

Article

# Postoperative Acute Kidney Injury in Infectious Endocarditis: Outcomes and Risk Factors

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## Abstract

**Background:** We conducted the following study to analyze the risk factors of postoperative acute kidney injury (AKI) in patients diagnosed with infectious endocarditis (IE) and their impact on outcomes. **Methods:** We retrospectively analyzed patients with IE treated surgically. We use a contingency table method and logistic regression analysis for investigation of the relationship with perioperative risk factors, Kaplan Meier analysis for survival rate, logarithmic rank test for inter group survival rate differences, Spearman analysis for the correlation of two variates, receiver operating characteristic (ROC) analysis for the diagnostic value of risk factors, and the Youden index for the optimal value. **Results:** 848 patients were enrolled and divided into a group with AKI ( $n = 272$ ) and a group without AKI ( $n = 576$ ). The incidence of postoperative AKI was 32.1% (272/848). Male gender ( $p < 0.001$ ), preoperative aortic regurgitation ( $p < 0.001$ ), paravalvular leak ( $p < 0.001$ ), cardiopulmonary bypass length  $\geq 120$  minutes ( $p < 0.001$ ), aortic occlusion duration  $\geq 90$  minutes ( $p < 0.001$ ), mechanical ventilation length  $\geq 72$  hours ( $p < 0.001$ ), contrast iodine ( $p = 0.048$ ), and vancomycin ( $p < 0.001$ ) were found to be risk factors of postoperative AKI in IE. A positive relationship exists between cardiopulmonary bypass length and postoperative AKI ( $r = 0.406$ ,  $p < 0.001$ ). A value of cardiopulmonary bypass length  $> 161$  minutes was 70.6% sensitive and 83.3% specific for the diagnosis of postoperative AKI ( $p < 0.001$ ). Long-term survival in the group with AKI was significantly less than that in the group without AKI. **Conclusions:** Postoperative AKI in IE contributes to an apparent increase in in-hospital and long-term mortality. Optimization of the management of AKI will improve the short- and long-term outcomes of postoperative an AKI in IE.

## Keywords

AKI; IE; short- and long-term mortality; risk factors

## Introduction

Infectious endocarditis (IE) remains a complicated disease with significant morbidity and an overall mortality rate ranging from 20 to 25% in most series despite advances in diagnostic and therapeutic strategies. Epidemiological changes have occurred in high-income countries, with a significant and steady increase in the number of cases related to prosthetic valves and intravascular devices [1–4].

Acute kidney injury (AKI) is a serious and usual complication occurring in approximately 40% of cardiac surgery patients. AKI is related to an increased mortality rate, worsening prognosis, increased duration of mechanical ventilation, and prolonged hospital stays [5–7]. IE patients usually have a risk of kidney damage, and their kidney function may be further impaired due to cumulative damage before, during, and after surgery [8].

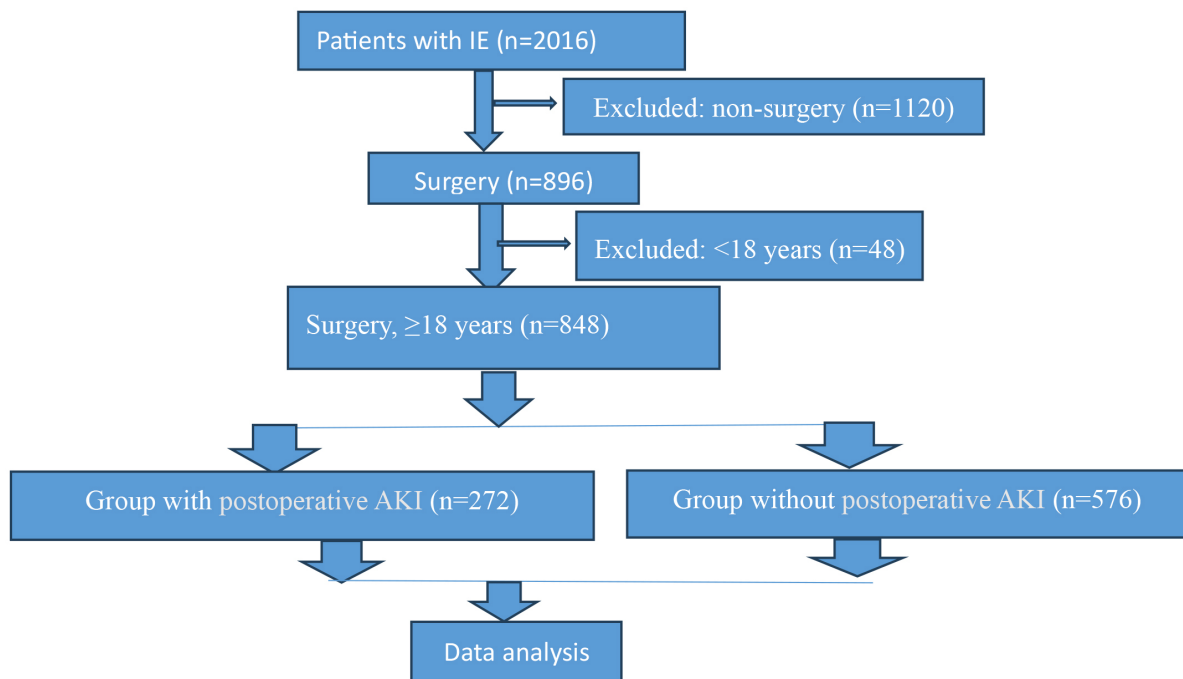
We hypothesized that improving the prevention and treatment of AKI after cardiac surgery could decrease in-hospital and long-term mortality. We conducted the study to analyze the risk factors of postoperative AKI in patients with IE and their impact on patient outcomes.

## Methods

### Study Design

We retrospectively analyzed the patients with IE aged  $\geq 18$  years treated surgically between January 2006 and November 2022 at our hospital (Fig. 1). The inclusion criteria included patients aged  $\geq 18$  years diagnosed with infective endocarditis undergoing cardiac surgery during the study period at our hospital. The exclusion criteria included patients not receiving cardiac surgery including multiorgan failure at admission, medical therapy alone, and refusal of surgery. All patients aged  $< 18$  years were excluded.





**Fig. 1. Flow diagram of clinical trial.** AKI, acute kidney injury; IE, infectious endocarditis.

### Diagnosis

Patients in our hospital were diagnosed on the basis of the modified Duke criteria [9] and surgical and pathological results were reviewed to confirm preoperative diagnosis. Based on Kidney Disease Improving Global Outcomes (KDIGO) classification, a patient is classified as having AKI if serum creatinine rises by  $\geq 26.5 \mu\text{mol/L}$  ( $0.3 \text{ mg/dL}$ ) within 48 hours, or serum creatinine is 50% greater than the baseline within the first 7 days, or urine output is less than  $0.5 \text{ mL/kg/hour}$  for 6 hours [10].

### Variables Investigated

A survey was conducted on the variables (Supplementary Materials).

The interval from symptoms to operation refers to the duration of time from the onset of symptoms to the date of the operation.

The in-hospital mortality rate is defined as death within 30 days after surgery or during the same hospitalization period.

### Follow-up

We followed up all discharged patients until the end of the investigation. All patients undergo echocardiography, electrocardiogram, and chest X-ray examination every three to twelve months. During the final follow-up, we contacted the patient via phone or WeChat, or conducted an interview directly at the outpatient department.

### Statistical Analyses

Continuous variables are presented as means  $\pm$  SE. We performed a normality test for all variates in the research using the Kolmogorov-Smirnov test and evaluated the relationship between preoperative variables and selected intraoperative, and postoperative variates by chi square test, Kruskal Wallis test, or Wilcoxon rank sum test (depending on the situation). We used the contingency table method and logistic regression analysis to investigate the relationship with perioperative risk factors. Kaplan Meier analysis was used for survival rate, and logarithmic rank test was used for inter group survival rate differences. The correlation of two variates was determined by the Spearman correlation coefficient. We plotted receiver operating characteristic (ROC) curves and their corresponding area under the curve (AUC) to investigate the diagnostic value of risk factors, and adopted the Youden index to investigate the optimal critical value in subject operating characteristic analysis. A  $p$ -value  $< 0.05$  is considered to be statistically significant. IBM SPSS version 24.0 software (IBM Corp., Armonk, NY, USA) was used to perform all analyses.

### Results

#### Characteristics of Patients

848 patients ( $\geq 18$  years) with IE treated surgically were assigned to the group with ( $n = 272$ ) and without ( $n = 576$ ) postoperative AKI (Fig. 1).

### Preoperative Data

Age ( $48.6 \pm 0.7$  vs.  $42.3 \pm 0.6$  years,  $p < 0.001$ ), weight ( $59.1 \pm 0.76$  vs.  $50.6 \pm 0.46$  kg,  $p < 0.001$ ), size of vegetation ( $13.1 \pm 0.40$  vs.  $8.95 \pm 0.25$  mm,  $p < 0.001$ ), preoperative left ventricular end diastolic dimension (LVEDD) ( $63.8 \pm 0.49$  vs.  $59.8 \pm 0.39$  mm,  $p < 0.001$ ), preoperative aortic valve dysfunction ( $8.16 \pm 0.49$  vs  $4.36 \pm 0.23$  cm<sup>2</sup>,  $p < 0.001$ ), preoperative serum creatinine ( $108.82 \pm 2.56$  vs.  $39.13 \pm 0.77$   $\mu$ mol/L,  $p < 0.001$ ), contrast iodine (52.9% vs. 33.3%,  $p < 0.001$ ) and vancomycin (27.9% vs. 16.1%,  $p < 0.001$ ) in the AKI group were apparently greater than those in the non-AKI group (Table 1). Preoperative left ventricular ejection fractions (LVEF) ( $60.6 \pm 0.49$  vs.  $62.6 \pm 0.30\%$ ,  $p < 0.001$ ) and preoperative tricuspid insufficiency ( $4.18 \pm 0.18$  vs.  $4.88 \pm 0.21$  cm<sup>2</sup>,  $p = 0.04$ ) in the AKI group were less than those in the non-AKI group (Table 1).

### Mortality and Postoperative AKI

272 patients developed postoperative AKI (32.1%, 272/848), 152 (55.9%) classified as KDIGO stage 1, 52 (19.1%) as KDIGO stage 2, and 68 (25%) as KDIGO stage 3. 68 (25%) required hemodialysis. 48 in-hospital deaths occurred. The mortality rate of the group with AKI was markedly larger than that of the group without AKI (18.0% vs. 0.34%,  $p < 0.001$ ) (Table 1).

### Intra- and Post-Operative Data

Aortic occlusion time ( $103.24 \pm 2.20$  vs.  $79.08 \pm 1.30$  minutes,  $p < 0.001$ ), cardiopulmonary bypass length ( $171.59 \pm 2.59$  vs.  $127.0 \pm 1.99$  minutes,  $p < 0.001$ ), intubation length ( $95.56 \pm 4.91$  vs.  $27.48 \pm 1.24$  hours,  $p < 0.001$ ), intensive care unit retention length ( $7.06 \pm 0.20$  vs.  $3.74 \pm 0.09$  days,  $p < 0.001$ ), postoperative 24-hour serum creatinine ( $133.24 \pm 2.71$  vs.  $68.9 \pm 0.95$   $\mu$ mol/L,  $p < 0.001$ ), postoperative serum creatinine levels at 48 hours ( $190.53 \pm 3.85$  vs.  $66.51 \pm 0.83$   $\mu$ mol/L,  $p < 0.001$ ), chest drainage ( $683.54 \pm 24.41$  vs.  $599.49 \pm 15.81$  mL,  $p < 0.001$ ), postoperative LVEDD ( $49.06 \pm 0.32$  vs.  $47.45 \pm 0.31$  mm,  $p = 0.002$ ), fresh-frozen plasma ( $722.94 \pm 23.66$  vs  $577.18 \pm 19.65$  mL,  $p < 0.001$ ) and red blood cell transfusion ( $4.71 \pm 0.27$  vs.  $1.85 \pm 0.07$  units,  $p < 0.001$ ) in the AKI group were markedly greater than those in the non-AKI group (Table 1).

Fluid balance on the day of surgery in the AKI group ( $-266.47 \pm 50.01$  vs.  $-763.59 \pm 28.45$  mL,  $p < 0.001$ ) was less negative than that in the non-AKI group. Fluid balance on the first day postoperative in the AKI group ( $-732.35 \pm 104.30$  vs.  $-565.38 \pm 24.94$  mL,  $p = 0.034$ ) and the fluid balance on the second day ( $-682.35 \pm 61.89$  vs.  $-487.18 \pm 21.65$  mL,  $p < 0.001$ ) were more negative than those in the non-AKI group (Table 1). Postoperative left LVEF of the

AKI group ( $57.88 \pm 0.35$  vs.  $59.39 \pm 0.29\%$ ,  $p = 0.003$ ) was lower than that of the non-AKI group (Table 1).

Risk factor in-hospital deaths and complications postoperative in IE is showed in Table 2.

### Risk Factors of AKI Postoperative

By univariate analysis, factors are found to be related to AKI postoperative, including male gender (odd ratio: 4.56, 95% CI: 1.368–8.654,  $p < 0.001$ ), age (odd ratio: 0.925, 95% CI: 0.913–0.937,  $p < 0.001$ ), preoperative aortic regurgitation (odd ratio: 3.106, 95% CI: 2.289–4.214,  $p < 0.001$ ), paravalvular leak (odd ratio: 3.964, 95% CI: 2.470–6.362,  $p < 0.001$ ), cardiopulmonary bypass (CPB) length  $\geq 120$  minutes (odd ratio: 5.833, 95% CI: 4.101–8.298,  $p < 0.001$ ), aortic occlusion duration  $\geq 90$  minutes (odd ratio: 5.551, 95% CI: 4.062–7.587,  $p < 0.001$ ), mechanical ventilation length  $\geq 72$  hours (odd ratio: 9.273, 95% CI: 6.004–14.321,  $p < 0.001$ ), contrast iodine (odd ratio: 1.65, 95% CI: 1.28–1.96,  $p < 0.001$ ), and vancomycin (odd ratio: 2.67, 95% CI: 2.14–3.56,  $p < 0.001$ ).

Multivariate analysis demonstrated that male gender (odd ratio: 5.67, 95% CI: 1.90–7.07,  $p < 0.001$ ), age (odd ratio: 0.88, 95% CI: 0.86–0.90,  $p < 0.001$ ), preoperative aortic regurgitation (odd ratio: 2.23, 95% CI: 1.60–3.12,  $p < 0.001$ ), paravalvular leak (odd ratio: 3.17, 95% CI: 1.93–5.21,  $p < 0.001$ ), CPB length  $\geq 120$  minutes (odd ratio: 2.346, 95% CI: 1.428–3.854,  $p < 0.001$ ), aortic occlusion duration  $\geq 90$  minutes (odd ratio: 3.549, 95% CI: 2.262–5.570,  $p < 0.001$ ), mechanical ventilation length  $\geq 72$  hours (odd ratio: 9.753, 95% CI: 6.045–15.737,  $p < 0.001$ ), contrast iodine (odd ratio: 8.833, 95% CI: 1.023–16.28,  $p = 0.048$ ), and vancomycin (odd ratio: 1.86, 95% CI: 1.45–2.65,  $p < 0.001$ ) were related to postoperative AKI (Table 3).

### Follow-up Results

The follow-up completion rate was 95.8% (766/800), with 800 survivors discharged and 766 being successfully followed up. The average follow-up duration was  $77.73 \pm 1.85$  months. 87 cases (87/766, 11.4%) died within one year after discharge due to recurrent IE or brain hemorrhage. 658 patients fell into the New York Heart Association class I (658/766, 85.9%), and 21 were categorized as class II (21/766, 2.7%) (Table 1).

The follow-up duration of the group with AKI ( $69.1 \pm 4.0$  vs.  $81.4 \pm 2.0$  months,  $p = 0.002$ ) was significantly less than that of the group without AKI, which may have resulted from the higher overall mortality rate in the group with AKI. Compared to the group without AKI, the group with AKI had a significantly increased overall mortality rate (22.8% vs. 6.9%,  $p < 0.001$ ) (Table 1).

**Table 1. Characteristics of patients and operative and follow-up results (n = 848).**

| Variable                                              | Total (n = 848) | Group with AKI (n = 272) | Group without AKI (n = 576) | p value |
|-------------------------------------------------------|-----------------|--------------------------|-----------------------------|---------|
| <b>Characteristics</b>                                |                 |                          |                             |         |
| Male gender, n (%)                                    | 560 (66.1%)     | 224 (82.4%)              | 336 (53.8%)                 | <0.001  |
| Age, years                                            | 44.6 ± 0.48     | 48.6 ± 0.70              | 42.3 ± 0.60                 | <0.001  |
| Weight, kg                                            | 56.76 ± 0.36    | 59.1 ± 0.76              | 50.6 ± 0.46                 | <0.001  |
| Time between symptoms and surgery, months             | 2.46 ± 0.08     | 2.46 ± 0.12              | 2.46 ± 0.09                 | 0.993   |
| Coronary heart disease, n (%)                         | 18 (2.1%)       | 7 (2.6%)                 | 11 (1.9%)                   | 0.531   |
| Hypertension, n (%)                                   | 36 (4.2%)       | 11 (4.0%)                | 25 (4.3%)                   | 0.842   |
| Diabetes mellitus, n (%)                              | 17 (1.9%)       | 6 (2.2%)                 | 11 (1.9%)                   | 0.774   |
| Neurological complications before surgery, n (%)      | 112 (13.2%)     | 37 (13.6%)               | 75 (13.0%)                  | 0.815   |
| Vegetation length, mm                                 | 10.58 ± 0.23    | 13.1 ± 0.40              | 8.95 ± 0.25                 | <0.001  |
| Preoperative LVEDD, mm                                | 61.13 ± 0.32    | 63.8 ± 0.49              | 59.8 ± 0.39                 | <0.001  |
| Preoperative LVEF, n (%)                              | 61.92 ± 0.27    | 60.6 ± 0.49              | 62.6 ± 0.30                 | <0.001  |
| Preoperative aortic insufficiency, cm <sup>2</sup>    | 5.82 ± 0.11     | 8.16 ± 0.49              | 4.36 ± 0.23                 | <0.001  |
| Preoperative mitral insufficiency, cm <sup>2</sup>    | 7.06 ± 0.21     | 7.74 ± 0.28              | 7.06 ± 0.27                 | 0.136   |
| Preoperative tricuspid insufficiency, cm <sup>2</sup> | 4.89 ± 0.16     | 4.18 ± 0.18              | 4.88 ± 0.21                 | 0.040   |
| Serum creatinine before surgery, μmol/L               | 83.32 ± 1.34    | 108.82 ± 2.56            | 39.13 ± 0.77                | <0.001  |
| <i>S. aureus</i> endocarditis, n (%)                  | 98 (11.6%)      | 39 (14.3%)               | 59 (10.2%)                  | 0.082   |
| Streptococci endocarditis, n (%)                      | 161 (19.0%)     | 59 (21.7%)               | 102 (17.7%)                 | 0.167   |
| Contrast iodine, n (%)                                | 336 (39.6%)     | 144 (52.9%)              | 192 (33.3%)                 | <0.001  |
| Vancomycin, n (%)                                     | 169 (19.9%)     | 76 (27.9%)               | 93 (16.1%)                  | <0.001  |
| <b>Operative</b>                                      |                 |                          |                             |         |
| In-hospital deaths, n                                 | 48 (5.7%)       | 46 (18.0%)               | 2 (0.34%)                   | <0.001  |
| Aortic occlusion time, minutes                        | 86.75 ± 1.17    | 103.24 ± 2.20            | 79.08 ± 1.30                | <0.001  |
| Cardiopulmonary bypass length, minutes                | 141.43 ± 1.75   | 171.59 ± 2.59            | 127.0 ± 1.99                | <0.001  |
| Intubation time, hours                                | 50.5 ± 2.10     | 95.56 ± 4.91             | 27.48 ± 1.24                | <0.001  |
| ICU retention time, days                              | 4.89 ± 0.10     | 7.06 ± 0.20              | 3.74 ± 0.09                 | <0.001  |
| Postoperative hospitalized time, days                 | 18.98 ± 0.27    | 18.35 ± 0.48             | 19.21 ± 0.31                | 0.131   |
| Postoperative serum creatinine 24 h, μmol/L           | 91.11 ± 1.47    | 133.24 ± 2.71            | 68.9 ± 0.95                 | <0.001  |
| Postoperative serum creatinine 48 h, μmol/L           | 108.80 ± 2.40   | 190.53 ± 3.85            | 66.51 ± 0.83                | <0.001  |
| Fluid balance on operation day, mL                    | -613.40 ± 27.47 | -266.47 ± 50.01          | -763.59 ± 28.45             | <0.001  |
| Fluid balance on 1st day following operation, mL      | -635.85 ± 38.10 | -732.35 ± 104.30         | -565.38 ± 24.94             | 0.034   |
| Fluid balance on 2nd day following operation, mL      | -558.49 ± 25.53 | -682.35 ± 61.89          | -487.18 ± 21.65             | <0.001  |
| Chest drainage, mL                                    | 645.47 ± 13.75  | 683.54 ± 24.41           | 599.49 ± 15.81              | <0.001  |
| LVEDD, mm                                             | 48.08 ± 0.24    | 49.06 ± 0.32             | 47.45 ± 0.31                | 0.002   |
| LVEF postoperative, %                                 | 58.79 ± 0.23    | 57.88 ± 0.35             | 59.39 ± 0.29                | 0.003   |
| Fresh-frozen plasma, mL                               | 646.00 ± 16.10  | 722.94 ± 23.66           | 577.18 ± 19.65              | <0.001  |
| Red blood cells transfusion, units                    | 2.83 ± 0.11     | 4.71 ± 0.27              | 1.85 ± 0.07                 | <0.001  |
| <b>Follow-up</b>                                      |                 |                          |                             |         |
|                                                       | Total (n = 766) | Group with AKI (n = 228) | Group without AKI (n = 538) | p value |
| Length of follow-up, months                           | 77.73 ± 1.85    | 69.10 ± 4.00             | 81.40 ± 2.00                | 0.002   |
| All-time mortality, n (%)                             | 89 (11.6%)      | 52 (22.8%)               | 37 (6.9%)                   | <0.001  |

LVEDD, left ventricular end diastolic dimension; LVEF, left ventricular ejection fractions; ICU, intensive care unit; *S. aureus*, *Staphylococcus aureus*.

#### Relationship Between Cardiopulmonary Bypass Length and Postoperative AKI

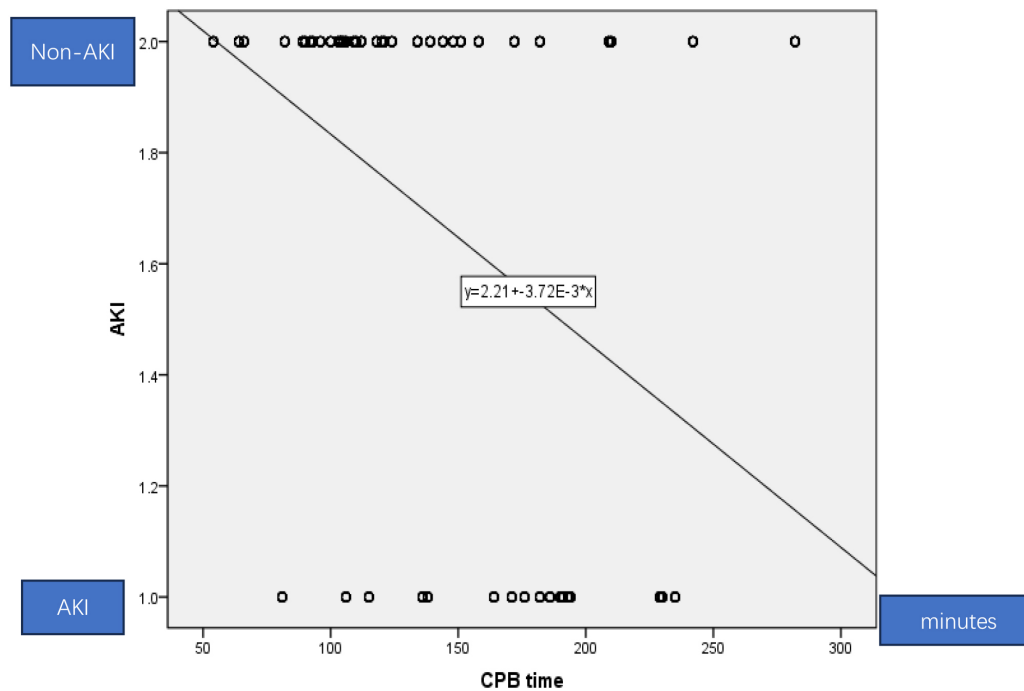
We found an apparent positive relationship between cardiopulmonary bypass length and postoperative AKI ( $r = 0.406$ ,  $p < 0.001$ ) by Spearman correlation analysis (Fig. 2).

An apparent positive relationship between cardiopulmonary bypass length and postoperative AKI ( $r = 0.406$ ,  $p < 0.001$ ) by Spearman correlations analysis ( $r = 0.406$ ,  $p < 0.001$ ) was demonstrated.

#### The ROC Curve of Diagnostic Accuracy with Cardiopulmonary Bypass Length for Predicting the Rate of Incidence of Postoperative AKI

A value of cardiopulmonary bypass length >161 minutes was 70.6% sensitive and 83.3% specific for the diagnosis of postoperative AKI, with an AUC 0.770 (95% CI: 0.735–0.804;  $p < 0.001$ ) and a Youden index 0.539 (Fig. 3).

The ROC curve with the AUC were plotted to investigate the diagnostic value of the risk. The optimal cutoff was assessed by using Youden's index in ROC analysis.



**Fig. 2. Relationship between cardiopulmonary bypass length and postoperative AKI.** CPB, cardiopulmonary bypass.

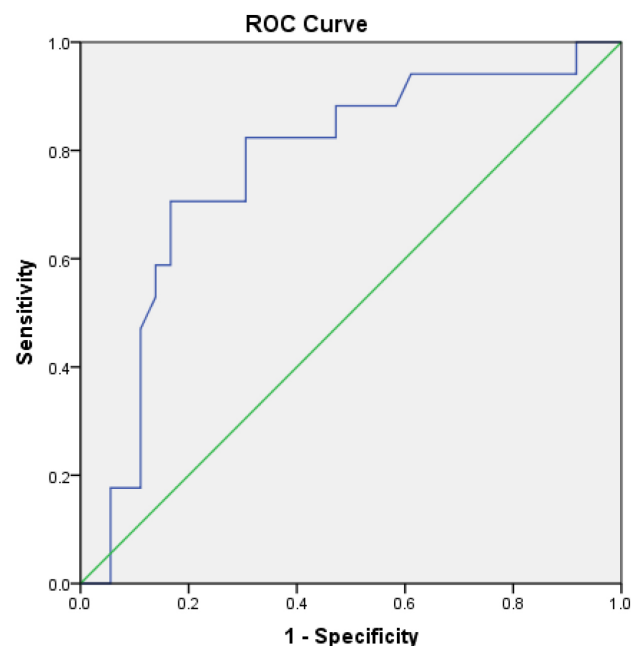
**Table 2. In-hospital deaths and complications postoperative in IE (n = 848).**

| Variable                                                                          | Value       |
|-----------------------------------------------------------------------------------|-------------|
| Operations                                                                        |             |
| Aortic valve replacement alone, n (%)                                             | 176 (20.8%) |
| Mitral valve surgery alone, n (%)                                                 | 368 (43.4%) |
| Double valve operation, n (%)                                                     | 256 (30.2%) |
| Bentall + mitral valve replacement, n (%)                                         | 16 (1.9%)   |
| Extracorporeal membrane oxygenation, n (%)                                        | 3 (3.5%)    |
| Causes of in-hospital deaths                                                      |             |
| Paravalvular leak + AKI + cardiogenic shock + septicemia + hepatic failure, n (%) | 32 (3.8%)   |
| Hemorrhage in brain, n (%)                                                        | 16 (1.9%)   |
| Postoperative complications                                                       |             |
| AKI, n (%)                                                                        | 272 (32.1%) |
| Intubation time >48 h, n (%)                                                      | 352 (41.5%) |
| Hepatic failure, n (%)                                                            | 39 (4.6%)   |
| Respiratory failure, n (%)                                                        | 142 (16.7%) |
| Ventricular fibrillation, n (%)                                                   | 33 (3.9%)   |

Using 161 minutes as a cutoff level, a value of cardiopulmonary bypass length >161 minutes was 70.6% sensitive and 83.3% specific for the diagnosis of postoperative AKI, with an AUC 0.770 (95% CI: 0.735–0.804;  $p < 0.001$ ) and a Youden index 0.539.

### Long-Term Survival

Long-term survival in the group with AKI was markedly lower than that in the group without AKI (Log Rank test,  $p = 0.009$ ) (Fig. 4).



**Fig. 3. The ROC curve of diagnostic accuracy with cardiopulmonary bypass length for predicting the incidence of postoperative AKI.** ROC, receiver operating characteristic.

### Discussion

AKI is a disease characterized by acute deterioration of renal function, characterized by a decrease in glomerular filtration rate, as a usual complication following heart

**Table 3. Analysis of risk factors of AKI postoperative for IE.**

| Model                                                       | Odd ratio | 95% CI       | p value |
|-------------------------------------------------------------|-----------|--------------|---------|
| Univariable analysis of risk factors of AKI postoperative   |           |              |         |
| Male gender                                                 | 4.560     | 1.368–8.654  | <0.001  |
| Age                                                         | 0.925     | 0.913–0.937  | <0.001  |
| Aortic regurgitation preoperative                           | 3.106     | 2.289–4.214  | <0.001  |
| Paravalvular leak                                           | 3.964     | 2.470–6.362  | <0.001  |
| CPB length $\geq 120$ minutes                               | 5.833     | 4.101–8.298  | <0.001  |
| Aortic occlusion duration $\geq 90$ minutes                 | 5.551     | 4.062–7.587  | <0.001  |
| Mechanical ventilation length $\geq 72$ hours               | 9.273     | 6.004–14.321 | <0.001  |
| Contrast iodine                                             | 1.650     | 1.280–1.960  | <0.001  |
| Vancomycin                                                  | 2.670     | 2.140–3.560  | <0.001  |
| Multivariable analysis of risk factors of AKI postoperative |           |              |         |
| Male gender                                                 | 5.670     | 1.900–7.070  | <0.001  |
| Age                                                         | 0.880     | 0.860–0.900  | <0.001  |
| Aortic regurgitation preoperative                           | 2.230     | 1.600–3.120  | <0.001  |
| Paravalvular leak                                           | 3.170     | 1.930–5.210  | <0.001  |
| CPB length $\geq 120$ minutes                               | 2.346     | 1.428–3.854  | <0.001  |
| Aortic occlusion duration $\geq 90$ minutes                 | 3.549     | 2.262–5.570  | <0.001  |
| Mechanical ventilation length $\geq 72$ hours               | 9.753     | 6.045–15.737 | <0.001  |
| Contrast iodine                                             | 8.833     | 1.023–16.280 | 0.048   |
| Vancomycin                                                  | 1.860     | 1.450–2.650  | <0.001  |

CI, confidence interval.

operation with an incidence rate of 6.7% to 39% [11–13]. It is related to increased mortality, a stay in an intensive care unit (ICU), hospitalization duration, and the amount of resources consumed [14–16]. Renal replacement therapy (RRT) is needed in 1.6%–7.7% following heart surgery. It has been reported that risk factors of AKI following heart surgery include advanced age, diabetes, high EuroSCORE, transfusion of blood, time from angiography to surgery, increased preoperative serum creatinine, and the use of nephrotoxic drugs [4,11,16–18]. The accumulation of damage including infection, systemic inflammation related to extracorporeal circulation, and the use of nephrotoxic drugs further elevates the risk of postoperative AKI in IE patients [8].

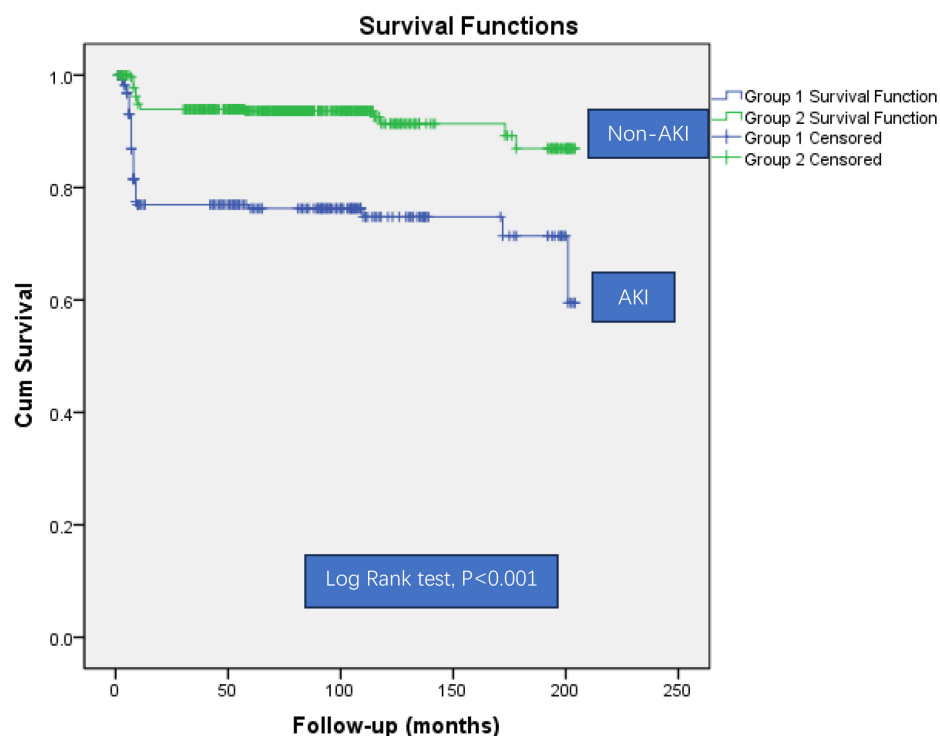
Our investigation showed that the incidence of postoperative AKI is 32.1% (272/848). Male gender, preoperative aortic regurgitation, paravalvular leak, cardiopulmonary bypass length  $\geq 120$  minutes, aortic occlusion duration  $\geq 90$  minutes, mechanical ventilation length  $\geq 72$  hours, contrast iodine, and vancomycin were found to be risk factors of postoperative AKI. A positive relationship exists between cardiopulmonary bypass length and postoperative AKI. A value of cardiopulmonary bypass length  $>161$  minutes was 70.6% sensitive and 83.3% specific for the diagnosis of postoperative AKI. Long-term survival in the group with AKI was significantly lower than that in the group without AKI.

Epidemiological research data show that gender is an important factor in the incidence rate of active aortic IE, and the incidence rate in males is higher. Healthy natural valves

are protected by intact endothelium from bacterial invasion; The endothelium of patients with endocarditis is no longer a fused monolayer, and bacteria adhere to the surface, leading to the formation of biofilms. Due to its encapsulation effect, bacterial biofilms have inherent resistance to antimicrobial agents. Cysts include bacteria that produce extracellular polymers and proteolytic enzymes damaging nearby tissues and enhancing infection. Estrogen protects endothelial cells, which explains the difference in the incidence rate of endocarditis between men and women. Due to the reduction of junction proteins between endothelial cells, estrogen deficiency and lobular migration are more pronounced [19].

Vancomycin as a nephrotoxic agent has been described as having nephrotoxicity to IE and critically ill patients. High serum trough concentration of vancomycin is related to an increased risk of AKI [8]. It is generally needed to maintain a high trough concentration due to the high minimum inhibitory concentration in severe cases of methicillin-resistant *Staphylococcus aureus* infection. Antibiotics of lower nephrotoxicity in IE patients deserve further assessment [20–22]. We should balance the advantages of preoperative enhanced computed tomography or angiography with the risks of iodine contrast and renal function [8].

Preoperative aortic regurgitation can reduce glomerular filtration rate and lead to AKI. We advocate for timely diagnosis and intervention of IE to avoid severe preoperative aortic regurgitation, as IE is a progressive, complicated, and life-threatening disease. Early surgical treatment can reduce the risk of stroke and death in IE patients [2,3,23].



| Patients at risk  |     |     |     |     |     |     |
|-------------------|-----|-----|-----|-----|-----|-----|
| Months            | 0   | 50  | 100 | 150 | 200 | 250 |
| Group with AKI    | 228 | 128 | 77  | 23  | 6   | 0   |
| Group without AKI | 538 | 423 | 150 | 43  | 16  | 0   |

Blue line, Group 1: Group with AKI; Green line, Group 2: Group without AKI

**Fig. 4. Kaplan-Meier curve.** Long-term survival in in group with AKI was apparently less than that in group without AKI (Log Rank test,  $p < 0.001$ ).

Paravalvular leakage can develop into complications of valve replacement or repair surgery, and can manifest as symptomatic valve regurgitation, heart failure, or hemolysis. It is believed that the abnormal high-speed impact of mitral or aortic regurgitation tract on the artificial valve annulus or lining area is the cause of red blood cell damage, which hinders the endothelialization of the artificial valve annulus surface. High shear residual mitral regurgitation is currently recognized as an important cause of postoperative hemolysis [24,25]. High shear force can be caused by annular leakage of artificial valves, the influence of blood flow on the rough surface of the artificial materials, and turbulence resulted from reflux beams such as impact, split and acceleration. When the shear force increases beyond the maximum stress that the red blood cell membrane can withstand, it can lead to cell rupture. However, valve leakage in IE patients remains a challenging issue for cardiac surgeons [26–28]. We also found cardiopulmonary bypass length  $\geq 120$  minutes and aortic occlusion duration  $\geq 90$  minutes to be risk factors of postoperative AKI. Improvements in surgical and perfusion techniques can reduce the incidence of perivalvular leakage, shorten cardiopulmonary bypass

length and aortic occlusion duration, which have significance in decreasing the incidence and degree of postoperative AKI.

All in all, our study identified modifiable risk factors for AKI. How to optimize these modifiable risk factors? Timely diagnosis and treatment are recommended to avoid larger aortic valve regurgitation. Improvement in the understanding of the diseases and surgical techniques can reduce the occurrence of perivalvular leakage. We should do our best to improve surgical and anesthesia techniques, and minimize extracorporeal circulation and aortic occlusion time as much as possible. We can also optimize and adjust the use of antibiotics while ensuring therapeutic efficacy with a reasonable dosage of vancomycin. Further research is needed to determine whether coronary angiography is necessary for patients with IE, as iodine can cause damage to kidney function.

#### Limitations of the Study

The retrospective nature of the study introduces inherent biases, such as selection bias and recall bias, which may limit the generalizability and reliability of the findings.

Furthermore, conducting the study in a single tertiary referral center reduces the external validity and may not reflect the broader population with IE and postoperative AKI. Programs to reduce in-hospital morbidity and mortality resulting from postoperative AKI are recommended. Prospective cohort studies are required. Strategies to mitigate these biases in future studies (e.g., propensity score matching or multicenter data collection) would strengthen this discussion.

## Conclusions

Postoperative AKI in IE contributes to an increase in in-hospital and long-term mortality. We should optimize the management of AKI to improve short- and long-term outcomes of postoperative AKI in IE.

## Abbreviations

AKI, acute kidney injury; CPB, cardiopulmonary bypass; ICU, intensive care unit; LVEF, left ventricular ejection fractions; LVEDD, left ventricular end diastolic dimension.

## Availability of Data and Materials

The materials of the study can be obtained from the corresponding author on the basis of reasonable request.

## Author Contributions

ZH and JH designed the research study. ZH, JH, CL, and ZW performed the research. CL, and ZW contributed to the acquisition and interpretation of data. ZH and JH analyzed the data. All authors have participated sufficiently in the work. All authors contributed to editorial changes in the manuscript. All authors read and approved the final manuscript. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Ethics Approval and Consent to Participate

The study was carried out in accordance with the guidelines of the Declaration of Helsinki and approved by the Ethics Committee of The People's Hospital of Guangxi Zhuang Autonomous Region (Protocol No. PHGX08862021). The study obtained written informed consent from all patients.

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## Conflict of Interest

The authors declare no conflict of interest.

## Supplementary Material

Supplementary material associated with this article can be found, in the online version, at <https://doi.org/10.59958/hsf.8201>.

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