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A protocol for a Systematic Review and Meta-analysis of External Diaphragm Pacing Alone and Combined Adjunctive Therapies for Respiratory Function in Patients With Stroke

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Data analysis.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 22 March 2026 and was last updated on 22 March 2026.

INTRODUCTION

Review question / Objective The aim of this systematic review and meta-analysis is to evaluate the effectiveness of external diaphragmatic pacing (EDP), used alone or in combination with adjunctive therapies, for improving respiratory function and diaphragmatic function in patients with stroke. The review will address the following question: compared with the same background rehabilitation without EDP, or compared with EDP alone, does EDP or adjunctive therapy plus EDP improve pulmonary function and diaphragmatic outcomes in patients with stroke?

Rationale Respiratory dysfunction is common after stroke and may contribute to impaired pulmonary ventilation, diaphragmatic dysfunction, reduced cough effectiveness, prolonged hospitalization, and poorer rehabilitation outcomes. External diaphragmatic pacing has been increasingly applied in neurological rehabilitation settings, either as an add-on to conventional rehabilitation or in combination with other adjunctive interventions, such as inspiratory muscle training, respiratory training, postural training, abdominal electrical stimulation, and repetitive peripheral magnetic stimulation. However, the available evidence remains heterogeneous in terms of patient populations, intervention protocols, comparator frameworks, and measurement conditions of diaphragmatic outcomes. Therefore, a systematic review and meta-analysis is needed to synthesize the current randomized evidence and clarify the effectiveness of EDP alone or in combination with adjunctive therapies in patients with stroke.

Condition being studied Stroke-related respiratory dysfunction, including reduced pulmonary ventilation and/or impaired diaphragmatic function, in patients with ischemic stroke or hemorrhagic stroke at different rehabilitation stages.

METHODS

Search strategy A systematic search will be conducted in PubMed, Embase, Cochrane Library, Web of Science Core Collection, China National

Knowledge Infrastructure (CNKI), Wan Fang Database, Chinese Scientific Journal Database (VIP), and China Biology Medicine (CBM) from inception to [date]. The search strategy will combine terms related to stroke (e.g., "stroke", "cerebrovascular accident", "hemiplegia"), diaphragmatic/phrenic stimulation (e.g., "external diaphragmatic pacing", "diaphragm pacing", "phrenic nerve stimulation"), and randomized trials. No language restrictions will be imposed. The detailed search strategies for each database will be reported in the final review.

Participant or population Patients diagnosed with stroke, including ischemic stroke and hemorrhagic stroke, who have respiratory dysfunction, impaired diaphragmatic function, tracheostomy, or other indications for pulmonary rehabilitation or respiratory muscle rehabilitation.

Intervention External diaphragmatic pacing (EDP) or transcutaneous phrenic nerve stimulation, used either alone on top of the same background treatment or as part of a combined intervention with adjunctive therapies.

Comparator Eligible comparators will include: (1) the same background rehabilitation or supportive treatment without EDP, for analyses assessing the incremental effect of EDP; and (2) EDP alone, for analyses assessing the additional effect of adjunctive therapies combined with EDP.

Study designs to be included Only randomized controlled trials will be included.

Eligibility criteria Studies will be eligible if they: (1) enroll patients with stroke; (2) include EDP or transcutaneous phrenic nerve stimulation as an intervention; (3) fit one of the two predefined comparison frameworks; (4) report at least one prespecified core outcome, including FEV1, FVC, diaphragm excursion (DE), or diaphragm thickness (DT); and (5) use a randomized controlled trial design. Studies will be excluded if they are non-randomized studies, observational studies, case reports, reviews, protocols, dissertations, duplicate reports, or if the intervention/comparator framework does not match the predefined review question.

Information sources Electronic databases to be searched will include PubMed, Embase, Cochrane Library, Web of Science Core Collection, China National Knowledge Infrastructure (CNKI), Wan Fang Database, Chinese Scientific Journal Database (VIP), and China Biology Medicine (CBM). Additional sources will include the reference lists of eligible studies and relevant reviews. No language restrictions will be applied.

Main outcome(s) The primary outcomes will be forced expiratory volume in one second (FEV1), forced vital capacity (FVC), diaphragm excursion (DE), and diaphragm thickness (DT).

Data management Two reviewers will independently screen studies, extract data, and cross-check the extracted information. Any disagreement will be resolved by discussion or consultation with a third reviewer.

Quality assessment / Risk of bias analysis Risk of bias of the included randomized controlled trials will be assessed independently by two reviewers using the Cochrane Risk of Bias 2.0 tool, covering bias arising from the randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result.

Strategy of data synthesis Meta-analysis will be performed using Review Manager and/or other statistical software as appropriate. For continuous outcomes, standardized mean differences (SMDs) with 95% confidence intervals will be calculated because the included studies are expected to use different measurement scales and units. A random-effects model will be applied due to anticipated clinical and methodological heterogeneity.

Subgroup analysis Subgroup analyses are planned according to: (1) tracheostomy status (tracheostomy vs non-tracheostomy) in the main comparison; and (2) type of adjunctive intervention in the combined-treatment comparison, including physical neuromodulation, active training-based interventions, and other adjunctive therapies if applicable.

Sensitivity analysis Sensitivity analyses will be performed by excluding studies with high risk of bias, excluding studies with extreme effect sizes, and, where applicable, comparing different definitions or measurement conditions of diaphragmatic outcomes.

Language restriction No language restrictions will be applied.

Country(ies) involved China.

Keywords stroke; external diaphragmatic pacing; phrenic nerve stimulation; respiratory function; diaphragm; systematic review; meta-analysis.

Dissemination plans The findings of this review will be disseminated through peer-reviewed publication and conference presentation.

Contributions of each author

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