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REVIEW ARTICLE

Rehabilitation of Patients with Post-COVID-19 Syndrome: A Narrative Review

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Objectives: We aimed to review the most recent articles on the rehabilitation of patients after coronavirus disease 2019 (COVID-19) and to identify the methods and effects of rehabilitation on such patients. **Methods**: A literature search was conducted using PubMed and Web of Science from study inception to October 2022 using the following search terms to identify meta-analyses and randomized controlled studies with abstracts written in English: ["COVID-19" or "COVID 19" or "2019-nCoV" or "SARS-CoV" or "novel coronavirus" or "SARS-CoV-2"] and ["rehabilitation"]. Publications investigating the effects of pulmonary and physical rehabilitation on patients with COVID-19 were extracted. **Results:** The extraction process selected four meta-analyses, two systematic reviews, two literature reviews, and two randomized controlled trials. Pulmonary rehabilitation recovered forced vital capacity (FVC), 6-min walk distance (6MWD), health-related quality of life (HRQOL), and dyspnea. Pulmonary rehabilitation increased predicted FVC, distance in the 6MWD test, and HRQOL score compared with baseline values. Physical rehabilitation, comprising aerobic exercises and resistance training, effectively improved fatigue, functional capacity, and quality of life with no adverse events. Telerehabilitation was an effective tool to provide rehabilitation for patients with COVID-19. **Conclusions:** Our study suggests that rehabilitation after COVID-19 should be considered an effective therapeutic strategy to improve the functional capacity and quality of life of patients with COVID-19.

Key Words: activity of daily living; meta-analysis; randomized controlled trial; respiratory function

INTRODUCTION

Patients with coronavirus disease 2019 (COVID-19) who require prolonged intensive care may experience muscle atrophy and loss of muscle mass, as well as decreased respiratory function caused by multiple organ failure or sepsis. These patients require comprehensive, multidisciplinary rehabilitation to regain their capacity for activities of daily living.[1–9] The survival rate of patients with COVID-19 varies depending on the strain, with infection with the Omicron strain resulting in a higher survival rate than that with the Delta strain. Recently, the overall survival rate of patients with COVID-19 has increased because of the prevalence of the Omicron strain. For these patients, the acute phase progresses into the subacute phase and many recover; however, some patients may experience a condition known as post-COVID-19 condition.[10] Post-COVID-19 symptoms include fatigue, reduced physical capacity, anxiety, dyspnea, post-traumatic stress disorder, amnesia, arthralgia, and depression.[11–13] Symptoms appear 30–90 days after the onset of COVID-19, with the highest incidence at about 60 days.[13] Post-COVID-19 symptoms are not exclusive to patients with severe cases but also manifest in those with relatively mild cases, and more than 60% of those infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) experience post-COVID-19 symptoms. These findings indicate the need for rehabilitation according to the level of impairment caused by post-COVID-19 symptoms.

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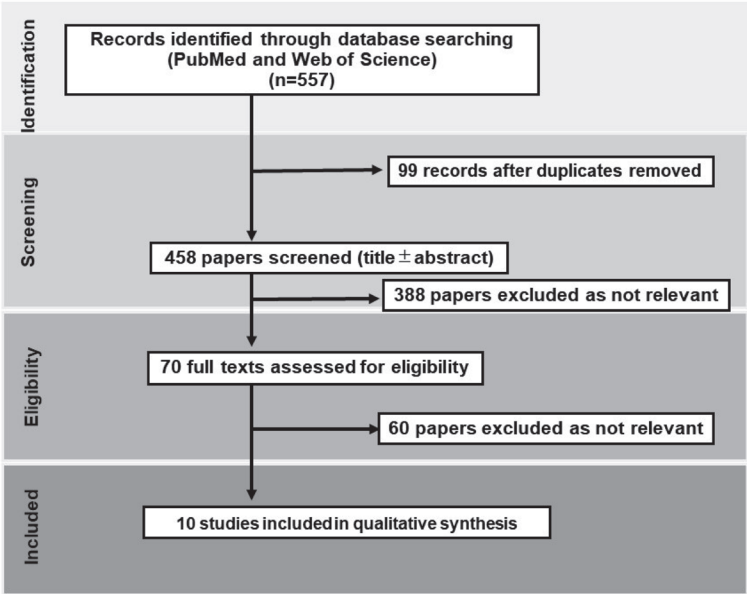

Fig. 1. Flow chart of review selection process.

The most common respiratory manifestations of post-COVID-19 conditions include considerably decreased DLCO (diffusing capacity of the lung for carbon monoxide) and associated interstitial lung damage.[14,15] These persistent respiratory complications cause morbidity, long-term disability, and even death because of progressive lung fibrosis. Furthermore, cardiac complications, especially arrhythmias and myocardial injury, may result from post-COVID-19 conditions.[16–18]

Pulmonary rehabilitation (PR) has been proposed for decades to provide comprehensive care and improve the functional status of patients with respiratory diseases.[19] The consensus statement for rehabilitation after COVID-19 is being developed based on data obtained from a previous coronavirus outbreak because the long-term results for COVID-19 are not available. Therefore, we should consider the type, intensity, duration, and effectiveness of rehabilitation for post-COVID-19 conditions. In this study, we reviewed articles on the rehabilitation of patients with COVID-19 and examined the characteristics and effectiveness of PR.

MATERIALS AND METHODS

For this review, a literature search was conducted using PubMed and Web of Science from inception until October 31, 2022, using the following search terms: [“COVID-19” or “COVID 19” or “2019-nCoV” or “SARS-CoV” or “novel coronavirus” or “SARS-CoV-2”] and [“rehabilitation”]. Meta-analyses and randomized controlled studies written in English were included. The inclusion criteria were articles about rehabilitation for patients with COVID-19. We excluded articles in which rehabilitation was provided to patients with diseases other than COVID-19 during the COVID-19 pandemic or those that did not include the actual rehabilitation. The articles were first screened by reading titles and abstracts. Full-text reviews were conducted for articles that remained unclear from the title or abstract screening (**Fig. 1**). Because this was a literature review, ethical approval and informed consent were not required.

RESULTS

PubMed and Web of Science database searches yielded 557 articles, of which 99 were removed because of duplication. Of those remaining, 388 were excluded based on their titles and abstracts, and 70 reports were read in full. Finally, 10 articles were extracted for the review (**Fig. 1**). These included 4 meta-analyses, 2 systematic reviews, 2 randomized controlled trials (RCTs), 1 literature review focusing on pulmonary and physical rehabilitation (**Table 1**), and 1 literature review on recommendations for risk management.

Demeco et al. recommend respiratory rehabilitation interventions be individualized, especially for patients with comorbidities, advanced age, obesity, multiple diseases, or single or multiple organ complications.[20] The rehabilitation team needs to focus on patient-specific problems to develop

Table 1. Outcomes of the reviewed studies (n=9)

Study and country	Type	Study participants	ICU/MV history	Exclusion criteria	Control	Intervention	One session (min)	Frequency (times/week)	Duration/week (min)	Duration	Methods	Respiratory function	Dyspnea	Physical capacity	HRQOL
Reina-Gutierrez et al.[21] Spain	Systematic review Meta-analysis	11 studies 637 participants	ILD Severe COVID-19	Not listed	Usual care Weekly telephone support	Respiratory muscle training Aerobic exercises (ergometer, walking, treadmill) Resistance training (10–15 RM)	20–45	2–6	40–150	3–12 weeks	Supervised	FVC	Borg RPE mMRC	6MWD	HRQOL
Ahmed et al.[22] Turkey	Systematic review Meta-analysis	8 studies 449 participants	Mild-to-severe COVID-19	Not listed	Usual care	Respiratory muscle training Aerobic execises	10–60	1–5	20–180	1–12 weeks	Supervised or telerehabilitation	FVC, FEV1%	Dyspnea	6MWD	HRQOL
McNarry et al.[23] UK	RCT	281 participants	Self-reported COVID-19 With breathlessness >18 years	Dementia Cardiac disease High risk of falls	Usual care	8-week IMT	20	3	60	8 weeks	Unsupervised	MIP SMIP	K-BILD domains for breathlessness TDI, FIT	Estimated V' O2 max	-
Chen et al.[24] China	Systematic review Meta-analysis	3 studies 233 participants	Mild-to-moderate COVID-19	Not listed	Education	Respiratory muscle training (device-based: threshold PEP) 1 study: +lower limb muscle exercises	10–40	2–4	120–300	2–6 weeks	Home exercises	FVC, FEV1%	DSI mMRC (one study)	6MWD	Physical HRQOL Mental HRQOL (two studies)
Ahmadi Hekmartikar et al.[26] Iran	Systematic review	7 studies 286 participants	Mild-to-moderate COVID-19	Not listed	Post-ICU vs. non-ICU Post vs. non-hospitalized	Aerobic exercise (3–5 on modified Borg scale) Resistance training (10–20 RM)	15–30	2–7	60–105	10 days to 12 weeks	Supervised	Not assessed	Fatigue (one study) Depression (one study)	6 MWD or hand grip strength 30-s sit-to-stand test	HRQOL
Jimeno-Almazan et al.[25] Spain	RCT	39 participants	Post-COVID-19 condition Symptoms lasting 12 weeks Not hospitalized >18 years	Cardlac disease COPD SpO2<94%, Breath frequency 23 bpm	Unsupervised self-management Following WHO guidelines	Tailored and supervised program Two days: resistance training+MIVT Third day: monitored LICT	30–60	3	90–180	8 weeks	Supervised	-	CFQ-11	Estimated V' O2 max	Physical HRQOL

Table 1. *Continued*

Study and country	Type	Study participants	ICU/MV history	Exclusion criteria	Control	Intervention	One session (min)	Frequency (times/week)	Duration/week (min)	Duration	Methods	Respiratory function	Dyspnea	Physical capacity	HRQOL
Nambi et al.[27] Saudi Arabia	RCT	76 participants	Men aged 60–80 years Post-COVID-19 sarcopenia	Respiratory, cardiac, or neurological problems, fractures	Low (40%–60% of HR max) vs. High (60%–80% of HR max)-intensity aerobic exercises	15 min of warm-up (stretching) 30 min low- or high-intensity aerobic exercises 15 min cool down (stretching and breathing)	30	4	120	8 weeks	Supervised	Not assessed	Not assessed	Hand grip strength Muscle quantity Tampa scale Kinesiophobia	HRQOL
Huang et al.[28] China	Systematic review Meta-analysis	7 studies 652 participants	Patients with COVID-19 >18 years	Not listed	No treatments or usual care	Breathing, aerobics, or strength exercises	Web-based 10 exercises	3–7	-	1–6 weeks	Web-based or online	-	Borg RPE Multidimensional dyspnea-12	Muscle strength 30-s sit-to-stand test	-
Vieira et al.[29] Brazil	Systematic review	6 trials 323 participants	Mild-to-moderate COVID-19 >18 years	Not listed	No treatments or usual care	Breathing, aerobics, or strength exercises	Web-based Not listed	3–7	-	1–12 weeks	Web-based or online	FVC, FEV1%	Borg RPE	6 MWD 30-s sit-to-stand test	Physical HRQOL

ICU/MV, intensive care unit/mechanical ventilation; ILD, interstitial lung disease; RM, repetitive maximum; FVC, forced vital capacity; 6MWD, 6-min walk distance; HRQOL, health-related quality of life; Borg RPE, Borg rating of perceived exertion; mMRC, modified Medical Research Council dyspnea scale; K-BILD, King's brief interstitial lung disease; TDI, transition dyspnea index; DSI, dyspnea severity index; CFQ-11, Chader fatigue questionnaire; DSQ-14, DePaul symptom questionnaire short form; COPD, chronic obstructive pulmonary disease; MIP, maximal inspiratory presssure; SMIP, sustained maximal inspiratory pressure; MIVT, moderate-intensity various training; LICT, light-intensity continuous training; FIT, fatigue index test.

individualized programs and to monitor patients throughout the respiratory rehabilitation process, including the use of different techniques; some recommendations for discharged patients are listed in **Table 2**.

Reina-Gutiérrez et al. reported that PR and physical exercises, including resistance and aerobic exercises, increased the predicted forced vital capacity (FVC) by 5.5%, increased the 6-min walk distance (6MWD) by 44.55 m, and increased the health-related quality-of-life (HRQOL) score by 3.9 points compared with the respective baseline values in patients with interstitial lung disease (ILD), including those with severe COVID-19 and severe respiratory symptoms.[21] Although data from cases of ILD and COVID-19 with critical illness were included, respiratory muscle training, aerobic exercises, and muscle strengthening improved respiratory function, physical function, and respiratory distress in critically ill patients.[21] Ahmed et al. have also reported that respiratory muscle training and aerobic exercises provided under supervision or by telerehabilitation improved FVC, respiratory function and dyspnea, 6MWD, and HRQOL scores in patients with mild-to-severe COVID-19.[22]

In a systematic review, McNarry et al. reported that home-

Table 2. Principal recommendations for discharged patients

Consideration	Description
Exclusion criteria	(1) Heart rate>100 beats/min; (2) blood pressure<90/60 mmHg or>140/90 mmHg; (3) blood oxygen saturation ≤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.
Rehabilitation evaluation	Clinical evaluation: physical examination, imaging, laboratory tests, lung function tests. Evaluation of exercise and respiratory function: (1) Respiratory muscle strength: maximum inspiratory pressure/maximum expiratory pressure. (2) Muscle strength (Medical Research Council), isokinetic muscle testing. (3) Joint range-of-motion measurement. (4) Balance function evaluation: Berg Balance Scale. (5) Aerobic exercise capacity: 6MWT. (6) Physical activity assessment: international physical activity level tables (International Physical Activity Questionnaire), physical activity scale for the elderly. 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 exercises for patients such as walking, brisk walking, jogging, and swimming, starting from low intensity, gradually increasing the intensity and duration: 3–5 times per week for 20–30 min 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 2–3 times per week, with a training period of 6 weeks and a weekly increase of 5%–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, and difficulty with sputum discharge, they must begin breathing and sputum training and breathing mode training including body management, adjusting breathing rhythm, thoracic 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 ADL: assess ability to perform daily activities such as training transfer, grooming, toileting, and bathing, and provide rehabilitation guidance for daily life obstacles. (2) Instrumental ADL: assess the ability of instrumental daily activities, identify obstacles in task participation, and conduct targeted intervention under the guidance of an occupational therapist.

based inspiratory muscle training (IMT) for 281 adults recovering from self-reported COVID-19 who had been randomized (4:1) to an 8-week IMT or "usual care" (control) group was effective for producing clinically meaningful improvements in the King's Brief Interstitial Lung Disease (K-BILD) domains for breathlessness and the Transition Dyspnea Index for breathlessness, as well as in respiratory muscle strength and estimated aerobic fitness.[23] However, no difference was observed between the groups in terms of the K-BILD total score after intervention.[23]

According to a systematic review and meta-analysis by Chen et al., PR significantly improved 6MWD and physical QOL in individuals with post-COVID-19 conditions and exhibiting lung impairment.[24] They analyzed three studies that employed device-based home respiratory muscle training for 233 post-COVID patients and one study that employed lower limb muscle strength exercises. They reported that PR could improve dyspnea, mental QOL, and exercise capacity among patients with mild-to-moderate lung impairment after COVID-19, although they did not consider the heterogeneity of the intervention design and duration and different outcomes.[24]

Jimeno-Almazán et al. compared the outcomes of patients with post-COVID-19 undergoing supervised therapeutic exercise intervention with those following the self-management WHO rehabilitation leaflet in an RCT of 39 patients in the chronic symptomatic phase lasting more than 12 weeks.[25] Patients were randomly assigned to a tailored multicomponent exercise program based on concurrent training for 8 weeks [two supervised sessions per week of resistance training combined with aerobic training (moderate-intensity variable training) plus a third day of monitored light-intensity continuous training] or to a control group that followed the WHO guidelines for rehabilitation after COVID-19. The levels of the cardiovascular and strength markers significantly increased in the exercise group: VO_2 max, +5.7%; sit-to-stand, −22.7%; load-velocity profiles in bench press, +6.3%; and half squat, +16.9% ($P<0.05$).[25]

Ahmadi Hekmatikar et al. conducted a systematic review to evaluate the effect of resistance or aerobic exercises on post-COVID-19 patients after hospital discharge.[26] Their review showed that 7 of 381 studies reported that exercise programs consisting of resistance exercises [e.g., one or two sets of 8–10 repetitions at 30%–80% of one repetition maximum (1RM)] and aerobic exercise (e.g., 5–30 min at moderate intensity) may improve functional capacity and QOL (reduce stress and the incidence of mental disorders) in post-COVID-19 patients. They demonstrated that the exercise intensity could range from 30% to 80% of 1RM for resistance exercises, from 3 to 5 on the modified Borg Scale, and from 40% to 60% of maximum heart rate for the aerobic exercises without any adverse events or without the need for hospital re-admission.[26]

Nambi et al. reported on men aged 60–80 years with post-COVID-19 sarcopenia who received resistance training.[27] Patients were randomized into two groups: low-intensity aerobic training group (40%–60% of maximum heart rate, n=38), and high-intensity aerobic training group (60%–80% of maximum heart rate, n=38) for 30 min per session, one session per day, 4 days/week for 8 weeks. At the end of the 6-month follow-up, handgrip strength, kinesiophobia level, and QOL showed improvement in both groups, with more improvement in the low-intensity aerobic training group than in the high-intensity aerobic training group.[27]

After a meta-analysis of RCTs, Huang et al. reported the superiority of telerehabilitation over no treatment or usual care for dyspnea (Borg Scale) in terms of limb muscle strength, ambulation capacity, and depression, with no significant difference in terms of anxiety or QOL.[28] The interventions included online, web-based, or app-based exercise programs including PR, PR and strengthening exercises, stretching, or a combination of these methods.[28]

Vieira et al. also conducted a systematic review of randomized trials that assessed the effects of telerehabilitation delivered as a website exercise program, an app-based exercise program, or a video exercise program.[29] They found that breathing exercises or aerobic exercises and lower limb muscle strength exercises delivered via telerehabilitation improved the scores of the 6MWDT, the 30-s sit-to-stand test, Multidimensional Dyspnea-12 questionnaire, and 0–10 Borg Scale compared with those in the control group with no intervention in six trials with 323 participants.[29]

DISCUSSION

We reviewed articles on the rehabilitation of patients with COVID-19 and examined the characteristics and effectiveness of PR. The rehabilitation was targeted to patients post-COVID-19 and included a variety of patients, from those with self-reported COVID-19 to those with severe COVID-19. COVID-19 can range in severity, from involving home recuperation to requiring intensive care. The goal of rehabilitation is to restore the pre-COVID-19 level of activity and improve the QOL. Patients with severe disease require treatment from the time they are admitted to the intensive care unit until they return home, where they must be sup-

ported until they can return to society. In contrast, post-COVID symptoms occur not only in severely ill patients but also in mild-to-moderately ill patients, presenting with symptoms such as breathlessness and fatigue.

A systematic review that compared the prevalence of long-COVID symptoms according to relevant SARS-CoV-2 variants in COVID-19 survivors showed that the patients infected with Omicron variants (B.1.1.529/BA.1) showed fewer long-COVID symptoms than those infected with the Alpha (B.1.1.7) and Delta (B.1.617.2) variants.[10] However, the number of patients with long-term COVID varies with the infection rate and characteristics of the variants. Considering that the Omicron variants cause less severe disease with higher survival rates and higher transmission rates, the prevalence of the Omicron variants results in an increased number of patients.[10]

The rehabilitation for post-COVID-19 symptoms included respiratory muscle strengthening, breathing techniques, resistance training for lower extremity muscles, resistance exercises, and aerobic exercises. PR has been suggested for decades to provide comprehensive care and improve the functional status of patients with respiratory diseases.[30] Effective exercises can be planned according to the frequency, intensity, time, and type of exercises.[31] The provided PR for COVID-19 varied in frequency, intensity, time, and type of exercises and showed improvements in FVC in respiratory function, subjective respiratory symptoms such as breathlessness and fatigue, and physical activity measures such as 6MWD or sit-to-stand test and HRQOL scores.

Rehabilitation must be provided safely and effectively. Ahmadi Hekmatikar et al. demonstrated that exercise intensity of 30%–80% of 1RM for resistance and 3–5 on the modified Borg Scale with 40%–60% of maximum heart rate for aerobic exercise could be performed without adverse events or hospital re-admission.[26] In other studies, resistance exercises were also performed at 10–20 RM, which was the equivalent of 65%–80% of 1RM or at the level of 3–5 on the modified Borg Scale. The exclusion criteria of the studies included comorbidities of respiratory, cardiac, or physical diseases. Respiratory and cardiac complications should be considered because patients with or after COVID-19 may have some degree of disability and functional limitations, including those resulting from decreased respiratory function or particularly arrhythmias and myocardial damage.[16,17,32] An initial assessment of pulmonary and physical functional impairment is recommended to ensure that rehabilitation can be conducted safely. Patients with COVID-19 who require oxygen therapy in the acute setting should undergo chest radiography, chest computed tomography, and pulmonary function tests. Cardiac symptoms and potential impairment should be investigated regardless of disease severity together with functional assessment of residual musculoskeletal impairment because rehabilitation after COVID-19 often includes patient-directed exercise during and after hospitalization, home therapy sessions, and telemedicine treatment.

Nambi et al. reported that low-intensity aerobic training exercises were more effective in improving clinical and psychological measures than high-intensity aerobic training in patients with post-COVID-19 sarcopenia.[27] It is reported that acute exercise can induce an increase in inflammatory cytokines and oxide synthase markers after exercise.[33] Although exercise is essential for the rehabilitation of COVID-19 to improve respiratory and physical function, the appropriate intensity of exercise should be further examined in larger populations and in populations with different backgrounds.

It is likely to be more effective to provide the appropriate amount of exercise with a tailor-made program to the patients with supervised rehabilitation than with self-training. However, the rehabilitation of patients with post-COVID-19 is usually performed after discharge from the hospital and there are difficulties in providing guidance. Although there were no cases of worsening of symptoms after rehabilitation, it is desirable to monitor patients with severe symptoms and the progress of their symptoms. It is also advisable to monitor progress during rehabilitation of patients with mild symptoms and those with severe symptoms, along with an evaluation of their condition.[19]

Telerehabilitation improved shortness of breath, physical performance, and physical quality of life. It was provided with the use of videos or app-based or web-based programs or delivered by physiotherapy professionals via telecom/Internet network services. Telemedicine has served as a conventional method to provide rehabilitation since the latter part of the twentieth century, although its application has spread slowly.[34–36] Nevertheless, the use of digital and remote technologies unexpectedly increased in society after the COVID-19 pandemic and has also become a revolutionary aspect of healthcare. Telemedicine has become increasingly convenient for its ability to avoid infection transmission and clustering, low cost, short waiting times, and reduction of unnecessary commutes to receive treatment.[37] Telemedicine with rehabilitation offers patients a variety of benefits, including reduced costs, convenient access, and time to visit a hospital. Although further research on the type, intensity, and duration of exercise is warranted, telemedicine is promising for rehabilitation. However, safety

management in telerehabilitation is difficult owing to limitations imposed by distance. Depending on patient condition, it may be necessary to consider conducting the rehabilitation or checking vital signs using telemedicine devices during online consultation.[38]

The most common respiratory manifestation of COVID-19 is a marked decrease in DLCO and associated interstitial lung damage. One year after moderate COVID-19, the incidence of decreased DLCO and persistent lung damage still exceeds 30%. Persistent respiratory complications can cause considerable population morbidity, long-term disability, and even death as a result of progressive lung fibrosis. The incidence of lung fibrosis caused by COVID-19 can be estimated based on a 15-year observational study of lung pathology after SARS-CoV infection.[39] Most infected patients with fibrotic lung injury recovered within the first year and remained healthy thereafter. However, in 20% of cases, significant fibrosis progression was observed after 5–10 years. Therefore, fibrosis is expected to be a major long-term complication of COVID-19, even in asymptomatic individuals. Currently, despite the best efforts of the global medical community, a cure for COVID-induced pulmonary fibrosis is yet to be established. Nevertheless, rehabilitation should be provided, and the long-term course of respiratory symptoms should be monitored.[39]

There are some limitations to this study. The first is that this is a narrative review, which may have introduced some bias in the selection of studies. The second is that the heterogeneity of the studies and rehabilitation caused by different rehabilitation interventions was not determined. Because the long-term course of post-COVID-19 symptoms is still unknown, further long-term studies are needed for comprehensive evaluation of post-rehabilitation effects.

CONCLUSION

This narrative study confirms that rehabilitation for post-COVID-19 is an effective therapeutic strategy to improve the respiratory and functional capacity, subjective dyspnea, and QOL of patients after COVID-19.

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CONFLICTS OF INTEREST

The authors declare no conflict of interest.

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