# INPLASY

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Department of Respiratory and Critical Care Medicine, Beijing Institute of Respiratory Medicine, Beijing Chao-Yang Hospital, Capital Medical University, Beijing, 100020, China. Effect of prolonged prone positioning in intubated COVID-19 patients with acute respiratory distress syndrome: a systematic review and meta-analysis

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## **ADMINISTRATIVE INFORMATION**

**Support** - This work was funded by the research Grant 2023YFC0872500 from the Ministry of Science and Technology of the People's Republic of China.

**Review Stage at time of this submission -** Formal screening of search results against eligibility criteria.

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 21September 2023 and was last updated on 21 September 2023.

## INTRODUCTION

Review question / Objective Prone positioning (PP) has been considered a feasible treatment for intubated coronavirus disease 2019 (COVID-19) patients with acute respiratory distress syndrome (ARDS). However, the optimal duration of PP remains uncertain. This meta-analysis aims to assess the efficacy and safety of prolonged PP on patients with ARDS due to COVID-19.

**Rationale** Relevant studies published from inception until September 21, 2023, were systematically searched. The primary outcomes were the mortality and change in the PaO2:FIO2 ratio; the secondary outcome was the incidence of complications. The random effects model was used to analyze the data.

**Condition being studied** Since 2019, the coronavirus disease 2019 (COVID-19) pandemic

has placed unprecedented pressure on global healthcare systems. Coronavirus disease has many clinical manifestations ranging from asymptomatic infection to critical illness. Approximately 10-20% of hospitalized patients with COVID-19 develop acute respiratory distress syndrome (ARDS) requiring intensive care unit (ICU) admission and invasive mechanical ventilation (IMV), which also have a high mortality rate[1-4]. Active interventions have been taken to reduce mortality risk in COVID-19 patients with ARDS, and the prone position is one of them.

## **METHODS**

**Search strategy** The Cochrane Library databases, Embase, and Pubmed were systematically searched from January 1, 2020, to September 21, 2023. The search terms were as follows: ("COVID-19" or "SARS-CoV-2") and ("prone position\*" or "Pron\*"). We did not apply language restrictions. The reference lists of the included studies were also reviewed to identify any additional relevant studies.

Participant or population Adults (≥18 years old) who developed acute respiratory distress syndrome due to COVID-19 and were in the intubated state.

**Intervention** Prolonged prone positioning (>24 hours) or standard prone position.

**Comparator** studies that compared the experimental group using prolonged prone positioning (>24 hours) with the control group using standard prone position.

**Study designs to be included** The inclusion criteria were as follows: 1) adults (≥18 years old) who developed acute respiratory distress syndrome due to COVID-19 and were in the intubated state; 2) studies that compared the experimental group using prolonged prone positioning (>24 hours) with the control group using standard prone position; 3) studies included required outcomes and the data could be directly extracted or calculated; 4) randomized controlled trials (RCTs) or observational studies.

Eligibility criteria The inclusion criteria were as follows: 1) adults (>18 years old) who developed acute respiratory distress syndrome due to COVID-19 and were in the intubated state; 2) studies that compared the experimental group using prolonged prone positioning (>24 hours) with the control group using standard prone position; 3) studies included required outcomes and the data could be directly extracted or calculated; 4) randomized controlled trials (RCTs) or observational studies. The exclusion criteria were as follows: 1) meta-analyses, reviews, case series, case reports, study protocols, or expert opinions; 2) cross-over trials; 3) insufficient data; 4) multiple publications or unpublished studies; 5) not related to intubated COVID-19 patients; 6) studies that enrolled patients younger than 18 years old or animals; 7) experimental group did not receive prolonged prone positioning; 8) control group did not receive standard prone position; 9) not reported the outcomes what we need.

**Information sources** The Cochrane Library databases, Embase, and Pubmed were systematically searched.

Main outcome(s) The primary outcomes included mortality and change in the PaO2:FIO2 ratio.

Additional outcome(s) The secondary outcomes were the incidence of complications in the prone position (pressure injuries, facial edema, loss of endotracheal tube, loss of vascular access, etc).

Quality assessment / Risk of bias analysis The risk of bias for included RCTs was evaluated by the Cochrane Collaboration Risk of Bias tool and rated as "low," "unclear," or "high" in each domain. The risk of bias for included observational cohort studies was assessed by the Newcastle-Ottawa scale. Studies with three or four stars in the selection domain, one or two stars in the comparability domain, and two or three stars in the outcome/exposure domain were considered good quality studies with a low risk of bias.

Strategy of data synthesis Review Manager Version 5.4 was used to finish all statistical analyses. We used the Mantel-Haenszel randomeffects model to analyze the results. The results were shown as the forest plots. Values for continuous outcomes were reported as the mean (standard deviation), and dichotomous outcomes were presented as the odds ratios (OR) with 95% confidence intervals (CI). I<sup>2</sup> testing was used to assess the statistical heterogeneity between studies. I<sup>2</sup> of more than 50% was regarded as moderate-to-high heterogeneity[16]. We used sensitivity analyses to explore the sources of heterogeneity. Sensitivity analyses were performed by sequentially excluding one study each time to identify the potential influence.

Subgroup analysis None.

**Sensitivity analysis** We used sensitivity analyses to explore the sources of heterogeneity. Sensitivity analyses were performed by sequentially excluding one study each time to identify the potential influence.

Country(ies) involved China.

**Keywords** Prolonged prone position; COVID-19; acute respiratory distress syndrome; PaO2/FiO2 ratio; mortality.

## **Contributions of each author**

Author 1 - Hanyujie Kang. Author 2 - Nuer Subi. Author 3 - Zhaohui Tong.