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Effects of respiratory muscular training in post-covid-19 patients: a systematic review and meta-analysis of randomized controlled trials

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Abstract

Background Post-Covid-19 syndrome is defined as non-self-sustaining signs and/or symptoms lasting more than 12 weeks, occurring during or after a Covid-19 infection. The primary outcome was the analysis of the respiratory muscle training (RMT) result in respiratory muscle strength, (maximum inspiratory pressure (MIP) e maximum expiratory pressure (MEP)); and the secondary results were the analysis of lung function, dyspnea, quality of life (QoL), fatigue and functional performance. Methods: The PICO description for this research was: P: patients diagnosed with post-Covid-19; I: RMT; C: Sham or simulated inspiratory or expiratory muscle training and usual care; O: MIP, MEP, Lung Function, level of dyspnea, QoL and functional performance. On January 15, 2024, the following databases were consulted: PubMed, Lilacs, Cochrane Library, PEDro and EMBASE. Randomized clinical trials were included without restrictions on year of publication or language. The data selection and extraction steps were carried out by two independent reviewers. Results: The search in the databases resulted in a total of 14,216 studies, and after the eligibility process, 7 studies were included with a sample of 527 patients. The MIP results suffered a statistically significant increase, that is, the RMT was favorable to improve the MIP (MD = 29.55cmH_2O IC 95%: 7.56cmH_2O to 51.54cmH_2O, $p = 0{,}00001$). For the MEP outcome, the results were statistically significant in favor of RMT (MD = 10.93cmH2O CI 95%: 3.65cmH_2O to 18.21cmH_2O, $p = 0.00001$). We also noticed a significant improvement for the group that received the RMT in the distance covered in the 6-Minute Walk Test (6MWT) MD = 40.70 m CI 95%: 18.23 m to 65.17 m%, $p = 0.01$). Conclusion: We noticed that RMT is being used in patients with respiratory diseases, including post-Covid-19. Our systematic review observed that this training provides an increase in inspiratory and expiratory muscle strength, a reduction in dyspnea levels, and an increase in the distance covered in the 6MWT and improved QoL in post-covid patients after intervention.

Keywords Long COVID, Covid-19, Respiratory muscle training, Randomized controlled trial, Post-COVID-19 syndrome

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Introduction

In the month of April 2021, more than 127 million cases of coronavirus infection (COVID-19) were reported worldwide [1]. The pandemic was caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), responsible for a new type of acute respiratory infection and atypical pneumonia with the potential to evolve into a severe acute respiratory syndrome (SARS), described for the first time in Wuhan Province, China [2].

The National Health Service (NHS - London) defines post-Covid-19 syndrome as non-self-sustaining signs and/or symptoms lasting longer than 12 weeks, occurring during or following a COVID-19 infection [3]. Additionally, the term COVID-19 has long been frequently used to describe signs and symptoms that continue or develop after acute Covid-19 [4–6].

For post-Covid hospitalized patients, there is an urgent need to develop new education and training programs focusing on interdisciplinary rehabilitation [7]. Previous studies confirm that physiotherapeutic interventions are especially relevant to combat respiratory and neuromuscular dysfunctions in these patients [7, 8].

The popularity of physical training in post-Covid-19 patients has increased significantly [9]. As the number of people recovering from the infection grows, physical rehabilitation has proven essential for restoring quality of life (QoL) and promoting overall health. Physical training is recognized for helping to improve cardiorespiratory capacity, muscle strength, and endurance, factors often compromised after coronavirus infection. This increase in popularity is due to the need to mitigate the residual effects of the disease, such as chronic fatigue, shortness of breath, and muscle weakness, which are common in many COVID-19 survivors [7–9].

The physiological adaptations to physical training in post-Covid-19 patients include a series of significant improvements in the cardiovascular, respiratory, and muscular systems [9]. Regular physical exercise can increase the efficiency of the heart and lungs, improving oxygenation and blood circulation [8, 9]. Additionally, resistance and strength training can contribute to the recovery of lost muscle mass and the improvement of muscle function, essential for performing daily activities [8, 9]. These adaptations are crucial to help patients resume their normal routines and reduce the incidence of long-term complications associated with Covid-19 [9].

Among the practices addressed in the rehabilitation of these patients is respiratory muscle training (RMT). Existing evidence supports the use of this practice within pulmonary rehabilitation programs, as this therapy has been shown to improve functional capacity, lung function and respiratory muscle strength in post-Covid-19 patients, hopefully to improve their QoL [10, 11]. However, it is still necessary to systematize the results of this treatment modality to guarantee and support its use.

Therefore, the aim of this study was to elucidate the effectiveness of controlled muscle training in post-Covid-19 patients. The primary outcome was the analysis of the RMT result in respiratory muscle strength (maximum inspiratory pressure (MIP) e maximum expiratory pressure (MEP)); and the secondary objectives were intervention responses on lung function, dyspnea, QoL, fatigue and functional performance.

Methods

Study registration

This systematic review of randomized controlled trials (RCT) is reported in line with the preferred reporting items for systematic review/meta-analysis (PRISMA) check list [12] and according to the Cochrane Handbook for Systematic Reviews methodology [13]. The protocol of this review is registered in the Open Science Framework (https://osf.io/h8gjm/and/or DOI https://doi.org/10.17605/OSF.IO/H8GJM) (Appendix I).

Eligibility criteria

PICOS for this study was defined as: P: Studies with patients who did or did not present symptoms after a previous infection with Covid-19, and currently classified with a diagnosis of post-Covid-19, Long Covid or Post-Covid Syndrome, of both sexes, regardless of age; and who did not have post-covid stroke, renal failure and/or myocardial infarction were included; I: RMT was considered any type of exercise to gain and/or maximize resistance and/or strength of the respiratory muscles. Equipment with progressive linear loads was considered, such as Threshold®, POWERbreathe® or any other equipment developed to make this training modality viable, regardless of being used in conjunction with other therapies; C: Sham or simulated inspiratory muscle training (IMT), expiratory muscle training (EMT), usual care (medication and/or education) were all used as comparators; S: RCT.

Search strategy and selection of articles

Searches were performed from baseline to January 15, 2024 (Appendix II), without date limits or language restrictions, in the following databases: Medline via PubMed (www.pubmed.gov), Lilacs via Virtual Health Library (www.bvsalud.org), CENTRAL through the Cochrane Library (www.cochranelibrary.com), Physiotherapy Evidence Database (PEDro) (https://www.pedro.org.au/) and EMBASE (https://www.embase.com/). ClinicalTrials.gov was evaluated to identify potential ongoing studies. In addition, the initial search was complemented by a manual search of the reference lists of retrieved articles. The terms used were related to "respiratory muscle

training", "Pos - covid" and "randomized controlled trials". To avoid publication bias, gray literature (Google Scholar) was also consulted.

Electronic searches were performed by two independent authors (DMX and RALA). The articles found in the databases were exported to Rayyan (http://rayyan.qcri.org) [14]. After, duplicates were removed. First, manuscripts were selected by titles and abstracts based on eligibility criteria. Then, the selected studies were read in full to confirm their eligibility. Disagreements about the inclusion process were resolved by a third reviewer (MGNJ).

Data extraction

Data were extracted by two independent reviewers (DMX and RALA). The authors of the articles were contacted to request missing or additional data when necessary.

The following information was extracted: author, year and country of studies, time of intervention, inclusion and exclusion criteria; characteristics of the population (age, gender and sports practice); intervention used (equipment used and characteristics of the intervention and comparator groups); lung function: respiratory muscle strength (MIP) e (MEP), Forced Expiratory Volume in 1 s (FEV_1), Forced Vital Capacity (FVC), Tiffenau Index (FEV_1/FVC); results of indexes evaluating the level of dyspnea, QoL and fatigue; and performance/physical test results.

We extracted post-intervention means, standard deviations (SD) and sample sizes for each of our interest groups. In the study, short-term effects were considered as follow-up up to three months after the beginning of the study; medium-term effects were considered follow-up after three months but less than twelve months, and long-term effects were considered follow-up of at least twelve months after baseline.

In cases where there was more than one follow-up point available in the same period, the point closest to the end of the intervention was chosen. The study was excluded from the quantitative analysis when the authors did not respond [12, 15].

Risk of bias in individual studies

Two independent reviewers (DMX and RALA) assessed the risk of bias of the included studies using the PEDro scale from 0 to 10. The third reviewer was asked to resolve existing discrepancies (MGDJ). Where available, we use existing scores from the PEDro database (https://pedro.org.au/).

Summary measures and summary of results

When possible, a meta-analysis was performed using Review Manager software version 5.4. Meta-analysis was produced when at least two studies reported sufficient data for the same outcome in the RMT and GC groups. Data regarding the mean difference and SD from baseline to post-intervention follow-up were collected. Effect sizes were expressed as final (or standardized) weighted mean differences post-intervention (for continuous data) and their 95% confidence intervals. Heterogeneity was assessed in a statistically randomized fashion using I^2 test, considering random-effects model if $I^2 \geq 30\%$ and fixed effects models if $I^2 < 30\%$. Subgroup analyzes were performed when sufficient data were available to investigate the impact between the types of programs used [16, 17].

Reliability of cumulative evidence

Two independent reviewers assessed the quality of the current evidence using the Grading of Recommendations Assessment (GRADE) approach [18, 19].

A Summary of Results (SoF) was created using GRADEPro GDT (McMaster University, ON, Canada) for each outcome that allowed meta-analyses. SoF tables were generated at the end of the analysis according to the certainty of evidence across studies and classified as high, moderate, low or very low certainty of evidence. When no reason was found to downgrade the evidence, it was classified as "no limitation". When any reason was found to downgrade the evidence, it was classified as "serious".

Results

In total, 14,216 potentially relevant articles were found in electronic databases, manual searches and gray literature. Duplicates were then removed and two reviewers carried out the eligibility assessment according to titles and abstracts, leaving a total of 126 articles. Afterwards, these 126 articles were read in full; A total of 119 manuscripts were excluded for different reasons (not RCT: ($n=24$), not population of interest: ($n=35$), not intervention of interest: ($n=29$), not comparison of interest: ($n=18$) and not results of interest: (n: 13). This left a total of 7 studies [11, 20–25] were included in the qualitative study in which 527 post-Covid 19 patients participated. Only two studies [10, 22] were excluded from the quantitative analysis because they presented their data differently from the others. Figure 1 shows the flowchart of the study selection process.

Description of studies and assessment of risk of bias

The studies included in this review were published between 2021 and 2023. The duration of the RMT programs ranged from six weeks to a maximum of 12 weeks. The sample size of the included studies ranged from 26 to 160 participants and the mean age ranged from 44 (11.28) to 50.40 (12.12). Data on the gender of participating athletes were reported in 6 studies, involving a total of 156 men and 223 women [20–25].

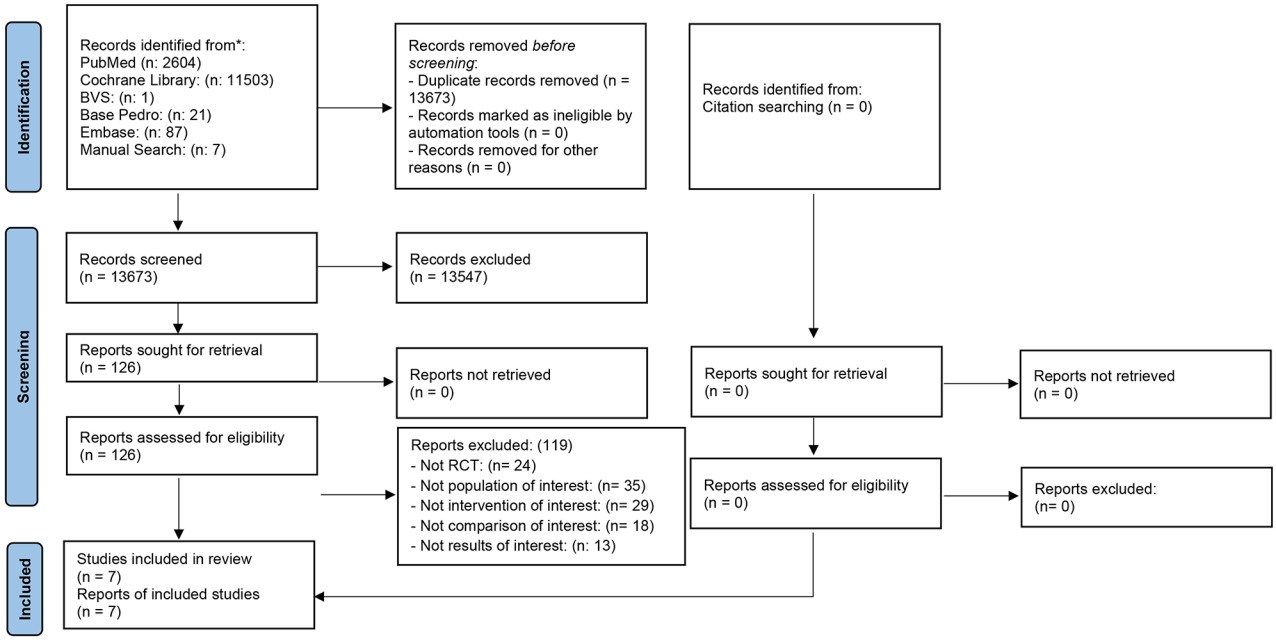

Fig. 1 Flow of studies through the review. RCT: randomized controlled trial; BVS: biblioteca virtual de saúde

The POWERbreathe® device was the most used among the studies. The load used to perform the RMT was most commonly performed between 25 and 80% of the MIP and/or MEP. Participants in the comparison group used sham RMT, usual care. Tables 1 and 2 show the main characteristics of the included studies, participants, interventions and clinical characteristics.

Five included studies were at low risk of bias; their PEDro scores were greater than 6. The main reasons for the reduction in risk of bias scores were: not blinding allocation (not blinding therapists and subjects (4 trials [100%])). Detailed characteristics of the risk of bias of included studies are presented in Appendix III.

Data extraction and meta-analysis

MIP

In a meta-analysis involving 4 studies [11, 21, 24, 25] the MIP results suffered a statistically significant increase in the medium term, that is, the RMT was favorable to improve the MIP (MD=29.55cmH_2O IC 95%: 7.56cmH_2O to 51.54cmH_2O, p=0,00001). Data present in Fig. 2.

MEP

The produced meta-analysis showed statistically significant results in the medium term in favor of the RMT (MD=10.93cmH_2O IC 95%: 3.65cmH_2O to 18.21cmH_2O, p=0,00001). Figure 3.

FEV_1

The meta-analysis produced included a total of three articles [21, 23, 25] and indicated that there was no statistically significant difference, in the medium term, between the intervention and GC groups after the RMT intervention in FEV_1 values (MD=0.30 95% CI: -0.07 to 0.67%, p=0.01). Figure 4.

FEV_1/FVC

The meta-analysis produced included a total of two articles [21, 25] indicated that there was no statistically significant difference, in the medium term, between the intervention and GC groups after the RMT intervention in FEV_1/FVC values (MD = -1.66 95% CI: -4.04 to 0.72%, p=0.01). Appendix IV.

FVC

The meta-analysis involving 3 studies [21, 23, 25] showed that there was no statistically significant difference, in the short term and medium term, after the RMT when comparing the intervention and control groups (MD=0.35 95% CI: -0.13 to 0.82%, p=0.01). Appendix V.

Performance and/or physical test

1-min sit-to-stand (1-min STS)

The 1-min STS test was used by two studies [21, 24]. In the meta-analysis produced, we can see that there was no statistically significant difference, medium term, between the CG and the intervention group after RMT (MD=1.79 95% CI: -0.99 to 4.57%, p=0.01). Appendix VI.

Table 1 Main methodological characteristics of the included studies

Author, Year	Country (cases)	Intervention time	Times a week	Inclusion criteria	Exclusion criteria
Abodonya et al., 2021	Saudi Arabia	2 wk	10 s/wk	Negative COVID, hemodynamically stable, respiratory rate < 25 breath/min, negative inspiratory force < − 25 cm H_2O, minute ventilation < 10 L/min, oxygen tension (PO_2)/fraction of inspired oxygen (FIO_2) > 200	Neurological, neuromuscular, and musculoskeletal limitations, cognitive dysfunction, end-stage of chronic diseases, and body mass index (BMI) > 35 kg/m^2
McNarry et al., 2022	UK	8 wk	3 s/wk	Prior self-reported COVID-19 infection, primary symptom of breathlessness and age ≥ 18 years	Dementia meaning, they could not follow commands/training, unstable cardiac disease, myocardial infarction or non-ST-elevation myocardial infarction within 6 weeks and/or high risk of falls
Palau et al., 2022	Spain	12 wk	14 s/wk	Symptomatic adult > 18 years old with a previous admission due to SARS-CoV-2 pneumonia; at least 3 months after discharge and provide informed consent	Inability to perform a maximal baseline exercise test; structural heart disease, valve heart disease or diastolic dysfunction estimated by two-dimensional echocardiography; previous ischemic heart disease, heart failure, myocardiopathy or myocarditis; effort angina or signs of ischemia during cardiopulmonary exercise testing; significant primary pulmonary disease, including a history of pulmonary arterial hypertension, chronic thromboembolic pulmonary disease or chronic obstructive pulmonary disease; treatment with digitalis, calcium channel blockers, β-blocker or ivabradine; chronic kidney disease (glomerular filtration rate < 60 mL/min/1.73 m^2); patients with pacemakers or previous history of atrial fibrillation; autoimmune, inflammatory or active neoplastic disease; anemia and pregnancy
Corral et al., 2022	Spain	8 wk	6 s/wk	Aged over 18 years who presented long-term post-COVID-19 symptoms of fatigue and dyspnea for at least 3 months after the COVID-19 diagnosis confirmed by positive reverse-transcription-polymerase chain reaction (RT-PCR) SARS-CoV-2 test from a nasopharyngeal or oropharyngeal swab or serological tests positive for SARS-CoV-2 antibodies	A diagnosis of progressive respiratory, neuromuscular or neurological disorders and/or psychiatric or cognitive conditions that hindered their ability to cooperate; any contraindication to respiratory muscle training treatment; lack of internet access; and previous inclusion in a rehabilitation programme for their long-term post-COVID-19 symptoms
Costa, 2022	Brazil	6wk	2 s/kw	18 years of age or older, with confirmed previous diagnosis of COVID-19 by polymerase chain reaction test (RT-PCR), who had respiratory sequelae after acute coronavirus infection such as dyspnea and desaturation at rest and/or at rest, in addition to not having chronic respiratory	Exertion intolerance, the emergence any disabling orthopedic or neurological condition

Table 1 (continued)

Author, Year	Country (cases)	Intervention time	Times a week	Inclusion criteria	Exclusion criteria
Jimeno-Almazán et al., 2023	Spain	8 wk	14 s/wk	18 years who had a confirmed microbiological diagnosis of COVID-19 by SARS-CoV-2 reverse transcription-polymerase chain reaction on an oropharyngeal-nasopharyngeal swab or a positive rapid antigen test, who presented a chronic symptomatic phase, lasting > 12 wk from the onset of symptoms, and had not been hospitalized because of the acute COVID-19 infection. Those with evidence of COVID-19 pneumonia needed a Brixia score ≤ 5 (20) and to show total recovery of pulmonary function and radiological follow-up. None must have received specific SARS-CoV-2 treatment	Pregnant women and those who had acute or unstable chronic diseases such as unstable myocardiopathy, ischemic heart disease, uncontrolled hypertension, asthma, or chronic obstructive pulmonary disease and those who had major surgery in the past 3 months
Gracelli, 2023	Brazil	6 wk	14s/wk	patients of any sex diagnosed laboratory test of COVID-19 by reverse transcription followed by chain reaction of real-time polymerase (RT-PCR) that were not in the window of transmissibility, people between 30 and 70 years old, who signed the TCLE and who did not previously perform IMT	patients unable to perform the evaluation tests, patients with orthopedic, visual and neurological problems that limited treatment with exercise, or who were unable to perform the IMT due to discomfort with the use of the device, patients with respiratory diseases, severe heart diseases and/or pre-existing COVID-19 neuromuscular disorders, participants who did not have 90% frequency of rehabilitation sessions, patients who required intubation orotracheal tube and use of Mechanical Ventilatory Assistance (AVM) or who had body mass index over 40

NR Not reported: yes, *N* no, *UK* United Kingdom, *COVID* Coronavirus disease, *Wk* weeks, *SARS-CoV-2* Severe acute respiratory syndrome Coronavirus *2*, *S* sessions, † Data extracted from abstracts

Six-minute walk test (6MWT)

The 6MWT was carried out in a study [23] and we noticed that there was a statistically significant improvement, in the short term, in favor of the intervention group when compared to the CG, demonstrating an improvement in functional capacity (MD = 40.70 m 95% CI: 18.23 m to 65.17 m %, $p = 0.01$).

Estimated V_{O2max}

V_{O2max} was measured in one study [11] (estimated by the Chester Step Test). After the intervention, we noticed a statistically significant improvement in the V_{O2max} of the participants who were in the intervention group (MD = 5.2mL·kg^{-1}·min^{-1} 95% CI: 1.78mL·kg^{-1}·min^{-1} to 8.62mL·kg^{-1}·min^{-1}%, $p = 0.01$).

Fatigue

Only one study [11] evaluated fatigue after intervention using the Fatigue Index Time (FIT). The results did not identify a statistically significant difference after the intervention between the CG and the RMT group (MD = 2.9 95% CI: -6.37 to 12.17%, $p = 0.01$).

QoL

The QoL was evaluated in four studies [11, 20, 22, 23] being quantified by 3 different instruments: Euro Quality 5Dimensions-3Levels (EQ-5D-3 L), The King's Brief Interstitial Lung Disease (K-BILD) and 12- item Short Form Survey (SF-12). The study by McNarry et al. [11] and Abodonya et al. [23] demonstrated an improvement in the QoL for participants in the RMT intervention group when compared to the CG: (MD = 16.10 95% CI: 11.59 to 20.61%, $p = 0.01$) and (MD = 8.00 95% CI: 3.14 to 12.86%, $p = 0.01$), respectively. The SF-12 was used by one study [20] however, only two domains were reported in the study (Physical Activity and mental health) and found no significant difference between groups after the intervention. In addition, the study by Palau et al. [22] demonstrated that after the intervention there were significant improvements in the dimensions of usual activities and anxiety/depression in the group that received the RMT.

Dyspnea

Four studies evaluated dyspnea [11, 20, 23, 25]. However, it was not possible to carry out any meta-analysis due to differences in the scales used and the method of disseminating the results. The scales used to quantify the results were: Transition Dyspnea Index (TDI), dyspnea severity index (DSI) and modified Medical Research Council (mMRC). In the study by Jimeno-Almazán et al. [20] and McNarry et al. [11] an improvement in dyspnea was observed after the RMT intervention. We noticed a

Table 2 Characteristics of the included studies

Year, Author	Age range (AR) / mean, years (SD)	Gender (M/F)	Intervention group (IG)	Comparison group (CG)	RMT equipment	Outcome measures	Time point
Abodonya et al., 2021	AR: NR 48.05 (8.85)	33/9	Each session has consisted of 6 inspiratory cycles; each cycle has remained around 5 min of resisted inspiration, followed by 60-second rest time intending to improve inspiratory muscle strength. At the fifth and sixth cycle, each patient was instructed to breath regularly as much as possible in tending to improve inspiratory muscle fitness. The inspiratory threshold was controlled by a device loading valve that provided a threshold load with 50% of the MIP	Incentive spirometer exercise	Respironics, Cedar Grove, NJ	Pulmonary function test; dyspnea severity index (DSI); QOL questionnaire: EuroQuality-5Dimensions-3Levels (EQ-5D-3 L); Functional performance: six-minute walk test (6-MWT)	Post-intervention: short term
McNarry et al., 2022	AR: NR / 46.6 (12.2)	NR	Three unsupervised IMT sessions per week, on nonconsecutive days, for 8 weeks, as in previous studies. Each session involved up to six blocks of six inspirations, with the rest periods interspersing each inspiration progressively decreasing from 40 to 10 s with each block, producing maximum session durations of 20 min. Participants completed as many inspirations as they could prior to failure, defined as not achieving 80% SMIP on three consecutive breaths	Usual care	PrO_2 (PrO_2Fit Health, Smithfield, RI, USA)	Health-related quality of life: King's Brief Interstitial Lung Disease (K-BILD) Perceived breathlessness: Baseline Dyspnea Index (BDI) and Transition Dyspnea Index (TDI) Inspiratory muscle strength; Physical fitness Estimated: V'O2max (mL·kg – 1 ·min – 1)	Post-intervention: short term
Palau et al., 2022	AR: NR / 50.4 (12.2)	15/11	Train at home twice daily, for 20 min each session, and for 12 weeks using a threshold inspiratory muscle trainer. After the first visit, the subjects will start home-based inspiratory training at a resistance equal to 25–30% of MIP for 1 week	Usual care	Threshold IMT, Respironics)	Lung function: spirometry; Physical test: VO_{2peak} test (mL/kg/min); Health-related Qo: European Quality of Life 5 Dimensions 3 Level Version (EQ-5D-3 L); Inspiratory muscle strength	Post intervention: short term
Corral et al., 2022	AR: NR	25/63	The regimen was 40 min/day, divided into two 20-min sessions (morning and afternoon), 6 times a week, for 8 weeks. The training load, regardless of whether participants performed IMT or RMT, was individually adapted and increased according to the same distribution scheme for inspiratory and expiratory muscle training; the IMT Group: only inspiratory muscle training; RMT group: training of inspiratory and expiratory muscles	Received a device without resistance (0 cm H_2O) because it lacked a threshold valve	POWERbreathe KH1© device (POWERbreathe International Ltd., Southam, UK)	Quality of life: EuroQol-5D questionnaire; Respiratory muscle function: inspiratory/expiratory muscle strength; inspiratory muscle endurance); Physical function: lower and upper limb strength [1-min Sit-to-Stand and handgrip force]; Lung function (forced spirometry); psychological status	Post-intervention: short term

Table 2 (continued)

Year, Author	Age range (AR) / mean, years (SD)	Gender (M/F)	Intervention group (IG)	Comparison group (CG)	RMT equipment	Outcome measures	Time point
Costa, 2022	AR: NR IG: 50.76 (11.28) CG: 44 (11.28)	13/20	Lung expansion therapy; muscle training Inspiratory: Threshold IMT with 40% of MIP in the 1st, 2nd and 3rd weeks, 50% of MIP in the 4th, 5th and 6th weeks, Three sets of ten repetitions; MMSS strengthening exercises; treadmill	fortnightly lectures, over the six-week period. These meetings were composed of lectures on education in health on various topics related to COVID-19, chronic diseases, quality of life healthy life and lifestyle	Threshold imt (Philips Respironics, EUA)	Lung Function; Dyspnea: Modified Medical Research Council Dyspnea Scale (mMRC)	Post-intervention: short term
Jimeno-Almazán et al., 2023	AR: NR / 45.30 (8.0)	50/110	CTRM: three-days-a-week concurrent training routine: two days of resistance training [50% 1RM (one-repetition maximum), 3 sets, 8 repetitions, 4 exercises (squat, bench press, deadlift, and bench pull)] followed by moderate intensity variable training [MIVT: 4–6 × 3–5 min at 70–80% heart rate reserve (HRR)/2–3 min at 55–65% HRR], and one day of a monitored autonomous light intensity continuous training (LICT: 30–60 min, 65–70% HRR); RM: 1 set of 30 repetitions [62.5 ± 4.6% of the PIM (maximum inspiratory pressure)], preceded by a warm-up set, twice a day, every day of the week	CT: same training as the CTMR group, but without respiratory training; CG: follow the WHO guidelines: "Support for Rehabilitation: Self-Management after COVID-19-Related Illness"	Power-Breathe Classic Heath Series	Anxiety and depression: General Anxiety Disorder Questionnaire-7 (GAD-7) and (Patient Health Questionnaire-9 (PHQ-9); Dyspnea: Modified Medical Research Council Dyspnea Scale (mMRC); Fatigue: Fatigue Severity Scale (FSS) and Chalder Fatigue Scale (CFS); Functional limitations: Post-COVID-19 Functional Status (PCFS)	Post-intervention: short term
Gracelli, 2023	AR: NR CG: 51.40 (12.80) IG: 52.0 (13.40)	20/10	IMT: for 6 weeks performing 2 sets of 30 repetitions daily using the POWERbreathe classic medic® device POWERbreathe InternationalLtd., Southam, UK). Patients exercised at 40% MIP at first week and 60% MIP in the subsequent 5 weeks; Performed respiratory physiotherapy, consisting of the following muscle-strengthening exercises: sitting down and standing up from a chair, abduction of upper limbs with elastic resistance, abduction of limbs lower limbs with elastic resistance and rowing with elastic resistance, were performed 03 series of 10 repetitions of each exercise	Performed respiratory physiotherapy, consisting of the following muscle-strengthening exercises: sitting down and standing up from a chair, abduction of upper limbs with elastic resistance, abduction of limbs lower limbs with elastic resistance and rowing with elastic resistance, were performed 03 series of 10 repetitions of each exercise	POWERbreatheKH2 (POWERbreathe K series KH2®, HaB International, Warwickshire, Reino Unido)	Respiratory muscle strength and endurance	Post-intervention: short term

NR Not reported, *Not used* NU, *IG* intervention group, *CG* control group, *MIP* maximum inspiratory pressure, *SD* standard deviation, *M* male, *F* female, *Md* Mediana; Interquartil range: {IQR}; Standard Deviation: (SD); Standar Error: [SE]; IMT: Inspiratory muscle training, *RMT* Respiratory muscle training, *wk* weekends, *min* minutes, *CTRM* Concurrent training program [with inspiratory muscle training, *CT* Concurrent training program, *RM* Inspiratory muscle training program

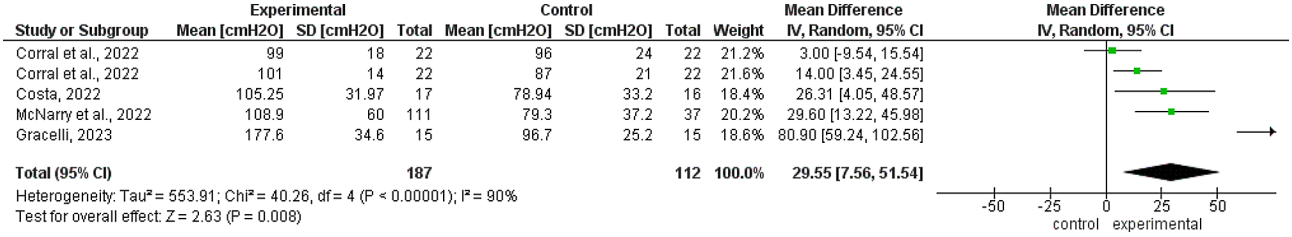

Fig. 2 Mean difference (and 95% confidence interval) of Maximum Inspiratory Pressure (MIP) between groups of RMT (respiratory muscle training) versus CG (Control group)

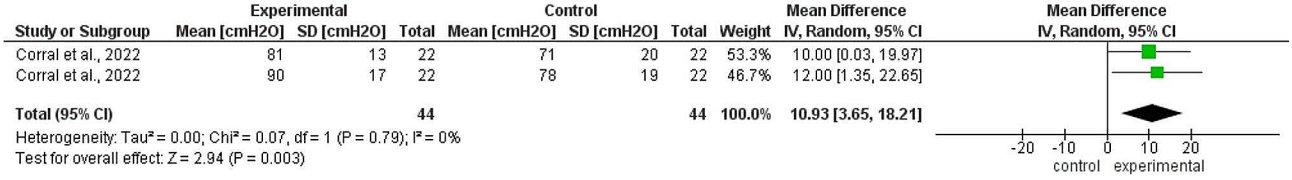

Fig. 3 Mean difference (and 95% confidence interval) of Maximum Expiratory Pressure (MEP) between groups of RMT (respiratory muscle training) versus CG (Control group)

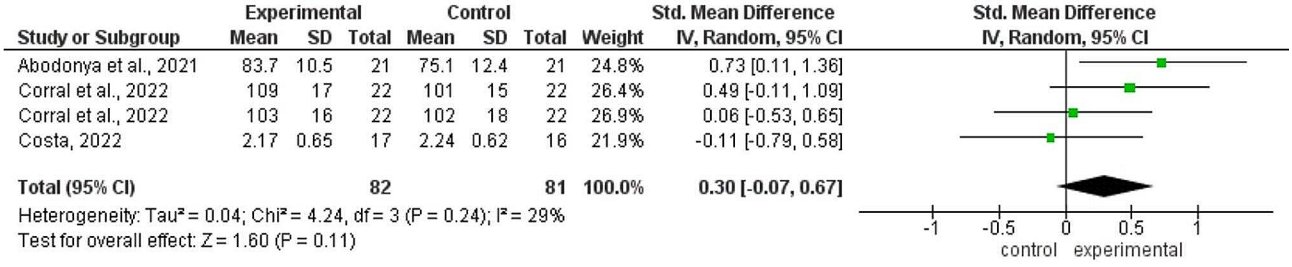

Fig. 4 Mean difference (and 95% confidence interval) of FEV_1 between groups of RMT (respiratory muscle training) versus CG (Control group)

reduction in the mMRC scale score after the intervention (MD = -1.45 95% CI: -1.94 to -0.96%, p=0.01) [25] and also in the DSI scale (MD = -2.90 95% CI: -5.44 to -0.36%, p=0.01) [23] after RMT, which is indicative of improvement in dyspnea symptoms.

Reliability of cumulative evidence

The assessment of the quality of evidence using GRADE showed very low quality of evidence for the results obtained in MIP and FEV_1/FVC; low certainty for FEV_1 and FVC; and moderate certainty of evidence for MEP and 1-min STS. The main reasons for the decrease in the certainty of the evidence of the evaluated outcomes were the possibility of inconsistency and imprecision (Appendix VII).

Discussion

The Covid-19 pandemic has brought significant challenges to global health, with many patients experiencing persistent sequelae even after recovering from the acute infection [2, 3, 5]. Among these sequelae, respiratory muscle weakness has been a growing concern, as it directly impacts the QoL and functional capacity of patients [3, 5, 9]. RMT has emerged as a potentially beneficial intervention to mitigate these adverse effects [9–11].

Post-Covid syndrome (also known as Long-Covid), can be defined as a syndrome that encompasses a prolonged course of different physical and neuropsychiatric symptoms that persist for more than 12 weeks without an alternative explanation [26]. In this systematic review, 7 studies were included to evaluate an RMT program as a complementary treatment option for patients with post-Covid syndrome. The main findings of this systematic review and meta-analysis indicate that RMT results in significant improvements in respiratory function (MIP, MEP), exercise capacity (6MWT, VO_{2max}) and QoL in post-Covid-19 patients. These results are consistent with previous studies demonstrating the effectiveness of RMT in populations with chronic respiratory diseases.

The number of weekly sessions in the studies ranged from 3 to 14 sessions, with a minimum duration of 2 weeks and a maximum of 12 weeks. The included studies only counted patients who were able to perform at least 70% of the RMT sessions.

RMT is already used in different types of health conditions that affect the respiratory system, such as chronic obstructive pulmonary disease (COPD) [27], cystic fibrosis [28] and asthma [29]. Our review observed that studies (RCTs) are being carried out from the year 2021 to the current year.

The most used device for RMT was the POWERbreathe®. This device is capable of adapting the inspiratory resistance to the pulmonary pressure curve, stabilizing the load during exercise, allowing training to be more comfortable; Furthermore, it is known that this equipment offers the possibility of introducing greater levels of load during exercise [30]. These facts could explain the choice of this device in most RCTs.

Respiratory muscle strength is a critical component of lung function and overall ventilatory capacity [8, 9]. In post-Covid-19 patients, respiratory muscle weakness has been identified as a significant sequela, contributing to persistent symptoms such as dyspnea and fatigue [7–9]. Our results showed an improvement in both inspiratory and expiratory muscle strength following TMR. This finding corroborates results from previous studies that have employed this type of training [29, 31]. These improvements can be explained by the principle that respiratory muscle groups, like other skeletal muscles, respond to training stimuli through adaptations when their fibers are stimulated to generate a state of overload [32, 33].

Moreover, previous studies involving participants with pulmonary diseases who underwent IMT also demonstrated an increase in MIP results, similar to what was observed in our review [34, 35]. The minimal clinically important difference for MIP in post-Covid-19 individuals has recently been established at 18cmH_2O [36]. Our results may be clinically significant, as we found values exceeding the established threshold following the intervention (MD = 29.55cmH_2O, 95% CI: 7.56 cmH_2O to 51.54cmH_2O, $p = 0.00001$).

The MEP is a crucial indicator of the strength and function of the muscles responsible for expiration [37]. Our study revealed that RMT, including EMT, has a substantial positive impact on MEP, highlighting the effectiveness of this approach in respiratory recovery. The observed increase in MEP across the included studies suggests that EMT can lead to significant gains in respiratory muscle strength and expiratory capacity, which are essential for the restoration of pulmonary function [10, 21]. These benefits are particularly relevant for patients who may have experienced a reduction in expiratory strength due to the prolonged impact of Covid-19, contributing to improved respiratory efficiency and greater comfort during daily activities [37].

We noticed that there were no statistically significant results between CG and intervention for FEV_1/FVC values. This difficulty in obtaining a significant improvement in this outcome can be explained by the pulmonary consequences that may occur due to Covid-19 [38, 39]. It has already been reported that Covid-19 can develop abnormalities in the bronchi, such as necrotizing bronchiolitis [38] bronchial or focal bronchiolar inflammation [40].

The QoL has been increasingly reported in studies involving patients with diseases involving the respiratory system. Studies have found that respiratory rehabilitation can improve the QoL of patients with COPD [40], cystic fibrosis [41], asthma [28]. These results corroborate the findings of this study since the scores of the questionnaires used after the intervention were favorable to the improvement of QoL. Several studies included in the analysis reported improvements in patients' QoL, measured by standardized questionnaires. These improvements were attributed to reduced dyspnea and increased ability to perform daily activities without excessive fatigue [11, 20, 23]. However, this outcome should be further explored; the standardization of instruments and their application may be important for future research to better describe the results of this intervention in these patients.

The 6MWT, a common measure of functional capacity, also showed significant improvements in the intervention groups [23]. The greater distance covered by patients who participated in RMT indicates an increase in endurance and aerobic capacity. Dyspnea is a common and debilitating symptom in post-Covid-19 patients. The increase in distance covered on the 6MWT after RMT suggests a reduction in dyspnea, allowing patients to maintain a higher level of activity without excessive respiratory distress. This fact corroborates the results presented by the study Abodonya et al. [23], since after intervention we observed a reduction in dyspnea and an increase in the distance covered.

Therefore, the results indicate that RMT can be an effective intervention to mitigate the prolonged respiratory effects of COVID-19, promoting the recovery of lung function and improving exercise capacity and QoL. The improvement in respiratory muscle strength likely contributes to a reduction in respiratory effort and greater respiratory efficiency, which may explain the improvements observed in the functional and subjective evaluations of the patients.

Study limitations

Several concerns should be considered as limitations of this study. Although the included studies had similar primary objectives, they exhibited substantial heterogeneity in terms of methodology, follow-up periods, and outcome assessments. Consequently, only a few studies were included in our meta-analyses. Additionally, despite our

conclusions being based on the analysis of experimental studies, the very small number of patients included in these analyses precludes the generalization of the results to the entire population with post-Covid syndrome. Furthermore, we were unable to assess publication bias due to the limited number of studies included.

However, despite these limitations, we believe that the scarcity of data underscores the need for future and additional investigations. This could serve as a positive impetus to enhance our understanding of the use of RMT in post-Covid syndrome.

Conclusion

There are a limited number of studies comparing post-covid patients undergoing RMT versus standard treatment. However, in our systematic review we found an increase in inspiratory and expiratory muscle strength in post-covid patients after intervention. The descriptive analysis suggests a reduction in dyspnea levels, an increase in the distance covered in the 6MWT, and an improvement in QoL. However, the conclusions remain uncertain as these results are based on very low to low quality evidence.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s13102-024-00954-x.

Supplementary Material 1

Supplementary Material 2

Supplementary Material 3

Supplementary Material 4

Supplementary Material 5

Supplementary Material 6

Supplementary Material 7

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Author contributions

D.M.X.: Conceptualization, Methodology, Formal analysis, Investigation, Writing - Original Draft; R.A.L.A.: Conceptualization, Methodology, Formal analysis, Investigation, Writing - Original Draft; F.G.C.: Methodology, Writing - Review & Editing; W.T.S.:Formal analysis, Writing - Review & Editing, Supervision; S.N.S.: Writing - Review & Editing; E.L.G.: Writing - Review & Editing; M.Ga.N.J.: Writing - Review & Editing, Supervision.

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Data availability

Data is provided within the manuscript or supplementary information files.

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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