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Original article

Assessment of fluid retention in patients with paroxysmal and long-standing persistent types of atrial fibrillation

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Abstract: Determining fluid retention in circulatory system currently remains a challenge. The *objective* of our study was to determine the sensitivity of individual symptoms and signs of chronic heart failure (CHF) and echocardiographic criteria for detecting fluid retention in patients with atrial fibrillation and invasively measured elevated atrial pressure.
Methods — We conducted a prospective study of adult patients with a history of cardiovascular disease (coronary artery disease or/and arterial hypertension in combination with atrial fibrillation [AF]) hospitalized for radiofrequency catheter ablation. All patients underwent expert ultrasound examination of the heart using Philips HD 15 and Philips iE33 devices, as well as invasive measurement of pressure in the left and right atria at rest (n=20).
Results — The sensitivity of dyspnea in patients with paroxysmal AF and long-standing persistent AF was 44.4% and 90.9%, respectively. The sensitivity of the mean E/e' ratio in patients with paroxysmal AF and long-standing persistent AF was 22.2% and 18.1%, correspondingly. According to the 2016 American Society of Echocardiography/European Association of Cardiovascular Imaging (ASE/EACVI) algorithm, only one patient (11.1%) in the group with paroxysmal AF and 54.5% of subjects in the group with a long-standing persistent AF type had two positive criteria. The sensitivity of lower limb edema was 0% in patients with paroxysmal AF and 57.1% in those with long-standing persistent AF. The sensitivity of IVC diameter >22 mm was 80% in patients with paroxysmal AF and 57.1% in the group with long-standing persistent AF. At the same time, the sensitivity of the IVC inspiratory collapse ≤50% was significantly lower in both groups: 60% in patients with paroxysmal AF and 42.9% in subjects with long-standing persistent AF.
Conclusion — Clinical symptoms and signs of chronic heart failure (CHF), as well as echocardiographic parameters reflecting an increase in the filling pressure of the heart chambers, are characterized by extremely low sensitivity in a cohort of patients with paroxysmal AF. The use of more stringent criteria for diagnosing congestion in this group of patients leads to a significant underdiagnosis of elevated filling pressure in the left chambers of the heart, which, in turn, increases the likelihood of insufficient prescription of diuretic therapy when it is objectively necessary.

Keywords: Chronic heart failure, echocardiography, fluid retention, invasive measurement of atrial pressure.

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Introduction

Despite advances in treatment [1], the prevalence of progressive heart failure is increasing worldwide, accounting for 1–10% of the total population of patients with chronic heart failure (CHF) [2, 3]. Most patients admitted to the hospital with symptoms and signs of heart failure have fluid retention [4, 5], which is an indication for diuretic therapy [4, 5]. However, the diagnostic significance of clinical symptoms and signs of CHF is low [6, 7]. E.g., the sensitivity and specificity of dyspnea at rest are 50% and 73%, respectively. During exercise, these numbers change to 66% and 52%, correspondingly. In this regard, there is an underestimation of symptoms and signs of fluid retention by clinicians in patients with CHF, which leads to the prescription of inadequate diuretic therapy [1] and resulting increase in the number of decompensated patients. In addition, the presence of atrial fibrillation (AF) leads to an even greater reduction in the sensitivity and specificity of clinical parameters, along with evaluated echocardiographic data, implying the presence of fluid stasis in the body [5]. The gold standard in diagnosing congestion is cardiac catheterization for direct measurement of atrial and pulmonary artery pressure with assessment of capillary wedge pressure. However, the invasiveness of the method significantly limits its application in clinical practice.

According to the conclusion of experts on the use of diuretics in patients with CHF, dynamic measurement of natriuretic peptide

(NUP) can be used to control fluid retention in CHF [8]. Instrumental studies have also been proposed for an objective assessment of euvolemia [6, 7]. Data, such as the presence of B-lines during ultrasonography of the lungs (according to the BLUE protocol), an increase in the echocardiographic parameter of E/e' mean (the mean ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity), and the diameter of the inferior vena cava (IVC) with an assessment of its inspiratory collapse are of diagnostic value. However, the above methods are either nonspecific or have low sensitivity and allow diagnosing blood stasis only at late stages [6]. An increased mean value of E/e' correlates with an increase in left ventricular filling pressure [9] and is one of the criteria for the algorithm of determining left ventricular diastolic dysfunction with elevated left atrial pressure according to the 2016 recommendations of the American Echocardiographic Society and European Association for Cardiovascular Imaging (ASE/EACVI) [10]. In addition, the 2021 European Society of Cardiology guidelines for the diagnosis and treatment of CHF [5] recommended using higher thresholds for indexed left atrial volume (iLAV) (>40 mL/m^2), E/e' mean (>15), and tricuspid regurgitation velocity (>3.4 m/s) at peak load for the diagnosis of CHF in patients with AF.

Objective of the study: to investigate the sensitivity of individual symptoms and signs of CHF, along with echocardiographic criteria (iLAP, E/e' mean, 2016 ASE/EACVI algorithm), for detecting fluid retention in the pulmonary circulation in patients with AF and invasively measured elevated pressure in the left atrium.

Material and Methods

A prospective study of adult patients with CHF and AF admitted to the Regional Arrhythmology Center for radiofrequency catheter ablation of the pulmonary veins (n=20) was performed.

The inclusion criteria were as follows: history of cardiovascular disease (coronary artery disease, arterial hypertension in combination with AF) and increased left atrial pressure during invasive measurement at rest (>10 mmHg). The exclusion criteria were acute coronary syndrome, pulmonary embolism, congenital and acquired valvular heart disease, thyroid disease, acute and severe chronic kidney disease, acute and chronic lung disease, and oncopathology.

The patients were distributed among two groups depending on the type of AF: Group 1 included patients with paroxysmal type of AF (n=9), Group 2 comprised patients with a long-standing persistent type of AF (n=11).

Before the ablation procedure, all patients underwent an expert ultrasound examination of the heart using Philips HD 15 and Philips iE33 devices by one specialist according to a standard protocol with obligatory measurement of IVC on inspiration and expiration, calculation of the mean E/e' ration and qualitative determination of elevated pressure in the left atrial cavity according to the 2016 ASE/EACVI algorithm, in which at least 2 of 3 criteria are positive (iLAV >34 mL/min, sPAP >35 mmHg, E/e' mean >14). During the intervention, direct measurement of pressure in both atria in systole and diastole was performed, followed by calculation of the mean pressure. All patients signed written informed consent to participate in the study, approved by the local ethics committee.

Statistical data processing was performed using the IBM SPSS Statistics software. The description of quantitative data was carried out in the form of a median and interquartile range (Me [Q25; Q75]) taking into account the non-normal distribution of signs. Qualitative values were presented in absolute and relative values (n [%]). Mann-Whitney U test was used to compare quantitative data between two independent samples. We used the analysis of contingency tables (Pearson's $\chi 2$ test and two-tailed Fisher's exact test) to determine the statistical significance of differences in nominal traits. Correlation analysis was performed using Spearman's rank correlation coefficient. The critical level of significance when testing statistical hypotheses was assumed at $p \leq 0.05$ (where p is the achieved level of significance).

Results

The general clinical characteristics of patients with paroxysmal and long-standing persistent types of AF are presented in *Table* 1. Patients of the studied groups did not significantly differ in gender, age and concomitant pathology. Patients with paroxysmal AF had a shorter history of arterial hypertension and smaller severity of symptoms and signs of heart failure, including a lower functional class (FC) of CHF sensu NYHA, compared with patients with a long-standing persistent type of AF (*Table* 1).

Table 1. Anamnestic data of patients with different types of atrial fibrillation

Parameter	*Paroxysmal AF (n=9)*	*Long-standing persistent AF (n=11)*	*p*
Gender M/F, n (%)	6 (66.7)/3 (33.3)	3 (27.3)/8 (72.7)	0.095
Age, n (%)	56 (48.5; 60.5)	60 (57; 70)	0.067
BMI, n (%)	27 (24; 32.5)	33 (26; 35)	0.112
AH, n (%)	7 (77.8)	8 (72.7)	0.604
AH experience, years	10 (6.5; 22.5)	20 (15; 25)	0.022
CAD, n (%)	6 (66.7)	8 (72.7)	0.574
PC, n (%)	0	0	
DM, n (%)	1 (11.1)	2 (18.2)	0.579
Stroke, n (%)	1 (11.1)	2 (18.2)	0.579
FC of CHF, n (%)			
I	5 (55.5)	0	0.008
II	3 (33.3)	7 (63.6)	0.185
III	1 (11.1)	4 (36.4)	0.221
IV	0	0	
AF experience, years	4 (1; 7)	5 (3; 7)	0.621
GFR, mL/min/1.73м^2	69.5 (61; 78.5)	69.5 (57; 82.75)	0.714
Weakness, n (%)	0	7 (70)	0.002
Fatigue, n (%)	2 (22.2)	6 (60)	0.157
Dyspnea, n (%)	4 (44.4)	10 (90.9)	0.038
Orthopnea, n (%)	0	1 (9)	0.550
Palpitation, n (%)	5 (55.5)	9 (81.8)	0.217
Edema, n (%)	0	6 (54.5)	0.012
Therapy			
RAAS inhibitors, n (%)	5 (55.5)	7 (63.6)	0.535
Beta blockers, n (%)	6 (66.6)	8 (72.7)	0.574
Aldosterone antagonists, n (%)	0	1 (9)	0.550
Diuretics, n (%)	2 (22.2)	6 (54.5)	0.157
Antiarrhythmic agents, n (%)	4 (44.4)	8 (72.7)	0.205

AF, atrial fibrillation; AH, arterial hypertension; BMI, body mass index; CAD, coronary artery disease; FC of CHF, functional class of chronic heart failure; DM, diabetes mellitus; GFR, glomerular filtration rate; PC, postinfarction cardiosclerosis; RAAS, renin-angiotensin-aldosterone system.

Table 2. Instrumental and laboratory characteristics of patients with different types of atrial fibrillation

Indicator	*Paroxysmal AF (n=9)*	*Long-standing persistent AF (n=11)*	*p*
LA, mm	40 (35.5; 45.5)	44 (42; 52)	0.049
LA volume, mL	68 (51.5; 92.5)	99 (82; 147)	0.031
iLAV, mL/m^2	35 (27.75; 41)	55 (43; 68)	0.026
MMI, g/ m^2	84 (78.75; 92.75)	104 (81; 107)	0.132
EF, %	65 (62.5; 68)	59 (35; 62)	0.016
sPAP, mmHg	25 (23.5;27)	39 (34;44.25)	<0.001
E/A	0.72 (0.67; 0.84)	0.81 (0.75; 0.89)	0.131
E/e' mean	6.8 (5.84; 7.82)	7 (5.88; 7.8)	0.664
IVC, mm	24 (21; 25.5)	20.5 (19; 24.2)	0.183
Invasively measured pressure in LA, mmHg	15 (13; 17)	16 (14; 17)	0.553
Invasively measured pressure in RA, mmHg	7 (5.5; 8.5)	7 (5.75; 8.5)	0.999

AF, atrial fibrillation; LA, left atrium; iLAV, indexed left atrial volume; MMI, myocardial mass index; EF; ejection fraction; sPAP, systolic pulmonary artery pressure; E/A, a marker of the function of the left ventricle; E/e' mean, the mean ratio of early diastolic mitral inflow velocity to early diastolic mitral annulus velocity; IVC, inferior vena cava; RA; right atrium.

Table 3. Sensitivity of symptoms, signs and echocardiographic criteria for diagnosing fluid stasis in patients with atrial fibrillation

Indicators	*Paroxysmal AF*	*Long-standing persistent AF*
Left ventricular failure (n=20)	n=9	n=11
Dyspnea	22.2%	90.9%
iLAV >34 mL/m^2	55.5%	90.9%
iLAV >40 mL/m^2	33.3%	81.8%
E/e'>14	22.2%	18.1%
2016 ASE/EACVI algorithm (iLAV>34, sPAP >35, E/e' mean>14): 2 or 3 positive criteria	11.1%	54.5%
Right ventricular failure (n=12)	n=5	n=7
Edema of the lower extremities	0	57.1%
Inferior vena cava:		
IVC diameter >22 mm	80%	57.1%
IVC inspiratory collapse ≤ 50%	60%	42.9%

AF, atrial fibrillation; iLAV, indexed left atrial volume; sPAP, systolic pulmonary artery pressure; IVC, inferior vena cava.

Echocardiography confirmed that patients with long-standing persistent AF differed from those with paroxysmal AF in greater dilatation of the left atrium and higher calculated systolic pulmonary artery pressure (sPAP) (*Table 2*). At the same time, patients with paroxysmal and long-standing persistent types of AF did not differ from each other in terms of the invasively measured pressure in the left and right atria (*Table 2*).

Considering that the study inclusion criterion was the presence of elevated left atrial pressure on invasive measurement, the frequency of occurrence of individual symptoms and signs of hypervolemia in the studied cohort is a sensitivity value for determining the presence of fluid retention. Thus, the sensitivity of dyspnea in patients with paroxysmal AF was only 44.4%, while in the group with long-standing persistent AF it was 90.9%. The mean E/e' indirectly reflected the pressure in the left atrium. Its sensitivity in patients with paroxysmal AF and long-standing persistent AF was 22.2% 18.1%, respectively. According to the 2016 ASE/EACVI algorithm (iLAV >34, sPAP >35, E/e' mean >14), in the group with paroxysmal AF, only one patient met the above two criteria (11.1%), while in in the group of patients with a long-standing persistent type, the proportion of such patients was 54.5% (*Table 3*). Hence, an extremely low detection rate of elevated pressure in the left atrium by symptoms and echocardiographic criteria was established in patients with paroxysmal AF, whereas a higher detection rate was demonstrated in patients with long-standing persistent AF.

In the study cohort, 12 patients had invasively recorded increased pressure in the right atrium (≥7 mmHg): in 55.5% (n=5) of patients with paroxysmal AF and in 63.6% (n=7) subjects with long-standing persistent AF (p=0.535). Based on the obtained data, the sensitivity of edema of the lower extremities and echocardiographic criteria (maximum IVC diameter >22 mm and IVC inspiratory collapse ≤50%) was determined in patients with invasively measured elevated pressure in the right atrium. The sensitivity of edema of the lower extremities in patients with paroxysmal AF was 0%, while in the group with long-standing persistent AF it was 57.1%. The sensitivity of IVC with a diameter >22 mm was 80% in patients with paroxysmal AF and 57.1% in patients with long-standing persistent AF. At the same time, the sensitivity of the IVC inspiratory collapse ≤ 50% was significantly lower in both groups: 60% in patients with paroxysmal AF and 42.9% in patients with long-standing persistent AF. Thus, the detectability of elevated pressure in the right atrium by signs and echocardiographic criteria in patients with AF was also insufficient, especially in the group with a long-standing persistent form. It should be noted that the detection of high blood pressure in the right atrium, according to the recommended echocardiographic criteria, is significantly higher than the detection of elevated blood pressure in the left atrium.

Correlation analysis in both study groups revealed a statistically significant relationship with invasively measured left atrial pressure and iLAV (r=0.42; p=0.049) (*Figure 1*). At the same time, no significant correlations with the linear size of the left atrium (r=0.25; p=0.288), non-indexed volume of the left atrium (r=0.28; p=0.223) and the calculated value of sPAP (r=0.2; p=0.378) were revealed.

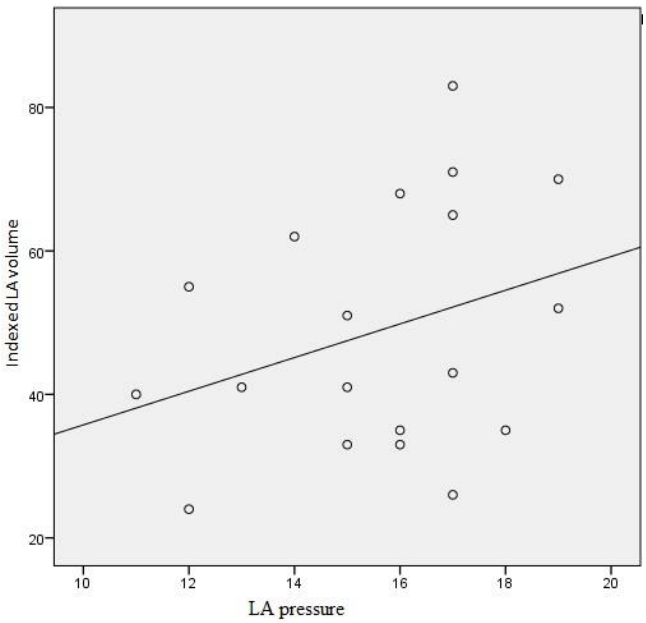

Figure 1. Correlation of invasively measured left atrial pressure with indexed left atrial volume in patients with atrial fibrillation based on echocardiography.

Discussion

Detection of fluid retention in the body by symptoms/signs and echocardiographic criteria was studied in comparison with the gold standard: invasively measured pressure in the heart chambers of patients with paroxysmal and long-standing persistent forms of AF. It is known that timely diagnosis of heart failure in patients with AF is an extremely important task, since the combination of these conditions is associated with a worse prognosis [11]. At the same time, it is currently proposed to use more stringent criteria for diagnosing heart failure in patients with AF [5]. The results of our study demonstrated that in patients with paroxysmal AF, the sensitivity of clinical symptoms and signs of fluid retention in the body was extremely low, and the recognized echocardiographic parameters made it possible to diagnose an increase in filling pressure in the heart chambers only in half of the patients. At the same time, an increase in the threshold values for diagnosing heart failure led to an even greater decrease in the number of detected cases of retention, which inevitably contributes to underdiagnosis and insufficient prescription of diuretic therapy in this category of patients. We discovered that of all echocardiographic parameters, the iLAV indicator exhibited the strongest relationship with the value of invasively measured pressure in the left atrium, which implied the need for closer attention to this indicator, especially in patients with paroxysmal AF.

The presented study had a number of limitations, primarily due to the small number of study groups, because of the limited clinical indications for invasive measurement of pressure in the heart chambers. However, as a result of the analysis, we were able to identify significant differences between patients with paroxysmal and long-standing persistent forms of AF regarding the sensitivity of clinical and echocardiographic parameters for the diagnosis of heart congestion. It is perhaps appropriate to use standard rather than more stringent echocardiographic criteria for diagnosing heart failure in patients with paroxysmal AF. Besides, it is necessary to develop new effective non-invasive procedures for assessing fluid retention in the pulmonary circulation in patients with CHF in combination with AF, allowing timely administration of diuretic therapy, preventing decompensation of heart failure. Our results need to be confirmed in larger multicenter studies.

Conclusion

Clinical symptoms and signs of CHF, as well as echocardiographic parameters reflecting an increase in the filling pressure of the heart chambers, were characterized by extremely low sensitivity in a cohort of patients with paroxysmal AF. The use of more stringent criteria for diagnosing congestion in this group of patients could lead to a significant underdiagnosis of elevated filling pressure in the left chambers of the heart, which, in turn, increases the likelihood of insufficient prescription of diuretic therapy when it is objectively necessary.

Conflict of interest

The authors of this article declared no conflicts of interest to report.

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