International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY

Efficacy of Extradiaphragmatic Pacing Combined with Rehabilitation Training on Pulmonary Function in Stroke Patients: A Meta-Analysis

INPLASY202530095
doi: 10.37766/inplasy2025.3.0095
Received: 23 March 2025
Published: 23 March 2025

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - The review has not yet started.

Conflicts of interest - None declared.

INPLASY registration number: INPLASY202530095

Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 March 2025 and was last updated on 23 March 2025.

INTRODUCTION

Review question / Objective To synthesize the existing evidence and assess the efficacy of extradiaphragmatic pacing (EDP) combined with rehabilitation training (Intervention) compared to rehabilitation training alone or standard care (Comparison) in improving pulmonary function outcomes (Outcome) among stroke patients (Population), based on randomized controlled trials (Study design).

PICO Breakdown:

P (Population): Stroke patients (with or without pre-existing pulmonary dysfunction).
I (Intervention): Extradiaphragmatic pacing (EDP) combined with rehabilitation training.
C (Comparison): Rehabilitation training alone, standard care, or placebo/sham intervention.
O (Outcome):
Primary outcomes: Forced expiratory volume in 1 second (FEV1), forced vital capacity (FVC), FEV1/FVC ratio.
Secondary outcomes: Respiratory muscle strength (maximal inspiratory/expiratory pressure), exercise tolerance, hospitalization duration, quality of life, and adverse events.

Condition being studied Post-stroke pulmonary dysfunction is a common and debilitating complication in stroke survivors, primarily caused by neurological damage to respiratory control centers (e.g., brainstem or motor cortex lesions) and secondary respiratory muscle weakness due to prolonged immobility. This condition leads to reduced lung capacity, impaired airway clearance, and heightened susceptibility to respiratory infections, significantly impacting recovery and quality of life. Conventional rehabilitation strategies, such as breathing exercises and aerobic training, aim to improve respiratory function but often fall short in patients with severe neuromuscular impairment, as they fail to adequately activate paralyzed or weakened respiratory muscles. Emerging therapies like extradiaphragmatic pacing (EDP), which directly stimulates the phrenic nerve to enhance

diaphragm contraction, hold potential to complement traditional rehabilitation by addressing both neurological deficits and deconditioning effects.

METHODS

Search strategy ("Stroke"[Mesh] OR "Cerebrovascular Disorders"[Mesh] OR "post-stroke"[tiab] OR "hemiplegia"[tiab])
AND
("Electric Stimulation Therapy"[Mesh] OR "phrenic nerve stimulation"[tiab] OR "EDP"[tiab])
AND
("Respiratory Function Tests"[Mesh] OR "pulmonary function"[tiab] OR “FEV1"[tiab]).

Participant or population Stroke patients with impaired pulmonary function undergoing rehabilitation training.

Intervention Extradiaphragmatic pacing (EDP) combined with structured rehabilitation training, including electrical stimulation of the phrenic nerve to enhance diaphragmatic contraction and standardized respiratory or physical exercises (e.g., breathing retraining, aerobic training, or resistance exercises).

Comparator Standard rehabilitation training alone (e.g., breathing exercises, aerobic/strength training) or conventional care (e.g., pharmacological management, routine physiotherapy) without extradiaphragmatic pacing (EDP).

Study designs to be included Randomized controlled trials (RCTs).

Eligibility criteria Inclusion:(1)Adult stroke patients (≥18 years) with or without pulmonary dysfunction.(2)Extradiaphragmatic pacing (EDP) combined with any form of rehabilitation training (e.g., respiratory exercises, physical therapy).(3)Rehabilitation training alone or standard care (e.g., routine physiotherapy, pharmacological treatment).(4)Peer-reviewed randomized controlled trials (RCTs) with quantitative outcome data.(5)At least one pulmonary function metric (e.g., FEV1, FVC) or respiratory muscle strength.

Exclusion:(1)Studies combining EDP with non-rehabilitation therapies (e.g., surgery, acupuncture).(2)Non-RCTs, reviews, case reports, or studies with incomplete data (e.g., conference abstracts without full text).(3)Duplicate reports or unpublished trials without peer review.(4)Research in languages other than Chinese or English.

Information sources CNKI, Wanfang, VIP, CBM, PubMed, Embase, Web of Science, and CochraneLibrary.

Main outcome(s) Pulmonary Function Metrics.

Additional outcome(s) (1)6-Minute Walk Test (6MWT): Exercise tolerance (meters).(2)Modified Barthel Index (MBI): Activities of daily living (ADL) capacity.(3)Hospitalization Duration: Days from admission to discharge.(4)Incidence of Respiratory Infections: Pneumonia or bronchitis events.(5)Patient-Centered Outcomes:(6)Quality of Life (QoL): Validated scales (e.g., SF-36, SGRQ).(7)Adverse Events: EDP-related complications (e.g., skin irritation, nerve injury).

Quality assessment / Risk of bias analysis The included studies were assessed for the RoB using the Cochrane risk-of-bias tool 2.0 in five domains: bias arising from the randomization process, bias due to deviations from intended interventions, bias due to missing outcome data, bias in measurement of the outcome, and bias in selection of the reported result. The possible source of each bias was explored. Each study was categorized as low risk, some concerns, or high risk. The overall RoB was also assessed.

Strategy of data synthesis Review Manager 5.3 and Stata17.0 will be used to perform meta-analyses. For continuous variables, the effect size measure will be the mean difference (MD), and for dichotomous variables, the risk ratio (RR) will be used. The Q test and I^2 statistic will be used to assess inter-study heterogeneity. A fixed-effects model will be adopted if no heterogeneity is found ($I^2$0.1); otherwise, a random-effects model will be used. Subgroup analyses will be conducted by different study characteristics to explore the sources of heterogeneity and better understand the effects of interventions.

Subgroup analysis (1)Stroke Characteristics(2)Intervention Parameters(3)Disease Phase(4)Baseline Pulmonary Severity(5)Control Group Type.

Sensitivity analysis
Sensitivity Analysis: To assess the robustness of the pooled results, we performed leave-one-out sensitivity analyses by iteratively excluding each individual study and recalculating the effect estimates. This approach aimed to identify whether any single study disproportionately influenced the overall findings.

Publication Bias:

Potential publication bias was evaluated using Egger's linear regression test (statistical significance threshold: $P < 0.05$) and visual inspection of funnel plots (symmetry assessment for primary outcomes). If asymmetry was detected, we further explored sources of bias using trim-and-fill analysis.

Language restriction Chinese, English.

Country(ies) involved China.

Keywords Stroke,Extradiaphragmatic pacing, Pulmonary function,Rehabilitation training, Respiratory rehabilitation.

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