

Klotho as an Early Marker of Acute Kidney Injury following Cardiac Surgery: A Systematic Review

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Center University of Rochester.**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202440021**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 04 April 2024 and was last updated on 04 April 2024.**INTRODUCTION**

Review question / Objective Population (P): Patients undergoing cardiac surgery Intervention (I): Measurement of postoperative serum Klotho levels Comparator (C): Standard postoperative monitoring without Klotho measurement Outcome (O): Incidence of acute kidney injury (AKI) post-cardiac surgery, sensitivity, specificity, and prognostic validity of Klotho levels for predicting CSA-AKI.

Review question: In patients undergoing cardiac surgery, how does the measurement of postoperative serum Klotho levels compare to standard postoperative monitoring without Klotho measurement in predicting the incidence of acute kidney injury?

Rationale Acute kidney injury (AKI) following cardiac surgery, affecting 35-40% of patients, has complex and poorly understood pathophysiology,

involving factors like renal hypoperfusion, microembolization, and exposure to nephrotoxins. Despite the majority recovering renal function, a subset experiences permanent damage, with even minor serum creatinine elevations impacting survival and increasing healthcare costs. Current renal function assessments, such as serum creatinine, are limited by delayed response and external influences, leading to potential underdiagnosis of AKI. This highlights the need for improved early detection methods, prompting our investigation into the efficacy of Klotho as a predictive biomarker for CSA-AKI.

Condition being studied Acute kidney injury (AKI) signifies a rapid reduction in renal function, leading to the accumulation of urea and other waste products, along with disturbances in fluid and electrolyte balance. The terminology has evolved from acute renal failure (ARF) to AKI to acknowledge the clinical significance of even

minor declines in renal function, which are linked to increased adverse outcomes. Uniform criteria for AKI have been established, focusing on changes in serum creatinine levels and urine output, facilitating the identification of AKI cases in research and clinical outcomes studies.

METHODS

Search strategy This review adhered to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines, with the search concluding on February 17, 2024. Four researchers systematically examined the PubMed/MEDLINE and CENTRAL/Cochrane databases to find studies on Klotho level measurements after cardiac surgery, using keywords related to cardiac surgery and Klotho.

Participant or population Patients undergoing cardiac surgery.

Intervention Measurement of postoperative serum Klotho levels.

Comparator Standard postoperative monitoring without Klotho measurement.

Study designs to be included Retrospective and prospective clinical studies.

Eligibility criteria Inclusion criteria were studies that investigated the link between α -Klotho levels and CSA-AKI, employed validated α -Klotho assays in blood, urine, or tissue samples, and documented the incidence of CSA-AKI as a primary outcome. Exclusions were made for studies not reporting α -Klotho levels in post-cardiac surgery AKI cases. Discrepancies were resolved through consensus discussions led by the lead author.

Information sources PubMed/MEDLINE and CENTRAL/Cochrane.

Main outcome(s) Incidence of postoperative AKI.

Additional outcome(s) Length of ICU and total hospital stay, mortality rates, and the duration of postoperative surveillance.

Data management Pre-piloted excel spreadsheets.

Quality assessment / Risk of bias analysis The Newcastle–Ottawa Quality scale will be used to evaluate the selected studies. A score of at least six indicated high quality. Two reviewers (PK, KSM)

independently rated all primary papers and any disagreements were resolved via discussion.

Strategy of data synthesis The selected studies will be assessed using the Newcastle–Ottawa Quality scale, where a score of six or above signifies high quality. The evaluation of all primary papers will be carried out independently by two reviewers with any discrepancies resolved through discussion.

Subgroup analysis N/A.

Sensitivity analysis N/A.

Language restriction No.

Country(ies) involved Greece, UK, Canada, Grenada, USA.

Keywords acute kidney injury; cardiac surgery; Klotho; serum; urine; biomarker; systematic review.

Dissemination plans *LinkedIn *ResearchGate *Twitter.

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