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CLINICAL RESEARCH

Pulmonary vein isolation with or without empiric superior vena cava isolation in patients undergoing ablation for paroxysmal atrial fibrillation: the randomized ESVCI-AF trial

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Aims The superior vena cava (SVC) has been implicated as a non-pulmonary vein trigger in the initiation and maintenance of atrial fibrillation (AF). However, the incremental benefit of empiric SVC isolation (SVCI) in addition to pulmonary vein isolation (PVI) for paroxysmal AF (PAF) remains inconclusive. This study aimed to determine whether adding empiric SVCI to PVI improves freedom from atrial arrhythmia (ATA) recurrence in patients with PAF.

Methods and results A total of 302 patients with PAF, aged 18–75 years, undergoing index ablation, were enrolled and randomized in a 1:1 ratio to either the PVI plus SVCI group or the PVI alone group between May 2021 and February 2024. In the PVI plus SVCI group, PVI was performed first, followed by empiric SVCI. In the PVI alone group, only PVI was performed. Among 302 randomized patients [median (IQR) age, 64.9 (56.0–70.0) years, 165 men (54.6%)], 302 (100%) completed the 3-month blanking period and contributed to the efficacy analysis. After a median follow-up of 20 months, the recurrence of rate of ATAs did not differ significantly between the PVI plus SVCI group (20/151 patients, 13.2%) and PVI alone group (29/151, 19.2%) without taking antiarrhythmic drugs (hazard ratio, 0.68, 95% confidence interval 0.38–1.20, $P = 0.182$). Subgroup outcomes analysis further demonstrated no significant interaction across subgroups.

Conclusion Among patients with PAF undergoing initial ablation, the addition of empiric SVCI to PVI, compared with PVI alone, did not significantly improve freedom from ATA recurrence.

Clinical trial registration This study was registered with Chinese Clinical Trials Registry: ChiCTR220005554.

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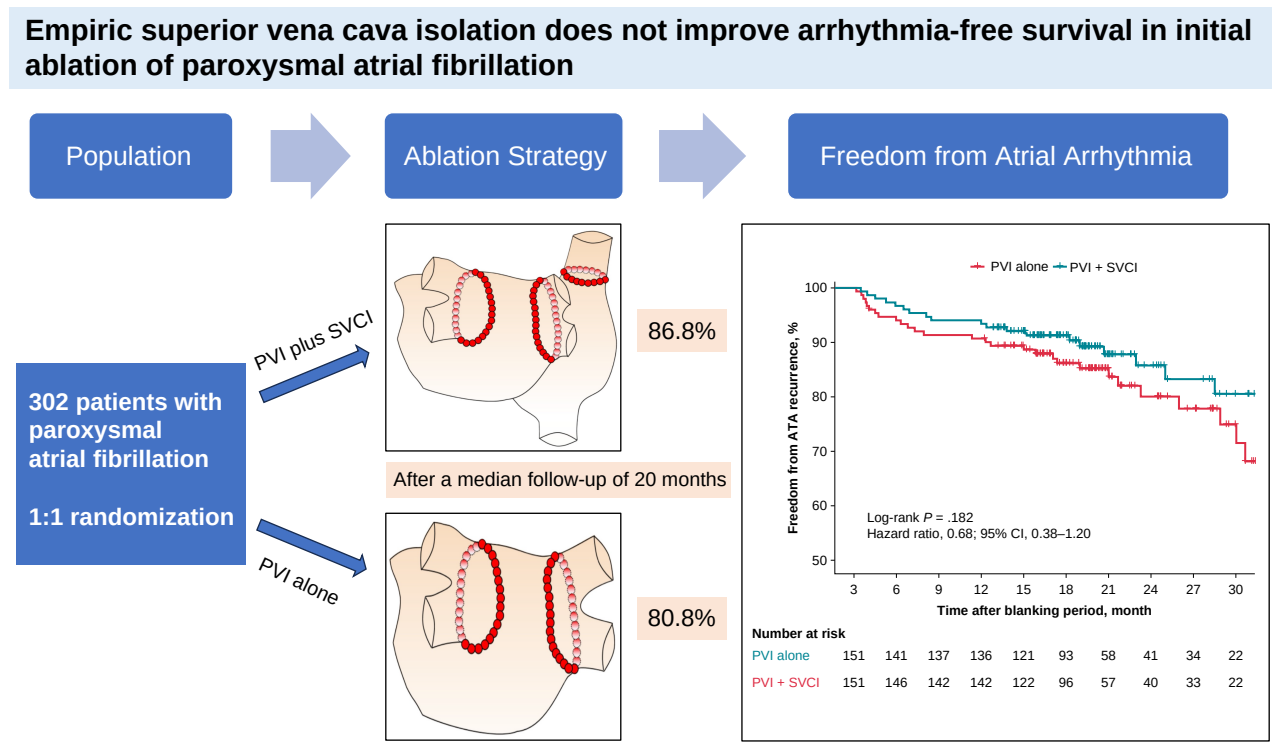
Graphical Abstract



Keywords Sinus vena cava • Radiofrequency ablation • Non-pulmonary vein trigger • Incidence • Recurrence

What's new?

- This is a prospective, multicentre, randomized trial evaluating the incremental benefit of empiric superior vena cava isolation (SVCI) in addition to pulmonary vein isolation (PVI) for patients with paroxysmal atrial fibrillation undergoing first-time ablation ($n = 302$).
- Over a median follow-up of 20 months, the addition of empiric SVCI did not result in a statistically significant reduction in atrial arrhythmia recurrence compared to PVI alone, suggesting a lack of value of routine empiric SVCI.
- A trend towards reduced recurrence with PVI plus SVCI in female patients was observed; however, limited sample size precludes definitive conclusions, underscoring the need for larger studies to explore sex-specific ablation strategies.

Introduction

Atrial fibrillation (AF) is the most prevalent sustained arrhythmia and is a major contributor to cardiovascular morbidity and mortality.[1,2] Pulmonary vein isolation (PVI) remains the cornerstone of catheter ablation for symptomatic paroxysmal AF (PAF), offering superior rhythm control compared to antiarrhythmic drugs.[3–5] Despite advances in ablation technology, a significant proportion of patients experience arrhythmia recurrence, which may be driven by triggers from non-pulmonary vein foci. These include the superior vena cava (SVC), crista terminalis, ligament of Marshall, coronary sinus (CS), and left atrium posterior wall.[6–8] Among these, the SVC has been identified as a frequent site of ectopic trigger, accounting for approximately 30% of non-PV triggers,[9,10] thus prompting interest in provocation protocols and adjunctive ablation strategies such as SVC isolation (SVCI).

Superior vena cava isolation was initially proposed as a strategy to mitigate AF recurrence in cases where the SVC serves as an arrhythmogenic source. However, the routine application of empiric SVCI in addition to PVI remains controversial, given the inconsistent findings across studies.[11–15] Notably, these prior investigations have varied considerably in study populations, ablation technologies, and procedural methodologies, thereby limiting the generalizability of their results. To address this uncertainty, we initiated a prospective, multicentre, randomized trial to evaluate whether PVI combined with empiric SVCI provides superior efficacy compared to PVI alone in patients with PAF.

Methods

Trial design and study population

The clinical trial was an investigator-initiated, multicentre, single-blind, randomized study in which the efficacy of PVI combined with empiric SVCI was assessed in patients with PAF. The study was conducted in eight tertiary hospitals in mainland China. The trial was developed by the first and last authors in collaboration with steering committee. The full protocol and statistical analysis are available in Supplementary material online, *Supplement S1*. All participants provided written informed consent before enrolment. Ethics approval was obtained from the institutional review boards of each participating centre. This study was conducted in accordance with the Consolidated Standards of Reporting Trials (CONSORT) guideline.

Patients were eligible for enrolment if they were age 18–75 years, diagnosed with PAF. Detailed inclusion and exclusion criteria are shown in Supplementary material online, *Supplement S1*. From May 2021 through February 2024, patients who provided informed consent for

radiofrequency catheter ablation were recruited and randomly assigned to undergo either PVI plus SVCI or PVI alone.

Randomization and blinding

Eligible patients were enrolled and randomized in a 1:1 ratio to either the PVI plus SVCI group or the PVI alone group using a centralized, computer-generated randomization sequence managed by Nanjing Drum Tower Hospital. This clinical trial was designed as a single-blind study. All patients were masked to their treatment assignment to minimize bias in symptom reporting, though operators cannot be blinded due to the procedural nature of the intervention.

Interventions

All antiarrhythmic medications were discontinued for five half-lives before the procedure. Patients assigned to PVI plus SVCI underwent PVI first, followed by SVCI. The geometry of the right atrium and SVC was constructed during sinus rhythm after PVI. The anatomical site of sinoatrial node was identified by activation mapping. Superior vena cava angiography was performed to confirm ostium of SVC combined with 3-D map of RA and SVC. High-voltage pacing (bipolar pacing 20 mA at 2 ms) was used to localize the course of the right phrenic nerve, which was marked on the 3-D map to minimize the risk of phrenic nerve injury (PNI). Superior vena cava isolation was performed 5–10 mm above sinoatrial node. On the free wall adjacent to phrenic nerve, high-power (40–45 W, contact force < 10 g), ablation index (AI)–guided ablation (AI target = 300) was applied cautiously. Further technical details have been described elsewhere[5,16] and in Supplementary material online, *Supplement S1*. The procedural endpoints were the achievement of bidirectional conduction block in both the pulmonary veins and the SVC. In both randomized groups, further ablation was performed if concomitant arrhythmia was identified, including atrial tachycardia, typical flutter and paroxysmal supraventricular tachycardias.

All ablations in the study were performed utilizing three-dimensional mapping system (CARTO3, Biosense-Webster Inc) with irrigated-tip, contact force catheters (ThermoCool SMARTTOUCH Catheter or ThermoCool SMARTTOUCH Surround Flow Catheter, Biosense-Webster Inc.) in power control mode. Ablation index was used to guide lesion quality, with target values of 500–550 for the anterior wall and 350–400 for the posterior wall in the PVs. An AI target of 350 was employed in SVC except at sites near the phrenic nerve.

Follow-up

Patients were discharged from the hospital within 48 h post-ablation. Oral anticoagulation therapy was maintained for a minimum of three months in all patients. Beyond this period, the decision to continue oral anticoagulation was guided by the patient's CHA_2DS_2-VASc score. Antiarrhythmic drugs were discontinued 3 months post-procedure. Continuous single-lead electrocardiographic monitoring was maintained for all patients throughout the duration of their hospitalization. The 24 h Holter recordings were performed at 3 and 6 months after the index procedure, and 7-day Holter recordings were employed at 12 months for all of the participants. In the subsequent years, clinic visits and 24 h Holter recordings were conducted every 6 months thereafter. Additional surface electrocardiograms (ECGs) or 24 h Holter monitoring were performed if patients reported symptoms suggestive of arrhythmic episodes. All follow-up assessments were conducted by the study personnel who were blinded to the treatment assignments.

Outcomes

The primary endpoint of the study was freedom from documented atrial arrhythmias (ATA) lasting >30 s without antiarrhythmic drugs following a single ablation procedure. Atrial arrhythmias included AF, atrial flutter, or atrial tachycardia, confirmed by 12-lead ECG or Holter monitoring during scheduled follow-up visits or symptomatic episodes reported by patients. During a 3-month blanking period, early recurrences were not counted as endpoint events. Arrhythmic events were adjudicated by an independent, blinded committee to ensure objectivity.

Secondary endpoints included the following: (i) freedom from ATA recurrence in prespecified subgroups defined by age, sex, hypertension, coronary artery disease (CAD), body mass index (BMI), and left atrial diameter (LAD); (ii) procedural characteristics, including total procedure time, radiofrequency application time, and fluoroscopy time; and (iii) safety outcomes, encompassing procedure-related complications.

Statistical analysis

The sample size for this study was determined to ensure sufficient power to compare participation between the PVI plus SVCI and PVI alone groups. Participants were equally allocated to the two randomization groups. Based on prior study,[17] and using PASS 15 software, a sample size of 137 participants per group was calculated, assuming an alpha level of 0.05, a power of 0.80, and a 12-month arrhythmia-free survival rate of 75% in the PVI alone group and 88% in the PVI plus SVCI group, respectively. To account for a potential dropout rate of 10%, this number was adjusted to 152 participants per group. Consequently, the total sample size required for the study was 304 participants.

The primary endpoint was performed according to the intention-to-treat (ITT) principle, including all randomized patients in their assigned groups regardless of protocol adherence. Kaplan–Meier survival curves were plotted, and log-rank test was used to evaluate cumulative recurrence incidence of ATA. Cox proportional hazards models were established to calculate hazard ratios (HRs) and 95% confidence intervals (CIs). Stratified analyses and interaction tests were performed across key demographic and clinical variables.

Secondary endpoints, including procedural characteristics and complication rates, were compared using descriptive statistics and appropriate tests. Baseline characteristics were summarized descriptively: continuous variables were reported as means with standard deviations (SDs) or medians with interquartile ranges (IQR), depending on distribution, and categorical variables as frequencies with percentages. Between-group comparisons of baseline data were used *t*-tests or Wilcoxon rank-sum tests for continuous variables and χ^2 or Fisher exact tests for categorical variables to confirm randomization balance. The interaction effects of Cox regression across different subgroups were analysed using subgroup MultiCOX function. Statistical significance was set at a two-sided $P < 0.05$. All Analyses were conducted using R (version 4.3.0).

Results

Baseline characteristics

A total of 302 patients [median (IQR) age, 64.9 (55.0–70.0) years, 165 men (54.6%)] were enrolled and randomized either to the PVI plus SVCI group or the PVI alone group (*Figure 1*). Among these patients, 302 (100%) completed the 3-month blanking period and were included in the primary analysis. The baseline demographic and clinical characteristics were well-balanced between PVI plus SVCI and the PVI alone (*Table 1*).

Primary outcomes

After a median follow-up of 20 months, the primary endpoint—freedom from documented ATAs lasting more than 30 s without antiarrhythmic drugs after a single ablation procedure—did not differ significantly between two groups. Atrial arrhythmia recurrence occurred in 20 of 151 patients (13.2%) in the PVI plus SVCI group and 29 of 151 patients (19.2%) in the PVI alone group (HR, 0.68; 95% CI, 0.38–1.20; $P = 0.182$). Kaplan–Meier analysis confirmed no significant divergence in arrhythmia-free survival between groups over the follow-up period (*Figure 2*).

Secondary outcomes

Procedural data were available for all 302 patients (*Table 2*). Procedural characteristics were comparable between the PVI plus SVCI and PVI alone groups. Concomitant ablation occurred in 7.9% vs. 9.9%. Median procedure time was 126.3 min (IQR, 110.0–150.0) vs. 120.0 min (IQR, 98.0–150.0), with SVCI adding 5.0 min (IQR, 3.5–6.0). Fluoroscopic time (5.0 vs. 4.0 min) and first-pass isolation rates (right pulmonary vein: 65.6% vs. 60.3%; left pulmonary vein: 55.1% vs. 56.3%) were similar. Radiofrequency delivery times between two groups showed no notable differences.

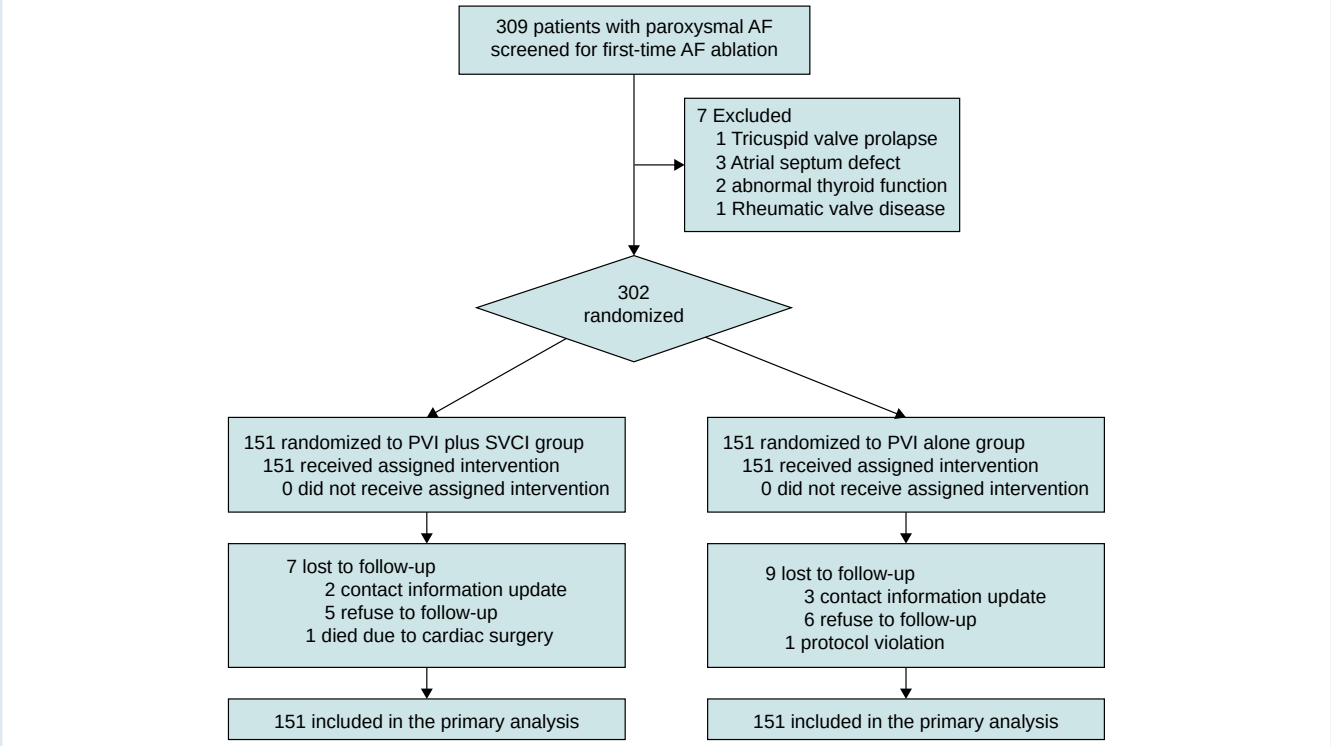


Figure 1 Patient enrolment and study flow.

Table 1 Baseline characteristics of the study population

Characteristic	No. (%)		*P* value
	PVI + SVCI (*n* = 151)	PVI alone (*n* = 151)	
Sex			
Male	88 (58.3)	77 (51.0)	0.204
Female	63 (41.7)	74 (49.0)	
Age, median (IQR), y	63.0 (55.0, 69.0)	65.9 (57.0, 71.0)	0.186
<65	83 (55.0)	68 (45.0)	0.084
≥65	68 (45.0)	83 (55.0)	
BMI, mean (SD)	24.6 (2.9)	24.7 (2.9)	0.897
<25	86 (57.0)	77 (51.0)	0.299
≥25	68 (43.0)	74 (49.0)	
LAD, median (IQR), mm	4.1 (3.7, 4.3)	4.0 (3.7, 4.4)	0.676
<45	124 (82.1)	119 (78.8)	0.468
≥45	27 (17.9)	32 (21.2)	
Hypertension	41 (27.2)	37 (24.5)	0.599
Diabetes	15 (9.9)	12 (7.9)	0.545
CAD	30 (19.9)	24 (15.9)	0.368
Ischaemic stroke or TIA	10 (6.6)	8 (5.3)	0.471
CHADS-VASc score, mean (SD)	2.6 (1.3)	2.3 (1.0)	0.853
LVEF, median (IQR), %	61.0 (58.2, 63.0)	60.3 (58.5, 63.0)	0.597
Concomitant arrhythmia	18 (11.9)	19 (12.6)	0.861

PVI, pulmonary vein isolation; SVCI, superior vena cava isolation; BMI, body mass index; LAD, left atrium diameter; CAD, coronary artery disease; TIA, transient ischaemic attack; LVEF, left ventricle ejection fraction.

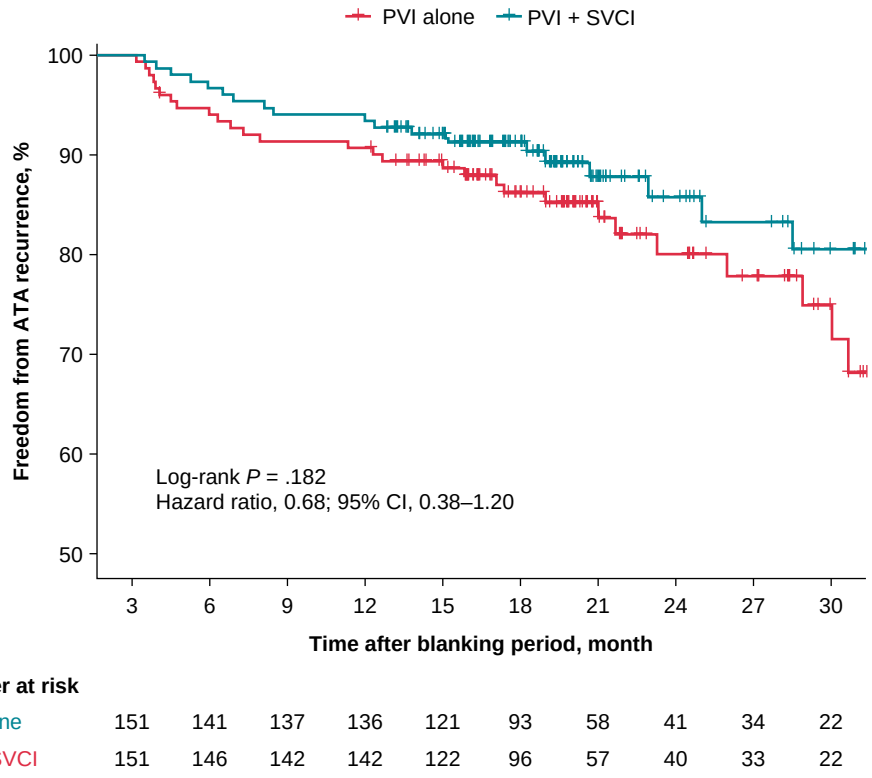


Figure 2 Kaplan–Meier curves of the primary outcome. The analysis was performed in randomized patients who remained in follow-up after the 3-month blanking period. Follow-up times are expressed in months following the end of the 3-month blanking period. Number at risk indicates the number of patients remaining at risk at the indicated follow-up times.

Table 2 Procedural characteristics

Characteristic	No. (%)		
	PVI plus SVCI ($n = 151$)	PVI alone ($n = 151$)	*P* value
Concomitant arrhythmia ablation	12 (7.9)	15 (9.9)	0.545
CTI ablation	5 (3.3)	7 (4.6)	0.556
Cardioversion after PVI	5 (3.3)	3 (2.0)	0.474
Total procedure time, median (IQR), min	126.3 (110.0, 150.0)	120.0 (98.0–150.0)	0.118
Total fluoroscopic time, median (IQR), min	5.0 (3.31, 6.66)	4.0 (3.0, 6.5)	0.023
First-pass isolation			
RPV	99 (65.6)	91 (60.3)	0.341
LPV	83 (55.1)	85 (56.3)	0.817
RPV RF delivery time, median (IQR), min	14.7 (12.0, 19.0)	15.0 (12.0, 20.0)	0.742
LPV RF delivery time, median (IQR), min	13.0 (10.4, 16.9)	14.0 (11.5, 17.0)	0.413
SVC RF delivery time, median (IQR), min	5.0 (3.5, 6.0)	0	*
Phrenic nerve paralysis during procedure	0	0	–

PVI, pulmonary vein isolation; SVCI, superior vena cava isolation; CTI, cavotricuspid isthmus; RF, radiofrequency; RPV, right pulmonary vein; LPV, left pulmonary vein.

Prespecified subgroup outcomes

Prespecified subgroup analyses of the primary outcome revealed no significant interactions (*Table 3*). In women, recurrence rates were 9 of 63 (14.3%) in the PVI plus SVCI group vs. 22 of 74 (29.7%) in the PVI alone group (HR, 0.47; 95% CI, 0.21–1.02; $P = 0.055$; interaction $P = 0.097$). For patients aged ≥65 years, recurrence was 8 of 68 (11.8%) vs. 19 of 83 (22.9%) (HR, 0.52; 95% CI, 0.23–1.19; $P = 0.121$). No significant differences emerged in patients with

Table 3 Primary outcomes in prespecified subgroups

Subgroup	No./total no.		HR (95% CI)	*P* value	Interaction *P* value
	PVI + SVCI ($n = 151$)	PVI alone ($n = 151$)			
Male	11/88	8/77	1.26 (0.51–3.14)	0.616	0.097
Female	9/63	21/74	0.47 (0.21–1.02)	0.055	
≥65 y	8/68	19/83	0.52 (0.23–1.19)	0.121	0.276
<65 y	12/83	10/68	0.98 (0.42–2.28)	0.966	
Hypertension	7/41	5/37	1.33 (0.42–4.23)	0.750	0.190
No hypertension	13/110	24/114	0.54 (0.28–1.06)	0.074	
CAD	4/30	1/24	2.44 (0.27–22.50)	0.431	0.185
No CAD	16/121	29/127	0.58 (0.31–1.06)	0.079	
BMI ≥ 25	9/65	15/74	0.67 (0.29–1.52)	0.336	0.939
BMI < 25	11/86	14/77	0.70 (0.32–1.54)	0.289	
LAD ≥ 45	3/27	8/32	0.34 (0.09–1.29)	0.234	0.339
LAD < 45	17/124	21/119	0.79 (0.42–1.50)	0.467	

PVI, pulmonary vein isolation; SVCI, superior vena cava isolation; HR, hazard ratio; CAD, coronary artery disease; BMI, body mass index; LAD, left atrium diameter.

hypertension (HR, 1.33; 95% CI, 0.42–4.23; $P = 0.633$) vs. without (HR, 0.54; 95% CI, 0.28–1.06; $P = 0.074$; interaction $P = 0.190$), nor across other subgroups including CAD, BMI, or LAD.

Safety outcomes

The periprocedural adverse events are shown in *Table 4*. The periprocedural complications were infrequent and comparable between groups. Cardiac tamponade occurred in two patients in the PVI plus SVCI group and in one patient in the PVI-alone group. One case in the PVI plus SVCI group required pericardiocentesis, while the remaining two cases were managed conservatively and resolved spontaneously under close observation. A single patient (0.6%) in the PVI plus SVCI group experienced post-procedural phrenic nerve paralysis, which fully resolved within 6 months.

Discussion

Main findings

In this multicentre, prospective, randomized clinical trial of patients with PAF undergoing initial ablation, the addition of empiric SVCI to PVI did not significantly improve freedom from ATA recurrence compared to PVI alone after a median follow-up of 20 months. Although this lack of benefit was consistently observed across all prespecified subgroups, a trend towards an AF recurrence reduction was observed among women in the PVI plus SVCI group. High-power ablation with a restricted AI during SVCI was associated with a reduced risk of PNI.

Outcome

The rationale for incorporating SVCI into PVI is based on the recognition of the SVC as a non-pulmonary vein trigger implicated in AF initiation and perpetuation,[18–20] as well as the myocardial sleeves within the SVC that exhibit automaticity and triggered activity.[21–23] Observational studies have frequently identified the SVC as a source of non-PV triggers contributing to AF recurrence and have reported the efficacy of SVCI in patients with AF.[12,20] However, small randomized trials investigating empiric SVCI have yielded conflicting results. A subgroup analysis from a randomized trial by Corrado *et al.*[24] showed that PVI combined with empiric SVCI was superior to PVI in patients with PAF, achieving a higher success rate over one year (90% vs. 77%, $P = 0.04$). By contrast, studies by Wang *et al.*[11] and Da Costa *et al.*[25] found no significant clinical benefit from adding empiric SVCI to PVI. This discrepancy may be attributed to differences in sample size, procedural methodology, and standardization. For example, Da Costa *et al.* used remote magnetic navigation, whereas Corrado *et al.* and Wang *et al.* utilized conventional manual ablation techniques. Our multicentre trial, with a robust sample size and extended follow-up, provides a higher level of evidence and supports the conclusion that empiric SVCI does not offer significant additional benefit over PVI alone in patients with PAF (*Figure 2*). Most recently, a meta-analysis from Mariani *et al.*[14] reported a 46% reduction in AF recurrence with PVI plus empiric SVCI compared to PVI alone. This significant reduction was largely driven by the inclusion of the recent study by Dong *et al.*,[15] which employed a provocation-guided approach and differed substantially in methodology from the three aforementioned trials, thereby introducing heterogeneity that may limit the generalizability of the pool effect. In comparison with the trial by Dong *et al.*, our study applied empiric SVCI without provocation testing, thus investigating the generalizability of empiric SVCI in broader PAF population, rather than its efficacy specifically in patients without SVC trigger. Despite these methodological differences, both studies consistently demonstrated no significant improvement in AF-free survival with empiric SVCI among PAF patients without identifiable SVC triggers or in the absence of provocation testing, underscoring the importance of individualized patient selection rather than routine application. Together, these complementary findings provided a more comprehensive perspective, enhancing our overall understanding of empiric SVCI in patients with PAF. Additionally, other energy sources have been explored to assess the efficacy and safety in SVCI. The CAVAC-AF trial demonstrated that cryoballoon-based SVCI isolation in conjunction with PVI did not improve 12-month freedom from atrial tachyarrhythmia and was associated with a significantly higher incidence of complications.[13] Taken together, these findings do not support routine SVCI during first-time catheter ablation in patients with PAF.

Clinical relevance in selected population

Although empiric SVCI did not demonstrate a universal benefit, it may be advantageous in selected patients with AF who exhibit specific

Table 4 Periprocedural adverse events

Adverse event	No. (%) PVI plus SVCI ($n = 151$)	No. (%) PVI alone ($n = 151$)	*P* value
Cardiac			
Tamponade	2 (1.3)	1 (0.6)	1.000
Needing pericardiocentesis	1 (0.6)	0	1.000
Needing cardiac surgery	0	0	–
Pericarditis	3 (2.0)	2 (1.3)	1.000
Atrioventricular conduction block	0	0	–
Vascular			
Pseudoaneurysm	3 (2.0)	2 (1.3)	1.000
Arteriovenous fistula	0	0	–
Deep venous thrombosis	0	1 (0.6)	1.000
Other			
Post-procedural fever	4 (2.6)	2 (1.3)	0.684
Drug-related sinus bradycardia	1 (0.6)	0	1.000
Phrenic nerve paralysis	1 (0.6)	0	1.000
Atrio-oesophageal fistula	0	0	–
Ischaemic stroke	0	0	–
Intracranial haemorrhage bleeding	0	0	–
Death	0	0	–

PVI, pulmonary vein isolation; SVCI, superior vena cava isolation.

arrhythmogenic or structural characteristics. A previous study from Chang *et al.*[26] reported a 73% rate of AF freedom at 5-year follow-up following a single SVCI procedure, without PVI, in patients with SVC-triggered AF. Similarly, Dong *et al.* observed a 93.3% of AF-free rate at 12-month follow-up in patients with PAF and identifiable SVC triggers who underwent SVCI in addition to PVI. Furthermore, studies of Dong *et al.*[15] and Higuchi *et al.*[27] reported that SVC triggers are more frequently observed in AF patients with longer SVC sleeves and larger SVC potentials. These findings suggested that the arrhythmogenic potential within SVC myocardial sleeves was heterogeneous rather than universally present. In our present study, subgroup analysis indicated a trend towards potential benefit of SVCI in female patients (29.7% vs. 14.3%; HR, 0.47; 95% CI, 0.21–1.02; $P = 0.055$). However, the limited number of female participants ($n = 137$) underscores the need for the larger studies to confirm this observation. Several prior studies have also investigated the predictors of an arrhythmogenic SVC. In a study by Lee *et al.*,[28] female sex was found to be the only independent risk associated with the presence originating from SVC ectopic firing. Collectively, these findings advocate for a more individualized approach in which SVCI is selectively applied based on optimized electrophysiological mapping, provocation testing or patient-specific characteristics, rather than routine empirical application in all individuals undergoing ablation.

Safety and complications

Safety outcomes in our study demonstrated a low rate of phrenic injury and no cases of sinus node injury (*Table 4*). Previous studies have reported PNI during SVCI in 0.17–2.1% of cases.[29,30] In our protocol, high-output pacing (20 mA) at the posterolateral site of SVC was used to localized the course of phrenic nerve, followed by high-power ablation (45 W, AI = 300) to minimize the risk of phrenic injury. In the present study, no cases of permanent PNI were observed. One patient developed phrenic nerve palsy post-ablation, which fully resolved within 6 months. Similarly, a study by Yamaji *et al.*[31] suggested that high-power, short-duration ablation (50 W, 7 s) may offer optimal protection, with no phrenic injuries observed in their cohort (0/160 patients). Pulsed electric field, a non-thermal novel energy source, for SVCI warrants further investigation as a potential approach to improve efficacy and safety.[32–35]

Limitations

Several limitations of this study should be acknowledged. First, the absence of continuous monitoring with invasive recorders may have underestimated the true incidence of ATA recurrence, especially asymptomatic episodes. Second is the lack of adenosine and isoproterenol testing to assess the durability of SVCI, which may have missed transient reconnections, potentially affecting the evaluation of SVCI efficacy. Third, although our multicentre design and sample size ($n = 302$) enhance the robustness and generalizability of the findings, the study was not powered for subgroup analyses, particularly in female patients ($n = 137$), limiting the conclusions about sex-specific effects. Finally, the single-blind design may introduce operator bias, a common challenge in ablation trials.

Conclusion

Among patients with PAF undergoing initial ablation, the addition of empiric SVCI to PVI, compared with PVI alone, did not significantly improve freedom from ATA recurrence. The present findings do not support routine empiric SVCI for the treatment of patients with PAF.

Supplementary material

Supplementary material is available at *Europace* online.

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Conflict of interest: none declared.

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Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

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