



## A Modern Approach to Risk Stratification in Patients with Heart Failure with Preserved and Reduced Ejection Fraction

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### ABSTRACT

A comparative analysis of left ventricular systolic dysfunction and heart failure with preserved left ventricular ejection fraction was carried out. 69 patients with heart failure FC III-IV according to NYHA were examined. In the group of chronic heart failure with preserved ejection fraction (40% of patients), women predominate, older people with a significantly higher body mass index, suffering from diabetes mellitus, anemia. In these patients, creatinine and cholesterol levels are significantly higher, and hemoglobin levels are significantly lower than in patients with left ventricular systolic dysfunction.

### Keywords:

chronic heart failure, preserved left ventricular ejection fraction, left ventricular systolic dysfunction.

### Introduction

Chronic heart failure is an urgent public health problem, given its prevalence and associated high mortality. Annually, 300 new patients with chronic heart failure are registered per 100 thousand of the population, the prevalence of chronic heart failure in the European population reaches 2%, in the USA - 2.2%, and in Russia - 6%, in Uzbekistan - 10% [1,8]. Mortality from chronic heart failure is 50% within 3 years from the start of medical supervision and within a year in severe failure [2,11]. The basis of chronic heart failure in the vast majority of cases is left ventricular dysfunction, which can be both systolic and diastolic. The most well studied features of the course and outcomes of systolic dysfunction of

the left ventricle, which is characterized by dilatation of its cavity and low ejection fraction. However, patients with preserved ejection fraction make up from one third to one half of patients with heart failure, and their total number has increased significantly in recent years [3,7]. The fundamental finding of recent studies is the discovery of a similar level of mortality in patients with preserved left ventricular ejection fraction, both in short-term and long-term follow-up. Moreover, if patients with systolic dysfunction have seen an improvement in survival over the past 10 years, the situation has not changed among patients with preserved ejection fraction [4,12]. To date, there is no proven therapeutic strategy that improves outcomes in patients with preserved

systolic function. Therefore, it is of great importance to study the links in the pathogenesis of chronic heart failure with preserved ejection fraction in order to develop an effective drug treatment.

### Objective

To conduct a comparative analysis between left ventricular systolic dysfunction and heart failure with preserved systolic function based on clinical, anamnestic, laboratory and instrumental parameters and evaluate the prognosis of life in patients with this pathology.

### Material and methods

69 patients with severe chronic heart failure were examined. 16 patients had NYHA FC III, 44 patients had NYHA FC IV. Mean age  $66.5 \pm 1.84$  years. There were 30 men, 39 women. The study took place on the basis of the Samarkand branch of the Republican Scientific Center for Emergency Medical Care and on the basis of the Cardiology Dispensary. All patients were admitted to hospital on an emergency basis due to decompensation of chronic heart failure in 2019, 2021. Anamnestic data were assessed: the main cause of chronic heart failure, what is the cause of decompensation, the duration of clinical manifestations of heart failure, previous therapy, comorbidities. The following laboratory parameters were studied: complete blood count, bilirubin, urea, creatinine, cholesterol, C-reactive protein, LDH1, MB - CPK, potassium, sodium, chlorine. To determine the variant of heart failure, all patients underwent Doppler echocardiography. The following indicators were studied: AO, mm (aorta); LP, mm (left atrium); IVS, mm (interventricular septum); ZS, mm (posterior wall of the left ventricle); CDR, mm (end diastolic size of the left ventricle); CSR, mm (final systolic size of the left ventricle); EF according to Simpson, % (ejection fraction according to Simpson); SDLA, mm Hg Art. (systolic pressure in the pulmonary artery). Patients with an ejection fraction of the left ventricle  $\geq 50\%$  were classified as having a preserved ejection fraction, those with an ejection fraction of less than 50% were classified as reduced. To diagnose diastolic dysfunction of the left ventricle, the transmitral

diastolic flow and the time of isovolumetric relaxation of the myocardium were studied. Normal diastolic function was diagnosed in the case of the ratio of the rate of passive filling to the rate of atrial filling E/A 1.0–1.5 and the time of isovolumetric relaxation 70–90 ms. Left ventricular diastolic dysfunction has not been evaluated in patients with atrial fibrillation. Life prognosis for patients with left ventricular systolic dysfunction was calculated based on the Seattle model of heart failure [5,14]. Predictors of mortality in this model are: advanced age, male sex, ischemic nature of chronic heart failure, low body mass index, decreased left ventricular ejection fraction, decreased blood pressure, decreased serum sodium, low cholesterol, low hemoglobin, decreased percentage of lymphocytes, high functional heart failure classes, elevated uric acid, increased creatinine, leukocytosis, use of a combination of loop and thiazide diuretics, use of allopurinol. Then, the calculated survival of patients was compared with the real one, as well as with the survival of patients with heart failure with preserved systolic function of the left ventricle. Statistical data processing was carried out using the Statistica 6.0 software package.

### Results and discussion

The causes of chronic heart failure in 84% of patients were coronary artery disease, in 16% - chronic rheumatic heart disease. The average duration of symptomatic CHF was  $5.0 \pm 4.4$  years. Mean functional class values (according to NYHA classification) did not differ between patients with normal and low left ventricular ejection fraction ( $3.6 \pm 1.1$  vs.  $3.6 \pm 1.0$ ). No differences were found in terms of physical examination of patients. All patients had peripheral edema, moist rales in the lungs, swollen jugular veins. 30% of patients associated decompensated heart failure with stress, 25% with acute respiratory viral infections, 24% with hypertensive crisis, 10% with excessive salt and fluid intake, 5% with alcohol intake, 3% with salbutamol, 3% with physical activity. In the study of routine biochemical parameters, the following changes were revealed: urea -  $11.6 \pm 0.6$  mmol / l

(increase in 68%), LDH1 -  $212 \pm 12.2$  U / l (increase in 43%), C-reactive protein -  $11.1 \pm 1.3$  mg/l (increase in 40%), creatinine —  $121.7 \pm 6.7$   $\mu$ mol /l (increase in 34%), bilirubin —  $20.5 \pm 2.0$   $\mu$ mol /l (increase in in 27%), MB-CK —  $27.6 \pm 5.0$  U /l (increase in 12%), cholesterol —  $4.6 \pm 0.1$  mmol /l (increase in 7%). Thus, indicators reflecting the development of nephroangiosclerosis most often increase . The increase in CRP in these patients confirms the role of endothelial dysfunction and systemic inflammatory response as a manifestation of the activation of pro- inflammatory cytokines in the pathogenesis of chronic heart failure. In the general group of patients, a correlation analysis was performed between the level of C-reactive protein and ejection fraction. No correlation was found (SR - 0.1; p = 0.57). LDH1 can serve

as a marker of heart failure decompensation in case of exclusion of acute coronary syndrome [9]. Although the majority of patients had ischemic heart failure, their average cholesterol levels were normal, which may reflect the development of liver failure and cardiac cirrhosis. When analyzing the ECG, atrial fibrillation (75% of patients) and complete blockade of the left bundle branch block (32%) were most often detected. Thus, the aforementioned arrhythmias and conduction disturbances may be unfavorable predictors of the progression of heart failure. 60% of patients had left ventricular systolic dysfunction (ejection fraction less than 50%), 40% of patients had heart failure with preserved ejection fraction. Comparative characteristics of patients are presented in Table 1.

Table 1 - Comparative characteristics of patients with CHF with low and normal left ventricular ejection fraction

Indicator	CHF with reduced left ventricular ejection fraction	CHF with preserved left ventricular ejection fraction
Gender composition	20 men, 11 women	10 men, 28 women
Duration of CHF	$5.0 \pm 0.7$ years	$5.1 \pm 1.1$ years
Average age	$64.5 \pm 9.4$ years	$69.7 \pm 7.6$ years
Arterial hypertension	In 53% of patients	In 50% of patients
BMI	$25.3 \pm 1.6$ kg/ m <sup>2</sup>	$28.6 \pm 1.6$ kg / m <sup>2</sup> *
history of MI	In 10% of patients	In 5% of patients
Anemia	In 8.4% of patients	In 29.7% of patients
COPD	In 11.2% of patients	In 4.2% of patients
Diabetes	In 16.7% of patients	In 30% of patients
LV diastolic dysfunction	In 14% of patients	In 20% of patients

\* - p < 0.005

Thus, chronic heart failure with preserved systolic function is more likely to affect women, older people with a significantly higher body mass index, diabetes mellitus and anemia. In this group, a significant (p < 0.005) decrease in hemoglobin was revealed -  $126 \pm 5.9$  g/l compared with  $138 \pm 3.6$  g/l in the group with a reduced ejection fraction. Therefore, for the treatment of heart failure in these patients,

adequate treatment of concomitant anemia should be carried out. Left ventricular systolic dysfunction is more common in men who have had myocardial infarction and who suffer from COPD.

A comparative analysis of echocardiographic parameters was carried out in patients with chronic heart failure (table 2)

Table 2 - Comparative analysis of echocardiographic parameters in patients with chronic heart failure

Indicator	Heart failure with reduced left ventricular ejection fraction	Heart failure with preserved left ventricular ejection fraction
PZh, mm	31.4 ± 0.9	30.2 ± 10.6
LP, mm	55.0±1.4	43.7 ± 1.6*
MZHP, mm	13.3±0.5	14.9±0.5*
ZS, mm	12.3±0.4	13.1 ± 0.45*
KDR, mm	62.8 ± 1.6	53.6 ± 1.8*
KSR, mm	49.7 ± 1.8	34.2 ± 1.4*
SDLA, mm	49.3 ± 1.2	41.5 ± 2.0*

\* -  $p < 0.005$

As can be seen from the data in Table 2, with systolic dysfunction of the left ventricle, dilatation of the left chambers of the heart and pulmonary hypertension are significantly more pronounced. In patients with heart failure with preserved systolic function, there is significantly more left ventricular hypertrophy. When conducting a Doppler study, it was revealed that hemodynamically significant mitral and tricuspid regurgitations in the group of patients with reduced ejection fraction are more common - in 100% and 75% versus 28% and 50%, respectively. The frequency of aortic regurgitation did not differ significantly (30% vs. 35%). Aortic stenosis occurred equally often

- in 10% in each group, mitral stenosis was detected in 5% in the group with a reduced fraction and in 3% in the group with preserved ejection fraction.

A comparison was made of the studied laboratory parameters (table 3).

Analysis of the data obtained showed that patients with preserved ejection fraction had a significantly higher level of creatinine, which indicates an unfavorable role of impaired renal function in the progression of heart failure, this should be taken into account in the treatment. Cholesterol in this group is also significantly higher. In the group with systolic dysfunction, a significantly higher level of C-reactive protein was obtained.

Table 3 — Comparative analysis of laboratory parameters in patients with CHF depending on the ejection fraction

Indicator	CHF with reduced EF	CHF with preserved EF
Potassium, mmol / l	4.63±0.1	4.8±0.13
Sodium, mmol / l	139.0±0.7	140.0±0.85
Chlorine, mmol / l	104.5±0.7	103.5±0.85
Urea, mmol / l	12.7 ± 1.1	11.7 ± 1.1
Creatinine, μmol / l	110.6 ± 6.8	138.7 ± 4.5*
CRP, mg/l	12.0± 1.7	9.5 ± 1.9
LDH1, u / l	222.8 ± 16.5	224.1 ± 14.1
MVKFK, units / l	20.0±1.7	17.5 ± 1.6
Cholesterol, mmol / l	4.38±1.3	4.92 ± 0.2*

\* -  $p < 0.005$

A correlation analysis was carried out between the value of the ejection fraction and laboratory parameters. In the group of patients with preserved systolic function, no significant correlation was obtained. In the group of patients with systolic dysfunction, a weak positive correlation (SR = 0.4;  $p = 0.03$ ) was found between the ejection fraction and the level of sodium in the blood serum, which may indicate an inverse relationship between stroke volume and the severity of dilution hyponatremia due to an increase in blood volume . circulating blood. A weak negative correlation was found between ejection fraction and creatinine level (SR = -0.4;  $p = 0.032$ ), which

is quite logically explained by the progression of glomerular filtration disorders. In addition, a significant negative correlation was found between the ejection fraction and the level of C-reactive protein (SR = -0.6;  $p = 0.042$ ).

The following survival rates were obtained for patients in the group with left ventricular systolic dysfunction, provided that they had not been treated: after a year - 68%, after 2 years - 46%, after 5 years - 16% of patients. Provided that patients received ACE inhibitors: after a year - 75%, after 2 years - 57%, after 5 years - 26%. Provided that beta-blockers were added to ACE inhibitors: after a year - 82%, after 2 years - 69%, after 5 years - 40%. If statins were added

to the above combination, the survival rate at one year would be 88%, after 2 years - 79%, after 5 years - 56%. If patients were introduced into the above treatment regimen with veroshpiron, the average survival rate after one year would be 91%, after 2 years - 83%, after 5 years - 64%. The real survival rate of patients in the group with systolic dysfunction over 2 years was 40% (8 out of 15 people died in 2019-2020), which is even less compared to the data obtained using the Seattle model - 46% (condition - no treatment). In the group of patients with heart failure with a preserved fraction, survival over 2 years was 56% (7 out of 16 people died). These data suggest a similar poor prognosis. When asking patients about what drugs they constantly took on an outpatient basis before admission to the hospital, the following data were obtained: ACE inhibitors - 48% of patients, beta-blockers - 28% of patients; veroshpiron - 28%; thiazide and loop diuretics - 62%; digoxin - 32%, statins - 6%. Thus, the actual practice is quite far from the theory. Systematic efforts aimed at early prescription of CHF pharmacotherapy, gradual achievement of optimal dosages of drugs, maintenance of the achieved therapy regimen should ensure long-term effectiveness of management of this category of patients,

### Conclusion

The main difficulty associated with addressing the issue of chronic heart failure with preserved ejection fraction is the lack of availability in the early diagnosis of this syndrome. It is required to introduce tissue Dopplerography to assess the diastolic function of the left ventricle everywhere and to apply the determination of brain natriuretic peptide in practical healthcare. Another problem is the lack of developed approaches to the treatment of diastolic CHF: despite the wide range of drugs that are potentially effective for the treatment of such patients, none of them can be considered ideal.

### Findings

1. The main cause of chronic heart failure is coronary artery disease. In patients with chronic heart failure FC III-IV according to

NYHA the incidence of systolic dysfunction of the left ventricle was 60%, the incidence of chronic heart failure with preserved ejection fraction was 40%.

2. In the group of patients with chronic heart failure with preserved ejection fraction, women predominate, older people with a significantly higher body mass index, suffering from diabetes mellitus, multifactorial anemia. Systolic dysfunction is more common in men who have had a myocardial infarction and who suffer from COPD.

3. Mean levels of creatinine and cholesterol are significantly higher, and hemoglobin levels are significantly lower in patients with preserved systolic function. The average level of C-reactive protein is significantly higher in patients with reduced left ventricular ejection fraction.

4. Therapy for chronic heart failure in real practice is far from optimal, which leads to a sharp deterioration in life prognosis.

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