Cardiac electrophysiological properties paroxysmal and chronic forms of atrial fibrillation

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Background Atrial fibrillation (AF) is one of the most common cardiac arrhythmias. In recent years approximately 0.4% of the population is diagnosed AF[9,17]. Presence of atrial fibrillation in a patient dramatically increases the likelihood of heart failure (HF), arrhythmogenic cardiomyopathy, thromboembolism, and death.

Nowadays there is a tendency towards population aging and an increase in the overall life expectancy, which in the future may lead to the increased number of patients with atrial fibrillation. Normally atrial fibrillation is associated with a number of symptoms such as palpitations, irregular heartbeats, dyspnoea, heart pain, fatigue, dizziness, and syncope, though both paroxysmal and persistent atrial fibrillation may not be accompanied by any evident symptoms or any significant reduction in the quality of life [1,2,3,6,8]. Atrial fibrillation is known to deteriorate the quality of life, contributing significantly to mortality and raising the mortality by 1.8-2 times [11-14,18], the major cause is stroke and heart failure progression [15-17]. Some authors have found that atrial fibrillation is an independent cardiac death predictor [19,20,21]. The works of several authors show that in patients with congestive heart failure atrial fibrillation is an independent predictor of all-cause and sudden mortality [23-26].

Mortality associated with atrial fibrillation is non to be not uniform and depends on concomitant diseases [27, 28, 29]. Patients with idiopathic asymptomatic atrial fibrillation are thought to have the lowest mortality rate, though the recent study [30,9] demonstrated that idiopathic atrial fibrillation may be an independent predictor of the death. Despite the fact that atrial fibrillation is a significant clinical problem, the data regarding the survival of patients with various forms of atrial fibrillation are scarce and sometimes contradictory [31, 32,33,34].

The recent clinical and experimental studies have demonstrated that frequent re-activation of the atrial myocardium plays a significant role in AF arrhythmogenesis, they also have shown the role of triggers in AF arrhythmogenesis.

Numerous hypotheses have been proposed about the factors that contribute to the AF presence for a long time.[35-37,40] One of them is that AF itself may be the cause of changes in the atrial myocardium, thus making this arrhythmia stable. This hypothesis was confirmed in animal experiments, and showed that there was a progressive remodeling of the atrial electrophysiological properties.[38, 39]

Most of the studies of AF pathophysiology conducted recently show renewed interest and insufficiency of our knowledge of this arrhythmia. Though recent observations have given some understanding of the mechanisms underlying AF development and course, clear evidence of the above hypotheses about a number of phenomena is still lacking.[41-43]

Despite the evident progress in AF management, the study of electrophysiological characteristics predicting the development of this arrhythmia and changes in the heart electrophysiological properties may contribute to the development of AF treatment methods based on the disease pathogenesis.[44-47]

This paper contains the analysis of the causes and conditions of paroxysmal AF development and its progression into the chronic form, the degree of remodeling of myocardial electrophysiological properties depending on AF duration and persistence.

Study objective: To study the regional changes of the atrial electrophysiological properties in patients with atrial fibrillation and to conduct a comparative analysis of the electrophysiological properties in patients with chronic and paroxysmal atrial fibrillation.

Materials and methods. The electrophysiology laboratory conducted electrophysiological studies (EPS) in 60 patients over the period from January 2012 to September 2016 within the Electrophysiology Program for AF patients. Group 1 included 20 patients with paroxysmal AF, group of 2 included 18 patients with persistent AF (duration of the last paroxysm that did not terminate spontaneously — from 8 to 90 (median 28) days; hereinafter this form is referred to as chronic AF). Group 3 that included 22 patients was assigned to a control group, these patients were conducted EPS after RFA for WPW syndrome, ectopic atrial tachycardia, or atrioventricular nodal tachycardia.

The main indications for EPS in treatment group 1 was to investigate the electrophysiological properties of atrial and cardiac conduction system, mapping of ectopic foci, and identification of slow or fragmented conduction areas to determine further treatment strategy. For group 2 patients the main indication for EPS was the restoration of sinus rhythm, assessing the risk of recurrence, and the study of the process of cardiac electrophysiological remodeling. Group 3 patients were performed EPS after RFA within the program developed for AF patients in order to compare the results obtained with the results in other treatment groups.

Clinical characteristics of patients are given in Table No.1 and Table No. 2.

All patients included in Group 2 had documented AF episodes in their ECGs, 3 patients (16.6%) had normosistolic AF form, and 15 patients had (83.3%) tachisystolic AF form. In 25% of patients (5 patients from Group 1) AF paroxysm occurred for the first time during EPS and the duration was from 2 to 30 (median 11) minutes. In the rest patients from Group 1 the paroxysm average duration was from 30 minutes to 6 hours (median 87 minutes). The duration of the current paroxysm in Group 2 patients was 8 to 90 day (median — 28 days).

Table No.1. Clinical profile of patients

	Group 1 (Persistent AF)	Group 2 (Chronic AF)	Group 3 (control)
Age, years	43±8.8	44.2*10.8	41.8±6.2
Gender (male/female)	13/7	10/8	10/12
Arrhythmia duration, years	from 2 to 27 (median –10)	from 0.5 to 8 (median — 2)	from 2 to 20 (median –10)*
Mean paroxysm duration, min	from 2 to 360 (median — 80)	Persistent paroxysm from 8 to 90 (median — 28)	from 0.5 to 120 (median - 80)*
Concomitant cardiac disease	50 (10)	83.3 (15)	9.09 (2)
History of cardiac surgery in the past	RFA 45%(9) Open –20% (4) 1 No-35%(7)	RFA-11,1%(2) Open –72.2% (13) No –16.6% (3)	100%(22)-RFA

*- in control group patient — parameters (history of arrhythmia, paroxysm frequency and duration) are typical for symptomatic arrhythmia observed in these patients.

In groups 1 and 3, the main complaints were: palpitation — in 26 (61.9%) patients, general weakness — in 21 (50%) patients, exertional dyspnea — in 12 (28.5%) patients, periodically occurred dizziness — in 9 (21.4%) patients, disruption of the heart rhythm — in 7 (16.6%), fatigue — in 6 (14.2%) patients. In group 2 patients complaints were: dyspnea upon mild exertion — in 14 (77.7%) patients, palpitation — in 11 (61%) patients, fatigue — in 10 (55.5%) patients, 13 (72.2%) patients undergone open heart surgery, 6 (33.3%) patients had the surgery some time ago — from 2 to 8 months ago. Mean paroxysm duration in operated patients was 11 ± 3.09 days.

Associated cardiac pathology included acquired heart valvular disease in 19 patients. Coronary heart disease (CHD) was in 5 patients. Congenital heart defects were in 3 patients (Table No.2).

Table No.2. Concomitant cardiac pathology.

	Group 1	Group 2	Group 3
Acquired heart disease			
Acquired mitral valve damage (MV)			
— stenosis	2	4	
— stenosis + failure		5	
Aortic valve damage (AV)			
— failure		2	
— stenosis + failure	2	4	
Tricuspid valve damage (TV)			
— failure		8	
Combined valvular damage			
MV + AV		3	
MV + TV		7	
Coronary heart disease			
Two-vessel disease		2	2
Three-vessel disease		1	
Congenital heart disease			
Aorta coarctation	1		
Double-chambered RV		1	
Atrial septal defect		2	
Heart failure as per NYHA classification			
0	6	0	13
I	10	8	9
II	4	4	

III	0	6	

43 (72.8%) patients had a history of treatment with antiarrhythmic drugs referred to I, II, III groups. An number of antiarrhythmic drugs taken varied from 1 to 3, on average it was 1.4 ± 0.5. Immediately before the electrophysiological study all patients with chronic AF received antiarrhythmics (Cordarone — 88.9%) on average for 7,4 ± 2,3 days to prevent early AF recurrence. In all other patients antiarrhythmic drugs were withdrawn 48-74 hours prior to the EPS, Cordarone was withdrawn 14-30 days, and digoxin — 3-5 days prior to the study. Apart from the antiarrhythmics 5 (20%) patients with paroxysmal AF and all patients with chronic AF were administered antiplatelet treatment (Aspirin 125 mg once daily) and antithrombotic treatment with Fenilin or Warfarin with monitoring of international normalized ratio (MHO) and prothrombin index (PTI) to keep them within the target ranges from 2 to 2.5 and from 35 to 50%, respectively.

All patients were performed a standard transthoracic echocardiography (echocardiography results are given in the table No.3), if paroxysm duration was greater than 48 hours, transesophageal echocardiography was performed to exclude any thrombus formation in the left atrial cavity, 15 (83.3%) patients were repeatedly performed echocardiography within 3 days after sinus rhythm restoration.

Table No.3. The results of echocardiography.

	Group 1 (Persistent AF)	**Group 2 (Chronic AF)**		**Group 3 (Control):**
		Prior to sinus rhythm restoration	**After sinus rhythm restoration**	
Left ventricular end-diastolic dimension, cm	5.04±0.7	4.9*0.25	4.3±0.15*	5.04±0.4
Left ventricular end-systolic dimension, cm	3.4±0.6	3.3±0.2	3.2±0.1*	3.2±0.4
Left ventricular end-systolic volume, mL	37.,3±12.9	43.5±7.8*	35.8±5.5*	Зб.6±13.3
Left ventricular end-diastolic volume, mL	107±41.3	107±9.9	94.6±26.3*	106.6±30.1
Ejection fraction, %	61.8±7.1*	59.6±6.0*	60±7.6	64.4±4.1
Stroke volume, mL	72.5*10.6	60.4±24.6	73.4±24.1	74.5±18 Д
Left atrial dimension, cm	3.7±0.6**	4.8±0.6	4.3±0.4**	3.64±0.48
Left atrial dimension, cm (transesophageal echocardiography)	-	4.9±1.2	-	-

-p<0,05, **-p£0,01 (*- comparison of group 1 patients and group 2 patients vs. control group); comparison of group 2 patients before and after sinus rhythm restoration).

All patients with chronic AF were performed endocardial cardioversion to restore the sinus rhythm. Endocardial defibrillation was effective in 94.4% of cases (17 patients) — the sinus rhythm was restored, one patient needed transthoracic electric cardioversion (TEC) with an energy of 360 J, as a result the sinus rhythm was restored.

In 3 cases (16.6%) there was bradycardia, which required stimulation conducted fore not more than 2 minutes in the automatic mode from ventricular electrode poles for endocardial defibrillation. The average defibrillation energy was 9.44 ± 1.1 J and input impedance was 50 ± 8,0 Ohm.

After sinus rhythm restoration 4 patients (22.2%) had AF recurrence after 4.9 ± 2.5 (median — 4) days. In one case sinus rhythm spontaneously restored after 2 hours, and in the rest cases repeated endocardial cardioversion was required.

Table No. 5. Concomitant cardiac arrhythmias

	Group 1	**Group 2**	**Group 3**
WPW syndrome	8		18
Atrioventricular nodal tachycardia AV rientri			4
Atrial tachycardia	1		
Atrial flutter (AFlu), type 1	2	1	
Atrial flutter (AFlu), type 2	6	3	
Ventricular extrasystole (VE), grade 2 to 3 as per Lown's grading VT	4	3	5
Atrial extrasystole	7	5	10

Concomitant cardiac arrhythmias were found in 36 (94.7%) patients with paroxysmal or chronic AF (Table No.5).

In order to achieve this objective all patients included in this study were performed comprehensive clinical and diagnostic, laboratory and functional examination. Patients were performed their examination stepwise: collection of clinical and anamnestic data, electrocardiographic, echocardiographic, and electrophysiologic test methods were applied.

Results.

Dysfunction of sinoatrial node, atrioventricular node and His-Purkinje system was not found in any treatment group.

The most significant conduction disorders were found in patients with chronic AF (P-wave duration increased by 29.6% and PQ interval increased by 22.9%, $p < 0.05$), and they were less significant in patients with paroxysmal AF (not more than 5.9%, $p<0.05$). Increased PQ interval in the respective groups was probably associated with the increased atrial component in this interval. No significant disorders of intraventricular conduction were found in any treatment group.

Disorders of inter- and intra-atrial conduction were observed in 100% of patients with chronic AF, in 12 (60%) patients with paroxysmal AF, and only in 4 (18.2%) patients in the control group.

The conduction time in patients with chronic AF vs. control group increased up to 77.2% in the right atrium and 65.8% in the left atrium ($p < 0.05$).

No statistically significant differences in the time of intra-atrial conduction in different parts of the atria were found between Group 1 and Group 3 ($p > 0.05$), patients with paroxysmal AF probably did not have any significant conduction disorders (Table No.6).

Table No.6. Intra- and interatrial conduction time

	A(HRA)-A(His)	A(HRA)-A(CSp)	A(HRA)-A(CSd)	A(CSp)-A(CSd)
Group 1 (paroxysmal AF)	24.5±12.3	49.5±8.1	67.8±10.1	18.5±4.8

Group 2 (chronic AF)	46.8±22.9*	69.9*20.7*	97.0±24.3*	27.7±15.7*
Group 3 (control)	26.4±12.2	52.8±11.6	69.3±13.4	16.7-**fc6,**5

* P <0.05 (* - comparison of group 2 patients vs. control group)

Disorders of local conduction, i.e., abnormal atrial electrograms after sinus rhythm restoration were found only in two patients (11.1%) with chronic AF, in once case electrogram duration increased up to 108 msec, it was recorded in the mid part of the right atrium along the border ridge, and in the second case it was a double atrial electrogram, recorded in the upper part of the right atrium.

A significantly greater number of abnormal atrial responses were recorded during programmed stimulation of various atrial part. Abnormal atrial electrograms were recorded in 6 patients (30%) with paroxysmal AF in different parts of the coronary sinus (CSp-3, CSm-2, CSd-1) and the lower part of the right atrium (2 patients); these were prolonged and fractionated electrograms, wherein in two patients abnormal electrograms were recorded at several sites of the right and left atrium.

In patients with chronic AF abnormal electrograms were found in 12 cases (66.7%), wherein only one patient had abnormal activity recorded only at one site, i.e. the proximal coronary sinus, in all the other patients abnormal atrial responses were recorded at several sites, depending on the location and the stimulation program. The most frequent location of abnormal atrial response was lower part of the right atrium (52.3%), the remaining electrograms were localized in different parts of the coronary sinus. In addition, patients in chronic AF group vs. paroxysmal AF group had much wider area of induction of abnormal atrial responses or atrial tachyarrhythmias (69 ± 30.35 msec and 22 msec ± 15,49, respectively, p = 0.006).

Atrial effective refractory period (ERP) was measured in patients of all three groups at three locations — upper (HRA) and lower (LRA) parts of the right atrium and in the distal coronary sinus (CSd) of the left atrium. Programmed stimulation was conducted sequentially using two basic stimulation lengths — 600 and 450 msec to assess atrial ERP adaptation depending on the basic stimulation length (Table No.7).

Table No.7. Effective refractory period in various atrial parts.

	Refractory period efficacy		Refractory period efficacy		Refractory period efficacy CSd	
	600 msec	450 msec	600 msec	450 msec	600 msec	450 msec
Group 1 (paroxysmal AF)	183.8+30.2*	181.5+26.1*	190+21.2*	179.2+22.5*	228.5+28.2	220.8±26.6
Group 2 (chronic AF)	**188Д**±24.0*	200+22.8*	223.6±31.1#*	210±25.7# *	190.9±25.5**	190.9+24.3*
Group 3 (control)	194±34.6	190.6±35.1	191.3±17.7	181.3*20.3	211.3+27.5	199.3+21.2

-p<0,05 (- comparison of Group 1 patients and group 2 patients vs. control group); *-p<0,05, *„-p<0,001 (”- comparison between Group 1 patients and Group 2 patients).

Variance for effective refractory period (ERP) was calculated in all three treatment groups to assess spatial distribution of atrial ERP and physiological adaptation of atrial ERP.

Our patient population did not have any difference in ERP in the upper right atrium (HRA) between AF patients (persistent AF and chronic AF) and the controls (p<0.05). Still, ERP measured in the distal coronary sinus was significantly shorter in patients with chronic AF than in those with persistent AF (190.9 +± 25.5 and 228.5 ms ± 28.2 ms, respectively, p <0.001).

Conversely, in the lower part of the right atrium (LRA) in treatment Group 2 EPG was significantly

greater than EPG in treatment Group 1 and 3 (31.1 msec + 223.6 and 191,3 ± 17.7 msec, respectively, p <0.05).

The spatial distribution of atrial ERP values differed in different treatment groups. In the control group and in the group of patients with paroxysmal AF maximum ERP was recorded in the distal CS, and the minimum one — in the lower or upper parts of the right atrium (i.e. CSd> HRA> LRA; p <0.05). CSd>HRA>LRA; p<0,05).

It should be noted that in the group of patients with paroxysmal AF 6 (30%) patients had spatial ERP distribution that differed from the average, whereas in the control group only 2 (9.1%) patients had spatial ERP distribution that differed from the average. In patients with chronic AF minimum ERP values were recorded in distal CS and in the upper part of the right atrium, and ERP value in the lower right atrium was much greater than ERP values elsewhere (i.e. LRA> CSd> HRA; p <0.05). Disorders of ERP physiological adaptation (i.e. increase in ERP with an increase in heart rate or decrease the duration of the basic stimulation cycle duration (CD)) were observed in 17 (85%) patients with paroxysmal AF, in 12 (66.6%) patients with chronic AF, and only in 4 (18.2%) patients in the control group. Moreover, most disorders of ERP physiological adaptation were observed in the lower right atrium (LRA) and distal CS (CSd) (47% and 38%, respectively), whereas in the upper right atrium (HRA) such disorders were found only in 15% of cases.

The maximum difference between the atrial effective refractory period at three different locations, i.e the upper (the HRA) and bottom (the LRA) parts of the right atrium and distal coronary sinus (dispersion of refractoriness) in Group 1 was 49.1 ± 27 msec (basic stimulation length — 600 msec) and 31,8 ± 21,8 (basic stimulation length — 450 msec), in Group 2 — 60 ± 19.2 msec and 53.8 ± 19.8 msec (basic stimulation lengths — 600 msec and 450 msec, respectively) and in Group 3 — 46 ± 23.8 msec and 42 ± 23.1 msec (basic stimulation lengths — 600 msec and 450 msec, respectively) (p <0.05).

Assessment of the dispersion of refractoriness in our patient population showed that this parameter in patients with chronic AF was significantly higher than in the rest treatment groups (p <0.05). Thus, in patients with paroxysmal AF the refractory dispersion was by 22.5% and 38.7% less than in patients with chronic AF, while in the control group it was by 30.4% and 28.1% less than in patients with chronic AF (p <0.05) at the basic stimulation cycle length, i.e. 600 and 450 msec, respectively.

The process of electrophysiological remodeling was studied in patients with chronic AF. Remodeling of electrophysiological properties was characterized by reduced atrial conduction in 100% of patients, local block in 12 (66.7%) patients, and conduction dispersion, reduced atrial ERP, and loss of ERP physiological adaptation in 12 (66.7%). The most significant alterations of the electrophysiological properties were observed in the left atrium (distal coronary sinus) and the lower part of the right atrium. This suggests a significant role of these parts of the heart in AF pathogenesis.

The assessment of echocardiographical data showed that along with echocardiographical alterations there are concomitant anatomic changes in the left atrium and ventricle associated with atrial fibrillation (i.e. structural remodeling of the heart due to AF).

Structural LV remodeling due to AF was accompanied by the development of arrhythmogenic cardiomyopathy — in our patient population the ejection fraction in case of chronic AF was 59,6 ± 6,0%, which was by 3.8% less than in the control group (p <0.05), and Left ventricular end-systolic volume was by 18.8% greater than in case of chronic AF (p <0.05), suggesting an increase in the residual volume and reduced left ventricular contractility.

Structural alterations in the left atrium were much more significant. The average LA dimension before sinus rhythm restoration was 4.8 ± 0.6 cm, which was by 33.3% greater than in the control group and by 29.7% greater than in patients with paroxysmal AF (P <0.05).

After sinus rhythm restoration 4 patients (22.2%) had AF recurrence after 4.9 ± 2.5 days. In one case sinus rhythm spontaneously restored after 2 hours, and in the rest cases repeated endocardial cardioversion was required. Although intra- and interatrial disorders were less significant in the group of patients with the recurrence compared to the group with the preserved sinus rhythm ($p < 0.05$), in all atrial parts investigated pathological changes of effective refractory period were more severe in Group 1 ($p < 0.05$). In addition, assessment of the dispersion of atrial refractoriness in these groups showed that the dispersion of refractoriness in AF recurrence group was significantly greater than in the group with sinus rhythm of 70.1 ± 29.4 msec and ± 38.6 ± 16.8 msec, respectively ($p < 0.05$). As for physiological adaptation of atrial ERP the impaired ERP physiological adaptation was found in 100% of patients in AF recurrence group and in 57.1% (8) of patients in the group with the preserved sinus rhythm.

Echocardiographic parameters did not differ between the treatment groups: the left atrium dimension and ejection fraction in AF recurrence group were 4,8 ± 0,5 cm and 60,7 ± 3,3%, respectively, and in patients with the preserved sinus rhythm the left atrium dimension and ejection fraction were 4,6 ± 0, 35 cm and 59,3 ± 7,1%, respectively ($p < 0.05$).

Electrical cardioversion caused reverse remodeling of the cardiac structural changes — the size of the left atrium decreased to 4,3 ± 0,4 cm, which was by 11.6% less than during AF (before electrical cardioversion mean LA dimension in these patients was 4.8 ± 0.6 cm) ($p < 0.05$), LV end-diastolic volume decreased from 107 ± 9.9 mL to 94.6 ± 26.3 mL, i.e. by 13.1%, and LV end-systolic volume decreased by 21.5% — from 43.5 ± 7.8 mL to 35.8 ± 5.5 mL ($p < 0.05$), still no significant findings were obtained regarding the improvement of left ventricular contractility after sinus rhythm restoration.

Result discussion.

Thus, our study results have confirmed the assumption that multiple re-entries make up the the main mechanism of atrial fibrillation. Micro-re-entry is supposed to be the main factor determining long AF duration. Micro re-entry wavelength is comprised of the atrial conduction velocity and atrial effective refractory period, therefore, the stability of micro re-entry wavelength is affected by atrial conduction disorders and reduced atrial effective refractory period. According to many authors, critical number of waves required for AF maintenance is six, in addition, critical mass of the atrial myocardium should be involved in the pathological process to maintain micro re-entry. All patients in the chronic AF group had significant disorders of atrial conduction and reduced effective refractory period in the left atrium.

All patients with chronic AF had local disorders of atrial conduction resulting in the development of abnormal (extended, fragmented, double) electrograms during sinus rhythm and in response to stimulation. These electrograms may appear due to slow, dissociated conduction as a result of local sclero-degenerative changes in the atrial myocardium.

In our patient population the most frequent sites where such abnormal electrograms were recorded were the left atrium (distal coronary sinus) and the lower part of the right atrium. This may be associated with the anatomic factors predisposing the development of these areas in the atrial myocardium (Marshall ligament in the distal coronary sinus and the embryonic venous sinus that precedes the formation of the right atrium). Such local atrial conduction disorders cause of longitudinal dissociation, the formation of daughter micro re-entry wavelets resulting consequently in persistent AF.

Long AF duration may be accompanied by a remodeling of the electrophysiological and structural properties of the atrial myocardium. Electrophysiological atrial remodeling is characterized by the reduced effective refractory period of the myocardium in the left atrium, increased atrial refractory dispersion, and loss of physiological adaptation in response to increased stimulation frequency. In patient population AF reoccurred after sinus rhythm restoration in patients with the effective refractory period in the left atrium significantly less compared to other patients with chronic AF, besides, these patients had more significantly

increased dispersion of atrial refractoriness. All patients with chronic AF had more significant increase in left atrial dimension. Echocardiography results showed that AF patients had a greater left ventricular end-diastolic and end-systolic volumes and reduced left ventricular ejection fraction. These changes were caused by the structural remodeling of the heart (arrhythmogenic cardiomyopathy) during AF, resulting mainly in the dilation of the left atrium and abnormal left ventricular systolic and diastolic function.

Conclusions.

1. The most significant atrial conduction and refractory disorders were found in the distal part of the atrial coronary sinus and in the lower part of the right atrium. These areas play a crucial role in the development of chronic atrial fibrillation.

2. Local atrial conduction disorders are typical for patients with chronic atrial fibrillation, they are caused by slowing, blocking, fragmentation, and dispersion of the electric pulse.

3. Long-lasting atrial fibrillation may be accompanied by remodeling of electrophysiological properties of the atrial myocardium, characterized by shortening of the atrial effective refractory period, loss of physiological adaptation, and increased dispersion of atrial refractoriness.

4. Changes in the effective refractory period in various parts of the atria and increased dispersion of atrial refractoriness are known to be important prognostic for the recurrence of atrial fibrillation, disorders of atrial conduction and left ventricular contractile function.

5. Electrophysiological remodeling in atrial fibrillation may be accompanied by the development of arrhythmogenic cardiomyopathy (structural remodeling of the heart), resulting in the increased left atrial dimension and reduced left ventricular systolic and diastolic function, after sinus rhythm restoration reverse structural remodeling of the heart may occur leading to the decreased left atrial and left ventricular dimensions.

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