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Altered Cardiac Performance Following Catheter Ablation in Patients with Non-Recurrence Persistent Atrial Fibrillation

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Abstract

We aimed to elucidate the relationship between echocardiographic data after ablation and atrial fibrillation (AF) recurrence, and to examine the difference in this relationship between paroxysmal and persistent AF. We enrolled 105 patients (72 men, paroxysmal/persistent 56/49, mean age 67 years) who underwent a single radiofrequency catheter ablation procedure. The transthoracic echocardiographic parameters were measured before ablation and at 3 days/6 months after ablation. Recurrence was observed in 30 patients (29%) at 12 months (paroxysmal 18%, persistent 41%). Stroke volume index (SVI) increased significantly in recurrence-free patients only with persistent AF shortly after ablation. Patients with persistent AF showing an increase in tricuspid regurgitation pressure gradient (ΔTRPG>0) exhibited an increase in SVI after ablation and a lower incidence of recurrence at 12 months than those with ΔTRPG<0. At 6 months after ablation, the altered levels of TRPG, but not SVI, were restored to the levels before ablation. In conclusion, a persistent increase in SVI associated with transiently increased TRPG at 3 days after ablation in patients with persistent AF, but not with paroxysmal AF, represents preserved cardiac performance of the entire heart and not just the left atrium, possibly related to the incidence of recurrence thereafter in patients with persistent AF.

Keywords: Tricuspid regurgitation pressure gradient; Recurrent atrial fibrillation; Stroke volume; Cardiac compliance; Stiff left atrial syndrome

Introduction

Recurrent atrial fibrillation (AF) is common despite advances in ablation techniques. Advanced age, hypertension, and enlarged left atrial (LA) diameter are well-known risk factors for AF [1,2]. However, there are multiple factors causing AF recurrence after a successful ablation [3]. Echocardiographic examination of LA performance might play an important role in predicting AF recurrence after cardioversion [3-5]. LA enlargement has been proven to be associated with AF recurrence after cardioversion [6]. Patients with moderately enlarged LA show a different response to ablation, and patients with severely enlarged LA have been identified to be at a high risk for AF recurrence [7]. Structural factors of the LA myocardium have been linked to arrhythmogenic substrates, leading to AF recurrence [8-11]. In contrast, dynamic cardiac changes other than changes in LA performance shortly after ablation for AF, and their relation to recurrence, are poorly defined. Cardiac performance after cardioversion, evaluated according to echocardiographic data such as stroke volume and pulmonary arterial dynamics in addition to LA performance, remains unclear. Furthermore, the long-term success rates vary among different studies because of the differences in AF type and ablation procedure. The aim of this study was to elucidate the relationship between altered echocardiographic data shortly after radiofrequency catheter ablation and AF recurrence at 12 month follow up, and to examine the difference in this relationship between patients with paroxysmal AF (ParAF) and patients with persistent AF (PerAF).

Methods

Patient selection

We enrolled consecutive 105 patients (72 men, ParAF/PerAF 56/49, mean age 67 years) who underwent a single radiofrequency catheter ablation procedure. The patients had symptomatic AF that was refractory to drugs. Medical histories were obtained by reviewing the patients' medical records for electrocardiograms (ECGs) and Holter recordings of AF episodes. Oral anticoagulation therapy was necessary for at least 1 month before and 3 months after ablation. Blood samples were obtained before ablation. The study protocol adhered to the Declaration of Helsinki and was approved by the institutional review board of our hospital. Written informed consent was obtained from all patients before catheter ablation.

Ablation procedure

After trans-septal puncture, a bolus of heparin was administered (5000–6000 IU, according to the patient's weight), followed by additional boluses, to maintain an activated clotting time of 300–350 s. By using double OPTIMA catheters (St. Jude Medical, St. Paul, MN, USA), we performed the electroanatomical mapping-guided extensive encircling pulmonary vein isolation (EEPVI) method. Three-dimensional mapping was performed with the NavX system (St. Jude Medical). Continuous circumferential ablation lines were created around the left- and right-sided pulmonary veins by using a 3.5 mm tip irrigated CoolFlex catheter (St. Jude Medical) at a maximum power of 30 W for 30 s at each site. The EEPVI endpoint was the absence or dissociation of local electrograms inside the entire surrounded region, together with exit block by means of pacing within the pulmonary vein

ostia. Additional ablation lines (LA roof and bottom) were performed only in patients with PerAF. Patients were treated per the physician's discretion and according to current guidelines.

Echocardiographic examination

The transthoracic echocardiographic parameters (Aprio 400, Toshiba Medicals, Tokyo, Japan) were measured before, 3 days after, and 6 months after ablation and were analyzed retrospectively. Measurements of echocardiographic parameters such as chamber size (LA dimension (LAD), LA volume index (LAVI), and left ventricular end-systolic and end-diastolic dimensions), left ventricular ejection fraction (LVEF), stroke volume index (SVI), tricuspid regurgitation pressure gradient (TRPG), transmitral flow velocity (E wave), and tissue Doppler images of the mitral annular septal and lateral area (mean e') were obtained according to the American or European Society of Echocardiography criteria [12-14]. The index was calculated by dividing with the body surface area. In patients showing AF rhythm, we paid careful attention to the appropriate cardiac cycle length and equivalence to obtain their echocardiographic data [15]. The heart rate was 72 ± 12 beats per min in patients with PerAF before ablation. The echocardiographic measurements were compared between recurrence-free patients (sinus rhythm maintained for >12 months) and those with recurrence. Transesophageal echocardiography was performed in all patients before ablation, to exclude the presence of LA thrombus [16].

Follow-up

The incidence of clinical recurrence was evaluated as follows: Follow-up 12-lead ECGs at 1, 3, 6, 9, and 12 months after the initiation of the assigned intervention were analyzed. Twenty-four-hour Holter monitoring was performed at 3, 6 and 12 months of follow-up. The time to first documented AF or atrial tachyarrhythmia lasting >30 s was defined as recurrence, after the 3-month blanking period.

Statistical analysis

Continuous variables were expressed as mean ± standard deviation, and categorical variables were presented as frequency and percentage. Differences in categorical variables between the groups were compared by using the chi-square test, and differences in continuous variables between the groups were compared with an unpaired t-test or a paired t-test appropriately. A P-value of <0.05 was considered significant.

Results

Clinical data before ablation and 12-month recurrence

The laboratory and echocardiographic data before ablation in the ParAF and PerAF groups are shown in Table 1. There were significant differences in brain natriuretic peptide level and echocardiographic data such as LVEF, SVI, LAD, and LAVI between patients with ParAF and those with PerAF; however, no difference was observed in renal function between the two groups. Recurrence was clinically observed in 30 patients (29%) at 12 months after ablation (ParAF 18%, PerAF 41%). The incidence of recurrence was significantly higher in patients with PerAF than in those with ParAF (P=0.009). Although not shown, recurrence-free patients had lower values of LAD (P = 0.005), LAVI (P<0.001), and TRPG (P<0.001) than those with recurrence in all patients. A significant positive correlation was observed between TRPG and LAD, LAVI, or E/e' before ablation (P<0.001 each).

	ParAF	PerAF	P value
	n=56	n=49	
Age, years	67.2 ± 9.6	67.2 ± 8.6	0.996
Men, n (%)	35 (63)	37 (76)	0.154
Laboratory data			
CRP, mg/dL	0.24 ± 0.55	0.15 ± 0.27	0.317
FBS, mg/dL	106 ± 16	116 ± 32	0.063
eGFR, mL/min/1.73 m^2	67.6 ± 13.7	64.9 ± 17.2	0.382
BNP, pg/mL	102 ± 123	193 ± 137	<0.001
Echocardiographic data			
LVDd, mm	47.6 ± 4.4	46.9 ± 2.0	0.506
LVDs, mm	30.2 ± 4.2	31.3 ± 6.0	0.279
LVEF, %	65.8 ± 6.9	61.6 ± 10.0	0.012
SVI, mL/m^2	41.3 ± 8.2	35.1 ± 6.8	<0.001
LAD, mm	39.2 ± 7.0	45.0 ± 4.9	<0.001
LAVI, mL/m^2	33.1 ± 13.5	43.5 ± 14.1	<0.001
E/e'	9.2 ± 3.3	10.7 ± 3.2	0.076
TRPG, mmHg	21.5 ± 5.7	23.3 ± 6.0	0.201

Table 1: Laboratory and echocardiographic data before ablation; Data are mean ± SD or number of patients (percent). P values represent the comparison between ParAF and PerAF patients. CRP: C-reactive protein; FBS: Fasting Blood Sugar; eGFR: estimated Glomerular Filtration Rate; BNP: Brain Natriuretic Peptide; LVDd: Left Ventricular end-diastolic Dimension; LVDs: Left Ventricular end-systolic Dimension; LVEF: Left Ventricular Ejection Fraction; SVI: Stroke Volume Index; LAD: Left Atrial Dimension; LAVI: Left Atrial Volume Index; TRPG: Tricuspid Regurgitation Pressure Gradient; ParAF: Paroxysmal Atrial Fibrillation; PerAF: Persistent Atrial Fibrillation.

Altered echocardiographic data after ablation and 12-month recurrence

SVI, but not TRPG or E/e', increased significantly in patients with PerAF without recurrence at 3 days after ablation when almost all patients were in sinus rhythm (P = 0.004, Table 2). Most of PerAF patients exhibited increased SVI, but most of ParAF patients showed decreased SVI shortly after ablation, irrespective of their clinical outcome at 12 months. A positive but weak correlation was found between the changes in TRPG (ΔTRPG) and SVI (r = 0.305, P = 0.049) or E/e' (r = 0.346, P = 0.097). Although TRPG before ablation was smaller in recurrence-free patients than in those with recurrence in both the PerAF and ParAF groups (Table 2), patients with increased TRPG (ΔTRPG>0) associated with increased SVI at 3 days after ablation exhibited a lower incidence of recurrence than those with reduced TRPG (ΔTRPG<0) only in the PerAF group (Table 3). There were similar differences in LAD, LAVI, and TRPG between recurrence-free patients and those with recurrence at 6 months after ablation in both the PerAF and ParAF groups (Table 4), as compared with those before ablation (Table 2), showing that the change in TRPG

was transient. In contrast, the increase in SVI after 3 days persisted at 6 months after ablation in recurrence-free PerAF, but not ParAF, patients unlike the case of TRPG (Tables 2 and 4).

A, ParAF	Recurrence-free		P value	Recurrent		P value
	Before ablation	3 days after ablation		Before ablation	3 days after ablation	
LVDd, mm	48.0 ± 4.3	46.4 ± 4.6	0.153	45.7 ± 4.9	42.8 ± 4.6	0.267
LVDs, mm	30.7 ± 4.2	29.6 ± 4.4	0.289	27.9 ± 3.8	26.3 ± 3.5	0.424
LVEF, %	65.0 ± 6.9	65.7 ± 7.9	0.698	69.7 ± 5.5	69.7 ± 2.8	0.998
SVI, mL.m^2/Kg	41.7 ± 8.1	39.3 ± 8.1	0.224	37.0 ± 8.6	35.2 ± 6.1	0.265
LAD, mm	38.8 ± 6.7	38.5 ± 6.8	0.866	41.4 ± 8.2	40.2 ± 7.4	0.767
LAVI, mL.m^2/Kg	31.2 ± 9.5	30.5 ± 8.8	0.777	41.0 ± 23.0	44.8 ± 37.5	0.808
E/e'	9.1 ± 3.3	9.9 ± 3.2	0.321	9.9 ± 3.5	9.3 ± 3.1	0.767
TRPG, mmHg	20.7 ± 5.3	22.7 ± 6.1	0.189	27.8 ± 5.2	20.8 ± 4.6	0.07

Table 2A: Differences in the altered echocardiographic data before and after ablation between patients with and without recurrence; ParAF: Recurrent-Before ablation, 3 days after ablation.

B, PerAF	Recurrence-free		P value	Recurrent		P value
	Before ablation	3 days after ablation		Before ablation	3 days after ablation	
LVDd, mm	46.7 ± 5.1	47.6 ± 4.1	0.524	47.3 ± 5.1	46.8 ± 5.0	0.79
LVDs, mm	31.4 ± 5.4	30.8 ± 4.6	0.682	31.2 ± 6.9	31.2 ± 4.6	0.998
LVEF, %	61.0 ± 9.0	64.8 ± 7.4	0.127	62.5 ± 11.5	62.3 ± 7.8	0.945
SVI, mLm^2/Kg	34.2 ± 6.2	39.3 ± 4.9	0.004	36.4 ± 7.5	37.2 ± 7.0	0.555
LAD, mm	43.9 ± 3.9	45.2 ± 5.4	0.361	46.6 ± 5.9	47.5 ± 6.1	0.67
LAVI, mLm^2/Kg	40.2 ± 14.2	43.6 ± 13.4	0.423	48.2 ± 13.0	47.2 ± 11.7	0.828
E/e'	10.1 ± 2.6	11.5 ± 4.3	0.289	12.0 ± 4.1	10.3 ± 2.5	0.287
TRPG, mmHg	21.1 ± 4.9	25.1 ± 7.4	0.056	26.0 ± 6.2	22.2 ± 3.8	0.068

Table 2B: Differences in the altered echocardiographic data before and after ablation between patients with and without recurrence; PerAF: Recurrent--Before ablation, 3 days after ablation.

	ParAF		P value	PerAF		P value
	ΔTRPG>0	ΔTRPG<0	ΔTRPG>0	ΔTRPG<0		
LVEF, %	3.0 ± 8.0	-2.3 ± 4.3	0.079	5.4 ± 6.3	0.7 ± 10.5	0.214
SVI, mL/m^2	-1.1 ± 6.3	-5.2 ± 5.0	0.123	5.1 ± 4.6	-0.4 ± 7.0	0.044
LAD, mm	-1.0 ± 3.5	-1.6 ± 3.9	0.717	-0.5 ± 5.4	-2.9 ± 2.9	0.197
LAVI, mL/m^2	-1.7 ± 5.4	-4.6 ± 6.2	0.299	-2.0 ± 13.6	-3.4 ± 8.2	0.781
E/e'	1.4 ± 3.6	-2.0 ± 3.7	0.067	1.0 ± 2.0	-0.7 ± 4.2	0.512

Recurrence, %	0	20	0.114	18	64	0.03

Table 3: PerAF: ΔTRPG>, ΔTRPG<0; Altered echocardiographic data and recurrence rate between patients with and without increased TRPG after catheter ablation. Delta data were obtained from the echocardiographic data at 3 days after ablation subtracted by those before ablation. Data are mean ± SD or percent. Abbreviations are as shown in Table 1.

	ParAF		P value	PerAF		P value
	Recurrence-free	Recurrent		Recurrence-free	Recurrent	
LVDd, mm	46.7 ± 4.8	43.3 ± 7.3	0.111	47.6 ± 4.0	44.1 ± 6.2	0.063
LVDs, mm	29.6 ± 3.8	27.7 ± 5.2	0.244	30.1 ± 3.7	27.8 ± 5.3	0.161
LVEF, %	66.3 ± 5.8	65.9 ± 6.1	0.857	66.0 ± 5.4	67.0 ± 5.4	0.645
SVI, mL/m^2	40.2 ± 9.0	35.3 ± 13.8	0.222	39.8 ± 6.2	35.4 ± 8.7	0.106
LAD, mm	37.9 ± 7.1	43.6 ± 8.2	0.057	40.1 ± 4.8	45.4 ± 4.7	0.006
LAVI, mL/m^2	29.3 ± 9.7	40.3 ± 18.6	0.021	34.4 ± 12.3	45.6 ± 13.6	0.028
E/e'	8.7 ± 2.3	9.8 ± 1.6	0.343	9.9 ± 4.2	8.8 ± 2.7	0.48
TRPG, mmHg	21.8 ± 4.9	31.8 ± 12.5	0.001	22.6 ± 7.3	28.3 ± 7.7	0.067

Table 4: Echocardiographic data 6 months after ablation in patients with and without recurrence. Data are mean ± SD. Abbreviations are as shown in Table 1.

Discussion

SVI, but not TRPG, increased significantly in recurrence-free PerAF group shortly after ablation. Patients with ΔTRPG>0 associated with the increased SVI 3 days after ablation exhibited a lower incidence of recurrence than those with ΔTRPG<0 in the PerAF group. The increase in SVI after 3 days persisted at 6 months after ablation in recurrence-free PerAF patients unlike the case of TRPG, which represented a good dynamic cardiac state after conversion from atrial to sinus rhythm in patients with PerAF, but not with ParAF, without recurrence.

Altered cardiac performance in recurrence-free PerAF patients

Pulmonary vein reconnection is a main cause of AF recurrence after ablation and may be related to LA remodeling. However, non-pulmonary vein trigger is another main cause of recurrence in PerAF patients and may be more related to LA remodeling [17]. Since TRPG was positively correlated with LAD, LAVI and E/e', high TRPG levels before ablation in recurrent patients may represent the measurable progression of cardiac remodeling. It would be different in the pathophysiological significance between the absolute value of TRPG before ablation and the transient change in TRPG shortly after ablation. As SVI increased significantly associated with mild increases in TRPG and E/e' shortly after ablation in the recurrence-free PerAF patients, the changes in TRPG and E/e' may be a secondary phenomenon in relation to SVI increase after sinus conversion. The altered cardiac performance of the entire heart and not just the LA after sinus conversion in the recurrence-free PerAF patients would indicate the lesser extent of cardiac remodeling at that time, possibly leading to the lesser incidence of pulmonary vein reconnection or non-pulmonary vein trigger thereafter, thus resulting in favorable outcome after 1 year.

Reported LA performance related to AF recurrence

Catheter ablation can lead to scarring of the atrium, which can cause LA diastolic dysfunction leading to elevated pulmonary pressure [18]. Stiff LA syndrome can occur after ablation [19]. However, the changes in the dynamic cardiac state shortly after ablation, observed in patients with PerAF with or without recurrence in this study, were different from the characteristics of this syndrome. Although LA size parameters such as LAD and LAVI tended to be reduced shortly after ablation in patients with PerAF recurrence, TRPG and E/e' were reduced as compared with the values before ablation. In patients with PerAF without recurrence, SVI increased significantly shortly after ablation associated with increased TRPG and E/e'. In favorable cardiac performance, the increase in TRPG would be associated with SVI increase, which is essentially different from that of stiff LA syndrome. Patients with ParAF exhibited much smaller LAD and LAVI than patients with PerAF, and their LA remodeling may not be progressive before ablation. TRPG and E/e' increased shortly after ablation, associated with the absence of SVI increase especially in patients with ParAF without recurrence. Stiff LA syndrome may occur in these patients.

As LA pressure increases after AF ablation [20], the changes in echocardiographic parameters immediately after ablation would be important to elucidate the characteristic alterations in cardiac performance. However, we performed echocardiographic examination at 3 days after ablation because of the individual differences in the extent of volume overload occurring during the procedures. More than 2 weeks of maintained sinus rhythm after cardioversion might be necessary for a complete restoration of LA function. At 3 days after ablation, the altered cardiac performance due to AF remains

unchanged, and we can evaluate the altered variables of cardiac compliance in relation to AF recurrence after ablation.

Limitations

It is unclear why some patients had more or less changes in compliance parameters than other patients; however, the possible reasons may be related to the number, extent, and location of the ablated lesions. We did not evaluate the time of recurrence in each patient and the changes in dynamic cardiac performance at the time of recurrence. Since we did not undergo redo ablations to determine the cause of recurrence, our findings cannot favor LA remodeling and PV reconnection as the cause of recurrence. In this sense, the echocardiographic parameters may be markers of clinical factors favoring recurrences. The present study was a single-center study, and the possibility that other centers may achieve different results with different patient cohorts cannot be excluded. Further prospective studies are needed to understand the relationship between the incidence of AF recurrence and the pre-ablation levels and/or their acute changes in cardiac performance parameters such as stroke volume, TRPG and E/e' after ablation, in addition to the possible changes in atrial performance.

Conclusions

The altered cardiac performance of the entire heart and not just the LA shortly after sinus conversion may indicate the lesser extent of cardiac remodeling at that time, possibly resulting in favorable outcome after 12 months in patients with persistent AF.

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