INPLASY PROTOCOL

To cite: Ru et al. Incidence,Mortality and Predictors of Acute Kidney Injury in Patients with Heart Failure: A Systematic Review and Meta-analysis. Inplasy protocol 2022120095. doi: 10.37766/inplasy2022.12.0095

Received: 23 December 2022

Published: 23 December 2022

Corresponding author:
Li ZhiJuan

13838836086@163.com

Author Affiliation:
Department of Cardiology, the First Affiliated Hospital of Henan University of Science and Technology.

Support: **None to declare.**

Review Stage at time of this submission: **Completed but not published.**

Conflicts of interest:
None declared.

Incidence,Mortality and Predictors of Acute Kidney Injury in Patients with Heart Failure: A Systematic Review and Meta-analysis

Ru, SC[1]; Lv, SB[2]; Li, ZJ[3].

Review question / Objective: **The PICOS principle was adopted when we confirmed the study eligibility. The inclusion criteria were as follows: (1) The study subject was adult patients with adequate diagnosis of heart failure; (2) exposure: patients with a confirmed diagnosis criteria for acute kidney injury; (3) presented the incidence, mortality and predictors of acute kidney injury in patients with heart failure or could be calculated by the available data from the article; (4) study design: observational study (cohort study or cross-sectional study). Articles that were reviews, case reports, comments, correspondences, letters or only abstracts were excluded.**
Information sources: **Records identified through database searching (n = 35414), Included PubMed (n =4499), Cochrane (n =3790), Embase (n =5242), Web of Science (n =17577), Medline (n=4306) and additional records identified through other sources (n = 0), studies searched from database creation to October 2022, with search strategies designed and implemented by experienced library staff. The subject terms used in the searches were "acute kidney injury" or "AKI" and "heart failure" or "HF". Detailed search strategies for each database are given in the Appendix.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 23 December 2022 and was last updated on 23 December 2022 (registration number INPLASY2022120095).

INTRODUCTION

Review question / Objective: **The PICOS principle was adopted when we confirmed the study eligibility. The inclusion criteria were as follows: (1) The study subject was adult patients with adequate diagnosis of heart failure; (2) exposure: patients with a confirmed diagnosis criteria for acute kidney injury; (3) presented the incidence, mortality and predictors of acute kidney injury in patients with heart failure or could be calculated by the available data from the article; (4) study design: observational**

study (cohort study or cross-sectional study). Articles that were reviews, case reports, comments, correspondences, letters or only abstracts were excluded.

Rationale: The definition of Acute Kidney Injury (AKI) has varied over the last two decades with the recognition that a serum creatinine ≥0.3 mg/dL above baseline has a negative impact on survival. Many other definitions have been invoked to define and stage AKI, such as the Risk of Injury and Failure (often referred to as RIFLE), AKI Network (Acute Kidney Injury Network) (often referred to as AKIN) criteria), and the Kidney Disease Prognosis Improvement Global Organization (often referred to as KDIGO). Differences in AKI definitions are one of the most important factors contributing to the heterogeneity in the incidence of AKI reported by heart failure patients. However, the essence of all the definitions appears to be similar. The incidence and impact on outcomes of AKI in heart failure patients have been examined in many studies, but few summarized data have been obtained. The Meta-analysis in this paper collects data from observational studies to determine the prevalence of AKI in patients with heart failure and its influence on patient survival, and to identify risk factors for AKI occurring in patients with heart failure by combining multifactorial variable analysis.

Condition being studied: AKI is a common event in the natural history of patients with heart failure and the exact mechanism by which it occurs is unclear. It may be as follows: acute heart failure is characterized by reduced left ventricular systolic function and inadequate cardiac output, triggering compensatory mechanisms such as the renin-angiotensin-aldosterone system, the sympathetic nervous system, and other local mediators, which interact to maintain fluid volume. The imbalance between these compensatory mechanisms is unable to maintain adequate cardiac output, resulting in volume overload. In addition, renal perfusion is reduced, combined with nephrotoxic drugs and excessive diuresis, ultimately leading to AKI in this kind of patient.

An increasing number of studies report that renal impairment is common in heart failure and is associated with poor outcomes. Conversely, renal disease is independently associated with increased cardiovascular morbidity and mortality. The clinical manifestation of bidirectional cardiac-renal interactions is known as Cardio-renal syndrome (CRS). In CRS, heart failure leads to renal dysfunction and/or vice versa through a number of interactive pathways between the heart and kidneys.

Given the lack of effective treatment for AKI, early prevention and early detection are crucial, especially early intervention in high-risk patients and their associated risk factors, which is significant to improve the prevention and treatment of AKI in heart failure patients.

METHODS

Search strategy: All methods used in this Meta-analysis met the PRISMA criteria for observational studies, and a comprehensive search was conducted to Embase, Medline, PubMed, Cochrane and Web of Science for studies searched from database creation to October 2022, with search strategies designed and implemented by experienced library staff. The subject terms used in the searches were “acute kidney injury” or “AKI” and “heart failure” or “HF”. Detailed search strategies for each database are given in the Appendix.

Two authors independently reviewed the titles and abstracts of the searched literature, and two investigators independently screened the literature, extracted information and cross-checked it. Disagreements, if any, were resolved through discussion or consultation with a third party. The literature was screened by first reading the titles and, further reading the abstracts and full text to determine inclusion after eliminating clearly irrelevant literature. If necessary, the authors of the original studies were contacted by email or telephone to obtain information that was not identified but was essential to the study herein..

Participant or population: Studies involving 3,533,583 patients with heart failure, of which 774,887 had AKI, classified according to study type: prospective (n=14), retrospective (n=23); diagnostic criteria: KDIGO (n=18), AKIN (n=7), RIFLE (n=7); heart failure type: acute heart failure (n=30), chronic heart failure (n=4) 4); geographical classification: Asia (n=21), Europe (n=9), American region (n=6), Australia (n=1); inpatient unit classification: intensive care unit (n=5), coronary care unit (n=5), emergency ward(n=3).

Intervention: None.

Comparator: Exposure: patients with a confirmed diagnosis criteria for acute kidney injury.

Study designs to be included: observational study (cohort study or cross-sectional study).

Eligibility criteria: Studies were excluded if they did not include incidence,mortality and predictors associated with AKI in heart failure patients or if there were insufficient data for analysis. There were no language or geographical restrictions on published studies, and as full manuscripts were included in the analysis.

Information sources: Records identified through database searching (n = 35414), Included PubMed (n =4499), Cochrane (n =3790), Embase (n =5242), Web of Science (n =17577), Medline (n=4306) and additional records identified through other sources (n = 0), studies searched from database creation to October 2022, with search strategies designed and implemented by experienced library staff. The subject terms used in the searches were “acute kidney injury” or “AKI” and “heart failure” or “HF”. Detailed search strategies for each database are given in the Appendix.

Main outcome(s): Of the 3,533,583 patients with heart failure in the 37 included studies, 774,887 had AKI, a combined incidence of 33%(95% CI: 32-35%), Patients with AKI had a higher in-hospital mortality than those without AKI, as assessed by 12 studies (risk ratio [RR (Relative Risk)] 3.57, 95% CI: 2.99-4.27, p=0.843). At one-year follow-up after the onset of AKI, mortality assessed in five studies remained significantly higher RR 1.85, 95% CI: (1.54, 2.22, p=0.757). In 13 studies analyzed a total of 16 admission variables, containing Diabetes mellitus (OR:1.70, 95% CI: 1.37,2.11, p <0.001), hypertension(OR: 1.81, 95% CI: 1.19,2.74, p = 0.005), pre-CKD(OR: 3.63 , 95% CI: 2.49,5.31, p <0.001), CHF Systolic and age(), NT-proBNP(OR: 2.53, 95% CI: 1.43,4.49, p 1.0 mg/dl(OR:1.76, 95% CI: 1.14,2.71, p = 0.011), eGFR index < 60 ml/min/1.73 m2(OR: 1.64, 95% CI: 1.23,2.18, p 24 mg/dl(OR: 2.67, 95% CI: 1.64,4.34, p <0.001), Serum albumin(0.96, 95% CI: 0.94,0.98, p <0.001),and Intravenous dobutamine(2.82, 95% CI: 1.76,4.52, p <0.001) were the statistically significant predictors of acute kidney injury occurs in patients with heart failure.

Data management: Literature data were extracted by two researchers using a self-made Excel sheet, which were collected for each study on author, study design type, site, year of publication, definition of AKI used, patient demographics, follow-up period and outcome indicators. Conflicts in data extraction were referred to the original articles and resolved by consensus between authors.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa scale was used independently by two researchers to assess the quality of each of the selected studies for analysis. It consisted of three main categories, cohort selection, comparability between groups, and outcome measures, with eight entries, and full marks of three categories were four, two, and three respectively. For each question, a score of one was assigned if the study met the criteria, except for comparability of study groups, and a score of two if the study controlled for age, gender, or other confounding factors (Supplementary Table 1). A total cumulative literature quality assessment score of ≥7 was defined as high-quality literature, and studies with a score ≤6 were considered low-quality ones. Any discrepancies were

resolved by re-assessing the relevant articles jointly and finally reaching consensus between authors.
Study heterogeneity was assessed according to I^2 and Q tests, and if $I^2 < 50\%$, Q test P value > 0.05, adopting fixed effect model (FDM) to analyze; If $I^2 \geq 50\%$ and Q-test P-value < 0.05, a random effect model (REM) was used. For studies with large heterogeneity, sensitivity analyses were used to explore sources of heterogeneity or performed targeted subgroup analysis. The publication bias of studies with ≥10 publications were analyzed using funnel plots and Egger's test, with P<0.1 being a statistically significant difference.

Strategy of data synthesis: The number of patients with acute kidney injury in heart failure was extracted from each study and Meta-analysis was performed using Stata 16.0 software to calculate the prevalence of AKI and the corresponding 95% confidence interval (CI), with data weighted according to sample size in each study. Mortality at different time points was extracted to derive risk ratios (RRs) and 95% CIs for mortality in patients with AKI versus those without AKI, and hazard ratios (HRs) and corresponding 95% CIs at different time points were obtained directly from literature extraction. Predictor variables for AKI adjusted for confounders were selected and their ORs and 95% CIs were combined. the Z test was used to determine the correlation between the incidence of AKI, mortality and associated predictors of AKI and patients with heart failure, with P<0.05 being a statistically significant difference.

Subgroup analysis: Therefore, in this Meta-analysis, subgroup analyses were performed by type of heart failure, diagnostic criteria for acute kidney injury, geographic region, type of study enrolled and unit of admission. It was found that the AKI prevalence was slightly lower in prospective studies (30%) than in retrospective studies (36%); the AKI prevalence was significantly higher in patients admitted to intensive care unit wards (51%) than in coronary care units (33%) and emergency wards (31%). In terms of geography, the incidence of AKI in heart failure patients was not significantly different between Europe (28%) and the Americas (26%) but was significantly higher in Asia (38%) than in Europe and the US; notably, the incidence of AKI in heart failure patients (47%) was 1.8 times higher than the AKIN criteria (26%) using the RIFLE criteria.
The study herein found that AKI not only predicted a poorer prognosis during hospitalization and a more than three-fold increased risk of in-hospital mortality in heart failure patients, but that the risk of death remained higher in these surviving hospitalized patients at the subsequent one-year follow-up; an increasing number of studies report that renal impairment is common in heart failure and is associated with poor outcomes.

Sensitivity analysis: For studies with publications ≥3, sensitivity analysis was performed by eliminating one literature successively, which showed that the each combined effect sizes after deletion of individual literature were not significantly different from the total combined RR values, indicating more reliable results.

Language restriction: No limits.

Country(ies) involved: China.

Keywords: Incidence, Mortality, Predictors, Acute Kidney Injury, Heart Failure, Systematic Review and Meta-analysis..

Contributions of each author:
Author 1 - Ru Song-Chao - were responsible for screening and extracting the studies, study quality assessment, statistical analysis, draft the manuscript.
Email: 302527907@qq.com
Author 2 - Lv Shu-Bin - were responsible for screening and extracting the studies, study quality assessment, statistical analysis.
Author 3 - Li Zhi-Juan - were responsible for statistical analysis, study design and review.
Email: 13838836086@163.com