INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Effect of different levels of PEEP on mortality in ICU patients without acute respiratory distress syndrome: a systematic review and meta-analysis

Shao, S[1]; Kang, H[2]; Wang, Q[3]; Qian, Z[4]; Tong, Z[5].

Review question / Objective: **To determine whether higher positive end- expiratory pressure (PEEP) could decrease mortality of patients without acute respiratory distress syndrome (ARDS) compared with lower PEEP.**
Condition being studied: **Invasive mechanical ventilation (IMV) is one of the most frequently applied lifesaving strategies among the intensive care unit (ICU) patients. However, inappropriate IMV can aggravate ventilator–induced lung injury (VILI). Patients with acute respiratory distress syndrome (ARDS) could benefit from ventilation with a higher positive end expiratory pressure (PEEP). However, in patients without ARDS, the benefit of PEEP may be diminished because they receive spontaneous ventilation more frequently and have less atelectasis than patients with ARDS. Previous study showed that higher PEEP could decrease the risk of ARDS and improve oxygenation index than lower PEEP. While in the latest RCT, no survival benefits were found. In order to develop suggestions for doctors regarding the usage of higher or lower PEEP in patients without ARDS, there is a need to collect and pool the results of eligible studies comprehensively. Therefore, we plan to construct a systematic review and meta-analysis to compare the effects of different levels of PEEP among patients without ARDS.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 17 February 2021 and was last updated on 17 February 2021 (registration number INPLASY202120052).

INTRODUCTION

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METHODS

Participant or population: ICU Patients without ARDS at onset of ventilation.

Intervention: Higher PEEP.

Comparator: Lower PEEP.

Study designs to be included: Randomized Controlled Trial.

Eligibility criteria: (1) RCTs; (2) adult patients without ARDS; (3) received mechanical ventilation in ICU setting; (3) higher PEEP was applied in the intervention arm; (4) lower PEEP should be applied among control arm; (5) similar Vt and fraction of inspiration O2 (FiO2) should be applied between these two groups.

Information sources: Medline, Embase, Cochrane Library, Web of Science, and Wanfang database.

Main outcome(s): Primary outcomes will be all-caused mortality and 28-day mortality.

Additional outcome(s): Secondary outcomes will be duration of mechanical ventilation (MV), duration of hospital, duration of ICU, pulmonary complications (ARDS, pneumonia, atelectasis, barotrauma, hypoxemia, and hypotension), arterial blood gas(PaO2) / FiO2 ratio, blood pressure, heart rate (HR), cardiac index (CI), systemic vascular resistance index (SCRI), cardiac output (CO).

Quality assessment / Risk of bias analysis: We will use the Cochrane Collaboration risk of bias tool to examine the risk of bias in the included trials and judge the risk of bias as “low risk,” “unclear,” or “high risk” in each domain specified by the tool.

Strategy of data synthesis: We will evaluate dichotomous variables using the RR and 95% CI. We will generate summary estimates of the mean and standard deviation (SD) for continuous outcomes. Meta-analysis will be performed using Mantel-Haenszel (M-H) random-effect models or, if the heterogeneity is not significant, fixed-effects models. A correction factor (1.0) will be applied to zero-event trials to enforce the effect of RR . We will assesse the heterogeneity among trials by using I 2 testing (where a value of >50% is regarded as indicating substantial heterogeneity). If a primary or secondary outcome has heterogeneity, we will performe subgroup analysis or sensitivity analysis to find the source of heterogeneity. We will judge the publication bias by creating a funnel plot and applying traditional statistical methods (Egger’s test) when there were more than five trials 29 . The results will be considered statistically significant if the p value < 0.05. We will use the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to judge the quality of evidence for the primary outcomes and secondary outcomes.

Subgroup analysis: We will perform the subgroup analysis to juedge the potential source of heterogeneity. The predefined

analysis wil be constructed based on the risk of bias, type of patients, PEEP gradient of control group (high versus zero PEEP). A test of interaction will be used to judge the differences in treatment effect across these subgroups.

Sensitivity analysis: In outcomes with moderate-to-high heterogeneity, we will perform sensitivity analysis by sequentially excluding the inclusion studies to assess the potential source of heterogeneity.

Country(ies) involved: China.

Keywords: positive end- expiratory pressure, acute respiratory distress syndrome, mortality, meta-analysis, intensive care unit.

Contributions of each author:

Author 1 - Shuai Shao developed the initial idea of this study and conducted a comprehensive search of four databases. Shuai Shao and Quanying Wang took responsibility for selecting the study. Shuai Shao extracted data and drafted the manuscript.
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Author 2 - Hanyujie Kang reviewed this article and provided suggestion for it. All of the authors have carefully examined this manuscript and agreed with the ideas presented in the article.
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All of the authors have carefully examined this manuscript and agreed with the ideas presented in the article.