Effects of Respiratory Muscle Training on Respiratory Function, Respiratory Muscle Strength and Exercise Tolerance in Post-Stroke Patients: A Systematic Review with Meta-Analysis

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REVIEW ARTICLE (META-ANALYSIS)

Effects of Respiratory Muscle Training on Respiratory Function, Respiratory Muscle Strength, and Exercise Tolerance in Patients Poststroke: A Systematic Review With Meta-Analysis

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Abstract

Objective: To examine the effects of respiratory muscle training on respiratory function, respiratory muscle strength, and exercise tolerance in patients poststroke.

Data Sources: We searched MEDLINE, Cochrane Library, Embase, SciELO, Physiotherapy Evidence Database (PEDro), and CINAHL (from the earliest date available to November 2015) for trials.

Study Selection: Randomized controlled trials (RCTs) that examined the effects of respiratory muscle training versus nonrespiratory muscle training in patients poststroke. Two reviewers selected studies independently.

Data Extraction: Extracted data from the published RCTs. Study quality was evaluated using the PEDro Scale. Weighted mean differences (WMDs), standard mean differences (SMDs), and 95% confidence intervals (CIs) were calculated.

Data Synthesis: Eight studies met the study criteria. Respiratory muscle training improved maximal inspiratory pressure WMDs (7.5; 95% CI, 2.7−12.4), forced vital capacity SMDs (2.0; 95% CI, 0.6−3.4), forced expiratory volume at 1 second SMDs (1.2; 95% CI, 0.6−1.9), and exercise tolerance SMDs (0.7; 95% CI, 0.2−1.2). No serious adverse events were reported.

Conclusions: Respiratory muscle training should be considered an effective method of improving respiratory function, inspiratory muscle strength, and exercise tolerance in patients poststroke. Further research is needed to determine optimum dosages and duration of effect.

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Impaired motor function is one of the most frequent and persistent consequences of stroke.[1] Not only are peripheral muscles involved in poststroke disability, but respiratory muscle weakness, low thorax expansion, and postural trunk dysfunction may also play an important role in exercise capacity and the ability to carry out activities of daily living.[2-6]

Respiratory muscle strength can be reduced in patients poststroke,[7,8] which reasonably justifies the use of respiratory muscle training in this population. However, despite the fact that certain effects of respiratory muscle training in patients poststroke have been shown in previous reviews,[9,10] evidence regarding the efficacy of respiratory muscle training is inconclusive and controversial. Xiao et al[9] concluded that there was insufficient evidence to support inspiratory muscle training after stroke. Pollock et al[10] concluded that respiratory muscle training can improve inspiratory but not expiratory muscle strength in neurologic conditions, but that its clinical benefit remains unknown.

Martín-Valero et al[11] recently published a systematic review with meta-analysis and reported that respiratory muscle training

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can improve strength and endurance of respiratory muscles in patients poststroke. However, they included in the meta-analysis studies that were not randomized controlled trials (RCTs) and studies that did not used respiratory muscle training as an intervention. In addition, the literature search for this meta-analysis was up to November 2014, and a number of new studies have been completed and published since.

Since previous reviews were published,[9-11] RCTs have been completed, but as far as we know, there is no published meta-analysis on the effects of respiratory muscle training in patients poststroke. This systematic review and meta-analysis aimed to analyze the published RCTs that investigated the effects of respiratory muscle training on respiratory function, respiratory muscle strength, and exercise tolerance in patients poststroke.

Methods

This meta-analysis was completed in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines.[12]

Eligibility criteria

This systematic review included all RCTs that studied the effects of respiratory muscle training in patients poststroke. Studies were considered for inclusion regardless of their publication status, language, or size. To be eligible, each trial should have randomized patients poststroke (independent of time since stroke [ie, acute, subacute, or chronic stages]) to at least 1 group of respiratory muscle training.

Respiratory muscle strength training was defined as the application of inspiratory muscle training, expiratory muscle training, or the combination of inspiratory and expiratory muscle training. We included all RCTs that studied the effects of respiratory muscle training compared with no respiratory muscle training or sham respiratory muscle training.

Decisions regarding what health outcomes to include in the systematic review were made by examining what outcomes were studied in previously conducted RCTs and systematic reviews on stroke rehabilitation. These key indicators consisted of the following: forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV_1) as a measure of respiratory function; maximal inspiratory pressure (MIP) and maximal expiratory pressure (MEP) as a measure of respiratory muscle strength; and peak oxygen consumption, exercise time, or maximum workload during a cardiopulmonary exercise test or maximal distance in walk tests as a measure of exercise tolerance.

List of abbreviations:

CI	**confidence interval**
FEV_1	**forced expiratory volume in 1 second**
FVC	**forced vital capacity**
MEP	**maximal expiratory pressure**
MIP	**maximal inspiratory pressure**
PEDro	**Physiotherapy Evidence Database**
RCT	**randomized controlled trial**

Information sources and search

We searched for references on MEDLINE, Embase, SciELO, CINAHL, Physiotherapy Evidence Database (PEDro), and the Cochrane Library up to November 2015 without language restrictions. A standard protocol for this search was developed, and whenever possible, controlled vocabulary (Medical Subject Heading terms for MEDLINE and Cochrane, and Emtree terms for Embase) was used. Keywords and their synonyms were used to sensitize the search.

The optimally sensitive search strategy developed by Higgins and Green[13] was used to identify RCTs in PubMed/MEDLINE. To identify RCTs in Embase, a search strategy using similar terms was adopted, in which there were 4 groups of keywords: study design, participants, interventions, and outcome measures.

We checked the references of the articles included in this meta-analysis to identify other potentially eligible studies. For ongoing studies or when the confirmation of any data or additional information was needed, the authors were contacted by e-mail.

Data collection and analysis

The previously described search strategies were used to obtain titles and abstracts of studies that might be relevant for this review. Each abstract identified in the research was independently evaluated by 2 authors. If at least 1 of the authors considered 1 reference eligible, the full text was obtained for complete assessment. Two reviewers independently evaluated the full-text articles for eligibility using inclusion and exclusion criteria. In the event of any disagreement, each of the authors discussed the reasons for their decisions, and a final decision was made by consensus.

Two authors independently extracted data from the published reports using standard data extraction forms adapted from the Cochrane Collaboration[13] model. Aspects of the study population, types of intervention performed, follow-up and loss to follow-up, outcome measures, and results were reviewed. Disagreements were resolved by 1 of the authors. Any further information required from the original author was requested by e-mail.

Quality of meta-analysis evidence

There are several scales for assessing the quality of RCTs, and the quality of evidence generated by this meta-analysis was classified using the PEDro Scale. The PEDro Scale assesses the methodologic quality of a study based on important criteria (eg, concealed allocation, intention-to-treat analysis, adequacy of follow-up). These characteristics make the PEDro Scale a useful tool for assessing the quality of physical therapy and rehabilitation trials.[14]

Methodologic quality was independently assessed by 2 researchers. Studies were scored on the PEDro Scale based on a Delphi list[15] that consisted of 11 items. One item on the PEDro Scale (eligibility criteria) is related to external validity and is generally not used to calculate the method score, leaving a score range of 0 to 10.[16]

Data synthesis and analysis

Pooled effect estimates were obtained by comparing the least squares mean percentage change from baseline to the end of the study for each group and were expressed as the weighted mean difference between groups. When the SD of change was not available, the SD of the baseline measure was used for the meta-analysis. Calculations were made using a fixed and random-effects models, and 1 comparison was made: respiratory muscle training versus nonrespiratory muscle training group. An α value of .05 was considered significant. Statistical heterogeneity of the treatment effect among studies was assessed using Cochran Q test and the inconsistency I^2 test, in which values >25% and 50% were considered indicative of moderate and high heterogeneity, respectively.[17] All analyses were conducted using Review Manager Version 5.3.[a]

Results

Description of selected studies

The initial search led to the identification of 309 abstracts, 19 of which were considered potentially relevant and were retrieved for detailed analysis. Seven studies met the eligibility criteria. Figure 1 shows the Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram of studies in this review.

The remaining 7 articles[18-24] were fully analyzed, approved by both reviewers, and had their data extracted. Each of the articles was scored using the PEDro Scale methodology by both reviewers. Studies included in this review had PEDro scores of 4 through 8; the mean methodologic quality of the included studies was 6.1. The results of the assessment of the PEDro Scale are presented individually in table 1.

Study characteristics

The number of participants in the included studies ranged from 18[22] to 109.[19] The mean age of the participants ranged from 54 to 65 years. All of the studies included patients of both sexes, but there was an overall predominance of men. Two studies[19,20] included patients within 2 weeks of stroke onset, whereas others[18,21-24] included patients with >6 months of stroke. Four studies[19,20,23,24] evaluated the initial MIP, and 3 studies[19,20,24] evaluated the initial MEP. The average of the initial MIP was 47.4cmH_2O, and the average of the initial MEP was 61.6cmH_2O. Table 2 summarizes the respiratory muscle training characteristics of the included studies.

The parameters used in the application of respiratory muscle training were reported in most studies. In all of the studies, 3 to 18 weeks of respiratory muscle training programs were performed.[19,23] Further, sessions were performed 3 to 6 times per week.[21-24] The intensity of resistance exercise was adjusted by the MIP assessment.

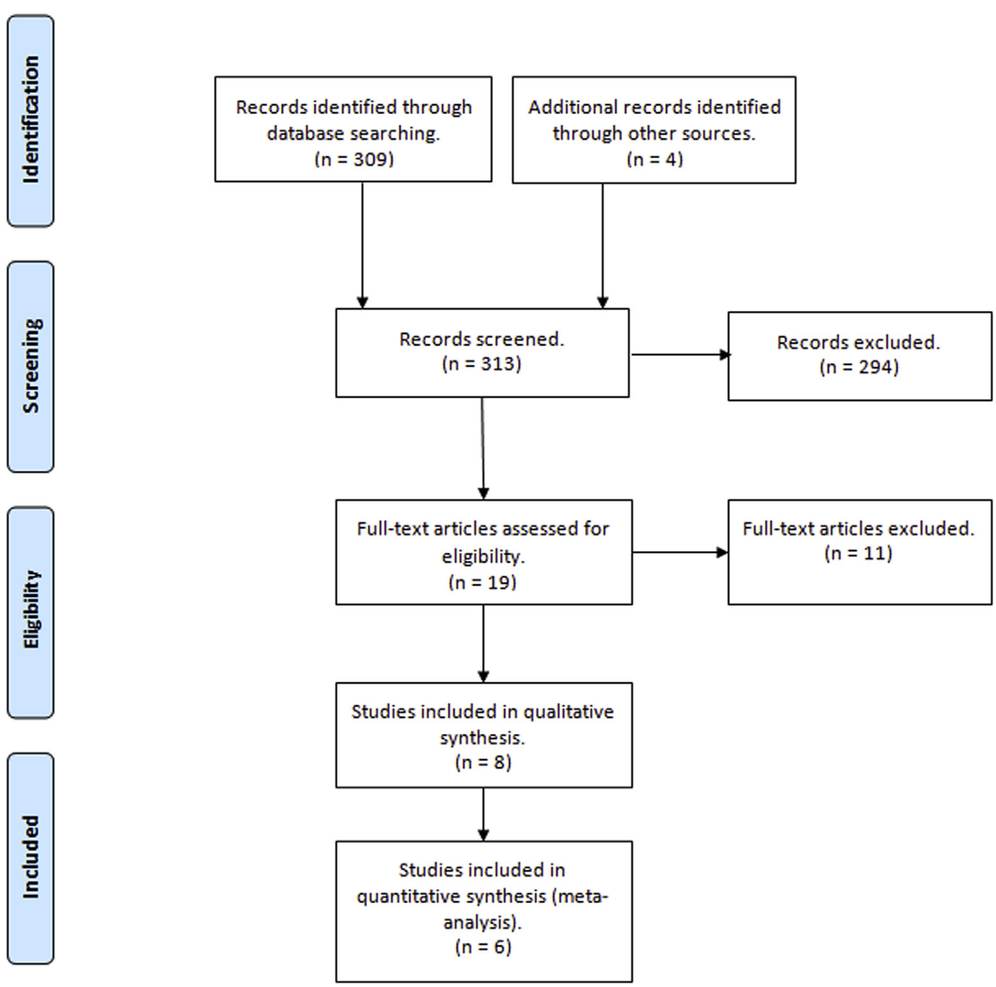

Fig 1 Search and selection of studies for systematic review according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 1 Study quality on the PEDro Scale

Study	PEDro Scale 1*	2	3	4	5	6	7	8	9	10	11	Total
Britto et al[23]	✓	✓	✓	✓			✓	✓		✓	✓	7
Jung et al[22]		✓		✓				✓		✓	✓	5
Kim et al[18]	✓	✓		✓			✓			✓	✓	5
Kim et al[21]		✓		✓						✓	✓	4
Kulnik et al[20]	✓	✓	✓	✓			✓		✓	✓	✓	7
Messaggi-Sartor et al[20]	✓	✓	✓	✓	✓		✓	✓		✓	✓	8
Sutbeyaz et al[24]	✓	✓	✓	✓			✓	✓		✓	✓	7
Mean												6.1

NOTE. 1, eligibility criteria and source of participants; 2, random allocation; 3, concealed allocation; 4, baseline comparability; 5, blinded participants; 6, blinded therapists; 7, blind assessors; 8, adequate follow-up; 9, intention-to-treat analysis; 10, between-group comparisons; 11, point estimates and variability.

* Item 1 does not contribute to the total score.

Most respiratory muscle training programs used an inspiratory threshold loading device,[20,22] but 1 study used a flow-dependent device,[18] which was adjusted according to the patient's effort (not exceeding moderate effort). The loads used in the selected studies ranged from 30% to 60% of the MIP. In most studies, loads of 30% to 40% were used initially,[22-24] reaching 60% of the MIP at the end of the training period. Some authors used 2 to 6 sets with 10 repetitions. Messaggi-Sartor,[19] Kulnik,[20] and colleagues

Table 2 Characteristics of the included studies

Study	Patients (no. analyzed, age, sex)	Outcome Measures: Pulmonary Function	Respiratory Muscle Strength	Exercise Tolerance	Key Findings
Britto et al[23]	N=21, 54y, 52% men Stroke >9mo	NA	MIP, IME	Cycloergometer maximum workload	MIP and IME improved in RMT group compared with non-RMT group ($P<.05$)
Jung et al[22]	N=18, 54.44y, 61.1% men	FVC, FEV_1, PEF, FEF	NA	NA	FEV_1 and PEF improved in RMT group in comparison with before and after the intervention ($P<.05$)
Kim et al[18]	N=37; 59.1y; 45.94% men Stroke >9mo	FVC, FEV_1	NA	NA	FVC and FEV_1 improved in RMT group compared with non-RMT group ($P=.05$)
Kim et al[21]	N=20; 54y Stroke >9mo	FVC, VEF1, PEF	NA	6MWT	FVC, VEF1, PEF, and 6MWT improved in RMT group compared with non-RMT group ($P<.05$)
Kulnik et al[20]	N=63; 64.4y; 60.33% men 2wk of stroke onset	NA	MIP, MEP	NA	MIP and MEP not improved in RMT group compared with non-RMT group ($P<.01$)
Messaggi-Sartor et al[20]	N=109; 65.5y; 57.8% men 2wk of stroke onset	NA	MIP, MEP	NA	MIP and MEP improved in IEMT group compared with non-IEMT group ($P<.01$)
Sutbeyaz et al[24]	N=45, 61.83y, 53.33% men Stroke during the previous 12mo	FVC, FEV_1, VC, $FEF_{25\%-75\%}$, PEF, MVV	MIP, MEP	Ergometer test VO_2peak	FVC, FEV1, VC, $FEF_{25\%-75\%}$, MVV, MIP, and VO_2peak improved in RMT group compared with non-RMT group ($P<.01$)

Abbreviations: 6MWT, 6-minute walking test; FEF, forced expiratory flow rate; $FEF_{25\%-75\%}$, forced expiratory flow rate 25%–75%; IEMT, inspiratory and expiratory muscle trainer; IME, inspiratory muscular endurance; MEP, muscular expiratory pressure; MIP, muscular inspiratory pressure; MVV, maximum voluntary ventilation; NA, not assessed; PEF, peak expiratory flow rate; RMT, respiratory muscle training; VC, vital capacity; VEF1, forced expiratory volume in 1 second; VO_2peak, peak oxygen uptake.

also performed expiratory muscle training. Training loads in the Messaggi-Sartor study[19] were set to a pressure equivalent to 30% of the MEP; in the Kulnik study,[20] the load was set at 50% of the MEP. The duration of the sessions varied from 15 to 30 minutes.[18,23,24] The characteristics of respiratory muscle training in included studies are provided in table 3.

Effect of respiratory muscle training on inspiratory and expiratory muscle strength

Four studies assessed MIP as an outcome.[19,20,23,24] Because of heterogeneity between studies, meta-analysis was performed with the random-effects model. The meta-analyses showed significant improvement in MIP at 7.55cmH_2O (95% confidence interval [CI], 2.7−12.4; n=167) for participants in the respiratory muscle training group compared with the nonrespiratory muscle training group (fig 2A).

Two studies assessed MEP as an outcome.[19,20] Because of the absence of heterogeneity between studies, meta-analysis was performed with the fixed-effects model. The meta-analyses showed a nonsignificant difference in MEP at 5.49cmH_2O (95% CI, −4.48 to 15.6; n=119) in participants in the respiratory muscle training group compared with the nonrespiratory muscle training group (fig 2B).

Effect of respiratory muscle training on pulmonary function tests

Four studies assessed FEV_1 as an outcome.[18,21,22,24] Because of the heterogeneity between studies, meta-analysis was performed with the random-effects model. The meta-analyses showed significant improvement in FEV_1 of 1.22mL (95% CI, 0.57−1.88; n=93) for participants in the respiratory muscle training group compared with the nonrespiratory muscle training group (fig 3A).

Four studies assessed FVC as an outcome.[18,21,22,24] Because of the heterogeneity between studies, meta-analysis was performed with the random-effects model. The meta-analyses showed significant improvement in FVC of 1.99 (95% CI, 0.57−3.42; n=93) for participants in the respiratory muscle training group compared with the nonrespiratory muscle training group (fig 3B).

Effect of respiratory muscle training on exercise tolerance

Three studies assessed exercise tolerance as an outcome.[21,23,24] Because of the difference between instruments used in the assessment of exercise tolerance, the cardiopulmonary exercise test[23,24] and the 6-minute walk test,[21] a meta-analysis was performed using the standardized mean difference. Because of the heterogeneity between studies, a meta-analysis was performed with the random-effects model. The meta-analyses showed significant improvement in exercise tolerance of .71 (95% CI, 0.21−1.2; n=68) for participants in the respiratory muscle training group compared with the nonrespiratory muscle training group (fig 4).

Discussion

The main results of our systematic review indicate that respiratory muscle training is effective in increasing MIP, respiratory function, and exercise tolerance in patients poststroke. These findings highlight the importance of including respiratory muscle assessment as part of the evaluation and selection of patients who might benefit from respiratory muscle training.

This systematic review with meta-analysis is important because it analyzes respiratory muscle training as a potential coadjuvant modality in the neurologic rehabilitation of patients poststroke. Functional recovery is a high priority in the health care system and also to enable independence of patients poststroke.[25] Furthermore, decreased levels of respiratory muscle strength and exercise tolerance are important because they have been associated with an increased risk of stroke and mortality.[26,27]

Patients poststroke have decreased respiratory muscle strength and consequent diaphragm and abdominal dysfunction.[10,28] Studies have shown that patients also show decreased respiratory function.[28,29] Khedr et al[30] report decreased diaphragmatic excursion in 41% of patients and reduced FVC and FEV_1 by as much as 50% of values predicted for unaffected individuals. Tomczak et al[31] also demonstrated that patients poststroke presented lower values of FVC, FEV_1, and tidal volume when compared with predictive values, which justifies the use of respiratory muscle training in patients poststroke. Respiratory muscle training resulted in an increased FEV_1 and FVC. This improvement can be associated with increased respiratory muscle strength.

Our systematic review showed that respiratory muscle training is effective in increasing inspiratory muscle strength. In our meta-analysis, the mean of the MIP in the analyzed studies was 50.6cmH_2O at baseline, being 70.4cmH_2O at the end of the intervention. Specifically, the weighted mean difference in the MIP was 7.5cmH_2O, favoring respiratory muscle training, which represents an improvement of 40%. A minimal clinically

Table 3 Characteristics of the respiratory muscle trainer intervention in the trials included in the review

Study	Modality	Intensity	Time/Repetitions	Frequency (times per wk)	Length (wk)	Supervision
Britto et al[23]	IMT	30% of MIP	30min	5	8	No
Jung et al[22]	IMT	30% of MIP	20min	3	4	Yes
Kim et al[18]	IMT	NA	15min	5	6	Yes
Kim et al[21]	IMT	NA	20min	3	4	Yes
Kulnik et al[20]	IMT EMT	50% of MIP and MEP	5 sets of 10 repetitions	7	4	Yes
Messaggi-Sartor et al[20]	IEMT (IMT plus EMT)	IEMT: 30% of MIP and MEP plus 10cmH_2O each week	5 sets of 10 repetitions	5	3	Yes
Sutbeyaz et al[24]	IMT	40%−60% of MIP	30min	6	6	Yes

Abbreviations: EMT, expiratory muscle trainer; IEMT, inspiratory and expiratory muscle trainer; IMT, inspiratory muscle trainer; NA, not assessed.

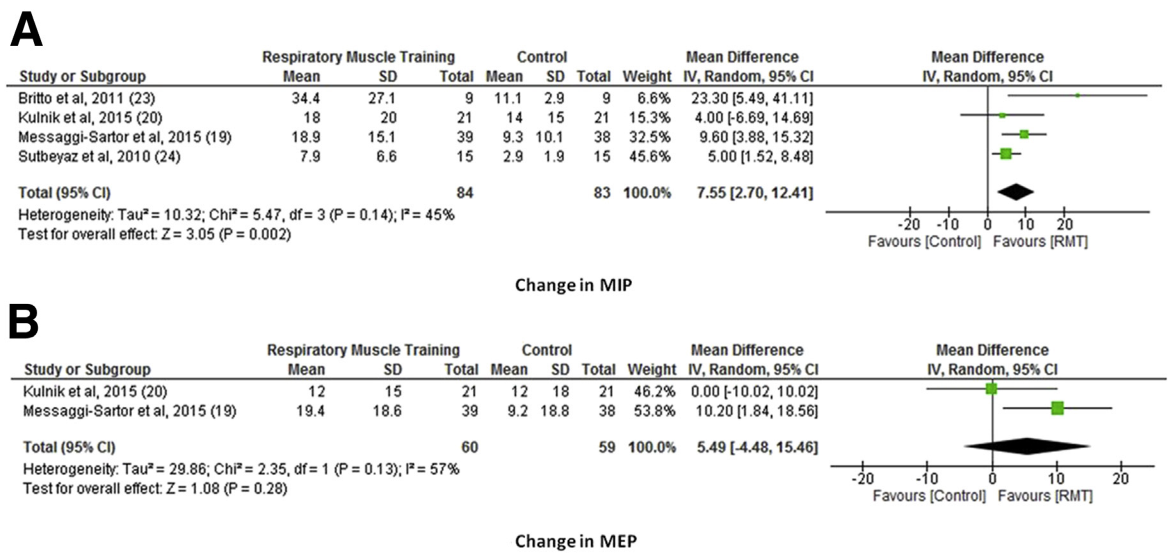

Fig 2 RMT versus non-RMT: inspiratory and expiratory muscle strength. (A) Change in MIP. (B) Change in MEP. Abbreviation: RMT, respiratory muscle training.

important difference for respiratory muscle strength in patients poststroke is not available. However, the gains were >30%, which likely represent clinically meaningful strength gains. The results of this review are in accordance with the findings of previous systematic reviews on patients poststroke,[9,11] patients with Parkinson disease, and patients with multiple sclerosis.[32]

The detected improvement in respiratory muscle strength is also important because respiratory muscle strength is an important determinant of exercise tolerance in patients with stroke.[33] Intolerance to exercise in patients poststroke may be in part because of respiratory impairment, resulting from decreased lung volumes and decreased inspiratory and expiratory strength. Respiratory muscle training has notably positive effects on pulmonary function and exercise tolerance, which ultimately can help patients carry out their activities of daily living more easily.[34]

Respiratory muscle training has also been shown to have positive effects on pulmonary function, inspiratory muscle strength, exercise tolerance, and activities of daily life in the context of other chronic diseases.[35,36]

The increased exercise tolerance may have been linked to certain key factors (eg, enhanced aerobic capacity of the inspiratory muscles), enabling greater minute ventilation and reduced time to fatigue during exercise. In addition, reduced respiratory muscle strength, elastic recoil of the lungs, and chest wall compliance can lead to reduced exercise tolerance.[32,37,38] Therefore, the benefit obtained from respiratory muscle strength and pulmonary function may improve exercise tolerance.

The loads used in the analyzed studies ranged from 30% to 60% of the MIP. Loads <30% of the MIP seem insufficient to

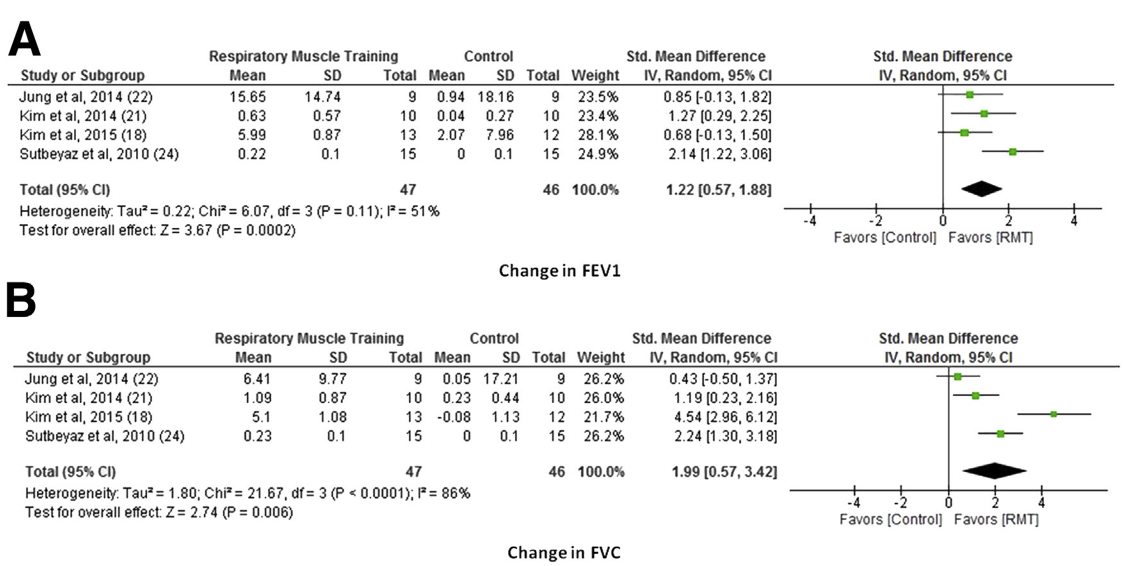

Fig 3 RMT versus non-RMT: FEV_1 and FVC. (A) Change in FEV_1. (B) Change in FVC. Abbreviation: RMT, respiratory muscle training.

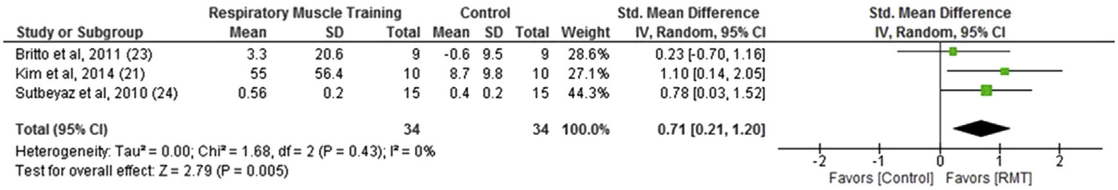

Fig 4 RMT versus non-RMT: exercise tolerance. Abbreviation: RMT, respiratory muscle training.

achieve improvements in inspiratory muscle strength and exercise tolerance.[39,40] Higher loads are more commonly associated with better functional outcomes than lower loads.[41]

Another relevant aspect is pretraining respiratory muscle strength. Four of the included studies[19,20,23,24] reported respiratory muscle strength at baseline as <70% of the predicted value of the MIP, or $<60cmH_2O$.[42,43] The American Thoracic Society and the European Respiratory Society show MIP values of considerably $<80cmH_2O$, the threshold for clinically meaningful weakness.[44] In a recent systematic review, Montemezzo et al[38] concluded that patients with heart failure who had weaker inspiratory muscles at baseline showed greater improvements in maximal and submaximal exercise capacities after inspiratory muscle strength training. Patients with greater respiratory muscle weakness respond better to respiratory muscle training. However, because this hypothesis was not specifically evaluated in the reviewed studies, it should be tested in future studies.

An assessment of respiratory muscle strength should be considered in patients poststroke before commencement of a rehabilitation program.[45] This will help professionals identify patients with low respiratory muscle strength, and to propose respiratory muscle training to enhance functional abilities.

Study limitations

Given the small pool of available studies, some caution is warranted when interpreting our results. A notable limitation of the included studies is the small sample sizes in the studies. Finally, the different protocols used to evaluate the patients and to apply the respiratory muscle training also limited the number of studies in this meta-analysis. Further investigation is required to explore how the positive effects of respiratory muscle training can be sustained over time and to determine optimum dosages, duration, and outcomes when used in combination with peripheral muscle training. Clearly, the value of respiratory muscle training in the survival of patients poststroke deserves special attention in future studies.

Conclusions

Taking into account the available studies, this systematic review with meta-analysis showed that respiratory muscle training should be considered an efficient method of improving MIP, respiratory function, and exercise tolerance in patients poststroke. More well-designed RCTs are necessary to determine the most appropriate methods (device, intensity, frequency, and duration) to optimally tailor the respiratory training to the particular characteristics of a patient subgroup or individual patient.

Supplier

a. Review Manager Version 5.3; The Cochrane Collaboration.

Keywords

Exercise; Rehabilitation; Stroke

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