ORIGINAL ARTICLE

Effects of additional ablation of low-voltage areas after Box isolation for persistent atrial fibrillation

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Abstract

Background: Previous studies reported that ablation of low-voltage areas (LVAs) after pulmonary vein isolation (PVI) improves the success rate in persistent atrial fibrillation (PerAF) patients with LVAs. However, the need for LVA ablation in addition to the posterior left atrial isolation, Box isolation (BOXI), for PerAF is unclear. We evaluated the effects of LVA ablation after BOXI for PerAF with LVAs.

Methods: In 115 patients with PerAF (75 longstanding PerAF), LA voltage maps were created during sinus rhythm after PVI. Subsequently, BOXI was performed. In 61 patients without LVAs (<0.5 mV), BOXI alone was performed. Fifty-four patients with LVAs were randomly assigned to BOXI plus LVA ablation (33 patients) or BOXI alone (21 patients).

Results: The rate of AF termination or cardioversion after BOXI was significantly higher than that after PVI (100% vs 88%, $P < 0.001$). The inducibility of atrial tachyarrhythmia after BOXI was significantly lower than that after PVI (27% vs 100%, $P < 0.001$). During 24 ± 9 months of follow-up after a single procedure, atrial tachyarrhythmia-free rate in the patients with LVAs, was significantly lower than that without LVAs (65% vs 82%, $P = 0.043$). However, the success rate was not significantly different between the BOXI plus LVA ablation group and the BOXI alone group of patients with LVAs (67% vs 62%, $P = 0.722$).

Conclusion: BOXI facilitates AF termination and its non-inducibility. Among patients with PerAF, BOXI alone may be adequate in cases without LVAs. Although cases with LVAs have higher risk of AF recurrence, additional LVA ablation does not improve the outcomes much.

KEYWORDS
atrial fibrillation, Box isolation, catheter ablation, low voltage area, pulmonary vein isolation

1 | INTRODUCTION

The joint professional society consensus statements support that pulmonary vein isolation (PVI) is the cornerstone of catheter ablation of atrial fibrillation (AF).[1] PVI is highly effective in paroxysmal AF, however, it may not be adequate to suppress persistent AF (AF). Further modification of the atrial substrate maintaining AF seems necessary in patients with persistent AF. Both the PVs and posterior left atrium (LA) develop from the sinus venosus, which has many pacemaker cells.[2] The posterior

LA has been implicated in the AF substrate including conduction delay and block.[3-6] Non-PV triggers and rotors mainly existing in the posterior LA have been reported.[7,8] Recently, late gadolinium enhancement of left atrial magnetic resonance imaging has been shown to be highly distributed in the posterior LA.[9] These findings support that isolation of not only the PVs but also the posterior LA can result in a much better suppression rate in persistent AF. Therefore, we developed an approach for a complete isolation of the posterior LA including all PVs, namely the Box isolation (BOXI).[10,11]

Furthermore, an individualized approach for AF ablation based on low-voltage areas (LVAs), which are correlated with atrial fibrosis, has been provided.[12-16] Previous studies reported that LVA ablation after PVI improved the success rate in persistent AF patients with LVAs.[12-16] However, the necessity of LVA ablation in addition to the BOXI for persistent AF with LVAs is less clear.

Although an additional benefit of the BOXI over PVI in the treatment of persistent AF has been reported in previous studies,[16-23] the mechanism of the beneficial effect of the BOXI is still unclear. Therefore, we evaluated the additional effect of the BOXI in addition to PVI on the termination and inducibility of AF and the additional benefit of LVA ablation over the BOXI for persistent AF with LVAs.

2 | METHODS

2.1 | Study population

One-hundred fifteen consecutive patients with persistent AF (n = 40) and longstanding persistent AF (n = 75) underwent catheter ablation of AF from September 2014 to February 2017.

Persistent AF was defined as AF that was sustained for more than 7 days but which required pharmacologic or electrical cardioversion. Longstanding persistent AF was defined as continuous AF that had lasted for more than 1 year. Written informed consent was obtained from all patients. The study was approved by the Fukuoka Sanno Hospital's Institutional Review Board.

2.2 | Preparation

A venous access site in the right internal jugular vein was used to introduce a duo-decapolar catheter (Bee-AT, Japan-Lifeline Co., Ltd., Tokyo, Japan), of which the distal 10-poles were positioned in the coronary sinus while the proximal 10-poles were placed along the crista terminalis for internal cardioversion. After a double transseptal puncture, a 20-pole circular mapping catheter (Optima™ or Reflexion HD™; St. Jude Medical, St. Paul, MN) and irrigated-tip ablation catheter (Cool Flex™ or FlexAbility™; St. Jude Medical) were inserted into the LA for the mapping and ablation. A 3D geometry of the LA was created and fused with the preoperative 3DCT using an EnSite NavX™ system (St. Jude Medical). A temperature monitoring probe (SensiTherm™; St. Jude Medical) was inserted into the esophagus.

2.3 | Pulmonary vein isolation

Pulmonary vein isolation was performed using the irrigation catheter. Radiofrequency (RF) energy was applied in a dragging fashion with a temperature limit of 40°C, and a power limit of 40 W on the anterior wall, 30 W on the posterior wall, and 20 W near the esophagus. PVI was confirmed using a circular mapping catheter.

2.4 | Voltage mapping

After PVI, AF was internally cardioverted with 10 J. When AF was not cardioverted, the energy was increased up to 20 J. In cases that could not be cardioverted even with 20 J, BOXI was subsequently performed during AF. After BOXI, cardioversion was performed again in the same way. After a 15 minutes waiting interval before the mapping, LA voltage maps were constructed from the contact bipolar electrograms obtained from a steerable 20-pole circular mapping catheter with a 1-mm electrode length and 2-mm interelectrode spacing (Reflexion HD™; St. Jude Medical) during sinus rhythm (SR) with a mean number of sampling points of 524 ± 204. The mapping catheter was manipulated through an SL0™ sheath. The distance between a mapping point and the geometry surface was set at 5 mm. The maximum distance between the mapping points was set at 10 mm. Bipolar intracardiac electrograms were filtered by a band pass to frequencies between 30 and 300 Hz.

LVAs were defined as areas with bipolar peak-to-peak voltage amplitudes of <0.5 mV[12-16] and covering >5% of the LA body surface area. Regarding the analysis of the distribution of the LVAs, the LA was divided into six parts including the anterior wall, roof, septum, posterior wall, inferior wall, and lateral wall. In patients who subsequently underwent BOXI during sustained AF after PVI, only LVAs outside the posterior LA region were evaluated.

2.5 | Box isolation

After voltage mapping, AF was induced by rapid pacing for 20 beats while shortening the cycle length by 10 mseconds from 250 to 180 seconds from the coronary sinus, then BOXI was subsequently performed during AF. Ablation of the LA roof and floor was performed by creating a contiguous line to isolate the posterior LA. RF energy was applied in a dragging fashion with a temperature limit of 40 W on the roof, 30 W on the floor, and 20 W near the esophagus. If the esophageal temperature was higher than 40°C, RF applications were interrupted. When electrograms were found within Box lesion using the ablation catheter or the circular mapping catheter placed on the posterior LA, they were ablated until the complete absence of electrograms. Entrance block of Box lesion was confirmed by the complete electrical silence on the posterior LA (Figure 1A).

When AF still sustained after BOXI, AF was internally cardioverted again in the same way. Exit block of Box lesion was confirmed during SR. Gaps along the ablation lines were detected and closed using high output (10 V) pacing through the ablation catheter.[11] In

FIGURE 1 A, An example of Box isolation in the group without low-voltage areas (LVAs).Voltage mapping on the anterior (left) and posterior walls (right). The color gradient indicates the serial changes in the electrogram amplitude from purple at >0.5 mV to gray at <0.1 mV. The brown tags indicate the ablated lesions, and gray lesion indicates the complete electrical silence on the Box lesion (right). B, An example of the LVA ablation group with LVAs. In this case, LVAs were found on the anterior wall (left). LVAs were circumferentially ablated (brown tags) and linear lesions were created to connect the LVAs to the right PV and mitral annulus. The gray lesion indicates the Box lesion (right). AP, anteroposterior; PA, posteroanterior
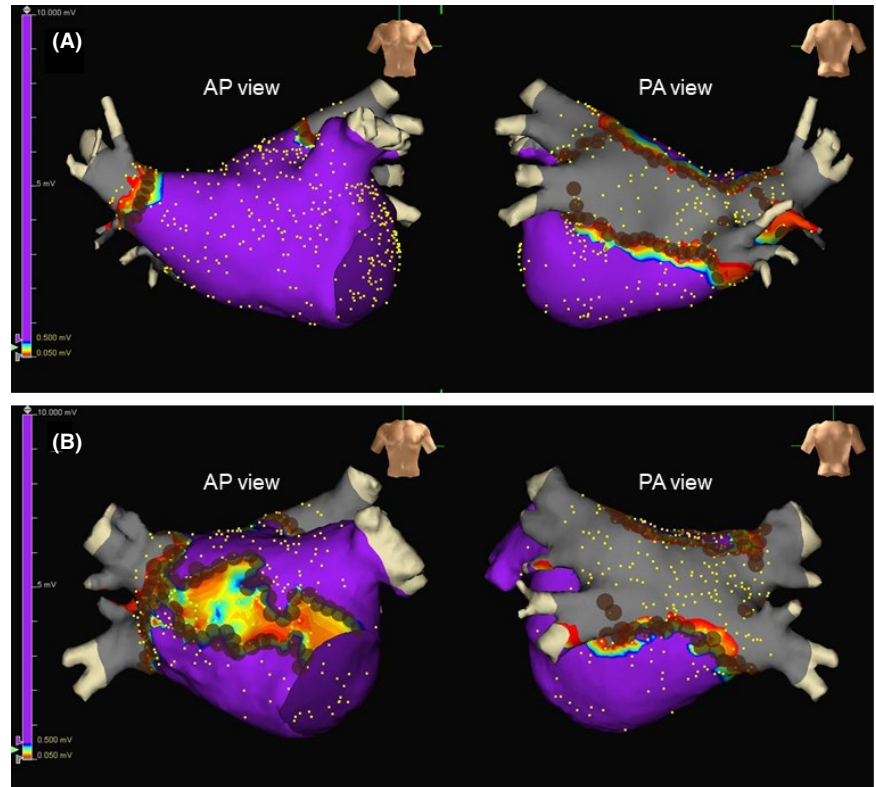
case of pacing capture, RF energy was delivered simultaneously while pacing from the tip of the ablation catheter. The endpoint of BOXI was defined as bidirectional conduction block, that is, both a lack of potentials in the posterior LA and the loss of pacing capture.[11]

After the completion of BOXI in SR, re-inducibility of AF was assessed by rapid pacing in the same way. When atrial arrhythmias were not induced, isoproterenol (5-10 μg) was injected. When AF from the superior vena cava (SVC) was induced, SVC isolation was performed. When cavotricuspid isthmus (CTI) dependent atrial flutter, mitral flutter and atrial tachycardia were induced, CTI linear ablation, mitral isthmus ablation, and focal ablation were performed.

2.6 | LVA ablation

Patients with LVAs (n = 54) were randomly assigned to ablation with BOXI plus LVAs ablation group (LVAabl, n = 33; Figure 1B) or BOXI alone group (LVAnon-abl, n = 21; Figure 2). For the LVAabl group, the LVA ablation was subsequently performed after BOXI during AF with a temperature limit of 40 W. When AF was not induced, the LVA ablation was performed during SR. LVAs were circumferentially ablated in a dragging fashion. The linear lesions were created to connect the LVAs to anatomical obstacles including the PVs, roofline and mitral annulus to prevent the creation of narrow, proarrhythmic channels (Figure 1B). The endpoint was the complete isolation of the LVAs as confirmed by the lack of potentials in the LVAs and loss of pacing capture using high output (10 V) pacing at the ablation site during SR.

2.7 | Periprocedural care and follow-up

All patients were taking a direct oral anticoagulant before the ablation. Transesophageal echocardiography was performed 1 day before the procedure in all patients. All antiarrhythmic drugs were stopped at least five half-lives before the procedure. Amiodarone was not prescribed in any patients. Patients were discharged with prescription for antiarrhythmic drugs, which was continued for up to 3 months (blanking period) and then discontinued.

The patients were monitored for the recurrence of arrhythmias by a general practitioner every month and a questionnaire survey every 3 months. Hospital visits were also scheduled at 3, 6, and 12 months and then every 6 months thereafter. A 7-day Holter monitor was performed at 6 and 12 months. A telemetry ECG recorder (HCG-801, Omron, Japan) was also used to document symptomatic episodes and to record ECG once per week regardless of symptoms. A recurrence was defined as any atrial arrhythmias documented by ECG, Holter monitoring, or event recorder >30 seconds in duration 3 months after the ablation.

2.8 | Statistical analysis

All statistical data analyses were performed with SAS 9.4 software (SAS Institute Inc., Cary, NC). Categorical variables were compared between groups by a χ^2 analysis or Fisher's exact test. Continuous variables were compared between groups by the Student's *t*-test or Wilcoxon rank-sum test, and data are presented as the mean ± SD. Atrial tachyarrhythmia-free survival curves were estimated by the
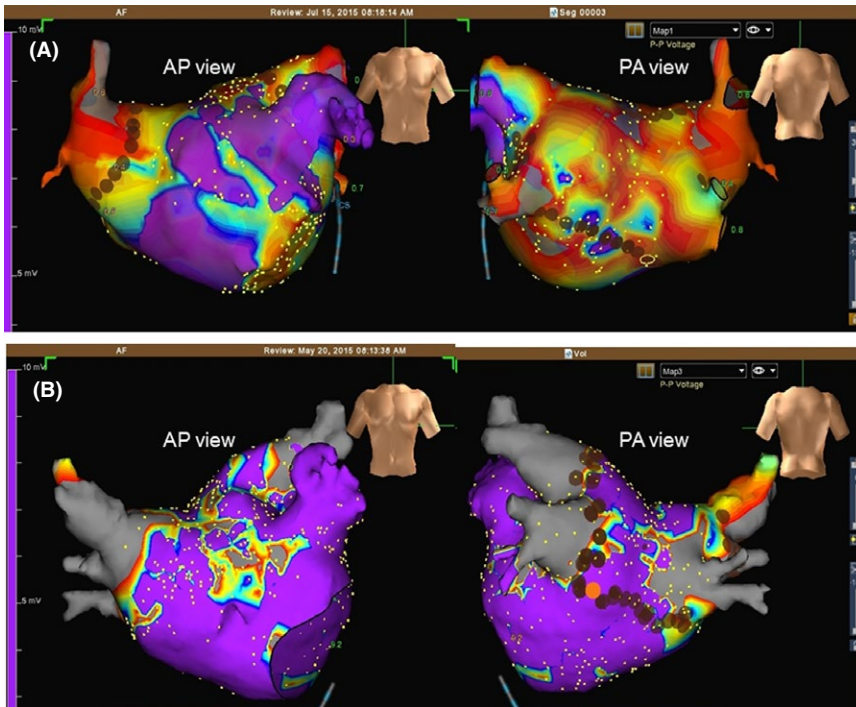
FIGURE 2 Two cases of atrial fibrillation termination during Box isolation in the low-voltage area (LVA) non-ablation group with LVAs. A, In this case, LVAs were identified on the anterior (left) and posterior (right) walls. B, In this case, LVAs were found only on the anterior wall (left). In both cases, despite the LVAs existed on the anterior wall, AF terminated during Box isolation. AP, anteroposterior; PA, posteroanterior

Kaplan-Meier method, and a log-rank test was used for comparisons between groups. Cox proportional hazard regression was used to calculate the hazard ratio (HR) and 95% confidence interval (CI). A multivariable Cox regression was used to identify the significant predictors of arrhythmia recurrence. Statistical significance was set at a $P < 0.05$.

3 | RESULTS

3.1 | Additional effects of BOXI added to the PVI

Figure 3 shows the flow chart of the study. Among the 115 patients with persistent AF, AF directly converted to SR in six patients during the PVI. After the PVI, SR was restored by cardioversion with 10 or 20 J in 95 patients, but not even with 20 J in 14 patients. Among the 101 patients (88%) with AF termination or cardioversion after the PVI, LVAs were identified in 40 patients. Fourteen patients without AF termination or cardioversion after the PVI had LVAs and were randomly assigned to ablation with BOXI plus LVAs ablation group (n = 7) or BOXI alone group (n = 7). AF was induced in all patients by rapid pacing at 207 ± 25 mseconds. The inducibility of atrial tachyarrhythmia in patients successfully cardioverted following PVI was 100% (Figure 3).

Box isolation was performed during AF in all patients. AF terminated in 15 (13 + 2) patients, in whom AF directly terminated into SR in 14 and converted to atrial flutter in 1. Of those patients, LVAs were found in seven patients (Figure 2), but not in eight patients. In the remaining 100(88 + 12) patients with sustained AF after the BOXI, AF was successfully cardioverted with 10 or 20 J. The rate of AF termination or cardioversion after BOXI was significantly higher than that after PVI (100% vs 88%, $P < 0.001$).
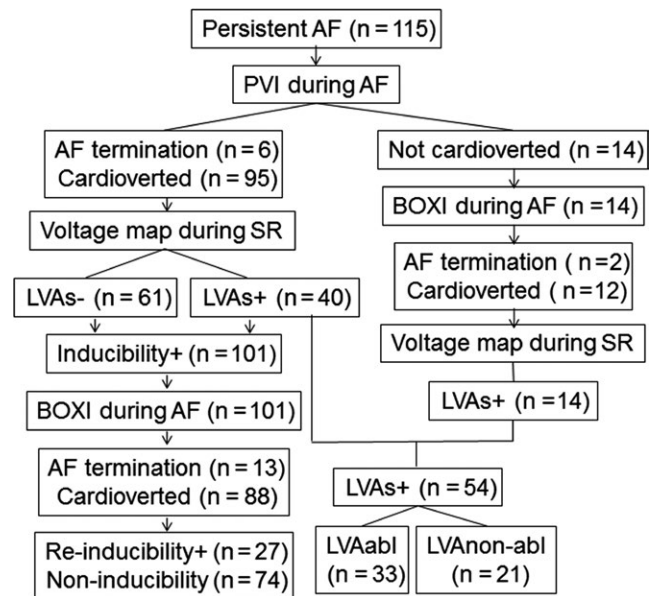
FIGURE 3 Flow chart of the study. abl, ablation; AF, atrial fibrillation; BOXI, Box isolation; LVAs, low-voltage areas; PVI, pulmonary vein isolation; SR, sinus rhythm

Box isolation was completely achieved in all patients. After BOXI, the re-inducibility of AF was assessed in 101 patients with induced AF after PVI (Figure 3). AF was induced in eight patients and atrial flutter/tachycardia was induced in 19, including CTI dependent flutter in 10 patients, perimitral flutter in five and atrial tachycardia in four. Of those 27 patients (27%), LVAs were found in 15 patients, but not in 12 patients. The inducibility of atrial tachyarrhythmia after BOXI was significantly lower than that after PVI (27% vs 100%, $P < 0.001$).

TABLE 1 Baseline characteristics of LVA− and LVA+ patients with and without LVA ablation

		LVAs+				
	LVAs− (n = 61)	Total (n = 54)	P value[a]	LVAabl (n = 33)	LVAnon-abl (n = 21)	P value[b]
Age, y	60 ± 10	65 ± 8	0.003	65 ± 8	65 ± 10	0.98
Female, n (%)	4 (7)	15 (28)	<0.001	8 (24)	7 (33)	0.47
CHADS$_2$	0.8 ± 0.8	0.8 ± 0.9	0.91	0.9 ± 0.8	0.8 ± 1.0	0.66
Persistent AF, n (%)	20 (33)	20 (37)	0.63	11 (33)	9 (43)	0.48
Long-perAF, n (%)	41 (67)	34 (63)		22 (67)	12 (57)	
LAd (mm)	44 ± 5	46 ± 5	0.08	46 ± 5	46 ± 5	0.89
LVEF (%)	59 ± 8	61 ± 7	0.06	61 ± 7	61 ± 8	0.71
CTI ablation, n (%)	38 (62)	34 (63)	0.94	21 (64)	13 (62)	0.90
SVC isolation, n (%)	8 (13)	9 (17)	0.59	5 (15)	4 (19)	0.71
RF energy, ×10^4 J	8.0 ± 2.5	8.4 ± 3.5	0.73	9.4 ± 3.4	6.7 ± 3.0	0.007
RF time (min)	49 ± 13	54 ± 24	0.30	62 ± 23	41 ± 18	<0.001
Procedure time (min)	115 ± 30	127 ± 40	0.07	143 ± 33	103 ± 39	<0.001
Fluoroscopic time (min)	33 ± 9	35 ± 11	0.36	39 ± 10	30 ± 11	0.002

abl, ablation; AF, atrial fibrillation; CTI, cavotricuspid isthmus; LAd, left atrial diameter; Long-perAF, longstanding persistent AF; LVA, low-voltage area; LVEF, left ventricular ejection fraction; RF, radiofrequency; SVC, superior vena cava.
[a]LVAs+ vs LVAs−.
[b]LVAabl vs LVAnon-abl.

Thus, the addition of BOXI to PVI facilitated AF termination and non-inducibility regardless of the presence or absence of LVAs.

3.2 | Additional effects of LVA ablation added to the BOXI

Table 1 shows the baseline characteristics of patients. The patients with LVAs were significantly older and more often females than those without LVAs. There were no significant differences in the patient characteristics, and the distribution and area of the LVAs between the LVAabl and LVAnon-abl groups (Tables 1 and 2). LVAs were frequently identified on the anterior LA wall and septum in both groups (Table 2). The LVAabl group had higher RF energy and longer RF, procedure, and fluoroscopic times as compared with the LVAnon-abl group (Table 1).There were no significant differences in AF termination during PVI (2 [6.1%] patients in LVAabl vs 2 [9.5%] patients in LVAnon-abl, P = 0.953) and BOXI (6 [18%] patients in LVAabl vs 3 [14%] patients in LVAnon-abl, P = 0.508), and AF inducibility after BOXI (10 [30%] patients in LVAabl vs 5 [24%] patients in LVAnon-abl, P = 0.604) between LVAabl and LVAnon-abl groups.

In the LVAabl group (n = 33), LVA ablation was performed during AF in 22 patients and AF terminated in three, in whom AF directly terminated into SR in one, was converted to CTI dependent flutter in one, and to atrial tachycardia in one. In the remaining 11 patients, LVA ablation was performed during SR. The complete isolation of the LVAs was achieved in 29 of 33 patients (88%). In 4 patients, the LVAs were not entirely ablated due to the wide area, but the anterior lines across the LVA were created.

TABLE 2 Comparison of distribution and area of LVAs between LVAabl and LVAnon-abl groups

| Variables	LVAabl (n = 33)	LVAnon-abl (n = 21)	P value
Anterior, n (%)	27 (82)	17 (81)	0.936
Septum, n (%)	18 (55)	11 (52)	0.876
Roof, n (%)	15 (45)	8 (38)	0.593
Posterior, n (%)	15 (45)	12 (50)	0.402
Inferior, n (%)	10 (30)	10 (48)	0.199
Lateral, n (%)	7 (21)	5 (24)	0.823
LVA (cm^2)	33 ± 19	39 ± 21	0.368
LVA/LA surface area (%)	30 ± 17	37 ± 17	0.174

abl, ablation; LA, left atrium; LVA, low-voltage area.

3.3 | Procedural complications

One patient in the group without LVAs had a pericardial effusion, but no surgical intervention was required. No major complications occurred in any of the groups.

3.4 | Ablation outcomes

After a single procedure, 50 (82%) of 61 patients without LVAs, 35 (65%) of 54 patients with LVAs, 22 (67%) of 33 patients in the LVAabl group, and 13 (62%) of 21 patients in the LVAnon-abl group had no recurrence of atrial tachyarrhythmia during 24 ± 9 months of follow-up (Figure 4). A rate of freedom from atrial tachyarrhythmia in the
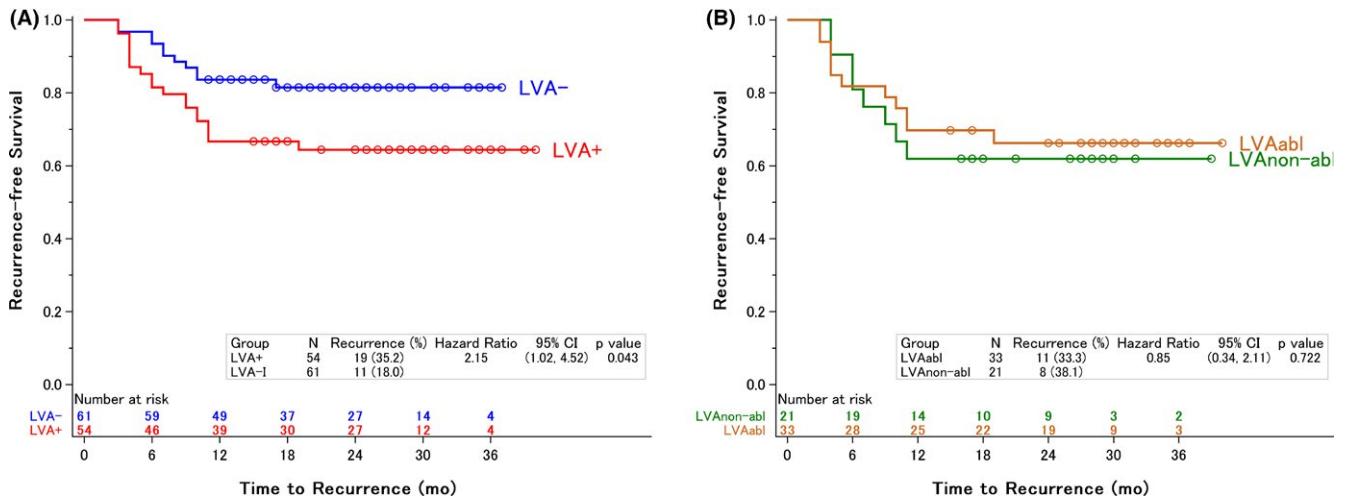
FIGURE 4 Kaplan-Meier survival curves showing the cumulative atrial tachyarrhythmia-free survival in the patients with and without low-voltage areas (LVAs) (A), LVA ablation (LVAabl) and LVA non-ablation (LVAnon-abl) groups (B) after a single procedure

overall patients with LVAs, was significantly lower than that in the patients without LVAs ($P = 0.043$, Figure 4A). However, the survival curves of the LVAabl and LVAnon-abl groups crossed in the early follow-up period (<12 months), and atrial tachyarrhythmia-free rate was not significantly different between the two groups ($P = 0.722$, Figure 4B). The patients with inducible atrial tachyarrhythmias had a significantly higher AF recurrence rate than those without inducible atrial tachyarrhythmias (41% vs 20%, $P = 0.017$).

Among the 11 patients in the group without LVAs who had recurrence, 10(91%) had AF and 1 (9%) had atrial flutter. A second procedure was performed in 7 of 11 patients with recurrence, in whom a re-BOXI was performed in six, SVC isolation in four, and mitral isthmus ablation in one. Among the 11 patients in the LVAabl group who had a recurrence, nine (82%) had AF and two (18%) had atrial flutter. A second procedure was performed in 6 of 11 patients with recurrence, in whom a re-BOXI was performed in four, SVC isolation in six, and mitral isthmus ablation in one. Among the eight patients in the LVAnon-abl group who had a recurrence, six (75%) had AF and two

(25%) had atrial flutter. A second procedure was performed in five of eight patients with recurrence, in whom a re-BOXI was performed in two, SVC isolation in four, and mitral isthmus ablation in one.

After the second procedure, a total of 56 patients (92%) in the group without LVAs, 41 (76%) in the overall patients with LVAs, 26 (79%) in the LVAabl group, and 15 (71%) in the LVAnon-abl group had no recurrence during 20 ± 10 months of follow-up (Figure 5). A rate of freedom from atrial tachyarrhythmia in the overall patients with LVAs, was significantly lower than that in the patients without LVAs ($P = 0.022$, Figure 5A). However, atrial tachyarrhythmia-free rate was not significantly different between the LVAabl and LVAnon-abl groups ($P = 0.603$, Figure 5B).

3.5 | Predictors of atrial tachyarrhythmia recurrence

The results of the univariate and multivariate analysis are shown in Table 3. An LVA was a univariate predictor of an atrial tachyarrhythmia recurrence. After adjusting for baseline characteristics,
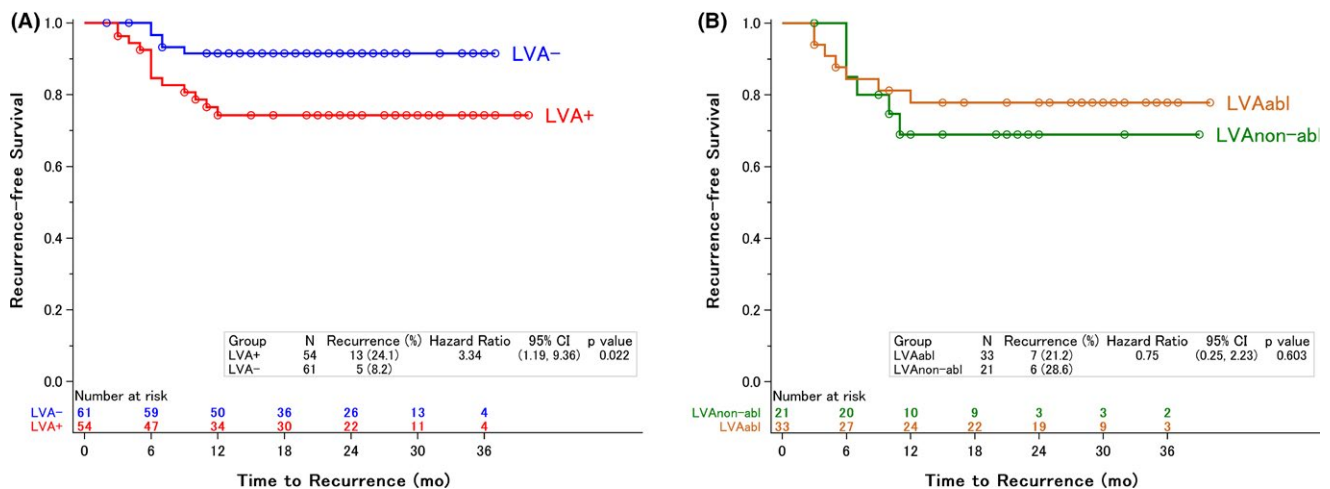
FIGURE 5 Kaplan-Meier survival curves showing the cumulative atrial tachyarrhythmia-free survival in the patients with and without low-voltage areas (LVAs) (A), LVA ablation (LVAabl), and LVA non-ablation (LVAnon-abl) groups (B) after a second procedure

longstanding persistent AF was an independent predictor of an atrial tachyarrhythmia recurrence. The patients with longstanding persistent AF were 2.9 times more likely to fail at the follow-up (HR 2.88, 95% CI 1.03-8.05, *P* = 0.044).

4 | DISCUSSION

4.1 | Main findings

The present study demonstrated that (a) the addition of BOXI to PVI facilitated AF termination and its non-inducibility regardless of the presence or absence of LVAs, (b) BOXI alone was adequate in patients without LVAs, and (c) patients with LVAs have higher risk of AF recurrence, however, the addition of LVA ablation to BOXI did not improve atrial tachyarrhythmia-free rate in persistent AFpatients.

4.2 | Benefits of BOXI over the PVI in persistent AF

The STAR AF II trial demonstrated that both linear ablation and ablation of complex fragmented atrial electrograms showed no benefit over PVI in patients with persistent AF.[24] In contrast, it has been shown that BOXI in addition to PVI results in a better outcome than PVI alone in patients with persistent AF.[16-23] BOXI can reduce the critical mass for the maintenance of AF by eliminating the potential triggers and rotors within the posterior LA. In the present study, BOXI facilitated AF termination and its non-inducibility. Therefore, BOXI should be considered in patients with persistent AF.

4.3 | Additional effects of adding the LVA ablation to the BOXI

Previous studies reported that LVA ablation after PVI markedly improved success rate in persistent AF patients with LVAs (LVAabl group vs LVAnon-abl group: 70% vs 27% in Rolf et al,[12] 72% vs 6% in Yamaguchi et al[15]). However, we found that addition of LVA ablation to BOXI after PVI did not significantly improve the success rate in persistent AF patients with LVAs (LVAabl group vs LVAnon-abl group: 67% vs 62%). Therefore, our finding suggests that the additional benefit of BOXI may prevent AF recurrence even in patients with LVAs.

It is possible that BOXI may eliminate the triggers in the posterior LA. Moreover, BOXI can serve as LVA ablation when LVAs are localized to the posterior LA. However, it is not clear why the LVAs outside of the posterior LA were not related to the outcomes. Cutler et al[16] performed BOXI only when LVAs were found in the posterior LA and achieved a sufficient success rate (80%) without having to ablate the other LVAs, which are generally identified more commonly on the anterior LA wall. Those results suggest that the LVAs outside of the posterior LA may be bystanders. Recently, Sakata et al[25] revealed that rotors and multiple wavelets assumed as AF drivers did not always coincide with LVAs. It is possible that there may be active LVAs, which should be targeted for ablation and dormant LVAs. Thus, the necessity of additional ablation of LVAs outside of the posterior LA is controversial. Moreover, the voltage depends on the thickness of the atrial myocardium, contact of the electrode with the tissue, size of the electrode, and inter-electrode distance. Therefore, LVAs may not always represent the presence of fibrotic tissue.

In patients with large LVAs, an entire regional LVA ablation is impractical, incomplete ablation may cause atrial tachycardia, and extensive anterior LA ablation may decrease the LA systolic function. Even if all LVAs are completely ablated, subclinical LVAs (0.6-1.0 mV) may later progress to obvious LVAs. However, a randomized study demonstrated that patients without LVAs did not need further substrate modification and could avoid excessive ablation.[26] Therefore, BOXI alone may be adequate in persistent AF patients without LVAs. Moreover, additional LVA ablation after BOXI may not always be necessary during the first procedure.

4.4 | Study limitations

This was a single center study, and it is possible that a solid conclusion may not be reached regarding the effects of LVA ablation on the recurrence due to a relatively small sample size. However, two previous studies compared the outcome of LVAabl and LVnon-abl groups in addition to PVI in similar sample sizes (LVAabl group vs LVAnon-abl group: 47 vs 26 patients in Rolf et al,[12] 39 vs 16 patients in Yamaguchi et al[15]). It took a long time to collect the patients with LVAs which were found in about 40% of the patients with persistent AF.

It is possible that asymptomatic recurrences were missed. An implanted loop recorder would give the highest sensitivity detection,

TABLE 3 Predictors of atrial tachyarrhythmia recurrence

Variables	Univariate		Multivariate	
	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age	1.01 (0.96-1.05)	0.83	0.99 (0.95-1.04)	0.82
Male gender	0.46 (0.17-1.21)	0.12	0.62 (0.21-1.83)	0.39
Long-perAF	2.67 (0.99-7.21)	0.053	2.88 (1.03-8.05)	0.044
LA size	1.01 (0.93-1.09)	0.78	1.00 (0.92-1.09)	0.98
LVA	2.47 (1.05-5.83)	0.039	2.39 (0.90-6.30)	0.079

CI, confidence interval; HR, hazard ratio; LA, left atrium; Long-perAF, longstanding persistent atrial fibrillation; LVA, low-voltage area.

but may be cost-prohibitive. Also, a monitoring frequency bias may exist in symptomatic patients but all patients with longstanding persistent AF in the present study were asymptomatic.

5 | CONCLUSIONS

Box isolation facilitates AF termination and its non-inducibility regardless of the presence or absence of LVAs. Among the patients with persistent AF, BOXI alone may be adequate in cases without LVAs. Although cases with LVAs have higher risk of AF recurrence, additional LVA ablation did not improve the outcomes much.

CONFLICT OF INTEREST

The authors declare no conflict of interests for this article.

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