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Abstract

Atrial fibrillation (AF) is a common disease that changes cardiac morphology, especially in the left atrium (LA). It is now known that certain categories of functional mitral regurgitation (MR) are associated with AF; however, the influence of AF on right cardiac morphology is not fully understood. Our aim in this study was to investigate the association between AF and right cardiac morphology. This was a retrospective cohort study of 86 patients with persistent AF without other cardiac disease who underwent catheter ablation (CA). Seventy-one patients had sustained sinus rhythm (SR) (SR Group) and 15 patients had sustained AF (AF Group) during the study period. We compared the changes in the right cardiac dimensions and tricuspid regurgitation (TR) between the groups 12 months after CA. Patients' baseline echocardiographic assessments revealed that the LA volume index was significantly smaller in the SR group than in the AF group (46.8 ± 11.9 ml/m^2 vs 59.3 ± 12.8 ml/m^2, respectively; $p < 0.01$). Comparing baseline data with the 12-month follow-up data, in the SR group, right atrial area (RAA, cm^2), tricuspid annular diameter (mm), and tricuspid regurgitant jet area (cm^2) were significantly decreased compared with the AF group (19.5 ± 4.5–15.5 ± 3.6 vs 20.7 ± 3.6–19.7 ± 2.3; 30.5 ± 4.9–26.4 ± 3.9 vs 28.7 ± 4.0–28.8 ± 3.1; and 1.4 [interquartile range (IQR) 0.7–2.6]–0.6 [IQR 0.2–1.2] vs 1.2 [IQR 1.1–1.5]–0.9 [IQR 0.4–1.3], respectively). On multivariate analysis, change in RAA correlated with the reduction in tricuspid regurgitant jet area ($R = 0.51$, $p < 0.001$). In conclusion, successful CA for persistent AF led to right heart

	reverse remodeling, and our findings suggested that persistent AF was associated with RAA dilatation and TR.
Keywords (separated by '-')	Atrial fibrillation - Atrial tricuspid regurgitation - Right atrium - Echocardiography
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ORIGINAL ARTICLE

Successful catheter ablation of persistent atrial fibrillation is associated with improvement in functional tricuspid regurgitation and right heart reverse remodeling

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Abstract

Atrial fibrillation (AF) is a common disease that changes cardiac morphology, especially in the left atrium (LA). It is now known that certain categories of functional mitral regurgitation (MR) are associated with AF; however, the influence of AF on right cardiac morphology is not fully understood. Our aim in this study was to investigate the association between AF and right cardiac morphology. This was a retrospective cohort study of 86 patients with persistent AF without other cardiac disease who underwent catheter ablation (CA). Seventy-one patients had sustained sinus rhythm (SR) (SR Group) and 15 patients had sustained AF (AF Group) during the study period. We compared the changes in the right cardiac dimensions and tricuspid regurgitation (TR) between the groups 12 months after CA. Patients' baseline echocardiographic assessments revealed that the LA volume index was significantly smaller in the SR group than in the AF group (46.8 ± 11.9 ml/m^2 vs 59.3 ± 12.8 ml/m^2, respectively; $p < 0.01$). Comparing baseline data with the 12-month follow-up data, in the SR group, right atrial area (RAA, cm^2), tricuspid annular diameter (mm), and tricuspid regurgitant jet area (cm^2) were significantly decreased compared with the AF group (19.5 ± 4.5–15.5 ± 3.6 vs 20.7 ± 3.6–19.7 ± 2.3; 30.5 ± 4.9–26.4 ± 3.9 vs 28.7 ± 4.0–28.8 ± 3.1; and 1.4 [interquartile range (IQR) 0.7–2.6]–0.6 [IQR 0.2–1.2] vs 1.2 [IQR 1.1–1.5]–0.9 [IQR 0.4–1.3], respectively). On multivariate analysis, change in RAA correlated with the reduction in tricuspid regurgitant jet area ($R = 0.51$, $p < 0.001$). In conclusion, successful CA for persistent AF led to right heart reverse remodeling, and our findings suggested that persistent AF was associated with RAA dilatation and TR.

Keywords Atrial fibrillation · Atrial tricuspid regurgitation · Right atrium · Echocardiography

Introduction

Atrial fibrillation (AF) is the most common arrhythmia, and as societies age, AF is being diagnosed more commonly [1, 2]. Catheter ablation (CA) can restore sinus rhythm more stably for patients with AF. Recent advances in CA for AF helped identify AF as a cause of atrioventricular functional regurgitation [3, 4], termed "atrial mitral regurgitation" (MR) and "atrial tricuspid regurgitation" (TR). Gerts et al. showed that suppressing AF by CA reduced left atrial size, mitral annular diameter, and the severity of MR [5] suggesting that dilatation of the mitral annulus and left atrium were possible mechanisms underlying atrial MR. TR secondary to AF was termed atrial TR in the 2017 Guidelines of the joint report by the American Society of Echocardiography and the Society for Cardiovascular Magnetic Resonance [6]. However, it is unknown whether mechanisms reported in *left heart* remodeling can be applied to right heart remodeling because the description of atrial TR is based on retrospective observational studies [7–11]. Therefore, there is a lack of evidence to confirm a causal relationship between AF and right heart remodeling leading to atrial TR.

Recently, TR has attracted considerable interest in the field of the cardiovascular medicine because evidence indicates a negative impact of TR on the prognosis of patients with both primary TR and functional TR (FTR) [11–27]. FTR is the major type of TR and is secondary to various

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concomitant cardiovascular diseases such as heart failure, left-sided valvular heart diseases, cardiomyopathies, and pulmonary artery hypertension. Atrial TR is a type of FTR. Recent guidelines recommend integrative management of TR based on the need for left-sided valve surgery, the cause of TR, the severity of TR, signs of right-heart failure, and right-heart morphology [28, 29]. An understanding of the precise mechanisms underlying FTR is needed to manage the condition appropriately.

We hypothesized that restoring sinus rhythm (SR) in patients with persistent AF would positively influence *right cardiac* morphology and TR. This study aimed to investigate the influence of AF on the morphology and function of the right heart as it might relate to FTR (atrial TR). Therefore, we performed a retrospective cohort study of patients with persistent AF who underwent initially successful CA. We compared the changes in right cardiac morphology and FTR between patients with sustained SR and patients with sustained AF for 12 months after CA.

Methods

Study population

This was a retrospective cohort study. We reviewed data for 127 consecutive patients with persistent AF who underwent CA at Hiroshima University Hospital between April 2011 and March 2015. Persistent AF was defined as AF sustained for > 1 year. In all patients, CA successfully restored SR at the end of the procedure. Exclusion criteria were as follows: primary tricuspid regurgitation, ischemic heart disease, more than moderate left-sided valvular heart disease, cardiomyopathy, congenital heart disease, previous history of cardiac surgery, ventricular pacing, and pulmonary arterial hypertension. We also excluded patients with no electrocardiographic data at the 3-month and 12-month follow-ups.

Clinical and geographic data, namely, AF risk factors, preprocedural medications, and AF duration were collected from patients' clinical records. Baseline oral medications were continued at discharge from hospital following CA, and blood pressures were measured at the end of each echocardiographic examination.

CA procedure for AF

All patients underwent proximal antral pulmonary vein isolation guided by intracardiac echocardiography and circular multipolar electrode catheter recordings. All four pulmonary veins were isolated, and the cavotricuspid isthmus was also isolated routinely with and without the clinical presence of atrial flutter. All patients' rhythms following ablation were converted to SR, and all patients were routinely treated with antiarrhythmic medications for 3 months after CA.

Echocardiography

Transthoracic echocardiography (TTE) was performed within 6 months before CA as a baseline evaluation and at the 12-month follow-up using commercially-available equipment (iE33, Phillips Medical Systems, Andover, MA, USA; Artida and Artida2, Toshiba, Tokyo, Japan; Vivid7 and Vivid E9, GE Medical Systems, Milwaukee, WI, USA). Four board-certified echocardiographers performed comprehensive echocardiographic examinations according to American Society of Echocardiography (ASE) guidelines [6, 30, 31]. One researcher blinded to patients' clinical information analyzed the echocardiographic data, offline.

Left atrial volume (LAV) at end-systole was measured in apical two- and four-chamber views using the method of discus. Left ventricular (LV) volumes and LV ejection fraction (LVEF) were measured in apical two- and four-chamber views using the method of discus, and LA and LV volumes were indexed to body surface area. Transmitral early diastolic inflow (E) wave data were acquired in the three-chamber view. Pulsed-wave tissue Doppler early diastolic and systolic mitral annular velocities (e', s') were measured at the septal annular site, and the ratio of E to e′ (E/e′) was calculated. The averages of measurements from 3 to 5 cardiac cycles were used in the analysis. Figure 1a shows patients' AQ1 echocardiographic measurements of the *right heart*. Right atrial (RA) area (RAA) was traced from the lateral aspect of the tricuspid annulus to the septal aspect, excluding the area between the leaflets and annulus, following the RA endocardium, in the apical four-chamber view at the end of ventricular systole. The RA long- and short- axis diameters at the end of ventricular systole were also measured in the apical four-chamber view. RA long-axis diameter (RA LAXd) was defined as the distance from the center of the tricuspid annulus to the center of the superior RA wall. RA short-axis diameter (RA SAXd) was defined as the distance from the midlevel of the RA free wall to the interatrial septum, perpendicular to the long axis. End-systolic mitral and tricuspid annular diameters were also measured in the apical four-chamber view. Right ventricular (RV) area, RV long-axis diameter (RV LAXd), and RV short-axis diameter (RV SAXd) were also measured in the four-chamber apical view at end-diastole. RV LAXd was defined as the distance from the plane of the tricuspid annulus to the RV apex. In this study, we defined RV SAXd diameter as the midcavity diameter measured in the middle third of the right ventricle at the level of the LV papillary muscles [31].

Comprehensive evaluation of MR and TR were performed according to the ASE guidelines [6]. Patients with less than moderate MR who had small MR jet areas,

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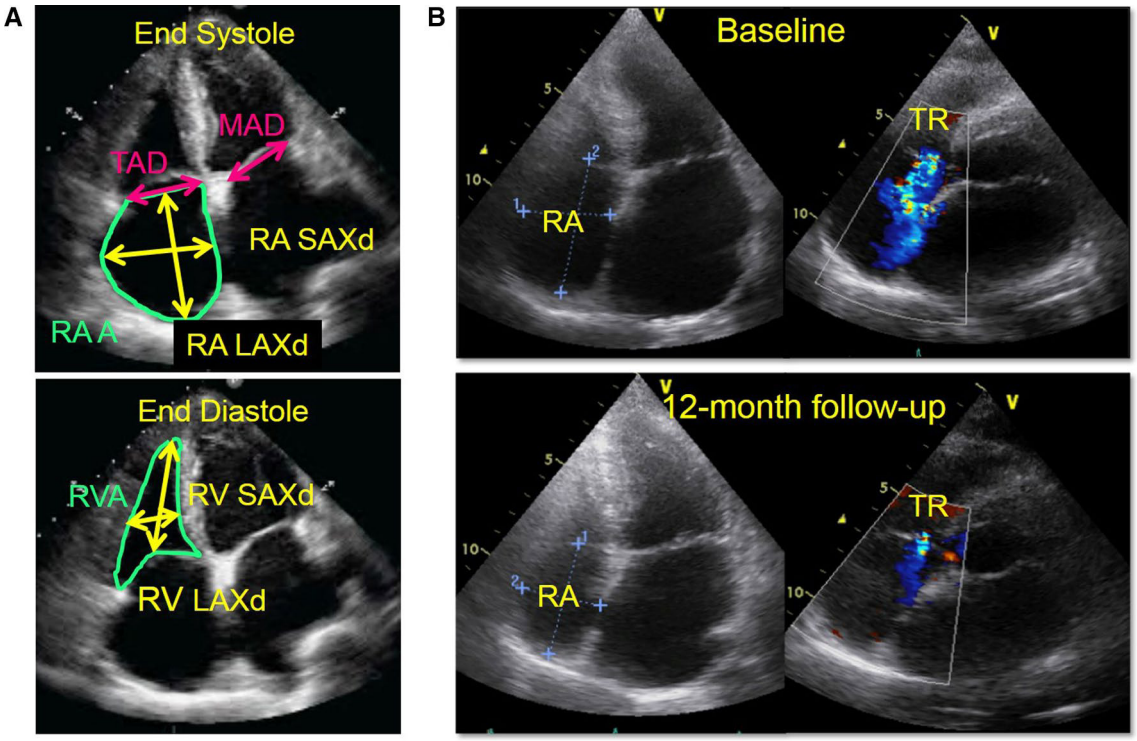

Fig. 1 XXX

normal leaflet morphology, narrow vena contracts, and no- or small-flow convergence were included in this study. TR severity was determined by integrative assessment using multiple parameters such as TR jet area (TRJA), the ratio of TRJA to RAA, continuous Doppler contour, hepatic vein flow pattern, and jugular venous pulse. TRJA was measured either in the apical four-chamber view or as the parasternal short-axis in the basal RV view; whichever view identified the clearest and largest TRJA. TR pressure gradient was calculated from TR velocity, and we adopted the highest value [6]. RA pressure was also estimated by inferior vena cava (IVC) diameter and respiratory change (IVC diameter < 2.1 cm that collapses > 50%; 3 mm Hg, IVC diameter > 2.1 cm that collapses < 50%; 15 mmHg, the others; 8 mm Hg). Finally, right ventricular systolic pressure was determined from TR pressure gradient and RA pressure [31].

Patient follow-up

Patients were clinically evaluated as outpatients 3 months and 12 months after CA. We asked patients about their symptoms and performed 12-lead electrocardiograms and blood laboratory evaluations at both follow-ups. Patients underwent echocardiographic assessment at the 12-month follow-up.

Statistical analysis

We categorized patients with SR at both the 3-month and 12-month follow-up into the SR Group and those with AF at both the 3-month and 12-month follow-up into the AF Group. We analyzed differences between groups using Student's t test, Wilcoxon's rank-sum test, the χ^2 test, or repeated measures analysis of variance, as appropriate. The Bonferroni correction was adopted for the post hoc analysis.

Continuous normally distributed parameters are presented as mean ± standard deviation. Ordinal and skewed data are presented as median (interquartile range (IQR)). $p < 0.05$ was considered statistically significant, and all statistical analyses were performed using JMP 13 (SAS Institute, Cary, NC, USA).

Results

Patient registration

Figure 2 shows the entry of patients into this study; 127 patients underwent a first ablation for persistent AF at our institution between April 2011 and March 2015. We excluded three patients because of ischemic heart disease, post-aortic valve replacement, or moderate aortic regurgitation. Another 23 patients were excluded because they did not undergo

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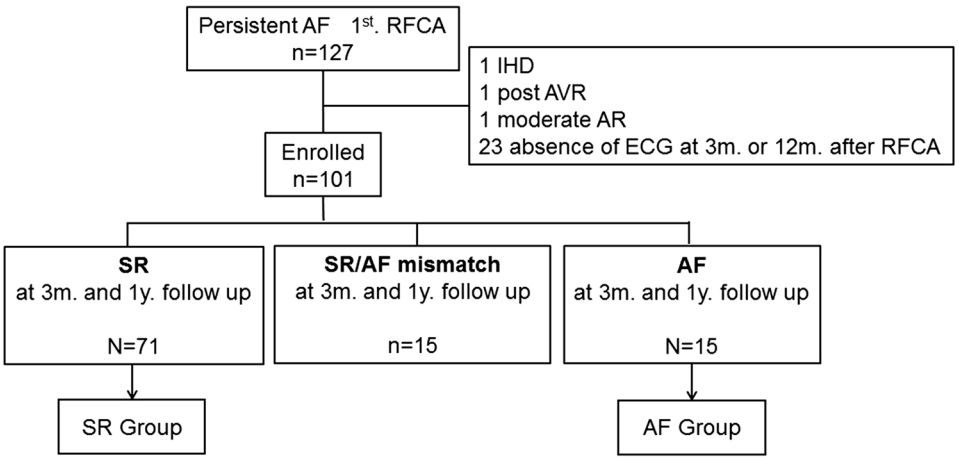
Fig. 2 XXX



electrocardiography either at the 3-month or 12-month follow-up, and 15 patients with mismatched rhythm status at 3-month and 12-month follow-up were also excluded. Finally, we analyzed data for 86 patients, in this study; 71 (70.3%) patients were categorized into the SR Group, and 15 (14.9%) patients were categorized into the AF Group.

Baseline patients' clinical characteristics and echocardiographic findings

Table 1 shows patients' baseline clinical characteristics and demographic data. The AF group had higher body mass index and longer AF duration. The prevalence of hypertension, diabetes mellitus, thyroid disorders, and previous history of stroke showed no significant difference between the two groups. ß-blockers were used more frequently in the AF Group, but diuretic use was similar between the groups. All patients had been routinely treated with antiarrhythmic medication for 3 months after CA. Baseline N-terminal pro-brain natriuretic peptide levels were similar between the groups.

Regarding the echocardiographic parameters, only LA volume index (LAVI) differed significantly difference between the two groups. The prevalence of mild MR was similar between the two groups at baseline: 42 (59.2%) in the SR group and 9 (60.0%) in the AF group. We found no differences in right cardiac morphology, including RAA and TAD, between the two groups. Similarly, the right ventricular systolic pressure were similar between the two groups. There was no patient who has significant TR (TRJA; SR group 1.4 [interquartile range (IQR) 0.7–2.6] vs AF group 1.2 [IQR 1.1–1.5]), but 80 (93.0%) patients has some of TR.

Serial changes in patients' echocardiographic parameters before and after CA

The serial changes in patients' echocardiographic parameters from baseline to the 12-month follow-up examinations are summarized in Table 2; total of 79/86 (91.9%), 65/71 (91.5%) in SR Group and 14/15 (93.3%) in AF Group, patients underwent echocardiographic examination at the 12-month follow-up (median [IQR], 12 [12–14] months), and we analyzed the serial echocardiographic measurements by repeated measures analysis of variance testing.

Comparing the SR group with the AF group, LVEF and s′ were significantly increased in the left cardiac parameters. In contrast, in the right heart, RAA, RA diameter, TAD, and RV long-axis diameter were significantly decreased after CA in the SR Group. RV showed no significant change in both groups (Fig. 3).

Table 3 shows the association between patients' baseline factors and the change in RAA. No factor had a significant relationship with changes in RAA, but restoring SR after CA and the duration of AF rhythm before CA were related to changes in RAA.

Right cardiac morphology and tricuspid regurgitation

TRJA decreased significantly in the SR group compared with the AF group. Figure 1b shows data for a representative patient in the SR group who had sustained SR for 12 months and decreased RAA and TRJA.

We tested the association between change in TRJA and changes in right cardiac morphology by univariate linear regression analysis. As shown in Table 4, changes in RAA and RA diameters were significantly correlated with changes in TRJA. On multivariate analysis, change in RAA was independently associated with the change in

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Table 1 Patients' baseline clinical characteristics and echocardiographic assessments

Variables	SR group, $n=71$	AF group, $n=15$	p value
Age, years	60.8 ± 9.7	58.0 ± 7.2	n.s
Male, *n* (%)	56 (78.9)	14 (93.3)	n.s
BMI, kg/m2	24.3 ± 3.3	27.4 ± 5.2	0.004
Heart rate, bpm	78.3 ± 17.1	81.5 ± 13.9	n.s
SBP, mmHg	126.1 ± 15.3	129.1 ± 19.8	n.s
DBP, mmHg	83.8 ± 11.8	89.8 ± 16.2	n.s
Duration of AF, years	2.8 ± 2.8	5.5 ± 3.7	0.002
Comorbidities, *n* (%)			
Hypertension	35 (49.3)	10 (66.7)	n.s
Diabetes mellitus	9 (12.7)	3 (20.0)	n.s
Thyroid disorder	10 (14.1)	2 (13.3)	n.s
Prior stroke or TIA	7 (9.9)	0 (0.0)	n.s
Medications, *n* (%)			
Anti-arrhythmic drug	71 (100)	15 (100)	n.s
β blocker	21 (29.6)	9 (60.0)	0.020
Calcium blocker	8 (11.3)	3 (20.0)	n.s
ACEI/ARB	24 (33.8)	8 (53.3)	n.s
Diuretics	13 (18.3)	3 (20.0)	n.s
NT-pro BNP, pg/ml, median (IQR)	454.0(291.0–737.5)	471.0 (262.0–1242.5)	n.s
Echocardiography			
LAVI, ml/m^2	46.9 ± 11.9	59.3 ± 12.8	< 0.001
LV EDVI, ml/m^2	50.5 ± 12.4	52.0 ± 16.0	n.s
LV ESVI, ml/m^2	23.3 ± 8.6	23.5 ± 10.9	n.s
LV EF, %	55.1 ± 7.5	56.3 ± 7.9	n.s
E, cm/s	82.3 ± 22.8	94.5 ± 32.1	n.s
e', cm/s	8.7 ± 2.3	8.6 ± 2.0	n.s
s', cm/s	5.9 ± 1.4	5.6 ± 1.2	n.s
E/e'	10.2 ± 4.4	11.5 ± 5.3	n.s
MAD, mm	35.2 ± 3.3	36.1 ± 3.4	n.s
Mild MR, n (%)	42 (59.2)	9 (60.0)	n.s
RA area, cm^2	19.5 ± 4.5	20.7 ± 3.6	n.s
RA LAXd, mm	58.1 ± 6.6	60.2 ± 5.0	n.s
RA SAXd, mm	40.2 ± 6.4	39.4 ± 4.6	n.s
RV area, cm^2	10.0 ± 2.6	9.8 ± 2.1	n.s
RV LAXd, mm	51.6 ± 5.6	53.9 ± 6.4	n.s
RV SAXd, mm	23.8 ± 3.9	24.0 ± 4.2	n.s
TAD, mm	30.5 ± 4.9	28.7 ± 4.0	n.s
TRJA, cm^2: median (IQR)	1.4 (0.7–2.6)	1.2 (1.0–1.6)	n.s
RVSP, mmHg	30.5 ± 8.6	27.5 ± 5.3	n.s

Values are mean ± standard deviation, median (IQR) or number (%)

ACEI angiotensin converting enzyme inhibitor, *AF* atrial fibrillation, *ARB* angiotensin II receptor blocker, *BMI* body mass index, *DBP* diastolic blood pressure, *E* early diastolic trans mitral flow velocity, *e'* early diastolic mitral annular velocity, *EDVI* end-diastolic volume index, *EF* ejection fraction, *ESVI* end-systolic volume index, *IQR* interquartile range, *LAD* left atrial diameter, *LAVI* left atrium volume index, *LAXd* long axis diameter, *LV* left ventricle, *MAD* mitral annular diameter, *NT-pro BNP* N-terminal pro-brain natriuretic peptide, *RA* right atrium, *RV* right ventricle, *s'* systolic mitral annular velocity, *SAXd* short axis diameter, *SBP* systolic blood pressure, *SR* sinus rhythm, *TAD* tricuspid annular diameter, *TIA* transient ischemic attack, *TRJA* tricuspid regurgitation jet area, *RVSP* right ventricular systolic pressure

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Table 2 Comparison of the serial echocardiographic measurements at baseline and after 12-months' follow-up within each group and between the groups

Variables	SR group, $n=71$		AF group, $n=15$		p value for time-group interaction
	Baseline	12-month	Baseline	12-month	
Left-side					
LAVI, ml/m^2	46.8 ± 11.9	40.5 ± 12.3	59.3 ± 12.8	53.0 ± 10.2	0.61
LVEDVI, ml/m2	50.3 ± 12.4	52.1 ± 9.6	52.0 ± 16.0	47.8 ± 11.8	0.15
LVESVI, ml/m2	23.3 ± 8.6	19.6 ± 4.5	23.5 ± 10.9	20.6 ± 7.2	0.73
LV EF, %	55.1 ± 7.5	62.7 ± 3.6	56.3 ± 7.9	58.0 ± 6.1	0.01
E, cm/s	82.3 ± 22.8	64.6 ± 15.5	94.5 ± 32.1	84.4 ± 21.7	0.27
e', cm/s	8.7 ± 2.3	7.2 ± 2.2	8.6 ± 2.0	8.3 ± 1.5	0.03
s', cm/s	5.9 ± 1.4	7.2 ± 1.3	5.6 ± 1.2	5.8 ± 1.6	0.03
E/e'	10.1 ± 4.4	9.5 ± 2.7	11.5 ± 5.3	10.3 ± 2.5	0.63
MAD, mm	35.2 ± 3.3	34.7 ± 3.4	36.1 ± 3.4	35.9 ± 3.6	0.28
Right-side					
RA area, cm^2	19.5 ± 4.5	15.3 ± 3.6	20.7 ± 3.6	19.7 ± 2.3	0.01
RA LAXd mm	58.1 ± 6.6	53.0 ± 5.9	60.2 ± 5.0	58.7 ± 3.3	0.01
RA SAXd, mm	40.2 ± 6.4	35.7 ± 6.5	39.4 ± 4.6	40.9 ± 4.1	0.01
RV area, cm^2	10.0 ± 2.6	9.1 ± 2.3	9.8 ± 2.1	8.9 ± 1.9	0.91
RV LAXd, mm	51.6 ± 5.6	50.7 ± 5.8	53.9 ± 6.4	51.2 ± 5.6	0.03
RV SAXd, mm	3.8 ± 3.9	22.2 ± 3.7	24.0 ± 4.2	22.4 ± 3.5	0.69
TAD, mm	30.5 ± 4.9	26.4 ± 3.9	28.7 ± 4.0	28.8 ± 3.1	0.01
TRJA, cm^2: median (IQR)	1.4 (0.7–2.6)	0.6 (0.2–1.2)	1.2 (1.1–1.5)	0.9 (0.4–1.3)	0.02
RVSP, mmHg	30.5 ± 8.6	27.7 ± 7.0	27.5 ± 5.3	27.2 ± 7.7	0.19

Values are mean ± standard deviation or median (interquartile range)

AF atrial fibrillation, *E* early diastolic trans mitral flow velocity, *e'* early diastolic mitral annular velocity, *EDVI* end-diastolic volume index, *EF* ejection fraction, *ESVI* end-systolic volume index, *LAD* left atrial diameter, *LAVI* left atrium volume index, *LAXd* long axis diameter, *LV* left ventricle, *MAD* mitral annular diameter, *RA* right atrium, *RV* right ventricle, *s'* systolic mitral annular velocity, *SAXd* short-axis diameter, *SR* sinus rhythm, *TAD* tricuspid annular diameter, *TRJA* tricuspid regurgitation jet area, *RVSP* right ventricular systolic pressure

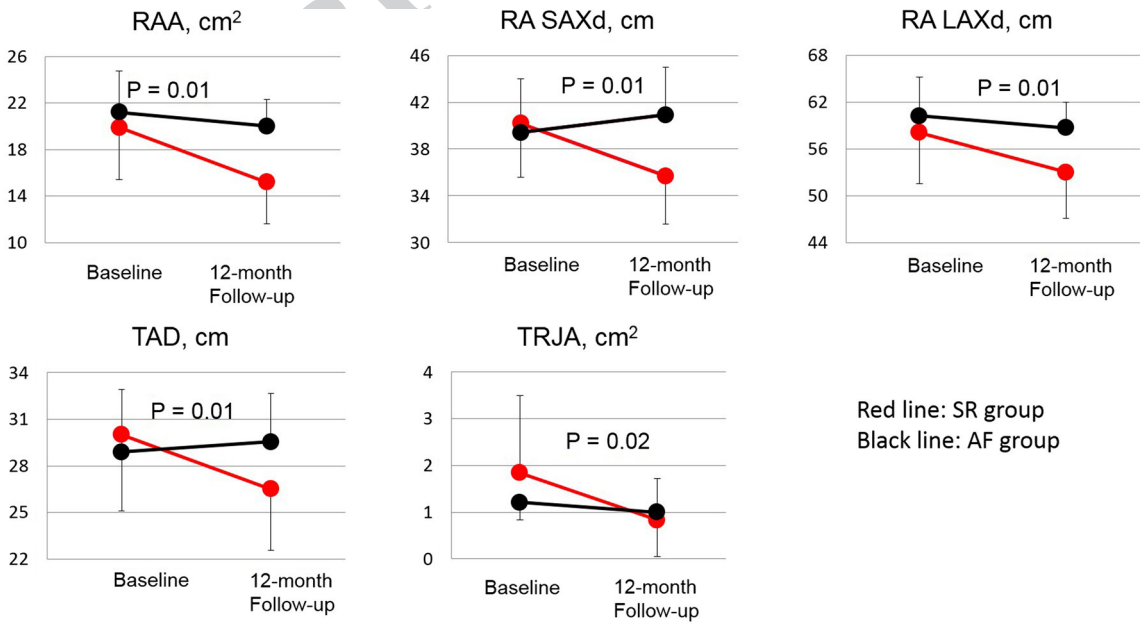

Fig. 3 XXX

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Table 3 Correlation between patients' parameters and the change in RAA

Variables	Univariate liner regression analysis	
	R (95% CI)	*p* value
Age, years	0.14 (−0.04 to 0.18)	0.20
Male, *n* (%)	−0.14 (−4.22 to 0.97)	0.22
BMI, kg/m^2	−0.06 (−0.37 to 0.22)	0.62
Heart Rate, bpm	−0.05 (−0.08 to 0.05)	0.68
Duration of AF rhythm, years	−0.24 (−0.65 to −0.03)	0.03
β blocker medication	0.04 (−1.76 to 2.50)	0.73
Diuretic medication	0.01 (−2.57 to 2.67)	0.97
Baseline LAVI, ml/m^2	0.13 (−0.02 to 0.07)	0.27
Baseline LVEF, %	−0.07 (−0.18 to 0.09)	0.53
SR group, *n* (%)	0.28 (0.70 to 5.87)	0.01

Values are mean ± SD, number (%) or median (IQR)

AF atrial fibrillation, *BMI* body mass index, *CI* confidence interval, *LAV* left atrial volume, *LVEF* left ventricular ejection fraction, *RAA* right atrial area, *SR* sinus rhythm

TRJA. Figure 4 shows the relationship between change in TRJA and change in RAA in the SR group.

Discussion

This was a retrospective cohort study to investigate the impact of AF on right heart morphology. The major findings were as follows: (1) restoring SR from persistent AF reduced RAA, RA diameter, and TAD; and (2) the change in RAA correlated with the change in TRJA. These findings may help explain how atrial fibrillation causes FTR through right atrial remodeling.

Study population

All of our study patients had persistent AF and were divided into two groups based on their heart rhythm after CA. Among the patients, AF duration was relatively homogeneous for at least 1 year before CA because of our inclusion criteria. However, AF duration in the AF group was longer than in the SR group. In some studies evaluating the effect of restoring SR by CA on cardiac morphology, the duration of AF was more heterogeneous than in our study: 30–60% of study participants had paroxysmal AF in these studies [5, 32]. Additionally, the duration of exposure to AF after CA was considered a critical factor to evaluate the impact of AF on cardiac morphology. Therefore, in the present study, we tried to resolve the heterogeneity of AF duration before and after CA. We confirmed patients' heart rhythm 3 and 12 months after CA by electrocardiography. Using frequent heart rhythm evaluation, the duration of AF after CA was also considered to be relatively homogenous among the patients in the AF group. This was an advantage of the present study: homogenizing the duration of exposure to AF before and after CA within each group.

In the present study, 76/101 (75.2%) patients undergoing CA for persistent AF had sustained SR for 12 months. This result was consistent with a previous report [33].

At baseline, body mass index, AF duration, and the use of β-blockers differed between the two groups, but these factors did not correlate with the change in RAA. The longer AF duration in the AF group could explain the larger LAVI value in the AF group vs the SR group at baseline. LAVI in both groups decreased similarly after CA without a time–group interaction. In contrast, all right heart parameters were similar between the two groups at baseline.

Table 4 Univariate and multivariate analysis of the association between changes in the right heart parameters and changes in TRJA

Variables	Univariate analysis		Multivariate analysis	
	R (95% CI)	*p* value	*β* (95% CI)	*p* value
Δ RAA, cm2	0.49 (0.06 to 0.17)	<0.001	0.43 (0.02 to 0.17)	0.01
Δ RA LAXd, mm	0.34 (0.02 to 0.11)	0.001	0.09 (−0.04 to 0.07)	0.52
Δ RA SAXd mm	0.30 (0.01 to 0.10)	<0.001	0.05 (−0.04 to 0.06)	0.73
Δ RV area, cm2	0.15 (−0.06 to 0.19)	0.28		
Δ RV LAXd, mm	0.25 (−0.01 to 0.22)	0.07		
Δ RV SAXs, mm	0.03 (−0.09 to 0.12)	0.83		
Δ TAD, mm	0.13 (−0.03 to 0.08)	0.35		

CI confidence interval, *Δ* change, *LAXd* long axis diameter, *LV* left ventricle, *RA* right atrium, *RAA* right atrial area, *RV* right ventricle, *SAXd* short-axis diameter, *SAXs* short-axis diameter, *TAD* tricuspid annular diameter, *TRJA* tricuspid regurgitant jet area

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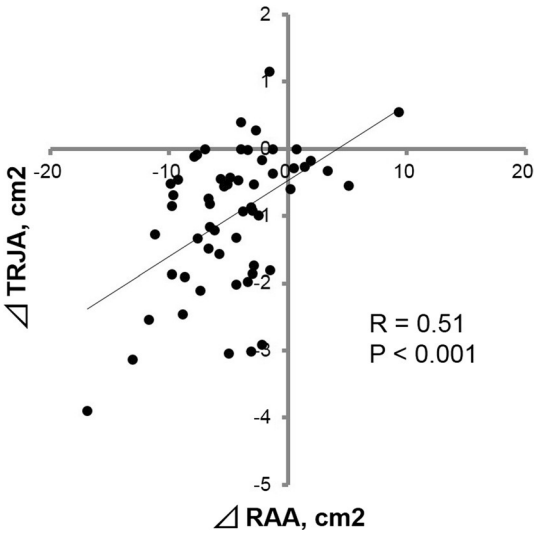

Fig. 4 XXX

Impact of atrial fibrillation on right heart morphology

Our results supported the concept that AF causes right atrial expansion and tricuspid annular dilatation leading to functional TR, and our results also confirmed that restoring SR from persistent AF by CA reduced RAA and TAD. In contrast, in the AF group, we saw no change in right heart morphology. Our findings suggested that AF rhythm itself had an impact on both left- and right heart morphology.

Previous studies reported a relationship between restoring SR and left-sided cardiac parameters. Shin et al. reported that restoring SR by CA decreased left atrial volume [32]. Gerts et al. [5] reported that patients with AF with more than moderate functional MR showed a reduction in MR after restoring SR. The authors also reported that patients with sustained SR showed significant reduction in left atrial volume and mitral annular diameter [5]. However, the precise mechanisms involved in remodeling the left atrium and mitral annulus induced by AF remain to be elucidated. A similar situation exists regarding the relationship between right heart remodeling and AF; further study is needed to elucidate the precise mechanism of AF in cardiac remodeling.

The effect of restoring SR on TR

Our results showed that persistent AF could be a cause of FTR because restoring SR by CA decreased right cardiac size, especially RAA, and that the change in RAA correlated with the change in TRJA in patients with persistent AF.

It is now recognized that TR is independently related to cardiac events [11–27], and chronic AF is considered an important cause of FTR. Previous studies suggested an influence of AF on right cardiac morphology and function leading to FTR [34, 35]. Other studies demonstrated that 6–12% of patients with severe TR had no diseases associated with TR such as tricuspid valve leaflet abnormality, pulmonary hypertension, RV dysfunction, or left-sided heart disease, and the authors also discussed a relationship between isolated FTR and chronic AF [7, 8, 21]. Utsunomiya et al. reported that 13% of patients with more than moderate FTR had AF because of TR, according to three-dimensional transesophageal echocardiography [9]. As in these studies, FTR caused by AF is described in the ASE guidelines [6], and our findings also support this finding.

In the present study, among the parameters describing right cardiac morphology, change in RAA was the only parameter related to the change in TRJA, using multivariate analysis; change in TAD was unrelated. However, Badano et al. previously reported that tricuspid annular dilatation caused by AF is a mechanism underlying functional tricuspid valve regurgitation [18]. We speculated that this discrepancy was caused by the difficulty of measuring TAD by two-dimensional TTE.

Limitations

The limitations of the present study were as follows: First, this was a single-center retrospective study with a relatively small sample size, and we measured right heart morphology by two-dimensional TTE. Because the RA, RV, and annular diameters were measured offline, we could not use the RV-focused view for measurements in all patients. In addition, it is well known that two-dimensional TTE may cause errors in right heart measurements. To increase measurement accuracy, multicenter prospective studies using three-dimensional TTE are necessary.

Second, there were several differences in patients' baseline data between the two groups. Because of the retrospective cohort study design and the inclusion of consecutive patients, patients were not equally divided into the SR group (70%) and AF group (15%), which may have influenced outcomes. In particular, LAVI at baseline was larger in the AF group, and this could explain why patients in the AF group had progressive AF compared with patients in the SR group. However, the similar RAA and TRJA values in both groups at baseline helps lessen this importance of this limitation.

Third, we collected heart rhythm data only at the electrocardiogram evaluation follow-up points; we did not have heart rhythm data throughout the study period. Some patients whom we classified into the SR group might have had AF. However, we can reasonably rely on the classification process because LAVI decreased noticeably in the SR group. Additionally, patients in the AF group might have had

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SR, especially for some time after CA, which may explain the reduction in LA volume in the AF group.

Fourth, all patients enrolled in this study had less than mild TR. We do not know whether our findings also apply to patients with AF and severe TR.

Conclusions

Our findings support the concept that persistent AF has a substantial impact on right cardiac morphology and is a cause of FTR.

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Compliance with ethical standards

Conflict of interest Kiho Itakura declares that she has no conflict of interest. Takayuki Hidaka declares that she has no conflict of interest.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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