Biatrial strain as a new predictive marker of successful pulmonary vein ablation in patients with atrial fibrillation and preserved left ventricular function

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Introduction The rate of atrial fibrillation (AF) recurrence after a single radiofrequency catheter ablation (RFCA) procedure is reported to be as high as 30% to 50%. Multiple factors have been identified as related with AF relapse after RFCA; however, their predictive value is rather small.[1] Therefore, new predictors of procedural outcome are needed for better identification of patients who will benefit the most from RFCA.

Left atrial (LA) structural and functional remodeling has been recognized as an important risk factor for AF recurrence. On the other hand, AF is a biatrial disease and the enlargement of the right atrium (RA) contributes to AF relapse to a similar degree as LA remodeling.[2] Although RA fibrosis and remodeling have been reported in patients with paroxysmal AF,[3] and structural biatrial remodeling has been shown to be significantly correlated with this arrhythmia,[4] the impact of RA and both LA and RA function on AF recurrence after RFCA has not been investigated. Subtle cardiac dysfunctions can be recognized on 2-dimensional speckle tracking echocardiography (2D-STE), even when they are not yet visible on conventional echocardiographic analysis. Hence, application of 2D-STE before RFCA can improve identification of myocardial alterations linked to AF recurrence. We hypothesized that the extent of remodeling of both atria, and not the LA alone, would be associated with AF relapse after RFCA. The aim of the study was to evaluate the predictive value of LA and RA size and function on AF recurrence after RFCA. To minimize the impact of the left ventricle (LV) on atrial deformation, only patients with LV ejection fraction (LVEF) of 50% or more were included in the analysis.

Methods This single-center prospective study included 41 patients with paroxysmal or persistent nonvalvular AF who underwent initial RFCA between January 2014 and December 2017. Only patients in sinus rhythm and with LVEF of 50% or more were eligible for enrollment. Follow-up visits with 12-lead electrocardiogram (ECG) and 24-hour Holter recording were scheduled at 3 and at least 6 months after RFCA at an outpatient arrhythmia clinic. Each outpatient who developed symptoms suggestive of AF was advised to undergo immediate ECG recording. The RFCA procedure was considered successful if during the follow-up, after a blanking period of 3 months, there was no recurrence of AF lasting more than 30 seconds, as detected on serial ECG or 24-hour Holter monitoring.

A detailed description of the RFCA procedure and echocardiographic study with strain measurements can be found in the supplementary material.

Statistical analysis Variables were compared with the *t* test for independent values, Mann–Whitney test, χ^2 test with Yates correction, or

TABLE 1 Baseline clinical and echocardiographic characteristics of the whole study group and patients classified according to atrial fibrillation recurrence after pulmonary vein isolation (continued on the next page)

Parameter	Total (n = 41)	Group without AF recurrence after PVI (n = 26)	Group with AF recurrence after PVI (n = 15)	*P* value[a]
Age, y, mean (SD)	55 (11)	54 (11)	55 (11)	0.96
Male sex, n (%)	25 (61)	18 (69)	7 (47)	0.27
BMI, kg/m^2, mean (SD)	29 (4)	29 (4)	29 (4)	0.55
Persistent AF, n (%)	7 (17)	2 (8)	5 (33)	0.09
History of AF, y, median (IQR)	3 (2–7)	3 (2–7)	5 (3–8)	0.22[c]
Documented AFl, n (%)	6 (15)	3 (12)	3 (20)	0.78
Hypertension, n (%)	21 (51)	13 (50)	8 (53)	0.91
Hypercholesterolemia, n (%)	11 (27)	5 (19)	6 (40)	0.28
Obesity (BMI >30 kg/m^2), n (%)	15 (37)	10 (38)	5 (33)	0.99
Type 2 diabetes, n (%)	2 (5)	2 (8)	None	0.73
Stable CAD, n (%)	2 (5)	2 (8)	None	0.73
CTI ablation, n (%)	1 (2)	1 (4)	None	0.78
AVRT/AVNRT ablation, n (%)	2 (5)	2 (8)	None	0.73
CHA_2DS_2-VASC score, n (%)				
Score 0	10 (24)	6 (23)	4 (27)	0.76[b]
Score 1	15 (37)	11 (42)	4 (27)	
Score 2	10 (24)	6 (23)	4 (27)	
Score 3	6 (15)	3 (12)	3 (20)	
Pharmacotherapy, n (%)				
Amiodarone	6 (15)	3 (12)	3 (20)	0.78
Sotalol	8 (20)	8 (31)	None	<0.05
Class I C antiarrhythmic drugs	15 (37)	7 (27)	8 (53)	0.18
No antiarrhythmic drugs	12 (29)	8 (31)	4 (27)	0.94
β-Blockers	18 (44)	9 (35)	9 (60)	0.21
Calcium antagonists	8 (20)	7 (27)	1 (7)	0.16
ACEIs/ARBs	16 (39)	9 (35)	7 (47)	0.67
Statins	18 (44)	12 (46)	6 (40)	0.96
Aldosterone antagonists	5 (5)	1 (4)	4 (27)	0.10
Echocardiographic results				
Heart rate, bpm, mean (SD)	61 (10)	63 (12)	59 (6)	0.70
IVS, mm, mean (SD)	11 (2)	11 (1)	10 (2)	0.73
PW, mm, median (IQR)	10 (9–11)	10 (9–10)	10 (9–11)	0.24[c]
LV end-diastolic volume, ml, mean (SD)	97 (21)	99 (23)	94 (18)	0.50
LV end-systolic volume, ml, median (IQR)	36 (30–45)	37 (31–45)	34 (30–44)	0.87[c]
LVEF, %, mean (SD)	62 (6)	63 (5)	59 (7)	0.10
LV-GLS, %, mean (SD)	–20 (3)	–20 (2)	–19 (4)	0.30
RV end-diastolic area, cm^2, median (IQR)	19 (17–22)	19 (18–22)	18 (17–19)	0.12[c]
s'RV, cm/s, mean (SD)	1.3 (0.4)	1.4 (0.3)	1.2 (0.3)	0.07

TABLE 1 Baseline clinical and echocardiographic characteristics of the whole study group and patients classified according to atrial fibrillation recurrence after pulmonary vein isolation (continued from the previous page)

Parameter	Total (n = 41)	Group without AF recurrence after PVI (n = 26)	Group with AF recurrence after PVI (n = 15)	*P* value[a]
RV strain, %, mean (SD)	–21 (5)	–21 (5)	–20 (5)	0.32
LA diameter, mm, mean (SD)	40 (5)	39 (5)	40 (5)	0.50
Minimum LA volume, ml, mean (SD)	43 (18)	36 (11)	47 (15)	<0.01
Maximum LA volume, ml, mean (SD)	80 (23)	72 (16)	86 (21)	0.03
LAVI, ml/m^2, mean (SD)	40 (12)	37 (10)	44 (12)	0.05
LAEF, %, mean (SD)	47 (11)	50 (10)	42 (10)	0.01
LA strain, %, mean (SD)	25 (6)	27 (5)	21 (6)	<0.01
RAVI, ml/m^2, median (IQR)	27 (24–30)	26 (24–32)	27 (24–29)	0.90[c]
RA strain, %, mean (SD)	31 (10)	33 (11)	29 (10)	0.23
Biatrial strain, %, mean (SD)	22 (8)	28 (6)	21 (5)	<0.001
E, m/s, mean (SD)	0.7 (0.2)	0.7 (0.1)	0.8 (0.3)	0.09
E/e', mean (SD)	8 (3)	7 (3)	8 (3)	0.40

a Group with vs without AF recurrence after PVI; *P* values were calculated with the χ^2 test with Yates correction, *t* test for independent values; Fisher Exact test (**b**) or Mann–Whitney test (**c**) where appropriate. A *P* value of less than 0.05 was considered significant.

CHA_2DS_2-VASc score: congestive heart failure, hypertension, age >75 years, diabetes mellitus, history of stroke or thromboembolism, vascular disease, age 65 to 74 years, female sex

Abbreviations: ACEI, angiotensin-converting enzyme inhibitor; AF, atrial fibrillation; AFl, atrial flutter; ARB, angiotensin II receptor blocker; AVNRT, atrioventricular nodal reentrant tachycardia; AVRT, atrioventricular reentrant tachycardia; BMI, body mass index; CAD, coronary artery disease; CTI, cavo-tricuspid isthmus; E, early transmitral flow velocity by pulsed-wave Doppler; e', early diastolic mitral annulus velocity by spectral tissue Doppler; IQR, interquartile range; IVS, interventricular septum; LA, left atrial; LAEF, LA emptying fraction; LAVI, LA volume index; LV, left ventricular; LVEF, LV ejection fraction; LV-GLS, LV global longitudinal peak strain; PVI, pulmonary vein isolation; PW, posterior wall; RA, right atrium; RAVI, RA volume index; RV, right ventricular; s'RV, peak systolic velocity of tricuspid annulus by spectral tissue Doppler

Fisher exact test, as appropriate. Receiver operating characteristic (ROC) curves were constructed to calculate adjusted cut-off values of variables for predicting AF recurrence after RFCA. The logistic regression analysis was applied to identify variables that independently predicted AF relapse. The variables with univariate *P* value of 0.1 or less and no colinearity between each other were included in the multivariate logistic regression model. For that reason only 1 parameter determining the LA function or size was taken into consideration in multivariate analysis. A *P* value of less than 0.05 was considered statistically significant. The STATA software (version 15.1, StataCorp LLC, College Station, Texas, United States) was used for statistical calculations.

Results and discussion Clinical and preprocedural echocardiographic characteristics of the study population are listed in TABLE 1. Bidirectional electrical pulmonary vein isolation was completed in all patients. During a mean (SD) follow-up of 13 (7) months after the RFCA procedure, 15 patients (37%) presented with recurrence of AF, while 26 (63%) were free from AF. There were no significant differences in clinical characteristics or pharmacotherapy between the 2 groups apart from sotalol use, which was more frequent in the group with AF recurrence.

The mean LV and right ventricular size and function were normal (TABLE 1). Both the LA and RA were mildly enlarged with slightly reduced function (mean [SD] LA strain, 25% [6%]; mean [SD] RA strain, 31% [10%]).

In the univariate analysis, LA minimal and maximal volumes, LA emptying fraction (LAEF), LA strain, and biatrial strain were predictors of AF recurrence (Supplementary material, *Table S1, Figure S1*).

In the ROC analysis, the respective cut-off values for sinus rhythm maintenance after RFCA were LA minimal volume of less than 35 ml (sensitivity, 87%; specificity, 46%; area under the curve [AUC], 0.69), LA maximal volume of less than 69 ml (sensitivity, 62%; specificity, 40%; AUC, 0.51), LAEF of more than 41% (sensitivity, 81%; specificity, 53%; AUC, 0.73), LA strain of more than 22% (sensitivity, 89%; specificity, 60%; AUC, 0.76), and biatrial strain of more than 24.75% (sensitivity, 74%; specificity, 80%; AUC, 0.80).

In multivariate analysis, biatrial strain was the main independent predictor of AF recurrence after RFCA (odds ratio, 1.21; 95% CI, 1.05–1.41; *P* = 0.011) (Supplementary material, *Table S1*).

Our study indicates that in patients with an LVEF of more than 50% undergoing the first RFCA for AF, larger LA volumes and worse atrial function (LAEF, LA strain, biatrial strain) identified the group at risk of AF relapse. We found that preprocedural biatrial strain was an independent predictor of arrhythmia elimination and the value of more than 24.75% best identified patients who maintained the sinus rhythm after RFCA (supplementary material, *Figure S1*).

Recently, 2D-STE has become widely accepted as an innovative and valuable method of subtle cardiac dysfunction evaluation. Atrial reservoir function, determined by LA strain, not only reflects the atrial wall distensibility, but is also related to chamber stiffness and fibrosis.[5] So far, LA strain measured by 2D-STE showed higher predictive value for RFCA efficacy than the LA size or type of AF.[6,7] We also found that LA strain allows the prediction of arrhythmia recurrence after RFCA with adequate sensitivity and specificity.

To the best of our knowledge, this is the first study that determines the impact of both LA and RA function assessed by biatrial strain using 2D-STE on AF elimination after RFCA. This atrial strain analysis reflects biatrial reservoir function. There is evidence supporting the relationship between LA and RA remodeling due to AF as it results in biatrial enlargement, and structural changes in both atria are significantly correlated.[4] Stiles et al[3] reported on the presence of biatrial electroanatomical abnormalities (atrial enlargement, conduction abnormalities, and sinus node dysfunction) even in patients with paroxysmal lone AF who remained in sinus rhythm and were studied remote from arrhythmia. Akutsu et al[2] analyzed patients with paroxysmal AF using a multidetector computed tomography and showed that apart from the LA structural remodeling, the RA remodeling defined as RA enlargement was equally associated with the outcome of RFCA. Moreover, they indicated that the assessment of combined atrial volumes had the highest diagnostic accuracy. The present study demonstrated that biatrial strain, representing LA and RA functional remodeling, is an important parameter predicting arrhythmia recurrence after RFCA. However, we found that LA strain was superior to RA strain for predicting AF recurrence. Our results indicate that RA functional changes contribute to AF-related atrial remodeling to a lesser extent. We think that the determinant of RA remodeling in our study was AF itself as we excluded all factors which might contribute to RA remodeling, such as LV systolic dysfunction, myocardial disease involving the RV, lung disease, or pulmonary hypertension.

In our study, biatrial strain turned out to be the best predictor of AF recurrence after RFCA, and this finding may have a few possible explanations. Yasuda et al[8] reported that LA strain measured on the LA lateral wall by 2D-STE might be the most useful parameter for predicting successful AF ablation, as it represents pure LA contractile function. Biatrial strain, which combines lateral walls of both atria, can be more sensitive to atrial wall remodeling than LA strain itself. In addition, we believe that evaluation of atrial free wall deformation can lead to a more precise assessment of true atrial function, as it allows to avoid artifactual dropout of the atrial septum in the 4-chamber view. Moreover, in accordance with the results of Akutsu et al,[2] we may suspect that combined LA and RA dysfunction may better reflect a more remarkable overall functional remodeling than individual atrial remodeling alone.

The limitation of our study is the possibility of overlooking silent AF episodes after RFCA, as continuous rhythm monitoring was not available.

SUPPLEMENTARY MATERIAL

Supplementary material is available at www.mp.pl/kardiologiapolska.

ARTICLE INFORMATION

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CONFLICT OF INTEREST None declared.

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