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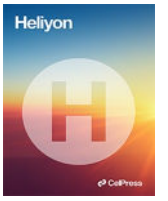

Research article

Effect of respiratory muscle training in patients with stable chronic obstructive pulmonary disease: A systematic review and meta-analysis

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ABSTRACT

Objectives: Chronic obstructive pulmonary disease (COPD) is a prevalent respiratory disorder characterized by progressive airflow limitation. This meta-analysis aims to evaluate the effectiveness of respiratory muscle training (RMT) on key pulmonary function parameters, inspiratory muscle strength and quality of life in patients with stable COPD.

Methods: A comprehensive search was conducted in the databases including PubMed, Cochrane, Web of Science, Embase, and ClinicalTrials.gov, from their inception to June 12, 2023. Randomized controlled trials (RCTs) evaluating the impact of RMT on stable COPD were included for meta-analysis.

Results: In total, 12 RCTs involving 453 participants were included in the meta-analysis. RMT demonstrated a significant increase in maximal inspiratory pressure (PImax, MD, 95% CI: 14.34, 8.17 to 20.51, $P < 0.001$) but not on maximal expiratory pressure (PEmax). No significant improvement was observed in 6-Min walk test (6MWT), dyspnea, forced expiratory volume in 1 s (FEV_1), forced vital capacity ratio (FVC) and quality of life between RMT and control groups. However, subgroup analysis revealed a significant negative effect of RMT alone on FEV_1/FVC (MD, 95% CI: 2.59, −5.11 to −0.06, $P = 0.04$). When RMT was combined with other interventions, improvements in FEV1/FVC and FEV1 were found, although not statistically significant.

Conclusion: RMT can effectively improve maximal inspiratory pressure in stable COPD patients, but the effect is slight in improving lung function, dyspnea and quality of life. It is recommended

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to combine with other treatment strategies to comprehensively improve the prognosis of COPD patients.

1. Introduction

Chronic obstructive pulmonary disease (COPD) is a progressive respiratory condition characterized by airflow limitation and persistent respiratory symptoms, such as cough, sputum production, and dyspnea [1]. It is a major global health issue and a leading cause of morbidity and mortality, imposing a substantial burden on individuals, healthcare systems, and society at large [2]. Despite advancements in pharmacological interventions and pulmonary rehabilitation, the management of COPD remains challenging, necessitating the exploration of additional treatment strategies.

Respiratory muscle weakness is a common feature in patients with COPD, leading to impaired respiratory muscle function, reduced exercise tolerance, and diminished quality of life [3]. The respiratory muscles, including the diaphragm and intercostal muscles, play a vital role in generating the necessary forces for breathing [4]. In COPD, these muscles undergo structural and functional alterations, contributing to respiratory muscle dysfunction and impairing overall respiratory function [5]. Respiratory muscle training (RMT), through various techniques such as inspiratory muscle training (IMT) and expiratory muscle training (EMT), aims to improve the strength, endurance, and coordination of respiratory muscles [6]. It involves a regimen of repetitive exercises targeting the inspiratory and/or expiratory muscles to enhance their performance [7].

Several studies have investigated the potential benefits of RMT in patients with stable COPD. However, the evidence regarding its effectiveness and clinical implications remains inconclusive [8]. The variability in study designs, intervention protocols, and outcome measures contributes to the conflicting findings reported in the literature. To provide a comprehensive evaluation of the existing literature and establish a more robust understanding of the impact of RMT on COPD outcomes, a systematic review and meta-analysis are warranted.

The objective of this study is to conduct a systematic review and meta-analysis to assess the effect of RMT in patients with stable COPD. By synthesizing the available evidence from randomized controlled trials (RCTs), we aim to determine the magnitude of RMT's impact on respiratory muscle function, exercise capacity, dyspnea severity, health-related quality of life, and other relevant outcomes. Furthermore, we will explore potential sources of heterogeneity across studies, evaluate the methodological quality of the included studies, and identify research gaps that warrant further investigation.

The findings of this study are expected to provide valuable insights into the role of RMT in the management of stable COPD. By elucidating the effects of RMT on respiratory muscle function and patient-centered outcomes, we can optimize treatment strategies and potentially enhance patient outcomes, ultimately leading to reduced healthcare costs associated with COPD management.

2. Methods

This systematic review was conducted according to the PRISMA guidelines [9].

2.1. Search strategy

A comprehensive search was performed in multiple databases, including PubMed, Cochrane, Web of Science, Embase, and ClinicalTrials.gov, covering the period from their inception to June 12, 2023. The search strategy included a combination of Medical Subject Headings (MeSH) and Emtree terms, tailored to each specific database, along with free keywords. Boolean operators "AND" and "OR" were used to combine the search terms. The detailed search strategy was shown in Supplementary Table S1. Only studies evaluating the impact of RMT on stable COPD were considered for inclusion in the meta-analysis.

2.2. Eligibility criteria

The inclusion criteria were as follows: (1) patients diagnosed with COPD and having a stable respiratory condition; (2) interventions involving RMT; (3) randomized controlled trials (RCTs) comparing RMT with a non-exercising intervention (Control) or comparing RMT plus other interventions with other intervention alone; (4) assessment of outcomes related to dyspnea, quality of life, key pulmonary function parameters, and inspiratory muscle strength.

The exclusion criteria were as follows: (1) duplicate publications; (2) Conference abstracts, letters, editorials, reviews, meta-analysis, and case reports; (3) studies without sufficient data; (4) publications written in languages other than English.

2.3. Study selection, data extraction and study quality assessment

Study selection was independently assessed by 2 researchers using the eligibility criteria, and the differences were resolved through consult with the third researcher. Relevant data were extracted from the selected studies, including name of first author, year of publication, country, study design, groups with sample sizes, evaluation time, number and percentage of males, mean age, and baseline forced expiratory volume in 1 s to forced vital capacity ratio (FEV_1/FVC) [10–21]. The risk of bias was assessed using the Cochrane Collaboration tool [22].

2.4. Data analysis

All data analysis were conducted using Review Manager software (Version 5.3; Cochrane, Oxford, United Kingdom). The data were presented as mean with standard deviation (SD). Mean Difference (MD) was calculated for outcomes measured using the same scales, while Standardized Mean Difference (SMD) was used for outcomes assessed using different scoring systems. Both MD and SMD were accompanied by their respective 95% confidence intervals (CI). Heterogeneity among the included studies was assessed by the Chi-square test, and the inconsistency was measured using the I^2 statistics. The random effects (Chi-square test $P \leq 0.10$) or fixed-effects (Chi-square test $P > 0.10$) model was used based on the significance of the Chi-square test. The statistical significance of the pooled estimates was determined using Z-test, with a P value of <0.05 considered as statistically significant. Publication bias was assessed by visualizing a funnel plot.

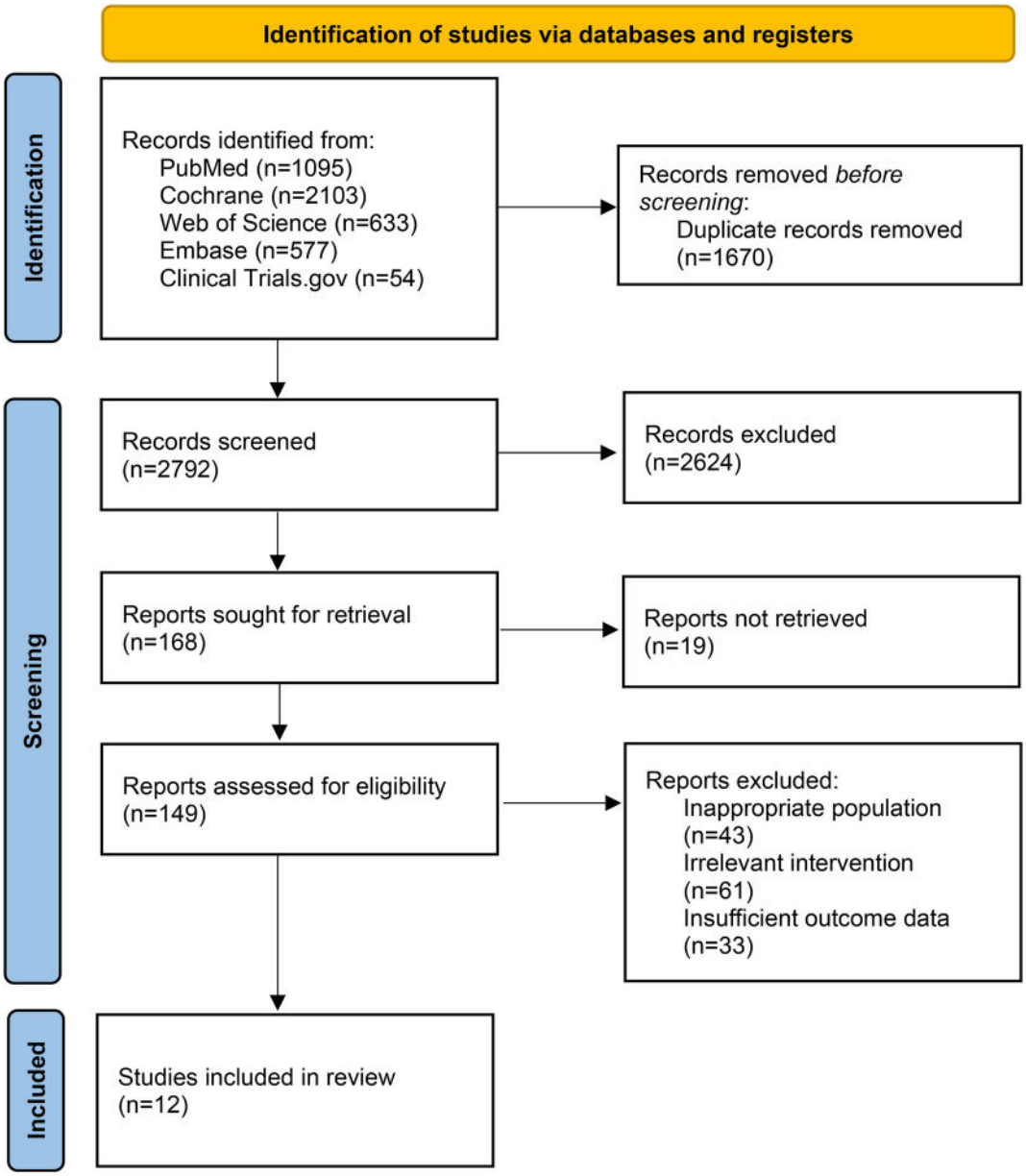

Fig. 1. Flow diagram for the selected studies.

3. Results

3.1. Study properties

A total of 4462 articles were included from 5 databases. After excluding duplicates and ineligible articles, finally 12 RCTs consisting of 453 COPD patients were selected for meta-analysis (Fig. 1). The studies compared various RMT interventions including inspiratory muscle training (IMT), respiratory muscle endurance training (RMET), expiratory muscle training, pranayama breathing training, to control groups with sham training or health education. Some studies also included combination interventions like IMT + cycle ergometry training (CET) and pulmonary rehabilitation (PR) + IMT. The selected RCTs were published between 1999 and 2022, and conducted in various countries (see Table 1). The quality of the included methodological quality RCTs was assessed using the Cochrane risk of bias tool. The assessment highlighted a limitation in terms of allocation concealment, which can be attributed to the inherent challenges of blinding the patients to their allocation in interventions involving RMT. As RMT necessitates active engagement and physical exercises, complete blinding becomes challenging since participants are likely to be aware of the specific intervention they are receiving (Fig. 2A and B).

Table 1
Characteristics of the included studies.

	Country	Study design	Groups (n)	Evaluation time	Male sex, n (%)	Age(year)	FEV_1/FVC baseline(%)
Larson 1999	USA	RCT	IMT, n = 13 CET, n = 14 CET + IMT, n = 14 ED, n = 12	4 months	35 (66.04)	IMT, 66 ± 5 CET, 66 ± 6 CET + IMT, 68 ± 6 ED, 62 ± 7	IMT, 44 ± 9 CET, 39 ± 9 CET + IMT, 40 ± 9 ED, 42 ± 16
Sánchez Riera 2001	Spain	RCT	Group T (IMT), n = 10 Group C (Control), n = 10	6 months	18 (90)	IMT, 67 ± 4 Control, 67.6 ± 5	NR
Beckerman 2005	Israel	RCT	IMT, n = 21 Control, n = 21	1 year	32 (76.19)	IMT, 67.7 ± 3.6 Control, 66.9 ± 3.3	<70
Hill 2006	Australia	RCT	H-IMT, n = 18 S-IMT, n = 17	8 weeks	22 (62.86)	H-IMT, 69.4 ± 7.2 S-IMT, 66.6 ± 9.8	H-IMT, 38.7 ± 9.3 S-IMT, 37.2 ± 10.4
Koppers 2006	Netherlands	RCT	RMET, n = 18 Control Group, n = 18	5 weeks	17 (47.22)	RMET, 54.4 ± 7.7 Control Group, 57.0 ± 8.5	RMET, 46 ± 13 Control Group, 50 ± 14
Mota 2007	Spain	RCT	Expiratory training, n = 10 Sham training, n = 6	5 weeks	16 (100)	Expiratory training, 66 ± 7 Sham training, 62 ± 7	Expiratory training, 32 ± 2 Sham training, 32 ± 4
Yamaguti 2012	Brazil	RCT	TG, n = 15 CG, n = 15	4 weeks	22 (73)	TG, 66.5 CG, 66.4	TG, 40.3 CG, 39.9
Majewska-Pulsakowska 2016	Poland	RCT	Group 1 (IMT), n = 8 Group 2 (CET), n = 9 Group 3 (IMT + CET), n = 13 Group 4 (Control), n = 13	8 weeks	22 (58.14)	Group 1, 63.4 ± 9.8 Group 2, 62.3 ± 5.2 Group 3, 61.5 ± 6.1 Group 4, 65.5 ± 7.0	NR
Kaminsky 2017	USA	RCT	Pranayama group, n = 21 Control group, n = 22	12 weeks	17 (39.53)	Pranayama group, 68 ± 7 Control group, 68 ± 9	NR
Cutrim 2019	Brazil	RCT	Control, n = 11 IMT, n = 11	12 weeks	17 (77.27)	Control, 70 ± 8.0 IMT, 66 ± 8.5	NR
Yekefallah 2019	Iran	RCT	Control, n = 25 Upper limb exercise, n = 25 Breathing exercise, n = 25	1 month	55 (73.33)	Control, 64.2 ± 13.4 Upper limb exercise, 65.5 ± 11.3 Breathing exercise, 68.8 ± 16.1	NR
Noor 2022	Pakistan	RCT	Group A (Pulmonary rehab along with IMT), n = 26 Group B (Pulmonary rehab only),n = 26	4 weeks	NR	Group A, 30.46 ± 6.94 Group B, 29.57 ± 6.21	NR

FEV_1, forced expiratory volume in 1 s; FVC, forced vital capacity; RCT, randomized controlled trial; IMT, inspiratory muscle training; CET, Cycle ergometry training; ED, Health education; m ± SD, mean ± standard deviation; NR, not reported; H-IMT, high-intensity IMT; S-IMT, sham IMT; RMET, respiratory muscle endurance training; TG, training group; CG, control group; Pulmonary rehab, Standardized pulmonary rehabilitation program; COPD, chronic obstructive pulmonary disease.

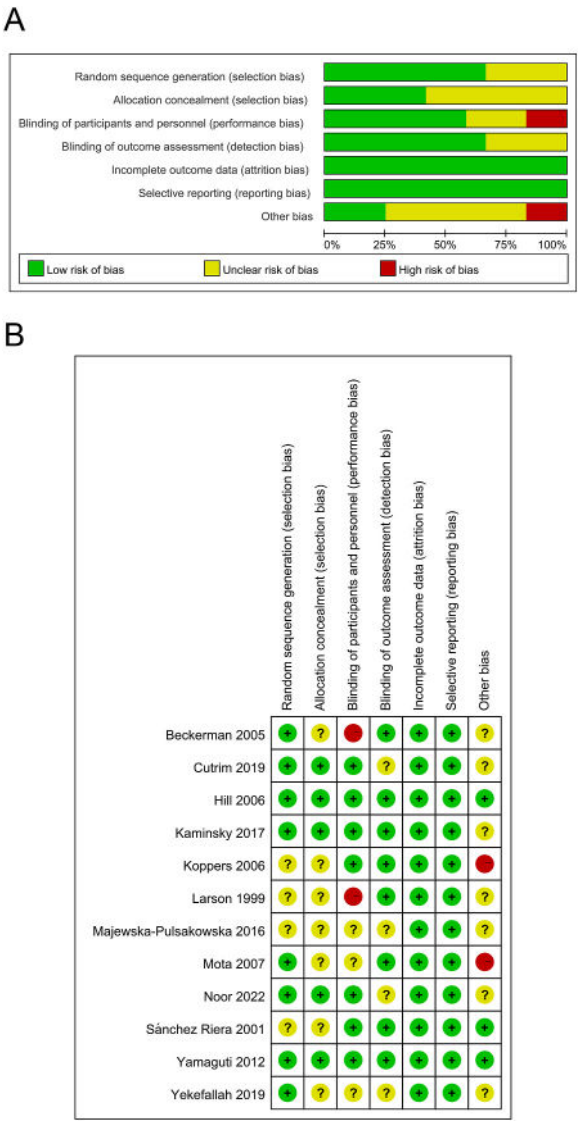

Fig. 2. Risk of bias assessment. (A) Risk of bias graph; (B) Risk of bias summary.

3.2. 6-Min walk test (6MWT)

In total, 7 RCTs analyzed 6MWT. The results showed that value of 6MWT was not significantly changed after RMT compared with the control group (MD, 95% CI: 10.27, −8.04 to 28.59, P = 0.27) (Fig. 3).

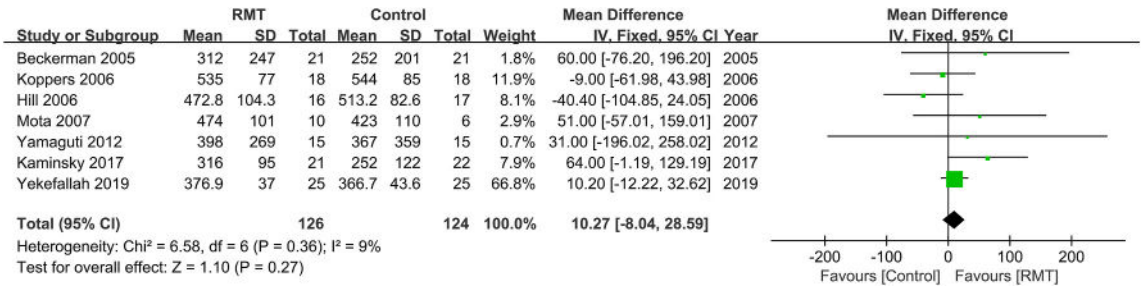

Fig. 3. Effect of RMT on 6-Min walk test (6MWT) in patients with stable COPD.

3.3. Dyspnea

Of the 12 studies, 6 RCTs analyzed the dyspnea during exercise using Borg scale or modified Borg scale, 5 RCTs assessed the dyspnea in daily life with dyspnea dimension of Chronic Respiratory Questionnaire (CRQ) or modified Medical Research Council (mMRC) scale. No significant difference was observed neither in dyspnea during exercise (MD, 95% CI: 0.37, −1.17 to 0.43, P = 0.36) nor dyspnea in daily life (CRQ: SMD, 95% CI: 0.62, −0.85 to 2.08, P = 0.41; mMRC: MD, 95% CI: 0.24, −0.73 to 0.24, P = 0.33) between patients receiving RMT or sham training (Fig. 4A–C).

3.4. Pulmonary function

In Fig. 5A–C, the results indicated that there was no significant improvement in FEV_1/FVC, FEV_1 and FVC among stable COPD patients receiving RMT treatment (all P > 0.05). Then, subgroup analysis further revealed that RMT alone had a significant negative effect on FEV_1/FVC (MD, 95% CI: 2.59, −5.11 to −0.06, P = 0.04), while no significant effects were observed on FEV_1 and FVC (both P > 0.05). However, when RMT was combined with other interventions, there were improvements in FEV_1/FVC and FEV_1 compared to the interventions used alone, although these differences did not reach statistical significance.

3.5. Inspiratory muscle strength

As depicted in Fig. 6A, there was a significant increase in maximal inspiratory pressure (PImax) among stable COPD patients receiving RMT alone compared to the control group (MD, 95% CI: 14.34, 8.17 to 20.51, P < 0.001). However, there were no significant changes observed in maximal expiratory pressure (PEmax; MD, 95% CI: 10.44, −7.63 to 28.52, P = 0.26) (Fig. 6B).

3.6. Quality of life

Only 5 RCTs assessed the impact of RMT on quality of life in stable COPD patients using CRQ or St. George's Respiratory Questionnaire (SGRQ). There was a tendency towards improvement in patients' quality of life after receiving RMT, while the differences were not statistically significant (CRQ: SMD, 95% CI: 0.51, −0.34 to 1.37, P = 0.24; SGRQ: MD, 95% CI: 5.64, −13.92 to 2.65, P = 0.18) (Fig. 7A and B).

3.7. Publication bias

The analysis did not identify any significant publication bias (Fig. S1). Due to the limited number of studies providing data for each

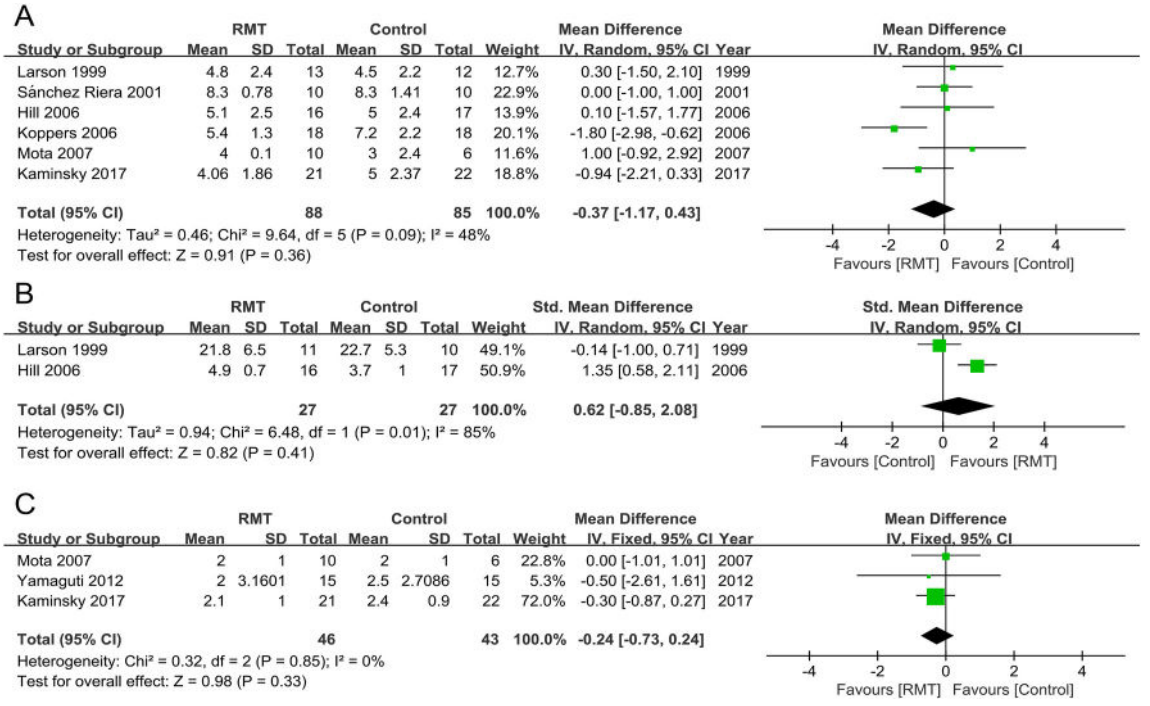

Fig. 4. Effect of RMT on dyspnea in patients with stable COPD. (A) dyspnea during exercise assessed using Borg scale or modified Borg scale; (B) dyspnea in daily life assessed using dyspnea dimension of CRQ; (C) dyspnea in daily life assessed using Mmrc scale.

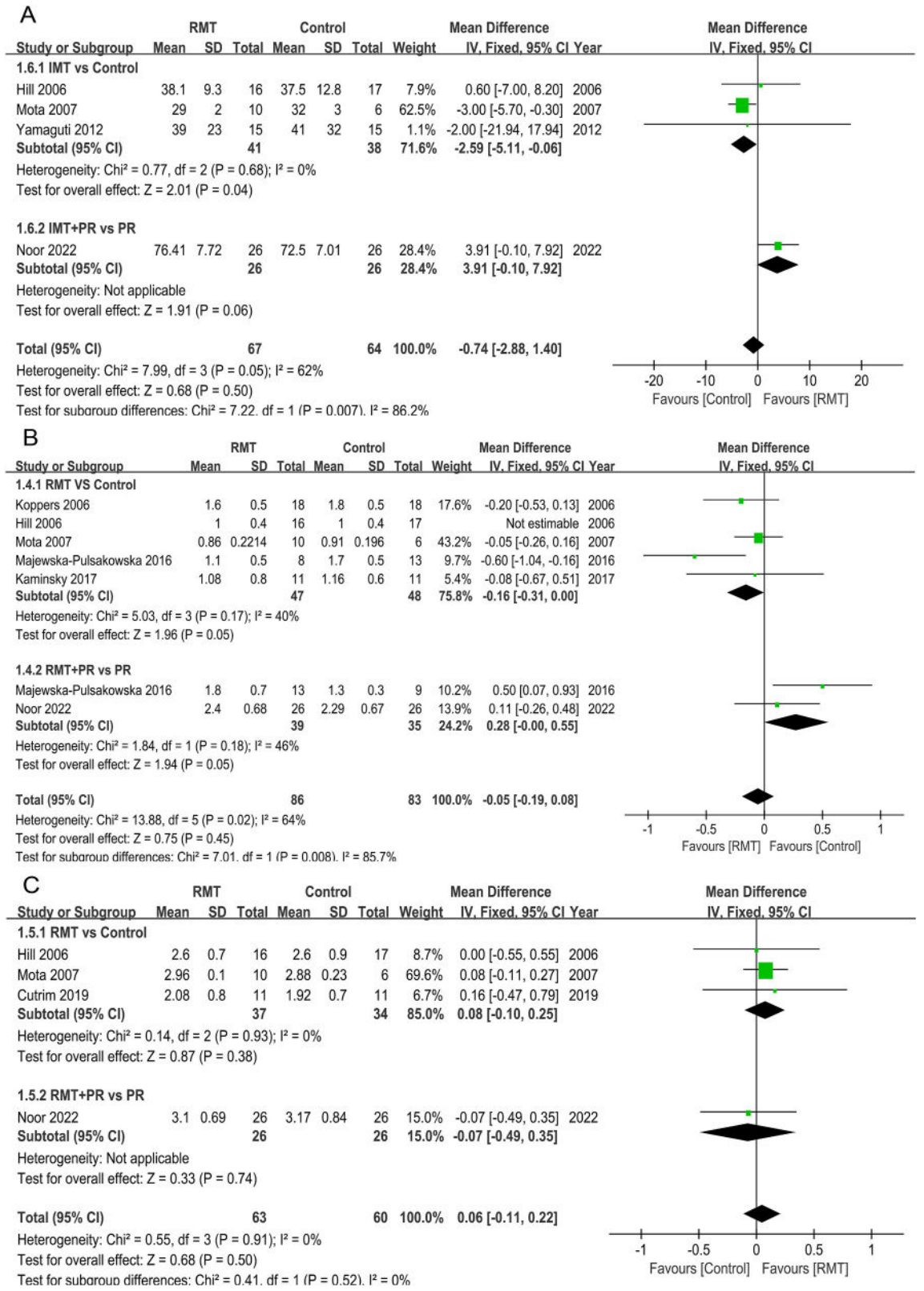

Fig. 5. Effect of RMT on pulmonary function in patients with stable COPD. (A) FEV_1/FVC; (B) FEV_1; (C) FVC.

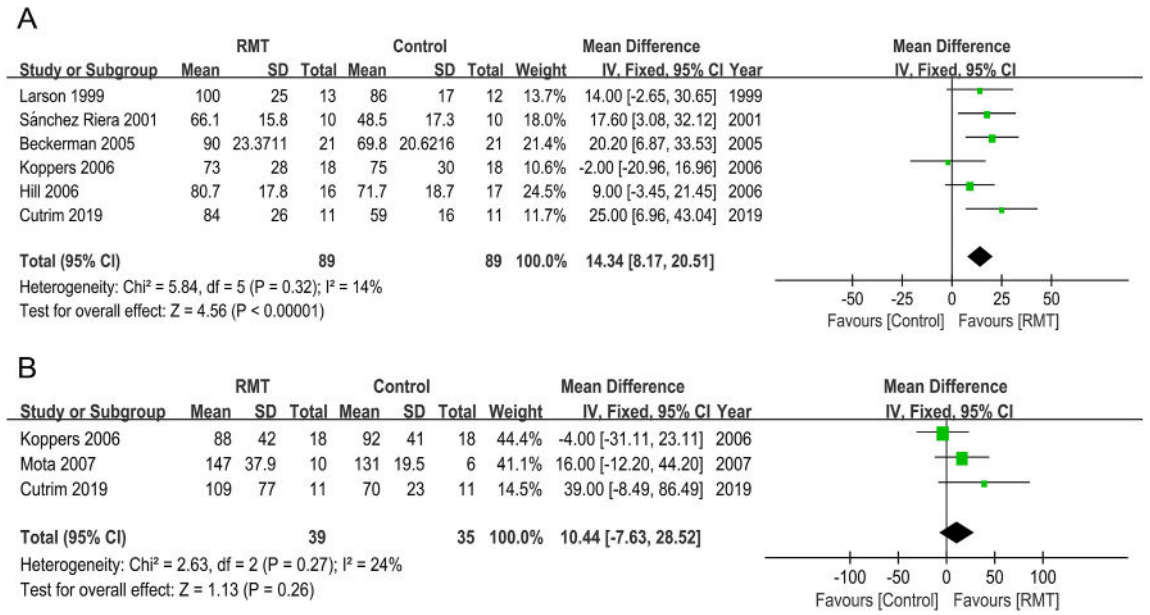

Fig. 6. Effect of RMT on inspiratory muscle strength in patients with stable COPD. (A) PImax; (B) PEmax.

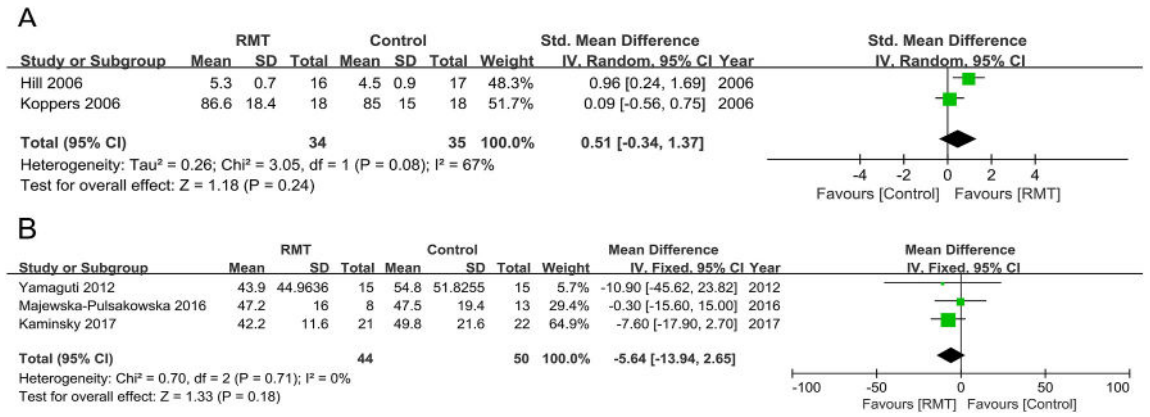

Fig. 7. Effect of RMT on quality of life in patients with stable COPD. (A) quality of life assessed using CRQ; (B) quality of life assessed using SGRQ.

outcome (less than 10 studies), Begg's or Egger's tests were not performed to formally assess publication bias.

4. Discussion

This meta-analysis was a comprehensive review of studies examining the effectiveness of RMT in patients with stable COPD, with a focus on evaluating the impact of RMT on key pulmonary function parameters, inspiratory muscle strength, and quality of life. The study found that RMT significant improved PImax in stable COPD patients and had a slightly positive effect on improving dyspnea and quality of life. In addition, RMT combined with PR or exercise training also has a certain impact on improving lung function.

The strengthening of inspiratory muscles play a crucial role in supporting respiratory mechanics [1]. Enhanced inspiratory muscle strength can lead to improved respiratory muscle endurance and reduced dyspnea during daily activities [6]. Our meta-analysis demonstrated a significant increase in PImax following RMT, while PEmax tend to increase while did not reach statistical significance, which may be related to the small sample size included. Dyspnea is a major symptom that significantly impacts the quality of life of COPD patients [23]. This meta-analysis evaluated dyspnea during both exercise and daily life. The results showed that RMT did not significantly improve dyspnea in COPD patients, contradicting some previous meta-analyses which have demonstrated benefits of RMT on dyspnea [24,25]. The lack of significant dyspnea improvement could potentially be attributed to the limited sample size and heterogeneity of RMT protocols and outcome measures used across the small number of included studies [7]. Furthermore, dyspnea is a complex multidimensional symptom with sensory-perceptual, affective distress, and impact aspects [26]. Use of comprehensive, validated multidimensional dyspnea assessment tools may better capture RMT effects on dyspnea compared to single-item ratings

[27]. Further large, high-quality RCTs employing multidimensional dyspnea assessment are warranted to clarify the effects of RMT on dyspnea burden in COPD patients.

COPD patients often experience impaired lung function, and FEV_1/FVC is widely recognized as an important indicator of airflow limitation and obstruction in patients with COPD [28]. RMT targets the respiratory muscles responsible for inhalation, including the diaphragm and intercostal muscles, which play a crucial role in generating inspiratory and expiratory forces during breathing. Strengthening these muscles through training can enhance their contractility and coordination, resulting in improved lung function parameters such as FEV_1/FVC [29]. Second, RMT may help improve the overall mechanics of breathing, leading to better airflow dynamics and reduced air trapping, which are common in COPD [7]. Lastly, the increased strength and endurance of the respiratory muscles achieved through RMT may contribute to improved respiratory efficiency, leading to a more favorable FEV_1/FVC ratio [30]. However, in contrast to the expected improvement, this study found that FEV_1/FVC significantly decreased in COPD patients after RMT, suggesting a potential further decline in lung function. This result might be related to the severity of COPD in the included patients. COPD is a progressive chronic disease, and lung function gradually declines with the disease's progression. In patients with already significant lung function impairment, respiratory muscle training may not be able to reverse the existing lung function damage. Additionally, RMT might require sufficient time to demonstrate improvements in lung function parameters. The RCTs included in this analysis evaluated patients over relatively short intervention periods, which might have limited the observation of potential effects on lung function parameters. Therefore, the positive effects of respiratory muscle training on COPD lung function cannot be entirely ruled out. Further research and more rigorous randomized controlled trials are warranted to comprehensively assess the impact of respiratory muscle training on lung function parameters in COPD patients. Furthermore, comprehensive treatment strategies, such as medication, rehabilitation plans, and respiratory support, may play a more crucial role in improving COPD patients' lung function. One of the included studies in this meta-analysis indicated that RMT combined with PR had a better effect on FEV_1/FVC compared to PR alone [21].

COPD not only affects physical health but also has a substantial impact on mental well-being and overall quality of life [31]. RMT may alleviate dyspnea, enhance exercise capacity, and improve patients' overall well-being by targeting inspiratory muscles and respiratory mechanics [13,14,17]. Although in this study, the improvements in quality of life observed in different quality of life assessment scales after RMT did not reach statistical significance, there is a positive trend. COPD is influenced by various factors, including airflow limitation, inflammation, lung damage, and systemic effects [1]. While respiratory muscle training can improve respiratory muscle strength, the improvement in quality of life may require combination with other treatments, such as medication, rehabilitation plans, and nutritional support.

Nevertheless, this study has certain limitations. Firstly, the number of included RCTs was limited, which may have an impact on the reliability of the results. Additionally, the inability to blind participants in the included studies due to the nature of the intervention introduces the potential for bias in outcome assessment. Future studies should aim to minimize bias through blinding of outcome assessors and incorporation of rigorous study designs.

5. Conclusions

Our meta-analysis suggests that RMT has been shown to effectively improve maximal inspiratory pressure in COPD patients, but its effects on lung function, dyspnea and quality of life are relatively modest. Further research is necessary to investigate its impact on additional outcomes and to explore optimal protocols and patient selection criteria for the implementation of RMT in clinical practice.

Funding statement

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Ethics approval statement and patient consent statement

All analyses in this study were based on previously published results and did not require ethical approval or patient consent.

Data availability statement

No data was used for the research described in the article.

CRediT authorship contribution statement

Zhongjie Huang: Writing – original draft, Validation, Supervision, Data curation. **Zhibin Li:** Writing – review & editing, Investigation, Formal analysis. **Meihao Yan:** Writing – review & editing, Validation, Supervision, Methodology. **Jianming Zheng:** Writing – original draft, Software. **Wencheng Huang:** Writing – review & editing, Validation, Software, Conceptualization. **Liyue Hong:** Writing – original draft, Validation, Supervision, Software, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Qiuxiang Lu:** Validation, Supervision, Software. **Limin Liu:** Writing – original draft, Validation, Investigation, Data curation. **Xincheng Huang:** Validation, Software, Formal analysis. **Hongtao Fan:** Writing – original draft, Software, Methodology, Investigation. **Weiping Su:** Validation, Methodology, Investigation, Conceptualization. **Xiaoping Huang:** Visualization, Software, Methodology. **Xiaoyan Wu:** Visualization, Supervision, Software, Investigation. **Zhixiong Guo:** Writing – review & editing,

Supervision, Methodology. **Caiting Qiu:** Writing – original draft, Software. **Zhaodi Zhao:** Visualization, Software. **Yuancheng Hong:** Writing – review & editing, Writing – original draft, Supervision.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e28733.

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