Features of the Remodeling of Atria and Pulmonary Veins in CHF Patients with Paroxysmal AF and Permanent AF

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Abstract

Research objective: the aim is to study the features of the remodeling of the left atrium and pulmonary veins in CHF patients with paroxysmal AF, with permanent AF, and without arrhythmia (n=225). Materials and methods. The features of the remodeling of the left atrium and pulmonary veins were studied echocardiographically in patients having chronic heart failure with paroxysmal AF (n=38) and permanent AF (n=36) and without arrhythmia (n=225). Results. Structural changes of the left atrium and pulmonary veins in patients with chronic heart failure having permanent atrial fibrillation were significantly more distinct than those in patients with paroxysmal atrial fibrillation, in patients without arrhythmia, and in the control group. Thus, respectively, LA in the left lateral position was 46.35±1.93, 41.26±1.49, 38.60±0.90, and 29.57±0.68 mm; LAVI was 67.16±6.14, 58.81±5.92, 44.28±1.34, and 23.64±0.47; the maximum diameter of the left inferior pulmonary vein was 23.91±1.07, 22.21±0.69, 20.64±0.41, and 13.51±0.16 mm; the minimum diameter of the pulmonary vein was 15.10±1.06, 13.15±1.07, 10.51±0.41, and 5.70±0.09 mm, with higher E/e' values of 14.78±1.45, 11.34±1.81, 10.03±0.47, and 6.26±0.28 mm. Conclusion. A more evident dilatation of the left atrium with the dilatation of pulmonary veins was diagnosed in patients with permanent AF as compared to that in patients with paroxysmal AF and patients having CHF without arrhythmia.

Introduction

Atrial fibrillation (AF), being one of the most frequent types of arrhythmia in clinical practice, affects the course of chronic heart failure (CHF). Patients with both CHF and AF have poor prognosis, including higher mortality regardless of the parameters of the LV ejection fraction (LV EF) [1, 2]. The fact that AF often develops in many patients with CHF is due to common risk factors and similar pathophysiological mechanisms [3] including cardiac structural remodeling, activation of neurohormonal mechanisms, and impairment of the left ventricular function during ventricular flutter.

Drug and non-drug approaches to the management of patients are applied today in order to reduce the frequency of atrial fibrillation or to restore sinus rhythm [4]. However, there is a view that an obvious beneficial effect of sinus rhythm maintenance with the use of antiarrhythmic drugs is annihilated by unfavorable and often fatal results, namely a 49% increase in mortality risk [5]. The non-drug approach to managing patients with AF is radiofrequency ablation (RFA). The sinus rhythm is successfully maintained in 20-80% of patients within a year after RFA [6, 7]. Despite the development of the RFA technique, the relapse of rhythm breakdown [8, 9] indicates the necessity of detecting the mechanisms that promote the relapse.

An increased left atrial size is a well-established, independent predictor of AF [10, 11]. Atrial remodeling is associated with slower and more heterogeneous atrial conduction and increased PV firing. Paroxysmal forms show a predominance of local triggers/drivers, particularly from pulmonary veins (PVs) [12]. As AF becomes more persistent and eventually permanent, reentry substrates (initially functional and then structural) predominate. It is known that 90% of paroxysmal AFs are driven by PV sources and respond well to

PV-directed ablation procedures; as AF progresses, atrial substrates become more complicated and require more complex ablation procedures [4].

Research objective : The aim is to study the features of the remodeling of the left atrium and pulmonary veins in CHF patients with paroxysmal AF, with permanent AF, and without arrhythmia.

Materials and methods . The study retrospectively recruited 299 patients with chronic heart failure of the II-III New York Heart Association (NYHA) functional classes and 132 practically healthy people aged 35.08±1.80 (control group), examined in Klinika Uralskaya, LLC (Ekaterinburg, Russia). Patients with CHF were divided into three groups: group 1 (n=225) included patients with chronic heart failure without atrial fibrillation; group 2 (n=38) consisted of patients having chronic heart failure with paroxysmal atrial fibrillation; group 3 (n=36) was represented by patients having chronic heart failure with permanent atrial fibrillation. Chronic heart failure was diagnosed in accordance with the latest recommendations on CHF diagnostics [13]. Transthoracic echocardiography was recorded using a Philips HD-15 device (USA) according to the standard protocol with the additional determination of the maximum and minimum diameters of the visualized pulmonary vein in order to diagnose pulmonary venous hypertension [14]. The informed consent for research was obtained from all the patients. All the patients gave a written consent for participation in the study, which was approved by the local ethic committee of the Institute of Medical Cell Technologies (Ekaterinburg, Russia).

The investigation results were statistically processed according to the Student's criterion in connection with the normal data distribution with the use of the Microsoft Excel spreadsheet program. Consistency with the normal distribution was checked by the visualization method and the Pearson test of fit. The differences were considered statistically significant at $p<0.05$. The data is presented as M±m, where M is the average of the measured values and m is the error.

Results

The groups were comparable in the number and age of patients, associated pathologies, and the severity of chronic heart failure evaluated according to the stages and NYHA functional classes. In the group of patients with permanent atrial fibrillation, male gender prevailed as compared to other groups, probably, due to men's late medical consultation. Table 1 presents a general characteristic of the patients.

Table 1. Characteristic of CHF patients with permanent atrial fibrillation, with paroxysmal one, and without atrial fibrillation

Parameter	Control values (n=132)	CHF patients without AF (n=225)	P	Patients with paroxysmal AF (n=38)	P	P'	Patients with permanent AF (n=36)	P	P'
Gender (male)	40 (30.3%)	62 (27.5%)		7 (18.4%)			18 (50%)		
Age, years	35.08±1.80	65.01±1.45	0.001	70.31±3.04	0.001	0.002	69.28±3.48	0.001	0.03
AH	-	225(100%)		38(100%)			36(100%)		
CAD	-	29 (12.9%)		4(10.5%)			4(11.1%)		
Type 2 DM	-	11(4.9%)		4(10.5%)			3(8.3%)		
AS	-	9(4%)		1(2.6%)			2(5.6%)		

Parameter	Control values (n=132)	CHF patients without AF (n=225)	P	Patients with paroxysmal AF (n=38)	P	P'	Patients with permanent AF (n=36)	P	P'
Inferolateral wall of the left ventricle, mm	7.73±0.16	11.20±0.2	0.001	10.95±0.65	0.001	0.45	11.50±0.64	0.001	0.49
Interventricular septum thickness, mm	8.11±0.22	12.18±0.36	0.001	12.11±0.80	0.001	0.901	12.27±0.61	0.001	0.81
Inferior wall of the right ventricle, mm	4.22±0.72	7.95±0.76	0.001	7.34±0.42	0.001	0.17	8.88±1.29	0.001	0.20
Myocardial mass index, g/m^2	82.35±2.90	107.93±3.82	0.001	108.63±7.62	0.001	0.900	105.19±8.92	0.001	0.60
Right atrium volume, ml	33.69±1.07	53.74±2.28	0.001	54.14±5.23	0.001	0.93	101.21±12.35	0.001	0.001
Left atrium in the left lateral position, mm	29.57±0.68	38.60±0.90	0.001	41.26±1.49	0.001	0.003	46.35±1.93	0.001	0,001
Left atrium volume, ml	42.94±1.44	85.51±3.20	0.001	103.41±10.63	0.001	0.002	124.65±10.63	0.001	0.001
LAVI	23.64±0,47	44.28±1.34	0.001	58.81±5.92	0.001	0.001	67.16±6.14	0.001	0.001

Parameter	Control values (n=132)	CHF patients without AF (n=225)	P	Patients with paroxysmal AF (n=38)	P	P'	Patients with permanent AF (n=36)	P	P'
Left ventricular end-diastolic volume, ml	93.31±4.13	107.56±6.10	0.001	109.38±11.54	0.01	0.86	110.62±13.89	0.02	0.69
Left ventricular end-systolic volume, ml	29.94±1.66	35.35±3.08	0.001	33.52±4.31	0.11	0.44	48.21±9.98	0.001	0.02
Stroke volume, ml	62.88±2,81	72.54±3.62	0.001	74.41±6.55	0.001	0.49	62.41±5.86	0.85	0.001
Simpson's ejection fraction, %	66.67±0.95	67.28±0.95	0.31	68.71±1.45	0.02	0.09	58.38±4.00	0.001	0.001
Systolic pressure in the pulmonary artery, mm Hg	14.74±0.51	23.43±1.24	0.001	26.05±3.25	0.001	0.12	34.82±3.34	0.001	0.001
IVC, mm	18.83±0.52	17.13±0.44	0.001	16.79±0.99	0.001	0.59	19.75±1.00	0.07	0.001
TAPSE, mm	22.43±0.42	22.19±0.53	0.46	21.40±1.04	0.06	0.18	16.50±1.42	0.001	0.001
Average E/e'	6.26±0.28	10.03±0.47	0.001	11.34±1.81	0.001	0.16	14.78±1.45	0.001	0.001
Maximum pulmonary vein diameter, mm	13.51±0.16	20.64±0.41	0.001	22.21±0.69	0.001	0.001	23.91±1.07	0.001	0.001

Parameter	Control values (n=132)	CHF patients without AF (n=225)	P	Patients with paroxysmal AF (n=38)	P	P'	Patients with permanent AF (n=36)	P	P'
Minimum pulmonary vein diameter, mm	5.7±0.09	10.51±0.41	0.001	13.15±1.07	0.001	0.001	15.10±1.06	0.001	0.001

Note: AH is arterial hypertension; CAD is coronary artery disease; Type 2 DM means type 2 diabetes mellitus; AS is acute stroke; LAVI is the left atrial volume index; IVC is the inferior vena cava; TAPSE is tricuspid annular plane systolic excursion; Average E/e' is the ratio of the early-diastolic blood flow velocity to the average between the velocity of the lateral part and the medial part of the fibrous ring of the mitral valve.

P indicates the significance of the differences between each group of patients and the control group; P' indicates the significance of the differences between the group of patients with paroxysmal AF and the group of CHF patients without AF, and also the differences between the group of patients with permanent AF and the group of CHF patients without AF; P" indicates the significance of the differences between the group of patients with permanent AF and the group of patients with paroxysmal AF.

The patients with chronic heart failure, regardless of the absence or presence of paroxysmal or permanent atrial fibrillation, have structural changes in the heart, as compared to the control group, which were detected echocardiographically ($P<0.05$). These changes are as follows: myocardial hypertrophy of the walls of both ventricles (the LV inferolateral wall thickness is 11.20±0.20, 10.95±0.65, 11.50±0.64, and 7.73±0.16 mm, respectively; the interventricular septum thickness is 12.18±0.36, 12.11±0.80, 12.27±0.61, and 8.11±0.22 mm; the RV wall thickness is 7.95±0.76, 7.34±0.42, 8.88±1.29, and 4.22±0.72 mm), increased myocardial mass index (107.93±3.82, 108.63±7.62, 105.19±8.92, and 82.35±2.90 g/m^2), dilatation of the right and left atria (the right atrium volume is 53.74±2.28, 54.14±5.23, 101.21±12.35, and 33.69±1.07 ml; the left atrium volume is 85.51±3.20, 103.41±10.63, 124.65±10.63, and 42.94±1.44 ml), LAVI (44.28±1.34, 58.81±5.92, 67.16±6.14, and 23.64±0.47), increased systolic pressure in the pulmonary artery (23.43±1.24, 26.05±3.25, 34.82±3.34 and 14.74±0.51 mm Hg), dilatation of the left lower pulmonary vein of the maximum (20.64±0.41, 22.21±0.69, 23.91±1.07, and 13.51±0.16 mm) and minimum (10.51±0.41, 13.15±1.07, 15.10±1.06, and 5.70±0.09 mm) diameters.

The patients with chronic heart failure having paroxysmal or permanent atrial fibrillation, as compared to patients without atrial fibrillation, have significantly more distinct structural changes in the heart. They are more evident left atrium dilatation (LA in the left lateral position is 41.26±1.49, 46.35±1.93, and 38.60±0.90 mm, respectively; left atrium volume is 103.41±10.63, 124.65±10.63, 85.51±3.20 ml; LAVI is 58.81±5.92, 67.16±6.14, and 44.28±1.34), dilatation of the left lower pulmonary vein of the maximum (22.21±0.69, 23.91±1.07, and 20.64±0.41 mm) and minimum (13.15±1.07, 15.10±1.06, and 10.51±0.41 mm,) diameters (Table 1).

Differences in myocardial remodeling in the patients with different forms of atrial fibrillation have been detected. The patients with permanent AF, as compared to the patients with paroxysmal AF, are noted to have larger LA dilatation (LA in the left lateral position is 46.35±1.93 vs. 41.26±1.49 mm; the left atrium volume is 124.65±10.63 vs. 103.41±10.63 ml; LAVI is 67.16±6.14 vs. 58.81±5.92) with larger dilatation of the left lower pulmonary vein of the maximum (23.91±1.07 vs. 22.21±0.69 mm) and minimum (15.10±1.06 vs. 13.15±1.07 mm) diameters with higher average E/e' (14.78±1.45 vs. 11.34±1.81 mm). Besides, the dilatation

of right atrium (the right atrium volume is 101.21±12.35 vs. 54.14±5.23 ml), more evident LV myocardial hypertrophy (LV inferolateral wall thickness is 8.88±1.29 vs. 7.34±0.42 mm), together with increased systolic pressure in the pulmonary artery (34.82±3.34 vs. 26.05±3.25 mm Hg) at a lower LV preserved ejection fraction (58.38±4.00 vs. 68.71±1.45%) and a decreased systolic function of the right ventricle (TAPSE is 16.50±1.42 vs. 21.40±1.04 mm), were detected in the CHF patients having permanent atrial fibrillation.

Discussion.

The study of myocardial remodeling in the patients with chronic heart failure without arrhythmia and those having paroxysmal or permanent atrial fibrillation has shown structural changes in the heart, as compared to the control group, in the form of the increased wall thickness of both ventricles, increased myocardium mass index, dilatation of both atria, the increased maximum and minimum diameters of the left lower pulmonary vein, and elevated systolic pressure in the pulmonary artery. The structural changes in the heart were the same in each group regardless of the presence or absence of arrhythmia.

The study of myocardial remodeling in the patients with chronic heart failure having atrial fibrillation has shown more evident structural impairments of the heart walls and chambers as compared to those in the patients without arrhythmia; this manifested itself in a more pronounced dilatation of the left atrium, with a pulmonary vein flowing into it. According to other researchers, PVs are critical in AF initiation and maintenance [15].

The study of myocardial remodeling in the patients with chronic heart failure having permanent atrial fibrillation has shown more evident structural impairments of the heart chambers and hemodynamics as compared to those in the patients having paroxysmal atrial fibrillation; this manifested itself in a more pronounced dilatation of the left atrium, with a pulmonary vein flowing into it, the value of the average E/e' ratio being higher. Besides, the CHF patients with permanent AF had a dilatation of the right atrium with greater hypertrophy of the RV inferolateral wall, together with increased systolic pressure in the pulmonary artery and the RV systolic dysfunction estimated according to TAPSE. Both the left atrium and the right atrium possess structural features contributing to the pathogenesis of AF [16].

Thus, the CVD patients with CHF have left atrial dilatation with dilatation of pulmonary veins as distinct from the control group. Paroxysmal AF in the patients with CHF is likely to associate due to the further myocardial remodeling of the atria in the form of an even greater dilatation of the left atrium and pulmonary veins flowing into it. The maximum atrial volumes and pulmonary vein diameters have been detected in the patients having CHF and permanent AF.

Besides, the obtained results confirm that AF evolves from paroxysmal to persistent and permanent forms through the influence of atrial remodeling progression caused by arrhythmia [17, 18]. Remodeling-induced atrial dilatation promotes AF by increasing circuit path space, so that larger reentry circuits can be supported and/or a larger number of circuits can be maintained [17]. The study included 1,219 patients with paroxysmal AF. Progression of AF occurred in 178 (15%) patients. Multivariate analysis has shown that heart failure, age, previous transient ischemic attack or stroke, chronic obstructive pulmonary disease, and hypertension are the only independent predictors of AF progression. The factors known to cause atrial structural remodeling (age and underlying heart disease) are independent predictors of AF progression. With consideration of the nature of these factors and in view of the fact that they are associated with future cardiovascular events, researchers conjecture that structural rather than electrical remodeling of the atria is involved in AF progression [18]. Underlying diseases might cause chronic stretch and atrial dilatation, which seem to be important stimuli for chronic atrial structural remodeling (cellular hypertrophy, fibroblast proliferation, and tissue fibrosis), and this enables the maintenance of AF [19].

Conclusion. Thus, more significant dilatation of the left atrium with pulmonary veins flowing into it, with their increasing dilatation in the association of paroxysmal AF and its transition into permanent AF has been detected in patients with chronic heart failure having atrial fibrillation.

Conflict of interests

We confirm that there is no financial support or conflict of interests to be reported.

References

Wang TJ, Larson MG, Levy D, Vasan RS, Leip EP, Wolf PA, D'Agostino RB, Murabito JM, Kannel WB, Benjamin EJ. Temporal relations of atrial fibrillation and congestive heart failure and their joint influence on mortality: the Framingham Heart Study. Circulation 2003;107:2920–2925.

Mamas MA, Caldwell JC, Chacko S, Garratt CJ, Fath-Ordoubadi F, Neyses L. A

meta-analysis of the prognostic significance of atrial fibrillation in chronic heart failure. Eur J Heart Fail 2009;11:676–683.

Kotecha D, Piccini JP. Atrial fibrillation in heart failure: what should we do? Eur

Heart J. 2015;36:3250–3257.

1. Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomstrom-Lundqvist C, Boriani G, Castella M, Gheorghe-Andrei Dan, Polychronis E. Dilaveris, Fauchier L, Filippatos G, Kalman JM, Meir M, Lane DA, Lebeau J-P, Lettino M,. Lip GYH, Pinto FJ, Thomas GN, Valgimigli M, Van Gelder IC, Van Putte BP, Watkins CL. 2020 ESC Guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). European Heart Journal. 2020;00:1-125.
2. AFFIRM Investigators. Atrial Fibrillation Follow-up Investigation of Rhythm Management. Baseline characteristics of patients with atrial fibrillation: the AFFIRM Study. Am Heart J. 2002;143(6):991-1001.
3. Perez FJ, Lung TH, Ellenbogen KA, Wood MA. Is time to first recurrence of atrial fibrillation correlated with atrial fibrillation burden? Am J Cardiol 2006;97(9):1343-5.
4. Ganesan AN, Shipp NJ, Brooks AG, Kuklik P, Lau DH, Lim HS, Sullivan T, Roberts-Thomson KC, Sanders P. Long-term outcomes of catheter ablation of atrial fibrillation: a systematic review and meta-analysis. J Am Heart Assoc. 2013;2:e004549.
5. Spragg DD, Dalal D, Cheema A, Scherr D, Chilukuri K, Cheng A, Henrikson CA, Marine JE, Berger RD, Dong J, Calkins H. Complications of catheter ablation for atrial fibrillation: incidence and predictors. J. Cardiovasc. Electrophysiol. 2008; 19: 627-631.
6. Baman TS, Jongnarangsin K, Chugh A, Suwanagool A, Guiot A, Madenci A, Walsh S, Ilg KJ, Gupta SK, Latchamsetty R, Bagwe S, Myles JD, Crawford T, Good E, Bogun F, Pelosi F, Morady F, Oral H. Prevalence and predictors of complications of radiofrequency catheter ablation for atrial fibrillation. J. Cardiovasc. Electrophysiol. 2011; 22: 626-631.
7. Kannel WB, Wolf PA, Benjamin EJ, Levy D. Prevalence, incidence, prognosis, and predisposing conditions for atrial fibrillation: population-based estimates. Am J Cardiol. 1998;82:2N–9N.
8. Vaziri SM, Larson MG, Benjamin EJ, Levy D. Echocardiographic predictors of nonrheumatic atrial fibrillation. The Framingham Heart Study. Circulation. 1994;89:724–30.
9. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Métayer P, Clémenty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in the pulmonary veins. N Engl J Med. 1998; 339:659–666..
10. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ et al. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC) Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European Heart Journal. 2016; 37(27): 2129–2200.
11. Kirillova VV. Rannyaya ultrazvukovaya diagnostika venoznogo zastoya v malom kruge krovoobrashcheniya u patsiyentov s khronicheskoy serdechnoy nedostatochnostyu. Journal of Cardiac failure=Zhurnal Serdechnaya nedostatochnost. 2017;18(3):208-212. doi: 10.18087/RHFJ.2017.3.2315. (In Russ.)
12. Haissaguerre M, Jais P, Shah DC, Takahashi A, Hocini M, Quiniou G, Garrigue S, Le Mouroux A, Le Me´tayer P, Cle´menty J. Spontaneous initiation of atrial fibrillation by ectopic beats originating in

the pulmonary veins. N Engl J Med. 1998;339:659–666.
13. Lin YJ, Tai CT, Kao T, Tso HW, Huang JL, Higa S, Yuniadi Y, Huang BH, Liu TY, Lee PC, Hsieh MH, Chen SA. Electrophysiological characteristics and catheter ablation in patients with paroxysmal right atrial fibrillation. Circulation. 2005;112:1692–1700.
14. Nattel S, Burstein B, Dobrev D. Atrial remodeling and atrial fibrillation: mechanisms and implications. Circ Arrhythm Electrophysiol. 2008; 1:62–73.
15. de Vos CB, Pisters R, Nieuwlaat R, Prins MH, Tieleman RG, Coelen RJ, van den Heijkant AC, Allessie MA, Crijns HJ. Progression from paroxysmal to persistent atrial fibrillation clinical correlates and prognosis. J Am Coll Cardiol. 2010; 55:725–731.
16. Eckstein J, Verheule S, Groot NM, Allessie M, Schotten U. Mechanisms of perpetuation of atrial fibrillation in chronically dilated atria. Prog Biophyss Mol Biol. 2008;97:435-451.