Consequences of chronic heart failure in the diagnosis of bronchial asthma

Shukhrat Xudayberdiyevich Ziyadullayev
Institute of Immunology and Human Genomics of Academy of Sciences of Uzbekistan
Jamshid Abduraimovich Ismailov
Shukhrat Suyun o'g'li Aliev
Xumora Urinova
Samarkand State Medical University

Abstract: Bronchial asthma is a prevalent chronic respiratory disorder characterized by episodic and reversible airflow obstruction, airway hyperresponsiveness, and chronic inflammation. It affects millions of people worldwide, significantly impacting quality of life and posing a substantial public health burden. The pathophysiology of asthma involves complex interactions between genetic predisposition and environmental factors, leading to the hallmark symptoms of wheezing, coughing, shortness of breath, and chest tightness.

Keywords: bronchial asthma, chronic heart failure, treatment, pro-BNP, endothelium

Background. Studies by the European Society of Cardiology show that among hospitalised and ambulatory patients, all-cause mortality rates are 17% and 7%, respectively, and hospital admissions are 44% and 32%, respectively [1,3,5]. Most deaths in patients with CHF (both hospitalised and outpatients) are related to cardiovascular causes, which are associated with sudden cardiac death (primary cardiac arrest) and worsening of the course of CHF. Different levels of CHF have been identified in hospitalised patients with complications of AD and have caused difficulties in treatment. Therefore, the development of therapeutic strategies for the treatment of pathology complicated by BA with CHF is particularly relevant [4,6] .

The data on diagnosis, modern methods of treatment, as well as the author's approach to the scientific solution of this problem are analysed. The above cases show the relevance of the problem of internal diseases and encourage the study of issues of practical importance [2,7].

Materials and methods. Based on the aim of the study, the anamnesis and age history of the patients were studied in three comparative groups. According to the results of the study 110 patients with CHS and BA II-III stages made up the first initial group: 34 women (30.9%) and 76 men (69.09%). In the second reference

group, 50 patients with CHF were examined, including 21 women (42%), 29 men (58%) and 30 healthy people in the third reference group, including 15 men (50%) and 15 women (50%).

This study is based on the results of examination of 110 patients of the main group with CHF and BA stage II-III: 34 women (30.9%), 76 men (69.09%). In the second control group 50 patients with CHF were examined, including 21 women (42%), 29 men (58%), 30 healthy people in the third control group, including 15 men (50%) and 15 men. 50%).

From 2019 to 2021, the patients who came to the therapeutic room of the emergency room were examined in the first therapeutic department .

Based on the aim of the study, the history and age history of the patients were studied in two comparative groups.

The first (main) group consisted of 60 patients under 50 years of age (20 women 33.33%; 40 men 66.66%). There were 50 patients older than 50 years (14 women 28%; 36 men 72%).

The second (control) group consisted of 30 patients under 50 years of age (12 females 40%; 18 males 60%). There were 20 patients over 50 years of age (9 women 45%; 11 men 55%).

The first group of patients under 50 years of age was 21-50 years old, with a mean age of 36.8 ± 0.7 years; the age of patients over 50 years old was 51-76 years old, with a mean age of 61.0 ± 0.6 years. compact.

The second group of patients younger than 50 years old was 20-50 years old, mean age 35.6 ± 0.6 years, patients older than 50 years old was 51-70 years old, mean age 56.0 ± 0.7 years. years. compact.

50 лет - 51-70 лет, средний возраст $56,0 \pm 0,7$ года. лет. компактный.

Table 1

Clinical features of patients of the main group

Indicators		Average age	Minimum age	Maximum age
Age		48.9	21	76
		Number of patients	% of the total number of patients in the group	
Floor	Men	76	69.09%	
	Women	34	30.9%	
Body mass index kg/m2		27.8 (25.2; 29.7)		
CHF	NYHA I FC	20	18.18%	
	NYHA II FC	38	34.54%	
	NYHA III FC	52	47.27%	
Average number of hospitalizations per year		3		
BA	I degree	23	20.9%	
	II degree	53	48.18%	
	III degree	34	30.9%	
Smoking duration		32 [28; 36]		
Emphysema		41	37.27%	

Pulmonary hypertension (EchoCG)	I degree	38	34.54
	II degree	9	8.18
	III degree	3	2.72

Results. The first main group examined 110 patients with AD complicated by chronic heart failure. The first control group consisted of 50 patients with CHF and the second control group consisted of 30 healthy subjects. The use of static methods to assess differences required the creation of groups according to sex, age, duration and severity of the disease.

In the initial phase of the study, a cross-sectional analysis of all patient groups was performed to determine the characteristics of CHF in treatment-naive patients with AD complicated by chronic heart failure.

The main correlations were characteristic for CHF: proBNP ($r = -0.73$), CCN Clinical Status Assessment Scale (CSAS) ($r = 0.71$), 6-minute walk test, LV EF and LVEF, and questionnaire for EQ-5D-5L - there was a correlation relationship.

Interestingly, the correlation between the BODE proBNP index and the EQ-5D-5L health assessment questionnaire, which characterises the ICU, is of great interest, and it is important to determine proBNP in the ICU. We present the results of correlation analysis of left ventricular post-systolic and post-diastolic parameters with functional tests, reflecting the interdependence of parameters characterising the functional class of CHF. LV EF ($r = 0.93$) showed moderate and strong direct correlation between the main tests.

Patients admitted to the hospital presented complaints inherent to both CHF and BA: palpitations on physical and psychoemotional stress, unpleasant sensations behind the sternum, dyspnoea, constant intake of short-acting b2-agonists, peripheral edema, general weakness, rapid breathing. Taking into account the necessity of differential diagnostics of dyspnoea symptoms in BA and CHF, NT-proBNP level in blood was determined in all patients.

NT-proBNP levels were determined to determine the functional class of CCN. These results are described in Table 2.

Table 2

NT-proBNP levels in the group with CHF

1 group		
(n=110)	EF>40% (n=76)	EF<40% (n=34)
2755 [1260; 3781]	1068 [1025-2062]	1793 [1010-2358]
P<0.01		
2 группа		
(n=50)	EF>40% (n=28)	EF<40% (n=22)
2593 [978; 3714]	1028 [979-1699]	1401 [1065-1789]
P<0.01		

Significant increases in the levels of fibrinogen and proinflammatory cytokines were observed in both groups during analysis for signs of inflammation. Moreover, these changes were more pronounced in group 1, indicating a more pronounced systemic inflammatory response in AD patients. All inflammatory symptoms were slightly higher in the 2nd main subgroup, but significant differences were noted only for fibrinogen and IL-6. Elevated levels of pro-inflammatory cytokines were also found, but significant differences were noted in both groups only for IL - 8, indicating a lack of anti-inflammatory potential (Table 3).

Cytokine activity was significantly increased in patients with AD complicated by CHF and the comparable group with CHF, in contrast to the group with healthy subjects. Significant decrease of IL-6 and 8 levels in patients in the main group was noted against the background of treatment with inhaled corticosteroids, which at the end of treatment did not differ from that in the group of healthy people. Thus, it is possible to fix the balance of the system of proinflammatory cytokines.

Table3

Results of immunological analysis

Control groups	Fibrinogen	CRP	IL - 6	IL - 8
1 - group (110)	5,48±1,4	53,3±17,41	135,0±20,81	225,0±20,8
2 - group (50)	4,35±1,5	38,3±10,81	59,1±11,41	63,2±10,5
3 - group (30)	2,57±0,3	2,8±0,5	2,4±0,5	28,4±8,4
Norm	2-4 mg/l	0-5 mg/l	7 pg/ml	0-62 pg/ml

The mean NT-proBNP level at the time of inclusion in the study in group 1 was 2755 [1260; 3781] and group 2 was 2593 [978; 3714]. These values show no significant differences in NT-proBNP levels between the two groups ($p > 0.05$). Patients with LVEF less than 40% had significantly higher NT-proBNP levels in the within-group analysis, which was associated with the severity of CHF ($p < 0.05$).

The above data show that patients of both main groups had approximately the same exercise tolerance at the initial stage. The results of these functional tests show that the symptoms of CHF were predominant in both groups. No significant statistical differences were found between groups ($p < 0.05$), although the mean distance was greater in correlation with the 6-minute walk test in group 2. Thus, the assessment of the functional class of CHF was based on laboratory parameters, data obtained from the patient's history, and functional tests that complemented each other and showed similar results. This is a test with six-minute walking and on the SCOX scale - assessment of the clinical condition of a patient with CHF.

At the stages of the study, EchoCG was used to assess cardiac activity of all patients and to determine central haemodynamics. Comparative analysis of haemodynamics in the studied groups showed reliable changes in both groups. Dilatation of the left atrium and left ventricle, increase in the posterior wall of the left ventricle, increase in the thickness of the interventricular septum were observed.

However, high left ventricular and pulmonary artery pressures were in both groups of CHF. These changes were associated with the severity of the condition of the patients with CHF and BA. Echocardiographic findings complement previous laboratory and functional examination methods and represent the distribution of patients with chronic heart failure by functional class, as well as the severity associated with the presence of pulmonary hypertension. Table 5 presents the main echocardiographic parameters of patients in this group.

The level of pro-BNP was determined in all patients of the 1st and 2nd groups. High levels of this enzyme were found in the first and second groups and were not statistically different. The level of pro-BNO in the main group with BA and CHF and in the second group with CHF it was high, indicating the presence of heart failure in both groups. Some additions to the diagnostic and treatment standards are required to address the problem of CHF with BA phenotype.

Patients were evaluated for NT-proBNP, 6-minute walk test, SHOCS questionnaire, performance of EchoCG and spirometry, performance of EQ-5D-5l and SGRQ, and evaluation of BODE index.

Determination of proBNP level after 6 months of therapy showed the following results

Table 4

ProBNP levels after 6 months of therapy

1 - группа (110)			
Indicators	(n=110)	EF>40% (n=76)	EF<40% (n=34)
In the initial phase of the inspections	2755 [1260; 3781]	1068 [1025-2062]	1793 [1010-2358]
After 6 month	1564 [1200-3863]	1035 [1020-3050]	1079 [1018-1140]
p	$_{1-2}$ >0,05	$_{1-2}$ >0,05	$_{1-2}$ >0,05
2 - group (50)			
Indicators	(n=50)	EF >40% (n=28)	EF<40% (n=22)
In the initial phase of the inspections	2593 [978; 3714]	1028 [979-1699]	1401 [1065-1789]
After 6 month	1239 [978; 1500]	1037 [902-1712]	1045 [1015-2083]
p	$_{3-4}$ <0,05	$_{3-4}$ <0,05	$_{3-4}$ <0,05
	$_{2-4}$ <0,05	$_{2-4}$ <0,05	$_{2-4}$ <0,05

When analysing the obtained results, no significant differences in the dynamics of NT-proBNP levels in the main group and in the first control group were revealed. There was an increase in the NT-proBNP parameter when assessing the main group in patients with CHF>40% and CHF <40%, but there was no statistical difference. This result does not show a significant positive clinical outcome in stable CHF clinic. After 6 months in the first control group i.e. in patients with CHF only, a significant positive trend was observed. Reliability of differences was also important when assessing this index in the group with CHF> 40% (p <0,05), but the mean values of NT-proBNP were approximately the same. There was a more pronounced reduction

in NT-proBNP value by 40% in the group with CHF <40%. ARNI-adjuvanted therapy in the groups of patients with CHF and with BA and CHF had a greater effect on patients with a less favourable prognosis.

Distribution of groups into subgroups with CHF >40% and CHF <40%. The dynamics of these patients are quite different, and clinical evaluation should be performed with more accurate data. The presented data showed that the mean NT-proBNP levels in groups 1 and 2 were 2755 pg/mL and 2593 pg/mL, respectively. In patients with CHF <40%, divided into the second group according to the criteria of CHF, this index was 1239 pg / ml after 1564 months of therapy, which dramatically changed the approach to this category of patients. The dynamics of NT-proBNP levels helps the physician in the choice of therapy tactics and especially in the assessment of its effectiveness. The details are shown in Figures 2 and 3.

Valsartan/sacubitril complex showed better results than treatment with IAPP. Significant laboratory dynamics in the form of decreased NT-proBNP levels were observed in patients with CHF <40%, which affects the pathogenetic mechanisms associated with the formation and development of CHF. The obtained results significantly influenced the increase of exercise tolerance in patients with chronic obstructive pulmonary disease complicated by chronic heart failure. Narrowing of the PP cavity and reduction of LA pressure indicate not only regression of AD, but also regression of CHF. The use of IF-channel inhibitors in the treatment of patients with obesity and chronic obstructive pulmonary disease complicated by chronic heart failure reduces bronchoobstructive syndrome in these patients and significantly reduces the number of attacks.

In 75 (80%) patients such blood lipid parameters as plasma cholesterol, triglycerides, very low density lipoproteins, significant increase in low density lipoproteins and decrease in high density lipoproteins were initially disturbed.

After six months of treatment, no significant positive dynamics were observed in both groups. Some reduction of total cholesterol and its atherogenic fractions was shown, which led to a decrease in the atherogenicity index by 14.9% and by 17.4% in the first and second groups (Fig. 4). The use of statins in the treatment scheme of obese patients with chronic obstructive pulmonary disease complicated by chronic heart failure has a metabolically neutral effect. Blockers of neurohormonal system of RAAS help to improve the profile of lipid metabolism due to their vasoprotective, antioxidant effects and synergy, which, in turn, helps to improve vascular permeability and, thus, reduce clinical manifestations of heart failure.

The levels of fibrinogen and proinflammatory cytokines decreased in both groups after treatment. In addition, the changes were more significant in both groups (Table 5).

In patients with chronic obstructive pulmonary disease complicated by chronic heart failure against the background of long-term therapy the activity of cytokines was significantly reduced. Thus, it is possible to fix the balance of the system of proinflammatory cytokines during remission of BA.

Table 5

Results of immunological analysis

Control group	Fibrinogen	CRP	IL - 6	IL - 8
1 - group (110)	4,8±1,4	32,2±15,1	62,0±20,81	48,0±9,2
2 - group (50)	4,2±1,4	15,3±10,81	9,1±1,41	30,2±3,1
3 - group (30)	2,52±0,3	2,8±0,5	8,4±2,5	25,4±8,4

The dynamics of the 6-minute walk test and clinical status rating scale after 6 months are presented in Table 6.

Table 6

6-minute walk test and SHOCS

1 - group (110)		
6-minute walk test		
Indicators	(n=110)	CHF>40% (n=76)	CHF<40% (n=34)
After 6 month	226,0 [232,0; 374,0]	300,0 [220,0-420,0]	245,0 [240,0-250,0]
p	1-2 <0,05	1-2 <0,05	1-2 <0,05
SHOCS		
Indicators	(n=50)	CHF>40% (n=28)	CHF<40% (n=22)
After 6 month	10 [6; 10]	5 [4; 6]	7,5 [7; 8]*
p	3-4 <0,05	3-4 <0,05	3-4 <0,05
2 - group (50)		
6-minute walk test		
Indicators	(n=50)	CHF>40% (n=28)	CHF<40% (n=22)
After 6 month	254,0 [225,0; 310,0]	220,0 [180,0-280,0]	210,0 [120,0-240,0]
p	5-6 <0,05	5-6 <0,05	5-6 <0,05
	2-6 >0,05		
SHOCS		
Indicators	(n=50)	CHF>40% (n=28)	CHF<40% (n=22)
After 6 month	9 [5; 9]	4 [3-5]	9 [7-9]
p	7-8 <0,05	7-8 <0,05	7-8 <0,05
	4-8 >0,05		

Inclusion of proBNP level determination in the diagnostic standards for patients with BA also serves as an effective method for early detection and early initiation of treatment of chronic heart failure and prevention of its worsening.

CONCLUSION

1. Bronchial asthma in obese patients complicated by chronic heart failure is characterised by the predominance of pathogenetic mechanisms of endothelial dysfunction depending on the stage of BA and the stage of CHF. The more severe the course of BA, the higher the levels of proinflammatory cytokines, which indicate the severity of endothelial dysfunction. Also, the higher the stage of CHF, the higher the level of proBNP.

2. The use of if-receptor blocker in patients with stable CHF is characterised by improvement of quality of life on the basis of SGRQ and EQ-5D-5L questionnaires, as well as SQRS. The conducted analysis of if-receptor blocker therapy efficacy on endothelial function, markers of cytokine inflammation, NUP level, haemostasis system showed significant improvement of all parameters in patients with BA complicated by CHF.

3. Using ARNI, pro-BNP levels can be used not only for the assessment of CHF, but also for the prognosis of patients with BA complicated by CHF, as there is a strong correlation with both parameters of the disease. Pro-BNP levels decreased on long-term ARNI therapy in both groups.

References

1. Fiseselmann J.F., Richerson H.B: Respiratory diseases // Basic and Clinical Immunology. — 8th ed. / Ed. by D.P. Stites, Al. Terr, T.G. Parslow. — Norwalk, CT: Appleton & Lange, 2014. — P. 528-540.

2. Saini G, Porte J, Weinreb PH et al. $\alpha v \beta 6$ integrin may be a potential prognostic biomarker in interstitial lung disease. ERJ Express, 2015, March 5.

3. Ziyadullaev S. et al. The effect of budesonide on the quality of life in patients with bronchial asthma //European Journal of Molecular & Clinical Medicine. - 2020. - Т. 7. - №. 2. - С. 1760-1766.

4. Fazilova G. et al. The role of certain regulatory cytokines in the immunopathogenesis of extrinsic allergic alveolitis. - 2018.

5. Ismailov J. A. et al. O'SOK va yurak yetishmovchiligi patogenezining zamonaviy tushunchalari //Science and Education. - 2023. - Т. 4. - №. 6. - С. 71-81.

6. Ismailov J. A., Urinova X., Zokirova F. Bronxoobstruktiv sindromda surunkali yurak yetishmovchiligini davolashning samaradorligi //Science and Education. - 2023. - Т. 4. - №. 6. - С. 110-128.

7. Зиядуллаев Ш. X. и др. Генетические маркеры гиперреактивности бронхов при бронхиальной астме //Академический журнал Западной Сибири. - 2014. - Т. 10. - №. 3. - С. 19-19.