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ORIGINAL PAPER

Successful radiofrequency catheter ablation of atrial fibrillation is associated with improvement in left ventricular energy loss and mechanics abnormalities

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Abstract
Dissipative energy loss (EL), an index of inefficient blood flow, has not been studied in patients with atrial fibrillation (AF). We therefore assessed the effect of AF and of successful catheter ablation on left ventricular (LV) EL and global longitudinal strain (GLS) to explore the effect of inefficient blood flow on LV remodeling. In 53 patients undergoing catheter ablation for AF (AF group), LV EL (in mW/m) was evaluated by vector flow mapping (VFM) during systole (ELsys), early diastole (ELed) and atrial contraction phase (ELac), and GLS was calculated by two-dimensional tissue tracking (2DTT). Of the 53 patients, 37 patients who sustained sinus rhythm and completed echocardiographic evaluation at baseline and at 3 and 6 months follow-up were examined for change in EL and GLS. The latter parameters also were assessed in 44 age- and sex-matched controls. At baseline in AF group, ELsys and ELed were significantly higher (3.97 ± 2.29 vs. 3.14 ± 1.01; and 9.22 ± 5.01 vs. 3.89 ± 1.51; both $P < 0.05$, respectively), and GLS was lower (-16.66 ± 3.50 vs. -19.95 ± 2.40, $P < 0.05$) than in controls. During follow-up after catheter ablation, ELsys and ELed significantly improved at 3 months, and almost normalized at 6 months (both $P < 0.05$); GLS also improved significantly ($P < 0.05$). In multivariate logistic regression analysis, ELed was the only independent predictor for maintenance of sinus rhythm at 1-year follow-up (hazard ratio, 1.254; 95% confidence interval 1.073–1.467). VFM and 2DTT revealed impaired LV EL and GLS in patients with AF. Successful catheter ablation appeared to ameliorate impairment in intraventricular flow and mechanics.

Keywords Energy loss · Vector flow mapping · Atrial fibrillation · Strain · Catheter ablation

Introduction

Atrial fibrillation (AF), the most frequent among long lasting arrhythmias, is associated with adverse cardiovascular outcomes, including thromboembolic stroke, heart failure and higher mortality [1]. Radiofrequency catheter ablation (RFCA) is superior to drug therapy in suppressing AF refractory to at least one antiarrhythmic drug and improves patient's symptoms and quality of life [2]. Successful RFCA promotes subsequent left atrial (LA) and left ventricular (LV) remodeling which may contribute to the aforementioned benefits; however, the exact underlying mechanisms remain undefined, especially in terms of intracardiac flow pattern which via its effects on tissue might substantially impair remodeling onset [3].

Normal intracardiac flow pattern boosts inflow into ventricles, limits energy dissipation, preserves momentum, and redirects flow outwards [4]. Ischemic heart disease and valvular heart disease interfere with the normal flow pattern thereby increasing dissipative energy loss (EL) and affecting disease outcome [5]. Vector flow mapping (VFM), a new echocardiographic technology, allows visualization of the intracardiac flow velocity vector using color Doppler and speckle tracking measurement, and to quantify flow EL [6]. In addition, LV global longitudinal strain (GLS) allows

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detection of more subtle abnormalities in LV systolic function [7].

Accordingly, the present study evaluated: (1) the difference in LV EL during cardiac cycle by VFM and in GLS by two-dimensional tissue tracking (2DTT) in patients with AF undergoing RFCA; and (2) the effects of successful RFCA for AF on LV EL and GLS.

Methods

Study design

The present study was approved by the institutional Ethics Committee, and written informed consent was obtained from all participants. Between May 2016 and December 2016, 53 patients with AF aged 35–76 years old (AF group) who underwent RFCA at our hospital, and 44 age- and sex-matched healthy volunteers (controls) aged 32–73 years old, were enrolled. Study inclusion criteria were paroxysmal AF (PaAF) in sinus rhythm before ablation, or persistent AF (PerAF) in sinus rhythm within 72 h after ablation. Exclusion criteria were poor quality echocardiographic images, inadequately controlled blood pressure (blood pressure > 140/90 mmHg) and blood glucose (fasting glucose > 7.0 mmol/L), myocardial infarction, significant valvular stenosis or regurgitation, rheumatic disease, congenital heart disease, hyperthyroidism, asthma, neoplastic disease, renal failure and hepatic cirrhosis.

Baseline information, including body weight and height for computing BSA and blood pressure (BP), was collected. For AF, pertinent information was collected from medical histories to calculate the CHA_2DS_2-VASc score [1]. Laboratory tests were performed for all participants, including determination of levels of total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol and fasting glucose.

Electrophysiological mapping and radiofrequency catheter ablation

The procedure was performed by the same doctor. A circular pulmonary vein (PV) mapping catheter (Lasso, Biosense-Webster Inc.) was used for 3D electroanatomical map (NavX, St. Jude Medical Inc.; CARTO 3, Johnson and Johnson, Inc.). An open-irrigation 3.5 mm-tip deflectable catheter (Celsius, Johnson and Johnson, Inc.; Coolflex, St. Jude Medical Inc.; 30–35 W, 47 °C) was used for RFCA. All patients underwent circumferential PV isolation, and patients with PerAF routinely underwent bidirectional blocks of isthmus and roof lines. Operators could opt to perform additional ablation of non-PV foci, complex atrial fractionated electrograms or the superior vena cava, and after that, electrical cardioversion would be performed if sinus rhythm was not attained [8].

Post-ablation management and follow-up

After RFCA, patients were discharged on anti-arrhythmic drugs, namely oral amiodarone 0.2 g/day or propafenone 0.45 g/day for 3 months, and other cardiovascular drugs. Patients were followed up at the outpatient clinic at 1, 3, 6, and 12 months after the procedure with evaluation by electrocardiography and 24 h-Holter monitoring. During follow-up, patients underwent echocardiographic evaluations at 3 and 6 months if without atrial tachyarrhythmia recurrence, which was defined as atrial tachyarrhythmia developing after 3 months and lasting at least 30 s.

Transthoracic echocardiography

All patients underwent transthoracic echocardiography (TTE) prior to RFCA for PaAF patients and 24–72 h after RFCA for PerAF patients, and at 3 and 6 months after procedure for patients with sustained sinus rhythm at follow-up. TTE was performed using a UST-52105 probe (1–5 MHz) on a ProSound F75 ultrasound device (Hitachi Aloka Medical Ltd., Tokyo, Japan), and following recommended procedure [9]. Conventional LV systolic and diastolic parameters were measured. The LA maximal volume index (LAVI), LV end-diastolic volume (LVEDV), LV end-systolic volume (LVESV), and LV ejection fraction (LVEF) were calculated using the biplane Simpson's method. Pulsed-wave Doppler was used to measure transmitral flow velocities of early diastolic (E) and atrial contraction (A) phase of LV filling, calculating the deceleration time (DT) and E/A ratio. Tissue Doppler measurement was used to determine the e′, and to calculate the E/e′ ratio. Two-dimensional (2D) cineloop images in A4C, A2C and A3C, set to at least 55 frames/s, were stored for 2DTT; 2D color Doppler cineloop images with VFM configuration in A4C, set to at least 22 frames/s, were stored for calculating EL. All echocardiographic parameters were acquired as the average value of three consecutive cardiac cycles.

Analysis of energy loss

The stored 2D color Doppler cineloop images were measured with VFM analysis software (DAS-RS1, Hitachi Aloka Medical Ltd, Tokyo, Japan). The software calculated the velocity and obtained intracardiac flow EL based on the equation [6]. Dealiasing was manually performed for those exhibiting aliasing. The endocardial border was manually traced at the maximal volumes of LV, and then automatically obtained for the remaining frames. After automatic tracing, LV EL was measured at every frame during one

cardiac cycle and then summed up as total EL (measurement in mW/m) (Fig. 1). The average EL was calculated by dividing the total EL by the number of frames. EL was determined during systole (ELsys), early diastole (ELed) and atrial contraction (ELac).

Analysis of LV global longitudinal strain

2DTT analysis was performed using the same software (DAS-RS1, Hitachi Aloka Medical Ltd, Tokyo, Japan). The endocardial border was traced as described above. The software automatically generated curves of the LV longitudinal strain (Fig. 2). The peak GLS was measured in A4C, A2C and A3C, and the average GLS was calculated using three views.

Reproducibility

In ten randomly selected subjects, intra-observer variation was determined at least 2 weeks after the initial analysis. Inter-observer variation was evaluated with the same quantitative methods by a blinded second observer.

Statistical analysis

Continuous variables are expressed as mean ± standard deviation (SD), and were compared using the Student's or the paired sample *t* test. Categorical variables are expressed as number and percentage, and were compared using the χ^2 test. Univariate and multivariate regression analyses (significance level set at $P < 0.10$ for inclusion into model) were performed to determine independent sociodemographic, clinical, GLS, and echocardiographic parameters associated with: (1) EL at baseline in AF group; (2) EL difference between baseline and 6 months after successful RFCA; and (3) atrial tachyarrhythmia recurrence during 1-year follow-up. All data analyses were performed using SPSS version 22.0 (IBM Corporation, Armonk, NY). The significance level was set at $P < 0.05$.

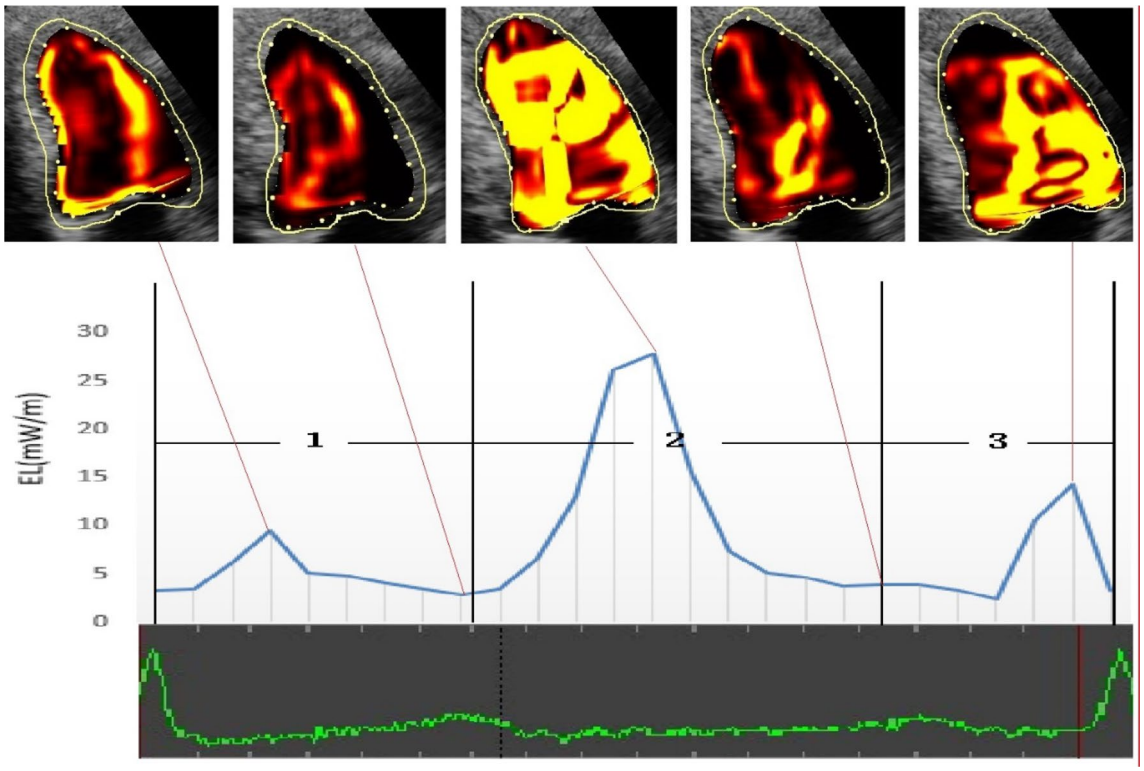

Fig. 1 Diagram of the curve and images of EL in a patient. The upper graph depicts EL images. Brightness represents the magnitude of EL. From left, the time phases are mid-systole, isovolumetric relaxation phase, early diastole, mid-diastole and atrial contraction phase. The lower graph depicts the change of EL during one cardiac cycle which is divided into three phases, where 1 represents systole (from the peak of the R wave to the peak of the T wave); 2 represents early diastole (from the peak of the T wave to the onset of the P wave); and 3 represents atrial contraction phase (from the onset of the P wave to the peak of the R wave). The peak during systole is because of flow acceleration through the left ventricular outflow tract. The peak during early diastole is originated by the dissipative transmitral inflow. The peak of atrial contraction phase is generated by the atrial contraction

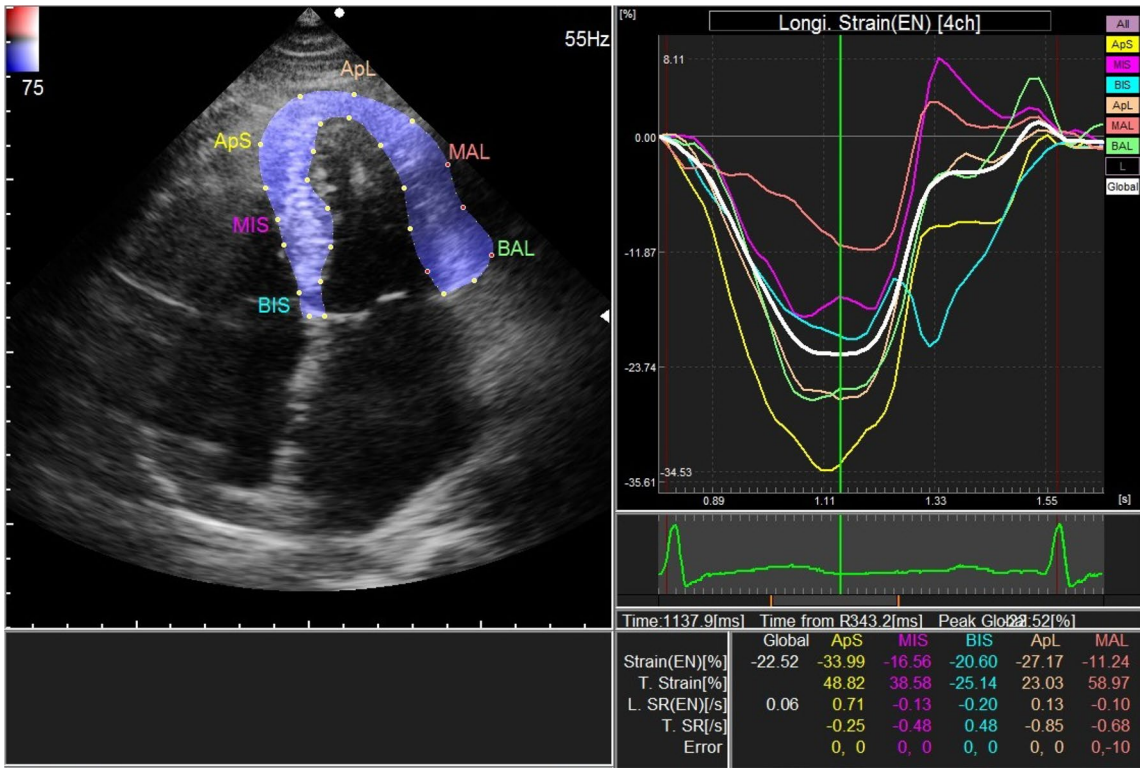

Fig. 2 LV global longitudinal strain was measured at the peak of its curve

Results

Out of the 53 patients in AF group, 13 patients developed atrial tachyarrhythmia recurrence and 3 patients were lost to follow-up. Therefore, 37 patients with sustained sinus rhythm and who completed echocardiographic examination at baseline and at 3 and 6 months post RFCA were included for evaluation of change of EL and GLS during follow-up. Baseline characteristics, except for BSA, were similarly distributed between patients in AF group and controls (Table 1). The majority of patients had PaAF (34 patients, 64.20%), with mean AF duration (from initial diagnosis to ablation) of 3.34 ± 5.18 years. The CHA_2DS_2-VASc score was 2.04 ± 1.41. Pertinent cardiovascular comorbidities were congestive heart failure (2/53, 3.77%), hypertension (29/53, 54.72%), diabetes (13/53, 24.53%), stroke (4/53, 7.55%) and vascular disease (20/53, 37.74%). During follow-up, 20 (37.74%) patients were on angiotensin converting enzyme inhibitors or angiotensin II receptor blockers (ACEI/ARB), and 23 (43.40%) on statins.

Table 1 General characteristics of patients with AF and controls

	Controls (n = 44)	AF group (n = 53)	*P* value
Male (%)	61.36%	64.15%	0.777
Age (years)	55.6 ± 10.0	58.4 ± 9.80	0.172
HR (bpm)	71.7 ± 9.8	67.6 ± 11.6	0.063
BSA (m^2)	1.75 ± 0.15	1.87 ± 0.15	< 0.001
SBP (mmHg)	121.8 ± 11.5	123.7 ± 9.7	0.364
DBP (mmHg)	74.3 ± 8.2	72.9 ± 6.6	0.378
TC (mmol/L)	4.18 ± 0.48	4.09 ± 0.92	0.548
TG (mmol/L)	1.40 ± 0.40	1.50 ± 0.74	0.370
HDL (mmol/L)	1.18 ± 0.25	1.17 ± 0.25	0.823
LDL (mmol/L)	2.47 ± 0.59	2.66 ± 0.68	0.154
Plasma glucose	5.19 ± 0.74	5.13 ± 0.93	0.718

Data are shown as mean ± standard deviation

BSA body surface area, *DBP* diastolic blood pressure, *HDL* high-density lipoprotein, *HR* heart rhythm, *LDL* low-density lipoprotein, *SBP* systolic blood pressure, *TC* total cholesterol, *TG* triglycerides

Echocardiographic changes during follow-up

Comparisons of echocardiographic parameters between controls and AF group are shown in Table 2, while Table 3 lists changes in said parameters during follow-up. Briefly, in AF group vs. controls, LA diameter and LAVI were larger (both $P < 0.001$), with slight improvement during follow-up reaching a significant difference at 6 months (both $P < 0.05$). There also was significant impairment in LVEDV and LVESV (both $P < 0.001$), which improved at 6 months relative to baseline (all $P < 0.05$). In AF group, LVEF was lower

Table 2 EL, GLS and echocardiographic parameters in controls and AF group

	Controls (n = 44)	AF group (n = 53)	*P* value
ELsys (mW/m)	3.14 ± 1.01	3.97 ± 2.29	0.022
ELed (mW/m)	3.89 ± 1.51	9.22 ± 5.01	< 0.001
ELac (mW/m)	4.15 ± 1.94	4.33 ± 2.69	0.708
GLS (%)	19.95 ± 2.40	16.66 ± 3.50	< 0.001
LAD (mm)	31.58 ± 3.11	40.19 ± 5.28	< 0.001
LAVI (mL/m^2)	25.34 ± 5.38	36.49 ± 10.45	< 0.001
LVEDV (mL)	80.43 ± 13.23	93.55 ± 18.80	< 0.001
LVESV (mL)	30.59 ± 6.67	37.91 ± 10.13	< 0.001
LVEF (%)	62.1 ± 5.6	59.7 ± 5.0	0.049
E (cm/s)	83.28 ± 14.06	87.04 ± 27.68	0.391
A (cm/s)	72.68 ± 12.30	64.17 ± 24.43	0.029
E/A	1.17 ± 0.24	1.70 ± 1.23	0.004
e′ (cm/s)	12.94 ± 2.60	9.66 ± 2.18	< 0.001
E/e′	6.65 ± 1.52	9.40 ± 3.54	< 0.001
DT (ms)	193.89 ± 23.85	178.59 ± 38.34	0.019

Data are shown as mean ± standard deviation

DT deceleration time, *EL* energy loss, *ELsys* EL during systole, *ELed* EL during early diastole, *ELac* EL during atrial contraction, *GLS* global longitudinal strain, *LA* left atrial, *LV* left ventricular, *LAD* LA diameter, *LAVI* LA volume index, *LVEDV* LV end-diastolic volume, *LVESV* LV end-systolic volume, *LVEF* LV ejection fraction

than in controls ($P = 0.049$), and decreased numerically but not significantly from baseline to 6 months ($P = 0.053$). As for diastolic function, there was marked impairment in E/A and DT (both $P < 0.05$), with normalization during follow-up (both $P > 0.05$ relative to controls).

LV energy loss and mechanics

Figure 1 illustrates a typical diagram of EL in a patient during a cardiac cycle, and Supplementary Table 1 compares LV EL and GLS between patients with PaAF and those with PerAF. ELed in patients with PerAF was numerically but not significantly higher than in patients with PaAF ($P = 0.052$). Table 2 summarizes LV EL and GLS in controls and AF group, and Table 3 the changes in LV EL and GLS during follow-up after successful RFCA. Briefly, ELsys and ELed in AF group were significantly higher than in controls (both $P < 0.05$), improved at 3 months follow-up, and almost normalized at 6 months follow-up after successful RFCA. In addition, compared with controls, GLS was significantly lower in AF group ($P < 0.001$), and improved from baseline to 3 months ($P = 0.005$) (Fig. 3).

Regression analysis

To determine independent predictors of EL, factors in AF group reaching significance level of < 0.10

Table 3 EL, GLS and echocardiographic parameters during follow-up

	Controls (n = 44)	AF at baseline (n = 37)	AF at 3 months (n = 37)	AF at 6 months (n = 37)
ELsys (mW/m)	3.14 ± 1.01	4.18 ± 2.36*	3.13 ± 1.15$^{\#}$	3.09 ± 1.12$^{\#}$
ELed (mW/m)	3.89 ± 1.51	8.99 ± 3.84*	5.19 ± 2.67$^{*,\#}$	4.24 ± 1.74$^{\#,\&}$
ELac (mW/m)	4.15 ± 1.94	4.29 ± 2.67	3.71 ± 2.50	3.63 ± 2.57
GLS (%)	19.95 ± 2.40	16.82 ± 3.79*	18.01 ± 3.39$^{*,\#}$	18.49 ± 3.40$^{*,\#}$
LAD (mm)	31.58 ± 3.11	39.96 ± 5.52*	38.36 ± 4.70$^{*,\#}$	37.46 ± 4.72$^{*,\#,\&}$
LAVI (mL/m^2)	25.34 ± 5.38	36.59 ± 10.61*	34.20 ± 11.55*	33.59 ± 10.43$^{*,\#}$
LVEDV (mL)	80.43 ± 13.23	94.24 ± 18.59*	92.62 ± 18.25*	89.62 ± 17.95$^{*,\#}$
LVESV (mL)	30.59 ± 6.67	37.62 ± 9.91*	37.11 ± 12.70*	37.93 ± 11.11*
LVEF (%)	62.1 ± 5.6	60.5 ± 5.0	60.7 ± 7.7	58.4 ± 6.2$^{*,\&}$
E (cm/s)	83.28 ± 14.06	84.64 ± 26.46	75.26 ± 18.12$^{*,\#}$	72.63 ± 18.62$^{*,\#}$
A (cm/s)	72.68 ± 12.30	63.49 ± 22.68*	64.54 ± 17.21*	66.79 ± 15.33
E/A	1.17 ± 0.24	1.56 ± 0.88*	1.21 ± 0.29$^{\#}$	1.13 ± 0.36$^{\#}$
e′ (cm/s)	12.94 ± 2.60	10.02 ± 2.31*	9.74 ± 2.25*	9.31 ± 2.21*
E/e′	6.65 ± 1.52	8.83 ± 3.41*	8.24 ± 3.48*	8.13 ± 2.8*
DT (ms)	193.89 ± 23.85	174.38 ± 34.48*	205.41 ± 49.71$^{\#}$	203.57 ± 36.59$^{\#}$

Data are shown as mean ± standard deviation

DT deceleration time, *EL* energy loss, *ELsys* EL during systole, *ELed* EL during early diastole, *ELac* EL during atrial contraction, *GLS* global longitudinal strain, *LA* left atrial, *LV* left ventricular, *LAD* LA diameter, *LAVI* LA volume index, *LVEDV* LV end-diastolic volume, *LVESV* LV end-systolic volume, *LVEF* LV ejection fraction

*$P < 0.05$ vs. controls

#$P < 0.05$ vs. AF at baseline

&$P < 0.05$ vs. AF at 3 months

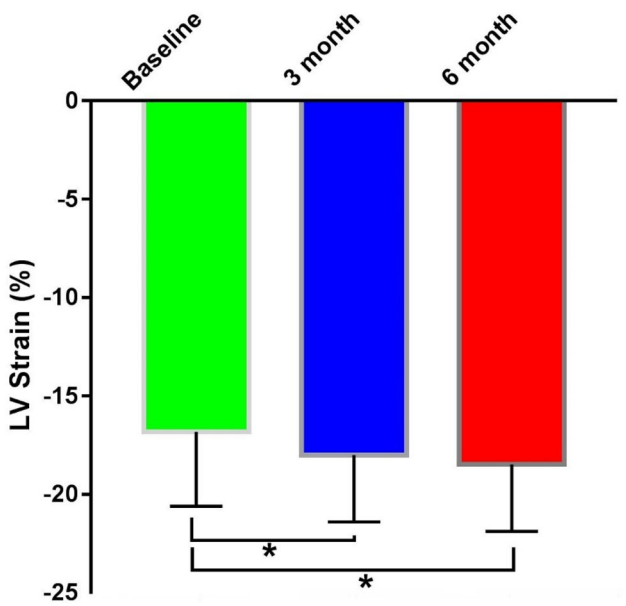

Fig. 3 Change in GLS during follow-up after successful RFCA in 37 patients. (*$P<0.05$)

in univariate analysis (Supplementary Table 2) were incorporated into the model for stepwise multivariate linear regression analyses. The independent predictors of EL were: for ELsys, CHA_2DS_2-VASc score ($P=0.023$) and LVESV ($P=0.003$), with the regression equation: $\text{ELsys} = 6.271 + 0.468 \times \text{CHA}_2\text{DS}_2\text{-VASc score} - 0.086 \times \text{LVESV}$ (adjusted R^2 0.232, $P=0.001$); for ELed, E/A ($P<0.001$), with the regression equation: $\text{ELed} = 5.094 + 2.432 \times \text{E/A}$ (adjusted R^2 0.342, $P<0.001$); and for ELac, CHA_2DS_2-VASc score ($P=0.019$) and A ($P=0.008$), with the regression equation: $\text{ELac} = 0.734 + 0.574 \times \text{CHA}_2\text{DS}_2\text{-VASc score} + 0.038 \times \text{A}$ (adjusted R^2 0.214, $P=0.001$). Likewise, univariate (Supplementary Table 3) and multivariate analyses were conducted to determine the independent predictors of the difference in EL between baseline and 6 months. The independent predictors were: for ELsys, E/e′ ($\beta=-0.337$, $P=0.041$); for ELed, E/A ($\beta=0.525$, $P=0.001$); and for ELac, e′ ($\beta=0.25$, $P=0.009$).

In univariate and multivariate logistic regression analysis, ELed was the only independent predictor for maintenance of sinus rhythm at 1-year follow-up: hazard ratio, 1.254; 95% CI 1.073–1.467 (Table 4).

Reproducibility

Bland–Altman analysis demonstrated good reproducibility of intra- and inter-observer variability (Table 5).

Discussion

In the present study, 53 patients were studied to explore the influence of AF on LV EL and GLS; among them, 37 with sustained sinus rhythm at 1 year after RFCA were studied to evaluate the effects of successful RFCA on LV EL and GLS. Compared with controls, LV ELsys, ELed and GLS were impaired in patients with AF; 3 months after RFCA, a significant improvement in ELsys and ELed, and GLS was observed, with almost normalization of ELsys and ELed at 6 months follow-up.

Left ventricular systolic function after successful catheter ablation

The positive effect of successful catheter ablation on LV systolic function has been proved in patients with LV systolic dysfunction [10]. However, the advantageous effect of successful catheter ablation on LV systolic function, in patients with preserved LV systolic function, is less evident [11]. In the present study, 37 patients with sustained sinus rhythm post RFCA had numerically lower LVEF at 6-month follow-up (60.5 ± 5.0 vs. 58.4 ± 6.2, $P=0.053$), which might be secondary to comorbidities and to a less favorable effect of RFCA in patients with normal LV systolic function [12]. Interestingly, GLS improved significantly at 3-month follow-up in the present study. GLS, detected by 2DTT, was introduced as a reliable method to detect subtle LV systolic dysfunction. In a study by Tops and colleagues of 78 patients with AF and normal LVEF undergoing catheter ablation, successful catheter ablation significantly improved GLS at 1-year follow-up without significant improvement in LVEF [7]. The present study further verified the favorable effect of successful RFCA on subtle LV systolic function during the early phase.

Left ventricular energy loss

EL is generated by transformation of kinetic energy into thermal energy secondary to friction between flow and ventricular wall [13]. The higher the dispersion of velocity or shear angle between blood flow and wall, the higher the EL [6]. Naturally, the blood flow pattern in the heart is asymmetrically redirected to avoid excessive energy dissipation by restricting flow separation and instability [4], therefore only producing little EL [14]. Under pathological conditions, resulting in the deformation of LV geometry and impairment of LV diastolic function and LA pressure, LV flow patterns would be adversely affected as would the efficiency of ventriculoatrial coupling leading to additional and excessive EL during filling. In the patients with AF studied, the high

Table 4 Predictors of atrial tachyarrhythmia recurrence at 1-year follow-up

Variables	Univariate regression Hazard ratio (95% CI)	*P* value	Multivariate regression Hazard ratio (95% CI)	*P* value
Age	0.985 (0.924–1.051)	0.654		
Sex	1.161 (0.319–4.227)	0.821		
ELs	0.157 (0.928–1.584)	0.157		
ELed	1.270 (1.093–1.477)	0.002	1.254 (1.073–1.467)	0.005
ELac	1.106 (0.885–1.382)	0.377		
GLS	0.958 (0.799–1.149)	0.644		
HR	0.999 (0.946–1.055)	0.97		
BSA	0.099 (0.001–8.247)	0.306		
CHA2DS2-VASc score	1.323 (0.848–2.063)	0.217		
AF duration	1.144 (0.993–1.319)	0.062	1.098 (0.953–1.265)	0.194
Type of AF	1.780 (0.497–6.374)	0.375		
LAD	1.069 (0.945–1.210)	0.290		
LAVI	1.037 (0.978–1.100)	0.219		
LVEDV	0.977 (0.940–1.015)	0.225		
LVESV	0.963 (0.901–1.030)	0.276		
LVEF	9.787 (0.000–435686.967)	0.676		
E	1.013 (0.990–1.036)	0.281		
A	0.994 (0.968–1.020)	0.631		
E/A	1.339 (0.831–2.157)	0.230		
e′	1.250 (0.929–1.683)	0.141		
E/e′	1.004 (0.840–1.200)	0.965		
DT	0.991 (0.974–1.009)	0.327		

BSA body surface area, *DT* deceleration time, *EL* energy loss, *ELsys* EL during systole, *ELed* EL during early diastole, *ELac* EL during atrial contraction, *GLS* global longitudinal strain, *HR* heart rhythm, *LAD* LA diameter, *LAVI* LA volume index, *LVEDV* LV end-diastolic volume, *LVESV* LV end-systolic volume, *LVEF* LV ejection fraction

Table 5 Results of reproducibility

Variables	Mean difference	LOA	ICC
Intra-observer			
LVELsys	0.01	1.07	0.986
LVELed	0.22	1.70	0.990
LVELac	0.19	1.93	0.975
GLS	−0.80	5.00	0.900
Inter-observer			
LVELsys	0.23	2.02	0.946
LVELed	0.16	1.41	0.991
LVELac	0.06	1.56	0.985
GLS	−0.40	6.30	0.826

EL energy loss, *ELsys* EL during systole, *ELed* EL during early diastole, *ELac* EL during atrial contraction, *GLS* global longitudinal strain, *ICC* interclass correlation coefficient, *LOA* limits of agreement

EL was observed during both systolic and early diastolic phases, manifesting as highly spatially dispersed and inefficient intraventricular blood flow [6]. Notably, EL during the latter two phases improved significantly at 3 months post successful RFCA relative to baseline.

According to a previous study in healthy volunteers, ELsys is mainly affected by preload and afterload in LV, i.e., the high velocity of ejected flow [14, 15]. According to the multivariate regression analysis in the present study, ELsys was influenced by CHA_2DS_2-VASc score ($P=0.023$) and LVESV ($P=0.003$), suggesting that comorbidities, such as hypertension, deteriorate the ELsys. On the other hand, diastolic LV EL is mainly affected by LV diastolic function. Upon mitral valve opening, there is high velocity flow into the LV cavity because of the pressure gradient between LA and LV and active relaxation of LV myocardium, promoting vortex formation. However, LV diastolic dysfunction in patients with AF [8] apparently affects vortex formation [16], leading to high diastolic LV EL [17, 18]. In the present study, ELed was largely generated by the abnormal E/A mainly secondary to impaired atrial systolic capacity in AF. Abnormal E/A apparently affects intracardiac flow pattern by interfering with formation of the normal vortex and increasing its dissipation, leading to excessive collision between inflow and ventricular wall, thereby producing more EL [19]. In another study, after conversion of AF, E/A almost reversed at about 5–8 weeks [20] especially for restrictive pattern [21]. We found that successful RFCA

effectively reversed E/A to recover early diastolic LV EL at follow-up. Moreover, the larger the E/A at baseline, the greater the ELed benefits, suggesting that successful RFCA has a beneficial impact on ELed, i.e., the intracardiac flow pattern during early diastole. As for ELac, it was mainly affected by the systolic capacity of LA. Atrial contraction would help to shape the late intracardiac vortex promoting LV kinetic energy and decreasing EL dissipation [13]. However, in the present study, there was no significant difference between controls and AF group for impairment of A wave velocity. According to the multivariate regression analysis, ELac was affected by A wave velocity and CHA_2DS_2-VASc score, and the comorbidities may counteract the influence of A wave velocity on ELac.

Interaction between left ventricular energy loss and structural remodeling

EL is fundamentally kinetic energy shifted into thermal energy due to viscosity-driven friction. Under physiological conditions, EL is low (about 10%) compared with the kinetic energy [14], and its role is undefined. However, in pathological situations, the proportion would increase reflecting an adverse change in intraventricular flow pattern, which may in turn affect cardiac tissue eventually leading to cardiac adaptive–maladaptive remodeling from local wall to whole ventricle [3]. Studies that used VFM to evaluate LV EL, especially diastolic EL, in patients with diabetes [17] and end-stage renal disease [18] revealed that LV EL may be a better tool to identify preclinical LV remodeling secondary to suboptimal disease management.

In the present study, LV ELed was the only independent predictor for maintenance of sinus rhythm which indicated that high ELed may result in severely adverse LV remodeling and subsequently increased risk of atrial tachyarrhythmia recurrence. On the other hand, successful ablation was associated with early reversal of LV EL at 3 months before significant amelioration in LV structure became apparent at 6 months. The current viewpoints attribute the improvement in LV remodeling to the normalization of the heart rate or recovery of the efficient LV filling, however, the mechanism remains unveiled. Improvement in LV flow pattern (based on decrease in EL) after successful RFCA may be secondary to subsequent reverse LV structural remodeling propitiated by the more harmonious interaction between tissue and flow [3].

In conclusion, VFM is a feasible and reproducible tool for evaluating dissipative EL in patients with AF in sinus rhythm. LV ELsys and ELed were both impaired in patients with AF. An increase in ELed may increase the risk of atrial tachyarrhythmia recurrence after catheter ablation. Successful RFCA in AF may first favor the recovery of the intracardiac flow pattern and then ameliorate structural remodeling during sustained sinus rhythm.

Study limitations

This study has several limitations. Firstly, the included patients were selected to undergo RFCA, which might introduce bias even though study enrolment was prospective and consecutive. Nonetheless, the patients studied constituted a typical target population for AF ablation in real-world practice [22]. Secondly, management of comorbid cardiovascular conditions, including for instance use of ACEI/ARBs and statins, may improve LV EL or GLS. To this end, ACEI/ARBs have a beneficial effect on LV strain in patients with hypertension [23] or heart failure [24] and on LV remodeling [25], while the effect remains undetermined in AF. Moreover, relevant studies on LV EL have not been performed. In ad hoc analysis in the present study, while not an independent predictor, ACEI/ARB appeared to be associated with improvement in ELed. Further studies designed to explore these possible associations are warranted. Thirdly, the relatively small number of patients and controls limits the interpretation of findings, such as the influence of AF type on EL; again, larger studies with more diverse populations are warranted.

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Compliance with ethical standards

Conflict of interest The authors declare that there is 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.

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