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REVIEW

The effect of exercise rehabilitation on COVID-19 outcomes: a systematic review of observational and intervention studies

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Abstract

Purpose Disturbance to physical and psychological characteristics among COVID-19 survivors are not uncommon complications. In the current systematic review, we aimed to investigate the role of exercise rehabilitation programs, either in acute or post-acute phase, on COVID-19 patients' outcomes.

Methods A systematic search was conducted in November 2021 of Web of Sciences, PubMed-Medline, Google Scholar, and Scopus. Observational and intervention studies on COVID-19-infected patients undergoing a rehabilitation program including any type of exercise were included if they reported physical or psychological factors as outcomes. The Cochrane risk of bias tool for randomized controlled trials and Joanna Briggs Institute (JBI) critical appraisal checklist were used by two independent reviewers.

Results A total number of 469, and 957 patients were included in 9 intervention studies, and 14 observational studies, respectively. Most factors reported by studies as outcomes fell in the categories of exercise capacity, respiratory function, as well as psychological aspects. The reported outcomes in almost all studies, disclosed the overall beneficial role of exercise rehabilitation in improving the outcomes.

Conclusion The current review demonstrated that exercise rehabilitation generally could have a beneficial role in improvement of both physical and psychological related outcomes. As the best onset time, and FITT components are not yet completely clear, further large, well-designed RCTs are suggested to provide details of exercise rehabilitation program.

Keywords Exercise · Rehabilitation · SARS-Cov-2 · COVID-19 · Systematic review

Abbreviations

BI	Barthel index
CPET	Cardio-pulmonary exercise test
DLCO	Diffusing capacity for carbon monoxide
FEV1	Force expiratory volume in 1 s
FITT	Frequency, intensity, time and type
FVC	Forced volume capacity
hACE-2	Human angiotensin-converting enzyme-2
MCID	Minimal clinically important difference
MEP	Maximum expiratory pressure
mMRC	Modified Medical Research Council
MP	Maximum inspiratory pressure
NICE	The National Institute for Health and Care Excellence
PEFR	Peak expiratory flow rate
PEmax	Maximum expiratory pressure
PImax	Maximum inspiratory pressure
PRISMA	The Preferred Reporting Items for Systematic Reviews and Meta-Analyses
ROBVIS	Results of the risk of bias visualization
SARS	Severe acute respiratory syndrome
SPPB	Short physical performance battery
STS	Step test score
STSS	Sit to stand score
TLC	Total lung capacity
TLCO%	Transfer factor for lung carbon monoxide
6MWT	Six minutes' walk test
30STS	Thirty-second sit-to-stand test

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Introduction

By the end of February 2021, more than 430 million people have been recognized as confirmed cases with SARS-CoV2 infection. In addition, after almost 2 years of COVID-19 pandemic, this ongoing public health problem has been responsible for more than 5.9 million deaths globally [1].

As the number of confirmed cases with COVID-19 increases, the pressure posed to global health and economy will become more evident [2, 3]. Not only is this due to increase in mortality, but also the result of increase in long-term health consequences among recovered cases [3].

A significant number of patients with COVID-19 suffer from prolonged symptoms [4]. Existing research indicates that patients with different age group as well as diverse severity of disease may experience persistent symptom [5].

Although the evidence suggests that efficacious and trustworthy vaccines may play a crucial role in terminating the pandemics [6], potential of high mutation rate within SARS-CoV-2 genome could make it more challenging [7]. Furthermore, long COVID still seems to exist as a significant complication of the disease [5].

Finding the most effective therapeutic interventions is still emerging with a variety of ongoing studies [8]. Besides that, it is likely, along with the primary prevention i.e., using vaccine, to combat the pandemic [7], the rehabilitation programs as a tertiary prevention could help to alleviate the huge health adverse effects due to COVID-19 [9], and to decrease the disease burden [10].

The evidence suggest that exercise could play a fundamental role in rehabilitation and restoring the normal life among COVID-19 survivors. In this sense, improvement in lung function, immunity enhancement by cytokine regulation, reduction in oxidative stress, as well as intestinal flora modulation were theoretically introduced [2]. On the other hand, inactivity has proposed as a novel risk factor for increasing COVID-19 duration [11]. In addition, sports participation was associated with lower rate of COVID-19 complication [12].

As the deterioration in physical and psychological characteristics among COVID-19 survivors are not uncommon complications [10], we aimed in this systematic review to investigate the role of exercise rehabilitation programs, either in acute or post-acute phase, on physical and psychological outcomes among COVID-19 patients.

Methods

This systematic review was undertaken using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines [13]. The protocol was registered to PROSPERO (CRD42022301087).

Search strategy

Web of Sciences, PubMed-Medline, Google Scholar, and Scopus were searched systematically between December 2019 and November 2021 in English language. The combination of ("physical activity" OR "exercise" OR "physical inactivity" OR "sedentary behavior" OR "life-style" OR "sports") with ("COVID-19" OR "SARS-CoV-2" OR "SARS-CoV-2") were defined as the search strategy.

Inclusion and exclusion criteria

All published observational and intervention studies on COVID-19-infected patients undergoing an exercise rehabilitation program were included if they met the following inclusion criteria: 1—Studies conducted on patients with confirmed diagnosis of COVID-19 regardless of the severity, either with or without comorbidity. 2—Rehabilitation programs included any type of exercise regardless of onset time, and duration of program. 3—Studies have reported either physical or psychological factors as outcome. All other study types (e.g., case reports, case series, qualitative, reviews, commentaries and editorials) were excluded.

Eligibility and data extraction

The title and abstract of studies, found based on the above strategy, were screened by two independent investigators (FH & BM) and a third one (MS) as consultant in specific disagreement cases. Full texts of eligible studies were reviewed.

The previously designed data extraction sheet including the name of first author, study design, sample size, methodology, sex and age range of patients, onset and type of rehabilitation, outcome definition and assessment time was used.

Quality assessment

For intervention and observational studies, the Cochrane risk of bias tool for randomized controlled trials [14] and Joanna Briggs Institute (JBI) [15] critical appraisal checklist were used, respectively. Two independent reviewers (BM & BT) were involved in quality assessment.

Results

As seen in Fig. 1, 5035 studies were identified initially through Web of Sciences, PubMed-Medline, Google Scholar, and Scopus databases. After duplicate removal, 3332 studies were remained. Title/abstract screening excluded another 3245 studies and 87 studies were selected for full-text review. Finally, 23 studies including fourteen observational and nine intervention studies met the inclusion criteria. Most factors reported by studies as outcomes fell in the categories of exercise capacity, respiratory function, as well as psychological aspects.

Risk of bias assessment revealed variation in scores of different domains through all studies. Table 1 and Fig. 2 illustrate the results of quality assessment of observational, and intervention studies, respectively. Results of The Risk of Bias VISualization (ROBVIS) [16] was utilized to demonstrate the results of quality assessment of intervention studies.

Intervention studies

A total number of 469 patients were included in nine intervention studies [17–25] (Table 2). The duration of rehabilitation programs was within the range of 5–42 days. Acute and post-acute rehabilitation were considered in six and three studies, respectively.

According to the National Institute for Health and Care Excellence (NICE), acute and post-acute phases were defined as within the first 4 weeks of symptoms onset, and more than 4 weeks of symptoms onset, respectively [26]. However, acute phase was considered as the first 40 days of

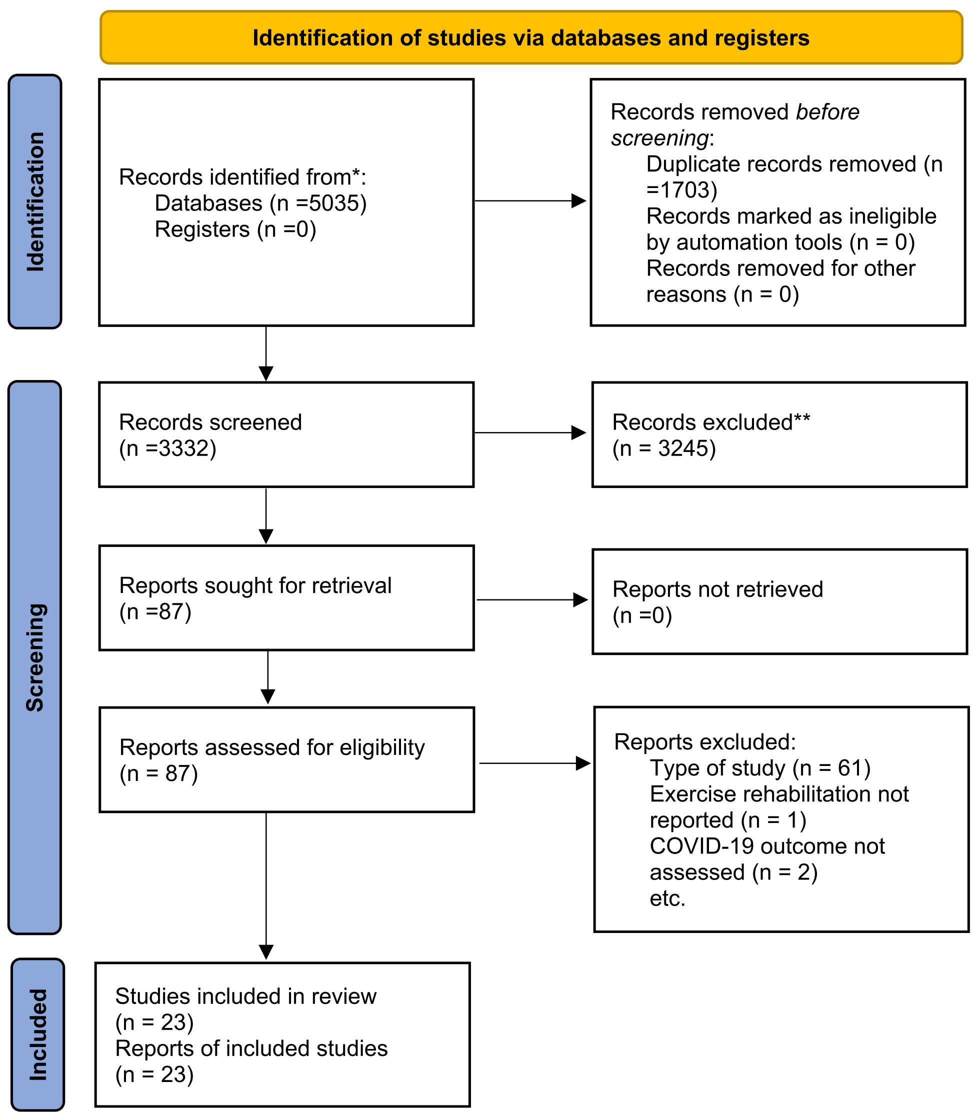

Fig. 1 PRISMA flowchart of systematic literature search on exercise rehabilitation and COVID-19 outcomes

Table 1 Results of quality assessment of included observational studies using the Joanna Briggs Institute (JBI) critical appraisal checklist

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8			
Cross-sectional											
Evaraerts et al. 2021	No	Yes	Yes	Yes	No	No	Yes	Yes			
Maniscalco et al. 2021	No	Yes	Yes	Yes	No	No	Yes	Yes			
Olezene et al. 2021	No	Yes	Yes	Yes	No	No	Yes	Yes			
Rosen et al. 2020	No	Yes	Yes	Yes	No	No	Yes	Yes			
Zampogna et al. 2021	Yes	Yes	Yes	Yes	No	No	Yes	Yes			
Zhang et al. 2021	Yes	Yes	Yes	Yes	No	No	No	Yes			
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11
Cohort											
Chikhanie et al. 2021	No	Yes	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Daynes et al. 2021	No	Yes	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Hameed et al. 2021	Yes	Yes	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Jiandani et al. 2020	Yes	Yes	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Li et al. 2021	No	Yes	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Martin et al. 2021	Yes	Yes	Yes	Yes	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Udina et al. 2021	Yes	Yes	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes
Zha et al. 2020	No	No	Yes	No	No	Yes	Yes	Not applicable	Yes	Yes	Yes

symptoms onset in studies by Gonzalez-Gerez et al. [18], and Rodriguez-Blanco et al. [24]. This discrepancy was due to problems related to diagnostic testing caused by collapses in their health systems.

The reported outcomes in eight studies of nine disclosed the overall beneficial role of exercise rehabilitation in improving the outcomes.

Five studies by Gonzalez-Gerez et al. [18], Liu et al. [21], Mohamed et al. [22], Ozlu et al. [23], and Rodriguez-Blanco et al. [24] demonstrated the beneficial effects of acute exercise rehabilitation among COVID-19 patients. The reported severity was within mild to moderate in these studies.

In studies by Abodonya et al. [17], Liu et al. [20], and Tang et al. [25] exercise rehabilitation in post-acute phase was significantly effective in improving the physical (including both exercise capacity, and respiratory function) and psychological outcomes among the patients with either mild-to-moderate severity or severe to critically ill.

Andre et al. revealed that inpatient rehabilitation (including unsupervised physical activity) among older hospitalized patients with COVID-19 was ineffective to improve neither exercise capacity nor psychological aspects [19].

Rehabilitation and exercise capacity

Six minutes' walk test (6MWT), and thirty-second sit-to-stand test (30STS) were the most common tests evaluated as exercise capacity in included studies. The results demonstrated a significant improvement in favor of rehabilitation group. Sit to stand test, semi-tandem and side by side stand, as well as walking speed were considered as outcomes in study by Andre et al. [19] They have not reported significant difference between two groups.

Rehabilitation and respiratory function

Spirometry outcomes and dyspnea scale were considered as the most common outcomes. Spirometry-related factors consisted of force expiratory volume in one second (FEV1), forced volume capacity (FVC), FEV/FVC%, and transfer factor for lung carbon monoxide (TLCO%). Borg scale and modified Medical Research Council (mMRC) were considered as dyspnea scale in two and one studies, respectively. All factors were significantly improved in favor of rehabilitation group.

Rehabilitation and psychological aspects

Outcomes in this field generally were related to the quality of life, anxiety, and depression measured via questionnaire-based approach.

Other outcomes

Only in one study, blood immune markers including leukocytes, lymphocytes, interleukins, IgA, and TNF-alpha were considered as outcomes. Although only changes in leukocytes, lymphocytes and IgA were reached statistical difference, improvement in all investigated factors was seen. All

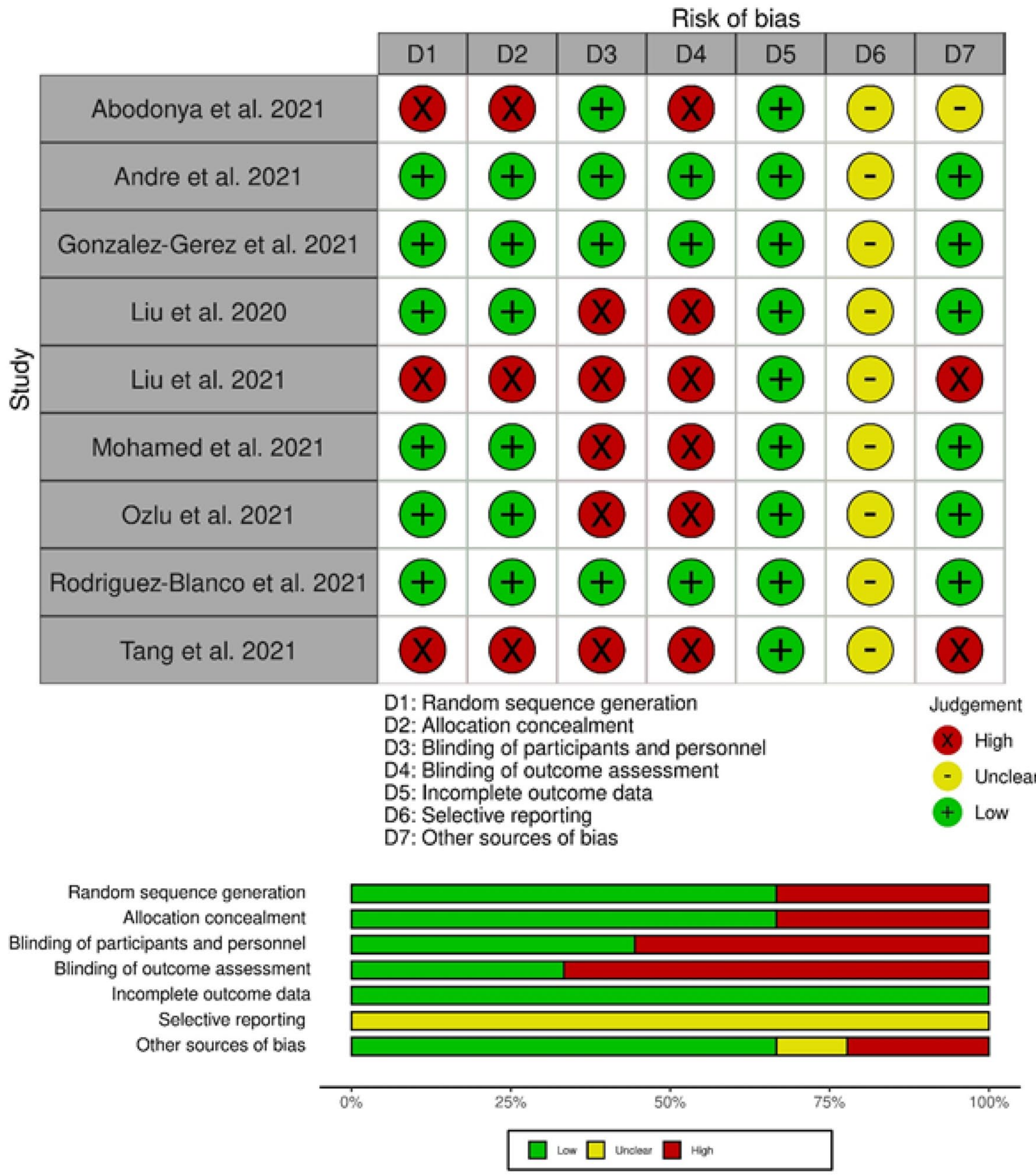

Fig. 2 Results of quality assessment of included intervention studies using the Cochrane risk of bias tool. **a** Traffic light plot and **b** summary plot

differences were in favor of exercise rehabilitation except TNF-alpha [22].

Observational studies

A total number of 957 patients were included in 14 observational studies [27–40] (Table 3).

The duration of rehabilitation programs was within the range of 1–42 days. Acute and post-acute rehabilitation were considered in five and nine studies, respectively. The reported outcomes in all studies disclosed the overall beneficial role of exercise rehabilitation in improving the outcomes. All types of disease severity from mild to severe and critically ill patients were included in the studies. Only one study dealt with the rehabilitation of patients with persistent symptoms.

Rehabilitation and exercise capacity

Factors related to aerobic capacity, as well as strength and balance capacity were measured as outcomes in this field. Aerobic capacity-related factors, including 6MWT, shuttle

Table 2 Summary of intervention studies

Author and year	Design	Sample size (intervention/control ratio)	Age (year); mean (SD)	Participants	Exercise rehabilitation versus comparator	Rehabilitation duration	Onset of rehabilitation	Outcome(s)
Abodonya et al. 2021 [17]	Pilot clinical trial	42 (ratio: 1:1)	48.05 (8.85)	ICU admitted patients	IBE + IMT [6 inspiratory cycles, threshold load with 50% of the MIP] vs. IBE	2 weeks	Post-acute phase	Exercise capacity (walking distance in 6MWT) [$P = 0.028$] Psychological aspect (Eq-5D-3L score) [$P = 0.021$] Respiratory function (FEV1%, FVC, DSI) [$P = 0.041$, $P = 0.043$, $P = 0.032$] All significant in favor of IMT group
Andre et al. 2021 [19]	Pilot clinical trial	11	86.6 (6.3)	Hospitalized patients	MATCH intervention: unsupervised validated physical activity	Mean: 9.3 days	Acute phase	Exercise capacity (including Sit to stand test, semi-tandem and side by side stand, walking speed) Psychological aspects (including ADL, HAD anxiety/depression) Non-significant
Gonzalez-Gerez et al. 2021 [18]	Pilot randomized clinical trial	38 (ratio: 1:1)	Intervention: 40.79 (9.84), Control: 40.32 (12.53)	Mild cases	Home breathing exercise vs. control	7 days	Acute phase (within the first 40 days), outpatient	Exercise capacity (including 6MWT, 30STST) Respiratory function (including MD12, Borg Scale) All significant in favor of exercise group ($P < 0.05$)

Table 2 (continued)

Author and year	Design	Sample size (intervention/control ratio)	Age (year); mean (SD)	Participants	Exercise rehabilitation versus comparator	Rehabilitation duration	Onset of rehabilitation	Outcome(s)
Liu et al. 2020 [20]	Randomized clinical trial	72 (ratio: 1:1)	Intervention: 69.4 (8), Control: 68.9 (7.6)	Hospitalized patients	Respiratory muscle training, cough exercise, diaphragmatic training, stretching, and home exercise, (two sessions/week, once a day for 10 min) vs. no rehabilitation	6 weeks	Post-acute phase	Exercise capacity (including 6MWT) Psychological aspects (including SF36, SAS) Respiratory function (including FEV1, FVC, FEV/FVC%, TLCO%) All significant in favor of intervention group ($P < 0.05$)
Liu et al. 2021 [21]	Randomized clinical trial	140 (ratio: 1:1)	NA	Hospitalized mild COVID-19	Group psychological intervention + pulmonary rehabilitation exercise (including five-tone breathing and Baduanjin exercises) vs. conventional nursing methods	1 month	Acute phase	Psychological aspects (including SAI [$P < 0.001$] and PSQI Scores [$P < 0.01$]) All significant in favor of intervention group
Mohamed et al. 2021 [22]	Pilot randomized clinical trial	30 (ratio: 1:1)	Intervention: 44.56 (4.25) Control: 35.25 (3.96)	Mild and moderate cases	Aerobic exercise with moderate intensity (3 sessions per week with duration of 40 min)	2 weeks	Acute phase	Psychological aspects (WURSS) blood immune biomarkers significant difference (WURSS, leukocyte, lymphocyte, and IgA) and non-significant difference (IL-6, IL-10, TNF-alpha) in favor of intervention group

Table 2 (continued)

Author and year	Design	Sample size (intervention/control ratio)	Age (year); mean (SD)	Participants	Exercise rehabilitation versus comparator	Rehabilitation duration	Onset of rehabilitation	Outcome(s)
Ozlu et al. 2021 [23]	Randomized clinical trial	67 (ratio: 33: 34)	Intervention: 36.48 (11.63) Control: 33.15 (11.90)	Hospitalized COVID-19 patients	The progressive and supervised muscle relaxation training, (twice a day) vs. routine care	5 days	Acute phase	Psychological aspects (including SAI, RCSQ) All significant in favor of intervention group ($P < 0.05$)
Rodriguez-Blanco et al. 2021 [24]	Pilot randomized clinical trial	36 (ratio: 1:1)	Intervention: 39.39 (11.74) Control: 41.33 (12.13)	Mild-to-moderate cases	Resistance and strength training vs. control	1 week	Acute phase (within the first 40 days), outpatient	Exercise capacity (including 6MWT, 30STST) Respiratory function (Borg Scale) All significant in favor of exercise group ($P < 0.05$)
Tang et al. 2021 [25]	Clinical trial	33	43.2 (10.4)	28 mild/ moderate, 5 severe/critical cases	Liuzijue exercise (a type of traditional Chinese mind body exercise including breathing training), once a day, 20 min	4 weeks	Post-acute phase	Exercise capacity (walking distance in 6MWT [$P = 0.02$]) Psychological aspects (including QOL: SF36-PF [$P = 0.014$], SF36-RP [$P = 0.009$], Anxiety: HAMA [$P < 0.001$], Depression: HAMD [$P = 0.0032$]) Respiratory function (including MIP [$P < 0.001$], PIF [$P < 0.001$], diaphragmatic movement in deep breathing [$P = 0.009$], Dyspnea: mMRC [$P = 0.022$]) All significant in favor of intervention group

Table 2 (continued)

ADL, activities of daily living score; *DSI*, Dyspnea Severity Index; *Eq-5D-3L*, EuroQuality-5-dimensions-3-levels; *FEV1*, forced expiratory volume in one second; *FIM*, Functional Independence Measure Scale; *FVC*, forced vital capacity; *HAD*, Hospitalized Anxiety and Depression Scale; *HAMA*, Hamilton Anxiety Rating Scale; *HAMD*, Hamilton Depression Rating Scale; *IBE*, incentive breathing exercise; *IMT*, inspiratory muscle training; *MD12*, multidimensional dyspnoea-12; *MIP*, maximal inspiratory pressure; *mMRC*, modified British Medical Research Council; *PSQI*, Pittsburgh Sleep Quality Index Scale; *QOL*, quality of life; *RCSQ*, The Richards–Campbell Sleep Questionnaire; *SAI*, State Anxiety Inventory; *SAS*, Self-rating Anxiety Scale; *SDS*, Self-rating Depression Scale; *SF-36*, 36-Item Short Form Health Survey; *SF36-PF*, SF36-Physical Functioning; *SF36-RP*, SF-36-Role-Physical; *SPPB*, Short Physical Performances Battery; *WURSS*, Wisconsin Upper Respiratory Symptom Survey; *6MWT*, six-minutes walking test; *30STST*, thirty-second sit-to-stand test

test, cardio-pulmonary exercise test (CPET), sit to stand score (STSS), step test score (STS), and 10-m walk test were measured in seven studies. Significant improvement in hand grip and quadriceps muscle strength reported in cohort and cross-sectional studies on 21, and 22 patients with severe–critically ill COVID-19, respectively. Tinetti balance test, Berg Balance Scale, Short Physical Performance Battery (SPPB), and Barthel Index (BI) were considered as balance factors in included studies. The overall results demonstrated significant improvement in favor of rehabilitation groups.

Rehabilitation and respiratory function

Dyspnea scores including Borg dyspnea scale, and spirometry factors including FEV1%, FVC%, total lung capacity (TLC), diffusing capacity for carbon monoxide (DLCO), maximum inspiratory pressure (MIP), maximum expiratory pressure (MEP), P/F ratio, peak expiratory flow rate (PEFR), maximum inspiratory pressure (PImax), maximum expiratory pressure (PEmax), as well as acute symptoms and oxygen requirement were considered as parameters of respiratory function in included observational studies.

Rehabilitation and psychological aspects

Questionnaire-based measurement of quality of life, anxiety, and depression were generally regarded as psychological outcomes. Improvement in psychological aspects were observed in all studies, although statistical significance was not reached in some studies.

Discussion

The current systematic review aimed to figure out the role of exercise rehabilitation on COVID-19 patients' outcomes. Results of included studies generally have revealed the benefits of exercise rehabilitation. Overall, both physical and psychological related outcomes have improved by exercise rehabilitation.

The results are contrary to that of Connoly et al. who found that the benefit of post-discharge exercise-based rehabilitation on exercise capacity and health-related quality of life among 483 ICU survivors were inconclusive [41], but are broadly consistent with earlier systematic review study conducted by Goodwin et al., which has postulated that exercise and mobilization could have a substantial role in improving the outcomes among critical care admitted patients with severe respiratory illness. As they generalized the results to the cases with COVID-19 infection, they have concluded that exercise could make a significant

Table 3 Summary of observational studies

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Chikhanie et al. (27) 2021	Cohort	42 including 21 COVID patients	70.9 (10.6)	Severe COVID patients with at least one comorbidity including obesity, diabetes, cardiovascular, respiratory as well as cancer	Respiratory exercises, strengthening, and balance training. In some cases, walking, cycling and gymnastics may also be done	Mean: 27.6 (14.2) days	Post-acute phase	Significant ($P < 0.05$) improvement in Exercise capacity (Tinetti balance test, 6MWD, Handgrip and Quadriceps isometric (Kg)), Psychological aspects (Fatigue, Anxiety, Depression), and Respiratory function (FEV1%, FVC%, PImax, PEmax) Non-significant improvement in Psychological aspects (Quality of life, post-traumatic stress), Respiratory function (Percent of patients needed Oxygen therapy, Minimal SpO2 (%), End-of-test dyspnea (Borg))

Table 3 (continued)

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Daynes et al. 2021 [28]	Cohort	30	58	26 hospitalized patients (21 patients with mechanical ventilation)	Two sessions weekly, supervised rehabilitation program including aerobic exercise (walking/treadmill based), strength training of upper and lower limbs and online educational discussions	6 weeks	Post-acute (mean of 125 days post infection)	Significant improvement in Exercise capacity (Incremental Shuttle Walking Test $P<0.01$, Endurance Shuttle Walking Test $P<0.01$) Psychological aspects (Montreal Cognitive Assessment $P<0.01$ Non-significant in Hospital Anxiety and Depression Scale $P=0.5$ Hospital Anxiety and Depression Scale $P=0.1$)
Everaerts et al. 2021 [29]	Cross-sectional	22	54.5 (47–61)	Hospitalized patients (15 ICU admitted patients)	Progressive endurance and resistance training including treadmill, cycle/ arm ergometer, stair climbing, step, leg and chest press	12 weeks	Acute phase	Significant improvement in Exercise capacity (including 6MWD, hand grip force, quadriceps force, work load and peak VO2 via CPET) and Respiratory function (including FEV1, TLC, DLCO, MIP, MEP). $P<0.05$ Deterioration in Psychological aspects (including HADS anxiety and depression score, MoCA, return to work)

Table 3 (continued)

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Hameed et al. 2021 [30]	Cohort	106 (44: VPT/25: HPT/17:IE/20: no rehabilitation)	VPT: 60 (14), HPT: 57 (14), IE: 59 (20), none: 58 (18)	Persistent COVID-19 patients including mild to critically severe cases	Tele-medicine rehabilitation program including VPT, HPT, IE Vs. no rehabilitation	2 weeks	Post-acute phase	Data on 53 patients with follow-up visits showed improvement in Exercise capacity (STSS, STS) in VPT, and HPT groups. In addition, STS changes were significant in IE group. Neither STSS changes nor STS changes were significant among patients with no rehabilitation
Jiandani et al. 2020 [31]	Cohort	278	ICU: 54.82 (13.09), SDU: 51.71 (14.57)	COVID-19 patients admitted in ICU and a step-down unit (SDU) of the hospital	Position change, Respiratory physiotherapy consist of deep breathing exercises, paced breathing, active cycle of breathing technique (ACBT), and diaphragmatic breathing	7 days	Post-acute phase	Significant improvement in ICU mobility score (IMS) among ICU patients ($P = 0.00$) and SDU patients ($P = 0.00$)
Li et al. 2021 [32]	Cohort	13	Age range (50–85)	Severe and critical COVID-19 cases	Respiratory physiotherapy, positioning, mobility and IMT exercises	A rang of 3–21 days, 2 sessions of 30–40 min in a day	Acute phase	Improvement in Respiratory function (P/F ratio, PEFR, MIP, and Borg Dyspnea Scale), and Functional outcomes (Medical Research Council Sum Score, the Physical Function in Intensive Care Test score, De Morton Mobility Index, and Modified BI)

Table 3 (continued)

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Maniscalco et al. 2021 [33]	Cross-sectional	95 (49 without comorbidity, 46 with comorbidity)	Comorbid patients: 65.3 (1.2), non-comorbid patients: 61.5 (1.6)	COVID-19 patients with and without comorbidity	6 sessions/week: pulmonary rehabilitation program including progressive exercise training (upper and lower extremity strength and flexibility training, treadmill and outdoor walking and stationary cycling at moderate-to-high intensity according to dyspnea and fatigue symptoms), dietary and psychosocial counselling	5 weeks (30 sessions)	Post-acute phase	Improvement in Exercise capacity (6MWD) and Respiratory function (FEV1, FVC, and DLCO%) in both groups of patients with or without comorbidity
Martin et al. 2021 [34]	Cohort	27 (14: 13)	61.5 (10.5) Case: 60.8 (10.4), control: 61.9 (10.7)	Severe, and critically ill cases	The synchronous telerehabilitation program including endurance exercises, upper and lower body strength training. Encouragement to perform unsupervised exercises three times a week, using the provided templates	6 weeks	Post-acute phase	Significant difference of exercise capacity (STST change) between rehabilitation group and control ($P=0.004$) Non-significant difference of respiratory function (dyspnea) between rehabilitation group and control ($P=0.56$)

Table 3 (continued)

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Olezene et al. 2021 [35]	Cross-sectional	29	60 (50.5–67.5)	Severe	At least three hours per day, five days per week, individualized rehabilitation	Mean: 16.7 ± 7.8 days	Post-acute phase	Significant improvement in Exercise capacity (including Berg Balance Scale $P < 0.001$, 10-m walk test $P < 0.0001$, 6 MWTD $P < 0.001$, gait speed $P < 0.001$), Functional independence (including transfer and ambulation independence $P < 0.001$), and Functional communication measures. $P < 0.05$
Rosen et al. 2020 [36]	Cross-sectional	12	Median: 56	COVID-19 inpatients	Inpatient telerehabilitation (included patient education, therapeutic exercises, and breathing techniques)	1–2 sessions	Acute phase	None of the patients required increased oxygen supplementation or medical care after rehabilitation
Udina et al. 2021 [37]	Cohort	33	66.2 (12.8)	Survived COVID-19 patients. 60.6% of them were ICU admitted	A 30-min daily multicomponent exercise training including resistance, endurance and balance training	Up to 10 days	Post-acute phase	Significant improvement in Exercise capacity (including SPBB, BI, ability to walk unassisted, and single leg stance). $P < 0.05$

Table 3 (continued)

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Zampogna et al. 2021 [38]	Cross-sectional	140	71 (61.5–78)	Recovered patients with negative RT-PCR test for SARS-CoV-2	Individually tailored training including both group and personal exercise programs with one or more of the following trainings; mobilization, active exercises and free walking, limb muscle activities, shoulder, and full arm circling, callisthenic, strengthening, balance exercise, paced walking, cycle-ergometer at low-intensity exercises (< 3.0 METs), and chest physiotherapy	Median: 24.0 (19.0–34.0) days, 60 (38–84) sessions, 2.8 (1.0–3.8) daily sessions	Post-acute phase	Significant improvement in exercise capacity (including SPPB, $P < 0.00$ and BI, $P < 0.001$) were identified. Also, the authors revealed significant reduction ($P < 0.001$) in the proportion of patients were unable at admission to stand, to rise from a chair, and to walk
Zha et al. 2020 [39]	Cohort	60	54 (38–62)	mild, and no CT evidence of pneumonia on admission	The modified rehabilitation exercise (MRE), including Overhead Chest and Shoulder Stretch, Heel Raises and Upper Body Acupressure, Upper Body Rotation, and Hand Acupressure Massage	NA	Acute phase	Improvement in All respiratory symptoms (including dry cough, productive cough, difficulty in expectoration and dyspnea)

Table 3 (continued)

Author and year	Design	Sample size (case/control ratio)	Age (years) [mean (SD)/median (IQR)]	Participants	Exercise rehabilitation vs. comparator (if available)	Rehabilitation duration	Onset of rehabilitation	Outcomes
Zhang et al. 2021 [40]	Cross-sectional	91	NA	Mild cases or common clinical types	Baduanjin exercise	NA	Acute phase	Correlation between higher frequency of Baduanjin exercise and improvement in Psychological aspects including HAD anxiety ($P=0.65$) and depression ($P<0.01$)

BI, Barthel Index; *CPET*, CardioPulmonary Exercise Test; *DLCO*, Diffusing Capacity for Carbon monoxide; *FEV1*, Forced Expiratory Volume in One second; *FVC*, Forced Vital Capacity; *HADS*, Hospital Anxiety and Depression Scale; *HPT*, home physical therapy; *IE*, independent exercise program; *MEP*, Maximal Expiratory Pressure; *MIP*: Maximal Inspiratory Pressure; *MoCA*, Montreal Cognitive Assessment; *MRC*, Medical Research Council; *PEFR*, Peak Expiratory Flow Rate; *PEmax*, Maximal Expiratory Pressure; *PImax*, Maximal Inspiratory Pressure; *P/F ratio*, PaO2/FIO2; *SpO2*, Pulse Oximeter Oxygen Saturation; *SPPB*, Short Physical Performances Battery; *STS*, Step Test Score; *STSS*, Sit To Stand Score; *STST*, Sit To Stand Test; *TLC*, Total Lung Capacity; *VO2*, oxygen consumption; *VPT*, virtual physical therapy; *6MWD*, 6-min walking distance

contribution to improve the physical outcomes. However, their finding regarding quality of life was under debate [42].

In a 2022 study by Barman et al., respiratory rehabilitation including either aerobic or respiratory muscle training has a positive effect on exercise capacity as well as pulmonary function among patients with Severe Acute Respiratory Syndrome (SARS) [43]. With respect to the minimal clinically important difference (MCID) of 20–30 m established for 6MWD, analysis of pooled data in the mentioned study revealed that 6MWD as a valid tool to determine the exercise capacity had been improved significantly higher than MCID. [43] The amount of such increase in all included studies were higher than previously reported MCID except in study by Tang et al. [25]

It is worth noting that a wide variety in the rehabilitation onset were used in included studies in our review. Although most of intervention studies focus on acute rehabilitation, post-acute rehabilitation was considered as a dominant approach in observational studies.

It seems there is still big controversy over the appropriate time of rehabilitation onset among COVID-19 patients. Chinese and Italian societies of rehabilitation did not recommend acute rehabilitation due to probable decrease in oxygen blood saturation [44, 45]. A similar conclusion was reached by Demeco et al. [46] In their study, severe and critically ill patients were recommended to postpone the respiratory rehabilitation until their status become more stable. In contrast, the results of the study by Goodwin et al. focusing on acute rehabilitation in critical care setting were pleasant [42].

The results of the current review revealed that acute rehabilitation in either mild to moderate [18, 21, 22, 24, 39, 40] or severe patients [8, 23, 29, 36] were associated with successful outcomes.

In addition, components of exercise prescription including frequency, intensity, time and type (FITT) were broadly varied through the studies. It is not yet completely clear what FITT components are of interest to COVID-19-affected patients.

Wittmer et al. have sounded a note of caution on exercise prescription for COVID-19 patients [47]. They concluded that exercise intensity must be adapted according to clinical status and stage of illness. Neither too much to be problematic nor too little to be ineffective. The challenges to determine the intensity are twofold. First, it should be compatible with patients with muscle strength decrement [48]. Second, the intensity should not be as vigorous as it poses a further pressure to respiratory system for the reason that SARS could happen to some mild-moderate patients [49].

The results of observational studies included in study by Wittmer et al. demonstrated that low-to-moderate intensity and low intensity were associated with good results in mild, and moderate COVID-19 patients, respectively. Early mobilization was also related to better prognosis in severe to critical COVID-19 patients [47]. Similarly, included studies in our review revealed that progressive mild-to-moderate intensity could bring positive results.

Hassanodin et al. demonstrated that comorbidities should be considered in any rehabilitation. It is clearly affect the participation or progression of program [50]. It seems individualized rehabilitation approach is rational. According to position statement of Taiwan Academy, rehabilitation programs for patients with COVID-19 should adjusted according to clinical statuses. COVID-19 patients were categorized into the following groups: 1—mild severity without any risk factor, 2—mild severity with established risk factor, 3—moderate-to-severe severity, 4—ventilator-assisted cases without cognitive problem, and 5- ventilator- assisted cases with cognitive problem [51].

As there was a huge heterogeneity regarding the components of rehabilitation training, it is not possible to compare the results within the different frequency and duration of programs. Also, a large modes of workouts including breathing exercise, muscle relaxation training, aerobic, strengthening, stretching as well as balance training were used as exercise rehabilitation in included studies.

It is thought that the broad expression of Human Angiotensin-Converting Enzyme-2 (hACE-2) receptors in multiple organs could lead to wide extra-pulmonary manifestations in COVID-19 [52]. Most outcomes have been addressed by included studies were related to cardiopulmonary, and psychological factors. It seems the remaining extra-pulmonary manifestations including neurologic, gastrointestinal, hematologic, hepatic, and renal involvement should be more considered in future studies. Although study by Mohammed et al. demonstrated the benefits of exercise on some hematologic factors [52], the role of exercise in coagulopathy is relatively scarce. Previous research introduced the coagulopathy as the most important feature of hematologic manifestations in COVID-19 [53]. In this regard, Zadow et al. reported that mild-to-moderate exercise training might improve the coagulopathy problems associated with COVID-19. However, probably the opposite effect could be observed in high intensity exercise [54].

Limitation

In current study, there were huge heterogeneity in included studies. In addition to differences in FITT components of exercise, large variation in disease severity, as well as rehabilitation onset was observed. In addition, the measured outcomes were broadly different in each study. In light of these considerations, meta-analysis could not be performed. We have also included all studies determining the effect of exercise as a part of rehabilitation on COVID-19 outcomes. As the other non-exercise component of rehabilitation programs including either nutritional, or psychological consultation have been neglected, the results should be interpreted with some cautions.

Conclusion

Exercise rehabilitation generally could have a beneficial role in improvement of both physical and psychological related outcomes. As the best onset time, and FITT components are not yet completely clear, further large, well-designed RCTs are mandatory to provide details of exercise rehabilitation program.

Author contributions FH devised the project, the main conceptual ideas and proof outline. He also revised the drafted manuscript critically for important intellectual content. BM, MS, and BT contributed to study implementation. They drafted the manuscript. All the authors have read and approved the final version of the manuscript.

Declarations

Competing interests The authors declare no competing interests.

Conflict of interest All authors declare that they have no conflict of interest.

Ethical approval This study is a review type and ethical approval is not required.

Informed consent For this type of review study informed consent is not required.

References

1. WHO Coronavirus Disease (COVID-19) Dashboard. Available from https://covid19.who.int/. Accessed 29 Feb 2022
2. Bo W, Xi Y, Tian Z (2021) The role of exercise in rehabilitation of discharged COVID-19 patients. Sports Med Health Sci 3(4):194–201
3. Barker-Davies RM, O'Sullivan O, Senaratne KPP, Baker P, Cranley M, Dharm-Datta S et al (2020) The Stanford Hall consensus statement for post-COVID-19 rehabilitation. Br J Sports Med 54(16):949–959
4. Gloeckl R, Leitl D, Jarosch I, Schneeberger T, Nell C, Stenzel N, et al (2021) Benefits of pulmonary rehabilitation in COVID-19: a prospective observational cohort study. ERJ Open Res https://doi.org/10.1183/23120541.00108-2021
5. Gaffney AW (2022) The long-COVID conundrum. Am J Med 135:5–6
6. Kaplan RM, Milstein A (2021) Influence of a COVID-19 vaccine's effectiveness and safety profile on vaccination acceptance. Proc Natl Acad Sci 118(10): e2021726118

7. Peng X-L, Cheng J-S-Y, Gong H-L, Yuan M-D, Zhao X-H, Li Z, et al (2021) Advances in the design and development of SARS-CoV-2 vaccines. Milit Med Res 8(1):1–31
8. Li C-X, Noreen S, Zhang L-X, Saeed M, Wu P-F, Ijaz M, et al (2021) A critical analysis of the SARS-CoV-2 (COVID-19) pandemic, emerging variants, therapeutic interventions, and vaccination strategies. Biomed Pharmacother 146:112550
9. Nieman DC (2021) Exercise is medicine for immune function: implication for COVID-19. Curr Sports Med Rep 20(8):395–401
10. Li J, Xia W, Zhan C, Liu S, Yin Z, Wang J, et al (2021) A telerehabilitation programme in post-discharge COVID-19 patients (TERECO): a randomised controlled trial. Thorax. https://doi.org/10.1136/thoraxjnl-2021-217382
11. Tavakol Z, Ghannadi S, Tabesh MR, Halabchi F, Noormohammadpour P, Akbarpour S, et al (2021) Relationship between physical activity, healthy lifestyle and COVID-19 disease severity; a cross-sectional study. J Public Health. https://doi.org/10.1007/s10389-020-01468-9
12. Halabchi F, Mazaheri R, Sabeti K, Yunesian M, Alizadeh Z, Ahmadinejad Z et al (2020) Regular sports participation as a potential predictor of better clinical outcome in adult patients with COVID-19: a large cross-sectional study. J Phys Act Health 18(1):8–12
13. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD et al (2021) The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. Int J Surg 88:105906
14. Higgins J, Altman D, Sterne J (2011) Assessing risk of bias in included studies. In: Higgins JPT, Green S (eds) Cochrane handbook for systematic reviews of interventions version 5.1.0 (updated March 2011). The Cochrane Collaboration, 2011. Available from handbook cochrane org, pp 243–96
15. Moola S, Munn Z, Tufanaru C, Aromataris E, Sears K, Sfetcu R, et al (2017) Systematic reviews of etiology and risk. Joanna Briggs institute reviewer's manual The Joanna Briggs Institute, p 5
16. McGuinness LA, Higgins JPT. Risk-of-bias VISualization (robvis): An R package and Shiny web app for visualizing risk-of-bias assessments. Research Synthesis Methods. https://doi.org/10.1002/jrsm.1411
17. Abodonya AM, Abdelbasset WK, Awad EA, Elalfy IE, Salem HA, Elsayed SH (2021) Inspiratory muscle training for recovered COVID-19 patients after weaning from mechanical ventilation: a pilot control clinical study. Medicine 100(13):e25339
18. Gonzalez-Gerez JJ, Saavedra-Hernandez M, Anarte-Lazo E, Bernal-Utrera C, Perez-Ale M, Rodriguez-Blanco C (2021) Short-term effects of a respiratory telerehabilitation program in confined COVID-19 patients in the acute phase: a pilot study. Int J Environ Res Public Health 18(14):7511
19. Laurine A, Rolland Y, Gerard S, Kergoat M-J, Peyrusqué E, Aubertin-Leheudre M (2021) Feasibility and effect of implementing physical activity program implementation during COVID-19 in hospitalized positive COVID-19 older adults. J Nutr Health Aging 25(6):724–726
20. Liu K, Zhang W, Yang Y, Zhang J, Li Y, Chen Y (2020) Respiratory rehabilitation in elderly patients with COVID-19: a randomized controlled study. Complement Ther Clin Pract 39:101166
21. Liu Y, Yang Y-Q, Liu Y, Pei S-L, Yang H-H, Wu J-J, et al (2021) Effects of group psychological intervention combined with pulmonary rehabilitation exercises on anxiety and sleep disorders in patients with mild coronavirus disease 2019 (COVID-19) infections in a Fangcang hospital. Psychol Health Med 27:333–342
22. Mohamed AA, Alawna M (2021) The effect of aerobic exercise on immune biomarkers and symptoms severity and progression in patients with COVID-19: a randomized control trial. J Bodyw Mov Ther 28:425–432
23. Özlü İ, Öztürk Z, Karaman Özlü Z, Tekin E, Gür A (2021) The effects of progressive muscle relaxation exercises on the anxiety and sleep quality of patients with COVID-19: a randomized controlled study. Perspect Psychiatr Care 57(4):1791–1797
24. Rodriguez-Blanco C, Gonzalez-Gerez JJ, Bernal-Utrera C, Anarte-Lazo E, Perez-Ale M, Saavedra-Hernandez M (2021) Short-term effects of a conditioning telerehabilitation program in confined patients affected by COVID-19 in the acute phase. A pilot randomized controlled trial. Medicina 57(7):684
25. Tang Y, Jiang J, Shen P, Li M, You H, Liu C, et al (2021) Liuzijue is a promising exercise option for rehabilitating discharged COVID-19 patients. Medicine. 100(6): e24564
26. Shah W, Hillman T, Playford ED, Hishmeh L (2021) Managing the long term effects of covid-19: summary of NICE, SIGN, and RCGP rapid guideline. BMJ 372:n136
27. Al Chikhanie Y, Veale D, Schoeffler M, Pépin J, Verges S, Hérengt F (2021) Effectiveness of pulmonary rehabilitation in COVID-19 respiratory failure patients post-ICU. Respir Physiol Neurobiol 287:103639
28. Daynes E, Gerlis C, Chaplin E, Gardiner N, Singh SJ (2021) Early experiences of rehabilitation for individuals post-COVID to improve fatigue, breathlessness exercise capacity and cognition—a cohort study. Chron Respir Dis 18:14799731211015692
29. Everaerts S, Heyns A, Langer D, Beyens H, Hermans G, Troosters T et al (2021) COVID-19 recovery: benefits of multidisciplinary respiratory rehabilitation. BMJ Open Respir Res 8(1):e000837
30. Hameed F, Palatulan E, Jaywant A, Said R, Lau C, Sood V et al (2021) Outcomes of a COVID-19 recovery program for patients hospitalized with SARS-CoV-2 infection in New York City: a prospective cohort study. PM&R 13(6):609–617
31. Jiandani MP, Salagre SB, Kazi S, Iyer S, Patil P, Khot WY, et al (2020) Preliminary observations and experiences of physiotherapy practice in acute care setup of COVID 19: a retrospective observational study. J Assoc Physic India 68:18–24
32. Li L, Yu P, Yang M, Xie W, Huang L, He C, et al (2021) Physical therapist management of COVID-19 in the intensive care unit: the West China Hospital experience. Phys Therapy 101(1):pzaa198
33. Maniscalco M, Fuschillo S, Ambrosino P, Martucci M, Papa A, Matera MG et al (2021) Preexisting cardiorespiratory comorbidity does not preclude the success of multidisciplinary rehabilitation in post-COVID-19 patients. Respir Med 184:106470
34. Martin I, Braem F, Baudet L, Poncin W, Fizaine S, Aboubakar F et al (2021) Follow-up of functional exercise capacity in patients with COVID-19: it is improved by telerehabilitation. Respir Med 183:106438
35. Olezene CS, Hansen E, Steere HK, Giacino JT, Polich GR, Borg-Stein J et al (2021) Functional outcomes in the inpatient rehabilitation setting following severe COVID-19 infection. PLoS ONE 16(3):e0248824
36. Rosen K, Patel M, Lawrence C, Mooney B (2020) Delivering telerehabilitation to COVID-19 inpatients: a retrospective chart review suggests it is a viable option. HSS J 16(1_suppl):64–70
37. Udina C, Ars J, Morandi A, Vilaró J, Cáceres C, Inzitari M (2021) Rehabilitation in adult post-COVID-19 patients in post-acute care with therapeutic exercise. J Frailty Aging 10(3):297–300
38. Zampogna E, Paneroni M, Belli S, Aliani M, Gandolfo A, Visca D et al (2021) Pulmonary rehabilitation in patients recovering from COVID-19. Respiration 100(5):416–422
39. Zha L, Xu X, Wang D, Qiao G, Zhuang W, Huang S (2020) Modified rehabilitation exercises for mild cases of COVID-19. Ann Palliat Med 9:3100–3106
40. Zhang X-B, Zhang J-L, Li M-X, Yuan Y-P, Sun J (2021) Baduanjin exercise can alleviate anxiety and depression of patients with COVID-19 in Square cabin hospital: a cross-sectional survey. Medicine 100(32):e26898

41. Connolly B, Salisbury L, O'neill B, Geneen L, Douiri A, Grocott MP, et al (2016) Exercise rehabilitation following intensive care unit discharge for recovery from critical illness: executive summary of a Cochrane Collaboration systematic review. J Cachexia Sarcopenia Muscle. 7(5):520–526
42. Goodwin VA, Allan L, Bethel A, Cowley A, Cross JL, Day J et al (2021) Rehabilitation to enable recovery from COVID-19: a rapid systematic review. Physiotherapy 111:4–22
43. Barman A, Sinha MK, Sahoo J, Jena D, Patel V (2022) Respiratory rehabilitation in patients recovering from severe acute respiratory syndrome: a systematic review and meta-analysis. Heart Lung 53:11–24
44. Xi ZJHHH, Zhi Z (2020) Chinese Association of Rehabilitation Medicine, Respiratory rehabilitation committee of Chinese Association of Rehabilitation Medicine, Cardiopulmonary rehabilitation Group of Chinese Society of Physicai Medicine and Rehabilitation. In: Recommendations for respiratory rehabilitation of COVID-19 in adults, vol 432020, p E029
45. MEDICA EM (2020) Rehabilitation and respiratory management in the acute and early post-acute phase. “Instant paper from the field” on rehabilitation answers to the COVID-19 emergency
46. Demeco A, Marotta N, Barletta M, Pino I, Marinaro C, Petraroli A et al (2020) Rehabilitation of patients post-COVID-19 infection: a literature review. J Int Med Res 48(8):0300060520948382
47. Wittmer VL, Paro FM, Duarte H, Capellini VK, Barbalho-Moulim MC (2021) Early mobilization and physical exercise in patients with COVID-19: a narrative literature review. Complement Ther Clin Pract 43:101364
48. Rayegani SM, Raeissadat SA, Fakharian A, Babaee M, Nezamabadi M, Boland Nazar NS, et al (2021) Role of rehabilitation medicine in the COVID-19 pandemic: an Iranian consensus. Eur J Phys Rehabil Med 57: 309–310
49. Vitacca M, Carone M, Clini EM, Paneroni M, Lazzeri M, Lanza A et al (2020) Joint statement on the role of respiratory rehabilitation in the COVID-19 crisis: the Italian position paper. Respiration 99(6):493–499
50. Hasanudin H, Sukartini T, Makhfudli M, Rosyid AN, Revita NCT, Aini HN (2022) The effectiveness of pulmonary rehabilitation on pulmonary function among adults patients of COVID-19 survivors: a systematic review. J Respir 8(1):15–25
51. Cheng Y-Y, Chen C-M, Huang W-C, Chiang S-L, Hsieh P-C, Lin K-L et al (2021) Rehabilitation programs for patients with COronaVIrus Disease 2019: consensus statements of Taiwan Academy of Cardiovascular and Pulmonary Rehabilitation. J Formos Med Assoc 120(1):83–92
52. Thakur V, Ratho RK, Kumar P, Bhatia SK, Bora I, Mohi GK et al (2021) Multi-organ involvement in COVID-19: beyond pulmonary manifestations. J Clin Med 10(3):446
53. Higgins V, Sohaei D, Diamandis EP, Prassas I (2021) COVID-19: from an acute to chronic disease? Potential long-term health consequences. Crit Rev Clin Lab Sci 58(5):297–310
54. Zadow EK, Wundersitz DWT, Hughes DL, Adams MJ, Kingsley MIC, Blacklock HA, et al., editors. Coronavirus (COVID-19), coagulation, and exercise: interactions that may influence health outcomes. Seminars in thrombosis and hemostasis; 2020: Thieme Medical Publishers

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