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Research Article



# Remodeling of the Left Atrium and the Possibility of Predicting Recurrences of Atrial Fibrillation in Various Variants of Sinus Rhythm Restoration

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**OBJECTIVE:** to compare the dynamics of left atrial remodeling in patients with AF with various CP recovery options and to identify the most reliable predictors of AF recurrence.

**MATERIALS AND METHODS:** 153 patients with non-valvular AF lasting from 24 hours to 6 months were examined. All patients were divided into 3 groups depending on the type of cardioversion: the 1<sup>st</sup> group included 49 patients whose CP was restored against the background of drug therapy; the 2<sup>nd</sup> group included 57 patients after electro-pulse therapy (EIT); the 3<sup>rd</sup> group included 47 patients who underwent radiofrequency isolation of the pulmonary veins (RFI LV). All patients underwent ECHO-cardiographic examination (ECHO KG) at the time of AF, as well as on 1, 3, 5, 15 days and 6 months after CP recovery with an assessment of indexed indicators of linear left atrium size (LP), LP volume, LP function recovery time by the rate of peak A transmittal flow (TMF) and LP filling pressure in relation to E/E' with the help of a fabric Doppler imaging.

**RESULTS:** it was revealed that the absence of AF paroxysms in any variant of cardioversion for 2 weeks is a reliable predictor of maintaining CP after 6 months ( $p < 0.001$ ) and reducing the number of AF paroxysms for 6 months ( $p < 0.001$ ). Accordingly, relapses of AF during the first 2 weeks indicate an increase in their probability within 6 months [OR (risk ratio) = 15.37]. A significant relationship was found between the timing of recovery of LP function (peak A  $> 0.5$  m/sec) and recurrence of AF during 2 weeks and 6 months of follow-up ( $p < 0.05$ ). In patients after LV RF, the linear size and volume of LP significantly decreased in dynamics while maintaining CP in comparison with those who had AF relapses for 6 months ( $p < 0.05$ ). In patients after conservative cardioversion and RF ILV, LP filling pressure (E/E') significantly decreased after 14 days ( $p < 0.05$ ) in the absence of AF relapses and did not change significantly by 6 months of follow-up ( $p < 0.05$ ). While in the presence of repeated paroxysms of AF, this indicator did not change significantly by 6 months of follow-up. In the EIT group, no reliable dynamics of the estimated parameters of LP remodeling was found.

**CONCLUSIONS:** The peak A  $> 0.5$  m/s measured by TMF on 1 day after the rhythm restoration is a reliable predictor of CP retention for 6 months in any variant of cardioversion ( $p < 0.001$ ). The absence of AF paroxysms within 2 weeks after CP recovery reduces the likelihood of their occurrence also within 6 months with any choice of cardioversion ( $p < 0.001$ ). In patients with CP recovery on the background of drug therapy and after RF ILV, the absence of recurrence of arrhythmia for 6 months is associated with a significant decrease in the size of LP (ILP and IOLP), ( $p < 0.05$ ). A decrease in LP filling pressure (E/E') 2 weeks after conservative cardioversion and LV RFI can be considered a reliable predictor of maintaining sinus rhythm by 6 months ( $p < 0.05$ ).

**Keywords:** atrial fibrillation; thromboembolic complications; cardioversion; restoration of sinus rhythm.

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Научная статья

# Ремоделирование левого предсердия и возможности прогнозирования рецидивов фибрилляции предсердий при различных вариантах восстановления синусового ритма

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**Цель** — сравнить динамику ремоделирования левого предсердия у пациентов с фибрилляцией предсердий (ФП) при различных вариантах восстановления синусового ритма (СР) и выявить наиболее достоверные предикторы рецидивирования ФП.

**Материалы и методы.** Обследовано 153 пациента с неклапанной формой ФП продолжительностью от 24 часов до 6 месяцев. Все пациенты делились на 3 группы в зависимости от вида кардиоверсии: в 1-ю группу вошли 49 пациентов, у которых СР восстанавливался на фоне медикаментозной терапии; во 2-ю — 57 пациентов после электроимпульсной терапии (ЭИТ); в 3-ю — 47 пациентов, которым проводилась радиочастотная изоляция легочных вен (РЧИ ЛВ). Всем пациентам проводилось ЭХО-кардиографическое исследование на момент ФП, а также на 1, 3, 5, 15-е сутки и через 6 месяцев после восстановления СР с оценкой индексированных показателей линейного размера левого предсердия (ЛП), объема ЛП, времени восстановления функции ЛП по скорости пика А трансмитрального потока (ТМП) и давления наполнения ЛП по отношению  $E/E'$  с помощью тканевой доплерографической визуализации.

**Результаты.** Выявлено, что отсутствие пароксизмов ФП при любом варианте кардиоверсии в течение 2 недель является достоверным предиктором сохранения СР через 6 месяцев ( $p < 0,001$ ) и уменьшения количества пароксизмов ФП в течение 6 месяцев ( $< 0,001$ ). Соответственно, рецидивы ФП в течение первых 2 недель свидетельствуют о повышении их вероятности в течение 6 месяцев [OR (отношение риска) = 15,37]. Обнаружена достоверная взаимосвязь между сроками восстановления функции ЛП (пик А  $> 0,5$  м/с) и рецидивированием ФП в течение 2 недель и 6 месяцев наблюдения ( $< 0,05$ ).

У пациентов после РЧИ ЛВ в динамике достоверно уменьшались линейный размер и объем ЛП при сохранении СР в сравнении с теми, у кого регистрировались рецидивы ФП в течение 6 месяцев ( $p < 0,05$ ).

У пациентов после консервативной кардиоверсии и РЧИ ЛВ давление наполнения ЛП ( $E/E'$ ) достоверно снижалось через 14 дней ( $p < 0,05$ ) при отсутствии рецидивов ФП и существенно не менялось к 6 месяцам наблюдения ( $p < 0,05$ ), в то время как при наличии повторных пароксизмов ФП данный показатель существенно не менялся к 6 месяцам наблюдения. В группе ЭИТ не обнаружено достоверной динамики оцениваемых показателей ремоделирования ЛП.

**Выводы.** Измеренный по ТМП пик А  $> 0,5$  м/с в 1 сутки после восстановления ритма является достоверным предиктором сохранения СР в течение 6 месяцев при любом варианте кардиоверсии ( $p < 0,001$ ). Отсутствие пароксизмов ФП в течение 2 недель после восстановления СР снижает вероятность их возникновения так же в течение 6 месяцев при любом выборе кардиоверсии ( $p < 0,001$ ).

У пациентов при восстановлении СР на фоне медикаментозной терапии и после РЧИ ЛВ отсутствие рецидивирования аритмии в течение 6 месяцев сопряжено с достоверным уменьшением размеров ЛП (ИЛП и ИОЛП), ( $p < 0,05$ ). Снижение давления наполнения ЛП ( $E/E'$ ) через 2 недели после консервативной кардиоверсии и РЧИ ЛВ можно считать достоверным предиктором сохранения синусового ритма к 6 месяцам ( $p < 0,05$ ).

**Ключевые слова:** фибрилляция предсердий; тромбэмболические осложнения; кардиоверсия; восстановление синусового ритма.

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## LIST OF ABBREVIATIONS

LA — left atrium  
 AF — atrial fibrillation  
 SR — sinus rhythm  
 LV — left ventricle  
 NYHA — HF I-II FC  
 LV SF — systolic function of the left ventricle  
 AH — arterial hypertension  
 LAI — left atrial index  
 LAVI — left atrial volume index  
 ET — electropulse therapy  
 RPVI — radiofrequency pulmonary vein isolation  
 RFA PV — radiofrequency ablation of pulmonary veins  
 FR MV — fibrous ring of the mitral valve  
 ApD of LA — anterior-posterior dimension of the left atrium  
 TF — transmission flow  
 TEC — thromboembolic complications  
 AAT — antiarrhythmic therapy  
 LVEF — left ventricular ejection fraction  
 HD — hypertonic disease  
 DM — diabetes mellitus  
 DF — diastolic function  
 MI — myocardial infarction  
 EMD — electromechanical dissociation

As is known, atrial fibrillation (AF) is the most common of all arrhythmias and the most dangerous due to the high risk of hemodynamic and thromboembolic complications (TEC) [1, 2].

Recently, numerous studies have been devoted to both the probability of predicting and recurring AF, and to the assessment of the morphology of the left atrium (LA) and its dysfunction, which may determine the predisposition to TEC in certain groups of patients [3–5, 28].

Back in 1989, W. Manning et al. found that when sinus rhythm is restored, the normalization of the mechanical function of the atria does not occur immediately: in 38–80% of patients with atrial fibrillation (AF) duration of more than 7 days, the phenomenon of "stunning" of the atrial myocardium is observed [6].

This phenomenon has become the basis of the concept of electromechanical dissociation of LA and may be the reason for TEC development.

"Stunning" of LA is often observed after spontaneous, pharmacological or electrical cardioversion, as well as after radiofrequency pulmonary vein isolation of the (RPVI) [7].

As a rule, atrial mechanical function gets to be restored in the period from several hours to 4 weeks in certain groups of patients, depending on the duration of the current AF paroxysm, on the method of rhythm restoration, as well as on the initial characteristics of the LA [8, 9].

The choice of sinus repair method is not a predictor of the presence or absence of subsequent arrhythmia recurrences [10]. According to various sources, in 50–60%

of patients with AF, recurrent paroxysms can occur within 4 weeks after cardioversion, and the risk of their recurrence within a year varies from 20 to 80% [11, 12].

Over the past decades, many studies have demonstrated the complex pathophysiology of AF. The main trigger for the onset of AF is the presence of ectopic foci in the pulmonary veins, whereas LA structural remodeling is identified as the main factor in the progression of arrhythmia [13, 29]. Recent studies have also demonstrated that left atrial volume correlates with the degree of atrial fibrosis [14, 15].

Since the advent of the method of Doppler tissue imaging, the algorithm for assessing LV diastolic function (DF) has included such a mandatory parameter as the calculated ratio of the maximum rate of transmitral blood flow (E) and the peak rate of early myocardial relaxation in the early LV filling phase (E/E'), which proved to correlate with the magnitude of pressure in the LA. The E/E' index > 15 is highly likely to indicate the presence of LV diastolic dysfunction and increased pressure in the left atrium [16].

According to Kusunose et al., this indicator can also be assessed in patients with AF and does not change significantly when measured over several cardiac cycles. It has also been proven that the E/E' ratio correlates well with the level of natriuretic peptide, which is a reliable predictor of heart failure. However, researchers have not confirmed the correlation of this indicator with the presence of LV diastolic dysfunction in patients with AF [17]. The work of M. Caputo et al. associates an increase in this parameter with a more frequent recurrence of AF in patients after successful electrical cardioversion [18].

However, despite a large number of studies, to date there are no reliable predictors of maintaining sinus rhythm after cardioversion, regardless of the method of restoration of SR and the choice of antiarrhythmic therapy (AAT).

The search for new opportunities to identify the risk of recurrence of AF and prevent associated AF remains extremely relevant.

The purpose of this study was to study the features of left atrial remodeling and to find the predictors of atrial fibrillation recurrence in various types of SR restoration.

## SCIENTIFIC NOVELTY OF THE RESEARCH

This research demonstrates new data in the prediction of atrial fibrillation recurrence with various methods of rhythm restoration. It has been shown that the absence of atrial contractility on the first day after any type of cardioversion is associated with AF recurrence within 2 weeks and 6 months after rhythm restoration. It was also found that the absence of AF paroxysms after SR restoration for 14 days is a significant predictor of maintaining sinus rhythm up to 6 months and reducing the number of AF relapses with any type of cardioversion. It was demonstrated that a decrease in dynamics 2 weeks after reversion to sinus rhythm in such

parameters of LA remodeling as the volume index and filling pressure (E/E') turned out to be prognostically favorable in terms of maintaining of sinus rhythm for 6 months after drug cardioversion and radiofrequency ablation of pulmonary veins. In turn, the absence of dynamics of these indicators or their increase, on the contrary, may be associated with a high risk of atrial fibrillation recurrence.

The data obtained can be used in cardiology and arrhythmology for the selection of antiarrhythmic therapy, determining the duration of anticoagulant therapy in patients without a high risk of TEC and/or at high risk of bleeding in controversial clinical situations.

## MATERIALS AND METHODS

The study included 153 patients, namely 83 men (54.2%) and 70 women (45.7%), mean age was 62.7 (36–81) with non-valvular AF lasting from 24 hours to 6 months with systolic function of the left ventricle (LV SF) > 40%. Distribution into 3 groups was made: the first included 49 patients in whom SR was restored in a sign of drug therapy; the second one included 57 patients who underwent electrical cardioversion; the third one encompassed 47 patients who underwent radiofrequency pulmonary vein isolation (RPVI). The exclusion criteria were LV EF < 40%, HF I-II FC (NYHA), valvular heart disease. Initially, the comparison groups did not have significant differences in age and the presence of such diseases as stable forms of coronary artery disease I-II FC, hypertension (AH), type 2 diabetes mellitus (DM) in the compensation stage, HF I-II FC (NYHA)) (Table 1).

All patients underwent a transesophageal echocardiographic study (TEECHO CG) right before rhythm restoration to rule out thrombi in the LA auricle. Patients received anticoagulants in accordance with

the recommended scale CHA2DS2VASc. All patients received antiarrhythmic therapy (AAT) with Propafenone (in the absence of contraindications to class 1C) or Amiodarone before cardioversion and as maintenance therapy after effective SR restoration. The choice of AAT did not significantly affect the predictions for the presence or absence of AF relapses in the study groups (Table 2). ET was carried out according to the standard method in ICU. RPVI was performed in patients with current AF paroxysm using the CARTO electroanatomical mapping system. During the procedure, an anatomical map of the LA was constructed, followed by circular antral isolation of the left and right PVs using magnetic navigation with verification of the conduction block using a Lasso catheter.

All patients underwent an ECHO-cardiographic study (Echo-CG) on ultrasonic Vivid q, (GE) against the background of AF, on the 1<sup>st</sup>, 3<sup>rd</sup>, 5<sup>th</sup>, 15<sup>th</sup> days and 6 months after the restoration of SR. During the study, LV systolic and diastolic function, myocardial wall thickness, indexed LA dimensions, as well as LA function according to TF were evaluated. The function of the atrial myocardium was considered effective in the presence of peak A > 0.5 m/sec. LVEF was assessed in a two-dimensional mode according to the Simpson method, the analysis of LV diastolic function (DF) was performed by the traditional method of measuring the transmitral flow (TF) in pulsed wave Doppler mode (E), as well as using Doppler tissue imaging with an assessment of early peak diastolic velocity (E') and the E/E' ratio, reflecting the pressure in the LA cavity and the LV filling pressure, the LA volume index was determined by the biplane method. The frequency of AF recurrence was assessed according to the history data, using ECG at the time of control, as well as according to the data of 24-hour Holter ECG monitoring in the period from 3 to 6 months after cardioversion. Arrhythmia recurrence was

**Table 1.** Clinical and demographic indicators and features of anamnesis in patients in the study groups

Parameters	Cons. (n = 49)	ET (n = 57)	R (n = 47)	p
Men	21 (42.9%)	40 (70.2%)	22 (46.8%)	> 0.05
Women	28 (57.1%)	17 (29.8%)	25 (53.2%)	< 0.05
AH	29 (59.2%)	41 (72%)	27 (57.5%)	> 0.05
IHD	4 (13.8%)	7 (17.1%)	3 (11.1%)	> 0.05
DM	3 (10.3%)	2 (12.5%)	3 (11.1%)	> 0.05
CHF I-II FC	5 (17.2%)	2 (12.5%)	8 (29.6%)	> 0.05

Notes: Cons. — group of conservative therapy; ET — group of electropulse therapy; R — RPVI group; AH — arterial hypertension; IHD — ischemic heart disease; DM — Type II diabetes mellitus; CHF I-II FC — chronic heart failure I-II FC (NYHA).

**Table 2.** Antiarrhythmic therapy (AAT)

Medication	Cons. (n = 49)	ET (n = 57)	R (n = 47)	p
Propafenone	16 (32.7%)	11 (19.3%)	14 (29.8%)	> 0.05
Cardarone	33 (67.3%)	46 (80.7%)	33 (70.2%)	> 0.05

defined as the presence of symptomatic or asymptomatic episodes of AF lasting more than 30 seconds.

The clinical results obtained during the study were processed using the STATISTICA for Windows software system (version 10 License BXXR310F964808FA-V). Comparison of the frequency characteristics of qualitative indicators was carried out using non-parametric methods 2, 2 with the Yates correction (for small groups) and the Fisher criterion. When comparing quantitative parameters, the Mann-Whitney test, median chi-square, and ANOVA were used. The evaluation of the studied parameters in dynamics after the treatment and in follow-up was carried out using the Signs criterion and the Wilcoxon criterion. Statistical significance was considered at  $p < 0.05$ .

## RESULTS

The studied groups initially did not differ in age and comorbidities (Table 1). However, the number of women whose rhythm was restored with the help of ET turned out to be almost 2 times less than in the groups of conservative therapy and RPVI (Table 1).

When assessing echocardiographic data in patients with restored SR on conservative therapy, LVEF was significantly higher than in the groups of ET and RPVI (Table 3).

In addition, there were differences in the measurement of LA volume in the study groups. The LA volume index initially turned out to be higher in the group of patients who underwent radiofrequency PV isolation. Differences were also found in the analysis of the parameters of LV diastolic function. Thus, the initial value of the peak E TF was lower in the group of patients with RFA PV, and the peak A TF, measured on the first day after the restoration of SR, was significantly higher among patients in the group of drug cardioversion; the E' index was higher in patients in the ET group, and the E/E' ratio in the group of radiofrequency PV isolation exceeded this parameter in other groups (Table 3). The assessment of these parameters reflects a more significant impairment of LV diastolic function in patients in the RFA PV group.

A TMP peak, measured 1 day after SR restoration, was the highest in the drug cardioversion group. This makes it possible to conclude a higher LA contractility in this group and, as a result, a decrease in the frequency of AF recurrence in the long term in these patients (Table 3).

It should also be noted that the study groups did not differ in the duration of the current arrhythmia paroxysm at the time of cardioversion (Table 4).

It was found that the absence of AF paroxysms after the restoration of sinus rhythm for 2 weeks was associated

**Table 3.** Baseline echocardiographic parameters in the examined patients

Parameters	Cons. (n = 49)	ET (n = 57)	R (n = 47)	p
Age	64.12 (48; 81)	61.33 (45; 77)	63.11 (36; 80)	> 0.05
BSA	1.86 (1.48; 2.17)	2.07 (1.69; 2.72)	1.91 (1.56; 2.36)	> 0.05
LV EF (Biplan)%	66.14 (56; 75)	62.05 (43; 76)	62.78 (46; 77)	< 0.05
EDS	48.66 (38; 64)	50.18 (41; 64)	51.89 (42; 80)	> 0.05
ESS	32.21 (23; 45)	32.56 (25; 56)	35.00 (24; 64)	> 0.05
IVS	11.93 (8; 16)	12.95 (9; 18)	11.81 (9; 15)	> 0.05
WS	11.38 (8; 16)	12.69 (9; 18)	11.33 (8; 15)	> 0.05
ILS	24.85 (17.9; 30.4)	23.13 (15.6; 29.3)	25.03 (18.9; 33.3)	> 0.05
LAVI	38.23 (26.3; 62.5)	38.05 (25.7; 60.9)	45.71 (27.2; 81.7)	< 0.05
Peak E	94.06 (70; 132)	96.72 (69; 180)	79.43 (55; 120)	< 0.05
Peak A 1d	52.02 (0; 79)	34.88 (0; 104)	27.76 (0; 100)	< 0.05
DT	161.55 (99; 230)	162.85 (77; 240)	167.42 (125; 286)	> 0.05
E'	11.78 (6; 16)	12.61 (7; 19)	7.88 (4; 20)	< 0.05
E/E'	8.28 (5; 13.3)	8.10 (4; 18)	12.04 (6; 20)	< 0.05

Note: Cons. — group of conservative therapy; ET — group of electropulse therapy; R — RPVI group; BSA — body surface area; LV EF (Biplan)% — left ventricular ejection fraction; measured according to Simpson; EDS — LV end diastolic size; ESS — LV end systolic size; IVS — interventricular septum; WS — posterior wall; ILS — index of the linear size of the left atrium; LAVI — index of the volume of the left atrium; Peak E — the maximum rate of early filling of the left ventricle; Peak A 1d — the maximum rate of late filling of the left ventricle; measured on day 1; after the restoration of sinus rhythm; DT — deceleration time of early diastolic filling; E' — the maximum speed of the early diastolic wave of movement of the fibrous ring of the mitral valve (FR MV); E/E' — the ratio of the maximum speed of early filling of the LV to the maximum speed of the early diastolic wave of movement of the FR MV.

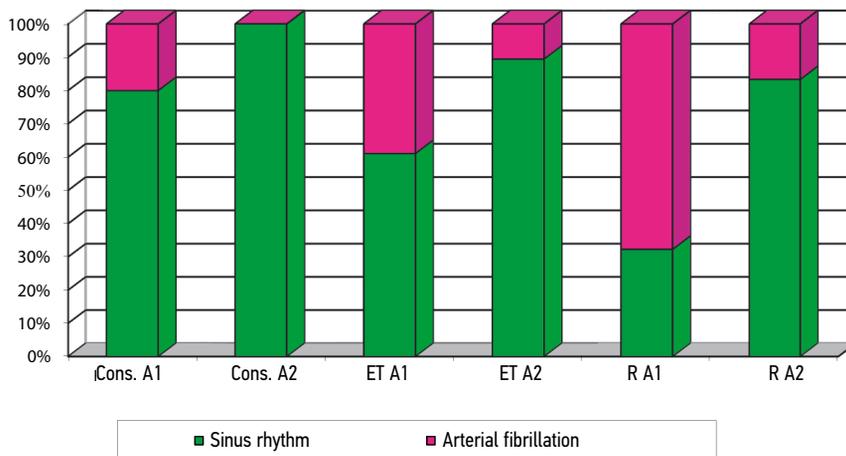
with a decrease in the likelihood of arrhythmia recurrence within 6 months in all observation groups ( $p < 0.001$ ).

Accordingly, the occurrence of early AF paroxysms during the first 2 weeks after the restoration of SR also indicates their higher probability of their appearance within 6 months [RR (risk ratio) = 15.37].

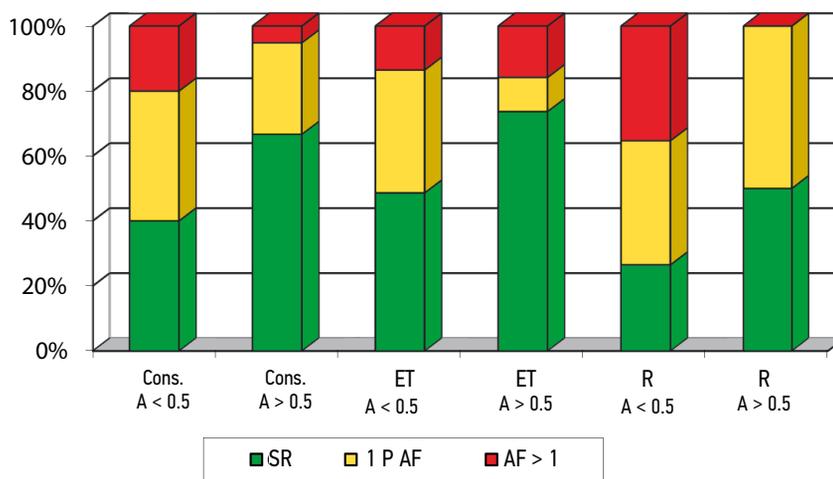
A significant relationship was also found between the restoration time of LA contractility (peak A > 0.5 m/sec) and the frequency of AF recurrence during 6 months of follow-up. So, in the group of medical cardioversion in 39 (80%) patients, effective LA systole (peak A > 0.5 m/sec)

was recorded on the first day after the restoration of sinus rhythm, and by the 15<sup>th</sup> day of observation, sinus rhythm was maintained in all patients of this group (Fig. 1). In addition, arrhythmia did not recur within 6 months of observation in most of these patients (26 (66.7%) people), and only in 13 (33.3%) patients in the long-term period 1 or more AF paroxysms were observed (Fig. 2).

Out of 10 patients in the group of drug-induced rhythm restoration with no atrial contractility on the first day after cardioversion (peak A < 0.5 m/sec), AF relapses were recorded in 2 patients by day 15. Within 6 months, arrhythmia recurred



**Fig. 1.** The frequency of AF relapses in the observation groups for 15 days, depending on the restoration of atrial systole on the first day after cardioversion. A1 — A < 0.5 m/s; A2 — A > 0.5 m/s; Cons. — group of conservative therapy; ET — electrical cardioversion group; R — RPVI group



**Fig. 2.** The frequency of AF recurrence in groups within 6 months depending on atrial contractility on the first day after SR restoration (A > or < 0.5 m/s). SR — sinus rhythm; 1 P AF — 1 paroxysm of atrial fibrillation; AF > 1 — more than 1 paroxysm of AF; Cons. — group of conservative therapy; ET — electrical cardioversion group; R — RPVI group

**Table 4.** Duration of the current AF paroxysm in the study groups

Duration of AF paroxysm	Cons. (n = 49)	ET (n = 57)	R (n = 47)	p
24 h–7 days	17	15	14	> 0,05
7–30 days	20	24	18	> 0,05
30 days–6 months	12	18	15	> 0,05

in 6 patients of this subgroup (60%; significance of differences in the appearance of the sign compared with patients who restored atrial systole on the first day after cardioversion is  $p < 0.005$ ; Fig. 2). However, after 6 months in all patients after medical restoration of SR, regardless of the timing of normalization of atrial contractility, SR was recorded.

In the ET group, peak A  $> 0.5$  m/sec on the first day after cardioversion was recorded in 19 (34.5%) patients, of which 17 (89.5%) by the 15th day of observation maintained stable SR; relapses of AF were registered only in 2 (10.5%) people;  $p < 0.05$ . After 6 months, in 14 (73.7%) patients of this subgroup SR was stable, and relapses were noted only in 5 (26.3%) people.

On the first day after ET in 36 (65.5%) patients peak A was not recorded or was less than 0.5 m/sec. Of these, 14 (39%) people had AF paroxysms within 15 days after cardioversion, which was more common than in patients with good LA contractility on the first day after rhythm restoration;  $p < 0.05$  (see Fig. 2).

In the group of radiofrequency PV isolation, only 12 (26%) patients had peak A  $> 0.5$  m/sec on the first day after SR restoration. As well as in groups 1 and 2, in most of these patients (10 (83.3%)) by the 15th day of observation, SR continued, and AF relapses were observed in only 2 (16.7%) patients (see Fig. 1). Within 6 months, half of this subgroup (6 (50%)) had persistent SR, and the remaining 6 people had repeated paroxysms of AF within 6 months.

After RFA PV in most patients (34 (74%)) on the first day after the restoration of SR, peak A was not recorded or was  $< 0.5$  m/sec, which was much more frequent than in groups 1 and 2;  $p < 0.01$ . At the same time, by day 15 after RFA, arrhythmia recurred in 23 (67.6%) patients, while SR continued in the remaining 11 (32.4%) patients; significance of differences in comparison with patients who had effective atrial systole on the first day after restoration of HR  $p < 0.001$  (see Fig. 1).

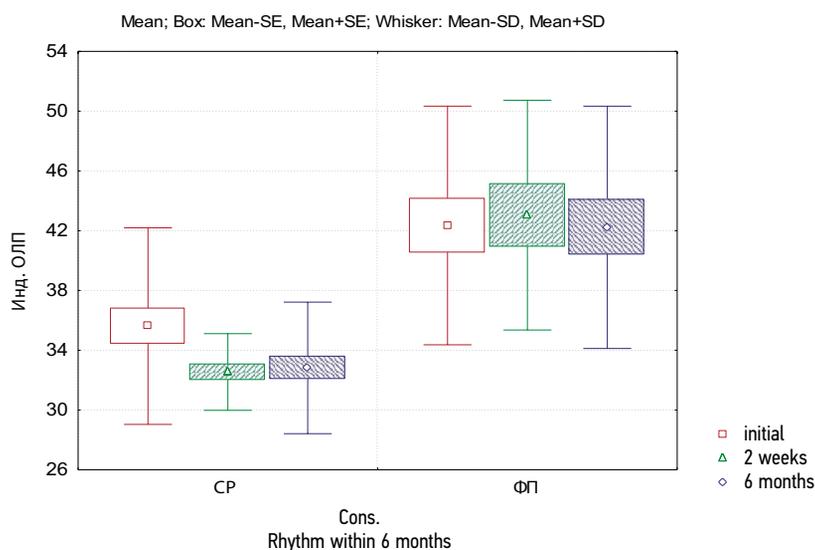
After 6 months, this subgroup also showed a greater number of patients with AF: arrhythmia recurrences were recorded in 25 (73.5%) of them; significance of differences in comparison with patients who had an effective LA systole on the first day after SR restoration was  $p < 0.005$  (see Fig. 2).

## DYNAMICS OF THE LINEAR SIZE OF LA

When measuring the indexed linear size of the LA, there was no significant dynamics of this indicator in the groups of medical and electrical cardioversion during the control after 6 months of observation, regardless of the presence or absence of AF relapses during this period. In the group of conservative therapy in patients without recurrence of arrhythmia for 6 months (30 people), the initial LAI was  $25.1 \pm 2.8$  ml/m<sup>2</sup>, and after 6 months there was only a slight tendency to decrease ( $23.8 \pm 2.8$  ml/m<sup>2</sup>,  $p > 0.05$ ). In patients with recurrent AF (19 people), LAI did not change: the initial indicator was  $24.4 \pm 2.8$  ml/m<sup>2</sup>, after 6 months it was  $24.1 \pm 2.1$  ml/m<sup>2</sup>,  $p > 0.05$  respectively.

In the group of patients with ET with persistent SR for 6 months (32 people), the mean values of LAI initially amounted to  $23.3 \pm 2.1$  ml/m<sup>2</sup> and  $23.3 \pm 2.6$  ml/m<sup>2</sup> by 6 months of observation ( $p > 0.05$ ). In patients with recurrent AF after ET (25 people), the initial LAI was  $22.9 \pm 3.4$  ml/m<sup>2</sup>, after 6 months it did not change significantly either ( $23.5 \pm 2.7$  ml/m<sup>2</sup>;  $p > 0.05$ ).

However, in the RPVI group, there was a significant decrease in LAI by 6 months of follow-up in patients without arrhythmia recurrence. With persistent SR after RFA PV ( $n = 14$ ), the baseline LAI was  $25 \pm 3.2$  ml/m<sup>2</sup> and significantly decreased to  $20.4 \pm 1.8$  ml/m<sup>2</sup> after 6 months ( $p < 0.001$ ), while in patients with recurrence of AF within 6 months ( $n = 33$ ) the LAI was initially equal to  $26 \pm 2.8$  ml/m<sup>2</sup> and on average did not change after 6 months —  $25.3 \pm 4.4$  ml/m<sup>2</sup> (Fig. 3).



**Fig. 3.** Dynamics of the LA linear size index (LAI) in the RFA PV group depending on the presence or absence of AF relapses within 6 months

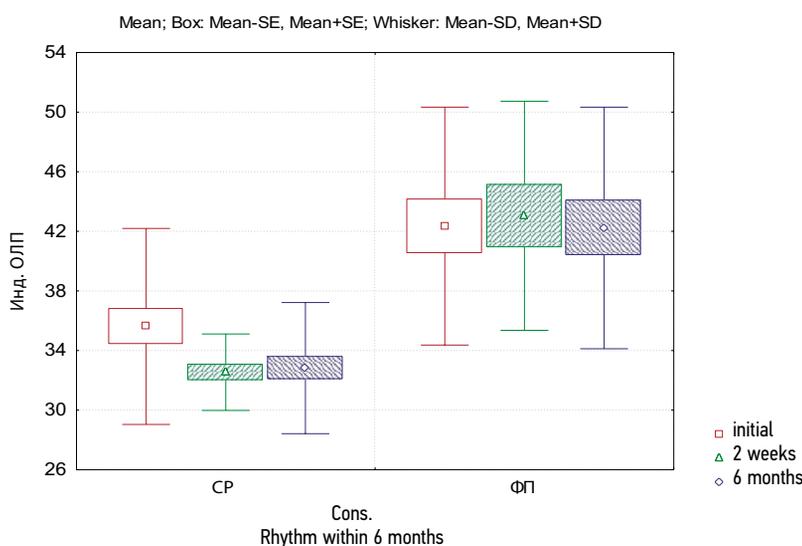
## LP VOLUME DYNAMICS

In the group of SR drug restoration, there were initial differences in indexed LA volumes in patients depending on the presence or absence of AF paroxysms within 6 months. In the absence of recurrences of arrhythmia for 6 months in 30 patients of this group, the initial LAVI index was  $35.6 \pm 6.6$  ml/m<sup>2</sup>, while in 19 people with subsequent recurrences of AF after SR restoration, this parameter initially turned out to be significantly higher ( $42.3 \pm 8$  ml/m<sup>2</sup>,  $p < 0.05$ ).

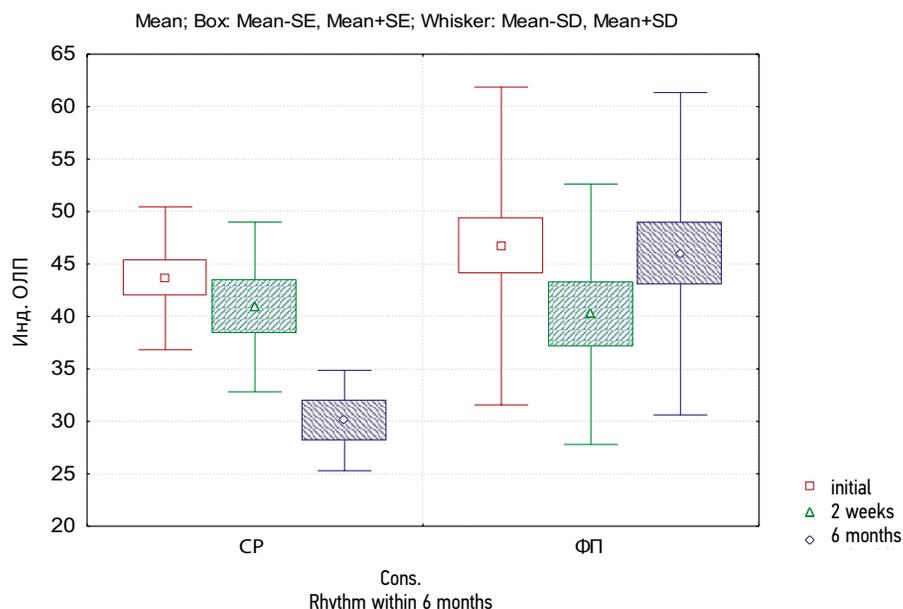
After 2 weeks of observation, patients after drug cardioversion showed a slight trend towards a decrease in the LAVI to  $32.5 \pm 2.6$  ml/m<sup>2</sup> in the absence of arrhythmia

recurrences during this period, without significant further dynamics ( $32.8 \pm 4.4$  ml/m<sup>2</sup> after 6 months;  $p > 0.05$ ). In patients with AF recurrence within 6 months, this indicator did not change significantly in dynamics: by the 2<sup>nd</sup> week of observation, the LAVI was  $43 \pm 8$  ml/m<sup>2</sup>, by 6 months it was  $42.2 \pm 8.1$  ml/m<sup>2</sup>;  $p > 0.05$  (Fig. 4).

In the group of patients after ET, this parameter also did not change significantly during 6 months of observation, regardless of the presence or absence of recurrence of arrhythmia: LAVI in patients with persistent SR was  $38.8 \pm 9.2$  ml/m<sup>2</sup> and  $40.2 \pm 11.9$  ml/m<sup>2</sup> at 2 weeks and 6 months, respectively ( $p > 0.05$ ), and in patients with recurrent AF it was  $37.1 \pm 8.9$  ml/m<sup>2</sup> and  $34.8 \pm 12$  ml after 2 weeks and 6 months, respectively ( $p > 0.05$ ).



**Fig. 4.** Index of LA volume in the group of medical cardioversion depending on the presence or absence of AF relapses within 6 months after SR restoration



**Fig. 5.** Changes in the LA volume index in the RFA PV group depending on the presence or absence of recurrent AF within 6 months

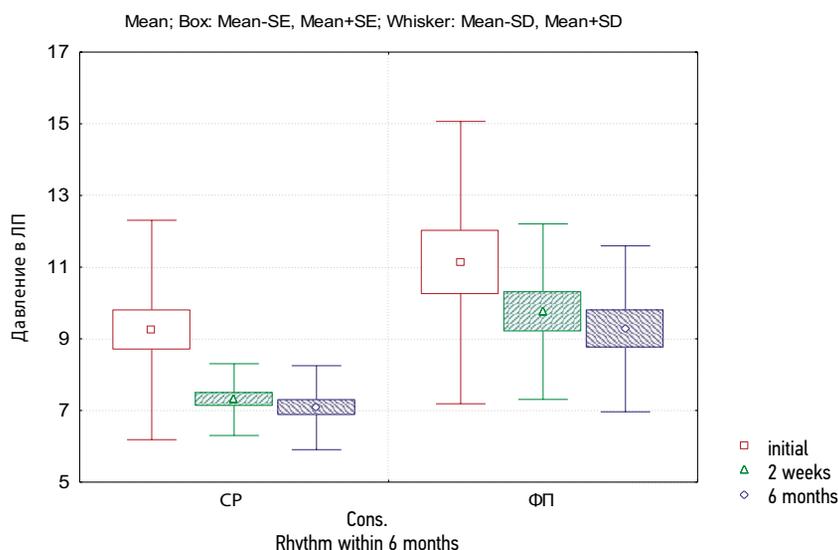
However, in the group of patients after RFA PV in the absence of arrhythmia recurrence (14 people), by 6 months the LAVI decreased on average from the initial  $42.9 \pm 7 \text{ ml/m}^2$  to  $30.1 \pm 15.4 \text{ ml/m}^2$ ;  $p < 0.001$ . While in patients with recurrent AF, this indicator did not change significantly: the initial LAVI was  $46.8 \pm 14.7 \text{ ml/m}^2$ , and after 2 weeks and 6 months it was  $41.3 \pm 12$  and  $46 \pm 15.4 \text{ ml/m}^2$ , respectively;  $p > 0.05$ . (Fig. 5).

## DYNAMICS OF E/E'

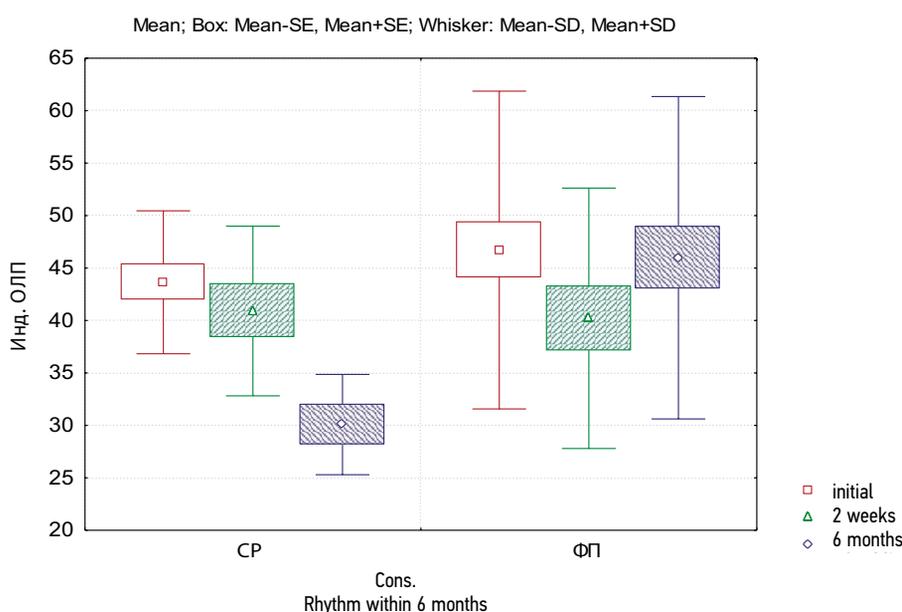
The value of the E/E' ratio in the group of patients with medical SR restoration significantly decreased after 2 weeks in the absence of arrhythmia paroxysms after

cardioversion from  $9.2 \pm 3$  to  $7.3 \pm 3$  ( $p < 0.05$ ) without further significant dynamics within 6 months ( $7.0 \pm 1.2$ ). In patients with recurrent AF in this group, this parameter did not change significantly after 2 weeks ( $11.1 \pm 3.9$  and  $9.8 \pm 2.5$ , respectively;  $p > 0.05$ ), however, it significantly decreased after 6 months (from  $11.1 \pm 3.9$  to  $9.2 \pm 2.5$ ;  $p < 0.05$ ) (Fig. 6).

In the group of patients after ET, the E/E' indicator did not change significantly during 6 months of observation, regardless of the presence or absence of AF relapses during observation up to 6 months: in 32 patients without repeated paroxysms of arrhythmia, the indicator was  $8.1 \pm 2.5$  in the first days after cardioversion;  $8.1 \pm 3.7$  — after 2 weeks and  $7.7 \pm 4.1$  — after 6 months;  $p > 0.05$ . In patients with



**Fig. 6.** E/E' indicator in the drug cardioversion group depending on the presence or absence of AF recurrence within 6 months



**Fig. 7.** Dynamics of the E/E' indicator in the group of patients after RFA PV depending on the preservation of SR or the presence of AF recurrence within 6 months

arrhythmia recurrence, no dynamics of this parameter was also found: E/E' initially amounted to  $8.0 + 1.9$ , after 2 weeks —  $8.6 + 2.2$  and after 6 months —  $9.5 + 2.8$ .

However, in patients after RFA PV, a statistically significant decrease in E/E' was observed in the absence of arrhythmia recurrence, both, after 2 weeks (initially, E/E' was  $20.1 + 7.6$ , and after 2 weeks it decreased to  $14.3 + 2.8$  ( $p < 0.05$ )), and after 6 months of observation — with a decrease in the indicator to  $8.3 + 3.1$ ;  $p < 0.05$ . And in patients with AF paroxysms, the E/E' ratio did not change significantly during 6 months: on the first day after RFA, the IPV and restoration of the rhythm E/E' averaged  $12.5 + 7.1$ ; after 2 weeks —  $13 + 7.4$ ; with a slight downward trend after up to 6 months of observation —  $10.5 + 5$  (Fig. 7).

## DISCUSSION

It is known that “stunning” of the left atrium is associated with the processes of thrombosis in the LA appendage, and the longer the electromechanical dissociation of the LA persists, the higher the risk of delayed thromboembolism [13]. This must also be taken into account when deciding on the timing of anticoagulant therapy,

Some authors consider atrial systole ineffective in the complete absence of wave A of the transmural blood flow (Mahbubul A. et al., 1992), while others consider this concept with any decrease in the speed of peak A less than 0.5 m/s (Hariai K. et al., 1998). Mahbubul A. et al. (1992) also describe the dependence of the timing of restoration of atrial contractility on the linear size of the LA in patients with AF. In their opinion, an LA size of 50 mm or more is associated with the absence of an LA systole lasting more than 4 hours, and in the presence of an LA size of less than 50 mm, atrial contractility is usually restored within the first 4 hours after effective cardioversion [14]. Other studies have demonstrated that atrial systole in patients with AF can restore within seconds to weeks after cardioversion [15].

Other authors also describe the relationship between the timing of the restoration of wave A TF and the duration of arrhythmia: if the duration of paroxysm AF is less than 2 weeks, the peak A TF is restored, as a rule, within 24 hours; with paroxysm from 2 to 6 weeks, EMD persisted for about 7 days, and if the arrhythmia lasts more than 6 weeks atrial contractility could be absent for up to 1 month [16]. But at the same time, there are studies that do not confirm the relationship between the duration of EMD and the duration of AF paroxysm and the size of the LA [17].

In this issue, the work, which includes 112 patients with AF and medical restoration of SR, who were observed for 6 months in order to search for predictors of arrhythmia recurrence, deserves special attention. Atrial systole restoration was assessed based on wave A TF on days 1, 7, and 21 after cardioversion. And conclusions were drawn that the absence of a TF A peak in the first 24 hours after

rhythm restoration was the most significant predictor of AF recurrence [18].

As a result of our analysis, we also concluded that the absence of wave A of the TF (or at its value less than 0.5 m/s) on the first day after cardioversion significantly correlates with the occurrence of AF paroxysms within 2 weeks and 6 months. with various methods of restoration of SR. The absence of AF paroxysms in the first 2 weeks after cardioversion in all groups in relation to reducing the likelihood of their occurrence in the period up to 6 months also turned out to be significant.

Also, in recent years, a large number of studies has been conducted aimed at finding the relationship between the size of the LA and the likelihood of recurrence of AF.

The work of F.M. Costa et al. reflects the results of a study of 809 patients with AF of various durations. The paper proved that the most significant predictors of recurrent AF paroxysms are LA volume, female sex and the duration of the current episode of arrhythmia. Moreover, the LA volume most significantly correlated with the likelihood of arrhythmia recurrence than the duration of the current episode of arrhythmia [19].

In a study by Marchese et al. data were obtained on 411 patients with AF after electrical cardioversion: after 12 months, 250 of them had repeated episodes of arrhythmia and they also had a significantly larger initial indexed volume of the left atrium compared to those who did not have arrhythmia during the year [20].

It has been proven that fibrosis is a hallmark of LA structural remodeling and is associated with an increased risk of stroke, worsening of the results of catheter ablation, and an increase in the frequency of arrhythmia recurrences [25–27].

In turn, Shin S.H. et al. studied patients with atrial fibrillation before RFA: LV dimensions, LV systolic function, and both atrial dimensions were assessed. They concluded that only the volume of the left atrium was an independent predictor of the occurrence of recurrent arrhythmia episodes during follow-up up to 6 months ( $p < 0.01$ ) [21].

In our study, the indexed linear size and volume of the left atrium in patients after RFA PV were also independent predictors of AF recurrence for 6 months, and reverse LA remodeling after six months was associated with a decrease in the likelihood of recurrent episodes of arrhythmia during this period.

Also, relatively recently, such a parameter of LA remodeling and a criterion of LV diastolic function as E/E' began to be evaluated, including in patients with AF to assess the dynamics of LA filling pressure.

The value of this indicator is also being studied by researchers in relation to assessing the probability of predicting arrhythmia recurrence. M. Caputo et al. analyzed the echocardiographic parameters of the left atrium in patients with AF, and the ratio E/E' was an independent predictor of the occurrence of recurrent AF paroxysms during the year [22].

Other authors also proved the significance of this criterion in patients with AF after RPVI [23]. Li et al. analyzed the E/E' ratio in 103 patients with AF before radiofrequency LV isolation, and it turned out that the value of 11.2 was an independent predictor of arrhythmia recurrence within 3 months after surgery [24].

According to our data, the value of E/E' also proved to be prognostically significant in relation to arrhythmia recurrence in the groups of medical cardioversion and RFA of the LV when observed up to 6 months. Moreover, the greatest prognostic value was not the initial values of E/E', but their dynamics after 14 days. Thus, a significant decrease in this parameter by 2 weeks after the restoration of SR in the groups was a significant predictor of the preservation of SR for 6 months.

While in the group of patients with electro-pulse therapy (EPT), there were no significant differences in the dynamics of LA sizes and the E/E' ratio for 6 months, regardless of the presence or absence of recurrent arrhythmias.

## CONCLUSIONS

Our data allow us to conclude that peak A, measured by transmitral blood flow, exceeding 0.5 m/s on the 1st day after rhythm restoration can be considered a significant criterion for maintaining SR for up to 6 months with any choice of cardioversion ( $p < 0.05$ ). In addition, one of the predictors of maintaining sinus rhythm by month 6, according to our data, may be the absence of AF paroxysms during the first 2 weeks after SR restoration ( $p < 0.001$ ).

Also, a decrease in dynamics after 2 weeks of such parameters of LA remodeling as the volume index and filling pressure (E/E') can serve as predictors of maintaining sinus rhythm for 6 months in patients with atrial fibrillation after successful medical cardioversion and radiofrequency ablation of the pulmonary veins. Whereas the absence of dynamics in these indicators or an increase, on the contrary, is associated with a high risk of recurrence of atrial fibrillation.

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