Clinical outcomes of left atrial circumferential ablation and box ablation for paroxysmal atrial fibrillation

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Running title: LACa versus BOXa for PAF

ABSTRACT

Purpose: Left atrial circumferential ablation (LACa) and box ablation (BOXa) are common treatments for paroxysmal atrial fibrillation (PAF). However, few studies have compared both strategies. This study aimed to compare the clinical outcomes of these two therapeutic modalities.

Methods: Patients with PAF undergoing catheter ablation were randomly assigned to the LACa or BOXa groups and were followed up for 6 months. The primary outcomes were the rate of AF recurrence at 6months and changes in left atrial ejection fraction (LAEF) measured by magnetic resonance imaging from baseline to follow-up. The secondary outcomes included the frequency of supraventricular premature beats (SPBs) and short supraventricular runs (SVRs) on a 24-hr electrocardiogram at follow-up.

Results: Forty patients were randomized into the LACa group (n=21) or the BOXa group (n=19). There were no significant between-group differences regarding patient characteristics and LAEF at baseline, rate of AF recurrence at 6 months (LACa, 4.8% [1/21] vs. BOXa, 5.3% [1/19]; *P*=0.94), and changes in LAEF at 3 and 6 months. However, SPB and SVR frequency at 6 months were significantly lower in the LACa group than in the BOXa group (0.2 [-0.2, 0.50]/24hr vs. 0.8 [0.5, 1.2]/24hr, *P*=0.01; 2.2 [-4.2, 8.7]/24hr vs. 11.9 [4.8, 18.9]/24hr, *P*=0.04, respectively).

Conclusion: Although LACa and BOXa were comparable in terms of the rate of AF recurrence and changes in LAEF, the higher incidence of SPBs and SVRs at 6 months in the BOXa group indicates that BOXa showed no advantage in treatment of patients with PAF.

Keywords: atrial fibrillation, catheter ablation, left atrium function, recurrence rate, supraventricular premature beats

INTRODUCTION

There is an increase in the prevalence of atrial fibrillation (AF) globally (1). It is known that patients with AF are at increased risk of ischemic stroke and heart failure, with the latter occurring in approximately 40% of patients (2-4). In patients with AF, catheter ablation is more effective in reducing cardiovascular events and mortality compared to anti-arrhythmic drug therapy (5, 6). These findings have led to more widespread application of catheter ablation for AF, particularly in patients with paroxysmal AF (PAF) (2-6). However, the specific method of catheter ablation that is most effective for treating PAF remains unknown. Moreover, the effects of catheter ablation on left atrial function, including ejection fraction, remain unclear. Left atrial circumferential ablation (LACa) and box ablation (BOXa) are among the methods recently used to treat PAF (7, 8). Previous studies involving small cohorts reported that both strategies were beneficial in terms of acute success and procedural complication rates (9, 10). However, few studies have directly compared both strategies. Therefore, this study aimed to evaluate the efficacy, safety, and effect on atrial function of LACa and BOXa in the management of PAF.

SUBJECTS AND METHODS

Study design

This study was a prospective, randomized, single-blind, single-center trial (Clinical Trial Registration: UMIN-CTR, UMIN000028470) that included patients with PAF recruited between October 2017 and August 2018. The study was conducted per the Declaration of Helsinki and was approved by the Institutional Review Board of Showa University Northern Yokohama Hospital (approval number: 17H032). Written informed consent was obtained from all participants. Since there is no previous study, we planned 80 cases with reference to the study of

20 registrants who calculated left atrial ejection fraction (LAEF) by magnetic resonance imaging (MRI). However, due to the capacity of MRI in our hospital, the registration was completed with 40 cases (11).

Patients (20–80 years old) diagnosed with PAF and referred for catheter ablation due to refractory symptoms as well as patients with de novo PAF were included. Refractory symptoms were defined as the failure of symptom resolution after using more than one class I or III antiarrhythmic drugs or beta-blockers. Patients with the following characteristics were excluded: history of congenital heart disease; contraindications to MRI; and requiring hemodialysis treatment. After enrollment, patients were randomly assigned to undergo LACa or BOXa. The flow chart of the study is presented in Figure 1. Patients not having sinus rhythm when analyzed by MRI are not appropriate to measure accurate LAEF. Similarly, if it is not sinus rhythm, the values of 24-h Holter monitor and biomarker would be inappropriate. Therefore the cases with AF recurrence after catheter ablation were excluded from the analyses of MRI, 24-hr Holter monitor and biomarker.

Interventions

An electro-anatomical mapping system (CARTO® 3, Biosense Webster, CA, USA; EnSite™ NavX™, Abbott, IL, USA; EnSite™ Velocity, Abbott, IL, USA) was used to create a three-dimensional model of the left atrium (LA). First, a transeptal puncture was performed under fluoroscopic and intracardiac echocardiographic guidance. A circulatory mapping catheter (Inquiry™ AFocusII™, Irvine Biomedical Inc., CA, USA; or PentaRay®, Biosense Webster, Inc., CA, USA) was placed inside the pulmonary veins, and a wide antral ablation line was created around each pair of ipsilateral pulmonary veins using a radiofrequency ablation catheter

(TactiCath™, Abbott, IL, USA; or THERMOCOOL SMARTTOUCH®, Biosense Webster, CA, USA: 30–35 W, 30–40 sec, 10–20 g). LACa was defined as completion of the procedure described above. In the BOXa group, after complete pulmonary vein isolation, a “roof line” was created between the top of each contralateral set of lesions, and a “floor line” closed the posterior wall that connected the base of each set of the contralateral lesion in a “box” fashion. The endpoint of both procedures was complete isolation of the posterior wall, dissociation of the potentials in the posterior wall using a high-density mapping catheter (inquiry™ AFocusII™, Irvine Biomedical Inc., CA, USA; or PentaRay®, Biosense Webster, Inc., CA, USA), and the inability to capture the atrium by 10-V pacing in the posterior wall after regaining sinus rhythm. Power titration was performed according to the esophageal temperature, and radiofrequency lesions were interrupted when ≥39° was reached.

Outcome measures

The primary outcomes in the comparison of BOXa and LACa were the rate of AF recurrence (lasting more than 30 sec) at 6months and changes in LAEF measured by MRI from baseline to follow-up. The secondary outcome was the frequency of supraventricular premature beats (SPBs) and short supraventricular runs (SVRs). The laboratory data, the frequency of SPBs and SVRs, and LAEF using MRI were evaluated at baseline and at 3- and 6 months after the procedure. Early recurrence of AF within the first 90 days after ablation is not considered as recurrence, because it may result from inflammation or incomplete lesion healing, which is common and is not necessarily predictive of long-term outcomes (12). Recurrent arrhythmias managed with anti-arrhythmic drugs or cardioversion within the blanking period were therefore excluded from the number of AF recurrence. The frequency of SPBs was defined as the

SPB/total heart rate on a 24-hr Holter monitor. SVRs were defined as >3 consecutive supraventricular beats with an accelerated cycle length lasting <30 s (13).

Patients were placed in a supine position and cardiac MRI was performed using a 3.0-T scanner (GE Medical Systems, Milwaukee, WI, USA). After localizing the scans, electrocardiography-gated cine images of the heart were obtained in two standard long axes and multiple short-axis slices, with a slice thickness of 8 mm and an interslice distance of 2 mm from the base to the apex of the heart. All images were analyzed offline using Ziostation 2 (Ziosoft Inc., Tokyo, Japan). The LA maximum was defined as the frame immediately preceding mitral valve opening. We defined LA maximun as Left atrial diameter maximum (LAD maximum). The LA minimum was defined as the frame immediately following mitral valve closure. The volumes were measured in both two- and four-chamber views by two experienced operators. The endocardial border of the LA was traced manually. Excluding the LA appendage, the anterior border was located at the mitral annular plane, while the posterior border at the ostia of the pulmonary veins. LA volumes were calculated using the area–length method (volume = 0.85 × area2/length), and the LAEF was calculated using the formula: [(LA max – LA min)/LA max] × 100%. Additionally, the LA total emptying volume was calculated (reservoir function) using LA max – LA min, and the LA conduit volume was calculated using LV stroke volume – LA total emptying volume (14).

Study follow-up

Hospital visits were scheduled at 3- and 6 months following the ablation procedure. At each visit, the medical history, MR images, blood examination, and 24-hr Holter monitoring records were obtained. All follow-up assessments were performed by study personnel who were blinded to the treatment assignments.

Statistical analysis

We were unable to calculate the minimum number of patients required for this study because there are limited data on LA function in patients with AF who have undergone catheter ablation. Therefore, we enrolled 40 patients as per our procedure volume. The primary hypothesis was that BOXa using radiofrequency ablation was inferior to LACa in terms of LAEF.

Continuous variables were reported as medians and interquartile ranges (IQR), representing the 25th to 75th percentiles of the distribution data and compared using the Mann-Whitney U test. Categorical variables were presented as percentages and compared using the chi-square test or Fisher's exact test, as appropriate. A multiple linear regression analysis was performed to examine the predictors of SVRs including variables when a $P<0.10$ was obtained for the single regression analysis or if the relationship was demonstrated by previous studies. The regression coefficient and 95% confidence interval (CI) were calculated. Multicollinearity was assessed using the variance inflation factor (analysis of variance). Statistical significance was set at $P<0.05$. All data were analyzed using JMP software (SAS Institute, Inc., Cary, NC, USA).

RESULTS

A total of 40 patients (LACa: 21, BOXa: 19) were included in this study. No significant between-group differences were observed regarding patient characteristics and baseline LAEF (Table 1). Among the procedure variables, only ablation time significantly differed between the two groups; ablation time was significantly shorter in patients treated with LACa than in those treated with BOXa (43.8 [39.5, 47.9]min vs. 49.1 [44.3, 53.8]min, *P*=0.047). Notably, the AF recurrence rate at 6 months following the procedures was similar in both groups (LACa, 4.8% [1/21] vs. BOXa, 5.3% [1/19]; *P*=0.94). The LAEF at 3- and 6 months also did not significantly differ between the LACa and BOXa groups (26.4 [23.1, 29.7]% vs. 25.0 [20.2, 29.8]%, *P*=0.60; 25.4 [22.8, 29.7] % vs. 25.9 [21.1, 30.8] %, *P*=0.85, respectively) (Table2, Figure 2).

No significant difference was observed in the changes in LAEF between the patients treated with LACa and those treated with BOXa at 3 months (0.1 [-3.9, 4.1]% vs. 1.2 [-5.0, 7.4]%, *P*=0.75) and at 6 months (-0.8 [-5.8, 4.1]% vs. 2.1 [-3.2, 7.5]%, *P*=0.41), respectively (Table 2, Figure 3). Brain natriuretic peptide (BNP) level at 3 months (32.0 [18.6, 45.4]pg/ml vs. 46.2 [27.4, 65.0]pg/ml, *P*=0.16) and 6 months (38.2 [20.7, 43.3]pg/ml vs. 41.9 [23.4, 60.4]pg/ml, *P*=0.72) were not significantly different between the two groups. LAD maximum at 3 months (40.4 [39.0, 41.9]mm vs. 39.9 [38.3, 41.4]mm, *P*=0.58) and 6 months were not significantly different between the two groups (39.6 [38.2, 41.0]mm vs. 39.8 [38.2, 41.3]mm, *P*=0.86). At 6 months, the frequencies of SPBs (0.2 [-0.2, 0.50]/24hr vs. 0.8 [0.5, 1.2]/24hr, *P*=0.01) and SVRs (2.2 [-4.2, 8.7]/24hr vs. 11.9 [4.8, 18.9]/24 hr, *P*=0.04) were significantly lower in the LACa group than in the BOXa group (Table 2). The multiple regression analysis revealed that BOXa was an independent predictor of the frequency of SVRs (regression coefficient=18, 95% CI, 2.37–33.7, *P*=0.03) (Table 3).

DISCUSSION

This study compared the efficacy of LACa and BOXa for treating PAF. No significant differences were observed between the LA function and AF recurrence rate between the two treatment modalities. However, frequencies of SPBs and SVRs were significantly lower in the LACa group than in the BOXa group.

Atrial contraction causes additional blood flow (~20–30%) across the mitral valve, thereby contributing to the total diastolic volume. Insufficient filling of the left ventricle due to loss of atrial contraction can reduce cardiac output. Considering this, identifying the effect of radiofrequency ablation on the LA function of patients with AF is important. Our findings revealed no changes in the LAEF of patients pre- and post-ablation. Similarly, changes in LAEF were similar between the two groups. The small area of ablation or an anatomic reason during BOXa is speculated to cause an absence of posterior wall contractility. No significant differences in the biomarkers for the LA wall stress were consistent with the findings of the LAEF on cardiac MRI. We removed the LAA during the LAEF measurement. The reason is that the ejection fraction of LAA cannot be measured well by MRI due to technical problems. So our study did not reveal the impact of LAA on LAEF.

The rate of AF recurrence was similar between the two groups. In patients with persistent AF, BOXa may be associated with a decrease in the recurrence of AF (15). In contrast, Kim et al. demonstrated the inferiority of BOXa linear ablation in addition to LACa in reducing the recurrence rate in patients with PAF (16). Their results were different from our study result. We thought that the causes were the short follow-up period of 6 months and the small study population. But long-term follow-up may give different results. Furthermore, We thought it is highly possible that roof and floor lines for BOXa reconnect to LA. Thomas et al. reported linear ablation (BOXa and anterior linear ablation) in addition to LACa did not improve clinical outcomes in patients with PAF because they reported that complete bidirectional conduction block rate was 68.0% in the linear ablation (17).

At 6 months postoperatively, the frequencies of SPBs and SVRs were significantly higher in patients treated with BOXa than in those treated with LACa in our study result. We expected SPBs and SVRs to decrease if they were the perfect lines for all BOXa cases. Because the initial box lesion was speculated to generate atrial tachycardia (AT) through electrical gaps. Thomas et al. reported that the roof line often becomes the major problem area for creating posterior LA isolation because of the deeper muscle bundles on the roof (17). In addition, another study demonstrated that the floor line was a major limitation in achieving posterior LA isolation (18). The major recurrence sites at the floor line were adjacent to the esophagus; to avoid esophageal injury, radiofrequency energy was not delivered to the LA sites in contact with the esophagus. Choi et al. suggested that SPBs and SVRs were associated with an increase in the rate of AF recurrence rate (19). AT is common after ablation and is symptomatic and refractory to antiarrhythmic drugs (20, 21). Furthermore, previous studies suggested that an electrical gap along the ablation line resulted in a conduction delay in the LA, leading to an excitable gap that might present as macro-reentrant AT (22, 23). An incomplete conduction block of linear ablation increases the risk of recurrent AT (24). Our study found no benefit from additional ablation and the cause was unknown. Similarly, Atul Verma et al. reported that among patients with persistent atrial fibrillation, they found no reduction in the rate of recurrent atrial fibrillation when either linear ablation (left atrioventricular roof + mitral valve annulus) or ablation of complex fractionated electrograms (CFAE) was performed in addition to LACa (25). Atul Verma et al. reported that a wider range of ablation was incompletely line-ablated and additional ablation could cause new iatrogenic areas of arrhythmia development (25). In a report comparing LACa+

left atrial linear ablation (left atrioventricular roof + mitral valve annulus) and LACa in patients with PAF, extensive line ablation for electrically normal atrial fibrillation might increase iatrogenic arrhythmias and negated the benefits of reduced recurrence rates of atrial fibrillation (26). Our study also attributed the increase in SVB SVR to the emergence of new iatrogenic areas of arrhythmia due to incomplete line ablation gap and unnecessary incomplete additional ablation. It has also been reported that both frequent PAC and long PAC run at 6 months after ablation are independent predictors of late recurrence (27). Our results of long-term follow-up might have made a difference in AF recurrence rates.

Limitation

There are some limitations in this study. First, the study involved a single-center with a small cohort, which may have limited the power to detect associations and the ability to control confounders in the multivariate models. Second, a universal method for measuring cardiac MRI has not been established; therefore, inconsistencies in the results of cardiac MRI may be observed in each method of measurement. Finally, there is no established cut-off point regarding the frequency of SPBs that is considered pathological.

Conclusion

In conclusion, although LACa and BOXa were comparable in terms of AF recurrence rates and LAEF changes, BOXa exhibited a higher frequency of SVBs and SVRs at 6 months compared to LACa. BOXa may be associated with an increase in AT after ablation. BOXa showed no advantage in patients with PAF. Therefore, treatment of PAF with LACa may be more beneficial than BOXa treatment and may not require additional ablation. Further studies are required to confirm the effects of each catheter ablation strategy on LA function and the recurrence of atrial arrhythmias in patients with PAF.

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W.I., Y.A., J.S., Y.O., K.Y., N.I., and M.Ochiai treated the patients and collected the data and helped draft the manuscript. M.Y. helped perform the statistical analysis. M.Ochiai. N.I. T.O. and M.Ono participated in the study design and coordination and helped draft the manuscript. M.Ono and T.O. participated in the study design and wrote the manuscript. All authors have read and approved submission of the manuscript.

Conflict of Interest Disclosure: The authors have no competing interests to declare.

REFERENCES

1. Chugh SS, Havmoeller R, Narayanan K, *et al.* Worldwide epidemiology of atrial fibrillation: a Global Burden of Disease 2010 Study. *Circulation*. 2014;**129**:837–847.
2. Gómez-Outes A, Lagunar-Ruíz J, Terleira-Fernández AI, *et al.* Causes of death in anticoagulated patients with atrial fibrillation. *J Am Coll Cardiol*. 2016;**68**:2508–2521.
3. Zafrir B, Lund LH, Laroche C, *et al.* Prognostic implications of atrial fibrillation in heart failure with reduced, mid-range, and preserved ejection fraction: a report from 14 964 patients in the European Society of Cardiology Heart Failure Long-Term Registry. *Eur Heart J*. 2018;**39**:4277–4284.
4. Okabe T, Yakushiji T, Kido T, *et al.* Poor prognosis of heart failure patients with in-hospital worsening renal function and elevated BNP at discharge. *ESC Heart Fail*. 2020;**7**:2912–2921.
5. Marrouche NF, Brachmann J, Andresen D, *et al.* Catheter ablation for atrial fibrillation with heart failure. *N Engl J Med*. 2018;**378**:417–427.
6. Turagam MK, Garg J, Whang W, *et al.* Catheter ablation of atrial fibrillation in patients with heart failure: a meta-analysis of randomized controlled trials. *Ann Intern Med*. 2019;**170**:41–50.
7. Kettering K, Yim DH, Benz A, *et al.* Catheter ablation of paroxysmal atrial fibrillation: circumferential pulmonary vein ablation: success rates with and without exclusion of areas adjacent to the esophagus. *Clin Res Cardiol*. 2017;**106**:743–751.
8. Yang CH, Chou CC, Hung KC, *et al.* Comparisons of the underlying mechanisms of left atrial remodeling after repeat circumferential pulmonary vein isolation with or without additional left atrial linear ablation in patients with recurrent atrial fibrillation. *Int J*

Cardiol. 2017;**228**:449–455.

9. Lee JM, Shim J, Park J, *et al.* The electrical isolation of the left atrial posterior wall in catheter ablation of persistent atrial fibrillation. *JACC Clin Electrophysiol*. 2019;**5**:1253–1261.
10. Steinbeck G, Sinner MF, Lutz M, *et al.* Incidence of complications related to catheter ablation of atrial fibrillation and atrial flutter: a nationwide in-hospital analysis of administrative data for Germany in 2014. *Eur Heart J*. 2018;**39**:4020–4029.
11. O. Rodevand, R. Bjornerheim1, M. Ljosland, *et al.* Left atrial volumes assessed by three- and two-dimensional echocardiography compared to MRI estimates. *Int J Cardiovasc Imaging*. 1999;15:397-410.
12. Calkins H, Kuck KH, Cappato R, *et al.* 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: *Heart Rhythm*. 2012;**9**:632–696.e21.
13. Kochhäuser S, Dechering DG, Dittrich R, *et al.* Supraventricular premature beats and short atrial runs predict atrial fibrillation in continuously monitored patients with cryptogenic stroke. *Stroke*. 2014;**45**:884–886.
14. Pellicori P, Zhang J, Lukaschuk E, *et al.* Left atrial function measured by cardiac magnetic resonance imaging in patients with heart failure: clinical associations and prognostic value. *Eur Heart J*. 2015;**36**:733–42.
15. Bai R, Di Biase L, Mohanty P, *et al.* Proven isolation of the pulmonary vein antrum with or without left atrial posterior wall isolation in patients with persistent atrial fibrillation. *Heart Rhythm*. 2016;**13**:132–140.
16. Kim TH, Park J, Park JK, *et al.* Linear ablation in addition to circumferential pulmonary

vein isolation (Dallas lesion set) does not improve clinical outcome in patients with paroxysmal atrial fibrillation: a prospective randomized study. *Europace*. 2015;**17**:388–395.

17. Thomas SP, Lim TW, McCall R, *et al.* Electrical isolation of the posterior left atrial wall and pulmonary veins for atrial fibrillation: feasibility of and rationale for a single‑ring approach. *Heart Rhythm*. 2007;**4**:722–730.
18. Higuchi S, Sohara H, Nakamura Y, *et al.* The feasibility of a Box isolation strategy for non-paroxysmal atrial fibrillation in elderly patients. *J Arrhythm*. 2016;**6**:198–203.
19. Choi JI, Pak HN, Park JS, *et al.* Clinical significance of early recurrences of atrial tachycardia after atrial fibrillation ablation. *J Cardiovasc Electrophysiol*. 2010;**21**:1331–1337.
20. Chae S, Oral H, Good E, *et al.* Atrial tachycardia after circumferential pulmonary vein ablation of atrial fibrillation: mechanistic insights, results of catheter ablation, and risk factors for recurrence. *J Am Coll Cardiol*. 2007;**50**:1781–1787.
21. Takigawa M, Derval N, Frontera A, *et al.* Revisiting anatomic macroreentrant tachycardia after atrial fibrillation ablation using ultrahigh-resolution mapping: implications for ablation. *Heart Rhythm*. 2018;**15**:326–333.
22. Horlitz M, Schley P, Shin DI, *et al.* Atrial tachycardias following circumferential pulmonary vein ablation: observations during catheter ablation. *Clin Res Cardiol*. 2008;**97**:124–130.
23. Harrison JL, Sohns C, Linton NW, *et al.* Repeat left atrial catheter ablation: cardiac magnetic resonance prediction of endocardial voltage and gaps in ablation lesion sets. *Circ Arrhythm Electrophysiol*. 2015;**8**:270–278.

24. Anousheh R, Sawhney NS, Panutich M, *et al.* Effect of mitral isthmus block on development of atrial tachycardia following ablation for atrial fibrillation. *Pacing Clin Electrophysiol*. 2010;**33**:460–468.

25. Atul V, Chen-yang J, Timothy R, *et al*. Approches to Catheter Ablation for Persistent Atrial Fibrillation. *NEJM*. 2015;**372**:1812-1822.

26. Navinder S, Ramtin A, Wei C, *et al*. Circumferential Pulmonary Vein Ablation With Additional Linear Ablation Results in an Increased Incidence of Left Atrial Flutter Compared With Segmental Pulmonary Vein Isolation as an Initial Approach to Ablation of Paroxysmal Atrial Fibrillation. *Circ Arrhythm Electrophysiol*. 2010;**3**:243-248.

27. Hiroyuki I, Nobuaki T, Koji T, *et al*. Burden and Long Firing of Premature Atrial Contraction Early After Catheter Ablation Predict Late Recurrence of Atrial Fibrillation. *Circ Journal*. 2020;**84**:894-901.

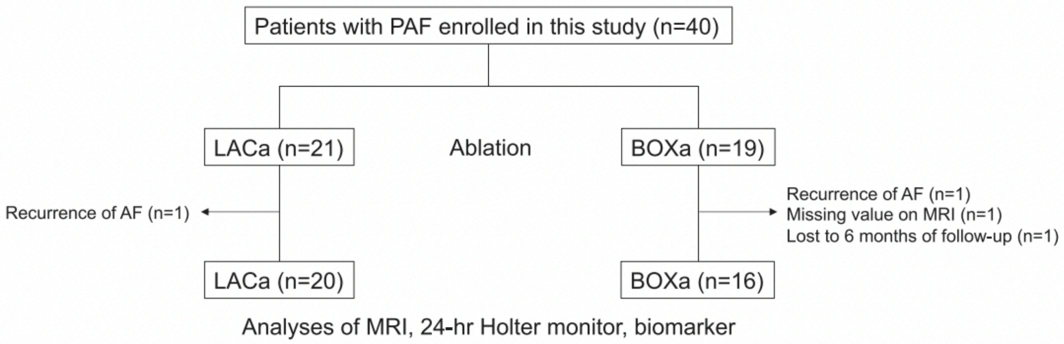

Fig. 1. Study flowchart

Table 1. Patient and procedural characteristics

	LACa (n=21)	BOXa (n=19)	*P*-value
Age, years	65.3 [61.3, 69.2]	68.3 [62.7, 73.7]	0.35
Female	7 (33.3)	5 (26.3)	0.62
BMI, kg/m^2	22.6 [20.8, 24.4]	22.4 [21.1, 23.6]	0.83
Hypertension	10 (47.6)	9 (47.4)	0.98
Diabetes	4 (19.1)	3 (15.8)	0.78
Hyperlipidemia	9 (42.9)	7 (36.8)	0.69
Smoking	9 (42.9)	5 (26.3)	0.27
Alcohol intake history	5 (23.1)	4 (21.1)	0.83
$CHADS_2$ score	0.8 [0.3, 1.2]	1.4 [0.9, 1.8]	0.09
Heart failure	1 (4.8)	1 (5.3)	0.94
LVEF, %	66.8 [63.5, 69.9]	63.1 [56.8, 69.5]	0.24
Hb, mg/dl	14.1 [13.5, 14.8]	14.3 [13.6, 15.0]	0.74
Creatinine, mg/dl	0.9 [0.07, 0.8]	0.8 [0.08, 0.7]	0.49
BNP, pg/ml	61.3 [48.1, 172.1]	110.1 [40.1, 81.9]	0.06
Procedural characteristics			
Radioscopic time, min	78.5 [68.1, 88.9]	73.7 [62.0, 85.4]	0.54
Dose radiation, mGy	517 [360, 638]	438 [302, 574]	0.38
Procedure time, min	214 [196, 232]	217 [197, 238]	0.79
Ablation time, min	43.8 [39.5, 47.9]	49.1 [44.3, 53.8]	0.047

Values are expressed as medians, interquartile ranges, or no. (percentage)
BOXa, box ablation; BMI, body mass index; Hb, hemoglobin; LACa, left atrial circumferential ablation; LVEF, left ventricular ejection fraction

Table 2. Primary and secondary outcomes in the LACa and BOXa groups

	LACa (n=20)	BOXa (n=16)	*P* Value
LAEF at baseline, %	26.3 [21.8, 30.7]	23.8 [18.0, 29.8]	0.46
LAEF at 3 months, %	26.4 [23.1, 29.7]	25.0 [20.2, 29.8]	0.60
LAEF at 6 months, %	25.4 [22.8, 29.7]	25.9 [21.1, 30.8]	0.85
ΔLAEF (3 months-baseline), %	0.1 [−3.9, 4.1]	1.2 [−5.0, 7.4]	0.75
ΔLAEF (6 months-baseline), %	−0.8 [−5.8, 4.1]	2.1 [−3.2, 7.5]	0.41
LAD maximum at baseline	40.7 [38.7, 42.7]	41.7 [39.6, 43.9]	0.48
LAD maximum at 3 months, mm	40.4 [39.0, 41.9]	39.9 [38.3, 41.4]	0.58
LAD maximum at 6 months, mm	39.6 [38.2, 41.0]	39.8 [38.2, 41.3]	0.86
BNP at 3 months, pg/ml	32.0 [18.6, 45.4]	46.2 [27.4, 65.0]	0.16
BNP at 6 months, pg/ml	38.2 [20.7, 43.3]	41.9 [23.4, 60.4]	0.72
3-month SPB, /day	0.3 [0.02, 0.5]	0.48 [0.2, 0.7]	0.18
3-month SVR, /day	3.5 [−0.1, 7.1]	8.5 [4.4, 12.5]	0.06
6-month SPB, /day	0.2 [−0.2, 0.50]	0.8 [0.5, 1.2]	0.01
6-month SVR, /day	2.2 [−4.2, 8.7]	11.9 [4.8, 18.9]	0.04

Values are expressed as medians and interquartile ranges

LAEF, left atrial ejection fraction; ΔLAEF, changes in the LAEF; LACa, left atrial circumferential ablation; BNP, brain natriuretic peptide; BOXa, BOX ablation; PAC, premature atrial contraction; LAD, left atrium diameter measured by MRI

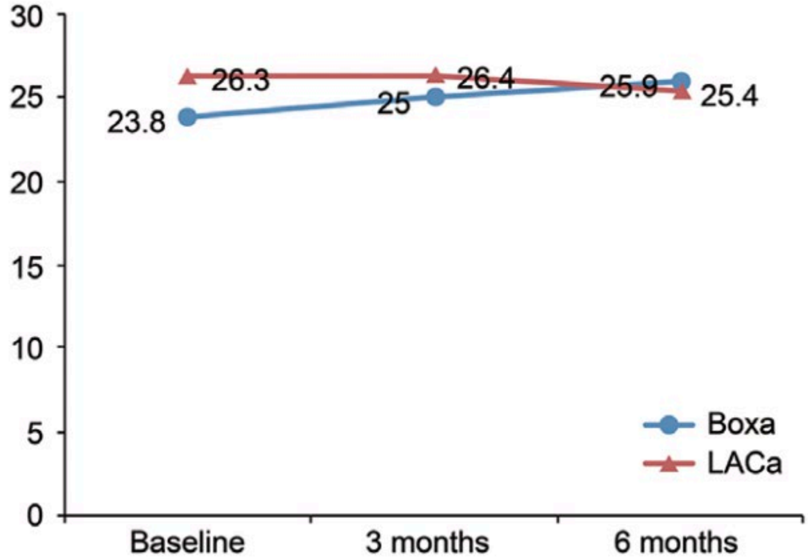

Fig. 2. Differences in the LAEF between the BOXa and LACa groups
(Red) LAEF of the LACa group over 6 months; (blue) LAEF of the BOXa group over 6 months
BOXa, box ablation; LACa, left atrial circumferential ablation; LAEF, left atrial ejection fraction

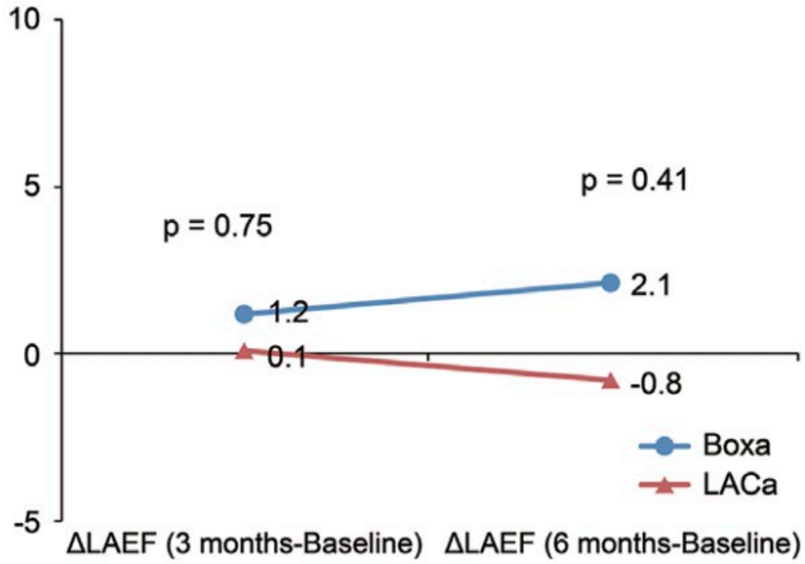

Fig. 3. Differences in the Δ LAEF between the BOXa and LACa groups

(Red) Change in the LAEF of the LACa group over 6 months ; (blue) change in the LAEF of the BOXa group over 6 months

BOXa, box ablation ; LACa, left atrial circumferential ablation ; LAEF, left atrial ejection fraction

Table 3. Multivariate regression analysis of the relations between the frequency of short supraventricular runs (SVRs) and variables

Covariate	Regression coefficient	95% Confidence interval	*P*-value
Age, years	1.41	[−0.34, 3.15]	0.11
Female	6.98	[−9.56, 23.52]	0.39
BNP at baseline, pg/ml	−0.17	[−0.36, 0.01]	0.07
BOXa	18.0	[2.37, 33.7]	0.03
LAD maximum at 6 months, mm	1.64	[−4.03, 7.32]	0.56

BNP, brain natriuretic peptide ; BOXa, BOX ablation ; LAD, left atrium diameter