INPLASY PROTOCOL

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None declared.

Association of serum uric acid with all-cause and cardiovascular mortality in peritoneal dialysis patients: a systematic review and meta-analysis of observational studies

Xue, X[1]; Lu, CL[2]; Jin, XY[3]; Liu, XH[4]; Yang, M[5]; Wang, XQ[6]; Cheng, H[7]; Yuan, J[8]; Liu, Q[9]; Zheng, RX[10]; Liu, JP[11].

Review question / Objective: **Types of participants: All participants who had received peritoneal dialysis (PD) for more than 3 months. There was no restriction on the type of PD, including continuous ambulatory PD, intermittent PD, automated PD, continuous cyclic PD and tidal PD. Exposure factor: Hyperuricemia in PD patients was the exposure factor of this study. Either categorization according to baseline serum uric acid (SUA) level or time-average SUA concentration was acceptable. Definition of hyperuricemia and the categorization for the SUA level was based on the definition in each included article respectively. Types of outcome measures: Primary outcome: all-cause mortality. The death was determined by the hospital medical record and death certificate. Secondary outcome: cardiovascular (CV) mortality. The definition of "CV events": coronary events (myocardial infarction, unstable angina), cardio myopathy, cardiac arrest, cardiac dysrhythmia, congestive heart failure, ischemic brain injury, cerebrovascular accident and peripheral vascular disease. The cause of death was determined through medical history, hospital medical records and death certificates.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 05 April 2021 and was last updated on 05 April 2021 (registration number INPLASY202140020).

INTRODUCTION

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Condition being studied: Hyperuricemia is common in end-stage renal disease patients with PD. The relationship between serum uric acid (SUA) level, all-cause and CV mortality in PD patients is currently controversial. This study aimed to systematically analyze the correlation between SUA level and mortality from current observational studies to inform clinical practice and further research.

METHODS

Participant or population: All participants who had received PD for more than 3 months. No restriction is applied on sex or race of participants.

Intervention: Hyperuricemia in PD population was the exposure factor of this study.

Comparator: Hyperuricemia in PD population was the exposure factor of this study. So non-hyperuricemia was comparator.

Study designs to be included: Cohort studies and case-control studies were identified.

Eligibility criteria: (1) All participants who had received PD for more than 3 months. (2) Cohort studies and case-control studies. (3) Hazard ratio (HR) and its corresponding 95% confidence interval (CI) (or other data to calculate them) of all-cause or CV mortality for 1mg/dl change in SUA level, or for the highest versus lowest SUA category or the lowest versus highest category can be obtained from the original article.

Information sources: We will search the following Chinese and English databases from their inception to January 2021. Chinese databases include China National Knowledge Infrastructure (CNKI), Wan Fang, Chinese Science and Technology Journal Database (VIP), and SinoMed Database. English databases include PubMed, EMBASE, the Cochrane Library, and Web of Science. Trial registers including Clinical Trials. gov and the World Health Organization International Clinical Trials Registry Platform are also searched. Additionally, related reviews, conference papers, references lists and gray literatures also are searched manually to minimize the missed detection rate. No language or publication type is imposed. Taking 'PubMed' as an example, the retrieval strategy is as follows: ("Uric Acid" [Mesh] OR "Uric Acid" OR "serum uric acid") AND ("Mortality" [Mesh] OR "Mortality") AND ("Peritoneal Dialysis" [Mesh] OR "Peritoneal Dialysis" OR "PD" OR "continuous ambulatory PD" OR "CAPD" OR "intermittent PD" OR "IPD" OR "automated PD" OR "APD" OR "continuous cyclic PD" OR "CCPD" OR "tidal PD" OR "TPD").

Main outcome(s): Primary outcome: all-cause mortality. The death was determined by the hospital medical record and death certificate.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Quality Assessment Scale (NOS) was used to assess the quality

of observational studies. NOS allocated a maximum of 9 points for quality of selection, comparability, and outcome of study population. Two investigators assessed and validated the quality of included studies independently. Any disagreements were resolved by discussion with professor JP Liu. Overall study quality scores were defined as poor (0–3), fair (4–6), or good (7–9).

Strategy of data synthesis: SUA was analyzed not only as a categorical variable, but also as a continuous variable in the included studies. The statistical analysis for the overall association between SUA levels and death risk (all-cause and CV mortality) were based on random effects model and on comparisons of highest versus lowest category of SUA level, or by increase of 1mg/dl. HR and 95% CI were used as effect indicators. HR and corresponding 95% CI of each study were transformed to their natural logarithm (lnHR, lnlCI and lnUCI), and overall HR and its 95% CI was calculated by exponentiation of the pooled lnHR, lnlCI and lnUCI. If data of cases, person-years, and HR and 95% CI for each category were available in included studies, then a dose-response analysis would be performed to further explore the relationship between SUA and mortality. The potential non-linearity association was examined by modeling SUA levels using restricted cubic splines with three knots at 25, 50, and 75% of the distribution. We assigned the median or middle point of the upper and lower boundaries in each category as the corresponding dose to the related HR for each study. In case of P value$>$0.05, the linear regression model should be considered. square (I2) was applied to test the statistical heterogeneity among studies (Higgins and Thompson, 2003). When I2$>$85%, we believed that the results could not be poolled. Data not suitable for statistical pooling were synthesized qualitatively. STATA16.0 software (StataCorp, College Station) was used for data analysis.

Subgroup analysis: To explore the source of heterogeneity among studies, subgroup analyses were conducted according to study design, study location, publication years, adjustment for sex, adjustment for DM and adjustment for albumin. Additionally, the meta-regression analysis was also performed to detect potential heterogeneity based on the above variables when about 10 studies were included.

Sensitivity analysis: Sensitivity analysis was performed with removing one study at a time to explore the robustness of results if data were available.

Country(ies) involved: Only in China.

Keywords: Serum uric acid, all-cause mortality, cardiovascular mortality, peritoneal dialysis, systematic review.

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