INPLASY PROTOCOL

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Conflicts of interest:
None declared.

Comparison of Clinical Outcomes between Aggressive and Non-aggressive Intravenous Hydration for Acute Pancreatitis: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Review question / Objective: **To compare the clinical outcomes between aggressive and non-aggressive intravenous hydration in severe and non-severe acute pancreatitis.**
Condition being studied: **Patients with acute pancreatitis probably have the increased risk of mortality, and an early intravenous fluid supplement is the cornerstone therapy for acute pancreatitis. However, the treatment effects between aggressive and non-aggressive intravenous hydration remain controversial.**
Information sources: **We will search the PubMed, Embase and the Cochrane Library to identify the relevant randomized controlled trials without the language limitation from the database inception to November 23, 2022. The updated search will be performed, if necessary. The search strategy will be developed by the evidence-based medicine researcher and senior librarian. The important keywords with MeSH terms include "acute pancreatitis", "normal saline" and "Lactated Ringer's solution". To make our search more comprehensive, we will manually review the reference lists from the included studies, the previous review articles and published guideline of acute pancreatitis.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 15 November 2022 and was last updated on 29 December 2022 (registration number INPLASY2022110068).

INTRODUCTION

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increased risk of mortality, and an early intravenous fluid supplement is the cornerstone therapy for acute pancreatitis. However, the treatment effects between aggressive and non-aggressive intravenous hydration remain controversial.

METHODS

Participant or population: Adults with severe or non-severe acute pancreatitis.

Intervention: Aggressive intravenous hydration.

Comparator: Non-aggressive intravenous hydration.

Study designs to be included: Randomized controlled trials.

Eligibility criteria: Two reviewers will independently identify the included studies based on the following inclusion criteria: (1) participants: adults with acute pancreatitis; (2) interventions: aggressive intravenous fluid resuscitation defined as a. fluid administration (predominant normal saline or Lactated Ringer's solution) at a rate greater than 5-10 ml/kg/hour as the initial management; b. fluid bolus 20 ml/kg for 2 hours then 2-3 ml/kg/hour in the first 24 hours; c. 250–500 ml/h of isotonic crystalloid for the first 12–24 h or d. fluid administration ≧ 4,000 ml in the first 24 hour; (3) comparisons: non-aggressive intravenous fluid resuscitation defined as a. fluid administration at a rate lower than 5-10 ml/kg/hour; b. fluid bolus 10 ml/kg for 2 hours then 1.5 ml/kg/hour in the first 24 hour or c. fluid administration < 4,000 ml in the first 24 hour; (4) primary outcome: all-cause death; (5) design: randomized controlled trials. For the discrepancy of study selection, another senior author will make the final judgment.

Information sources: We will search the PubMed, Embase and the Cochrane Library to identify the relevant randomized controlled trials without the language limitation from the database inception to November 23, 2022. The updated search will be performed, if necessary. The search strategy will be developed by the evidence-based medicine researcher and senior librarian. The important keywords with MeSH terms include "acute pancreatitis", "normal saline" and "Lactated Ringer's solution". To make our search more comprehensive, we will manually review the reference lists from the included studies, the previous review articles and published guideline of acute pancreatitis.

Main outcome(s): We define all-cause death as the primary study outcome. Other secondary study outcomes, such as the rate of clinical improvement (a composite outcome required the SIRS subsides, decrease in hematocrit, blood urea nitrogen, and creatinine from baseline, decrease in epigastric pain degree and tolerance of oral nutrition) within 48 hours, fluid-related complications (such as abdominal compartment syndrome, pulmonary and peripheral edema) in non-severe acute pancreatitis and the changes of Acute Physiology and Chronic Health Evaluation II (APACHE II) scores for severe acute pancreatitis, sepsis, acute respiratory failure, acute kidney failure, pancreatitis necrosis, SIRS subsides, persistent SIRS>48 hours, clinical progression (persistent organ failure defined by revised Atlanta classification), total hospitalization days, hematocrit changes and blood urea nitrogen changes will be also evaluated if they have been reported from the included studies.

Quality assessment / Risk of bias analysis: The risk-of-bias assessment will be performed by two independent reviewers. We will use the Cochrane Collaboration's tool 2.0 which contains randomization process, deviations from intended interventions, missing outcome data, measurement of the outcome, selection of the reported result, and overall bias, to evaluate the methodological quality of the included randomized controlled trials.

Strategy of data synthesis: We will use the Review Manager Version 5.3 to conduct a random-effects meta-analysis. We will separately calculate the pooled risk ratio

(RR) and mean difference (MD) with a 95% confidence interval (CI) for categorical and continuous outcomes, respectively, in severe and non-severe acute pancreatitis. The I2 statistic will be used to determine the extent of statistical heterogeneity among the included randomized controlled trials, and a value > 50% is considered as significant heterogeneity. Funnel plots will be constructed to visually examine the presence of publication bias if there were at least 10 included randomized controlled trials in the meta-analysis.

Subgroup analysis: We will perform the subgroup analyses based on study countries, mean or median age and fluid volume of early aggressive hydration during the first 24 hours of treatment.

Sensitivity analysis: We will replicate all the analyses by only including studies with the goal-directed fluid therapy as the sensitivity analyses to determine the result robustness.

Country(ies) involved: Taiwan.

Keywords: acute pancreatitis; hydration; systematic review and meta-analysis.

Contributions of each author:

Author 1 - Xiu-Wei Li - Author 1 conducted the study selection, data extraction, risk-of-bias assessment, meta-analysis and drafted the manuscript.
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