

Improved Kidney Outcomes and Reduced Mortality Achieved with AKI Care Bundles: A Systematic Review and Meta-Analysis

INPLASY202370043

doi: 10.37766/inplasy2023.7.0043

Received: 12 July 2023

Published: 12 July 2023

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See, CY¹; Pan, HC²; Chen, JY³; Wu, CY⁴; Liao, HW⁵; Wu, VC⁶; Ostermann, M⁷.**ADMINISTRATIVE INFORMATION****Support** - None.**Review Stage at time of this submission** - Completed but not published.**Conflicts of interest** - None declared.**INPLASY registration number:** INPLASY202370043**Amendments** - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 12 July 2023 and was last updated on 12 July 2023.**INTRODUCTION**

Review question / Objective Population: patients who are at risk of kidney injury
Intervention: novel biomarker-guided implementation of the care bundle. Comparison: conventional biomarker-guided implementation of a care bundle or without using a care bundle. Outcomes: major adverse kidney events and mortality.

Rationale As novel biomarkers allow earlier detection of acute kidney injury, we are interested in whether patients' outcomes after the implementation of a care bundle based on novel biomarkers are significantly better.

Condition being studied Acute kidney injury (AKI) is an abrupt deterioration of kidney function that results in nitrogenous waste product accumulation and dysregulation of extracellular volume, electrolytes, and acid-base balance. AKI is common among hospitalized patients, especially patients in intensive care or surgical units. AKI can

lead to unfavorable long-term consequences, such as chronic kidney disease, cardiovascular events, and death.

METHODS**Search strategy** Pubmed searching strategy:

No. Query Results (6781)

("acute kidney injury"[MeSH Terms] OR ("acute"[All Fields] AND "kidney"[All Fields] AND "injury"[All Fields]) OR "acute kidney injury"[All Fields] OR ("acute kidney injury"[MeSH Terms] OR ("acute"[All Fields] AND "kidney"[All Fields] AND "injury"[All Fields]) OR "acute kidney injury"[All Fields] OR ("acute"[All Fields] AND "renal"[All Fields] AND "failure"[All Fields]) OR "acute renal failure"[All Fields]) OR ("acute kidney injury"[MeSH Terms] OR ("acute"[All Fields] AND "kidney"[All Fields] AND "injury"[All Fields]) OR "acute kidney injury"[All Fields] OR ("acute"[All Fields] AND "kidney"[All Fields] AND "failure"[All Fields]) OR "acute kidney failure"[All Fields]) OR (("kidney"[MeSH Terms] OR "kidney"[All Fields] OR "kidneys"[All Fields] OR "kidney s"[All Fields]) AND ("injurie"[All Fields] OR

"injured"[All Fields] OR "injuries"[MeSH Subheading] OR "injuries"[All Fields] OR "wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields] OR "injurious"[All Fields] OR "injury s"[All Fields] OR "injured"[All Fields] OR "injurs"[All Fields] OR "injury"[All Fields]) OR (("renal"[All Fields] OR "renals"[All Fields]) AND ("injurie"[All Fields] OR "injured"[All Fields] OR "injuries"[MeSH Subheading] OR "injuries"[All Fields] OR "wounds and injuries"[MeSH Terms] OR ("wounds"[All Fields] AND "injuries"[All Fields]) OR "wounds and injuries"[All Fields] OR "injurious"[All Fields] OR "injury s"[All Fields] OR "injured"[All Fields] OR "injurs"[All Fields] OR "injury"[All Fields])) OR ("acute kidney injury"[MeSH Terms] OR ("acute"[All Fields] AND "kidney"[All Fields] AND "injury"[All Fields]) OR "acute kidney injury"[All Fields] OR ("acute"[All Fields] AND "renal"[All Fields] AND "insufficiency"[All Fields]) OR "acute renal insufficiency"[All Fields]) OR ("renal insufficiency"[MeSH Terms] OR ("renal"[All Fields] AND "insufficiency"[All Fields]) OR "renal insufficiency"[All Fields]) AND ("prevent"[All Fields] OR "preventability"[All Fields] OR "preventable"[All Fields] OR "preventative"[All Fields] OR "preventatively"[All Fields] OR "preventatives"[All Fields] OR "prevented"[All Fields] OR "preventing"[All Fields] OR "prevention and control"[MeSH Subheading] OR ("prevention"[All Fields] AND "control"[All Fields]) OR "prevention and control"[All Fields] OR "prevention"[All Fields] OR "prevention s"[All Fields] OR "preventions"[All Fields] OR "preventive"[All Fields] OR "preventively"[All Fields] OR "preventives"[All Fields] OR "prevents"[All Fields] OR ("protect"[All Fields] OR "protected"[All Fields] OR "protecting"[All Fields] OR "protection"[All Fields] OR "protections"[All Fields] OR "protective agents"[Pharmacological Action] OR "protective agents"[MeSH Terms] OR ("protective"[All Fields] AND "agents"[All Fields]) OR "protective agents"[All Fields] OR "protectant"[All Fields] OR "protectants"[All Fields] OR "protective"[All Fields] OR "protectively"[All Fields] OR "protectiveness"[All Fields] OR "protectives"[All Fields] OR "protects"[All Fields]) OR ("KDIGO"[All Fields] AND ("patient care bundles"[MeSH Terms] OR ("patient"[All Fields] AND "care"[All Fields] AND "bundles"[All Fields]) OR "patient care bundles"[All Fields] OR ("care"[All Fields] AND "bundle"[All Fields]) OR "care bundle"[All Fields]) OR ("patient care bundles"[MeSH Terms] OR ("patient"[All Fields] AND "care"[All Fields] AND "bundles"[All Fields]) OR "patient care bundles"[All Fields] OR ("care"[All Fields] AND "bundle"[All Fields]) OR "care bundle"[All Fields]) OR ("bundle"[All Fields] OR "bundle s"[All Fields] OR "bundled"[All Fields]

OR "bundles"[All Fields] OR "bundling"[All Fields]) AND ("biomarker s"[All Fields] OR "biomarkers"[MeSH Terms] OR "biomarkers"[All Fields] OR "biomarker"[All Fields] OR ("lipocalin 2"[MeSH Terms] OR "lipocalin 2"[All Fields] OR ("neutrophil"[All Fields] AND "gelatinase"[All Fields] AND "associated"[All Fields] AND "lipocalin"[All Fields]) OR "neutrophil gelatinase associated lipocalin"[All Fields] OR "NGAL"[All Fields] OR ("tissue s"[All Fields] OR "tissues"[MeSH Terms] OR "tissues"[All Fields] OR "tissue"[All Fields]) AND ("antagonists and inhibitors"[MeSH Subheading] OR ("antagonists"[All Fields] AND "inhibitors"[All Fields]) OR "antagonists and inhibitors"[All Fields] OR "inhibitors"[All Fields] OR "inhibitor"[All Fields] OR "inhibitor s"[All Fields]) AND "metalloproteinase-2"[All Fields] AND "x"[All Fields] AND ("insulin like growth factor binding protein related protein 1"[Supplementary Concept] OR "insulin like growth factor binding protein related protein 1"[All Fields] OR "insulin like growth factor binding protein 7"[All Fields])) OR "TIMP-2IGFBP7"[All Fields] OR ("cell cycle"[MeSH Terms] OR ("cell"[All Fields] AND "cycle"[All Fields]) OR "cell cycle"[All Fields])

EMBASE

No. Query Results (309)

((angiotensin AND converting AND enzyme AND inhibitors OR angiotensin) AND receptor AND blocker OR renin) AND angiotensin AND aldosterone AND system AND blockers OR 'renin angiotensin') AND system AND blockade AND ((acute AND kidney AND injury OR acute) AND renal AND failure OR mortality OR advanced) AND kidney AND disease

Cochrane searching strategy:

No. Query Results (344)

(acute kidney injury OR acute renal failure OR acute kidney failure OR acute renal insufficiency OR renal insufficiency) in ALL TEXT AND (Prevention OR Protection OR KDIGO care bundle OR care bundle) in ALL TEXT AND (Biomarker OR NGAL OR neutrophil gelatinase-associated lipocalin OR TIMP-2 · IGFBP7 OR cell cycle OR tissue inhibitor metalloproteinase-2 x insulin-like growth factor-binding protein 7) in ALL TEXT.

Participant or population Hospitalized patients, mostly in the intensive care units and surgical department.

Intervention Biomarker-guided implementation of AKI care bundle proposed by KDIGO 2012.

Comparator Conventional patient care.

Study designs to be included Systemic review and meta-analysis.

Eligibility criteria Participants aged 18 years or older of any ethnic origin or sex, and study published in English were included. The exclusion criteria were as follows: (1) studies including patients with preexisting chronic kidney disease (CKD) [estimated glomerular filtration rate (eGFR) ≤ 60 ml/min/1.73m²], chronic dialysis-dependence or previously received dialysis, or kidney transplantation; (2) studies including pregnant or lactating patients; and (3) editorials, letters, review articles, conference or case reports.

Information sources The sources of the literature review were electronic databases, including PubMed, EMBASE, and Cochrane Library.

Main outcome(s) The main outcomes were major adverse kidney events (MAKE) including advanced AKI (defined as KDIGO AKI stage 2 to 3), receipt of renal replacement therapy, and mortality.

Data management Microsoft Excel spreadsheet was used to record and organize information from the literature.

Quality assessment / Risk of bias analysis The risk of bias analysis was assessed according to the Cochrane Handbook for Systemic Reviews of Interventions. The quality of evidence was assessed using the GRADE system.

Strategy of data synthesis Review Manager software package (RevMan) version 5.4.1 (The Nordic Cochrane Centre, Copenhagen, Denmark, 2020) was used for outcome analyses. Forest plots of the outcomes were created using Mantel Haenszel statistical method and random effect analysis model due to the diverse methodologies used in the included studies. Funnel plots were constructed to examine any exaggeration of effect estimates from low-quality studies. MetaInsight V4.0.0 [National Institute for Health and Care Research (NIHR) – Complex Reviews Support Unit (CRSU), United Kingdom, 2023] (7), a tool adapted from the R software to conduct network meta-analysis. Surface under the cumulative ranking curve (SUCRA) was used to show the hierarchy of the treatment effects in a rank-heat plot, with the preferential treatment having the highest SUCRA value.

Subgroup analysis Subgroup analysis included surgical patients, particularly those who underwent cardiovascular surgery was performed.

Sensitivity analysis Nil.

Language restriction English.

Country(ies) involved Taiwan.

Keywords acute kidney injury, care bundles, biomarkers.

Contributions of each author

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