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ORIGINAL INVESTIGATION

Improvement of left ventricular function after successful radiofrequency catheter ablation in persistent atrial fibrillation with preserved left ventricular ejection fraction: a comprehensive echocardiographic assessment using two-dimensional speckle tracking analysis

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Abstract

Background A limited number of studies have investigated the effects of radiofrequency catheter ablation (RFCA) on left ventricular (LV) function and the left atrial (LA) size in patients with atrial fibrillation (AF). The purpose of this study was to conduct a comprehensive assessment of LV function in patients with AF with preserved left ventricular ejection fraction (LVEF) before and after RFCA.

Method A total of 30 consecutive patients with no recurrences after RFCA for persistent AF (age, 57.7 ± 8.4 years) were enrolled. Transthoracic echocardiography was performed at the baseline and 6 months after the final RFCA using speckle tracking derived LV strain analysis.

Results After RFCA, we measured decreases in the LA volume index (33.7 ± 10.4 ml/m^2 vs. 24.6 ± 8.6 ml/m^2, $p < 0.0001$), while we observed improvements in systolic indices such as LVEF (56.8 ± 9.8% vs. 65.1 ± 9.1%, $p < 0.0001$), global longitudinal strain (− 16.8 ± 4.4% vs. − 18.8 ± 3.4%, $p = 0.0055$) and twist (8.12 ± 3.66° vs. 12.33 ± 6.75°, $p = 0.0050$), and also in diastolic indices such as strain rate during early diastole (SR_E) (0.73 ± 0.10 s^{-1} vs. 1.32 ± 0.29 s^{-1}, $p < 0.0001$) and early transmitral inflow velocity (E)/SR_E (1.11 ± 0.36 m vs. 0.61 ± 0.19 m, $p < 0.0001$). Logistic regression analysis showed that $\Delta E/SR_E$ was a contributing factor for improvement in LVEF (odds ratio 126.9; $p = 0.021$).

Conclusion In persistent AF with preserved LVEF, further improvement in LVEF and reverse remodeling of the LA are achieved after RFCA. LV filling pressure may play significant roles in the mechanisms.

Keywords Strain · Strain rate · Reverse remodeling · Atrial fibrillation · Radiofrequency catheter ablation

Introduction

Radiofrequency catheter ablation (RFCA) is highly successful in maintaining sinus rhythm, and studies have reported improvements in cardiac dimensions and function after RFCA in patients with atrial fibrillation (AF) and left ventricular (LV) dysfunction [1, 2] or congestive heart failure [3]. Several meta-analyses have supported these findings [4–8]. Current guidelines recommend the use of RFCA in symptomatic patients with heart failure and/or reduced LV ejection fraction (LVEF) [9, 10]. However, there is another type of AF, namely, AF with normal LVEF. A number of investigations regarding the effects of RFCA on LV function and left atrial (LA) volume in those patients have been conducted. However, to this day, the favorable effects of RFCA

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on LV function in AF with normal LVEF have not been confirmed [11–14], although reverse remodeling of the left atrium is well documented [15–20]. Recently, Zhu et al. [21] reported a meta-analysis, which concluded that RFCA could improve LV systolic function in AF patients with low LVEF or persistent AF patients.

Two-dimensional speckle tracking echocardiography (STE) is a recently developed imaging modality that can sensitively detect LV systolic dysfunction [22]. It evaluates LV systolic function by measuring LV deformations, such as global longitudinal, radial, and circumferential strains [23], and assessing LV synchronicity [24] or torsion [25]. STE can also provide other tools to evaluate LV diastolic function by measuring the global longitudinal strain rate [26]. However, STE analysis has so far only been deployed in a few studies involving RFCA for AF [15, 16, 27]. Therefore, the purpose of this study was to conduct a comprehensive assessment of the improvement of left ventricular function by RFCA in persistent AF with preserved LVEF using STE, and to evaluate the clinical significance of LV deformations, dyssynchrony, torsion and diastolic function on the improvement of LVEF.

Methods

Patients with persistent AF who underwent RFCA at the Japan Self-Defense Forces Central Hospital between 2009 and 2013 were prospectively recruited for this study. Patients with any known structural heart disease, history of congestive heart failure, severely reduced LVEF ($\leq 45\%$) in accordance with a previous study [3], and poor image quality during the baseline transthoracic echocardiography (TTE) were excluded. At the medical visit 6 months after single or multiple (maximum three times) RFCA procedures, patients with no recurrences of AF and stable sinus rhythm were considered to have had a successful RFCA (the index RFCA procedure) and were enrolled in this study. The final cohort of this study consisted of a total of 30 consecutive patients with no recurrences of AF and a maintenance of stable sinus rhythm after undergoing RFCAs for persistent AF (age, 57.7 ± 8.4 years; males, 27). Serum brain natriuretic peptide (BNP) level was measured at the baseline and at the medical visit 6 months after the index RFCA. Written informed consent was obtained from all participants. The study protocol was approved by the Institutional Review Board of Japan Self-Defense Forces Central Hospital. The study conformed to the principles outlined in the Declaration of Helsinki.

All patients underwent baseline TTE upon admission before the first RFCA. TTEs were repeated at 6 months after the index RFCA procedure. The TTE study was performed using a Vivid 7 system with an M4S probe (GE Vingmed Ultrasound, Horten, Norway) in order to collect two-dimensional echocardiographic parameters, such as LVEF, left ventricular and left atrial dimensions (LAD), left atrial volume index (LAVI), left ventricular end-diastolic volume (LVEDV), left ventricular end-systolic volume (LVESV), stroke volume (SV), and left ventricular mass index (LVMI) in accordance with the current guidelines for two-dimensional echocardiography [28]. The left atrial volume was calculated using the area-length approximation ($8/3\pi\{(A1)(A2)/(L)\}$). Left atrial length (L) was defined as the shorter of the two long axes measured in the apical two- and four-chamber views. A1 and A2 are the corresponding left atrial areas. The LV mass was calculated using the Cube formula ($0.8 \times 1.04 \times \{(\mathrm{IVS} + \mathrm{LVID} + \mathrm{PWT})^3 - \mathrm{LVID}^3\} + 0.6$) in which "IVS" is interventricular septum, "LVID" is LV internal diameter, and "PWT" is inferolateral wall thickness. The modified biplane Simpson method was used to calculate LV volumes and LVEF. Cardiac output (CO) was calculated with the formula: SV × heart rate. Assessments of diastolic indices including transmitral inflow and septal mitral annular velocities were performed using conventional and tissue-doppler echocardiography. However, statistical comparisons between the baseline variables and the variables 6 months after the index RFCA were not conducted, since all patients had AF rhythm at the baseline which was successfully treated by RFCA, and had maintained normal sinus rhythm 6 months later. Conventional assessment of LV diastolic function was performed using Doppler and tissue-Doppler echocardiography in accordance with the current guidelines [29].

To obtain LV global longitudinal strain (GLS), global radial strain (GRS), global circumferential strain (GCS), systolic global longitudinal strain rate (SR_{SYS}), global longitudinal strain rate during early diastole (SR_E), global longitudinal strain rate during atrial contraction (SR_A), dyssynchrony and torsion, digitalized image acquisition was performed during normal sinus rhythm without ectopic beats. Speckle tracking analysis was performed by two independent cardiologists using the commercially available software package EchoPac (GE Vingmed Ultrasound). As previously described [22], two-dimensional grayscale images were acquired in the standard parasternal and apical (apical four-chamber, apical two-chamber, and apical long-axis) views at a frame rate of 40–60 frames/s. In total, three cardiac cycles were recorded. Parasternal short-axis views were acquired at 3 levels: the mitral valve level, the papillary muscle level, and at the apex. All images were stored digitally for offline analysis. In each of the apical four-chamber, apical two-chamber, and long-axis views, a longitudinal strain curve was obtained, with all LV myocardial segments considered as the region of interest [22]. The average values of peak systolic longitudinal strain from the three apical views were then calculated as the GLS. Peak systolic radial strain values

were obtained from all 16 segments from the three short-axis views and averaged to obtain the GRS. Similarly, peak systolic circumferential strain values were obtained from the three short-axis views and averaged to obtain the GCS. Peak global longitudinal SR_{SYS}, SR_E and SR_A were calculated by averaging the values of each of the 18 segments, which were derived from the 6 segments of each of the 3 apical views (four-chamber, two-chamber, and apical long-axis views). The ratio of early mitral inflow velocity (*E*) and SR_E was used as a diastolic index to estimate LV filling pressure (E/SR_E) [26]. To assess LV dyssynchrony, radial strain was used as previously described [24]. LV radial strain curves from the six segments at the level of the papillary muscle were acquired. Time to peak strain from each of the six regional curves was measured. The dyssynchrony index was expressed using the maximal time delay measured from the first and last segments to reach the peak S_r. A cutoff value of ≤ 130 ms was used for the diagnosis of LV dyssynchrony, as previously described [24]. To assess LV torsion, radial strain was used as previously described [25]. LV radial strain curves of the average of the basal and apical rotations in six myocardial segments and their net differences at each corresponding time point were obtained. LV twist, twist rate, and untwist rate were measured as surrogates for LV torsion.

We performed extensive encircling pulmonary vein isolation. If AF persisted after pulmonary vein isolation, additional ablation procedures, such as linear ablation of the left atrium roof, superior vena cava isolation, and ablation of continuous fractionated atrial electrocardiograms, were performed. Finally, if AF did not resolve, cardioversion was performed to obtain sinus rhythm. A caval-tricuspid isthmus line ablation was performed in all patients. After discharge, the patients were followed up at 2–4 weeks after the index RFCA and then every 3 months at the outpatient clinic by a cardiologist. Holter ambulatory ECG monitoring was performed at least till 2 years after the index RFCA in order to detect the recurrence of AF. An additional RFCA procedure was performed when patients experienced recurrences after 3 months as a blanking period, depending on the clinical judgement of the cardiologist.

Numerical data are presented as the mean ± standard deviation and as numbers (%) for categorical variables. For comparison of continuous variables between two groups, the unpaired Student's *t* test was used. For comparison of categorical variables, the Chi square test was used. For repeated measurements, the paired Student's *t* test was used. Logistic regression analysis was used to evaluate potential predictors of maintaining stable sinus rhythm 2 years after the index RFCA among the echocardiographic variables at the baseline and 6 months after the index RFCA. We defined significant improvements in LVEF as an increase of $\geq 9\%$, which is the mean difference in LVEF between the baseline and 6 months after the index RFCA, and reverse remodeling of the left atrium (LA) as a decrease of ≥ 10 ml, which is the mean difference in LAVI between the baseline and 6 months after the index RFCA. To uncover the factors contributing to improvement of LVEF by RFCA, we compared the changes of LV functional indices between the patients with and without the improvement of LVEF by logistic regression analysis. To uncover the factors contributing to reverse remodeling of the LA by RFCA, we compared the changes in LV function indices between the patients with and without the reverse remodeling of the LA using logistic regression analysis. The change in each variable was calculated as a Δ value (value 6 month after RFCA—baseline value). We first used univariate analysis and then entered all variables with $p < 0.1$ into the multivariable regression model (forward selection method). All statistical analyses were performed using SPSS 19.0 (SPSS, Chicago, IL), and p values of < 0.05 were considered significant.

Results

Baseline demographic data are summarized in Table 1. Medical backgrounds included systemic hypertension in 14 cases (46%), dyslipidemia in 8 cases (27%), diabetes mellitus in 6 cases (20%), and cerebral embolism in 2 cases (7%). No known structural heart disease including coronary artery disease, valvular heart disease and cardiomyopathies, or history of congestive heart failure was included. Patients in 13 cases (43%) were taking an angiotensin converting enzyme inhibitor or angiotensin II receptor blocker as an anti-hypertensive

Table 1 Demographic variables

	Total, $n = 30$
Age, years	57.7 ± 8.4
Male sex	27 (90%)
AADs before ablation	29 (90%)
ACE inhibitor/AT II receptor blocker	13 (43%)
Statin	8 (27%)
Systemic hypertension	14 (46%)
Dyslipidemia	8 (27%)
Diabetes mellitus	6 (20%)
Coronary artery disease	0 (0%)
Congestive heart failure	0 (0%)
Cerebral embolism	2 (7%)
$CHADS_2$ score	0.67 ± 1.03
Stable SR 6 months after the index RFCA	30 (100%)
After 1st RFCA procedure	22 (73%)
After 2nd RFCA procedure	7 (23%)
After 3rd RFCA procedure	1 (3%)

AAD antiarrhythmic drug, *ACE* angiotensin converting enzyme, *AT* angiotensin, *RFCA* radiofrequency catheter ablation, *SR* sinus rhythm

medication. In all cases, baseline heart rhythm was characterized by AF, but with stable sinus rhythm 6 months after the final RFCA (the index RFCA). To obtain stable sinus rhythm, a single RFCA procedure was needed in 22 patients (73%), a second RFCA was needed in 7 patients (23%), and a third RFCA was needed in 1 patient (3%).

Echocardiographic data and serum BNP levels are shown in Table 2. Although 6 patients had transient sinus rhythm, rest 24 patients had AF rhythm at the baseline echocardiographic assessment. Baseline LAVI was 33.7 ± 10.4 ml/m^2 and LVMI was 98.5 ± 28.7 g/m^2. Both values were within the normal range, but close to the upper limit values of LAVI (34 ml/m^2) and LVMI (102 g/m^2) [26]. Baseline LVEDV and LVESV were 89.0 ± 24.4 ml and 41.6 ± 17.3 ml, and were within the range of 2 standard deviations (62–150 ml for men, 46–106 ml for women; 21–61 ml for men, 14–42 ml for women, respectively) [25]. Baseline LVEF was 56.8 ± 9.8%, which was also within the normal range (≥ 53%) [26]. At the baseline, GLS, GRS and GCS were − 16.8 ± 4.4%, 28.1 ± 11.8%, and − 14.1 ± 5.1%, respectively. These values were lower than the lower limit values reported in normal subjects with sinus rhythm (GLS: − 15.9% to − 22.1%, GRS: 35.1% to 59.0%, GCS: − 20.9% to − 27.8%) [26]. There was no patient with LV dyssynchrony at the cutoff value of ≥ 130 ms [23]. Diastolic indices such as early mitral annular velocity (*e′*) and the ratio of early transmitral inflow velocity (*E*) and *e′* (*E*/*e′*) were under the cutoff values of the current guidelines (0.07 m/s and 14, respectively) [27].

Table 2 Echocardiographic variables at baseline and 6 months after the index radiofrequency catheter ablation

	Baseline	6 months after the index RFCA	*p* value
Heart rate, beats per minute	70.2 ± 21.1	65.4 ± 11.1	NS
Sinus rhythm at the ultrasound study	6 (20%)	30 (100%)	NA
BNP, pg/ml	91.5 ± 78.3	28.2 ± 22.0	< 0.0001
LAVI, ml/m^2	33.7 ± 10.4	24.6 ± 8.6	< 0.0001
E, m/s	0.80 ± 0.24	0.78 ± 0.23	NS
A, m/s	NA	0.45 ± 0.15	NA
E/A	NA	1.83 ± 0.97	NA
DT, ms	206 ± 56	227 ± 62	NS
e′ (septal), m/s	0.080 ± 0.027	0.073 ± 0.019	NS
E/*e′*	10.86 ± 4.27	11.08 ± 3.78	NS
LVMI, g/m^2	98.5 ± 28.7	78.5 ± 26.6	0.0020
LVEDV, ml	89.0 ± 24.4	86.2 ± 23.7	NS
LVESV, ml	41.6 ± 17.3	33.5 ± 16.0	0.0087
LVEF, %	56.8 ± 9.8	65.1 ± 9.1	< 0.0001
SV, ml	49.2 ± 13.0	55.1 ± 15.9	0.0581
CO, ml/min	3.43 ± 1.23	3.57 ± 1.01	NS
GLS, %	− 16.8 ± 4.4	− 18.8 ± 3.4	0.0055
GRS, %	28.1 ± 11.8	33.2 ± 19.0	NS
GCS, %	− 14.1 ± 5.1	− 11.1 ± 17.0	NS
SR_{SYS}, s^{-1}	− 1.03 ± 0.31	− 1.13 ± 0.19	NS
SR_E, s^{-1}	0.73 ± 0.10	1.32 ± 0.29	< 0.0001
SR_A, s^{-1}	NA	0.68 ± 0.31	NA
E/SR_E, m	1.11 ± 0.36	0.61 ± 0.19	< 0.0001
Dyssynchrony index ≥ 130 ms	0 (0%)	0 (0%)	NA
Dyssynchrony index, ms	9.8 ± 16.9	7.4 ± 20.0	NS
Twist, °	8.12 ± 3.66	12.33 ± 6.75	0.0050
Twist rate, °/s	64.01 ± 8.23	78.17 ± 38.74	0.0584
Untwist rate, °/s	− 61.78 ± 41.81	− 77.85 ± 50.37	NS

RFCA radiofrequency catheter ablation, *BNP* brain natriuretic peptide, *LAVI* left atrial volume index, *E* early transmitral inflow velocity, *A* transmitral inflow velocity during atrial contraction, *DT* Deceleration time of early transmitral inflow, *e′* early mitral annular velocity, *LVMI* left ventricular mass index, *LVEDV* left ventricular end-diastolic volume, *LVESV* left ventricular end-systolic volume, *LVEF* left ventricular ejection fraction, *SV* stroke volume, *CO* cardiac output, *GLS* global longitudinal strain, *GRS* global radial strain, *GCS* global circumferential strain, SR_{SYS} systolic strain rate, SR_E strain rate during early diastole, SR_A strain rate during atrial contraction, *NS* not significant, *NA* not applicable

6 months after the index RFCA, the morphologic parameters of the left-sided cardiac chambers, such as LAVI and LVESV, decreased significantly (33.7 ± 10.4 ml/m^2 vs. 24.6 ± 8.6 ml/m^2, $p < 0.0001$; and 41.6 ± 17.3 ml vs. 33.5 ± 16.0 ml, $p = 0.0087$, respectively), and the surrogates of LV systolic function, such as LVEF, GLS, twist, improved significantly ($56.8 \pm 9.8\%$ vs. $65.1 \pm 9.1\%$, $p < 0.0001$; $-16.8 \pm 4.4\%$ vs. $-18.8 \pm 3.4\%$, $p = 0.0055$; and $8.12 \pm 3.66°$ vs. $12.33 \pm 6.75°$, $p = 0.0050$, respectively). Diastolic indices such as SR_E, and E/SR_E improved significantly (0.73 ± 0.10 s^{-1} vs. 1.32 ± 0.29 s^{-1}, $p < 0.0001$; and 1.11 ± 0.36 m vs. 0.61 ± 0.19 m, $p < 0.0001$, respectively). Serum BNP levels improved significantly from 91.5 ± 78.3 pg/ml to 28.2 ± 22.0 pg/ml ($p < 0.0001$).

We obtained clinical data during the follow-up period for all patients until 2 years after the index RFCA. At the follow-up visit 2 years after the index RFCA, 22 patients had maintained stable sinus rhythm. The logistic regression analysis showed that the baseline value of *e′* was selected for a predictor of maintaining stable sinus rhythm (odds ratio 37.093; confidence interval 7.032–78.071, $p = 0.015$; Table 3). Among the echocardiographic variables at 6 months after the index RFCA, the logistic regression analysis showed that the value of LAVI 6 months after the index RFCA was a predictor of maintaining stable sinus rhythm (odds ratio 0.793; confidence interval 0.664–0.946; $p = 0.010$; Table 4).

Sixteen patients (53%) showed significant improvements in LVEF (i.e., they experienced an increase of $\geq 9\%$). Fifteen patients (50%) exhibited significant reverse remodeling of LA (i.e., experienced a decrease in LAVI of ≥ 10 ml) 6 months after RFCA.

Among the changes of each echocardiographic variable including both systolic and diastolic LV function indices, the logistic regression analysis showed that ΔE and $\Delta E/SR_E$ was a contributing factor for significant improvement in LVEF (odds ratio 0.981; confidence interval 0.965–0.998; $p = 0.026$; odds ratio 126.9; confidence interval 2.1–7762.3; $p = 0.021$, respectively; Table 5). However, the logistic regression analysis did not show any significant contributing factors in reverse remodeling of the LA, although ΔLVEF

Table 3 Baseline variables predicting maintenance of stable sinus rhythm 2 years after the index radiofrequency catheter ablation

Baseline variables	Stable SR 2 years after the index RFCA			Odds ratio (95% CI)	*p* value
	Yes ($n = 22$)	No ($n = 8$)	*p* value		
$CHADS_2$ score	0.46 ± 0.30	1.25 ± 1.39	0.0596		
LAVI, ml/m^2	31.7 ± 10.7	38.8 ± 8.01	0.0987		
e′ (septal), m/s	0.088 ± 0.025	0.058 ± 0.020	0.0044	37.093 (7.032–78.071)	0.015
E/e′	9.67 ± 3.88	14.14 ± 3.67	0.0084		
LVMI, g/m^2	90 ± 20	122 ± 36	0.0050		
LVEF, %	58.8 ± 10.5	51.3 ± 4.8	0.0632		
GRS, %	30.9 ± 12.1	22.1 ± 9.9	0.0771		

RFCA radiofrequency catheter ablation, *CI* confidence interval, *LAVI* left atrial volume index, *e′* early mitral annular velocity, *E* early transmitral inflow velocity, *LVMI* left ventricular mass index, *GRS* global radial strain

Table 4 Variables at 6 months after the index RFCA predicting maintenance of stable sinus rhythm 2 years after the index radiofrequency catheter ablation

Variables 6 months after the index RFCA	Stable SR 2 years after the index RFCA			Odds ratio (95% CI)	*p* value
	Yes ($n = 22$)	No ($n = 8$)	*p* value		
LAVI, ml/m^2	21.6 ± 7.5	32.8 ± 5.4	0.0007	0.793 (0.664–10.946)	0.010
e′ (septal), m/s	0.077 ± 0.020	0.063 ± 0.015	0.0719		
E/e′	10.2 ± 2.8	13.6 ± 5.0	0.0239		
LVMI, g/m^2	72.4 ± 21.3	95.4 ± 33.5	0.0337		
GLS, %	-19.5 ± 3.3	-17.1 ± 3.6	0.0973		
GRS, %	40.0 ± 11.3	29.4 ± 11.3	0.0304		
SR_{SYS}, s^{-1}	-1.18 ± 0.19	-1.01 ± 0.15	0.0327		
SR_A, s^{-1}	0.74 ± 0.31	0.51 ± 0.27	0.0711		
E/SR_E, m	0.57 ± 0.15	0.71 ± 0.25	0.0636		

RFCA radiofrequency catheter ablation, *CI* confidence interval, *LAVI* left atrial volume index, *e′* early mitral annular velocity, *LVMI* left ventricular mass index, *GLS* global longitudinal strain, *GRS* global radial strain, SR_{SYS} systolic strain rate, SR_A strain rate during atrial contraction, *E* early transmitral inflow velocity, SR_E strain rate during early diastole

Table 5 Factors contributing to improvement in left ventricular ejection fraction

	Improvement in LVEF			Odds ratio (95% CI)	*p* value
	Yes ($n=16$)	No ($n=14$)	*p* value		
ΔLAVI, ml/m^2	−6.2 ± 5.0	−11.6 ± 7.8	0.0346		
Δ*E*, m/s	0.404 ± 0.11	−0.08 ± 0.20	0.0490	0.981 (0.965–0.998)	0.028
ΔDT, ms	−12.4 ± 65.8	50.1 ± 64.8	0.0141		
Δ*E*/SR$_E$, m	−0.35 ± 0.22	−0.63 ± 0.31	0.0094	126.9 (2.1–7762.3)	0.021

LVEF left ventricular ejection fraction, *CI* confidence interval, *LA* left atrial volume index, *E* early transmitral inflow velocity, *DT* Deceleration time of early transmitral inflow, *SR$_E$* strain rate during early diastole

did show a tendency towards contribution ($p=0.057$, Table 6).

Discussion

In this study, we performed comprehensive LV functional assessment in patients with persistent AF and preserved LVEF who underwent RFCA. We then evaluated LV deformation as global strains (GLS, GRS, and GCS), SR, dyssynchrony, and torsion by using STE. The three main findings of our study are as follows: (1) in persistent AF with preserved LVEF and no heart failure symptoms, further improvement in LVEF (16/30, 53%) along with improvements of LV deformation and torsion was observed within 6 months after RFCA; (2) the predictor of maintaining stable sinus rhythm 2 years after the index RFCA was the baseline value of *e′* and the value of LAVI 6 months after the index RFCA; (3) ΔE/SR$_E$ contributed to patients being able to experience significant improvement in LVEF after RFCA.

In our study, further improvement in LVEF was observed and the improvements in LV deformation, torsion, and diastolic function within 6 months after RFCA were confirmed by STE. Three studies have evaluated LV function in AF with preserved LVEF using STE. In two studies, GLS and GCS were reported to have been restored by RFCA, although no LVEF improvement was observed [10, 15]. Conversely, Zhang et al. reported impaired all three strains as well as in the LVEF and their restoration after RFCA for AF [25], which was similar to our study results. Currently, GLS is recommended as a sensitive marker of subclinical LV dysfunction [20]. Longitudinal myocardial fibers, which are located mainly in the sub-endocardium, are more vulnerable to fibrosis due to hypertension or myocardial ischemia and are impaired earlier than circumferential fibers (which are mostly located in the mid-wall), or radial fibers (which are mostly located in the subepicardium). Thus, in most cases with subclinical cardiovascular disease, radial and circumferential strains are usually preserved [30, 31]. Therefore, it is possible that the patients in our cohort were at a slightly more advanced stage of AF-induced LV dysfunction.

In our study, the baseline value of septal *e′* and the value of LAVI 6 months after the index RFCA were long-term predictors of maintaining stable sinus rhythm. The septal *e′*, which is one of the LV diastolic function indices, was found to be a long-term predictor. Patients with recurrent AF after RFCA had a higher incidence of LA scarring than did those without such recurrence [32]. Left ventricular diastolic dysfunction is associated with LA remodeling [33] with increasing atrial fibrosis and decreased LA voltage [34] and this initiates the recurrence of AF after RFCA. There have been a few reports that describe LV diastolic dysfunction as an independent predictor of AF recurrence after RFCA [34, 35]. The present findings are concordant with these studies and further confirm the importance of LV diastolic function in the treatment of AF. Reverse remodeling of the LA after RFCA for isolated AF is well documented [15, 36]. Moreover, morphological and functional recovery of the LA is regarded as a strong predictor for maintenance of stable sinus rhythm after RFCA for AF [16, 36–40]. The results of our study are also concordant with those studies.

In our study, LV systolic function indices such as LVEF, LVESV, strains, strain rate, dyssynchrony, and torsion were not found to be predictors of maintenance of stable sinus rhythm after RFCA. Recently, Liao et al. reported that reverse remodeling of the LV with a decrease in LV

Table 6 Factors contributing to reverse remodeling of the left atrium

	Reverse remodeling of LA			Odds ratio (95% CI)	*p* value
	Yes ($n=15$)	No ($n=15$)	*p* value		
ΔBNP, pg/ml	−85.8 ± 95.8	−340.7 ± 31.1	0.0940		
ΔLVEF, %	4.9 ± 8.8	11.5 ± 7.8	0.0399	0.902 (0.810–1.003)	0.057

LA left atrium, *CI* confidence interval, *BNP* brain natriuretic peptide, *LVEF* left ventricular ejection fraction

endo-systolic dimension is also predictive of maintenance of stable sinus rhythm as well as reverse remodeling of the LA after RFCA for AF [41]. In a study with a larger sample size, LV systolic function indices, such as GLS and LVEF, may have the power to predict the patient's prognosis.

In our study, $\Delta E/SR_E$ conversely contributed to improvement in LVEF, and a smaller decrease of E/SR_E was associated with significant improvement of LVEF. Several clinical studies have reported favorable factors for LVEF improvements after RFCA for AF, such as the maintenance of stable sinus rhythms after RFCA [42] and the favorable baseline characteristics such as the existence of persistent AF or low LVEF [21]. Ling et al. [43] reported that diffuse fibrosis in the LV could be detected in AF patients with LV dysfunction using cardiac magnetic resonance imaging. In AF patients with mild LV fibrosis and lower LV filling pressure, there is greater improvement in the LVEF than in AF patients with severe LV fibrosis and higher LV filling pressure. Therefore, it can be postulated that pre-existent or acquired LV fibrosis after the initiation of AF [44] might attenuate the favorable effect of RFCA for AF on LVEF.

Theoretically, potential mechanisms of LVEF improvement after RFCA for AF might involve the restoration in atrial contractility, the maintenance of synchronic atrioventricular contractions, and the prevention of a high ventricular heart rate [3]. However, it remains unclear what mechanism contributes the most. As our cohort experienced no changes in the ventricular heart rate between baseline and follow-up, it can be excluded as a potential mechanism in this study. Tops et al. [18] mentioned that the improvement in LV function after catheter ablation may be more related to restoration and long-term maintenance of sinus rhythm than to normalization of the heart rate since significant changes in GCS, GLS and SR were only noted in the patients who maintained sinus rhythm during follow-up. Kucukdurmaz et al. [20] claimed that a potential mechanism of the recovery of ventricular dysfunction associated with this arrhythmia could be similar to the improvement after ablation of frequent ventricular ectopic beats in patients with regular heart rates. Our postulation is similar to those of previous studies, which indicated that the restoration in atrial contractility and maintenance of synchronic atrioventricular contraction improve LV hemodynamics and lead to the improvements of LV function, including LVEF, LV deformations and torsion.

In our study, no significant contributing factors in the reverse remodeling of the LA were observed, although ΔLVEF showed only a tendency towards contribution. In a study with a larger sample sizes, common contributing factors for both LVEF improvement and reverse remodeling of the LA after RFCA may be uncovered. LV diastolic function indices such as $\Delta E/SR_E$ might be one of the candidates.

Since the sample size in our cohort was small and the data were obtained from a single center, it is possible that there may be an institutional bias. Therefore, the results and conclusions from this study may not be generalized to other institutions. Further study in a larger cohort is necessary especially to confirm the prognostic values of LV functional indices for maintenance of stable sinus rhythm, for significant improvement in LVEF, and for significant reverse remodeling of the LA after RFCA.

Conclusion

In persistent fibrillation with preserved LVEF and no heart failure symptoms, LV deformation, torsion and diastolic function can be restored by RFCA with improvement in LVEF as well as reverse remodeling of the LA. LV filling pressure may play significant roles in the mechanisms. Further investigations are necessary on a large-scale and in multiple institutions to confirm these findings and elucidate the main mechanism of this phenomenon.

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Author contributions All authors conceived the study concept and study design. TN, AH, and JA complied and synthesized the data. TN and JA performed statistical analysis. HT supervised the research project. TN wrote the first version of the draft. All authors participated in the interpretation of the results and the reports, and approved the final version.

Compliance with ethical standards

Conflict of interest Tomoo Nagai, Junko Arakawa, Akira Hamabe, and Hirotsugu Tabata declare that they have no conflict of interest.

Ethical statements All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1964 and later revisions.

Informed consent Informed consent was obtained from all patients for being included in the study.

References

1. Kato K, Ejima K, Fukushima N, et al. Catheter ablation of atrial fibrillation in patients with severely impaired left ventricular systolic function. Heart Vessels. 2016;31:584–92.
2. Gentlesk PJ, Sauer WH, Gerstenfeld EP, et al. Reversal of left ventricular dysfunction following ablation of atrial fibrillation. J Cardiovasc Electrophysiol. 2007;18:9–14.
3. Hsu LF, Jaïs P, Sanders P, et al. Catheter ablation for atrial fibrillation in congestive heart failure. N Engl J Med. 2004;351:2373–83.

4. Marrouche NF, Brachmann J, Andresen D, et al. Catheter Ablation for Atrial Fibrillation with Heart Failure. N Engl J Med. 2018;378:417–27.
5. Al Halabi S, Qintar M, Hussein A, et al. Catheter ablation for atrial fibrillation in heart failure patients: a meta-analysis of randomized controlled trials. JACC Clin Electrophysiol. 2015;1:200–9.
6. Ganesan AN, Nandal S, Lüker J, et al. Catheter ablation of atrial fibrillation in patients with concomitant left ventricular impairment: a systematic review of efficacy and effect on ejection fraction. Heart Lung Circ. 2015;24:270–80.
7. Dagres N, Varounis C, Gaspar T, et al. Catheter ablation for atrial fibrillation in patients with left ventricular systolic dysfunction. A systematic review and meta-analysis. J Card Fail. 2011;17:964–70.
8. Wilton SB, Fundytus A, Ghali WA, Veenhuyzen GD. Meta-analysis of the effectiveness and safety of catheter ablation of atrial fibrillation in patients with versus without left ventricular systolic dysfunction. Am J Cardiol. 2010;106:1284–91.
9. Calkins H, Kuck KH, Cappato R, et al. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. Europace. 2012;14:528–606.
10. Kirchhof P, Benussi S, Kotecha D, et al. 2016 ESC guidelines for the management of atrial fibrillation developed in collaboration with EACTS. Eur Heart J. 2016;37:2893–962.
11. Lutomsky BA, Rostock T, Koops A, et al. Catheter ablation of paroxysmal atrial fibrillation improves cardiac function: a prospective study on the impact of atrial fibrillation ablation on left ventricular function assessed by magnetic resonance imaging. Europace. 2008;10:593–9.
12. Reant P, Lafitte S, Bougteb H, et al. Effect of catheter ablation for isolated paroxysmal atrial fibrillation on longitudinal and circumferential left ventricular systolic function. Am J Cardiol. 2009;103:232–7.
13. Kosiuk J, Buchta P, Gaspar T, et al. Prevalence and predictors of worsened left ventricular diastolic dysfunction after catheter ablation of atrial fibrillation. Int J Cardiol. 2013;168:3613–5.
14. Machino-Ohtsuka T, Seo Y, Ishizu T, et al. Efficacy, safety, and outcomes of catheter ablation of atrial fibrillation in patients with heart failure with preserved ejection fraction. J Am Coll Cardiol. 2013;62:1857–65.
15. Reant P, Lafitte S, Jaïs P, et al. Reverse remodeling of the left cardiac chambers after catheter ablation after 1 year in a series of patients with isolated atrial fibrillation. Circulation. 2005;112:2896–903.
16. Marsan NA, Tops LF, Holman ER, et al. Comparison of left atrial volumes and function by real-time three-dimensional echocardiography in patients having catheter ablation for atrial fibrillation with persistence of sinus rhythm versus recurrent atrial fibrillation 3 months later. Am J Cardiol. 2008;102:847–53.
17. Sacher F, Corcuff JB, Schraub P, et al. Chronic atrial fibrillation ablation impact on endocrine and mechanical cardiac functions. Eur Heart J. 2008;29:1290–5.
18. Tops LF, Den Uijl DW, Delgado V, et al. Long-term improvement in left ventricular strain after successful catheter ablation for atrial fibrillation in patients with preserved left ventricular systolic function. Circ Arrhythm Electrophysiol. 2009;2:249–57.
19. Nori D, Raff G, Gupta V, et al. Cardiac magnetic resonance imaging assessment of regional and global left atrial function before and after catheter ablation for atrial fibrillation. J Interv Card Electrophysiol. 2009;26:109–17.
20. Kucukdurmaz Z, Kato R, Erdem A, et al. Catheter ablation for atrial fibrillation results in greater improvement in cardiac function in patients with low versus normal left ventricular ejection fraction. J Interv Card Electrophysiol. 2013;37:179–87.
21. Zhu P, Zhang Y, Jiang P, et al. Effects of radiofrequency catheter ablation on left ventricular structure and function in patients with atrial fibrillation: a meta-analysis. J Interv Card Electrophysiol. 2014;40:137–45.
22. Reisner SA, Lysyansky P, Agmon Y, et al. Global longitudinal strain: a novel index of left ventricular systolic function. J Am Soc Echocardiogr. 2004;17:630–3.
23. Yingchoncharoen T, Agarwal S, Popovic ZB, et al. Normal ranges of left ventricular strain: a meta-analysis. J Am Soc Echocardiogr. 2013;26:185–91.
24. Suffoletto MS, Dohi K, Cannesson M, et al. Novel speckle-tracking radial strain from routine black-and-white echocardiographic images to quantify dyssynchrony and predict response to cardiac resynchronization therapy. Circulation. 2006;113:960–8.
25. Notomi Y, Lysyansky P, Setser RM, et al. Measurement of ventricular torsion by two-dimensional ultrasound speckle tracking imaging. J Am Coll Cardiol. 2005;45:2034–41.
26. Wang J, Khoury DS, Thohan V, et al. Global diastolic strain rate for the assessment of left ventricular relaxation and filling pressures. Circulation. 2007;115:1376–83.
27. Zhang JQ, Sun JP, Liu XY, et al. Left ventricular synchronization and systolic function estimated by speckle tracking echocardiography pre-and post-radiofrequency ablation in patients with atrial fibrillation. Int J Cardiol. 2014;172:217–9.
28. Lang RM, Badano LP, Mor-Avi V, et al. Recommendations for cardiac chamber quantification by echocardiography in adults: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2015;28:1–39.
29. Nagueh SF, Smiseth OA, Appleton CP, et al. Recommendations for the evaluation of left ventricular diastolic function by echocardiography: an update from the American Society of Echocardiography and the European Association of Cardiovascular Imaging. J Am Soc Echocardiogr. 2016;29:277–314.
30. Sanderson JE. Heart failure with a normal ejection fraction. Heart. 2007;93:155–8.
31. Fang ZY, Leano R, Marwick TH. Relationship between longitudinal and radial contractility in subclinical diabetic heart disease. Clin Sci (Lond). 2004;106:53–60.
32. Chang SL, Tai CT, Lin YJ, Wongcharoen W, et al. Biatrial substrate properties in patients with atrial fibrillation. J Cardiovasc Electrophysiol. 2007;18:1134–9.
33. Kim TH, Shim CY, Park JH, et al. Left ventricular diastolic dysfunction is associated with atrial remodeling and risk or presence of stroke in patients with paroxysmal atrial fibrillation. J Cardiol. 2016;68:104–9.
34. Hu YF, Hsu TL, Yu WC, et al. The impact of diastolic dysfunction on the atrial substrate properties and outcome of catheter ablation in patients with paroxysmal atrial fibrillation. Circ J. 2010;74:2074–8.
35. Cha YM, Wokhlu A, Asirvatham SJ, et al. Success of ablation for atrial fibrillation in isolated left ventricular diastolic dysfunction: a comparison to systolic dysfunction and normal ventricular function. Circ Arrhythm Electrophysiol. 2011;4:724–32.
36. Casaclang-Verzosa G, Gersh BJ, Tsang TS. Structural and functional remodeling of the left atrium: clinical and therapeutic implications for atrial fibrillation. J Am Coll Cardiol. 2008;51:1–11.
37. Pump A, Di Biase L, Price J, et al. Efficacy of catheter ablation in nonparoxysmal atrial fibrillation patients with severe enlarged left atrium and its impact on left atrial structural remodeling. J Cardiovasc Electrophysiol. 2013;24:1224–31.
38. Motoki H, Negishi K, Kusunose K, et al. Global left atrial strain in the prediction of sinus rhythm maintenance after catheter ablation for atrial fibrillation. J Am Soc Echocardiogr. 2014;27:1184–92.

39. Montserrat S, Gabrielli L, Bijnens B, et al. Left atrial deformation predicts success of first and second percutaneous atrial fibrillation ablation. Heart Rhythm. 2015;12:11–8.
40. Park HC, Lee Y, Lee D, et al. Left atrial functional reservoir: predictive value for outcome of catheter ablation in paroxysmal atrial fibrillation. Int J Cardiovasc Imaging. 2014;30:1423–34.
41. Liao YC, Liao JN, Lo LW, et al. Left atrial size and left ventricular end-systolic dimension predict the progression of paroxysmal atrial fibrillation after catheter ablation. J Cardiovasc Electrophysiol. 2017;28:23–30.
42. Nedios S, Sommer P, Dagres N, et al. Long-term follow-up after atrial fibrillation ablation in patients with impaired left ventricular systolic function: the importance of rhythm and rate control. Heart Rhythm. 2014;11:344–51.
43. Ling L, Kistler PM, Ellims AH, Iles L, et al. Diffuse ventricular fibrosis in atrial fibrillation: noninvasive evaluation and relationships with aging and systolic dysfunction. J Am Coll Cardiol. 2012;60:2402–8.
44. Avitall B, Bi J, Mykytsey A, Chicos A. Atrial and ventricular fibrosis induced by atrial fibrillation: evidence to support early rhythm control. Heart Rhythm. 2008;5:839–45.