Background. According to the national registries of European countries and epidemiological studies, the prevalence of chronic heart failure (CHF) among adults is 2.0–5.0%, and increases due to age, in people aged over 70 years old it is 10.0–20.0%.

Objective. To find out the specific features of remodeling of the left atrium and change of vasodilation factors in ischemic heart failure with reduced and preserved left ventricular ejection fraction and to establish correlation relationships.

Methods. A full clinical examination of 153 patients with CHF (105 men and 48 women) was conducted to achieve this objective. The surveyed patients underwent clinical examinations; spectrophotometric parameters: quantification of markers of vasodilation, metabolites of monoxide nitrogen — nitrates and nitrites with Gris reagent; content of endothelial nitric oxide synthase (eNos) in serum — ELISA for the set of Nitric Oxide Synthase 3, Endothelial (NOS3) Human ELISA Kit (Cloud-Clone Corp, USA). Electrocardiographic (ECG) examination was conducted in 12 standard conventional leads on electrocardiograph by the Hungarian production Heart Screen 112 D.

Results. The 1st group of the examined patients with reduced LV eF prevails in (significant) degree LA dilatation in 33 (70.21%) cases, II (moderate) degree of LA dilatation was determined in 14 (29.78%), and I (initial) degree was not defined at all. In the 2nd group of the patients with preserved LV EF mainly the II degree of LA dilatation was determined in 44 (44.51%) cases, and decreased LA dilation in 39 (36.79%) cases (p<0.01), and III degree of LA dilation was defined in 23 (21.69%) cases (p<0.01). In patients with stable coronary heart disease, complicated by heart failure with reduced LV EF and II degree of LA dilatation, eNOS levels in the serum was 449.00±39.91 pg/ml, whereas in patients with stable coronary heart disease, complicated by heart failure with preserved LV EF and II stage of LA dilatation — 673.56±50.98 pg/ml (p<0.01). At III stage of LA dilatation in patients of the 1st group level eNOS was 344.20±51.98 pg/ml in the patients of the 2nd group — 616.90±36.49 pg/ml (p<0.01). At the same degree and with LA dilation in the patients of the 2nd group eNOS was 750.27±99.85 pg/ml.

Conclusions. The structural and functional changes of the left atrium and changing factors of vasodilation in patients with stable coronary artery disease of II-III functional classes complicated by heart failure of I-III functional classes are studied. It is established that in the examined patients with stable coronary heart disease complicated by heart failure with reduced left ventricular ejection fraction mainly III (significant) degree of dilatation of the left atrium was determined, while in patients with stable coronary heart disease, complicated by heart failure with preserved left ventricular ejection fraction mainly II (moderate) degree of dilation of the left atrium was determined. In comparison with the results of research among the patients with stable coronary heart disease, complicated by heart failure with reduced left ventricular ejection fraction, and a group of patients with preserved left ventricular ejection fraction, it was determined a significant decrease in eNOS, nitrites, total amount of nitrites and nitrates.

KEY WORDS: heart remodeling factors of vasodilation, heart failure.
with or even is caused by this disease. Analysis of prognostic value of LVH in patients with CHF with preserved ejection fraction proves that the high risk of lethal outcome is observed in patients with left ventricular myocardial mass that exceeds 400 g [3]. It is established that at the progression of diastolic dysfunction an increased risk of sudden cardiac death in 80.0% occurs [4, 15]. Endothelial dysfunction is very important in development of CHF. The cause of nitric oxide (NO) synthesis inhibition by endothelium as a major component of its dysfunction at CHF is free radical stress [11]. The main cause of CHF is negative impact of free radical factors that leads to lower ventricular myocardial contractile function followed by entire body hypoxia, endothelial dysfunction with the appropriate activation of cellular factors [17]. These processes can lead to increasing of blood coagulation capacity, which is one of the causes of thrombotic complications in patients with CHF [12]. Biosynthesis of NO from L-arginine occurs in three major isofoms of NO-synthase, two constitutive: neuronal (nNOS) and endothelial (eNOS), and inducible one (iNOS) [6].

**The objective of the study** is to find out the specific features of left atrium remodeling and vasodilation factors changes in case of ischemic heart failure with reduced and preserved left ventricular ejection fraction and to establish correlation relationships.

**Material and Methods**

To achieve this objective a full clinical examination of 153 patients with CHF (105 men and 48 women) was conducted; they were treated in the Department of Cardiology for patients with arrhythmias of Vinnita Regional Centre of Cardiovascular Disorders (Ukraine). All patients were divided into 2 groups: group 1 consisted of patients with stable coronary heart disease complicated by heart failure with reduced LV EF (n=47); group 2 — patients with stable coronary heart disease complicated by heart failure with preserved LV EF (n=106). The control group consisted of 30 healthy individuals. The diagnoses of CH and FC was made due to clinical, laboratory and instrumental criteria, as recommended by the European Society of Cardiology (2012) and the Association of Cardiologists of Ukraine (2012) [16]. Diagnosis and treatment of clinical forms of coronary artery disease were made by order of the Ministry of Health of Ukraine № 152 from 03.02.2016 [9]; functional class (FC) CH — by NYHA classification.

**Results and Discussion**

The decrease in left atrium (LA) dilation degree in patients with stable coronary heart disease complicated by heart failure with reduced and preserved LV EF is presented in Table 1.

In Table 1 the 1st group of the examined patients with reduced LV EF prevails III (significant) degree of LA dilatation in 33 (70.21%) cases, II (moderate) degree of LA dilatation in 14 (29.78%), I (initial) degree is not defined at all. In the 2nd group of patients with preserved LV EF the degree of dilatation II LA was determined in 44 (44.51%) cases, and slightly decreased degree of LA dilatation in 39 (36.79%) cases (p<0.01), III degree of LA dilatation in 23 (21,69%) cases (p<0.01).
Remodeling of myocardium, including hypertrophy and dilation of left ventricle with a change of its geometry and a contraction violation precedes clinical skim CHF manifestations [7]. Thus, remodeling is a harbinger of heart activity decompensation [7, 13]. The features of myocardial remodeling are studied the most in patients after myocardial infarction with heart failure development [7, 8, 14].

These results are consistent with the data that myocardial ischemia may be accompanied by its dysfunction [7].

The study of factors of vasodilation levels and degrees of LA dilatation in patients with stable coronary heart disease complicated by heart failure with reduced and preserved LV EF is presented in Table 2.

In patients with stable coronary heart disease complicated by heart failure with reduced LV EF and II degree of LA dilatation, eNOS levels in the serum is 449.00±39.91 pg/ml, whereas in patients with stable coronary heart disease complicated by heart failure with preserved LV EF and II stage of LA dilatation — 673.56±50.98 pg/ml (p<0.01). At III stage of LA dilatation in patients of group 1 the eNOS level is 344.20±51.98 pg/ml in patients of groups 2 — 616.90±36.49 pg/ml (p<0.01). At the same degree and with LA dilatation in patients of group 2 eNOS is 750.27±99.85 pg/ml. Thus, in the examined patients with the progression of heart failure the endothelial factors decrease, e.g. eNOS.

In the study of levels of metabolites of nitrogen monoxide — nitrites and nitrates in blood serum the following data were obtained: in patients with stable coronary heart disease, complicated by heart failure with reduced LV EF and II and III stage of LA dilatation, the total level of nitrates and nitrites in serum was significantly lower than in patients with stable coronary heart disease, complicated by heart failure with preserved LVEF and II and III stage of LA dilatation (p<0.01).

Among the patients of group 1 with reduced LV EF with the progression of LA dilatation degree from II (moderate) stage to III (large) one, eNOS levels in blood serum decreased by 23.34%.

### Table 1. Remodeling of left atrium in case of stable coronary heart disease complicated by heart failure with reduced and preserved left ventricular ejection fraction

<table>
<thead>
<tr>
<th>Degree of LA dilatation LA</th>
<th>Patients with heart failure with reduced LV EF group 1, n=47</th>
<th>Patients with heart failure with preserved LV EF group 2, n=106</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (initial) LA from 40.0 to 45.0 mm</td>
<td>0</td>
<td>39 (36.79%)</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>II (moderate) LA from 45.1 mm to 50.0 mm</td>
<td>14 (29.78%)</td>
<td>44 (41.51%)*</td>
<td>p&lt;0.01</td>
</tr>
<tr>
<td>III (significant) LA from 50.1 mm and more</td>
<td>33 (70.21%)*</td>
<td>23 (21.69%)*</td>
<td>p&lt;0.01</td>
</tr>
</tbody>
</table>

Notes: LA — the size of the left atrium; * p<0.01 — reliable change index.

### Table 2. Vasodilating factors at different stages of left atrium dilatation in case of stable coronary heart disease complicated by heart failure with reduced and preserved left ventricular ejection fraction (M±m)

<table>
<thead>
<tr>
<th>Indices</th>
<th>Patients with heart failure with reduced LV EF group 1, n=47</th>
<th>Patients with heart failure with preserved LV EF group 2, n=106</th>
</tr>
</thead>
<tbody>
<tr>
<td>eNOS, pg/ml</td>
<td>449.00±39.91</td>
<td>344.20±51.98</td>
</tr>
<tr>
<td>Nitrite+nitrate, mmol/l</td>
<td>16.75±0.75</td>
<td>16.05±0.94</td>
</tr>
<tr>
<td>Nitrite, mmol/l</td>
<td>4.41±0.21</td>
<td>3.95±0.32</td>
</tr>
<tr>
<td>Nitrate, mmol/l</td>
<td>12.34±0.59</td>
<td>12.09±1.13</td>
</tr>
</tbody>
</table>

Notes:
* — comparison of patients with stable coronary heart disease complicated by heart failure with reduced LV EF and preserved LV EF and II degree of left atrium dilatation (p<0.01);
* — comparison of patients with stable coronary heart disease complicated by heart failure with reduced LV EF and preserved LV EF and III degree of left atrium dilatation (p<0.01).
Among the patients of group 2 with preserved LV EF with the progression of LA dilatation from I (initial) stage to II one, the level of eNOS in blood serum decreased by 12.89%, and with the progression of the II stage to III one LA dilation reduced by 8.41%.

In the examined patients with stable coronary artery disease complicated by heart failure with reduced left ventricular ejection fraction, the correlation analysis between indicators of linear dimensions of LA and eNOS levels in the blood serum a direct correlation of medium strength (r=0.38) (p<0.01) was established. Carrying out a similar correlation analysis for patients with stable coronary heart disease complicated by heart failure with preserved LV EF also allowed to establish a direct correlation of weak force (r=0.21) (p<0.01).

Progressive hypertrophy and dilatation of heart was followed by subsequent first diastolic disruption and then systolic ventricular dysfunction, increased myocardial oxygen demand, changes in subendocardial blood flow, myocardial bioenergy disorders and increased risk of life-threatening ventricular arrhythmias [1].

Recent research proved instrumental and morphological parallels, so we expand on the remodeling of heart as a single clinical and morphological syndrome that is important for making prognosis in patients with coronary heart disease [18].

Conclusions
In patients with stable coronary heart disease complicated by heart failure with reduced left ventricular ejection fraction III (significant) degree of left atrium dilatation was mainly determined, while in patients with stable coronary heart disease complicated by heart failure with preserved left ventricular ejection fraction II (moderate) degree of left atrium dilatation was mainly determined.

In the patients with stable coronary heart disease complicated by heart failure with reduced left ventricular ejection fraction in comparison with the group of patients with preserved left ventricular ejection fraction, the significant reduction of eNOS, nitrites, total of nitrites and nitrates was defined during the study.

The research allowed to establish the direct correlation of medium strength (r=0.38) between parameters of linear left atrial size and eNOS levels in blood serum of the patients with stable coronary artery disease complicated by heart failure with reduced left ventricular ejection fraction (p<0.01) and the direct correlation of weak force (r=0.21) in the examined patients with stable coronary artery disease complicated by heart failure with preserved left ventricular ejection fraction (p<0.01).

References
7. Zakirova AN, Oganov RG, Zakirova NE, Klochkova GR, Musina FS. Myocardial remodeling in ischemic heart disease. Rational Pharmacotherapy in Car-
16. ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure 2012: The Task Force for the Diagnosis and Treatment of Acute and Chronic Heart Failure 2012 of the European Society of Cardiology. Developed in collaboration with the Heart Failure association (HFA) of the ESC. European Heart Journal 2012; 33: 1718–1847.