

Consensus Report

Pulmonary rehabilitation principles in SARS-COV-2 infection (COVID-19): The revised guideline for the acute, subacute, and post-COVID-19 rehabilitation

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Received: April 21, 2021 Accepted: May 10, 2021 Published online: May 25, 2021

ABSTRACT

Coronavirus disease 2019 (COVID-19) is a contagious infection disease, which may cause respiratory, physical, psychological, and generalized systemic dysfunction. The severity of disease ranges from an asymptomatic infection or mild illness to mild or severe pneumonia with respiratory failure and/or death. COVID-19 dramatically affects the pulmonary system. This clinical practice guideline includes pulmonary rehabilitation (PR) recommendations for adult COVID-19 patients and has been developed in the light of the guidelines on the diagnosis and treatment of COVID-19 provided by the World Health Organization and Republic of Turkey, Ministry of Health, recently published scientific literature, and PR recommendations for COVID-19 regarding basic principles of PR. This national guideline provides suggestions regarding the PR methods during the clinical stages of COVID-19 and post-COVID-19 with its possible benefits, contraindications, and disadvantages.

Keywords: COVID-19, guideline, post-COVID-19, pulmonary rehabilitation, severe acute respiratory syndrome.

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Cite this article as:

Kurttaş Aytür Y, Köseoglu BF, Özyemişçi Taşkıran Ö, Kutay Ordu Gökçaya N, Ünsal Delialioğlu S, Sonel Tur B, et al. Pulmonary rehabilitation principles in SARS-COV-2 infection (COVID-19): The revised guideline for the acute, subacute, and post-COVID-19 rehabilitation. Turk J Phys Med Rehab 2021;67(2):129-145.

Turkish Society of Physical Medicine and Rehabilitation Specialists Cardiopulmonary Rehabilitation Study Group

On behalf of

Turkish Society of Physical Medicine and Rehabilitation Specialists

Turkish Society of Physical Medicine and Rehabilitation

April, 2021

Version 2.0

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Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome-coronavirus-2 (SARS-CoV-2), a newly emergent coronavirus, that was first recognized in Wuhan, China, in December 2019.^[1] The first case in Turkey was identified on March 11th, 2020.^[2] The World Health Organization (WHO) declared COVID-19 as a pandemic on March 12th, 2020.^[3]

SARS-CoV-2 is a beta-coronavirus with a genetic sequence highly similar to SARS virus.^[3] Angiotensin-converting enzyme 2 (ACE-2) found in the lower respiratory airways of humans is a cellular receptor for SARS-CoV and has been shown to play a role in the spread from one human being to another and in cross-transmission.^[4,5] The ACE-2 is mainly associated with cardiovascular diseases and it is a type I membrane protein expressed by the lungs, heart, kidneys, and bowel.^[6]

While most individuals with COVID-19 develop only mild (40%) or moderate (40%) disease, approximately 15% develop severe disease which requires oxygen support, and 5% have critical disease with complications such as respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, thromboembolism, and/or multi-organ failure, including acute kidney injury and cardiac injury (Tables 1, 2).^[3]

Elderly individuals and individuals with underlying health conditions (diabetes, hypertension, cardiac disease, chronic lung, kidney and hepatic disease, obesity and cancer) are more prone to infection and more inclined to ARDS and severe consequences

that may be related to cytokine storms.^[7,8] Among hospitalized COVID-19 patients, approximately 33% develop ARDS, 26% require transfer to an intensive care unit (ICU), 16% receive invasive mechanical ventilation (IMV), and 16% die.^[9]

As in cases of ARDS due to other causes, age and comorbid disease states are reported as risk factors for COVID-19, as well. In multivariate analysis, advanced age, a high Sequential Organ Failure Assessment (SOFA) score, and an elevated D-dimer level at the time of admission were associated with higher mortality.^[3] In COVID-19, the mortality rate was reported as 40% in patients admitted to ICU, 59% of those who received IMV, and 45% in COVID-19-associated ARDS.^[9]

Autopsies were performed in 10 African American decedents aged 44 to 78 years with a cause of death attributed to COVID-19. Important findings included the presence of thrombosis and microangiopathy in the small vessels and capillaries of the lungs, with associated hemorrhage, that significantly contributed to death. Pathological features of diffuse alveolar damage including hyaline membranes were reported even in patients who had not been on IMV. There were also cardiac findings, such as individual cell necrosis without lymphocytic myocarditis.^[10]

The long-term sequelae of COVID-19 are still unknown. Lessons from past viral epidemics reveal that, after recovery, patients with viral pulmonary infections can suffer from irreversible pulmonary dysfunction and demonstrate residual imaging or functional abnormalities. Residual ground-glass opacities, consolidations, reticular and linear opacities,

TABLE 1
Symptoms and risk factors associated with COVID-19^[3]

Clinical presentation	<p>Presenting signs and symptoms of COVID-19.</p> <p>Fever (83-99%), cough (59-82%), fatigue (44-70%), anorexia (40-84%), shortness of breath (31-40%), myalgia (11-35%).</p> <p>Other non-specific symptoms; sore throat, nasal congestion, headache, diarrhea, nausea, vomiting, loss of smell (anosmia) or loss of taste (ageusia).^[1,62-67]</p> <p>Older people and immunosuppressed patients in particular may present with atypical symptoms such as fatigue, reduced alertness, reduced mobility, diarrhea, loss of appetite, delirium, and absence of fever.^[68-70]</p> <p>In pregnant women, symptoms such as dyspnea, fever, gastrointestinal (GI) symptoms or fatigue due to physiologic adaptations, adverse pregnancy events, or other diseases such as malaria, may overlap with symptoms of COVID-19^[71]</p> <p>Children might not experience fever or cough as frequently as adults^[72]</p>
Risk factors for severe disease	<p>Age older than 60 years (increasing with age).</p> <p>Underlying non-communicable diseases (NCDs): diabetes, hypertension, cardiac disease, chronic lung disease, cerebrovascular disease, chronic kidney disease, immunosuppression and cancer have been associated with higher mortality.</p> <p>Smoking.</p>

TABLE 2
COVID-19 disease severity^[3]

Mild disease		Symptomatic patients meeting the case definition for COVID-19 without evidence of viral pneumonia or hypoxia.
Moderate disease	Pneumonia ^[73]	Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) but no signs of severe pneumonia, including SpO ₂ ≥90% on room air.
Severe disease	Severe pneumonia ^[73]	Adolescent or adult with clinical signs of pneumonia (fever, cough, dyspnea, fast breathing) plus one of the following: respiratory rate >30 breaths/min; severe respiratory distress; or SpO ₂ <90% on room air.
Critical disease	Acute respiratory distress syndrome (ARDS) ^[74-76]	Onset: Within one week of a known clinical insult (i.e. pneumonia) or new or worsening respiratory symptoms. Chest imaging: (radiograph, CT scan, or lung ultrasound): Bilateral opacities, not fully explained by volume overload, lobar or lung collapse, or nodules. Origin of pulmonary infiltrates: Respiratory failure not fully explained by cardiac failure or fluid overload. Need objective assessment (e.g. echocardiography) to exclude hydrostatic cause of infiltrates/edema if no risk factor present. Oxygenation impairment in adults: 200 mmHg < PaO ₂ /FiO ₂ ^a ≤300 mmHg (with PEEP or CPAP ≥5 cmH ₂ O). ^b
Critical disease	Sepsis ^[77,78]	Adults: Acute life-threatening organ dysfunction caused by a dysregulated host response to suspected or proven infection. Signs of organ dysfunction include: altered mental status, difficult or fast breathing, low oxygen saturation, reduced urine output, fast heart rate, weak pulse, cold extremities or low blood pressure, skin mottling, laboratory evidence of coagulopathy, thrombocytopenia, acidosis, high lactate, or hyperbilirubinemia.
	Septic shock ^[77,78]	Adults: Persistent hypotension despite volume resuscitation, requiring vasopressors to maintain MAP ≥65 mmHg and serum lactate level >2 mmol/L.

See the WHO website for most up-to-date case definitions.^[79]
SpO₂: Pulse oxygen saturation; CT: Computed tomography; PaO₂: Partial pressure arterial oxygen; FiO₂: Fraction of inspired oxygen; PEEP: Positive end-expiratory pressure; CPAP: Continuous positive airway pressure; MAP: Mean arterial pressure; ^a: If altitude is higher than 1000 m, then the correction factor should be calculated as follows: PaO₂/FiO₂ × barometric pressure/760; ^b: When PaO₂ is not available, SpO₂/FiO₂ ≤315 suggests ARDS (including in non-ventilated patients).

residual crazy paving pattern, melted sugar sign, and parenchymal fibrotic bands are typical features found in the late or remission stages of COVID-19. These radiological findings can be observed weeks after the symptom onset, even after hospital discharge, and they may or may not correlate with clinical manifestations.^[11]

Currently, there is no specific antiviral drug for COVID-19. Although there is no approved antiviral regimen, drugs including lopinavir/ritonavir, remdesivir, favipiravir, umifenovir, emtricitabine, chloroquine and hydroxychloroquine, azithromycin, immunomodulators (i.e., tocilizumab, anakinra, interferon-β-1a), and plasma therapy are being used.^[3]

As of March 2021, there are more than 300 vaccine candidates at different development stages.^[12] An efficacious vaccine is essential to prevent further morbidity and mortality. Several technological methods (e.g., DNA, RNA, inactivated, viral vector,

protein subunit) are available for vaccine development.^[13] Vaccination has started in many countries worldwide with several different vaccines.

The guidelines by the Republic of Turkey, Ministry of Health define the patients complying with the diagnoses of pneumonia and severe pneumonia and the indications for admission to ICU for our country in detail.^[14]

As there is no adequate data about the long-term results, the degree of damage or sequela after the active disease is not known. Being the main target, respiratory system seems to be one of the most vulnerable systems for the unforeseen damage or sequela. This situation requires a good planning of post-COVID-19 management in the long-term setting, including pulmonary rehabilitation (PR).

In a patient-specific manner, PR is planned based on a detailed patient assessment including but not limited to training, exercise, and behavioral

changes, since it aims at improving the physical and psychological status of individuals with chronic respiratory disease and focuses on comprehensive interventions for long-term commitment to health improvement attitudes.^[15] Although PR has classically been defined for the treatment of chronic pulmonary diseases, it is also needed and implemented during the course of different pulmonary diseases and during immobility, surgery, and systemic, neurological, and musculoskeletal diseases which impair breathing.

Pulmonary rehabilitation procedures will definitely be necessary for the right patient at the right time.^[16-18] In patients with COVID-19 pneumonia or ARDS, multidisciplinary and holistic approach in COVID-19 management encompasses the PR with the selection of appropriate components according to the individual needs. Although indications of PR specific to COVID-19 are not clear, general indications can be listed as follows, when the effects of the disease on the respiratory system and its consequences are taken into consideration:

1. During the acute disease, dyspnea, cough, difficulty in expectoration, respiratory failure, gas exchange abnormalities and immobility
2. Difficulty in daily life activities due to decreased functional status
3. Nutritional deficiency
4. Deterioration in quality of life
5. Psychosocial problems
6. Fatigue and chronic respiratory symptoms in the long term
7. Decrease in work performance
8. Increase in the utilization of medical resources such as hospital admission due to chronic respiratory problems secondary to COVID-19.

The scope of standard PR includes the following components:

1. Education of the patient, family or caregiver
2. Smoking cessation
3. Exercise training; respiratory and peripheral muscle training
4. Breathing strategies; bronchial hygiene techniques and breathing retraining
5. Occupational therapies
6. Nutritional evaluation and support
7. Psychosocial evaluation and support
8. Oxygen support

9. Utilization of non-invasive and invasive mechanical ventilation

Among the elements of PR, exercise training is the most effective and compulsory method in achieving the goals of PR. Exercise and other rehabilitation approaches are demonstrated in Table 3.

Protection

The most important routes of transmission for COVID-19 between humans are close contact and droplet spread. Therefore, healthcare workers (HCWs) who provide service to these patients are regarded as having a high risk of transmission and the protection of HCWs is one of the most important priorities. There are guidelines issued by both WHO^[3,19] and the Republic of Turkey Ministry of Health^[20] concerning the use of personal protective equipment (PPE). According to these guidelines, HCWs having contact with possible/confirmed COVID-19 patients have to use PPE appropriate for droplet, contact, and aerosolization type routes of transmission. For all the patients diagnosed with COVID-19, HCWs need to use surgical masks, gowns, gloves, goggles/shields during patient care/treatment. During procedures with the potential of aerosol transmission of the virus (respiratory tract sampling, close distance examinations, all types of invasive procedures, respiratory secretion aspirations, etc.) HCWs should definitely use particle-blocking masks (N95). In the guideline issued by the Republic of Turkey Ministry of Health, risk stratification has not been made for PR bronchial drainage techniques such as assisted coughing techniques, respiratory exercises, postural drainage and percussion. However, some of the published guidelines state that all these procedures will lead to aerosol production and that the HCW should definitely use an N95 mask.^[21,22] The HCWs should also respect the sequencing rules when donning/doffing of PPE.

The Purpose of the Guideline

This national guideline was prepared to inform primarily the physical medicine and rehabilitation (PMR) specialists and other physicians who follow COVID-19 patients. This guideline provides suggestions regarding the PR methods during the clinical stages of COVID-19 and post-COVID-19 with its possible benefits, contraindications and disadvantages.

The Scope of the Guideline

This guideline is prepared in the light of COVID-19 diagnosis and treatment guidelines of WHO and the Republic of Turkey, Ministry of Health, Public Health General Directorate,^[3,18] of published articles

TABLE 3
Exercise components of pulmonary rehabilitation

Respiratory muscle training	<ul style="list-style-type: none"> a. Inspiratory muscle training: <ul style="list-style-type: none"> • Voluntary isocapnic hyperpnea or normocapnic hyperventilation • Inspiratory resistive loading • Inspiratory threshold loading • Tapered threshold loading b. Expiratory muscle training
Breathing strategies	<ul style="list-style-type: none"> a. Controlled breathing techniques <ul style="list-style-type: none"> • Pursed lip breathing • Segmental breathing (lateral costal breathing) • Diaphragmatic breathing (abdominal breathing) • Slow and deep breathing • Alternate nostril breathing • Frog breathing (Glossopharyngeal breathing) • Head-down (Trendelenburg) and bending forward postures • Abdominal girdle • Relaxation exercises b. Bronchial hygiene-airway clearance techniques <ul style="list-style-type: none"> • Forced expiration techniques <ul style="list-style-type: none"> ◦ Controlled cough maneuver ◦ Huffing • Incentive spirometry (sustained maximal inspiration-SMI) • Flutter breathing (devices applying vibrations to the inside of mouth) • Postural drainage, percussion, vibration • Positive expiratory pressure (PEP) • Active cycle of breathing techniques (ACBT) • Autogenic drainage • Mechanical Insufflator-Exsufflator (MI-E) • Intrapulmonary percussive ventilation (IPV) • High-frequency chest wall oscillation (HFCWO) • Cough increasing techniques <ul style="list-style-type: none"> ◦ Maximum Insufflation Capacity Maneuver (MIC) ◦ Glossopharyngeal breathing ◦ Manually assisted cough (MAC) ◦ MI-E and IPV
Aerobic/endurance	<ul style="list-style-type: none"> • Continuous/intermittent training • Bicycle with a single leg • Scandinavian/Nordic walking training • Non-assisted walking training
Strengthening/resistance	
Other	<ul style="list-style-type: none"> Upper extremity and shoulder girdle exercises Exercises in water Balance training Neuromuscular electrical stimulation (NMES): (the diaphragm, abdominal muscles and extremity muscles) Nonlinear exercise training Whole-body vibration Yoga training Tai Chi exercises

on COVID-19 treatment and published expert opinion recommendations on PR for COVID-19. It contains recommendations for adult patients. The guideline includes PR recommendations for different clinical presentations of COVID-19 and prolonged symptoms and impairments after COVID-19 to help patients recover the disease. At the time of establishment of these recommendations, the transmissibility of

COVID-19, the principle of a limited number of HCWs having contact with the patient and the level of benefits to be provided by PR were taken into account.

Method for Guideline Development

For the purpose of developing a PR guideline to be used in the treatment of COVID-19 patients, PMR specialists who are experienced in the field of

cardiopulmonary rehabilitation were invited to work together under the coordination of the Cardiopulmonary Rehabilitation Study Group of Turkish Society of Physical Medicine and Rehabilitation Specialists. The same group published the “Pulmonary Rehabilitation after COVID-19” short guideline on March 25th, 2020, as an expert opinion.^[23] Following this quick and brief guideline, preparation of a more detailed PR clinical practice guideline was decided on March 30th, 2020. The Turkish Society of Physical Medicine and Rehabilitation and Turkish Society of Physical Medicine and Rehabilitation Specialists together prepared the guideline and Cardiopulmonary Rehabilitation Study Group of the Turkish Society of Physical Medicine and Rehabilitation Specialists drafted the guideline on behalf of these two associations.^[24] Finally, the new version including PR recommendations for post-COVID-19 was developed. The steps listed below were followed in the preparation of the guideline:

1. AGREE II framework was followed in the development of the guideline.^[25]
2. The literature search was conducted on PubMed, CINAHL, Google Scholar, Cochrane and related online databases. In the literature review, guidelines and recommendations during the last decade, meta-analyses, systematic reviews, randomized studies, and websites of relevant agencies such as WHO and the Republic of Turkey, Ministry of Health were analyzed. The language of the literature search was English. Furthermore, references translated into Turkish were used. Keywords were identified as “*Coronavirus pneumonia*”, “*Rehabilitation AND Coronavirus infection*”, “*COVID-19*”, “*SARS-CoV-2*”, “*ARDS*”, “*SARS*”, “*MERS*”, “*Influenza pneumonia*”, “*Pulmonary rehabilitation AND Pneumonia*”, “*Pulmonary rehabilitation after COVID-19*”, “*Respiratory rehabilitation AND respiratory failure*”, “*Rehabilitation AND Critically ill patient*”.
3. After all the participants reviewed the data obtained by this search, key research questions were prepared in accordance with the PICO framework.^[26] The prepared questions were individually reviewed by five of the authors (FK, NKOG, SÜD, TT, YKA), similar questions were combined and the questions were arranged for a common language and for the sake of clarity. The questions were tailored according to the Delphi technique and the final version was approved unanimously by the five-member group.
4. One hundred and ninety questions were prepared and sent to all the participants with the Qualtrics Program to be reviewed by the Delphi technique. In the light of scientific publications and personal experience, the participants were asked to mark each question as “Yes”, “No” or “Do not know/Neutral”. The questions receiving more than 70% of the common view were approved as research questions and those receiving less than 70% of consensus were re-evaluated by the participants. In the second round, the questions approved with a rate of 65% were accepted as research questions.
5. Based on the results obtained from the research questions, six authors (BST, FK, NKOG, ÖÖT, SÜD, YKA) developed the recommendations.
6. For the post-COVID-19 recommendations, 38 questions were prepared and sent to all the participants with the Qualtrics Program to be reviewed by the Delphi technique. The same methodology explained in the 4th item was applied for these questions.
7. The recommendations in the previous version (v 1.1) were reviewed by all the authors. Six of the authors (BST, FK, NKOG, ÖÖT, SÜD, YKA) revised these recommendations considering the expert reviews, new knowledge and gained experience about COVID-19.
8. Finally, new recommendations and the final version of the guideline was presented for the approval of all the participants.

RECOMMENDATIONS

The vast majority of the literature data on the definition of PR and the effectiveness of different methods on mortality and morbidity are based on experiences in chronic pulmonary disease and mainly chronic obstructive pulmonary disease (COPD). There is still no literature with high-quality evidence about the use of PR for acute respiratory failure/ARDS, COVID-19 and similar acute infectious conditions. Therefore, while preparing a PR guideline for COVID-19, there was a need to consider the characteristics of this disease and its transmissibility together with the results of other methods whose efficacy were investigated for chronic diseases to prioritize condition appropriate and individualized recommendations. In the preparation of the

recommendations for PR applications, the following topics were emphasized:

- Recommendations for acute, post-acute, and post-COVID-19 stages of COVID-19 are presented.
- Each patient should be evaluated individually before PR. Evaluation methods may vary in a wide range from standard clinical examination to telemedicine and similar technological means, according to the patient's disease and transmission status and whether he/she is inpatient or at home. For the selected patients, individualized PR program is planned by the PMR specialist, regarding general rehabilitation principles and holistic approach.
- Given the fact that all types of rehabilitation practices entail high levels of transmission risk, rehabilitation services should be planned based on the isolation and protection principles, the source of PPE, the staff and infrastructure characteristics of the COVID-19 center. Due to similar concerns, rehabilitation services can also be provided through visual materials or tele-rehabilitation.
- Assessments requiring any equipment such as pulmonary function tests or cardiopulmonary exercise tests are not recommended in the acute and subacute phase, when there is a risk of contagiousness.
- Psychosocial and nutritional status of the patient should be taken into account, since all these may affect the outcome of PR intervention.
- Bronchial hygiene techniques, such as assisted cough, postural drainage and percussion, breathing exercises and mobilization that may induce cough, carry the risk of aerosolization and healthcare workers should wear appropriate PPE.
- Certain PR and general rehabilitation applications may lead to clinical deterioration by increasing respiratory workload in the acute COVID-19 infection. Rehabilitation programs should be individualized and closely monitored. Close communication with the primary physician of the patient about the clinical course is recommended.
- Other systemic involvements, particularly cardiac and neurological involvement

secondary to COVID-19 should be taken into consideration, while planning the PR program.

- Patients and their families or caregivers should be educated regarding PR program.
- COVID-19 patients with severe lung involvement are expected to develop physical, functional, cognitive and psychosocial sequelae. It is important to organize rehabilitation programs to address these impairments.
- During all assessments and rehabilitation interventions, PPE complying with standard definitions of the Republic of Turkey, Ministry of Health should be used.
- COVID-19 survivors may report persistent restrictive ventilation deficits, regardless of disease severity; there is only sparse and low-quality evidence concerning the efficacy of any rehabilitation intervention to promote functional recovery.

1. MILD DISEASE

RECOMMENDATION 1.1

Comprehensive pulmonary rehabilitation in COVID-19 during the mild disease is not necessary, but relevant health measures should be taken into account.

Clinical symptoms are mild at this clinical condition. It is important that these individuals stay home and achieve a balance between rest and physical activity by paying attention to their symptoms. At a time when it is compulsory for these individuals to stay at home, indoor exercises such as marching on spot, joint range of motion (ROM), posture, balance and coordination exercises in conformity with the existent physical activity guidelines and criteria to symptom limit such as fatigue, dyspnea, dizziness etc. are suggested to refrain from adverse effects of physical activity restriction.^[27,28] During the mild disease, preventive measures such as cessation of smoking, sleep hygiene, nutritional balance, adequate fluid intake, and supportive measures recommended by the health authorities and guidelines should be taken.^[29-34]

Individuals with special conditions (i.e., older age, immunocompromised, neurological, pulmonary, cardiovascular, musculoskeletal, metabolic or other systemic diseases) can be evaluated by a PMR specialist and their rehabilitation program should be planned and revised accordingly, in case of a recent functional deterioration.

2. MODERATE DISEASE

PNEUMONIA

RECOMMENDATION 2.1

It is recommended to apply an individualized pulmonary rehabilitation program for the patients diagnosed with COVID-19 pneumonia when deemed appropriate after assessment.

When the first version of this guideline was published in Turkey, patients diagnosed with COVID-19 pneumonia with moderate disease were mostly hospitalized. However, as the knowledge accumulated about the nature and progress of the disease and the capacity with the variety of options of health services became clearer, hospitalization criteria changed. According to recent guidelines of the Republic of Turkey, Ministry of Health^[35] most of the patients of moderate disease stay at home with the appropriate treatment plans and are followed by health personnel via telemedicine and home visits, if needed. Thus, Recommendation 2.1 should be interpreted according to the designated treatment option of the patient.

For the hospitalized patient:

- Patients without prominent respiratory difficulty and/or patients with low-level oxygen requirement (≤ 5 L/min for $SpO_2 \geq 90\%$), who have non-productive cough or are able to clear secretions independently do not need specific PR interventions; such as breathing strategies and bronchial hygiene techniques.
- In patients with difficulties in secretion clearance due to their respiratory or neuromuscular comorbidity (e.g., cystic fibrosis, neuromuscular disease, spinal cord injury, stroke, chronic pulmonary diseases) PR interventions for airway clearance should be applied.
- Patients who have exudative consolidation and cough with sputum, but cannot clear his/her secretions should have PR interventions for airway clearance.
- Possible progression of the disease should be taken into account and rehabilitation interventions should be withdrawn in case of high fever (38°C); worsening dyspnea; respiratory rate >30 breaths/min; Borg dyspnea score >3 , $SpO_2 <90\%$ on oxygen therapy, respiratory distress, and other systemic symptoms such as arterial hyper/hypotension (blood pressure [BP] $<90/60$ mmHg or $>180/90$

mmHg), bradycardia or tachycardia (heart rate [HR] <40 beat/min or >120 beat/min), intercurrent arrhythmias, profuse sweating, evidence of radiological lesion progression ($>50\%$) within 24 to 48 h or other conditions that may be indication of clinical worsening and general contraindications for exercise.^[36,37]

For the patients followed at home:

- It is recommended to apply same treatment guidelines and instructions mentioned above for the patients. Although there is no such infrastructure at the moment, the symptoms may be questioned via telemedicine (mostly phone calls, and home visits, when needed) and patients in the need of PR may be selected and further information may be supplied and supported with booklets, videos, social media applications or other available telerehabilitation methods.

All patients, either in hospital or at home, should be recommended to perform ROM and mobilization activities to the limit of fatigue and other symptoms. Pulmonary rehabilitation program may include the utilization of devices for individual use such as incentive spirometry, flutter breathing devices, positive expiratory pressure (PEP) and having sputum expelled with controlled cough and huffing maneuvers and finally breathing strategies. As these activities result in aerosol formation, necessary measures should be taken to prevent spreads to the environment (i.e., collecting the sputum in closed plastic bags, patient wearing a mask while performing breathing strategies and cough maneuvers, in negative pressurized rooms).^[38]

Although aerobic exercises, respiratory and general muscle strengthening exercises were also recommended in some earlier guidelines,^[36-41] at the acute pneumonia stage, it is not recommended to routinely apply these exercises.^[42,43]

Pulmonary rehabilitation to be used at this stage is thought to help to manage problems such as dyspnea, cough and sputum, anxiety and depression;^[44] however, there are no such data in the context of evidence-based medicine for COVID-19.^[36,37,41,45]

RECOMMENDATION 2.2

All patients who have prolonged immobility, frailty, multiple comorbidities such as stroke, spinal cord injury, cardiac or respiratory diseases, functional decline in daily activities should have rehabilitation interventions for breathing strategies, mobilization, and ROM exercises.

These individuals should be evaluated by a PMR specialist and the patient's still ongoing home-based rehabilitation program should be revised or a new program should be recommended tailored to the needs of the patient, and various methods such as booklets or telemedicine can be used.

RECOMMENDATION 2.3

The use of individual devices, mobilization techniques and exercises prescribed by the PMR specialist should be instructed to the patient by one of the rehabilitation team members. These practices can be performed by PMR specialist or existing healthcare personnel (nurse, physiotherapist, occupational therapist, physiotherapy technician, etc.) depending on the present conditions, and availability of human resources and PPE at the facility.^[46] The frequency of PR interventions should be planned according to the patient's status. It is recommended to perform a regular follow-up of the rehabilitation program and revised accordingly considering the patient's clinical status.

The PR programs can be offered by the use of printed and visual materials, videos, social media, telerehabilitation in the presence of eligible infrastructure.

3. SEVERE DISEASE

SEVERE PNEUMONIA

RECOMMENDATION 3.1

It is recommended to plan an individualized pulmonary rehabilitation program for patients with severe COVID-19 pneumonia and to start implementing the program after the patient becomes medically stable and fulfills the following criteria:

- Initial diagnosis time or symptom onset ≥ 7 days; initial onset of dyspnea ≥ 3 to 5 days
- Respiratory system^[36,37]
 - $FiO_2 \leq 0.6$
 - $SpO_2 \geq 90\%$ on oxygen therapy
 - Respiratory rate ≤ 40 breaths/min
 - PEEP ≤ 10 cmH₂O
 - Absence of ventilator resistance
- Cardiovascular system
 - BP $\geq 90/60$ or $\leq 180/90$ mmHg
 - HR ≥ 40 and ≤ 120 beats/min
 - Absence of new arrhythmia or myocardial ischemia

- Absence of shock with lactic acid level ≥ 4 mmol/L
- Absence of new unstable deep vein thrombosis and pulmonary embolism
- Nervous system; able to cope with the rehabilitation program regarding the patient's consciousness and cognitive status.
- Others
 - Absence of new progressively worsening hepatic/renal impairment
 - Temperature $\leq 38^\circ C$

After the assessment of the general condition, fever, respiratory symptoms such as dyspnea, cough, respiratory rate, SpO_2 , blood tests, radiological findings, ROM, respiratory and peripheral muscle strength, functional capacity, exercise capacity and other comorbid disease states, a rehabilitation program appropriate for the current impairments of the patient should be planned.

Many guidelines and expert recommendations suggest that PR should be applied to COVID-19 patients with severe pneumonia. Although it is thought that PR to be implemented during this period will help to manage symptoms such as dyspnea, cough, sputum, weaknesses of respiratory and peripheral muscles, immobilization, anxiety and depression; there is still no such data in the context of evidence-based medicine. The evidence obtained from studies evaluating the effectiveness of PR is mostly derived from research performed on individuals with chronic pulmonary diseases.^[15,35,43,47] Research related to rehabilitation in COVID-19 is still sparse.^[48] Yet, the studies mainly focus on the clinical presentation of COVID-19 rather than the efficacy of rehabilitation intervention and their level of evidence is either category 3 or 4.^[49]

RECOMMENDATION 3.2

It is recommended to discontinue PR, if the following conditions occur:^[18,21,22,38,41,50,51]

- Respiratory system
 - Progression in chest imaging $>50\%$ within 24 to 48 hours
 - $SpO_2 < 90\%$ or decrease by $>4\%$ from baseline
 - Respiratory rate >40 breaths/min
 - Ventilator resistance
 - Artificial airway dislodgement or migration

- Cardiovascular system
 - BP <90/60 or >180/90 mmHg, or >20% change compared with baseline
 - HR <40 or >120 beats/min,
 - New arrhythmia and myocardial ischemia
- Nervous system
 - Loss of consciousness
 - Irritability
 - Unable to cope with the program or follow instructions
- Others
 - Body temperature >38.0°C
 - Indication of clinical worsening and general contraindications for exercise
 - Discontinuation of any treatment or removal of monitoring tube connected to the patient
 - Patient-perceived heart palpitations
 - Exacerbation of dyspnea or shortness of breath, and intolerable fatigue.
- For patients having sputum and productive cough, airway clearance techniques should be used. The patient should be taught how to expel the sputum that has accumulated and the central airways should be cleared by maneuvers such as controlled cough and huffing. Devices for personal use such as incentive spirometry, flutter breathing devices, and PEP may also be prescribed to mobilize sputum to central airways and maneuvers such as controlled cough and huffing should be repeated.
- Controlled breathing techniques including diaphragmatic breathing, alternate breathing, and pursed-lip breathing may be used. However, it should be kept in mind that the use of these techniques may increase the respiratory workload during the acute stage and further lead to deterioration of the patient's condition.

RECOMMENDATION 3.4

The use of individual devices, mobilization techniques and exercises prescribed by the PMR specialist should be instructed to the patient by one of the rehabilitation team members. These practices can be performed by PMR physician or existing healthcare personnel (nurse, physiotherapist, occupational therapist, physiotherapy technician, etc.) depending on the present conditions, and availability of human resources and PPE at the facility.^[46] The frequency of PR interventions should be planned according to the patient's status. It is recommended to perform a regular follow-up of the rehabilitation program and revised accordingly considering the patient's clinical status.

Rehabilitation interventions such as positioning, mobilization, ROM exercises can be performed by a team member. Training of PR interventions which require active participation of the patient (such as controlled breathing techniques, using of devices) should be provided by a team member, individually. PR programs may be offered by the use of printed and visual materials, videos, social media, telerehabilitation in the presence of eligible infrastructure.

4. CRITICAL DISEASE

ACUTE RESPIRATORY DISTRESS SYNDROME

RECOMMENDATION 4.1

Comprehensive PR in COVID-19 during ARDS is not required, but rehabilitation principles to avoid adverse effects of immobilization and for secretion management should be followed.

RECOMMENDATION 3.3

Although the PR program is individualized according to the condition of the patient, it should basically include similar techniques used in all other non-COVID-19 pneumonia types.

- During this period, the signs and findings listed in Recommendation 3.2 should be closely followed.
- Positioning in bed and frequent position changes should be made; in cases with severe pneumonia and/or using non-invasive mechanical ventilators (NIMVs), a semi-sitting or sitting position is recommended to prevent the risk of aspiration. While positioning, aids such as pillows can be used to minimize effort.
- Active or active-assisted ROM exercises can be applied.
- Mobilization as soon as possible (sitting position in bed, sitting on the edge of the bed, transfer to the chair, and standing with the help of assistive devices, such as walker, tilt table, etc.) should be ensured.
- Progressive ambulation of patients who can tolerate mobilization with the help of walking aids should be attempted.
- Airway clearance techniques should not be used in patients who have a dry cough and no sputum.

Pulmonary rehabilitation is not appropriate or safe for ARDS patients in respiratory stress whose $\text{PaO}_2/\text{FiO}_2 < 300$ mmHg (on ventilator settings or PEP/continuous positive airway pressure (CPAP) of > 5 cmH_2O), and mostly have fever ($> 38^\circ\text{C}$), respiratory rate of > 40 breaths/min, oxygen saturation of $< 90\%$ despite oxygen support, HR < 40 or > 120 beats/min, or have variable arrhythmia, BP $< 90/60$ or $> 180/90$ mmHg, who are in shock, deep sedation and who has radiological progression more than 50% in the last 24-48 hours.^[21,22,38,41,50,51]

- Pulmonary rehabilitation is not appropriate and safe in ARDS patients who are in prone position which is preferred to increase oxygenation for 12 to 16 hours.
- During the following rehabilitation interventions, vital and respiratory stress signs should be closely monitored.
- In patients requiring secretion management, these procedures should be done in negative pressure rooms and/or isolated rooms and closed systems, as this may cause aerosol formation. Mechanical insufflator and exsufflator (MI-E) and oscillating devices, which are other airway cleaning techniques used in the intensive care, should be used very carefully considering the benefit/harm due to aerosol formation.
- Patients should be carefully inspected for pressure ulcers. Attention should be paid to the proper positioning.
- Range of motion exercises in 10-15 repetitions/day for each joint should be performed when the patient is in the supine position. When the patients can participate, they can do active or assisted exercises.
- Mobilization exercises and self-care activities can be started when the general condition and cooperation of the patient allows.
- Electrical stimulation modalities such as NMES can be used in patients with muscle weakness for large muscle groups at an intensity that will not cause any burns.

RECOMMENDATION 4.2

The patient who is recovering and/or in the weaning period should be evaluated together with the PMR physician and the ICU physicians about the eligibility and the timing of rehabilitation. If the patient fulfills the eligibility criteria for PR (Recommendation 3.1 and 3.2) the recommendations

for COVID-19 patients with severe pneumonia should be followed.

RECOMMENDATION 4.3

After the critical disease and ICU period, the patient who has functional limitations, such as difficulty in mobility or other activities of daily living, and persistent symptoms should be evaluated and a patient-specific rehabilitation program is planned by the PMR specialist.

During the evaluation process, the general condition of the patient, the blood tests, radiological findings, respiratory parameters, joint ROM, muscle strength, respiratory muscle strength, activities of daily living, functional capacity and other existing comorbid conditions are considered. At this transition stage, respiratory muscle exercises (inspiratory muscle training, expiratory muscle training), breathing strategies (controlled breathing techniques, airway clearance techniques) and aerobic training, progressive resistive exercises and shoulder girdle and upper extremity exercises can be progressively recommended only if the patient's status allows. For PR, criteria outlined in above recommendations should be followed.

PULMONARY REHABILITATION AFTER COVID-19

RECOMMENDATION 5.1

Comprehensive PR is indicated for individuals with ongoing fatigue, respiratory symptoms, diminished activities of daily living, reduced exercise tolerance, and limited functionality 6 to 8 weeks following discharge.

As of April 15th, 2021, the number of individuals infected with SARS-CoV-2 virus over the world exceeded 136 million. At the beginning of the pandemic, COVID-19 was thought of as a disease that affects primarily the pulmonary system. Soon after, it has been understood that, it is a multisystem disease with complications affecting the cardiac, renal, gastrointestinal, nervous, endocrine and musculoskeletal systems. However, pulmonary involvement still remains significant. A more serious prognosis is expected in patients who have complications related to pulmonary involvement. In many studies, prolonged symptoms of fatigue, dyspnea and breathlessness are reported in patients besides symptoms related to other systems.^[52-54] These complications, particularly pulmonary related problems, have the potential to impair the patient's quality of life by limiting their daily living activities,

and reduce exercise capacity. Thus, all these reveal the need for comprehensive PR in patients after COVID-19.

The current guidance for routine post-exacerbation PR for COPD is 4 weeks post discharge; however, the recommendation to delay PR for COVID-19 patients until 6 to 8 weeks post-discharge was based upon the following considerations. First, there is a lack of data about the decay of the levels of infection in the COVID-19 survivor. Second, there is data suggesting that, a proportion of physical recovery will have occurred in ARDS survivals in two months.^[55] Also, it may be a burden for services to recruit patients at an earlier time after discharge.^[56] Hospitalized patient with COVID-19 including the survivors of acute respiratory failure should be evaluated at 6 to 8 weeks following hospital discharge. Multiple re-assessments may be required at different time points such as 3 and 6 months after discharge, and a PR program can be initiated according to the individual needs of the patient.

RECOMMENDATION 5.2

Patients who exhibit signs of respiratory impairment whether accompanying musculoskeletal, swallowing, functional, cognitive or psychosocial problems exist or not are the main candidates for a comprehensive PR program. A detailed information on comprehensive PR program exists in the introduction section.

Particular attention should be paid to the following criteria:

1. Patients who have been treated in the ICU either with or without IMV.
2. Patients who needed high level of oxygen therapy and who have been treated with or without non-invasive ventilation.
3. Patients with persisting respiratory symptoms and diminished respiratory function due to COVID-19 either treated in hospital or at home.
4. Individuals with special conditions (older age, immunocompromised, having neurological, pulmonary, cardiovascular, metabolic and other systemic diseases etc.).

PR candidates may also have:

1. Joint contractures, muscle weakness, physical deconditioning
2. Widespread pain

3. Limitation in activities of daily living
4. Neurological conditions and complications due to COVID-19 such as critical-illness neuromyopathy, stroke, tremor
5. Cardiac conditions and complications due to COVID-19
6. Swallowing and communication impairments
7. Psychosocial impairments
8. Impaired quality of life

Patients with the following criteria should be excluded:

1. Patients with suspected active COVID-19 infection.
2. Patients who predominantly have unstable systemic problems such as neurological, cardiac, renal etc. due to COVID-19.
3. Patients with musculoskeletal difficulties that preclude exercise (e.g., severe arthritis or severe peripheral vascular disease).
4. Patients with severe frailty in the need of palliative care.
5. General contraindications for PR such as angina pectoris, recent myocardial infarction, severe pulmonary hypertension, congestive heart failure, unstable diabetes, inability to do exercise due to orthopedic or other reasons, psychiatric illness, dementia, cognitive dysfunction.^[57]
6. Severe exercise-induced hypoxemia which cannot be corrected with O₂ supplementation.
7. Lack of motivation, non-adherence, unwilling to give consent.

PR program should be withdrawn or adjusted in the following conditions:

1. Body temperature >37.2°C at rest^[58]
2. Worsening dyspnea
3. Borg dyspnea score >3 at rest
4. Exercise is interrupted if the patient develops severe dyspnea (eg, Borg score ≥7)^[59]
5. Respiratory rate >30 breaths/min at rest
6. Resting SpO₂ <90% on oxygen therapy
7. Oxygen should be supplemented or titrated when SpO₂ <88% or a relative reduction of 2%-5% occurs^[59]
8. Resting BP <90/60 or >180/90 mmHg
9. Resting HR <40 or >120 beat/min

10. Intercurrent arrhythmias
11. Other conditions that may be indication of clinical worsening and general contraindications for exercise.

RECOMMENDATION 5.3

Comprehensive PR should be applied in a well-appointed PR setting. After the assessment and program prescription by the PMR physician, an approach can be made with a core rehabilitation team consisting of PMR physician, nurse, physiotherapist and occupational therapist, as well as with a wider rehabilitation team including psychologist, nutritionist, speech and swallowing therapist, etc. according to the identified deficits and problems of the patient.

Although the core rehabilitation team is mostly sufficient, individualized protocols with expanded, systematic and organized determinants are one of the most important steps of a successful PR.

RECOMMENDATION 5.4

The PR setting for the post-COVID-19 patients should be chosen based on the clinical status, existing impairments and characteristics of the patients.

Inpatient rehabilitation may be indicated in patients with tracheostomy, CPAP or bilevel positive airway pressure (BIPAP) therapy, requiring high levels of oxygen therapy at rest, extra-pulmonary comorbidities or severe limitations in the activities of daily life. PR as an outpatient setting may be appropriate for the patients who are sufficient to handle their daily activities and without transportation limitations. A home setting may be used in clinically stable patients and who do not require monitorization by a health professional during sessions.

The delivery of PR program may vary due to the PR setting and the ongoing risk of contagiousness such as the usual face-to-face intervention, visual tools including brochures, booklets, and telemedicine interventions. Since telerehabilitation is a novel approach for many healthcare facilities, special considerations should be taken into account for the implementation of PR via telerehabilitation. In patients who are appropriate for home-based PR, telerehabilitation could be used, when there is a need for social distancing, there are accessibility, transportation or cost issues, or there is no available PR program. For the implementation of telerehabilitation, there should be sufficient technological set-up both at the facility and the patient's home and adequate caregiver support if

needed; the patient should be capable of understanding and following instructions via technological means, and vital parameters (SpO₂, HR, BP, respiratory rate) and the symptoms should be recorded by the patient/caregiver before the telerehabilitation session, and informed and monitored.

RECOMMENDATION 5.5

The patients should be questioned to ensure that they do not have any symptoms of recurrent COVID-19 and any of the exclusion criteria for PR before the assessment and rehabilitation program.

In case they have symptoms of COVID-19, they should be advised to self-isolate for 10 days or in line with the current guidance. If there are no symptoms indicating a new infection, patient can start the program. The contagiousness of COVID-19 is shown to be lasting up to 10 days usually and up to 30 days in some severe cases. Since the assessments and rehabilitation program are planned to be performed 6 to 8 weeks after the discharge, there is no need for swab testing unless recurrent/new infection is suspected. Currently, results of antibody testing should not change the program planning.

RECOMMENDATION 5.6

All patients should be thoroughly assessed as recommended by the PR guidelines before the PR program, and multi-system examination using biopsychosocial approach should be performed considering the various impacts of COVID-19, as well.

Assessments are done mainly on six domains:

1. Symptoms
 - a. Dyspnea (e.g., rated perceived exertion by Borg, or Medical Research Council).
 - b. Fatigue
 - c. Pain
 - d. Weakness
2. Pulmonary function testing
3. Physical capacity assessment
 - a. Exercise test/Cardiopulmonary exercise test (ET/CPET)
 - b. Field tests of exercise (e.g., 2-min/6-min walk tests; shuttle test)
 - c. Peripheral and inspiratory muscle strength^[60]
 - d. Balance

4. Functionality
 - a. Activities of daily living; (e.g., Post-COVID-19 Functional Status Scale, Barthel, Functional Independence Measure-FIM, Katz Index of Independence in Activities of Daily Living)
 - b. Bedside assessments (e.g., Chelsea Physical Assessment Tool, Short Physical Performance Battery Test, sit-to-stand test).^[61]
5. Psychological status
 - a. Hospital Anxiety Depression Scale, Beck Depression Inventory/Beck Anxiety Inventory, etc.
6. Quality of life
 - a. EuroQol-5 Dimension (EQ-5D), St. George's Respiratory Questionnaire (SGRQ), etc.

According to the severity of the disease and length of hospitalization, there may be symptoms and impairments other than those of the respiratory system. Therefore, each patient's further evaluation should be individual based on the existing impairments and symptoms and may include nutritional, cognitive, orofacial including swallowing and speech, systemic, particularly cardiac and neurological assessments. Vocational assessment and returning to work strategies should be also considered.

RECOMMENDATION 5.7

During the assessments and rehabilitation program, guidelines should be followed regarding the prevention of spread of the disease such as social distancing, hygiene of the patient and the facility, even if the patient is considered to be non-contagious.

All HCWs involving in the PR process of COVID-19 patients should wear appropriate PPE using proper techniques to avoid self-contamination. Even if the patients considered to be non-contagious, eye protection, donning of gloves and disposable gown besides face masks should be used during aerosol-generating procedures. All patients should wear surgical masks during rehabilitation. If possible, exercise testing rooms should be equipped with negative pressure systems and HEPA filters. Otherwise, exercise testing rooms should be aerated well after each patient and there should be at least 30 min between two patients' tests and assessments. All surfaces should be sanitized after each patient's assessment and rehabilitation

session. A unique set of principles should be implemented for the exercise areas, as well. The number of patients rehabilitated at the same time should be limited to allow social distancing and depends on the field's size. The waiting room and appointments should be arranged accordingly to ensure necessary social distancing.

The Strengths of the Guideline

The number of COVID-19 cases in our country has been increasing, similar to the world. This guideline is prepared by taking the health practices in our country into consideration. It aims to provide guidance primarily to PMR specialists and to all physicians. PMR specialists taking part in the development of this guideline are experienced in PR and they rehabilitate COVID-19 patients in both acute and chronic stages in different hospitals across Turkey. Some have gained experiences in treating COVID-19 patients as their primary physicians, as well. This guideline will create an opportunity for sharing experiences in line with COVID-19 treatment guidelines.

The Limitations of the Guideline

This guideline was prepared with the aim of incorporating the principles of PR with scientific data pertaining to the COVID-19 pandemic which has started nearly a year ago. Although the knowledge and experience about rehabilitation in acute COVID-19 have accumulated, scientific quality is not adequate for a strong level of evidence. Yet, research concerning rehabilitation outcomes on chronic COVID-19 symptoms in long term or outcomes of tele-rehabilitation are still scarce in number. Recommendations may need adaptations according to the condition of the patients, available resources and experience of the healthcare professionals.

The Time and Method for Revision

Following the publication of this second version of the guideline, we aim at revising it, if new evidence about the PR emerges and after evaluating the results of clinical applications and long-term results of the patients within a period of 6 to 12 months.

Acknowledgement

We would like to thank to the PMR specialists who participated in the Delphi round for the development of Recommendation 5, namely Koray Aydemir, Sibel Başaran, Sibel Çağlar, Gülin Fındıkoğlu, İsmail Güneş Gökmen, Gülçin Kaymak Karataş, Nur Kesiktaş, Serap Tomruk Sütbeyaz, Hanife Baykal Şahin, and Zeynep Turan.

Declaration of conflicting interests

The authors declared no conflicts of interest with respect to the authorship and/or publication of this article.

Funding

The authors received no financial support for the research and/or authorship of this article.

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