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Rehabilitation strategies and neurological consequences in patients with COVID-19: part I

Nilufer Cetisli-Korkmaz[a], Furkan Bilek[b], Tuba Can-Akman[a], Emre Baskan[a], Ilke Keser[c], Esra Dogru-Huzmeli[d], Mehmet Duray[e], Bahar Aras[f] and Buse Kilinc[g]

[a]School of Physiotherapy and Rehabilitation, Pamukkale University, Denizli, Turkey; [b]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Firat University, Elazig, Turkey; [c]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Gazi University, Ankara, Turkey; [d]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Hatay Mustafa Kemal University, Hatay, Turkey; [e]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Suleyman Demirel University, Isparta, Turkey; [f]Faculty of Health Sciences, Department of Physiotherapy and Rehabilitation, Kutahya Health Sciences University, Kutahya, Turkey; [g]School of Health Sciences, Department of Physiotherapy and Rehabilitation, KTO Karatay University, Konya, Turkey

ABSTRACT

Background: The 2019 novel coronavirus disease (COVID-19) pandemic has triggered a devastating effect worldwide. In addition to cardiovascular, pulmonary, and musculoskeletal deconditioning, reports of neurological consequences (e.g. stroke, critical illness polyneuropathy, myopathy, vertigo, headaches, facial palsy, and delirium) are growing increasingly common.
Objectives: Part I of this review of rehabilitation strategies and neurological consequences in patients with COVID-19 sought to consider potential rehabilitation strategies for managing the emerging neurological consequences of COVID-19.
Methods: An exploratory review was conducted that comprised a narrative synthesis in two parts. Part I focused on neurological consequences and physiotherapy and rehabilitation approaches. Part II focused on the general principles of rehabilitation interventions and precautions that should be considered. Literature on the use of the neurorehabilitation approaches was also included in the review.
Results: Rehabilitation services include inpatient and outpatient rehabilitation services. With respect to the recovery of mobility and function, an interdisciplinary approach was generally involved.
Conclusions: A thorough assessment and the development of an individualized, progressive treatment and rehabilitation plan should be implemented by focusing on existing function, any disabilities, the desire to return to participation in society, and maximizing function and quality of life. It should be noted that neurorehabilitation should not be delayed and be completed for all patients with COVID-19 of all levels in need.

KEYWORDS
COVID-19; neurological consequences; physiotherapy and rehabilitation; neurorehabilitation; exercise; telerehabilitation

1. The 2019 novel coronavirus disease

The 2019 novel coronavirus disease (COVID-19) pandemic is driving a devastating effect worldwide. According to currently available data and clinical expertise, older adults and people with immune system problems or who have underlying chronic medical conditions may be at higher risk for developing severe illness from the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) responsible for COVID-19 [1]. One of the most worrying aspects of the COVID-19 epidemic is linked to the involvement of people with fragility, vulnerability, disabilities, multiple comorbidities, or chronic disease [2]. There is a vicious cycle that appears between comorbid symptoms and COVID-19. In patients with neurological conditions, the presence of heart disease, chronic lung disorders, and diabetes increases the risk of experiencing a more serious case of COVID-19 [3]. Meanwhile, both patients who remain hospitalized for a long time after battling COVID-19 and those without COVID-19 but who have a limited capacity to move independently and to care for themselves are at high risk for many health problems [4].

After an incubation period of about five days, a variety of symptoms can appear in patients infected with SARS-CoV-2. The most common symptoms reported were fever, cough, and fatigue, while other symptoms include headache, hemoptysis, and dyspnea [3]. The clinical severity of COVID-19 has been classified into the following four main groups [5]:

CONTACT Nilufer Cetisli-Korkmaz nkorkmaz@pau.edu.tr, niluferc75@yahoo.com School of Physiotherapy and Rehabilitation, Pamukkale University, Denizli, Turkey

Table 1. Symptoms to be assessed before starting rehabilitation and during each rehabilitation session [8,14,15,17].

Virus-related Symptoms	
Neurologic Symptoms	Some Other Symptoms
Stroke	High-grade fever
Upper motor neuron symptoms such as spasticity	Dry cough
Fatigue	Shortness of breath
Headaches	Acute respiratory distress syndrome
Disturbed consciousness	Sepsis/septic shock
Delirium	Multiorgan failure
Seizures	Acute kidney injury
Absence of smell and taste	Peripheral respiratory failure
Paresthesia	Restrictive lung disease
Neuropathy	Peripheral cardiac failure such as arrhythmia, cardiac insufficiency
Myopathy	Troponin I elevation
Contractures	Severe myocarditis with reduced systolic function
Issues with attention, visuospatial abilities, memory	
Executive function problems	
Decreased muscle strength	
Facial palsy	
Vertigo	
Balance problems	
Decreased cardiopulmonary capacity	
Decreased physical activity level	
Decreased participation in daily living activities	

1. Mild: clinical symptoms are mild and there are no abnormal radiological findings.
2. Medium: pneumonia is apparent via thoracic computer tomography (CT); fever, cough and other symptoms are present.
3. Severe: the patient is in respiratory distress, with a respiratory rate of 30 breaths/min or greater, oxygen saturation (SpO_2) level of 93% or less, and partial oxygen pressure in arterial blood/fraction of inspired oxygen (PaO_2/FiO_2) concentration of 300 mmHg or less.
4. Critical: acute respiratory distress syndrome (ARDS) occurs and mechanical ventilation is required; septic shock or multiorgan failure develops [5].

2. Rehabilitation of patients with neurological consequences secondary to COVID-19

Research indicates that the SARS-CoV-2 can spread from the respiratory tract to the central nervous system (CNS) [3], accessing the CNS through the olfactory bulb, causing inflammation and demyelination, then eventually entering individual cells by binding to angiotensin-converting enzyme 2 (ACE-2) receptors. It reaches the brain first by infecting the endothelial and epithelial cells in the blood–brain barrier and blood–cerebrospinal fluid (CSF) or through leukocytes and, second, *via* the retrograde axonal route; this transportation usually takes place through the III, V, IX, and X cranial nerves or peripheral nerves [6]. Isolating SARS-CoV-2 from CSF and autopsies of COVID-19 victims may clarify the role of this virus in observed neurological consequences [7].

Unfortunately, it is known that the COVID-19 pandemic significantly increases and will continue to increase the burden of disease and disability [8]. As SARS-CoV-2 spreads to CNS, neurological consequences such as febrile seizures, convulsions, changes in mental status, encephalitis, headache, dizziness, impaired consciousness, ataxia, seizure, meningeal signs, loss of smell and taste, neuropathic pain, variants of Guillain–Barré syndrome (GBS), and skeletal muscle injury may be found in affected patients. The prevalence rates of specific symptoms have been reported with wide variety in the current literature [3,7,9,10]. More recently, acute ischemic stroke, cerebral venous sinus thrombosis, and cerebral hemorrhage were also reported as associated events [10]. In addition to cardiovascular, pulmonary, and musculoskeletal deconditioning, affective disorders (e.g. depression and posttraumatic stress disorder), postintensive care syndrome (e.g. critical illness polyneuropathy and myopathy), and other neurological consequences of the fatigue brought on by the virus are also reported to be common among patients with a history of COVID-19 (Table 1) [8,9,11,12]. Following the COVID-19 process, it is appropriate to pursue neurorehabilitation as the treatment of virus-related neurologic symptoms, especially the treatment of stroke-related symptoms is crucial for good outcomes [8,13–15]. The main recommendations when deploying physiotherapists to commence rehabilitation for patients with COVID-19 is for the physiotherapists to wear appropriate personal protective equipment (PPE) before undertaking screening and assessment prior to initiating mobilization and relevant exercise prescriptions [16].

2.1. Stroke

Although the cause of stroke related to COVID-19 has not been fully elucidated, the possibility of CNS

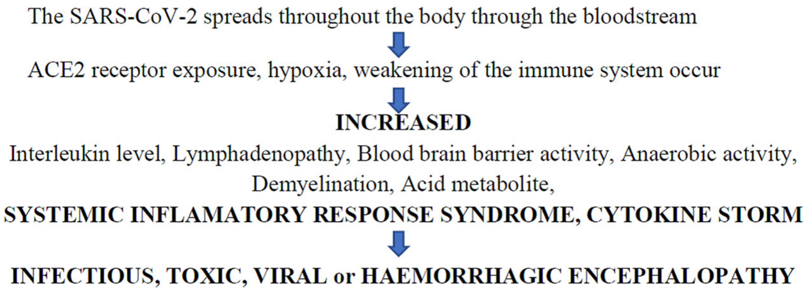

Figure 1. The mechanism of stroke in patients with COVID-19 [18,19].

involvement is high [7,18]. However, because of the virus's effect of expressing of vascular endothelial cells on receptors, potential vascular complications can arise [14]. The presence of hyperemia and edema in the CNS during the autopsy of patients with COVID-19 indicates the tendency for cerebrovascular events [18]. Because of the potential for severe stroke- and COVID-19–related symptoms, the World Stroke Organization drew attention to the importance of deploying effective and rapid treatment in patients with stroke related to COVID-19 [18]. The mechanism of stroke in patients with COVID-19 as defined by existing studies is shown in Figure 1.

Stroke is also considered as a medical emergency in the ongoing pandemic process. So, stroke management, which also includes early rehabilitation is essential. During this process, rehabilitation suggestions for stroke continue to be evidence-based as is usual. Evidence-based stroke management efforts should not be ceased, because the benefits include reductions in the risk of mortality and death from stroke, acceleration of hospital discharge, and relief of burden on the health system [20,21]. Establishing rapid and effective stroke-rehabilitation strategies are extremely important to achieve maximum functional recovery and control of neurological symptoms in patients undergoing hospitalization after triage [22]. A management protocol focusing on five target items called **CORONA** has been published for patients with stroke and unknown COVID-19 status. Under this initiative, the goals for patients with stroke are as follows:

- (*) **CO**ordination of action protocols in ensuring access to hospital care
- (*) **R**ecognition of potentially infected patients with stroke
- (*) **OR**ganization of patient management to prevent infection among health care professionals
- (*) **A**voiding procedures that may increase the risk of infection; performing (*) safe and early discharge and follow-up of patients [22]

Physiotherapy is an integral part of the care of patients with COVID-19 associated stroke [14]. In the COVID-19 epidemic process, the access of patients with stroke to rehabilitation has been severely restricted. Currently, many patients who receive inpatient stroke rehabilitation are being discharged earlier than is appropriate. However, to manage the negative effects of long-term disability, including neuroplastic care, is vital for patients with stroke to be able to continue progressing in their inpatient or outpatient rehabilitation [8,21,23].

Patients with an increased mortality risk associated with stroke are first admitted to intensive care, where patients with COVID-19 are also admitted. This raises the concern that patients with stroke undergoing intensive care rehabilitation may experience more serious neurological and viral effects [21]. As such, respiratory functions, especially dyspnea, thoracic activity, diaphragmatic activity and amplitude, respiratory muscle strength, and respiratory patterns should be specially addressed from the beginning of rehabilitation in patients with stroke. Comprehensive assessment and the treatment of any issues with the cardiac, respiratory, metabolic, and other systems in the intensive care unit (ICU) should be followed up with during inpatient rehabilitation [13]. Patients who have had a transient ischemic attack could be followed up *via* telehealth if it is not feasible to follow them up at home [22]. Patients, families, and caregivers should be educated about strategies and resources for self-management and stroke management [21]. During the neurological assessment, observation (mental state, speech and etc.), cranial nerve, motor (limb movements, coordination, and gait), and sensory examinations could also be performed.

Using sphygmomanometers and glucometers during the rehabilitation program is recommended to ensure safety [21]. Position changes, activities and mobility in bed, sit-to-stand exercises, limb exercises, neuromuscular electrical stimulation, and aerobic reconditioning with overland walking are adopted to prevent possible complications and to facilitate recovery. Balance, endurance, strength exercises, and occupational and speech therapy should be included as well [13]. Meanwhile, regional/country laws relating to lockdown around the world have constrained the rehabilitation services in outpatients and home or community visits as well as putting strain on inpatient activities, in order to reduce the viral spread. Two-way audiovisual or at least telephone communication with family members should be encouraged to limit social isolation in rehabilitation facilities during inpatient rehabilitation. Patients with stroke who need inpatient rehabilitation services often need to be discharged earlier than normal during the ongoing pandemic process, due to the strain on services and increased risk of infection for both staff and patients, especially with the close physical contact required during rehabilitation. So, home orientation, including the training of caregivers, should be provided. Along these lines, telerehabilitation services should be developed rapidly to support continued rehabilitation with outpatient treatment [23]. During the ongoing COVID-19 pandemic in 2020 and beyond, telerehabilitation (telestroke) has been easily accepted to maintain physical distance and reduce the risk of nosocomial viral transmission. Institutions without a telestroke system, on the other hand, can adopt different telerehabilitation modalities such as video-conferencing software or telephone consultancy [21].

2.2. Neuropathy

Posterior reversible encephalopathy syndrome causing headache, confusion, seizures, and vision loss is a potential complication of COVID-19 [24]. Previous research indicates that the SARS virus can induce neurological diseases such as polyneuropathy, viral encephalitis, and ischemic stroke. Almost one-fifth of patients who contracted Middle East Respiratory Syndrome (MERS), showed neurological symptoms such as changes in consciousness, stroke, ischemic stroke, GBS, infectious neuropathy, or seizure [13,25]. While polyneuropathy has been reported with other beta coronavirus infections (SARS and MERS), limited studies focusing on GBS associated with COVID-19 exist [25].

Critical illness polyneuropathy (CIP) is a mixed sensorimotor neuropathy leading to axonal degeneration that may occur after COVID-19 [24,26,27]. In a study of patients hospitalized in the ICU, 46% of patients were reported to have CIP [27]. CIP causes mechanical ventilation separation difficulties, distal symmetrical weakness (rather than proximal, but including diaphragmatic weakness), sensorial losses, atrophy, decreased or loss of tendon reflexes and range of motion, pain, fatigue, incontinence, difficulty in swallowing, anxiety, depression, posttraumatic stress disorder, and cognitive loss [26,27]. CIP syndrome remains present after discharge from the intensive care unit and is also associated with low functional capacity, decreased respiratory function and inspiratory muscle strength, and weakness in knee extension, the upper extremities and grip. Therefore, recovery may take up to one year or more [28].

Considering these findings, respiratory rehabilitation is crucial. In a systematic review, aerobic exercise or the combination of aerobic exercise and resistance exercise for at least five weeks led to significant improvements in cardiorespiratory fitness, strength, body composition, and quality among patients with human immunodeficiency virus [29]. The goals of rehabilitation in individuals diagnosed with neuropathy during the ongoing pandemic are to maximize functional capacities, increase or maintain independent function and mobility, and prevent physical deformity. The treatment is symptom-specific because of the many different symptoms that may occur; however, sensorial, pain and musculoskeletal treatment, strengthening, maintenance of range of motion and respiratory capacity are the most basic practices [30]. In particular, transcutaneous electrical nerve stimulation (TENS) can be used in neuropathic pain management as well as medical treatment. Naderi Nabi et al. stated that TENS therapy is effective in reducing pain among patients who cannot respond to amitriptyline therapy [31]. Because of the pandemic, home-based exercises should consist of those that the individual can do on his/her own as much as possible.

2.3. Guillain-Barré syndrome

GBS is an umbrella term of an acute, immune-mediated polyradiculoneuropathy with a wide range of clinical and pathologic manifestations. GBS is usually triggered by an infection that induces an aberrant autoimmune response that targets peripheral nerves and their spinal nerve roots [32]. Respiratory infections are usually mentioned as initial symptoms in two-thirds of patients with GBS. Meanwhile, the most common symptoms of COVID-19 are respiratory in nature. Therefore, GBS should be considered as one of the neurological complications of SARS-CoV-2 [33]. As GBS is an infection-related disease, recent studies have confirmed that COVID-19 can play a role in the emergence of GBS [12,33,34]. In an observational study from Northern Italy, Toscana et al. reported five patients were diagnosed with GBS five to 10 days after the beginning of COVID-19 symptoms. The first symptoms of four patients were lower-limb weakness and paresthesia, while, in one patient, GBS began with facial diplegia, followed by ataxia and paresthesia. Dysautonomia was not observed in any of these patients. During the fourth week of treatment, two patients remained in the ICU and were receiving mechanical ventilation, two had flaccid paraplegia and minimal upper-limb movement, and one had been discharged and could walk independently [12]. In a systematic review of case reports; eight studies and 12 patients with GBS and COVID-19 were identified. It should be noted however, that the clinical presentation of these patients was highly heterogeneous [35].

GBS is a potentially life-threatening disease that necessitates urgent medical care and immunological treatment. In patients with GBS, physiotherapy and rehabilitation programs should begin immediately after diagnosis with the aim of facilitating recovery, reducing complications, and decreasing the occurrence of long-term disability. Rehabilitation encompasses an interdisciplinary team approach and includes respiratory rehabilitation, a graduated mobility program in the acute phase of the disease, range-of-motion exercises, strengthening and flexibility exercises, orthotic applications, balance and functional training, and fatigue and pain management [36].

2.4. Myopathy

Although most people who contract COVID-19 experience mild symptoms, some instead develop severe disease requiring hospitalization and treatment in the ICU. Early clinical reports suggest that the length of ICU stay appears to be long in many patients with COVID-19, most of whom remain intubated for one week or longer [37]. In general, regardless of their underlying disease, ICU survivors often develop muscle weakness unrelated to the primary pathology responsible for ICU admission [38]. In a recent study, Puthucheary et al. observed a 20% reduction in the cross-sectional area of the rectus femoris muscle within the first 10 days of ICU admission [39]. This condition is known as ICU-acquired weakness and can be the result of various factors including prolonged bed rest, physical deconditioning, and neuromuscular disorders such as critical illness polyneuropathy, critical illness myopathy (CIM), or both [38].

In COVID-19 survivors, CIM is one of the possible complications of a prolonged stay in the ICU. Patients with CIM often demonstrate generalized muscle weakness with more prominent involvement of the limbs and respiratory muscles with intact sensory functions. The proximal muscles are typically more affected than the distal muscles [27]. The observed weakness of the respiratory muscles can delay weaning from mechanical ventilation and prolong the hospital stay further, with increased associated health costs [1]. Although most patients recover from CIM weakness within several weeks, in severely affected individuals, CIM can have a long-lasting effect that persists for months to years following ICU discharge [40]. CIM occurs in 25% to 63% of patients who receive mechanical ventilation for seven days or longer [41]. The diagnosis of CIM can be made *via* muscle strength evaluations, electrophysiologic testing, muscle ultrasound measurements, and muscle biopsy [42]. Although the pathophysiology of CIM is not fully understood, it is thought to involve electrical, microvascular, metabolic, and bioenergetic pathophysiological mechanisms. The decrease in muscle strength and mass inherent in CIM was found to be the result of the distortion of protein to DNA ratio, muscle protein synthesis, and an increase in catabolic proteolysis (which increases muscle catabolism) [43].

A major goal for health care professionals is to reduce the risk of CIM as it results in marked reduction in both the physical and functional capacity of patients, leading to greater dependence on others when performing activities of daily living and reductions in quality of life [44]. There is a clear consensus that adopting physiotherapy and rehabilitation strategies early is an important approach to treating CIM and will help to facilitate long-term recovery and greater functional independence among patients [37]. Existing physiotherapy and rehabilitation interventions include early mobilization, inspiratory muscle training, range-of-motion exercises (i.e. passive, active-assisted, or active), neuromuscular electrical stimulation, cycle ergometry, strength and mobility training (e.g. bed activities such as rolling, bridging, sitting and standing from a lying position and walking), interactive video-gaming, and balance training [45,46]. Physiotherapy and rehabilitation should be initially tailored according to each patient's needs and adapted as needed to the persisting physical, cognitive, and mental status of the patient as well as continued after discharge from the hospital.

2.5. Vertigo

Although COVID-19 is known to cause neurological symptoms, there is no definitive evidence regarding its effect on vertigo. It has been noted that the vertigo is observed in some case reports with COVID-19. It can be assumed that COVID-19 has the potential to cause auditory neuropathy spectrum disorder, as coronavirus can cause peripheral neuropathy, including sensory neuropathy [47]. In a case series, Karimi-Galougahi et al. reported that some cases with COVID-19 experienced acute-onset hearing loss and/or vertigo [48]. The affected patients were young (age range: 22–40 years) and had no prior relevant medical history concerning vertigo or hearing loss, so they concluded that vertigo and hearing loss may accompany COVID-19. However, existing studies are not sufficiently specific for such symptoms to be considered vestibular in origin [47]. Publications on vertigo and COVID-19 include low-quality cases and further studies are needed.

Pathologies associated with the vestibular system result in vertigo, with the primary associated symptom generally expressed as dizziness. Because vertigo causes balance problems, it is known that it limits the ambulation of patients and facilitates a more sedentary lifestyle. This itself will result in decreased muscle strength, normal joint movement limitations, and gradually deteriorating balance. Cumulatively, vertigo and resulting sedentary lifestyle will cause the quality of life to deteriorate. Therefore, vestibular rehabilitation for vertigo is extremely important [49,50].

Vestibular, visual, and somatosensory systems are responsible for ensuring balance. Therefore, both the visual and somatosensory systems should be stimulated and included in the vertigo rehabilitation plan. Eye-related Cawthorne–Cooksy exercises, balance coordination exercises, and dual task exercises can be offered to patients with vertigo. The ability to conduct additional exercises such as standing on one leg, walking on a tandem, looking all around the wall as if looking around outside while walking, sitting up while looking at a steady object, and following a moving object with one's eyes should be done. Exercises should also be prescribed to increase gaze stability; in one example, the gaze is flicked to a target, while the head is moved horizontally and vertically. Other activities such as taking an object placed on the ground and behind it with the eyes following the object can be performed. Based on the experiences of Benlidayi, and also Batuk and Aksoy, it has been suggested that vestibular adaptation exercises could be performed four to five times a day for a total of 20 to 40 min a day in order to activate the adaptive and compensatory mechanisms in the brain, to increase the independence in daily activities, and to develop compensatory strategies in coping dizziness and anxiety [49,50].

2.6. Headache

To date, the literature has revealed that some patients with COVID-19 have symptoms similar to intracranial infections such as headache, epilepsy, and disturbed consciousness [19]. In studies of patients with COVID-19, it was found that headaches were observed at varying rates [9]. Headache rehabilitation should be considered because headache affects the well-being and quality of life. Some physiotherapy methods such as spinal joint manipulation/mobilization, soft tissue interventions, therapeutic exercises, neurostimulation, and needling therapies have been proposed to be effective for the management of headaches. Also, small lifestyle changes (e.g. stopping caffeine, increasing exercise, managing stress, and improving sleep hygiene) might be put into practice with headache rehabilitation [51,52]. Neurostimulation by methods such as using a single-pulse transcranial magnetic stimulator is a potential treatment option for patients and is effective in headache therapy. Noninvasive vagus and occipital nerve stimulation and sphenopalatine ganglion stimulation methods are other stimulation methods that may be trialed [51–53].

2.7. Facial palsy

Cranial nerve involvement could potentially be seen in patients with COVID-19. Detailed neurological examinations should be performed to eliminate concomitant cranial nerve involvement (e.g. trigeminal or vestibulocochlear nerve palsies), especially in patients with isolated facial nerve palsy. Facial nerve palsy should not be assumed to be idiopathic as it is commonly due to, or associated with, a viral infection. In addition to magnetic resonance imaging, CSF analysis can be helpful for identifying CNS infection, inflammation, and other secondary causes [9,11,12]. In a case report of a 27-year-old male patient with COVID-19, weakness in the left facial muscles, left retro-auricular pain, and dysgeusia started on the sixth day of the disease. The neurological examination revealed involvement of the left frontalis, orbicularis oculi, buccinators, and orbicularis orris, consistent with a left lower motor neuron–type facial nerve palsy. Corneal reflex was present and no hyperacusis was noted. Magnetic resonance imaging of the brain showed enhancement of the left facial nerve [54].

While the physiotherapy and rehabilitation process is very important in patients with COVID-19 associated facial palsy, some problems in the rehabilitation of patients with facial paralysis for different reasons during the ongoing COVID-19 pandemic period persisted and there is no clear explanation in the literature. To establish optimal physiotherapy and rehabilitation approaches, such as neuromuscular electrical stimulation and proprioceptive neuromuscular facilitation applications, close contact with the affected patient is needed. Physiotherapists should take all necessary precautions given the risk of contamination during the rehabilitation of acute patients. To avoid increasing the risk of transmission and contamination, home exercise programs, facial mimic exercises in front of the mirror, taping, remote patient observation, and telerehabilitation could be selected as techniques in addition to medical treatment for chronic patients. It provides a useful solution to ensure that patients performing exercise schedules at home respect the instructions. Meanwhile, Fieux et al. researched favorable effects on the quality of care during the ongoing COVID-19 pandemic. In the study by Fieux et al, outcomes following telemedicine consultation showed the patients' overall satisfaction with telemedicine consultation was 87% [55]. Tan et al. reported that telemedicine could provide follow-up of patients with peripheral facial palsy, although certain assessments using the House and Brackmann or Sunnybrook scales still remains a problem in this context [56]. However, telerehabilitation remains a useful solution in the context of the COVID-19 pandemic among patients with peripheral facial paralysis to follow exercise schedules at home with respect to the ocular protection instructions [55,56].

2.8. Delirium

Psychosocial stresses may increase psychiatric problems. It was reported that more than 50% of patients infected by SARS and MERS experienced psychological distress [57]. It is also known that COVID-19 can cause viral encephalitis, while brain tissue edema and partial neuronal degeneration have been observed in deceased patients [19,58]. Although the sum of effects of COVID-19 remain unclear, cognitional and emotional problems may reduce immunity and compromise recovery [59]. Delirium may be seen in 80% of ICU settings [17,60]. Cognitive impairment following ARDS has been noted to affect the majority of survivors (39 – 51%) at the time of hospital discharge. It was 13% to 79% at 3- to 6-month follow-up, and 10% to 71% of impairments are persistent through one-year follow-up [17,59]. Neuropsychological impairments are typically multidimensional and affect memory, attention, and higher-order executive functions [59]. Delirium is associated with worse functional outcomes from all reasons mentioned above.

The prevalence of consciousness disorders in patients with COVID-19 is 3.8% [61]. Loss of consciousness is higher especially among patients with comorbidity. The duration of impaired consciousness is, on average eight days long and longer than those of other neurological symptoms [9]. Impaired consciousness has also been shown to be associated with both symptoms of COVID-19 [62] and other underlying diseases. There are helpful tools for the evaluation and follow-up of patients with delirium such as PREdiction of DELIRium in ICU (PRE-DELIRIC) and the Confusion Assessment Method for the ICU (CAM-ICU) [63,64]. Meanwhile, "Guidelines for the Provision of Intensive Care Services" specify that patients must be routinely screened for delirium [65]. Also, "Guidelines for Detection, Prevention and Treatment of Delirium", "Awakening and Breathing Co-ordination, Delirium Monitoring/Management and Early Exercise/Mobility Bundle" (ABCDE), "Clinical Practice Guidelines for the Management of Pain, Agitation and Delirium in Adult Patients in the Intensive Care Unit", "NICE Delirium: Prevention, Diagnosis, and Management" encompass core standards for patients in the intensive care unit with delirium [65–67]. Different screening tools have a variety of sensitivities and specificities. The time needed to complete the assessments also adds to the complexity of delirium detection. Gusmao-Flores et al. analyzed 11 studies and found that the CAM-ICU is an excellent diagnostic tool in critically ill ICU patients, whereas Bergeron N et al. stated that the "Intensive Care Delirium Screening Checklist" (ICDSC) has moderate sensitivity and good specificity [68,69].

Symptoms that indicate the presence of possible delirium include inattention, confusion or disorganized thinking, fluctuation in levels of consciousness, altered psychomotor activity (e.g. restlessness, agitation, and decreased motor activity), rapid fluctuations in emotions, and the presence of auditory and/or visual hallucinations. Monitoring, treatment and follow-up of all these holds are of great importance during the course of COVID-19, especially when a patient is found to have one or more of the symptoms [70]. Multi-interventional approaches and bundles are reported as successful tools in reducing the number of days with delirium and the length of the hospital stay. The key components of these bundles have been listed as spontaneous breathing trials, daily sedation holds, addressing pain relief, early mobilization, and normalization of a daily routine. Although there has been limited research regarding the role of rehabilitation within this patient group, the study of cognitive therapy and functional tasks in patient populations such as patients with stroke and those receiving elderly care emphasizes its importance in those who may benefit from it. It was underlined that patients in ICU have similar rehabilitation requirements and may benefit from similar treatment approaches and additional therapeutic activities in reducing the duration of delirium [71]. Improving sleep, normalizing patients' day, increasing mobility, and conducting passive movement exercises may be helpful, too [72]. Qigong exercise can also be used as a meditative movement to treat mental conditions such as mood disorders and cognitive impairment [73]. Additionally, telerehabilitation platforms for exergaming and physical, language, and cognitive rehabilitation enable remote supervision and the collection of patient-reported outcomes [74].

3. Conclusions

While the physiotherapy and rehabilitation process is very important in patients with neurological consequences of having COVID-19, for different reasons during the pandemic period to date some problems have persisted. As yet, there is no clear explanation in the literature as to why that should be. Part I of this review has focused on the possible neurological consequences of COVID-19 and some rehabilitation approaches for them, which could help the rehabilitation team in their clinical decision-making and close the gap in the available scientific literature. Close attention must be given to possible neurologic consequences that may affect function and cause long-lasting disability in patients with COVID-19 and their identification and mitigation are crucial during and after the treatment of patients with COVID-19.

A framework which lists the rehabilitation interventions, monitors progress, and reviews the efficacy and results of long-term follow is still lacking. Thus further studies, with high level evidence are needed. Neurological consequences are reported to present often in the acute stage and rehabilitation applications could be planned within the framework of existing guidelines for the treatment of patients with COVID-19. Moreover, rehabilitation programs should be available for patients at all levels of function. In this regard, urgent action needs to be taken by leaders and policymakers to ensure the continuity and deliverability of physiotherapy and rehabilitation services to patients with COVID-19 [75]. Though the ongoing COVID-19 pandemic currently limits access to rehabilitation services, continuing studies focusing on the effects of rehabilitation are warranted.

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Notes on contributors

Nilufer CETISLI-KORKMAZ, PT.PhD.Prof. She is experienced in neurological rehabilitation, geriatric rehabilitation, community-based rehabilitation, technology and electrophysical agents in physiotherapy and rehabilitation, and has publications in prestigious journals. nkorkmaz@pau.edu.tr

Furkan BILEK, PT.MSc.Lecturer He continues his studies in the fields of neurological rehabilitation, geriatric rehabilitation and cardiopulmonary. His area of interest is physiotherapy and rehabilitation in Multiple Sclerosis. fbilek@firat.edu.tr

Tuba CAN-AKMAN, PT.PhD.Lecturer She is interested in adult neurological rehabilitation such as multiple sclerosis, polyneuropathy and burden of care. tubacan@pau.edu.tr

Emre BASKAN, PT.PhD.Lecturer He is interested in neurological rehabilitation, geriatric rehabilitation and sports in individuals with disabilities. ebaskan@pau.edu.tr

Ilke KESER, PT.PhD.Prof. Special interest areas are neurological rehabilitation, oncological rehabilitation, lymphedema rehabilitation and geriatric rehabilitation. ilkekeser@gazi.edu.tr

Esra DOGRU-HUZMELI, PT.PhD.Assoc.Prof. She is working in patients with Parkinson's Disease, stroke and multiple sclerosis. Her last publications about effect of deep brain stimulation in Parkinson's Disease Patients. She has many publications in prestigious journals. esradogru001@hotmail.com

Mehmet DURAY, PT.PhD.Lecturer His special interests were neurological rehabilitation, geriatric rehabilitation, pain management, and pediatric rehabilitation. mehmetduray@sdu.edu.tr

Bahar ARAS, PT.PhD.Lecturer She continues her studies as a teaching fellow in the fields of neurological rehabilitation and pediatric rehabilitation. bahar.aras@ksbu.edu.tr

Buse KILINC, PT. Her research interests were physiotherapy and rehabilitation, neurological rehabilitation and diabetes mellitus. buse.kilinc@karatay.edu.tr

ORCID

Nilufer Cetisli-Korkmaz http://orcid.org/0000-0003-3471-8240
Furkan Bilek http://orcid.org/0000-0003-1567-7201
Tuba Can-Akman http://orcid.org/0000-0001-5230-2009
Emre Baskan http://orcid.org/0000-0001-7069-0658
Ilke Keser http://orcid.org/0000-0001-6999-4056
Esra Dogru-Huzmeli http://orcid.org/0000-0002-7025-8192
Mehmet Duray http://orcid.org/0000-0002-3764-215X
Bahar Aras http://orcid.org/0000-0002-3669-9461
Buse Kilinc http://orcid.org/0000-0001-9822-0965

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