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SYSTEMATIC REVIEW

Evaluation of respiratory muscle training interventions on pulmonary function in critical care: a systematic review and meta-analysis

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Abstract

Background: A meta-analysis of randomized controlled trials (RCTs) up to July 2024 evaluated the efficacy of respiratory muscle training (RMT) on pulmonary function in critically ill patients. **Methods**: The Ovid Medline was searched for RCTs (in English) examining RMT or related interventions (*e.g.*, inspiratory/expiratory muscle training, non-invasive support) on respiratory muscle strength (*e.g.*, maximum inspiratory (PI_{max}), maximum expiratory (PE_{max}) and clinical outcomes. Methodological quality followed Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines. Effect sizes and 95% confidence intervals (CI) were calculated using a random-effects model, with heterogeneity assessed using I^2 statistics. **Results**: Data from six RCTs, encompassing a total of 299 participants, were included in the analysis, among whom 152 were allocated to intervention groups and 147 to control groups. Despite the heterogeneity of the interventions, all shared the common objective of enhancing pulmonary function parameters, particularly PI_{max} and PE_{max}, which serve as indicators of respiratory muscle strength. A high degree of heterogeneity (I^2 = 99%) was observed, likely due to variations in patient populations, the types of intervention modalities employed (*e.g.*, high-flow oxygen therapy, non-invasive ventilation modes, electrical stimulation) and differences in treatment durations. Nonetheless, the overall effect size was positive (13.26, 95% CI: 3.08 to 23.44), suggesting that these interventions effectively improve pulmonary function. **Conclusions**: This meta-analysis demonstrates that RMT interventions significantly improve pulmonary function in critically ill patients. However, the diversity of interventions and reliance on a single database (Ovid Medline) may limit the comprehensiveness of the findings. Future research should employ a more targeted Population, Intervention, Comparison, Outcomes and Study design (PICOS) framework, incorporate additional databases such as Cochrane Central, and standardize intervention protocols to enhance the clarity and comparability of outcomes. **Clinical Trial Registration**: INPLASY2024100041.

Keywords

Lung; Respiratory interventions; Pulmonary function; Exercise capacity; Meta-analysis

1. Introduction

Pulmonary function is an essential determinant of clinical outcomes in patients admitted to intensive care units (ICUs), as critically ill individuals often experience significant respiratory muscle weakness due to factors such as prolonged mechanical ventilation and systemic inflammation [1, 2]. This decline in muscle strength not only compromises pulmonary function but also increases the risk of prolonged ventilator dependence and worsened recovery outcomes. In response to these challenges, interventions targeting pulmonary function, particularly those involving inspiratory and expiratory muscle training, have garnered growing interest, and unlike previous studies that incorporated both observational studies and randomized controlled trials (RCTs), this systematic review and meta-analysis investigated only RCTs to ensure a higher level of evidence, thereby addressing the inconsistencies and limitations associated with prior research.

Recent epidemiological data report respiratory failure as a leading cause of ICU admissions globally [3, 4], and has necessitated the use of therapies such as non-invasive ventilation (NIV) and high-flow nasal cannula (HFNC) to reduce the reliance on invasive mechanical ventilation [5–7]. Simultaneously, advancements in the interpretation of pulmonary function tests (PFTs) have highlighted the need for individualized approaches tailored to the physiological and clinical characteristics of ICU patients [8]. Thus, maintaining and enhancing pulmonary function is important for both immediate survival during the ICU stay and long-term recovery after discharge.

Given the substantial burden of respiratory muscle weakness in critically ill patients, which is strongly associated with extended ventilator dependence and diminished quality of life, there is increasing interest in interventions such as respiratory muscle training (RMT) [9, 10]. Preliminary studies have demonstrated the potential benefits of RMT, particularly through inspiratory and expiratory muscle exercises, in improving respiratory muscle strength [11, 12]. However, the lack of systematic analyses exclusively based on RCTs has limited the generalizability and applicability of these findings in clinical practice [13].

To address these gaps, this meta-analysis aims to evaluate the effectiveness and safety of RMT interventions in ICU patients using only RCTs for robust and reliable conclusions. Furthermore, this study seeks to explore the underlying mechanisms through which RMT enhances pulmonary function and reduces complications, while also providing evidence-based recommendations for optimizing rehabilitation strategies in critical care. Overall, the findings could provide insights into resolving previous inconsistencies and a comprehensive understanding of the role of RMT in improving outcomes for critically ill patients.

2. Methods

This systematic review and meta-analysis evaluated the impact of RMT interventions on pulmonary function in critically ill patients using the structured population, intervention, comparison, outcome and study design (PICOS) framework. The study population comprised critically ill adult patients, the intervention included RMT or related strategies designed to enhance respiratory muscle strength, the comparison involved standard care versus no intervention, the outcomes focused on pulmonary function metrics, such as PI$_{max}$ and PE$_{max}$ and only RCTs were included.

2.1 Methodological quality assessment

The quality of the included studies was rigorously evaluated using the Cochrane Risk of Bias tool, which assesses multiple domains, including selection bias, performance bias, detection bias, attrition bias and reporting bias. Two reviewers independently assessed each study, and any disagreements were resolved through discussion or consultation with a third reviewer. Sensitivity analyses were conducted to examine the influence of study quality on the pooled effect estimates, ensuring that the overall quality of evidence was integrated into the final meta-analysis results.

2.2 Study guidelines

This meta-analysis was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. The protocol was registered in the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) under the registration number INPLASY2024100041, which is accessible online at https://inplasy.com/inplasy-2024-10-0041/.

2.3 Literature search

The Ovid Medline database was searched comprehensively for relevant studies published up to July 2024 [14]. The complete search strategy, including all keywords and Medical Subject Headings (MeSH) terms, is provided in the **Supplementary material**, and due to resource constraints, the search was limited to the Ovid Medline database. While this limitation may have introduced selection bias by excluding studies indexed in other databases, it was necessary given the preliminary nature of this investigation. To address this issue in future research, additional databases such as Cochrane Central were incorporated to improve the comprehensiveness of the search and reduce the risk of bias.

2.4 Inclusion and exclusion criteria

To ensure methodological rigor, only RCTs were included in this meta-analysis. Eligible studies had to meet the following criteria: (1) they were RCTs; (2) they were published up to July 2024; (3) they had no geographical restrictions; and (4) they were published in English. Studies were excluded if they were observational studies, case reports, case series, expert opinions, or if they contained severely incomplete data. Additionally, studies that did not provide sufficient data on the primary outcomes (PI$_{max}$ and PE$_{max}$) for effect size calculation or lacked adequate reporting of interventions and outcome measures required for data extraction were excluded from the analysis.

2.5 Data extraction

Two independent researchers initially screened the titles and abstracts to identify potentially relevant studies after removing duplicates. Full texts of the shortlisted articles were then reviewed to confirm their eligibility based on the inclusion and exclusion criteria. Data extraction was performed using a standardized Excel spreadsheet, and key details such as the first author, publication year, sample size, participant age, disease type, study design, intervention specifics (including mode and dosage), treatment duration and follow-up period were retrieved. Additionally, the type and extent of respiratory support provided (*e.g.*, mechanical ventilation settings, high-flow nasal cannula) were recorded to contextualize the clinical applications of the interventions.

2.6 Data analysis

The primary outcomes, PI$_{max}$ and PE$_{max}$, were used as indicators of respiratory muscle strength, and efficacy was defined as significant improvements in these metrics. Effect sizes were calculated using Cohen's *d*. For studies with missing data, corresponding authors were contacted to request the necessary information. If data remained unavailable, the studies were excluded from the quantitative synthesis to maintain the validity of the meta-analysis. To account for variability in treatment durations across studies, effect sizes were standardized using a random-effects model to accommodate differences in intervention lengths and population characteristics. The potential influence of varying treatment durations on overall effect estimates was also assessed, heterogeneity among studies was determined using I^2 and Tau^2 statistics, and the results were interpreted to quantify variability in effect sizes. All statistical analyses were performed using RevMan software (version 5.4.1, The Cochrane Collaboration, London, UK).

3. Results

3.1 Study selection and characteristics

The systematic search initially identified 65 records, comprising 60 from database searches and 5 from other sources. After removing duplicates, 63 were screened, leading to the full-text review of 13 articles, and following the exclusion of 7 articles, 6 studies that met the inclusion criteria were included in both the qualitative synthesis and quantitative meta-analysis (Fig. 1).

The six included studies (Table 1) involved a total of 299 critically ill patients with impaired pulmonary function requiring intensive care, comprising 152 in the intervention groups and 147 in the control groups. The interventions tested all aimed at enhancing and While the in approach, they were selected providing a broad. The mean age of participants across the studies ranged from 54 to 71.5 years.

Methodological quality was assessed using the Cochrane Risk of Bias tool, which indicated a low to moderate risk of bias in most studies, supporting the reliability of the included evidence. The detailed results of the quality assessment are presented in Fig. 2.

3.2 Pulmonary function outcomes

The primary outcomes, PI_{max} and PE_{max}, demonstrated statistically significant improvements, indicating enhanced respiratory muscle strength among participants receiving RMT-related interventions. However, substantial heterogeneity was observed ($I^2 = 99\%$), reflecting variability in the interventions, patient populations and treatment durations across the included

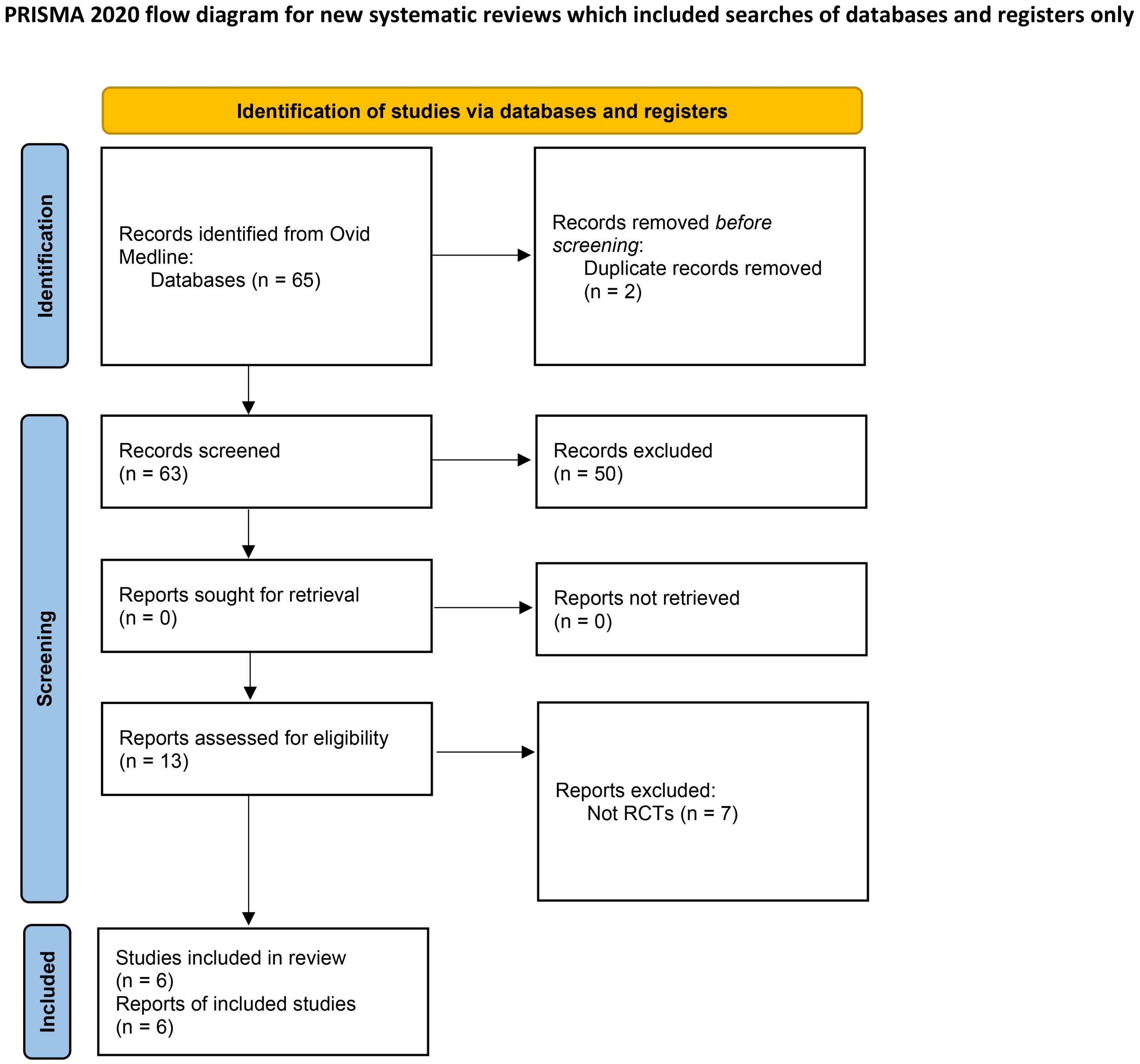

FIGURE 1. Flowchart of the screening process. RCTs: randomized controlled trials.

TABLE 1. Basic characteristics of included studies.

Authors, yr	Total No. of patients	Age, mean, yr	Study type	Intervention/ Control	Quantity, dose	Route of administration	Treatment duration
Vitaceae, 2020	171	71.5 (8.1)	Randomized controlled study	HFOT/Venturi mask	20 sessions	Nasal cannula/Mask	4 wk
Kelly, 2014	23	54 (41–61)	Randomized crossover trial	iVAPS/standard PS	iVAPS: 5–18 cmH_2O/standard PS: 10 cmH_2O	Not specified	1 mon
Zanotti, 2003	24	65.4 (6.2)	Randomized controlled study	ALM + ES/ALM	30 min bid	Electrical Stimulation/N.A.	4 wk
Marchesan, 2000	45	67.9 (5.5)	Randomized observer-blinded crossover trial	FDP/Placebo	FDP: 150 mg/kg/d Placebo: 100 mg/kg/d	Intravenous	7 d
Johnson, 1993	21	59 (22–84)	Double-blind crossover design	$MgSO_4$/Placebo	6 g IV over 16 h/Placebo	Intravenous	2 d
Cropp, 1987	15	58 (2)	Randomized controlled trial	Negative pressure ventilation/No intervention	20–25 cmH_2O	Non-invasive ventilator/N.A.	3 d

Abbreviations: HFOT: high-flow oxygen therapy; iVAPS: intelligent volume-assured pressure support; PS: pressure support; ALM: active limb mobilization; ES: electrical stimulation; FDP: fructose-1,6-diphosphate; IV: Intravenous; N.A.: not applicable; $MgSO_4$: magnesium sulfate.

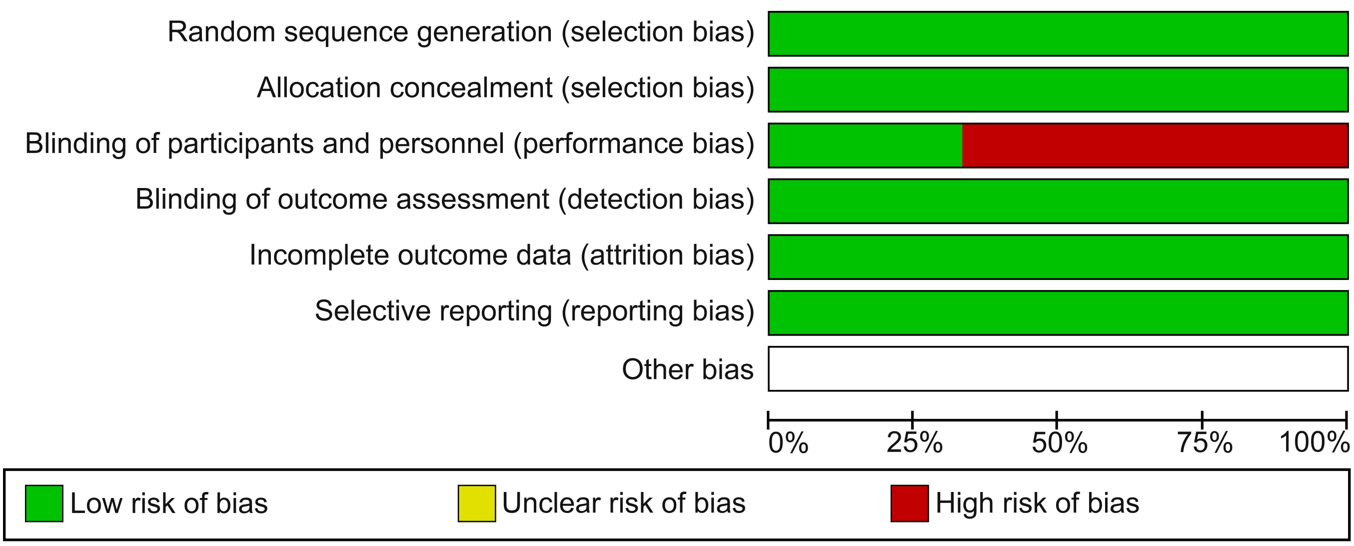

FIGURE 2. Risk of bias analysis.

studies, which complicated direct comparisons between individual study results. Despite these challenges, the pooled effect estimate was positive, suggesting that interventions incorporating RMT components can significantly improve respiratory muscle strength in critically ill patients. The individual study effect sizes ranged from 0.00 [15] to 34.60 [16].

3.3 Heterogeneity and sensitivity analysis

Substantial heterogeneity was observed across the included studies (I^2 = 99%, τ^2 = 156.1529, $p < 0.01$), indicating considerable variability in patient characteristics, intervention modalities and study designs (Fig. 2), and the need for cautious interpretation of the pooled results, thereby highlighting the importance of tailoring treatment strategies to individual patient needs in critical care settings. Moreover, sensitivity analysis identified potential sources of this variability; however, no single factor was identified as the primary contributor to the observed heterogeneity.

3.4 Respiratory muscle strength

Fig. 3 presents the forest plot summarizing the meta-analysis results. Analysis using the random effects model revealed significant heterogeneity across studies ($I^2 = 99\%$, $\tau^2 = 156.1529$, $p < 0.01$). The overall effect estimate from the random effects model was 13.26 (95% CI: 3.08 to 23.44), indicating a statistically significant positive impact of RMT interventions on respiratory muscle strength. Individual study effect sizes varied widely, ranging from 0.00 (Kelly, 2014) to 34.60 (Johnson, 1993). Among the included studies, those conducted by Vitacca (2020), Marchesan (2000), and Johnson (1993) demonstrated the largest effect sizes, whereas studies by Kelly (2014) and Zanoitti (2003) reported minimal effects. Notably, the common effect model estimate was 2.23 (95% CI: 1.65 to 2.81), differing substantially from the random effects model, further underscoring the high degree of heterogeneity among the studies, which might have been due to differences in study designs, patient populations and intervention protocols. Overall, the lack of a standardized approach to RMT highlights the need for refining future study selection criteria and implementing uniform intervention protocols for more consistent and interpretable outcomes.

4. Discussion

The findings of this RCT-only meta-analysis suggest that targeted interventions to enhance respiratory muscle strength can significantly improve pulmonary function in critically ill patients. However, the inclusion of a wide range of interventions, such as non-invasive ventilation methods and adjunctive therapies, poses challenges to the interpretability of the pooled results, and future systematic reviews could focus on specific intervention types, such as inspiratory muscle training alone, and expand their literature searches to include additional databases, such as Cochrane Central, for more comprehensive results.

The interventions evaluated included high-flow oxygen therapy, intelligent volume-assured pressure support, active limb mobilization combined with electrical stimulation and pharmacological treatments, and the results showed an overall positive impact on pulmonary function and exercise capacity [15–20]. This multifaceted approach highlights the importance of addressing functional outcomes in critical care [21]. Moreover, the analysis revealed varied effects across different outcome measures; for instance, some interventions showed significant improvements in parameters such as PI_{max} and PE_{max}, while others demonstrated more modest effects on measures such as the 6-minute walking distance [22], highlighting the complexity of managing critically ill patients and emphasizing the necessity of tailoring treatment strategies to individual patient profiles.

Although the studies included in this meta-analysis were based on robust RCT designs, offering high-quality evidence to support the effectiveness of the interventions, the substantial heterogeneity observed ($I^2 = 99\%$) highlights significant variability among the included studies, which could influence the reliability of the pooled effect estimates. This variability might have been due to differences in patient characteristics, intervention methods, and treatment durations across the studies. These findings underscore the complexity of implementing respiratory muscle training interventions in critically ill patients and suggest that a standardized, one-size-fits-all approach may not be suitable. Instead, these results emphasize the importance of developing personalized treatment strategies tailored to the specific needs and conditions of individual patients to achieve optimal pulmonary function outcomes.

The substantial heterogeneity observed in this meta-analysis also supports the critical need for greater standardization in future studies. Using consistent intervention protocols, uniform outcome measures, and comparable patient populations could enhance the ability to draw accurate comparisons and synthesize results across studies. Additionally, the limited number of included studies and the exclusion of grey literature may have introduced publication bias, potentially skewing the findings. While efforts were made to mitigate this bias by screening reference lists and relevant reviews, the possibility of unpublished studies remains [23]. Thus, expanding future research to include a larger pool of studies would provide a more

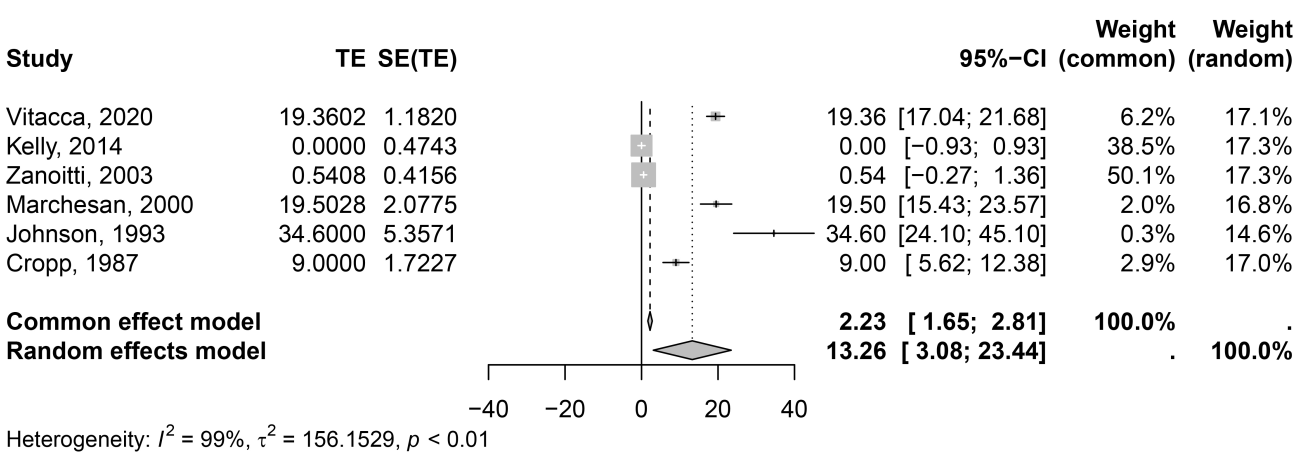

FIGURE 3. Effect size for interventions versus control. TE: treatment effect; SE: standard error; CI: confidence interval.

comprehensive understanding of the sources of heterogeneity and improve the generalizability of findings.

Despite the promising results reported in this meta-analysis, several limitations should be considered. First, the inclusion of a broad range of interventions and the reliance on a single database (Ovid Medline) may have limited the comprehensiveness of the search and introduced selection bias, and studies indexed in other databases, such as Cochrane Central or Web of Science, were not included, potentially affecting the generalizability of the findings. To enhance the robustness and comprehensiveness of the evidence base, future research should incorporate multiple databases. Second, the inherent heterogeneity among the studies, including variations in participant characteristics, intervention types, and outcome measures, could have influenced the results. Additionally, restricting the analysis to English-language studies may have introduced language bias. The short duration of interventions in some studies further limits the ability to detect long-term effects of respiratory muscle training. Longer follow-up periods should be prioritized in future studies to evaluate the sustainability of pulmonary function improvements. Addressing these limitations would enhance the validity and applicability of meta-analytic findings in this field. Although sensitivity analyses are valuable for assessing the robustness of meta-analytic results, their utility was limited in this study by the small number of included studies. The overall methodological quality of the studies, while generally low to moderate risk of bias, also constrained the ability to exclude studies with higher risk of bias without compromising statistical power. Therefore, additional sensitivity analyses excluding higher-risk studies were not performed. Future meta-analyses with a larger number of high-quality studies could more effectively utilize sensitivity analyses to validate their findings.

In summary, the findings of this study indicate that targeted interventions can significantly enhance pulmonary function and exercise capacity in critically ill patients. However, the substantial heterogeneity and varied effect sizes observed across studies indicate the need for further research to identify the most effective interventions for specific patient populations and to establish standardized treatment protocols. Future investigations should emphasize longer-term follow-up periods and more consistent outcome measures to improve the comparability and clinical relevance of findings.

5. Conclusions

This study demonstrates that respiratory interventions, particularly those targeting pulmonary function, are effective in the critical care setting, with a multifaceted approach incorporating diverse intervention modalities being beneficial in managing respiratory failure in critically ill patients. However, the substantial heterogeneity observed across studies suggests the importance of developing personalized treatment strategies to optimize patient outcomes. Further research is needed to establish standardized protocols and determine the most effective interventions for specific patient populations in the ICU.

AVAILABILITY OF DATA AND MATERIALS

The authors declare that all data supporting the findings of this study are available within the paper, and any raw data can be obtained from the corresponding author upon request.

AUTHOR CONTRIBUTIONS

XFZ—designed and conducted the study, supervised data collection. XLZ—collection, analyzed the data, and prepared the manuscript for publication. MLZ—interpreted the findings, prepared the manuscript for publication, and reviewed its draft. All authors have read and approved the final manuscript.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

This article does not contain any studies with human participants or animals performed by any of the authors. Hence, no ethical approval was required.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

SUPPLEMENTARY MATERIAL

Supplementary material associated with this article can be found, in the online version, at https://oss.signavitae.com/mre-signavitae/article/1909444093032710144/attachment/Supplementary%20material.docx.

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