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Persistence of left atrial abnormalities despite left atrial volume normalization after successful ablation of atrial fibrillation

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Abstract

Background: Left atrial volume index (LAVI) of >34 mL/m^2 is the cutoff value for identifying an enlarged left atrium. The definition of left atrial (LA) reverse remodeling after atrial fibrillation (AF) ablation is undetermined. We hypothesized that patients with LA dilatation who achieve normal LA volume (LAVI<34 mL/m^2) after AF ablation have better long-term outcomes than those who do not. Furthermore, we investigated whether patients with a normal LA volume can also achieve normal LA function with AF ablation.

Methods: We enrolled 140 AF patients with baseline LAVI of ≥34 mL/m^2, without AF recurrence for 1 year after the initial AF ablation. We acquired conventional and speckle-tracking echocardiographic parameters within 24 hour and at 1 year after the procedure. To define the normal range of LA function, age- and sex-matched controls without a history of AF were also enrolled.

Results: After restoration of sinus rhythm, LA structural and functional parameters significantly improved, and 75 patients (54%) had normal LA volume. During a median follow-up of 44 (31-61) months, 32 patients (23%) experienced a late recurrence of AF (AF recurrence >1 year). Patients who achieved normal LA volume after AF ablation had fewer late recurrences than those who did not ($P < .01$). However, LA abnormalities, especially LA dysfunction, persisted in AF patients even when the LA volume was normalized compared with controls.

Conclusion: Patients who achieved normal LA volume had better long-term outcomes of AF ablation than those who did not; however, LA abnormalities persisted even after successful ablation of AF.

KEYWORDS
atrial fibrillation, atrial remodeling, catheter ablation, echocardiography, recurrence

1 | INTRODUCTION

Atrial fibrillation (AF) is the most common arrhythmia encountered in clinical practice, and its prevalence is increasing due to the aging population.[1, 2] AF initiates self-perpetuating changes in the structural, functional, and electrophysiological properties of the atrium and promotes atrial remodeling (AF begets AF).[3]

It is well known that left atrial (LA) structural remodeling is associated with cardiac morbidity and cardiovascular outcomes, including heart failure, stroke, cardiac death, and AF development.[4-7] Regarding parameters assessed with cardiovascular imaging techniques, LA volume assessed using transthoracic echocardiography has been established as a robust and useful marker for LA remodeling since echocardiography is the most frequently used imaging technique in clinical practice. Recent guidelines demonstrate the normal ranges and severity partition cutoffs of LA volume abnormality assessed by echocardiography; the upper normal limit of LA volume index (LAVI) of 34 mL/m^2 is thought to correlate well with a risk-based approach for discrimination of cutoffs between a normal and an enlarged left atrium.[8]

In the past decade, catheter ablation has become an established non-pharmacological therapy for AF. Many studies have revealed a reduction in LA enlargement after restoration of sinus rhythm by catheter ablation (reverse remodeling).[9-20] Reverse remodeling has also been thought to be a useful predictor for not only acute recurrence (AF recurrence ≤1 year) but also late recurrence (AF recurrence >1 year) following procedures.[12-16] However, there is no clear definition of LA reverse remodeling after AF ablation because the degree of reverse remodeling varies among individuals and studies. Moreover, the association between the degree of LA reverse remodeling and long-term outcomes of AF ablation has not been fully investigated. In addition, it is unknown whether the LA function is reversible in parallel with LA structural remodeling.

Thus, we hypothesized that patients who achieved normal LA volume (LAVI <34 mL/m^2) with restored sinus rhythm had better long-term outcomes of AF ablation than patients who still had enlarged LA volume (LAVI ≥34 mL/m^2). Furthermore, we investigated whether the LA function recovered to the normal range in patients with normal LA volume.

2 | METHODS

2.1 | Study population

Figure 1 shows the selection of patients for the present study. We retrospectively identified 286 consecutive patients with AF who underwent initial radiofrequency catheter ablation (RFCA) and echocardiography within 24 hour at the Ehime University Hospital between November 2011 and April 2017. As nine patients were excluded because of atrial tachyarrhythmia during echocardiography (n = 3) and inability to perform strain analysis or acquire interpretable images from baseline echocardiography (n = 6), 277 patients whose baseline echocardiography was evaluated during sinus rhythm were selected. Of these 277 patients, 123 patients were excluded for the following reasons: no LA dilatation (LAVI <34 mL/m^2) at baseline (n = 29), loss to follow-up (n = 5), and AF recurrence within 1 year after initial RFCA (acute recurrence) (n = 89) because one of the aims of this study was to investigate the impact of LA reverse remodeling on the long-term outcome of RFCA for AF. At the 1-year follow-up, 154 patients maintained sinus rhythm after the initial RFCA even though LA remodeling existed at baseline. Of these 154 patients, follow-up echocardiography was performed for 140 patients. Thus, the final analysis was based on data obtained from 140 patients. Table A.1 shows comparison characteristics and ablation procedures between the study population (n = 140) and patients excluded due to acute recurrence of AF (n = 89). Except for baseline LAVI, there were no significant differences in almost all parameters between the two groups. Patients with acute recurrence of AF (excluded patients) had significantly larger LAVI than those without acute recurrence of AF (study population).

In addition, age- and sex-matched patients without a history of AF and structural heart disease were randomly selected as the control group from the echocardiographic database in our hospital. In the control group, the main reason for performing echocardiography was to screen for preoperative risks.

This study was approved by the Research Ethics Committee of the Ehime University Graduate School of Medicine.

2.2 | Ablation procedure

All patients underwent extensive pulmonary vein isolation (PVI) guided by electroanatomical mapping combined with image integration.[21] Briefly, after transseptal punctures, three-dimensional electroanatomic maps were constructed (CARTO XP or CARTO 3; Biosense Webster). One or two 7-Fr decapolar circumferential catheters (Lasso, Biosense Webster) were placed within the ipsilateral superior and inferior pulmonary veins (PVs). Circumferential ablation lines were created around both ipsilateral PVs using a 3.5-mm tip-irrigated catheter (Navistar Thermocool or Thermocool SmartTouch; Biosense Webster). Radiofrequency energy was delivered with a maximum power of 30 W for 30 seconds, and the maximum temperature was limited to 41°C. The endpoint of PVI was defined as the establishment of a bidirectional conduction block between the LA and PVs. Following PVI, adenosine triphosphate was administered as an intravenous bolus of 20-30 mg to evaluate dormant PV-atrial conduction. If dormant PV–atrial conduction occurred during adenosine testing, additional ablation was performed at the reconnection sites. Isoproterenol was subsequently infused to induce and detect non-PV foci. When a non-PV focus was identified, ablation was performed at the focus, except for those in the superior vena cava (SVC) where segmental isolation of the SVC was performed. Substrate modifications were not routinely performed in these patients during the initial procedure. Cavo-tricuspid isthmus ablation was performed in patients with documented and/or inducible cavo-tricuspid isthmus-dependent atrial flutter.

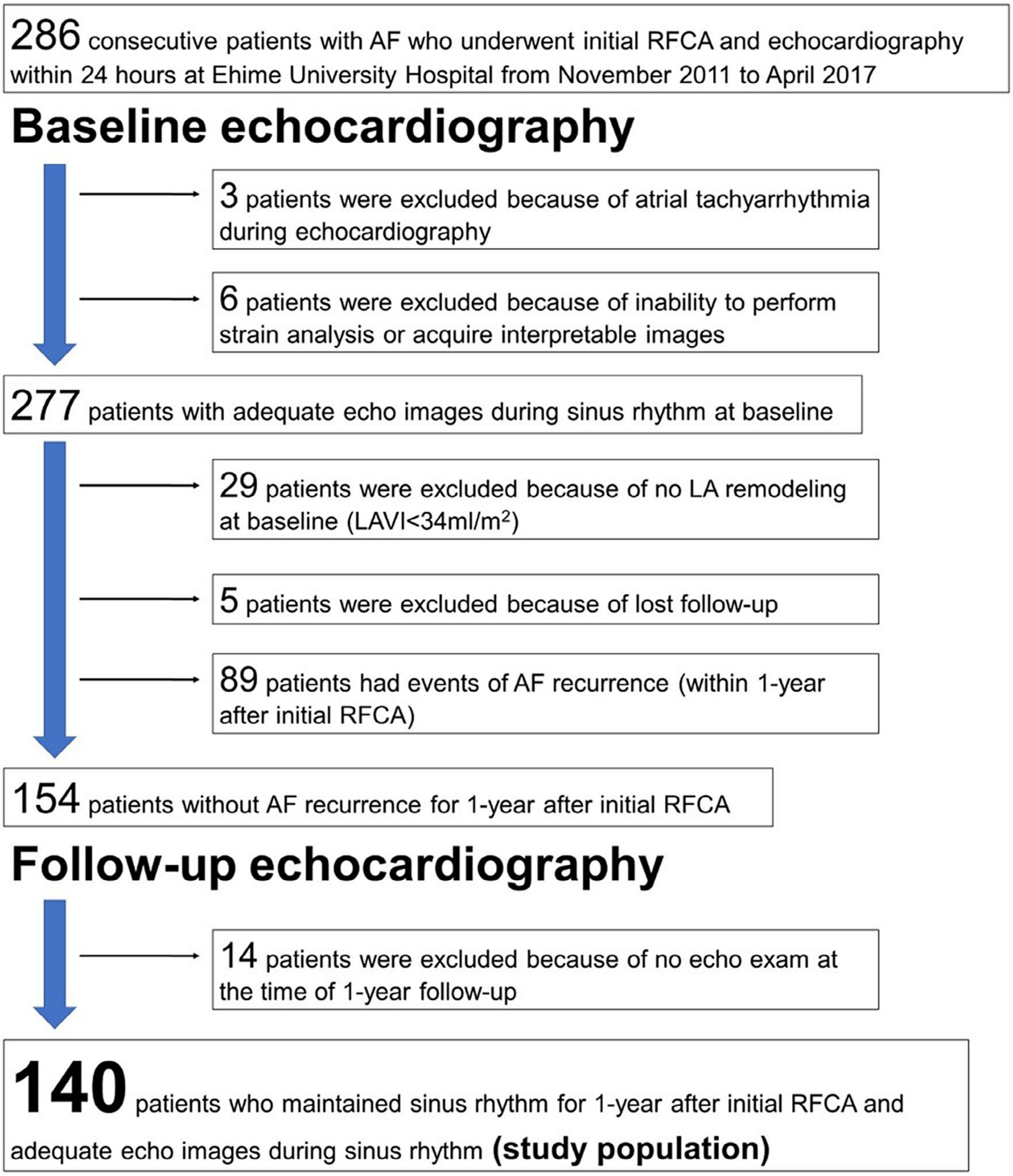

FIGURE 1 Selection of patients in this study. The final analysis was based on data from 140 patients who maintained sinus rhythm for 1 y after initial AF ablation and were evaluated by adequate echocardiography at baseline and the time of follow-up. AF, atrial fibrillation; LAVI, left atrial volume index; RFCA, radiofrequency catheter ablation

2.3 | Conventional and speckle-tracking echocardiography

All echocardiographic examinations were performed by experienced sonographers using the Aplio i900 and Artida ultrasound system (Canon). Conventional echocardiographic parameters were measured according to the recommendations of the American Society of Echocardiography.[8, 22] Early diastolic mitral annular tissue velocity (e′) was measured in the apical four-chamber view, with the sample volume positioned at both the septal and lateral mitral annuli, as the average of these two values. LA volume was calculated using the biplane method of disks (Simpson's modified rule) and indexed to body surface area (LAVI), and abnormal LA volume was graded according to the guidelines.[8] To evaluate the LA function, we measured LA reservoir and LA pump strains. LA reservoir strain corresponds to the reservoir function, which is modulated by the left ventricular systolic function, atrial size, and compliance.[23] LA pump strain corresponds to the contractile function, which is modulated by atrial contractile reserve, atrial preload, and afterload.[23] All LA strain parameters were assessed using speckle-tracking imaging with a two-dimensional wall motion tracking application (Canon). All images with a frame rate of >50 frames were selected for speckle tracking.

After manual tracing of the LA endocardial border, the dedicated software automatically tracked the myocardium throughout the cardiac cycle. The reference point for image analysis was taken at the onset of the QRS complex (R-R gating) (Figure A.1), and LA reservoir and LA pump strains were averaged from the apical four-chamber and two-chamber views (Figure 2).[23] Since the standard values of LA strain have not been clearly defined in the guideline, we defined the standard values of LA reservoir and LA pump strains as 40% and 17%, respectively, on the basis of recent studies.[24, 25]

Patients without interpretable images, such as those with incomplete strain measurements, were excluded from the study (Figure 1). In all patients, conventional and strain parameters were obtained in sinus rhythm, and all measurements were performed by experienced investigators.

2.4 | Follow-up

All patients were reviewed at 2-4 weeks after AF ablation and 1-3 months thereafter at the outpatient clinic. At each hospital visit, patients underwent physical examination, 12-lead electrocardiography (ECG), and questioning regarding any arrhythmia-related symptoms. A 24-hour Holter ECG was performed 6 and 12 months after AF ablation. If patients reported palpitations, an event recorder (available for 14 days) and/or portable ECG monitoring were also performed. Any detectable atrial tachyarrhythmia lasting for >30 seconds beyond a 3-month blanking period after the procedure was considered as recurrence.[26] Almost all patients discontinued antiarrhythmic drugs after ablation; however, patients with AF recurrence during the blanking period were treated temporarily with antiarrhythmic drugs, and discontinuation was attempted again when the recurrent AF disappeared on treatment. If sinus rhythm could be maintained, these drugs were permanently discontinued. Late recurrence was defined as AF recurrence >1 year after RFCA.

2.5 | Statistical analysis

Continuous variables are expressed as medians (interquartile range), and categorical variables are shown as percentages. The significance of differences between the groups was assessed using an unpaired or paired t-test for data with normal distribution, and the Mann–Whitney U test was used for data that were not normally distributed. For categorical variables, the χ^2 test or Fisher's exact test was used, as appropriate. Univariable and multivariable logistic regression analyses were used to evaluate the association between normalized LAVI at the time of follow-up and other clinical and echocardiographic parameters. Univariable and multivariable Cox regression analyses were used to identify the determinant of late recurrence of AF following initial RFCA. The independence and robustness of LA volume normalization were examined using several models. Survival was estimated using the Kaplan-Meier method, and differences in survival between groups were assessed using the log-rank test and adjusted using the Bonferroni method.

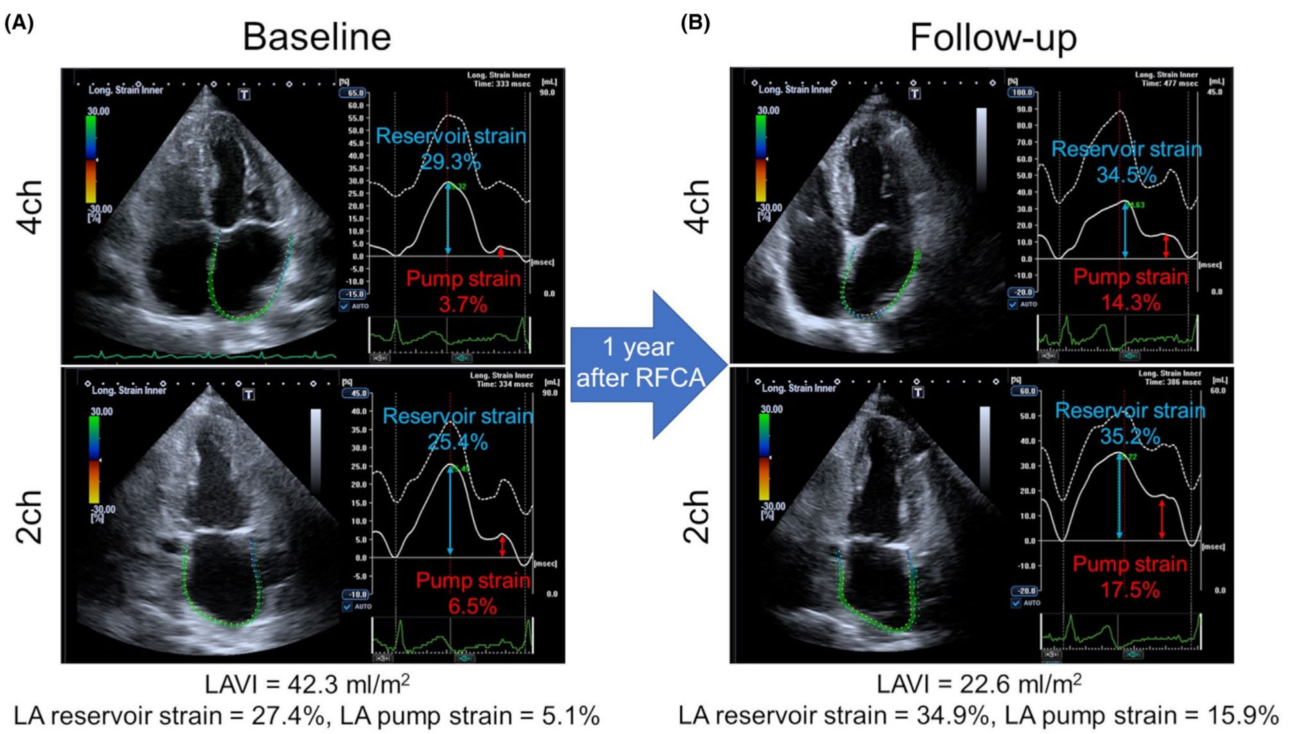

FIGURE 2 A representative case of LA reverse remodeling by restored sinus rhythm after initial AF ablation. LA volume was normalized (LAVI<34 mL/m^2) and both LA pump and LA reservoir strains were improved at the time of follow-up. AF, atrial fibrillation; LA, left atrium; LAVI, left atrial volume index

Reproducibility was assessed in 30 randomly selected patients. Interobserver and intraobserver variability were evaluated by having the same observer, and another experienced reader repeated the analysis; these were reported as inter-class correlation coefficients (ICCs). In addition, the mean differences and limits of agreement between measurements were assessed using Bland–Altman plots.

All statistical analyses were performed using a standard statistical software package (SPSS version 27, SPSS Inc), and statistical significance was defined as a *P*-value of <0.05.

3 | RESULTS

3.1 | Patient characteristics

The baseline characteristics and details of RFCA are summarized in Table 1. The median age was 64 (58-71) years, and most patients had a low $CHADS_2$ score (median 1 [1-2]). Of the 140 AF patients, 67 (48%) had non-paroxysmal AF. Although LA parameters were impaired, left ventricular parameters were within the normal range. PVI was performed in all patients, and cavo-tricuspid isthmus ablation and focal ablation of non-PV foci were additionally performed in 41 (29%) and 22 (16%) patients, respectively. Substrate modification, including linear ablation, was performed in only three (2%) patients. After initial RFCA, all patients maintained sinus rhythm for 1 year.

3.2 | LA remodeling at baseline

At baseline, LA structural parameters (LA diameter and LAVI) were increased and LA functional parameters (LA pump and LA reservoir strains) were decreased (Table 1 and Figure 3). Baseline LA volume abnormalities are shown in Figure 4. Of 140 patients, 35 patients (25%) were classified as having a moderately abnormal LA volume, and 55 patients (39%) were classified as having a severely abnormal LA volume (Figure 4). On the other hand, baseline LA functional abnormalities are shown in Figure A.2. Both LA reservoir and LA pump strains in most patients (99% and 98%) were abnormal when using the cutoff value of 40% for LA reservoir strain and 17% for LA pump strain (Figure A.2).

3.3 | LA reverse remodeling after RFCA

Figure 3 shows the changes in LA structural and functional parameters between the baseline and follow-up. After maintaining sinus rhythm for 1 year, all LA parameters were significantly improved (all $P < .01$). Regarding LA structural reverse remodeling, the LA diameter was significantly shorter and LAVI significantly decreased (Figure 3). Importantly, the median LAVI improved to the normal range at the time of follow-up. Regarding LA functional reverse remodeling, both LA reservoir and LA pump strains were significantly improved (Figure 3). A representative case of LA structural and functional reverse remodeling is shown in Figure 2.

3.4 | Changes in LA volume and functional abnormalities

Figure 4 shows the changes in LA volume abnormalities from baseline to follow-up. Of 140 patients, 114 (81%) showed improvement in LA volume abnormalities, but 26 patients (19%) did not. Importantly, more than half of the patients (54%) had a normal LA volume at the time of follow-up. Based on the results, all patients were divided into three groups as follows: group 1, patients who achieved normal LA volume (LAVI <34 mL/m^2); group 2, patients who achieved LA volume reduction but in whom LA volume abnormality persisted (LAVI ≥34 mL/m^2); and group 3, patients who did not achieve LA volume reduction compared with baseline. On the other hand, Figure A.2 shows the changes in LA functional abnormalities from baseline to follow-up. Unlike LA volume, both LA reservoir and LA pump strains were still abnormal in 99% and 94% of patients, respectively, despite the sinus rhythm being maintained in all patients for 1 year after initial RFCA. These findings suggested that LA functional improvement was incomplete despite LA structural reverse remodeling.

3.5 | Association of the degree of LA reverse remodeling with long-term RFCA outcomes

Over a median of 44 (31-61) months following the initial RFCA, 32 patients (23%) experienced a late recurrence of AF. The Kaplan-Meier curve shows the differences in long-term recurrence-free periods after the initial RFCA in the three groups (Figure 5). Patients who achieved normal LA volume (group 1) had significantly better long-term outcomes than those in the other two groups (groups 2 and 3) (both $P < .01$). However, there was no significant difference between groups 2 and 3, although group 2 patients achieved LA volume reduction ($P = .25$). The univariable and multivariable Cox regression analyses revealed that LA volume normalization was significantly and independently associated with the long-term outcome of initial RFCA (Table A.2). In addition, Figure A.3 shows the distribution of patients with and without late recurrence of AF in the four groups classified by both LA structural and functional standard values at the time of follow-up. Although there were very few patients with both LA structural and functional normalization, all of them maintained sinus rhythm after the initial RFCA.

3.6 | Association between baseline characteristics and LA volume normalization after RFCA

The baseline characteristics and details of RFCA in patients with and without normalized LA volume are summarized in Table 1. At baseline, patients who achieved normal LA volume were younger and had fewer comorbidities and lower $CHADS_2$ scores than those who did not. Furthermore, baseline LA structural and functional remodeling were milder in patients who achieved normal LA volume than

TABLE 1 Baseline characteristics

	All patients	Normalized LA volume at the time of follow-up YES	NO	
	N = 140	N = 75	N = 65	*P* value
Demographics				
Age, years	**64.0 (58.0-71.0)**	**63.0 (55.0-68.0)**	**68 (62-73)**	**<.01**
Age >75 years	17 (12)	6 (8)	11 (17)	.11
Male	95 (68)	55 (73)	40 (61)	.14
BSA, m^2	1.7 (1.6-1.9)	1.7 (1.6-1.9)	1.7 (1.5-1.9)	.24
BMI, kg/m^2	24.9 (22.7-27.1)	24.4 (22.7-26.3)	25.6 (22.7-27.8)	.13
Never smoker	70 (50)	32 (43)	38 (58)	.06
Non-paroxysmal AF	67 (48)	35 (47)	32 (49)	.76
$CHADS_2$ score	**1.0 (1.0-2.0)**	**1.0 (0.0-2.0)**	**1.0 (1.0-2.0)**	**<.01**
Comorbidities				
History of heart failure	24 (17)	11 (15)	13 (20)	.40
Hypertension	**82 (59)**	**36 (48)**	**46 (71)**	**<.01**
Diabetes mellitus	30 (21)	12 (16)	18 (28)	.09
History of stroke/TIA	**19 (14)**	**6 (8)**	13 (20)	**.04**
Vascular disease	14 (10)	7 (9)	7 (11)	.78
Medication				
ACE inhibitors or ARBs	**59 (42)**	**23 (31)**	**36 (55)**	**<.01**
β-blockers	75 (54)	37 (49)	38 (58)	.28
Prior class 1 or 3 AAD	103 (74)	53 (71)	50 (77)	.40
Echocardiographic parameters				
LVEF, %	62.6 (58.3-67.9)	62.4 (58.0-66.7)	62.8 (58.9-68.1)	.25
E velocity, cm/sec	78.5 (61.2-90.8)	76.0 (61.1-89.0)	80.0 (62.0-92.1)	.32
e′, cm/sec	7.0 (6.0-8.3)	7.2 (6.2-9.0)	6.8 (5.6-8.0)	.12
E/e′	10.7 (8.7-13.3)	10.4 (8.7-12.1)	11.8 (8.6-13.6)	.10
LA diameter, mm	**42.0 (38.0-46.0)**	**40.0 (36.0-43.0)**	**43.0 (40.0-49.0)**	**<.01**
LAVI, mL/m^2	**43.6 (39.1-54)**	**40.3 (35.6-43.6)**	**52.0 (45.3-62.6)**	**<.01**
LA pump strain, %	**5.5 (3.1-8.3)**	**6.0 (2.9-8.8)**	**4.7 (3.2-8.1)**	**<.01**
LA reservoir strain, %	**16.5 (12.1-21.0)**	**17.0 (14.0-21.6)**	**15.2 (11.1-19.5)**	**.02**
Ablation procedure				
PVI	140 (100)	75 (100)	65 (100)	1.00
CTIA	41 (29)	25 (33)	16 (25)	.26
Focal ablation (including SVCI)	22 (16)	12 (16)	10 (15)	.92
Substrate modification	3 (2)	1 (1)	2 (3)	.48
Outcome				
Late recurrence of AF (>1 year after RFCA)	**32 (23)**	**6 (8)**	**26 (40)**	**<.01**

Note: Data are expressed as median (interquartile range) and number (percentage).

Statistically significant values are indicated in bold.

Abbreviations: AAD, antiarrhythmic drug; ACE, angiotensin-converting enzyme; AF, atrial fibrillation; ARB, angiotensin receptor blocker; BMI, body mass index; BSA, body surface area; CTIA, cavo-tricuspid isthmus ablation; LA, left atrium; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; PVI, pulmonary vein isolation; SVCI, superior vena cava isolation; TIA, transient ischemic attack.

**P* value compared with patients.

in those who did not. In the univariable logistic regression analysis, LA volume normalization was associated with baseline age, $CHADS_2$ score, E/e′, LAVI, and LA reservoir strain (Table 2). Multivariable logistic regression analysis revealed that baseline LAVI was independently associated with LA volume normalization after the initial RFCA (Table 2).

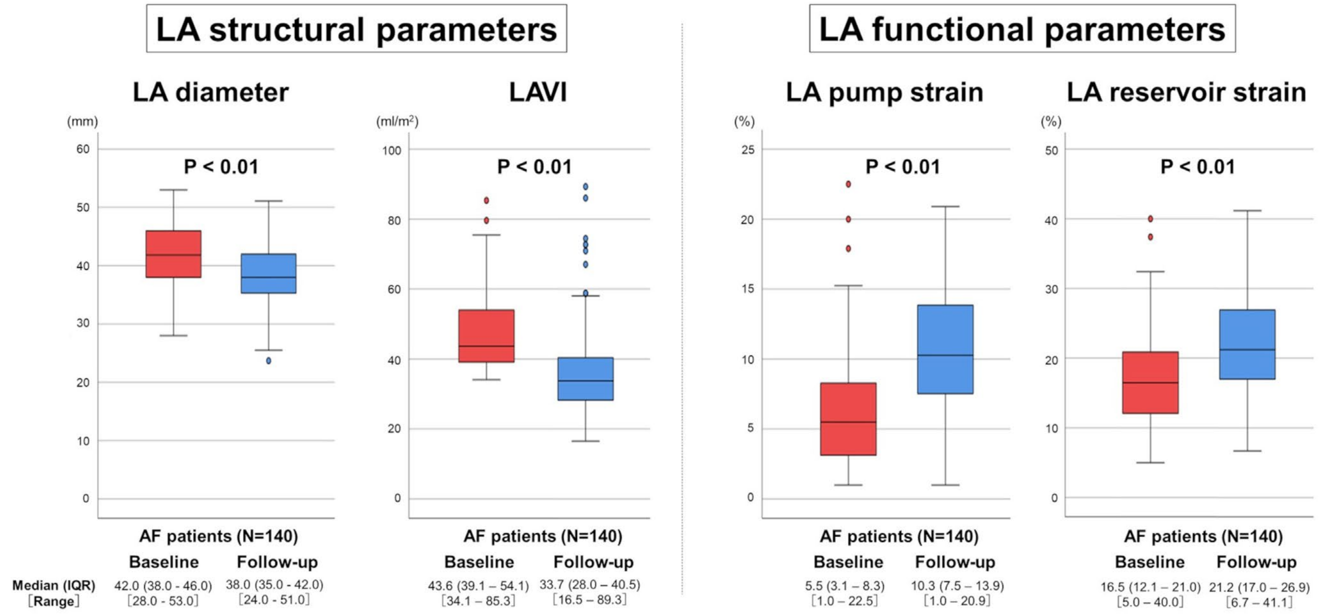

FIGURE 3 LA structural (LA diameter and LAVI) and functional parameters (LA pump and LA reservoir strains) at baseline and follow-up. All LA parameters were significantly improved after initial AF ablation. AF, atrial fibrillation; LA, left atrium; LAVI, left atrial volume index

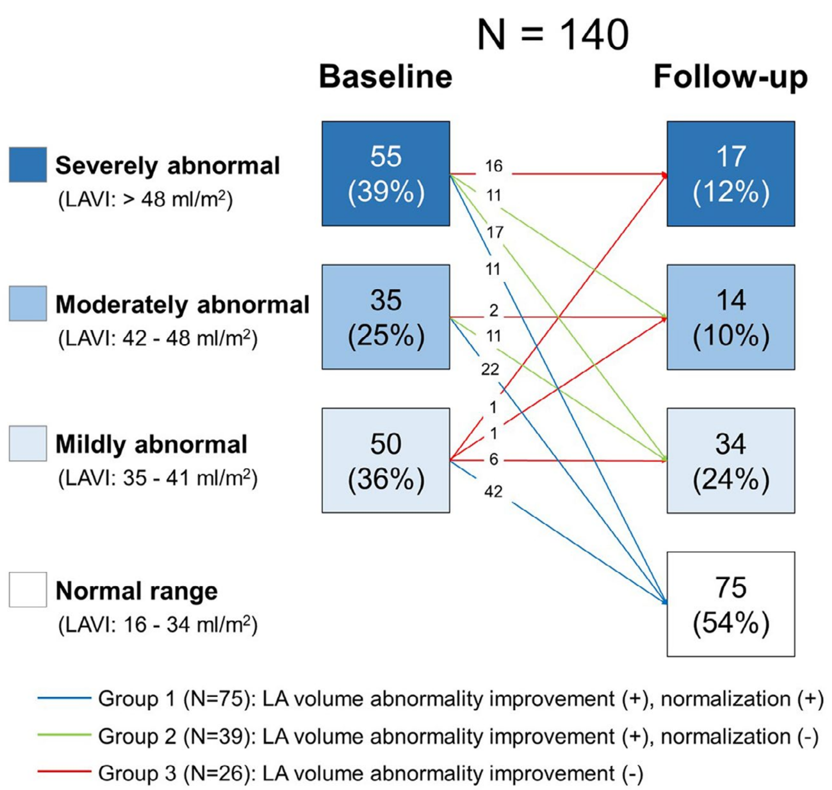

FIGURE 4 Time course of LA volume abnormality at baseline and follow-up. After initial AF ablation, 114 patients (81%) achieved LA volume improvement, and 75 patients (54%) achieved normal LA volume at the time of follow-up. There were 26 patients (19%) with no change or deterioration of LA volume abnormality. AF, atrial fibrillation; LA, left atrium; LAVI, left atrial volume index

3.7 | LA parameter comparison between controls and patients with AF who achieved a normal LA volume

To assess the efficacy of RFCA for AF patients who had LA remodeling, we compared LA parameters between AF patients who achieved normal LA volume (n = 75) and age- and sex-matched controls without a history of AF (n = 75). The clinical characteristics of patients with AF and control subjects are summarized in Table A.3. There were no significant differences in body mass index, $CHADS_2$ score, and most comorbidities between the two groups. Echocardiographic parameters of both groups are summarized in Table A.4. In controls, the median LA volume was within the normal

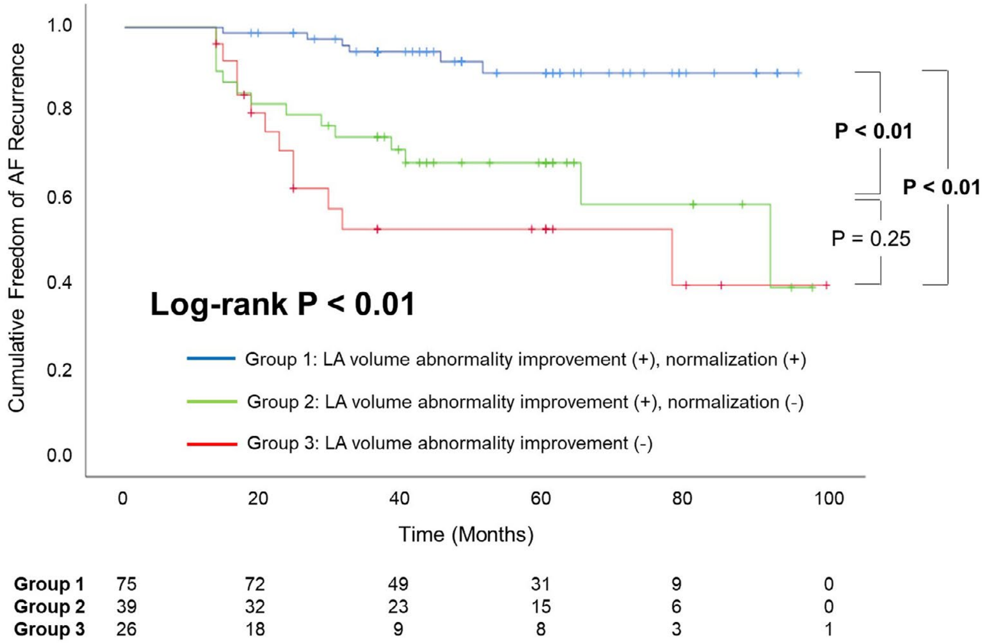

FIGURE 5 Kaplan-Meier event-free curves in 140 patients after initial AF ablation. Patients were divided into three groups based on the course of LA volume abnormality after initial AF ablation shown in Figure 3. AF, atrial fibrillation; LA, left atrium

TABLE 2 Univariate and multivariate logistic regression analyses associations with LA volume normalization at the time of follow-up echocardiography after RFCA

	Univariable		Multivariable	
	OR (95% CI)	*P* value	OR (95% CI)	*P* value
Age, years	**0.94 (0.90-0.97)**	**<.01**	0.99 (0.92-1.06)	.74
Male	1.72 (0.84-3.51)	.14	0.75 (0.25-2.29)	.62
Non-paroxysmal AF	0.90 (0.46-1.76)	.76	2.50 (0.67-9.33)	.17
$CHADS_2$ score	**0.52 (0.37-0.74)**	**<.01**	0.67 (0.43-1.03)	.07
LVEF, %	0.97 (0.93-1.02)	.25	0.94 (0.88-1.01)	.08
E/e′	**0.89 (0.80-0.99)**	**.03**	1.03 (0.88-1.19)	.74
LAVI, mL/m^2	**0.85 (0.81-0.90)**	**<.01**	**0.82 (0.76-0.89)**	**<.01**
LA pump strain, %	1.04 (0.95-1.14)	.36	0.86 (0.69-1.07)	.18
LA reservoir strain, %	**1.07 (1.01-1.13)**	**.02**	1.12 (0.99-1.28)	.08

Statistically significant values are indicated in bold.

Abbreviations: AF, atrial fibrillation; CI, confidence interval; LA, left atrium; LAVI, left atrial volume index; LVEF, left ventricular ejection fraction; OR, odds ratio; RFCA, radiofrequency catheter ablation.

range and the median values of LA reservoir and LA pump strains were comparable to the standard values as reported in previous studies.[24,25] Figure 6 shows comparisons of LA parameters, demonstrating that there were significant differences in all LA parameters between control subjects and AF patients at baseline (all $P < .01$). After restoration of sinus rhythm, both LA structural and functional parameters were significantly improved in patients with AF (all $P < .01$). As a result, there was no significant difference in LA diameter between AF patients and control subjects ($P = .17$), but statistical differences remained in LAVI between the two groups ($P = .04$). Furthermore, regarding the LA function, there were significant and large differences in LA pump and LA reservoir strains between AF patients and control subjects (both $P < .01$) (Figure 6). These results suggested that LA abnormalities, especially LA dysfunction, persisted even if AF patients achieved a normal LA volume as a result of successful AF ablation.

3.8 | Reproducibility

The ICC values for intraobserver variability for LA pump strain and LA reservoir strain were 0.92 (95% CI 0.84-0.96) and 0.89

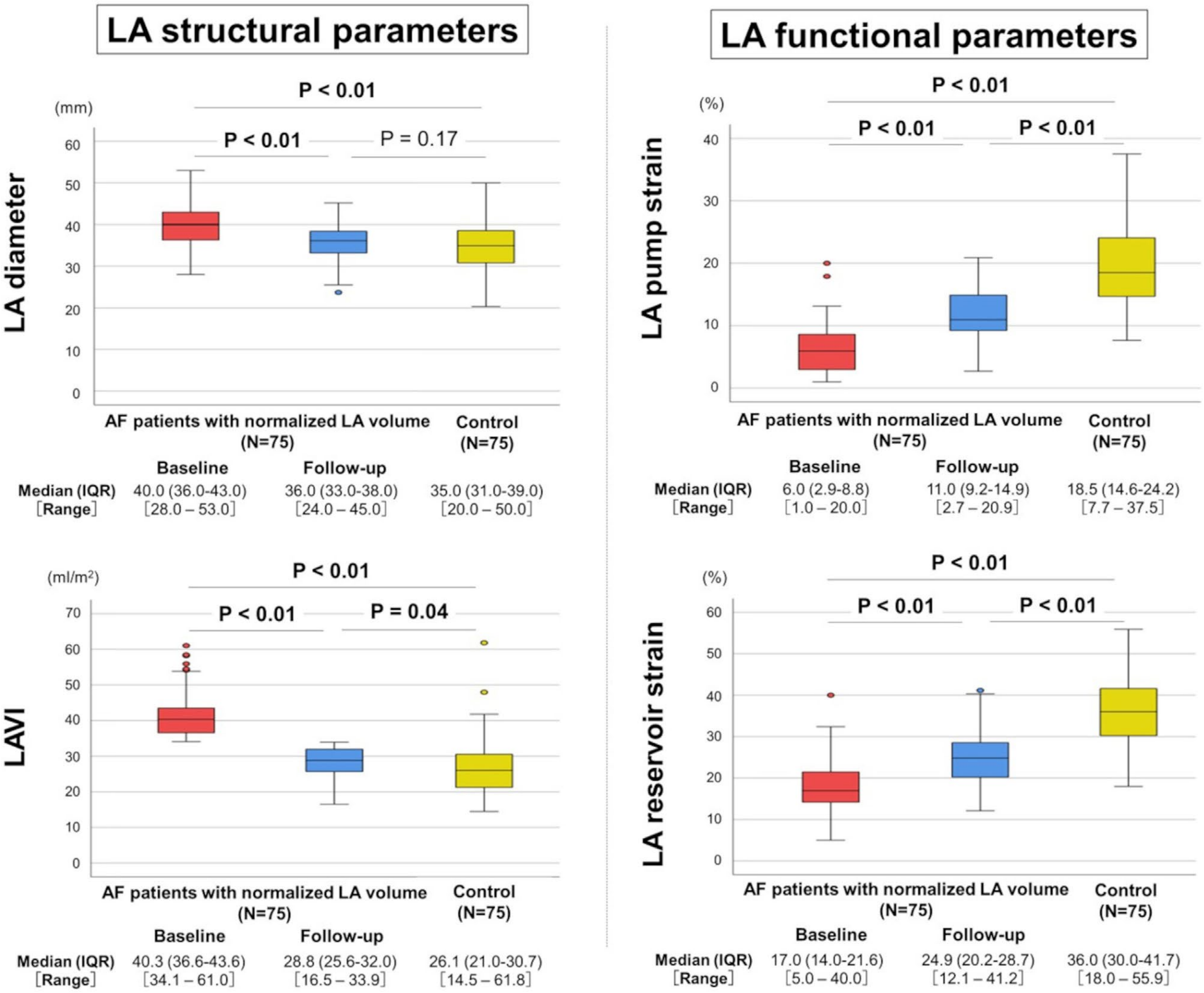

FIGURE 6 Comparison of LA structural (LA diameter and LAVI) and functional (LA pump and LA reservoir strains) parameters between AF patients and control subjects. AF, atrial fibrillation; LA, left atrium; LAVI, left atrial volume index

(0.78-0.94), respectively. The ICC values for interobserver variability were 0.93 (95% CI 0.69-0.97) and 0.91 (0.81-0.95), respectively. The Bland–Altman plots are shown in Figure A.4.

4 | DISCUSSION

The main findings of our study are as follows: First, overall LA structural and functional parameters were significantly improved by restoring and maintaining sinus rhythm after initial RFCA for AF. Especially, the degree of LA reverse remodeling in structural parameters was larger than that in functional parameters. Second, more than half of the patients (54%) had a normal LA volume at the time of follow-up, and these patients had better long-term outcomes after RFCA than those without a normal LA volume. Third, mild LA enlargement at baseline was significantly associated with LA volume normalization. Fourth, LA abnormalities, especially LA dysfunction, persisted despite LA volume normalization after RFCA compared with control subjects without AF.

4.1 | LA reverse remodeling after successful AF ablation

Since the establishment of PVI due to advances in catheter technologies and techniques, numerous studies have demonstrated LA reverse remodeling due to restoration and maintenance of sinus rhythm after PVI.[9-20, 27-31] Regarding LA structural reverse remodeling, meta-analyses revealed that LA diameter and LA volume were significantly decreased by AF ablation.[18, 19] On the other hand, although the LA function was also improved by successful RFCA, several studies have reported persistent LA functional abnormalities after effective ablation.[14, 20, 27, 31] Lin et al investigated LA functional reverse remodeling using a speckle-tracking technique and identified sustained LA dysfunction in patients who underwent AF ablation compared with control subjects without AF.[31] Teh et al performed repetitive atrial electroanatomic mapping in patients who underwent AF ablation and revealed that electrophysiologic substrate did not completely reverse even after successful RFCA, similar to control subjects without AF.[27] The same group also reported that LA strain assessed by speckle-tracking echocardiography is a potent surrogate for sustained electrophysiologic abnormalities.[14] In the present study, the increase in LA volume was improved in approximately 80% of patients, and more than half of the patients (54%) had normal LAVI after restoration of sinus rhythm for 1 year after initial RFCA. However, the LA function did not normalize in most patients even though all patients maintained sinus rhythm for 1 year after initial AF ablation. These results are consistent with those of previous studies, which suggested that LA structural remodeling can be reversible, but functional remodeling is irreversible.

4.2 | Clinical significance of LA volume normalization on long-term RFCA outcomes

Although LA reverse remodeling has been thought to be a useful predictor of long-term outcome of RFCA,[12-16] there is no clear definition of LA reverse remodeling and no data on the impact of LA reverse remodeling on long-term outcomes. In the present study, we investigated these unresolved clinical questions using the criteria of LA enlargement according to the guidelines and showed that LA volume normalization at follow-up was significantly associated with better long-term outcomes of AF ablation. Our results suggested that LAVI of 34 mL/m^2 may be a clear cutoff value for determining LA structural reverse remodeling in patients undergoing AF ablation. We also revealed that the degree of LA enlargement at baseline was significantly associated with LA volume normalization after initial RFCA. Similarly, previous studies suggested that mild LA enlargement and dysfunction before RFCA[10, 12, 13] are predictors of LA reverse remodeling after the procedure. These findings could answer a clinical question regarding the optimal timing to consider RFCA in patients with AF and suggest that early intervention provides better outcomes than late intervention in patients with AF. Indeed, the latest randomized trial demonstrated that early rhythm-control therapy was associated with a lower risk of cardiovascular outcomes than usual care among patients in the early phase of AF.[32]

4.3 | LA abnormalities persisted even after LA volume normalization

We showed that LA abnormalities, especially LA dysfunction, still remained even when AF patients achieved a normal LA volume as a result of successful AF ablation when compared with control subjects without a history of AF. These findings suggested that the risk of AF could not be completely eliminated by RFCA. An optimal strategy for follow-up after AF ablation has not yet been established. Many physicians carefully monitor patients because discontinuation of anticoagulants may increase the risk of thromboembolic events in patients with a high risk of recurrence. The results of our study suggested that late recurrence of AF is not rare and that LA abnormalities cannot be improved even in patients who achieve a normal LA volume after successful ablation. Thus, physicians should carefully consider long-term follow-up and residual AF risks, regardless of sinus rhythm restoration by RFCA.

5 | LIMITATIONS

Our study had several limitations. First, this was a single-center retrospective study, and the study population was relatively small. Second, despite the use of Holter or event recorder monitoring, we may have underestimated the recurrence rate of AF following initial catheter ablation because asymptomatic cases could have been missed. Third, baseline echocardiographic examination was performed after RFCA (within 24 hour). Therefore, LA contraction did not recover partly due to atrial stunning, even if sinus rhythm was restored electrically in patients with persistent AF. In addition, our results may have been influenced by radiofrequency power. However, we did not perform LA substrate modification in most patients; therefore, we believe that the adverse effect of ablation on the LA structure and function was minimal. Fourth, although we selected control subjects without a history of AF, some may have had a short duration of asymptomatic AF because a few people had remodeled the left atrium in the control group. Fifth, regarding LA volume, we did not compare echocardiographic data with cardiac computed tomographic data. It is well known that LA volume measured by echocardiography tends to be underestimated.[33] Finally, strain imaging, similar to other imaging techniques, is an operator-dependent method.

6 | CONCLUSIONS

Patients who achieve normal LA volume have better long-term outcomes of AF ablation than those who do not. Although AF ablation promotes beneficial effects on the LA structure and function, LA remodeling, especially functional abnormality, cannot be normalized even in patients who achieve normal LA volume after successful ablation. Thus, physicians should carefully consider long-term follow-up and residual AF risks, regardless of sinus rhythm restoration by RFCA.

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CONFLICT OF INTEREST

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.

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