

Assessment of left atrial function and dyssynchrony by real time three-dimensional echocardiography predicts recurrence of paroxysmal atrial fibrillation after radiofrequency ablation

Y. HONGNING¹, X. RUIQIN², W. JING¹, H. GAOJIE¹, Z. XUQIAN¹,
Z. HONG¹, M. YAJING¹, L. FAN², L. JINGCHAO², M. CHENGLONG², C. WEI²

¹Department of Echocardiography, The Second Hospital of Hebei Medical University, Shijiazhuang, P.R. China

²Department of Cardiology, The Second Hospital of Hebei Medical University and Institute of Cardiocerebrovascular Disease of Hebei Province, Shijiazhuang, P.R. China

Abstract. – OBJECTIVE: Left atrial volume and function are associated with recurrence of paroxysmal atrial fibrillation (AF) after radiofrequency ablation. A relationship between left atrial mechanical dyssynchrony and AF recurrence is presently unclear. The aim of this study was to investigate whether left atrial volume, function, and dyssynchrony were associated with AF recurrence in patients with normal left ventricular function, and normal or mildly enlarged left atrium, if assessed by the Real-time three-dimensional echocardiography (3DE).

PATIENTS AND METHODS: We included 88 patients with AF who had their first pulmonary vein isolation. There were 67 patients without and 21 patients with AF recurrence after radiofrequency ablation. Real-time 3DE was performed in the sinus rhythm the day before radiofrequency ablation. Left atrial volumes (maximum, minimum and preA), functions (passive, active and reservoir) and dyssynchrony were calculated. The latter was quantified by the standard deviation of time to minimum systolic volume (Tmsv-SD) from the end-diastole.

RESULTS: There was no difference between left atrial volume and function in patients with or without AF recurrence. However, significant differences in left atrial Tmsv-SD were observed in patients with AF recurrence.

CONCLUSIONS: In patients with normal left ventricular function, and normal/mildly enlarged left atrium, left atrial Tmsv-SD assessment by Real-time 3DE is a useful predictor of AF recurrence after radiofrequency ablation.

Key Words

Atrial fibrillation, Left atrium, Three-dimensional echocardiography, Atrial dyssynchrony.

Abbreviations

2DE = two-dimensional echocardiography; 3DE = three-dimensional echocardiography; AF = atrial fibrillation; LAEFactive = active atrial emptying fraction; LAEFpassive = passive atrial emptying fraction; LAEFtotal = total atrial emptying fraction; LAmx = left atrial maximum volume; LAmin = left atrial minimum volume; LApreA = left atrial volume before atrial active contraction; LVEF = left ventricular ejection fraction; ROC = receiver-operating characteristic curve; STE = speckle tracking echocardiography; Tmsv-SD = standard deviation of time to minimum systolic volume.

Introduction

Atrial fibrillation (AF) is the most common arrhythmia in clinical practice. Its prevalence increases with advanced age. While rare in people younger than 50 years old, AF prevalence rises to about 9% in those aged above 80 years old¹. AF is a strong risk factor for ischemic stroke and congestive heart failure, and thereby leads to reduced quality of life and increased economical burden²⁻⁴.

Radiofrequency catheter ablation is an important treatment option for patients with symptomatic drug-refractory AF. Unfortunately, the post-ablation recurrence rate of AF can be as high as 52% in a long-term follow-up⁵. Careful patient selection for radiofrequency catheter ablation may decrease the AF recurrence rate. In this regard, it is interesting that atrial tissue

fibrosis, a tissue remodeling parameter associated with AF, can serve as a predictor for AF, such as when estimated by delayed-enhancement magnetic resonance imaging^{6,7}. Specifically, it has been demonstrated that atrial tissue fibrosis is associated with recurrent AF after radiofrequency ablation⁸. Unfortunately, utilization of magnetic resonance imaging in diagnostics of atrial tissue fibrosis is limited by the high cost and general inconvenience of this diagnostic method.

A possible diagnostic alternative is echocardiography. Left atrial fibrosis leads to reduce left atrial function. Analysis of left atrial mechanics by echocardiography may give insights into the status of left atrial fibrosis and may, therefore, be of predictive value for AF.

Left atrial fibrosis can be documented in form of left atrial strain and dyssynchrony by speckle tracking echocardiography (STE) applied to the analysis of chamber function⁹⁻¹¹. This is a highly reproducible method. Real-time three-dimensional echocardiography (3DE) has recently been developed; it is more accurate in measuring the volume and function of left atrium than two-dimensional echocardiography (2DE)^{12,13}. Recent investigations¹⁴⁻¹⁶ proved that measurement of left atrium strain and dyssynchrony using 3DE shows good reproducibility, and is quicker and simpler than 2DE.

There is still controversy about the merit of left atrial dyssynchrony as a predictor of the recurrence of AF after radiofrequency ablation. To address this, we conducted the present study to measure the left atrial volume, function and standard deviation of time to minimum systolic volume (Tmsv-SD) in patients with AF, normal left ventricular function, and normal or mildly enlarged left atrium.

Patients and Methods

Patients

From January 2012 to March 2014, 158 patients with AF underwent radiofrequency ablation in our center. Written informed consent was given by all study participants. The study was approved by the Ethical Committee of the Second Hospital of Hebei Medical University.

AF was defined as paroxysmal atrial fibrillation that terminated spontaneously or after intervention within 7 days of onset¹⁷. Indications for radiofrequency ablation were symptomatic drug-refractory AF, or intolerance of at least

one Class I or III antiarrhythmic medication. Of the enrolled patients, 128 patients had initial onset of AF. The echocardiographic recordings of these patients were reviewed. The patients were included in the study if they had normal systolic function (left ventricular ejection fraction, LVEF > 50%), and normal or mildly increased left atrial size (volume index < 42 mL/m²).

Exclusion criteria were poor image quality, structural heart disease, history of previous myocardial infarction, heart surgery, bundle branch block, moderate to severe valvular dysfunction, ongoing atrial fibrillation, or other sustained arrhythmias. Forty patients were excluded on the basis of these exclusion criteria. Thereby, 88 patients with AF were included in this study. The median time since the AF onset was 24 months.

2D Transthoracic Echocardiography and Tissue Doppler Imaging

Conventional echocardiographic examination and 2D STE were performed using a standard ultrasound machine (iE33, Philips Medical Systems, Amsterdam, The Netherlands) with a X5-1 transducer. Standard techniques were used to obtain M-mode, 2D and Doppler measurements in accordance to the American Society of Echocardiography guidelines. Transmitral flow velocities were determined using pulsed-wave Doppler echocardiography. Furthermore, mitral flow parameters, including peak velocities during early and late diastole, and deceleration time of early diastole, were measured. Tissue doppler imaging from the apical four-chamber view was performed with a frame rate of 80 to 120 frames/sec. Tissue doppler-derived peak systolic, early and late diastolic velocities were derived from the septal mitral annulus. The mitral ratio of early diastole/early diastolic velocity was subsequently calculated. Left ventricular end-systolic volume, end diastolic volume, and ejection fraction were calculated by the modified Simpson's method from apical four and two chamber views.

2D STE

For 2D STE, apical four-chamber and two-chamber images were obtained using 2DE. All images were recorded with a frame rate of >50 frames/s. Three reference points were placed at septal mitral annulus, lateral mitral annulus, and left atrial roof at the end-diastole in the apical four-chamber. The software automatically tracked the contours on subsequent frames. Then, three reference points were placed at anterior

mitral annulus, posterior mitral annulus and left atrial roof at the end-diastole in apical two-chamber, and the software automatically tracked the contours on the subsequent frames. The left atrial longitudinal strain was defined as the left atrial peak ventricular systolic longitudinal strain, which was calculated by averaging the values of the 12 left atrial segments, measured from apical four-chamber and two-chamber views. Then, the values were averaged.

Real-Time 3D STE

The apical full-volume acquisition was performed to visualize the entire left atrium in a volumetric image. While retaining the entire left atrium within the pyramidal volume, depth and sector width were decreased as much as possible to improve the temporal and spatial resolution of the image, resulting in a volume rate of >15 volumes/s. The images were obtained during an end expiratory breath-hold, lasting 6 to 8 s. Three-dimensional data sets were stored in a raw-data format for offline analysis and exported to the Q-lab workstation (Q-lab, version 9.0, 3DQ(A); Philips Medical Systems, Amsterdam, The Netherlands). This software performs 3D endocardial border tracking throughout the cardiac cycle, to provide a mathematical model of the left atrial volume. The left atrial volume and function parameters were calculated using equations published previously¹³. The left atrial maximum volume (LA_{max}) was defined at the end systole, when left atrium was maximal, just before the mitral valve opening. The left atrial minimum volume (LA_{min}) was defined at the end diastole when the left atrial volume was the smallest, just before the mitral valve closure. The left atrial volume before atrial active contraction (LA_{preA}) was measured at the time of the P wave on the electrocardiogram (Fig-

ure 1). All left atrial volumes were normalized to the body surface area.

The left atrial function was derived from the left atrial volumes and expressed using the following formulas:

- 1) Total atrial emptying fraction, $LAEF_{total} = [(LA_{max} - LA_{min}) / LA_{max}] \times 100$;
- 2) Active atrial emptying fraction, $LAEF_{active} = [(LA_{preA} - LA_{min}) / LA_{preA}] \times 100$ (considered an index of left atrial active contraction);
- 3) Passive atrial emptying fraction, $LAEF_{passive} = [(LA_{max} - LA_{preA}) / LA_{max}] \times 100$ (considered an index of left atrial conduit function).

Left atrium mechanical dyssynchrony was quantified by Real-time 3DE. A 3D model of left atrium was created, and the model was divided into 16 segments. Time volume curves were generated for each of the 16 segments. To quantify left atrial dyssynchrony, times to peak contraction (LA_{min}) in 16 segments were measured. The left atrial Tmsv-SD was defined as the standard deviation of these timings (Figure 2). The left atrial synchronicity parameters were calculated for curves as previously described¹⁸. Higher grades of dyssynchrony were recognized as larger values of left atrial Tmsv-SD.

All echocardiographic studies were performed by an experienced cardiologist who was blinded to the patients' clinical information. Intra- and inter-observer variability of left atrial Tmsv-SD were assessed, and found minimal.

Electrophysiological Study and Radiofrequency Ablation

A 6-F decapolar catheter (Biosense Webster Inc., Diamond Bar, CA, USA) was positioned in the coronary sinus via the right femoral vein. A double trans-septal puncture into the left atrium was performed under the guidance of two SL0 sheaths.

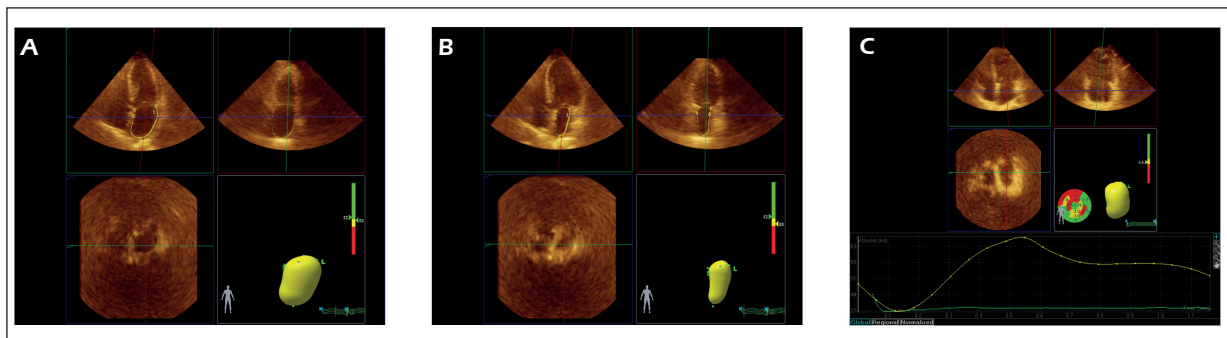


Figure 1. Real-time three-dimensional echocardiography. (A) Left atrial maximum volume, LA_{max} , (B) Left atrial minimum volume, LA_{min} , (C) Left atrial time volume curve. Left atrial volume before atrial active contraction (LA_{preA}) was measured at the time of P wave on electrocardiogram.

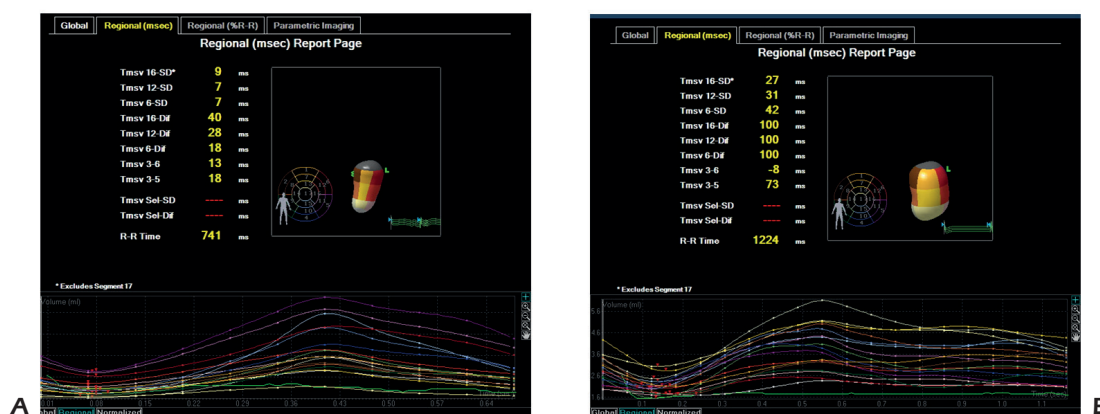


Figure 2. Left atrial (LA) time volume curves in patients without (A) or with (B) atrial fibrillation recurrence after radiofrequency ablation. The LA Tmsv-SD (the standard deviation of times to LA minimum volume) was defined as the standard deviation of times from end-diastole (the R wave on the electrocardiogram) to peak contraction (minimum volume) in 16 segments.

A Lasso circular mapping catheter (Biosense Webster Inc., Diamond Bar, CA, USA) and a 3.5-mm tip irrigated ablation catheter (Navistar Thermocool, Biosense Webster Inc., Diamond Bar, CA, USA) were placed into the left atrium. A 3D electroanatomical map was created by the Carto-3 system (Biosense Webster Inc., Diamond Bar, CA, USA). The ablation strategy was encircling of ipsilateral pairs of pulmonary vein antra using a maximum power of 30-35 watts. If necessary, a complete pulmonary vein isolation was applied. The end point of the procedure was pulmonary vein isolation, including exit block verified by the Lasso catheter.

Clinical Follow-Up

Patients were assessed at 3, 6, and 12 months after radiofrequency ablation. The follow up comprised outpatient visits for clinical examination, electrocardiogram, and 24-hour Holter monitoring to detect asymptomatic atrial fibrillation episodes. Oral antiarrhythmic medication and anticoagulation were taken at least 3 months after radiofrequency ablation and then discontinued if no atrial fibrillation episodes were detected, and if there were no subjective AF episodes. The procedure was considered successful if during the follow up, there were no AF episodes lasting > 30 s up, after a blanking period of 3 months^{19,20}.

Statistical Analysis

Continuous variables were presented as mean \pm SD (parametric data) or as median (interquartile range) (nonparametric data). Categorical variables were expressed as numbers and percentages. The χ^2 , unpaired Student's *t*-test, or Wilcoxon

rank sum tests were used to respectively compare categorical, parametric or non-parametric variable. The statistical software used was SPSS (version 21, SPSS Inc., Armonk, NY, USA).

A logistic regression analysis was applied to identify independent prognostic value of left atrial Tmsv-SD for predicting AF. Age, left atrial volumes, e' , and left atrial Tmsv-SD were also tested as predictors in a multivariate logistic regression analysis. The area under the receiver-operating characteristic (ROC) curve was calculated for left atrial Tmsv-SD. The value closest to the upper left corner of the ROC curve determined the optimal sensitivity and specificity to discriminate between patients with and without arrhythmic events.

Reproducibility was expressed as an intra-class correlation coefficient. The *p*-values (two tailed tests) of < 0.05 were considered significant.

Results

The baseline clinical and echocardiographic characteristics of 88 patients with AF are summarized in Table I. Of these, 67 had no AF recurrence during the follow-up, while 21 had recurrent episodes after one radiofrequency ablation therapy. No difference in age, sex, weight, height, body mass index, comorbidities, duration of AF, and stroke risk were observed between patients with and without recurrence of AF.

The first recurrence episode of AF took place after 8 ± 4 months in the recurrence group. The total follow-up of patients without AF recurrence was 13 ± 2 months.

Table I. Clinical characteristics.

Clinical characteristic	Patients without AF recurrence (n = 67)	Patients with AF recurrence (n = 21)	p
Age (years)	59.75±8.50	54.38±11.71	0.06
Male, n (%)	42 (63)	10 (48)	0.22
Heart rate (bpm)	68.19±13.67	65.48±7.97	0.39
Height (cm)	167.60±7.32	166.67±7.61	0.62
Weight (kg)	73.67±11.04	74.00±7.75	0.90
BSA (m ²)	1.93±0.17	1.92±0.12	0.97
Duration of AF, months	12 (7, 60)	24 (11, 48)	0.13
Hypertension, n (%)	30 (45)	9 (75)	0.88
SBP (mm Hg)	129.27±4.83	128.86±11.39	0.91
DBP (mm Hg)	79.27±10.39	80.48±8.46	0.83
Diabetes mellitus, n (%)	7 (10)	1 (5)	0.68
Coronary artery disease, n (%)	4(6)	2(10)	0.63
Stroke, n (%)	10 (15)	1 (5)	0.45
CHADS2 score for atrial fibrillation stroke risk			
Score 0, n (%)	28 (42)	11 (52)	0.39
Score 1, n (%)	25 (37)	8 (38)	0.95
Score 2, n (%)	8 (12)	0 (0)	0.19
Score 3, n (%)	6 (9)	2 (10)	1.00

Footnote: Data are expressed as mean ± SD (parametric data), median (25%-75%), and numbers (%) (categorical data). AF, atrial fibrillation; BSA, body surface area; DBP, diastolic blood pressure; SBP, systolic blood pressure.

The left atrial volume, left ventricular volume and LVEF of enrolled patients were within the normal range. Patients with AF recurrence showed higher left atrial Tmsv-SD compared

with the patients without recurrence ($p < 0.001$; Table II). There was no difference, though, in left atrial volumes and LAEF between patients with and without AF recurrence (Table II).

Table II. Echocardiography parameters.

Parameter	Patients without AF recurrence (n = 67)	Patients with AF recurrence (n = 21)	p
LVIDd/BSA (mm/m ²)	24.35±2.50	24.42±2.06	0.90
LVIDs/BSA (mm/m ²)	13.95±2.22	13.75±2.38	0.73
LV EDV/BSA (mL/m ²)	45.68±10.85	45.94±6.96	0.92
LV ESV/BSA (mL/m ²)	14.12±3.59	14.87±2.94	0.39
LVEF (%)	68.78±5.83	67.62±3.96	0.40
E velocity (cm/s)	63.90±15.91	70.89±19.33	0.10
DT (ms)	216.40±39.50	221.10±30.63	0.62
A velocity (cm/s)	70.67±17.38	71.34±19.89	0.88
e' (cm/s)	5.91±1.54	6.38±1.81	0.26
E/e'	11.3±3.40	11.6±3.40	0.72
LA GLS (%)	36.81±8.42	37.45±9.95	0.77
LA Tmsv-SD (ms)	12.0±4.83	15.5±5.57	<0.001
LA diameter/BSA (mm/m ²)	35.27±4.71	35.95±4.38	0.56
LA maximum volume/BSA (ml/m ²)	26.97±8.49	27.31±7.17	0.87
LA minimum volume/BSA (ml/m ²)	10.66±5.55	11.05±4.79	0.77
LA volume preA /BSA (ml/m ²)	21.22±7.73	21.18±6.07	0.98
LA total emptying fraction (%)	61.68±12.35	60.47±8.55	0.68
LA passive emptying fraction (%)	22.02±9.02	22.67±7.22	0.76
LA active emptying fraction (%)	50.91±14.66	48.50±11.87	0.50

Footnote: Data are shown as mean ± SD. AF, atrial fibrillation; BSA, body surface area; DT, deceleration time; EDV, end-diastolic volume; EF, ejection fraction; ESV, end-systolic volume; GLS, global longitudinal strain; LA, left atrial; LV, left ventricle; LVIDd, left ventricular internal diameter diastole; LVIDs, left ventricular internal diameter systole; Tmsv-SD, the standard deviation of times to LA minimum volume.

Table III. AF determinants

	Univariate logistic regression			Multivariate logistic regression		
	<i>p</i>	OR	95% CI	<i>p</i>	OR	95% CI
Age (years)	0.22	0.65	0.32, 1.31	0.06	0.38	0.14, 1.04
LA maximum volume/BSA (ml/m ²)	0.65	0.85	0.42, 1.71	0.93	1.04	0.45, 2.39
e' (cm/s)	0.94	1.07	0.20, 5.75	0.16	0.19	0.02, 1.93
LA Tmsv-SD (ms)	<0.001	6.19	2.07, 18.55	<0.001	7.14	2.32, 22.0

Footnote: BSA, body surface area; CI, confidence interval; LA, left atrial; MD, mechanical dispersion; OR, odds ratio; AF, atrial fibrillation.

Similarly, there was no difference in left ventricular dimensions or volumes, or left ventricular diastolic function parameters, including mitral early and late diastole velocities, their ratio, deceleration time, early diastolic velocity, and early diastole/early diastolic velocity ratio between the two groups (Table II).

The left atrial Tmsv-SD was found to be an independent predictor of AF in a multivariate logistic regression analysis (Table III). The ROC analysis demonstrated that the left atrial Tmsv-SD of 14.5 msec was the optimal cut-off value to discriminate between patients with recurrent AF and patients without AF recurrence (area under the curve = 0.88; Figure 3). The sensitivity and specificity were, respectively, 95.2% and 68.7% (Figure 3).

The intra- and inter-observer intra-class correlation was performed in 10 randomly selected patients. There was good reproducibility (respec-

tively, *p* = 0.933 and 0.763) of left atrial Tmsv-SD measurements.

Discussion

Here we report that (1) patients with recurrent AF after radiofrequency ablation demonstrate greater left atrial Tmsv-SD compared with patients without such recurrence, (2) left atrial Tmsv-SD measured by real-time 3DE is useful to predict AF recurrence, normal left ventricular function, and normal or mildly enlarged left atrium, and (3) indices of left atrial volumes and functions do not correlate with the recurrence of AF after radiofrequency ablation.

These results suggested that mechanical dyssynchrony of left atrium manifests in early stages of left atrium remodeling in patients with AF. Previous reports showed that left atrial mechanical dyssynchrony and disorder may arise from the regional left atrial tissue scar and fibrosis. These morphological changes, as documented by delayed-enhancement magnetic resonance imaging, are closely related to AF recurrence⁶⁻⁸. The left atrial mechanical dyssynchrony can be used to predict the recurrence of AF and the onset of new AF in patients with heart failure, in both cases using tissue doppler imaging and 2D STE^{9,21-23}.

There are, however, limitations in the clinical practice because of angle dependence in Tissue Doppler Imaging and one plane assessment in 2D STE. Theoretically, 3D STE has advantage over Tissue Doppler Imaging and 2D STE in assessment of left atrial mechanical dyssynchrony. This is confirmed by the recent studies. Mochizuki et al²⁴ showed that assessment of left atrial strain and dyssynchrony by 3D STE was feasible, reproducible, and more advantageous compared with the assessment by 2D STE. Kobayashi et al²⁵ demonstrated that left atrial strain was lower and dyssynchrony was higher, compared with con-

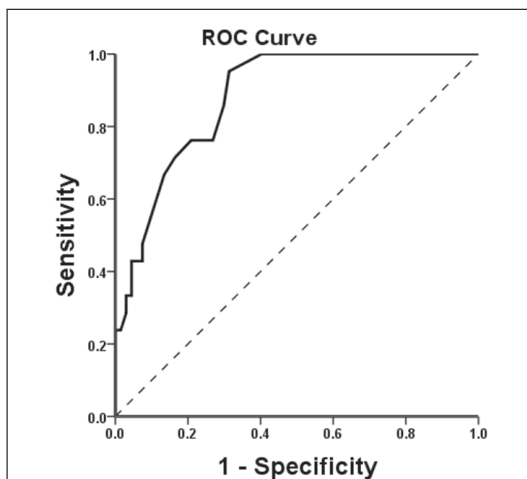


Figure 3. The Receiver-Operator Curve (ROC) analyses for the ability of left atrial Tmsv-SD (the standard deviation of times to left atrial minimum volume) to discriminate patients with or without recurrence of atrial fibrillation recurrence after radiofrequency ablation.

trols, in patients with AF, when assessed by 3D STE, and that left atrial dyssynchrony improved 3 months following radiofrequency ablation. Our study showed that left atrial dyssynchrony significantly correlated with the recurrence of AF after radiofrequency ablation. There was not difference in left atrial volumes, LAEFs and left atrial global longitudinal strain between patients with or without recurrence. Yet, left atrial Tmsv-SD of recurrent patients was much higher than in patients without this recurrence. It is confirmed that left atrial contractile remodeling occurs earlier than structural remodeling, and that left atrial dyssynchrony assessed by real-time 3DE is more accurate in predicting AF recurrence than assessment of left atrial volumes and LAEF. We further think that 3D STE can predict the recurrence of AF after radiofrequency ablation better than 2D STE.

Sarvari et al²¹ investigated AF recurrence in patients with normal left ventricular function, and normal or mildly enlarged left atrium. They found that left atrial mechanical dispersion estimated by 2D STE was more pronounced in patients with AF recurrence compared with those without such recurrence, and that left atrial mechanical dispersion could predict AF recurrence. However, there is still disagreement whether an association exists between left atrial dyssynchrony and AF recurrence. Mochizuki et al¹⁴ reported that left atrial strain determined by 3D STE was a better predictor of AF recurrence than when determined by 2D STE. Yet the association of AF recurrence with indices of left atrial synchrony and volume was not significant.

The mathematical formulas for left atrial dyssynchrony measurement were different in previous studies. Specifically, left atrial dyssynchrony was quantified by the standard deviation of time to peak strain of 16 LA segments from end-diastole (the R wave on the electrocardiogram) by area tracking of 3D STE. As an index of left atrial dyssynchrony, standard deviation of time to peak strain of the area tracking was computed and expressed as a percentage of the R-R interval^{14,15}. Sarvari et al²¹ measured the duration of the left atrial contraction from the peak of the P wave on electrocardiography to the maximum left atrial shortening by strain. Standard deviation of contraction durations in 18 left atrial segments was defined as left atrial dyssynchrony. In our study, we used a method similar to that applied in a previous study¹⁶. The left atrial 3D endocardial border was tracked throughout the cardiac cycle to provide a mathematical model of left atrial volume. This

volume was segmented into 16 subvolumes corresponding to the standard myocardial segments to derive volume curves for each time. The left atrial Tmsv-SD was defined as a standard deviation of this timing. Wang et al²⁶ reported that left atrial wall is thin (about 3-5 mm). Thus, the number of speckles in left atrial wall is significantly less than in the left ventricular wall, and the accuracy of left atrial strain assessed by both 2D and 3D STE can also be affected. In theory, the thinness of the left atrial wall has a smaller impact on left atrial dyssynchrony measured by left atrial volume time curves by 2D or 3D STE.

At present, left atrial dyssynchrony has been quantified in a different phase, including ventricular systole and atrial active systole, respectively representing left atrial reservoir function and bumping function^{14,21,24,25}. Our study focused on left atrial dyssynchrony during atrial systole. Cho et al²⁷ reported that left atrial strain determined by 3D STE was a better predictor of AF recurrence than that determined by 2D STE. Yet, the association of recurrence with indices of left atrial synchrony and volume was not significant. For this reason, we think there is left atrial dyssynchrony not only in the left atrial reservoir phase, but also in the active contraction phase.

The Real-time 3DE can quickly assess left atrial dyssynchrony, which enabled noninvasive estimation of left atrial electrical remodeling and substrate, and therefore reflect the mechanism for increased risk of AF recurrence after radiofrequency ablation.

We demonstrate that left atrial Tmsv-SD assessment by Real time 3DE can predict AF recurrence in patients with normal left ventricular (function, and normal or mildly enlarged left atrium after radiofrequency ablation. This assessment is more accurate compared with that by 2D STE. Therefore, the left atrial Tmsv-SD may be useful to guide the medication, with the focus on long-term use of the antiarrhythmia and anticoagulant drugs after radiofrequency ablation.

Previous reports^{9,22,23} assessed the merit of left atrial enlargement and reduced left atrial strain in predicting AF recurrence in these patients. We observed that left atrial dyssynchrony exists in patients with AF before left atrium becomes dilated, and left atrial strain decreases. Certainly, more investigations is needed to clarify whether earlier and more aggressive treatment is necessary to slow the progression of atrial dysfunction, reduce paroxysmal AF recurrence, and prevent the development of permanent AF.

Some limitations of our study may need to be mentioned. For example, the data of left atrial dyssynchrony after radiofrequency ablation were not included in our study. Therefore, we did not compare the changes in the left atrial dyssynchrony. In addition, patients with heart failure, structural heart disease, and increased left atrial size were excluded in this study. Clinical implications of these findings remain to be determined. Also, we applied the Real-time 3DE analysis software designed for left ventricular analysis to left atrial analysis. The relatively low volume rates in time resolution and spatial resolution of real time 3DE affect the accurate identification of left atrial dyssynchrony. In addition, our patient population did not include patients with persistent and permanent AF. Also, the reservoir and conduit phases of left atrium were not assessed, as we focused on the active atrial systole phase. Finally, this work was a small, single-center study with a relatively short follow-up period. Further larger scale, multicenter researches with longer follow-up times are needed to confirm our results.

Conclusions

We found that assessment of the left atrial Tmsv-SD by Real-time 3DE is more accurate, compared with the left atrial strain assessed by 2D STE, in predicting AF recurrence in patients with normal left ventricular function, and normal or mildly enlarged left atrium. Therefore, the left atrial Tmsv-SD assessment by real-time 3DE is a useful predictor of AF recurrence.

Conflict of Interest

The Authors declare that they have no conflict of interests.

References

- 1) FREEDMAN JE, GERSH BJ. Atrial fibrillation and stroke prevention in aging patients: what's good can be even better. *Circulation* 2014; 130: 129-131.
- 2) LAKSHMINARAYAN K, ANDERSON DC, HERZOG CA, QURESHI AI. Clinical epidemiology of atrial fibrillation and related cerebrovascular events in the United States. *Neurologist* 2008; 14: 143-150.
- 3) HEALEY JS, CONNOLLY SJ, GOLD MR, ISRAEL CW, VAN GELDER IC, CAPUCCI A, LAU CP, FAIN E, YANG S, BAILLEUL C, MORILLO CA, CARLSON M, THEMELES E, KAUFMAN ES, HOHNLOSER SH. Subclinical atrial fibrillation and the risk of stroke. *N Engl J Med* 2012; 366: 120-129.
- 4) ZONI BERISSO M, LANDOLINA M, ERMINI G, PARRETI D, ZINGARINI GL, DEGLI ESPOSTI L, CRICELLI C, BORIANI G. The cost of atrial fibrillation in Italy: a five-year analysis of healthcare expenditure in the general population. From the Italian Survey of Atrial Fibrillation Management (ISAF) study. *Eur Rev Med Pharmacol Sci* 2017; 21: 175-183.
- 5) KNECHT S, STICHERLING C, VON FELTEN S, CONEN D, SCHAEER B, AMMANN P, ALTMANN D, OSSWALD S, KUHNE M. Long-term comparison of cryoballoon and radiofrequency ablation of paroxysmal atrial fibrillation: a propensity score matched analysis. *Int J Cardiol* 2014; 176: 645-650.
- 6) MAHNKOPF C, BADGER TJ, BURGON NS, DACCARETT M, HASLAM TS, BADGER CT, MCGANN CJ, AKOUM N, KHOLMOVSKI E, MACLEOD RS, MARROUCHE NF. Evaluation of the left atrial substrate in patients with lone atrial fibrillation using delayed-enhanced MRI: implications for disease progression and response to catheter ablation. *Heart Rhythm* 2010; 7: 1475-1481.
- 7) COCHET H, MOURIES A, NIVET H, SACHER F, DERVAL N, DENIS A, MERLE M, RELAN J, HOCINI M, HAISSAGUERRE M, LAURENT F, MONTAUDON M, JAIS P. Age, atrial fibrillation, and structural heart disease are the main determinants of left atrial fibrosis detected by delayed-enhanced magnetic resonance imaging in a general cardiology population. *J Cardiovasc Electrophysiol* 2015; 26: 484-492.
- 8) MARROUCHE NF, WILBER D, HINDRICKS G, JAIS P, AKOUM N, MARCHLINSKI F, KHOLMOVSKI E, BURGON N, HU N, MONT L, DENEKE T, DUYSCHAEVER M, NEUMANN T, MANSOUR M, MAHNKOPF C, HERWEG B, DAOUD E, WISSNER E, BANSMANN P, BRACHMANN J. Association of atrial tissue fibrosis identified by delayed enhancement MRI and atrial fibrillation catheter ablation: the DECAAF study. *JAMA* 2014; 311: 498-506.
- 8) CAMELI M, MANDOLI GE, LOIACONO F, SPARLA S, IARDINO E, MONDILLO S. Left atrial strain: a useful index in atrial fibrillation. *Int J Cardiol* 2016; 220: 208-213.
- 10) MONTERRAT S, GABRIELLI L, BIJNENS B, BORRAS R, BERRUEZO A, POYATOS S, BRUGADA J, MONT L, SITGES M. Left atrial deformation predicts success of first and second percutaneous atrial fibrillation ablation. *Heart Rhythm* 2015; 12: 11-18.
- 11) MOTOKI H, NEGISHI K, KUSUNOSE K, POPOVIC ZB, BHARGAVA M, WAZNI OM, SALIBA WI, CHUNG MK, MARWICK TH, KLEIN AL. Global left atrial strain in the prediction of sinus rhythm maintenance after catheter ablation for atrial fibrillation. *J Am Soc Echocardiogr* 2014; 27: 1184-1192.
- 12) ANWAR AM, SOLIMAN OI, GELEUNSE ML, NEMES A, VLETTER WB, TEN CATE FJ. Assessment of left atrial volume and function by real-time three-dimensional echocardiography. *Int J Cardiol* 2008; 123: 155-161.
- 13) MIYASAKA Y, TSUJIMOTO S, MAEBA H, YUASA F, TAKEHANA K, DOTE K, IWASAKA T. Left atrial volume by real-time three-dimensional echocardiography: validation by 64-slice multidetector computed tomography. *J Am Soc Echocardiogr* 2011; 24: 680-686.
- 14) MOCHIZUKI A, YUDA S, FUJITO T, KAWAMUKAI M, MURANAKA A, NAGAHARA D, SHIMOSHIGE S, HASHIMOTO A, MIURA T. Left atrial strain assessed by three-dimensional speckle tracking echocardiography predicts atrial fibrillation recurrence after catheter ablation in patients with paroxysmal atrial fibrillation. *J Echocardiogr* 2017; 15: 79-87.

- 15) CHO KI, KIM BJ, CHA TJ, HEO JH, KIM HS, LEE JW. Impact of duration and dosage of statin treatment and epicardial fat thickness on the recurrence of atrial fibrillation after electrical cardioversion. *Heart Vessels* 2015; 30: 490-497.
- 16) DENG Y, GUO SL, SU HY, WANG Q, TAN Z, WU J, ZHANG D. Left atrial asynchrony and mechanical function in patients with mitral stenosis before and immediately after percutaneous balloon mitral valvuloplasty: a real time three-dimensional echocardiography study. *Echocardiography* 2015; 32: 291-301.
- 17) JANUARY CT, WANN LS, ALPERT JS, CALKINS H, CIGARROA JE, CLEVELAND JC, JR., CONTI JB, ELLINOR PT, EZEKOWITZ MD, FIELD ME, MURRAY KT, SACCO RL, STEVENSON WG, TCHOU PJ, TRACY CM, YANCY CW. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines and the Heart Rhythm Society. *Circulation* 2014; 130: 2071-2104.
- 18) AZAR F, PEREZ DE ISLA L, MORENO M, LANDAETA A, REFOYO E, LOPEZ FERNANDEZ T, MACAYA C, ZAMORANO J. Three-dimensional echocardiographic assessment of left atrial size and function and the normal range of asynchrony in healthy individuals. *Rev Esp Cardiol* 2009; 62: 816-819.
- 19) CALKINS H, KUCK KH, CAPPATO R, BRUGADA J, CAMM AJ, CHEN SA, CRIJNS HJ, DAMIANO RJ, JR., DAVIES DW, DIMARCO J, EDGERTON J, ELLENBOGEN K, EZEKOWITZ MD, HAINES DE, HAISSAGUERRE M, HINDRICKS G, IESAKA Y, JACKMAN W, JALIFE J, JAIS P, KALMAN J, KEANE D, KIM YH, KIRCHHOF P, KLEIN G, KOTTKAMP H, KUMAGAI K, LINDSAY BD, MANSOUR M, MARCHLINSKI FE, MCCARTHY PM, MONT JL, MORADY F, NADEMANEE K, NAKAGAWA H, NATALE A, NATTEL S, PACKER DL, PAPPONE C, PRYSTOWSKY E, RAVIELE A, REDDY V, RUSKIN JN, SHEMIN RJ, TSAO HM, WILBER D. 2012 HRS/EHRA/ECAS expert consensus statement on catheter and surgical ablation of atrial fibrillation: recommendations for patient selection, procedural techniques, patient management and follow-up, definitions, endpoints, and research trial design. *J Interv Card Electrophysiol* 2012; 33: 171-257.
- 20) CAMM AJ, KIRCHHOF P, LIP GY, SCHOTTEN U, SAVELIEVA I, ERNST S, VAN GELDER IC, AL-ATTAR N, HINDRICKS G, PRENDERGAST B, HEIDBUCHEL H, ALFIERI O, ANGELINI A, ATAR D, COLONNA P, DE CATERINA R, DE SUTTER J, GOETTE A, GORENEK B, HELDAL M, HOHLÖSER SH, KOLH P, LE HEUZEY JY, PONIKOWSKI P, RUTTEN FH. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). *Europace* 2010; 12: 1360-1420.
- 21) SARVARI SI, HAUGAA KH, STOKKE TM, ANSARI HZ, LEREN IS, HEGBOM F, SMISETH OA, EDVARDSEN T. Strain echocardiographic assessment of left atrial function predicts recurrence of atrial fibrillation. *Eur Heart J Cardiovasc Imaging* 2016; 17: 660-667.
- 22) MA XX, BOLDT LH, ZHANG YL, ZHU MR, HU B, PARWANI A, BELYAVSKIY E, RADHA KRISHNAN AK, KRISPER M, KOHNCKE C, OSMANOGLU E, KROPF M, LACOUR P, BLASCHKE F, EDELMANN F, TSCHOPE C, HAVERKAMP W, PIESKE-KRAIGHNER E, PIESKE B, MORRIS DA. Clinical relevance of left atrial strain to predict recurrence of atrial fibrillation after catheter ablation: a meta-analysis. *Echocardiography* 2016; 33: 724-733.
- 23) YASUDA R, MURATA M, ROBERTS R, TOKUDA H, MINAKATA Y, SUZUKI K, TSURUTA H, KIMURA T, NISHIYAMA N, FUKUMOTO K, AIZAWA Y, TANIMOTO K, TAKATSUKI S, ABE T, FUKUDA K. Left atrial strain is a powerful predictor of atrial fibrillation recurrence after catheter ablation: study of a heterogeneous population with sinus rhythm or atrial fibrillation. *Eur Heart J Cardiovasc Imaging* 2015; 16: 1008-1014.
- 24) MOCHIZUKI A, YUDA S, OI Y, KAWAMUKAI M, NISHIDA J, KOUZU H, MURANAKA A, KOKUBU N, SHIMOSHIGE S, HASHIMOTO A, TSUCHIHASHI K, WATANABE N, MIURA T. Assessment of left atrial deformation and synchrony by three-dimensional speckle-tracking echocardiography: comparative studies in healthy subjects and patients with atrial fibrillation. *J Am Soc Echocardiogr* 2013; 26: 165-174.
- 25) KOBAYASHI Y, OKURA H, KOBAYASHI Y, OKAWA K, BANBA K, HIROHATA A, TAMADA T, OBASE K, HAYASHIDA A, YOSHIDA K. Assessment of atrial synchrony in paroxysmal atrial fibrillation and impact of pulmonary vein isolation for atrial dyssynchrony and global strain by three-dimensional strain echocardiography. *J Am Soc Echocardiogr* 2014; 27: 1193-1199.
- 26) WANG K, HO SY, GIBSON DG, ANDERSON RH. Architecture of atrial musculature in humans. *Br Heart J* 1995; 73: 559-565.
- 27) CHO GY, JO SH, KIM MK, KIM HS, PARK WJ, CHOI YJ, HONG KS, OH DJ, RHIM CY. Left atrial dyssynchrony assessed by strain imaging in predicting future development of atrial fibrillation in patients with heart failure. *Int J Cardiol* 2009; 134: 336-341.