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## Improving the diagnosis of structural and morphological changes of the heart in patients with combined cardiorespiratory pathology (new approach)

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### Abstract

The research deals with the examining of the diagnostic and prognostic role of individual homeostasis Cardiostrophin pool cytokine-1 (CT-1) in the definition of myocardial hypertrophy and heart remodeling parameters in 72 patients with acute exacerbation of chronic obstructive pulmonary disease (COPD) of III<sup>rd</sup> degree of severity in combination with stable ischemic heart disease (SIHD), stable exertional angina (SIHD SEA) I-II FC. A significant increase of CT-1 levels was discovered in patients with myocardial hypertrophy depending on the type of remodeling of the heart.

**Keywords:** COPD, IHD, cardiac remodeling, cardiostrophin-1

### 1. Introduction

According to the current knowledge of the etiopathogenesis of COPD – this disease is seen as a chronic diffuse nonallergic inflammation of the bronchi, parenchyma and blood vessels of the lungs, the clinical picture is dominated by the obstructive type of respiratory failure with irreversible or partially reversible obstruction of the airways that occurs with systemic effects or comorbidities [1]. Today there is no objection that the long course of COPD is accompanied by increased levels of proinflammatory cytokines and some "acute phase proteins" inflammation in the tissues, blood, epithelial lining fluid and other fluids, indicating systemic inflammation as a response to risk factors [2, 3]. Bronchial obstruction and excessive amounts of inflammatory mediators (cytokines, C-reactive protein, etc.) in the blood and heart tissues is accompanied by the development of endothelial dysfunction in coronary arteries and structural changes of cardiomyocytes that leads to the formation of chronic cor pulmonale and comorbide coronary artery disease [4]. An important thing today is early diagnosis of any change in structures and coronary vessels of the heart, because they allow to detect cardiovascular disease and to determine adequate drug therapy. Today there is a shortage of the publication of special heart exam results (echocardiography, Doppler echocardiography, Computer Tomography, etc.), and their clinical interpretation under normal and under cardiorespiratory pathological conditions (CRP) [5]. Moreover, it is recognized that scientific publications on this subject are sometimes controversial so the development and introduction into clinical practice of new establishing diagnostic morphological and functional changes in the heart are current.

It is important to emphasize that the cytokine system, affecting the growth, differentiation, angiogenesis and the repair can accelerate reparative processes what is important in acute coronary disease, including myocardial infarction and is associated with excessive proliferation of intercellular matrix. Previously conducted studies indicate the ability of Cardiostrophin-1 which is a protein with a molecular weight of 21.5 KD and is a representative of the superfamily of interleukin (IL-6) with severe proliferative properties, to induce hyperplasia and hypertrophy of cardiomyocytes as in vivo, and in vitro, defining its role in the formation and progression of myocardial remodeling [6-8]. The biological role of CT-1 is implemented through its binding to a specific heterodimeric receptor of glycoprotein (gp) 130/receptor), which is widely expressed in various tissues, including heart, kidney, skeletal muscle and liver [9-11]. So, one of the promising areas in diagnosis of structural and morphological changes from the side of the heart is the definition of CT-1 levels in patients with combined cardiorespiratory pathology.

### 1.1 Objective of the study

to study the diagnostic value of Cardiostrophin-1 (CT-1) indicators to establish the structural and morphological changes of the heart in patients with acute exacerbation of COPD of III<sup>rd</sup> degree of severity when combining with SIHD SEA I-II FC.

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## 2. Materials and methods

A prospective phase of the research based on the results of the study, which was randomized and met the criteria of evidence-based medicine. According to a specific purpose and tasks of scientific research in a hospital were examined 72 patients with acute exacerbation of COPD of III<sup>rd</sup> degree of severity combining with SIHD SEA I-II FC. All patients were divided by randomization into two groups. The first group consisted of 28 patients with an isolated course of COPD of III<sup>rd</sup> degree of severity, the average age was (57, 7±8, 1) years. The second group included 44 patients with combined cardiorespiratory pathology, whose average age was (58, 3±6, 2) years. Depending on the clinical course of combined cardiorespiratory pathology the second group of patients was divided into two subgroups: basic subgroup (26 patients with combined COPD of III<sup>rd</sup> degree of severity and SIHD SEA I-II FC with a stable course) and subgroup of comparisons (18 patients with COPD III severity level when combined with the threat of destabilization of course SIHD SEA I-II FC. The control group consisted of 28 practically healthy people (PHP), whose average age was (47, 6±3, 9) years.

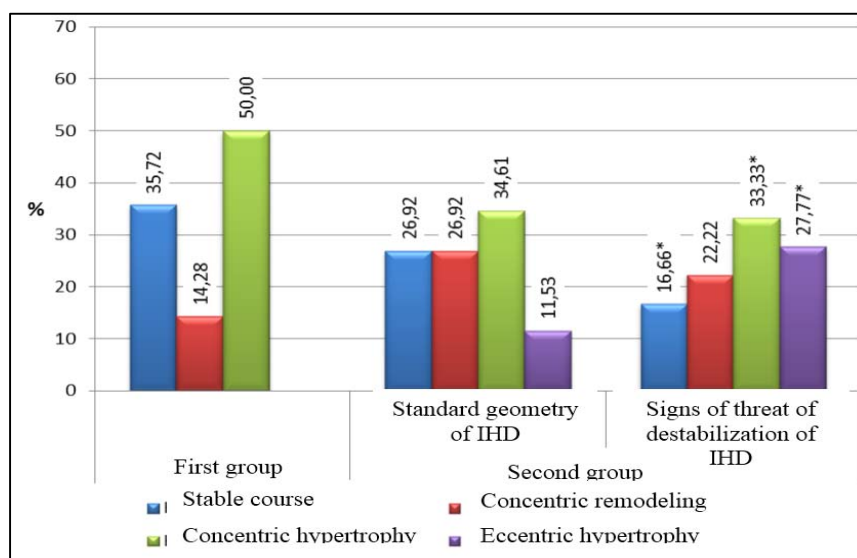
Patients passed the examination and got treatment in specialized branches of Regional Clinical Hospital of Ivano-Frankivsk. In the complex of additional and specialized studies were included ECG in 12 leads, ECG monitoring, echocardiography and

doppler echocardiography with the study protocol of left and right ventricles.

The concentration of Cardiotrophin-1 in serum was established by enzyme-linked immunosorbent assay method in terms of clinical laboratory of Regional Clinical Hospital of Ivano-Frankivsk. For this purpose, the kit "RayBio® Human CT-1-001" ELISA was used.

## 3. Results of the study and their discussion

Analysis of the structural and functional state of left parts of heart in patients with an isolated course of COPD of III<sup>rd</sup> degree of severity and the combination of SIHD SEA I-II FC showed significant differences in separate parameters of echocardiography and Doppler echocardiography. In patients with combined cardiorespiratory pathology were established probable deviations of echocardiographic indicators of left ventricle (LV EDD, LV ESD, LVEDV, LVESV, LVMI, IVST, LWPWT), which manifested an increase in their size and decrease in functional parameters (EF, CI, ΔS %). The course of COPD of III<sup>rd</sup> degree of severity in combination with comorbid SIHD SEA I-II FC led to the development of various types of compensatory hypertrophy of left ventricle, which showed the beginning of maladaptive remodeling character (Fig. 1.1).



**Fig 1:** Types of LV remodeling in patients with isolated COPD of III<sup>rd</sup> degree of severity and combination with cardiorespiratory pathology: \* - significant difference in performance ( $p < 0,05$ ) between the first and the second group of patients.

Thus, normal LV geometry which is fixed by the comparison of indicators LV MI, LVPWT, IVST and ESD and EDD, was diagnosed in 10 (35.72%) patients with isolated course of COPD, while in patients with COPD when combined with SEA I-II FC and under the threat of destabilization of course SEA I-II FC a form of structural and morphological state of left heart was observed in 7 (26, 92%) and 3 (16.66%) patients, respectively. Concentric hypertrophy (CH) of LV often occurred in the first group of patients (50.0%) and significantly fewer in patients of the main subgroup – 9 (34.61%) and subgroup of comparison – 6 (33.33%). In contrast, concentric remodeling (CR) of left heart is seen in (26, 92%) patients of main subgroup, in 9 (14.28%) patients in the first group and 11 (61.11%) patients of group of comparison ( $\chi^2=10,28, p < 0.05$ ). Eccentric hypertrophy (EG) of LV occurred only in patients with combined cardiorespiratory pathology, in 3 (11.53%)

patients in the main subgroup and 5 (27.77%) patients in the subgroup of comparison, confirming the unfavorable course of comorbidity [12]. Correlation analysis of individual indicators of echocardiographic study of left heart with duration of COPD disease was performed. A weak negative correlation between the duration of COPD and EDD and LV EDV ( $r=-0,30 - (-0,28); p < 0.05$ ), was found respectively.

At a later stage, special attention was paid to the study of diastolic function (DF) of LV as diastolic disorders affect more the severity of the clinical condition, the degree of reduction in stress tolerance and quality of life of patients than the changes of systolic phase of the heart. To verify diastolic dysfunction were used impulsive, continuous and color Doppler effect modes and the study of transmitral flow and regurgitation. Indicators of Doppler Echocardiography study of left heart shown in Table. 1.

**Table 1:** Indicators of Doppler Echocardiography study of left heart in patients with an isolated course of COPD of III rd degree of severity in acute exacerbation and when combining with SIHD SEA I-II FC.

Indicators	Group AH, (n=28)	First group, (n=28)	Second Group (COPD+SIHD), (n=94)	
			Main group, (n=51)	Group of comparison, (n=43)
E <sub>LV</sub> , mc	0,88±0,02 ***●●●●●	0,76±0,01	0,68±0,01 ××	0,64±0,01
A <sub>LV</sub> , mc	0,70 ± 0,02 ●●●●●	0,74±0,01	0,78±0,01 ××	0,85±0,02
E/A	1,28 ± 0,11 ●●●●●	1,18±0,04	0,87±0,01 ×××	0,75±0,01
DT <sub>LV</sub> , mc	182,0 ± 3,2 ●●	184,60±3,21	188,65±3,64	196,40±3,81
IVRT <sub>LV</sub> , mc	81,4±1,8 ***●●●●●	105,30±1,44	116,40±2,41 ××	127,80±2,38

**Notes.** Reliability of difference of parameters: \* - between indicator values of AH group and first group: \* - ( $p < 0.05$ ); \*\* - ( $P < 0.01$ ); \*\*\* - ( $P < 0.001$ ); ● - between indicators of AH group and the main subgroup: ● - ( $p < 0.05$ ); ●● - ( $p < 0.01$ ); ●●● - ( $p < 0.001$ ); ■ - between indicators of AH group and subgroup of comparison: ■ - ( $p < 0.05$ ); ■■ - ( $p < 0.01$ ); ■■■ - ( $p < 0.001$ ); × - between indicators of main subgroup and subgroup of comparison: × - ( $p < 0.05$ ); ×× - ( $p < 0.01$ ); ××× - ( $p < 0.001$ ).

According to the results of Doppler echocardiographic study in patients with COPD when combined with steady progress SEA I-II FC is found the reduction of peak amplitude E of ( $0,68 \pm 0,01$  m / s ( $t = 8,94$ ;  $p < 0,001$ ), an increase of peak height to ( $0,78 \pm 0,01$  m / s ( $t = 3,58$ ;  $p < 0,001$ ) and a decrease in the ratio E / A < 1 ( $0,87 \pm 0,01$ ) RVU ( $T = 3,71$ ;  $p < 0,001$ ). At the same time rates DT LV were increased to ( $188, 65 \pm 3, 64$ ) m / s ( $t = 1, 37$ ;  $p > 0, 05$ ) and rates IVRT LV decreased to ( $116, 40 \pm 2, 41$ ) m / s, ( $t = 11, 63$ ;  $p < 0,001$ ).

In patients with signs of destabilization threat of SEA I-II FC was noted the possible decreasing of the maximum speed of early diastolic filling (E) LV to 27,28% ( $t = 10,73$ ;  $p < 0,001$ ) and possible reduction of the maximum speed atrial diastolic filling (A) to 17.65% compared to the figures in the AH group ( $t = 5,30$ ;  $p < 0,001$ ). Indicator E / A was ( $0, 75 \pm 0, 01$ ) ms and was significantly lower compared to the AH group ( $t = 4, 80$ ;  $p < 0,001$ ), indicating the development of diastolic dysfunction (DD) LV. The confirmation of this was likely the extension of isovolumic relaxation time of the left ventricle (IVRT) to 26.31% compared to the AH group ( $t = 15, 55$ ;  $p < 0,001$ ), which is natural for such restrictive DD. In general, according to a study of LV diastolic function in patients with COPD of III<sup>rd</sup> degree of severity in combination with SEA was found a violation for type I in 22 (43.13%) patients and for the second type – in 11 (21.56%) patients. In rest of the examined patients Doppler echocardiographic indicators were close to normal. In the subgroup of comparison DD for the first type was found in 12 (27.90%) patients, type II – in 19 (44.18%) patients. A violation of left ventricular diastolic function for the second variant, perhaps, may be a sign of threat destabilization of course SEA I-II in patients with COPD.

According to the results of echocardiography of right heart were found changes in structural and functional characteristics as RA and RV. Thus, in patients of the main subgroup was defined increase in anteroposterior size RA, on average, to ( $40,3 \pm 0,07$ ) mm in patients of subgroup of comparison, this indicator was 1.11 times more likely than in the group of PHP ( $t = 50.85$ ,  $p < 0.001$ ).

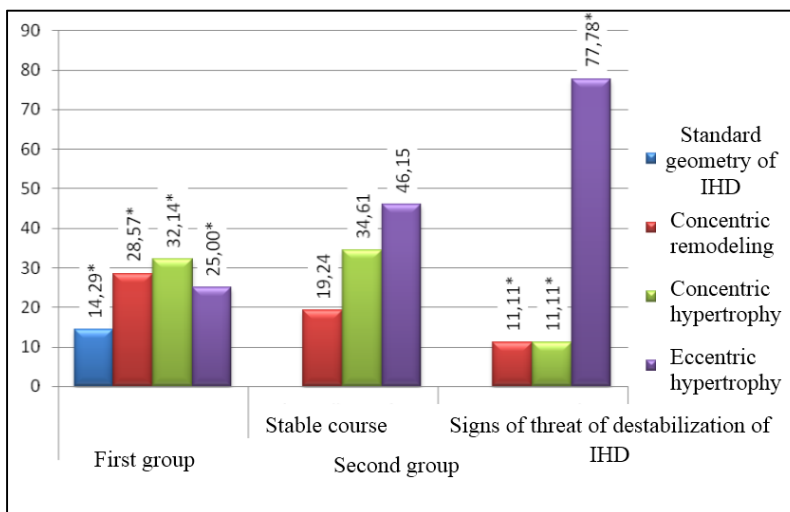
Remodeling of right heart developed through hypertrophy of RV and its dilatation. In patients with isolated COPD the average RVAWth was ( $0, 45 \pm 0, 07$ ) mm. The greatest thickness of the anterior wall of RV (RVAWth) was recorded in patients with combined cardiorespiratory pathology. Thus,

RVAWth in patients of the main subgroup was, on average, ( $0, 58 \pm 0, 04$ ) mm, that is 31.04% significantly higher compared to the PHP group ( $t = 3, 18$ ;  $p < 0.001$ ) and according to the level of statistical trends is higher than in patients of subgroup of comparisons ( $t = 1, 94$ ;  $p < 0.1$ ). Smaller indicators of RVAWth ( $0, 51 \pm 0, 04$ ) mm are in patients of subgroup of comparison due, perhaps, to the development of dilatation processes in RV because RVEDD in these patients is the highest and is ( $27, 9 \pm 0,05$ ) mm. In general, the hypertrophy of anterior wall of RV was detected in 45 (88.23%) patients in the main subgroup and in 27 (62.79%) patients of subgroup of comparison. It was established a negative correlation of medium force size of RVAWth in patients of main subgroup with indicators such as COPD disease duration ( $r = -0,38$ ;  $p < 0,05$ ), FEV1 ( $r = -0,54$ ;  $p < 0,05$ ) and pO2 ( $r = -0,52$ ;  $p < 0,05$ ) and average force positive correlation with the index of Mean Pulmonary Artery Pressure (MPAP) ( $r = 0,44$ ;  $p < 0,05$ ). Evidence of the formation of primary dilatation in patients of subgroup of comparison is the increase of the index RVAWth / RVEDD to ( $0,023 \pm 0,008$ ) cu at a rate of ( $0,017 \pm 0,007$ ) cu ( $T = 0, 56$ ;  $p > 0, 05$ ).

It was established an increase in end-diastolic volume of RV in all patients of studied groups compared to a group of PHP. In particular, in the subgroup of comparison the indicator of EDO was ( $136, 38 \pm 4, 32$ ) ml, that is 1.06 times more improbable than in the group of Practically Healthy People ( $t = 1, 37$ ;  $p > 0.1$ ) and 1, 01 times more compared to the main group ( $t = 0, 33$ ;  $p > 0.1$ ). It was established a medium force negative correlation between RV ejection fraction and severity of COPD in patients of the main subgroup, which was ( $r = -0, 36$ ;  $p < 0, 05$ ), between RV ejection fraction and oxygen saturation ( $r = -0, 28$ ;  $p < 0, 05$ ) between RVEF and thickness of the anterior wall of RV ( $r = -0, 24$ ;  $p < 0, 05$ ). Thus, the course of COPD of III rd degree of severity in combination with SEA I-II FC in most patients is accompanied by the development of compensatory hypertrophy of myocardium and dilatation of the RV.

According to results of the contractile function of the RV was found a probable decrease of ejection fraction in 13.76% in patients in the subgroup of comparison, which was ( $47, 4 \pm 0, 89$ ) % ( $t = 5, 12$ ;  $p < 0,001$ ), while in patients with isolated course of COPD of III rd degree of severity ejection fraction was higher and was ( $49, 86 \pm 1,22$ )% ( $t = 4,28$ ;  $p < 0,001$ ).

The results of the study of type RV remodeling by echocardiography data shown in Fig. 2



**Fig 2:** Types of RV remodeling according to echocardiography data in patients with isolated course of COPD and combined with IF: \* - significant difference of distribution by types of remodeling ( $p < 0.05$ ).

According to the analysis of data that are shown in Fig. 2, various types of remodeling of right heart were defined. The normal geometry of right heart was found only in patients with isolated COPD course the proportion of this type of remodeling was small and was noted in 4 (14.29%) patients. In contrast, concentric remodeling (CR) of right heart was found in patients of both groups of the study. In patients of the first group CR RV was found in 28.57% of patients, in the main subgroup of patients – in 19.27%, in patients of the subgroup comparison - in 11, 11%. Concentric hypertrophy (COG) of RV was detected by comparing the indicators of RVAWth and index RVAWth/

EDD in 9 (32.14%) patients of the first group, 9 (31.64%) patients of the main subgroup and in 2 (11.11%) patients of subgroup of comparison. As we know, the most unfavorable variant of cardiac remodeling is eccentric hypertrophy (EG). According to our data, EG RV was found in 7 (25.00%) patients of the first group, in 12 (46.15%) patients of the main subgroup and in 14 (77.78%) patients of subgroup comparison, confirming the presence of the most highly unfavorable type RV remodeling. The research results of diastolic function of RV are given in Table. 2.

**Table 2:** Inter-group comparative analysis of parameters of diastolic function of the right ventricle in patients with isolated course of COPD of III<sup>rd</sup> degree of severity in the acute phase and when combined with SIHD SEA I-II FC

Indicators	PHP group, (n=28)	First group, (n=28)	Second group (COPD+SCAD), (n=44)	
			Main group, (n=26)	Subgroup of comparison, (n=18)
ERV, mc	0,72±0,01 ***●●●●●	0,48±0,01	0,43±0,01	0,41±0,01
ARV, mc	0,55±0,02 ●●●	0,52±0,01	0,49±0,01 xx	0,42±0,01
E/A	1,25±0,04 ●●●●●	1,14±0,13	0,87±0,04	0,78±0,03
DT <sub>RV</sub> , mc	176,6±3,62 ***●●●●●	248,38±3,89	259,23±4,83	264,65±4,78
IVRT <sub>RV</sub> , mc	81,1±1,94 ***●●●●●	98,60±3,18	106,70±2,46 x	115,70±2,78

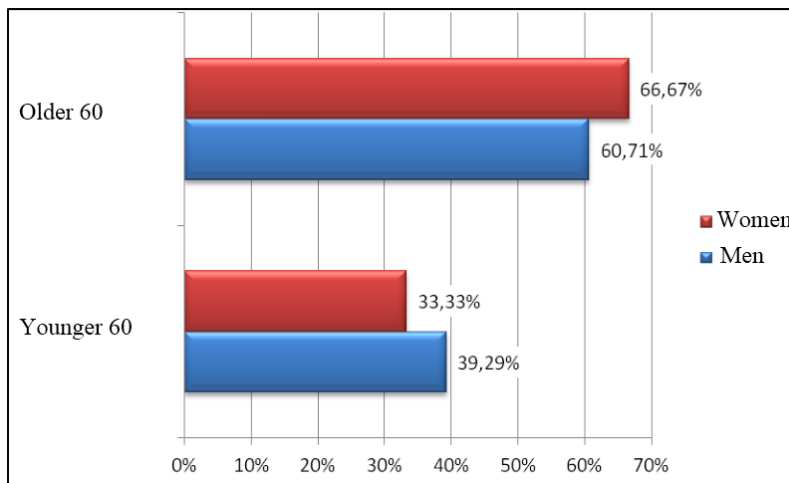
**Notes.** Reliability of difference in parameters: \* - between indicator values of PHP group and of the first group; \* - ( $p < 0.05$ ); \*\* - ( $P < 0.01$ ); \*\*\* - ( $P < 0.001$ ); ● - between indicators of PHP group and the group with stable course SEA I-II FC: ● - ( $p < 0.05$ ); ●● - ( $p < 0.01$ ); ●●● - ( $p < 0.001$ ); ■ - between indicators of PHP group and the group with signs of destabilization threats SEA I-II FC: ■ - ( $p < 0.05$ ); ■■ - ( $p < 0.01$ ); ■■■ - ( $p < 0.001$ ); × - between indicators of the group with a stable flow of SEA I-II FC and the group with signs of destabilization threats SEA I-II FC: × - ( $p < 0.05$ ); xx - ( $p < 0.01$ ); xxx - ( $p < 0.001$ ).

The study showed that in patients of the first group IVRT rate was (98,60 ± 3,18) mc., in patients of the main subgroup (106,70 ± 2,46) ms., respectively, while in patients of subgroup of comparison - (115,70 ± 2,78) ms. Thus, the increase of time IVRT was noted in all patients with COPD, and in patients with combined cardiorespiratory pathology these indicators are significantly higher compared to the group of PHP, ( $t = 8,17-10,0$ ;  $p < 0,001$ ). Indicator DT RV in patients of subgroup of comparison was (264, 65 ± 4, 78) ms. and (259, 23 ± 4, 83) ms. in patients of main subgroup that are statistically significantly higher than in the group of PHP ( $t = 14, 6-28, 8$ ;  $p < 0.001$ ). In addition, during the study of blood flow in the outflow tract of

RV was noted the probable drop of E indicator in patients of all groups of the study ( $t = 24, 2-31, 3$ ;  $p < 0.001$ ) and probable reduction of parameter of maximum speed peak of early diastolic filling (A) in patients with combined cardiorespiratory pathology ( $t = 2, 83-6, 14$ ;  $p < 0, 05-0,001$ ). Ratio E / A in patients of subgroup of comparison was (0, 78±0, 03) cu and (0, 87 ± 0, 04) cu. in the main group of patients that is lower than in the PHP group ( $t = 9, 40$  and  $6.72$ , respectively;  $p < 0.001$ ). In these conditions, diastolic dysfunction (DD) in most patients with COPD of III<sup>rd</sup> degree of severity when combined with SIHD SEA I-II FC was according to the first type of ("delayed relaxation"), leading to a redistribution of diastolic filling

ventricle for atrial component, and showed a decrease in the amplitude of the maximum speed of early diastolic filling, an increase of the height of the maximum rate of late diastolic filling and a decrease in the ratio E / A <1. Overall, on admission

to hospital the symptoms and signs of right ventricular heart failure were found in 28 (63.63%) patients with COPD of III rd degree of severity, and at the same time was noted an increase of its frequency with age and gender. (Fig. 3).

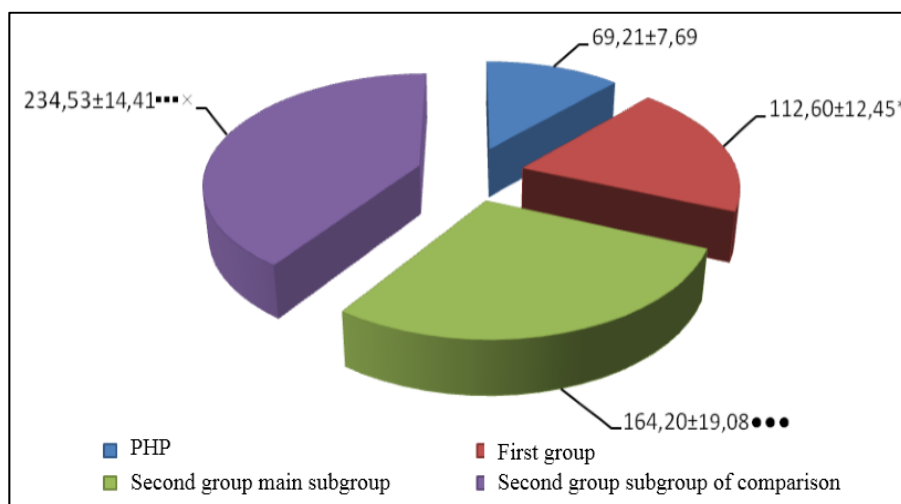


**Fig 3:** The frequency of right ventricular heart failure in patients with combined CRP depending on age and gender.

Thus, in patients who are over 60, the incidence of right ventricular failure in men clearly predominated the number of cases compared to the group of patients younger than 60 years and in female patients. Consequently, carried analysis of echocardiography and Doppler echocardiography shows the differences in the structural and functional characteristics of heart and central hemodynamics depending on the features of COPD of IIIrd degree of severity. In patients with isolated COPD course as the earliest recorded structural changes increase the size and volume of the left atrial (LA). However, in patients with COPD in combination with comorbid SIHD SEA I-II FC dominate systolic and diastolic dysfunctions on the part of the left and right ventricles with the presence of II nd type

range of transmitral and tricuspid flow of blood. With the increase of the duration of the combined CRP course, especially in patients older than 60, the incidence of right ventricular failure in men prevails the number of cases compared to the group of patients younger than 60. A violation of left ventricular diastolic function for the second variant, perhaps, may be a diagnostic sign of threat of destabilization of course SEA I -II FC in patients with COPD.

To determine the role of immunological parameters in the diagnosis of structural and morphological changes of myocardium was carried the determination of the concentration of CT-1 in blood plasma. Results of the study CT-1 shown in Fig. 4.



**Fig 4:** The levels of Cardiotrophin-1 in plasma of patients with COPD of III rd degree of severity in the exacerbation phase and combined cardiorespiratory pathology \* - significant difference between the indicators of the first group and the group of PHP: \* - ( $p < 0.05$ ); \*\* - ( $P < 0.01$ ); \*\*\* - ( $P < 0.001$ ); ● - between indicators of PHP and the main subgroup: ● - ( $p < 0.05$ ); ●● - ( $p < 0.01$ ); ●●● - ( $p < 0.001$ ); ■ - between indicators of PHP and subgroup of comparison: ■ - ( $p < 0,05$ ); ■■ - ( $p < 0,01$ ); ■■■ - ( $p < 0.001$ ); × - between the indicators of main subgroup and subgroup of comparison: × - ( $p < 0,05$ ); ×× - ( $p < 0,01$ ); ××× - ( $p < 0.001$ ).

The results of the analysis showed that patients with COPD of IIIrd degree of severity in the exacerbation phase in combination with SEA I-II level of Cardiotrophin FC-1 were

significantly higher than in patients with isolated course of COPD. Thus, in patients with isolated course of COPD the level of Cardiotrophin-1, was in average (112,60 ± 12,45) pg / ml,

which is 1.45 times less likely than in patients of the main subgroup ( $164,2 \pm 19,08$ ) pg / ml ( $t = 2,26; p < 0,05$ ) and 2.08 times less likely compared to levels in patients of subgroup of comparison ( $234,53 \pm 14,41$ ) pg / ml ( $t = 6,40; p < 0,001$ ). We found of moderate force positive correlation between levels of Cardiotrophin-1 in plasma and certain structural and morphological parameters of the heart in patients with acute exacerbation of COPD of IIIrd degree of severity, in the exacerbation phase combining with SIHD SEA I-II FC, particularly between LVPWT and LVMI and IVST ( $r = + 0,32, p < 0,05; r = + 0,34, p < 0,05; r = + 0,38, p < 0,05$ , respectively).

#### 4. Conclusions

1. Syntrophy of COPD of III<sup>rd</sup> degree of severity, and comorbid SIHD SEA I-II FC makes a significant contribution to the structure and function of the heart. Combined course of both clinical conditions leads to a hypertrophy of the left and right atria. The possible increase of such echocardiographic indicators as LVEDD to ( $51,17 \pm 3,03$ ) mm LVESD to ( $37,28 \pm 2,02$ ) mm IVST to ( $10,6 \pm 0,04$ ) mm, LVESV to ( $62,3 \pm 5,88$ ) ml and LVEDV to ( $136,0 \pm 5,09$ ) ml ( $p < 0,05 - p < 0,01$  for these indicators) points to the development of hypertrophy and dilatation of the left ventricle, helping its remodeling.
2. According to the results of Doppler echocardiography in patients with COPD of III<sup>rd</sup> degree of severity, in the exacerbation phase in combination with SIHD SEA I-II FC is set a development of diastolic function of the right heart, which appears as a likely decline in average indicators of peak amplitude E of ( $0,68 \pm 0,01$ ) m / s, increasing of the height of the average indicators of peak A to ( $0,74 \pm 0,01$ ) m / s and a decrease in the ratio  $E/A < 1$  ( $0,91 \pm 0,01$ ), ( $p < 0,05 - 0,01$  all indicators). At the same time the average indicators of the RV IVRT increase to ( $196, 40 \pm 3, 81$ ) m/s and reduce the average indicators of the RV DT to ( $116, 40 \pm 2, 41$ ) m/s ( $p < 0,05 - 0,01$  all indicators).
3. Diastolic dysfunction of RV of type I was found in 42.30% of patients, of type II - in 22.72% of patients. The identified functional impairment and structural changes in the heart structure worsen significantly the prognosis for patients of the appropriate category, and some indicators can be regarded as markers of threat of destabilization of SIHD SEA I-II FC course.
4. Indicators of Cardiotrophin-1 level in plasma in the presence of myocardial hypertrophy is higher than without it, and confirm the possibility of using it in patients with COPD of III<sup>rd</sup> degree of severity in the exacerbation phase as at isolated course, so as when combined with SIHD SEA I-II FC, to identify hypertrophic processes in myocardium.

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