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Rehabilitation of patients post-COVID-19 infection: a literature review

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Abstract

Rehabilitation is important for patients with coronavirus disease 2019 (COVID-19) infection. Given the lack of guidelines in English on the rehabilitation of these patients, we conducted a review of the most recent reports. We performed this literature review using the principal research databases and included randomized trials, recommendations, quasi-randomized or prospective controlled clinical trials, reports, guidelines, field updates, and letters to the editor. We identified 107 studies in the database search, among which 85 were excluded after screening the full text or abstract. In total, 22 studies were finally included. The complexity of the clinical setting and the speed of spread of the severe acute respiratory syndrome coronavirus 2, which leads to rapid occupation of beds in the intensive care unit, make it necessary to discharge patients with COVID-19 who have mild symptoms as soon as possible. For these reasons, it is necessary to formulate rehabilitation programs for these patients, to help them restore physical and respiratory function and to reduce anxiety and depression, particularly patients with comorbidities and those who live alone or in rural settings, to restore a good quality of life.

Keywords

Rehabilitation, coronavirus disease 2019, intensive care, respiratory function, physical function, review

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Introduction

The coronavirus disease 2019 (COVID-19) outbreak initially appeared in Wuhan, Hubei Province, China in December 2019, and it has quickly evolved into a worldwide pandemic.[1]As of 28 July 2020, there were

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16,465,707 reported cases of COVID-19 (according to case definitions and testing strategies in the countries concerned).[2] There is growing understanding of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) with respect to virology, epidemiology, and clinical management. However, no drugs to treat or vaccines against SARS-CoV-2 have been officially approved owing to a lack of adequate evidence.[3]

As the pandemic is ongoing, there are limited data on the clinical and prognostic factors of patients with COVID-19.[4,5] COVID-19 is a highly infectious respiratory infection disease, which leads to respiratory, physical, and psychological dysfunction in affected patients.[6] Because COVID-19 is highly infectious, patients are isolated to limit the spread of SARS-CoV-2. This leads to substantial reduction in social interactions, which makes patients feel lonely and isolated.[6,7]

In many cases, patients remain bedridden in the intensive care unit (ICU) for extended periods. Patients often remain in a prone position for many hours, which can cause post-ICU dysphagia, muscle weakness, myopathy, and neuropathy owing to critical illness, as well as reduced joint mobility, pain in the neck and shoulders, difficulty standing, and impaired balance and gait, with consequent limitations in activities of daily living.[7,8]

Owing to lung fibrosis as a sequela of pneumonia, some patients experience severe respiratory failure requiring respiratory rehabilitation.[6,7] Many recommendations regarding respiratory rehabilitation have reported made in the published literature; however, these are not based on experiences among patients with COVID-19. A rehabilitation program is considered necessary for these patients, but the setting remains unclear. Therefore, in this study, we reviewed the most recent articles addressing rehabilitation in patients with COVID-19 infection, to examine the various proposed rehabilitation programs and provide concrete evidence of program efficacy as well as suggestions regarding measures that health care organizations can take to treat patients with COVID-19 in the post-acute phase.

Methods

The present literature search was conducted through April 21, 2020 using PubMed, ScienceDirect, and Google Scholar, with the following search terms: ["COVID-19" or "COVID 19" or "2019-nCoV" or "SARS-CoV" or "novel coronavirus" or "SARS-CoV-2"] and ["Rehabilitation"]. Randomized trials, recommendations, quasi-randomized or prospective controlled clinical trials, reports, guidelines, field updates, and letters to the editor were included, in English and Chinese.

The articles were initially screened by title and abstract. Articles that remained unclear from the title or abstract were reviewed according to the selection criteria in a full-text review. Two authors who were blinded to each other independently extracted data from the studies that met the inclusion criteria.

The guidelines of the Cochrane Handbook were followed to assess the risk of bias. The quality of the study, such as selection bias, performance bias, detection bias, attrition bias, selective reporting of results, and other biases, were independently evaluated by two reviewers (Figure 1). Differences between the extracted data and disagreements in quality assessment were discussed with a third and fourth author, to reach consensus.

This study was conducted in accordance with the Preferred Reporting Item for Systematic Review and Meta-analysis (PRISMA-P) statement[9] (Figure 2). Ethics approval and informed consent were not required as this was a literature review.

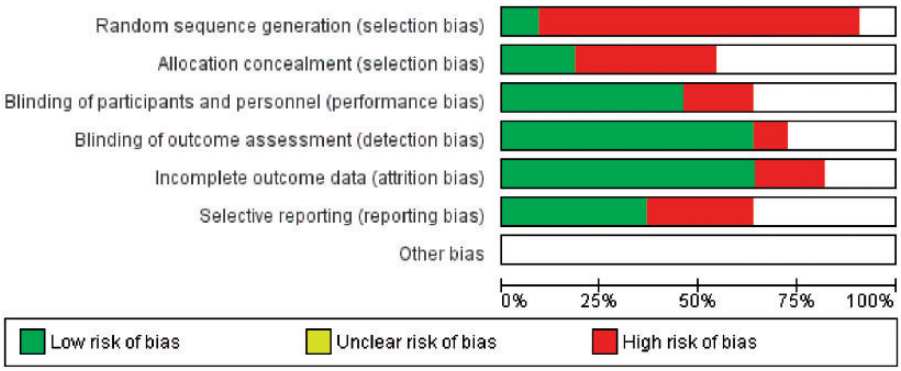

Figure 1. Bias risk.

Results

In the database search, we identified 107 studies; among these, 85 were excluded after screening the full text or abstract. A total of 22 studies were finally included in the review (Figure 2). Partly owing to the rapid onset of the COVID-19 pandemic, there is currently little scientific evidence to guide the approach to rehabilitation in patients with COVID-19. Most publications (16/22) were letters, reports, and editorials, with one clinical case (patient sample size of 2) and four clinical recommendation documents. Two publications were written by the same authors and their conclusions were similar. This lack of high-quality evidence published in peer-reviewed journals presents a challenge to the formulation of recommendations.

Given the high percentage of hospitalized patients requiring intensive care, it is likely that in the weeks and months following an increase in the number of acute patients admitted to hospitals and ICUs, there will be a considerable number of COVID-19 survivors requiring rehabilitation.[10] For this reason, it is a common opinion that a rehabilitation program must be developed that is tailored to the specific needs of each patient.

Yang[11] proposed a general pulmonary rehabilitation method based on the principle of 4S (simple, safe, satisfy, save) for patients with pneumonia caused by the novel coronavirus. The Chinese Association of Rehabilitation Medicine made the first recommendation based on expert opinions, differentiating between patients with mild or critical illness and discharged patients. Liu[12] concluded that a 6-week respiratory rehabilitation program significantly improves respiratory function, quality of life, and anxiety in older patients with COVID-19.

A primary concern is regarding the timing of when to start a rehabilitation protocol in the face of the real threat of COVID-19 spread. For Stam et al., there is a clear consensus that early rehabilitation is an important strategy for the treatment of polyneuropathy and myopathy in critical disease, to facilitate and improve long-term recovery and patients' functional independence, and to reduce the duration of assisted ventilation and hospitalization.[13] In the acute phase, which is mainly characterized by respiratory disorders, early respiratory rehabilitation is encouraged, to be performed at the patient's bedside and continued in a specialized rehabilitation unit, to improve the chances of recovery.[14,15] Early active mobilization is important for

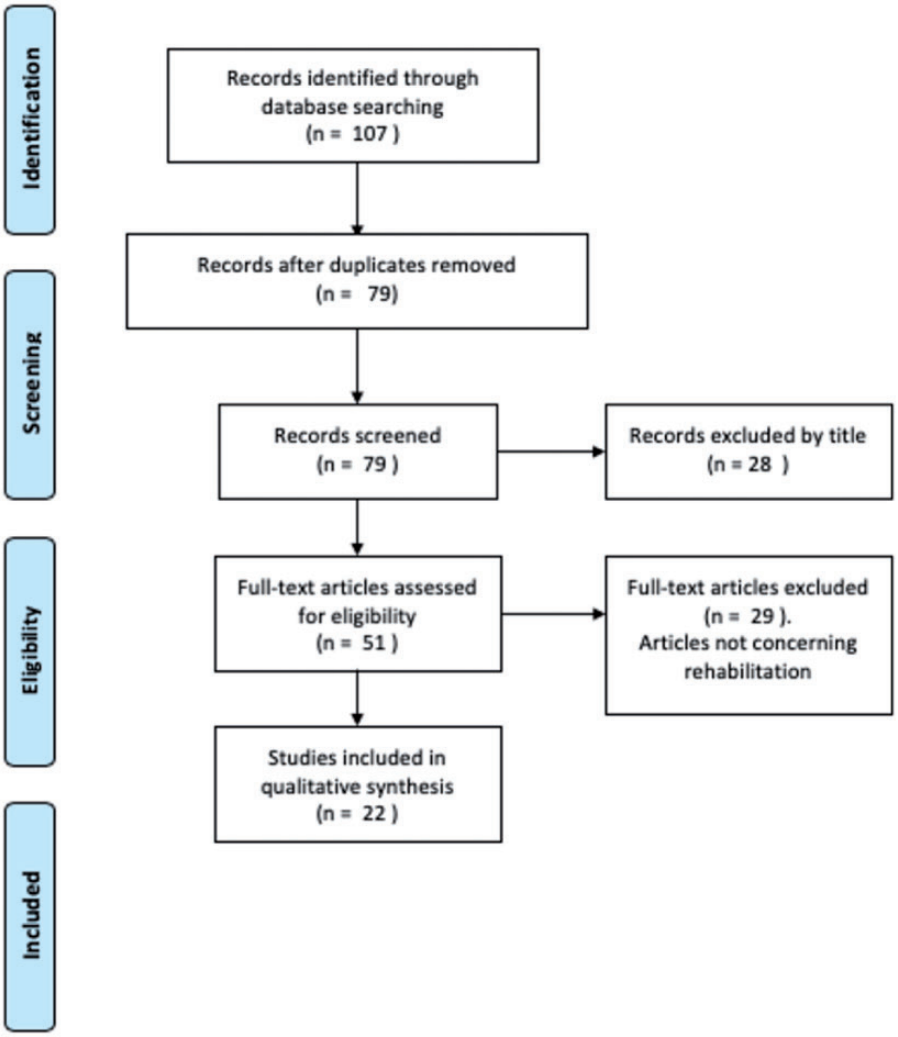

Figure 2. PRISMA flowchart.
PRISMA, Preferred Reporting Item for Systematic Review and Meta-analysis.

improving muscle strength, promoting better mobility when the patient is discharged from the hospital and better quality of life outside of the hospital.[8]

In contrast, the Chinese Association of Rehabilitation Medicine and the Italian PRM Association have concluded that early respiratory rehabilitation is not recommended[6] because it is not well tolerated, resulting in rapid desaturation.[7] The evidence in the field indicates that considerable reorganization of services is required with acute emergencies taking precedence over rehabilitation, which may involve complete conversion of beds, wards, and even hospice facilities. Rehabilitation beds are often used for the care of acutely ill patients, with physiatrists being sent to emergency rooms[16] and in some cases becoming directly involved in the care of

patients with COVID-19, detracting them from rehabilitation care.[10]

McNeary proposed the Conditions, Actions, Needs (CAN) model, used to prepare for natural disasters, such as the COVID-19 pandemic.[17] Given the prevalence and magnitude of physical impairments after critical illness, many survivors recovering from COVID-19 could benefit from physiotherapy after hospital discharge.[18] However, the typical needs in rehabilitation, such as human and physical contact, as well as social interaction among patients, groups, family and caregivers, are necessarily eliminated, greatly limiting the work of physiotherapists.[19]

In the context of the COVID-19 pandemic, virtual outpatient care may be preferable to face-to-face interactions for multiple reasons.[8] Among solutions between early care and rehabilitation services are telemedicine and other e-health applications.[13] A tele-rehabilitation system, with a physiotherapist following patients who perform rehabilitation exercises for 20 minutes, can be easily developed using a combination of technologies. Tele-rehabilitation could be a very useful tool, regardless of whether it is used in hospitals or in the community, to address the social difficulties associated with the ongoing pandemic.[20]

Huang et al.[21] proposed an online/offline multidisciplinary epidemic management model, which has demonstrated some success in the management of mild cases and screening serious cases, using online communication that leads to continuous monitoring of the symptoms reported by patients. However, virtual care also has many limitations, such as ready availability of equipment, technical malfunctions, the potential for involuntary disclosure of personal data, and the limited scope for physical examination. In addition, such a process is largely based on whether the patient is able to participate in sessions and can communicate and interact accordingly.[8,16,22]

Discussion

COVID-19 is a highly infectious respiratory disease that leads to respiratory, physical, and psychological dysfunction in patients. In most patients (81%), COVID-19 infection confers mild disease with fever (88.7%), cough (57.6%), and dyspnea (45.6%). However, for a considerable number of patients, generally, those age > 65 years with comorbidities such as hypertension and diabetes, the infection can have very serious sequelae. Among patients requiring hospitalization, a relatively high percentage (20.3%) require management in the ICU, often for acute respiratory distress syndrome (ARDS);[8] these patients can also experience multiorgan failure.[14]

Isolation is an effective method of reducing transmission of highly contagious SARS-CoV-2. Most patients have fever, fatigue, muscle pain, and may remain bedridden for a long period. This leads to a reduction in muscle strength, which causes poor sputum expulsion and significantly increases the risk of deep vein thrombosis.[6] Patients in the ICU can have several complications owing to extended immobilization and many hours in the prone position;[7,23,24] these include neuromuscular complications, severe muscle weakness and fatigue, joint stiffness, dysphagia, psychological problems, reduced mobility, severely impaired quality of life, frequent falls, and even quadriparesis.[13,19] In addition, persistent mental health impairment is commonly described following treatment in the ICU, with pooled estimates showing a high prevalence of depression (29%).[8] The longer a patient remains in the ICU, the greater the risk of long-term physical, cognitive, and emotional complications.[13] Home quarantine and closure of day care facilities are likely to have a negative impact on fragile patients,[25] who may feel physically uncomfortable, frightened, alone, and depressed;[21]

therefore, these patients tend to give up treatment or develop other psychological problems.[6]

In hospitalized patients with COVID-19, the aim of respiratory rehabilitation is to improve symptoms of dyspnea, relieve anxiety and depression, reduce complications, prevent and improve dysfunction, reduce disability, preserve function to the maximum extent, and improve quality of life.[6] As of this writing, there remains a lack of evidence about rehabilitation programs in patients with COVID-19. Owing to poor knowledge about this infection, most published articles are based on past literature and have mostly considered general symptoms related to COVID-19, such as neuromuscular, psychological, and respiratory symptoms owing to post-acute syndrome and anxiety related to the idea of being infected with the novel coronavirus. Published studies do not specifically report results in patients with COVID-19 but rather focus on the sequelae of infection.

In the present review, we identified two lines of thought; the first is based on consolidated principles of early respiratory rehabilitation, including mobilization and psychological support, to be started during the acute phase of illness. The second viewpoint is based on the Chinese and Italian experience, countries that had to face the seriousness of COVID-19 pathology early during the pandemic and that experienced a crisis in rehabilitation services.

Based on the results of this review, early respiratory rehabilitation is not recommended for severely and critically ill patients during periods of possible and progressive deterioration. The timing for beginning respiratory rehabilitation should be determined after ruling out contraindications, and attention to all precautions is needed to avoid the spread of infection. For hospitalized patients in an isolation ward, it is recommended to use videos, brochures, or remote consultations to follow patients in rehabilitation, to conserve resources of personal protective equipment and avoid cross-infection. Patients who have recovered and tested negative for COVID-19 infection can undergo respiratory rehabilitation, according to their clinical condition.

Respiratory rehabilitation interventions must be personalized, particularly for patients with comorbidities, advanced age, obesity, multiple diseases, and complications of single or multiple organs. The rehabilitation team should focus on the patient's specific problems to develop an individualized program.[6,7,26] Patients should be monitored throughout the respiratory rehabilitation process, such as with the use of various technologies.[8,20,21]

From the outset, the pandemic has had an enormous impact on health systems worldwide, particularly the emergency, intensive care, laboratory, and imaging departments. As the pandemic progresses, nearly all health sectors will become involved, including the areas of post-acute care and rehabilitation. In this difficult context, a balance of rigor and professional pragmatism is needed. Normal rehabilitation protocols simply do not apply because patients must be discharged earlier than usual to make hospital beds available; this means identifying patients who are "nearly ready to be discharged" and who have good caregiver support.[17] Mainly for this reason, the best recommendation is to formulate a rehabilitation program for discharged patients, with greater attention paid to patients with comorbidities[10] and those who live alone or in rural settings.[27]

Based on current evidence in discharged patients with SARS and Middle East respiratory syndrome (MERS) as well as the clinical experience of patients with ARDS, patients discharged after COVID-19 infection may have poor fitness and have breathing difficulties after exertion

as well as muscle wasting (including of the respiratory and trunk muscles) and psychological disorders such as post-traumatic stress disorder.[6] For these reasons, patients with mild pulmonary dysfunction should be prescribed a rehabilitation program to restore fitness and reduce anxiety and depression.[6] Patients who are

Table 1. Principal recommendations for discharged patients.

Exclusion criteria	(1) Heart rate $>$ 100 beats/minute; (2) blood pressure $<$ 90/60 mmHg or $>$ 140/90 mmHg; (3) blood oxygen saturation $\leq$95%; (4) other diseases in which exercise is unsuitable.
Exercise termination criteria	(1) Fluctuations in body temperature $>$ 37.2°C; (2) respiratory symptoms and fatigue worsen and are not relieved after rest; (3) stop activities immediately and consult a doctor if the following symptoms occur: chest tightness, chest pain, breathing difficulties, severe cough, dizziness, headache, blurred vision, palpitations, sweating, trouble standing, and other symptoms.
Rehabilitation evaluation	(1) *Clinical evaluation*: physical examination, imaging, laboratory, lung function, and so on. (2) *Evaluation of exercise and respiratory function*: ① Respiratory muscle strength: maximum inspiratory pressure/maximum expiratory pressure (MIP/MEP). ② Muscle strength (Medical Research Council), isokinetic muscle testing (IMT). ③ Joint range of motion (ROM) measurement. ④ Balance function evaluation: Berg Balance Scale. ⑤ Aerobic exercise capacity: 6-minute walk test (6MWT). ⑥ Physical activity assessment: international physical activity level tables (International Physical Activity Questionnaire, IPAQ), physical activity scale for the elderly (PASE), and so on. 3) *Assessment of daily living ability*: assessment of activities of daily living (ADL) (Barthel index).
Respiratory rehabilitation interventions	*Patient education*: (1) Manuals or video materials to explain the importance of respiratory rehabilitation; (2) healthy lifestyle education; (3) encourage patients to participate in family and social activities. *Recommendations for respiratory rehabilitation*: (1) Aerobic exercise for patients such as walking, brisk walking, jogging, swimming, and so on, starting from low intensity, gradually increasing the intensity and duration: 3 to 5 times per week for 20 to 30 minutes each time. Intermittent exercise can be used in patients who are prone to fatigue. (2) Strength training: progressive resistance training is recommended for strength training with a frequency of 2 to 3 times per week, with a training period of 6 weeks and a weekly increase of 5% to 10%. (3) Balance training: Patients with balance dysfunction should undergo balance training, including hands-free training and balance training using a device, under the guidance of a physiotherapist. (4) Breathing training: if patients have shortness of breath, wheezing, difficulty with sputum discharge, and so on, they must begin breathing and sputum training and breathing mode training including body management, adjusting breathing rhythm, thorax activity training, and mobilizing breathing muscle group participation. Sputum training: first, patients can use breathing techniques to help reduce sputum and energy consumption in coughing; second, patients may need to be assisted with positive expiratory pressure (PEP)/oscillatory PEP and other equipment. *ADL guidance*: (1) Basic activities of daily living (BADL): assess the patient's ability to perform daily activities such as training transfer, grooming, toileting, bathing, and so on, and provide rehabilitation guidance for daily life obstacles. (2) Instrumental activities of daily living (IADL): assess the ability of instrumental daily activities, identify obstacles in task participation, and conduct targeted intervention under the guidance of an occupational therapist.

seriously ill with COVID-19 and who have passed the critical phase of lung infection, and have been discharged but have symptoms of pulmonary dysfunction, should undergo respiratory rehabilitation.[6,13]

Recently, results of the first randomized controlled trial assessing a respiratory rehabilitation regimen for patients discharged after COVID-19 infection were published. The findings showed a significant improvement in respiratory function, quality of life, and anxiety in a group of older patients who participated in the following respiratory rehabilitation program: respiratory muscle training, coughing exercises, diaphragmatic training, stretching exercises, and home exercises comprising two sessions per week for 6 weeks, once a day for 10 minutes.[12]

Given the exceptional work of clinical services and the extremely valuable role that rehabilitation can play in this pandemic, some recommendations for discharged patients are shown in Table 1. Considering the many aspects of COVID-19 pneumonia, it is important that health care providers and individual professionals provide the highest standards of clinical care. Post-acute care facilities will be increasingly challenged by an increasing influx of patients with varying degrees of disability. Open communication among rehabilitation centers is needed for the exchange of knowledge, allowing centers that currently do not offer home-based programs to quickly learn from other centers where this practice has been successfully implemented.[28] In this scenario, telemedicine has great potential. It is a tool for connecting patients and health care professionals, while respecting social safety restrictions. There are few data available, but the initial results are encouraging. Digital health interventions can help provide self-monitoring tools, field updates, exercise protocols, and psychological support.[6,7,21]

To date, interest has been focused on the management of critically ill patients in acute care settings. Less attention has been given to the ability of the post-acute health care system to manage many patients after COVID-19 infection, that is, when patients move from the hospital to a long-term care facility or return home. For this reason, in the gradual return to normal, rehabilitation will have to be focused on screening programs. It is essential to establish adequate screening opportunities. This can be done by a general practitioner alone or by a multi-professional team consisting of a physiatrist, a physiotherapist, a psychologist, an ICU physician, and others. The choice of a screening technique (including telemedicine and other e-health applications) depends on the available resources, the local health care infrastructure, and the availability of further rehabilitative interventions.[13]

A large number of COVID-19 patients will need outpatient and home rehabilitation care, and the negative impact that COVID-19 has had on rehabilitation medicine units can cause difficulties in meeting patients' needs. Remodeling of hospitals with reduced hospital rehabilitation services could increase waiting lists and the need to resort to a private office. Where appropriate, repurposing of clinics and athletic facilities or gyms to establish temporary post-acute care facilities could rapidly expand the available space for adapted physical activity.

Conclusion

Considering the high number of people affected by COVID-19 infection worldwide, based on the limited scientific knowledge and evidence available at the moment, it can be expected that physiatrists and physiotherapists will be increasingly involved in the care of these patients, to improve pulmonary function, physical and psychological efficiency, and to restore a good patient quality of life. Timely preparation and thoughtful planning can help to limit any impact that arises from this unprecedented situation.

Author contributions

A. Demeco and N. Marotta conceived the research. M. Barletta, I. Pino, and C. Marinaro performed the investigation. A. Demeco and N. Marotta curated the data. A. Ammendolia supervised the project. A. Demeco and N. Marotta wrote the original draft. A. Petraroli, L. Moggio, and A. Ammendolia reviewed and edited the draft. Authors whose names appear on this submission have contributed substantially to the scientific work and therefore share collective responsibility and accountability for the results.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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