NEGATIVE ASPECTS OF THE COMORBID COURSE OF COPD AND CHF

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Abstract. *The paper focuses on challenges in the diagnosis and treatment choice for patients with CHF and COPD. It is underlined that in the pathogenesis of both diseases there are common processes of systemic inflammation, oxidative stress, and endothelial dysfunction. One of the main systemic inflammation markers is highly sensitive C-reactive protein (hs-CRP). The fact that N-terminal pro-brain natriuretic peptide (NT-proBNP) is a standard laboratory biomarker of CHF, but the adverse effect of COPD on the cardiovascular system can also affect its level in blood serum is also stressed. The study was aimed to assess the impact of COPD on the level of NT-proBNP, hs-CRP and the functional status of patients with CHF. The results obtained demonstrate that combination of COPD and CHF amplifies systemic inflammation and myocardial remodeling processes determined by the level of NT-proBNP. A negative effect of COPD on the functional status of patients with CHF with different left ventricular ejection fraction was reported. The results obtained contribute to expansion of the diagnostic capabilities, and prognosis and effectiveness of pharmacotherapy in patients with COPD and CHF.*

Keywords: *CHF, COPD, NT-proBNP, hs-CRP, 6MWT.*

Introduction. Nowadays we are observing an increase in the number of patients with chronic heart failure (CHF). CHF decompensation is the main reason for hospitalization in cardiology departments, especially among patients over 65 [1]. New CHF management algorithms made it possible to increase the survival rate; nevertheless, the annual mortality rate of this group of patients is 7%, and severe decompensation reaches 17% [2]. It is also worth noting that the comorbidity of CHF and chronic obstructive pulmonary disease (COPD) significantly worsens the prognosis for such patients.

Difficulties in the diagnosis and treatment choice for patients with CHF and COPD determine the increased scientific interest in the study of the cardiorespiratory state in recent years. Currently available data indicate that COPD affects 25% - 42% of patients with CHF. Such patients are at increased risk of readmission and death [3].

In the pathogenesis of both diseases, there are common processes of systemic inflammation, oxidative stress, and endothelial dysfunction [4]. One of the main systemic inflammation markers is highly sensitive C-reactive protein (hs-CRP) that could be identified in the systemic circulation. In turn, N-terminal pro-brain natriuretic peptide (NT-proBNP) is a standard laboratory biomarker of CHF, but the adverse effect of COPD on the cardiovascular system can also affect its level in blood serum.

The aim of the study was to assess the impact of COPD on the level of NT-proBNP, hs-CRP and the functional status of patients with CHF with different left ventricular ejection fraction.

Material and methods. Participants' recruitment for the study was conducted using the CHF registry of the Voronezh region. From two thousand patients of the register, the study included 240 patients aged from 40 to 70 years with ischemic CHF (of which - 134 men and 106 women, average age 71.4 ± 8.4 years). The patients were divided into two groups: the first group (n = 160) - patients with isolated CHF (86 men and 74 women, mean age - 73.2 ± 8.8 years) who had no signs of the lung diseases, the second group (n = 80) - patients with a comorbid course of

CHF and COPD, including 48 men (60.0%) and 32 women (40.0%), the mean age is 67.5 ± 5.9 years.

The main criterion for dividing patients into subgroups was the left ventricular ejection fraction, which was measured using echocardiography. Consequently, each of the two groups (with an isolated course of CHF, with a comorbid course of COPD and CHF) was divided into two subgroups. Patients with CHF with borderline ejection fraction (40-50%) and reduced ejection fraction (<40%) were combined into a group of patients with chronic heart failure with reduced ejection fraction (CHFrEF) (ejection fraction <50%). Subgroup 1 included 69 patients with an isolated course of CHFpEF (EF ≥50%), subgroup 2 - 91 patients with CHFrEF (EF <50%). Subgroup 3 consisted of 36 patients with COPD and CHFpEF (EF≥50%) and subgroup 4 consisted of 44 patients with COPD and CHFrEF (EF <50%).

All participants were examined by a cardiologist and a pulmonologist every week from the moment of inclusion. This was used to control the absence of symptoms of CHF decompensation and COPD exacerbation. After 12 weeks, the study participants underwent 6-minute walk test (6MWT) and standard examination. We used a complex of cardiorespiratory analysis to assess exercise tolerance and 6MWT. The result was expressed in meters and compared with the proper 6-minute walk distance (6MWD (i)). The formula for calculating 6MWD (i) for men: 6MWD (i) = 1140 - 5.61 x BMI-6.94 x age. For women - 6MWD (i) = 1017 - 6.24 x BMI - 5.83 x age [5]. In addition to general clinical laboratory studies, enzyme immunoassays of blood were used to determine the levels of NT-proBNP and hs-CRP.

Statistical analysis was carried out using the STATISTICA 10.0. The data normality was assessed using the Shapira-Wilk and Kolmogorov-Smirnov test. Continuous variables are presented as M ± SD (M - mean, SD - standard deviation). Comparison of unrelated groups was performed in the case of normal distribution using Student's t-test. The null hypothesis was rejected at a significance level of p <0.05. All quantitative data have a normal distribution.

Results. The data obtained show that CHFrEF was accompanied by an increased level of NT-proBNP regardless of the presence or absence of COPD (Table 1). However, it should be noted that the combination of COPD and CHF (1512 ± 229 ng / L) in patients of the second group was accompanied by a statistically higher level of NT-proBNP than in patients with isolated CHF 1004 ± 174 ng / L (p = 0.042).

The hs-CRP level was measured to assess the severity of endogenous inflammation. In patients with CHFpEF the level of hs-CRP was 3.7 ± 0.62 mg / L, while in patients with CHFrEF it was significantly lower - 2.6 ± 0.59 mg / L (p <0.001). It was also lower in patients with COPD and CHFpEF (third subgroup) (4.9 ± 0.85 mg / l) then in patients from the fourth subgroup (4.4 ± 0.74 mg / L.), (p <0.001).

Table 1. Comparison of laboratory parameters in the studied patients

Indicator	Subgroup 1 (CHFpEF)	Subgroup 2 (CHFrEF)	p1 value	Subgroup 3 (COPD and CHFpEF)	Subgroup 4 (COPD and CHFrEF)	p2 value
NT-proBNP, ng/L	813 ± 127 ng / L	1171 ± 191	<0.001	1228 ± 206	1876 ± 254	<0.001
hs-CRP, mg / L	3.7 ± 0.62	2.6 ± 0.59	<0.001	4.9 ± 0.85	4.4 ± 0.74	<0.001

Note: data are presented as "Mean ± standard deviation"; CHFpEF – chronic heart failure with preserved ejection fraction; CHFrEF - chronic heart failure with reduced ejection fraction; COPD - chronic obstructive pulmonary disease; hs-CRP - highly sensitive C-reactive protein; NT-proBNP - NT-terminal fragment of natriuretic peptide.

The results obtained during 6MWT in patients with COPD and CHF, regardless of LVEF, were less than in patients with CHF (p1 = 0.04; p2 = 0.03). It can be explained by a combination of both types of breathing disorders in patients with a comorbid CHF and COPD: obstructive and restrictive. At the same time, in patients with an isolated course of CHF, there are no significant obstructive breathing disorders.

Calculation of the 6MWD / 6MWD (i) ratio allowed us to establish that in patients

with CHF and COPD, this indicator is lower than in patients with CHF, regardless of LVEF. The results are shown in Table 2.

Heart rate (HR) before and immediately after 6MWT did not differ significantly in the subgroups. In addition, the device did not record an excess of submaximal values during the test in the subjects.

The SpO2 level was the same in the studied subgroups before the start of the test. When assessing this parameter after the test, significantly lower indicators were recorded in patients with a comorbid course of CHF and COPD, regardless of LVEF. Exercise tolerance was assessed also by using the Borg scale for assessing the severity of dyspnea after 6MWT. In patients with comorbid CHF and COPD, the higher scores were obtained compared to subgroups 1 and 2 (with isolated CHF) (Table 2).

Table 2. Comparison of 6MWT parameters in the studied patients

Indicator	Subgroup 1 (CHFpEF)	Subgroup 3 (COPD and CHFpEF)	p1 value	Subgroup 2 (CHFrEF)	Subgroup 4 (COPD and CHFrEF)	p2 value
6MWD, m	301,5±153,5	264,6±120,6	0,04	251,5±183,5	202,4±130,2	0,03
6MWD, % from the proper	53,0±29,2	47,2±25,6	0,01	48,1±30,5	42,8±22,4	0,02
HR before test, beats / min	76,1±15,2	77,8 ± 17,3	0,18	86,1±15,2	87,8 ± 17,3	0,16
HR after test, beats / min	102,4±17,5	107,3 ± 18,8	0,15	109,4±17,2	115,1 ± 14,8	0,15
SpO2 before test, %	97,9±2,0	97,5±2,1	0,12	95,2±2,4	94,9±2,6	0,26
SpO2 after test, %	95,5±3,0	93,3±3,1	0,001	94,1±3,3	91,2±2,5	0,001
Dyspnea according to Borg, points	2,41±0,17	3,22±0,29	0,01	3,83±0,32	5,19±0,37	0,001

Note: data are presented as "Mean ± standard deviation"; 6MWD - distance covered in the six-minute walk test; CHFpEF – chronic heart failure with preserved ejection fraction; CHFrEF - chronic heart failure with reduced ejection fraction; COPD - chronic obstructive pulmonary disease; HR – heart rate; SpO2 - blood oxygen saturation.

Discussion. The manifestation of CHF means unfavourable prognosis for the patient, but early diagnosis makes it possible to more effectively restrain the disease progression.

A number of articles have been published on the effectiveness of determining the level of NT-proBNP in patients with CHF and COPD. There are results that indicate that NT-proBNP is an independent predictor of death in patients with COPD [6]. Conversely, there is evidence that an increase in NT-proBNP allows CHF to be suspected in patients with COPD and should be accompanied by further examination [7]. Similar results were obtained in our study: this biomarker does not lose its diagnostic value in the case of a combined course of COPD and CHF. It was also noted that in patients with a combination of COPD and CHF, the NT-proBNP level was statistically significantly higher than in patients with isolated CHF.

In addition, there are data that indicate an increased risk of CHF in patients with COPD with an increased level of CRP that indicates the processes of endogenous inflammation [8].

Previously, we found that in patients with COPD, a decrease in physical activity is apparently associated not only with lung dysfunction at rest, but also depends on a number of other factors. Thus, in patients with COPD, a decrease in lean body mass is often observed. It is a consequence of systemic inflammation and muscle atrophy due to low physical activity [3]. Therefore, it can be assumed that one of the components that reduce exercise tolerance in such patients is the activation of systemic endogenous inflammation, leading, among other things, to a decrease in muscle mass.

Conclusion. Patients with CHFpEF have higher levels of hs-CRP in comparison with patients with CHFrEF. The combination of COPD and CHF amplifies systemic inflammation and myocardial remodeling processes, determined by the level of NT-proBNP, in comparison with the isolated course of CHF. A negative effect of COPD on the functional status of patients with CHF with different LVEF was established, which is manifested by lower 6MWT values, the 6MWD / 6MWD ratio (i). With further study, the results ob-

tained will expand the diagnostic capabilities, as well as assess the prognosis and effectiveness of pharmacotherapy in patients with COPD and CHF.

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НЕГАТИВНЫЕ АСПЕКТЫ КОМОРБИДНОГО ТЕЧЕНИЯ ХОБЛ И ХСН

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Аннотация. *Статья посвящена проблемам диагностики и выбора лечения больных ХСН и ХОБЛ. Подчеркивается, что в патогенезе обоих заболеваний присутствуют общие процессы системного воспаления, окислительного стресса и эндотелиальной дисфункции. Одним из основных маркеров системного воспаления является высокочувствительный С-реактивный белок (вч-СРБ). Также обращает на себя внимание тот факт, что N-концевой промозговой натрийуретический пептид (NT-proBNP) является стандартным лабораторным биомаркером ХСН, но неблагоприятное влияние ХОБЛ на сердечно-сосудистую систему может сказываться на его уровне в сыворотке крови. Целью исследования было оценить влияние ХОБЛ на уровень NT-proBNP, вч-СРБ и функциональное состояние больных ХСН. Было установлено, что сочетание ХОБЛ и ХСН усиливает системное воспаление и процессы ремоделирования миокарда, определяемые уровнем NT-proBNP. Отмечено негативное влияние ХОБЛ на функциональное состояние больных ХСН с различной фракцией выброса левого желудочка. Полученные результаты способствуют расширению диагностических возможностей, прогноза и эффективности фармакотерапии больных ХОБЛ и ХСН.*

Ключевые слова: *ХСН, ХОБЛ, NT-proBNP, hs-CRP, 6MWT.*