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Systematic Review

Effects of physical rehabilitation interventions in COVID-19 patients following discharge from hospital: A systematic review

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ABSTRACT

Background: Hospitalized patients recovering from coronavirus disease 2019 (COVID-19) may experience disability and suffer from significant physical and mental impairment requiring physical rehabilitation following their discharge. However, to date, no attempt has been made to collate and synthesize literature in this area.
Objective: This systematic review examines the outcomes of different physical rehabilitation interventions tested in COVID-19 patients who were discharged from hospital.
Search strategy: A systematic search of MEDLINE/PubMed, CINAHL, Scopus and medRxiv was conducted to identify articles published up to March 2022.
Inclusion criteria: This systematic review included studies of outpatient rehabilitation programs for people recovering from COVID-19 who received physical activity, exercise, or breathing training to enhance or restore functional capacity, pulmonary function, quality of life, and mental health or function.
Data extraction and analysis: Selection of included articles, data extraction, and methodological quality assessments were conducted by two review authors respectively, and consensus was reached through discussion and consultation with a third reviewer. Finally, we review the outcomes of studies based on four categories including: (1) functional capacity, (2) pulmonary function, (3) quality of life, and (4) mental health status.
Results: A total of 7534 titles and abstracts were screened; 10 cohort studies, 4 randomized controlled trials and 13 other prospective studies involving 1583 patients were included in our review. Early physical rehabilitation interventions applied in COVID-19 patients who were discharged from the hospital improved multiple parameters related to functional capacity, pulmonary function, quality of life and mental health status.
Conclusion: Physical rehabilitation interventions may be safe, feasible and effective in COVID-19 patients discharged from the hospital, and can improve a variety of clinically relevant outcomes. Further studies are warranted to determine the underlying mechanisms.
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Contents

1. Introduction

Human infections with zoonotic coronaviruses including severe acute respiratory syndrome coronavirus (SARS-CoV), Middle East respiratory syndrome coronavirus, also known as severe acute respiratory syndrome coronavirus-1 (SARS-CoV-1), and a novel coronavirus (2019-nCoV, also called SARS-CoV-2) have become global public health concerns [1]. Coronavirus disease 2019 (COVID-19), the disease caused by SARS-CoV-2, was declared a pandemic in March 2020 and has led to an unprecedented rise in morbidity and mortality globally [1,2]. Among discharged COVID-19 patients without any prior motor or functional limitations, health-related quality of life is poor, and the patients often suffer from varying degrees of parenchymal lung damage, cognitive disturbance, or significant physical or psychological impairments [3–6]. Several studies have shown that early post-acute physical rehabilitation programs, including mobilization and respiratory physiotherapy, may significantly improve the recovery of COVID-19 patients after their discharge from hospital [7–10]. Therefore, it would be beneficial for discharged COVID-19 patients to have a safe, effective and comprehensive physical rehabilitation program. Accordingly, several international guidelines and recommendations have been proposed for COVID-19 patients at the time of hospital discharge to support their return to normal life [11–15]. Timely multidisciplinary physical rehabilitation interventions may improve prognosis, maximize functional preservation, and improve quality of life in recovering COVID-19 patients [16].

Additionally, it has been shown that a high proportion of patients discharged after COVID-19-related pneumonia have residual abnormalities in pulmonary CT scans and reduced lung function [17]. Importantly, persistent impairment of pulmonary function and functional capacity has lasted for months or even years in SARS-CoV-2 survivors after their discharge from hospital [18–21].

Several studies have shown that physical rehabilitation programs for COVID-19 patients discharged from hospital can improve physiological, functional and psychological parameters [4,18,22–26]. However, to date, no attempt has been made to review and synthesize this literature. Therefore, this systematic review examines the outcomes of physical rehabilitation programs administered to COVID-19 patients following their discharge from hospital.

2. Methods

We performed a systematic review, in accordance with methodological guidelines from the Cochrane Handbook for Systematic Reviews, of studies that reported the effects of physical exercise and breathing training on factors related to COVID-19 post-hospitalization. The study was conducted based on the guidelines and principles outlined by the *Preferred Reporting Items for Systematic Review and Meta-Analyses* (PRISMA) statement and checklist [27].

2.1. Search strategies

The current systematic review used a literature search of 5 electronic databases, including MEDLINE/PubMed, Cumulative Index to Nursing and Allied Health Literature (CINAHL), Scopus and medRxiv, executed by two researchers (MR and MMS), up to March 2022 to identify studies that examined the influence of physical activity and exercise training on physiological and mental factors related to post-COVID-19 rehabilitation. The search syntax was as follows: ("severe acute respiratory syndrome coronavirus 2" or "novel coronavirus" or "COVID-19" or "2019-nCoV" or "SARS-CoV-2") and ("post-hospitalization" or "hospitalization" or "intensive care") and ("physical activity," or "exercise training," or "physical training," or "exercise activity" or "respiratory training," or "breathing exercise") and ("rehabilitation," or "telerehabilitation," or "physiotherapy," or "quality of life," or "pulmonary function," or "lung function," or "mental health," or "physical function," or "functional capacity") (Supplementary file). Additionally, literature cited by included studies was also searched for other eligible articles.

2.2. Eligibility criteria

The eligibility criteria followed population, intervention, comparison and outcome (PICO) criteria (Table 1). We included studies that tested the effects of physical activity, exercise or breathing training on COVID-19 patients after their discharge from hospital that reported at least one of the following outcomes: functional capacity, pulmonary function, quality of life and mental status. The present systematic review excluded editorials, letters, commentaries, abstracts with insufficient data, and studies that employed rehabilitation programs during the hospitalization period of COVID-19.

2.3. Data extraction

First, titles and abstracts of articles identified in database searches were screened by two investigators (MR and MMS) for relevance. When there were disagreements or ambiguity, consensus was reached through discussion and consultation with a third reviewer (AK). Second, the full text of relevant articles was reviewed for inclusion, and the following data were extracted from eligible studies, where available: author's name, country, study design, participants' age and gender, rehabilitation program, and related outcomes. In all stages, discrepancies were solved before conducting a systematic review.

Table 1
PICO criteria for the included studies.

Item	Contents
Population (P)	COVID-19 patients discharged from hospital
Intervention (I)	Any physical rehabilitation intervention
Comparison (C)	Identify the best physical activity protocol for rehabilitation
Outcome (O)	Any score for functional capacity, pulmonary function, quality of life and mental status

COVID-19: coronavirus disease 2019; PICO: population, intervention, comparison and outcome.

2.4. Quality assessment

The Newcastle-Ottawa Scale (NOS) was used to assess the quality of retrospective cohort and prospective studies. The NOS includes 3 domains (quality of selection, comparability, and quality of outcome and adequacy of follow-up), with a maximum score of 9 points. Studies with NOS scores of 0 to 3, 4 to 6, and 7 to 9 were considered low, moderate, and high quality, respectively [28]. We also used the Cochrane Collaboration's tool to assess the risk of bias for randomized controlled trials (RCTs). This allows evaluation of risk of bias as high, low, or unclear for the following domains: selection, attrition, detection, performance, reporting, and others [29].

2.5. Analysis

To categorize interventions, we sorted the studies into four categories: (1) functional capacity, (2) pulmonary function, (3) quality of life, and (4) mental health status. Additionally, a narrative synthesis was undertaken and structured by intervention type.

3. Results

3.1. Study identification and characteristics

A total of 7534 potentially relevant articles were identified in our literature search. Among them, 558 studies remained after removing duplicates. After screening titles and abstracts, 499 research articles were excluded. Of these 59 research articles, another 32 articles were excluded. Finally, 27 articles met the eligibility criteria and were included in the systematic review (Fig. 1).

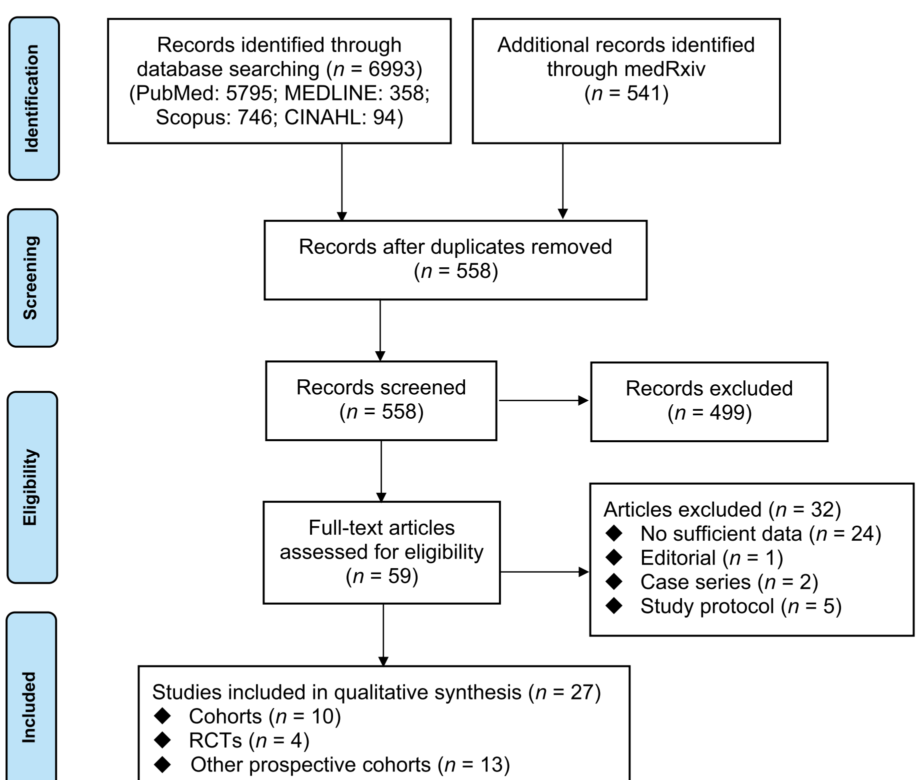

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram of study selection. RCT: randomized controlled trial; CINAHL: Cumulative Index of Nursing and Allied Health Literature.

3.2. Description of the included studies and characteristics of the interventions

The characteristics of the included studies and their rehabilitation features are listed in Table 2. The present systematic review included 27 studies (10 cohort studies, 4 RCTs, and 13 other prospective studies), involving 1583 COVID-19 patients discharged from hospital. Regarding the COVID-19 severity, 10 studies included only hospitalized COVID-19 patients [6,8,22,25,30–35], 7 studies included COVID-19 patients who were admitted to intensive care unit (ICU) [7,9,26,36–39], and 10 studies included COVID-19 patients who were hospitalized or admitted to ICU [3–5,10,23, 24,40–43]. The study sample size ranged from 7 to 183 COVID-19 survivors, and the mean age ranged from 38 to 72 years. The 6-minute walking test (6MWT), Barthel index, sit-to-stand test (STST), functional independent measurement (FIM), and handgrip strength were used to assess the functional capacity of the COVID-19 survivors before and after the interventions. The following parameters related to pulmonary function were measured in some reports: forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), diffusing lung capacity for carbon monoxide (DLCO), and dyspnea severity. European Quality of Life-5 Dimensions-3 Levels (EQ-5D-3L), EQ-5D-5L, and short-form 36- and 12-item health survey (SF36/SF12) questionnaires were used as health-related quality of life measures. Hospital Anxiety and Depression Scale, Generalized Anxiety Disorder-7, Patient Health Questionnaire, Hamilton Depression Rating Scale and Hamilton Anxiety Rating Scale were used in some reports to assess the mental health status of COVID-19 survivors before and after the interventions. In addition, the Montreal Cognitive Assessment was used in some reports to assess cognitive function. Only one study reported the rate of the symptoms related to post-intensive care syndrome, and 85% of the patients were identified with this syndrome [41]. Additionally, only one study was conducted in community-based patients after COVID-19 infection; this study reported significant improvement in skeletal muscle strength and quality of life [32]. Most of the included studies were of moderate quality with NOS scores between 5 and 6 (Table 3). According to the Cochrane Collaboration's tool, all RCT studies were rated as "low risk of bias" (Table 4).

3.3. Physical rehabilitation features of the included studies

Telerehabilitation programs were employed in 6 studies as a treatment intervention, while a supervised physical rehabilitation program was employed in 21 other studies. Aerobic training, resistance training and breathing exercise were used as the main training protocols in most studies. Balance training [6,9,39], Liuzijue exercise [34] and yoga [42] were also used in some reports. The duration of the physical rehabilitation period varied from 1 to 12 weeks. The frequency of interventions varied between 2 and 10 sessions per week. The duration of the physical rehabilitation session varied from 20 to 120 min and the most common duration was 30 min.

Aerobic training included outdoor walking, walking and running on the treadmill, and biking on a cycle ergometer. The training intensity in aerobic interventions was based on the Borg scale, reaching a perceived exertion between 4 and 6, which is considered moderate-intensity exercise.

Resistance training programs included upper body and lower body exercises using body weight, resistance training devices, TheraBands, and materials available in the home. The criteria for the intensity of resistance training varied between 30% to 85% of participants' one repetition maximum. The number of repetitions for resistance exercises varied between 8 and 12. Also, the number of sets was between 2 and 3 sets of resistance training for each exercise. Additionally, calisthenics and gymnastics were employed in some reports as a resistance training intervention.

The breathing exercise program included diaphragm recruitment and chest-abdomen coordination exercises to improve lung function. The intensity of respiratory and breathing intervention training was based on the Borg scale, reaching a perceived exertion between 4 and 10.

3.4. Summary of evaluated outcomes in the included studies

3.4.1. Functional capacity

Out of 27 studies included, 18 studies, with a total of 1104 participants, reported significant improvement for 6MWT [3,4,6–9, 23,24,30,31,33–38,41,42]; 6 studies, with a total of 369 participants [5,6,9,36,39,41], reported significant improvement for Barthel index; 3 studies, with a total of 263 participants [5,10,40], reported significant improvement for 1-minute STST; 3 studies, with a total of 94 participants [30,33,42], reported significant improvement for 30-second STST; one study, with a total of 140 participants [6], reported significant improvement for 5 times STST; 3 studies, with a total of 309 participants [26,37,38], reported significant improvement for FIM in post-hospital discharge COVID-19 patients after a physical rehabilitation intervention; 6 studies, with a total of 365 participants, assessed skeletal muscle strength using a handgrip device, and all of these [4,5,26,32,35], except one [42], reported significant improvements after a physical rehabilitation intervention.

3.4.2. Pulmonary function

Of the 27 studies included, 10 reports, with a total of 762 patients [4,7,23,24,31,35,37,38,41,42] assessed pulmonary function using standard spirometry and lung volume measurements, and except for one study [42], all of them reported significant improvements in FVC and FEV1 after a physical rehabilitation intervention in post-hospital discharged COVID-19 patients. Four reports involving 325 patients assessed DLCO before and after a physical rehabilitation intervention in post-hospital discharged COVID-19 patients. Among them, 3 studies [37,38,41] reported significant improvement in DLCO, whereas one study failed to observe a significant change [42]. Dyspnoea severity was another pulmonary function that improved in 11 reports, with a total of 548 patients [3,7,9,10,30,31,34–36,40,42].

3.4.3. Quality of life

Out of the 27 studies included in this review, significant improvements were reported after a physical rehabilitation intervention in post-hospital discharged COVID-19 patients in EQ-5D-3/5L (4 reports, involving 169 patients [7,8,24,43]) and SF36/SF12 (7 reports, involving 587 patients [3,10,23,32,34,35,37]).

3.4.4. Mental health status

Of the 27 studies included in this review, 7 reports, with a total of 449 participants [4,22,24,25,34,37], examined anxiety and depression, and 3 reports, with a total of 129 participants [22,23,26], examined cognitive deficits after a physical rehabilitation intervention in discharged COVID-19 patients and reported significant improvements.

4. Discussion

The present systematic review included 27 studies, with a total of 3761 COVID-19 patients, after their discharge from hospital. The results showed that physical rehabilitation activities, which mainly involved aerobic training, resistance training and breathing exercise, may improve functional capacity, pulmonary function, quality

Table 2
General characteristics of included studies.

Author and country	Study design	Sample size	Age (year, mean ± SD)	Study type	Type of exercise	Training program	Rehabilitation protocol feature	Outcomes
Abodonya et al. 2021 [7], Saudi Arabia	Prospective	*N* = 42 (inspiratory muscle training: 17 M and 4 F; Control: 16 M and 5 F)	50.6 ± 10.9	RehP	BE	2 weeks, 8 sessions/week; duration: 30 min	Six inspiratory cycles with 5 min of duration per cycle and 1-minute rest between each.	6MWT: ↑; FVC: ↑; FEV1: ↑; Dyspnoea Scale: ↓; EQ-5D-3L: ↑
Ahmed et al. 2021 [3], Pakistan	Prospective	*N* = 10 (6 M and 4 F)	38.0 ± 10.3	RehP	AT	5 weeks; 3 sessions/week; duration: 20 min	AT: 50%–70% of heart rate maximum according to the age of individuals. Rate of perceived exertion between 4 and 6.	6MWT: ↑; SF36: ↑; Dyspnoea Scale: ↓
Betschart et al. 2021 [8], Switzerland	Cohort	*N* = 12 (8 M and 4 F)	61.5 ± 1.6	RehP	AT and RT	8 weeks; 2 sessions/week; duration: 60 min	AT: warm-up 4 min at 15% peak work rate. High intensity: 4 min 50% peak work rate (4 ×); BS 4–6. Mild intensity: 3 min 20%–30% peak work rate (3 ×) cooling-down 3 min at 15% peak work rate. RT: 10–12 repetitions, 50%–85% of one-repetition maximum three rounds per device.	6MWT: ↑; Eq-5D-5L: ↑
Curci et al. 2021 (a) [9], Italy	Prospective	*N* = 32 (22 M and 10 F)	72.6 ± 10.9	RehP	Balance exercises and BE	3 weeks; 10 sessions/week; duration: 30 min	Static and dynamic balance exercises and pulmonary rehabilitation exercises.	6MWT: ↑; Barthel index: ↑; Dyspnoea Scale: ↓
Curci et al. 2020 (b) [36], Italy	Prospective	*N* = 41 (15 M and 16 F)	72.2 ± 11.1	RehP	AT, RT and BE	3 weeks; 10 sessions/week; duration: 30 min	BE: breath control, confinement, and release. RT: strengthening the muscles of the upper and lower limbs and trunk. RT was performed in 2–4 sets between 8 to 12 repetitions.	6MWT: ↑; Barthel index: ↑; Dyspnoea Scale: ↓
Dalbosco-Salas et al. 2021 [10], Spain	Prospective	*N* = 115 (non-hospitalized: 14 M and 44 F; hospitalized: 35 M and 22 F)	64.1 ± 3.2	TelR	AT, RT and BE	9 weeks; 3 sessions/week; duration: 40 min	Moderate- to high-intensity training: BS 3–6. RT was performed with elastic bands.	1-minute STST: ↑; SF36: ↑; Dyspnoea Scale: ↓
Daynes et al. 2021 [22], United Kingdom	Cohort	*N* = 30 (16 M and 14 F)	58.1 ± 1.6	RehP	AT and RT	6 weeks; 2 sessions/week; duration: 30 min	AT: walking/treadmill. RT: exercises for upper and lower limbs.	Incremental shuttle walking test: ↑; cognitive deficits: ↓; depression: ↓; anxiety: ↓
Everaerts et al. 2021 [4], Belgium	Prospective	*N* = 22 (15 M and 7 F)	66.3 ± 2.2	RehP	AT and RT	12 weeks; 3 sessions/week; duration: 90 min	The program started at 60%–75% of maximal individual performance. Progressive overload was obtained by increasing both intensity and duration, based on symptom scores (target Borg dyspnoea and fatigue score 4–6/10).	6MWT: ↑; handgrip strength: ↑; FVC: ↑; FEV1: ↑; depression: ↓; anxiety: ↓
Gloeckl et al. 2021 [23], Germany	Cohort	*N* = 50 (moderate COVID-19: 5 M and 20 F; critical COVID-19: 17 M and 8 F	57.0 ± 10.0	RehP	AT, RT and BE	3 weeks; 5 sessions/week; duration: 110 min	AT: 60%–70% of peak work. RT: leg press, knee extension, pull-down, and push-down; 15–20 repetitions for each calisthenics.	6MWT: ↑; FVC: ↑; FEV1: ↑; SF36: ↑; depression: ↓; anxiety: ↓; cognitive deficits: ↓
Gonzalez-Gerez et al. 2021 [30], Australia	RCT (pilot)	*N* = 38 (breathing: 10 M and 9 F; control: 11 M and 8 F)	41.0 ± 13.0	TelR	BE	1 week; 7 sessions/week; duration: 20 min	Ten exercises on the BS 4 for 10 min, the BS 8 for 20 min, and the BS 10 for 30 min.	6MWT: ↑; 30 s of STST: ↑; Dyspnoea Scale: ↓
Hayden et al. 2021 [24], Germany	Prospective	*N* = 108 (acute severe: 34 M and 21 F; severe: 21 M and 11 F; mild: 4 M and 17 F)	68.9 ± 10.2	RehP	AT and RT	3 weeks; 3 sessions/week; duration: 120 min	AT: ergometer bicycle. BS 4–6. RT: 8 exercises, 12 repetitions in 3 sets.	6MWD: ↑; FVC: ↑; FEV1: ↑; Eq-5D-5L: ↑; depression: ↓; anxiety: ↓
Ibrahim et al. 2021 [25], Malaysia	Cohort	*N* = 43 (group A: 4 M and 17 F; group B: 6 M and 15 F)	67.7 ± 10.2	RehP	RT	4 weeks; 7 sessions/week; duration: 30 min	Exercise for neck, chest, shoulder, upper back, lower back, abdomen, thigh, and ankle.	Depression: ↓; anxiety: ↓
Imamura et al 2021 [26], Brazil	Prospective	*N* = 27 (20 M and 7 F)	53.7 ± 13.3	RehP	RT and BE	3 weeks; 3 sessions/week; duration: 50 min	BE: include tail holding, breathing, and exhaling. RT: functional and resistance exercises.	FIM: ↑; handgrip strength: ↑; walking capacity: ↑; cognitive deficits: ↓
Li et al. 2021 [35], China	RCT	*N* = 120 (intervention: 27 M and 32 F; control: 26 M and 35 F)	44.8 ± 11.0	TelR	AT, RT and BE	6 weeks; 4 sessions/week; duration: 40–60 min	BE: breathing control and thoracic expansion; RT: lower limb exercises.	6MWT: ↑; handgrip strength: ↑; FEV1: ↑; FVC: ↑; SF12: ↑; Dyspnoea Scale: ↓
Maniscalco et al. 2021 [31], Italy	Prospective	*N* = 95 (group 1: 41 M and 8 F; group 2: 39 M and 7 F)	58.5 ± 10.6	RehP	AT and RT	5 weeks; 6 sessions/week; duration: 30 min	AT: treadmill walking. The intensity of exercise was moderate to high. RT: exercises for the upper and lower extremities.	6MWT: ↑; FEV1: ↑; FVC: ↑; Dyspnoea Scale: ↓

(*continued on next page*)

Table 2 (*continued*)

Author and country	Study design	Sample size	Age (year, mean ± SD)	Study type	Type of exercise	Training program	Rehabilitation protocol feature	Outcomes
Martin et al. 2021 [40], Belgium	Prospective	*N* = 48 (TelR: 11 M and 3 F; control: 6 M and 7 F)	66.2 ± 12.8	TelR	AT and RT	3 weeks; 2 sessions/week; duration: 50 min	The intensity of the endurance training was fixed based on a 6-point score on the BS. The upper and lower body muscle training was performed with materials available in the home (bottles of water and a chair). The participants were instructed to do 2–3 series of 8–12 repetitions for each exercise.	1-minute STST: ↑; Dyspnoea Scale: ↓
Nambi et al. 2022 [32], Egypt	RCT	*N* = 76 (28 M and 20 F)	71.0 ± 14.1	RehP	AT and RT	3 weeks; 3 sessions/week; duration: 60 min	AT: 30 min of low-intensity aerobic training exercises, which includes 20 min of the treadmill and 10 min of cycle ergometer. RT: 11 exercises (10 repetitions for three sets with a rest period of 60 s.	Handgrip strength: ↑; SarQol: ↑
Piquet et al. 2021 [5], France	Cohort	*N* = 100 (66 M and 34 F)	50.6 ± 10.9	RehP	AT and RT	3 weeks; 10 sessions/week; duration: 20 min	AT: bicycle ergometer at submaximal intensity; RT: general motor strengthening with body weight training (sit-to-stand, tiptoe stands, and squats) with 3 sets of 10 repetitions.	Barthel index: ↑; 1-minute STST: ↑; handgrip strength: ↑
Puchner et al. 2021 [41], Austria	Cohort	*N* = 23 (16 M and 7 F)	65.3 ± 1.2	RehP	AT, RT and BE	3 weeks; 7 sessions/week; duration: 50 min	AT: 20 min with 30% of individual Pmax intensity; RT: devices, body weight, and elastic bands.	6MWT: ↑; FVC: ↑; FEV1: ↑; Barthel index: ↑; DLCO: ↑
Rodriguez-Blanco et al. 2021 [33], Brazil	RCT (pilot)	*N* = 36 (exercise: 9 M and 9 F; control: 8 M and 10 F)	61.5 ± 10.5	TelR	RT	1 week; 7 sessions/week; duration: 50 min	Depending on the score obtained on the BS during the assessment, patients performed 4 (BS 7–10), 8 (BS 5–7), or 12 (BS 1–5) repetitions per exercise.	6MWT: ↑; 30 s STST: ↑
Spielmanns et al. 2021 (a) [37], Switzerland	Cohort	*N* = 183 (123 M and 60 F)	64.1 ± 3.2	RehP	AT and RT	4 weeks; 6 sessions/week; duration: 35 min	AT: cycling; RT: 3 sets of 3–5 exercises with 8–12 repetitions; gymnastics and outdoor walking.	FIM: ↑; 6MWT: ↑; FVC: ↑; FEV1: ↑; DLCO: ↑; depression: ↓; anxiety: ↓
Spielmanns et al. 2021 (b) [38], Switzerland	Cohort	*N* = 99 (57 M and 42 F)	66.3 ± 2.2	RehP	AT and RT	3 weeks; 6 sessions/week; duration: 35 min	AT: low-intensity ergometer (55%–70% of maximum heart rate). RT: 3 sets of 3–5 exercises with 8–12 repetitions. Gymnastics, outdoor walking, and respiratory training.	FIM: ↑; 6MWT: ↑; FVC: ↑; FEV1: ↑; DLCO: ↑
Stavrou et al. 2021 [42], Greece	Cohort	N = 20 (15 M and 5 F)	64.1 ± 9.9	RehP	AT and yoga	8 weeks; 3 sessions/week; duration: 100 min	Each training session included (1) warm-up (5 min), (2) recovery set (5 min) with flexibility and mobility exercises, (3) AT with walking (50 min), (4) the set with yoga exercises for breathing and/or proprioception (20 min), and (5) the set with multi-joint strength exercises (20 min).	6 MWT: ↑; FVC: ↔; FEV1: ↔; DLCO: ↔; 30 s STST: ↑; Handgrip strength: ↔; Dyspnoea Scale: ↓
Tang et al. 2021 [34], China	Prospective	*N* = 33 (moderate: 14 M and 14 F; severe: 2 M and 3 F)	57.0 ± 10.0	RehP	Liuzijue exercise	4 weeks; 7 sessions/week; duration: 20 min	Liuzijue exercise: xu, he, hu, si, chui and xi.	6WMT: ↑; SF36: ↑; Dyspnoea Scale: ↓; anxiety: ↓; depression: ↓
Tanguay et al. 2021 [43], Canada	Prospective (pilot)	*N* = 7 (4 M and 3 F)	42.0 ± 13.0	TelR	AT and RT	8 weeks; 7 sessions/week; duration: 30 min	AT: walking; RT: using material available in participant's home setting.	Eq-5D-5L: ↑
Udina et al. 2021 [39], Spain	Cohort	*N* = 33 (ICU: 10 M and 10 F; non-ICU: 4 M and 9 F)	68.9 ± 10.2	RehP	AT, RT and balance training	8 weeks; 7 sessions/week; duration: 30 min	AT: up to 15 min of aerobic training with a cycle ergometer, steps, or walking. RT: 1–2 sets with 8–10 repetitions each (intensity between 30% and 80% of the repetition maximum. Balance training: walking with obstacles, changing directions, or on unstable surfaces.	Barthel index: ↑; balance: ↑
Zampogna et al. 2021 [6], Italy	Prospective	*N* = 140 (95 M and 45 F)	67.7 ± 10.2	RehP	AT, RT and balance training	8 weeks; 2 sessions/week; duration: 30 min	Intensity and duration of training were selected according to age, length of immobility of the patient, and severity of the disease. Physical exercises include calisthenic, strengthening, balance exercise and paced walking (BS 4–5).	4MWT: ↑; Barthel index: ↑; balance: ↑; 5 times STST: ↑

AT: aerobic training; BE: breathing exercise; BS: Borg scale; DLCO: diffusing lung capacity for carbon monoxide; EQ-5D-3L: European Quality of Life-5 Dimensions-3 Levels (dyspnea severity); F: female; FEV1: forced expiratory volume in 1 second; FIM: functional independent measurement; FVC: forced vital capacity; ICU: intensive care unit; M: male; 6MWT: 6-minute walking test; Pmax: maximum power; RCT: randomized controlled trial; RehP: rehabilitation program; RT: resistance training; SarQol: Sarcopenia and Quality of Life questionnaire; SD: standard deviation; SF36/SF12: short-form 36- and 12-item health survey; STST: sit-to-stand test; TelR: telerehabilitation. ↔: unchanged or not changed in response to training period; ↓: decrease; ↑: increase.

Table 3
Summary of the Newcastle-Ottawa Scale for risk of bias assessment of cohort and prospective studies.

Author	Selection				Comparability		Outcome			Total
	Representativeness of exposed cohort	Selection of non-exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at the start of the study	Study control for adherence and tolerability	Additional factors; controlled for ≥ 2 variables including comorbidities	Assessment of outcome	Was follow-up long enough for outcomes to occur?	Adequacy of follow-up of cohorts	
Cohort study										
Betschart et al. 2021 [8]	1	0	1	1	1	1	0	1	0	6
Daynes et al. 2021 [22]	1	0	1	1	0	0	0	1	1	5
Ibrahim et al. 2021 [25]	1	0	1	1	1	0	0	1	0	5
Gloeckl et al. 2021 [23]	1	0	1	1	1	1	0	1	1	7
Piquet et al. 2021 [5]	1	0	1	1	0	0	0	1	1	5
Puchner et al. 2021 [41]	1	0	1	1	1	0	0	1	1	6
Spielmanns et al. 2021 [37] (a)	1	0	1	1	0	1	0	1	1	6
Spielmanns et al. 2021 [38] (b)	1	0	1	1	0	1	0	1	1	6
Stavrou et al. 2021 [42]	1	0	1	1	1	0	0	1	1	6
Udina et al. 2021 [39]	1	0	1	1	0	1	0	1	1	6
Prospective study										
Abodonya et al. 2021 [7]	1	1	1	1	1	0	1	1	1	8
Ahmed et al. 2021 [3]	1	0	1	1	0	0	0	1	1	5
Curci et al. 2021 (a) [9]	1	0	1	1	0	1	0	1	1	6
Curci et al. 2020 (b) [36]	1	0	1	1	0	1	0	1	1	6
Dalbosco-Salas et al. 2021 [10]	1	0	1	1	0	1	0	1	0	5
Everaerts et al. 2021 [4]	1	0	1	1	0	0	0	1	1	5
Hayden et al. 2021 [24]	1	0	1	1	1	0	0	1	1	6
Imamura et al 2021 [26]	1	0	1	1	0	1	0	1	1	6
Maniscalco et al. 2021 [31]	1	0	1	1	0	1	0	1	1	6
Martin et al. 2021 [40]	1	1	1	1	0	0	0	1	1	6
Tang et al. 2021 [34]	1	0	1	1	0	0	0	1	1	5
Tanguay et al. 2021 [43]	1	0	1	1	0	1	0	1	1	6
Zampogna et al. 2021 [6]	1	0	1	1	0	0	0	1	1	5

Table 4
Risk of bias assessment of RCT studies.

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment	Incomplete outcome data	Selective reporting	Other sources of bias	Total
Gonzalez-Gerez et al. 2021 [30]	Low	Low	Low	Low	Moderate	Low	Moderate	Low
Li et al. 2021 [35]	Low	Low	Low	Low	Moderate	Low	Moderate	Low
Nambi et al. 2022 [32]	Low	Low	Low	Low	Moderate	Low	Moderate	Low
Rodriguez-Blanco et al. 2021 [33]	Low	Low	Low	Low	Moderate	Low	Moderate	Low

RCT: randomized controlled trial.

of life and mental health. Functional capacity is defined as the ability to perform tasks and activities necessary in daily life [23]. Muscle strength and aerobic fitness are factors in maintaining performance capacity. Functional limitations can develop in patients with COVID-19 during treatment and hospitalization. Muscle weakness, cardiovascular complications, and severe weight loss are among these complications [44,45]. According to the Dallas bed rest study [46], a reduction of 30% in the maximum cardiovascular capacity is observed after 3 weeks of bed rest. In addition, patients may face some pathophysiological problems associated with COVID-19, and this can cause secondary organ damage that affects functional capacity and disrupts daily activities [47,48].

Decreased muscle strength due to muscle hypoxia, prolonged immobility, and extended use of steroids and other neuromuscular blocking agents can cause post-hospitalization polyneuropathy and myopathy [49]. Studies show that many acute respiratory distress syndrome survivors experience muscle weakness after their discharge from hospital, which is accompanied by an impairment in walking ability, performance of daily activities, and a lower quality of life [50]. Simultaneous use of aerobic and resistance training during COVID-19 rehabilitation has been effective in improving handgrip strength in most studies [4,5,26,32,42]. Due to the proposed relationship between maintaining muscle mass and strength and positive immune system responses [51,52], COVID-19 patients will likely recover faster by maintaining muscle strength [53]. This, along with other factors, will improve the performance capacity of patients discharged from hospital [54]. The results of the current systematic review show that a physical rehabilitation program applied in primary health care is feasible and effectively improves functional capacity in adult survivors of COVID-19.

Pulmonary injuries, especially hypoxic respiratory failure, appear to be a major complication of COVID-19 [55,56]. Prolonged mechanical ventilation in severe cases of the disease can cause secondary lung damage such as edema and pneumonia [56,57]. Significant changes in diffusion capacity and lung volume are also observed following the disease [17]. Approximately half of patients may experience obstructive pulmonary patterns and develop restrictive pulmonary patterns after hospitalization [47,48]. These respiratory effects may decrease functional capacity and quality of life in these patients and confirm the need for pulmonary rehabilitation. The studies presented in this review make it clear that the use of breathing exercises can be an essential part of the rehabilitation process of patients, and has been effective in improving respiratory capacity. This systematic review shows that multiple lung functional parameters, including FVC, FEV1, DLCO, and dyspnea severity, significantly improved following a physical rehabilitation program in adult survivors of COVID-19.

The present study results also show the positive effects of physical rehabilitation on mental health, especially anxiety and depression. COVID-19 can be associated with psychological and cognitive disorders, and in some cases, survivors of the disease may also experience psychological trauma [58,59]. It seems that applying exercise training, especially aerobic and resistance training, can effectively improve psychological responses during COVID-19 rehabilitation.

However, the present systematic review findings have some limitations. First, because most of the studies included in our analysis did not report comorbidities associated with severe COVID-19 outcomes, the beneficial effects of physical rehabilitation with adverse COVID-19 outcomes may be more exaggerated than indicated. Second, in some included studies, it is unknown if the observed effects result from physical rehabilitation or non-specific factors other than the intervention, such as psychological rehabilitation program and time. More prospective and well-organized studies are needed to determine the beneficial roles of physical rehabilitation in discharged COVID-19 patients and evaluate the impact of different etiologies and clinical factors on outcomes. Third, most of the included studies were limited by the absence of a control group. Forth, some of the outcome measures in the included studies were related to the quality of life and mental health status, which were self-reported and potentially introduced recall and social desirability bias into the findings. Fifth, different outcome measures (including different measures for functional capacity, pulmonary function, quality of life and mental health) used across the included studies impose different levels of validity, reliability and sensitivity. Sixth, one of the major limitations of the included studies lies with the different types, intensities and durations of the tested physical rehabilitation programs. Future research should provide a more consistent physical rehabilitation program for discharged COVID-19 patients to provide a clearer view on the dose–response relationship of physical activity and functional and mental outcomes in this setting. Finally, we did not perform a meta-analysis because of the absence of a control group, different physical rehabilitation programs, and different outcome measures used in the included studies. Therefore, further studies should consider evaluating the impact of specific types of physical rehabilitation in discharged COVID-19 patients.

5. Conclusion

In summary, our systematic review suggests that physical rehabilitation interventions might be safe, feasible and effective in patients after COVID-19, thereby improving various physical, clinical and psychological relevant outcomes.

Authors' contribution

MR, MMS, JIS and LS developed the idea, designed the study, had full access to all data in the study, and take responsibility for the integrity of the data and the accuracy of the data analysis. MR and MMS ran the search strategy. MR, WW, AK, SWL and

DKY evaluated the quality of the literature. MR and MMS wrote the manuscript, while WW, AK, SWL, DKY, JIS and LS edited it. All listed authors reviewed and approved the final manuscript.

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Declaration of Competing Interest

The authors declare that there are no conflicts of interests.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.joim.2023.01.003.

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