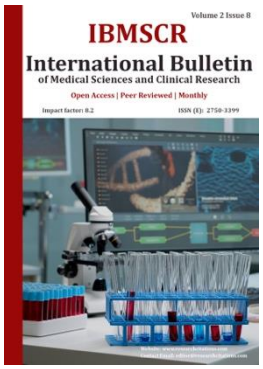

CHANGES IN THE CARDIOVASCULAR SYSTEM AND IMPAIRMENTS IN THE QUALITY OF LIFE OF PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

G.T.Madjidova
Samarkand State Medical University
2nd Assistant of the Department of Internal Medicine
Samarkand Uzbekistan
G.I.Sunnatova
Samarkand State Medical University
2nd Assistant of the Department of Internal Medicine
Samarkand Uzbekistan
D.N.Adilova
Doctor's office, Samarkand branch of the
Republican Scientific Center for Urgent Ambulance
Samarkand Uzbekistan.
F.H.Safarova
Doctor's office, Samarkand branch of the
Republican Scientific Center for Urgent Ambulance
Samarkand Uzbekistan.
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A NNOTATION. The relevance of the topic is undeniable. COPD is one of the 3 leading causes of death in the world. In this article comorbid cardiovascular disorders, including pulmonary hypertension, affecting the quality of life in patients with COPD, were studied in 45 patients. It was found that in patients with COPD the following disorders prevail: severe course of the disease, expiratory dyspnea, irreversible bronchial obstruction, airway emphysema, which is accompanied by chronic respiratory insufficiency. In 14.8±4.5 years from the disease onset, COPD patients show signs of pulmonary hypertension, mean pulmonary artery pressure increases up to 32.1±1.2 mm Hg and more, accompanied by moderate gas exchange disorders. The progression of the disease (the number of exacerbations per year was 5.12±2.3 times) in patients with COPD is accompanied by a gradual decrease in the parameters of tolerance to physical activity and quality of life. Thus, the analysis of integral quality of life indicators in the main group revealed a significant decrease to 55.7±0.8% of physical and to 38.2±0.8% of mental quality of life components. Walked distance in 6-minute walking test in patients with COPD was 60.7±0.6% of proper, which was the ground for establishing moderate restrictions of mobility in patients with COPD and caused disability in about 50% of patients with COPD (disability group 3 was established).

Relevance: According to the World Health Organization (WHO), non-communicable diseases have become the number one cause of death globally [1]. COPD is one of the 3 leading causes of death in the world and accounts for 90% of deaths when they occur in low- and middle-income countries. Currently, 380 million people worldwide suffer from moderate to severe COPD. Experts estimate that 3 million people die from this disease every year . The incidence of COPD is 574.1 per 100,000 adults. In 2019, 13,670 patients with COPD were observed in

the republic, in 2,901 cases the diagnosis was established for the first time [4]. Distance walked in the 6-minute walk test (MWT) is the primary outcome of this validated test, given its reliability and validity, and its strong association with clinical outcomes in patients with COPD [4]. Despite the active role of systemic and local inflammation in the progression of COPD, the high significance and frequency of changes in the cardiovascular system in COPD, their relationship with the development of exercise intolerance and the quality of life of patients with COPD remain insufficiently studied.

Goal: to identify comorbid cardio -respiratory disorders in COPD, assess exercise tolerance and quality of life of patients.

Materials and methods of research.

The study included 45 patients. The patients were comparable in age and body mass index. To solve the purpose and objectives of this study, all patients of the compared groups underwent a set of instrumental research methods (body plethysmography , ECG, EchoCG , 6-minute walk test, laboratory research methods - general and biochemical blood tests). Patients in the main and control groups received basic therapy for the underlying disease in accordance with clinical protocols for the diagnosis and treatment of respiratory diseases. Statistical processing of the results was carried out using the Statistica 6.0 program . The significance of differences between two independent samples was determined by parametric statistics using Student's t-test or non-parametric statistics (Mann-Whitney U-test). Differences were considered significant at $p < 0.05$. For indicators characterizing qualitative characteristics, the absolute number and relative value as a percentage were indicated.

Research results. The study included 45 patients, incl . 20 people with COPD, average age - 59.7±1.72 years, which formed the main group (MG) and 25 patients with chronic non-obstructive bronchitis (CNB), average age - 50.3±2.6 years, who formed the control group (CG) . Main group 1 (OG1) – 20 patients with COPD. Of these, 13 (65.0%) were men, 7 (35.0%) were women. The age of the patients ranged from 21 to 69 years, the average age was 59.7±1.72 years . The duration of illness of patients with COPD was 14.8±4.5 years.

Clinical and anamnestic data in the compared groups are presented in Table 1.

Table 1 Characteristics of patients included in the study

Options	OG, n =20	CG, n =25	R
Floor: male, n (%) female, n (%)	 11(65.0%) 5(35.0%)	 5(20.0%) 20(80.0%)	-
Age, years	43.7±1.7	50.3±2.6	< 0.01
BMI, kg/ m^2	26.4± 0.9	29.1 ±1.6	-
Smoking index, packs/years	11.3±3.5	3.4±2.9	<0.001
Smoking experience, years	15.2±3.8	6.2±3.6	<0.05
Duration of illness, years	11.7 ±4.5	4.7 ±1.4	<0.05
Number of exacerbations/year	4.12±2.3	1.1±0.1	-

Note: data are presented as M ± SD or n (%)

Patients in the main group smoked 10 people (50%), the smoking index was 14.3±3.5 packs/years, smoking experience was 17.2±3.8 years; 10 people (50%) did not smoke. All patients (100%) complained of increased shortness of breath, 12 people. (60.0%) - for cough

with an increase in sputum volume. 10 patients (50.0%) were exposed to adverse effects of industrial pollutants (prolonged inhalation of chlorine, gasoline, phenols, dust, fertilizers) and cold working conditions at the workplace. Patients with COPD had concomitant diseases: ENT organs – 5 people. (25.0%); kidneys (urolithiasis, kidney cysts) – 1 person. (5.0%); cardiovascular system, incl . coronary heart disease (CHD) – 10 people. (50.0%), arterial hypertension (AH) - 4 people. (20.0%).

Control group (CG) – 25 patients with CNB. Of these, 5 (20.0%) were men, 20 (80.0%) were women. The age of the patients ranged from 21 to 69 years, on average 50.3±2.6 years. The duration of the patients' illness was 4.7±1.4 years. The average smoking experience was 6.2±3.6 years, the smoking index was 3.4±2.9 packs/years. Patients complained of increased shortness of breath - 20 people. (80.0%), for cough with an increase in sputum volume - 19 people. (76.0%). The number of patients who were exposed to adverse effects of industrial pollutants (prolonged inhalation inhalation) was 5 people (20.0%). The patients had concomitant diseases: ENT organs – 7 people. (28.0%); diabetes mellitus type II – 2 people. (8.0%); autoimmune thyroiditis – 1 person. (4.0%); kidney diseases (urolithiasis, kidney cysts) – 2 people. (8.0%); diseases of the cardiovascular system, incl . IHD – 10 people. (40.0%), AG - 3 people. (12.0%).

There was a statistically significant predominance of disease duration in patients of the main group with COPD, which amounted to 14.7±4.5 years ($p < 0.05$), smoking experience - 17.2±3.8 years ($p < 0.05$), pack/year index - 14.3±3.5 ($p < 0.05$), as well as the frequency of exacerbations of the underlying disease - 5.12±2.3 times. The results of a comprehensive study of external respiration function are presented in Table 2.

Statistically significant dynamics of the main indicators characterizing lung ventilation in the CG compared to the CG was revealed. Severe obstructive disorders were identified in OG patients . This was manifested by a decrease in FEV_1 to 43.5±5.12% of the predicted value. Patients in the CG had normal group average values of FEV_1 up to 93.5±3.2%. In patients in the OG there was also a decrease in the FEV_1 / FVC ratio to 51.0 ± 3.5% of the predicted value, which corresponded to a severe course of the disease according to the GOLD classification , and in the CG this ratio was normal and amounted to 79.8 ± 1.6 % of predicted ($p < 0.001$).

Spirometry indicators reflected the increase in irreversible bronchial obstruction as the duration and severity of the disease increased. In patients with COPD, there was a significant decrease in the $MOS_{75\ indicator}$ - to 17.1±2.8% of the predicted value in the OG and to 62.6±6.2% of the predicted value in the CG ($p < 0.001$). There was also a decrease in MOS_{50} - to 19.5±3.9% of the expected value in the OG ($p < 0.001$ compared to the CG), MOS_{25} - to 28.5±6.3% of the expected value in the OG ($p < 0.001$ compared to the CG). compared to CG). An increase in bronchial resistance (BR) in the OG was detected to 197.7±0.2% of the expected value compared to the CG - up to 81.3±0.9 ($p < 0.001$). Data indicate the presence of irreversible bronchial obstruction in patients with severe COPD .

Table 2 Results of spirometry, body plethysmography and studies of lung diffusion capacity in patients with COPD

Options	OG, n =20	CG, n= 25	p_1
FEV_1 , % of debt .	43.5±5.12	93.5±3.2	<0.001
FEV_1 /FVC, % of expected .	51.0±3.5	79.8±1.6	<0.001

MOS $_{25}$, % of debt .	28.5±6.3	92.9±4.6	<0.001
MOS $_{50}$, % of debt .	19.5±3.9	77.4±4.9	<0.001
MOS $_{75}$, % of debt .	17.1±2.8	62.6±6.2	<0.001
SOS2575, % of debt .	20.4±3.9	80.9±5.7	<0.001
BStotal , % of debt .	197.7±0.2	81.3±0.9	<0.001
OOL, % of debt .	184.7±1.3	137.2±0.7	<0.001
OOL/OEL, % of debt .	145.4±0.8	109.8 ±4.3	<0.001
DSL/ AO , % of debt .	60.4±4.2	81.8±6.9	<0.05

Notes: FEV1 - post-bronchodilation forced expiratory volume in 1 second, FEV $_1$ /FVC - post-bronchodilation ratio of forced expiratory volume in 1 second to forced vital capacity of the lungs, BStotal , BSvd , BSvyd - total bronchial resistance, on inhalation and exhalation , ROL – residual lung volume, ROL/OEL – ratio of residual volume to total lung capacity, Evd./OEL – ratio of inspiratory capacity to total lung capacity, DSL – diffusion capacity of the lungs

It was found that with the progression of COPD in the MG, the residual volume (VR) significantly increased - up to 184.7 ± 1.3% of the expected value and the ratio of the residual volume to total lung capacity (RVL/TLC) - up to 145.4 ± 0.8% from what should be compared to the CG - to 137.2±0.7% and 109.8±4.3%, respectively (p<0.001). An increase in the ratio of OO, TB/TEL (1.3 times compared to normal values) indicates the presence of moderate signs of pulmonary emphysema and gas exchange disorders in patients with COPD. An increase in the BStotal indicator in patients in the MG compared to the CG . up to 197.7±0.2% indicates the presence of expiratory dyspnea. The severity of shortness of breath in patients in the group was characterized by an MRC indicator of 4.2 ± 0.4 points, which was higher than in patients in the control group of 1.3 ± 0.4 points (p < 0.05). In severe COPD, there was no increase in the diffusion capacity of the lungs (DLCA), amounting to 60.4 ± 4.2% of the expected value , which may be due to the preservation of the number of functioning alveoli and the total surface of the functioning lung tissue. However, the level of DLSO in patients in the group corresponded to moderate disturbances in gas exchange due to the presence of pulmonary emphysema.

To determine the degree of respiratory failure, a study of the gas composition of capillary blood (PaO $_2$, PaCO $_2$) and pulse oximetry (SaO $_2$) was carried out. At the same time, the level of metabolites (lactate) and acid-base status (ALS) were recorded . The results are presented in Table 3.

In patients suffering from COPD, a decrease in arterial blood saturation was detected by 4.7% - to 91.1 ± 1.3% in the CG (p < 0.01 compared with the CG - to 95.6 ± 0.3%).

Table 3 Gas composition of capillary blood, saturation, lactate level

Options	OG, n = 24	KG, n=21	R
SaO2 , %	91.1±1.3	95.6±0.3	<0.01
pH	7.34±0.01	7.41±0.001	<0.001
PaCO $_2$, mm Hg. Art.	39.6±1.5	36.0±0.9	<0.05
PaO2 , mm Hg . Art.	62.1±2.8	72.3±1.4	<0.05
Lactate, mmol/l	2.46±0.3	1.5±0.13	<0.05

A significant (p <0.05 compared to CG1) increase in arterial blood lactate to 2.46±0.3 mmol /l was established, which indicates pronounced signs of lactic acidosis in patients with

COPD from the MG. Against this background, normal levels of $PaCO_2$ indicators were observed - 39.6 ± 1.5 mm Hg. Art. and PaO_2 - 62.1±2.8 mm Hg. Art. ($p < 0.05$ compared with CG). This indicates the initial signs of chronic respiratory failure, which manifests itself mainly during physical activity or walking. Thus, with the progression of COPD, there is a tendency for patients with severe COPD to develop moderate hypoxemia and respiratory acidosis in the absence of manifestations of respiratory failure at rest.

As the disease progresses in patients with COPD, along with the development of cardiorespiratory disorders, there is a gradual decrease in exercise tolerance (ETT). This is manifested by a decrease in the distance in the 6-minute walk test by 44.5% and 17.2%, respectively. Indicators of physical fitness in patients with COPD are shown in Table 4. The distance covered in patients with COPD in the 6-minute walk test was 60.7±0.6% of the predicted value, which indicated a decrease in exercise tolerance and the development of mobility limitations in patients from the OG , and in 10 patients of them (50.0%) the third disability group was established.

Table 4 Indicators of exercise tolerance

Load test indicators	OG, n =20	CG, n =25	R
SBP, mm Hg .	137.2±1.2	130.3±0.8	< 0.05
DBP, mm Hg .	84.9±0.7	81.7±0.9	<0.01
Heart rate, beats per minute	105.1±1.2	81.4±0.7	<0.001
Walking distance, % of duty .	60.7±0.6	109.9±1.7	-

Indicators of blood pressure and heart rate in the CG, measured 5 minutes after the stress tests, did not exceed normal values, but were significantly higher compared to the CG ($p < 0.05$), which emphasizes the formation of moderate limitations in life activity in patients with COPD.

When conducting psychological expert -rehabilitation diagnostics, we assessed the quality of life of patients in the main and control groups (Table 5). It was found that in patients with COPD from the MG there was a significant decrease in IPF - up to 55.7±0.8 % ($p >0.05$ compared to the CG) and a decrease in IPPI - up to 38.2±0.8 % ($p <0.001$ compared with CG). When analyzing integral indicators of quality of life in the main group, a significant decrease in the physical and slight decrease in the mental components of the quality of life was established.

Table 5 Integral indicators of quality of life in patients

Integral indicators	OG, n =20	CG, n =25	R
FA, %	70.0±1.2	40.0±0.8	<0.001
RF, %	14.3±1.4	25.0±2.5	<0.01
HP, %	64.3±0.6	66.7±4.2	-
JS, %	65.0±0.6	65.8±1.2	-
SA, %	39.3±3.3	37.5±0.7	-
RE, %	42.9±2.0	66.7±3.3	<0.001
PV, %	56.5±2.0	56.2±0.5	-
IPFZ, %	38.2±0.8	54.6±0.7	<0.001

IPPV, %	55.7±0.8	55.0±0.4	-

Note: FA - indicator of physical activity , RF - the role of physical problems in limiting life activity, OH - general perception of health , VC - vitality , SA - social activity , RE - the role of emotional problems , MH - mental health , IPF - integral indicator of physical health , IPPI - an integral indicator of mental health

Patients from the MG and CG had a low RF rate - up to 14.3±1.4 % and 25.0±2.5 %, respectively, and this figure was significantly lower in patients with COPD from the CG ($p < 0.01$ compared to CG). A decrease in ER was noted in patients from the MG and CG , but the value of this indicator was significantly lower in patients with COPD from the MG ($p < 0.001$ compared to the CG). The PA indicator was significantly lower in patients with COPD from the MG ($p < 0.001$ compared to the CG), which is due to the initial level of disability in this category of patients.

Discussion. Comorbid cardiovascular disorders were studied , including pulmonary hypertension, which affects the quality of life of patients with COPD. It has been established that in patients with COPD the following prevail: severe course of the disease, expiratory shortness of breath, irreversible bronchial obstruction, emphysema of the respiratory tract, which is accompanied by chronic respiratory failure. After 14.8±4.5 years from the onset of the disease, signs of pulmonary hypertension appear in patients with COPD, the average pressure in the pulmonary artery increases to 32.1±1.2 mm or more Hg , which is accompanied by moderate disturbances in gas exchange. As the disease progresses (the number of exacerbations per year was 5.12±2.3 times), patients with COPD experience a gradual decrease in the parameters of exercise tolerance and quality of life. Thus, when analyzing the integral indicators of quality of life in the main group, a significant decrease to 55.7±0.8% in the physical and up to 38.2±0.8% in the mental components of the quality of life was established. The distance covered in the 6-minute walk test in patients with COPD was 60.7±0.6% of the expected distance , which was the basis for establishing moderate mobility restrictions in patients with COPD and caused disability in about 50% of patients with COPD (it was established 3 disability group).

Conclusions:

In patients with severe exacerbation of COPD, an increase in leukocytes was found to $12.9±3.6*10^{9}$ cells/l, ESR to 15.2±3.3 mm/h, C-reactive protein to 6.3±2.1 g/l, which, along with moderate hypercholesterolemia (cholesterol levels above 6.5 mmol /l), determined the presence of an active inflammatory process both in the respiratory tract and in the vascular component and were predictors of the development of atherosclerosis of the coronary arteries and pulmonary arterial hypertension.

Based on the results of a comprehensive study of the function of external respiration, as well as hemodynamic parameters of the pulmonary circulation, the presence of pulmonary arterial hypertension was established in patients with severe COPD against the background of irreversible bronchial obstruction, expiratory dyspnea, and emphysema.

As the disease progresses in patients with COPD, there is a gradual decrease in exercise tolerance parameters. Thus, the distance covered in the 6-minute walk test in patients with COPD was 60.7±0.6% of the expected distance , which was the basis for establishing moderate mobility restrictions in patients with COPD and caused disability about 50% of patients

(disability group 3) . When analyzing the integral indicators of the quality of life of patients with COPD, a significant decrease in the physical and slight decrease in the mental components of the quality of life was found.

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