The Incidence, Risk Factors and Outcomes of Acute Kidney Injury in Critically Ill Patients Undergoing Emergency Surgery: A Prospective Observational Study

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Research

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Abstract

Background

Postoperative acute kidney injury (AKI) is associated with higher morbidity, mortality, and economic burden. However, there is a lack of evaluation of postoperative AKI in highly heterogeneous critically ill patients undergoing emergency surgery. To explore the incidence, risk factors, and prognosis, to clarify the epidemiological status, and to improve the early identification and diagnosis of postoperative AKI, this study was taken.

Methods

A prospective observational study was conducted in the general intensive care units of Guangdong Provincial People's Hospital from January 2014 to March 2018. Preoperative variables, intraoperative variables, postoperative variables, and postoperative prognosis data were collected. The diagnosis and staging of postoperative AKI were based on the Kidney Disease: Improving Global Outcomes criteria. They were divided into two groups according to whether postoperative AKI occurred: AKI group and non-AKI group. The baseline characteristics, postoperative AKI incidence, AKI stage, and in-hospital prognosis in all enrolled patients were analyzed prospectively. Multivariate logistic forward stepwise (odds ratio, OR) regression was used to determine the independent risk factors of postoperative AKI. Results were presented using the OR with 95% confidence intervals (CIs).

Results

A total of 383 critically ill patients undergoing emergency surgery, 151 (39.4%) patients among them developed postoperative AKI. Postoperative reoperation, postoperative Acute Physiology and Chronic Health Evaluation (APACHE II) score, postoperative serum lactic acid (LAC), postoperative serum creatinine (sCr) were independent risk factors for postoperative AKI in critically ill patients undergoing emergency surgery, with the adjusted OR (ORadj) of 1.854 (95% CI, 1.091 - 3.152), 1.059 (95% CI, 1.018 - 1.102), 1. 239 (95% CI, 1.047 - 1.467), and 3.934 (95% CI, 2.426 - 6.382), respectively. Duration of mechanical ventilation, renal replacement therapy, ICU and hospital mortality, ICU and hospital length of stay, total ICU and hospital costs were higher in the AKI group than in the non-AKI group.

Conclusions

The independent risk factors which included postoperative reoperation, postoperative APACHE II score, postoperative LAC, and postoperative sCr could improve the early diagnosis and prevention of postoperative AKI and identify the higher risk of adverse outcomes in critically ill patients undergoing emergency surgery.

Introduction

Acute kidney injury (AKI) was a common postoperative complication, with the incidence ranged from 0.8–39% reported by previous studies [1–3]. The incidence of postoperative AKI ranges varies considerably, which might be related to the diagnostic criteria of AKI and the type of surgery [4, 5]. Studies had shown that the incidence of AKI in critically ill patients was between 31.6% and 67% [6–9]. We speculate that the incidence of postoperative AKI will be high in critically ill patients who have undergone emergency surgery. Whereas, the incidence and risk factors of AKI after emergency surgery in critically ill patients has not been well described.

Postoperative AKI could be potentially fatal which was mainly manifested by increased hospital mortality, prolonged hospital stays, the occurrence of chronic kidney disease (CKD), and accelerated progression to end-stage renal disease (ESRD) [10–12]. Simple accurate risk scores that utilize accessible routine data to predict outcomes would improve these clinical benefits [13–15]. Therefore, it is always a hot topic to clarify the clinical characteristics of postoperative AKI and take effective measures for corresponding prevention and intervention, which is of great clinical significance for improving the safety of patients during the perioperative period. But, for now, most postoperative AKI research focuses on cardiac surgery [16–19], non-cardiac surgery [20–22], or neurosurgery [23, 24] at present. In meanwhile, most of the risk factors related to postoperative acute kidney injury are concentrated in specialized operations, so the operation population and operation type are single, which can not reflect the heterogeneities. Hence, prospective study about the incidence, risk factors, and consequences of postoperative AKI in the critically ill population undergoing emergency surgery was scarce. And it might lead to an unacceptable delay in initiating any therapy regimens. A better knowledge of the morbidity and risk factors of postoperative AKI after emergency surgery might help develop efficacious intervention of this complication. Therefore, we conducted a prospective, observational study in the adult intensive care units (ICUs) to explore the incidence of postoperative AKI after emergency surgery, identify perioperative risk factors, and clarify the relationship between postoperative AKI and clinical outcomes.

Methods

Study Design and Participants

This prospective observational study was conducted in the general ICUs in Guangdong Provincial People's Hospital. Patients who underwent noncardiovascular emergency surgery and admitted to the ICUs between January 2014 and March 2018 were included. The exclusion criteria included younger than 18 years, refusal of consent, preexisting ESRD, presence of AKI before emergency surgery, or missing admission data. The primary outcome was the occurrence of AKI according to the Kidney Disease: Improving Global Outcomes (KDIGO) criteria within 7 days after noncardiovascular emergency surgery. And the secondary outcome comprised postoperative duration of mechanical ventilation, postoperative reintubation, postoperative RRT during ICU stay, ICU and hospital mortality, length of ICU and hospital stay, as well as ICU and hospital costs. The protocol was in accordance with STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines [25]. All experiments were performed under the approved protocols, guidelines, and regulations, and all patients (or appropriate surrogates for patients unable to consent) provided written informed consent simultaneously. This study was approved by the Ethics Committee of the Guangdong Provincial People's Hospital and carried out in accordance with the Declaration of Helsinki.

Data Collection

Clinical and demographic characteristics and outcomes of these patients were collected once they were admitted to the ICU. The following variables were recorded: age, gender, body mass index (BMI), preexisting clinical conditions [hypertension, diabetes mellitus, CKD, cerebrovascular disease, and coronary artery disease (CAD)], American Society of Anesthesiologist (ASA) classification, classification of New York Heart Association (NYHA) heart function, preoperative medication including the preoperative use of nephrotoxic drugs [nonsteroidal anti-inflammatory drug (NSAID), angiotensin-converting enzyme inhibitor (ACEI), angiotensin receptor blocker (ARB), immunosuppressant, aminoglycoside, vancomycin, acyclovir, or amphotericin] and the preoperative administration of radiographic contrast, surgery group (neurosurgical surgery, noncardiovascular chest surgery, abdominal surgery, or others), and incision type. Laboratory values were obtained, including the level of preoperative hemoglobin, baseline serum creatinine (sCr), baseline estimated glomerular filtration rate (eGFR), and concentration of postoperative sCr, hemoglobin, and the lactic acid (LAC) at ICU admission. Blood samples were measured at the central laboratory of the Guangdong Provincial People's Hospital using a standard protocol. sCr and hemoglobin were measured before the operation, and then measured after the operation at ICU admission, and thereafter at least once a day as a part of routine clinical care during ICU hospitalization. Postoperative LAC was measured at ICU admission. We also recorded the hourly urine output (UO) of each patient from enrollment to ICU discharge. The baseline eGFR was calculated by the CKD-Epidemiology Collaboration Equation [26]. The postoperative Acute Physiology and Chronic Health Evaluation (APACHE Ⅱ) score which was used to evaluate the overall condition of the patient, was assessed immediately after patients had recovered from the anesthetic. Postoperative reoperation within 7 days after the first noncardiovascular emergency surgery was recorded as an indicator of postoperative AKI. Surgical data including general anesthesia, duration of surgery, intraoperative estimated blood loss, lowest mean arterial pressure (MAP; i.e. lowest MAP for at least 5 continuous minutes) during anesthesia, radiographic contrast, intraoperative UO, amount and type of intraoperative fluids administered (crystalloid and artificial colloid), intraoperative transfusions [red blood cells (RBCs), platelets, and plasma] were recorded. Outcome variables were also recorded, including duration of postoperative mechanical ventilation, the incidence of postoperative tracheal reintubation and RRT, ICU and in-hospital mortality, length of stay in hospital and ICU, and total ICU and in-hospital costs.

Definitions

According to the KDIGO criteria [27], patients with an increase in sCr by ≥ 0.3 mg/dL (≥ 26.5 μmol/L) within 48 hours (h), or increase in sCr to ≥ 1.5 times baseline within one week, or urine output < 0.5 mL/(kg/h) for 6 hours were diagnosed with AKI within one week after surgery. AKI stages were graded according to the following KDIGO criteria. AKI stage 1was defined as the increase of sCr to 1.5–1.9 times from baseline, or ≥ 0.3 mg/dl (≥ 26.5 μmol/l), or urine output < 0.5 ml/kg/h for 6–12 hours. The definition of AKI stage 2 was the increase of sCr to 2.0–2.9 times from baseline, or urine output < 0.5 ml/kg/h for ≥ 12 h. With the 3 times increase of sCr from baseline or ≥ 4.0 mg/dl (≥ 353.6 μmol/l) increase of sCr or initiation of RRT, or urine output < 0.3 ml/kg/h for ≥ 24 h or anuria for ≥ 12 h were the standard of AKI stage 3. However, since the urine output criteria had limited sensitivity when diuretics were administrated [28], the AKI diagnosis was based on sCr in this study. Established postoperative AKI was defined as the diagnosis of postoperative AKI at the time of admission to ICU, and later-onset postoperative AKI indicated no postoperative AKI diagnosis on entry but meeting the KDIGO criteria during the following one week after admission.

A baseline sCr was determined by using the following rules ranked in descending order of preference as previously described [29–31]: (1) the most recent pre-ICU value between 30 and 365 days before ICU admission; (2) a stable pre-ICU value > 365 days for patients aged < 40 years, (stable defined as within 15% of the lowest ICU measurement) before ICU admission;(3) pre-ICU value > 365 days before ICU admission and less than the initial sCr on ICU admission ; (4) a pre-ICU value (between 3 and 39 days before ICU admission) less than or equal to the initial sCr on-admission to ICU and not distinctly in AKI ; (5) the lowest serum creatinine upon initial admission to ICU, the last ICU value, or the minimum value at follow-up up to 365 days.

Sample Measurements

All samples were collected simultaneously within 1 hour (h) after ICU admission and analyzed at the central laboratory of the Guangdong Provincial People's Hospital using standard protocols. The concentrations of samples were measured using commercially available multiplex assays and enzyme-linked immunosorbent assays according to the manufacturer's instructions.

Statistical Analysis

As reported previously described by Harrell [32], events per variable (EPV) > 10 was an important issue for the estimation of multivariable regression coefficients. To avoid a biased estimation of regression coefficients, EPV = 10 would be required of interest in our outcome model. Thus, to fit a model with 5 covariates, we would require approximately 50 outcome events. We calculated the sample size based on an estimated AKI incidence of 15%, which was found by previous studies that the incidence of AKI fluctuated from 0.8–39% due to different surgical types. Therefore, a sample size of 334 cases was required. Considering a possible dropout rate of 10%, we would need at least 368 cases.

The statistical analyses were performed with SPSS version 16.0 software program (SPSS Inc., Chicago, Illinois, USA). A two-sided P-value of less than 0.05 was considered to indicate statistical significance. Continuous variables were presented as mean ± standard deviation (SD), median and interquartile range (IQR), and categorical variables were presented as percentages. For continuous variables, normally distributed variables were compared using the *t*-test, and non-normally distributed variables were compared using the Wilcoxon rank-sum test. Categorical variables were compared using the chi-square test or Fisher's exact test. Univariate logistic regression analysis was performed to examine the association between each of the indicators and postoperative AKI separately. We also conducted multivariate logistic regression to determine the variables that were independently associated with postoperative AKI. A criterion of $P < 0.10$ in the univariate analysis entered into multivariate analysis. Multivariate logistic forward stepwise (odds ratio, OR) regression was then used to determine the most efficient predictors of postoperative AKI. Results were presented using the OR with 95% confidence intervals (CIs).

Results

Preoperative baseline characteristics of the patients

Figure 1 presented the protocol and flow diagram of the screening process. Among 412 patients enrolled for the study, 29 were excluded for the following reasons: younger than 18 years ($n = 2$), refusal of consent($n = 4$), end-stage renal disease ($n = 2$), presence of AKI before emergency procedure ($n = 14$), and missing data ($n = 7$). A total of 383 patients were involved in the study. Of them, 151 (39.4%) patients occurred in postoperative AKI basing on the KDIGO criteria. Of those patients who evolved into postoperative AKI, 92 patients (60.9%) developed to stage 1, 40 patients (26.5%) were progressed to stage 2, and 19 patients were evolved into stage 3 (12.6%). Among the 151 postoperative AKI patients, 110 (72.8%) developed postoperative AKI in the first day after the operation, 25 (16.6%) on the second day, 6 (4.0%) on the third day, and 10 (6.6%) patients beyond 3 days. Thus, 93.4% of the patients reached postoperative AKI within 3 days after emergency operations.

Presented by Table 1, the patients who were along with the preexisting clinical conditions of hypertension, undergoing the neurosurgical surgery or abdominal surgery were at a higher risk of developing to postoperative AKI. Moreover, with a higher the ASA classification and Classification of NYHA heart function, patients were at a higher risk of involving in postoperative AKI. Whereas, there were no significant differences in age, sex, BMI, part of the preexisting clinical conditions (including diabetes mellitus, CKD, cerebrovascular disease, CAD), preoperative hemoglobin concentration, baseline sCr, baseline eGFR, preoperative medication of radiographic contrast, some varieties of surgery group (containing noncardiovascular chest surgery, others) and incision type between patients with and without postoperative AKI. It was interesting to note that there were no markedly difference between postoperative AKI patients and non-postoperative-AKI patients in the preoperative medication of nephrotoxic drugs.

Table 1
Preoperative baseline characteristics of the patients.

Characteristics	All patients (n = 383)	Non-AKI (n = 232)	AKI (n = 151)	*P* value
Age, years	60(49,71)	59(49,71)	61(49,71)	0.996
Gender (male), n (%)	247(64.5)	149(64.2)	98(64.9)	0.892
BMI, kg/m2	23.9(22.1,25.5)	23.8(22.1,25.4)	24.1(22.0,25.6)	0.173
Preexisting clinical conditions, n (%)				
Hypertension	161(42.0)	86(37.1)	75(49.7)	0.015
Diabetes mellitus	37(9.7)	17(7.3)	20(13.2)	0.055
CKD	11(2.9)	4(1.7)	7(4.6)	0.176
Cerebrovascular disease	157(41.0)	103(44.4)	54(35.8)	0.093
CAD	35(9.1)	18(7.8)	17(11.3)	0.245
ASA classification, n (%)				0.002
I	31(8.1)	19(8.2)	12(7.9)	
II	139(36.3)	102(44.0)	38(24.5)	
III	154(40.2)	86(37.1)	68(45.0)	
IV	49(12.8)	23(9.9)	26(17.2)	
V	5(1.3)	1(0.4)	4(2.6)	
Classification of NYHA heart function				0.015
I	175(45.7)	115(49.6)	60(39.7)	
II	181(47.3)	107(46.1)	74(49.0)	
III	27(7.0)	10(4.3)	17(11.3)	
Preoperative hemoglobin, g/L	123.0(99.3,138.5)	123.8(105.2,139.6)	121.0(92.0,135.5)	0.063

The continuous variables were expressed as mean ± SD or median (25th percentile–75th percentile, IQR). Categorical variables were expressed as a number (%). aIncludes any of the following medications administered within 5 days before the operation: nonsteroidal anti-inflammatory drug, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, immunosuppressant, aminoglycoside, vancomycin, acyclovir, amphotericin. Abbreviations: AKI, Acute Kidney Injury; ASA classification, American Society of Anesthesiologists Classification; BMI, Body Mass Index; CAD, Coronary Artery Disease; CKD, Chronic Kidney Disease; eGFR, Estimated Glomerular Filtration Rate; IQR, Interquartile Range; NYHA, New York Heart Association; SD, Standard Deviation.

Characteristics	All patients (n = 383)	Non-AKI (n = 232)	AKI (n = 151)	*P* value
Baseline serum creatinine, mg/dl	0.78(0.62,1.01)	0.79(0.64,0.99)	0.72(0.59,1.07)	0.373
Baseline eGFR, ml/min/1.73 m^2	94.75(72.79,107.95)	94.0(75.4,106.8)	95.3(68.2,110.3)	0.852
Preoperative medication, n (%)				
Nephrotoxic drugs[a]	37(9.7)	17(7.3)	20(13.2)	0.055
Radiographic contrast	100(26.1)	63(27.2)	37(24.5)	0.564
Surgery group, n (%)				
Neurosurgical surgery	187(48.8)	124(53.4)	63(41.7)	0.025
Noncardiovascular chest surgery	6(1.6)	4(1.7)	2(1.3)	1.000
Abdominal surgery	161(42.0)	82(35.3)	79(52.3)	0.001
Others	29(7.6)	22(9.5)	7(4.6)	0.080
Incision type				0.614
I	258(67.4)	160(69.0)	98(64.9)	
II	104(27.2)	61(26.3)	43(28.5)	
III	21(5.5)	11(4.7)	10(6.6)	

The continuous variables were expressed as mean ± SD or median (25th percentile–75th percentile, IQR). Categorical variables were expressed as a number (%). aIncludes any of the following medications administered within 5 days before the operation: nonsteroidal anti-inflammatory drug, angiotensin-converting enzyme inhibitor, angiotensin receptor blocker, immunosuppressant, aminoglycoside, vancomycin, acyclovir, amphotericin. Abbreviations: AKI, Acute Kidney Injury; ASA classification, American Society of Anesthesiologists Classification; BMI, Body Mass Index; CAD, Coronary Artery Disease; CKD, Chronic Kidney Disease; eGFR, Estimated Glomerular Filtration Rate; IQR, Interquartile Range; NYHA, New York Heart Association; SD, Standard Deviation.

Intraoperative characteristics of the patients

Table 2 demonstrated the intraoperative parameters of patients in this cohort. During the intraoperation, the patients who were at a higher risk of developing postoperative AKI with a longer duration of surgery, more estimated blood loss and lower minimum MAP. Meanwhile, postoperative AKI patients had a higher rate of radiographic contrast when compared with non-AKI patients. In addition, the patients who received total artificial colloid or blood transfusion (RBCs, plasma, platelets) during the operation were more likely to develop postoperative AKI. However, the general anesthesia, intraoperative UP, and total crystalloid of intraoperative fluids were the inconspicuous difference for postoperative AKI.

Table 2
Intraoperative characteristics of the patients.

Variables	All patients (n = 383)	Non-AKI (n = 232)	AKI (n = 151)	*P* value
General anesthesia, n (%)	370(96.6)	224(96.6)	146(96.7)	0.942
Duration of surgery, minute	196(141,270)	189(131,256)	200(151,295)	0.015
Estimated blood loss,ml	50.0(5.0,250.0)	50.0(5.0,200.0)	100.0(10.0,400.0)	0.003
Minimum MAP, mm Hg	75.0(67.0,80.0)	77.0(68.5,81.0)	73.0(63.0,80.0)	0.003
Radiographic contrast, n (%)	92(24.0)	64(27.6)	28(18.5)	0.043
Intraoperative UO, ml/kg/h	1.15(0.41,2.64)	1.28(0.23,2.82)	0.98(0.47,2.18)	0.235
Intraoperative fluids				
Total crystalloid, per 500 ml	1.0(1.0,2.0)	1.0(1.0,2.0)	1.0(1.0,3.0)	0.285
Total artificial colloid, per 500 ml	2.0(1.0,2.0)	2.0(1.0,2.0)	2.0(1.0,3.0)	0.020
RBCs, n (%)	121(31.6)	55(23.7)	66(43.7)	< 0.0001
Plasma, n (%)	102(26.6)	45(19.4)	57(37.7)	< 0.0001
Platelets, n (%)	13(3.4)	4(1.7)	9(6.0)	0.025

Continuous variables were presented as mean ± SD or median (25th percentile–75th percentile, IQR). Categorical variables were expressed as a number (%). Abbreviations: AKI, Acute Kidney Injury; MAP, Mean Arterial Pressure; IQR, Interquartile Range; RBC, Red Bood Cell; SD, Standard Deviation; UO, Urine Output.

Postoperative characteristics of the patients

Revealing by Table 3, patients who were more potential to progress to the postoperative AKI had the following features: the higher APACHE II score which reflected the severity of the disease and the overall situation of the patient, the higher concentration of postoperative sCr and postoperative LAC concentration. Compared with patients without postoperative AKI, patients who experienced postoperative AKI were having a greater likelihood to have lower UP and undergo reoperation after the first emergency procedure. As for postoperative indicators, there was only postoperative hemoglobin was the unapparent difference for postoperative AKI.

Table 3
Postoperative characteristics of the patients.

Variables	All patients (n = 383)	Non-AKI (n = 232)	AKI (n = 151)	*P* value
APACHE II score	18(13,22)	16(12,21)	20(16,25)	< 0.0001
Serum Cr, mg/dl	0.96(0.74,1.37)	0.85(0.69,1.09)	1.28(0.89,1.86)	< 0.0001
Hemoglobin, g/L	110.0(95.0,121.6)	112.7(97.0,122.7)	107.0(89.0,121.0)	0.086
Lactic acid,mmol/L	1.5(0.9,2.4)	1.2(0.8,2.1)	1.8(1.1,3.3)	< 0.0001
UP, ml/kg/h	1.79(1.17,2.41)	1.85(1.24,2.45)	1.58(1.04,2.38)	0.033
Postoperative reoperation, n (%)	97(25.3)	52(22.4)	45(29.8)	0.048

Continuous variables were expressed as mean ± SD or median (25th percentile–75th percentile, IQR). Categorical variables were expressed as a number (%). Postoperative reoperation, underwent the second emergency operation within 7 days after the first emergency procedure. Abbreviations: AKI, Acute Kidney Injury; APACHE II, Acute Physiology and Chronic Health Evaluation II; Cr, Creatinine; IQR, Interquartile Range; UP, Urine Output Within The First 24 Hours After Operation; SD, Standard Deviation.

Multivariable analysis of risk factors that are related to postoperative AKI

Risk factors that were significantly correlated with the incidence of postoperative AKI were depicted in Table 4. Postoperative reoperation, postoperative APACHE II score, the concentration of postoperative LAC, and concentration of postoperative sCr were the independent risk factors for postoperative AKI. Intraoperative estimated blood loss might increase the rate of postoperative AKI occurrence in an amount-dependent manner, with every 100 ml estimated blood loss increasing the odds of postoperative AKI 1.04-fold. Postoperative reoperation was an independent risk factor of postoperative AKI with the adjusted OR (ORadj) of 1.854 (95% CI, 1.091–3.152). We also found that higher postoperative APACHE II score could predict postoperative AKI occurrence [ORadj 1.059 (95% CI, 1.018–1.102)]. Additionally, This study demonstrated that higher postoperative LAC could predict postoperative AKI occurrence [ORadj 1. 239 (95% CI, 1.047–1.467)]. Each unit increment in postoperative sCr was independently associated with postoperative AKI [ORadj 3.934 (95% CI, 2.426–6.382)] after adjustment for clinical covariates.

Table 4
Multivariable logistic regression analysis of factors that are related to postoperative AKI in emergency operation for critically ill patients.

Variable	ORunadj	ORadj	95% CI	*P* value
Postoperative reoperation	1.595	1.854	1.091–3.152	0.022
Postoperative APACHE II score	1.098	1.059	1.018–1.102	0.005
Postoperative lactic acid,mmol/L	1.392	1.239	1.047–1.467	0.013
Postoperative serum creatinine, mg/dl	5.195	3.934	2.426–6.382	< 0.0001

Postoperative reoperation, reoperation within 7 days after the first emergency operation.
Abbreviations: AKI, Acute Kidney Injury; APACHE II, Acute Physiology and Chronic Health Evaluation; CI, Confidence Interval; ORadj, Odds Ratio Adjusted.; ORunadj, Odds Ratio Without Adjusted.

Clinical outcomes of postoperative patients

Elucidated by Table 5, the occurrence of postoperative AKI would lead to higher rates of postoperative RRT, ICU mortality, and in-hospital mortality. Moreover, patients with postoperative AKI had a more likely to go through the long duration of postoperative mechanical ventilation, therefore resulted in prolonging ICU and hospital length of stay, higher total ICU costs, and higher hospital ICU costs. But there was no marked difference between postoperative AKI and reintubation.

Table 5
Clinical outcomes of postoperative patients.

Outcomes	All patients (n = 383)	Non-AKI (n = 232)	AKI (n = 151)	*P* value
Duration of mechanical Ventilation, hours	12(4,68)	9(2,22)	36(10,145)	< 0.001
Reintubation, n (%)	44(11.5)	21(9.1)	23(15.2)	0.064
RRT, n (%)	21(5.5)	3(1.3)	18(11.9)	< 0.001
ICU mortality, n (%)	72(18.8)	31(13.4)	41(27.2)	0.001
Hospital mortality, n (%)	77(20.1)	33(14.2)	44(29.1)	< 0.001
ICU length of stay, days	4(2,9)	2(1,6)	8(4,15)	< 0.001
Hospital length of stay, days	14(9,25)	12(8,19)	21(12,34)	< 0.001
Total ICU cost, CNY	34038(14132,77231)	20081(11415,40776)	60909(34338,126413)	< 0.001
Total Hospital cost, CNY	98793(59651,173582)	80639(50722,126803)	151384(87973,223422)	< 0.001

Continuous variables were expressed as mean ± SD or median (25th percentile–75th percentile, IQR); Categorical variables were expressed as a number (%).Abbreviations: AKI, Acute Kidney Injury; CNY, Chinese Yuan; ICU, Intensive Care Unit; IQR, Interquartile Range; RRT, Renal Replacement Therapy; SD, Standard Deviation.

Discussion

In this prospective study, we found that the morbidity of postoperative AKI was as high as 39.4% in critically ill patients undergoing emergency surgery, and the occurrence of postoperative AKI would further lead to adverse hospitalization results. Compared with previous studies, there was a little distinction for the morbidity of postoperative AKI, while the high risk of adverse hospitalization results was consistent [33–35]. On account of the heterogeneousness of the population in critically ill patients undergoing emergency surgery, and the numerous kinds of operations, so the incidence of postoperative AKI found in our study was higher than in previous studies. Furthermore, our study found that 93.4% of the patients reached postoperative AKI within 3 days after emergency operations, so physicians must take early surveillance and early intervention for those people who were at high risk of postoperative AKI. Therefore, with a large sample size, high population heterogeneity, and a wide range of surgeries, our research results have strong applicability and popularization in the clinic.

The independent risk factors of postoperative AKI occurrence included postoperative reoperation, postoperative APACHE II score, postoperative LAC, postoperative sCr. The risk factors for postoperative AKI varied in different clinical situations, and four of the above risk factors were identified in this emergency surgery cohort. Manifested by this study, postoperative reoperation was an independent risk factor for the occurrence of postoperative AKI, which was consistent with previous studies [23, 36]. Although the mechanism of postoperative AKI caused by reoperation had not been fully elucidated, a logical assumption was that reoperation involved in many factors related to the occurrence of postoperative AKI, such as hemodynamic damage and bleeding. In this condition, the body was overexcited by the sympathetic-adrenal medulla system, which promoted the increase of plasma catecholamine concentration and caused the dysfunction of neurohumoral regulation. Then, epithelial cells were degenerated and necrotic due to ischemia and hypoxia, and eventually, postoperative AKI occurred [37].

The APACHE II scoring system was usually used to assess the severity and prognosis of general diseases, which could more objectively reflect and comprehensively evaluate the current pathophysiology of patients [38]. The higher APACHE II score indicated that the more severity of the patient's overall condition and the greater risk of death [39], which might make the patient susceptible to surgery and lead to a higher risk of postoperative AKI. As expected, the postoperative APACHE II score of the AKI group in this study was higher than that of the non-AKI group. Corrected by multivariate regression, the postoperative APACHE II score was still an independent risk factor for postoperative AKI, which was consistent with the previous study [23]. We considered that a high postoperative APACHE II score indicated a serious condition. Under these circumstances, the body might be insufficiently perfused during emergency surgery, and the blood flow to the kidneys would be significantly reduced while ensuring the blood supply to important organs such as the heart and brain. Eventually, the kidneys were prone to develop postoperative AKI.

Similar to our study, some studies had also shown that the initial increase in LAC was related to the occurrence of AKI [40, 41]. Elevated LAC was often accompanied by hypoxia and hypoxia in tissues and organs, and insufficiency of systemic perfusion, so the patient's mortality rate increased significantly. The increase of serum LAC level after emergency surgery was generally related to the preoperative, intraoperative, and postoperative hypoxia and hypoperfusion [42], which caused the increase of catecholamines to accelerate glycolysis, the release of systemic inflammatory mediators and the reduction of liver and kidney clearance. In this study, the LAC level in the postoperative AKI group was significantly increased, suggesting that the ischemia and hypoxia in the postoperative AKI group were more serious, which represented a lower level of tissue perfusion. Above these were the predisposing factors for postoperative AKI.

It has been testified that high postoperative sCr would increase the incidence of postoperative AKI and the mortality of patients. A retrospective cohort study reported by Bihorac et al [43], which had involved 10,518 patients with AKI after major surgery, indicated that even small changes in sCr levels during hospitalization were associated with long-term mortality risk. What is more, according to a study of 19,982 AKI patients, an increase in sCr > or = 0.5 mg/dl was associated with a 6.5-fold increase in the odds of death, a 3.5-day increase in the length of stay, and nearly 7500 dollars in excess hospital costs [44]. Increased postoperative sCr has become an independent risk factor for the morbidity of postoperative AKI and the poor prognosis, and our study got the same result.

More and more studies had shown that even relatively mild renal injury drugs were associated with increased risk of AKI morbidity and mortality [13]. In our study, we also analyzed commonly prescribed medications that predispose to renal impairment, including NSAID, ACEI, ARB, immunosuppressants, aminoglycosides, vancomycin, acyclovir, and amphotericin. Even though nephrotoxic drugs were well known for their kidney damage, the use of them had little to do with the occurrence of AKI in this study. The one reason we were unable to obtain statistically significant conclusions might be due to the small number of patients using these drugs in our cohort. Simultaneously, physicians in ICU took more attention to carefully evaluate drugs in their potential injury to renal function and structure to avoid the damage in the kidney, which was consistent with the KDIGO standard.

Postoperative AKI was closely related to adverse hospital outcomes. To prevent the occurrence of complications, this study aimed to discuss the risk factors and morbidity of postoperative AKI in critically ill patients undergoing emergency surgery, which had important clinical significance. Despite the lack of effective treatment options, assessing the risk factors and morbidity of postoperative AKI might help formulate new strategies to prevent the occurrence of postoperative AKI. Therefore, we identified the risk factors and timeline that could induce postoperative AKI in advance. It was worth noting that all the above-identified risk factors and morbidity in our study were verifiable. Before translating our research into clinical applications, further intervention studies should be conducted to prove the effectiveness of these modifiable risk factors.

Compared with previous studies, this was the first prospective observational study on postoperative AKI in critically ill patients undergoing emergency surgery, which provided a basis for clarifying the epidemiological status of postoperative AKI in critically ill patients undergoing emergency surgery and improving clinical prevention strategies. However, our study still had some limitations and shortcomings. First, this was a single-center prospective study, and the number of cases was small. The influence of some confounding factors could not be completely ruled out, which might further lead to a certain deviation in the judgment of incidence, influencing factors, and prognosis. To reduce bias, it needed to be verified by a large sample, multi-center prospective study. Secondly, the data of this study were collected from the general ICU and did not fully represent all postoperative ICU patients, especially those patients who were undergoing cardiovascular surgery. Moreover, this study lacked long-term follow-up after discharge and fails to count kidney long-term prognosis.

Conclusion

The morbidity of postoperative AKI in critically ill patients undergoing emergency surgery according to the KDIGO standard was 39.4%, and 93.4% of the patients reached postoperative AKI within 3 days after emergency operations. Postoperative reoperation, postoperative APACHE II score, postoperative LAC, and postoperative sCr were independent risk factors of the occurrence of postoperative AKI in critically ill patients undergoing emergency surgery. Postoperative AKI was closely related to adverse hospital outcomes. Therefore, this study had important clinical significance for critically ill patients undergoing emergency surgery who were at risk of postoperative AKI.

Abbreviations

ACEI, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; APACHE II, Acute Physiology and Chronic Health Evaluation; ARB, angiotensin receptor blocker; ASA, American Society of Anesthesiologist; BMI, body mass index; CAD, coronary artery disease; CI, confidence interval; CKD, chronic kidney disease; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; h, hour; ICU, intensive care units; IQR, interquartile range; KDIGO, Global Thorne Disease Prognosis Organization; LAC, lactic acid; MAP, mean arterial pressure; NSAID, nonsteroidal anti-inflammatory drug; NYHA, New York Heart Association; OR, odds ratio; ORadj, adjusted odds ratio; RBC, red blood cell; RRT, renal replacement therapy; sCr, serum creatinine; SD, standard deviation; STROBE, Strengthening the Reporting of Observational Studies in Epidemiology; UO, urine output; UP, Urine Output Within The First 24 Hours After Operation.

Declarations

Ethics approval and consent to participate

The Ethics committee of the Guangdong Provincial People's Hospital supervised the study, including the study design, protocol, ethical issue, and data and sample collection. Written informed consent was obtained from each patient or the appropriate guardian.

Consent for publication

Not applicable. No individual personal data were included in the study. All patients provided necessary consent to participate in the present study.

Availability of data and materials

The datasets generated and/or analyzed during this study are not publicly available, owing to currently ongoing research studies, but the data are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

LH, LG, and DZ equally contributed to the design of the research and interpretation of the data. CC, LH, LG, DZ, and YH contributed to the conception and design of the research as well as interpretation of the data and critically revised the manuscript. LH, LG, DZ, YH, and YD performed the research and collected data. LH and LG analyzed the data. All authors contributed to the acquisition and analysis of the data, drafted the manuscript, and agreed to be fully accountable for ensuring the integrity and accuracy of the work. All authors read and approved the final manuscript.

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Figures

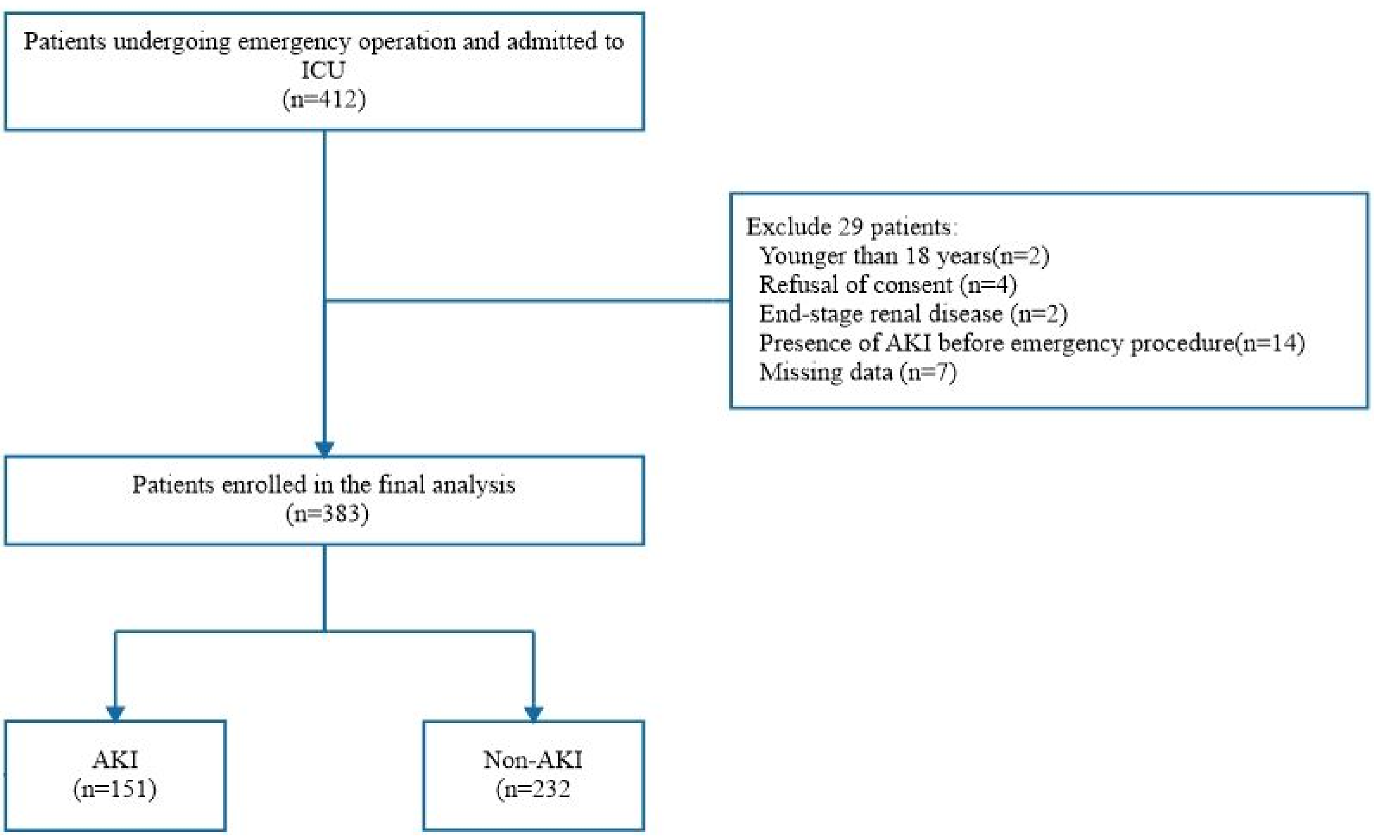

Figure 1

Flow chart from recruitment to the outcome. Abbreviations: ICU, intensive care unit; AKI, acute kidney injury.