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Effects of extracorporeal carbon dioxide removal in implementing ultra-protective ventilation strategies for patients with acute respiratory distress syndrome: A systematic review and meta-analysis

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ADMINISTRATIVE INFORMATION

Support - None.

Review Stage at time of this submission - Completed but not published.

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 17 July 2025 and was last updated on 17 July 2025.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aims to evaluate the role of ECCO2R in facilitating the application of ultraprotective ventilation strategies in ARDS patients.

Condition being studied Despite proven mortality benefits of low tidal volume ventilation in acute respiratory distress syndrome (ARDS), overall mortality remains high (30-40%). Ultraprotective ventilation (≤4 ml/kg predicted body weight) may further reduce ventilator-induced lung injury but risks severe hypercapnia. Extracorporeal carbon dioxide removal (ECCO2R) could enable ultraprotective ventilation by managing carbon dioxide retention, though evidence remains limited.

METHODS

Search strategy "extracorporeal carbon dioxide removal", "ECCO2R", "acute respiratory distress syndrome", "ARDS", "ultraprotective ventilation", and "low tidal volume ventilation".

Participant or population Patients with acute respiratory distress syndrome (ARDS) meeting the Berlin Definition.

Intervention $ECCO_2R$-assisted ultraprotective ventilation (tidal volume ≤4 ml/kg predicted body weight [PBW]).

Comparator Pretreatment.

Study designs to be included Randomized controlled trials (RCTs), quasi-experimental studies, cohort studies, and case-control studies.

Eligibility criteria Inclusion criteria comprised: (1) population: patients with acute respiratory distress syndrome (ARDS) meeting the Berlin Definition; (2) intervention: $ECCO_2R$-assisted ultraprotective ventilation (tidal volume ≤4 ml/kg predicted body weight [PBW]); (3) study designs: randomized

controlled trials (RCTs), quasi-experimental studies, cohort studies, and case-control studies; and (4) outcomes: respiratory mechanics parameters, ventilation variables, patient-centered outcomes, and complication rates.

Information sources PubMed, Embase, Web of Science, and the Cochrane Library.

Main outcome(s) Respiratory mechanics parameters, ventilation variables, patient-centered outcomes, and complication rates.

Quality assessment / Risk of bias analysis Methodological quality was assessed with differentiated tools: the Cochrane Risk of Bias Tool for randomized controlled trials, evaluating domains including randomization process, allocation concealment, blinding, missing data management, and outcome measurement bias; the Newcastle-Ottawa Scale (NOS) for cohort and case-control studies, scored across three dimensions: selection of study groups, comparability of cohorts, and assessment of exposure/outcomes.

Strategy of data synthesis For continuous variables, the weighted mean difference (WMD) with 95% confidence intervals (95%CI) was used as the pooled effect measure. Dichotomous outcomes were analyzed using proportion with 95% CI. Given anticipated heterogeneity across studies in design characteristics, sample profiles, and intervention protocols, all meta-analyses employed a random-effects model.

Subgroup analysis Prespecified subgroup analyses stratified by study design, patient age, and sex were conducted, with between-subgroup differences tested for statistical significance using interaction tests.

Sensitivity analysis Sensitivity analysis using the leave-one-out method was performed to evaluate the robustness of pooled estimates and heterogeneityindices.

Language restriction Chinese and English.

Country(ies) involved China.

Keywords extracorporeal carbon dioxide removal; ultra-protective ventilation; acute respiratory distress syndrome; systematic review; meta-analysis.

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