

# The epidemiology of acute kidney injury in critically ill patients in the Gansu Province: the EACG Study

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## Research

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# Abstract

**Objective:** To investigate the epidemiology of acute kidney injury and to clarify the risk factors associated with the prognosis of acute kidney injury in critically ill patients in the Gansu Province.

**Methods :** This was a multicenter, retrospective study. The clinical data of all patients from January 1, 2017, to December 31, 2019, in the intensive care unit of the selected hospitals were screened. Descriptive statistical analysis was performed first, and then the patients were divided into a survival group and a nonsurvival group based on survival status at discharge. Logistic regression analyses were used to determine the risk factors for in-hospital mortality in patients with acute kidney injury.

**RESULTS :** (1) Among the 8106 patients admitted, a total of 3019 patients were excluded according to the exclusion criteria. Among the included patients, 890 patients met the diagnostic criteria for AKI, with an incidence of 17.5% and mortality of 41.3%. The etiology of acute kidney injury was 64% prerenal, 33% renal, and 2.7% postrenal. Prerenal AKI was the most common, among which cases caused by sepsis and septic shock accounted for 44.7%. Among the selected AKI patients, AKI stage I accounted for 22.02%, AKI stage II accounted for 31.01%, AKI stage III accounted for 46.97%, and 35.8% of the AKI patients received renal replacement therapy. (2) Logistic regression analysis showed that sex , age, AKI stage, RRT, infection, cardio-pulmonary resuscitation, cardiac output, mechanical ventilation, diuretics, white blood cells, platelets, blood urea nitrogen, prothrombin time and activated partial thromboplastin time were significantly associated with the prognosis of acute kidney injury ( $P < 0.05$ ). Further analysis showed that male sex, old age, high AKI stage, RRT treatment, low cardiac output, mechanical ventilation, elevated leukocyte count, reduced platelet count and reduced serum albumin were independent risk factors for a poor prognosis of acute kidney injury.

**Conclusions :** Large-scale epidemiological data from several representative general hospitals in the Gansu Province showed that the incidence and mortality of acute kidney injury in intensive care units were still very high. Sepsis and septic shock are the main causes of AKI.

## Background

Acute kidney injury (AKI) is a common critical illness among in-hospital patients, especially critically ill patients.[1-3] Broadly speaking, AKI is a sudden decrease in glomerular filtration rate (GFR) caused by a variety of etiologies and clinical symptoms. Currently, no consensus has been reached on the exact definition of AKI, and more than 30 definitions have been used to diagnose AKI.[4] Due to the different criteria used, the incidence of AKI in critically ill patients has reported to be between 3.2% and 78%.[5] Moreover, the diversity of AKI definition criteria led to an incomparability among the results of various studies and the inability to accurately evaluate the therapeutic effects of different treatment regimens and interventions for AKI. Although we have made great progress in basic research and the identification and treatment of AKI, the prognosis of AKI is still poor. [6, 7] The incidence and mortality of AKI show significant differences among countries due to the different backgrounds of AKI patients and the diversity

of AKI definitions. [8, 9] The latest study reported that the incidence of AKI in patients admitted to the Mayo clinic was 6.7% and that in critically ill patients was 16.9% between 2006 and 2014[10]. Two other multinational prospective studies found that the incidence of AKI was 5.7% and 57.3%.[11, 12] However, there are few AKI epidemiological studies among critically ill patients in China, especially in western China, and the data are basically nonexistent. Therefore, this study intends to select three tertiary hospitals in the Gansu Province to obtain epidemiological data of AKI in critically ill patients to infer the epidemiology of AKI in critically ill patients in western China.

## Data And Methods

This is a multicenter retrospective observational study about the epidemiology of AKI in ICU patients in Gansu, China. The Ethics Committee of Lanzhou University Second Hospital approved this study. The Chinese Clinical Trial Registry number is ChiCTR1800016945. All patients admitted to the ICU in three participating tertiary hospitals in the Gansu Province from January 1, 2017, to December 31, 2019, were retrospectively analyzed.

### Inclusion criteria

During the study period (January 1, 2017 to December 31, 2019), all patients admitted to the ICU in three participating tertiary hospitals in the Gansu Province were enrolled.

### Exclusion criteria:

- Chronic kidney disease.
- History of nephrectomy.
- Kidney transplantation history within 3 months before ICU admission.
- Readmission to the ICU during the same hospitalization period.

### DESIGN

The data were recorded in Microsoft Excel, and the research was divided into five steps:

First, all patients admitted to the hospital in 2017 and 2019 were recruited using the Hospital Information System (HIS).

In the second step, the medical records and laboratory examinations were checked one by one for all patients, and patients who met the exclusion criteria were excluded.

The third step was to check the medical records of all AKI patients and extract the data.

The fourth step was to sort out the collected data and import them into Excel.

The fifth step was to import the data into SPSS software for statistical analysis.

## **Statistics**

SPSS software 21.0 (SPSS Inc. Chicago, IL, USA) was used for statistical analysis. Descriptive statistical analysis was conducted on the enumeration data, and statistical charts were drawn. Then, the characteristics of AKI patients were grouped according to their survival status at discharge. If the measurement data followed a normal distribution, the mean  $\pm$  standard deviation ( $\bar{x} \pm s$ ) was used. The t-test was used to compare the two groups, and the q-q normal probability graph was used for the normality test. If the measurement data did not follow a normal distribution, the median M and quartic interval (Qu, QL) were used. Comparisons between the two groups were conducted by the Mann-Whitney U test in the Spearman nonparametric test. Enumeration data were expressed as n (%), Pearson's chi-square test was used to compare binary classification data between the two groups, and the Mann-Whitney U test was used for ordered multiclassification. Logistic regression analysis was used to evaluate the risk factors. First, univariate logistic regression analysis was performed on the demographic data, AKI stage, etiology classification, basic diseases, risk factors, vital signs, laboratory examination results and whether RRT affected the prognosis of AKI patients, and a collinear judgment was made. Then, the variables with statistical significance in the univariate analysis were analyzed by multivariate logistic regression. If the variables were collinear and there were significant differences in the univariate logistic regression analysis, one of the variables was selected for multivariate logistic regression analysis. All tests were bilateral, with  $P < 0.05$  defined as statistically significant.

## **Results**

### **Basic data and general information of the AKI patients**

A total of 8,106 patients were admitted to the ICUs of the three hospitals. Of the 3019 patients excluded, the reasons were as follows: 517 patients were  $< 18$  years old, 1831 patients were admitted to the ICU for  $< 24$  hours, 482 patients had chronic kidney disease, 16 patients had nephrectomy, 5 patients underwent kidney transplantation within 3 months before admission to the ICU, 52 patients were re-admitted to the ICU during the same hospital stay, and 116 patients had missing needed data for the study (Fig. 1). The characteristics of the AKI patients are shown in Table 1.

## **Incidence of AKI**

According to the KIDGO criteria, a total of 890 ICU patients developed AKI, with an incidence of 17.5% (890/5087).

## **AKI stage**

According to the KIDGO criteria, AKI can be divided into KIDGO stages (I, II, III), as shown Table 2; this study included 22.02% (196/890) stage I cases, 31.01% (276/890) stage II cases, and 46.97% (418/890) stage III cases.

## **Etiology of AKI**

To clarify the etiology of AKI, the AKI patients were divided into three categories according to etiology: prerenal, renal substantive and postrenal, among which 64% (570/890) had pre-renal failure. The main causes included 255 cases of sepsis and septic shock, accounting for 44.7%; 130 cases of reduced cardiac output, accounting for 22.8%; 113 cases of fluid loss from various causes, accounting for 19.8%. A total of 33% (294/890) had renal substantial renal failure; 16.3% (48) had renal vascular and glomerular diseases, 75.9% (223) had renal tubular and interstitial diseases, 7.8% (23) had other unknown renal injury sites, and 2.7% (24) had postrenal failure. The main causes were 37.5% (9) cases of urinary tract stones, 25% (6) cases of urinary tract tumors, and 29.2% (9) cases of ureteral strictures, followed by prostate disease and neurogenic bladder.

## **Continuous renal replacement therapy**

Currently, the main treatment methods for AKI include identifying and removing causes and risk factors, treating the primary disease, improving renal insufficiency, providing kidney-preserving drugs, and administering continuous renal replacement therapy (CRRT). CRRT has been an important supportive therapy for patients with AKI, and there are multiple treatment models available based on different mechanisms. Of the 890 AKI patients, 35.8% (319/890) received CRRT, including 6.3% (20/319) stage I patients, 21.6% (69/319 stage II patients), and 72.1% (230/319) stage III patients. The higher the AKI stage was, the more patients received CRRT.

## **Outcomes of AKI**

The AKI patients were divided into two groups according to outcome: the survival group and the non-survival group. Of the patients with AKI hospitalized in the ICU, there are 368 deaths during hospitalization, and the mortality rate was 41.3% overall, 16% (59) for stage I AKI, 31.5% (116) for stage II AKI, and 52.4% (193) for stage III AKI; the higher the AKI stage was, the worse the prognosis. (Table 2) The mortality of patients without RRT was 37.1% (212), and 48.9% (156) of patients with RRT died ( $p=0.001$ ).

Further analysis showed that patients treated with RRT had a higher AKI stage and more severe disease than those without RRT.

## **Risk factors for death in AKI patients**

### **1. Univariate analysis**

Univariate logistic regression analysis showed that male sex, old age, high AKI stage, RRT, infection, cardio-pulmonary resuscitation, reduced cardiac output, mechanical ventilation, diuretics, and reduced white blood cells, platelets, blood urea nitrogen, serum albumin prothrombin time (PT) and activated partial thromboplastin time (APTT) were significantly correlated with death in AKI patients (all P values were less than 0.05). (Table 3)

### **2. Multivariate analysis**

Multivariate logistic regression analysis showed that old age, male sex, high AKI stage, reduced cardiac output, mechanical ventilation, RRT, elevated leucocyte count, reduced platelet count, and reduced serum albumin were all independent risk factors for AKI death. (Table 4)

## **Septic AKI**

Sepsis and septic shock were the most common causes of AKI in critically ill patients. Among the AKI patients enrolled in this study, 28.7% (255/890) had AKI caused by sepsis and septic shock, which were the major causes of AKI. The main infection sites were the lung, abdomen, urinary system, skin and soft tissue. Among the patients with AKI caused by sepsis and septic shock, 92 patients received RRT, accounting for 28.8% of the total patients treated with RRT. A total of 136 patients with sepsis and septic shock AKI died, leading to a mortality of 53.3%.

## **Discussion**

Acute kidney injury is a major clinical problem in critically ill patients that leads to high medical costs and poor prognosis. AKI can arise from a variety of causes and is an important risk factor for chronic kidney disease (CKD). Recently, a southern medical university [13] conducted epidemiological studies on AKI in ICU inpatients in 9 hospitals in different regions of China, but this study did not include the northwest region. Epidemiological investigations have shown that the occurrence and development of diseases will be affected by different regional environments, different study populations, different economic levels and different medical conditions.[14-16] Here, we considered several representative hospitals in the Gansu Province in northwest China as investigation points to conduct a multicenter and retrospective study of 8106 patients admitted to a comprehensive ICU.

The results showed that the incidence of AKI was 17.5% overall, 22.02% for stage I, 31.01% for stage II, and 46.97% for stage III, and the mortality was 41.3%. A southern medical university study found that, on the basis of the KIDGO diagnostic criteria, the incidence of AKI among ICU inpatients was 30.04%, and AKI stages I, II, and III accounted for 52.1%, 19.7% and 28.2% of the patients, respectively. Another regional retrospective study that included five ICU centers in southwest China's Sichuan province reported an incidence of AKI of 37.8% and hospital mortality as high as 51.8%.[17] In our study, in comparison, the incidence of AKI was lower, and stage III AKI had for the highest incidence of all stages. The reason may be that AKI lacks specific symptoms and is mainly diagnosed by monitoring the changes in serum creatinine in the short term. A low awareness of AKI would lead to repeated low serum creatinine readings, and the low recognition rate of AKI will cause treatment delays and speed up AKI progression. According to a multicenter survey, the repeated serum creatinine detection rate of hospitalized patients in mainland China was only 29.8%, which is lower than the number reported by developed countries (63.2-67.6%)[18]. Therefore, it is reasonable to believe that the incidence of AKI in the relatively underdeveloped northwest region may be underestimated.

It is noteworthy that this study found an increased risk of death in male AKI patients compared to in female AKI patients, which was inconsistent with previous studies that showed no significant impact from sex on the prognosis of AKI patients, but a recent study also showed that the male sex was a risk factor for poor prognosis in AKI patients[19]. Further studies are needed to confirm the effect of sex on the prognosis of AKI patients.

In addition, in our study, we also found that RRT is one of the risk factors for AKI. Further analyses of the study results showed that RRT in patients with stage III AKI caused most patients to suffer from severe illness, resulting in high mortality. However, according to existing studies, RRT is an important treatment for AKI in ICU patients. Over time, the incidence of AKI patients requiring dialysis increases, but mortality gradually decreases[20, 21]. This is inconsistent with the results of our study, which may be related to the degree of renal injury, RRT dose, the timing of RRT initiation and other factors that affect the prognosis of AKI patients. There is no unified conclusion at present, and further studies are needed to confirm this hypothesis.

## Limitations And Strengths

1. This study selected three hospitals that can represent the medical situation of the Gansu Province. From the perspective of epidemiological sampling, there is sampling bias, which may affect the epidemiological results for AKI. In the future, more data from hospitals of different regions and levels can be collected for further research. 2. Our study is a retrospective study and thus cannot accurately monitor the urine volume of patients. Therefore, the diagnosis of acute kidney injury is mainly based on serum creatinine changes, which may underestimate the incidence of acute kidney injury. Although this study has some shortcomings, it is also innovative and practical, which is of great benefit for guiding clinical treatment. First, epidemiological studies on acute kidney injury in critically ill patients are mostly single-center, small-sample studies with poor representativeness. Our study is a multicenter study with a large

sample size, which is closer to the overall sample size. The results of our study are more conducive to guiding clinical treatment and scientific research. Second, laboratory indicators were added to the analysis of prognostic risk factors in our study, and these indicators were simple and economical to obtain and had good clinical application prospects. At present, most scholars are committed to studying the pathogenesis of AKI and the risk factors affecting the occurrence of AKI, while research on the factors affecting the prognosis of acute kidney injury has relatively lagged behind. In the future, predicting the prognosis of AKI will arouse the interest of many researchers. Most importantly, with the rapid development of big data in medicine, an increasing number of people will realize the importance of data science. The development of medical science and technology is also inseparable from big data. Specialized development, collation and analysis of big data may bring unexpected benefits to our scientific research. Therefore, our research "The epidemiology of acute kidney injury in critically ill patients in the Gansu Province (EACG)" series (Chinese clinical trial registration number: ChiCTR1800016945) will further expand upon the data collected from critically ill patients with AKI in the Gansu Province, establish a database and build a cross-field data sharing platform to help more clinical and scientific researchers interested in AKI quickly obtain clinical data and process these data. Furthermore, data from China, the world's largest developing country, will provide valuable information for improving the current situation and economic burden of acute renal impairment worldwide.

## **Conclusions**

Large-scale epidemiological data from several representative general hospitals in the Gansu Province showed that the incidence and mortality of acute kidney injury in intensive care units were still very high. Sepsis and septic shock are the main causes of AKI.

## **Declarations**

### **Ethics approval and consent to participate**

The Ethics Committee of Lanzhou University Second Hospital approved this study, and the number was 2018-043. Written informed consent was obtained from individual or guardian participants.

### **Consent for publication**

Not applicable.

### **Availability of data and materials**

All data generated or analysed during this study are included in this published article.

## Competing interests

All authors declare that there are no competing interests.

## Funding

Not applicable.

## Authors' contributions

Conducted the study: YC, FF.

Collected all data: DL, YY, ML, J-jY, C-hM, C-mD.

Did the statistical analysis: YC, X-nC.

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## Tables

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## Figures

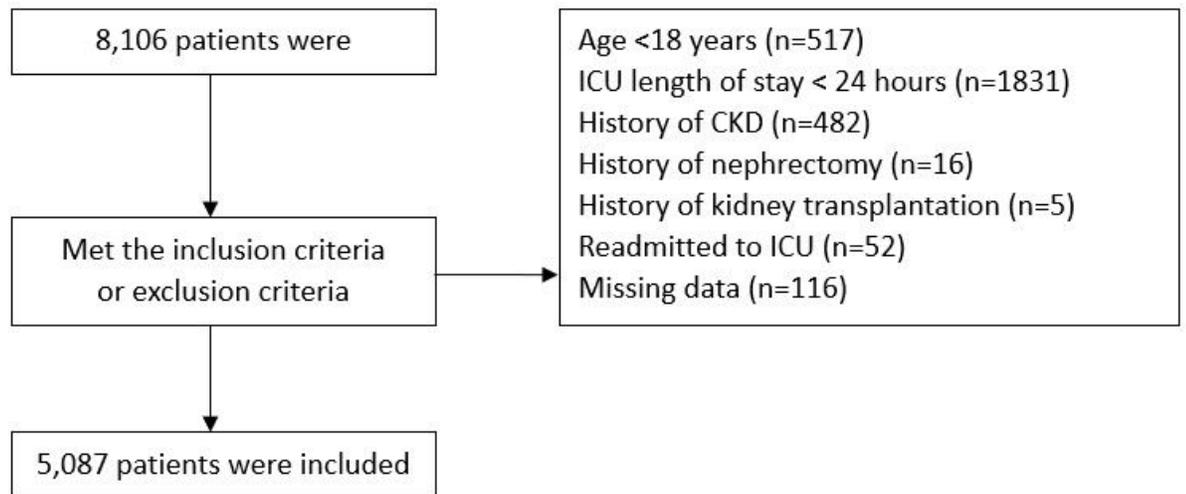


Fig. 1 Flow chart

## Figure 1

Flow chart

## Supplementary Files

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