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EVALUATION OF FUNCTIONAL STATE OF THE CARDIORESPIRATORY SYSTEM IN PATIENTS AFTER THE COVID-19 PNEUMONIA DURING MEDICAL REHABILITATION AT THE RESORT

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Key words: medical rehabilitation, COVID-19 pneumonia, resort, physical performance, cardiorespiratory system.

Annotation. The purpose of this study is to evaluate the efficiency of medical rehabilitation in resort conditions of patients, who were affected by the COVID-19 pneumonia, through the assessment of functional state of the cardiorespiratory system. Rehabilitation measures were conducted on the base of the S.M. Kirov Sanatorium of the FSBI NCFSCC of the FMBA of Russia located in Pyatigorsk for 29 patients affected by the COVID-19 pneumonia. The research program included two-time (at the beginning and at the end of treatment) examination of heart rhythm variability (HRV), degree of dyspnea according to mMRC scale, motor activity in the 6-minute walking test, determining oxygen saturation in blood by the pulse oxymetry method. As a result of two-week complex spa treatment, patients affected by the COVID-19 pneumonia have shown a decrease of vegetative imbalance, an increase of tolerance of cardiorespiratory system to physical loads.

Introduction. In 2020 and currently the object of interest of the healthcare system and the world society is the COVID-19 pandemic, which took over almost all world's countries [1, 2, 3]. In the Russian Federation, the first COVID-19 incidence rate was registered in March of 2020. The use of quarantine measures in many world countries, including Russia, caused the slowdown of coronavirus infection's incidence tempo since late March, but a decrease of cases of infected and

deceased was registered only in August-September according to the website "stopcoronavirus.rf". At the end of September of 2020, there was a rapid increase of incidence rate, and by the middle of October the number of SARS-CoV-2 cases exceeded the peak value, which was registered earlier in the first decade of May.

The most common clinical (nosological) manifestation of the new coronavirus infection is an acute respiratory disease of the upper airways, provided that the most patients with severe process of COVID-19 have a developing bilateral pneumonia, 3-4% of patients with pneumonia have a development of an acute respiratory distress syndrome [4, 5, 6, 7]. Approximately 10-15% of mild and moderate cases (81-82% of all infected) turn into severe ones, approximately 15-20% of severe cases become extremely severe. The SARS-CoV-2 virus affects not only lungs, but also the cardiovascular system, causing the development of myocarditis and worsening the process of given pathology (coronary heart disease (CHD), hypertonic disease etc.) After the COVID-19 infection convalescents had to endure such severe after-effects as respiratory failure, formation of pronounced astheno-neurotic and immunosuppressive syndromes, and multimorbidity [8, 9].

Results of foreign and national studies about research of epidemiological and clinical features of infection's process are used for updating and including additional information to clinical guidelines for medical rehabilitation of patients affected by the COVID-19 pneumonia [1, 10, 11]. Three pre-suggested stages of medical rehabilitation for patients affected with COVID-19, which were conducted according to the disease period including the after-treatment period, remain unchanged. The second stage of rehabilitation is conducted during the convalescence period, the durability of which depends on the severity of the disease's process during the active period, the extent area of lung tissue damage, the involvement of other organs into the pathological process and the presence of chronic diseases, which is why it can last 14 days to several months.

Medical rehabilitation of patients affected with the new COVID-19 infection is aimed at the recovery of damaged functional systems of organs and to overcome after-effects related to hypoxia, damage of external respiration and blood flow, which cause a risk of developing aggravations of cardiovascular and bronchopulmonary systems [12, 13, 14].

The purpose of the study. To evaluate the efficiency of medical rehabilitation in resort conditions of patients affected by the COVID-19 pneumonia through the assessment of functional state of the cardiorespiratory system and physical performance.

Methods and organization. Rehabilitation measures were conducted in the S.M. Kirov Sanatorium of the FSBI NCFSCC of the FMBA of Russia located in

Pyatigorsk during the Territorial State Guarantee of Free Medical Care to the Citizens of the Russian Federation throughout 14 days. After signing an informed written consent the patients were involved into the single-center cohort study. Criteria of participating into the study were patients affected by the coronavirus infection caused by the COVID-19 virus; the virus was identified by the ICD-10 (confirmed by laboratory testing) with the code U07.1. According to the data of the discharge summary from covid in-patient facility, all patients had complications in form of the virus pneumonia. Total number of examined patients was 29 (8 men and 21 women), 32 to 69 years old, who were affected by the pneumonia associated by the new coronavirus infection. Patients were sent to the second stage of medical rehabilitation not earlier than 14 days after the end of treatment in the in-patient stationary, with 2 negative results of swab tests for SARS-CoV-2 performed by using the polymerase chain reaction (PCR) method. Moreover, one of contraindications for including people for rehabilitation was the generally accepted list of diseases included in the list of contraindications for spa treatment. All epidemic-prevention measures, including gatekeeping, two-fold COVID-19 test monitoring and thermometry.

The examination program included the determination of anthropometric indicators, such as body mass, body mass index (BMI) and the two-fold (at the beginning and at the end of rehabilitation events) study of physical performance and functional state of the cardiorespiratory system. Patients were filling forms in order to assess a degree of dyspnea on the «Medical Research Council» scale (mMRC) [13]. Oxygen saturation level in blood (SpO_2) was determined by the pulse oxymetry. Tolerance to physical loads was examined using the 6-minute walking test under the pulse oxymetry control, heart rate (HR), respiratory rate (RR), blood pressure (BP) level. the 6-minute walking test was conducted in accordance with guidelines of conducting stress tests [14]. 30-meter-long track with 1-meter divisions was highlighted with colored tape and bounded with road triangles in the center of the 50-meter-long corridor. Each patient was given an oral instruction on how to perform the test. A researcher registered a distance walked by the patient in 6 minutes. Before and after the 6-minute walking test an assessment of vegetative balance was performed based on cardiointervalography (CIG) records for 5 minutes using the R.M. Bayevsky method [15]. Patients with movement limitations related to diseases of joints and blood vessels of lower extremities or with arrhythmia were not included in the test. The CIG was performed 1 hour after having a light breakfast, before taking medications and therapeutic physical factors.

Records of electrocardiopotentials were made on the “VNS-Spectre” apparatus (registration certificate № FSR2011/10309), patients were sitting during the recording, and electrodes were placed on their wrists (the 1st standard lead). The

"Neurosoft" software automatically processed results of heart rhythm variability (HRV). Indicators of variance and time, amplitude and frequency characteristics of HRV were analyzed: HR, RRNN, SDNN, MxDMn, MxRMn, RMSSD, AMo, Range (R), VBI – AMo/R, IARP – AMo/Mo, VIR, Stress Index (SI) – AMo/2R*Mo, Total Power (TP) – total power in range of frequencies of 0,003-0,4 Hz; High Frequency (HF) – in range of high frequencies of 0,15-0,4 Hz and wavelength of 2,5-6,5 s; Low Frequency (LF) – in range of low frequencies of 0,04-0,15 Hz and wavelength of 2,5-6,5 s; Very Low Frequency (VLF) – in range of very low frequencies ≤ 0,04 Hz and wavelength more than 25 s. Received values of examined indicators are presented as absolute (ms^2) and relative (%) values. Norm units of LF (norm, %) and HF (norm, %) were received by the division of LF and HF by TP. LF/HF coefficient characterizes relation of power of low-frequency oscillations of RR intervals in range of 0,04-0,15 Hz, ms^2, to power of high-frequency oscillations of RR intervals in range of 0,15-0,4 Hz, ms^2.

The set of therapeutic measures includes: a sparing training regime of motor activity – dosed walking on route of the terrenkur № 1 (forest area of Mashuk Mountain), at the beginning of therapy the route length is 1200 m, the walking tempo is slow (3-4 km/h) with 5 to 10-minute-long pauses, then the route should be elongated up to 2400-3600 m; therapeutic nutrition according to the standard diet's general version; oral administration of weak carbonate sulphate-hydrocarbonate, calcium-natrium mineral water "Slavyanovskaya" with low water mineralization level (3,2-3,8 g/l), 3-3,5 ml for 1 kg of body mass, 3 times a day, 40 minutes before meals, warm; exercise therapy (ET) for diseases of respiratory organs and organs of blood circulation; mechanotherapy (training devices) with the use of sparing method for diseases of bronchopulmonary and cardiovascular systems, 8 sessions for the therapy course; normobaric oxygenation with the use of oxygen chamber (Oxysys 4500, made by MEDICONET, Korea), 8 sessions; halotherapy in salt room, 8 sessions; "Rotokan" therapeutic inhalations, 8 sessions for the therapy course; ribcage massage, 8 sessions.

Data processing was made using non-parametric criteria of statistical analysis. In order to compare dependent variables, Wilcoxon criteria, the t-test and the two-way analysis of variance (two-way ANOVA) were used. Quantity indicators, distribution of which was different from normal, were described using median value (Me), lower and upper quartile (Q1; Q3).

Results and discussion. 29 patients affected with pneumonia associated with COVID-19, 55 (51;60) years old, received medical rehabilitation on the in-patient stage in resort conditions, 5 of them suffered from a severe form of the disease, 21 of them suffered from a moderate form of the disease. During entrance all patients

were complaining about pronounced general fatigue and fast fatigability, 13 of them were complaining about dyspnea when coming to the 5th floor, 5 of them (17,2%) noted slight cough with poor mucous sputum, 6 of them (20,6%) noted dizziness. The body mass index (BMI) of all patients was above normal, the overweight body mass was noted in 7 patients (24,1%), class I obesity – in 10 patients (34,5%), class II obesity – in 6 patients (20,7%) and class III obesity – in 6 patients (20,7%). Comorbidity was characterized by the presence of I-II degree of arterial hypertension (AH) with risks of cardiovascular complications 2-4 in 13 patients (44,8%), including 7 patients (24,1%), who also have 2nd type of diabetes, and 5 patients (17,2%), who also have chronic bronchitis. According to the ECG data, various types of moderate disorders of conduction in form of disorders of intraventricular conduction (deceleration of atrioventricular conduction and incomplete right bundle branch block) or processes of repolarization in inferior wall of left ventricular.

During evaluation of stress of adaptation processes, according to the CIG data all examined patients revealed high initial values of SI related to an increase of the amount of intervals of the same type of duration (increase in the AMo indicator), with simultaneously high indicators of VBI, indicating a predominance of sympathetic activity in regulation of cardiac activity and vegetative imbalance. Moreover, before conducting the 6-minute walking test in the initial state indicators of relation of power of low-frequency oscillations to high-frequency oscillations of durability of RR intervals (LF/HF), exceeded the standard values on average by 2-3 times, which is typical for a predominance of sympathetic suprasegmentary impact over the parasympathetic one. A difference in the LF/HF indicator was noted, according to which 10 patients were characterized with normotonia (LF/HF < 2 c.u.), 19 patients were characterized with sympathotonia (LF/HF > 2 c.u.). BMI of patients with normotonia was higher than BMI of patients with sympathotonia, and it was 40 (36,9; 44,1) c.u. and 32,5 (28,6; 34,1) c.u., p=0,0048. There were also differences in breathing frequency, oxygen saturation in blood (SpO2, %) and length of covered distance according to the data of the 6-minute walking test depending on sympathetic tonus. Change of breathing frequency (BF) depending on predominance of regulatory effect of sympathotonia or normotonia on HRV and covered distance in the 6-minute walking test was examined with the use of the two-way analysis: A – initial state before the 6-minute walking test (F=3,8, p=0,0612); B – shortly after the 6-minute walking test (F=4,7, p=0,0384), see on Fig. 1.

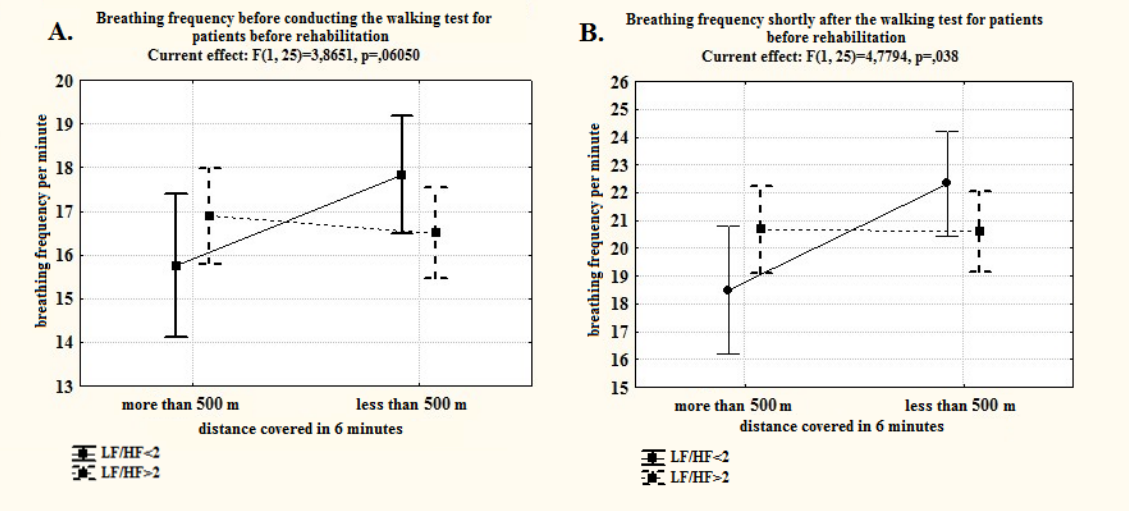

Fig.1. Breathing frequency and covered distance in the 6-minute walking test of examined patients depending on the type of vegetative regulation (normotonics – LH/HF<2, sympathotonics – LH/HF>2) before rehabilitation: A – in the initial rest state, before conducting the test, and B – after conducting the test

Breathing frequency of patients with normotonia, who walked 500 meters and more during the 6-minute walking test, was less before and shortly after the load than the breathing frequency of patients, who walked less than 500 meters, however, oxygen saturation level in blood is higher, while differences of breathing frequency and SpO_2 depending on the covered distance in the 6-minute walking test wasn't determined in patients with sympathotonia.

Data of SpO_2 level 10 minutes after the 6-minute walking test, taking the covered distance and the type of vegetative regulation into account with the use of the two-way analysis (F=4,4, p=0,0427), are presented in Fig. 2.

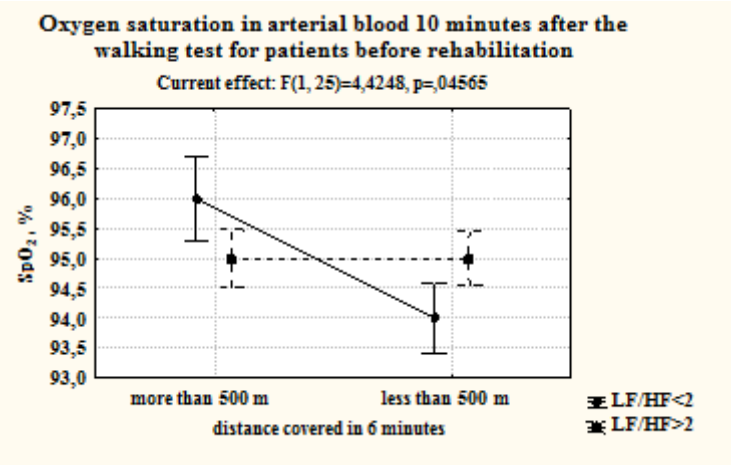

Fig. 2. Oxygen saturation in blood and the covered distance in the 6-minute walking test depending on vegetative regulation type (normotonics – LH/HF<2, sympathotonics – LH/HF>2) before rehabilitation: 10 minutes after the 6-minute walking test

Positive dynamics of indicators, which characterize functional state of the cardiorespiratory system during physical loads, are revealed in 79,3% of patients

affected with the COVID-19 pneumonia after the conducted complex therapy in resort conditions. Screening indicators of respiratory and cardiovascular systems (the walking test, HR, BF, SBP, DBP, SpO_2, %) did not significantly change, however, an increase of the covered distance in the 6-minute walking test was registered (Table 1).

Table 1

Dynamics of indicators of breathing frequency, pulse, arterial blood pressure level and level of oxygen saturation in blood in treated patients according to the data of the 6-minute walking test and cardiointervalography (n=29)

Indicators	Before rehabilitation			After rehabilitation		
	Before the 6-minute walking test	After the 6-minute walking test	10 minutes after the 6-minute walking test	Before the 6-minute walking test	After the 6-minute walking test	10 minutes after the 6-minute walking test
Distance covered in the 6-minute walking test, m	490 (458; 530)			520 (468;550)*		
Ps, min	80 (74; 87)	88 # (79; 96)	80 (75; 88)	78 (74; 84)	86# (83; 100)	81# (74; 90)
BF, min	16 (16; 18)	20# (18; 22)	18# (16; 22)	16 (16; 18)	22# (18; 23)	18# (16; 20)
SBP, mm of mercury	120 (115; 130)	140# (135; 150)	120 (110; 130)	120 (110; 130)	135# (125; 150)	120 (110; 125)
DBP, mm of mercury	80 (75; 80)	80 (70; 90)	80 (70; 85)	75 (70; 80)	80# (70; 90)	80 (70; 85)
SpO_2,%	95 (94; 96)	95 (95; 96)	95 (94; 96)	95 (94; 96)	96 (95;96)	95 (94; 96)

Note: *- p<0,001 – statistically significant differences between the distance covered in 6 minutes before and after rehabilitation; #- p<0,001 – statistically significant differences between indicators before and after the walking test, results are presented in form of median value (Me), lower and upper quartile (Q1; Q3).

Table 2

Dynamics of indicators of the variable-based spectral analysis of cardiointervalography before and after the 6-minute walking test of treated patients (n=29)

Indicators	Before rehabilitation		P-level	After rehabilitation		P-level
	Before the 6-minute walking test	After the 6-minute walking test		Before the 6-minute walking test	After the 6-minute walking test	
Time and variation characteristics						

HR, beats/min	80 (72; 89)	85 (77; 92)	0,0003	81 (74;87)	85 (80;93)	0,0002
RRNN, ms	745 (675; 777)	702 (653; 784)	0,0008	739 (688; 810)	707 (642; 748)	0,00004
SDNN, мс	21,5 (15; 30)	21,4 (14,7; 25)	-	20 (14,7; 25,5)	17,3 (13,7; 27)	0,009
MxDMn, мс	100 (74; 136)	96 (64; 114)	-	90 (68; 116)	74 (62; 122)	-
RMSSD	11,2 (7,9; 15)	12,6 (8,1; 16,3)	-	13,8 (8,1; 16,3)	8,8 (5; 11,2)	-
CV, %	2,8 (2,2;4)	2,7 (2,1; 3,7)	-	2,4 (2; 3,4)	2,4 (1,9; 3,6)	-
Mo	0,73 (0,68; 0,78)	0,73 (0,68; 0,78)	-	0,73 (0,68; 0,83)	0,73 (0,63; 0,78)	
AMo, c.u.	71,5 (55;81)	63,4 (52,6;82,8)	0,003	67 (61,2; 76)	66 (54; 75)	0,0008
VBI, c.u.	735 (403;1092)	654 (518;1131)	-	709 (514; 1221)	841 (452; 1202)	-
IARP	92,4 (73;112,6)	85,9 (78,6;114,2)	-	96 (79;106)	91,2 (69;112)	-
VIR	12,9 (9,2;21,2)	14,1 (11,9;23,9)	-	13,8 (11,8; 21)	18,6 (11,3; 22,2)	-
IC	0,65 (0,44;1)	0,6 (0,34;0,9)	-	0,65 (0,43; 1,1)	0,56 (0,39; 0,92)	-
SI, c.u..	471 (275;761)	471 (365;838)	-	456 (365; 892)	594 (318; 829)	-
Amplitude and frequency characteristics of spectral analysis						
TR, ms^2	424 (208;722)	264 (145;508)	0,02	375 (210;545)	199 (146;517)	-
VLF, ms^2	186 (109;373)	151 (78,5;276)	-	217 (108; 329)	143 (83; 282)	-
LF, ms^2	112 (53,4;191)	80,7 (32,7;153)	0,02	78 (54; 174)	50 (36; 109)	0,06
HF, ms^2	43 (12;124)	17,5 (10;43)	0,0002	30,4 (12; 47,6)	18,8 (5,2; 35,2)	0,009
VLF, %	61 (49;69,6)	62,6 (52,7;74,5)	-	60 (47,8; 70)	64 (52; 72)	-
LF,%	26 (19;37,7)	26 (20,2;35,2)	-	28 (21; 33)	27 (16,7; 34,7)	-
HF,%	10,7 (4,4;16,3)	6,8 (3,7;15,6)	-	6,7 (4,4; 14,3)	5,8 (3,7; 11)	0,03
LF norm, %	75 (60,6;81)	79,3 (65,3;87)	0,08	77 (63; 85)	82 (66; 91)	0,009
HF norm, %	25 (19;39,4)	20,7 (13;34,7)	0,08	22,7 (14,6; 37)	18,1 (9,3; 34)	0,009
LF/HF	3 (1,4;4,2)	3,7 (1,4;6,4)	-	2,8 (1,6; 5,4)	4,5 (1,7; 9,8)	0,01

Note: P-level – value of type 1 error during comparison of indicators of heart rhythm variability before and after the 6-minute walking test; HR – heart rate; RRNN – mean value of RR interval's duration; SDNN – standard deviation of average duration of cardiac cycle; MxDMn – difference between maximum and minimum values of cardiointervals; MxRMn – relation of a cardiointerval with a maximum value of duration to a cardiointerval with a minimum value of duration; RMSSD – square root of the sum of squares of differences between values of consequential pairs of NN intervals; Mo – mode, the most common cardiointerval value; AMo – mode amplitude; R – range; VBI – vegetative balance index; IARP – indicator of adequacy of regulation processes; VIR – vegetative indicator of rhythm; IC – index of centralization; SI – stress index; TP (Total Power) – total power in range of 0,003-0,4 Hz frequencies; HF – in range of high frequencies of 0,15 to 0,4 Hz; LF – in range of low frequencies of 0,04 to 0,15 Hz; VLF – in range of very low frequencies ≤ 0,04 Hz; LF/HF – vegetative coefficient.

By the end of the rehabilitation period symptoms of fatigue and dizziness in all patients were gone in 1 week, the cough stopped. Favorable dynamics of indicators characterizing the adaptation potential of the cardiovascular system (CVS) during physical loads were registered in 79,3% of patients. Based on results of the questionnaire, according to the mMRC scale, a decrease of 2nd and 3rd degree of dyspnea down to the 1st degree in y 38,5% of patients and its complete disappearance in the rest of the group was revealed.

The examined decrease of power in total frequency range (TP) of 0,003 to 0,4 Hz, mainly due to low and high frequencies, did not go through significant changes during the rehabilitation course. Dynamics were determined only in high frequency specter and characterized by the change of norm indicators with an increase of LF norm, %, and a decrease of HF norm, %, which indicates a decrease of parasympathetic tonus and an increase of sympathetic activation leading to formation of adaptation mechanisms with an increase of tolerance to physical loads (Table 2).

A pilot study of 29 patients affected by the mostly moderate (72,4%) and severe (17,2%) COVID-19 pneumonia, who also had comorbidities (obesity, arterial hypertension, I type diabetes) in their past medical history, showed that amplitude characteristics of the HRV were decreased along with the low variation indicator, which is SDNN (standard deviation of average duration of cardiac cycle), in comparison with values of healthy people of the same age [17]. Values of total power in range of 0,003 to 0,4 Hz and indexes of variation and time in those patients were close to values typical for heart failure [18]. Taking into the account the fact, that all patients affected with the COVID-19 pneumonia had a decreased tolerance to physical loads, which was characterized by the 1-3 degree of dyspnea on the mMRC scale, low motor activity according to the data of the walking test, which corresponds to the I class of functional state, and accompanying comorbidity, they were recommended a sparing training regime of motor activity in the form of walking on terrenkur (forest area of Mashuk mountain), at the beginning of treatment the length

should not be more than 1200 m, walking tempo should be slow (3-4 km/h). By the end of the 2nd week of rehabilitation, the route length increased up to 2500-3000 m, which allowed achieving a training effect. The use of terrenkur with exercise therapy, aimed at strengthening respiratory muscles, mechanotherapy with elements of respiratory gymnastics in the set with massage and halotherapy for patients, support the recovery of breathing biomechanics, which, according to the given data in literature, can cause improvement of ventilation-perfusion function of lungs [19]. Normobaric oxygenation was included in the rehabilitation set for patients on order to overcome consequences of chronic hypoxia and activation of metabolism combined with the course of oral administration of weak carbonate sulphate-hydrocarbonate calcium-natrium mineral water "Slavyanovskaya". An increase of the covered distance in the 6-minute walking test by 30 m in average, after a course of complex medical rehabilitation in resort conditions, is an objective indicator of an increase of physical performance and improvement of state of patients.

Conclusion. Results of conducted studies showed that patients affected with the COVID-19 pneumonia, who arrived on the second stage of medical rehabilitation in resort conditions, have a decreased physical performance, stress of adaptation processes with predominant sympathetic activity and vegetative imbalance, 1-3 degree of dyspnea on the mMRC scale, some of patients with normotonia had a decreased level of SpO_2 of blood to 92%.

Complex rehabilitation measures with the use of natural and preformed therapeutic physical factors (drinking mineral waters, mechanotherapy, halotherapy, normobaric oxygenation, ribcage massage, inhalations), due to their sanogenetic and adaptogenic effect on regulatory systems of various levels of biological integration, supported an increase of general adaptation potential, improvement of functional state of cardiorespiratory system, correction of vegetative imbalance and increase of tolerance to physical loads.

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