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Effectiveness of Threshold-Pressure Inspiratory Muscle Training on Pulmonary Rehabilitation in Children and Adolescents with Asthma

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Objective: The objective of this systematic review and meta-analysis was to assess the effectiveness of TIMT on pulmonary function in children and adolescents with asthma.

Method: We searched for randomized controlled clinical trials in the MEDLINE, Embase, the Cochrane Library, Web of Science, CINAHL, Sino Med, Wan fang, CNKI, and VIP until March 2024. In addition, the references included in the literature and the relevant systematic evaluation were manually traced in order to avoid the omission of any relevant literature. These trials compared TIMT against blank TIMT and conventional care. Eligible studies were assessed in terms of risk of bias and quality of evidence using RoB II tool. Where feasible, data were pooled and subjected to meta-analysis. The mean difference (MD) and 95% confidence interval (CI) were estimated by fixed effect models or random effect models.

Result: Six studies were included in the present meta-analysis involving 337 children and adolescents ranged from 4 to 18 years. The meta-analysis showed that TIMT could significantly improve lung function. Compared to the control group, TIMT can significantly improve FEV1 (MD 4.63 mL, 95% CI 2.64 to 6.62 mL, $I^2 = 4\%$), FVC (to the control group (MD 7.46 mL, 95% CI 5.09 to 9.82 mL, $I^2 = 0\%$), FEV1/FVC (MD 7.33%, 95% CI: 5.01 to 9.65%) and ACT (MD 1.86, 95% CI 0.96 to 2.75 mL, $I^2 = 12\%$) of patients at the end of intervention. There was no significant heterogeneity in these meta-analyses.

Conclusion: In conclusion, the results of this systematic review and meta-analysis support the effectiveness of TIMT training in restoring lung function and relieving asthma symptoms of asthmatic children. More high-quality and RCTs with large sample size are urgently required to verify the conclusion.

Keywords: threshold-pressure inspiratory muscle training, children, asthma, systematic review

Introduction

Asthma is the most common chronic airway disease in childhood, The prevalence of asthma in children has risen from 11.1%to 13.2% globally in the last 10 years, and is much higher than in adults.[1] It is responsible for considerable global morbidity and health-care costs.[2] Asthma is a heterogeneous disease, usually characterized by chronic airway inflammation. It is defined by the history of respiratory symptoms such as wheezing, shortness of breath, chest tightness and cough that vary over time and in intensity, together with variable expiratory airflow limitation.[3] Restricted expiratory airflow results in the lung expansion, which subsequently alters the shape and position of the diaphragm and impairs the functionality of the respiratory muscles.[4]

Inspiratory muscle training (IMT) is a technique used to increase strength or endurance of the diaphragm and accessory muscles of inspiration.[5] There are three types of IMT, normocapnic hyperpnoea, flow resistive loading and

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pressure threshold loading, threshold-pressure inspiratory muscle training (TIMT) is the most widely used IMT method because it is portable and easy to use.[6]

TIMT is a form of exercise that involves applying pressure to ensure that the intensity of the training remains at a certain level.[7] It differs from traditional respiratory training as it enables the specific targeting of inspiratory muscle groups for strength training purposes.[8] This pressure is used to exercise the relevant inspiratory muscles, with the aim of strengthening the muscle strength and endurance. Previous studies have demonstrated that TIMT reduces respiratory muscle weakness and enhances respiratory pressure, exercise capacity[9,10] However, the results of the studies that have reported the effects of TIMT on lung function in people with asthma are controversial.[9,11] Therefore, we systematically reviewed the available evidence from RCTs to assess the effectiveness of TIMT in improving lung function in children with asthma. The 39 participants in Lage's study were randomized into two groups: IMT group performed inspiratory muscle training 5 days a week for 8 weeks, consisting of six sets of 30 breaths per day with a training load ≥50% of maximal inspiratory pressure, plus an educational program; the controlgroup only received the educational program. There were no significant differences between groups at postintervention in predicted values for forcedexpiratory volume in the first second, forced vitalcapacity, or peak expiratory flow. The same result was found in Yang's study.[10] However, the opposite findings emerged from the Duruturk's study. It is important to synthesize the evidence obtained on such techniques. To our knowledge, no systematic review on this topic has been published previously. Thus, within this review, we aimed to summarise and assess evidence from randomised controlled trials (RCTs) regarding the the effectiveness of TIMT in improving lung function in children with asthma.

Methods

The protocol of this system review and meta-analysis was registered in the PROSPERO international prospective register of systematic reviews, and the reference number is CRD42024522137. We reported this systematic review and meta-analysis in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) statement.[12] No ethical approval was required for this study because there was no direct involvement of humans.

Literature Inclusion and Exclusion Criteria

Types of Studies

We included parallel randomized controlled trials (RCTs) that used an external inspiratory exerciser compared with a control.

Types of Participants

Children (0–9 years) and adolescents (10–19 years) with stable asthma as defined by internationally accepted criteria or objectively defined with a clinical diagnosis of asthma, have no other organ diseases.

Types of Interventions

The trial intervention group was threshold-pressure IMT rather than other type of IMT regardless of whether the intervention group had additional interventions. The control group intervention was either non-TIMT.

Outcome Indicators

The main outcomes were reported for at least one outcome among forced vital capacity (FVC), forced expiratory volume in the first second (FEV1), ratio of forced expiratory volume in the first second to forced vital capacity (FEV1/FVC), peak expiratory flow (PEF), and ACT (asthma control test).

Exclusion Criteria of Literature

(1) Conference abstracts, study plans, and literature for which the full text was not available; (2) The trial intervention group was other type of IMT rather than threshold-pressure IMT; (3) Literature for which data could not be accessed or converted; (4) Repeatedly published literature; (5) The recruitment of non-asthma patients or patients with other pulmonary diseases is sought for the aforementioned studies; (6) Neither Chinese nor English literature.

Search Strategy

We searched for literatures in the MEDLINE, Embase, The Cochrane Library, Web of Science, CINAHL, Sino Med, Wan fang, CNKI, and VIP. In addition, the references included in the literature and the relevant systematic evaluation were manually traced in order to avoid the omission of any relevant literature. The search period was from the establishment of the database to 1 March 2024. Detailed search strategies are provided in the appendix.

Screening and Extraction of Literature

Two authors independently evaluated the list of titles and abstracts from each database. If at least one of the reviewers considered one study eligible, the full text was obtained for complete assessment. Then, two reviewers independently assessed the full text of the selected studies to verify whether they met the eligibility criteria. The extracted literature was subjected to a comprehensive review, encompassing the following: (1) Basic information about the literature, including the year of publication, author, country of origin, and source of the literature; (2) Basic characteristics of the study population, such as age, gender, and sample size; (3) The specific content and frequency of the intervention; (4) Relevant outcome indicators. Any disagreements were resolved by discussion in the process of the full-text selection and data extraction.

Quality Assessment of Included Literature

The risk of bias (RoB) in the included trials was assessed independently by two investigators using the Cochrane Risk of Bias II tool. Quality was evaluated across the following domains:. For each indicator, “low risk”, “some concerns” and “high risk” were used for judgment. A third reviewer resolved any disagreements in rating the studies.

Statistical Analysis

Any outcome measure reported by more than two included studies was considered the primary outcome of the study, including FEV1, FVC, FEV1/FVC, ACT, FEF25-75 and PEF. Review Manager 5.3 were used for the analyses. The mean and SD of the outcome measure were reported for effectiveness evaluation. A significant effect requires that the mean difference (MD) for continuous data is not equal to 0, and the confidence interval does not include 0. The analysis model was selected based on the I-squared value. The random effect model was applied if I^2 was > 50%; otherwise, a fixed effect model was employed. The significance level was set at 0.05.

Result

Characteristic of Included Studies

One thousand eight hundred and seventy-eight studies were identified by the literature search. After screening these studies through use of the inclusion criteria, 6 studies were included in the present meta-analysis involving in 337 children and adolescents ranged from 4 to 18 years[13–18] (Figure 1). The characteristics of the randomized controlled trials are summarized in Table 1. The duration of intervention ranged from 4 to 12 weeks and the frequency ranged from 1 to 3 times per week. The common effect measures are FVC, FEV1, FEV1/FVC.

Quality Assessment of Included Studies

The risk of bias of included studies assessed by ROB II tool (Figures 2 and 3). The comprehensive RoB assessment of the included studies were all some concerns. This is mainly because the six studies were open-label trials, so randomization process and deviations from intended interventions is some concern in all studies. A half of studies were assessed as low risk in the field of missing data. All studies were assessed as low risk in the field of measurement of the outcome. The 66.7% were assessed as low risk in the field of selective reporting.

FVC

Five studies[13–18] reported the FVC as their measure of lung function. Both the intervention group and the control group, FVC of participants increased on completion of the intervention. Meta-analysis showed that FVC improvement was

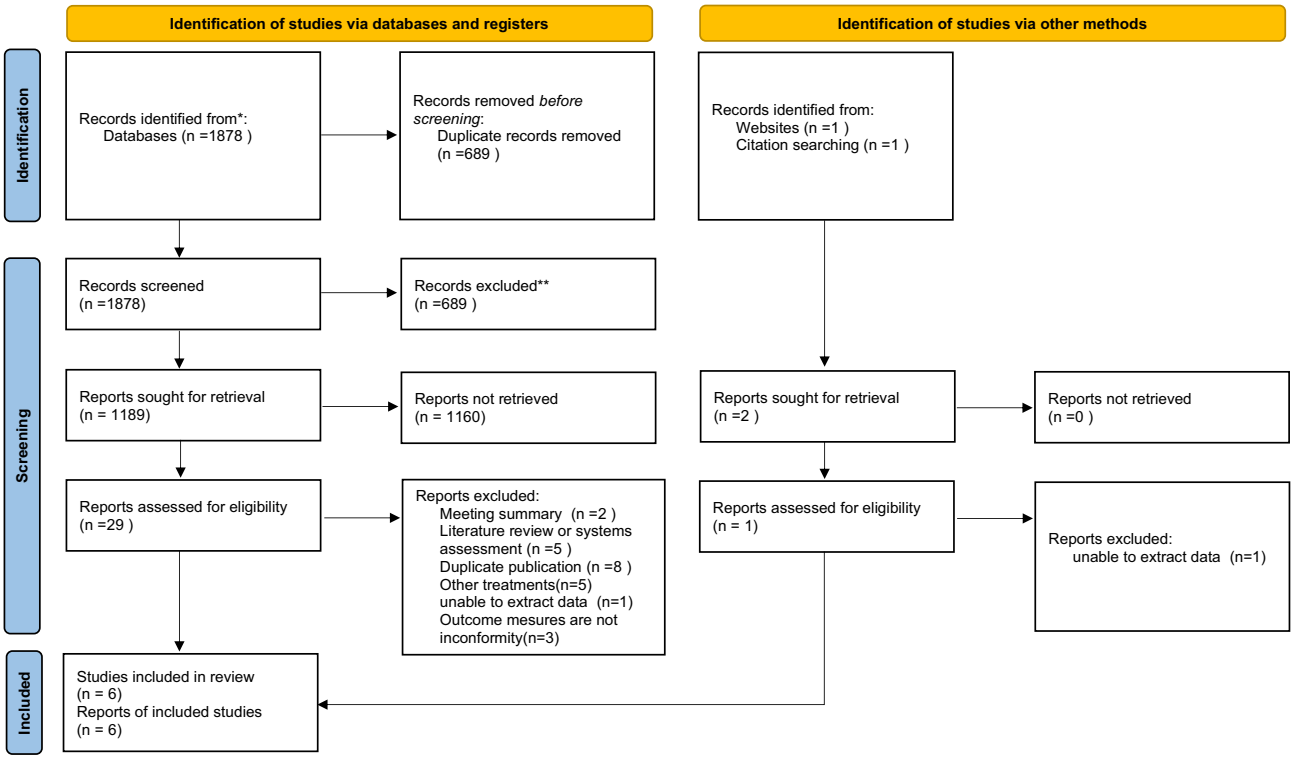

Figure 1 Flow chart of included studies.

significantly higher in the intervention group compared to the control group (MD 7.46 mL, 95% CI 5.09 to 9.82 mL, I^2 = 0%) (Figure 4).

FEV1

Totally 5 studies[13,15–18] evaluated FEV1 and their results suggested that FEV1 after intervention was higher than before intervention. Meta-analysis showed that FEV1 improvement was significantly higher in the intervention group compared to the control group (MD 4.63 mL, 95% CI 2.64 to 6.62 mL, I^2 = 4%) (Figure 5).

FEV1/FVC

Four studies[13,15–17] evaluated FEV1/FVC. Meta-analysis showed that FEV1/FVC was significantly higher in the intervention group compared to the control group (MD 7.33%, 95% CI: 5.01 to 9.65%) (Figure 6). Nevertheless, there is a medium heterogeneity in the meta-analysis (I^2 = 34%).

ACT

Two studies[16,17] evaluated ACT and their results suggested that ACT after intervention was higher than before intervention. Meta-analysis showed that ACT improvement was significantly higher in the intervention group compared to the control group (MD 1.86, 95% CI 0.96 to 2.75 mL, I^2 = 12%) (Figure 7).

PEF

Two studies[14,18] evaluated PEF and their results suggested that PEF after intervention was higher than before intervention. The meta-analysis has a great heterogeneity (I^2 = 98%). Based on random-effect model, the result showed that PEF improvement was not significantly for MIMT compared with the control group (MD 56.45 mL, 95% CI −33.10 to 146.00 mL) (Figure 8).

Table 1 Characteristics of Included Studies

Studies	Sample Size	Age	Region	Intervention	Control	Term	Time	Frequency	Effect Measure
Lima 2008[13]	25/25	8–12	Brazilian	A pressure threshold load of 40% of maximal inspiratory pressure	Medical follow-up and asthma education program	7W	50min	2 times a week	MIP, MEP, PEF
David 2018[14]	118/118	6–18	Croatia	IMT	Diaphragmatic breathing exercises	4W	/	At least 10 times a month	FVC, FEV1, PEF, PFM, MIP, Tlim
Elnaggar 2021[15]	17/17	12–16	SaudiArabia	IMT at 40% of the maximal inspiratory pressure(IPmax)	Placebo IMT at 5% of IPmax	12W	20min/ session	3 times a week	FVC, FEV1, FEV1/FVC, MIP, MEP, ACT
Liu 2022[16]	51/55	4–12	China	IMT	Only with drug use	12W	20–30min	1–2 times a week	FVC, FEV1, PEF, FEF25, FEF50, FEF75, quality of life, PedsQL
Elnaggar 2023[17]	17/17	12–18	SaudiArabia	30% load for inspiratory muscle strength	Placebo training no-load respiratory muscle training	12W	35min	3 times a week	FVC, FEV1, FEV1/FVC, MIP, MEP, ACT
Ozden 2023[18]	35/35	8–17	Istanbul	Threshold IMT, 30% of maximum inspiratory pressure	Only with drug use	6W	/	7 days/ 6 weeks	FVC, FEV1, FEV1/FVC, FEF25-75, MIP, MIP%, MEP, MEP%

FEF25-75

Two studies[13,15] reported FEF25-75 and their results suggested that FEF25-75 after intervention was higher than before intervention. Meta-analysis showed that PEF improvement was not significantly for MIMT compared with the control group (MD 56.45 mL, 95% CI −33.10 to 146.00 mL) (Figure 9).

Discussion

The findings of this systematic review and meta-analysis indicate that TIMT training demonstrates significant efficacy in the pulmonary rehabilitation of children with asthma, compared to traditional IMT. This advantage suggests that TIMT may be a potent tool for restoring lung function and relieving asthma symptoms of asthmatic children.

Recurrent respiratory tract infections significantly contribute to the morbidity of asthma in children.[19] These infections have a detrimental impact on the disease prognosis, often triggering asthma attacks.[20] Among pharmacological treatments for asthma, corticosteroids are considered the most effective method for controlling and managing the condition.[21,22] These medications decrease the presence of eosinophils, T lymphocytes, mast cells, and dendritic cells in respiratory inflammation. They also inhibit the production of proinflammatory cytokines, ultimately reducing the frequency of asthma exacerbations.[9,23] While inhaled corticosteroids are commonly prescribed for asthma treatment and effectively control most symptoms, they may not prevent symptoms from occurring, especially in at-risk children over an extended period of time. These medications suppress various inflammatory markers associated with asthma but may not be sufficient to prevent the development of inflammation.[24] Therefore, there is a need for additional strategies to manage asthma more effectively.

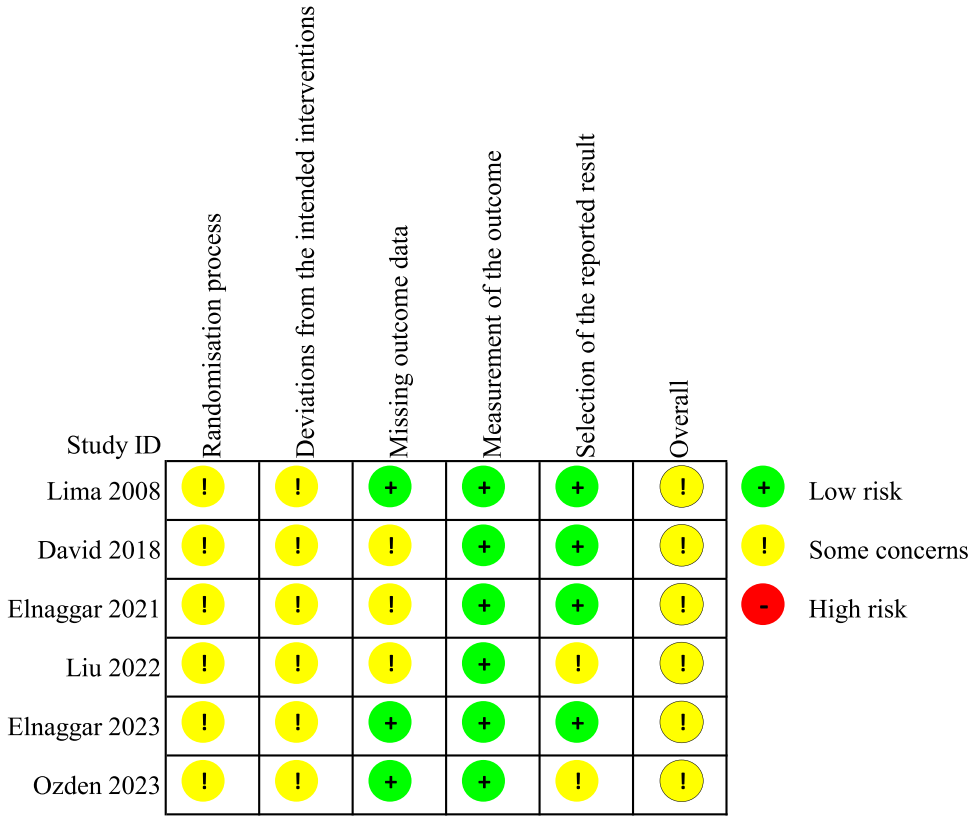

Figure 2 Risk of bias assessment for included studies.

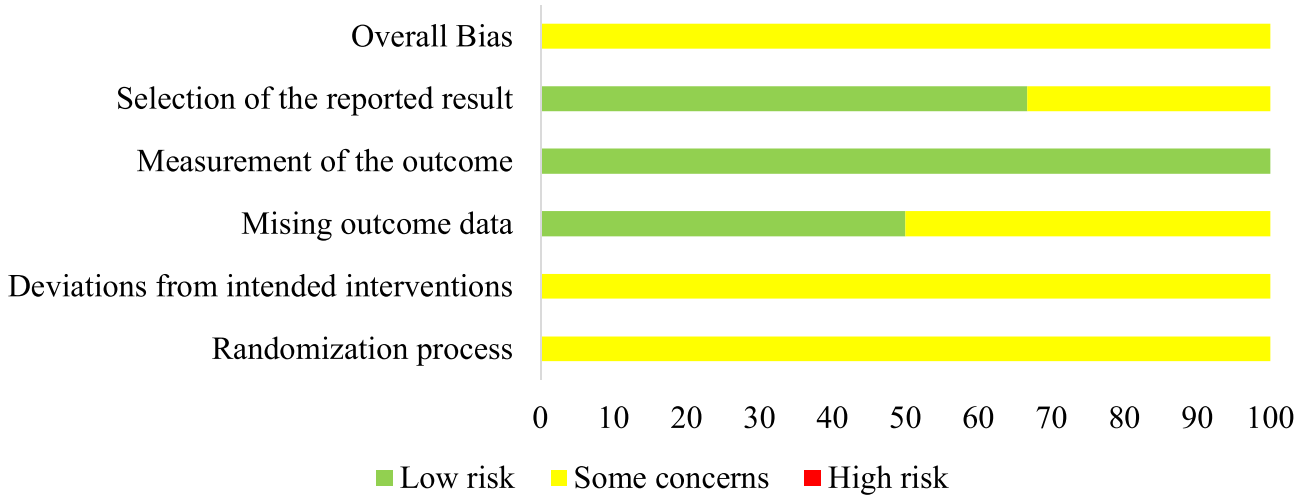

Figure 3 Summary plot for risk of bias assessment for included studies.

Exercise-assisted medical therapy has been identified as an essential component of asthma management.[25] Combining traditional pharmacological treatments with low-cost adjunct treatments has been shown to yield better disease management outcomes. Non-pharmacological interventions also play a significant role in asthma treatment.[26] Silva[27] et al found that a statistically significant increase in inspiratory muscle strength, measured by maximal inspiratory pressure (PImax). In addition, the results of Lista-Paz's study show that inspiratory muscle training (IMT) had beneficial effects on maximal inspiratory pressure (PImax: mean difference [MD] 21.95 cmH2O, 95% CI: 15.05; 28.85).[6] In line with these findings, our study focused on the effect of threshold-pressure inspiratory muscle training (IMT) as a non-

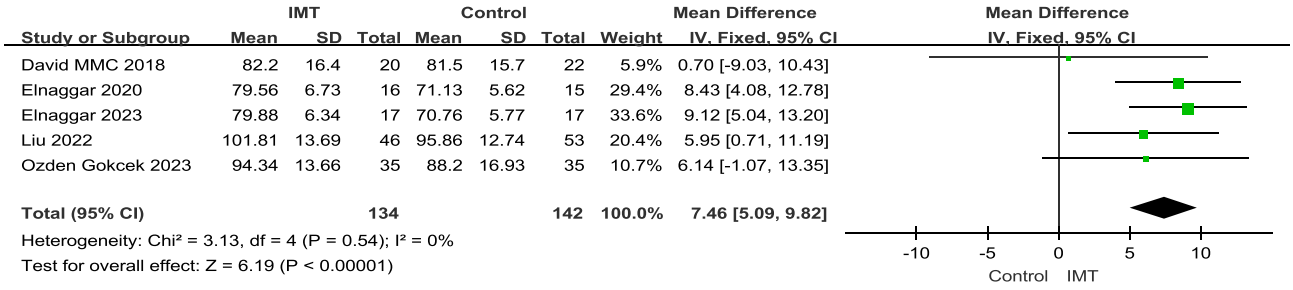

Figure 4 Meta-analysis for FVC after intervention between IMT group and control.

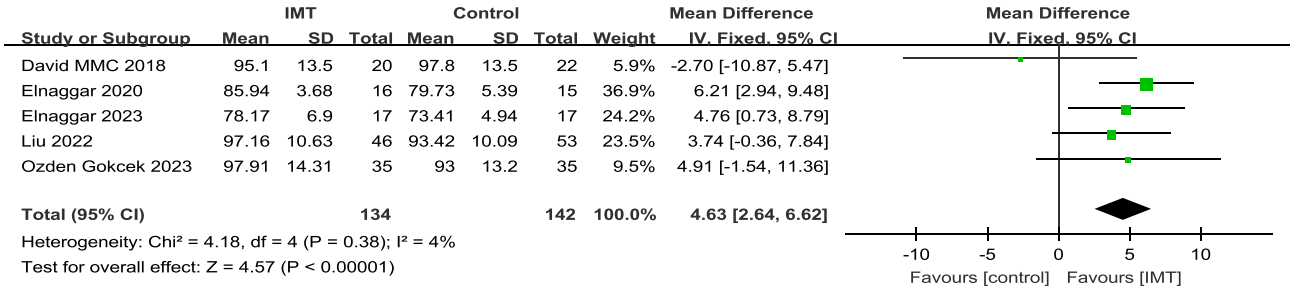

Figure 5 Meta-analysis for FEV1 after intervention between IMT group and control.

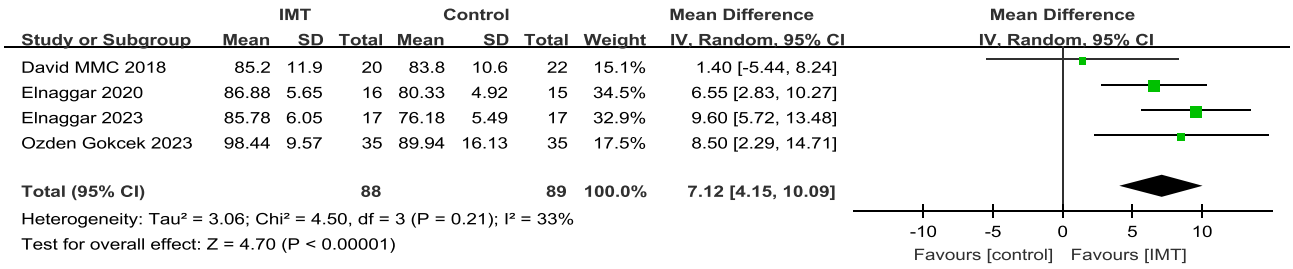

Figure 6 Meta-analysis for FEV1/FVC after intervention between IMT group and control.

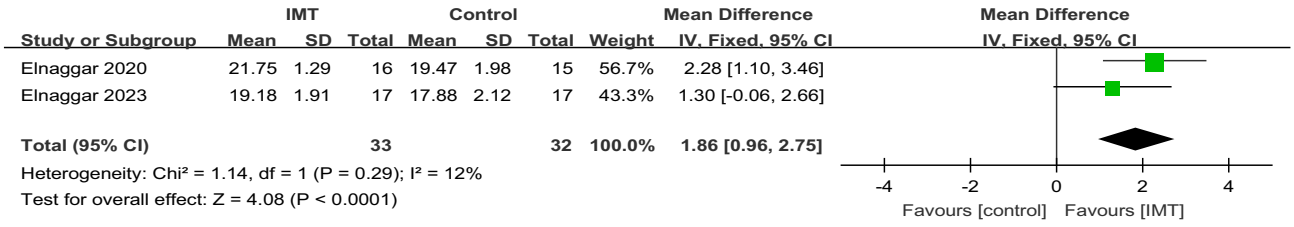

Figure 7 Meta-analysis for ACT after intervention between IMT group and control.

pharmacological intervention in the pulmonary rehabilitation of children with asthma. We observed improvements in both FVC and FEV1 after intervention, indicating the potential benefits of this training method in enhancing lung function.

IMT can also improve lung function in patients with other diseases. For example, Basbug[28] and his college explored effects of inspiratory muscle training in adolescents with idiopathic scoliosis. They found that IMT is beneficial for patients with AIS for achieving further improvements in respiratory function, respiratory muscle strength and functional capacity compared to conventional exercise program alone. Another study of patients with chronic kidney disease also showed that IMT significantly improved lung function and patient life quality.[29]

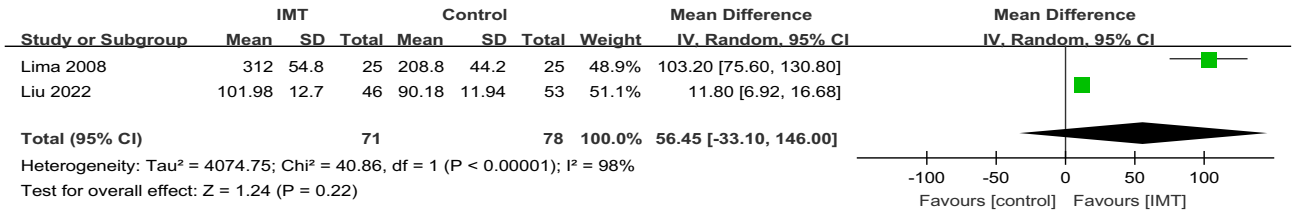

Figure 8 Meta-analysis for PEF after intervention between IMT group and control.

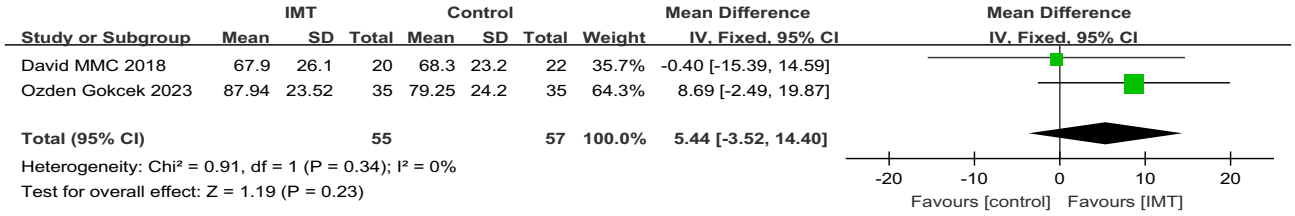

Figure 9 Meta-analysis for FEF25-75 after intervention between IMT group and control.

In this study, the results of the meta-analysis for PEF may not be reliable, on the one hand, because only two studies were included in this meta-analysis, and on the other hand, both of these studies reported significant results. For the meta-analysis of FEF25-75, both two studies reported the non-significant results between the IMT group and the control group. But authors did not give a reasonable explanation. This may be due to the limited sample size and short intervention period. Fry[30] et al conducted a 10-week randomized controlled trial and observed a significant improvement of IMT on FEF25-75. Meanwhile, in another study, 45 subjects were randomly assigned to BRT, IMT, and control groups. After 6 weeks of intervention, the IMT group showed a significant improvement in FEF25-75 compared with the other two groups.[31] These outcomes suggest the importance of a multimodal approach to asthma management, combining both pharmacological and non-pharmacological interventions. By incorporating interventions TIMT into a comprehensive treatment plan, clinicians can offer a more holistic approach to asthma care, addressing both the pharmacological control of inflammation and the improvement of respiratory muscle function.

The significant benefits of TIMT for pulmonary rehabilitation in children with asthma can be credited to its distinctive training approach. This technique involves establishing a specific level of respiratory resistance, which challenges the respiratory muscles to work against increased loads, ultimately boosting their strength and endurance. By enhancing the function of these respiratory muscles, this training method may help alleviate breathing issues in children with asthma, leading to an overall improvement in their quality of life. Furthermore, TIMT have a positive impact on the pulmonary function of asthmatic children. Studies have shown that this training method can increase key pulmonary function indicators such as vital capacity and peak expiratory flow rate in asthmatic children. These improvements may be associated with the strengthening of respiratory muscles, reduction in airway inflammation, and increased alveolar ventilation.

However, this review also has certain limitations. Firstly, the sample size of each study included in the meta-analysis is relatively small, and the number of studies is relatively small. This may affect the accuracy and reliability of the results. Secondly, this study only conducted a meta-analysis on lung function indicators, and did not include other indicators such as quality of life, symptoms, and cost-effectiveness. This limits the comprehensiveness of the analysis and may affect the accuracy of the results. Thirdly, this study did not perform publication bias testing and subgroup analysis, which cannot eliminate the impact of selection bias. This may lead to inaccurate conclusions. Fourthly, the results of this study may be affected by other factors such as confounding factors, geographical differences.

Future research should focus on the specific mechanisms of threshold-pressure inspiratory muscle training in the pulmonary rehabilitation of children with asthma, in order to provide a more solid theoretical foundation for clinical

practice. Additionally, large-scale, high-quality multicenter studies are needed to verify the efficacy of threshold-pressure inspiratory muscle training in the pulmonary rehabilitation of asthmatic children.

Conclusion

In conclusion, the results of this systematic review and meta-analysis support the effectiveness of TIMT training in restoring lung function and relieving asthma symptoms of asthmatic children. More high-quality and RCTs with large sample size are urgently required to verify the conclusion.

Data Sharing Statement

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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