Effects of Early-stage Phased Rehabilitation Training on Acute Respiratory Distress Syndrome: A Systematic Review and Meta-analysis

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Abstract [**Objectives**] To systematically evaluate the effects of early-stage phased rehabilitation training on the oxygenation index, ICU length of stay, duration of mechanical ventilation, and occurrence of complications (ventilator-associated pneumonia, pressure ulcers, delirium) in ARDS patients, thus contributing evidence for the clinical application of early-stage phased rehabilitation training. [**Methods**] The China National Knowledge Infrastructure (CNKI), Wanfang, and other databases were searched. Literature screening, data extraction, and systematic analysis of the included studies were performed using Revman software. [**Results**] Thirteen randomized controlled trials involving a total of 860 patients were included in this review. The results of the meta-analysis showed that compared to the traditional rehabilitation training group, the early-stage phased rehabilitation training group demonstrated a significant increase in the oxygenation index of ARDS patients [*SMD* = 1.18, 95% *CI* (1.01, 1.35), $P<0.01$], with statistically significant differences. Furthermore, there were significant reductions in ICU length of stay [*SMD* = -0.70, 95% *CI* (-0.90, -0.50), $P<0.01$], duration of mechanical ventilation [*SMD* = -1.15, 95% *CI* (-1.36, -0.94), $P<0.01$], and occurrence of complications [*OR* = 0.16, 95% *CI* (0.10, 0.26), $P<0.01$], all of which were statistically significant. [**Conclusions**] Early-stage phased pulmonary rehabilitation training for ARDS patients effectively improves the oxygenation index, shortens ICU length of stay and duration of mechanical ventilation, and reduces complications. These findings support the clinical application and promotion of early-stage phased rehabilitation training.

Key words Early-stage phased rehabilitation training, Acute respiratory distress syndrome (ARDS), Oxygenation index, Systematic review

1 Introduction

Acute respiratory distress syndrome (ARDS) is a common life-threatening condition in the field of critical care medicine. According to the American Thoracic Society International Conference, ARDS can be classified into mild, moderate, and severe based on the severity of hypoxia. The more severe the hypoxia, the longer the mechanical ventilation time and the higher the mortality rate for patients[1]. Foreign studies have shown that early pulmonary rehabilitation therapy for ARDS patients can effectively promote lung function recovery and reduce mortality. However, the timing, methods, and procedures for conducting such therapy are still under exploration[2]. Currently, pulmonary rehabilitation training focuses on chronic pulmonary diseases, such as chronic obstructive pulmonary disease (COPD) patients[3-5]. In critically ill patients, physical exercise of the limbs has been widely carried out in some intensive care units (ICUs). Due to constraints in concepts, medical environments, technologies, and human resources, pulmonary rehabilitation training for ICU patients is less frequently conducted. The limited literature reports often focus on individual measures and primarily target patients in the stable phase of hospitalization. Further exploration is needed on how to implement early-stage phased pulmonary rehabilitation exercise for critically ill ARDS patients.

Early-stage phased pulmonary rehabilitation exercise techniques play a crucial role in the care of ARDS[6]. However, the existing studies have small sample sizes and there is a lack of systematic evaluative research, resulting in low reference value of conclusions. Therefore, there is an urgent need for relevant meta-analyses and reports to analyze the specific effects of early-stage phased pulmonary rehabilitation exercise techniques in the care of ARDS. Based on this, we conducted a literature search, assessed the methodological quality of clinically relevant studies that met the criteria, and performed integrated analysis to provide evidence-based references for early-stage phased pulmonary rehabilitation therapy for ARDS.

2 Material and methods

2.1 Literature search We conducted a computer-based search of the following Chinese biomedical literature databases: China National Knowledge Infrastructure (CNKI), Wanfang Database, and Chongqing VIP Chinese Scientific Journals Database. The search timeframe included the establishment of the databases up to December 2021. The search language was Chinese, and the main search terms used were "acute respiratory distress syndrome" and "early-stage phased rehabilitation training".

2.2 Inclusion and exclusion criteria

2.2.1 Inclusion criteria. (i) The included studies must be randomized controlled trials (RCTs) or clinical controlled trials. (ii) The study subjects must meet the clinical diagnostic criteria for acute respiratory distress syndrome. (iii) The intervention in the experimental group must involve early-stage phased rehabilitation training, including ventilator ventilation strategies, airway management, positioning therapy, activity/respiratory exercises, *etc.*

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The control group should receive routine treatments, including mechanical ventilation and medication. (iv) The outcome measures must include at least one of the following: (a) oxygenation index, (b) ICU length of stay, (c) ventilator usage time, (d) occurrence of complications (ventilator-associated pneumonia, pressure ulcers, delirium).

2.2.2 Exclusion Criteria. (i) Review articles, master's theses, doctoral dissertations. (ii) Case reports, famous physician case studies, individual case reports. (iii) Conference proceedings papers. (iv) Animal research literature. (v) Duplicate articles obtained from different databases. (vi) Studies with interventions other than early-stage phased rehabilitation training. (vii) Studies with unobtainable data, including single-arm studies and related data or experimental protocols that cannot be accessed. (viii) Studies with inconsistent treatment duration between the experimental and control groups or outcome measures that do not match.

2.3 Data extraction and quality assessment

2.3.1 Data extraction. Two systematic review authors obtained relevant literature, extracted the information, and cross-checked it. Discrepancies were resolved through the involvement of a third party. The included literature was recorded using a standardized data extraction form. The extracted information for this study included the first author, publication year, number of cases, intervention measures for the experimental and control groups, treatment duration, outcome measures, and assessment of risk of bias.

2.3.2 Quality assessment of the literature. The risk of bias assessment table was created using RevMan 5.4 software. The selected literature was assessed for quality, including assessing the following aspects: correctness of random sequence generation; allocation concealment; implementation of blinding for the assessors and participants; blinding of outcome assessment; completeness of outcome data; selective reporting; and other biases.

2.4 Statistical methods RevMan 5.4 software was used to analyze the relevant data from the included literature. For binary data, odds ratios (*OR*) were used as the effect measure statistical unit, and for continuous data, standard mean differences (*SMD*) with a 95% confidence interval (*CI*) were used. $P \leqslant 0.05$ was considered statistically significant. Heterogeneity among the included studies was assessed using p-values and I^2. If $P \geqslant 0.1$ and $I^2 \leqslant 50\%$, it indicated low heterogeneity, and a fixed-effects model was used for meta-analysis. If there was significant heterogeneity ($P < 0.1$ and $I^2 > 50\%$), a random-effects model was used for combining the statistical measures.

3 Results and analysis

3.1 Literature selection results A total of 560 articles were obtained from different databases. After eliminating duplicate articles using EndNote, 307 duplicates were removed. A preliminary screening of titles and abstracts resulted in the exclusion of 87 irrelevant articles, including case studies, animal experiments, and renowned expert experiences. After reading the full texts and reviewing the data, 143 articles that did not meet the criteria of this study were excluded. Finally, 13 articles were included [7-31]. The search process is shown in Fig. 1.

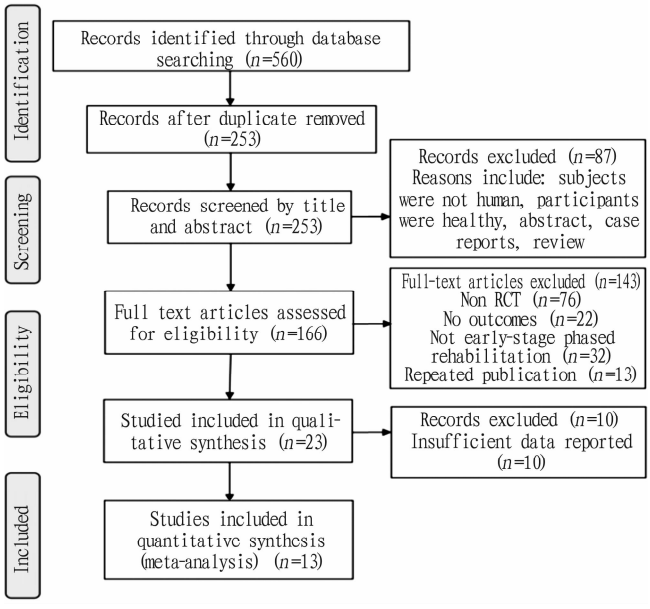

Fig. 1 PRISMA flowchart diagram of the search process

3.2 Quality evaluation of the included literature The included trials did not mention allocation concealment or blinding. Among them, random number table method was used in 10 studies, while the remaining literature only described it as random. All trials reported outcome evaluation indicators, and no selective reporting was observed. It is unknown whether the baseline data in the included literature is comparable. The risk of bias assessment for the included literature is shown in Fig. 2.

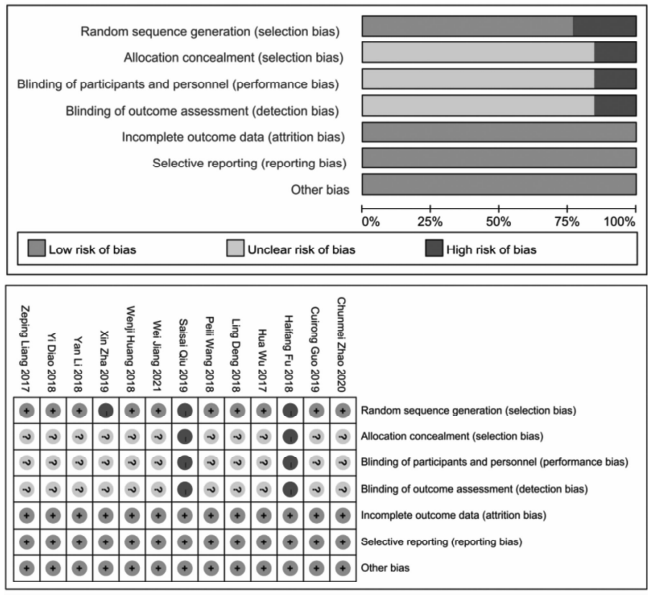

Fig. 2 Risk of bias summary

3.3 Main results According to the results of the meta-analysis, the early-stage phased rehabilitation training group, compared to the traditional rehabilitation training group, demonstrated a sig-

nificant increase in oxygenation index [*SMD* = 1.18, 95% *CI* (1.01, 1.35), *P* < 0.01] among ARDS patients. The difference was statistically significant (Fig. 3). Additionally, the ICU length of stay [*SMD* = −0.70, 95% *CI* (−0.90, −0.50), *P* < 0.01] (Fig. 4), duration of ventilator use [*SMD* = −1.15, 95% *CI* (−1.36, −0.94), *P* < 0.01] (Fig. 5), and incidence of complications [*OR* = 0.16, 95% *CI* (0.10, 0.26), *P* < 0.01] (Fig. 6) were significantly reduced, with statistically significant differences.

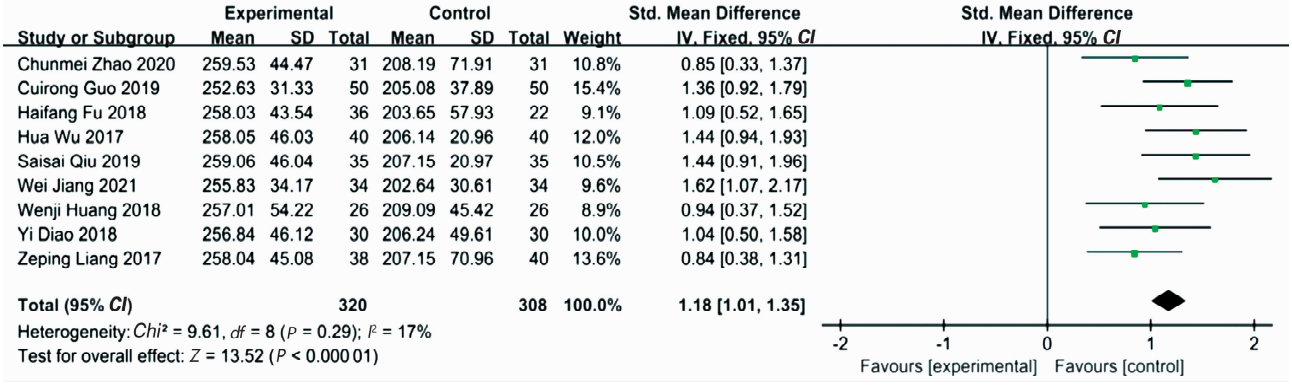

Fig. 3 Meta-analysis forest plot of the effects of early-stage phased rehabilitation training on oxygenation index in ARDS patients

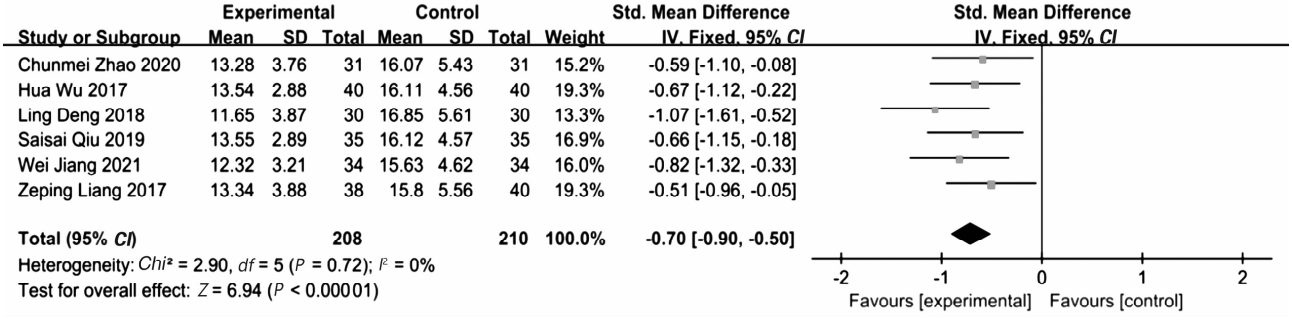

Fig. 4 Meta-analysis forest plot of the effects of early-stage phased rehabilitation training on the ICU length of stay in ARDS patients

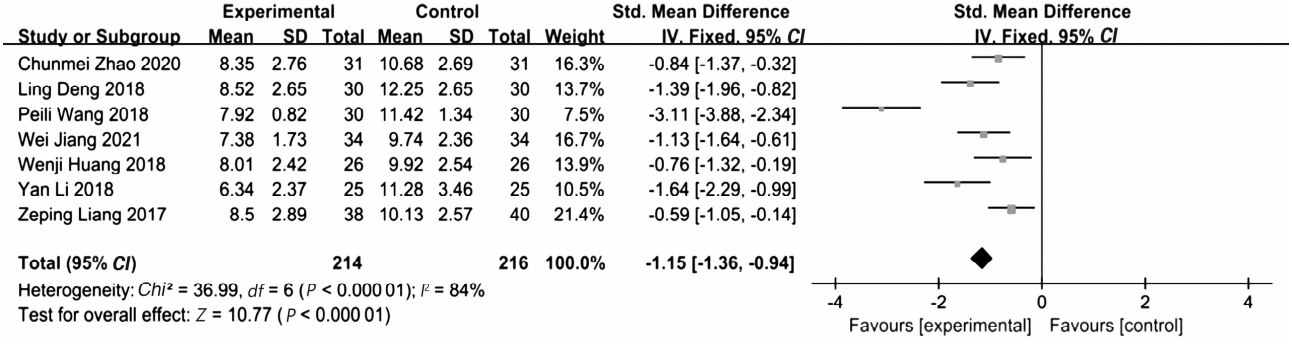

Fig. 5 Meta-analysis forest plot of the effects of early-stage phased rehabilitation training on the duration of ventilator use in ARDS patients

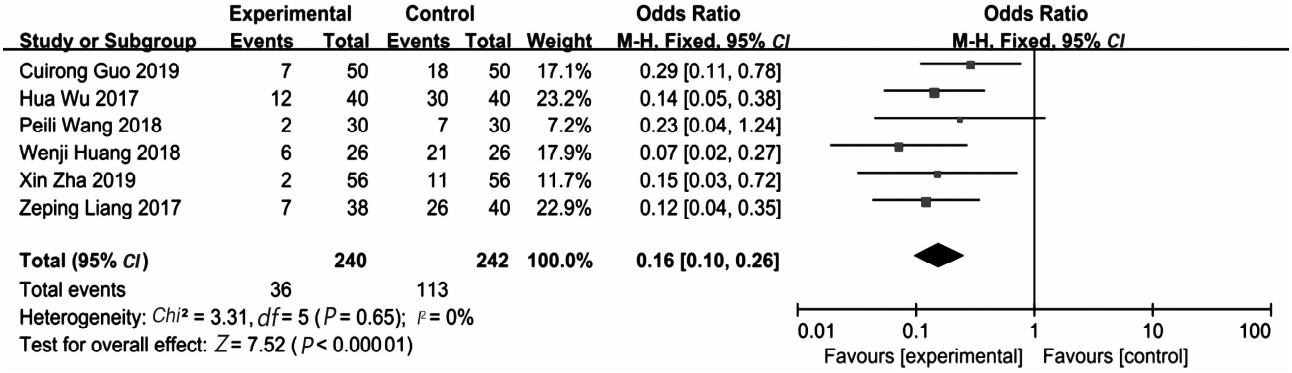

Fig. 6 Meta-analysis forest plot of the effects of early-stage phased rehabilitation training on the incidence of complications in ARDS patients

4 Discussion

The meta-analysis results suggest that early-stage phased pulmonary rehabilitation training in patients with acute respiratory distress syndrome (ARDS) can effectively improve the oxygenation index, shorten ICU length of stay and duration of ventilator use, and reduce complications. These findings indicate the potential clinical applicability and merits of implementing such interventions.

ARDS is a common respiratory distress syndrome characterized by progressively increased respiratory rate, persistent hypoxemia, and evident signs of oxygen deprivation, as well as pathological changes in lung function[7]. In clinical practice, ARDS is typically divided into four stages: (i) the lung injury stage, marked by increased respiratory rate; (ii) the relatively stable stage, characterized by dyspnea, hypoxemia, and pulmonary consolidation; (iii) the respiratory failure stage, necessitating the use of mechanical ventilation for respiratory support; and (iv) the end-stage, wherein severe oxygen deprivation and ineffective breathing occur, leading to disturbances in acid-base balance and circulatory failure[8]. Thus, early treatment of ARDS is essential to improve respiratory function, establish effective ventilation, and reduce the occurrence of complications[9].

The severity of ARDS is directly associated with higher mortality rates. Early initiation of rehabilitative care in patients can expedite lung function recovery and reduce mortality. Early-stage phased pulmonary rehabilitation exercise techniques involve developing targeted, phased rehabilitation plans based on the specific condition of each patient[10]. This approach transforms passive exercise into active exercise, effectively improving lung ventilation and exhalation functions. When combined with ventilator strategies, it significantly enhances the oxygenation index of patients and reduces the occurrence of complications such as ventilator-associated pneumonia[11]. Additionally, proper positional changes significantly improve patient oxygen saturation, while timely and effective airway management promotes the clearance of airway secretions and sputum. Early-stage phased pulmonary rehabilitation exercise techniques effectively prevent muscle atrophy and dysfunction. They are particularly beneficial for long-term bedridden patients and those receiving muscle relaxants or sedatives. This rehabilitation technique significantly reduces ICU length of stay, decreases hospital costs, alleviates the psychological burden and financial pressure on patients and their families, and effectively addresses the limitations of traditional nursing care[12].

When conducting pulmonary rehabilitation exercise in critically ill ARDS patients, in addition to implementing protective mechanical ventilation and medication treatment, the following issues should be considered. Firstly, the implementation of individualized plans: the content of operations varies among patients with different conditions, and even when following the same plan, the intensity (time and force) of treatment may differ. Secondly, assessment and observation during plan implementation: this technique may have certain effects on the patient's hemodynamics, therefore close monitoring of vital signs such as heart rate, blood pressure, and respiration is essential. Thirdly, the expertise of medical professionals: it has been reported that in the ICU, experienced healthcare workers achieve better treatment outcomes than less experienced or newly graduated ones[13]. Lastly, psychological issues after ICU discharge: Although ARDS survivors may have their lung function essentially restored, they often experience depression, anxiety, or other post-traumatic psychological disorders[14]. Survivors with low oxygenation index or prolonged mechanical ventilation are prone to develop anxiety disorders. Therefore, early psychological and physical rehabilitation therapy for ARDS survivors is important for improving their quality of life in the long term.

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