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Features of chronic heart failure depending on the left ventricular ejection fraction

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Aim. To assess clinical and demographic data, structural and functional features of the myocardium in patients with chronic heart failure (CHF) with a preserved ejection fraction in comparison with patients with CHF with an intermediate (CHFinEF) and a reduced ejection fraction (CHF-rEF).

Material and methods. The study included 186 patients with CHF I-IIB stages, I-III functional classes. One hundred and three patients had a preserved ejection fraction (EF) (≥50%), 43 — intermediate (40-49%) and 40 — reduced (<40%). All patients underwent a comprehensive clinical examination, as well as standard echocardiography.

Results. Among patients with CHF-rEF, remodeling of the left ventricular myocardium by the type of concentric hypertrophy was more often observed (69,9%), and among CHF-inEF and CHF-nEF patients — by the type of eccentric hypertrophy (88,4 and 87,5%, respectively). Restrictive diastolic dysfunction was observed in 2,0% of patients with CHF-rEF and in 21,7% of patients with EF less than 50%.

Conclusion. The severity of the clinical course of CHF does not depend on the left ventricular EF. Epidemiology and etiology of CHF-rEF has fundamental differences from CHF-inEF and CHF-nEF. CHF-rEF is more common among women over 60 years old with arterial hypertension and obesity. For patients with CHF-inFV, myocardial remodeling by the type of concentric hypertrophy and the prevalence of non-restrictive types of diastolic dysfunction are characteristic.

Key words: chronic heart failure, ejection fraction.

Conflicts of Interest: nothing to declare.

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According to Russian Federal State Statistics Service, since the 2000s, an increase in the average life expectancy of both men and women has been observed. Despite the advances in medicine, the general population aging is inevitably associated with an increase in cardiovascular diseases and, as result, chronic heart failure (CHF). According to Russian epidemiological studies, CHF prevalence in the general population is 7% (overt heart failure — 4,5%), increasing from 0,3% in the age group of 20-29 years to 70% in people over 90 years of age [1]. According to the prognosis of Headenreich PA, et al. (2011), an increase of CHF prevalence by 25% is expected in the next 20 years [2].

To date, unified approaches to the treatment and management of all CHF patients was discredited. It is obvious that CHF population is not homogeneous, and in order to reduce mortality, disability and the number of hospitalizations due to CHF decompensation, a differentiated approach to healthcare organization is required.

It is important to separate CHF patients based on ejection fraction (EF), since there are various etiology and pathogenesis of the disease. Without understanding it, this is impossible to develop effective diagnostic algorithms and treatment methods. In 2016, the European Society of Cardiology issued Guidelines for the diagnosis and treatment of acute and CHF [3], where for the first time, in addition to patients with CHF with preserved (CHF-pEF) (⩾50%) and reduced (CHF-rEF) (<40%) EF, a category of patients with mid-range EF (CHF-mrEF) (40-49%) was added. This separation allowed specifying the imbalance of diagnostic, therapeutic and interventional capabilities among CHF patients. Regarding patients with CHF-rEF, a great number of large-scale clinical trials was conducted and therapeutic agents with proven efficacy can be used. However the population of patients with CHF-pEF and CHF-mrEF is still poorly understood and the prognosis is unfavorable.

The aim of the study was to evaluate the clinical and demographic data, structural and functional features of the myocardium in patients with CHF-rEF in comparison with patients with CHF-mrEF and CHF-pEF.

Material and methods

The study included 186 patients with CHF of stage I-IIB (classification of Strazhesko M. D. and Vasilenko V. H.) and functional class (FC) I-III. Among this sample, 103 patients had a preserved ejection fraction (⩾50%), 43 — mid-range (40-49%) and 40 — reduced (<40%). The groups were comparable in stages and functional classes of CHF. The average age of the patients was 60,6±8,4 years. In 54 (29%) patients, CHF was a result of hypertension (HTN), in 132 (71%) — HTN in combination with coronary artery disease (CAD). A prerequisite for inclusion in the study, in addition to CHF, was a signed informed consent.

The study did not include patients with CHF which was a result of rhythm and conduction disturbances, congenital or acquired heart diseases and any inflammatory heart diseases (endocarditis, myocarditis, pericarditis). Patients with CHF decompensation (FC IV), history of acute coronary syndrome over the past three months, severe pulmonary, renal, hepatic pathology also did not include in the study.

After signing the informed consent, a complex examination was carried out for all patients. It included the collection of demographic and history data, physical examination with anthropometry, an assessment of the CHF severity (score of R. Cody, 1993 in V. Yu. Mareeva modification, 2000), one-dimensional, two-dimensional and Doppler echocardiography on the SonoScape 8000 (Korea).

During echocardiography, the following structural and functional parameters of the myocardium were evaluated: left ventricle (LV) EF (%), right ventricle (RV) dimension (mm), longitudinal dimension of right (RA) and left atrium (LA, mm), thickness of interventricular septum (IVS) and LV posterior wall (PW, mm), end-systolic (ESD) and end-diastolic (EDD) LV dimension (mm), LV volume parameters — end-diastolic (EDV) and end-systolic (ESV, ml). LV mass (LVM, g), left ventricular mass index (LVMI, g/m^2), and LV relative wall thickness (RWT, mm) were calculated using standard formulas. LV diastolic function was evaluated by transmitral blood flow.

The diagnosis of the main disease entities, including CHF, was established in accordance with current guidelines.

Statistical processing of the obtained data was carried out using Statistica 6.1 software (Statsoft.Inc, 2008). Qualitative characters are presented in the form of absolute and relative frequencies (n (%)); for quantitative characters having a normal distribution, the mean value and standard deviation (M±SD) were indicated. In the case of an abnormal distribution of a quantitative character, the median, upper and lower quartiles (Me [LQ;UQ]) were calculated. Comparison of quantitative characters with a normal distribution was carried out using parametric methods; in other

Table 1

General characteristics of CHF patients depending on EF

Parameter	CHF-pEF (n=103)	CHF-mrEF (n=43)	CHF-rEF (n=40)
Age (years), M±SD	60,4±7,4	61,1±11,3	60,6±6,7
Gender (men/women), n (%)	31 (30,1)/72 (69,9)	32 (74,4)/11 (25,6)	34 (85,0)/6 (15,0)
Etiology of CHF, n (%):			
• HTN	46 (44,7)	5 (11,6)	3 (7,5)
• HTN+CAD	57 (55,3)	38 (88,4)	37 (92,5)
Old myocardial infarction, n (%)	15 (14,6)	27 (62,8)	27 (67,5)
Diabetes, n (%)	19 (18,4)	8 (18,6)	6 (15,0)
Obesity (BMI), n (%):			
• no	28 (27,2)	29 (67,4)	25 (62,5)
• I class	38 (36,9)	8 (18,6)	9 (22,5)
• II class	25 (24,3)	2 (4,7)	5 (12,5)
• III class	12 (11,6)	4 (9,3)	1 (2,5)

Abbreviation: BMI — body mass index.

Table 2

Structural and functional myocardial characteristics in CHF patients depending on EF

Parameter	CHF-pEF (n=103)	CHF-mrEF (n=43)	CHF-rEF (n=40)	p_{1-2}	p_{1-3}	P_{2-3}
EF, %	66,0±7,6	44,2±3,4	32,6±3,6	<0,01	<0,01	<0,01
RV, мм	31,7±2,8	30,7±4,6	32,8±4,7	0,26	0,53	0,18
RA, мм	50,4±4,4	52,2±7,6	54,7±7,6	0,41	<0,01	0,19
LA, мм	51,6±6,8	53,9±10,7	58,7±12,4	0,27	0,04	0,23
EDD, mm	51,8±4,7	62,1±7,9	66,9±8,2	<0,01	<0,01	0,02
ESD, мм	33,1±5,1	48,9±5,4	55,3±8,2	<0,01	<0,01	<0,01
IVS, мм	13,4±1,3	11,8±2,2	11,0±1,8	<0,01	<0,01	0,18
PW, мм	11,8±1,4	10,3±1,6	9,3±1,8	<0,01	<0,01	0,04
RWT	0,49±0,06	0,36±0,07	0,31±0,05	<0,01	<0,01	<0,01
EDV, мл	130,1±26,9	198,7±54,2	234,8±64,0	<0,01	<0,01	0,02
ESV, мл	46,3±16,9	114,0±29,4	153,7±49,9	<0,01	<0,01	<0,01
EDVI, ml/m^2	67,4±11,8	100,3±22,1	120,8±34,2	<0,01	<0,01	0,02
ESVI, ml/m^2	23,7±7,6	58,0±11,9	79,2±26,4	<0,01	<0,01	<0,01
Stroke volume, ml	84,4±15,0	84,7±41,9	81,1±18,8	0,1	0,4	0,09
LVM, g	273,7±59,8	313,2±96,3	313,0±73,8	<0,01	0,02	0,89
LVMI, g/m^2	141,4±25,8	162,2±31,2	162,0±36,0	<0,01	<0,01	0,88

cases non-parametric methods were used. Differences were considered statistically significant if $p<0,05$.

Results

The general characteristics of patients with CHF depending on EF are given in Table 1.

According to the presented data, women over 60 years old with HTN and overweight predominate among patients with CHF-pEF. CHF-mrEF and CHF-rEF are more common in men without obesity in the same age group. HTN, as the single CHF etiological factor, is rarely observed among patients with

Table 3

Distribution of LV remodeling types in CHF patients depending on EF

Type of remodeling / Group	CHF-pEF (n=103)	CHF-mrEF (n=43)	CHF-rEF (n=40)
Concentric hypertrophy, n (%)	72 (69,9)	2 (4,6)	1 (2,5)
Eccentric hypertrophy, n (%)	18 (17,5)	38 (88,4)	35 (87,5)
Concentric remodeling, n (%)	9 (8,7)	3 (7,0)	1 (2,5)
Normal model, n (%)	4 (3,9)	0	3 (7,5)

EF less than 50%. However the proportion of patients with old myocardial infarction in this population increases sharply.

HTN (95,5%) and CAD (69,7%), as well as their combination (more than 50%), are the leading causes of CHF in Russia, Europe and United States [4, 5]. This is traced also in our study.

CHF symptoms and signs with the same prevalence were found in all groups. The most common clinical CHF manifestations were exertional dyspnea, pastosity, swelling of the feet and lower legs, palpitations, less often — congestive pulmonary rales, hepatomegaly.

An assessment of CHF severity (score of R. Cody, 1993 in V. Yu. Mareeva modification, 2000) also did not show differences between the groups: median in CHF-pEF group — 3,0 [3,0; 4,0] points, CHF-mrEF group — 3,0 [3,0; 4,0] points, CHF-rEF — 4,0 [3,0; 4,0] points ($p>0,05$).

The structural and functional myocardial parameters have a number of features depending on the EF. It implies the need for a differentiated approach to management of these patients (Table 2).

Table 2 shows that dilatation of the cardiac cavities is most outstanding in patients with reduced EF, thickness of LV walls — in patients with EF$\geqslant$50%. Patients with CHF-mrEF did not significantly differ from patients with CHF-rEF by the dimensions of the heart cavities, with the exception of lesser LV dilatation. By the extent of LV walls' thickening, patients with CHF-mrEF also had similar values with CHF-rEF patients. Differences of EDV and ESD were preserved between the groups even after indexing by body surface area.

Myocardial mass values and mass index increased with a decrease in EF less than 50%, however, with a further decrease in systolic function, significant differences between the groups were not obtained.

Based on the calculation of LVMI and LV RWT, LV geometric models (types of remodeling) were evaluated. According to the classification of Ganau A, et al. (1992), there are 4 types of structural and functional myocardial change: concentric hypertrophy, eccentric hypertrophy, concentric remodeling and the normal LV model [6]. According to the literature, patients with heart failure with the same provenance can have both concentric and eccentric LV hypertrophy [7]. The distribution of patients depending on the type of remodeling in the study groups is presented in Table 3.

Among patients with CHF-pEF, concentric hypertrophy was most common, while the vast majority of patients with CHF-mrEF and CHF-rEF had eccentric hypertrophy. High prevalence of concentric hypertrophy is characteristic of patients with CHF-pEF [8, 9] and is direct evidence of diastolic dysfunction [10], which plays a leading role in the development of this type of CHF. Volume overload and dilatation of heart cavities are more associated with the eccentric remodeling, which was observed in patients with EF less than 50%.

A number of studies have proved that LV concentric hypertrophy is the most unfavorable prognostic type of structural and functional myocardial change, which is associated with the greatest number of cardiovascular complications [11]. Thus, according to the literature [12, 13], risk of cardiovascular complications within 10 years in concentric LV hypertrophy is 30%, in eccentric hypertrophy — 25%, in concentric remodeling — 15%.

We also performed an analysis of echocardiographic parameters reflecting diastolic function. Noteworthy that there is diastolic dysfunction not only in patients with CHF-rEF, but also in the vast majority of patients with EF less than 50% [14]. In preserved EF, diastolic dysfunction predominates by hypertrophic type — 68 (66%) patients, less often by pseudonormal — 33 (32%) patients. As systolic dysfunction progresses, diastolic function worsens with an increase in the number of patients with restrictive type (21,7%) of diastolic dysfunction, which has the most unfavorable prognosis in patients with CHF [15].

Conclusion

Thus, the severity of the clinical course of CHF does not depend on LVEF. The epidemiology and etiology of CHF-pEF has fundamental differences from CHF-mrEF and CHF-rEF: CHF-pEF is more common among women over 60 with HTN and obesity. For patients with CHF-pEF, myocardial remodeling by concentric hypertrophy and the prevalence of non-restrictive types of diastolic dysfunction are characteristic.

Conflicts of Interest: nothing to declare

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