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L.D. Olesova, V.A. Makarova, M.A. Varlamova, S.I. Sofronova, E.N. Afanasyeva, A.N. Romanova

POST-COVID STATE OF EXTERNAL RESPIRATORY FUNCTION IN HOSPITALIZED AND OUTPATIENT PATIENTS

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A one-time medical and biological examination of the health status of 161 residents of Yakutsk aged 20 to 72 years who recovered from COVID-19 3-12 months ago during the first wave of the pandemic was carried out. Changes in lung function were detected in 29.5% of 139 patients who underwent spirometry. Among them, 7.2% of the surveyed revealed extremely severe changes. The appearance of symptoms and disturbances in the function of external respiration in the post-covid period did not have significant differences in hospitalized and outpatients, and were not associated with the post-covid period, the severity of lung damage in the acute period of the disease, smoking, and the presence of chronic diseases of the respiratory system. The obstructive and restrictive type of disorder was more often observed in women treated on an outpatient basis, which indicates a protracted recovery that requires the same rehabilitation measures that are carried out for hospitalized patients in order to eliminate multiple organ post-COVID complications.

Keywords: COVID-19, pneumonia, spirometry, external respiration.

Material and research methods. The study involved a total of 161 people who had been ill for 3-12 months. ago with a new coronovirus infection - COVID-19 at the age of 20 to 72 years. Of these, women - 101 (62.7%), men - 60 (37.3%). The average age of all examined was Me=51.1 years (41.5; 61.5), men – Me=50.9 years (40.0; 61.7), women – Me=53.7 years (42.0; 61.5).

According to the protocol of computed tomography (CT) from the anamnesis in the acute period of the disease, the subjects were divided according to the severity of lung damage into 5 groups: CT0 (zero) - no signs of viral pneumonia; CT1 (mild) - the presence of a ground-glass compaction zone, involvement of less than 25% of the lung volume; CT2 (moderate) - damage to the lungs from 25 to 50%; CT3 (severe) - damage to the lungs from 50 to 75%; CT4 (critical) - lung damage more than 75% (Table 2). According to the post-COVID period, they are divided into 4 groups: up to 3, up to 6, up to 9, up to 12 months ago (Table 1).

The study used a questionnaire that included questions about the presence of chronic diseases, complaints after suffering from COVID-19, and a questionnaire on the Hospital Anxiety and Depression Scale (HADS). The biomedical study included an appointment with a cardiologist, neurologist, rheumatologist, therapist, determination of hematological, biochemical and immunological parameters, ECG, anthropometry, spirometry. Spirometry was performed in 139 participants of the study using the diagnostic system "Valenta": 88 women (63.3%), the average age was Me - 50.9 (42.0; 61.0) and 51 men (36.7%), the average age - Me - 50.0 (40.0; 61.0). 22 participants were excluded due to contraindications and rejection of the study.

Yakut Scientific Center for Complex Medical Problems: **OLESOVA Lyubov Dygynovna** – Ph.D., leading researcher of the laboratories, oles59@mail.ru; **MAKAROVA Victoria Alekseevna** – therapist; **VARLAMOVA Maria Alekseevna** – neurologist; **SOFRONOVA Sargylana Ivanovna** – Candidate of Medical Sciences, head of the department; **AFANASYEVA Elena Nikolaevna** – nurse of the Clinic of YSC CMP; **ROMANOVA Anna Nikolaevna** – Doctor of Medical Sciences, Director

Table1

Groups according to the degree of lung damage (CT), abs. number / %

Groups	The severity of lung injury					Total
	CT0	CT 1	CT 2	CT 3	CT 4	
Men	7/13.7	15/29.4	12/23.5	15/29.4	2/3.9	51/100
Women	13/14.6	39/43.8	27/30.3	7/7.9	3/3.6	89/100

Note. Pearson chi-squared =11.908, df=4, p=0.018.

The function of external respiration was assessed in terms of VC, FVC, FEV1, Tiffno index (TI).

VC (vital capacity) - the maximum amount of air that can be exhaled after a maximum breath. FVC (forced vital capacity) is the volume of air that can be exhaled after a maximum inhalation at the maximum possible rate. FEV1 (forced expiratory volume in the first second) - the volume of air that the subject can exhale in the first second of maximum forced exhalation. Tiffno index - the ratio of FEV1 to VC, expressed in%. IT decreases with obstructive syndrome. The study was approved by the local committee on biomedical ethics at the Federal State Budgetary Scientific Institution YSC CMP No. 52 dated March 24, 2021 and was conducted subject to the voluntary informed consent of the participants.

Statistical processing was performed using the IBM SPSS Statistic 23 software package. The normality of the distribution of quantitative indicators was determined using the Kolmogorov-Smirnov test. The descriptive analysis values are presented as the median (Me) and the 25th and 75th quartiles (Q1-Q3) when the distribution is not normal. Nominal data are presented as absolute values and percentages, and their comparison in contingency tables was carried out using Pearson's chi-square. Correlation analysis was performed according to the method of Pearson and Spearman, where r is the correlation coefficient, p is the significance of the result. When testing statistical hypotheses, the critical level of significance (p) was taken at p<0.05.

Introduction. As time goes on, it becomes clear that one of the major problems associated with the SARS-CoV-2 pandemic is its long-term consequences. Recent studies have shown that those who have recovered from COVID-19 may experience certain symptoms that persist from 2 months to a year [7,12,14]. Symptoms persisting for more than 3 months are described as "post-COVID syndrome" [3]. In addition to problems of general well-being (fatigue, decreased performance, etc.), symptoms associated with the development of pathology of the respiratory and cardiovascular systems, gastrointestinal tract, and other organs appear, neurological, psychoemotional symptoms appear [21], i.e. . the novel coronavirus SARS-COV-2 is responsible for multiple organ syndrome [19].

At the same time, information often began to appear that post-COVID symptoms appear not only in patients with a severe course of the disease, but in people who have recovered from COVID-19 of mild and moderate severity [18,9]. The main severe manifestation of SARS-COV-2 infection is respiratory distress syndrome, the frequent development of extensive bilateral interstitial damage to the lung tissue, accompanied by thrombovasculitis of the microvasculature [22], which in turn is associated with a very high expression of the ACE2 protein receptor (angiotensin-converting enzyme-2) in the lung tissue, through which the SARS-CoV-2 virus penetrates into the cells of the alveolar epithelium, and replicates in the cytoplasm of cells [15]. In the future, continuing respiratory failure causes the development of hypoxia. In addition, damage to the alveolar epithelium and endothelium of the pulmonary vessels can cause the growth of fibroblasts, which is a factor in the formation of lung tissue fibrosis during the recovery period. Especially in men, smokers and the elderly [8].

Table2

Groups of men and women by post-COVID period, abs. number / %

Groups	Post-covid period, months				Total
	3	6	9	12	
Men	5/9.8	18/35.3	18/35.3	10/19.6	51/100
Women	9/10.2	40/45.5	28/31.8	11/12.5	88/100

Long-term hypoxia negatively affects the central nervous system and can cause anxiety and depressive disorders [2], increased fatigue, decreased performance, brain encephalopathy, stroke, muscle weakness, neuropathy (damage to the peripheral nerves of the extremities) with the development of motor paresis and paralysis, movement disorders, shortness of breath [23].

In this regard, in the absence of specific post-COVID symptoms and certain periods of their manifestation, which complicate diagnosis and treatment, the study of the long-term effects of COVID-19 on the respiratory system, regardless of the severity of the disease, is necessary to prevent severe complications and rehabilitate patients to maintain quality of life.

The aim of the study was a comparative assessment of symptoms and lung function after COVID-19 in hospitalized and non-hospitalized patients living in Yakutsk. Results and discussion. Earlier, in our published work, it was shown that the degree of lung damage (CT) in the acute period of COVID-19 disease was directly dependent on factors such as age (r=0.307; p<0.000), gender (r=-0.238; p<0.002), BMI (r=0.286; p<0.000) [5]. In addition, there was a dependence on the presence of arterial hypertension (r=0.373; p<0.000) and comorbidity (r=0.292; p<0.000).

The relationship between the severity of lung damage by the new SARS-CoV-2 coronavirus and gender is shown in Table 2. Among the subjects who underwent spirometry, mild and moderate lung tissue damage (CT1 and CT2) is more than 2 times more common in women, and vice versa, the incidence severe lung damage from 50 to 75% (CT3) was 2 times more common in men. There were only 6 people (3.7%) examined with CT4: 3 men and 3 women, since the survival rate of patients with critical lung disease (more than 75%) is extremely low.

Of the total number of those examined (n=161), 21 people had chronic respiratory diseases, which amounted to 13.46%. In them, 4 people (2.56%) suffer from bronchial asthma and 17 people (10.8%) suffer from chronic bronchitis. At the time of the examination, 13 people (8.33%) had chronic bronchitis in remission, and a prolonged exacerbation of bronchitis was observed in 4 people (2.56%). Pathology of the respiratory organs in the surveyed takes the 3rd place after diseases of the cardiovascular system (59.6%) and endocrine diseases (30.5%). Table 3 gives the frequency of pathologies in hospitalized and outpatient patients.

Frequent post-covid symptoms were sleep disturbance (48.2%), fatigue (43%), hair loss (33.1%), decreased performance (32.7%), shortness of breath (28.2%), weakness (26.6%) and sweating (25.5%). Symptoms such as shortness of breath, heaviness in the chest, a lump in the throat were indicated by 12.2%, 10.3% and 8.9%, respectively. Table 3 shows the prevalence of post-COVID symptoms in the hospitalized and outpatient groups. Post-covid symptoms were not only in patients with severe lung disease (hospitalized patients), but also in those who had mild to moderate COVID-19 and were treated on an outpatient basis (Table 4). There were 82 hospitalized patients (50.9%), outpatients - 79 (49.1%). One study showed that among hospitalized patients, the prevalence of ongoing symptoms ranged from 32.6% to 87%. [7].

In another study, among non-hospitalized patients, 37% complained of fatigue, 30% of cognitive impairment [11]. In a study including 433 non-hospitalized patients, 9.6 months after infection with SARS-CoV-2, signs of subclinical multiorgan damage associated with pulmonary, cardiac, thrombotic and renal functions were revealed. There were no signs of structural brain damage, neurocognitive impairments, or deterioration in the quality of life [17].

According to spirometry among the study participants, violations of the function of external respiration were revealed. Decreased value of VC, FVC, OVF1 was observed both in hospitalized and outpatients, and more often in women (Table 5).

The Tiffno index (FEV1 / VC, %) as a sensitive index of the presence or absence of deterioration in airway patency showed that cases of low values were detected in 24 people (17.3%): in 8 men, mostly hospitalized and 16 women, of which 7 were treated on an outpatient basis (Table 4). There were no significant differences in the frequency of ventilatory dysfunction between hospitalized and outpatients (p=0.248). It should be noted that men treated on an outpatient basis had fewer violations of respiratory function than women. Our data do not contradict the literature. X-ray studies of those who recovered after 3 months revealed pulmonary anomalies in 71% and functional disorders in 25%, despite the fact that only less than 10% had severe pneumonia, i.e. lung function abnormalities did not depend on the severity of the disease [16]. Lung function impairment among COVID-19 survivors 1 year after discharge is widespread, and persistent impairment of lung function has been

Table3

Frequency of pathologies among study participants, %

		1 group	2 group	Total	X^2 Pearson	df	p
Diseases respiratory system	Да	13/15.9	8/10.1	21/13.0	1.920	3	0.589
	Нет	69/84.1	71/89.9	140/87.0			
Diseases of the cardiovascular system	Да	53/64.6	32/40.5	85/52.8	15.106	1	**0.000**
	Нет	29/35.4	47/54.7.7	76/47.2			
Type II diabetes	Да	13/15.9	7/8.9	20/12.4	2.078	1	0.149
	Нет	69/84.1	72/91.1	141/87.6			
Obesity	Да	16/19.5	14/17.7	30/18.6	0.358	1	0.549
	Нет	66/80.5	65/82.3	131/81.4			
Anxiety	Да	18/22.2	20/25.7	38/	0.253	1	0.615
	Нет	63/77.8	58/74.4	121			
Depression	Да	22/26.8	17/21.5	39/24.2	0.620	1	0.431
	Нет	6073.2	62/78.5	122/75.8			

Note: 1 - hospitalised; 2-outpatients

Table4

Occurrence of post-convulsive symptoms in patients, units/%

gender	Groups	Symptoms				
		1	2	3	4	5
Men	hospitalized	12/61.9	14/73.7	12/66.7	5/100	9/64.3
	ambulatoryses	8/38.1	5/26.3	6/33.3	0/0.0	5/35.7
Women	hospitalized	27/46.6	12/38.7	21/42	6/42.8	13/43.3
	ambulatoryses	31/53.4	19/61.3	29/58	8/57.2	17/56.7

Note: 1-sleep disturbance, 2-decreased performance, 3-fatigue, 4 - labored breathing, 5 - shortness of breath.

Table5

The frequency of reduced values of spirometry, units/%

gender	Groups	VC, <80%	FVC, <80%	FEV1, <80%	FEV1/VC, <70%
Men	hospitalized	20/60.6	17/63.0	9/81.8	7/87.5
	ambulatoryses	13/39.4	10/37.0	2/18.2	1/12.5
Women	hospitalized	32/45.7	25/41.0	17/56.7	9/56.3
	ambulatoryses	38/54.3	36/59.0	13/43.3	7/43.7

Note: Pearson's chi-square=4.128, df=3, p=0.248.

Table6

The frequency of the decrease in respiratory function indicators at different time intervals, units /%

Indicators Functions of external respiration	Post-covid period, months				Total
	3	6	9	12	
VC, <80%	10/9.8	41/40.2	33/32.4	18/17.6	102/100
FVC, <80%	11/12.5	34/38.6	30/34.1	13/14.8	88/100
FEV1, <80%	4/8.7	23/50.0	12/26.1	7/15.2	46/100
FEV1/VC %,<70%	2/8.3	11/45.8	6/25.0	5/20.8	24/100

found in about 40% of survivors. The authors suggest that lung damage may be associated with pulmonary fibrosis [13].

The frequency of decrease in indicators of the function of external respiration was not associated with the post-COVID period (Table 6).

The decrease in the Tiffno index is mild, moderate and significant. Table 5 shows the incidence of severity of airway disorders according to the Tiffno coefficient in hospitalized and outpatient patients. There was a significant difference in the frequency of the decrease in this index among men: there was no moderate or significant decrease in IT in those treated on an outpatient basis.

The obstructive type of violation of the respiratory function (decrease in FEV1 and Tiffno index), due to the deterioration of the airway patency at any level, was in 20 people (14.4%), the restrictive type of violation of the respiratory function (decrease in FEV1, VC, FVC), due to a decrease in the functional tissue of the lungs, 37 people (26.6%) had Mixed type of violation of respiratory function, when all the listed indicators are lowered, was detected in 14 people (10.1%). In the group of men treated on an outpatient basis, obstructive and mixed disorders of respiratory function were not detected. Among persons with respiratory problems, non-smokers were 3.7-5.7% more (Table 8).

Thus, women treated on an outpatient basis had a moderate and significant decrease in airway patency. Also among women there are all types of violations of respiratory function. This is probably due to the fact that recovery in women is slow, and outpatients did not receive proper treatment and rehabilitation. It should be noted that CT of the lungs in dynamics is necessary for accurate diagnosis of violations of respiratory function.

Indications for obstruction were more common in patients with diseases of the endocrine and cardiovascular systems. In the group with a significant decrease in airway patency, only one person had a history of respiratory system pathology - chronic bronchitis with prolonged exacerbation, five had endocrine pathology (obesity, diabetes, hypothyroidism, goiter), two had coronary artery disease, hypertension, one had anxiety, the other - depression.

The lowest percentage of VC was found in patients with clinically pronounced depression. There is a significant decrease in the median VC in people with depression. This is also evidenced by a direct correlation between VC impairment and depression (r=0.257; p<0.002).

Table7

The severity of pulmonary ventilation disorders according to the Tiffno coefficient, units /%

gender	Groups hospitalized	FEV1/VC, (according to R.F. Kliment et al.)				Total
		1	2	3	4	
Men	ambulatoryses	19/63.3	5/16.7	3/10.0	3/10.0	30/100
	hospitalized	19/95.0	1/5.0	0/0.0	0/0.0	20/100
Women	ambulatoryses	28/71.8	8/20.5	0/0.0	3/7.7	39/100
	hospitalized	38/80.9	4/8.5	3/6.4	2/4.3	47/100

Pearson's chi-square =9.215, df=3, p=0.027. 1 - norm (M.: 84.2-109.6%, F-78.2 -113.3%); 2 - slight decrease (M<71.5%, W<73.1%); 3 - moderate decrease (M<65.1%, W<66.7%); 4 - significant decrease (M<52.4%, W<54%).

Table8

Types of violations of respiratory function in men and women, units /%

Type of violation of respiratory function, unit/%	Men			Women			Smoking	
	1	2	Total	1	2	Total	Yes	Not
obstructive	5/9.8	0/0.0	5/9.8	8/9.1	7/8.0	15/17.1	3/15	17/85
restrictive	7/13.7	2/1.4	9/15.1	16/18.2	12/13.6	28/31.8	8/21.6	29/78.4
Mixed	2/1.4	0/0.0	2/1.4	7/8.0	5/5.7	12/13.7	3/21.4	11/78.6

Note: 1 - hospitalised; 2-outpatients.

In our earlier published work, data on the frequency of anxiety and depressive disorders in study participants (161 people) are presented. More than 24% of the examined patients had anxiety and depressive disorders, regardless of the post-COVID period and the severity of lung damage. [6].

Frequent symptoms such as sleep disturbance, fatigue, decreased performance, especially in women, confirm the literature data that long-term neuropsychiatric disorders are an important part of the multisystem post-COVID syndrome [4] and the role of hypoxia in the mechanism of development of these symptoms is obvious, along with other factors, such as inflammatory pathogenesis (encephalopathy, myocarditis, pneumonitis); the immunological mechanism of development (consequences of the release of cytokines, activation of humoral and cellular immunity, the formation of circulating immune complexes) and impaired blood rheology (thromboembolic complications) [1,20]. Chaolin Huang et al's analysis of the 6-month follow-up of COVID-19 showed that the risk of anxiety or depression as an important psychological complication and impairment of lung diffusivity in patients treated in hospitals was higher in patients with more severe disease [10]. However, we did not find a significant difference in the incidence of these ailments between groups of inpatients and outpatients.

In the rehabilitation of patients with impaired lung function, especially for those with depressive disorder, osteopathy, massage, acupuncture, hirudotherapy, infusion therapy, the introduction of nootropic drugs, absorbable therapy, detoxification, the use of multivitamins and mineral complexes, the appointment of biostimulants will be useful for recovery [1].

Conclusion. In this study, we found that the post-COVID period in hospitalized and outpatient COVID-19 patients, the onset of symptoms and respiratory dysfunction had no significant differences and was not associated with the post-COVID period, the severity of lung damage in the acute period of the disease, smoking and with chronic diseases of the respiratory system. The obstructive and restrictive type of disorder is more common in women treated on an outpatient basis, which indicates a protracted recovery of the female body from post-COVID complications and requires the same rehabilitation measures that are now being carried out for patients treated for COVID-19 in hospitals.

Further long-term studies of long-term lung dysfunction associated with SARS-CoV-2 infection are needed to understand the underlying mechanisms and the con-

sequences of long-term lung dysfunction on other organs and body systems.

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