

The Predictive Value Of The Left Atrial Kinetic Energy For Atrial Fibrillation Recurrence

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Abstract

Introduction: Determining which patients will experience recurrence of atrial fibrillation (AF) is crucial for treatment modification.

Aim: This study aimed to investigate the value of left atrial kinetic energy (LAKE) in atrial fibrillation recurrence

Methods: A total of 120 consecutive patients who achieved sinus rhythm with electrical direct current cardioversion and met the inclusion criteria were included in the study. TTE and LAKE values were calculated on the first day after cardioversion. Rhythm control was performed with 12-lead electrocardiography in the first month follow-up. LAKE values calculated using TTE was compared between two groups of patients – those who remained in sinus rhythm and those who developed AF.

Results: While 81 (67.5%) patients were in sinus rhythm at one month, AF recurrence was detected in 39 (32.5%) patients. In the AF group, while AF duration, cardioversion energy, number of diabetic patients, left atrial (LA) diameter, LA pre A volume, LA minimum volume, and pulmonary artery pressure values were found to be significantly higher than those in the SR group, mitral A velocity and LAKE values were significantly lower. In multivariate regression analysis, AF duration (OR: 1.55 [CI: 95%; 1.23–1.95]; $p < 0.001$), LA diameter (OR: 1.36 [CI: 95%; 1.11–1.66]; $p = 0.003$) and LAKE (OR: 0.96 [CI: 95%: 0.94–0.99]; $p = 0.008$) were determined to be independent predictors of AF recurrence at one month.

Conclusions: LA diameter, AF duration, and LAKE were found to be significant predictors of AF recurrence after cardioversion. NCT05231967

Summary

Ensuring and maintaining normal sinus rhythm is critical for reducing negative outcomes in patients with atrial fibrillation (AF). Electrical direct current cardioversion is a frequently used method of restoring SR, but a significant proportion of patients later develop AF recurrence. Determining which of these patients is prone to recurrence is important for treatment modification. Left atrial kinetic energy (LAKE) is a parameter that shows left atrial mechanical function and can be calculated noninvasively by transthoracic echocardiography. LAKE is reduced in patients with AF recurrence. Due to the success of LAKE in showing 1-month short-term recurrences, AF recurrence may be prevented by applying more aggressive treatment in patients with low LAKE values.

Introduction

Atrial fibrillation (AF) is a common rhythm disorder among the general population and is associated with stroke, decreased exercise capacity, and increased mortality (1). Ensuring and maintaining normal sinus rhythm (SR) is critical for reducing these negative outcomes (2).

AF begins as a result of hemodynamic or structural changes in the left atrium (LA), and during this paroxysmal and persistent phase, LA dilatation occurs and mechanical functions gradually deteriorate (3, 4). An improved understanding of LA structure and function can help to predict the risk of developing AF and response to treatment (5). Electrical direct current cardioversion is a frequently used method of restoring SR, but a significant proportion of patients later develop AF recurrence (6). Determining which of these patients is prone to recurrence is important for treatment modification. For this reason, the ability to predict recurrence with simple and objective parameters is valuable to clinicians. In recent years, numerous studies have been conducted on noninvasive evaluation of LA size and mechanical function. LA function can be assessed using two-dimensional echocardiography, Doppler analysis of transmitral flow, and tissue Doppler assessment of LA myocardial velocities (7).

Left atrial kinetic energy (LAKE) is a parameter that shows left atrial mechanical function and can be calculated noninvasively by transthoracic echocardiography (TTE) (8). In this study, we aimed to investigate the effectiveness of LAKE in predicting recurrence in the first month of follow-up in AF patients converted to sinus rhythm with electrical direct current cardioversion.

Methods

Study population

The study was initiated after the ethics committee of Bursa Postgraduate Hospital approved the study protocol. A total of 120 consecutive patients aged 18 years and older who underwent successful electrical cardioversion following persistent AF were included in the study. Persistent AF was defined as continuous AF lasting longer than seven days in electrocardiography (ECG) follow-up (9). Patients with significant valvular disease, previous valve surgery, severe left ventricular systolic dysfunction (ejection fraction < 40%), severely dilated left atrium (> 5 cm), previous ablation of atrial fibrillation, or paroxysmal atrial fibrillation were excluded from the study.

The physical examination results, medications and laboratory results of all patients were recorded. Patients with systolic blood pressure \geq 140 mmHg and/or diastolic blood pressure \geq 90 mmHg or using antihypertensive medication were defined as hypertensive; patients with two consecutive fasting blood glucose measurements \geq 126 mg/dl or using oral antidiabetic/insulin were defined as diabetic. Cerebrovascular accident (CVA), chronic renal failure (CRF), chronic obstructive pulmonary disease (COPD) and peripheral arterial disease (PAD) were recorded. Electrocardiographic data (Cardiofax M ECG-1350K, Nihon Kohden, Tokyo, Japan) of the patients were recorded before and after cardioversion and one month later. The patients were divided into two groups – patients who remained in SR (group 1) and patients with AF recurrence (group 2) after one month of follow-up.

Echocardiography

All patients underwent routine TTE prior to cardioversion and transoesophageal echocardiography (TEE) (EPIQ 7 Echocardiography Machine, Philips Ultrasound, Netherlands) to exclude left atrial and left atrial

appendage thrombus. TTE was repeated using a 3.5-mHz probe in patients who remained in SR 24 hours after cardioversion. All standard measurements were taken from the parasternal long and short axes and apical two- and four-chamber windows. All assessments and measurements were made according to the American Society of Echocardiography (ASE) guidelines (10).

Left ventricular ejection fraction (LVEF) was calculated according to the modified biplane Simpson method (10). Mitral flow velocities were recorded from the apical four-chamber view with a sample volume of 5 mm placed at the level of the mitral valve tips using pulsed wave Doppler (PWD). Peak early (E) and late (A) mitral entry velocities were recorded.

LAKE values were calculated at the 24th hour after cardioversion. LAKE was defined as $0.5 \times \text{left atrium stroke volume (cm}^3, \text{ volume at the beginning of left atrial systole} - \text{left atrium minimal volume)} \times 1.06 \text{ (g/cm}^3, \text{ blood density)} \times (\text{peak A velocity})^2 \text{ (cm/sec, transmitral PWD A velocity)}$ (8).

Cardioversion

Pre-cardioversion anticoagulation with continuous intravenous (i.v.) heparin infusion was applied to all patients with an activated partial thromboplastin time (aPTT) 1.5–2 times the normal value. Patients without intracardiac thrombus on TTE and TEE were started on amiodarone infusion (15 mg/min i.v. loading dose infused in 10 minutes, followed by 0.5 mg/min infusion over 24 hours) and i.v. sedation with midazolam was used. Transthoracic electrical cardioversion was performed by giving synchronized biphasic direct current shocks of 150, 200 and 270 J, respectively, in the coronary intensive care unit. Cardioversion was considered successful if the atrial P-waves persisted five minutes after shock. Oral anticoagulants were given to patients with SR for at least 4 weeks after the procedure. The patients received antiarrhythmic treatment with oral amiodarone for a total of 4 weeks (600 mg/kg for 2 weeks and 200 mg/kg for the following 2 weeks). The patients were evaluated with physical examination and ECG measurements 1 month after the procedure; however, they were advised to come immediately if they had palpitations or symptoms of arrhythmia. If the patients had palpitation symptoms and the ECG records were SR, the patients were evaluated for AF with rhythm holter monitoring.

Statistical analysis

Statistical analysis was performed using the SPSS computer program (Statistical Package for the Social Sciences ver. 22., SPSS Inc, Chicago, Illinois, USA). Continuous variables were reported as mean \pm standard deviation, and categorical variables as percentages. Student's t test was used to compare the normally distributed variables, and the Mann Whitney U test was used to compare the non-normally distributed variables. Categorical variables were compared with the chi-square test or Fisher's exact test as appropriate. Univariate and multivariate logistic regression analyzes were used to identify significant predictors of AF recurrence following cardioversion. We performed two multivariate models for avoiding overfitting, first; include the parameters into the multivariate analysis if that's p-value smaller than 0.05, second; include the parameters into the multivariate analysis if that's p-value smaller than 0.01. A value of $p < 0.05$ was considered significant.

Results

In the study, which included 120 patients who underwent successful cardioversion, 81 patients (67.5%) remained in sinus rhythm at the end of the first month, while AF recurrence occurred in 39 (32.5%) patients. The duration of AF was found to be longer in group 2 than in group 1 (6.92 ± 3.15 vs. 4.74 ± 1.96 months; $p < 0.001$). Cardioversion energy was higher in the AF group (244.87 ± 34.01 vs. 226.66 ± 37.34 joules; $p = 0.01$). More patients with diabetes mellitus (DM) were detected in group 1 (19 (23.5%) vs. 2 (5.1%); $p = 0.01$). Other features were found to be similar between the two groups (Table 1).

Table 1
Baseline characteristics of the patients

	Group 1 (SR) n = 81	Group 2 (AF) n = 39	P value
Age	62.16 ± 7.39	63.07 ± 7.47	0.52
Gender n (%) (male / female)	26(% 32,1) / 55 (%67,9)	11(%28,2)/ 28(%71,8)	0.66
AF duration (months)	4.74 ± 1.96	6.92 ± 3.15	< 0.001
Heart rate (bpm)	109.46 ± 23.91	105.02 ± 25.27	0.35
Body mass index (kg/m ²)	29.12 ± 5.61	28.89 ± 5.02	0.83
Blood pressure (mmHg)			
Systolic	129.97 ± 18.04	132.25 ± 13.29	0.48
Diastolic	81.92 ± 13.58	80.71 ± 8.40	0.61
Hemoglobin (g/dl)	13.46 ± 1.40	13.47 ± 1.50	0.97
Urea (mg/ml)	34.46 ± 10.31	35.51 ± 7.69	0.57
Creatinin (mg/ml)	0.80 ± 0.26	0.80 ± 0.24	0.96
Cardioversion energy (j)	226.66 ± 37.34	244.87 ± 34.01	0.01
Comorbidities			
Diabetes mellitus	19 (23.5%)	2 (5.1%)	0.01
Hypertension	56 (69.1%)	25 (64.1%)	0.58
COPD	5 (6.2%)	4 (10.3%)	0.42
Coronary artery disease	10 (12.3%)	5 (12.8%)	0.94
Smoker	7 (8.6%)	3 (7.7%)	0.86
Medications			
Acetylsalicylic acid	55 (67.9%)	27 (69.2%)	0.88
Beta blocker	41 (50.6%)	25 (64.1%)	0.16
Calcium channel blocker	19 (23.5%)	8 (20.5%)	0.71
ACEI	26 (32.1%)	14 (35.9%)	0.67
ARB	22 (27.2%)	9 (23.1%)	0.63

ADEI: Angiotensin converting enzyme inhibitor; AF: Atrial fibrillation; ARB: Angiotensin receptor blocker; COPD: Chronic obstructive pulmonary disease; SR: Sinus rhythm.

	Group 1 (SR)	Group 2 (AF)	P value
	n = 81	n = 39	
Diüretic	3 (3.7%)	6 (15.4%)	0.06
ADEI: Angiotensin converting enzyme inhibitor; AF: Atrial fibrillation; ARB: Angiotensin receptor blocker; COPD: Chronic obstructive pulmonary disease; SR: Sinus rhythm.			

In Table 2, the pre-cardioversion values of the groups and the control echocardiographic measurements at the 24th hour after cardioversion are compared. LA diameter (44.99 ± 2.46 vs. 42.90 ± 3.58 mm; $p = 0.02$), LA minimal volume (31.46 ± 13.84 vs. 23.90 ± 8.06 ml; $p = 0.003$), pulmonary artery pressure (PAP) (39.64 ± 9.89 vs. 32.95 ± 8.54 mmHg, $p = 0.001$) while it was higher in the AF group; control mitral A velocity (0.62 ± 0.18 vs. 0.50 ± 0.13 m/s; $p = 0.001$), control left ventricle (LV) lateral Aa velocity (0.07 ± 0.02 vs. 0.05 ± 0.02 m/s; $p = 0.01$) and LA kinetic energy (53.60 ± 38.00 vs. 36.52 ± 20.48 kdynes.cm; $p = 0.002$) were higher in the SR group.

Table 2
Comparison of echocardiographic measurements of the groups before and after cardioversion

	Group 1 (SR) N = 81	Group 2 (AF) N = 39	P value
LV end-systolic diameter (mm)	30.56 ± 3.65	31.33 ± 4.28	0.31
LV end-diastolic diameter (mm)	48.08 ± 3.12	48.12 ± 2.80	0.95
Septal wall thickness (mm)	11.25 ± 1.22	11.30 ± 1.25	0.84
Posterior wall thickness (mm)	10.92 ± 0.84	10.97 ± 0.93	0.77
LV ejection fraction (%)	60.95 ± 6.16	59.17 ± 6.19	0.14
LA diameter (mm)	42.90 ± 3.58	44.99 ± 2.46	0.002
LA maximum volume (ml)	84.83 ± 25.25	90.73 ± 22.31	0.21
LA preA volume (ml)	33.29 ± 11.37	38.60 ± 12.73	0.02
LA minimum volume (ml)	23.90 ± 8.06	31.46 ± 13.84	0.003
Pulmonary artery pressure (mmHg)	32.95 ± 8.54	39.64 ± 9.89	0.001
Mitral E velocity (m/s)	1.02 ± 0.25	1.12 ± 0.28	0.06
LV lateral Ea velocity (m/s)	0.12 ± 0.03	0.13 ± 0.03	0.25
LV lateral E/Ea ratio	9.10 ± 4.33	9.18 ± 3.34	0.92
LV lateral S velocity (m/s)	0.07 ± 0.02	0.06 ± 0.02	0.35
Control mitral A velocity (m/s)	0.62 ± 0.18	0.50 ± 0.13	0.001
Control LV lateral Ea velocity (m/s)	0.12 ± 0.03	0.11 ± 0.03	0.51
Control LV lateral S velocity (m/s)	0.07 ± 0.03	0.08 ± 0.05	0.23
Control LV lateral Aa velocity (m/s)	0.07 ± 0.02	0.05 ± 0.02	0.01
LA kinetic energy (kdynes.cm)	53.60 ± 38.00	36.52 ± 20.48	0.002
AF: Atrial fibrillation; LA: Left atrium; LV: Left ventricle; SR: Sinus rhythm.			

In a univariate regression analysis DM [OR: 5.66 (CI, 95%: 1.24–25.73); p = 0.02], AF duration [OR: 1.39 (CI, 95%; 1.18–1.63); p < 0.001], cardioversion energy [OR: 1.01 (CI, 95%: 1.003– 1.02); p = 0.01], LA diameter [OR: 1.22 (CI, 95%: 1.07–1.39); p = 0.02], PAP [OR: 1.08 (CI, 95%: 1.03–1.12); p = 0.001] and LAKE [OR: 0.98 (CI, 95%: 0.96–0.99); p = 0.001] were found to be significant predictors of AF recurrence. In a multivariate regression analysis, AF duration [OR: 1.55 (CI, 95%: 1.23–1.95); p < 0.001], LA diameter [OR: 1.36 (CI, 95%: 1.11– 1.66); p = 0.003] and LAKE [OR: 0.96 (CI, 95%: 0.94–0.99); p = 0.008] were found to be independent predictors of AF recurrence at 1 month (Table 3). In the second multivariate logistic

regression model, again the AF duration (OR: 1.54 (CI, 95%: 1.22–1.93); $p < 0.001$), LA diameter (OR: 1.33 (CI, 95%: 1.10–1.61); $p = 0.002$) and LAKE (OR: 0.96 (CI, 95%: 0.94–0.99); $p = 0.007$) were independent predictors of AF recurrence at 1 month (Table 3).

Table 3

Evaluation of parameters with univariate and multivariate logistic regression analysis in terms of predicting AF recurrence in the first month

Variable	Univariate logistic regression analysis		Multivariate logistic regression analysis			
	OR (%95 CI)	P value	Model 1		Model 2	
			OR (%95 CI)	P value	OR (%95 CI)	P value
Age (year)	1.01 (0.96–1.07)	0.52				
Diabetes mellitus	5.66 (1.24–25.73)	0.02	7.55 (0.99–1.02)	0.06		
AF duration (months)	1.39 (1.18–1.63)	< 0.001	1.55 (1.23–1.95)	< 0.001	1.54 (1.22–1.93)	< 0.001
Cardioversion energy (j)	1.01 (1.003–1.02)	0.01	1.007 (0.99–1.02)	0.31		
LA diameter (cm)	1.22 (1.07–1.39)	0.002	1.36 (1.11–1.66)	0.003	1.33 (1.10–1.61)	0.002
LVEF (%)	0.95 (0.89–1.01)	0.16				
PAP (mmHg)	1.08 (1.03–1.12)	0.001	1.04 (0.97–1.10)	0.20	1.05 (0.99–1.12)	0.06
LAKE	0.98 (0.96–0.99)	0.001	0.96 (0.94–0.99)	0.008	0.96 (0.94–0.99)	0.007

AF: Atrial fibrillation; CI: Confidence interval; LA: Left atrium; LAKE: Left atrial kinetic energy; LVEF: Left ventricular ejection fraction; OR: Odds ratio; PAP: Pulmonary artery pressure.

Discussion

In this study, we investigated the value of LAKE, an indicator of left atrial mechanical function, in predicting AF recurrence 1 month later in patients with persistent AF who underwent SR by applying electrical direct current cardioversion. LAKE was found to be significantly lower in the AF group than in the SR group, and LAKE, LA diameter and AF duration were found to be independent predictors of AF recurrence at 1 month.

LAKE is an important indicator of the contribution of the left atrium in left ventricular filling. In patients with abnormal diastolic dysfunctions, such as hypertrophic cardiomyopathy, ventricular filling is impaired. As a compensatory mechanism to overcome this situation, left atrial contractility may increase

as a result of the Frank-Starling mechanism, which provides adequate left ventricular filling (11). Similarly, in patients with mitral stenosis, there is a compensatory increase in LA mechanical function against the stenotic valve before left atrial insufficiency develops (12). However, when mitral stenosis progresses and becomes symptomatic, LAKE gradually decreases instead of increasing due to persistent loading in the left atrium (13). Again, in patients with heart failure—especially in patients with mild to moderate heart failure symptoms—an increase in LA mechanical function occurs to compensate for the decreased left ventricular function (14). However, as heart failure progresses, left atrial function also deteriorates, and LAKE decreases (13, 15). In a study performed by Chrysohoou et al., 6-month follow-ups revealed a higher frequency of cardiovascular events in patients with newly diagnosed left ventricular failure and impaired LA mechanical function (16).

In a study comparing 2 groups consisting of paroxysmal AF patients and normal individuals, no significant difference was found between the 2 groups in terms of LAKE (17). One of the issues discussed in the study was the exclusion of persistent/permanent AF patients. This is an issue because deterioration in LA mechanical function is expected to be more common in the chronic stage.

As discussed above, LA is an attempt to compensate for the stroke volume by increasing its mechanical function as a result of Frank-Starling mechanisms in order to overcome the problems in the left ventricle or valve (11, 12). However, after a while, especially as the diseases progress, the LA structure begins to deteriorate, and mechanical function decreases (13). Deteriorated SoA is more prone to the development of atrial fibrillation. LAKE, which is an important indicator of LA mechanical function, also decreases over time. In our study, LAKE was found to be lower in patients with AF recurrence at 1-month follow-up after cardioversion.

LA diameter is one of the parameters that predicts AF recurrence at 1 month in multivariate analysis. Decreased atrial function and AF recurrence are expected to occur in patients with an enlarged LA diameter, and this has also been shown in previous studies (3, 4). The antero-posterior diameter of the LA was measured in our patients, but the 3-dimensional anatomy of the LA may provide more valuable information. The fact that LAKE is a predictor of AF recurrence independent of LA diameter is an indicator that LA function cannot be evaluated with LA diameter alone.

AF duration is another independent predictor of AF recurrence. As the duration of AF increases, LV mechanical function gradually worsens, atrial fibrosis increases, and AF recurrence increases in patients undergoing cardioversion. Especially in patients with an AF duration of 3 months or more, atrial functions begin to decrease, and AF recurrence increases (18). In our study, the AF duration was found to be longer in the group with AF recurrence. In addition, the high rate of AF recurrence (32.5%) seen at 1 month can be explained by the long AF durations in our study group. The duration of AF was 4.74 months in the SR group and 6.92 months in the AF group.

Clinical Implications

It has been shown that LAKE is reduced in patients with AF recurrence. Due to the success of LAKE in showing 1-month short-term recurrences, AF recurrence may be prevented by applying more aggressive treatment in patients with low LAKE values.

Limitations

The relatively small number of patients is the first limitation of our study. Due to this limited number of patients, the study may not be representative of the entire population. In addition, the follow-up period is as short as 1 month. It should be investigated whether the 1-month follow-up results are an indicator for the success of LAKE in predicting AF recurrence in long-term follow-ups.

Conclusions

LAKE, AF duration and LA diameter were found to be significant predictors of AF recurrence at 1 month after cardioversion. LAKE, an important indicator of left atrial mechanical function, predicts AF recurrence at 1 month after successful electrical cardioversion in patients with persistent AF. In patients with low LAKE values, a more aggressive treatment may be considered for the maintenance of SR. The results of this study, in which LAKE was identified as an independent predictor of AF recurrence, should be confirmed by studies with larger patient groups and longer follow-up periods.

Declarations

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Declaration of Competing Interest

The authors have no relevant conflicts of interest to disclose.

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Conflict of interest

The authors have no relevant conflicts of interest to disclose.

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