INPLASY PROTOCOL

To cite: Li et al. Association of preadmission metformin use and prognosis in patients with sepsis and diabetes mellitus: A systematic review and meta-analysis. Inplasy protocol 2021100113. doi: 10.37766/inplasy2021.10.0113

Received: 29 October 2021

Published: 29 October 2021

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Support: 2021HYTP053.

Review Stage at time of this submission: Piloting of the study selection process.

Conflicts of interest: None declared.

Association of preadmission metformin use and prognosis in patients with sepsis and diabetes mellitus: A systematic review and meta-analysis

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Review question / Objective: We search the studies about the relation between preadmission metformin use and prognosis in patients with sepsis and diabetes to solve the controversy, which whether preadmission metformin use could improve the mortality of patients with sepsis and diabetes.

Condition being studied: At present, some studies showed that preadmission metformin use could decrease the mortality of the patients with sepsis and diabetes, whereas other studies reported that preadmission metformin use did not decrease the mortality of patients with sepsis and diabetes. Importantly, data of the previuos meta-analysis was so small, so the conclusions may not credible.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 29 October 2021 and was last updated on 29 October 2021 (registration number INPLASY2021100113).

INTRODUCTION

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METHODS

Participant or population: Patients with sepsis and diabetes.

Intervention: Preadmission metformin use.

Comparator: Non-metformin use.

Study designs to be included: Observational study.

Eligibility criteria: (1) patients with sepsis and DM who used metformin were enrolled, (2) the control group was DM complicated with sepsis but not treated with metformin, (3) mortality in metformin and non-metformin users was measured, (4) all patients were adults, (5) observational studies from all settings (emergency department, hospital ward, or ICU) were included, and (6) the publications were written in English.

Information sources: We comprehensively searched PubMed, Cochrane, and Embase databases for English language articles published before August 08, 2021. We used a combination of MeSH/Emtree, title/abstract, and keyword terms. The search terms were "metformin", "sepsis" and "critically ill". Endnote x9 software was used for literature screening. We reviewed references to eligible articles to identify other potentially relevant studies. Literature retrieval was conducted independently by two researchers.

Main outcome(s): Mortality; levels of serum creatinine and lactic acid.

Quality assessment / Risk of bias analysis:

Using the Newcastle-Ottawa Scale (NOS) for cohort studies, the risk of bias was assessed for each outcome in all included studies. A maximum of nine points was

awarded on the basis of the cohort selection (maximum four points), the comparability of the cohort design and analysis (maximum two points), and the adequacy of the outcome measures (maximum three points). Seven to nine points were considered high quality (low risk of bias)The outcome quality was evaluated using the Newcastle-Ottawa Scale.

Strategy of data synthesis: The metaanalysis used the pooled effects of each outcome. To investigate the heterogeneity between studies, we used a randomeffects model to calculate ORs and 95% Cls for each outcome. Heterogeneity was assessed using I2 and P values.

Subgroup analysis: None.

Sensitivity analysis: Because all included studies were observational cohort studies with a low risk of bias, a sensitivity analysis based on the methodological criteria was not conducted. A sensitivity analysis was performed only to assess the influence of any one study on the pooled OR and 95% CI by omitting one individual study at a time.

Country(ies) involved: China.

Keywords: metformin; sepsis; mortality; systematic review; meta-analysis.

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