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The Effects of Radiofrequency Catheter Ablation for Atrial Fibrillation on Right Ventricular Function

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AUTHOR'S SUMMARY

This study examined the impact of radiofrequency catheter ablation (RFCA) on right ventricular (RV) function in patients with atrial fibrillation (AF). A total of 164 patients with paroxysmal AF (PAF), persistent AF (PeAF), and long-standing persistent AF (LSPeAF) were assessed using echocardiography pre- and post-RFCA. RV function were measured using fractional area change, and strain parameters (RV free-wall longitudinal strain, and RV 4-chamber strain including the ventricular septum). Results showed significant improvement in RV function, particularly in the PeAF group, compared to PAF and LSPeAF groups. These improvements were consistent across patients without recurrence and within the propensity-score matched cohort, indicating that RFCA is more effective in enhancing RV function in PeAF patients.

ABSTRACT

Background and Objective: The effects of radiofrequency catheter ablation (RFCA) for atrial fibrillation (AF) on right ventricular (RV) function are not well known.
Methods: Patients who underwent RFCA for AF and underwent pre- and post-procedural echocardiography were enrolled consecutively. Fractional area change (FAC), RV free-wall longitudinal strain (RVFWSL), and RV 4-chamber strain including the ventricular septum (RV4CSL) were measured. Changes in FAC, RVFWSL, and RV4CSL before and after RFCA were compared among paroxysmal AF (PAF), persistent AF (PeAF), and long-standing persistent AF (LSPeAF) groups.
Results: A total of 164 participants (74 PAF, 47 PeAF, and 43 LSPeAF; age, 60.8 ± 9.8 years; men, 74.4%) was enrolled. The patients with PeAF and LSPeAF had worse RV4CSL ($p<0.001$) and RVFWSL ($p<0.001$) than those with PAF and reference values. Improvements in RVFWSL and RV4CSL after RFCA were significant in the PeAF group compared with the PAF and LSPeAF groups (ΔRV4CSL, 8.4% [5.1, 11.6] in PeAF vs. 1.0% [−1.0, 4.1] in PAF, 1.9% [−0.2, 4.4] in LSPeAF, $p<0.001$; ΔRVFWSL, 9.0% [6.9, 11.5] in PeAF vs. 0.9% [−1.4, 4.9] in PAF, 1.0% [−1.0,

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Conflict of Interest
The authors have no financial conflicts of interest.

Data Sharing Statement
The data generated in this study is available from the corresponding author upon reasonable request.

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Author Contributions
Conceptualization: Kim M, Uhm JS; Data curation: Uhm JS, Park JW, Bae S, Jung IH; Formal analysis: Heo SJ; Investigation: Kim M, Park JW, Bae S, Jung IH; Methodology: Kim M, Heo SJ; Project administration: Uhm JS; Resources: Uhm JS, Kim D, Yu HT, Kim TH, Joung B, Lee MH; Software: Jung IH; Supervision: Uhm JS, Kim D, Yu HT, Kim TH, Joung B, Lee MH; Validation: Park JW, Bae S, Jung IH, Heo SJ, Kim D, Yu HT, Kim TH, Joung B, Lee MH; Visualization: Kim M; Writing - original draft: Kim M, Uhm JS; Writing - review & editing: Kim M, Uhm JS, Park JW, Bae S, Jung IH, Heo SJ, Kim D, Yu HT, Kim TH, Joung B, Lee MH.

3.6] in LSPeAF, p<0.001). In patients without recurrence, improvements in RVFWSL and RV4CSL after RFCA were significant in the PeAF group compared to the LSPeAF group.
Conclusions: RV systolic function is more impaired in patients with PeAF and LSPeAF than in those with PAF. RV systolic function is more improved after RFCA in patients with PeAF than in those with PAF or LSPeAF.

Keywords: Atrial fibrillation; Catheter ablation; Right ventricle; Strain; Ventricular function, right

INTRODUCTION

The prevalence of atrial fibrillation (AF) is gradually increasing over time, which is attributed to prolongation of the average lifespan and enhanced surveillance of AF.[1] Radiofrequency catheter ablation (RFCA), as a treatment option of rhythm control for symptomatic AF, improves left ventricular (LV) ejection fraction (LVEF) in patients with heart failure and significantly reduces left atrial (LA) size after successful restoration of sinus rhythm.[2][3] Although LVEF is normal in patients with AF, they may have significant diastolic dysfunction compared to heart failure patients with sinus rhythm, and this can result in structural changes in the right heart due to chronic increase in right ventricular (RV) systolic pressure and decreased atrial function.[4][5] In previous studies, investigations into right-sided heart changes following RFCA in patients with AF showed evidence of reverse remodeling.[6] However, there were small sample sizes, and no study has examined the improvement of RV function according to AF types and timing of RFCA.

Regarding the assessment of RV systolic function analysis, due to the complex geometry of the RV compared to the LV, there is no standardized method as there is for LVEF.[7][8] Recently, RV strain analysis using speckle tracking echocardiography has been utilized to evaluate RV function and to predict prognosis in various conditions such as pulmonary arterial hypertension, pulmonary embolism, and tricuspid regurgitation.[9-12] Therefore, we aimed to investigate the effects of RFCA on RV function by dividing AF patients into 3 groups of paroxysmal AF (PAF), persistent AF (PeAF), and long-standing persistent AF (LSPeAF) and to evaluate changes in RV function before and after RFCA using RV strain analysis.

METHODS

Ethical statement

The present investigation adhered to the updated 2013 Helsinki Declaration and obtained approval from our hospital's Institutional Review Board (9-2023-0018). Given the retrospective nature of the study, the need for informed consent was waived.

Study participants

In a single referral hospital, we conducted a retrospective cohort study from May 2020 to July 2022, enrolling patients consecutively who underwent RFCA for AF and had pre- and post-procedural echocardiography. Inclusion criteria was as follows: 1) age ≥19 years, 2) patients who underwent RFCA for AF, 3) patients who underwent echocardiography before and after RFCA. The following individuals were excluded from the study: 1) patients with complex congenital heart disease, 2) those who did not undergo pre- or post-echocardiography.

Among 174 patients who underwent the RFCA procedure, 10 did not undergo pre- or post-echocardiography. Finally, 164 participants were enrolled in the present study. PAF was defined as AF that terminates spontaneously within 7 days of onset. PeAF was defined as AF that continues beyond 7 days. LSPeAF was defined as continuous AF >12 months' duration.[13)]

Radiofrequency catheter ablation for atrial fibrillation and follow-up

All patients initially underwent electrical isolation of the 4 pulmonary veins and bidirectional block of the cavotricuspid isthmus using 3-dimensional electroanatomical mapping system (CARTO; Johnson & Johnson Inc., Diamond Bar, CA, USA). In patients with PeAF or LSPeAF, we additionally conducted electrical isolation of the posterior box, anterior line, perimitral line, or non-pulmonary vein trigger ablation at the operator's discretion. The endpoint of the procedure was electrical isolation of the 4 pulmonary veins and bidirectional block of the cavotricuspid isthmus with or without bidirectional block of the additional lines or no non-pulmonary vein triggers.

All patients were followed at the outpatient clinic at 1, 3, 6, 9, and 12 months post-RFCA and then every 3–6 months. Electrocardiogram (ECG) was performed at every visit and whenever the patients complained of palpitation. Regular smart watch ECG monitoring was performed at least once a week after RFCA and whenever patients complained of palpitation. If any ECG-documented AF episode occurred within the 3-month blanking period during follow-up, patients were diagnosed with early recurrence; any AF recurrence thereafter was diagnosed as clinical recurrence. In cases of early recurrence and clinical recurrence, antiarrhythmic drugs were prescribed at physicians' discretion.

Data collection

The demographic data of the patients for age; sex; blood pressure; body mass index; and medical history, including hypertension, diabetes mellitus, chronic kidney disease, vascular disease, heart failure, stroke, or transient ischemic attack, were acquired by medical chart review. The definition of heart failure includes the following criteria: LVEF <50%, or the presence of symptoms of dyspnea and evidence of pulmonary congestion, or N-terminal prohormone of brain natriuretic peptide (NT-proBNP) >375 pg/mL, or a Heart Failure Association-Pre-test assessment, Echocardiography & natriuretic peptide, Functional testing, Final aetiology (HFA-PEFF) score of 5 or higher, in cases where the LVEF is greater than or equal to 50%.[14)] We also collected hemoglobin, NT-proBNP, and creatinine as laboratory findings at the time between pre-procedural echocardiography and RFCA, and calculated the glomerular filtration rate using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation.[15)] The serial ECGs and Holter monitoring were reviewed and recurrence was identified by cardiac electrophysiologists (J.S.U. and J.W.P.). Transthoracic echocardiography examination was conducted using a commercially available echocardiographic machine (Vivid E9/E95; GE HealthCare, Horten, Norway). LA size was measured in both the anterior-posterior dimension and the LA volume index (LAVI). Other traditional echocardiographic parameters were collected based on the guideline.[16)] The timing of transthoracic echocardiography before and after the procedure was determined at the discretion of the physician.

Right ventricular function analysis and right ventricular longitudinal strain measurement

We measured the RV function of enrolled participants at the RV-focused apical 4-chamber view. Fractional area change (FAC), and traditional parameters for measuring RV function

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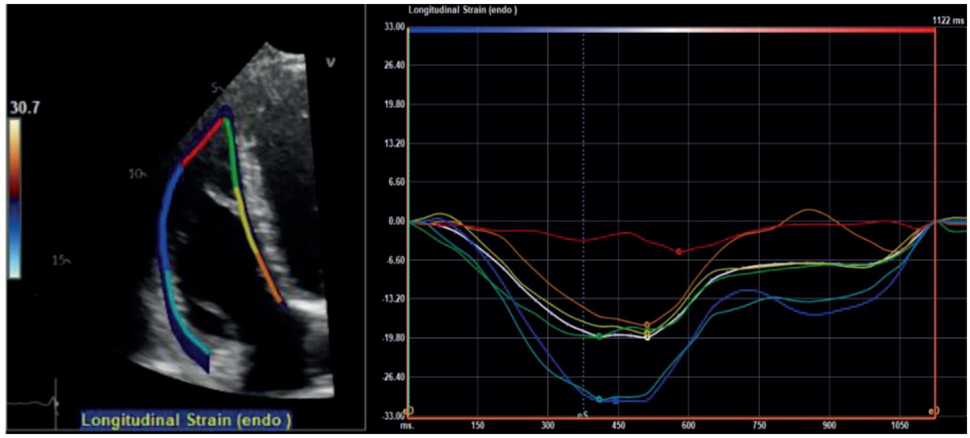

Figure 1. Right ventricular strain analysis using vendor-independent analysis software.

were obtained. Commercially available, vendor-independent analysis software (TomTec Imaging System, Munich, Germany) was used to measure RV longitudinal strain by an experienced sonographer blinded to participants' clinical information (**Figure 1**). In detail, end-diastolic (the starting point of the QRS complex or the largest RV size during the cardiac cycle) and end-systolic (the smallest RV volume during the cardiac cycle) periods were defined first. After the endocardial border of the RV was manually traced at end-systolic phase, the endocardial border of end-diastolic phase was traced semi-automatically by the speckle-tracking method. After the endocardial border at end-diastolic phase was selected, speckles along the RV endocardial border and myocardium were traced by the software throughout the cardiac cycle.

RV free-wall longitudinal strain (RVFWSL) and RV 4-chamber strain including the ventricular septum (RV4CSL) were measured according to the guideline.[17)] In brief, the region of interest is set between the endocardial and epicardial border. The RVFWSL measures the longitudinal strain values of the basal, mid, and apical segments of the RV free-wall, while the RV4CSL evaluates the longitudinal strain values of a total of 6 segments, including 3 from the RV portion of interventricular septum. FAC ≥35%, RV4CSL ≤−17.0%, and RVFWSL ≤−19.0% were considered normal RV function.[16)18)] Throughout the manuscript, RV strain values are consistently presented as absolute values for ease of comparison.

Measurement reproducibility

To demonstrate measurement reproducibility, we randomly selected 20 patients (7 PAF, 7 PeAF, and 6 LSPeAF patients) to evaluate intra- and inter-observer variability for FAC, RV4CSL, and RVFWSL. Intra-observer variability measurements were conducted with a minimum interval of 3 months and performed blinded to the previous results. Inter-observer variability measurements were conducted by an experienced imaging cardiologist (M.K.) who independently measured FAC, RV4CSL, and RVFWSL while blinded to the previous results.

Study endpoint

Our study aimed to investigate changes in RV function before and after RFCA in patients with PAF, PeAF, and LSPeAF. We also aimed to examine changes in RV function in the no-recurrence subgroup, defined as maintaining sinus rhythm without evidence of AF or atrial flutter or tachycardia after RFCA, across the 3 types of AF patients.

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Statistical analysis
The values of each continuous variable were presented as mean ± standard deviation or median (interquartile range; IQR), depending on whether normality is satisfied by the Shapiro-Wilk test. Categorical variables were presented as numbers and percentages and were compared using χ^2 test or Fisher's exact test. The homogeneity of variances was tested using Levene's test. Based on the test results, either one-way analysis of variance or Kruskal-Wallis test was performed to compare the differences of each variable among groups. Post-hoc analyses were performed using Dunnett T3 test with Bonferroni correction, when significant differences were observed among groups. Changes of echocardiographic parameters, including RV function, are presented as absolute difference (delta change), and improved RV function, defined as below the cutoff before the procedure and above the cutoff after the procedure, are presented as numbers and percentages. We conducted a receiver operating characteristics curve analysis to identify the best threshold of the absolute variation in RV strain parameters for predicting clinical recurrence using the Youden index. Three sensitivity analyses were conducted. Firstly, we assessed the improvement in RV function in the subgroup of patients who had no clinical recurrence and were in sinus rhythm during post-procedural echocardiography. Secondly, to adjust for the influence of heart rate on RV function, we analyzed patients who had a heart rate of 100 beats per minute or less during echocardiography.[19)] Thirdly, we excluded patients who were evaluated for RV function within 6 months of the procedure and performed the analysis. Fourthly, considering that the time interval between the procedure and the follow-up echocardiography might affect the improvement in RV function, we conducted a linear mixed model analysis. Statistical significance was defined as a 2-tailed p-value less than 0.05 or less than 0.017 with Bonferroni correction. The R (R Foundation for Statistical Computing, Vienna, Austria) version 4.1.2 software was utilized for all statistical analyses in this study.

RESULTS

Baseline characteristics
A total of 164 participants (74 PAF, 47 PeAF, and 43 LSPeAF; age, 60.8±9.8 years; men, 74.4%) who underwent RFCA and serial echocardiography before and after RFCA were enrolled. Among these participants, 13 individuals underwent a second RFCA procedure, and there were no significant differences observed in the rates of second RFCA among the PAF, PeAF, and LSPeAF groups, with 5 (6.8%), 5 (10.6%), and 3 (7.0%), respectively. Participants with PAF had a higher likelihood of being male; lower diastolic blood pressure; and lower incidence of diabetes mellitus, heart failure, and cerebrovascular accident (**Table 1**). Participants with PAF had higher estimated glomerular filtration rate than those with LSPeAF (p=0.004). The median NT-proBNP was 452.0 pg/mL (157.0–881.9), and participants with PAF had lower NT-proBNP than those with PeAF.

The conventional echocardiographic and strain values are summarized in **Table 2**. Among the participants, the prevalence of those who exhibited AF rhythm during the pre-procedural echocardiography was 16 (21.6%) in PAF, 41 (87.2%) in PeAF, and 40 (93.0%) in LSPeAF, respectively. The mean LVEF was 55.2±9.7% and participants with PAF had higher LV systolic function than those with PeAF or LSPeAF (p<0.001). The mean LA size was 45.5±18.4 mL/m^2, and participants with PAF had smaller LA than those with PeAF or LSPeAF (**Table 2**).

Table 1. Baseline characteristics of study participants

	PAF (n=74)	PeAF (n=47)	LSPeAF (n=43)	p value
Age (years)	59.7±10.8	62.2±9.1	61.3±8.6	0.377
Female sex	26 (35.1)	7 (14.9)	9 (20.9)	0.033*
Systolic BP (mmHg)	125.6±15.2	124.3±14.9	129.9±18.9	0.237
Diastolic BP (mmHg)	73.4±11.8	77.2±12.9	81.0±15.8	0.013†
Body mass index (kg/m^2)	25.1±2.9	26.5±3.4	25.7±3.3	0.244
Underlying disease				
Hypertension	42 (56.8)	27 (57.4)	29 (67.4)	0.487
Diabetes mellitus	10 (13.5)	12 (25.5)	19 (44.2)	0.001†
Chronic kidney disease	3 (4.1)	6 (12.8)	5 (11.6)	0.173
Vascular disease	8 (10.8)	6 (12.8)	2 (4.7)	0.397
Heart failure	16 (21.6)	36 (76.6)	31 (72.1)	<0.001*,†
HFrEF (LVEF <40%)	2 (2.7)	8 (17.0)	4 (9.3)	0.022*
Stroke or TIA	4 (5.4)	7 (14.9)	9 (20.9)	0.037*
CHA_2DS_2-VASc score	1.9±1.4	1.9±1.7	2.4±1.7	0.209
Medication history				
RAS inhibitor	34 (45.9)	33 (70.2)	32 (74.4)	0.003*,†
ARNI	4 (5.4)	11 (23.4)	10 (23.3)	0.006*,†
Beta-blocker	73 (98.6)	45 (95.7)	43 (100.0)	0.296
SGLT2i	5 (6.8)	11 (23.4)	13 (30.2)	0.003*,†
MRA	4 (5.4)	20 (42.6)	19 (44.2)	<0.001*,†
Antiarrhythmic drugs	74 (100)	47 (100)	43 (100)	>0.999
Class Ic	48 (64.9)	20 (42.6)	23 (53.5)	0.053
Class III	26 (35.1)	27 (57.4)	20 (46.5)	0.053
Laboratory findings				
Hemoglobin (g/dL)	14.2 (13.0–15.2)	14.7 (13.8–15.6)	14.8 (13.6–15.9)	0.202
eGFR (mL/min/1.73 m^2)	87.7 (72.5–102.3)	80.3 (73.2–91.2)	81.7 (66.6–89.7)	0.022
NT-proBNP (pg/mL)	487.4 (164.0–669.6)	702.0 (438.6–995.5)	662.7 (374.5–2,104.5)	0.002*,†

Continuous variables were presented mean ± standards or median (interquartile range), as appropriately. Categorical variables were presented as number (percent).
ARNI = angiotensin receptor-neprilysin inhibitor; BP = blood pressure; eGFR = estimated glomerular filtration rate; HFrEF = heart failure with reduced ejection fraction; LSPeAF = long-standing persistent atrial fibrillation; LVEF = left ventricular ejection fraction; MRA = mineralocorticoid receptor antagonist; NT-proBNP = N-terminal prohormone of brain natriuretic peptide; PAF = paroxysmal atrial fibrillation; PeAF = persistent atrial fibrillation; RAS = renin-angiotensin-aldosterone system; SGLT2i = sodium-glucose cotransporter-2 inhibitor; TIA = transient ischemic attack.
*Significant difference between PAF and PeAF, †Significant difference between PAF and LSPeAF, ‡Significant difference between PeAF and LSPeAF, as determined by post hoc analyses.

Table 2. Baseline echocardiographic parameters of study participants

	PAF (n=74)	PeAF (n=47)	LSPeAF (n=43)	p value
LA AP diameter (mm)	39.5 (36.0–43.0)	46.0 (43.0–49.5)	45.0 (41.0–49.0)	<0.001*,†
LAVI (mL/m^2)	35.6 (28.9–43.6)	48.5 (39.8–59.0)	49.2 (40.4–57.7)	<0.001*,†
LVEF (%)	60.0 (55.0–64.0)	53.0 (44.0–62.0)	55.0 (47.5–57.0)	<0.001*,†
Septal E/e’	8.7 (7.6–12.0)	9.9 (7.7–12.1)	9.6 (8.2–11.6)	0.529
Estimated PASP (mmHg)	26.1 (23.5–30.0)	28.0 (24.3–32.0)	27.1 (24.3–32.0)	0.257
HFA-PEFF score	3.0 (2.0–4.0)	4.0 (3.0–5.0)	4.0 (3.0–5.0)	<0.001*,†
HFA-PEFF score ≥5	7 (9.5)	17 (36.2)	13 (30.2)	<0.001*,†
FAC (%)	43.2±7.3	35.8±9.2	36.3±8.9	<0.001*,†
Patients with FAC <35%	7 (9.5)	20 (42.6)	18 (41.9)	<0.001*,†
RV4CSL (%)	22.8±4.7	12.9±4.3	13.6±4.3	<0.001*,†
Patients with FAC <35%	10 (13.5)	40 (85.1)	37 (86.0)	<0.001*,†
RVFWSL (%)	25.5±5.6	14.6±5.3	15.9±5.6	<0.001*,†
Patients with RVFWSL <19%	17 (23.0)	43 (91.5)	37 (86.0)	<0.001*,†

Continuous variables were presented as median (interquartile range). Categorical variables were presented as number (percent).
AP = anterior-posterior; FAC = fractional area change; HFA-PEFF = Heart Failure Association-Pre-test assessment, Echocardiography & natriuretic peptide, Functional testing, Final aetiology; LA = left atrial; LAVI = left atrial volume index; LSPeAF = long-standing persistent atrial fibrillation; LVEF = left ventricular ejection fraction; PAF = paroxysmal atrial fibrillation; PASP = pulmonary artery systolic pressure; PeAF = persistent atrial fibrillation;; RV4CSL = right ventricular 4-chamber strain including the ventricular septum; RVFWSL = right ventricular free-wall longitudinal strain.
*Significant difference between PAF and PeAF, †Significant difference between PAF and LSPeAF, ‡Significant difference between PeAF and LSPeAF, as determined by post hoc analyses.

The mean of baseline RV function measured by FAC was higher than the reference value of 35.0% in all 3 groups. Patients with PAF had higher FAC than those with PeAF or LSPeAF (p<0.001). Patients with PeAF and LSPeAF had worse RV4CSL (p<0.001) and RVFWSL (p<0.001) than those with PAF and reference values (**Table 2**). Among the total population in the baseline study, 97 patients were observed to have AF rhythm (16 with PAF, 41 with PeAF, and 40 with LSPeAF). There was no difference were observed with FAC among the 3 groups but significantly impaired in PeAF and LSPeAF patients compared to those with PAF when assessed using RV4CSL and RVFWSL in patients with AF rhythm during baseline study (**Supplementary Table 1**). In the total population, RV enlargement or annular dilation was observed in 12.8% (n=6) of the patients with PeAF (RV basal and mid diameter were 52.2±7.6 and 39.7±6.0) and 20.9% (n=9) of the patients with LSPeAF (51.8±5.7 [basal diameter] and 38.6±5.3 [mid diameter]) at baseline echocardiography. Even within the group with RV enlargement, no statistically significant differences in baseline RV function were observed between the 2 groups (31.9±9.4% [PeAF] vs. 32.9±8.2% [LSPeAF] in FAC, p=0.816; 12.5±3.1% vs. 13.1±2.0% in RV4CSL, p=0.660; 13.7±3.5% vs. 14.5±2.2% in RVFWSL, p=0.603).

Changes in left ventricular and right ventricular function before and after radiofrequency catheter ablation

The interval of echocardiography performed before and after RFCA was 360.5 days (216.0–544.5). The durations between RFCA and post-RFCA follow-up echocardiography were 98.0 (48.0–245.0), 180.0 (96.5–320.0), and 176.0 (91.0–366.0) days for each respective group. At the time of the post-procedural echocardiography following RFCA, a high proportion of patients were prescribed antiarrhythmic drugs, with 37 (50.0%) in PAF, 40 (85.1%) in PeAF, and 39 (90.7%) in LSPeAF respectively. Among a total of 164 participants, 92 showed improvements in LVEF (2.0%, [−2.0, 8.0], and 104 exhibited a decrease in LA size, referred to as reverse remodeling, based on LAVI (−2.4 mL/m^2, [−8.1, 2.4]). There were no statistically significant differences in improvement of LV function and reduction of LAVI among the groups (**Table 3**). The average HFA-PEFF score, a diagnostic algorithm used to

Table 3. Changes of echocardiographic parameters before and after RFCA

	PAF (n=74)	PeAF (n=47)	LSPeAF (n=43)	p value
ΔLA AP diameter (mm)	0.0 (−3.0, 2.0)	−2.0 (−4.0, 1.0)	−1.0 (−2.5, 1.0)	0.225
ΔLAVI (mL/m^2)	−1.1 (−8.0, 3.4)	−4.8 (−8.3, 1.0)	−1.9 (−8.1, 2.0)	0.249
ΔLVEF (%)	0.0 (−2.0, 5.0)	3.0 (−1.5, 10.5)	2.0 (−0.5, 8.0)	0.118
ΔSeptal E/e’	−0.1 (−1.8, 1.0)	0.2 (−1.6, 1.6)	1.5 (−0.4, 3.8)	0.071
ΔFAC (%)	1.0±7.8	7.9±9.6	3.1±6.6	<0.001*
ΔRV4CSL (%)	1.6±4.6	8.5±4.1	2.2±3.8	<0.001*,‡
ΔRVFWSL (%)	1.7±5.2	9.5±5.5	1.6±4.2	<0.001*,‡
Patients with improved FAC	7 (9.5)	15 (31.9)	10 (23.3)	0.008*
Patients with improved RV4CSL	10 (13.5)	36 (76.6)	11 (25.6)	<0.001*,‡
Patients with improved RVFWSL	10 (13.5)	37 (78.7)	7 (16.3)	<0.001*,‡
Patients with RV dysfunction after RFCA:FAC	0 (0.0)	7 (14.9)	8 (18.6)	<0.001*
Patients with RV dysfunction after RFCA:RV4CSL	0 (0.0)	5 (14.9)	26 (60.5)	<0.001*,†,‡
Patients with RV dysfunction after RFCA:RVFWSL	0 (0.0)	4 (8.5)	28 (65.1)	<0.001*,†,‡

Continuous variables were presented as median (interquartile range). Categorical variables were presented as number (percent).
AP = anterior-posterior; FAC = fractional area change; LA = left atrial; LAVI = left atrial volume index; LVEF = left ventricular ejection fraction; RV4CSL = right ventricular 4-chamber strain including the ventricular septum; RVFWSL = right ventricular free-wall longitudinal strain.
*Significant difference between PAF and PeAF, †Significant difference between PAF and LSPeAF, ‡Significant difference between PeAF and LSPeAF, as determined by post hoc analyses.

estimate heart failure with preserved ejection fraction, was 2.7 in PAF patients and 3.9 in both PeAF and LSPeAF patients. Moreover, a smaller proportion of PAF patients had an HFA-PEFF score of 5 or more compared to those with PeAF and LSPeAF.

There was a statistically significant difference in the change of RV function before and after the procedure among the 3 groups as measured by FAC, RV4CSL, and RVFWSL, and all groups showed improvement compared with the pre-RFCA state. In post-hoc analysis, the absolute change of RV function measured by FAC showed significant improvement in the PeAF group compared with the PAF and no significant difference between the PeAF and LSPeAF group ($p<0.001$ for PAF vs. PeAF, $p=0.048$ for PeAF vs. LSPeAF) (**Figure 2**, **Table 3**). However, in RV strain parameters, participants with PeAF showed a significant increase in RV function compared with both the PAF and LSPeAF groups after the procedure ($p<0.001$) (**Figure 2**, **Table 3**). Compared to pre-RFCA, the proportion of patients with RV dysfunction showed a decreasing trend in all measurement indices for the PeAF group (42.6% to 19.0% in FAC, 85.1% to 14.9% in RV4CSL and RVFWSL), whereas the decrease in RV dysfunction after the procedure was not significant for the LSPeAF group for FAC (41.9% to 25.6%) and RVFWSL (79.1% to 60.5%) (**Table 3**, **Supplementary Figure 1**). The proportion of patients who showed improved RV function was significantly higher in the PeAF group compared to the PAF and LSPeAF groups, as indicated by RV strain measurements (both RV4CSL and RVFWSL) (**Table 3**). In the subgroup of 15 patients with baseline RV enlargement, the RV mid diameter and tricuspid annular size decreased more in the PeAF group compared to the LSPeAF group (−6.5±2.6 vs. 0.0±4.1 mm in RV mid diameter, $p=0.005$; −5.7±4.7 vs. 0.4±4.0 in tricuspid annular size, $p=0.018$). Additionally, RV function showed more improvement in the PeAF group than in the LSPeAF group, similar to the total population, with greater changes in RV4CSL (5.9±3.7% vs.

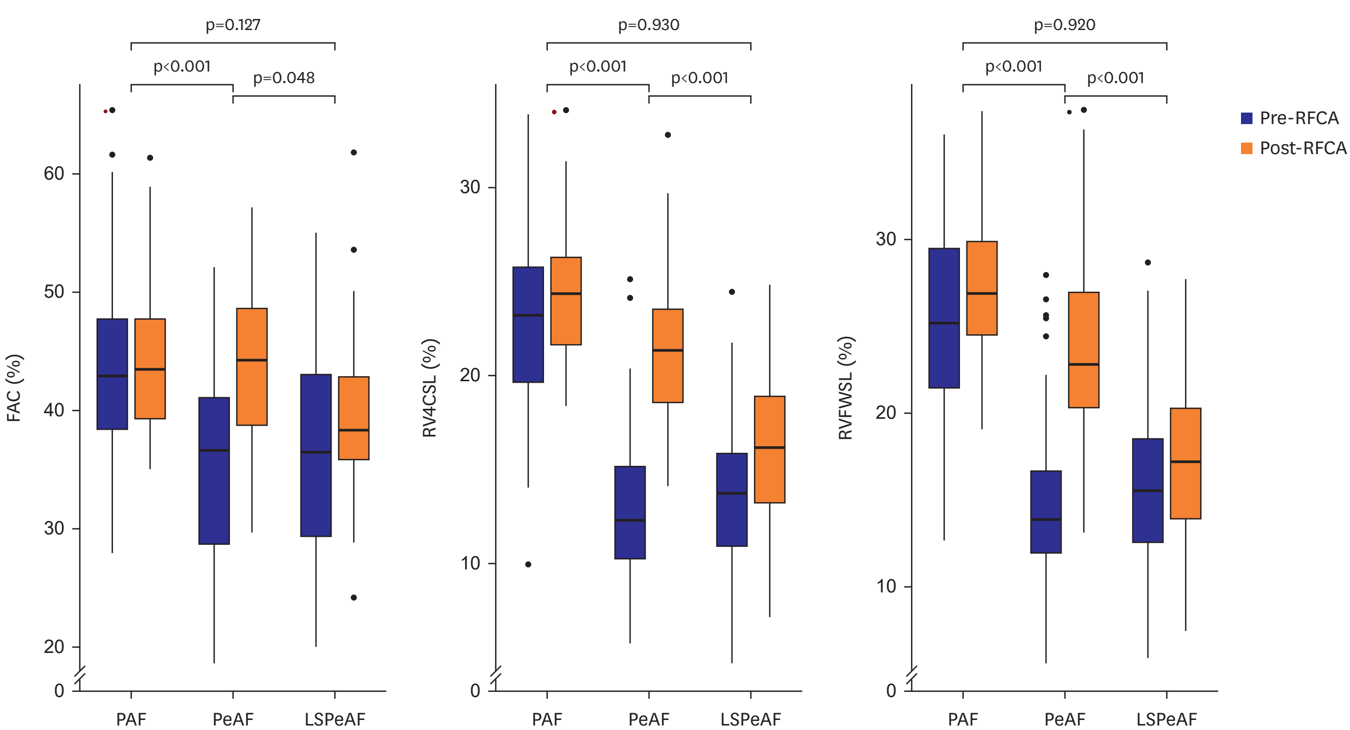

Figure 2. Changes in RV function as measured by FAC, RV4CSL, and RVFWSL before and after RFCA are shown for groups of PAF, PeAF, and LSPeAF in total population. FAC = fractional area change; LSPeAF = long-standing persistent atrial fibrillation; PAF = paroxysmal atrial fibrillation; PeAF = persistent atrial fibrillation; RV4CSL = RV 4-chamber strain including the ventricular septum; RVFWSL = RV free-wall longitudinal strain.

1.5±3.8%, p=0.045) and RVFWSL (7.0±3.1% vs. 1.4±4.3%, p=0.017). Of the 97 patients who exhibited AF rhythm on pre-procedural echocardiography, we assessed the changes in RV function in 39 participants who underwent post-procedural echocardiography within 60 days after RFCA. These participants were divided into 2 groups according to the presence or absence of clinical recurrence (mean follow-up period was 236.8±185.1 days), and in the group with clinical recurrence, the improvement of RV function, as measured by RV4CSL, was statistically significantly less pronounced (**Figure 3**, **Table 4**). The cut-off values for RV4CSL and RVFWSL in predicting clinical recurrence were determined using the Youden index method. Participants with a ΔRV4CSL of 3% or more (n=23) had a significantly lower rate of clinical recurrence compared to those with less (n=16) (4.3% vs. 31.2%, p=0.025). Similarly, participants with a ΔRVFWSL of 5% or more (n=15) had a significantly lower rate of clinical recurrence compared to those with less (n=24) (0% vs. 25.0%, p=0.040).

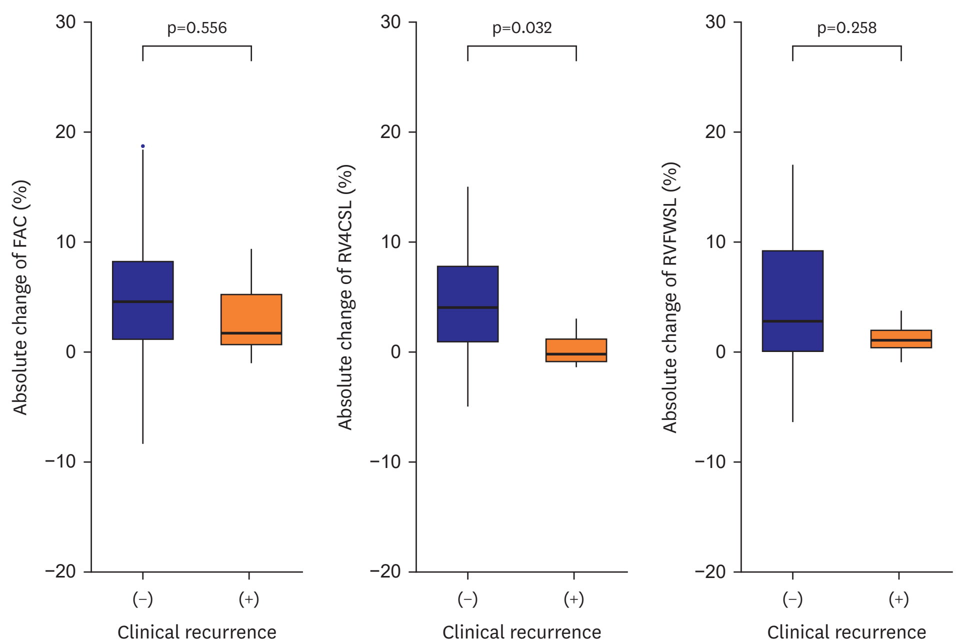

Figure 3. Changes of RV function parameters after RFCA based on clinical recurrence in patients with AF rhythm at preprocedural echocardiography.
AF = atrial fibrillation; FAC = fractional area change; RFCA = radiofrequency catheter ablation; RV = right ventricular; RV4CSL = right ventricular 4-chamber strain including the ventricular septum; RVFWSL = right ventricular free-wall longitudinal strain.

Table 4. Changes of RV function parameters after RFCA based on clinical recurrence in patients with AF rhythm during preprocedural echocardiography and underwent post-procedural echocardiography within 60 days after RFCA

	Clinical recurrence (+) (n=6)	Clinical recurrence (−) (n=33)	p value
ΔFAC (%)	1.7 (0.5, 6.3)	4.6 (1.2, 8.5)	0.556
ΔRV4CSL (%)	−0.2 (−0.9, 1.6)	4.1 (0.9, 7.8)	0.032
Patients with improved RV4CSL ≥3%	1 (16.7)	22 (66.7)	0.025
ΔRVFWSL (%)	1.1 (0.3, 2.1)	2.8 (0.1, 9.2)	0.258
Patients with improved RVFWSL ≥5%	0 (0)	15 (45.5)	0.040
Patients with RV dysfunction after RFCA	5 (83.3)	12 (36.4)	0.037

Numbers are presented as median (interquartile range) or number (percent).
AF = atrial fibrillation; FAC = fractional area change; RFCA = radiofrequency catheter ablation; RV = right ventricular; RV4CSL = right ventricular 4-chamber strain including the ventricular septum; RVFWSL = right ventricular free-wall longitudinal strain.

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Sensitivity analyses

First, among the total population, 128 (78.0%) participants had no clinical recurrence during the median 6.1 months (2.2–12.3) of follow-up. The proportion of patients without clinical recurrence was 83.8% in the PAF group, 78.7% in the PeAF group, and 67.4% in the LSPeAF group. Participants without clinical recurrence also showed improvement in LVEF and reduction in LAVI in a similar manner to the total population, with no significant differences observed among the groups. The change in RV function after RFCA was numerically greater in the no-recurrence group (**Figure 4**); similar to the total population, the improvement in RV function was significantly higher in the PeAF group compared to the PAF and LSPeAF groups (ΔRV4CSL, 8.5±4.1% in PeAF vs. 2.1±4.2% in PAF, 2.6±3.9% in LSPeAF, p<0.001; ΔRVFWSL, 9.6±5.9% in PeAF vs. 1.9±4.6% in PAF, 2.1±4.4% in LSPeAF, p<0.001) (**Supplementary Table 2**). Second, in baseline study, the median (interquartile ranges) heart rates for patients with different types of AF were 60.0 (54.0–71.0) in PAF, 72 (64.5–80.0) in PeAF, and 77.5 (68.0–83.0) in LSPeAF, showing a numerical difference but still lower than the criterion for rapid ventricular response of 100 beats per minute. We excluded 18 patients with heart rate >100 bpm at the time of pre- and post-RFCA transthoracic echocardiography, the analysis revealed a similar pattern to the total population (**Supplementary Table 3**). Third, to assess the long-term effects of RFCA on RV function, we analyzed 68 patients who had a follow-up period of more than 6 months post-procedure. While RV function assessed by FAC showed no difference between PeAF and LSPeAF, both the absolute improvement in RV function and the proportion of improvement above the reference value in RV4CSL and RVFWSL were higher in the PeAF group compared to LSPeAF. Additionally, the incidence of persistent RV dysfunction post-procedure was lower in the PeAF group than in LSPeAF (**Supplementary Table 4**). We performed linear mixed analysis for adjusting the impact of the time interval between the procedure and the follow-up examination on RV function improvement, and PeAF group had significantly improved RV function than those with PAF and LSPeAF (**Supplementary Table 5**).

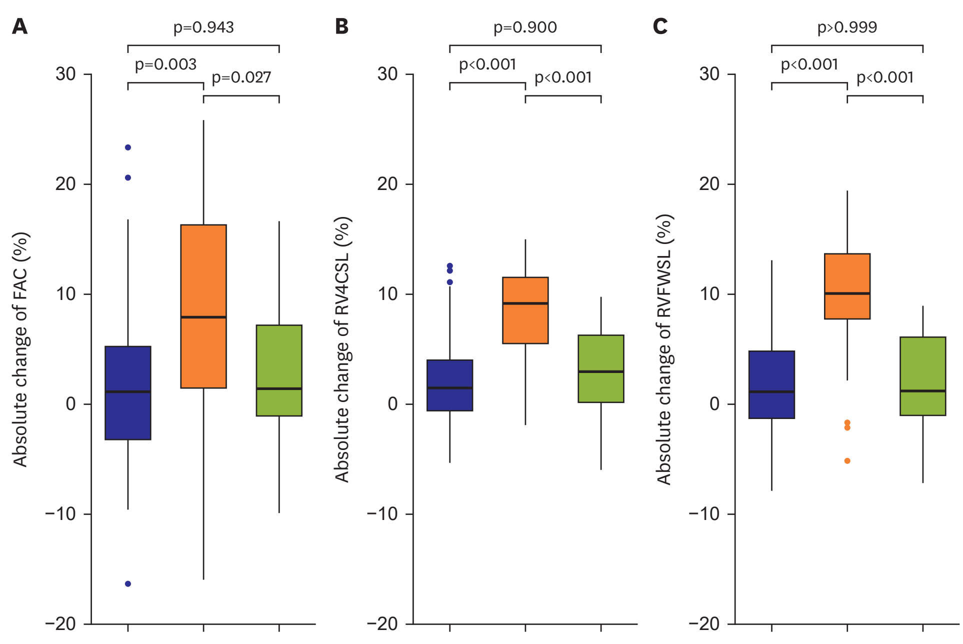

Figure 4. Changes of echocardiographic parameters before and after RFCA in participants without clinical recurrence. LSPeAF = long-standing persistent atrial fibrillation; PAF = paroxysmal atrial fibrillation; PeAF = persistent atrial fibrillation; RFCA = radiofrequency catheter ablation.

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Measurement reproducibility

The intra-observer variability of RV function measurement variables, assessed using the intraclass correlation coefficient (95% confidence interval [CI]), was high, indicating excellent agreement (FAC, 0.89 [0.75–0.96]; RV4CSL, 0.95 [0.87–0.98]; RVFWSL, 0.95 [0.87–0.98]). The intraclass correlation coefficient (95% CI) for FAC (0.78 [0.52–0.90]), RV4CSL (0.95 [0.89–0.98]), and RVFWSL (0.94 [0.86–0.98]) based on the RV function measurements independently performed by 2 observers was also very high, suggesting minimal inter-observer variability. The Bland-Altman plots depicting inter-observer and intra-observer variabilities in the measurements of FAC, RVFWSL, and RV4CSL are presented in **Supplementary Table 6**, **Supplementary Figures 2** and **3**.

DISCUSSION

The present study investigated changes in RV function, as assessed by FAC and RV strain parameters, specifically RVFWSL and RV4CSL, before and after RFCA for AF in 164 participants with PAF, PeAF, and LSPeAF over a median follow-up duration of 286 days. We found that RFCA resulted in significant improvement in RV function, particularly in patients with PeAF, compared to those with PAF or LSPeAF. These results were consistent in subgroups without clinical recurrence and the propensity score-matched cohort adjusted for baseline characteristics. To our knowledge, this is the first study to compare RV function using RV strain parameters before and after RFCA in 3 patient groups of PAF, PeAF, and LSPeAF. Our study suggests that timely RFCA intervention can improve clinical or subclinical RV dysfunction. A potential mechanism is blockage of prolonged AF duration, which may prevent myocardial fibrosis and RV dysfunction owing to persistently increased LV filling pressure.

RV function was not considered particularly important previously and was regarded simply as a conduit that supplies blood to the left-sided heart. However, in recent years, the importance of RV function has been emphasized in various studies.[9)20-23)] Impaired RV function in patients with LV failure after myocardial infarction significantly worsens their prognosis.[20)] Another study attempted to stage severe aortic stenosis and identified RV dysfunction as one of the parameters for staging classification.[21)] In addition, it is an important predictor of weaning of extracorporeal membrane oxygenation[24)] and to predict the long-term prognosis of patients with pulmonary embolism or pulmonary arterial hypertension.[22)23)] Focusing on studies about AF, RV structural remodeling and subclinical RV dysfunction, as measured by RVFWSL, were associated with the development of tricuspid regurgitation in patients with AF.[25)] In a previous study comparing left and right heart structural and functional changes in patients with PeAF who underwent RFCA (n=86), the group that maintained sinus rhythm showed lower LAVI, right atrial area, tricuspid annular diameter, and tricuspid regurgitation (TR) jet area compared to those with PeAF.[6)] Our study result is consistent with a previous finding that reduction of AF burden is associated with decreased loading condition of the right heart.[6)]

It remains unclear why the RV function remained impaired after successful RFCA and achieved maintenance of sinus rhythm in patients with LSPeAF. However, there are several potential mechanisms that could account for this phenomenon. One contributing factor might be poor ventricular rate control, which could detrimentally impact the overall cardiac function such as tachycardia-induced cardiomyopathy. Other consideration is the presence of irregular ventricular contractions, often exacerbated by the absence of atrioventricular (AV) synchrony, leading to decreased cardiac efficiency. The loss of atrial contraction can further contribute to the impairment in RV function. The higher proportion of LSPeAF patients with AF rhythm during the post-RFCA echocardiography might have contributed to the appearance of a sustained decrease in RV function, yet this could also explain the better RV function observed in our study among patients who recovered to sinus rhythm. Additionally, the prolonged duration of AF may lead to irreversible changes in the RV myocardium, such as fibrosis. Even with the restoration of sinus rhythm, these changes could be the underlying reason for the observed impaired RV function. While there is no direct research evidence in AF patients yet, in other conditions such as pulmonary hypertension and advanced heart failure, sustained pressure overload on the RV has been reported to potentially lead to RV fibrosis.[26)27)] Furthermore, studies have shown that this can be well-predicted using RVFWSL.[26)] There are some other studies indicating that patients who were exposed to a prolonged loading condition of the RV due to severe TR and who subsequently experience RV dysfunction have poor cardiovascular and postoperative prognoses.[9)10)] Insufficiently addressing the RV loading condition at the proper time could have led to irreversible RV dysfunction. However, further investigation using histological or other imaging techniques may be necessary to validate our study results.

The present study used FAC and RV strains to measure RV function before and after RFCA. Previous studies using RV strain analysis has been shown to be superior to traditional echocardiographic parameters such as FAC or tricuspid annular plane systolic excursion (TAPSE) and to have non-inferior performance compared to cardiac magnetic resonance, the gold standard for RV function analysis.[9)10)28)] TAPSE and tricuspid annulus S', traditional parameters for measuring RV function, are highly sensitive to the alignment of Doppler beam so that the reproducibility for TAPSE or S' velocity is very low.[29)] RV function assessed by strain, less angle dependent, may predict RV dysfunction earlier than conventional parameters TAPSE, tricuspid annulus s' or FAC.[10)]

According to previous studies demonstrating the relationship between AF and RV function, our study showed similar values of RVFWSL and RV4CSL in PeAF and LSPeAF.[4)30)] In the first study that investigated the structure and function of the whole cardiac chamber before and after the procedure, improvements in cardiac function and reverse remodeling were observed in both baseline sinus rhythm and AF patients after RFCA, and the more significant improvement in RV function measured by RV4CSL was seen in patients with PeAF than those with PAF.[30)] However, the sample size of PeAF patients was only 9 individuals, which limits the ability to analyze and differentiate between LSPeAF and PeAF or to re-analyze the clinical success group.

The present study has some limitations. First, since it was designed retrospectively and conducted at a single referral hospital, we have relatively small sample size and the power of the evidence may be weaker compared to that of a randomized control study or prospective cohort study. However, the sample size was sufficient to demonstrate significant difference between PeAF and LSPeAF, and the measured RV strain parameters were similar to those of previous studies.[4)30)] To generalize the results of this study, a prospective study with a larger number of patients is necessary. Second, heart rhythm on echocardiography could differ before and after RFCA. In many study patients with PeAF and LSPeAF, heart rhythm on echocardiography was AF before RFCA but sinus rhythm after RFCA. This might not be an issue as it is common in the real world. Third, the study endpoint was not a hard endpoint such as cardiovascular mortality, which may limit its clinical implications. The results of our study suggest that timely RFCA may prevent RV dysfunction, and future studies should be

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conducted to investigate the association between improved RV function after RFCA and long-term prognosis. Forth, the cutoff values of strain values for predicting AF recurrence merely serve as a tool to explore the relationship between RV parameters and prognosis, requiring external validation. Lastly, due to the limitations of a retrospective study, the time interval from RFCA to RV function analysis was not consistent across the groups.

In conclusion, RV systolic function is more impaired in patients with PeAF and LSPeAF than in those with PAF. RV systolic function is more improved after RFCA in patients with PeAF than in those with PAF or LSPeAF. Performing RFCA at an appropriate time may prevent irreversible RV dysfunction and warrants further investigations to validate the results and determine its clinical implications.

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SUPPLEMENTARY MATERIALS

Supplementary Table 1
Baseline echocardiographic parameters of study participants in patients with atrial fibrillation at pre-procedural echocardiography

Supplementary Table 2
Changes of echocardiographic parameters before and after RFCA in participants without clinical recurrence

Supplementary Table 3
Comparison of baseline echocardiographic parameters and their changes according different AF groups in patients with heart rate less than 100 beats per minute at pre- and post-RFCA echocardiography

Supplementary Table 4
Comparison of baseline echocardiographic parameters and their changes according different AF groups in patients with the interval between RFCA and post-procedural echocardiography more than 180 days

Supplementary Table 5
Changes of echocardiographic parameters before and after RFCA in linear mixed analysis

Supplementary Table 6
Limit of agreement in Bland-Altman analysis according to the parameters evaluating RV function

Supplementary Figure 1

Changes of echocardiographic parameters before and after RFCA in participants without clinical recurrence.

Supplementary Figure 2

Bland-Altman plot for comparing intra-observer variability of RV function measurement in FAC (A), RV4CSL (B), RVFWSL (C).

Supplementary Figure 3

Bland-Altman plot for comparing inter-observer variability of RV function measurement in FAC (A), RV4CSL (B), RVFWSL (C).

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