

# Pulmonary rehabilitation of patients with coronavirus infection COVID-19, clinical examples

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## Abstract

At the end of 2019, an outbreak of a new coronavirus infection was identified in the People's Republic of China centered in the city of Wuhan. The official name COVID-19 (COroNaVirus Disease 2019) was assigned to the infection caused by the novel coronavirus by the World Health Organization on February 11, 2020. The International Committee on Taxonomy of Viruses assigned the name to the causative agent of the infection – SARS-CoV-2 on February 11, 2020. The bilateral pneumonia is currently known to be the most common clinical manifestation of the variant of coronavirus infection. The development of acute respiratory distress syndrome was found in 3 – 4% of patients. As a result of pneumonia, patients develop ventilation and perfusion disorders, weakness of skeletal muscles. To recover patients after viral pneumonia, methods of pulmonary rehabilitation should be applied. This article represents the methods of pulmonary rehabilitation aimed to improve the blood circulation in the lungs, the ventilation-perfusion ratios, and to the restoration of the skeletal muscles.

**Key words:** new coronavirus infection COVID-19, SARS-CoV-2 infection, community-acquired pneumonia, pulmonary rehabilitation.

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# Легочная реабилитация пациентов, перенесших коронавирусную инфекцию COVID-19 (клинические примеры)

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## Резюме

В конце 2019 года в Китайской Народной Республике произошла вспышка новой коронавирусной инфекции с эпицентром в городе Ухань. Всемирная организация здравоохранения 11.02.20 присвоила официальное название инфекции, вызванной новым коронавирусом, COVID-19 (COroNaVirus Disease-2019). Международный комитет по таксономии вирусов 11.02.20 присвоил название возбудителю инфекции SARS-CoV-2. В настоящее время известно, что наиболее распространенным клиническим проявлением варианта коронавирусной инфекции является двусторонняя пневмония, у 3–4 % пациентов зарегистрировано развитие острого респираторного дистресс-синдрома. При пневмонии у пациентов развиваются вентиляционно-перфузионные нарушения, слабость скелетной мускулатуры. Для восстановления пациентов после вирусной пневмонии необходима легочная реабилитация. В данной статье приведены методы легочной реабилитации, направленные на улучшение кровообращения в легких, вентиляционно-перфузионных отношений, восстановление работы скелетной мускулатуры.

**Ключевые слова:** новая коронавирусная инфекция COVID-19, инфекция SARS-CoV-2, внебольничная пневмония, легочная реабилитация.

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At the end of 2019, an outbreak of a new coronavirus infection occurred in the People's Republic of China with an epicenter in the city of Wuhan.

On February 11, 2020, the World Health Organization assigned the official name to the infection caused by the new coronavirus, COVID-19 (Coronavirus Disease 2019). On 11 February 2020 the International Virus Taxonomy Committee assigned the name to the causative agent of the infection, SARS-CoV-2 [1].

It is now known that bilateral pneumonia is the most common clinical manifestation of the coronavirus infection variant; in 3 – 4% of patients the development of Acute Respiratory Distress Syndrome (ARDS) was recorded [1].

The epithelium of the upper respiratory tract and intestinal epithelial cells are the entrance gates of the pathogen. The initial stage of infection is the penetration of SARS-CoV-2 into target cells that have Type II Antiotensin

Converting Enzyme receptors (ACE2). ACE2 receptors are found on the cells of the respiratory tract, kidneys, esophagus, urinary bladder, ileum, heart, and central nervous system. However, the alveolar cells of type II (ACE2) of the lungs constitute the main and rapidly attainable target that determines the development of pneumonia. In the lungs in the early stage of the disease, the prevailing signs are acute bronchiolitis, the alveolo-hemorrhagic syndrome (inside alveolar hemorrhage); edema is an integral part of diffuse alveolar damage. A histological examination of this pathological process reveals the intra-alveolar edema; hyaline membranes line the contours of the alveolar passages and alveoli; the layers of cells of the alveolar epithelium are desquamated; accumulated fibrin can be found in part of the cavities of the alveoli; in a significant part of the cavities of the alveoli there is accumulation of red blood cells and there are signs of inflammation in interstitial cells the form of lymphocytic infiltration. Starting from Day 7 from the onset of the disease, at a later stage, single hyaline membranes, and fibrin and polypoid fibroblastic tissue in the lumens of the alveoli can be observed; the same can be observed in the part of the respiratory and terminal bronchioles (bronchiolitis obliterans organizing pneumonia, BOOP), squamous cell metaplasia alveolar epithelium; in the lumens of the alveoli there are accumulations of siderophages. Atelectasis and sometimes fibroatelectasis may occur [2, 3].

The interalveolar septa are characteristically thickened due to lymphoid infiltration and proliferation of type II alveolocytes. This causes further lung pathologies [4].

The formation of thrombus and changes in the rheological properties of blood leading to pathology of the cardiovascular system play an important part in the development of the disease. This is an essential aspect in the treatment and development of rehabilitation measures for patients. In addition, patients develop adynamia as they hardly ever move in hospital, and many patients have to be in a prone position to improve breathing. Prone positioning is necessary for patients to increase the surface of the lungs engaged in breathing. In this position, the lungs expand, and oxygen enters the parts of the lungs that were previously poorly ventilated. However, this position of the body causes even greater adynamia, damage to the skeletal muscles and (very importantly), the respiratory muscles [5, 6]. Pulmonary rehabilitation methods adopted according to clinical guidelines [7] can resolve the patients' problems.

## The concept of pulmonary rehabilitation

Patients who have undergone a new coronavirus (COVID-19), community-acquired pneumonia, need rehabilitation measures in order to recover the consequences of the disease [8].

In recent years, pulmonary rehabilitation methods have become a standard addition to drug therapy in patients with lung disease. The use of pulmonary rehabilitation methods improves the functioning of patients, reduces shortness of breath, improves the quality of life (QOL) of patients and reduces the number of hospitalizations and length of stay (the level of evidence A); the methods also

improve exercise tolerance and patient survival, and increase the bronchodilatory effect (the level of evidence B). Initially, pulmonary rehabilitation methods were developed for patients with chronic obstructive pulmonary disease. Further study of pulmonary rehabilitation methods has shown that the same principles apply to patients with other lung conditions. At present, it is impossible to provide full-fledged medical care for patients with lung diseases without the use of methods of pulmonary rehabilitation [9, 10].

The definition of pulmonary rehabilitation by the American Thoracic Society (ATS) Board of Directors given in December 2005 and the European Respiratory Society (ERS) Executive Committee in November 2005 is fundamental: pulmonary rehabilitation accompanies the main treatment of patients, and includes education, changes in the patient's lifestyle; it improves the physical and mental state of the patient with chronic respiratory diseases and contributes to long-term health improvement. The pulmonary rehabilitation program includes patient assessment, physical training, patient education, nutritional adjustments and psychological support. In a broader sense, pulmonary rehabilitation is a range of treatment strategies for patients with chronic lung disease throughout the patient's life; it involves active collaboration between the patient, their family and health care workers [11].

## Pulmonary rehabilitation for patients with a new coronavirus infection (COVID-19), community-acquired pneumonia

The goal of rehabilitation in patients who have undergone a new coronavirus infection (COVID-19), community-acquired pneumonia, is to improve respiratory function, relieve symptoms, reduce possible anxiety and depression, reduce the likelihood of complications, and normalize the work of the respiratory and skeletal muscles, and nutritional status.

The assessment of the patient's condition before rehabilitation is based on a general clinical assessment, (especially functional evaluation), including respiratory function, cardiac status, and the assessment of physical activity. It is necessary to control the state of the respiratory system, including the assessment of the functional activity of the lungs, and the amplitude of the diaphragm. It is important to evaluate the pathology of the cardiovascular system, the circulatory system and the nutritional status of the patient.

## Methods of pulmonary rehabilitation

### Inspiratory training

In coronavirus pneumonia, due to damage to the alveoli, it is necessary to influence the inspiratory muscles in order to reduce perfusion disturbances and decrease tidal volumes, in order to improve the ventilation capacity of the lungs. In training exercises, it is most important to influence all mechanisms of the respiratory system. The in-

spiratory muscles are active in the act of breathing and affect all aspects of pulmonary ventilation. By affecting the breathing pattern, the stress on the alveoli can be reduced by reducing the resistance in the bronchi and improving ventilation. This is especially important for patients who have to be prone positioned when the inspiratory muscles suffer. In order to restore the respiratory muscles, exercises can be used aimed at training the diaphragm: diaphragmatic breathing and exercises with training inhalation that should be done long enough (one-two-three) to improve ventilation and exhale with little resistance through closed lips (one-two-three-four) [11–13].

The use of training devices aimed at inspiratory muscles training (IMT), improves and restores lung function, and more intensively affects the restoration of the ventilation capacity of the lungs [14–16].

The use devices providing threshold resistance to the IMT is the most common approach to training the respiratory muscles. The devices used for training inspiratory muscles are Threshold IMT, Respironics (USA), and Powerbreathe Classic and Plus, Gaiam Ltd (UK).

The devices have a spring, a valve and a metered load. The valve opens only when the inspiratory pressure generated by the patient exceeds the resistance of the spring, and the exhalation occurs unimpeded through the expiratory movable valve. Stepped resistance is created in the devices that can be gradually increased during the training. The exercise increases lung capacity and improves lung function [17–19].

Various studies have been conducted to examine the efficacy of IMT, where IMT was used alone or combined with body training. A meta-analysis of IMT studies comparing with placebo or low resistance, showed that less than 30% in patients with COPD demonstrate a significant increase in strength and endurance of their respiratory muscles. In addition, the research showed significant and clinically significant reductions in dyspnea at home and an increase in the peak tidal flow. Improvements have also been shown in the 6 minute step test [20–24].

The use of IMT enables the influence on both the inspiratory muscles and the expiratory muscles that are activated after the inspiratory muscles. In order to enhance the discharge of sputum, (with the development of bronchitis), breathing machines with negative pressure during exhalation can also be applied, such as Flutters, Shakers, and Acapella devices. These devices do not train muscles, but they create additional resistance through the positive expiratory pressure during exhalation to give an impetus for coughing up phlegm, due to the opening of the airways. For example, the Threshold PEP trainer has a spring-loaded valve that creates positive pressure on exhalation, which is overcome by the patient by the expiratory muscles straining. However, the development of pneumonia associated with the coronavirus infection COVID-19 normally does not show any airway obstruction (unless the patient was diagnosed with bronchial asthma or COPD before the disease) and sputum discharge. Cough develops in response to damage to the alveoli, and not to the development of purulent bronchitis. Therefore, the use of these trainers for COVID-19 is not relevant.

## Vibration and percussion therapy

Considering the pathological inflammatory process that results from the development of viral pneumonia, and fibrin accumulation in the alveoli, the use of inspiratory training alone is not enough. The pathological process affects a large number of structures in the lungs, and the restoration of the ventilation capacity of the lungs and the reduction of fibrotic changes stipulates the use of high-frequency oscillation of the chest in conjunction with compression. This method combines the mechanical effect of high-frequency vibration and compression on the chest stimulating the restored drainage function of the lungs, and the improved blood supply to the lungs [25, 26]. The device providing this effect both affects the improvement of sputum discharge through the vibration exposure and is capable of affecting the functional and volume parameters of the lungs due to the compression effect of positive pressure, and of improving ventilation in the alveoli (as was shown in the studies of *A. Nicoloni et al.* and *R. Gloeck et al.* [27, 28]). In Russia there are two devices applied that have such characteristics: Hill-Rom Vest/Vest Airway Inc., USA, and Ventum Vest Vibration YK-800, China. Several international studies have demonstrated positive results regarding the effect of the device on the drainage function of the lungs by improving the MCC and functional changes in the lungs; the safety of this device was assessed in patients with RD. The vibration-compression apparatus consists of a vest connected by two tubes to an air pressure generator. The air pressure generator quickly builds and deflates the vest. A violent movement of the chest is created by compression and relaxation. The frequency of vibration and pressure is created by the individual adjustment of the device, but patients with coronavirus pneumonia need sufficiently significant compression and vibration (although the maximum indicators in the devices are quite safe); however, for patients with other lung pathology, vibration is primarily important. The use of vibration and compression therapy is counter-indicated in patients with suspected thromboembolism and bullous emphysema of the lungs; therefore, computed tomography of the lungs is mandatory before the rehabilitation program. In addition, when selecting modes of the procedure, a patient's comfort is essential as they experience discomfort during breathing and shortness of breath. The setting options vary in different devices. In some devices, the frequency is adjustable in the range from 1 to 20 Hz, the compression can be adjusted from 1 to 12 bar, and the time can be altered from 1 to 30 minutes. In other devices, the vibration frequency is 1 – 20 Hz, and the compression varies from 1 to 30 bar, the procedure can last from 1 to 99 minutes.

## Training for the upper and lower muscle groups

The restoration of the motor activity of the skeletal muscles (especially the upper muscle group) comprises an important stage of rehabilitation, since the muscles interact with the respiratory muscles. In addition, in severe pneumonia or with a considerable length of stay (more than 10 days), it becomes necessary to re-

store the strength of skeletal muscles [29, 30]. Patients rapidly lose muscle strength. For this, skeletal muscle training is used. Hand weights, weights, steppers, bicycle ergometers and treadmills can be used. During training, it is necessary to focus on the breathing pattern; all exercises should be performed slowly with a long inhalation and exhalation with resistance. For example, steppers are used depending on the patient's tolerance, but it is important to breathe correctly during exercise (a long inhale through the nose, and exhale through closed lips).

At the "IntegraMed" Respiratory Clinic, we have used all the presented rehabilitation methods with a positive effect. From March, 2020, 62 patients have undergone pulmonary rehabilitation under the program of patients who have had COVID-19 with pneumonia. All patients have been given a full course of rehabilitation during at least 10 sessions and continued further training of the upper and lower muscle groups and inspiratory training. After they were discharged from hospital, the patients began the course of therapy at different periods due to the different periods of quarantine, the patients' own wish to get out of the disease, as in addition to three patients (two with obesity syndrome and hypoventilation and one patient with hyperventilation syndrome), there were no issues with the respiratory organs and cardiovascular system. All patients, regardless of the quarantine timing, had similar complaints of chest congestion and difficulty in breathing, dry cough, migratory chest and back pains, pain in the trachea, and fear of death. After they completed the rehabilitation course, their complaints regressed. There is no doubt that pulmonary rehabilitation should be started already in the hospital; the earlier rehabilitation measures are commenced, the less manifestations of disturbances from the bronchopulmonary system and the faster the recovery of patients. According to the study of the function of external breathing, obstructive type of bronchial patency was not revealed in these patients; however, 53 patients showed a decrease in forced vital capacity (FVC). It was impossible to conduct bodyplethysmography and diffusion examination of the lungs at that time. These studies started only in July. In this paper we present the data of two clinical cases of patients with different types of pulmonary rehabilitation.

## Case 1

Patient K., 39 years old, got acutely ill on February 28, 2020, after returning from Italy (February 20, 2020). The patient's temperature rose to 37.4 – 38 °C; it decreased after taking paracetamol. On Day 4 of the disease, the temperature rose to 39 °C. From March 03, 2020, as prescribed by the therapist, the patient started taking amoxicillin. On March 04, due to a sharp deterioration in the patient's condition (the temperature was up to 39 °C, dry heavy cough, shortness of breath, and weakness), the patient turned to a private clinic, where they performed computed tomography (CT) of the lungs, and diagnosed bilateral polysegmental pneumonia.

The patient was immediately taken by an ambulance to be admitted to a hospital in Moscow. The patient was tested for

RNA 2019-SARS-CoV-2 as of March 04, 2020, the result was positive.

After a course of therapy, with a positive trend in the clinical state, two negative results for RNA 2019-SARS-CoV-2, (the last of which was dated March 13, 2020), the patient was discharged with recommendations for rehabilitation measures. According to the blood tests, the patient showed a sharp decrease in leukocytes and lymphocytes. The patient was discharged on March 24, 2020.

According to the CT scan of the chest organs dated March 10, 2020, there is a picture of bilateral polysegmental pneumonia of viral genesis. The lung damage was 65%.

The CT of the chest organs as of March 13, 2020, showed positive dynamics in the form of a decrease in the affected areas up to 50% (Figure 1).

The ultrasound of the pleural cavities as of March 09, 2020, showed minimal hydrothorax on the left, with a local decrease in the airiness of the lower lobe of the left lung.

The patient's history shows active sports (playing tennis 5 times a week). The patient does not smoke. There was an allergic reaction in the form of Quincke's edema to phenobarbital; no other allergy is noted.

According to the spirometry data as of March 25, 2020, no impairment of bronchial patency was revealed. Forced expiratory volume in 1 sec ( $FEV_1$ ) – 99%, FVC – 103%,  $FEV_1/FVC$  – 78%, mean forced expiratory flow during the 25% of FVC ( $MEF_{25}$ ) – 86%,  $MEF_{50}$  – 109%,  $MEF_{75}$  – 47%,  $MEF_{25-75}$  – 86%.

The ultrasound of the pleural cavity as of March 25, 2020, showed no signs of fluid in the pleural cavities.

After the patient was discharge from the hospital, there were complaints of dry cough, and tightness in the chest that greatly disturbed the patient.

The clinical blood test as of March 28, 2020, showed an increase in platelets up to 397 g/l, an increase in lymphocytes up to 43%, and the absolute indicators 2,24 thousand/ $\mu$ l.

From March 25, 2020, the patient was recommended therapy with Azithromycin (Sumamed) 250 mg one pill once a day, three times a week (Monday, Wednesday, Friday) during a month; Fluimucil 600 mg 2 times daily was prescribed as an antioxidant therapy.

Rehabilitation activities began on April 01, 2020, as since then the patient was able to visit the clinic.

The patient was prescribed training of the inspiratory muscles using a breathing device with an initial resistance of 40 mm H<sub>2</sub>O, 20 breathing movements 3 times daily.

High-frequency chest oscillation was performed using vibration-compression therapy with a 10 bar compression and a frequency of 13 Hz, for 30 minutes.

## Results

After three sessions of high-frequency oscillation of the chest, the patient stopped coughing, and the feeling of chest congestion disappeared. However, when the patient was unable to attend the therapy sessions for two days for family reasons, and the cough and tightness in the chest returned. The patient resumed therapy sessions. There were 10 sessions in total.

After ten therapy sessions using high-frequency oscillation of the chest, and an inspiratory trainer, inhalation of Fluimucil, and taking Sumamed, the patient's condition stabilized. The cough was stopped, the feeling of tightness in the chest does not resume.





Figure 1. Computer tomogram, patient K. 39 years old, 13.03.20  
Рис. 1. Компьютерная томограмма пациента К. 39 лет от 13.03.20



Figure 3. Computer tomogram, patient A. 52 years old, 01.05.20  
Рис. 3. Компьютерная томограмма пациента А. 52 лет от 01.05.20



Figure 2. Computer tomogram, patient K. 39 years old, 15.04.20  
Рис. 2. Компьютерная томограмма пациента К. 39 лет от 15.04.20

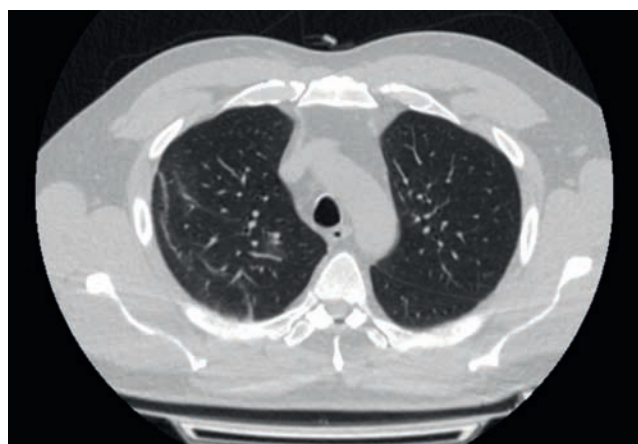


Figure 4. Computer tomogram, patient A. 52 years old, 10.06.20  
Рис. 4. Компьютерная томограмма пациента А. 52 лет от 10.06.20

According to the CT scan of the chest organs as of April 15, 2020, there was a drastic positive trend in the form of a significant decrease in the size and intensity of the foci of inflammation and ground glass opacities (Figure 2).

According to the spirometry data as of April 16, 2020, there was no improvement in bronchial patency.  $FEV_1$  – 103%, FVC – 98%,  $FEV_1/FVC$  – 85%,  $MEF_{25}$  – 111%,  $MEF_{50}$  – 101%,  $MEF_{75}$  – 92%,  $MEF_{25-75}$  – 107%.

The clinical blood test as of April 23, 2020, showed all indicators completely normalized, including the leukocyte formula.

As a result of the rehabilitation measures, there was a significant improvement in the patient's condition, the improvement of the drainage and ventilation functions of the lungs.

## Case 2

Patient A., 52 years old, on April 27, 2020, signs of ARVI appeared (myalgia, chills, body temperature increased to 38.2 °C, general weakness). On the third day, a dry cough appeared.

On May 30, the patient turned to a private clinic, where a CT scan of the chest organs was performed and upper lobe pneumonia was diagnosed.

According to the CT scan of the chest organs as of May 01, 2020, there were infiltrative changes and areas of ground glass

in the upper lobe of the right lung. On the visual scale, it corresponds to the CT-3 (Figure 3).

The blood tests as of May 03, 2020, showed CRP – 19.3 mg/L, ferritin – 886 ng/mL; leukocytes –  $3.6 \times 10^9/L$ ; fibrinogen – 4.7 g/L.

The CT scan was regarded as pneumonia caused by the viral infection COVID-19. The prescriptions were Azithromycin 500 mg per day, 7 days, hydroxychloroquine 200 mg, the first day 400 mg twice a day, then 200 mg twice a day, 7 days. Fluimucil was prescribed at a dose of 1,800 mg per day. During the treatment, the patient's body temperature varied in the range from 36.8 to 38 °C for 5 days. Then it returned to normal. Dry cough and fatigue persisted.

On May 09, 2020, high-quality IgM/IgG tests for SARS-CoV-2 were carried out, and turned out to be positive. The patient continued treatment with Fluimucil at a dose of 1,800 mg per day for 3 weeks.

According to the spirometry data as of May 28, 2020, no impairment of bronchial patency was revealed.  $FEV_1$  – 120%, FVC – 116%,  $FEV_1/FVC$  – 83%,  $MEF_{25}$  – 114%,  $MEF_{50}$  – 114%,  $MEF_{75}$  – 98%,  $MEF_{25-75}$  – 115%.

Rehabilitation started on May 28, 2020.

The patient was prescribed inspiratory muscles training using a breathing trainer with an initial resistance of 50 mm H<sub>2</sub>O, 30 respiratory movements twice a day.



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