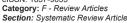
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# Physical Rehabilitation Therapy for Long COVID-19 Patient with Respiratory Sequelae: A Systematic Review

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#### **Abstract**

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BACKGROUND: Coronavirus disease 19 (COVID-19) infection has been a global pandemic since late 2019. Even though most COVID-19 patients recover fully from the disease, approximately 5-10% experience prolonged symptoms for several months following the acute COVID-19 phase, defined as long COVID-19 syndrome. Most of the sequelae are respiratory sequelae. Rehabilitation therapy is needed to overcome their respiratory sequelae and to improve their functional capacity.

AIM: This systematic review discusses rehabilitation therapy for long COVID-19 syndrome with respiratory sequelae.

METHODS: Using PubMed and Cochrane library, a systematic review was conducted based on PRISMA guidelines. The subject of this research was long COVID syndrome with respiratory sequelae. For rehabilitation therapy for long COVID-19 patients with respiratory sequelae, inclusion criteria were studied. Exclusion criteria were letters to the editor, editorial or commentary reports, and studies not available in full-text and not in English or Bahasa.

RESULTS: Nine studies are included in this systematic review comprising two consensus statements or recommendations, one cohort retrospective study, two case studies or case reports, one review, and three experimental studies. The recommended rehabilitation program pathway using a three-tier model depends on the severity of the disease. Several rehabilitation exercises for long COVID patients with respiratory sequelae include cardiorespiratory exercise, breathing exercise, therapeutic exercise, and even traditional Chinese fitness models such as Liuziiue exercise.

CONCLUSION: Rehabilitation therapy exercise helps to improve the breathing effort, improving dyspnea, and respiratory muscle strength in long COVID patients with respiratory sequelae.

# Introduction

The Coronavirus disease 19 (COVID-19) pandemic has become a worldwide health burden since first discovered in December 2019 in Wuhan, China. As of March 2022, around 6.1 million fatalities and 465 million recoveries from COVID-19 have been reported around the globe [1], [2]. In Indonesia, the COVID-19 cases reached 5.98 million cases with 154 thousand deaths as of March 2022 [3]. Some of the COVID-19 patients who recovered from the infection can still have some symptoms of infection, although they have tested negative. These symptoms are defined as long COVID syndrome. The National Institute for Health and Care Excellence (NICE) describes "post COVID-19 syndrome" or "Long COVID" as a set of persistent physical, cognitive, and psychological symptoms that continue for more than 12 weeks after illness and which are not explained by an alternative diagnosis [4]. Some of these symptoms include frequent shortness of breath, chest palpitations, headaches, joint pain, the ability to sense smell that is still not improving, tired quickly,

and excessive fear and anxiety. The pathophysiology of long COVID-19 syndrome is still unknown. The most common long COVID-19 syndrome was respiratory sequelae such as dyspnea and breathing difficulty. These symptoms are caused by residual COVID-19 infection in the form of fibrosis in the patient's lung [5].

In COVID-19 patients with moderate to severe infection, scar tissue can be established due to the virus infection in the lungs. Early epidemiological reports showed that 8.2% of the total cases presented with rapid and progressive respiratory failure, similar to acute respiratory distress syndrome (ARDS). Its treatment methods range from mechanical ventilation to extracorporeal membrane oxygenation in severe cases. The literature states that patients recovering from ARDS frequently develop significant long-term morbidity related to extrapulmonary complications [6], [7]. The literature states that 48% of patients do not return to work 1-year post-discharge and that 32% of patients die within 5 years [8]. In long COVID patients, although the patients have tested negative, the symptoms can be prolonged. Thus, some patients still need therapy for their symptoms [9]. The most common long COVID-19

syndrome in the post-COVID patient was dyspnea or respiratory sequelae. These patients still need treatments that are mostly related to rehabilitation to restore their functional capacity. Rehabilitation therapy can be done for long COVID patients as physical rehabilitation therapy [10], [11], [12], [13], [14], [15], [16], [17], [18]. Physical rehabilitation therapy is very necessary so that the residual symptoms of COVID-19 infection disappear completely. Thus, patients can carry out their activities as usual.

From the background above, it can be concluded that patient with long COVID syndrome, especially with respiratory sequelae, needs treatment to restore their breathing capacity. The respiratory sequelae can be improved through physical rehabilitation therapy such as breathing exercises, physical exercise, and fitness and relaxation exercises. Moreover, there is a clear need for guidance on the rehabilitation of COVID-19 survivors. Thus, our systematic review gathered studies and guidelines regarding physical rehabilitation therapy for long COVID-19 patients.

#### **Methods**

# Search strategy

We conducted an online literature search on an online journal database published in PubMed and Cochrane library from December 2019 to March 2022. We used Boolean operator with keyword [("physical rehabilitation" OR "rehabilitation therapy" OR "physical therapy") AND ("long COVID-19" OR "long COVID syndrome" OR "post COVID-19 infection)] to specify the finding result further.

# Study eligibility

We included a study with some eligibility criteria using a PRISMA diagram, as seen in Figure 1. We did literature screening from the online database based on the search strategy keywords in the first step. The irrelevant or duplicated study was eliminated. In the second step, the abstract and full-text version of the studies were evaluated and assessed according to the eligibility criteria. The inclusion criteria that we used were studied regarding physical rehabilitation or rehabilitation therapy for long COVID-19 patients or post-COVID-19 infection with respiratory sequelae. In contrast, the exclusion criteria were a letter to the editor or a commentary report, a study not available in full text and not in English or Bahasa Indonesia.

#### Data gathering

Two reviewers gathered data to choose a study that met our eligibility criteria. The selected research

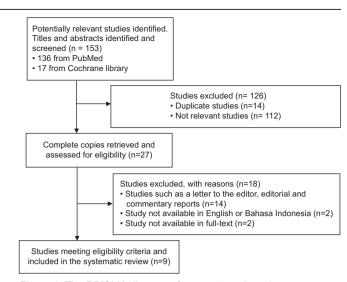


Figure 1: The PRISMA diagram of our systematic review

was then assessed for its evidence and included further analysis. All studies were read thoughtfully to extract the core idea of the literature.

### Study quality assessment

We used the Joanna Briggs Institute checklist for critical appraisal to assess the study's quality. We used a checklist according to each study design. Each item on the checklist had one point. A study is classified as good if it has a score equal to or more than half of the maximum total points [19].

# Data synthesis

relevant studies regarding physical rehabilitation or rehabilitation therapy for lona COVID-19 patients or post-COVID-19 infection were included in a narrative synthesis. Because this systematic review is a qualitative report, this study tried to gather information about physical therapy or physical rehabilitation guidelines or therapy for long COVID-19 patients or post-COVID-19 infection. The narrative synthesis was conducted systematically to conclude the range of physical rehabilitation therapy applied for long COVID-19 patients or post-COVID-19 infection.

#### Results

#### Study characteristics

One hundred and fifty-three studies were retrieved from the online database. After excluding duplicate studies and irrelevant titles, 27 pieces of the literature were assessed for the eligibility criteria.

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Eighteen studies did not meet the inclusion and exclusion criteria; only seven pieces of literature met the eligibility criteria and were included in the qualitative analysis. The nine included studies comprising two consensus statements or recommendations, one cohort retrospective study, two case studies or case reports, one review, and three experimental studies. Studies come from several countries, such as Brazil, China, Libya, Russia, Spain, Switzerland, the UK, and the USA. The experimental, cohort retrospective, and case series studies used post-COVID-19 patients as the subject. The analysis concludes that respiratory rehabilitation for long COVID patients is feasible and effective in relieving the sequelae, especially the respiratory sequelae. The detailed characterization of the study is described in Table 1.

#### Quality assessment result of the study

Quality assessment of the study using Joanna Briggs Institute checklist according to each study design. We used four types of checklists to assess the study quality: critical appraisal checklist for experimental study, case report, literature re, view and text, and opinion papers. Each item from the checklist contributed to one point. A study is considered good if it gets half or more maximum points and is regarded as low quality

if it gets less than the entire half-maximal point. The four reviewers (IMYP, DS, IPYP, and IBAPM) evaluated the quality of the study to avoid bias. A discussion was done to resolve any disagreement until we reached a common consensus. Of 11 studies involved, all were good quality, with a total point range from 5 to 7 [19].

# Long COVID-19 syndrome

The novel severe acute respiratory syndrome (SARS)-CoV-2 is highly infectious, causing a global pandemic since it was first discovered in Wuhan, China, in late 2019 [1]. COVID-19 dominantly affects the respiratory system. Still, evidence indicates that COVID-19 is a multisystem disease that is frequently severe and often causes death. COVID-19 can manifest in various medical conditions ranging from mild symptoms to severe conditions that require intensive care unit and ventilatory support. Some COVID-19 patients who tested negative and were discharged from the hospital still have some symptoms or sequelae [6]. Long-term sequelae of COVID-19 are unknown, but evidence from the previous coronavirus outbreaks demonstrates impaired pulmonary and physical function, reduced quality of life, and emotional distress. It is predicted that 45% of patients discharged from the hospital will require healthcare and social care support to do their

Table 1: Characteristic of study regarding physical rehabilitation for long COVID-19 patients

Study	Type of study	Study aim	Physical rehabilitation advice or intervention	Conclusion
Baker-Davies et al., 2020, UK	Consensus statement	Provide rehabilitation program recommendations.	Physical rehabilitation can be done according to the post-COVID-19 sequelae and should relieve dyspnea, psychological distress, physical function, and quality of life.	Rehabilitation for the post-COVID patient is patient-centered and individually based on the patient's sequelae [10].
Benzarti <i>et al.</i> , 2022, Libya	Recommendation	Provide cardiorespiratory rehabilitation (CRR) recommendations for long COVID patients.	CRR comprises at least 12 sessions, and Each session duration is about 50 min with four types of exercise.	The general practitioner should advise about CRR for post-COVID-19 patients with alteration of cardiorespiratory and muscular conditions [11].
Hermann <i>et al.</i> , 2020, Switzerland	Cohort retrospective	Evaluate the feasibility and potential benefit of cardiopulmonary rehabilitation for the post-COVID-19 patient.	Comprehensive CR consists of individualized exercise training, including aerobic and strength training, with 25–30 therapy sessions, 5–6 days per week.	Comprehensive CR for the post-COVID-19 patient is safe, feasible, and effective [12].
Kokhan <i>et al.</i> , 2021, Russia	Experimental	To assess the functional state of the post-COVID-19 patient before and after a course of physical rehabilitation.	The rehabilitation consists of physical therapy and breathing exercises held daily on an outpatient basis for 14 days for 30–60 min.	The functional state of post-COVID-19 patients after physical rehabilitation showed improvement in respiratory movements, oxygen saturation, the vital capacity of the lungs, and decreased heart rate [13].
Parkin <i>et al.</i> , 2021, UK	Case studies	Provide an integrated multidisciplinary comprehensive model of care of rehabilitation plan for the post-COVID-19 patient.	A rehabilitation plan for the post-COVID-19 patient can use three-tier model management. Level 1 needs a multidisciplinary team (MDT), level 2 needs community therapy teams, and level 3 needs a hospital or general practitioner (GP).	The three-tier model rehabilitation plan gives individualized interventions and comprehensive management for the post-COVID-19 patient [14].
Tang <i>et al.</i> , 2021, China	Experimental	Investigate the effects of Liuzijue exercise on the rehabilitation of COVID-19 patients.	Liuzijue exercises once per day for 20 min for 4 weeks.	Liuzijue exercise is a viable alternative home exercise program that can increase MIP, PIF, DM-DB, and quality of life in discharged patients with COVID-19 [15].
Tomato <i>et al</i> ., 2021, Brazil	Case report	Provide four different severity levels of post-COVID-19 syndrome treated with a cardiopulmonary rehabilitation program.	The cardiopulmonary rehabilitation program comprises a 6-min Walk Test, peripheral muscle strength, and double product at rest for a three-month rehabilitation protocol of at least 300 min/week.	The cardiopulmonary rehabilitation program gives a positive impact on these cases by improving functional capacity [16].
Udina <i>et al.</i> , 2021, Spain	Experimental	Effect of therapeutic exercise on a post-COVID-19 patient.	A 30-min daily multicomponent therapeutic exercise intervention combined resistance, endurance, and balance training.	Despite the previous admission to ICU, patients surviving COVID-19 seem to improve their functional status through a short, individualized, multicomponent therapeutic exercise intervention [17].
Yan <i>et al.</i> , 2021, China	Review	Provide follow-up and rehabilitation plans and management for each long COVID-19 syndrome.	The rehabilitation recommendation for long COVID-19 patients is based on the symptom severity. Mild require home surveillance and telemedicine; moderate require community therapy team with regular follow up, and severe need MDT care with regular follow up.	Early identification of long COVID-19 syndrome and early planning of rehabilitation programs are vital for their functional recovery and improved quality of life [18].

Abbreviation: CCRR: cardiorespiratory rehabilitation; GP: general practitioner; DM-DB: diaphragm movement in deep breathing; MDT: multidisciplinary team; MIP: maximal inspiratory pressure; PIF: peak inspiratory flow; UK: United Kingdom; USA: United States of America.

daily activity living. The National Institute for Health and Care Excellence (NICE) describes "post COVID-19 syndrome" or "Long COVID" as a set of persistent physical, cognitive, and psychological symptoms that continue for more than 12 weeks after COVID-19 infection and which are not explained by the alternative diagnosis. The long COVID-19 syndrome varies based on the virus's organ most affected the most. The COVID-19 sequelae can affect all of our system organs, such as respiratory, cardiovascular, musculoskeletal, neurological, hematological, digestive, renal, and even the patient's mental health [4].

# 1. Sequelae in respiratory

About 39% of COVID-19 patients discharged still have respiratory symptoms such as breathing discomfort, persistent cough, excessive sputum production, and sore throat. A postmortem study revealed extensive alveolus damage that supports the possibility of lung sequelae due to permanent lung damage and causing fibrosis.

#### 2. Sequelae in cardiovascular

Cardiovascular sequelae were reported in 13% of discharged COVID-19 patients. The symptoms are increasing resting heart rate, hypertension, extensive myocardium lesion, reduced systolic function, and arrhythmia. It is possibly caused by direct injury to cardiomyocytes, systemic inflammation, interstitial myocardium fibrosis, and hypoxia.

Sequelae in musculoskeletal
 Musculoskeletal sequelae include myalgia, fatigue, and joint pain. Muscular weakness, muscular imbalance, or even atrophy also can be seen in post-COVID-19 patients, particularly those who had long been bedridden in ICU.

#### 4. Sequelae in neurologic

Neurological sequelae in long COVID-19 syndrome include headaches, dizziness, paraesthesia, and sensory deficits such as olfactory and gustatory dysfunction. It is possibly caused by the direct spread of SARS-CoV-2 to the central nervous system through viral neurotropism.

### 5. Other sequelae

Other sequelae can involve other organs such as renal, digestive, reproductive systems, and mental health such as anxiety and depression [4], [5], [6].

# Pathway of rehabilitation program for long COVID-19 patient

The National Institute for Health and Care Excellence (NICE) recommends progressive rehabilitation programs are best initiated within the first 30 days (post-acute phase) to have the greatest impact on recovery [4]. From our study analysis, three studies

stated the pathway for a rehabilitation program in long COVID-19 patients [10], [14], [18]. The Stanford Hall consensus statement for post-COVID-19 rehabilitation said that rehabilitation is patient-centered and according to individual patient needs; any rehabilitation program should base on patient sequelae or symptoms that may affect a patient's progress or ability to partake in a program [10]. Parkin *et al.* also stated that after COVID-19 patients are discharged from the hospital, they should have follow-up regarding the symptoms or sequelae that the patients might experience through some questionnaire such as the COVID-19 Yorkshire Rehabilitation Scale (C19-YRS). Next, they should be classified into levels 1, 2, or 3 according to the three-tier model of management, as shown in Figure 2 [14].

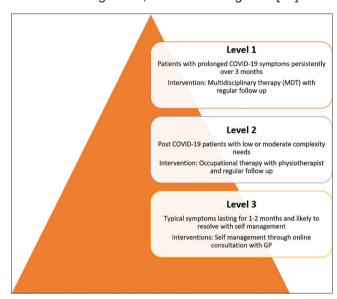


Figure 2: The three-tier model management for long COVID-19 syndrome rehabilitation program [10], [14], [18]

Patients with long COVID-19 symptoms or seguelae lasting between 1 and 2 months classified as Level 3 can be self-managed using online resources and consultation with a general practitioner (GP). In level 2, a classified patient with low/moderate complexity is supported by non-COVID-specific care and therapy services, such as community occupational and physiotherapy. Patients who meet the Level 1 criteria of having prolonged symptoms over 3 months with a clear need for more than one specialist role are eligible for referral into the Community COVID-19 MDT. The level 1 community covid-19 MDT consists of two allied health professional (AHP) pathway coordinators, two physiotherapists, two occupational therapists, and two consultants with specialisms in rehabilitation medicine, respiratory medicine, and cardiology; with specialist support from a respiratory nurse, respiratory physiotherapists, two dieticians, and two neurological occupational therapists [10], [14]. Yan et al. stated that the rehabilitation recommendation for long COVID-19 patients is based on the symptom severity. Mild require home surveillance and telemedicine, moderate require community therapy team with regular follow-up, and severe need MDT care with

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regular follow-up. Early identification of long COVID-19 syndrome and early planning of rehabilitation programs are vital for their functional recovery and improved quality of life [18].

# Rehabilitation exercise for long COVID-19 patient with respiratory sequelae

From our analysis, most of the studies recommend cardiorespiratory rehabilitation (CRR) as rehabilitation therapy for long COVID patients. A study by Benzarti et al. suggests CRR exercise that comprises four exercises with 50 min total duration: walking for 30 min, strength training for 10 min, balance posture for 5 min, and stretching for 5 min, as shown in Figure 3. Ideally, the CRR should be done in 12 sessions; it can be three sessions per week for 4 weeks. Before the CRR start, the doctor should evaluate the patient's dyspnea condition, give CRR content patient's education, respond to the patient's inquiries and provide psychological support. After the CRR exercise is done. the dyspnea will be re-evaluated. The patient also asks for their feedback, and the doctor encourages them for their next exercise [11]. Another study by Hermann et al. did rehabilitation through comprehensive CR consisting of individualized exercise training, including aerobic exercise and strength training with 25-30 therapy sessions; 5-6 days per week that is s safe, feasible, and effective. The exercise capacity was measured using the 6-min walk test (6-MWT), performed once at the beginning and once at the end of the CR program after 20 days. Both studies stated that CRR exercise effectively improves dyspnea and shortness of breath [12].



Figure 3: The cardiorespiratory rehabilitation exercise items [11]

Another study by Tozato *et al.* also advised CRR program consists of a 6-min Walk Test, peripheral muscle strength, and double product at rest for a three-month rehabilitation protocol of at least 300 min per week through four case reports. All of the patients from their case reports showed cardiovascular recovery as assessed by the double product, reduced exertion

dyspnea, increased peripheral muscle strength, and functional independence as reported and observed throughout the rehabilitation. The peripheral muscle strength was also increased, ranging from 20% to 6 times the baseline values [16]. Experimental study by Kokhan et al. focused on deep and slow breathing exercises, focusing on the respiratory rate of 12–15 times per min, breathing through slightly compressed lips. The exercise was held daily on an outpatient basis for 14 days for 30–60 min. The functional state of post-COVID-19 patients after physical rehabilitation showed improvement in respiratory movements, oxygen saturation, the vital capacity of the lungs, and decreased heart rate [13].

A study by Udina et al. recommends therapeutic exercise for the post-COVID-19 adult patient. Therapeutic exercise (TE) is a physical therapy technique used to improve or maintain a person's physical condition through resistance, endurance, flexibility, and balance training. The intensity, volume. progression, and type of exercise must be individualized based on the physical condition and tolerance during the execution of TE. Their study stated that most patients showed improved physical function after a relatively short therapeutic exercise intervention [17]. Last study by Tang et al. used Liuzijue exercise to rehabilitate COVID-19 patients. Liuziiue exercise is a traditional Chinese fitness method that helps to improve human health. Liuzijue involves inhalation and exhalation through different mouth patterns to regulate and control the rise and fall of the breath in the body. It is performed by producing six different sounds through expiration together with corresponding body movement. This study assessed MIP, PIF, DT, and DM-DB that reflect the respiratory muscle strength and function. After 4 weeks of the Intervention, the MIP, PIF, and DM-DB were significantly improved [15].

# **Discussion**

COVID-19 is a global pandemic affecting individuals to varying degrees, ranging from a few days of mild symptoms to respiratory distress requiring ICU treatment, including ventilatory support, and death. Although many COVID-19 patients recover fully from the disease, approximately 5–10% experience prolonged symptoms for several months following the acute COVID-19 phase [1], [4], [9]. This results in millions of people suffering from COVID-19 sequelae worldwide. After 6 months, the most frequent symptoms reported were fatigue, post-exertional malaise, and cognitive dysfunction. The survey found that 21% of patients were still experiencing severe symptoms after 6 months. Two-thirds required a reduced work schedule or no longer working due to illness [19].

From our qualitative analysis, we found that beneficial interventions urgently need to counteract these longterm COVID-19 consequences. There is a clear need to plan for post-acute and chronic rehabilitation of patients recovering from COVID-19. Exercise training should be one of the vital approaches in rehabilitating COVID-19 patients. Rehabilitation plays a major role in managing the health-related issue of COVID-19 patients for both hospitalized and discharged patients. However, rehabilitation interventions in this situation are guite complex and need well-trained professionals. As stated by Wise et al. and Nugraha et al., physical rehabilitation for post-COVID patients need the complex hygiene regulations, specific training, and personal protective equipment required to handle this particular group of patients [20], [21].

Our analysis result found that most of the recommended exercise for post-COVID rehabilitation programs comprises lung rehabilitation [22]. As we know, respiratory complication is the most COVID-19 sequelae found in discharged COVID-19 patients. Most complain of dyspnea exertion and breathing difficulty that alter their functional status in daily activity living [11], [12], [16]. Thus, a lung rehabilitation program aims to improve the lung's capacity and quality of life to overcome the symptoms and prevent deconditioning the airway tract and other system organs. COVID-19 is an interstitial lung disease that affects ventilation capacity and tissue oxygenation. An exercise that helps increase tissue oxygenation and improves exercise capacity is needed to improve oxygenation. But there are some contraindications for post-COVID-19 patient rehabilitation programs. Nugraha et al. stated that physical rehabilitation should be postponed if the heart rate is more than 100 times/min, oxygen saturation is below 95%, blood pressure is less than 90/60 mmHa or more than 140/90 mmHg and other diseases that disrupt the exercise program [21].

Long-term rehabilitation for COVID-19 patients with mild symptoms can be done through education, breathing exercises, physical exercise, airway clearance techniques, and anxiety management. As an essential part of post-acute care in COVID-19 patients, a study by Baker-Davies *et al.*, Kokhan *et al.*, and Tozato *et al.* stated that a cardiorespiratory rehabilitation program is feasible and effective in minimizing long-term disability and allows the post-COVID-19 patient to do their functional capacity back to normal [10], [13], [16].

# Conclusion

Based on our systematic review, we can conclude that rehabilitation programs for long COVID-19 syndrome, especially with respiratory sequelae, should be individually according to the patient's needs. The

recommended rehabilitation program pathway using a three-tier model depends on the severity of the disease. Rehabilitation exercises for long COVID patients include cardiorespiratory exercise, breathing exercise, therapeutic exercise, and traditional Chinese fitness models such as Liuzijue exercise. These exercises are feasible and effective in improving the patient's breathing effort and improving dyspnea and muscle strength.

#### **Author Contribution**

All authors contributed to the study, including conceptual framework, design, data collection, and data analysis to report study results for publication.

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