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Mechanical function of the left atrium within 28 days after restoration of sinus rhythm in patients with paroxysmal atrial fibrillation

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Abstract

Objective: Atrial fibrillation is a strong independent risk factor for cardioembolic stroke, with a significant impact on morbidity, mortality and healthcare costs. The aim of our study is to investigate left atrial mechanical function in healthy subjects and patients with atrial fibrillation paroxysms less than 48 hours with low risk of thromboembolic complications at 1 and 28 days after restoration of sinus rhythm.

Methods: Thirty-six healthy controls and patients with paroxysms of non-valvular atrial fibrillation less than 48 hours (n=25) with low-risk CHA_2DS_2VASc score were included in the study. The mechanical function of the left atrium (LA) was investigated by the 2D speckle tracking program. Transthoracic echocardiography was performed on the 1st and 28th days after restoration of sinus rhythm by pharmacological cardioversion.

Results: Despite the absence of differences in left ventricular systolic function and LA size between the groups, there was a significant decrease in LA deformation and strain rate on day 1 immediately after sinus rhythm recovery in the patients. In the pump phase, the decrease was about 3%, reservoir phase – 10%, and conduit phase – 7% compared to the control group. The strain rate also decreased in the patient group: -1.5 s-1 versus control: -2.14 s-1 ($p<0.0001$). On the 28th day after restoration of sinus rhythm, there were significant changes in reservoir and conduit functions in patients group in comparison with control group. Global longitudinal LA strain (reservoir phase) decreased to 7%, conduit phase decreased to 11% compared with the control group. In patients group we can see the dynamics during 28 days: pump phase and strain rate were significantly improved, however reservoir and conduit did not significantly change and were lower than in healthy.

Conclusion: Mechanical function of the LA in patients with non-valvular atrial fibrillation and low risk of thromboembolic complications, studied with speckle tracking on the first day was significantly impaired compared with the control group (reservoir phase and strain rate). By day 28, mechanical function improved compared to day 1, but reservoir phase remained significantly lower than normal.

Key words: atrial fibrillation, left atrium, strain, strain rate, cardioembolic stroke

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Introduction

Atrial fibrillation (AF) is the most common arrhythmia worldwide and is epidemic. AF is a strong independent risk factor for cardioembolic stroke, with a significant impact on morbidity, mortality and healthcare costs (1). Instruments assessing stroke risk in patients with AF are widely used in clinical practice to help select antithrombotic strategies. The clinical guidelines suggest the CHA_2DS_2VASc score (2) to assess the risk of thromboembolic events (both cerebral and peripheral), which includes left ventricular (LV) systolic dysfunction [LV ejection fraction (EF) <40%], arterial hypertension (systolic blood pressure over 140 mmHg st), age older than 65 years, diabetes mellitus (HbA1c level >6.5% and/or taking antidiabetic drugs), coronary artery disease (CAD), female sex, history of stroke or transient ischemic attack (TIA).

Left ventricular systolic dysfunction (LV EF<40%) is the single echocardiographic parameter in CHA_2DS_2VASc score. At the same time, in accordance with literature data, left atrial (LA) dilatation is an independent predictor of thromboembolic events in patients with AF (1).

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Functional echocardiographic analysis of the left atrium (LA) has been known for more than 30 years. The first studies supporting echocardiographic assessment of LA function were performed by using volumetric analyses such as the LA ejection fraction.

However, LA function is complex, consisting of three main components: systole (pump phase) (3), diastole (reservoir phase) (4) of the left atrium, and conduit phase (5), which corresponds to the protodiastolic phase of the LV. In recent years, a new echocardiographic examination method ``speckle tracking`` has been mentioned more and more often in the works on assessment of LA function. Obokata et al. study showed that global systolic LA deformation was independently associated with acute embolism in patients with paroxysmal and persistent AF (6). In another case-control study, reduced LV systolic strain was associated with an increased risk of stroke and TIA in patients with paroxysmal AF and low $CHADS_2$ scores (less than 1 point before stroke) (7). Thus, analysis of LA deformation may present a new prognostic tool for predicting the risk of thromboembolic complications in AF.

The aim of our study is to investigate left atrial mechanical function in healthy subjects and patients with atrial fibrillation paroxysms less than 48 hours with low risk of thromboembolic complications at 1 and 28 days after restoration of sinus rhythm.

Methods

Study design and population

Our study is prospective observational.

Patients with paroxysms of non-valvular AF less than 48 hours admitted in CICU of National Centre of Cardiology and Internal Medicine, Bishkek during January 2020 to May 2021 were included in the study. Inclusion criteria required the patient to have paroxysm of AF less than 48 hours, LV ejection fraction (EF) ≥50%, no valvular heart disease or a prosthetic valve, and low risk ($CHA_2DS_2VASc = 0$ for men, = 1 for women) by CHA_2DS_2VASc score. Due to the presentation of AF at the age 36.5 (33; 38) it was the first paroxysm for most of patients. Patients were excluded if images were of poor quality, or if image loops did not depict all LA segments. Signs of systolic dysfunction, valvular heart diseases and pregnancy were excluding criteria.

Healthy controls (n=36) were persons without any history of clinical and instrumental signs of hypertension, CAD, AF and systolic dysfunction with good physical activity.

Informed consent was taken before procedure from patients and healthy. This study complies with the Declaration of Helsinki and was performed according to the National Centre of Cardiology and Internal Medicine ethics committee approval.

Baseline variables

All patients underwent a full complex of clinical-laboratory and instrumental examinations, including history taking, clinical observation, and blood tests. Healthy and patients underwent electrocardiography (ECG) in 12 standard leads.

Echocardiography and strain rate imaging

Transthoracic echocardiography (TTE) included measurement of LV size, volumes (end-diastolic volume, end-systolic volume), LV systolic (LVEF, stroke volume) and LV diastolic (E/A, DT, e' laterale, e' mediale, e/e') functions, LA anteroposterior size, and indexed volume.

Healthy and patients were scanned in the left lateral decubitus position. Standard 2D gray scale and Doppler images were acquired using a commercially available system (Philips CX 50) equipped with 3.5 MHz transducers. All recordings and measurements were made according to current guidelines (8). Left ventricular end-systolic and end-diastolic volumes and LVEF were measured from the apical four- and two-chamber views, using the modified Simpson's biplane method (8). Digital loops were stored and analyzed offline (Xcelera, Philips Healthcare).

The mechanical function of the LA was investigated by the 2D Speckle Tracking software. The longitudinal deformation of the LA during three phases of the atrial cycle and strain rate (SRa) were studied. Longitudinal strain values were averaged from the 4-chamber and 2-chamber positions, measured in six segments of the LA during the pump, reservoir, and conduit phases. Calculations of LA function to assess conduit, reservoir, and booster functions were performed using definitions from previous studies (9, 10). Strain rate was measured during the pump phase, which was defined as the negative SRa wave recorded immediately after the P wave on the ECG. In healthy TTE was performed once, because their data were in normal ranges.

Therapy of AF and rhythm control

Therapy included beta-adrenoblockers, anticoagulants and ACE inhibitors accordingly to the guidelines (2). Pharmacological cardioversion of AF was performed with amiodarone IV. Amiodarone was administrated as 150 mg bolus, then infusion of 1 mg/kg. Sinus rhythm restored in 2-12 hours after amiodarone bolus. Our hospital has only two antiarrhythmics: amiodarone and lidocaine. That is why we performed administration of amiodarone.

TTE was performed on the 1st and 28th days after restoration of sinus rhythm by pharmacological cardioversion.

Statistical analysis

Statistical processing of the results was carried out taking into account the existing requirements for analysis of biomedical studies using "IBM SPSS Statistics 23" software package. The samples were checked for compliance with the normal distribution law using the Kolmogorov-Smirnov test. Student's t-test was used to analyze data subject to the normal law of distribution. Data having normal distribution law were described using mean and standard deviation (M(SD). We calculated median and quartiles (Me (Q1-Q3)) for data not having normal distribution law, where median (Me) characterized the central tendency and was analogous to the mean, and quartiles (Q1 and Q3) characterized the 50% scatter of values. For independent data not subject to the normal distribution law, the Mann-Whitney test was used as the criterion of probative statistics. A p value < 0.05 was considered statistically significant.

Results

In our study we studied a group of healthy and patients with paroxysmal atrial fibrillation less than 48 hours. Table 1 shows comparative characteristics of the control and the patients group on 1 day after sinus rhythm recovery. Left ventricular systolic and diastolic function in all groups corresponded to normal ranges. Diastolic function of the LV also corresponded to normal ranges.

Table 1. Baseline demographic and echocardiographic characteristics of controls and patients on the 1st day after sinus rhythm restoration

Variables	Control (n=36)	Patients (n=25) 1st day	p
Age, years	38.2 (36; 39)	36.50 (35; 38)	0.852
Sex F/M, %	48/52	39/61	0.068
BSA, m^2	1.9 (1.88; 2.12)	2.12 (2.12; 2.13)	0.005
SBP, mm Hg	110 (105;122)	124 (112; 130)	0.062
LV EF, %	60.25 (59.30; 61.87)	57.7 (51.4; 64)	0.925
ESV, ml	39.4 (34.3; 42.2)	74.5 (72.4; 76.6)	<0.0001
EDV, ml	102.1 (84.2; 116.5)	180 (158; 202)	<0.0001
SV, ml	65.3 (49.9; 72.95)	105 (81; 129)	<0.0001
E/A ratio	1.5 (1.5; 1.51)	1.37 (0.82; 1.93)	0.978
DT, sec	188 (182; 190)	204 (192; 216)	<0.0001
e' lat, cm/sec	12.4 (8.9; 13.8)	9.08 (7.96; 10.2)	0.023
e' med, cm/sec	9.8 (8.64; 12.1)	9.0 (6.8; 11.2)	0.109
E/e'	10.5 (9.2; 12.9)	8.87 (8.64; 9.1)	0.007
LA AP diameter, cm	3.71 (3.42; 4.0)	3.87 (3.65; 4.1)	0.179
LAVI, ml/m^2	34.6 (30.72; 39.65)	35.95 (31.8; 40.1)	0.593

A - late (atrial) transmitral flow velocity, BSA - body surface area, DT - deceleration time, E - early diastolic transmitral flow velocity, ESV - end systolic volume, EDS - end diastolic volume, e' lat - lateral e' velocity, e' med - septal e' velocity, EF - ejection fraction, F - female, LAVI - left atrial volume index, LA AP - left atrial antero-posterior, M - male, SBP - systolic blood pressure, SV - stroke volume

On the 28th day after sinus rhythm recovery, indices of LV systolic function were higher in the group of patients compared with day 1 but corresponded to normal indices (Table 2).

At the same time, despite the absence of differences in LV systolic function and LV size between the groups, there was a significant decrease in LA deformation and strain rate on day 1 immediately after sinus rhythm recovery in the patients. Table 3 shows the difference between regional longitudinal LA strain and LA strain rate of control and patients on day 1 after sinus rhythm recovery.

All values of deformation were significantly different between the groups. In the pump phase, the decrease was about 3%, reservoir phase – 10%, and conduit phase – 7% compared to the control group. The strain rate also decreased in the patient group: -1.5 s-1 versus control: -2.14 s-1 (p<0.0001).

There were no recurrent AF paroxysms during one month of follow-up.

Table 2. Baseline demographic and echocardiographic characteristics of controls and patients on the 28th day after sinus rhythm restoration

Variables	Control (n=36)	Patients (n=25) 28th day	p
Age, years	38.2 (36; 39)	36.50 (35; 38)	0.852
Sex F/M, %	48/52	39/61	0.068
BSA, m^2	1.9 (1.88; 2.12)	2.12 (2.12; 2.13)	0.005
SBP, mm Hg	110 (105;122)	121 (110; 123)	0.057
LV EF, %	60.25 (59.30; 61.87)	62.80 (58.5; 67.1)	0.546
ESV, ml	39.4 (34.3; 42.2)	60.1 (41.3; 78.9)	0.011
EDV, ml	102.1 (84.2; 116.5)	115 (104; 126)	0.011
SV, ml	65.3 (49.9; 72.95)	73.05 (61; 85.1)	0.108
EA	1.5 (1.5; 1.51)	1.07 (0.88; 1.26)	<0.0001
DT, sec	188 (182; 190)	196 (195; 197)	0.002
e' lat, cm/sec	12.4 (8.9; 13.8)	10.8 (10.5; 11.1)	0.142
e' med, cm/sec	9.8 (8.64; 12.1)	7.96 (7.75; 8.17)	<0.0001
E/e'	10.5 (9.2; 12.9)	8.23 (6.45; 10.01)	0.007
LA size, cm	3.71 (3.42; 4.0)	3.64 (3.57; 3.71)	0.689
LAVI, ml/m^2	34.6 (30.72; 39.65)	31.35 (29.3; 33.4)	0.003

A - late (atrial) transmitral flow velocity, BSA - body surface area, DT - deceleration time, E - early diastolic transmitral flow velocity, ESV - end systolic volume, EDS - end diastolic volume, e' lat - lateral
e' velocity, e' med - septal e' velocity, EF - ejection fraction, F - female, LAVI - left atrial volume index, LA AP - left atrial antero-posterior, M - male, SBP - systolic blood pressure, SV - stroke volume

Table 3. Left atrial regional longitudinal strain and strain rate in control and patients1 groups on the 1st day after restoration of sinus rhythm

Variables	Control (n=36)	Patients (n=25) 1st day	p
Pump phase, %	7.52 (6.61; 8.87)	4.33 (1.8; 6.86)	0.003
Reservoir phase, %	32.4 (27.93; 37.84)	22.42 (13.22; 31.63)	0.011
Conduit phase, %	25.64 (21.41; 29.36)	18.09 (11.42; 24.77)	0.011
Strain rate, SRa, s-1	-2.14 (-2.51; -1.79)	-1.5 (-1.79; -1.22)	<0.0001

On the 28th day after restoration of sinus rhythm, there was a significant decrease in reservoir function in patients group in comparison with control group (Table 4). Global longitudinal LA strain (reservoir phase) was decreased to 7%, conduit phase decreased to 11% compared with the control group. The strain rate in the dynamics by 28th day in the patient group returned back to normal and reached values typical for individuals without AF.

Table 4. Left atrial regional longitudinal strain and strain rate in control and patients` groups on the 28st day after restoration of sinus rhythm

Variables	Control (n=36)	Patients (n=25) 28th day	p
Pump phase, %	7.52 (6.61; 8.87)	8.94 (2.28; 15.6)	0.789
Reservoir phase, %	32.4 (27.93; 37.84)	25.41 (19.98; 30.84)	0.003
Conduit phase, %	25.64 (21.41; 29.36)	16.47 (15.24; 17.71)	0.001
Strain rate, SRa, s-1	-2.14 (-2.51; -1.79)	-2.27 (-2.7; -1.84)	0.423

In patients` group, we can see the dynamics during 28 days: pump phase and strain rate were significantly improved, however, reservoir and conduit did not significantly changed and were lower than in healthy controls (Table 5).

Table 5. Left atrial regional longitudinal strain and strain rate in patients` group on the 1st and 28th days after restoration of sinus rhythm

Variables	1st day (n=25)	28th day (n=25)	p
Pump phase, %	4.33 (1.8; 6.86)	8.94 (2.28; 15.6)	0.005
Reservoir phase, %	22.42 (13.22; 31.63)	25.41 (19.98; 30.84)	0.191
Conduit phase, %	18.09 (11.42; 24.77)	16.47 (15.24; 17.71)	0.188
Strain rate, SRa, s-1	-1.5 (-1.79; -1.22)	-2.27 (-2.7; -1.84)	0.004

Discussion

LV and LA functions in paroxysmal atrial fibrillation immediately after sinus rhythm restoration are not carefully studied. By current guidelines on AF management, anticoagulants are given during 28 days after sinus rhythm in low thromboembolic risk groups. But there are several studies where stroke developed in presence of low CHA_2DS_2VASc score (7). That is why we tried to study more precisely left atrial function using noninvasive method of left atrial evaluation: strain.

Strain can be described as a change in the relative position of individual myocardial points. The change in strain over time is referred to as strain rate and corresponds to the relative change in length per unit time. Measurements of LV deformation can be obtained using tissue Doppler and two-dimensional TTE with speckle tracking.

According to the literature, LA deformation in the reservoir phase corresponds to LA diastole, respectively, worsening of deformation indices means LA overload in diastole. Left atrial strain rate corresponds to LA systole, decreased strain rate in patients means decreased LA contractile function.

Deformation and strain rate in healthy individuals showed compliance with other similar studies, where the normal value of deformation in the reservoir phase > 30% and strain rate more than -2 s-1(11). Longitudinal LA strain and strain rate in our study showed reduction of mechanical function in the patients group immediately after sinus rhythm restoration.

The strain rate was significantly decreased in the patient group on the 1st day after sinus rhythm restoration, and on the 28th day it improved to the values of control group. Reservoir and conduit functions were decreased in comparison with the control group during 28 days after sinus rhythm recovery and were not significantly improved.

Study limitations

Patients with paroxysm of AF less than 48 hours and without systolic dysfunction, arterial hypertension are not frequently hospitalized. Most of them restore the sinus rhythm in pre-hospital phase and are not hospitalization. This moment is the limitation for taking more patients in period of 1.5 years. We will continue recruiting patients for more big data.

Conclusion

1.Systolic and diastolic functions of LV and LA in patients with non-valvular atrial fibrillation with low risk of thromboembolic complications were normal and did not differ from healthy (control group) parameters.

2.Mechanical function of the LA in patients with non-valvular atrial fibrillation and low risk of thromboembolic complications, studied with speckle tracking on the first day was significantly impaired compared with the control group (changes in reservoir phase and strain rate). By day 28, only pump and strain rate were improved , reservoir and conduit phases remained significantly lower than normal and were not improved during 28 days of sinus rhythm.

Ethics: Informed consent was taken before procedures from patients and healthy subjects. This study complies with the Declaration of Helsinki and was performed according to the National Centre of Cardiology and Internal Medicine ethics committee approval.

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Conflict of interest: None to declare

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