor Modulation (FIRM), Dominant Frequency (DF), Rotor Identification Index (RI)/Phase Map, Auto-CFAEs/VAVp, RRA, PRISM, and FaST, in addition to a manual location method. To assess for the presence of publication bias, funnel plots were used [9].

Outcomes of follow-up

Freedom from Atrial Fibrillation/Atrial Tachycardia/Atrial Flutter (FFATAs): The pooled analysis of fifteen controlled

studies revealed that the PVI+STDCA approach was significantly associated with an increased FFATAs (OR 2.10, 95% CI 1.44-3.05, $P=0.0001$, $I^2=70\%$) (Figure 2) without significant publication bias (Supplementary Figure 1), showing a higher prevalence of FFATAs at 69.0% compared to 52.4%. However, this effect was primarily driven by the non-FIRM subgroup of nine studies exhibiting low heterogeneity (OR 2.44, 95% CI 1.93-3.08, $P<0.00001$, $I^2=0\%$), which was further supported by RCTs (OR 2.43, 95% CI 1.81-3.26, $P<0.00001$, $I^2=0\%$) (Figure 3).

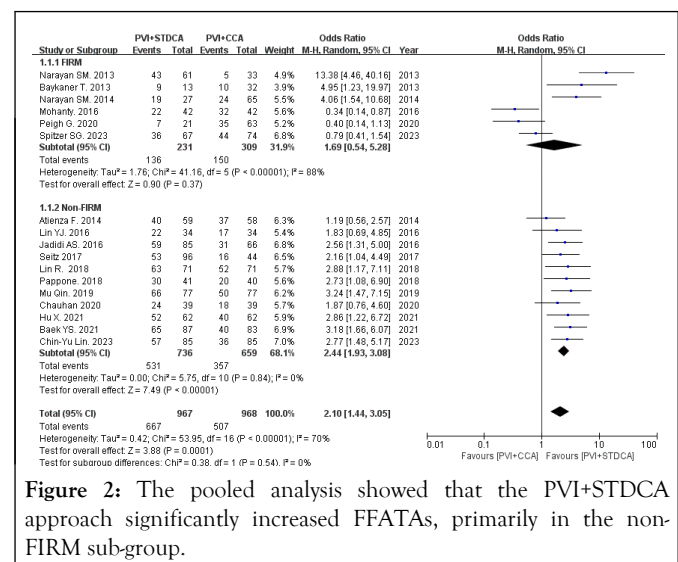


Figure 2: The pooled analysis showed that the PVI+STDCA approach significantly increased FFATAs, primarily in the non-FIRM subgroup.

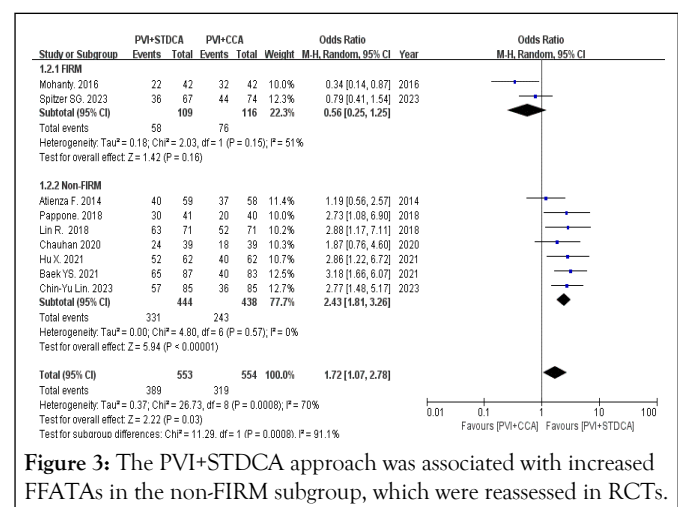
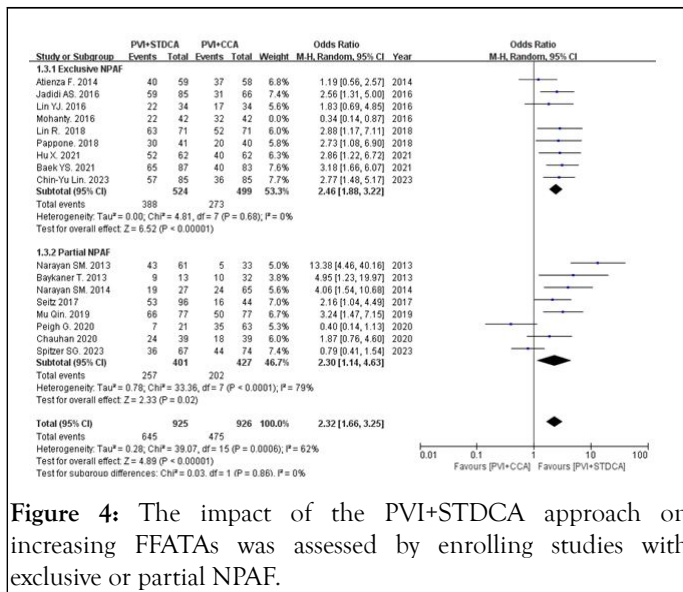


Figure 3: The PVI+STDCA approach was associated with increased FFATAs in the non-FIRM subgroup, which were reassessed in RCTs.

The efficacy of the PVI+STDCA approach was re-evaluated in a subgroup analysis based on AF type. After excluding Mohanty's study, which was the only source of heterogeneity in the exclusive NPAF subgroup, this novel approach consistently demonstrated a significant advantage with remarkable homogeneity (OR 2.46, 95% CI 1.88-3.22, $P<0.00001$, $I^2=0\%$). Similar findings were observed in the partial NPAF subgroup; however, substantial heterogeneity was present (OR 2.30, 95%CI 1.14-4.63, $P=0.02$, $I^2=79\%$) (Figure 4).



To explore the potential impact of the type of ablation catheter used, a sub-group analysis was conducted to reassess the comparison based on the utilization of force-sensing catheters (Figure 5). The pooled FFATs from ten studies in PVI+STDCA approach employing force-sensing catheter demonstrated a statistically favorable outcome (OR 2.08, 95% CI 1.41-3.07, $P = 0.0002$, $I^2 = 61\%$) compared to non-force-sensing catheter application (OR 2.32, 95% CI 0.85-6.33, $P = 0.10$, $I^2 = 84\%$).

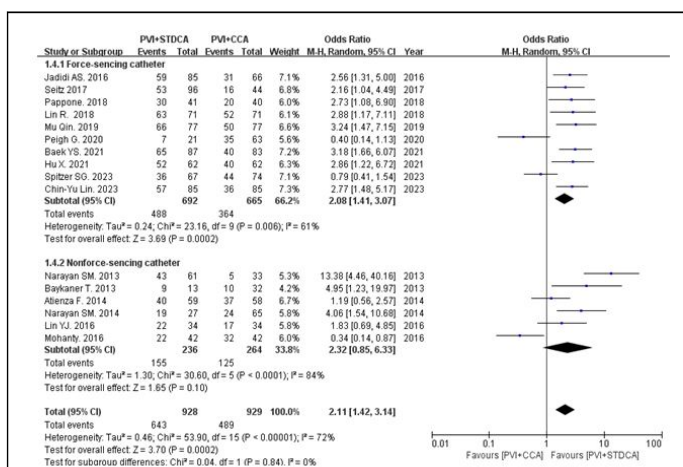


Figure 5: Reevaluating FFATs by subgroup analysis based on catheter type revealed a significant disparity within the force-sensing catheter sub-group.

To address potential bias arising from additional ablation strategies in the control group, we conducted a subgroup analysis based on adjunctive ablation in addition to PVI within the control group (Figure 6). The pooled data demonstrated that incorporating linear isolation alone targeting atrial tachycardia as an adjunctive ablation strategy to PVI+STDCA, yielded significant benefits in reducing post-procedural ATAs (OR 2.27, 95% CI 1.51-3.41, $P < 0.0001$, $I^2 = 68\%$). Conversely, other additional ablation strategies such as CFAE failed to achieve comparable outcomes (OR 1.58, 95% CI 0.58-4.32, $P = 0.38$, $I^2 = 80\%$).

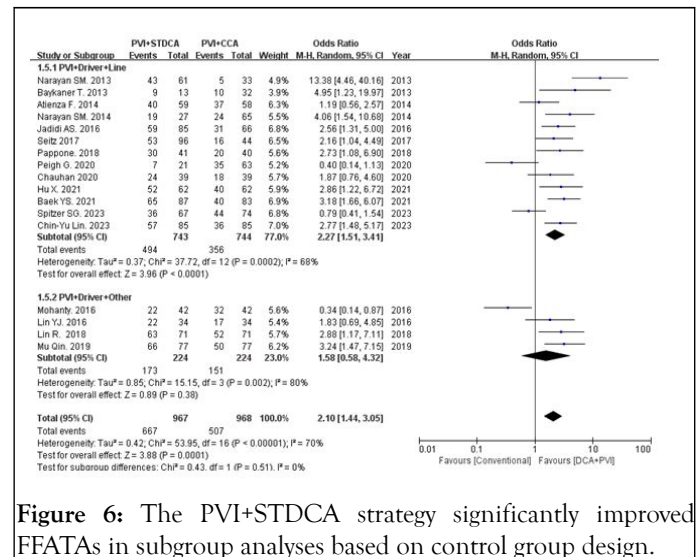


Figure 6: The PVI+STDCA strategy significantly improved FFATs in subgroup analyses based on control group design.

Freedom from Atrial Fibrillation (FFAF): The pooled data from thirteen controlled studies showed that the PVI+STDCA strategy was significantly associated with an increase in FFAF (OR 3.53, 95% CI 2.75-4.53, $P < 0.00001$, $I^2 = 43\%$) without significant publication bias (Supplementary Figure 2). This demonstrated a relative improvement to 82.2% compared to the conventional approach's 54.3% (Figure 7). Notably, this finding was supported by both RCTs (OR 2.71, 95% CI 1.94-3.76, $P < 0.00001$, $I^2 = 24\%$) and non-RCTs (OR 5.04, 95% CI 3.42-7.42, $P < 0.00001$, $I^2 = 29\%$), exhibiting low heterogeneity after excluding Narayan's study in 2013 as the primary source of heterogeneity. The consistent outcome remained regardless of whether the FIRM strategy was implemented (OR 11.01, 95% CI 4.59-26.39, $P < 0.00001$, $I^2 = 28\%$) or not (OR 3.87, 95% CI 2.49-6.02, $P < 0.00001$, $I^2 = 62\%$) (Figure 8).

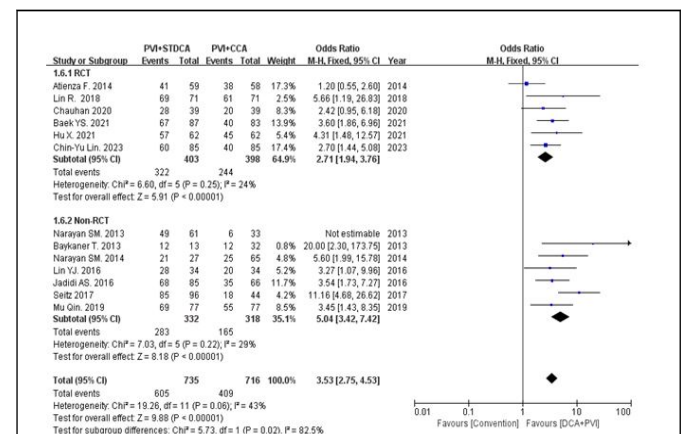


Figure 7: The PVI+STDCA strategy significantly improved FFAF in both RCTs and non-RCTs, with low heterogeneity.

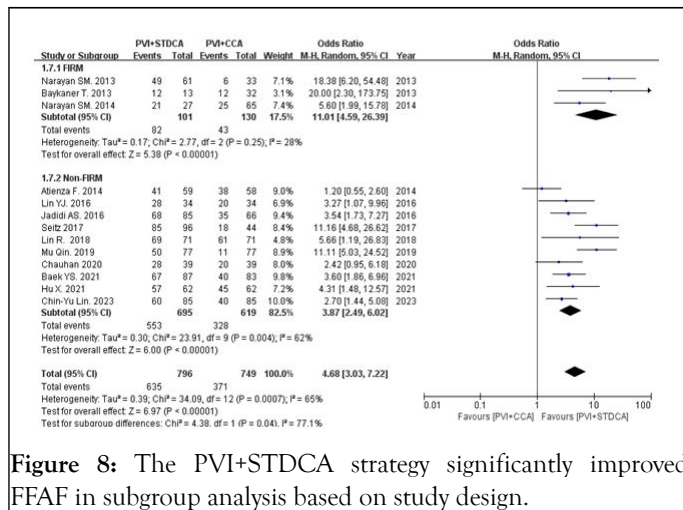


Figure 8: The PVI+STDCA strategy significantly improved FFAF in subgroup analysis based on study design.

Atrial Tachycardia (AT): However, there was no statistically significant difference observed in the incidence of post-procedural AT between the application of the strategy in PVI+STDCA and PVI+CCA across seven controlled studies (OR 1.01, 95% CI 0.59-1.75, $P=0.96$, $I^2=0\%$), which remained consistent in both RCTs (OR 1.03, 95% CI 0.55-1.95, $P=0.92$, $I^2=0\%$) and non-RCTs (OR 0.93, 95% CI 0.16-5.30, $P=0.93$, $I^2=62\%$) (Supplementary Figure 3). The occurrence rates were comparable at 7.3% vs. 7.2%.

Interprocedural characteristics

AF termination: The pooled analysis of the included studies revealed that the PVI+STDCA strategy yielded superior outcomes in terms of AF termination (OR 4.83, 95% CI 2.58-9.05, $P<0.00001$, $I^2=77\%$), which were further assessed in sub-groups of RCTs (OR 3.65, 95% CI 1.81-7.34, $P=0.0003$, $I^2=76\%$) and non-RCTs (OR 11.55, 95% CI 6.11-21.85, $P<0.00001$, $I^2=0\%$) (Figure 9). The AF termination rates were evaluated to be 61.0% and 28.2% for PVI+STDCA strategy and conventional protocol, respectively.

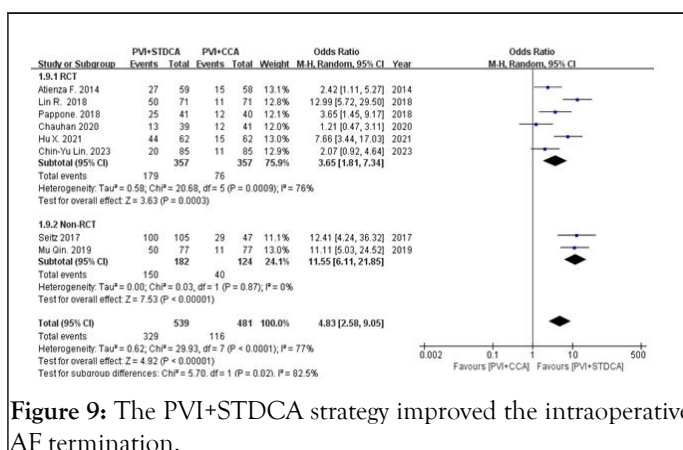


Figure 9: The PVI+STDCA strategy improved the intraoperative AF termination.

Radiofrequency (RF time): The pooled data of PVI+STDCA group exhibited a trend toward shorter RF time compared to the PVI+CCA group, with values of 43.6 ± 16.0 and 55.5 ± 35.5 respectively; however, there was no statistical difference between the two approaches with substantial heterogeneity (OR 4.95, 95% CI 2.33-12.43, $P=0.19$, $I^2=96\%$) (Supplementary Figure 4).

Serious Adverse Events (SAEs): Regarding Serious Adverse Events (SAEs), such as pericardial effusion/cardiac tamponade, cerebrovascular accident, atrial esophageal fistula, esophageal stent insertion, and vascular access site complications based on the included studies' reports, the incidence of SAEs was estimated to be 5.7% in the PVI+STDCA strategy compared to 4.4% in the conventional approach without statistically significant difference (OR 1.32; 95% CI 0.78-2.24; $P=0.30$; $I^2=0\%$) (Supplementary Figure 5).

DISCUSSION

Main findings

In this meta-analysis of 17 controlled clinical trials, we compared the PVI+STDCA strategy to the PVI+CCA protocol. Our findings revealed that the PVI+STDCA strategy improved clinical outcomes in NPAF over a one-year follow-up, with a safety profile comparable to that of traditional methods. This improvement was marked by increases in FFATAs, FFAF, and intraprocedural AF termination rates, with comparable SAEs and RF time.

This study, drawing on an extensive dataset, identified diverse outcomes associated with the mapping strategies employed. The "FIRM" approach, extensively studied, indicated benefits in FFAF but not in FFATAs within this meta-analysis, a pattern supported by RCTs. In contrast, other mapping techniques were found to be more effective in sustaining sinus rhythm. These findings suggest that advancements in mapping technology may potentially enhance the effectiveness of STD-guided ablation in AF.

Meanwhile, the efficacy of PVI+STDCA strategy was found to be associated with the utilization of force-sensing catheters. Previous studies conducted prior to 2016 using non-force sensing catheters failed to demonstrate similar favorable clinical outcomes.

Spatial/temporal dispersion activation pattern in AF

The phenomenon of Spatial/temporal dispersion activation pattern has been observed in numerous studies investigating the mechanisms of "rotor" and "driver", which are considered essential for maintaining Atrial Fibrillation (AF).

The CONFIRM study highlighted a specific type of atrial activation rotational activity referred to as rotors and ectopic focal activations as playing a crucial role in maintaining AF. The latter, which we are most familiar with, is attributed to Delayed after Depolarization (DAD) and Early after Depolarization (EAD). The former, as a concept gaining increasing attention, is attributed to a unique micro-reentrant circuit, leading to spiral-like activation surrounding phase singularities. The activation pattern, which relies on spatial frequency gradients to establish frequency-dependent functional barriers, sustains rotor activity through a unique mechanism of spatial and temporal dispersion. This mechanism, characterized by the maintenance

of spiral waves, was a key inclusion criterion for this meta-analysis.

These patterns were supported by experimental and computational data and were considered to be closely linked to atrial fibrillation. In 1990, spiral waves were first discovered *in vivo* sheep hearts, which exhibited rapid movement in the ventricle and subsequently led to ventricular fibrillation. In 1998, Gray et al.'s study recorded rotor-like activity through optical phase mapping conduction. Their visualized signal analysis suggested that the formation of spiral waves was associated with heterogeneity in tissue conduction and refractory periods, which could be understood as electrical remodeling of the atria. After that, Hansen et al. employed the optical mapping techniques using three high-resolution CMOS cameras to investigate activation patterns and transmural conduction in *ex vivo* human right atria in 2015, enabling the firstly capturing re-entrant drivers on sub-endo mapping and then the visualized re-entry or 'breakthrough' patterns on sub-Epi mapping. The study revealed a delay in active potential during transmural conduction, along with various forms of "rotor" between the endo- and epicardium, including spiral-wave re-entry patterns, stable foci, and breakthroughs, as well as spatially unstable breakthroughs.

Multi-electrode catheters were applied in manual mapping to detect and visually identify rotor-like activations. Narayan et al. pioneered the rotor-guiding ablation approach in clinical studies with the "Focal Impulse and Rotor Modulation (FIRM)" method, as published in the landmark 2012 CONFIRM study. This study employed a panoramic mapping system consisting of a 64-electrode basket catheter, coupled with the RhythmView analysis system. Subsequent advancements in mapping technology have facilitated the evaluation of the STD-guiding ablation strategy on various platforms, including ECVUE, CartoFinder, ECGI, RADAR, among others. These systems have contributed to the enhanced analysis of spatial/temporal dispersion activations and possess the potential to guide ablation strategy more effectively.

Mechanisms of STD ablation

In this meta-analysis, the additional STD-guided ablation suggested a higher incidence of FFATAs, FFAF, and AF termination compared to the conventional adjunctive ablation approach, implying potential mechanisms for intervening in the maintenance of AF.

With the application of FIRM, Shivkumar's study demonstrated that the rotor and focal drivers in the left atria were located adjacent to the PV antrum and posterior wall/coronary sinus in 39% and 28% of cases, respectively. In Haïssaguerre's study, using a noninvasive mapping system (ECVUE), the prevalence of reentrant drivers involving the left PV appendage and right PV regions was found to be 97% and 94%, respectively, revealing focal breakthroughs specifically originating from the PV ostia as well as both the right and left appendages. In the study by Ríos-Muñoz et al., utilizing ultra-high-density mapping, patients with focal and Rotational Activity (RAc) outside the region of Wide Area Circumferential Pulmonary Vein Isolation (WACPVI) exhibited a higher recurrence rate of atrial

fibrillation compared to those with all RAc confined within WACPVI or none.

The aforementioned studies indicated that the mechanisms of these conventional approaches, including PVI as a cornerstone of catheter ablation for atrial fibrillation, may be related to the ablation and isolation of the "drivers". This hypothesis is supported by the study of Kumagai et al., published in 2020. They performed posterior left atrial Box Isolation (BOXI) in addition to PVI for patients with NPAF, yielding significant findings. The results demonstrated that BOXI led to a decrease in observed rotors and multiple wavelets.

Therefore, "drivers" are considered to be one of the essential maintenance mechanisms of AF, manifesting in one form as spatial/temporal dispersion activation patterns.

The challenge of STD mapping

In our study, the statistical outcome of FFATAs was only observed in the non-FIRM sub-group, which may be attributed to differences in mapping systems. The five mapping systems we evaluated vary in terms of signal acquisition electrodes and matching algorithms, having evolved over the past decade. This variation contributes to discrepancies in identifying "drivers", which can be attributed to the diversity in pseudo "driver" filtration, potentially accounting for the substantial heterogeneity observed in rates of FFATAs, FFAF, and AF termination. It should be noted that not every identified "driver" we ablated resulted in AF termination, leading to academic controversy regarding electrical guided ablation despite some studies successfully establishing an association between post-procedural atrial arrhythmias and driver-guided ablation. Therefore, achieving accurate identification of active drivers and passive waves is crucial for effective electrical guided ablation. This imposes a higher demand on non-invasive panoramic active mapping systems, which are unable to directly measure intracardiac potentials.

With the electrical characteristics of rotor drift and the transition of endo-epicardial re-entrant-breakthrough-dissociated activation patterns, the collision of rotational core causes the regional frequency-dependent refractory period of rapid shift, which makes the positioning of the rotor dynamically change. This poses challenges in active rotor identification, particularly in the context of non-panoramic mapping approaches. The studies conducted by Jadidi, Kumagai, and Hu X adopted minimum potential capture durations of 5, 6 to 8, and 10 seconds, respectively. The brief duration of catheter placement at each site for precise STD localization remains a subject of controversy.

How to effectively perform a comprehensive mapping of STD is a crucial aspect, with easily overlooked areas such as the pulmonary vein ostia being one of the key regions. Diverse mapping strategies and experiences diversify mapping outcomes. The study conducted by Pappone et al., demonstrated a significantly higher rate of identification for 'drivers' near the pulmonary vein antra, with 40% compared to the 18% and 19% reported in the studies by Spitzer and Tilz, respectively.

Does homogenizing ablation have equivalent efficacy to area circumferential ablation in targeting the anatomical regional STD? The study by Tilz et al., revealed that employing a STD-guided ablation alone resulted in suboptimal outcomes, potentially attributed to the limited efficacy of driver ablation in precisely targeting deep regions within the PVs, which is otherwise comparable to segmental PVs isolation and susceptible to PVs stenosis. The randomized study conducted by Mohanty et al. demonstrated that the PVI+FIRM strategy resulted in a significant increase in AF/AT-free rates compared to the FIRM only group during a 12 ± 7 month follow-up period. Meanwhile, a part of studies included in this meta-analysis did not disclose the details of contact force irrigation catheters available, which impacted the outcomes related to the efficiency of PVI.

Thus, it is crucial not to overlook the deep drivers within the PVs, that are responsible for our proposed integrated approach of PVI plus STD-guided ablation.

Durable transmural injury following ablation is a crucial factor to consider. Park's study revealed that the lesions created by radiofrequency ablation exhibit a higher recovery rate than previously anticipated. Short-term recurrence rates were calculated as 72.3%, 30.2%, 41.0%, and 33.3% for the roof line, postero inferior line, anterior line, and left lateral isthmus line, respectively, indicating an inferior long-term effectiveness compared to ablation in the pulmonary vein antrum region. Consequently, the challenge lies in maintaining a durable transmural lesion while also striving to enhance the efficacy of radiofrequency ablation for STD targets. Novel ablation energy sources may hold greater promise STDCA.

CONCLUSION

The pooled estimate indicated that the PVI+STDCA strategy may confer benefits in maintaining sinus rhythm for patients with NPAF, compared to the PVI+CCA protocol, during mid- and long-term follow-up, while ensuring comparable safety. Improved driver mapping methods and robust data from RCTs are necessary.

LIMITATIONS

Although the PVI+STDCA approach has yielded promising results, it is crucial to consider certain limitations in our meta-analysis. Substantial heterogeneity was observed in a portion of the study's outcomes, primarily due to the development of STD recognition and mapping systems. To address this concern, we conducted subgroup analyses based on catheter type, control group variation, exclusive NPAF enrollment, and study design, aiming to minimize heterogeneity.

Meanwhile, the evaluation of the PVI+STDCA strategy was slightly compromised due to the unavailability of statistical analysis on PVs reconnection.

Additionally, this meta-analysis lacks an adequate number of high-quality RCTs, particularly those conducted in novel energy sources, which are essential for inclusion in our future studies.

AUTHOR CONTRIBUTIONS

The study was conceived and designed by Min Xu. Data extraction was performed by Qidong Gao, Sitai Liu and Yunfeng Di. Quality assessment and statistical analysis of the data were conducted by Hanlin Wang. The initial draft of the manuscript was prepared by Min Xu. Dayong Zhang critically reviewed the manuscript and provided valuable suggestions during revision. All authors contributed to writing this manuscript.

DISCLOSURES

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