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REVIEW ARTICLE (META-ANALYSIS)

Respiratory Muscle Training Reduces Respiratory Complications and Improves Swallowing Function After Stroke: A Systematic Review and Meta-Analysis

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Abstract

Objective: To investigate whether respiratory muscle training is capable of reducing the occurrence of respiratory complications and improving dysphagia (swallowing or cough function) after stroke.

Data Sources: Cochrane Library, Excerpta Medical Database (EMBASE), PUBMED, and Web of Science were searched for studies published in English; the China Biology Medicine (CBM), China Science and Technology Journal Database (VIP), China National Knowledge Infrastructure (CNKI), and Wanfang Database were searched for studies published in Chinese up to August 10, 2021.

Study Selection: Eleven randomized control trials (RCTs) (N=523) met the inclusion criteria were included in this systematic review.

Data Extraction: Data and information were extracted by two reviewers independently and disagreements was resolved by consensus with a third coauthor. Primary outcome was the occurrence of respiratory complications, secondary outcomes would be represented by swallowing and cough function. The quality of each included RCT were assessed by Cochrane risk-of-bias criteria and the GRADE evidence profile was provided to present information about the body of evidence and judgments about the certainty of underlying evidence for each outcome.

Data Synthesis: Respiratory muscle training reduced the risk of respiratory complications (relative risk, 0.51; 95% confidence interval [CI], 0.28-0.93; I^2=0%; *P*=.03; absolute risk difference, 0.068; number need to treat, 14.71) compared with no or sham respiratory intervention. It also decreased the liquid-type Penetration-Aspiration Scale scores by 0.81 (95% CI, −1.19 to −0.43; I^2=39%; *P*<.0001). There was no significant association between respiratory muscle training and Functional Oral Intake Scale (FOIS) scores, cough function: increased FOIS scores by 0.47 (95% CI, −0.45 to 1.39; I^2=55%; *P*=.32), decreased peak expiratory cough flow of voluntary cough by 18.70 L per minute (95% CI, −59.74 to 22.33; I^2=19%; *P*=.37) and increased peak expiratory cough flow of reflex cough by 0.05 L per minute (95% CI, −40.78 to 40.87; I^2=0%; *P*>.99).

Conclusion: This meta-analysis provided evidence that respiratory muscle training is effective in reducing the risk of respiratory complications and improving dysphagia by reducing penetration or aspiration during swallowing liquid bolus after stroke. However, there was no sufficient evidence to determine that respiratory muscle training improves cough function. Additional multicenter studies using larger patient cohorts are required to validate and support these findings. Furthermore, long-term follow-up studies should be performed to measure outcomes, while avoiding bias due to confounding factors such as heterogeneity of the etiologies of dysphagia.

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Dysphagia is a very common complication observed in stroke patients. The incidence rate is highly variable. It is lowest when identified using screening methods (ie, the water swallow test), with an incidence of approximately 37% to 45%, whereas it is highest when identified using instrumental testing (ie, videofluoroscopy), with an incidence rate of approximately 64% to 78%.[1] Aspiration is associated with an 11-fold increase in the risk of chest infections or pneumonia,[1] which is one of the most troublesome respiratory complications after stroke and may result in death.[2] Using pooled analysis from studies with sufficient data,

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the risk of pneumonia was found to be increased in patients with dysphagia, especially in patients with aspiration (relative risk [RR], 11.56; 95% confidence interval [CI], 3.36-39.77).[1] Furthermore, patients who develop pneumonia have higher mortality rates, longer hospitalization, poorer functional outcomes, and higher care needs.[2,3] Although some studies have reported that approximately 90% of patients with dysphagia usually improve spontaneously with a return of safe swallowing function within 2 weeks,[1,4] given the severity of poststroke respiratory complications, appropriate and effective early interventions for dysphagia is crucial.

Clinical therapy for dysphagia can be broadly divided into compensatory and remedial approaches. The compensatory approach aims to provide safer swallowing with control of food intake, material, viscosity, and the use of specific postures (eg, chin tuck, head rotation, and tilting).[5] However, the effect of this approach is partial and temporary. This is because the patient's secretions (saliva) mixed with bacteria are much more likely to cause pneumonia or chest infections compared with food intake.[6] The close association between the aspiration of bacteria-laden secretions and the development of pneumonia has been well documented.[6,7] Langdon et al[8] reported that of the 13 respiratory infections that were documented, 6 (46%) were observed in survivors who were ''nil by mouth." Hence, their infections were unlikely a result of aspirating food or fluids compared with their saliva secretions. Compared with compensatory-based approaches, remedial-based approaches to swallowing therapy focus on rehabilitating damaged neural and musculoskeletal structures that contribute to dysphagia through various exercises and maneuvers (eg, Mendelsohn maneuver, supraglottic swallowing, and neuromuscular electrical stimulation) in people with stroke.[9,10] Dysphagia in people with a history of stroke is often characterized by impairments in both swallowing efficiency and safety, as well as impairments in spatial and temporal pharyngeal swallowing kinematics.[1] Aspiration has been found to cause approximately 60% of poststroke pneumonia.[11] Hence, the pharyngeal phase is the most important, because aspiration is most likely to occur during this phase.[12]

Breathing and swallowing processes occur through similar anatomic pharyngeal structures and are controlled by the brainstem. The 2 processes must be closely coordinated because they cannot be performed simultaneously.[13] Also, the 2 coordinated processes provide important functions related to airway protection, such as forceful coughing. Evidence shows that reduced levels of cough flow indicate the need for assisted airway clearance and are associated with higher risk of aspiration, and therefore aspiration pneumonia in stroke.[14,15] However, weakness in the respiratory muscles and lack of the required coordination secondary to central nervous lesions can lead to swallowing impairment and ineffective cough after stroke. This predisposes patients to aspiration, secretion retention, pneumonia, or even respiratory failure.[16,17] Thus respiratory (inspiratory and/or expiratory) muscle training may be a therapeutic strategy to reduce aspiration risk and prevent respiratory complications to improve swallowing function and effective cough in stroke survivors.

To our knowledge, only 1 systematic review examined the effect of respiratory muscle training on reducing pneumonia incidence after stroke.[18] The likelihood of respiratory complications was observed to have reduced significantly in patients after intervention (RR, 0.38; 95% CI, 0.15-0.96; I^2=0%) compared with patients who received no or sham respiratory intervention. However, the study only included 2 trials[19,20] (N=179 participants) and failed to further explain the reason for lower pneumonia incidence after intervention. Three systematic reviews have examined the effect of expiratory muscle training on swallowing function.[21-23] The review by Renata et al[21] failed to find clear evidence due to heterogeneity in the etiologies and differences in the methods that summarized participant performance. The review by Marinda et al[22] included 3 studies using 4 different outcome measures (Penetration-Aspiration Scale [PAS], Functional Oral Intake Scale [FOIS], surface electromyography of suprahyoid muscle activity, and hyolaryngeal movement). This study demonstrated that expiratory muscle training resulted in decreased aspiration, with a large effect for fluids and a moderate effect for solids. The meta-analysis performed by Zhuo et al[23] included 5 studies that reported PAS scores. They found that patients in the expiratory muscle training group had a significant reduction in PAS scores (RR, −0.94; 95% CI, −1.27 to −0.61; P<.01) compared with the control group. With regard to cough function after stroke, very few systematic reviews have examined the effect of respiratory muscle training. The meta-analysis performed by Zhuo et al[23] included 4 studies that analyzed cough function, with 2 outcomes (ie, peak expiratory flow rate and cough volume acceleration [CVA]). However, this meta-review failed to observe any effect on peak expiratory flow rate (RR, 0.57; 95% CI, 0.62-1.77; P=.35) or CVA (RR, 33.87; 95% CI, −57.11 to 124.85; P=.47). The systematic review by Lucy et al[24] only included 2 trials that evaluated cough function in an adult population. No significant effect of expiratory muscle training on peak expiratory cough flow of voluntary cough (PECF-VC; increased by 4.63 L/min; 95% CI, −27.48 to 36.74; P=.78) was observed. However, all the reviews mentioned above analyzed patients with dysphagia from a variety of neurological diseases or from healthy adults. Therefore, heterogeneity of the etiologies confounded their findings. Furthermore, in addition to voluntary cough function, reflex cough function should also be examined. Several studies have demonstrated that reflex cough is also associated with pneumonia risk[14,15] and the function of reflex cough may be more important compared with voluntary cough in ensuring adequate airway protection and clearance after stroke.[25,26] Hence, there is a need for a more updated review of the current evidence on the effectiveness of respiratory muscle training.

The research questions for this systematic review were: (1) Does respiratory muscle training reduce the occurrence of respiratory complications in stroke survivors; and (2) Does respiratory muscle training improve dysphagia (swallowing and cough function) after a stroke?

List of abbreviations:

CI	**confidence interval**
CVA	**cough volume acceleration**
FOIS	**Functional Oral Intake Scale**
PAS	**Penetration-Aspiration Scale**
PECF-RC	**peak expiratory cough flow of reflex cough**
PECF-VC	**peak expiratory cough flow of voluntary cough**
RCT	**randomized controlled trial**
RR	**relative risk**

Methods

Search strategy

All searches were conducted before August 10, 2021 using Cochrane Library, Excerpta Medical Database (EMBASE), PUBMED, and Web of Science to locate studies published in

English, and using the China Biology Medicine (CBM), China Science and Technology Journal Database (VIP), China National Knowledge Infrastructure (CNKI), and Wanfang Database for studies published in Chinese. MeSH terms combined with free terms were used to search for potentially relevant articles across databases, and keywords were structured using the population, intervention approach, such as "Breathing Exercises," "Respiratory Muscle Training," "Maximal Respiratory Pressures," and "Stroke." Full search strategies are presented in appendix 1. This study conforms to all PRISMA guidelines and reports the required information accordingly. Using predetermined inclusion and exclusion criteria, 2 researchers who specialize in rehabilitation medicine independently screened each item for relevance by title and abstract. In cases where a decision could not be made as to whether the eligibility criteria were met based on the title and abstract, the full text of the article was obtained. More rigorous and comprehensive screening was used for 52 full texts by retrieving the study designs, specific interventions, characteristics of participants, and outcomes. After evaluating full-text articles, 41 studies failing to meet the inclusion criteria were excluded. Finally, 11 studies were included in this systematic review. Figure 1 outlines the flow of studies through the review. There was no potential for bias within the 2 researchers and disagreements or ambiguities were resolved by consensus with a third coauthor.

Eligibility criteria

The studies were included if they met the PICOS criteria as follows: (1) population (P; all of patients were adults older than 18 years diagnosed with stroke); (2) intervention (I): respiratory muscle training aimed at increasing strength of the inspiratory or expiratory muscles by using threshold resistance trainer or flow-oriented resistance trainer was considered as the intervention; (3) control (C): sham intervention without effective respiratory muscle training or no intervention was considered as the control; (4) outcomes (O): the occurrence of respiratory complications (lung infections or pneumonia) as primary outcome and swallowing function and cough function as secondary outcomes; and (5) study design (S): randomized controlled trials (RCTs). Studies were excluded if they were systematic reviews, tutorial articles, conference abstracts or single case reports; if the authors failed to obtain full texts or extract valid outcome data; if they were limited to describing immediate effects rather than outcomes after a course of treatment; if participants had swallowing dysfunction before stroke; and if, except for stroke, participants had other diseases that might affect outcomes, such as heart disease, chronic obstructive pulmonary disease, or spinal deformity.

Quality assessment

The Cochrane risk-of-bias criteria [27] for assessing the risk of bias was used to evaluate the methodological quality of each included RCT. There are 7 items that assess bias, including random sequence generation (selection bias), allocation concealment (selection bias), blinding of participants and personnel (performance bias), blinding of outcome assessment (detection bias), incomplete outcome data (attrition bias), selective reporting (reporting bias), and other bias. Each item was categorized as low, high, or unclear risk under the guidelines stated in the Cochrane Handbook. Other bias in this review was defined as trials in which baseline characteristics were not similar between different intervention groups. A GRADE evidence profile is a specific, tabular presentation of key information about all relevant outcomes of alternative health care interventions and it was provided to present information about the body of evidence and judgments about the certainty of underlying evidence for each outcome.

Data synthesis and analysis

Two reviewers independently extracted data and information. Basic information such as the first author's name, publication year, study design, patient characteristics, and intervention details was extracted and analyzed. Primary outcome is the occurrence of respiratory complications that was extracted as number of participants with diagnosis of pneumonia or lung infection after commencement of training. Secondary outcomes would be represented by swallowing and cough function, such as the PAS scores, FOIS scores, PECF-VC, and peak expiratory cough flow of reflex cough (PECF-RC). The PAS is a standard tool used by both researchers and clinicians to assess penetration, aspiration, and swallowing safety [28] Laryngeal penetration is defined as passage of material into the larynx, which does not pass below the vocal folds, and aspiration refers to material penetrating the larynx and entering the airway below the true vocal folds. The scale is divided into 8 levels based on the depth of material penetration into the airway and whether or not the material entering the airway is expelled. Higher levels indicate a greater degree of aspiration severity. Aspiration is judged to be more severe than penetration. Therefore, aspiration is scored 6, 7, or 8. Penetration, on the other hand, is scored either 2 or 3 if residue remains above the vocal folds and 4 or 5 if residue courses to the level of the vocal folds.[29]

The FOIS was developed by Crary et al[30] in 2005 as a tool with very good reliability, validity, and sensitivity to objectively determine and monitor the range of oral intake of patients with neurogenic dysphagia. It is an ordinal scale with 7 tiers that assesses the oral intake of food and liquids. Different ranges of nonoral feeding are subsumed in levels 1 through 3, whereas different ranges of oral feeding are included in levels 4 through 7. Level 1 indicates complete impairment of oral intake, whereas level 7 indicates that the patient has complete oral intake regardless of food consistency or type.

PECF was used as a surrogate marker for effective cough, which is an important defense against penetration and aspiration.[31] It was measured by having the patient inspire fully and then cough forcibly through a mask or mouthpiece attached to a peak flow meter. Voluntary cough was assessed by asking participants to make repeated maximal cough efforts into a tight-fitting face mask. Involuntary coughs were usually induced by the nebulization of escalating concentrations of capsaicin through the face mask. PECF less than 160 L per minute identifies patients with an ineffective cough. Patients with PECF between 160 and 270 L per minute are at risk of respiratory tract infections, which can further decrease muscle strength.[31-34]

The meta-analysis was performed using Review Manager 5.3 software[a] based on the preferred reporting items of the systematic review and meta-analysis guidelines. Heterogeneity was assessed by examining the clinical characteristics of the included studies and by formal statistical testing with chi-square and I^2 tests. For the assessment of swallowing function (PAS/ FOIS scores), inverse variance estimates with a fixed-effect analytical model preferred to be used to calculate the mean difference or standardized mean difference and their 95% CIs. For the occurrence of respiratory complications, the Mantel-Haenszel method with a fixed-effect analytical model preferred used to calculate relative risk (RR) and absolute risk difference and 95% CIs. If zero events were reported for one group in a

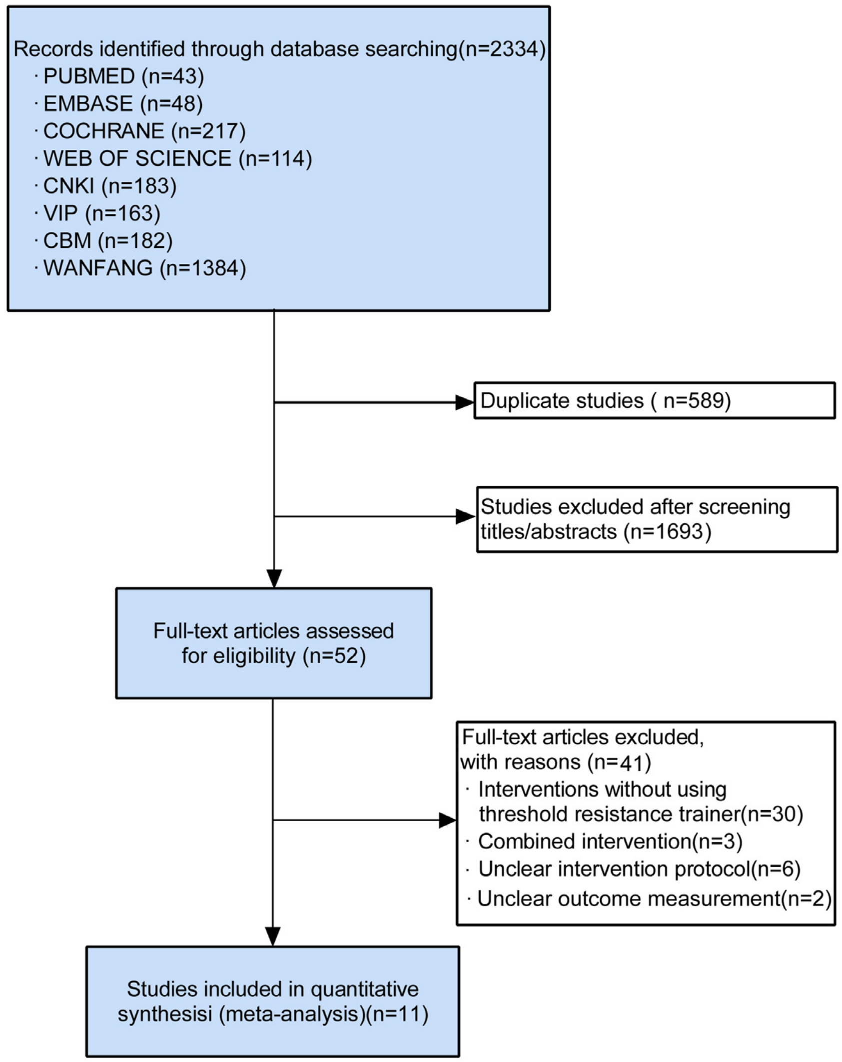

Fig 1 Flow of the search strategy.

comparison, a value of 0.5 was added to both groups for each such study. Based on the practice recommendation of the Cochrane Handbook,[27] trials with zero events in both the intervention and control groups were not included in the meta-analysis when RRs were calculated. If there was significant between-trial heterogeneity according to the judgment before the calculation, sensitivity analysis, subgroup analysis, or meta-regression was be used to try to explain the source of heterogeneity and resolve it. On the contrary, if resolution of heterogeneity failed, a randomized-effect analytical model was applied.

Results

Flow of trials through the review

The search strategy identified 2334 potentially relevant papers; 589 were found to be duplicates. After screening titles, abstracts, and reference lists, 52 potentially relevant full articles were screened. After evaluating full-text articles, 41 studies failing to meet the inclusion criteria were excluded, and 11 studies were included in this systematic review. Figure 1 outlines the flow of studies through the review.

Characteristics of included trials

The 11 included trials[13,19,20,35-42] involved 523 participants and investigated the effect of respiratory muscle training on respiratory complications (n=7), swallowing function (n=5), and cough function (n=4) after stroke. Ten studies performed respiratory muscle training with a threshold resistance trainer for inspiratory or expiratory muscle. The trainer was set to various pressures ranging from 30% to 60% maximal inspiratory pressure or 15% to 75% maximal expiratory pressure). One study performed respiratory muscle training with a flow-oriented resistance trainer, the resistance of which was adjusted according to tolerance. Two of included trials[19,36] were carried out with 3 arms of interest: inspiratory muscle training, expiratory muscle training, and sham training. For the outcomes of respiratory complications and cough function, data of each experimental subgroup were combined in different approaches to create a single comparison, following Cochrane recommendations.[27] Additional relevant characteristics of the included studies and intervention are shown in tables 1 and 2.

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Table 1 Characteristic of included trials

Study	Design	Intervention: Frequency and Duration	Intervention: Parameters	Outcome	Measurement of Rc or Cf
Eom et al,[35] 2017, Korea	RCT (NR) N=26	Exp (n=13): EMT 25 reps × 5/wk × 4 wk Con (n=13): sham (no loading) 25 reps × 5/wk × 4 wk	Muscles: expiratory Device: EMST150 Resistance: 70% MEP Progression: fixed	Swallowing function: PAS (0-8) (by VFSS) Timing: 0, 4 wk	—
Guillen-Solà et al,[13] 2016, Spain	RCT (computer-generated random list) N=33	Exp 1 (n=16): IEMT 50 reps × 2/d × 5/wk × 3 wk Con (n=17): nothing	Muscles: inspiratory + expiratory Device: Orygen-dual valve Resistance: 30% MIP + 30% MEP Progression: resistance increased weekly at intervals of 10 cmH2O	Respiratory complications: pneumonia Swallowing function: PAS (0-8) (by VFSS) FOIS (1-7) Timing: 0, 3, 12 wk	Rc: chest x-ray or by fever with abnormal respiratory signs (medical reports and/or telephone interview) Timing: 0, 12 wk
Wang et al,[36] 2019, China	RCT (NR) N=98	Exp 1 (n=33): EMT 50 reps × 4/wk × 90 d Exp 2 (n=32): IMT 50 reps × 4/wk × 90 d Con (n=33): sham (10% MIP/MEP) 50 reps × 4/wk × 90 d	Muscles: inspiratory or expiratory Device: NR Resistance: 50% MIP or 50% MEP Progression: resistance readjusted according to tolerance	Respiratory complications: pneumonia Cough function: PECF-VC (L/min) PECF- RC (L/min) Timing: 0, 28, 90 d	Rc: chest x-ray or by fever with abnormal respiratory signs (medical reports and/or telephone interview) Timing: 0, 90 d Cf: comprehensive lung function instrument (VIA-SYS, USA) VC: repeated maximal cough efforts RC: induced by capsaicin Timing: 0, 28, 90 d
Kulnik et al,[19] 2015, United Kingdom	RCT (random number) N=78	Exp 1 (n=27): EMT 50 reps × 7/wk × 4 wk Exp 2 (n=26): IMT 50 reps × 7/wk × 4 wk Con (n=25): sham (10% of maximal mouth pressure) 50 reps × 7/wk × 4 wk	Muscles: inspiratory or expiratory Device: NR Resistance: 50% MIP or 50% MEP Progression: resistance adjusted to 50% of maximal strength weekly	Respiratory complications: pneumonia Cough function: PECF-VC (L/min) PECF-RC (L/min) Timing: 0, 28, 90 d	Rc: temperature >37.5°C on 2 consecutive measurements or a single measurement of >38.0°C with chest symptoms, and ≥1 of the following: white cell count >11000/mL, pulmonary infiltrate on chest radiograph, positive microbiology cultures Timing: 0, 90 d Cf: calibrated pneumotachograph (PK Morgan Ltd, Rainham, England) VC: repeated maximal cough efforts RC: induced by the capsaicin Timing: 0, 28, 90 d
Liaw et al,[37] 2020, China (Taiwan)	RCT (random number) N=21	Exp (n=10): IEMT 30 reps × 1-2/d × 5/wk × 6 wk Con (n=11): nothing	Muscles: inspiratory + expiratory Device: Dofin breathing trainer Resistance: (30%-60%) MIP + (15%-75%) MEP Progression: resistance was adjusted according to tolerance	Swallowing function: FOIS (1-7) Cough function: PECF (L/min) Timing: 0, 6 wk	Cf: by a spirometer (Vitalograph, Serial Spirotrac, Buckingham, VA) per American Thoracic Society standards Timing: 0, 6 wk
Parreiras de Menezes et al,[38] 2018, Brazil	RCT (random number) N=37	Exp (n=19): IEMT 40 min × 7/wk × 8 wk Con (n=18): sham (0 cmH2O) 40 mins × 7/wk × 8 wk	Muscles: inspiratory+ expiratory Device: Orygen-dual valve Resistance: 50% MIP+ 50% MEP Progression: resistance adjusted to 50% maximal strength weekly	Respiratory complications Timing: 0.8, 12 wk	Rc: by asking the participants whether and how often they were admitted to a hospital due to respiratory reasons Timing: 0, 12 wk
Messaggi-Sartor et al,[20] 2015, Spain	RCT (random number) N=101	Exp (n=54): IEMT 50 reps × 2/d × 5/wk × 3 wk Con (n=47): sham (10 cmH2O) 50 reps × 2/day × 5/wk × 3 wk	Muscles: inspiratory+ expiratory Device: Orygen-dual valve Resistance: 30% MIP+ 30% MEP Progression: resistance increased 10 cmH2O weekly	Respiratory complications: lung infections Timing: 0, 3 wk, 6 mo	Rc: chest x-ray or fever with abnormal clinical respiratory signs (medical records and telephone interviews) Timing: 0, 6 mo
Moon et al,[39] 2017, Korea	RCT (NR) N=18	Exp (n=9): EMT 30 min × 5/wk × 4 wk Con (n=9): nothing	Muscles: expiratory Device: EMST150 Resistance: 70% MEP Progression: fixed	Swallowing function: PAS (0-8) (by VFSS) Timing: 0, 4 wk	—
Park et al,[40] 2016, Korea	RCT (random envelopes) N=27	Exp (n=14): EMT 25 reps × 5/wk × 4 wk Con (n=13): sham (no spring loading)	Muscles: expiratory Device: NR Resistance: 70% MEP Progression: fixed	Swallowing function: PAS (0-8) FOIS (1-7) Timing: 0, 4 wk	—
Yoo et al,[41] 2018, Korea	RCT (computer-generated random list) N=40	Exp (n=20): IMT + EMT 30 min × 2/day × 5/wk × 3 wk Con (n=20): nothing	Muscles: inspiratory+ expiratory Device: flow-oriented incentive spirometer +Acapella vibratory PEP device Resistance: not quantitative Progression: resistance was adjusted according to tolerance	Respiratory complications: pneumonia Timing: 0, 3 wk	Rc: clinical findings: new lung infiltration on imaging studies plus clinical evidence that the infiltrate was of infectious origin, which includes the new onset of fever, purulent sputum, leukocytosis, and a decline in oxygenation Timing: 0, 3 wk
Choi et al,[42] 2021, South Korea	RCT (NR) N=44	Exp (n=22): IMT + EMT 30 min × 5/wk × 4 wk Con (n=22): nothing	Muscles: inspiratory+ expiratory Device: POWERbreathe (POWERbreathe	Respiratory complications: pneumonia Cough function:	Rc: patient interviews and review of medical records for 1 y after acute stroke Timing: 0, 1 y

(*continued on next page*)

Table 1 (*Continued*)

Study	Design	Intervention: Frequency and Duration	Intervention: Parameters	Outcome	Measurement of Rc or Cf
			International Ltd) + Threshold IMT/PEP (Philips Respironics) Resistance: 5-10cm H_2O (POWERbreathe) + 50% MIP (Threshold IMT) + 50% MEP (Threshold PEP) Progression: pressure was increased by 2 cmH20 (IMT) and 1 cmH20 (EMT) as the patients became accustomed to the resistance	PECF-VC (L/min) Timing: 0, 4 wk	Cf: asthma mentor peak flow meter (Respironics) Timing: 0, 3 wk

Abbreviations: Cf, cough function; Con, control group; EMT, expiratory muscle training; Exp, experimental group; IEMT, inspiratory and expiratory muscle training; IMT, inspiratory muscle training; NR, not reported; Rc, respiratory complications; RC, reflex cough; reps, repetitions; VC, voluntary cough; VFSS, videofluoroscopic swallowing study.

Risk of bias assessment

The outcomes of quality assessment of the studies were input into the Review Manager 5.3 software according to the quality assessment judgment criteria (figs 2 and 3). The risk of bias was assessed as low, high, or unclear risk. Most of the studies had a low risk of bias for random sequence generation, allocation concealment, blinding of participants and personnel, and blinding of outcome data. All studies had a low risk of bias for incomplete outcome data, selective reporting, and other sources of bias. Seven trials were RCTs with a clear method of randomization,[13,19,20,37,38,40] and 4 trials were alleged RCTs but had unknown methodology and were thus defined as possible RCTs.[35,36,39,42]

Participants

The mean age of participants ranged from 34 to 86 years across trials. The mean time after stroke ranged from 8.8 days to 24 months. The majority of trials (87%) comprised participants who were within 3 months of stroke onset at the time of admission to the trial. In total, 242 stroke participants had dysphagia confirmed by videofluoroscopic swallowing study or bedside swallowing assessment.[19] Bedside swallowing assessment was performed by trained nursing staff, according to an algorithm and including evaluation of level of consciousness, oromotor function, and trials of water and food. Any concerns triggered review by a speech and language therapist.

Intervention

In all trials, the experimental intervention was respiratory muscle training delivered by a threshold resistance trainer or flow-oriented resistance trainer. The respiratory muscle training targeted the expiratory muscles,[20,35,39,40] a combination of inspiratory and expiratory muscles,[13,37,38,41,42] and inspiratory and expiratory muscles to separate participants.[19,36] Participants undertook training for 30 to 40 minutes (or 25 to 50 repetitions), 4 to 14 times per week for 3 to 13 weeks. In all trials, the control intervention was noor sham respiratory intervention.[19,20,35,36,38,40] Sham intervention was delivered via a threshold trainer with no resistance valve or a small resistance of the respiratory muscle strength (10% maximal inspiratory pressure/maximal expiratory pressure or 10c mH_2O).

Outcome measures

Occurrence of respiratory complications was measured in 7 trials[13,19,20,36,38,41,42]; it was reported as number of participants with pneumonia in 5 trials[13,19,36,41,42] and as number of participants with lung infections in 1 trial[20] after the commencement of training. In Menezes et al's trial,[38] there was no specific information about respiratory complications. Swallowing function was measured in 5 trials using the PAS (1-8 points) in 4 trials[13,35,39,40] and FOIS (1-7 points) in 3 trials.[13,37,40] Cough function was measured in 4 trials[19,36,37,42] using PECF-VC or PECF-RC.

Respiratory complications

The effect of respiratory muscle training on respiratory complications was examined by pooling the data from 7 trials.[13,19,20,36,38,41,42] With the consideration of the effect of clinical heterogeneity, the study by Parreiras de Menezes et al[38] was separated because of the time limitation (3 month $\leq$ time since stroke $\leq$5 year), which was completely at the chronic stage. Others were at the early stage (acute and subacute stage, $\leq$3 month). Therefore a total of 6 trials (n=394) were included in the meta-analysis. The likelihood of respiratory complications was significantly lower after respiratory muscle training (RR, 0.51; 95% CI, 0.28-0.93; I^2=0%; P=.03) compared with no or sham respiratory intervention (fig 4). The absolute risk difference was 0.068 and the number need to treat was 14.71.

Swallowing function

PAS

The effect of respiratory muscle training on swallowing function based on PAS was examined by pooling data from 4 trials.[13,35,39,40] However, complete data extraction failed in the Guillen-Solà et al trial.[13] Therefore a total of 3 trials (n= 71) were included in the meta-analysis. When a fixed-effects model was applied, respiratory muscle training decreased PAS scores by 0.81 (95% CI, −1.19 to −0.43; I^2=39%; P<.0001) compared with no or sham respiratory intervention (fig 5).

FOIS

The effect of respiratory muscle training on swallowing function based on FOIS was examined by pooling data from 3 trials.[13,37,40] In Guillen-Solà et al's trial,[13] there was no specific

Table 2 Characteristics of interventions

Study	Design	Participants	Stroke Site/ Hemiplegia	Exp (Exp 1/Exp 2)/ Con, n (%)	Stroke Etiology/Type	Exp (Exp 1/Exp 2)/ Con, n (%)
Eom et al,[35] 2017, Korea	RCT (NR) N=26	Exp (n=13): Age: 69.2±4.1 y Con (n=13): Age: 70.2±3.6 y Time since stroke: <3 mo All participants with dysphagia	Middle cerebral artery Basal ganglia Midbrain Frontal lobe Internal capsule Pons	9/9 0/1 1/0 1/1 1/1 1/1	—	—
Guillen-Solà et al,[13] 2016, Spain	RCT (computer-generated random list) N=33	Exp 1 (n=16): Age: 67.9±10.6 y Con (n=17): Age: 68.9±7.0 y Time since stroke: ≤1 to ≤3 wk All participants with dysphagia	Right Left Bilateral/ataxia	40%/38.1% 55%/57.1% 5%/4.8%	Atherosclerosis Cardioembolism Lacunar Other determined etiology Undetermined etiology Missing data	30%/28.6% 35%/33.3% 0%/9.5% 0%/0% 35%/23.8% 0%/4.8%
Wang et al,[36] 2019, China	RCT (NR) N=98	Exp 1 (n=33): Age: 66.43±13.95 y Exp 2 (n=32): Age: 62.67±14.39 y Con (n=33): Age: 64.07±10.82 y Time since stroke: ≤2 wk Dysphagia: NR	Left Right	14/17/13 19/15/20	Ischemic Hemorrhagic	26/23/29 7/9/4
Kulnik et al,[19] 2015, United Kingdom	RCT (random number) N=78	Exp 1 (n=27): Age: 65.7±15.4 y Unsafe swallow: 13 (48%) Exp 2 (n=26): Age: 62.5±14.6 y Unsafe swallow: 10 (38%) Con (n=25): Age: 65.1±13.9 y Unsafe swallow: 12 (48%) Time since stroke: ≤0.5 mo	Left Right Bilateral Cortical Subcortical Brainstem/cerebellar	10/8/11 17/17/14 —/1/— 12/10/11 14/12/8 1/4/6	Ischemic Hemorrhagic	22/23/24 5/3/1
Liaw et al,[37] 2020, China (Taiwan)	RCT (random number) N=21	Exp (n=10): Age: 66.80±11.47 y Swallowing disturbance: 6 (60.00%) Con (n=11): Age: 61.18±10.69 y Swallowing disturbance: 8 (66.67%) Time since stroke: 2.67±1.46 mo	Right Left	40.00%/33.33% 60.00%/66.66%	Hemorrhage Ischemic	40.00%/66.66% 60.00%/33.33%
Parreiras de Menezes et al,[38] 2018, Brazil	RCT (random number) N=37	Exp (n=19): Age: 60±14 y Con (n=18): Age: 67±11 y Time since stroke: ≤3 mo to ≤5 y Swallowing disorder: NR	Right Left Unknown	63%/32% 32%/58% 5%/10%	Ischemic Hemorrhagic Unknown	63%/79% 16%/16% 21%/5%
Messaggi-Sartor et al,[20] 2015, Spain	RCT (random number) N=101	Exp (n=54): Age: 65.6±11.4 y Dysphagia: 81.7% Con (n=47): Age: 67.6±10.9 y Dysphagia: 88.7% Time since stroke: <3 wk	Right Left	54%/59% 46%/41%	Cardioembolic Small vessel Undetermined Atherothrombotic	20.4%/24.5% 18.5%/18.9% 33.5%/30.2% 25%/18.9%
Moon et al,[39] 2017, Korea	RCT (NR) N=18	Exp (n=9): Age: 63.0±5.8 y Con (n=9): Age: 63.1±5.2 y Time since stroke: ≤1 mo All participants with dysphagia	Left Righ	4/5 5/4	Ischemic Hemorrhagic	6/7 3/2
Park et al,[40] 2016, Korea	RCT (random envelopes) N=27	Exp (n=14): Age: 64.3±10.7 y Con (n=13): Age: 65.8±11.3 y Time since stroke: ≤6 mo All participants with dysphagia	Middle cerebral artery Basal ganglia Midbrain Frontal lobe Internal capsule Corona radiate Pons	5/4 2/1 2/1 2/2 1/2 1/1 1/2	—	—
Yoo et al,[41] 2018, Korea	RCT (computer-generated random list) N=40	Exp (n=20): Age: 57 (34-82) y Aspiration: 10% Con (n=20): Age: 65 (34-86) y Aspiration: 10% Time since stroke: ≤3 mo	Right Left	11/9 9/11	Ischemic Hemorrhagic	11/12 9/8
Choi et al,[42] 2021, South Korea	RCT (NR) N=44	Exp (n=22): Age: 67.6±12.4 y Con (n=22): Age: 67.2±13.3 y Time since stroke: ≤2 wk Dysphagia: NR	Right Left Both None	5/7 15/11 2/3 0/1	Ischemic Hemorrhagic	16/15 6/7

NOTE. Outcome measures listed are only those that were analyzed in this systematic review.
Abbreviations: Con, control group; Exp, experimental group; NR, not reported.

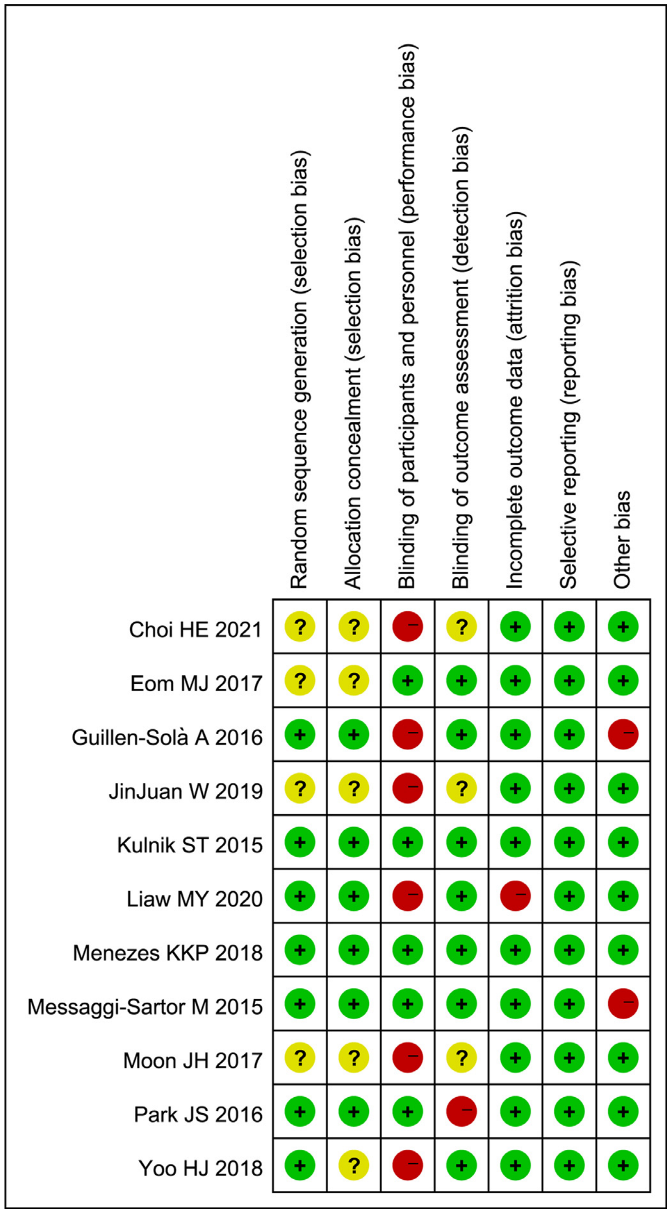

Fig 2 Risk of bias summary.

postintervention data and it was reported only that FOIS improved 0.76 (SD, 1.1) points after completing intervention and 1.76 (SD, 1.1) points at the 3-month follow-up. Therefore a total of 2 trials (n= 48) were included in the meta-analysis. When a random effects model was applied, there was no significant association between respiratory muscle training and the FOIS scores, which increased by 0.47 (95% CI, −0.45 to 1.39; I^2=55%; P=.32) compared with no or sham respiratory intervention (fig 6).

Cough function

PECF-VC

The effect of respiratory muscle training on cough function based on PECF-VC was examined by pooling data from 4 trials[19,36,37,42] (n=226), When a fixed-effects model was applied, there was no significant association between respiratory muscle training and PECF-VC, which decreased by 18.70 L per minute (95% CI, −59.74 to 22.33; I^2=19%; P=.37) compared with no or sham respiratory intervention (fig 7).

PECF-RC

The effect of respiratory muscle training on cough function based on PECF-RC was examined by pooling data from 2 trials[19,36] (n = 161). When a fixed-effects model was applied, there was no significant association between respiratory muscle training and PECF-RC, which increased by 0.05 L per minute (95% CI, −40.78 to 40.87; I2=0%; P>.99) compared with no or sham respiratory intervention (fig 8).

Discussion

Safe swallowing can prevent foreign materials from aspirating into the airway during the swallowing process. An effective and strong voluntary cough could reduce penetration and aspiration by

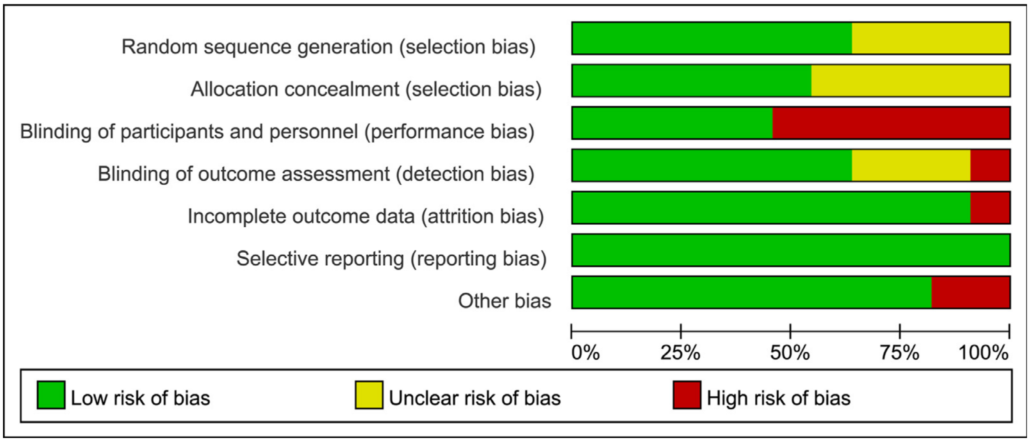

Fig 3 Risk of bias graph.

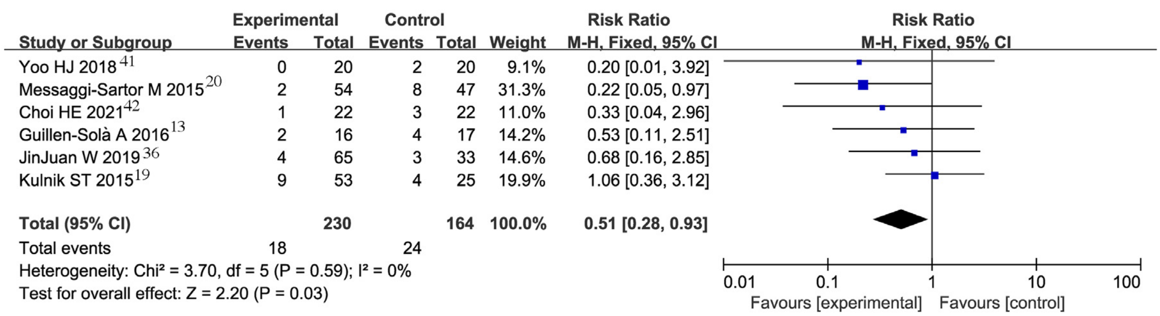

Fig 4 Respiratory complications forest plot showing RR (95% CI) of respiratory complications after respiratory muscle training versus no or sham respiratory intervention (n=394).

removing foreign materials, even after food enters the airway. Clinical interventions, such as improving swallowing or cough

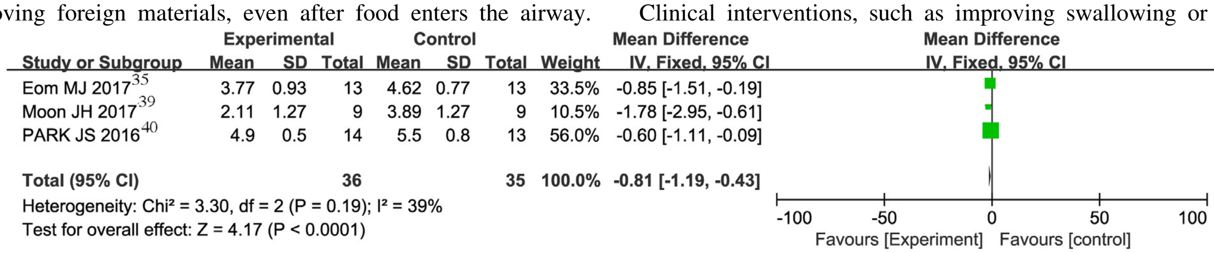

Fig 5 PAS forest plot showing the mean difference (95% CI) of the effect of respiratory muscle training versus no or sham respiratory intervention on PAS score (n=71).

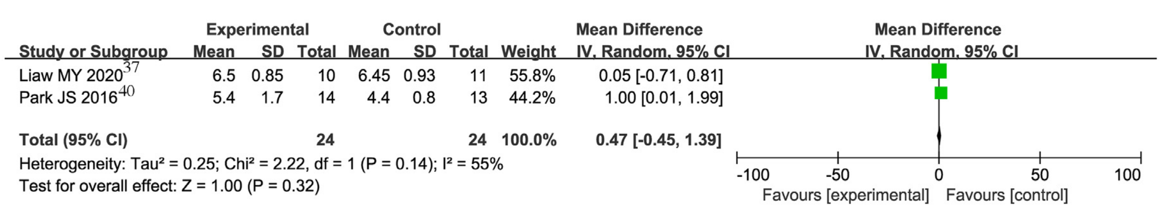

Fig 6 FOIS forest plot showing the mean difference (95% CI) of the effect of respiratory muscle training versus no or sham respiratory intervention on FOIS score (n=48).

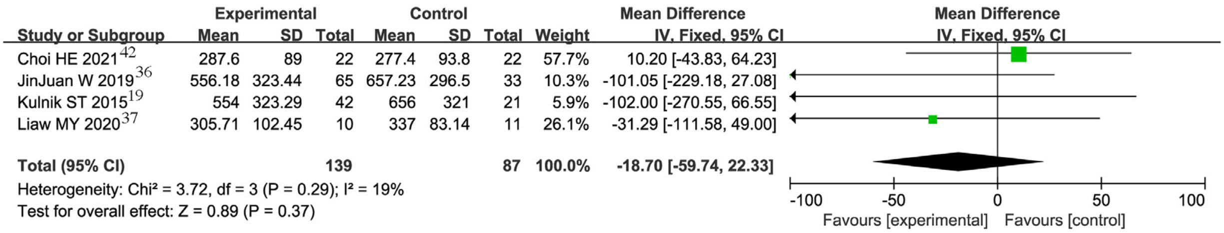

Fig 7 PECF-VC forest plot showing the mean difference (95% CI) of the effect of respiratory muscle training versus no or sham respiratory intervention on PECF-VC in L per minute (n=226).

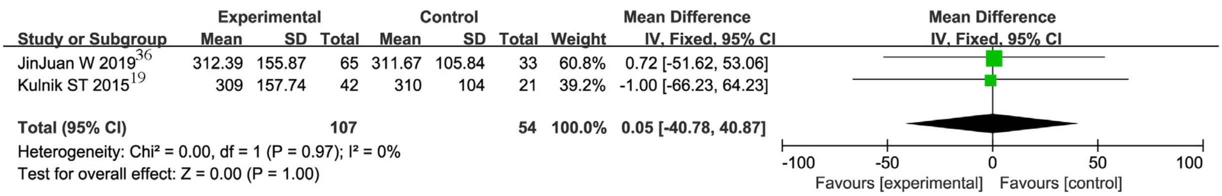

Fig 8 RC forest plot showing th mean difference (95% CI) of the effect of respiratory muscle training versus no or sham respiratory intervention on PECF-RC in L per minute (n=161).

function, could reduce the occurrence of respiratory complications. Based on this assumption, this review set out to answer 2 questions: (1) Does respiratory muscle training reduce the occurrence of respiratory complications after stroke; and (2) Does respiratory muscle training improve the swallowing function after stroke?

For the first question, this meta-analysis demonstrated that respiratory muscle training reduced the RR of respiratory complications immediately or 3 to 12 months after treatment initiation for the stroke participants who were at the early stage. However, we were unable to complete the meta-analysis for stroke participants who were at the chronic stage because only 1 study reported by Parreiras de Menezes et al[38] was included. This study reported that there was no significant between-group difference for respiratory complications. Although the power of analysis was increased by applying strict inclusion criteria, several limitations must be addressed. First, in the majority of trials, the incidence between the end of the intervention period and the final follow-up were captured, with some participants lost to follow-up, and only 1 trial[19] reported data on the intention to treat. Second, there are several independent risk factors for poststroke pneumonia.[3,43] Therefore, a statistical model that adjusted for potential confounders for respiratory complications was applied in analysis to ensure precise results. Third, even though the early and chronic stages were separated in analysis, this study failed to separate the early stage into acute and subacute stroke stages among the 6 studies. It is assumed that a higher occurrence of respiratory complications manifests during the acute stage.[1] Therefore, additional multicenter studies using larger patient cohorts and better methodological quality are required.

For the second question, sufficient data were not provided to determine whether respiratory muscle training was able to improve swallowing function based on FOIS scores. Based on the liquid-type PAS scores, preliminary evidence from 3 trials[35,39,40] demonstrated a reduction in the scores after respiratory muscle training. Possible explanations for this "seemingly contradictory result" could be due to several reasons. First, FOIS documents the functional level of oral intake food and liquid, as well as considering the use of enteral nutrition. Enteral nutrition may be necessary to avoid malnutrition in cases of severe dysphagia.[44] PAS as an objective evaluation describes fundamental aspects of dysphagia, but clinical outcome can be influenced by other important parameters (eg, awareness, collaboration, cognitive abilities, presence of apraxia, or speech impairment like aphasia), which can compromise the ability to understand language. The presence of these types of impairment can add further difficulties in the deglutition process and may reduce the success rate of swallowing treatment. Second, a previous cross-sectional study[45] demonstrated that FOIS, compared with PAS for identifying dysphagia for liquids, had a sensitivity of 6.3% and a specificity of 94.9%. For semisolids, the sensitivity was 6.1% and specificity was 95.5%. Thus, although the sensitivity of PAS is high, the specificity is lower than FOIS. Third, the sample size was small, with only 3 trials with 71 participants included. The results only reported liquid-type PAS scores, because most of the trials only assessed the effects of the training using standard thin liquid bolus. Only the trial performed by Park et al[40] evaluated training using semisolid bolus. After training, they found a significant difference in liquid-type PAS scores, but not for the semisolid type PAS scores (P=.03 and .32, respectively). Comparing the levels of change for both groups, significant differences were observed for only liquid-type PAS scores (P=.03) and not for semisolid type PAS scores (P=.38). Studies have shown that 62% of survivors were provided some form of modified diet or thickened fluids or were "nil by mouth" 2 days after hospital admission, which is comparable to the literature for patients with first-ever stroke.[46,47] Hence, it is important that future studies assess the swallowing function of oral intake of different bolus types to identify patterns of abnormal swallowing that may reflect different underlying etiologies of dysphagia.

However, the positive result of the liquid-type PAS scores suggested that respiratory muscle training reduced laryngeal penetration and aspiration during liquid bolus swallowing. This has potentially important implications for the management of dysphagia in stroke survivors. Similar results were observed in previous reviews[22,23] and showed that respiratory muscle training improved muscle and neural adaptations to recover swallowing function. Expiratory muscle training promotes the activation of the suprahyoid muscles that play a major role to elevate the hyolaryngeal complex and open the upper esophageal sphincter necessary for swallowing.[48] This is known to have a direct effect on decreasing aspiration and pharyngeal residues.[49] Furthermore, respiratory muscle training enhances the orofacial muscles, such as the submental, palatal, lingual, velopharyngeal, and pharyngeal musculature. This is important to coordinate bolus transport during swallowing, maintenance of swallowing safety and efficiency, and functional improvements.[48] Lastly, afferent stimulation of the sensory receptors of the tongue and oropharynx provided by respiratory muscle training may increase the activity of the swallowing center in the medulla oblongata of the brainstem.[50,51]

Based on a previous study,[52] voluntary coughs have been closely related to aspiration in terms of airway protection mechanism during swallowing. It was found that the intensity of coughing correlated with the risk of airway aspiration. The positive outcomes of respiratory muscle training on reducing PAS scores may indicate the ability to improve cough function. However, this meta-analysis failed to provide sufficient evidence to demonstrate any effects on PECF-VC or PECF-RC after respiratory muscle training. Possible explanations could be due to several reasons. First, even though the inspiratory and expiratory muscle strength after acute stroke patients was approximately half compared with healthy age-matched controls,[53] the weakness in cough observed in stroke patients was shown to be related to reduced cortical influences that modulate cough production, rather than peripheral muscle weakness.[53-55] In addition to respiratory muscle weakness, changes in chest wall kinematics could also be responsible for impaired cough after stroke.[55] Second, although an effective cough requires coordinated activation of inspiratory and expiratory muscles, PECF requires a short duration and isometric contraction of expiratory muscles to generate maximal pressure. This suggests that expiratory muscle strength is dominant in generating PECF. However, a previous meta-analysis[56] demonstrated that respiratory muscle training improves inspiratory, but not expiratory, muscle strength. This is because active inspiratory volume is a precondition for forceful expiration or cough flow. Hence, it seems reasonable that longer training is required for restoring expiratory muscle strength. Additionally, reflex cough is believed to originate primarily in the brainstem in response to food swallowing or inhalation of noxious substance. Several studies have demonstrated that reflex cough is more important than a voluntary cough in ensuring adequate airway protection and clearance after acute stroke.[26,25] However, reflex cough produced in the laboratory does not accurately replicate the response to aspirated fluids or food, which cannot be easily studied for safety reasons and patient discomfort considerations.[54] In addition, it is worth noting that peak expiratory cough flow is only one aspect to reflect cough function. Because the limitation of small sample size, other equally important measures were not included in this review, such as cough expired volume or cough volume acceleration. Thus, more studies evaluating the cough function comprehensively are recommended, before drawing definitive conclusions regarding clinically worthwhile effects in the future.

Lastly, in this meta-analysis review, one adverse event was reported in the trial conducted by Parreiras de Menezes et al.[38] A study participant who was in the experimental group terminated training after 2 weeks due to chest pain. The theoretical risks of elevated thoracic pressure or repeated Valsalva maneuvers performed in patients with stroke or cardiovascular comorbidities should be seriously considered during therapy.

Study limitations

The main limitations of this review can be deduced from the GRADE evidence profile. The small sample size was one of the most important factors leading to imprecision in this mete-analysis, especially for the outcome of PAS scores and FOIS scores as they only included 71 and 48 samples, respectively. In addition, from the total of 11 studies included in this systematic review, 6 only recruited unilateral stroke patients; 5 recruited both unilateral and bilateral stroke patients. There is no doubt that it is better to perform subgroup analysis to allow for more precise conclusions. However, the subgroup analysis was blocked in this study as we failed to obtain the original data. Also, although the power of analysis was increased by applying strict inclusion criteria, the presence of various of risk of bias for each included study such as the risk of performance bias, attrition bias, or detection bias became the other primary factors that lower the level of evidence. In view of the relative contradiction between enlarging the sample size and more rigorous studies' screening processes, more high quality RCTs are encouraged in the future to provide a high level of GRADE evidence.

Conclusions

This systematic review provides evidence that respiratory muscle training is effective in reducing the risk of respiratory complications (pneumonia, lung infection). Furthermore, it improved dysphagia by reducing penetration or aspiration during swallowing liquid bolus after stroke. The results of the meta-analysis indicated that 20 to 30 minutes of respiratory muscle training 5 times per week for 4 to 5 weeks could improve swallowing function and reduce the risk of respiratory complications after stroke. However, no significant effects of respiratory muscle training on improving cough function after stroke were observed. Additional multicenter studies using larger patient cohorts are required to validate and support these findings. Furthermore, long-term follow-up studies should be performed to measure outcomes, while avoiding bias due to confounding factors such as heterogeneity of the etiologies of dysphagia.

Supplier

a. Review Manager 5.3; Cochrane Training.

Keywords

Breathing exercises; Deglutition disorders; Rehabilitation; Stroke; Systematic review

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