



ORIGINAL ARTICLE

Pulmonary vein isolation plus left atrial posterior wall isolation and additional nonpulmonary vein trigger ablation using high-dose isoproterenol for long-standing persistent atrial fibrillation

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Abstract

Background: Little evidence exists regarding the endpoint and optimum approach to catheter ablation for long-standing persistent atrial fibrillation (LSPAF). We examined the efficacy of pulmonary vein isolation (PVI) plus left atrium posterior wall isolation (PWI) and additional non-PV trigger ablation using high-dose isoproterenol for LSPAF.

Methods: One-hundred and fifty-five patients (median AF duration, 36 months) underwent catheter ablation for LSPAF; After PVI plus PWI, they underwent provocation of non-PV triggers by high-dose isoproterenol and were divided into 3 groups based on the results: group A, PVI plus PWI alone, without induced non-PV triggers (single procedure: 105 patients, multiple procedures: 90 patients); group B, mappable non-PV triggers demonstrated and ablated (single procedure: 41 patients, multiple procedures: 45 patients); group C, if non-PV triggers were unmappable or could not be induced in repeated procedures, adjunctive complex fractionated atrial electrogram ablation was performed (single procedure: 9 patients, multiple procedures: 20 patients).

Results: The Kaplan-Meier estimate of the 1-year freedom from atrial tachyarrhythmias without antiarrhythmic drugs was 65% in all patients, (73%, 56%, and 11% in groups A, B, and C, respectively) after a single procedure, which improved to 86% in all patients (93%, 86%, and 53% in groups A, B, and C, respectively) after multiple procedures.

Conclusion: Even for LSPAF, in approximately 60% of patients, non-PV triggers were not elicited, and PVI plus PWI alone achieved good outcomes. Although the inducibility of non-PV triggers was associated with recurrence of atrial tachyarrhythmias, additional non-PV trigger ablation may improve the outcome after multiple procedures.

KEYWORDS

atrial fibrillation, catheter ablation, nonpulmonary vein triggers, posterior wall isolation, pulmonary vein isolation

1 | INTRODUCTION

Catheter ablation of patients with long-standing persistent atrial fibrillation (LSPAF) is challenging, and little evidence is available regarding the endpoint and optimum approach to catheter ablation.¹ To improve ablation outcomes, adjunctive ablation methods in addition to pulmonary vein isolation (PVI) have been described. However, the STAR AF II trial revealed that the outcomes of LSPAF patients are not improved with either empiric linear ablation or complex fractionated atrial electrogram (CFAE) ablation.² Furthermore, which patients respond to PVI alone and which additional ablation approach improves the outcome remain unclear. In contrast, left atrium posterior wall isolation (PWI) and nonpulmonary vein (PV) trigger ablation were reported as additional ablation methods.³⁻⁶ However, few studies have so far examined the efficacy of these methods for LSPAF. In this study, we examined the efficacy of PVI plus PWI with additional ablation of non-PV triggers induced by the administration of high-dose isoproterenol in patients with LSPAF.

2 | METHODS

2.1 | Patient population and data collection

The subjects of this retrospective study were 159 consecutive patients who underwent catheter ablation for drug-refractory LSPAF at our institution from January 2012 to June 2016. LSPAF was defined as continuous AF lasting ≥ 12 months. Of the 159 patients, 2 with less than 3 months' follow-up after the last ablation procedure and 2 who received antiarrhythmic drugs (AADs) for ventricular arrhythmia were excluded, leaving 155 patients. All patients gave their written informed consent for the ablation procedure and enrollment in our ablation registry. This study was approved by our institutional review board.

2.2 | Ablation protocol during the initial procedure

AADs were discontinued at least five half-lives before the procedure. All patients underwent a transesophageal echocardiogram before ablation to exclude left atrial thrombus. Warfarin was continued, and direct oral anticoagulant (DOAC) administration was interrupted just one dose before the procedure. The procedure was performed under deep sedation with midazolam and continuous infusion of propofol. Four venous access sites were obtained: 3 in the right femoral vein and 1 in the right subclavian vein. Heparin was administered to maintain an activated clotting time of 250-350 seconds during the procedure. A 20-pole catheter with intracardiac defibrillation capability

was inserted into the coronary sinus (CS) via the right subclavian vein. The distal portion was positioned in the CS and cavotricuspid isthmus (CTI), and the proximal portion was placed in the crista terminalis (CT) and superior vena cava (SVC). Following transseptal puncture, pulmonary venography, and esophagography, a 20-pole circumferential mapping catheter through the SLO sheath (St. Jude Medical) and a 3.5- or 4-mm open-irrigated-tip ablation catheter (ThermoCool/ThermoCoolSF, Biosense-Webster; or CoolPath/FlexAbility, St. Jude Medical) through a steerable sheath (Agilis; St. Jude Medical, Saint Paul, MN, USA) were introduced to the left atrium (LA). Catheter ablation was performed under the guidance of a three-dimensional electroanatomic mapping system (CARTO, Biosense-Webster; or Ensite NavX, St. Jude Medical). First, all patients underwent PVI plus PWI. Our ablation lesion set for PVI plus PWI was modified from that for extensive encircling PVI by combining the left and right posterior lines, forming a centerline, to avoid the ventral surface of the esophagus as much as possible using an esophageal temperature probe and esophagography; we named this method "centerline PVI" (Figure 1A). The endpoint of the PVI plus PWI procedure was defined as the absence of the local PV and left atrial posterior wall (PW) potentials; entrance block or local capture of the PV and PW without capture of the whole atrium when pacing by an ablation catheter positioned at the PV and PW; and exit block. If AF did not convert to sinus rhythm after PVI plus PWI, internal direct-current cardio version (DCC) was performed. Following PVI plus PWI, all patients underwent provocation of non-PV triggers using high-dose isoproterenol. At first, spontaneous AF initiation was evaluated to identify the AF trigger. If sinus rhythm was maintained, protocols to elicit PV and non-PV triggers were performed as follows: (a) high-dose isoproterenol infusion (5-15 $\mu\text{g}/\text{min}$ for 2 min) and (2) DCC of AF induced with rapid-burst atrial pacing following high-dose isoproterenol infusion. We defined non-PV triggers as the initiation of AF, atrial tachycardia, or frequent and repetitive atrial premature beats with a short run pattern (>3 beats) and a short coupling interval. If non-PV triggers were elicited, the earliest ectopic site was mapped by P-wave morphology and the activation sequence of the 20-pole catheter in the SVC/CT/CTI/CS (Figure 1B). Detailed mapping was performed by manipulating the circumferential mapping catheter and ablation catheter. Subsequently, we ablated the triggers with the endpoint of an inability to cause them by repeating the induction protocol. If such triggers originated from the SVC, isolation of the SVC was performed. If the non-PV triggers were eliminated or not induced by repeated provocation after ablation, they were defined as mappable non-PV triggers. In contrast, we determined unmappable non-PV triggers as non-PV triggers that could not be localized or eliminated because of multiplesources or unsuccessful trigger ablation. If unmappable non-PV triggers were present, adjunctive CFAE

FIGURE 1 (A) Approach of PVI plus PWI: Centerline PVI. (B) Positions of catheter at provocation of non-PV triggers. ESO: esophagus; CS: coronary sinus; CT: crista terminalis, CTI: cavotricuspid isthmus; LIPV: left inferior pulmonary vein; LSPV: left superior pulmonary vein; PIPV: right inferior pulmonary vein; RSPV: right superior pulmonary vein; SVC: superior vena cava; PVI: pulmonary vein isolation; PWI: posterior wall isolation

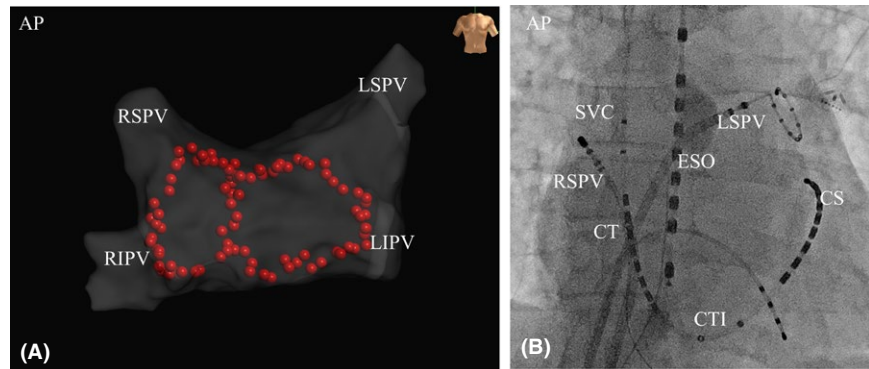
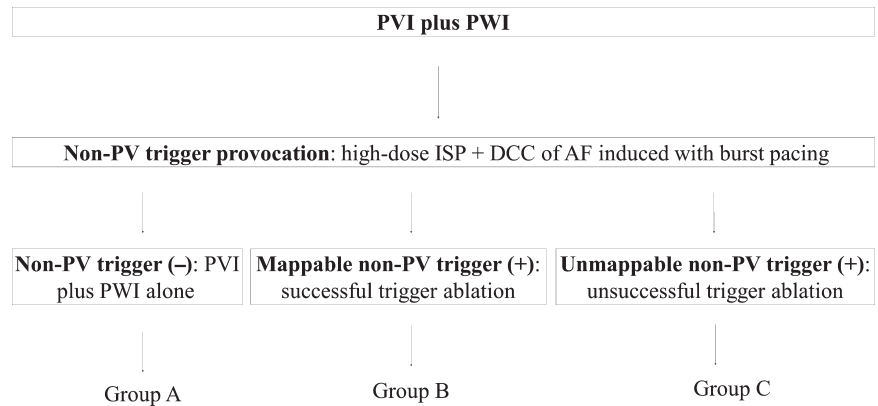


FIGURE 2 Methods of provocation and ablation for non-PV triggers. AF: atrial fibrillation; CFAE: complex fractionated atrial electrogram; DCC: direct current cardioversion; ISP: isoproterenol; PV: pulmonary vein; PVI: pulmonary vein isolation; PWI: left atrial posterior wall isolation



ablation was performed according to the judgment of the operator. CTI ablation for typical atrial flutter was performed according to the clinical history or the judgment of the operator.

The patients were divided into three groups according to the results of the provocation in the initial procedure, as follows (Figure 2): initial-group A, non-PV triggers were not induced and no additional ablation was performed (PVI plus PWI alone was performed); initial-group B, mappable non-PV triggers were demonstrated and ablated; and initial-group C, unmappable non-PV triggers were induced. Patients with both mappable and unmappable non-PV triggers were classified into initial-group C.

2.3 | Ablation protocol during repeat procedures

The patients experiencing recurrence of atrial tachyarrhythmias, such as AF and atrial tachycardia, after a blanking period (within 3 months after the last procedure) were encouraged to undergo a repeat procedure. The primary step in repeat procedures for recurrent atrial tachyarrhythmias was the assessment of reconnection of the PV or PW. All identified conduction gaps were ablated to achieve complete PVI plus PWI. If sustained atrial tachycardias were identified, we first performed mapping and ablation for them using activation and entrainment mapping. The provocation and ablation of non-PV triggers were performed in the same way as in the initial procedure. In the repeat procedures, we also determined whether or not unmappable non-PV triggers existed when the non-PV triggers could not be induced despite the absence of reconnection of the PV or PW.

Patients were divided into three groups according to the results of the provocation in multiple procedures, as follows (Figure 2): final-group A, non-PV triggers were not induced in each procedure (PVI plus PWI alone was performed); final-group B, mappable non-PV triggers were demonstrated and eliminated in any procedure; final-group C, unmappable non-PV triggers were identified in any procedure.

2.4 | Patient follow-up and the primary outcome

After ablation, anticoagulants were continued for 3 months or longer depending on the CHADS2 score. AADs were typically discontinued within 3 months after ablation if recurrence of atrial tachyarrhythmias was absent. All patients were scheduled to visit our hospital at 1, 3, 6, 9, and 12 months after the procedure and then every 6 months thereafter. A 12-lead electrogram (ECG) was obtained at each follow-up point. Twenty-four-hour Holter monitoring was performed at 3 and 12 months and 3 and 5 years after the procedure. This study's primary outcome was freedom from recurrence of atrial tachyarrhythmias (≥ 30 seconds) without AADs at 1 year after the last procedure. Episodes of atrial tachyarrhythmia only within the blanking period were not considered recurrences.

2.5 | Statistical analysis

Continuous variables are expressed as means with standard deviations or median with the interquartile range (Q1-Q3) as appropriate.

At the initial procedure	Initial-group A (N = 105)	Initial-group B (N = 41)	Initial-group C (N = 9)	P-Value
Age [y], median	60	64	65	0.2
Male gender [n] (%)	85 (81%)	32 (78%)	7 (78%)	0.8
Structural heart disease [n] (%)	15 (14%)	5 (12%)	1 (11%)	1
Hypertension [n] (%)	67 (64%)	24 (59%)	4 (44%)	0.4
Diabetes Mellitus [n] (%)	12 (11%)	3 (7%)	2 (22%)	0.4
Duration of persistent AF [mo], median	27	36	84	0.004
LVEF [%], median	63	60	64	0.6
LA diameter [mm], median	41	40	45	0.4
BNP [pg/mL], median	83	87	68	0.07
eGFR [mL/min/1.73 m ²], median	66	65	71	0.6

TABLE 1 Patient characteristics of each group at the initial procedure

Values are n (%) or the median. AF: atrial fibrillation; LA: left atrium; LVEF: left ventricular ejection fraction.

Categorical variables are expressed as frequencies and percentages. To compare each group, Fisher's exact test was used for categorical variables, and the Kruskal-Wallis test was used for continuous variables. The freedom from atrial tachyarrhythmia recurrence was calculated using a Kaplan-Meier analysis. The log-rank test with the Bonferroni post-hoc test was used for group comparison. Analyses were performed using the EZR software program, which is a graphical user interface for R.⁷ A $P \leq 0.05$ was considered statistically significant.

3 | RESULTS

3.1 | Patients' characteristics

Patients' characteristics are shown in Table 1. Of the 155 patients, there were 124 men (80%) with a mean age of 61 ± 9 years old. The mean LA diameter was 42 ± 6 mm. The median duration of persistent AF was 36 (Q1-Q3: 21-48) months.

3.2 | Ablation procedure

During the initial procedure, PVI plus PWI was achieved in 146 (94%) patients. In the remaining 9 (6%) patients, PVI was completed but not PWI. The 155 patients were divided into 3 groups according to the results of the provocation of non-PV triggers, as follows: non-PV triggers were not elicited, and no additional ablation was performed in 105 (68%) patients (initial-group A); mappable non-PV triggers were documented and ablated in 41 (26%) patients (initial-group B)—67 mappable non-PV triggers were induced in the initial procedure in the SVC in 19 patients, right atrium (RA) in 7 patients, interatrial septum in 17 patients, LA in 5 patients, and CS in 19 patients; unmappable non-PV triggers were provoked and adjunctive CFAE ablation performed in 9 (6%) patients (initial-group C) (Table 1). In 4 of the 9 patients in initial-group C, both mappable and unmappable non-PV

triggers were provoked. In the initial procedure, perimitral atrial flutter was documented, and mitral isthmus ablation was performed in 2 (1%) patients. The cavotricuspid isthmus (CTI) was blocked in 56 (36%) patients. During a median follow-up period of 755 (Q1-Q3: 554-1117) days after the initial procedure, a stable sinus rhythm without AADs was maintained in 90 of 155 (58%) patients. In the remaining 65 (42%) patients, atrial tachyarrhythmia recurrence was documented.

A total of 71 repeat procedures was performed in 53 (34%) patients with recurrent atrial tachyarrhythmia after the initial procedure (initial-group A, $n = 28$; initial-group B, $n = 20$; initial-group C, $n = 5$; Figure 3). In repeat procedures, 19 atrial tachycardias were targeted—, including 14 focal atrial tachycardias (LA, $n = 7$; IAS, $n = 6$; RA, $n = 1$), 4 macro reentry atrial tachycardias (LA roof dependent, $n = 2$; perimitral, $n = 1$; CTI dependent, $n = 1$), one atrial tachycardia was unprovoked during procedure. Among the 53 patients who underwent repeat procedures, the reconnection of the PVs and/or LAPW was observed and abolished in 38 (72%) patients in the overall population, 21 (75%) patients in initial-group A, 12 (60%) patients in initial-group B, and 5 (100%) patients in initial-group C. After completion of PVI plus PWI, the provocation of non-PV triggers was performed in the same way as in the initial procedure. New mappable non-PV triggers were revealed and ablated for the first time during the repeat procedures in 24 patients (initial-group A, $n = 14$; initial-group B, $n = 9$; initial-group C, $n = 1$). During the repeat procedures, adjunctive CFAE ablation was performed for unmappable non-PV triggers in 15 patients, with 7 undergoing it because non-PV triggers were not revealed despite the absence of reconnection of the PV and LAPW.

After the second procedure, the 155 patients were divided into 3 groups according to the results of the provocation of non-PV triggers, as follows: 90 patients (58%) underwent PVI plus PWI alone without non-PV triggers (Second-group A); 48 patients (31%) patients underwent non-PV trigger ablation in addition to PVI plus PWI (Second-group B); unmappable non-PV

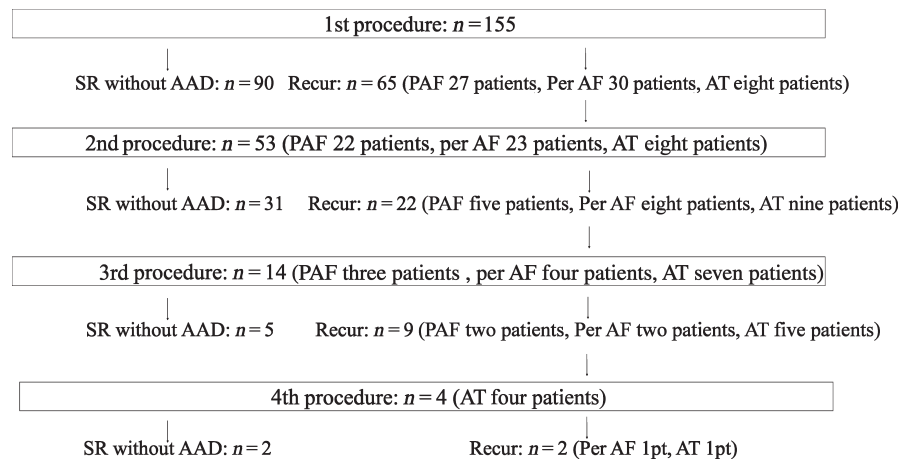


FIGURE 3 Flow chart describing the outcome after each procedure. AAD: antiarrhythmic drug; AT: atrial tachycardia; SR: sinus rhythm; PAF: paroxysmal atrial fibrillation; Per AF: persistent atrial fibrillation

triggers were present and adjunctive CFAE ablation was performed in 17 patients (11%) (Second-group C). After multiple procedures, the 155 patients were divided into 3 groups according to the results of the provocation of non-PV triggers as follows. PVI plus PWI alone was performed without non-PV triggers in 90 of 155 (58%) patients (final-group A). Non-PV trigger ablation in addition to PVI plus PWI was performed in 45 of 155 (29%: 8 patients from initial-group A, 37 patients from initial-group B) patients (final-group B)—106 mappable non-PV triggers were induced across multiple procedures in the SVC in 24 patients, RA in 16 patients, interatrial septum in 31 patients, LA in 11 patients, and CS in 24 patients. Unmappable non-PV triggers were present and adjunctive CFAE ablation was performed in 20 of 155 (13%: initial group A, n=7; initial-group B, n=4; initial-group C, n=9) patients (final-group C). Across multiple procedures, 15 patients underwent mitral isthmus block line ablation. CTI ablation was performed in 79 patients. In 15 of the 20 patients in final-group C, both mappable and unmappable non-PV triggers were provoked. The total number of procedures was 1.5 ± 0.7 in all patients and 1.4 ± 0.7 , 1.5 ± 0.6 , and 2.1 ± 1.3 in initial-group A, B, and C respectively. During a median follow-up period of 618 (Q1-Q3:416-866) days after multiple procedures, a stable sinus rhythm without AAD was maintained in 128 of 155 (83%) patients. In the remaining 27 (17%) patients, atrial tachyarrhythmia recurrence was documented.

3.3 | Characteristics and the ablation outcome in each group

We compared the baseline characteristics of each group after the initial procedure (Table 1) and after multiple procedures. After the initial procedure, the AF duration in initial-group C was significantly longer than that in initial-group A ($P = 0.004$) and initial-group B ($P = 0.03$). After multiple procedures, the AF duration in final-group C was significantly longer than that in final-group A ($P < 0.001$) and final-group B ($P < 0.001$). The LA diameter in final-group C was significantly larger than that in final-group A ($P = 0.04$).

The Kaplan-Meier estimates for freedom from atrial tachyarrhythmia recurrence without AADs after a single procedure (Figure 4), after a second procedure (Figure 5), and after multiple procedures (Figure 6) are shown. The freedom at 1 year after a single procedure was 65% in all patients (95% confidence interval [CI], 57-72) and 73% in initial-group A (95% CI, 64-81), 56% in initial-group B (95% CI, 40-70), and 11% in initial-group C (95% CI, 1-39). The single procedure outcome of initial-group A was significantly higher than that of initial-group B ($P = 0.03$) and initial-group C ($P < 0.001$). After a second procedure, the freedom at 1 year after the last procedure was 84% in all patients (95% CI, 78-89) and 93% in second-group A (95% CI, 86-97), 81% in second-group B ($n = 48$, 95% CI, 66-90), and 47% in second-group C (95% CI, 23-68). After multiple procedures, the freedom at 1 year after the last procedure was 86% in all patients (95% CI, 80-91) and 93% in final-group A (95% CI, 86-97), 86% in final-group B (95% CI, 72-94), and 53% in final-group C (95% CI, 28-72). After multiple procedures, the outcome of final-group C was significantly lower than that of final-group A ($P < 0.001$) and final-group B ($P < 0.001$).

3.4 | Procedure time and complications

The median procedure time was 183 (Q1-Q3; 155-220) minutes. Complications occurred in 7 of 226 (3%) procedures; 4 (2%) patients had pericardial effusion that required percutaneous drainage, 2 (1%) had gastroparesis, and 1 (0.4%) patient had an esophageal ulcer. All patients were conservatively treated without long-term sequelae.

4 | DISCUSSION

4.1 | Main findings

In this study, we demonstrated the efficacy of PVI plus PWI and additional ablation of non-PV triggers induced by the administration of high-dose isoproterenol for patients with LSPAF. The 1-year freedom from atrial tachyarrhythmia recurrence rate without AAD was 65% after a single procedure, which improved to 86% after multiple procedures (mean 1.5 per patient). Of note, the ablation outcomes were highly dependent

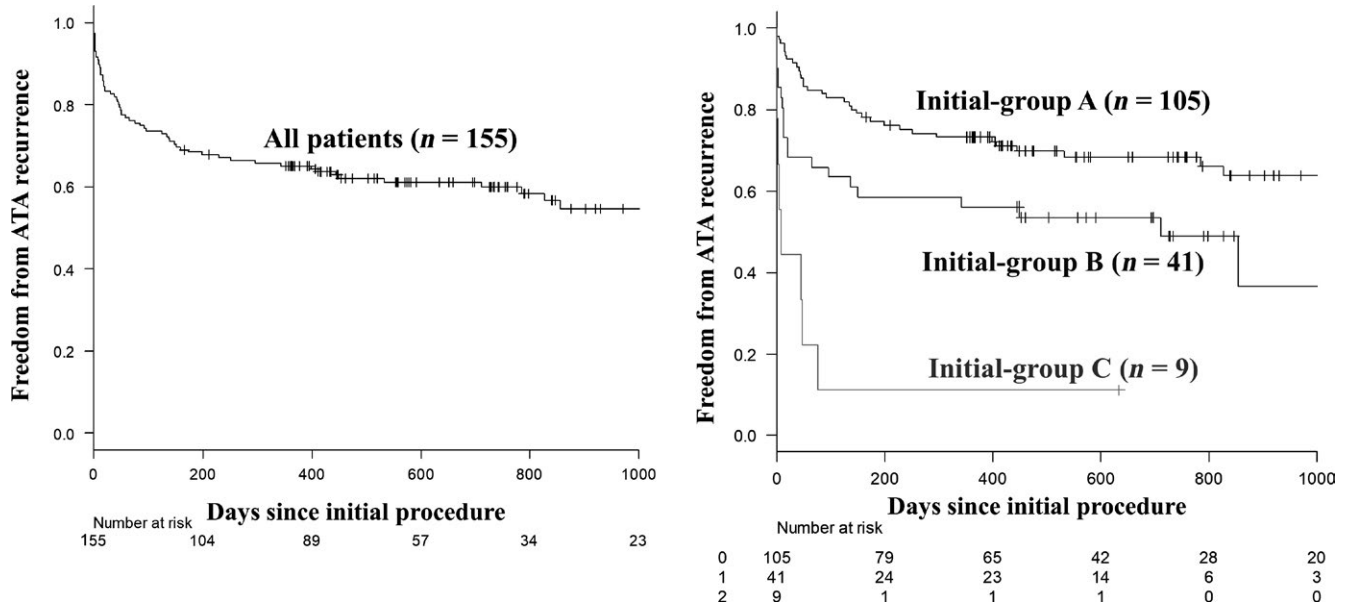


FIGURE 4 Freedom from recurrence of atrial tachyarrhythmias without antiarrhythmic drugs after single procedure. ATA: atrial tachyarrhythmias; AAD: antiarrhythmic drugs

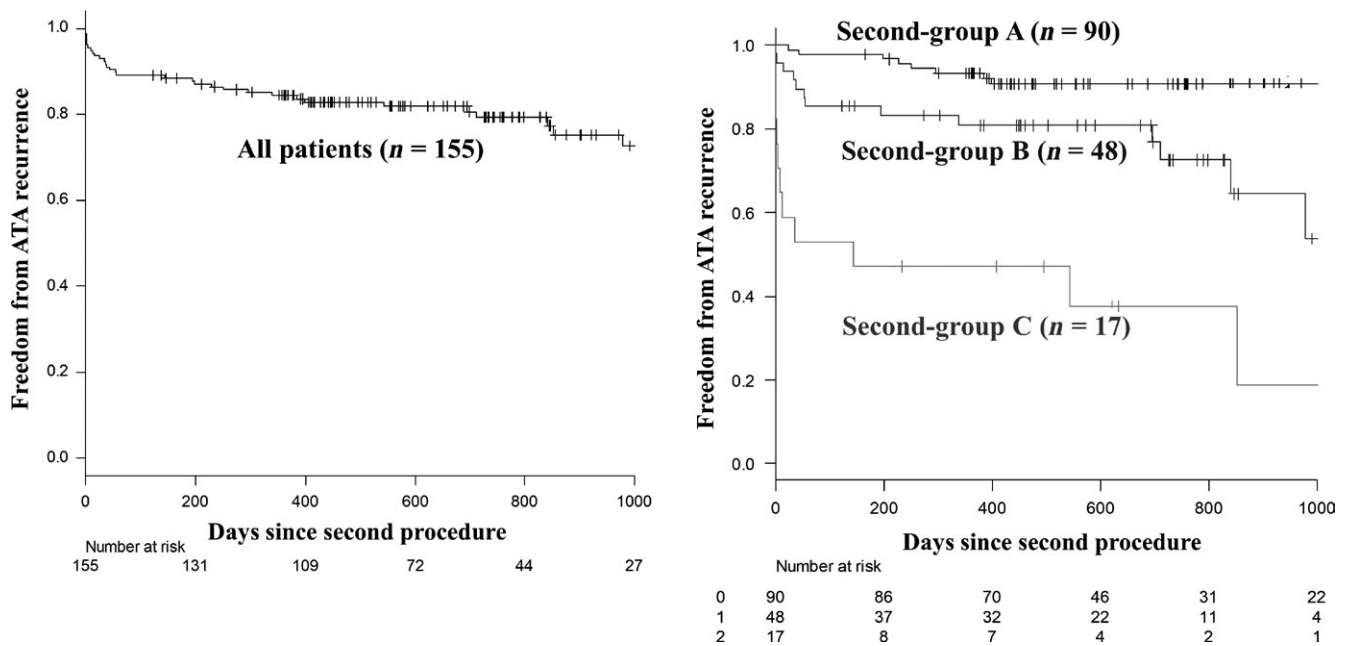


FIGURE 5 Freedom from recurrence of atrial tachyarrhythmias without antiarrhythmic drugs after second procedure. ATA: atrial tachyarrhythmias; AAD: antiarrhythmic drugs

on the presence of non-PV triggers. In approximately 60% of the LSPAF patients (group A), non-PV triggers were not induced using high-dose isoproterenol infusion, and PVI plus PWI alone achieved good outcomes (73% after a single procedure, 93% after multiple procedures). In approximately 30% of the patients (group B), mappable non-PV triggers were elicited, and the outcome of ablation of mappable non-PV triggers in addition to PVI plus PWI was 56% after a single procedure, which increased to 86% after multiple procedures. In contrast, approximately 10% of the patients (group C) had unmappable non-PV triggers and a poor outcome (11% after a single procedure, 53% after multiple procedures).

4.2 | Efficacy of PVI plus PWI for LSPAF

The efficacy of PVI for patients with paroxysmal AF (PAF) is well-established. In contrast, catheter ablation for LSPAF patients remains challenging.¹ Although some adjunctive ablation methods have been proposed,⁸⁻¹⁰ the optimum approach has not been elucidated. A recent meta-analysis reported that additional substrate ablation is associated with a worse outcome than PVI alone, although the single-procedure success rate of pulmonary vein antrum isolation alone for LSPAF is 57%.¹¹ In contrast, some studies reported the efficacy and

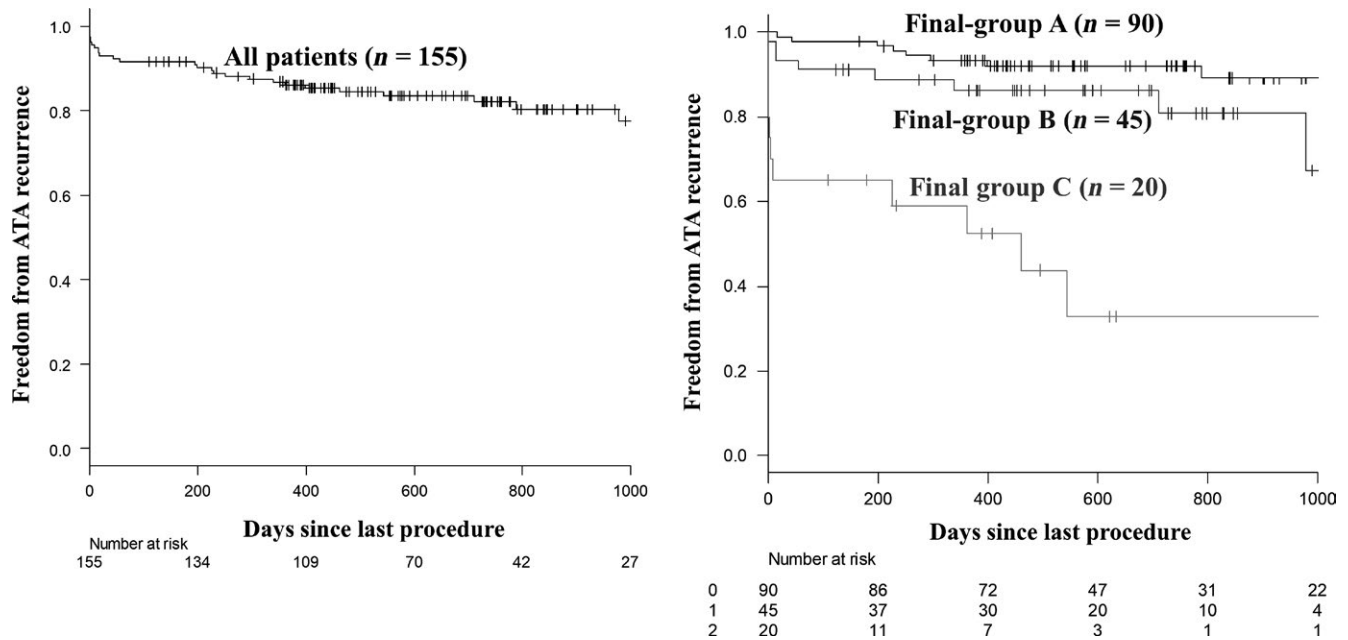


FIGURE 6 Freedom from recurrence of atrial tachyarrhythmias without antiarrhythmic drugs after multiple procedures. ATA: atrial tachyarrhythmias; AAD: antiarrhythmic drugs

benefits of PVI plus PWI in a significantly reduced AF recurrence rate compared with PVI alone.^{3,4} A systematic review reported that PVI plus PWI for LSPAF patients results in a drug-free success rate ranging from 42% to 50% at almost 2 years after a single procedure, which improves to 60% to 63% after repeat procedures (mean 1.4 per patient).¹² As an explanation for these results, several studies have suggested that the LAPW plays an important role in initiating and maintaining AF.¹³⁻¹⁶ However, there is little evidence regarding which LSPAF patients achieve sufficiently good outcomes from PVI plus PWI alone. Therefore, the endpoint of catheter ablation of LSPAF patients has never been determined. Several studies have proposed non-inducibility of AF by high-dose isoproterenol as a useful endpoint for catheter ablation in PAF patients.^{5,17,18} However, whether or not the same applies to LSPAF patients has been unclear. Our findings have shown that durable PVI plus PWI alone is sufficient therapy for patients without non-PV triggers induced by high-dose isoproterenol, and non-inducibility of non-PV triggers by high-dose isoproterenol is a useful endpoint for catheter ablation, even in LSPAF patients.

4.3 | Additional non-PV trigger ablation for LSPAF patients

The benefits of ablating non-PV triggers to improve the arrhythmia-free survival for PAF have been well-established in previous studies.^{5,19} In addition, a retrospective study on PVI and additional non-PV trigger ablation reported that non-PV triggers were elicited in 18% of patients either during the initial or repeat procedures, and 50% of patients maintained a normal sinus rhythm without AADs after a mean 1.3 procedures and a mean follow-up period of 39 months.⁶ In contrast, it has been reported that only 30% of non-PV triggers were able to be ablated because of difficulties in locating them, although the patients in whom

all non-PV triggers were eliminated had significantly better outcomes than those in whom non-PV triggers could not be ablated.²⁰

The prevalence of non-PV triggers in our study was higher than in previous studies. This difference might be explained by the definition of non-PV triggers, as ectopic beats initiating not only AF or atrial tachycardia but also frequent and repetitive atrial premature beats (>3 beats) were considered non-PV triggers in our study. The outcome of group B was significantly worse than that of group A after a single procedure but became comparable to that of group A after multiple procedures. Although the performance of re-PVI plus PWI as repeat procedures contributed to the improvement in the outcome after multiple procedures, our results indicate that it was difficult to induce and eliminate all non-PV triggers in a single procedure, suggesting the importance of repeat non-PV trigger ablation across multiple procedures. Careful ablation of mappable non-PV triggers may reduce the rate of ineffective extensive ablation and improve the arrhythmia-free survival. However, the presence of unmappable non-PV triggers significantly increases the rate of atrial tachyarrhythmia recurrence.

4.4 | Study limitations

This was a retrospective observational study; however, our approach to LSPAF ablation was consistent with the endpoint of PVI plus PWI with the elimination of non-PV triggers using high-dose isoproterenol infusion. Although the outcomes of patients who underwent PVI plus PWI with or without mappable non-PV triggers were comparable after multiple procedures, the efficacy of additional non-PV trigger ablation was uncertain because of the absence of a control group that underwent PVI plus PWI because provocation and ablation of non-PV triggers were not performed. The median LA diameter in our study was not as large as in some previous studies about LSPAF patients

but was larger than that described for a healthy Japanese population and in a previous study of Japanese paroxysmal AF patients. This may be because of the fact that Japanese hearts are relatively small.²¹ In our study, adjunctive CFAE ablation may have affected the ablation outcome, although it was performed not empirically but only if non-PV triggers were unmappable. Further studies with a control group of patients with inducible non-PV triggers who did not undergo ablation will be required to confirm that ablation of non-PV triggers has an incremental benefit over PVI plus PWI.

5 | CONCLUSION

In approximately 60% of LSPAF patients, non-PV triggers were not induced by high-dose isoproterenol infusion, and PVI plus PWI alone achieved good outcomes. Noninducibility of non-PV triggers by high-dose isoproterenol is a useful endpoint for catheter ablation, even in LSPAF patients. Although the inducibility of non-PV triggers after PVI plus PWI was associated with the recurrence of atrial tachyarrhythmias, the ablation of mappable non-PV triggers may improve the outcome after multiple procedures. However, the presence of unmappable non-PV triggers was significantly associated with poor outcomes.

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CONFLICT OF INTEREST

Dr. Takahashi and Dr. Goya received speaker honoraria from Biosense Webster and St. Jude Medical outside this study. The remaining authors have no disclosures.

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