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Original Article

Development and validation of AKI prediction model in postoperative critically ill patients: a multicenter cohort study

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Abstract: Background: Acute kidney injury (AKI) is a common complication, especially among postoperative critically ill patients. Early identification of AKI is essential for reducing mortality. Methods: Multicenter data were used to develop an AKI prediction model for critically ill postoperative patients. A total of 1731 patients admitted to intensive care units (ICUs) were divided into a development set (n=1196) and a validation set (n=535) according to the principle of 7:3 randomization. Multivariate logistic regression analysis was performed on the predictors identified by univariate analysis, and a nomogram was created based on the predictors. The area under the receiver operating characteristic curve (AUROC) was used to assess the discrimination of the model. Calibration curves were generated, and the Hosmer-Lemeshow (HL) goodness of fit test was carried out. Decision curve analysis (DCA) was performed to assess the net clinical benefit. Results: The final model included 7 predictors: age, emergency surgery, abnormal basal creatinine level (BCr), chronic kidney disease (CKD), use of nephrotoxic drugs, diuretic use, and the Sequential Organ Failure Assessment (SOFA) score. A nomogram was drawn based on the predictors. The AUROC of the model in the development set was 0.725 (95% confidence interval (CI): 0.696-0.754). In the validation set, the AUROC was 0.706 (95% CI: 0.656-0.744). The model showed good discrimination (>70%) in both sets, and the HL test indicated that the model fit was good (P>0.05). DCA showed that our model is clinically useful. Conclusion: The novel prediction model can be used to identify high-risk postoperative patients and provide a scientific and effective basis for clinicians to identify AKI early with a nomogram.

Keywords: Acute kidney injury, prediction model, postoperative, intensive care unit, predictors, nomogram

Introduction

Acute kidney injury (AKI) is a serious disease and complication [1] characterized by persistent oliguria and elevated serum creatinine (Scr) levels and is associated with high morbidity and mortality. AKI in postoperative critically ill patients [2] leads to an increased incidence of postoperative complications and mortality, as well as prolonged hospital stays and higher medical costs [3-6]. Critically ill patients are particularly prone to AKI following surgery [7]. Fluctuations in blood pressure caused by surgery and anesthesia may lead to a sharp deterioration in renal function [8]. In addition to fluid consumption and surgical consequences, many factors, such as neurohormonal compensatory responses to vasodilation induced by anesthetics [9, 10], perioperative blood loss [11] and intraoperative hypotension [12], may play an important role in the pathogenesis of AKI in postoperative patients [13]. As the etiological mechanism of AKI in surgical patients is significantly different from that in medical patients, postoperative AKI requires specific methods and management, especially in critically ill

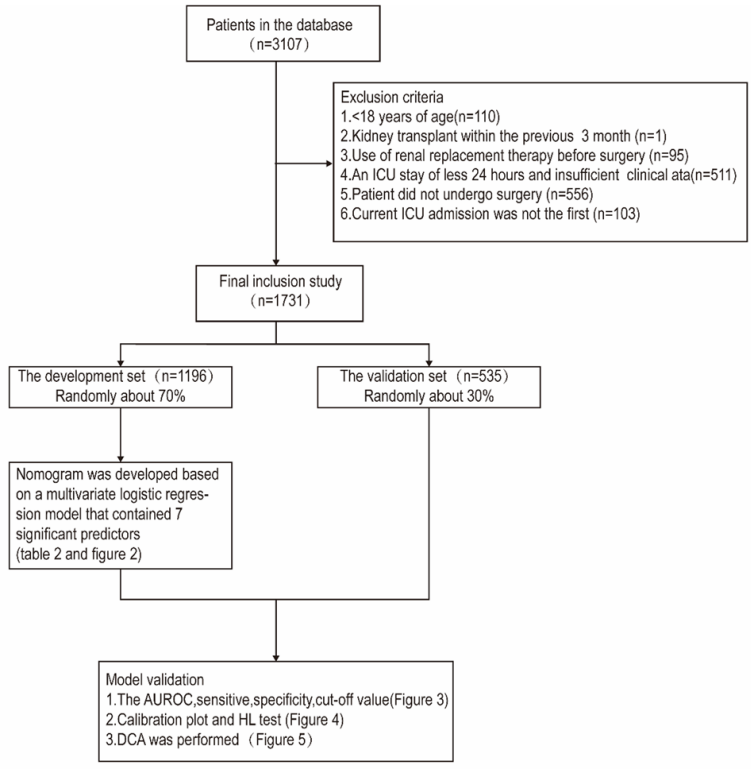

Figure 1. The flowchart of study. Prediction model data screening, model development and random split validation. RRT, Renal replacement therapy; ICU, Intensive care unit; AUC, Area under curve; HL, Hosmer-lemeshow; DCA, Decision curve analysis.

patients. Restricted by various factors, animal models cannot fundamentally simulate the pathogenesis of AKI in postoperative critically ill patients, and a sufficient understanding of its pathophysiology is still lacking. Given that no breakthroughs have been made in the field, physicians should not focus too much on specific surgeries or pathogeneses. Rather, our research focus should be on strengthening our ability to precisely identify kidney dysfunction soon after surgery to reduce the risk of perioperative AKI and reverse its pathological process. Improving the prognosis of this disease has important clinical implications.

A critical link in prognostic management is the early detection of AKI. We must determine whether early and active intervention is needed to prevent further deterioration of renal function [14]. Over the past decade, several models have been developed to predict AKI in specific clinical settings (e.g., cardiac surgery, contrast agent exposure, general and high-risk surgery) [15-24]. However, these models have some problems, such as using only single-center data, having a small sample size, and lacking internal or external verification [25-28]. Recently, a clinical predictive model for predicting AKI after non-cardiac surgery based on a multicenter cohort in Thailand was published [29]. The AKI prediction model for use after cardiac surgery has been reported in many studies. Critically ill postoperative patients may exhibit some characteristics that are different from those of critically ill non-surgical patients; thus, the main features of our study are the inclusion of all surgical patients in a prospective, multicenter database and the development and validation of a clinical prediction model for AKI in critical postoperative patients.

Materials and methods

Data sources

This study involved a retrospective analysis of a prospective multicenter database, the Beijing AKI Trial (BAKIT), which contains data from 30 different intensive care units (ICUs) in 28 large tertiary hospitals in Beijing, China. Trial registration: ChiCTR-ONC-11001875.

We consecutively included 3107 patients admitted to the ICU from March 1 to August 31, 2012. The exclusion criteria were as follows: (1) age <18 years (n=110); (2) kidney transplantation within the previous 3 months (n=1); (3) use of renal replacement therapy (RRT) before surgery (n=95); (4) an ICU stay of less than 24 hours or insufficient clinical data (n=511); (5) patient did not undergo surgery (n=556); and (6) the current ICU admission was not the first (n=103). Finally, 1731 patients were included in the study. Approximately 70% of the patients were randomly assigned to the development set to build the prediction model, and approximately 30% of the patients were assigned to the set used for model validation (**Figure 1**).

This study was approved by the Ethics Committees of Fuxing Hospital Affiliated with Capi-

tal Medical University (2010XM0501) and all other participating hospitals (online suppl. material). The institutional review board specifically approved the informed consent waiver because of the anonymous and purely observational nature of this study.

Relevant diagnostic criteria and definitions

We defined and staged AKI based on the 2012 Kidney Disease: Improving Global Outcomes (KDIGO) criteria (creatinine criteria).

Renal function (urea nitrogen, uric acid, serum creatinine): enzyme coupling rate method, uricase method, picric acid rate method.

Estimation of baseline serum creatinine (BCr): It can be assumed that the eGFR (mL/min* 1.73 m^2) can be estimated using the Modification of Diet in Renal Disease (MDRD) equation as follows: 186 × (Scr level)$^{-1.154}$ × (age)$^{-0.203}$ × 1.233 (× 0.742 female).

Definition and staging of AKI: Definition: The AKI criteria defined by the KDIGO guidelines are as follows: an increase in the Scr level within 48 hours ≥26.5 μmol/L; an increase in the Scr level to ≥1.5 times the baseline value that clearly occurred or was presumed to have occurred within the previous 7 days; or continuous 6-h urine output <0.5 ml/(kg·h).

Definition of postoperative AKI: Diagnosis of AKI based on the KDIGO criteria within 7 days after surgery.

Definition of postoperative critically ill patients: Adult patients admitted to the ICU for high-risk procedures primarily at the discretion of the surgeon and anesthesiologist without any intervention by the investigators.

Definition of nephrotoxic drugs: According to KDIGO guidelines, drug-induced nephrotoxic reactions can have direct toxic effects on the kidney or cause kidney damage through allergic reactions [1]. Such drugs mainly include NSAIDs, aminoglycosides, glycopeptides and antibiotics such as amphotericin B, contrast agents, mannitol, angiotensin-converting enzyme inhibitors (ACEIs)/angiotensin receptor blockers (ARBs), and statins.

Data collection and sorting

Clinical data were collected from March 1, 2012, to August 31, 2012. After data screening, a total of 1731 patients were included in the study.

The baseline data included sex, age, body mass index (BMI), primary diagnosis, emergency surgery, surgical classification [cardiovascular surgery, thoracic surgery, craniocerebral surgery, gastrointestinal surgery, orthopedic surgery, other surgery (surgery types other than those listed above)], basic diseases [hypertension, coronary heart disease, cardiac function class IV, diabetes, chronic kidney disease (CKD), malignant tumor, chronic liver disease, chronic obstructive pulmonary disease (COPD)], major organ damage [respiratory failure, cardiogenic shock, hypovolemic shock, septic shock, obstructive shock, disseminated intravascular coagulation (DIC), acute liver failure], use of the following drugs within 2 weeks before admission to the ICU [aminoglycoside antibiotics, glycopeptide antibiotics, amphotericin B, mannitol, contrast agents, partial vasoactive drugs (excluding vasodilators)] and use of nonsteroidal anti-inflammatory drugs (NSAIDs), ACEIs/ARBs, or statins.

Basic preoperative information for inclusion in the study after admission to the ICU included vital signs (temperature, respiratory rate, pulse rate, blood pressure), laboratory test results [white blood cell (WBC) count, hemoglobin, platelet count, bilirubin, international standardized ratio, creatinine, urea nitrogen, electrolytes, blood gas analysis-related indicators, oxygenation index (PaO_2/FiO_2)], and mechanical ventilation.

Based on the patient's worst physiological state at ICU admission, the Acute Physiology and Chronic Health Evaluation (APACHE II), Sequential Organ Failure Assessment (SOFA) score, and Simplified Acute Physiology Score (SAPS) II were used to evaluate the severity of the condition [15-17], Scr, the need for RRT, and presence of sepsis were recorded.

Statistical processing

Data analysis was performed using SPSS 26.0 (IBM Corp, Armonk, NY, USA) and R4.1.2 soft-

ware (Bell Labs, New Providence, NJ, USA). In this study, measurement data that were normally distributed and had homogeneity of variance are presented as the mean ± standard deviation (X ± SD). An independent sample t test was used for comparisons between the two groups. Measurement data that did not conform to a normal distribution are presented as the median (M) and interquartile range (Q25, Q75), and the Mann-Whitney U test was used for comparisons between the two groups. Count data are expressed as N (%), and dichotomous data between the two groups were compared using the chi-square test or Fisher's exact probability method. The cut-off value for statistical significance was $P<0.05$.

Multivariate logistic regression adopted the forward selection [likelihood ratio (LR)] method to screen the predictors for the AKI prediction model in postoperative critically ill patients (approximately 70% of the patients were randomly assigned to the development set for the prediction model, and approximately 30% of the patients were randomly assigned to the validation set). We included variables that were statistically significant at the $P<0.1$ level in the final multivariate logistic regression study, adjusted for sex. Then, the predictors were added to "R" software, and the "RMS" package was used to create the nomogram for the AKI prediction model for critically ill postoperative patients. By drawing receiver operating characteristic (ROC) curves, the areas under the curve (AUCs) of the model in the development and validation sets were calculated. The calibration curve was drawn by R software, and the Hosmer-Lemeshow (HL) test was used to assess the goodness of fit of the model. The clinical applicability was evaluated by decision curve analysis (DCA). This study is consistent with the Transparent Reporting of a Multivariable Prediction Model for Individual Prognosis or Diagnosis (TRIPOD) guidelines [30].

Results

Baseline data comparisons between the development and validation sets

The baseline data of the development and validation sets are presented in **Table 1**. A total of 1196 patients were enrolled in the development set, and 535 patients were enrolled in the validation set. The median patient ages were 61 [interquartile range (IQR), 50-73] years in the development set, which was composed of 61.7% (n=738) males, and 63 (IQR 50-74) years in the validation set, which was composed of 60.7% (n=325) males. The proportions of people over 65 years old in the development and validation sets were 40.1% (n=480) and 45.2% (n=242), respectively. There was no significant difference in sex between the two groups, while there was a significant difference in age ($P<0.05$).

Almost all of the demographic characteristics, complications, surgical classification, perioperative parameters, and interventions (**Table 1**) did not differ significantly between the two groups ($P>0.05$). The numbers of patients with AKI in the development and validation sets were 525 (43.9%) and 251 (46.9%), respectively, $P=0.243$, and the difference was not statistically significant.

The ICU mortality (8.8% vs. 1% in the development set and 10.8% vs. 1.8% in the validation set), 28-day mortality (15.4% vs. 3.3% in the development set and 14.7% vs. 4.2% in the validation set) and in-hospital mortality (12.4% vs. 3.0% in the development set and 12.4% vs. 3.0% in the validation set) of the AKI patients in the two groups were significantly higher than those of the non-AKI patients.

Development set prediction model construction

After univariate analysis and screening, 7 predictors were ultimately obtained by multivariate logistic regression (**Table 2**). Age, emergency surgery, abnormal basal creatinine (BCr) levels, CKD, nephrotoxic drugs, diuretic use, and the SOFA score were included as independent predictors of AKI in the prediction model for postoperative critically ill patients. Regression analysis (Forward, LR) of the model used the following equation: probability of AKI=$e^a/(1+e^a)$, where a=[-2.446 + (age × 0.009) + (emergency surgery × 0.485) + (abnormal BCr level × 1.379) + (CKD × 1.008) + (nephrotoxic drugs × 0.381) + (diuretic use × 0.616) + (SOFA score × 0.191)].

Nomogram of the AKI prediction model

We used R software to draw a nomogram based on the variables identified by logistic regression

Table 1. Baseline and prognostic values in the development and validation sets

Characteristics	Development (n=1159)	Validation (n=535)	*P*-value
Age (years)	61 (50-73)	63 (50-74)	0.030
Male [n (%)]	738 (61.7)	325 (60.7)	0.705
BMI (kg/m^2)	23.9 (21.9-26.1)	23.9 (21.9-26.1)	0.994
Abnormal BCr [n (%)]	36 (3.1)	12 (2.2)	0.324
Emergency surgery [n (%)]	270 (22.6)	124 (23.2)	0.782
Type of surgery			
Cardiovascular [n (%)]	413 (34.5)	186 (34.8)	0.924
Neurosurgery [n (%)]	133 (11.1)	50 (9.3)	0.267
Chest [n (%)]	73 (6.1)	26 (4.9)	0.303
Gastrointestinal [n (%)]	252 (21.1)	128 (23.9)	0.185
Orthopedic [n (%)]	106 (8.9)	63 (11.8)	0.059
Others [n (%)]	219 (18.3)	82 (15.3)	0.130
Comorbidities			
Hypertension [n (%)]	439 (36.7)	220 (41.1)	0.080
Diabetes mellitus [n (%)]	174 (14.5)	79 (14.8)	0.906
Coronary heart disease [n (%)]	153 (12.8)	78 (14.6)	0.312
Cardiac function level IV [n (%)]	27 (2.3)	12 (2.2)	0.985
CKD [n (%)]	34 (2.8)	15 (2.8)	0.964
Chronic liver disease [n (%)]	34 (2.8)	12 (2.2)	0.473
COPD [n (%)]	29 (2.4)	18 (3.4)	0.266
Malignancies [n (%)]	221 (18.5)	111 (20.7)	0.268
Major organ damage			
Respiratory failure [n (%)]	116 (9.7)	68 (12.7)	0.060
Cardiogenic shock [n (%)]	19 (1.6)	12 (2.2)	0.343
Hypovolemic shock [n (%)]	66 (5.5)	29 (5.4)	0.934
Septic [n (%)]	57 (4.8)	29 (5.4)	0.562
Obstructive shock [n (%)]	2 (0.2)	0 (0.0)	0.856
Acute liver failure [n (%)]	15 (1.3)	4 (0.7)	0.350
ICU score			
APACHE II	12 (9-17)	12 (9-17)	0.381
SAPS II	30 (23-38)	30 (25-38)	0.353
SOFA	5 (3-8)	6 (3-8)	0.722
GCS	12 (9-17)	12 (9-17)	0.338
Oxygenation index (24)	323 (230-475)	300 (214-443)	0.008
Oxygenation index <300 (24) [n (%)]	456 (44.1%)	239 (51.2%)	0.011
Mechanical ventilation [n (%)]	922 (77.1%)	417 (77.1%)	0.695
RRT [n (%)]	43 (3.6%)	25 (4.7%)	0.286
Diuretic use (24) [n (%)]	300 (25.1%)	138 (25.8%)	0.753
Fluid balance (24) [n (%)]	560 (-300-1486)	531 (-227-1380)	0.960
AKI	525 (43.9)	251 (46.9)	0.243
Nephrotoxic drugs			
Aminoglycosides [n (%)]	18 (1.5)	5 (0.9)	0.338
Glycopeptides [n (%)]	6 (0.5)	2 (0.4)	0.717
Contrast agent [n (%)]	51 (4.3)	26 (4.9)	0.579
Amphotericin B [n (%)]	1 (0.1)	0 (0.0)	0.503
Mannitol [n (%)]	38 (3.2)	11 (2.1)	0.194
NSAIDs [n (%)]	75 (6.3)	42 (7.9)	0.226

ACEIs/ARBs [n (%)]	288 (24.1)	117 (21.9)	0.315
Statins [n (%)]	179 (15)	79 (14.8)	0.914
Partial vasoactive drugs			
Dopamine [n (%)]	453 (37.9)	207 (38.7)	0.747
Epinephrine [n (%)]	138 (11.5)	61 (11.4)	0.934
Norepinephrine [n (%)]	182 (15.2)	70 (13.1)	0.245
Dobutamine [n (%)]	38 (3.2)	24 (4.5)	0.176
Outcomes			
ICU mortality [n (%)]	53 (4.4)	32 (6.0)	0.168
28-Day mortality [n (%)]	103 (8.6)	49 (9.2)	0.710
Hospital mortality [n (%)]	85 (7.1)	46 (8.6)	0.278

BMI, Body mass index; BCr, Basal creatinine; CKD, Chronic kidney disease; COPD, Chronic obstructive pulmonary disease; APACHE, Acute Physiology and Chronic Health Evaluation; SAPS, Simplified Acute Physiology Score; SOFA, Sequential Organ Failure Assessment; GCS, Glasgow Coma Scale; RRT, Renal replacement therapy; AKI, Acute kidney injury.

Table 2. AKI predictors by logistic regression in the development set

Variables	Univariable analysis result			Multivariable logistic model		
	β	OR (95% CI)	*P* value	β	OR (95% CI)	*P* value
Age	0.007	1.007 (1.002-1.013)	0.013	0.009	1.009 (1.001-1.017)	0.02
Emergency surgery	0.362	1.436 (1.146-1.799)	0.002	0.485	1.624 (1.192-2.214)	0.002
Abnormal BCr	1.749	5.749 (2.505-13.196)	0.000	1.379	3.971 (1.537-10.259)	0.004
CKD	1.610	5.001 (2.480-10.284)	0.000	1.008	2.740 (1.029-7.293)	0.044
Nephrotoxic drugs	0.595	1.813 (1.497-2.195)	0.000	0.381	1.464 (1.124-1.906)	0.005
SOFA score	0.223	1.250 (1.209-1.292)	0.000	0.191	1.210 (1.159-1.263)	0.000
Diuretic use	0.729	2.073 (1.686-2.549)	0.000	0.616	1.851 (1.379-2.485)	0.000
Respiratory failure	0.477	1.611 (1.185-2.191)	0.002			
Cardiogenic shock	1.285	3.616 (1.608-8.129)	0.002			
Septic shock	1.097	2.994 (1.871-4.793)	0.000			
Cardiac function level IV	0.693	2 (1.042-3.839)	0.037			
Hypertension	0.273	1.314 (1.081-1.596)	0.006			
Diabetes	0.234	1.264 (0.968-1.654)	0.086			
Sex	0.024	1.025 (0.843-1.245)	0.807			

BCr, Basal creatinine; CKD, Chronic kidney disease; SOFA, Sequential Organ Failure Assessment; OR, Odds ratio; β, Regression coefficient; CI, Confidence interval.

(**Figure 2**). The top of the figure is the scoring caliper. The corresponding score is obtained by matching the value of each item below it with the scoring caliper. The actual total score is calculated after the score of each item is obtained. The penultimate line and the last line are the total score calipers and the probability calipers, respectively. The calculated total score is used to find the corresponding probability value on the probability caliper through the total score caliper, and the probable value of AKI incidence in postoperative critically ill patients is finally obtained.

Validation of the model

Discrimination of the model: We calculated the area under the receiver operating curve (AUROC) values of the development and validation sets (**Figure 3**). The results showed that the AUROC values of the development and validation sets were 0.725 (95% CI: 0.696-0.754) and 0.706 (95% CI: 0.656-0.744), respectively. Of course, in addition to using random splitting for internal validation, we also used the bootstrap method (1000 replications) for internal validation and obtained a C-statistic, which had

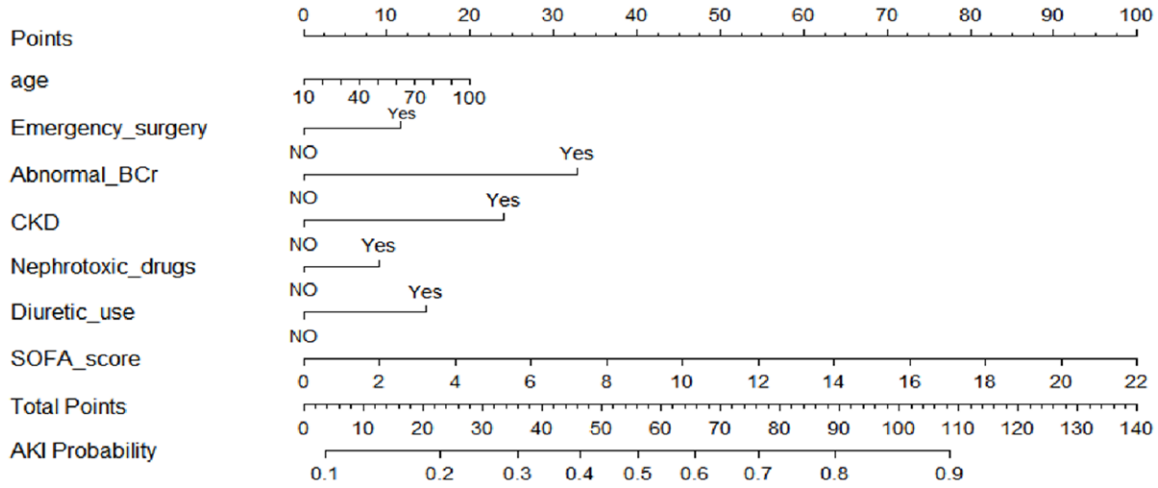

Figure 2. Nomogram score system. Base on logistic regression analysis, 7 predictors were screened to construct AKI prediction model in postoperative critically ill patients. To acquire the corresponding scores for each predictors, draw a vertical line upward to the "Points" axis, sum the score for all predictors and locate the final value on the "Total Points" axis. Draw a line straight down to the "Probability of AK" axis to determine the risk of AKI. Abbreviations: CKD, Chronic kidney disease; SOFA, Sequential organ failure assessment.

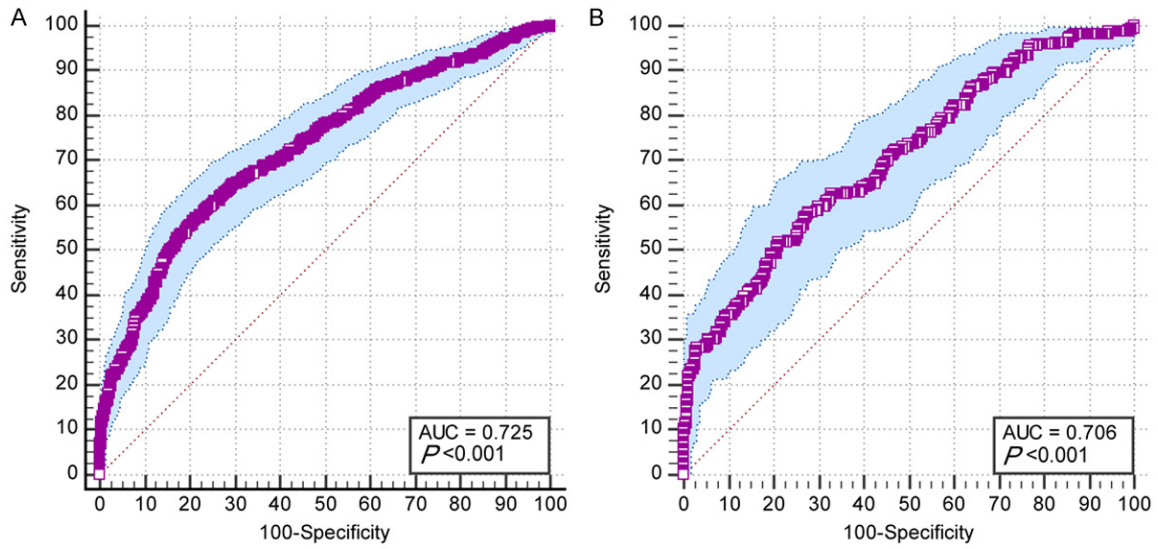

Figure 3. Discrimination of the AKI predictive model. A. Development set. B. Validation set. The ROC curve is plotted with the true positive rate (Sensitivity) as the vertical coordinate and the false positive rate (1-Specificity) as the horizontal coordinate.

an AUROC of 0.718. The AUROC was >0.7 for both the random split validation method and bootstrap method, indicating that the model had good discrimination. Comparing the AUROC values of the development and validation sets yielded a z-statistic of 0.626, P=0.5312, and the difference between the two groups was not statistically significant. Based on the maximum value of the Youden index, the optimal cutoff for the predicted probability of the AKI nomogram was set to 0.498 in the development set and 0.485 in the validation set. The sensitivity and specificity values of the model were 56.8% and 79.7% in the development set and 58.6% and 72.2% in the validation set, respectively.

The calibration degree of the model: The calibration plot showed that in both the development and validation sets, the model had a good

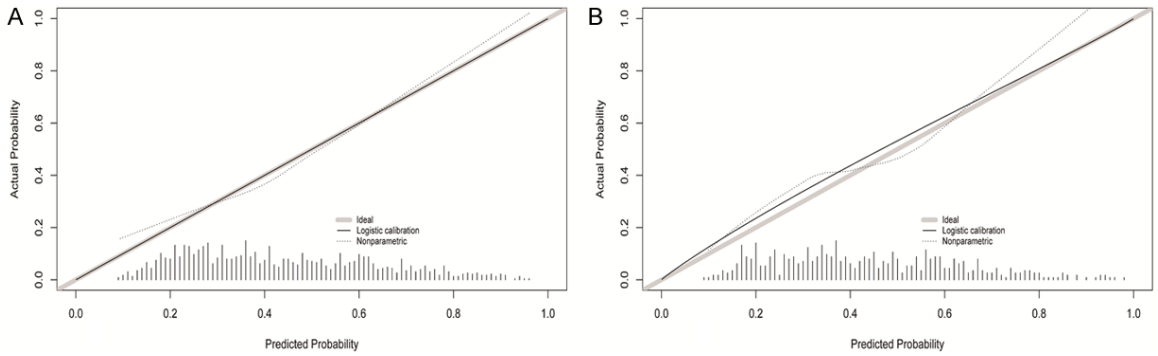

Figure 4. Calibration plot of the AKI predictive model. A. Development set. B. Validation set. The x-axis represents the predicted probability calculated by the model, and the y-axis is the observed actual probability of AKI. The clinodiagonal represents a perfect prediction by an ideal model. Logistic calibration represents how well the model fits. In the development set X^2=13.394, *P*=0.099. In the validation group, X^2=10.503, *P*=0.231. The results showed that the *P*-value of both sets were greater than 0.05, and the prediction model had good calibration ability.

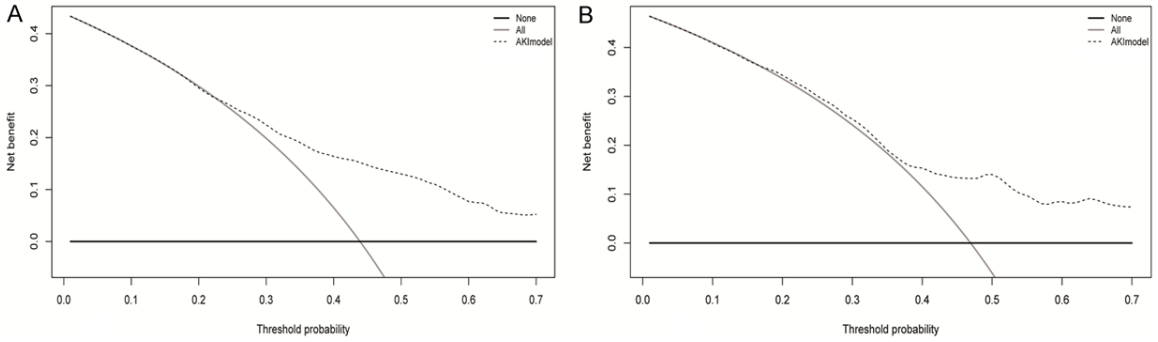

Figure 5. DCA of the AKI predictive model. A. Development set. B. Validation set. The horizontal axis (None) indicates that no one in the model received intervention, and the net benefit is 0. The slash (All) indicates that all received the intervention. In DCA, the AKI model line shows a more net benefit than full or no treatment across a threshold probability range. AKI, Acute kidney injury; DCA, Decision curve analysis.

fit (**Figure 4**). The calibration ability of the prediction model was evaluated by the Hosmer-Lemeshow goodness of fit test. The results showed that the *P* values of both sets were greater than 0.05, indicating that there was no statistically significant difference between the predicted value of the model and the actual observed value and that the prediction model had good calibration ability (development set, X^2=13.394, *P*=0.099; validation set, X^2= 10.503, *P*=0.231).

Decision curve analysis: DCA of the AKI prediction model for postoperative critically ill patients is shown in **Figure 5**. In DCA, the AKI prediction model (AKI model) showed potential clinical application in both cohorts. This model can guide clinicians in providing early aggressive treatment for potential AKI (true positive) patients, which will reduce the number of over-treatments (false positive) in non-AKI patients. The horizontal axis (None) indicates that no one in the model received intervention and that the net benefit is 0. The slash (All) indicates that all received the intervention. When the threshold probability of the development set is over 26%, the net benefit of the AKI model curve is significantly higher than that of the All curve, while for the validation set, the net benefit is significantly higher only when the threshold probability is more than 33%. The net benefit of the AKI prediction model decreases with increasing threshold probability.

Discussion

Acute kidney injury is associated with high morbidity and mortality, especially in postoperative critically ill patients. Clinically, 20-30% of AKI cases can be avoided or prevented if all risk

factors are identified and quantified [31]. To identify AKI earlier, it is necessary to study the prediction models for AKI. Existing models have strict limitations on the types of surgery involved. Most previous studies evaluated the prediction model for AKI after cardiac surgery [15-18], and some studies provided a prediction model after general surgery [23] or liver transplantation [24]. Most of these models included a single types of surgery, and the patient selection was biased. A prediction model for AKI in critically injured patients after multiple types of surgeries was reported in a recent large-scale multicenter prospective cohort study conducted in Thailand [29]. The study included 3474 patients admitted to the ICU after noncardiac surgery and obtained 6 predictors, some of which were consistent with the finding of our study, such as age, SOFA score, and emergency surgery. In the model, there were differences between the patients in the AKI group and non-AKI group who underwent nerve surgery and head and neck surgery vs. those who underwent abdominal colorectal surgery. The data in that study was of high quality; however, due to the early data collection, the definition and staging of AKI followed the Acute Kidney Injury Network (AKIN) standard, and the latest KDIGO diagnostic criteria were not used, so there may be problems in the promotion of the model. Regarding the above studies, we found that the reported models had some defect or other problems. Although Trongtrakul's model accounted for some defects and proposed some new predictors, it did not provide comprehensive predictors for all surgical types. Not all types of surgery (cardiac and noncardiac) were included. To address some shortcomings of previous studies, our study included all different types of surgeries and comprehensively analyzed the effects of the different surgical types on AKI in postoperative critically ill patients.

It is well known that cardiovascular surgery has an elevated risk of kidney injury [15-18]. However, the current study did not find this to be a risk factor, related to our prospectively designed experiment. Since this was a secondary analysis of the database, we did not limit the number of procedures included in the study at the time of data collection, so a relatively large proportion of cardiac procedures (approximately 35%) would have resulted in biased data selection if cardiac procedures had continued to be included in the statistical analysis. We found that the inclusion of cardiovascular surgery would have led to overfitting of the model although it would have improved the discrimination of the model by a small amount, so cardiovascular surgery was not included as a risk factor in the prediction model. In addition, the seven predictors included in the prediction model are more readily available in clinical practice, and the generalization of such a prediction model is easier.

The AUROCs of the AKI prediction model in the development and validation sets were 0.725 (95% CI: 0.696-0.754) and 0.706 (95% CI: 0.634-0.724), respectively. Both of these were greater than 0.7, indicating that the model had good discrimination. Some previous studies in which AKI prediction models were developed with different study populations and at different time periods have reported good diagnostic results. The AUROCs in most studies were greater than 0.80 [23, 29, 32]; however, most of these studies were single-center and retrospective studies, and some studies did not report the calibration degree of the model, which may have led to overfitting of the model.

An prediction model for AKI after major surgery has been reported. Bell et al. discussed the importance of AKI predictive models in patients undergoing orthopedic surgery and their impact on prognosis. The AUROC of that model was 0.74 (95% CI, 0.73-0.75) in the development set and 0.73 in the internally validation set. Another prediction model for AKI after noncardiac surgery was reported in the Simple Postoperative AKI Risk (SPARK) study [33], which had a large sample size and adopted an external validation method. The AUROC of the model was 0.80, and the AUROC of the external validation set was 0.72, indicating that the model had a good degree of discrimination. However, the problem with that study was that the model was developed using data from the retrospective study. Although there was a large amount of data, a data selection bias may have existed. In another study by Lei et al., who used preoperative data for the development of the model, the AUROC of 0.712 indicated a discrimination ability comparable to that of our study [34].

The low AUROC in our study was considered to be related to insufficient data collection in the perioperative period [34]. The American Society of Anesthesiology (ASA) score in the perioperative period was not collected in the current study, and urine volume and blood loss in the perioperative period were not included in the data, which may have led to the low AUROC of the prediction model. Thus, we need to design prospective cohorts in future studies with more comprehensive collection of perioperative data.

In our multicenter database study, we found that most of the variables were not significantly different between the development and validation sets ($P>0.05$). In addition, the incidence of AKI in postoperative critically ill patients can be predicted early with baseline characteristics and laboratory data after admission to the ICU. The 7 predictors, which were age, emergency surgery, abnormal BCr levels, CKD, nephrotoxic drugs, diuretics use, and the SOFA score, overlap with those in previous studies, such as nephrotoxic drugs [35]. Nephrotoxic drugs are well known to be predictors of AKI. The history of exposure to these drugs are an important predictor of AKI. This suggests that we should fully understand the pharmacological characteristics of the above drugs when treating patients to provide more accurate rescue treatment to patients.

Most studies have included age as a predictor, and increases in age can lead to an increase in the probability of AKI [21, 33, 35]. Our study is no exception. However, the cutoff values for age varied across studies. In some studies, the cutoff value is 65 years old [29], which is a commonly used and acceptable grouping method, but in others, 56 years old is used as the cutoff [21].

The effect of emergency surgery, which is also an important factor that affects the probability of AKI occurrence [21, 33], is determined by the characteristics of the surgery. Emergency patients usually cannot undergo relatively complete preoperative preparation. When they come to the hospital, most patients have abnormal hemodynamics and unstable circulation, which may increase the burden on the kidney and more easily lead to the occurrence of AKI.

CKD is a general term for heterogeneous diseases that cause abnormalities in renal structure and renal function [1]. Patients with CKD have a slow decline in renal function, and once AKI occurs, renal function shows a sharp deterioration. Even in the early stage of CKD, the occurrence of AKI may induce kidney disease to rapidly progress to end-stage renal disease [36]. The basal creatinine level is the prerequisite and basis for evaluating whether a patient meets the diagnostic criteria for AKI. In conclusion, CKD and abnormal basal creatinine values are effective predictors in AKI models.

The effectiveness of diuretics in the treatment of AKI is controversial and is complicated by inconsistencies in clinical settings, the timing of interventions, and differences in the endpoints used in clinical studies. There is experimental evidence that, despite normal or increased renal blood flow, changes in the microcirculation of the renal cortex or renal medulla may be associated with AKI through renal hypoxia and activation of inflammatory pathways [37]. Therefore, diuretic use is a predictor of AKI, consistent with our study.

For critically ill patients, the SOFA score is often used to assess the severity of disease and predict the mortality risk probability of patients [38]. SOFA includes respiratory system, platelet, bilirubin, circulatory system, Glasgow Coma Scale (GCS) and renal scores. To avoid overfitting of the model, we included only the SOFA score as a predictor in the model.

We included prospective multicenter data in this study; such cohort data are of high quality, and bias can be maximally controlled. Of course, our study also has some limitations. First, due to the short observation time and relatively small sample size, there may be deviations in statistical analysis. Second, to assess AKI in patients, we used the standard creatinine criteria, which may underestimate the actual prevalence of AKI and may ultimately affect the screening of model predictors. Due to the relatively large amount of included data, the collection of urine volume data was not complete, so we used only the KDIGO creatinine criteria as the reference for AKI, which could result in underestimation of the number of AKI diagnoses based on urine volume criteria. The actual incidence of AKI could be higher

than the level in the current study, which would certainly affect the screening of predictors [39]. Third, the lack of perioperative information led to incomplete factors in the AKI prediction model development, which may be the reason for the poor discrimination of the model. Fourth, the model lacks validation with external datasets, and thus, the model cannot be used with other populations.

Conclusion

The prediction model can identify high-risk postoperative patients and provide a scientific and effective basis for clinicians to identify AKI early. Visual scoring was performed for postoperative critically ill patients with the nomogram, and disease prevention and early intervention were performed according to the scores to improve the prognosis of patients.

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Disclosure of conflict of interest

None.

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References

[1] Inker LA, Astor BC, Fox CH, Isakova T, Lash JP, Peralta CA, Kurella Tamura M and Feldman HI. KDOQI US commentary on the 2012 KDIGO clinical practice guideline for the evaluation and management of CKD. Am J Kidney Dis 2014; 63: 713-735.

[2] Lewington AJ and Sayed A. Acute kidney injury: how do we define it? Ann Clin Biochem 2010; 47: 4-7.

[3] Adhikari NKJ, Fowler RA, Bhagwanjee S and Rubenfeld GD. Critical care and the global burden of critical illness in adults. Lancet 2010; 376: 1339-1346.

[4] Hobson C, Ozrazgat-Baslanti T, Kuxhausen A, Thottakkara P, Efron PA, Moore FA, Moldawer LL, Segal MS and Bihorac A. Cost and mortality associated with postoperative acute kidney injury. Ann Surg 2015; 261: 1207-1214.

[5] Pozzoli S, Simonini M and Manunta P. Predicting acute kidney injury: current status and future challenges. J Nephrol 2018; 31: 209-223.

[6] Silver SA and Chertow GM. The economic consequences of acute kidney injury. Nephron 2017; 137: 297-301.

[7] Chawla LS, Amdur RL, Amodeo S, Kimmel PL and Palant CE. The severity of acute kidney injury predicts progression to chronic kidney disease. Kidney Int 2011; 79: 1361-1369.

[8] Trongtrakul K, Sawawiboon C, Wang AY, Chitsomkasem A, Limphunudom P, Kurathong S, Prommool S, Trakarnvanich T and Srisawat N. Acute kidney injury in critically ill surgical patients: epidemiology, risk factors and outcomes. Nephrology (Carlton) 2019; 24: 39-46.

[9] Gameiro J, Fonseca JA, Neves M, Jorge S and Lopes JA. Acute kidney injury in major abdominal surgery: incidence, risk factors, pathogenesis and outcomes. Ann Intensive Care 2018; 8: 22.

[10] Sear JW. Kidney dysfunction in the postoperative period. Br J Anaesth 2005; 95: 20-32.

[11] Kim JM, Jo YY, Na SW, Kim SI, Choi YS, Kim NO, Park JE and Koh SO. The predictors for continuous renal replacement therapy in liver transplant recipients. Transplant Proc 2014; 46: 184-191.

[12] Sun LY, Wijeysundera DN, Tait GA and Beattie WS. Association of intraoperative hypotension with acute kidney injury after elective noncardiac surgery. Anesthesiology 2015; 123: 515-523.

[13] Kongsayreepong S, Chittawatanarat K, Thawitsri T, Chatmongkolchart S, Morakul S, Wacharasint P, Chau-In W, Poopipatpab S and Kusumaphanyo C. A multi-center Thai university-based surgical intensive care units study (THAI-SICU Study): outcome of ICU care and adverse events. J Med Assoc Thai 2016; 99: S1-S14.

[14] Mehta RL, Cerdá J, Burdmann EA, Tonelli M, García-García G, Jha V, Susantitaphong P, Rocco M, Vanholder R, Sever MS, Cruz D, Jaber B, Lameire NH, Lombardi R, Lewington A, Feehally J, Finkelstein F, Levin N, Pannu N, Thomas B, Aronoff-Spencer E and Remuzzi G. International society of nephrology's 0by25 initiative for acute kidney injury (zero preventable deaths by 2025): a human rights case for nephrology. Lancet 2015; 385: 2616-2643.

[15] Palomba H, de Castro I, Neto AL, Lage S and Yu L. Acute kidney injury prediction following elec-

tive cardiac surgery: AKICS score. Kidney Int 2007; 72: 624-631.
[16] Thakar CV, Arrigain S, Worley S, Yared JP and Paganini EP. A clinical score to predict acute renal failure after cardiac surgery. J Am Soc Nephrol 2005; 16: 162-168.
[17] Kristovic D, Horvatic I, Husedzinovic I, Sutlic Z, Rudez I, Baric D, Unic D, Blazekovic R and Crnogorac M. Cardiac surgery-associated acute kidney injury: risk factors analysis and comparison of prediction models. Interact Cardiovasc Thorac Surg 2015; 21: 366-373.
[18] Kiers HD, van den Boogaard M, Schoenmakers MC, van der Hoeven JG, van Swieten HA, Heemskerk S and Pickkers P. Comparison and clinical suitability of eight prediction models for cardiac surgery-related acute kidney injury. Nephrol Dial Transplant 2013; 28: 345-351.
[19] Aronson S, Fontes ML, Miao Y and Mangano DT; Investigators of the Multicenter Study of Perioperative Ischemia Research Group; Ischemia Research and Education Foundation. Risk index for perioperative renal dysfunction/failure: critical dependence on pulse pressure hypertension. Circulation 2007; 115: 733-742.
[20] Mehran R, Aymong ED, Nikolsky E, Lasic Z, Iakovou I, Fahy M, Mintz GS, Lansky AJ, Moses JW, Stone GW, Leon MB and Dangas G. A simple risk score for prediction of contrast-induced nephropathy after percutaneous coronary intervention: development and initial validation. J Am Coll Cardiol 2004; 44: 1393-1399.
[21] Inohara T, Kohsaka S, Abe T, Miyata H, Numasawa Y, Ueda I, Nishi Y, Naito K, Shibata M, Hayashida K, Maekawa Y, Kawamura A, Sato Y and Fukuda K. Development and validation of a pre-percutaneous coronary intervention risk model of contrast-induced acute kidney injury with an integer scoring system. Am J Cardiol 2015; 115: 1636-1642.
[22] Matheny ME, Miller RA, Ikizler TA, Waitman LR, Denny JC, Schildcrout JS, Dittus RS and Peterson JF. Development of inpatient risk stratification models of acute kidney injury for use in electronic health records. Med Decis Making 2010; 30: 639-650.
[23] Kheterpal S, Tremper KK, Heung M, Rosenberg AL, Englesbe M, Shanks AM and Campbell DA Jr. Development and validation of an acute kidney injury risk index for patients undergoing general surgery: results from a national data set. Anesthesiology 2009; 110: 505-515.
[24] Rueggeberg A, Boehm S, Napieralski F, Mueller AR, Neuhaus P, Falke KJ and Gerlach H. Development of a risk stratification model for predicting acute renal failure in orthotopic liver transplantation recipients. Anaesthesia 2008; 63: 1174-1180.
[25] Kheterpal S, Tremper KK, Englesbe MJ, O'Reilly M, Shanks AM, Fetterman DM, Rosenberg AL and Swartz RD. Predictors of postoperative acute renal failure after noncardiac surgery in patients with previously normal renal function. Anesthesiology 2007; 107: 892-902.
[26] Grimm JC, Lui C, Kilic A, Valero V 3rd, Sciortino CM, Whitman GJ and Shah AS. A risk score to predict acute renal failure in adult patients after lung transplantation. Ann Thorac Surg 2015; 99: 251-257.
[27] Kim WH, Park MH, Kim HJ, Lim HY, Shim HS, Sohn JT, Kim CS and Lee SM. Potentially modifiable risk factors for acute kidney injury after surgery on the thoracic aorta: a propensity score matched case-control study. Medicine (Baltimore) 2015; 94: e273.
[28] Cho E, Kim SC, Kim MG, Jo SK, Cho WY and Kim HK. The incidence and risk factors of acute kidney injury after hepatobiliary surgery: a prospective observational study. BMC Nephrol 2014; 15: 169.
[29] Trongtrakul K, Patumanond J, Kongsayreepong S, Morakul S, Pipanmekaporn T, Akaraborworn O and Poopipatpab S. Acute kidney injury risk prediction score for critically-ill surgical patients. BMC Anesthesiol 2020; 20: 140.
[30] Collins GS, Reitsma JB, Altman DG and Moons KG. Transparent reporting of a multivariable prediction model for individual prognosis or diagnosis (TRIPOD): the TRIPOD statement. BMJ 2015; 350: g7594.
[31] Kate RJ, Perez RM, Mazumdar D, Pasupathy KS and Nilakantan V. Prediction and detection models for acute kidney injury in hospitalized older adults. BMC Med Inform Decis Mak 2016; 16: 39.
[32] Slankamenac K, Beck-Schimmer B, Breitenstein S, Puhan MA and Clavien PA. Novel prediction score including pre- and intraoperative parameters best predicts acute kidney injury after liver surgery. World J Surg 2013; 37: 2618-2628.
[33] Park S, Cho H, Park S, Lee S, Kim K, Yoon HJ, Park J, Choi Y, Lee S, Kim JH, Kim S, Chin HJ, Kim DK, Joo KW, Kim YS and Lee H. Simple postoperative AKI risk (SPARK) classification before noncardiac surgery: a prediction index development study with external validation. J Am Soc Nephrol 2019; 30: 170-181.
[34] Lei VJ, Luong T, Shan E, Chen X, Neuman MD, Eneanya ND, Polsky DE, Volpp KG, Fleisher LA, Holmes JH and Navathe AS. Risk stratification for postoperative acute kidney injury in major noncardiac surgery using preoperative and intraoperative data. JAMA Netw Open 2019; 2: e1916921.
[35] Malhotra R, Kashani KB, Macedo E, Kim J, Bouchard J, Wynn S, Li G, Ohno-Machado L

and Mehta R. A risk prediction score for acute kidney injury in the intensive care unit. Nephrol Dial Transplant 2017; 32: 814-822.

[36] Dear JW and Yuen PS. Setting the stage for acute-on-chronic kidney injury. Kidney Int 2008; 74: 7-9.

[37] Ejaz AA and Mohandas R. Are diuretics harmful in the management of acute kidney injury? Curr Opin Nephrol Hypertens 2014; 23: 155-160.

[38] Godinjak A, Iglica A, Rama A, Tančica I, Jusufovič S, Ajanovič A and Kukuljac A. Predictive value of SAPS II and APACHE II scoring systems for patient outcome in a medical intensive care unit. Acta Med Acad 2016; 45: 97-103.

[39] Kellum JA, Sileanu FE, Murugan R, Lucko N, Shaw AD and Clermont G. Classifying AKI by urine output versus serum creatinine level. J Am Soc Nephrol 2015; 26: 2231-2238.