INPLASY PROTOCOL

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Support: **None.**

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

Conflicts of interest:
None.

Prognostic value of the level of gut microbe-generated metabolite trimethylamine-N-oxide in patients with heart failure: a meta-analysis and systematic review

Miao, L[1]; Qu, H[2]; Shi, D[3].

Review question / Objective: **The effect of TMAO on the prognosis of patients with heart failure is unknown, so this study was designed to observe the effect of TMAO on the prognosis of patients with heart failure P:patients with heart failure O:The relationship between plasma TMAO and all-cause mortality in patients with heart failure .The relationship between plasma TMAO and adverse outcomes was also extracted.**
Condition being studied: **Heart failure is a complex multifactor disease with a wide range of socio-economic consequences. Despite the latest development of new drugs and treatment strategies, HF related mortality and incidence rate is still high. Targeting the gut microbiome is a new strategy, as people are increasingly aware of its important role in overall health, one of which is heart failure. Trimethylamine nitrogen oxide (tmno) is considered to be a key mediator between intestinal microbiome changes and heart failure, and is associated with poor prognosis in patients with heart failure. We aimed to determine the prognostic value of TMAO in heart failure (HF).**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 13 October 2020 and was last updated on 13 October 2020 (registration number INPLASY2020100047).

INTRODUCTION

Review question / Objective: **The effect of TMAO on the prognosis of patients with heart failure is unknown, so this study was designed to observe the effect of TMAO on the prognosis of patients with heart failure P:patients with heart failure O:The relationship between plasma TMAO and all-cause mortality in patients with heart failure .The relationship between plasma TMAO and adverse outcomes was also extracted.**

Rationale: **Trimethylamine-N-oxide (TMAO), a metabolite of intestinal microbial origin, is considered to be the key mediator between the change of intestinal microflora**

and heart failure, and is associated with poor prognosis in patients with heart failure. The purpose of this meta-analysis was to systematically assess the relationship between plasma TMAO levels and the prognosis of heart failure. Cochrane Library, PubMed and EMBASE databases were searched for studies up to may 2020 was searched. Prospective studies reported that the relationship between TMAO plasma levels and all-cause mortality was included in this meta-analysis. The relative risk (RR) and 95% confidence interval (CI) of high TMAO were calculated by using the random effect model. The relationship between the plasma level of TMAO and the prognosis of patients with heart failure was studied systematically. A total of 7 clinical studies were included in the analysis, including 5519 heart failure patients. The major end point was the relationship between plasma TMAO and all-cause mortality in patients with heart failure. The secondary end point was the relationship between plasma TMAO and adverse outcomes. We aimed to determine the prognostic value of TMAO in heart failure (HF).

Condition being studied: Heart failure is a complex multifactor disease with a wide range of socio-economic consequences. Despite the latest development of new drugs and treatment strategies, HF related mortality and incidence rate is still high. Targeting the gut microbiome is a new strategy, as people are increasingly aware of its important role in overall health, one of which is heart failure. Trimethylamine nitrogen oxide (tmno) is considered to be a key mediator between intestinal microbiome changes and heart failure, and is associated with poor prognosis in patients with heart failure. We aimed to determine the prognostic value of TMAO in heart failure (HF).

METHODS

Participant or population: Patients with heart failure.

Intervention: None.

Comparator: None.

Study designs to be included: Prospective research.

Eligibility criteria: 1) Prospective research method is adopted, and complete data can be obtained from the literature; 2) Research methods were basically consistent between studies, with little inter-group heterogeneity and comparability between studies; 3) Outcome indicators should include the relationship between PLASMA TMAO and all-cause mortality.

Information sources: Cochrane Library, PubMed and EMBASE databases were searched for studies up to May 2020 was searched.

Main outcome(s): The relationship between PLASMA TMAO and all-cause mortality.

Additional outcome(s): The relationship between TMAO and adverse outcomes (cardiovascular mortality, MI, cardiovascular hospitalization, revascularization and stroke) in patients with heart failure.

Data management: Relevant data were extracted from each individual eligible study using a structured table. Two reviewers (Hua Qu and Lina Miao) extracted data independently and checked with each other. We contacted the authors to obtain the original data if the article lacked key information related to the investigation. Disagreement between the reviewers was resolved by consulting a third investigator (Dazhuo Shi). Basic information and research content were extracted for each study.

Quality assessment / Risk of bias analysis: Newcastle-Ottawa Scale was applied to evaluate the risk of bias for included studies based on study group selection, group comparability and ascertainment of exposure or outcome. Two reviewers independently assessed the quality of each study.

Strategy of data synthesis: The data were analyzed by Stata 12.0 meta analysis module.

Subgroup analysis: If necessary, we will evaluate the impact of TMAO level on outcome indicators according to the TMAO level before and after the patients themselves, and the TMAO level comparison results of heart failure patients and healthy people. And we will conduct subgroup analysis according to research design, gender, region, age of patients, BNP / NT proBNP level, ultrasound results, follow-up time, adjustment and other factors to determine the impact on outcome indicators.

Sensibility analysis: Sensitivity analysis can be used to judge the stability and reliability of research results. By eliminating the literature with high risk of bias and poor quality, meta analysis is carried out again, and the results before and after comparison are made to judge the stability and reliability of the results.

Language: No language limits be imposed on the search.

Country(ies) involved: China.

Keywords: Trimethylamine N-oxide, Heart Failure Cardiovascular events, Mortality, Meta-analysis.

Contributions of each author:
Author 1 - Lina Miao - Literature search, screening, data abstraction, analysis and writing the manuscript.
Author 2 - Hua Qu - Literature search, screening, data abstraction and analysis.
Author 3 - Dazhuo Shi - Conceptualization, methodology.