



EFFECT OF PHYSICAL THERAPY ON IMPAIRMENTS IN COVID-19 PATIENTS FROM INTENSIVE CARE TO HOME REHABILITATION: A RAPID REVIEW

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Objective: Guidelines regarding physical therapy for COVID-19 patients are often based on expert opinion. Recent clinical trials have reported effects on several rehabilitation outcomes in COVID-19 patients. This review summarizes the effects of physical therapy in COVID-19 patients.

Data sources: PubMed, Web of Science and Scopus databases were systematically searched for studies investigating the effect of any physical therapy modality on impairments in adult COVID-19 patients. Included studies were (non)-randomized controlled trials, pre-experimental studies, and cohort studies in which a pre-post analysis was performed.

Data extraction: After the screening process, data of interest were extracted from eligible studies and their risk of bias was assessed. Included outcome measures were divided into 3 groups: pulmonary function, physical function, and psychosocial function.

Data synthesis: A total of 15 studies were included in this review. Physical therapy seems to have positive effects on pulmonary function, physical function, and psychosocial function. However, these effects differ between clinical settings (e.g. home care, intensive care unit, inpatient units). Due to the low-to-moderate quality of the included studies, no robust conclusions can be drawn.

Conclusion: Further high-quality research is required, taking into account the different clinical settings, in order to draw conclusions about the effectiveness of physical therapy on impairments in COVID-19 patients.

Key words: COVID-19; physical therapy; rehabilitation.

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The coronavirus disease 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has been endangering global health since early 2020. Worldwide, over 237 million cases of COVID-19 have been registered, of

LAY ABSTRACT

Guidelines regarding physical therapy for COVID-19 patients are often based on expert opinion or on evidence from studies of physical therapy in patients with other diseases. More and more clinical studies are investigating the effect of physical therapy on the recovery of COVID-19 patients. Prior to this review, the importance of physical therapy for COVID-19 patients was not clear. This review summarizes the effects of physical therapy in COVID-19 patients. We reviewed and assessed the quality of the existing literature on this topic. Fifteen studies with a total of 1,341 COVID-19 patients were included in this review. Physical therapy appears to improve lung function, physical function, and psychosocial function in COVID-19 patients. However, the effect can differ between clinical settings; for example, home care, intensive care unit, or other inpatient units. Due to the low-to-moderate quality of the included studies, no robust conclusion can be drawn. Further high-quality research is needed, taking into account the different clinical settings.

whom over 4.8 million have died (1). However, this is probably an underestimation, as COVID-19 patients can be asymptomatic and thus remain unnoticed (1).

COVID-19 impacts, among other things, both the physical and mental well-being of patients. Approximately 14% of COVID-19 patients will require hospitalization, and extremely severe cases will need intensive care. Such patients can develop a range of dysfunctions, such as lung function impairments, neurological impairments, reduced physical capacity, muscle weakness, and psychological and cognitive impairments (2). Clinical practice guidelines state that these complications can be countered with appropriate physical therapy management as part of a multidisciplinary approach (3, 4). Research prior to the COVID-19 pandemic has shown that patients with acute lung injury may still have significant physical impairments, such as balance problems and muscle weakness, even years after discharge, which, in turn, can increase the risk of falls (5). Baricich et al.'s cross-sectional study (6) found that, 3–6 months after discharge, 32% of COVID-19 patients still had impaired physical performance. These findings emphasize the importance of rehabilitation, even after patients are discharged from hospital.

Several reviews and guidelines have summarized the role of physical therapy in rehabilitation of COVID-19 patients (7–9); however, due to the urgent need for guidelines on how to treat these patients, these are mostly based on expert opinion or on evidence from patients with other lung diseases, and not on evidence from recent literature concerning COVID-19. Meanwhile, many clinical trials about the rehabilitation of COVID-19 patients have already been conducted and published, highlighting the need for an update of the current guidelines. To the best of our knowledge, no systematic review has described the role of physical therapy in the rehabilitation of COVID-19 patients in both the acute and subacute phases of the disease. Therefore, the aim of this systematic review is to describe the role of physical therapy in the rehabilitation of COVID-19 patients in all phases of recovery.

METHODS

Study design

This rapid review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) statement for reporting systematic reviews.

Eligibility criteria

Studies were included in this review if they met following inclusion criteria:

- *Type of participants*: studies that included adult COVID-19 patients (> 18 years old).
- *Type of intervention*: studies that investigated the effect of any physical therapy modality (e.g. breathing exercises, aerobic training, muscle strengthening, relaxation) on COVID-19 impairments.
- *Type of outcome*: studies that assessed the pre–post and/or post-follow up effect of physical therapy on COVID-19 impairments. Outcomes were divided into 3 categories: pulmonary function (e.g. oxygen supplementation, oxygen saturation, forced vital capacity), physical function (e.g. 6-min walk test (6MWT), Barthel Index (BI), muscle strength), and psychosocial function (e.g. anxiety, depression, quality of life (QoL)).
- *Type of study design*: non-, quasi- or randomized controlled trials (RCTs), pre-experimental studies, or cohort studies were included. Non-clinical trials (e.g. guidelines, (systematic) reviews), case reports/case series, methodological papers and congress participations were excluded. Studies had to be published in English, Dutch or French.

Information sources and search strategy

Electronic searches were conducted using following 3 databases: PubMed, Web of Science and Scopus, with a final search date of 4 May 2021. The search strategy was developed by combining search terms related to the population (COVID-19-related keywords) and the intervention (keywords related to physical therapy interventions). To limit the number of studies to screen, some filters were used in all databases. In PubMed, the clinical trial filter was used. Reviews were already excluded in Web of Science and only experimental studies were included. In the

Scopus database, a filter was used to exclude reviews and to include only articles published in English, Dutch and French. The full electronic search is shown in Appendix S1.

Study selection

Identification and selection of eligible studies was performed with the use of the web-based application Rayyan (11). After excluding duplicates, titles and abstracts were screened to identify relevant studies. If studies were considered relevant or, in case of doubt, full paper copies were retrieved and their eligibility checked. If the full text was not available, the corresponding author was contacted to obtain a copy. If a copy could not be obtained, the study was excluded.

Data collection process and data items

The data items of interest were extracted by one reviewer (TP) using the Cochrane data extraction form template for RCTs and non-RCTs. This form was double-checked and completed by 2 other authors (RD and EDK). From each individual study, the following information was extracted: (i) patient characteristics (population, number, sex, age), (ii) therapy of the intervention group and, if applicable, the control group, (iii) outcome measures, and (iv) the setting (inpatient intensive care unit (ICU), inpatient no ICU, outpatient (home care)). Only outcomes for which the significance of the difference between the pre- and post-treatment values had been calculated, were included in the data extraction form. Other outcome measures were disregarded, since they do not reflect the effect of physical therapy. If important data were missing in a study, no assumptions were made, and no conclusions were drawn based on these data.

Risk of bias assessment

To assess the risk of bias, different tools were used, depending on the study design of the included article. To assess the risk of bias of a RCT, the second version of the Cochrane risk-of-bias tool for randomized trials (ROB II) was used (12). If the study was identified as either a non-RCT or a pre-experimental study, the Cochrane Risk Of Bias In Non-Randomized Studies tool (ROBINS-I) was used (13). Lastly, to assess the risk of bias in cohort studies, the Quality in Prognostic Studies (QUIPS) tool was utilized (14). Since the cohort studies included in this review could not be identified as prognostic studies, the domain “prognostic factor measurement” was not applicable and thus not included in the risk of bias assessment. No other adaptations were made to the tools used in this review.

RESULTS

Study selection

The total search yielded 2,863 relevant articles in PubMed, Web of Science and Scopus. Fig. 1 shows the flow diagram of the entire study selection process. In total, 15 studies were included, of which 2 were RCTs, 1 was a non-RCT, 6 were pre-experimental studies, and 6 were cohort studies.

Study characteristics

Table I and Table II list more detailed information about the study characteristics of the (non-) RCTs (Table I) and the pre-experimental and cohort studies (Table II).

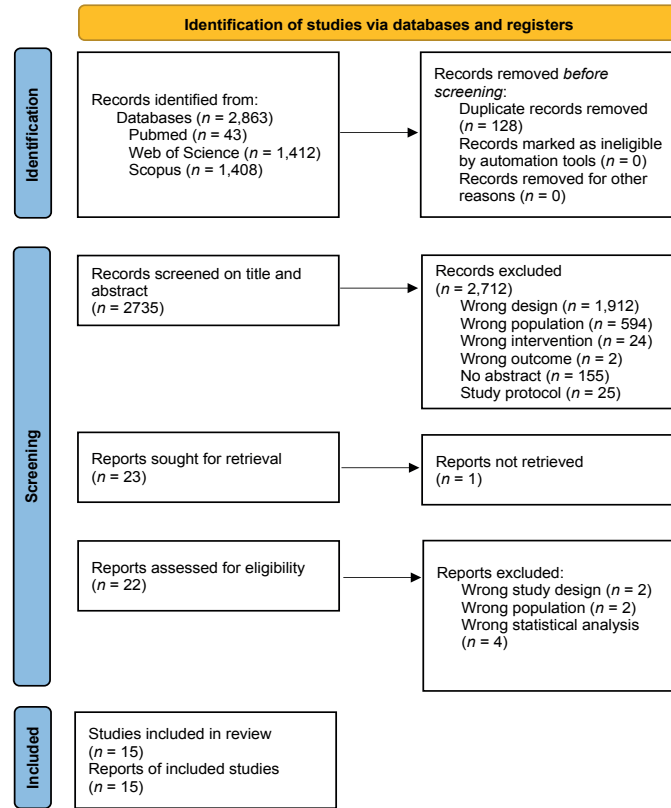


Table I. Characteristics of included (non-)randomized clinical trials assessing the effect of physical therapy on impairments in COVID-19 patients

Study	Intervention group					Control group					Setting			
	Population	N	%F	Age, years	Therapy	Population	N	%F	Age, years	Therapy	Outcomes	ICU	nICU	HC
RCT														
Liu et al. 2020 (15)	Elderly COVID-19 patients	36	33.3	69.4 (8.0)	(1) respiratory muscle training with threshold PEP 3×10 breaths, 60% MEP, 1 min rest (2) cough exercises 3×10 active coughs (3) diaphragmatic training 30 max. voluntary contractions with weight (1–3 kg) (4) stretching exercises respiratory muscles (5) home exercise: pursed lip breathing and cough training	Elderly COVID-19 patients	36	30.6	68.9 (7.6)	NI	FEV1 FVC DLCO 6MWT FIM SF-36 SAS SDS t0: baseline t1: 6 weeks			x
Özlü 2021 et al(16)	COVID-19 patients	33	36	36.48 (11.63)	2 sessions/day for 20–30 min progressive muscle relaxation exercises, taught via CD	COVID-19 patients	34	53	33.15 (11.90)	Usual care	STAI RCSQ t0: baseline t1: 5 days			x
Non-RCT														
Abodonya et al. 2021 (17)	Recovered COVID-19 patients weaned from ventilation	21	19.1	48.3 (8.5)	Incentive breathing exercises 2 sessions/day for 2 weeks + inspiratory muscle training: daily 2 sessions of 6 inspiratory cycles with 60 s rest afterwards, threshold set at 50% MIP	Recovered COVID-19 patients weaned from ventilation	21	23.8	47.8 (9.2)	Incentive breathing exercise 2×/day for 2 weeks	FVC FEV1 DSI EQ-5D-3L 6MWT t0: baseline t1: 2 weeks			x

Continuous values are reported as mean (SD). CD: compact disk; DLCO: diffusing capacity for carbon monoxide; DSI: dyspnoea severity scale; EQ-5D-3L: EuroQuality-5Dimensions-3Levels; %F: percentage female; FEV1: forced expiratory volume in 1 s; FIM: Functional Independence Measure; FVC: forced vital capacity; HC: home care; ICU: patients who stayed at the intensive care unit; max.: maximum; MEP: maximum expiratory pressure; MIP: maximum inspiratory pressure; N: number; NI: no information; nICU: patients who did not stay at the intensive care unit; PEP: positive expiratory pressure; RCSQ: Richards-Campbell Sleep Questionnaire; RCT: randomized controlled trial; SAS: self-rating anxiety scale; SDS: self-rating depression scale; SF-36: 36-Item Short Form Health Survey; 6MWT: 6-min walk test; STAI: State-Trait Anxiety Inventory.

Table II. Characteristics of included pre-experimental and cohort studies of the effect of physical therapy on impairments in COVID-19 patients

Study	Population	N	%F	Age, years, mean (SD)	Therapy	Outcomes	Setting		
							ICU	nICU	HC
<i>Pre-experimental study</i>									
Ahmed et al. 2021 (18)	Discharged COVID-19 patients who were admitted to inpatient units	10 (VENT-) 10 (VENT+)	40 30	38.0 (10.3) 41.2 (10.3)	Aerobic and breathing training 3 sessions/week for 5 weeks (1) aerobic training: 50–70% of max. heart rate, RPE: 4–6, first session 20 min duration increased, according to ACSM guidelines, to achieve 60 min on the final day (2) buteyko breathing exercises: "slow and reduced breathing" in combination with "control pauses" and "extended pauses".	6MWT mBORG SF-36 t0: baseline t1: 5 weeks			x
Chintamani et al. 2020 (19)	COVID-19 patients	50	NI	NI	Structured exercise protocol 2 sessions/day for 7 days: (1) deep breathing exercises, chest expansion exercises and prone lying for 30 min (2) ankle and toe movements, hand pumps and heel slides along with prone lying for 45 min (3) shoulder abduction movements, hip abduction and diaphragmatic breathing along with prone lying for 45 min	mBORG SpO2 Respiratory rate Heart rate Number of active cough extraction X-ray changes t0: baseline t1: 7 days		x	
Piquet et al. 2021 (20)	COVID-19 patients	100	34	66 (22)*	Two sessions/day (<20 min) 5 days a week: (1) motor strengthening with body weight exercises (sit-to-stand, tiptoe stands, squats), elastics and weights (3×10) (2) respiratory rehabilitation: controlled diaphragmatic breathing (3) aerobic training: bicycle ergometer at sub-max intensity + group sessions of 1 h if tolerated	Barthel Index Grip strength Sit-to-stand t0: baseline t1: discharge	x	x	
Sinha et al. 2020 (21)	COVID-19 patients from ICU to discharge	150	NI	NI	Stage I – ICU: deep breathing exercises, bed mobility exercises, functional mobility in and around bed (daily for 7 days) Stage II – Recovery ward: Stage 1 + graded upper and lower limb strengthening exercises and graded spinal exercises (daily for 7 days) Stage 3 – Home programme: Stage 1 + 2 + aerobic exercises	FIM Tinetti t0: baseline t1: 1 month	x	x	x
Tang (2021) (22)	Discharged COVID-19 patients	33	48.5	43.2 (10.4)	Liuzijue exercises 1 session/day for 20 min over 4 weeks: inhalation and exhalation through different mouth patterns to regulate and control the rise and fall of the breath in the body. It is performed by producing 6 different sounds through expiration together with corresponding body movements.	MIP PIF Diaphragm thickness Diaphragm movement SF-36 HAMA 6MWT mMRC t0: baseline t1: 4 weeks			x
Zampogna et al. 2021 (23)	COVID-19 patients	140	32.2	71 (61.5–78.0)	Multidisciplinary programme for pulmonary rehabilitation: type, intensity, timing and modality patient tailored starting with 20 min/day up to 2–3 session of 30 min/day	SPPB 6MWT Barthel Index t0: baseline t1: discharge		x	
<i>Cohort studies</i>									
Al Chikhanie et al. 2021 (24)	Severe COVID-19 patients post-ICU	21	33.33	70.9 (10.6)	Pulmonary rehabilitation: respiratory exercises, muscle strengthening, balance, walking, cycling, and gymnastics according to current recommendations	FEV1 – FVC MIP – MEP Tinetti – 6MWT SpO2 – Borg scale Strength (handgrip + quadriceps) QoL – Fatigue Anxiety Depression Post-traumatic stress t0: pre-PR t1: post-PR			x

Table II. *Conts.*

Study	Population	N	%F	Age, years, mean (SD)	Therapy	Outcomes	Setting		
							ICU	nICU	HC
Hermann et al. 2020 (25)	COVID-19 patients discharged from acute care hospitals	28 (total) 12 (VENT+) 16 (VENT-)	50 75 31.3	66.04 (9.3) 64.3 (8.9) 67.4 (9.7)	Cardiopulmonary rehabilitation, total of 25–30 session, 5–6 day/week for 2–4 weeks: (1) aerobic exercise: indoor/outdoor walking or stationary cycling (2) strength training: 3×20 repetitions with max load tolerated (3) respiratory physiotherapy: teaching breath control (pursed lip breathing, secretion mobilization, diaphragmatic breathing), energy-saving techniques, controlled coughing exercises (4) 2×/week (1 h), patients had an educational session	6MWT Feeling thermometer t0: baseline t1: 20 days		x	
Kofod et al. 2021 (26)	COVID-19 patients with hypoxemia	53	34	68 (57–78)	CPAP treatment: start with pressure of 10 cmH ₂ O; then observation of patient with focus on RR, SpO ₂ , mask leakage and compliance, pressure increased if SpO ₂ too low and pressure was decreased if RR was too high or if treatment was too demanding	PaO ₂ /FIO ₂ ratio RR Oxygen supplementation SpO ₂ Blood pressure Heart rate t0: baseline t1: acute effect CPAP t2: end CPAP		x	
Spielmanns et al. 2021 (27)	COVID-19 patients discharged from acute care hospitals	99	42.4	67.72 (10.23)	Multimodal program, total of 25–30 sessions, 5–6 day/week for 3 weeks: (1) exercise therapy: endurance training (cycling, treadmill), gymnastics, indoor and outdoor walking, strength training (2) respiratory physiotherapy: teaching breath control (pursed lip breathing, secretion mobilization, and diaphragmatic breathing), energy-saving techniques, and controlled coughing exercises (3) 2×/week (1h), patients had an educational session	6MWT FIM Feeling thermometer t0: baseline t1: 3 weeks			x
Udina et al. 2021 (28)	COVID-19 patients post-acute care	33 (total) 20 (ICU) 13 (nICU)	57.6 50 69.2	66.2 (12.8) 58.2 (7.9) 78.4 (8.1)	Multicomponent therapeutic exercise intervention, 30 min 7 days/week: (1) resistance training (2) endurance training: aerobic training with cycle ergometer, steps or walking (3) balance training: walking with obstacles, changing directions or on unstable surfaces) (4) others: when required, breathing exercises and manual therapy	Barthel Index SPPB FAC Single-leg stance t0: baseline t1: 10 days or discharge			
Verma et al. 2021 (29)	COVID-19 patients	433	31.17	53.88 (13.44)	Multicomponent therapeutic exercise intervention 1 session per day for 6 days a week: (1) relaxation and breathing control exercises (2) COVID awake repositioning/proning (3) exercises from supine to sitting to standing (4) spot marching (5) ambulation	Oxygen supplementation Heart rate t0: baseline t1: 2 weeks	x		x

Continuous values are reported as mean (SD) or median (IQR)*.

%F: percentage female; FAC: Functional Ambulation Category; FIM: Functional Independence Measure; HC: home care; ICU: patients who stayed at the intensive care unit; mBORG: modified BORG scale; mMRC: modified Medical Research Council; N: number; NI: no information; nICU: patients who did not stay at the intensive care unit; POMA: Performance Oriented Mobility Assessment; SF-36: 36-Item Short Form Health Survey; 6MWT: 6-min walk test; SpO₂: oxygen saturation; RPE: rating of perceived exertion; SPPB: Short Physical Performance Battery; VENT+: patients who received mechanical ventilation; VENT-: patients who did not receive mechanical ventilation.

Patient characteristics. In total, 1,341 COVID-19 patients were included (sample size: 10–433, a mean of 37% women, mean age range 33.1–78.4 years). One study focused specifically on elderly COVID-19 patients (≥65 years of age) (15). Six studies included active COVID-19

patients, of which 2 studies were on patients admitted to the ICU (19, 26), 2 studies were on patients admitted to other inpatient care units (16, 24), and 2 studies included both (20, 29). Five studies included recovered COVID-19 patients who were still receiving inpatient rehabilitation

Table III. Risk of bias assessment of the randomized controlled trials

Study	Risk of bias arising from randomization process	Risk of bias due to deviations from intended interventions	Risk of bias due to missing outcome data	Risk of bias in measurement of outcome	Risk of bias in selection of the reported studies	Overall risk of bias
Lui et al. 2020 (15)	+	-	?	+	+	-
Özlü Lui et al. 2021 (16)	+	?	-	?	+	-

+: low risk of bias; -: high risk of bias; ?: some concerns.

Table IV. Risk of bias assessment of the non-randomized controlled trials and pre-experimental studies

Study	Bias due to confounding	Bias in selection of the participants into the study	Bias in classification of interventions	Bias due to deviations from intended interventions	Bias due to missing data	Bias in measurement of outcomes	Bias in selection of the reported result	Overall
Abodonya et al. 2021 (17)	?	+	+	+	+	+	+	?
Ahmed et al. 2021 (18)	?	+	+	+	+	+	+	?
Chintamani et al. 2020 (19)	?	+	+	+	?	+	+	-
Piquet et al. 2021 (20)	?	-	+	+	?	+	+	-
Sinha et al. 2020 (21)	?	+	+	+	?	-	+	-
Tang et al. 2021 (22)	?	+	+	+	+	+	+	?
Zampogna et al. 2021 (23)	?	-	+	+	-	+	+	-

+: low risk of bias; -: high risk of bias; ?: some concerns.

Table V. Risk of bias assessment of the cohort studies

Study	Study participation	Study attrition	Outcome measurement	Study confounding	Statistical analysis and reporting
Al Chikhanie et al. 2021 (24)	-	+	?	?	+
Hermann et al. 2020 (25)	-	?	+	?	-
Kofod et al. 2021 (26)	-	+	?	?	+
Spielmanns et al. 2021 (27)	+	?	+	?	?
Udina et al. 2021 (28)	?	?	?	?	?
Verma et al. 2021 (29)	-	-	?	?	+

+: low risk of bias; -: high risk of bias; ?: some concerns.

(17, 18, 22, 25, 27), while 2 studies included discharged COVID-19 patients who received home care (18, 22). The remaining study investigated the effect of physical therapy on COVID-19 impairments in patients from ICU to home care (21).

Interventions. A variety of physical therapy interventions were included in the studies. Several subgroups could be distinguished: respiratory muscle training (strengthening and stretching) (15), breathing and cough exercises (15, 17), prone lying (19, 29), continuous positive airway pressure (CPAP) (26), aerobic training (18, 20, 21, 23, 25, 27, 28), physical exercises (muscle strengthening, mobilizations, bed mobility) (19–21, 23–25, 27–29), progressive muscle relaxation and educational sessions (25, 27).

Outcome measures. COVID-19 impairments were divided in 3 subgroups: pulmonary function, physical function, and psychosocial function. Several pulmonary outcome measures (e.g. forced expiratory volume, dyspnoea, breathlessness, oxygen saturation, heart rate)

were assessed in 8 studies (15, 17, 18, 19, 22, 24, 26, 29). Eleven studies assessed 1 or more physical outcome measures, such as the 6MWT, Functional Independence Measure, and grip strength (15, 17, 18, 20–25, 27, 28). Psychological outcomes were investigated in 8 studies and included questionnaires regarding QoL, anxiety and depression, sleep, fatigue, post-traumatic stress, and well-being (15–18, 22, 24, 25, 27).

Risk of bias assessment. The risk of bias of the RCTs, non-RCTs, pre-experimental studies and cohort studies are shown in Table III, Table IV and Table V.

One of the main limitations of most of the included studies was that no confounding variables were defined and accounted for (17–19, 24). Another prevalent badly scored item was the risk of bias due to missing outcomes. In some studies, this item scored poorly because more than 5% of the participants' data was missing and no appropriate analysis was conducted or it was not described how missing data were handled (15, 16, 27, 29). In other studies, no information was given about

Table VI. Results per outcome: pulmonary function

Study	Outcome	Study design	Results intervention group Pre – post value, mean (SD) <i>p</i> -value	Results control group (if applicable) Pre–post value, mean (SD) <i>p</i> -value	Between-group difference (if applicable) post values, mean (SD) <i>p</i> -value
<i>Respiratory volumes</i>					
Liu et al. 2020 (15)	FEV1 (l)	RCT	pre: 1.10 (0.08); post: 1.44 (0.25) $p < 0.05$; $t_0 < t_1$	pre: 1.13 (0.14); post: 1.26 (0.32) $p > 0.05$; $t_0 < t_1$	I: 1.44 (0.25); C: 1.26 (0.32) $p < 0.05$; I > C
Abodonya et al. 2021 (17)	FEV1 (%pred)	Non-RCT	pre: 76.2 (12.7); post: 83.7 (10.5) $p = 0.039$; $t_0 < t_1$	pre: 75.4 (12.2); post: 75.1 (12.4) $p = 0.871$	I: 83.7 (10.5); C : 75.1 (12.4) $p = 0.043$; I > C
Al Chikhanie et al. 2021 (24)		Cohort	pre: 66.7 (16); post: 81.2 (14.2) $p < 0.05$; $t_0 < t_1$	NA	NA
Liu et al. 2020 (15)	FVC (l)	RCT	pre: 1.79 (0.53); post: 2.36 (0.49) $p < 0.05$; $t_0 < t_1$	pre: 1.77 (0.64); post: 2.08 (0.37) $p > 0.05$; $t_0 < t_1$	I: 2.36 (0.49); C: 2.08 (0.37) $p < 0.05$; I > C
Abodonya et al. 2021 (17)	FVC (%pred)	Non-RCT	pre: 78.7 (13.5); post: 84.2 (10.3) $p = 0.047$; $t_0 < t_1$	pre: 77.2 (12.6); post: 76.8 (11.7) $p = 0.754$	I: 84.2 (10.3); C: 76.8 (11.7) $p = 0.041$; I > C
Al Chikhanie et al. 2021 (24)		Cohort	pre: 59.1 (15.2); post: 72.9 (15.2) $p < 0.05$; $t_0 < t_1$	NA	NA
Liu et al. 2020 (15)	FEV1/FVC%	RCT	pre: 60.48 (6.39); post: 68.19 (6.05) $p < 0.05$; $t_0 < t_1$	pre: 60.44 (5.77); post: 61.23 (6.43) $p > 0.05$; $t_0 < t_1$	I: 68.19 (6.05); C: 61.23 (6.43) $p < 0.05$; I > C
<i>Oxygen diffusion</i>					
Liu et al. 2020 (15)	DLCO%	RCT	pre: 60.3 (11.3); post: 78.1 (12.3) $p < 0.05$; $t_0 < t_1$	pre: 60.7 (12); post: 63 (13.4) $p > 0.05$; $t_0 < t_1$	I: 78.1 (12.3); C: 63 (13.4) $p < 0.05$; I > C
Chintamani et al. 2020 (19)	SpO ₂ (%)	Pre-experimental	pre: 90 (5); post: 98 (2) $p < 0.05$; $t_0 < t_1$	NA	NA
Kofod et al. 2021 (26)		Cohort	Full cohort pre: 90.7 (3.5); post: 92.7 (3.2) $p < 0.001$; $t_0 < t_1$ Excl. CPAP failure pre: 90.4 (3.5); post: 93.1 (2.5) $p < 0.001$; $t_0 < t_1$	NA	NA
Al Chikhanie et al. 2021 (24)		Cohort	pre: 85 (7); post: 89 (11) $p > 0.05$; $t_0 < t_1$	NA	NA
Kofod et al. 2021 (26)	Oxygen supplementation (l/min)	Cohort	Full cohort pre: 27.4 (13.3); post: 23.3 (10.7) $p < 0.001$; $t_0 < t_1$ Excl. CPAP failure pre: 27.9 (13.2); post: 23.3 (10.5) $p < 0.001$; $t_0 < t_1$	NA	NA
Verma et al. 2021 (29)		Cohort	pre: 60.9 (25.39); post: 34.76 (24.98) $p < 0.001$; $t_0 < t_1$	NA	NA
Kofod et al. 2021 (26)	PaO ₂ /FiO ₂	Cohort	Full cohort NI Excl. CPAP failure pre: 101 (36); post: NI $p = 0.02$; $t_0 < t_1$	NA	NA
<i>Dyspnoea</i>					
Abodonya et al. 2021 (17)	DSI (0–36)	Non-RCT	pre: 18.5 (4.3); post: 14.2 (3.5) $p = 0.001$; $t_0 > t_1$	pre: 17.8 (5.1); post: 17.1 (4.8) $p = 0.621$	I: 14.2 (3.5); C :17.1 (4.8) $p = 0.032$; I > C
Ahmed et al. 2021 (18)	mBORG – breathlessness (0–10)	Pre-experimental	pre: 4.5 (0.2); post: 3.1 (0.1) $p < 0.001$; $t_0 > t_1$	NA	Subgroup analysis +VENT: 3.1 (0.9) –vent: 3.1 (0.5) $p = 0.673$; +VENT<–vent NA
Chintamani et al. 2020 (19)		Pre-experimental	pre: 7 (3); post: 0 (1) $p < 0.001$; $t_0 > t_1$	NA	NA
Al Chikhanie et al. 2021 (24)		Cohort	pre: 4.4 (2.3); post: 4.1 (1.8) $p > 0.05$; $t_0 > t_1$	NA	NA
Tang et al. 2021 (22)	mMRC (0–4)	Pre-experimental	NI $p = 0.022$; $t_0 > t_1$	NA	NA
Chintamani et al. 2020 (19)	Respiratory rate (breaths/min)	Pre-experimental	pre: 45 (3); post: 20 (2) $p < 0.05$; $t_0 > t_1$	NA	NA
Kofod et al. 2021 (26)		Cohort	Full cohort pre: 28.6 (7.6); post: 26.9 (6.2) $p = 0.002$; $t_0 > t_1$ Excl. CPAP failure pre: 29.7 (7.1); post: 27.7 (5.7) $p = 0.001$; $t_0 > t_1$	NA	NA
Chintamani 2020 (19)	Number of active cough extraction	Pre-experimental	pre: 0 (1); post: 5 (2) $p < 0.001$; $t_0 < t_1$	NA	NA

Table VI. *Cont.*

Study	Outcome	Study design	Results intervention group Pre – post value, mean (SD) <i>p</i> -value	Results control group (if applicable) Pre–post value, mean (SD) <i>p</i> -value	Between-group difference (if applicable) post values, mean (SD) <i>p</i> -value
Chintamani et al. 2020 (19)	X-ray changes	Pre-experimental	NI <i>p</i> < 0.05; NI	NA	NA
Tang et al. 2021 (22)	MIP (cmH ₂ O)	Pre-experimental	MD: 13.46 (20.06) <i>p</i> < 0.001; t0 > t1	NA	NA
<i>Respiratory muscle function</i>					
Al Chikhanie et al. 2021 (24)		Cohort	pre: 42.7 (17.5); post: 62.9 (13) <i>p</i> < 0.05; t0 > t1	NA	NA
Tang et al. 2021 (22)	PIF (l/min)	Pre-experimental	MD: 0.74 (0.58) <i>p</i> < 0.001; t0 > t1	NA	NA
Tang et al. 2021 (22)	Diaphragm thickness (cm)	Pre-experimental	NI <i>p</i> > 0.05; NI	NA	NA
Tang et al. 2021 (22)	Diaphragm movement (cm)	Pre-experimental	NI <i>p</i> > 0.05; NI Deep breathing: MD: 0.57 (1.18) <i>p</i> = 0.009; t0 > t1	NA	NA
Al Chikhanie et al. 2021 (24)	MEP (cmH ₂ O)	Cohort	pre: 68.2 (30.3); post: 87.1 (30.3) <i>p</i> < 0.05; t0 > t1	NA	NA
Chintamani et al. 2020 (19)	Heart rate (beats/min)	Pre-experimental	pre: 100 (5); post: 69 (5) <i>p</i> < 0.05; t0 > t1	NA	NA
Kofod et al. 2021 (26)		Cohort (full cohort)	pre: 89.5 (24.4); post: 94.9 (18.9) <i>p</i> > 0.05; t0 > t1	NA	NA
Kofod et al. 2021 (26)		Cohort (excl. CPAP failure)	pre: 91.2 (26.8); post: 98.5 (19.4) <i>p</i> > 0.05; t0 > t1	NA	NA
Verma et al. 2021 (29)		Cohort	pre: 92.46 (14.93); post: 100.4 (13.25) <i>p</i> < 0.001; t0 < t1	NA	NA
Kofod et al. 2021 (26)	Blood pressure (mmHg)	Cohort	Full cohort pre: 133.6 (19.1); post: 129.3 (15.2) <i>p</i> > 0.05; t0 > t1 Excl. CPAP failure pre: 135.2 (21.5); post: 129.4 (15.2) <i>p</i> > 0.05; t0 > t1	NA	NA

Continuous values are reported as mean (SD). CPAP: continuous positive airway pressure; NA: not applicable; MD: mean difference; MEP: maximum expiratory pressure; MIP: maximum inspiratory pressure; NI: no information; PIF: peak inspiratory flow.

possible missing data or about how missing data would have been handled if present (19, 25). In some studies, the outcome measures were well defined and objective tools were used to measure these outcomes. However, in some studies, the way the outcome was measured was not well defined, or the tool used to measure the outcome was subjective. In addition, the participants and assessors were usually not blinded to intervention allocation (16, 24, 26). There was also missing information regarding the inclusion and exclusion criteria used to determine the eligibility of participants (23–25), or it was unclear when and where participants were recruited (28). These aspects can all lead to bias. Some of the studies were conducted retrospectively and individuals were selected after the outcome had been measured, both of which can lead to selection bias (20, 23–26, 29). This last factor can lead to an overestimation of the results, since the outcome measure is already measured and results are already known in a retrospective study. In most studies, the risk of reporting bias was low. However, in 3 studies, the risk of bias was scored moderate or high (25, 27, 28). In Udina et al.’s

study (28) only the results of the 6MWT of a subsample were reported. There was no information on how the whole sample scored on this test (28). In Hermann et al.’s study (25) there was inadequate reporting on which results were significant. Lastly, in Spielmanns et al.’s study the results of the pre-post analysis were not reported for all outcome measures mentioned (27). Lastly, checking the studies for publication bias was not always possible, since most of them were not registered and no pre-registered protocols were available. Researchers could only report the outcome measure on which physical therapy had a positive effect, which could lead to an overestimation of the benefits of physical therapy.

Overall, the risk of bias of the included studies is moderate-to-high. This means that the internal validity of the studies is low and conclusions drawn from these results should be interpreted with caution.

Qualitative synthesis of results

Pulmonary outcome measures were reported in 8 studies (15, 17–19, 22, 24, 26, 29), with in total 22 different

parameters. Detailed results of all included pulmonary outcome measures are shown in Table VI. Given the heterogeneity amongst the included outcome measures it was decided not to pool the results. Nevertheless, all studies reported significant improvements in pulmonary function after the physical therapy intervention (see Table VI). A variety of interventions were used to improve the pulmonary function of COVID-19 patients: (i) respiratory rehabilitation consisting of breathing and cough exercises, respiratory muscle training, stretching respiratory muscles and prone lying; (ii) CPAP treatment; (iii) physical rehabilitation consisting of motor strengthening, mobilizations, bed mobility exercises; and (iv) aerobic training.

Liu et al.'s RCT (15) demonstrated that 6 weeks of respiratory rehabilitation improved the forced vital capacity (pre: 1.79 (0.53) L; post: 2.36 (0.49) L; $p < 0.05$), the forced expiratory volume in 1 s (pre: 1.10 (0.08) L; post: 1.44 (0.25) L; $p < 0.05$), the Tiffeneau-index (pre: 60.48 (6.39) %; post: 68.19 (6.05) %; $p < 0.05$) and the diffusion capacity (pre: 60.3 (11.3) %; post: 78.1 (12.3) %; $p < 0.05$), in an elderly COVID-19 population (all patients > 65 years). The intervention group also scored higher post-intervention on these variables compared with the control group (15). Abodonya et al.'s non-RCT (17) also reported improvements in pulmonary function after only 2 weeks of inspiratory muscle training in an ICU COVID-19 population. The intervention group improved more over time than the control group (17). In Ahmed et al.'s pre-experimental study (18), 5 weeks of aerobic training in combination with breathing exercises seemed to be effective to improve dyspnoea experienced by COVID-19 patients (BORG score pre: 4.5 (0.2); post: 3.1 (0.1); $p < 0.001$) (18). Chintamani & Burungale (19) showed that a structured exercise programme can improve oxygen saturation (pre: 90 (5) %; post: 98 (2) %; $p < 0.05$), respiratory rate (pre: 45 (3); post: 20 (2); $p < 0.05$), dyspnoea (BORG score pre: 7 (3); post: 0 (1); $p < 0.001$) and heart rate (pre: 100 (5); post: 69 (5); $p < 0.05$) in ICU COVID-19 patients. The number of active coughs extractions (pre: 0 (1); post: 5 (2); $p < 0.001$) and the X-ray images from the lung also improved after 7 days (19). Tang et al.'s pre-experimental study (22) investigated the effect of a specific home exercise, namely Liuzijue, in discharged COVID-19 patients. After 4 weeks, the maxima inspiratory pressure (mean difference (MD): 13.46 (20.06) cmH₂O; $p < 0.001$) and peak inspiratory flow (MD: 0.74 (0.58) l/min; $p < 0.001$) increased, the movement of the diaphragm during deep breathing improved (MD: 0.57 (1.18) cm; $p = 0.009$) and dyspnoea decreased ($p = 0.022$) as well in these patients (22). The cohort study of Al Chikhanie et al. (24), determined the effect of pulmonary rehabilitation in general. The study showed that the forced expiratory volume in l/s (pre: 66.7 (16) %; post:

81.2 (14.2) %; $p < 0.05$), the forced vital capacity (pre: 59.1 (15.2) %; post: 72.9 (15.2) %; $p < 0.05$) and the maximal inspiratory pressure (pre: 42.7 (17.5) cmH₂O; post: 62.9 (13) cmH₂O; $p < 0.05$) and maximal expiratory pressure (pre: 68.2 (30.3) cmH₂O; post: 87.1 (30.3) cmH₂O; $p < 0.05$) improved significantly after pulmonary rehabilitation (24). Kofod et al.'s study (26) was the only one included in this review to examine the effect of CPAP in COVID-19 patients with respiratory failure. In the full cohort, both respiratory rate (pre: 28.6 (7.6); post: 26.9 (6.2); $p = 0.002$) and oxygen saturation (pre: 90.7 (3.5) %; post: 92.7 (3.2) %; $p < 0.001$) improved immediately after administering CPAP. Less oxygen supplementation was needed (pre: 27.4 (13.3) l/min; post: 23.3 (10.7) l/min; $p < 0.001$). The same conclusion could be drawn when the participants for whom CPAP failed were excluded from the study. The oxygenation index improved significantly over time ($p = 0.02$) in the CPAP success group, while it decreased significantly over time in the CPAP failure group ($p < 0.001$) (26). Finally, Verma et al.'s cohort study (29) proved that physical therapy improved heart rate (pre: 92.46 beats/min (14.93); post: 100.4 beats/min (13.25); $p < 0.001$) and that, after 2 weeks, less oxygen supplementation was needed (pre: 60.9 (25.39) l/min; post: 34.76 (24.98) l/min; $p < 0.001$).

Physical outcome measures. These were reported in 11 studies (15, 17, 18, 20–25, 27, 28), with, in total, 10 different parameters. Detailed results of all included physical outcome measures are shown in Table VII. Given the heterogeneity amongst the included outcome measures it was decided not to pool the results. However, all studies reported significant improvements in one or more physical outcome measures after the physical therapy intervention (see Table VII). A variety of interventions were used to improve the physical function of COVID-19 patients: (i) respiratory rehabilitation consisting of breathing and cough exercises, respiratory muscle training, stretching respiratory muscles, and prone lying; (ii) CPAP treatment; (iii) physical rehabilitation consisting of motor strengthening, mobilizations, bed mobility exercises; and (iv) aerobic training.

Liu et al.'s RCT (15) demonstrated that exercise endurance measured with the 6MWT improved (pre: 162.7 (72) m; post: 212.3 (82.5) m; $p < 0.05$) after 6 weeks of respiratory rehabilitation. The intervention group also scored higher post-intervention than the control group (I: 212.3 (82.5) m; C: 157.2 (71.7) m; $p < 0.05$). However, there was no improvement in functional independence (15). Abodonya et al. (17) reviewed the effect of 2 weeks of inspiratory muscle training on exercise capacity with a non-randomized controlled study design. There was a significant improvement after the intervention compared with the baseline assessment (6MWT pre: 332.6 (34.5) m; post:

376.5 (39.4) m; $p < 0.001$). The intervention group also improved more compared with the control group who received usual care (I: 376.5 (39.4) m; C: 334.8 (38.2)

m; $p = 0.028$) (17). Ahmed et al. (18) investigated the effect of aerobic training in combination with breathing exercises on exercise capacity in symptomatic

Table VII. Results per outcome: physical function

Study	Outcome	Study design	Results intervention group Pre-post value, mean (SD) <i>p</i> -value	Results control group (if applicable) Pre-post value, mean (SD) <i>p</i> -level	Between-group difference (if applicable) post values, mean (SD) <i>p</i> -value
Liu et al. 2020 (15)	Endurance 6MWT (m)	RCT	pre: 162.7 (72); post: 212.3 (82.5) $p < 0.05$; $t_0 < t_1$	pre: 155.7 (82.1); post: 157.2 (71.7) $p > 0.05$; $t_0 < t_1$	I: 212.3 (82.5); C: 157.2 (71.7) $p < 0.05$; I > C
Abodonya et al. 2021 (17)		Non-RCT	pre: 332.6 (34.5); post: 376.5 (39.4) $p < 0.001$; $t_0 < t_1$	pre: 329.7 (37.8); post: 334.8 (38.2) $p = 0.624$	I: 376.5 (39.4); C: 334.8 (38.2) $p = 0.028$; I > C
Ahmed et al. 2021 (18)		Pre-experimental	pre: 560.3 (11.3); post: 635.3 (11.6) $p < 0.001$; $t_0 < t_1$	NA	Subgroup analysis +VENT 602.9 (46) -VENT 667.8 (35.3) $p = 0.008$; +VENT < -VENT
Tang et al. 2021 (22)		Pre-experimental	MD: 17.22 (43.78) $p = 0.02$; $t_0 < t_1$	NA	NA
Zampogna et al. 2021 (23)		Pre-experimental	pre: 229 (102.5); post: 327.9 (97.8) $p < 0.01$; $t_0 < t_1$	NA	NA
Al Chikhanie et al. 2021 (24)		Cohort	pre: 138.7 (144.4); post: 343.4 (139.6) $p < 0.05$; $t_0 < t_1$	NA	NA
Hermann et al. 2020 (25)		Cohort	pre: 230.9 (153.6); post: 360.9 (134.6) $p < 0.05$; $t_0 < t_1$	NA	Subgroup analysis +VENT 386.7 (135.7) -VENT 341.6 (134.7) $p = 0.391$; +VENT > -VENT
Spielmanns et al. 2021 (27)		Cohort	pre: 176 (141); post: 357 (132) $p < 0.0001$; $t_0 < t_1$	NA	NA
Liu et al. 2020 (15)		Functional independence FIM	RCT	pre: 109.2 (13); post: 109.4 (11.1) $p > 0.05$; $t_0 < t_1$	pre: 109.3 (10.7); post: 108.9 (10.1) $p > 0.05$; $t_0 > t_1$
Sinha et al. 2020 (21)	Pre-experimental		pre: 72.4 (21.7); post: 91.2 (25.2) $p < 0.05$; $t_0 < t_1$	NA	NA
Spielmanns et al. 2021 (27)	Barthel Index	Cohort	pre: 100 (15.1); post: 111 (15) $p < 0.0001$; $t_0 < t_1$	NA	NA
Piquet et al. 2021 (20)		Pre-experimental	pre: 77.3 (26.7); post: 88.8 (24.5) $p < 0.01$; $t_0 < t_1$	NA	NA
Zampogna et al. 2021 (23)		Pre-experimental	pre: 55 (30-90)*; post: 95 (65-100)* $p < 0.001$; $t_0 < t_1$	NA	NA
Udina et al. 2021 (28)		Cohort	Full cohort MD: 18.5 (12.9) $p < 0.5$; $t_0 < t_1$ +ICU MD: 18.2 (124) $p < 0.05$; $t_0 < t_1$ -ICU MD: 18.8 (14.01) $p < 0.05$; $t_0 < t_1$	NA	NA
Zampogna et al. 2021 (23)		Pre-experimental	pre: 3.2 (3.7); post: 6.9 (3.8) $p < 0.01$; $t_0 < t_1$	NA	NA
Udina et al. 2021 (28)		Cohort	Full cohort SPPBt: MD: 3.7 (2.1) $p < 0.05$; $t_0 < t_1$ SPPBb: MD: 0.8 (1.1) $p < 0.05$; $t_0 < t_1$ SPPBg: MD: 0.3 (0.19) $p < 0.05$; $t_0 < t_1$ SPPBcs: MD: -14.1 (16.9) $p < 0.05$; $t_0 > t_1$	NA	Subgroup analysis SPPBt +ICU: MD: 4.4 (2.1) -ICU: MD: 2.5 (1.7) $p = 0.009$; +ICU > -ICU SPPBg: +ICU: MD: 0.4 (0.2) -ICU: MD: 0.2 (0.1) $p = 0.006$; +ICU > -ICU

Table VII. Cont.

Study	Outcome	Study design	Results intervention group Pre-post value, mean (SD) <i>p</i> -value	Results control group (if applicable) Pre-post value, mean (SD) <i>p</i> -level	Between-group difference (if applicable) post values, mean (SD) <i>p</i> -value
			+ICU SPPBt: MD: 4.4 (2.1) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 SPPBb: MD: 1.1 (1.2) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 SPPBg: MD: 0.4 (0.2) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 SPPBcs: MD: -15.3 (16.9) <i>p</i> < 0.05; <i>t</i> 0 > <i>t</i> 1 -ICU SPPBt: MD: 2.5 (1.7) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 SPPBb: MD: 0.2 (0.1) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 SPPBg: MD: 0.2 (0.1) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 SPPBcs: MD: -12.2 (17.6) <i>p</i> < 0.05; <i>t</i> 0 > <i>t</i> 1		
Udina et al. 2021 (28)	FAC	Cohort	Full cohort MD: 14 (42.4)* <i>p</i> < 0.05 ; <i>t</i> 0 < <i>t</i> 1	NA	NA
			+ICU MD: 7 (35)* <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 -ICU MD: 7 (53.8)* <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1		
Piquet et al. 2021 (20)	Muscle strength Sit to stand (Hz)	Pre-experimental	pre: 0.27 (0.16); post: 0.37 (0.16) <i>p</i> < 0.001; <i>t</i> 0 < <i>t</i> 1	NA	NA
Piquet et al. 2021 (20)	Grip strength (kg)	Pre-experimental	pre: 18.1 (9.25); post: 20.9 (8.9) <i>p</i> < 0.001; <i>t</i> 0 < <i>t</i> 1	NA	Subgroup analysis +ICU MD: 3.3 (3.1) -ICU MD: 0.99 (3.7) <i>p</i> = 0.049; +ICU > -ICU NA
Al Chikhanie et al. 2021 (24)		Cohort	pre: 18.1 (8); post: 23.5 (8.5) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1	NA	NA
Al Chikhanie et al. 2021 (24)	Quadriceps muscle strength (kg)	Cohort	pre: 14.2 (10.6); post 25.2 (11.7) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1	NA	NA
Sinha et al. 2020 (21)	Balance Tinetti	Pre-experimental	pre: 11.9 (3.6); post: 21.9 (5.5) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1	NA	NA
Al Chikhanie et al. 2021 (24)		Cohort	pre: 25 (3); post: 27.5 (1) <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1	NA	NA
Udina et al. 2021 (28)	Single-leg stance	Cohort	Full cohort MD: 10 (30.3)* <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 +ICU MD: 9 (45)* <i>p</i> < 0.05; <i>t</i> 0 < <i>t</i> 1 -ICU MD: 1 (7.7)* <i>p</i> > 0.05; <i>t</i> 0	NA	NA

Continuous values are reported as mean (SD) or N (%)*. FAC: functional ambulation category; +ICU: patients who stayed at the intensive care unit; -ICU: patients who did not stay at the intensive care unit; MD: mean difference; NA: not applicable; SPPBb: Short Physical Performance Battery balance score; SPPBcs: Short Physical Performance Battery chair stand time; SPPBg: Short Physical Performance Battery gait speed; SPPBt: Short Physical Performance Battery total score.

COVID-19 patients. The distance walked in 6 min also improved significantly in this study (pre: 560.3 (11.3) m; post: 635.3 (11.6) m; *p* < 0.001). Patients who had received mechanical ventilation improved less than patients who did not receive mechanical ventilation (+VENT: 602.9 (46) m; -VENT: 667.8 (35.3) m; *p* = 0.008) (18). Piquet et al.'s pre-experimental study

(20) showed that activities of daily living (ADL) (BI pre: 77.3 (26.7); post: 88.8 (24.5); *p* < 0.01), handgrip strength (pre: 18.1 (9.25) kg; post: 20.9 (8.9) kg; *p* < 0.001) and lower extremity strength (sit-to-stand frequency pre: 0.27 (0.16) Hz; post: 0.37 (0.16) Hz; *p* < 0.001) increased significantly after physical therapy in COVID-19 patients. Patients who were admitted to

the ICU showed greater improvement in grip strength compared with patients who were not admitted to the ICU (+ICU: MD 3.3 (3.1) kg; -ICU: MD 0.99 (3.7) kg; $p=0.049$) (20). The long-term effect of structured exercise was investigated in Sinha et al.'s pre-experimental study (21). Both independence (Functional Independence Measure (FIM) score pre: 72.4 (21.7); post: 91.2 (25.2); $p < 0.05$) and mobility (Tinetti score pre: 11.9 (3.6); post: 21.9 (5.5); $p < 0.05$) improved significantly after the intervention (21). Tang et al.'s study (22) investigated the effect of 4 weeks of Liuzijue

on exercise capacity and also reported improvements in the distance walked in 6 min (MD: 17.22 (43.78) m; $p=0.02$) (22). Zampogna et al. (23) showed that patient-tailored pulmonary rehabilitation, based on age, clinical severity, length of immobilization and comorbidities, has a positive effect on lower extremity function (Short Physical Performance Battery (SPPB) score pre: 3.2 (3.7); post: 6.9 (3.8); $p < 0.01$), exercise tolerance (6MWT pre: 229 (102.5) m; post: 327.9 (97.8) m; $p < 0.01$) and disability in COVID-19 patients who did not have any functional limitations

Table VIII. Results per outcome: psychosocial function

Study	Outcome	Study design	Results intervention group Pre – post value, mean (SD) p -value	Results control group (if applicable) Pre – post value, mean (SD) p -value	Between-group difference (if applicable) Post values, mean (SD) p -value
Liu et al. 2020 (15)	Quality of life SF36	RCT	$p < 0.05$; $t_0 < t_1$	$p > 0.05$	$p < 0.05$; I > C
Ahmed et al. 2021 (18)		Pre-experimental	$p < 0.005$; $t_0 < t_1$	NA	Subgroup analysis BP +VENT 65.5 (4.6) -VENT 68.8 (15.1) $p = 0.019$; +VENT < -VENT
Tang et al. 2021 (22)		Pre-experimental	PF: $p = 0.014$; $t_0 < t_1$ RP: $p = 0.009$; $t_0 < t_1$	NA	NA
Abodonya et al. 2021 (17)	EQ-5D-3L	Non-RCT	Pre: 38.6 (5.8); post: 59.4 (8.3) $p < 0.001$; $t_0 > t_1$	pre: 40.7 (6.2); post: 43.3 (6.5) $p = 0.173$	I: 59.4 (8.3); C: 43.3 (6.5) $p = 0.021$; I > C
Al Chikhani et al. 2021 (24)	Saint George respiratory questionnaire	Cohort	Pre: 37.2 (22.8); post: 22.3 (15.9) $p > 0.05$; $t_0 > t_1$	NA	NA
Liu et al. 2020 (15)	Anxiety Self-rating anxiety scale	RCT	Pre: 56.3 (8.1); post: 47.4 (6.3) $p < 0.05$; $t_0 > t_1$	pre: 55.8 (7.4); post: 54.9 (7.3) $p > 0.05$; $t_0 > t_1$	I: 47.4 (6.3); C: 54.9 (7.3) $p < 0.05$; I < C
Özlü et al. 2021 (16)	State-Trait anxiety scale	RCT	Pre: 62.33 (8.33); post: 44.67 (5.41) $p < 0.001$; $t_0 > t_1$	pre: 60.68 (9.17); post: 61.29 (7.95) $p = 0.652$	I: 44.67 (5.41); C: 61.29 (7.95) $p < 0.001$; I < C
Tang et al. 2021 (22)	Hamilton anxiety rating scale	Pre-experimental	NI $p < 0.001$; $t_0 > t_1$	NA	NA
Al Chikhani et al. 2021 (24)	Hospital anxiety and depression questionnaire	Cohort	Pre: 6.9 (4.6); post: 2.2 (3.2) $p < 0.05$; $t_0 > t_1$	NA	NA
Liu et al. 2020 (15)	Depression Self-rating depression scale	RCT	Pre: 56.4 (7.9); post: 54.5 (5.9) $p > 0.05$; $t_0 > t_1$	pre: 55.9 (7.3); post: 55.8 (7.1) $p > 0.05$; $t_0 > t_1$	I: 54.5 (5.9); C: 55.8 (7.1) $p > 0.05$; I < C
Tang et al. 2021 (22)	Hamilton depression rating scale	Pre-experimental	NI $p = 0.0032$; $t_0 > t_1$	NA	NA
Al Chikhani et al. 2021 (24)	Hospital anxiety and depression questionnaire	Cohort	Pre: 6.5 (4.8); post: 1.4 (2.4) $p < 0.05$; $t_0 > t_1$	NA	NA
Özlü et al. 2021 (16)	Sleep Richard-Campbell sleep questionnaire	RCT	NA	NA	I: 68.33 (14.53); C: 46.71 (19.71) $p < 0.001$; I > C
Al Chikhani et al. 2021 (24)	Fatigue Pichot questionnaire	Cohort	Pre: 12.1 (8.4); post: 4.3 (6.5) $p < 0.05$; $t_0 > t_1$	NA	NA
Al Chikhani et al. 2021 (24)	Post-traumatic stress Post-traumatic stress disorder checklist	Cohort	Pre: 29.7 (14.1); post: 22.7 (12.1) $p > 0.05$; $t_0 > t_1$	NA	NA
Hermann et al. 2020 (25)	Wellbeing feeling thermometer	Cohort	Pre: 40 (40-55)*; post: 80 (67.5-84)* $p < 0.05$; $t_0 < t_1$	NA	Subgroup analysis +VENT 80 (75-90)* -VENT 70 (60-80)* $p = 0.066$; +VENT > -VENT
Spielmanns et al. 2021 (27)		Cohort	Pre: 52.6 (15.5); post: 73.8 (14.5) $p < 0.0001$; $t_0 < t_1$	NA	NA

Continuous values are reported as mean (SD) or mean (CI)*. BP: bodily pain; C: control; EQ-5D-3L: EuroQuality-5Dimensions-3Levels; I: intervention; NA: not applicable; NI: no information; PF: physical functioning; RCT: randomized controlled trial; RP: role-physical; SF36: 36-Item Short Form Health Survey; +VENT: patients who endured mechanical ventilation; -VENT: patients who did not endure mechanical ventilation.

prior to the COVID infection (23). Al Chikhanie et al.'s cohort study (24) found that both walking performance (6MWT pre: 138.7 (144.4) m; post: 343.4 (139.6) m; $p < 0.05$) and muscle strength improved after pulmonary rehabilitation. Hermann et al.'s cohort study (25) showed that exercise capacity improved (6MWT pre: 230.9 (153.6) m; post: 360.9 (134.6) m; $p < 0.05$) after 20 days of cardiopulmonary rehabilitation and that there was no significant difference between patients who received mechanical ventilation and those who did not. Spielmanns et al. (27) concluded that, after 2 weeks of pulmonary rehabilitation, both exercise capacity (6MWT pre: 176 (141) m; post: 357 (132) m; $p < 0.0001$) and disability (FIM score pre: 100 (15.1); post: 111 (15); $p < 0.0001$) improved in COVID-19 patients. Once again, patients improved their distance walked in the 6MWT (27). Lastly, Udina et al. (28) investigated the effect of multicomponent therapeutic exercises in COVID-19 patients. The study assessed the total cohort, as well as patients who received ICU care and those who did not. After the intervention, both ADL activities and physical performance improved significantly in all groups. Only the balance item in the SPPB did not differ significantly from baseline in patients who received ICU care. Significantly more participants were able to walk unassisted and were able to perform the single-leg stance test. However, there was no significant difference in the number of patients who were able to perform the single-leg stance test among participants who did not receive ICU care (28).

Psychosocial function. Psychosocial function was reported in 8 studies (15–18, 22, 24, 25, 27), with a total of 14 different parameters. Detailed results of the psychosocial outcome measures are shown in Table VIII. Given the heterogeneity amongst the included outcome measures it was decided not to pool the results. All studies reported significant improvements in at least one or more psychosocial outcome measures after the physical therapy intervention (see Table VIII). A variety of interventions were used to improve the physical function of COVID-19 patients: (i) respiratory rehabilitation, consisting of breathing and cough exercises, respiratory muscle training, stretching respiratory muscles, and muscle relaxation exercises; (ii) physical rehabilitation, consisting of motor strengthening, mobilizations, bed mobility exercises; and (iii) aerobic training.

According to Liu et al.'s RCT (15), QoL and anxiety, but not depression, improved after 6 weeks of pulmonary rehabilitation in COVID-19 patients. The intervention group scored better post-intervention compared with the control group (15). Similar results for anxiety were found in Özlü et al.'s RCT (16). They concluded that, after 5 days of progressive muscle relaxation, the anxiety scores of COVID-19 patients improved in the interven-

tion group (State–Trait Anxiety Inventory (STAI) score pre: 62.33 (8.33); post: 44.67 (5.41); $p < 0.001$). No information regarding the pre-post difference in sleep quality was provided. Nevertheless, the intervention group scored higher post-intervention than the control group for both anxiety (STAI score I: 44.67 (5.41); C: 61.29 (7.95); $p < 0.001$) and sleep quality (RCSQ score I: 68.33 (14.53); C: 46.71 (19.71); $p < 0.001$) (16). Abodonya et al. (17) also investigated the effect of 2 weeks of inspiratory muscle training on QoL in a non-RCT. The intervention group had a better QoL post-intervention (EQ-5D-3L score pre: 38.5 (5.8); post: 59.4 (8.3); $p < 0.001$) and improvements were significantly higher compared with the control group (EQ-5D-3L score I: 59.4 (8.3); C: 43.3 (6.5); $p = 0.021$) (17). The pre-experimental study of Ahmed et al. (18) investigated the effect of aerobic training in combination with breathing exercises on QoL in symptomatic COVID-19 patients. Patients had a better QoL after 5 weeks of training (18). Tang et al.'s pre-experimental study of (22) showed that, after 4 weeks of Liuzijue training, QoL improved in discharged COVID-19 patients, but only in the physical functioning ($p = 0.014$) and in the role-physical aspect ($p = 0.009$) of the 36-Item Short Form Health Survey (SF-36) questionnaire. Patients also experienced less anxiety ($p < 0.001$) and depression ($p = 0.0032$) after the intervention (22). According to Al Chikhanie et al.'s cohort study (24) QoL and post-traumatic stress did not improve in COVID-19 patients after pulmonary rehabilitation. However, participants experienced less anxiety (HADS score pre: 6.9 (4.6); post: 2.2 (3.2); $p < 0.05$) and had fewer depressive feelings (HADS score pre: 6.5 (4.8); post: 1.4 (2.4); $p < 0.05$) after the intervention (24). In Hermann et al.'s cohort study (25), the effect of cardiopulmonary rehabilitation on the well-being of COVID-19 patients was investigated. Patients felt significantly better after the intervention. However, there was no significant difference between patients who received mechanical ventilation and those who did not (25). Lastly, Spielmanns et al.'s cohort study of (27) concluded that 2 weeks of pulmonary rehabilitation can improve well-being in COVID-19 patients (feeling thermometer pre: 52.6 (15.5); post: 73.8 (14.5); $p < 0.0001$).

DISCUSSION

This rapid review aimed to provide an overview of the effect physical therapy can have on impairments in COVID-19 patients. A variety of physical therapy interventions were provided to COVID-19 patients in different settings. Several interventions could be distinguished. While some interventions focused primarily on pulmonary rehabilitation, consisting of breathing and cough exercises, CPAP treatment,

respiratory muscle training and stretching, other interventions combined pulmonary rehabilitation with physical rehabilitation and/or aerobic training. Pulmonary rehabilitation, both with and without a physical/aerobic component, was found to positively affect the pulmonary, physical, and psychosocial functions of COVID-19 patients.

As the COVID-19 pandemic has evolved, long-term symptoms and functional problems related to the SARS-CoV-2 infection have become apparent. Approximately 5–10% of infected people experience prolonged symptoms, with the predominant symptoms being overall reduced physical capacity, fatigue and muscle weakness (30, 31). Since the start of the pandemic, the need for rehabilitation has been highlighted, and that patients with long-COVID (those who continue to experience COVID-19 symptoms for longer than usual after initially contracting the SARS-CoV-2 virus) may benefit from physical therapy interventions because of the severe impact on ADL, participation and QoL. However, the majority of the included studies focused on hospitalized COVID-19 patients, either in ICU or other inpatient units. Only 3 studies assessed the effect of physical therapy on discharged COVID-19 patients, which highlights the need for high-quality studies on rehabilitation interventions in this specific population. Currently, recommendations for the interventions are based on research performed in patients presenting similar difficulties, but caused by other diseases (chronic obstructive pulmonary disease (COPD), cancer rehabilitation, etc.). According to these recommendations, patients are advised to perform light aerobic and breathing exercises daily. However, such a generic “one-size-fits-all” physical therapy programme may not be suitable for every patient. In addition, due to long-COVID, patients’ feelings of fatigue, appropriate personalized and behavioural approaches are key to achieving optimal rehabilitation outcomes when implementing a physical training programme.

Besides the pulmonary and physical problems, most COVID-19 patients show some degree of dysphagia and malnutrition (32, 33). In addition, 37% (range 29–52%) of hospitalized COVID-19 patients have a weight loss of $\geq 5\%$, which defines cachexia. This COVID-19-induced cachexia is accompanied by muscle mass loss and relatively high percentage of fat tissue, which is also seen in other chronic illness-associated forms of cachexia. Moreover, the characteristics of COVID-19-related loss of taste and appetite, fever, inflammation, catabolic-anabolic imbalance and endocrine dysfunction further increase the risk of developing cachexia (33). A patient-tailored rehabilitation programme, combined with nutritional optimization and counselling, may therefore lead to a more rapid improvement in functional performance compared

with a standard physiotherapy programme in patients with long-term effects of COVID-19, and is worth implementing in future research.

Strengths and limitations

A strength of this rapid review is the broad scope of assessed outcome variables, providing readers a holistic view on the possible benefits of physical therapy in COVID-19 patients. Furthermore, the interventions administered to the patients were often described in detail, which makes replication and implementation easier. Lastly, relatively large sample sizes were used in the included studies, which gives these studies statistical power.

However, when interpreting the results, the moderate-to-poor methodological quality of the included studies must be taken into account. Another important key issue was the absence of a control group in most of the included studies. Hence, no causal relationship between an improvement in an outcome measure and the intervention can be determined. However, as stated in some studies, it is highly unethical to deny patients therapy when it is clearly recommended by experts in the field.

This rapid review is the first to discuss physical therapy in its entirety and the effect it has on COVID-19 patients. The new information provided by this review supplements previous reviews and guidelines, which are often based on expert opinion. However, many studies have already been conducted, and many more are still ongoing (124 studies are registered in clinicaltrials.gov; =covid+rehabilitation). Therefore, it is of great importance that the guidelines are reviewed regularly and, if necessary, updated to provide patients with the best possible care.

In conclusion, physical therapy is an important and necessary intervention at all stages of COVID-19 recovery. Pulmonary rehabilitation, both with and without a physical/aerobic component, can improve pulmonary, physical, and psychosocial functions in COVID-19 patients. However, this review shows that more high-quality research, focusing on all stages of COVID-19 recovery, is necessary to provide clinicians with clear evidence-based guidelines. Investigating more personalized and behavioural approaches, as well as the incorporation of other interventions, such as nutritional optimization and counselling, is highly recommended.

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Supplementary material to article by R. Debeuf et al. "Effect of physical therapy on impairments in COVID-19 patients from intensive care to home rehabilitation: A rapid review"

Appendix S1. Complete search strategy in the electronic database PubMed structured according to the Population Intervention Comparison Outcome (PICO) method

Search	PICO	Query
1	P	Coronavirus
2	P	SARS-CoV-2
3	P	COVID
4	P	COVID-19
5	P	Coronavirus patient*
6	P	SARS-CoV-2 patient*
7	P	COVID patient*
8	P	COVID-19 patient*
9	P	COVID-19 elderly patient*
10	P	"SARS-CoV-2"[MeSH]
11	P	1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7 OR 8 OR 9 OR 10
12	I	Physical therapy
13	I	Physiotherapy
14	I	Exercise therapy
15	I	Exercise
16	I	Endurance training
17	I	Chest physiotherapy
18	I	Respiratory physiotherapy
19	I	Respiratory physical therapy
20	I	Breathing exercises
21	I	Strength training
22	I	Strength exercise*
23	I	Rehabilitation
24	I	Pulmonary rehabilitation
25	I	Early rehabilitation
26	I	Early mobilisation*
27	I	Cardiopulmonary rehabilitation
28	I	Tele-rehabilitation
29	I	Exercise program
30	I	Training program
31	I	Geriatric rehabilitation
32	I	"Physical Therapy Modalities"[MeSH]
33	I	Aerobic exercise
34	I	12 OR 13 OR 14 OR 15 OR 16 OR 17 OR 18 OR 19 OR 20 OR 21 OR 22 OR 23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 30 OR 31 OR 32 OR 33
35	PI	11 AND 34

Search 35 was used to find eligible records. The same search strategy was used and adapted for the Web of Science and Scopus databases.