Phase-Adapted Rehabilitation for Acute Coronavirus Disease-19 Patients and Patient With Long-term Sequelae of Coronavirus Disease-19

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Abstract: Since the beginning of the COVID-19 pandemic in early 2020, many papers have highlighted the need for the rehabilitation of patients with SARS-CoV-2 infection. Most papers refer to the need for respiratory rehabilitation in the acute phase; however, the fact that the infection also affects other organ systems has to be considered in rehabilitation interventions. Long-term symptoms in many cases severely limit activity and participation and alter quality of life, leading to rehabilitation needs. This article proposes a phase-adapted model of linking the acute, postacute, and long-term symptoms of COVID-19 with the well-established matrix of acute, postacute, and long-term rehabilitation services. A review of currently available recommendations for phase-adapted rehabilitation strategies, including the relevance of prehabilitation within this context, is provided.

Key Words: Rehabilitation, COVID-19, SARS-CoV-2, Rehabilitation Services, Rehabilitation Interventions

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Since the beginning of the COVID-19 pandemic in early 2020, many papers have highlighted the need for rehabilitation for patients with SARS-CoV-2 infection. These studies include clinical recommendations and guidelines,[1,2] as well as papers highlighting the need to provide rehabilitation services.[1,3] Early papers referred to the critical illness myopathy as a result of COVID-19 as significant for rehabilitation care.[4,5] This factor reflects the need for rehabilitation in the acute phase, in particular for patients with severe respiratory symptoms and/or needing mechanical ventilation.[6,7] It soon became clear that the infection also affects other organ systems such as the cardiovascular and central nervous systems.[8] Later, long-term symptoms and functional deficits related to the SARS-CoV-2 infection were observed.[9,10] As these symptoms severely limit activity and participation and alter quality of life, rehabilitation is also indicated in this phase. However, many papers lack a clear distinction regarding what types of rehabilitation interventions are appropriate for which phases of the disease and through what kinds of rehabilitation services those treatments should be delivered.

This article recommends linking the acute and long-term symptoms of COVID-19 with the well-established matrix of acute, postacute, and long-term rehabilitation services and also reflects upon the possible relevance of prehabilitation within this context. This study aims at providing greater clarity for clinicians and healthcare planners who need to plan and provide rehabilitation services for patients with COVID-19. This work may also be helpful for structuring scientific papers dealing with the rehabilitation of these patients.

THE PATHOMECHANISM AND COURSE OF COVID-19

The principle *pathomechanisms* of SARS-CoV-2 that lead to COVID-19 have been elucidated, although many details are still unclear.[11] Airway infection via SARS-CoV-2 often includes the distal airways. This type of infection is related to a local immune reaction including epithelial cells, alveolar macrophages, and dendritic cells.[12] In addition, T-cell responses against coronaviruses have been described[13] and start from the antigen presentation of dendritic cells and macrophages. Furthermore, it has been observed that SARS-CoV-2 can directly infect dendritic cells and alveolar macrophages. Via the lymph system, the viral antigen can spread out and activate CD4+ and CD8+ T cells, followed by the activation of B cells producing antibodies.

In patients with severe COVID-19, generalized immune responses were reported, featuring low levels of T cells in the peripheral blood and the presence of proinflammatory cytokines, including. These responses include lymphopenia featuring low levels of T cells in the peripheral blood[14,15] and the presence of proinflammatory cytokines, including interleukin-6, interleukin-10, granulocyte-colony stimulating factor, monocyte chemoattractant protein 1, macrophage inflammatory protein 1α, and tumor necrosis factor-α.[14–16] This can be seen as the starting point of a very complex cascade in the immune response. In addition, high levels of d-dimer and fibrinogen levels have been detected in patients with severe COVID-19, which could explain the occurrence of thrombosis and pulmonary embolism. The response of the immune system and systemic inflammation may be responsible for multiorgan failure.

The predominant symptoms in the *first acute phase* are related to acute infection of the airways and consist of fever, cough, dry cough, sputum production, dyspnea, fatigue, anorexia, chest discomfort, and fever. Patients with severe oxygenation difficulties due to aggravation of the acute respiratory distress syndrome caused by COVID-19 pneumonia may need mechanical ventilation or extracorporeal membrane oxygenation.[17,18] In the *second acute phase* related to the hyperimmune reaction, a variety of symptoms may occur, such as fever, cough, dry cough, sputum production, dyspnea, chest discomfort, headache, fatigue, myalgia, anorexia, nausea, vomiting, abdominal pain, diarrhea, and other gastrointestinal symptoms.[19,20] As suggested by Yuki et al.

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in 2020,[11] the severity of symptoms can be classified as asymptomatic, mild, moderate, severe, or critical (Table 1).

In the *postacute and long-term phase*, besides respiratory insufficiency, a wide range of nonpulmonary manifestations and complications were detailed in a review by Lopez et al.,[21] including the following:

- Alterations in the *nervous system*, such as altered consciousness, headache, dizziness, ataxia, epilepsy, hypogeusia, hyposmia, peripheral nerve dysfunction, neuralgia,[22] agitation and confusion, dysexecutive syndrome, and corticospinal tract signs.[23] Acute cerebrovascular events and Guillain-Barré syndrome may also be related to SARS-CoV-2 infection.[24,25]
- Alterations in the *cardiovascular system*, including positive antiphospholipid antibodies, lower limb ischemia, hand-digit ischemia,[26] pulmonary embolism, other venous thromboembolic events, arterial thrombotic events (ischemic stroke),[27] myopericarditis and heart failure,[28] decompensation of underlying heart failure, ST-segment elevation, cardiogenic shock,[29] and acute cardiac injury.[30]
- *Musculoskeletal* complications such as rhabdomyolysis.[31,32]
- Alterations of *gastrointestinal tract* functions that include liver injury (aspartate aminotransferase, alanine aminotransferase, gamma-glutamyl transferase, or alkaline phosphatase level abnormality), pancreatic injury and diarrhea,[33] and digestive symptoms (decreased appetite, vomiting, diarrhea, and abdominal pain).[34]
- *Skin and eye* symptoms, such as erythematous rash, widespread urticaria, chickenpox-like vesicles,[35] and conjunctivitis.[36,37]

Predominant symptoms seem to include overall reduced physical performance, fatigue, alterations of taste and smell, concentration, and coordination.[19,20] In addition, chronic widespread pain, muscle weakness, and a depressive mood have been described to occur in many cases.[38,39] These symptoms and functional impairments were proposed by Kemp et al.[39] as features of post-COVID-19 syndrome. According to the study of Carfi et al.,[40] the most frequent symptoms in post-COVID follow-up patients are fatigue (53.1%), dyspnea (43.4%), joint pain (27.3%), and chest pain (21.7%). Another study also reported fatigue or muscle weakness (63%), sleep difficulties (26%), and anxiety and depression (23%) in patients 6 mos after being discharged from the hospital.[41]

The overall need for rehabilitation after severe and critical COVID-19 was demonstrated by Ahmed et al.,[42] who showed severe alteration of the health status in all dimensions of the Short Form-36 questionnaire. More detailed overviews of neurologic and neuropsychiatric complications were reported by Varatharaj et al.[43] and Ellul et al.,[44] including ischemic stroke, intracerebral hemorrhage, and cerebral venous sinus thrombosis, in most cases beginning 10 days after the onset of respiratory symptoms.[44] Guillain-Barre syndrome has also been observed during the acute phase of COVID-19. Furthermore, vasculitis of the central nervous system, unspecified encephalopathy, and clinical sign of encephalitis were observed.[43] Neuropsychiatric disorders like psychosis, neurocognitive (dementia-like) syndrome, and other psychiatric disorders were likewise described.[43] In a number of cases, nonspecific altered mental status occurred.[44]

TABLE 1. Classification of COVID-19 patients[9] (with permission)

Asymptomatic	COVID nucleic acid test positive. Without any clinical symptoms and signs and the chest imaging is normal
Mild	Symptoms of acute upper respiratory tract infection (fever, fatigue, myalgia, cough, sore throat, runny nose, sneezing) or digestive symptoms (nausea, vomiting, abdominal pain, diarrhea)
Moderate	Pneumonia (frequent fever, cough) with no obvious hypoxemia, chest CT with lesions.
Severe	Pneumonia with hypoxemia (SpO_2 <92%)
Critical	Acute respiratory distress syndrome, may have shock, encephalopathy, myocardial injury, heart failure, coagulation dysfunction, and acute kidney injury

PHASE MODEL FOR THE REHABILITATION OF PATIENTS DURING AND AFTER COVID-19

According to the World Health Organization, rehabilitation is an integral part of Universal Health Coverage and should be implemented in acute, postacute, and long-term care (including community-based rehabilitation services).[45] However, rehabilitation is not a part of Universal Health Coverage in many countries.[46,47]

Over the course of COVID-19, the symptoms and functional impairments evolve, and thus, rehabilitation approaches must be adapted to the various phases of the disease (Fig. 1).[48] Connected to this, interventions also must be described according to the services that are suitable to treat/rehabilitate patients according to the disease phase. In hospitals including intensive care, support for respiration functions and early mobilization have to be prioritized. In the postacute phase, which can be treated in either hospitals or postacute rehabilitation centers, pulmonary and cardiovascular training and further mobilization are of primary importance. Mental health support is also required in the case mental health–related issues are diagnosed.[49,50] In the long-term phase (e.g., in rehabilitation centers and community-based rehabilitation units), rehabilitation should focus on all persisting symptoms like fatigue, reduced performance, alterations of taste and smell, dysfunction of concentration and coordination, and musculoskeletal symptoms.

More specifically, the following phase model provides phase-adapted service types. Starting from the onset of the disease, in all severe and critical cases, *acute rehabilitation interventions* are needed.[7] These interventions predominantly aim at improving respiratory functions and preventing thrombosis, contractures, pressure sores, and cardiovascular deconditioning. In patients with mechanical ventilation, respiration therapy (optimally performed by specialized physiotherapists) is important. This should be started during ventilation and is crucial in the weaning phase. Other symptoms frequently occurring in patients with longer-lasting immobilization and mechanical ventilation are, among others, sarcopenia, contractures, cardiovascular dysregulation, and critical illness polyneuropathy. For prevention of these symptoms, daily physiotherapy and occupational therapy should be carried out.[51–54] After discharge from the intensive care unit or from the hospital, *postacute rehabilitation* should begin. Such interventions must be adapted to the individual symptoms and functional deficits and will mainly involve training in ventilation, improving physical fitness, treating psychiatric illness (mood and anxiety)[55] and

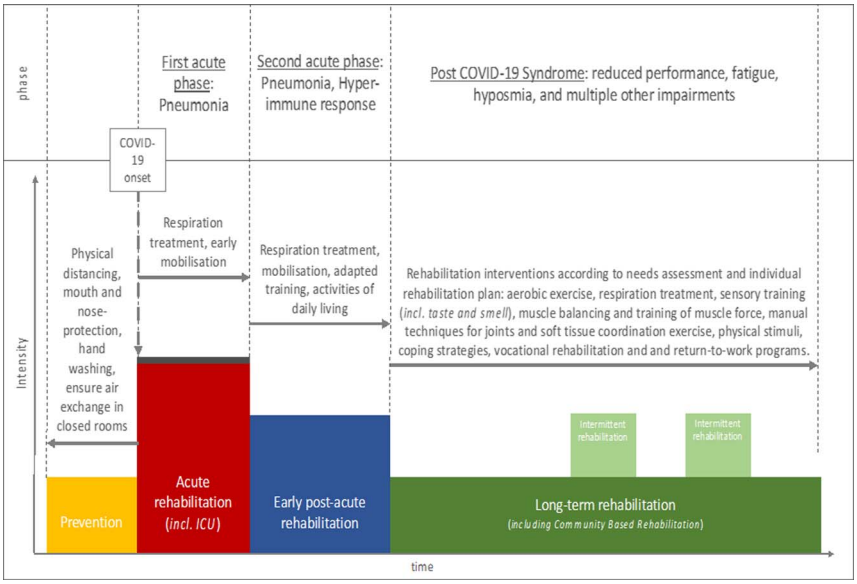

FIGURE 1. Model for phase-specific and phase adapted rehabilitation responses for patients with SARS-CoV-2 infection and Post-COVID-19-Syndrome (from Nugraha et al.,[48] modified with permission under a Creative Commons Attribution CC-BY-4.0 International License).

cognitive impairments (e.g., dysexecutive syndrome),[56] and helping patients cope with the disease.[1] Training of activities related to daily living will be one part of rehabilitation in this phase. Depending on local health system regulations and organization, postacute rehabilitation may be performed within the hospital or in independent rehabilitation units outside the hospital. If patients develop the so-called post-COVID syndrome, *long-term rehabilitation measures* will be needed. Here, rehabilitation strategies may address a wide range of symptoms and, therefore, must be tailored to the individual situation. Problems may include fatigue, reduced cardiovascular performance, respiratory insufficiency, depressive symptom, disturbances of smell and taste, muscle weakness and pain, deficits in concentration and coordinative functions, and others. Of course, in all phases, interventions must follow systematic assessment and assignment.

The above-described model will help medical professionals develop phase-adapted rehabilitation plans and interventions, as well as provide greater clarity for healthcare planners who have to adapt health services to the needs of individuals who have been affected by COVID-19.[3,57]

Looking at the literature and applying the principles of rehabilitation medicine, the following strategies and interventions can be linked to the above-described phases of patients with COVID-19 and post-COVID-19 syndrome:

- *Acute rehabilitation*: In the acute phase and during intensive care, treatments of respiratory functions are the most relevant.[1,7] Specific precautions for the prevention of virus spread must be followed, including use of appropriate personal protective equipment and avoiding respiration techniques with a high production of aerosols (e.g., no coughing techniques). Best practice recommendations for the early rehabilitation of COVID-19 patients has been proposed by Liebl et al.[7] The other interventions do not differ from the standards of rehabilitation techniques used in the intensive care unit.[58,59] Acute rehabilitation is strictly bound to the hospital and should be delivered there.
- *Postacute rehabilitation*: In the postacute phase, treatment of the acute phase should be continued. However, more active treatments can be applied, and the training level can be increased. The wide range of possible specific symptoms and functional deficits must be addressed by a multiprofessional rehabilitation team, including physical and rehabilitation medicine, physiotherapy, occupational therapy, speech and language therapy, psychotherapy and neuropsychology, social workers, and rehabilitation nursing (see Table 2). Table 2 was derived based on a pragmatic approach in this phase. Coping strategies must be supported, and perspectives for the upcoming period of life should be developed together with the patient. Postacute rehabilitation may be delivered in inpatient rehabilitation centers, day clinics, or well-equipped outpatient rehabilitation services.

As clinical trials and outcome studies on rehabilitation interventions have not been published yet (because of the short period of the existence of the disease), recommendations for rehabilitation interventions must be based on studies performed with patients presenting other diseases expressing similar symptoms and functional impairments. This is particularly true for long-term rehabilitation. Thus, the recommendations here are based on textbook standards and evidence from other patient groups showing similar dysfunctions.

- *Long-term rehabilitation care*: In long-term rehabilitation care, all persistent symptoms and functional deficits must be addressed (for an overview and a checklist, see Liebl et al.[7]). In the case of persisting symptoms, diagnostics must be done or repeated—that is, analysis of lung functions and cardiovascular function. Besides treating symptoms and increasing performance, vocational rehabilitation and return-to-work programs are significantly relevant. In principle, this phase can be seen as a continuation of the postacute rehabilitation phase. However, it may also be performed in outpatient or day clinic settings.

TABLE 2. Postacute and long-term rehabilitation in post-COVID-19 syndrome: Pragmatic approaches

No.	Symptoms, Dysfunctions, Tasks	Qualified Therapists	Interventions
1.	Overall alterations of bodily functions (including mental functions), activity limitations and participation restrictions, and socio-medical changes	Physical and rehabilitation medicine physician	Taking case history (anamnesis), physical examination, functional assessment, assessment questionnaires
2.	Assessing patient's needs and preferences, prioritization-informed consensus	Physical and rehabilitation medicine physician	Setting up rehabilitation plan assignment for interventions, team-integrated delivery of interventions, follow-up[60]
3.	Fatigue, reduced energy and drive, depressive symptoms, sleep disturbance	Physiotherapists, psychotherapists, occupational therapists	Medical training: aerobic training, hydrotherapy and thermotherapy, coping and ADL strategies (including management of energy and drive functions)[61]
4.	Disturbances in concentration and memory functions	Occupational therapists, neuropsychologists	Training of concentration and memory[62,63]
5.	Alterations of smell and taste	Speech and language therapists or occupational therapists	Training of smell and taste, smell/taste diaries with follow-up[64]
6.	Generalized body pain	Physiotherapists	Muscular balancing, medical training therapy (including aerobic training)[65]
7.	Alterations of coordination (including gait), disturbances of proprioception	Physiotherapists, occupational therapists	Balance training, gait training, postural training, sensory integration, training of activities of daily living[66,67]
8.	Muscle weakness, muscular pain (including muscle soreness, rhabdomyolysis)	Physiotherapists	Muscular balancing, movement exercises, dynamic muscle training, medical training therapy.[68,69] Soft-tissue techniques like Triggerpoint therapy, release techniques[70,71]
9.	Respiratory insufficiency (also including deterioration generation of voice)	Physiotherapists, speech and language therapists	Respiration therapy, medical training therapy (including aerobic training), speech therapy[72,73]
10.	Cardiovascular insufficiency, reduced aerobic capacity	Physiotherapists	Medical training therapy (including aerobic training)[74]
11.	Thrombo-embolic events		Treatment according to affected organs and functions[75]
12.	Gastrointestinal symptoms	Physiotherapists, massage therapists, dieticians	Bowel massage, connective tissue massage, massage devices, dietary advice[76]
13.	Dermal symptoms such as itching or disturbances of skin microcirculation	Physiotherapists, massage therapists	Carbon dioxide (CO_2) application (bath or "dry gas "application)[77]
14.	Manifestant depression, anxiety and other mental symptoms	Psychotherapists	Psychotherapy[78]
15.	Restrictions of vocational performance, unfitness to work	Occupational therapists, social workers	Vocational rehabilitation, social counselling[79]

Lastly, *prehabilitation interventions* may be useful for SARS-CoV-2 infections. Of course, before SARS-CoV-2 infection, prevention is the most important strategy, including physical distancing, hand washing, and wearing mouth and nose protection.[80] However, considering the risk factors for the severe and critical courses of the disease, other measures may be important, such as physical conditioning (i.e., aerobic exercise), increasing muscle fitness, and training of respiratory functions, which may help to mitigate the severity of COVID-19. This could be important advice for the general population, particularly those in lock-down situations. However, no evidence-based data is available yet to support such general recommendations.

Data published by World Health Organization show that around 63% of rehabilitation services have been disrupted worldwide.[81] Reasons for this disruption might include the need to use the capacities of rehabilitation centers to treat patients with COVID-19, the reduced availability of rehabilitation professionals due to COVID-infections, and a lack of personal protection materials. Priority shifts in financial management may also play a role. Even though no relevant studies are available yet, it can be assumed that the interruption of rehabilitation has had negative effects on patients in need, for example, those suffering from neurologic disorders, cancer or cancer after surgery, trauma, and cardiovascular events. Considering the risk of SARS-CoV-2 infection, there is no need to interrupt rehabilitation treatments as long as sufficient protection and hygiene are realized.

DISCUSSION

The applied framework distinguishing between acute, postacute, long-term rehabilitation and prehabilitation seems to be feasible for describing the different phases of rehabilitation needs and interventions over the course of COVID-19

(including post-COVID-19 syndrome). This framework is compatible with other frameworks for rehabilitation phases, such as the German phase model of neurorehabilitation.[82] Phase A is a part of acute care, phases B and C mainly reflect postacute rehabilitation, and phases D and E describe long-term rehabilitation interventions. However, the interfaces between the rehabilitation service phases may not be sufficiently defined. These phases also depend on the health system in a specific country. For acute rehabilitation, the start and end points are clearly defined, as they are connected to the definition of hospital care, which is bound to the need for 24-hr supervision and medical and nursing care.[83] Thus, postacute rehabilitation should start immediately (or soon) after discharge from the hospital. However, the end point of postacute rehabilitation and the starting point of long-term rehabilitation are not defined and are mainly related to the rules of service delivery in the respective health system. It is important to note that the question of whether a patient is still infectious should not be a contraindication for transferring to a postacute rehabilitation service, as long as appropriate infection prevention and control measures are followed.

With regard to planning and performing rehabilitation among patients with SARS-CoV-2 infection and post-COVID-19 syndrome, the linking of rehabilitation strategies and interventions to the phase model of rehabilitation is considered useful. By using this phase model, rehabilitation interventions required during the acute phase, featuring symptoms that are predominately related to airway infection and the early hyperimmune response, can be differentiated from the treatment of conditions and functional problems addressed as post-COVID-19 syndrome. This approach may lead to greater clarity for publications dealing with the rehabilitation of patients suffering from COVID-19 but also for clinicians and health care planners who need to plan and provide rehabilitation services.

REFERENCES

1. PAHO: Rehabilitation considerations during the COVID-19 outbreak. 2020. Available at: https://iris.paho.org/bitstream/handle/10665.2/52035/NMHMHCOVID19200010_eng.pdf?sequence=6&isAllowed=y. Accessed October 2, 2020
2. Cochrane: Cochrane rehabilitation REH-COVER (rehabilitation—COVID-19 evidence-based response) action. 2020. Available at: https://www.cochrane.org/news/cochrane-rehabilitation-reh-cover-rehabilitation-covid-19-evidence-based-response-action. Accessed October 2, 2020
3. Gutenbrunner C, Stokes EK, Dreinhofer K, et al: Why rehabilitation must have priority during and after the COVID-19-pandemic: A position statement of the Global Rehabilitation Alliance. *J Rehabil Med* 2020;52:jrm00081
4. Versace V, Sebastianelli L, Ferrazzoli D, et al: Case report: Myopathy in critically ill COVID-19 patients: A consequence of hyperinflammation? *Front Neurol* 2021;12:625144
5. Yonter SJ, Alter K, Bartels MN, et al: What now for rehabilitation specialists? Coronavirus disease 2019 questions and answers. *Arch Phys Med Rehabil* 2020;101:2233–42
6. Kiekens C, Boldrini P, Andreoli A, et al: Rehabilitation and respiratory management in the acute and early post-acute phase. "Instant paper from the field" on rehabilitation answers to the COVID-19 emergency. *Eur J Phys Rehabil Med* 2020;56:323–6
7. Liebl ME, Gutenbrunner C, Glaesener JJ, et al: Early rehabilitation in COVID-19—Best practice recommendations for the early rehabilitation of COVID-19 patients. *Phys Med Rehabilitationsmedizin Kurortmedizin* 2020;30:129–34
8. Romagnoli S, Peris A, De Gaudio AR, et al: SARS-CoV-2 and COVID-19: From the bench to the bedside. *Physiol Rev* 2020;100:1455–66
9. Salawu A, Green A, Crooks MG, et al: A proposal for multidisciplinary tele-rehabilitation in the assessment and rehabilitation of COVID-19 survivors. *Int J Environ Res Public Health* 2020;17:4890
10. Lopez C, Closa C, Lucas E: Telemedicine in rehabilitation: Post-COVID need and opportunity. *Rehabilitacion (Madr)* 2020;54:225–7
11. Yuki K, Fujiogi M, Koutsogiannaki S: COVID-19 pathophysiology: A review. *Clin Immunol* 2020;215:108427
12. Yoshikawa T, Hill T, Li K, et al: Severe acute respiratory syndrome (SARS) coronavirus-induced lung epithelial cytokines exacerbate SARS pathogenesis by modulating intrinsic functions of monocyte-derived macrophages and dendritic cells. *J Virol* 2009;83:3039–48
13. Fujimoto I, Pan J, Takizawa T, et al: Virus clearance through apoptosis-dependent phagocytosis of influenza A virus–infected cells by macrophages. *J Virol* 2000;74:3399–403
14. Qin C, Zhou L, Hu Z, et al: Dysregulation of immune response in patients with coronavirus 2019 (COVID-19) in Wuhan, China. *Clin Infect Dis* 2020;71:762–8
15. Zhou YG, Fu BQ, Zheng XH, et al: Pathogenic T-cells and inflammatory monocytes incite inflammatory storms in severe COVID-19 patients. *Natl Sci Rev* 2020;7:998–1002
16. Huang C, Wang Y, Li X, et al: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020;395:497–506
17. Barbaro RP, MacLaren G, Boonstra PS, et al: Extracorporeal membrane oxygenation support in COVID-19: An international cohort study of the Extracorporeal Life Support Organization Registry. *Lancet* 2020;396:1071–8
18. Haiduc AA, Alom S, Melamed N, et al: Role of extracorporeal membrane oxygenation in COVID-19: A systematic review. *J Card Surg* 2020;35:2679–87
19. Bennett S, Tafuro J, Mayer J, et al: Clinical features and outcomes of adults with coronavirus disease 2019: A systematic review and pooled analysis of the literature. *Int J Clin Pract* 2020;e13725. doi: 10.1111/ijcp.13725
20. Singhal T: A review of coronavirus disease-2019 (COVID-19). *Indian J Pediatr* 2020;87:281–6
21. Lopez M, Bell K, Annaswamy T, et al: COVID-19 guide for the rehabilitation clinician: A review of nonpulmonary manifestations and complications. *Am J Phys Med Rehabil* 2020;99:669–73
22. Mao L, Jin H, Wang M, et al: Neurologic manifestations of hospitalized patients with coronavirus disease 2019 in Wuhan, China. *JAMA Neurol* 2020;77:683–90
23. Helms J, Kremer S, Merdji H, et al: Neurologic features in severe SARS-CoV-2 infection. *N Engl J Med* 2020;382:2268–70
24. Toscano G, Palmerini F, Ravaglia S, et al: Guillain-Barre syndrome associated with SARS-CoV-2. *N Engl J Med* 2020;382:2574–6
25. Velayos Galan A, Del Saz Saucedo P, Peinado Postigo F, et al: Guillain-Barre syndrome associated with SARS-CoV-2 infection. *Neurologia* 2020;35:268–9
26. Zhang Y, Xiao M, Zhang S, et al: Coagulopathy and antiphospholipid antibodies in patients with COVID-19. *N Engl J Med* 2020;382:e38
27. Klok FA, Kruip MJHA, van der Meer NJM, et al: Incidence of thrombotic complications in critically ill ICU patients with COVID-19. *Thromb Res* 2020;191:145–7
28. Inciardi RM, Lupi L, Zaccone G, et al: Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020;5:819–24
29. Fried JA, Ramasubbu K, Bhatt R, et al: The variety of cardiovascular presentations of COVID-19. *Circulation* 2020;141:1930–6
30. Wang D, Hu B, Hu C, et al: Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. *JAMA* 2020;323:1061–9
31. Li YC, Bai WZ, Hashikawa T: The neuroinvasive potential of SARS-CoV2 may play a role in the respiratory failure of COVID-19 patients. *J Med Virol* 2020;92:552–5
32. Jin M, Tong Q: Rhabdomyolysis as potential late complication associated with COVID-19. *Emerg Infect Dis* 2020;26:1618–20
33. Wang F, Wang H, Fan J, et al: Pancreatic injury patterns in patients with coronavirus disease 19 pneumonia. *Gastroenterology* 2020;159:367–70
34. Han C, Duan C, Zhang S, et al: Digestive symptoms in COVID-19 patients with mild disease severity: Clinical presentation, stool viral RNA testing, and outcomes. *Am J Gastroenterol* 2020;115:916–23
35. Recalcati S: Cutaneous manifestations in COVID-19: A first perspective. *J Eur Acad Dermatol Venereol* 2020;34:e212–3
36. Loffredo L, Pacella F, Pacella E, et al: Conjunctivitis and COVID-19: A meta-analysis. *J Med Virol* 2020;92:1413–4
37. Chen L, Liu M, Zhang Z, et al: Ocular manifestations of a hospitalised patient with confirmed 2019 novel coronavirus disease. *Br J Ophthalmol* 2020;104:748–51
38. Rogers JP, Chesney E, Oliver D, et al: Psychiatric and neuropsychiatric presentations associated with severe coronavirus infections: A systematic review and meta-analysis with comparison to the COVID-19 pandemic. *Lancet Psychiatry* 2020;7:611–27
39. Kemp HI, Corner E, Colvin LA: Chronic pain after COVID-19: Implications for rehabilitation. *Br J Anaesth* 2020;125:436–40
40. Carfì A, Bernabei R, Landi F, Gemelli Against COVID-19 Post-Acute Care Study Group: Persistent symptoms in patients after acute COVID-19. *JAMA* 2020;324:603–5
41. Huang C, Huang L, Wang Y, et al: 6-month consequences of COVID-19 in patients discharged from hospital: A cohort study. *Lancet* 2021;397:220–32
42. Ahmed H, Patel K, Greenwood DC, et al: Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: A systematic review and meta-analysis. *J Rehabil Med* 2020;52:jrm00063
43. Varatharaj A, Thomas N, Ellul MA, et al: Neurological and neuropsychiatric complications of COVID-19 in 153 patients: A UK-wide surveillance study. *Lancet Psychiatry* 2020;7:875–82
44. Ellul MA, Benjamin L, Singh B, et al: Neurological associations of COVID-19. *Lancet Neurol* 2020;19:767–83
45. WHO: *Recommendations: Rehabilitation in Health Systems*. Geneva, WHO, 2017. Available at: http://apps.who.int/iris/bitstream/10665/254506/1/9789241549974-eng.pdf

46. Nugraha B, Tani K, Gutenbrunner C: Rehabilitation service assessment and workforce capacity building in Albania—A civil society approach. *Int J Environ Res Public Health* 2020;17:7300
47. Nugraha B, Setyono GR, Defi IR, et al: Strengthening rehabilitation services in Indonesia: A brief situation analysis. *J Rehabil Med* 2018;50:377–84
48. Nugraha B, Wahyuni LK, Laswati H, et al: COVID-19 pandemic in Indonesia: Situation and challenges of Rehabilitation Medicine in Indonesia. *Acta Med Indones* 2020;52:299–305
49. Yang Y, Sun S, Hu S, et al: Comparative effectiveness of multiple psychological interventions for psychological crisis in people affected by coronavirus disease 2019: A Bayesian network meta-analysis. *Front Psychol* 2021;12:577187
50. Putri DU, Tsai YS, Chen JH, et al: Psychological distress assessment among patients with suspected and confirmed COVID-19: A cohort study. *J Formos Med Assoc* 2021. doi: 10.1016/j.jfma.2021.02.014
51. Morley JE: Treatment of sarcopenia: The road to the future. *J Cachexia Sarcopenia Muscle* 2018;9:1196–9
52. Pattanshetty RB, Gaude GS: Critical illness myopathy and polyneuropathy—A challenge for physiotherapists in the intensive care units. *Indian J Crit Care Med* 2011;15:78–81
53. Morris DM, Jenkins GR: Preparing physical and occupational therapists to be health promotion practitioners: A call for action. *Int J Environ Res Public Health* 2018;15:392
54. Harvey LA, Katalinic OM, Herbert RD, et al: Stretch for the treatment and prevention of contracture: An abridged republication of a Cochrane systematic review. *J Physiother* 2017;63:67–75
55. Taquet M, Luciano S, Geddes JR, et al: Bidirectional associations between COVID-19 and psychiatric disorder: Retrospective cohort studies of 62 354 COVID-19 cases in the USA. *Lancet Psychiatry* 2021;8:130–40
56. Alonso-Lana S, Marquie M, Ruiz A, et al: Cognitive and neuropsychiatric manifestations of COVID-19 and effects on elderly individuals with dementia. *Front Aging Neurosci* 2020;12:588872
57. Jiang DH, McCoy RG: Planning for the post-COVID syndrome: How payers can mitigate long-term complications of the pandemic. *J Gen Intern Med* 2020;35:3036–9
58. Reid JC, Unger J, McCaskell D, et al: Physical rehabilitation interventions in the intensive care unit: A scoping review of 117 studies. *J Intensive Care* 2018;6:80
59. Parker A, Sricharoenchai T, Needham DM: Early rehabilitation in the intensive care unit: Preventing physical and mental health impairments. *Curr Phys Med Rehabil Rep* 2013;1:307–14
60. Melvin JL: 2.2 Rehabilitation: Rehabilitation as an intervention. *JISPRM* 2019;2:19
61. Wearden AJ, Dunn G, Dowrick C, et al: Depressive symptoms and pragmatic rehabilitation for chronic fatigue syndrome. *Br J Psychiatry* 2012;201:227–32
62. Nair RD, Lincoln NB: Cognitive rehabilitation for memory deficits following stroke. *Cochrane Database Syst Rev* 2007:CD002293
63. Spreij LA, Visser-Meily JM, van Heugten CM, et al: Novel insights into the rehabilitation of memory post acquired brain injury: A systematic review. *Front Hum Neurosci* 2014;8:993
64. Risberg-Berlin B, Ylitalo R, Finizia C: Screening and rehabilitation of olfaction after total laryngectomy in Swedish patients: Results from an intervention study using the nasal airflow-inducing maneuver. *Arch Otolaryngol Head Neck Surg* 2006;132:301–6
65. Nugraha B, Karst M, Engeli S, et al: Brain-derived neurotrophic factor and exercise in fibromyalgia syndrome patients: A mini review. *Rheumatol Int* 2012;32:2593–9
66. Jørgensen MB, Andersen LL, Kirk N, et al: Muscle activity during functional coordination training: Implications for strength gain and rehabilitation. *J Strength Cond Res* 2010;24:1732–9
67. Stewart KC, Cauraugh JH, Summers JJ: Bilateral movement training and stroke rehabilitation: A systematic review and meta-analysis. *J Neurol Sci* 2006;244(1–2):89–95
68. Forte R, Ditroilo M, Boreham CA, et al: Strength training and gross-motor skill exercise as interventions to improve postural control, dynamic functional balance and strength in older individuals. *J Sports Med Phys Fitness* 2021. doi: 10.23736/S0022-4707.21.11947-4
69. Zouita S, Zouhal H, Ferchichi H, et al: Effects of combined balance and strength training on measures of balance and muscle strength in older women with a history of falls. *Front Physiol* 2020;11:619016
70. Gulick DT: Influence of instrument assisted soft tissue treatment techniques on myofascial trigger points. *J Bodyw Mov Ther* 2014;18:602–7
71. Gulick DT: Instrument-assisted soft tissue mobilization increases myofascial trigger point pain threshold. *J Bodyw Mov Ther* 2018;22:341–5
72. Poletti V, Capozzolo A: Respiratory rehabilitation in the COVID-19 era. *Respiration* 2020;99:461–2
73. Vitacca M, Lazzeri M, Guffanti E, et al: Italian suggestions for pulmonary rehabilitation in COVID-19 patients recovering from acute respiratory failure: Results of a Delphi process. *Monaldi Arch Chest Dis* 2020;90
74. Fidalgo ASF, Farinatti P, Borges JP, et al: Institutional guidelines for resistance exercise training in cardiovascular disease: A systematic review. *Sports Med* 2019;49:463–75
75. Nagel C, Nasereddin M, Benjamin N, et al: Supervised exercise training in patients with chronic thromboembolic pulmonary hypertension as early follow-up treatment after pulmonary endarterectomy: A prospective cohort study. *Respiration* 2020;99:577–88
76. Akbas EUE, Ünver B: Efficacy of connective tissue manipulation on depression, anxiety and related gastrointestinal symptoms. *IJHSR* 2018;8:37–43
77. DeBruler DM, Blackstone BN, Baumann ME, et al: Inflammatory responses, matrix remodeling, and re-epithelialization after fractional CO_2 laser treatment of scars. *Lasers Surg Med* 2017;49:675–85
78. Eddington KM, Burgin CJ, Silvia PJ, et al: The effects of psychotherapy for major depressive disorder on daily mood and functioning: A longitudinal experience sampling study. *Cognit Ther Res* 2017;41:266–77
79. Nivorozhkin A: Overcoming barriers: Effects of entering vocational rehabilitation on labour market outcomes. *Int J Soc Welfare* 2019;28:260–70
80. WHO: Transmission of SARS-CoV-2: Implications for infection prevention precautions. 2020. Available at: https://www.who.int/news-room/commentaries/detail/transmission-of-sars-cov-2-implications-for-infection-prevention-precautions. Accessed October 2, 2020
81. WHO: COVID-19 significantly impacts health services for noncommunicable diseases. 2020. Available at: https://www.who.int/news-room/detail/01-06-2020-covid-19-significantly-impacts-health-services-for-noncommunicable-diseases. Accessed August 20, 2020
82. Schönle PW: *Neurological Rehabilitation in Germany—The Phase Model*. Boston, MA, Springer, 2000
83. Beyer JBM, Glaesener JJ, Liebl ME, et al: Positionspapier zur fachübergreifenden Früh rehabilitation—2. Aktualisierte Auflage. *Phys Med Rehabil Kuror* 2015;25:260–80