INPLASY PROTOCOL

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None declared.

Serum Amyloid A and the Risk of Cardiovascular or All-Cause Mortality in Chronic Kidney Disease: A Systematic Review and Dose-Response Meta-Analysis

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Review question / Objective: **Serum amyloid A (SAA) is one of the major acute-phase proteins, which is present in a wide range of mammals, including humans. Currently, numerous studies have indicated that inflammation is a key factor for major cardiovascular events and mortality risk in chronic kidney disease (CKD) patients. Therefore, SAA, which serves as an inflammatory marker, should be a promising prognostic biomarker candidate that has a biologically reasonable mechanism linked to CKD. However, the relationship between SAA with cardiovascular events and mortality risk have not received much study over the last few decades, and the results of several existing studies are even inconsistent. This meta-analysis was designed to explore the relationship of SAA with the risk of all-cause and cardiovascular mortality among patients with CKD. In particular, we aimed to examine their dose-response relationships.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 10 March 2022 and was last updated on 10 March 2022 (registration number INPLASY202230040).

INTRODUCTION

Review question / Objective: **Serum amyloid A (SAA) is one of the major acute-phase proteins, which is present in a wide range of mammals, including humans. Currently, numerous studies have indicated that inflammation is a key factor for major cardiovascular events and mortality risk in chronic kidney disease (CKD) patients.**

Therefore, SAA, which serves as an inflammatory marker, should be a promising prognostic biomarker candidate that has a biologically reasonable mechanism linked to CKD. However, the relationship between SAA with cardiovascular events and mortality risk have not received much study over the last few decades, and the results of several existing studies are even inconsistent. This meta-analysis was designed to explore the relationship of SAA with the risk of all-cause and cardiovascular mortality among patients with CKD. In particular, we aimed to examine their dose-response relationships.

Condition being studied: SAA is synthesized predominantly by the hepatocytes, and its circulating concentrations were significantly elevated in response to inflammatory stimuli or endothelial injury. Animal studies revealed that the administration of a certain SAA concentration to apo E-deficient mice model can contribute to early renal damage which is characterized by renal fibrosis and severe cardiovascular disease. In a recent study applying immunohistochemical assay, SAA protein deposition is widely distributed in the glomeruli and tubulointerstitium in both human and mouse with diabetic kidney disease. Fewer applications of SAA in clinical practice with respect to other inflammatory indicators, such as C-reactive protein (CRP), interleukin-6 (IL-6), may be due to the instability and relatively complicated techniques in measuring SAA.

METHODS

Participant or population: We will include CKD patients who had a minimum follow-up time of 1 year.

Intervention: Circulating SAA levels will be main Exposure/Interventions.

Comparator: Comparing the highest versus lowest SAA levels at baseline.

Study designs to be included: Prospective cohort studies, nested case-control studies or post hoc analysis of clinical trials.

Eligibility criteria: The eligibility criteria areas follows: (1) were prospective cohort studies, nested case-control studies or post hoc analysis of clinical trials; (2) included CKD patients regardless of dialysis; (3) evaluated the relationship of SAA with all-cause and/or cardiovascular mortality; (4) reported a multivariable-adjusted hazard ratio (HR) or relative risk (RR) or odds ratio (OR), and the corresponding 95% confidence interval (CI); (5) had a minimum follow-up time of 1 year; (6) were full-text articles written in English.

Information sources: The electronic databases including Pubmed, EMBASE, and Web of Science will be searched for the information sources.

Main outcome(s): The multivariable-adjusted hazard ratio (HR) and the corresponding 95% confidence interval (CI) will be pooled to estimate the associations of SAA with the risk of all-cause and cardiovascular mortality. Additionally, dose-response curves will be plotted for some of the included studies that provided adequate information.

Quality assessment / Risk of bias analysis: Study quality of the included studies will be assessed using the Newcastle-Ottawa Scale (NOS) for the included studies.

Strategy of data synthesis: The multivariate adjusted pooled effect estimates were calculated using random-effects models or fixed-effects models depending on heterogeneity among studies.

Subgroup analysis: Subgroup analysis will be conducted according to study location, study design, patient types, sample size, patient age, follow-up time, whether statistical adjustment for hypertension or blood pressure parameters, hs-CRP or CRP, or diabetes.

Sensitivity analysis: Sensitivity analyses were performed to confirm the stability of overall pooled HR by removing one study at a time.

Country(ies) involved: China.

Keywords: Serum amyloid A; chronic kidney disease; all-cause mortality; cardiovascular mortality; dose-response relationship; meta-analysis.

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