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CLINICAL STUDY

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Predictive role of estimated glomerular filtration rate prior to surgery in postsurgical acute kidney injury among very elderly patients: a retrospective cohort study

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ABSTRACT

Background: Acute kidney injury (AKI) is a common complication after surgery. Because of unpredictable and variable age-dependent physical decline, the incidence, risk factor of postsurgical AKI and the predictive power of estimated glomerular filtration rate prior to surgery (eGFRpreSurg) has not been fully elucidated in very elderly patients.

Methods: All discharged patients aged ≥80 years without chronic kidney disease who underwent surgery prior to intensive care unit (ICU) admission from 2017 through 2018 were included. Clinical, biological and surgical data were recorded. Mean of outpatient creatinine values from the year prior to ICU admission was used as the baseline value to determine the occurrence of AKI. Postoperative AKI was diagnosed according to Kidney Disease Improving Global Outcomes criteria.

Results: Among 243 very elderly postoperative patients admitted during the study period, 48 had AKI during their ICU stay. The occurrence of postsurgical AKI was associated with longer ventilation times ($p < .001$) and higher mortality ($p < .001$). The eGFRpreSurg, which is calculated based on the Modification of Diet in Renal Disease study equation, was a risk factor for postoperative AKI (OR = 2.662, $p = .010$). The incidence of postoperative AKI was significantly higher among patients with lower eGFRpreSurg than among those with an eGFRpreSurg ≥ 70 mL/min/1.73 m^2 ($p = .003$).

Conclusion: Postsurgical AKI in very elderly patients has a high incidence and is a risk factor for mortality. Our study confirmed that eGFRpreSurg could be used as an index for AKI risk stratification.

Abbreviations: AKI: Acute kidney injury; eGFRpreSurg: estimated glomerular filtration rate prior to surgery; CKD: chronic kidney disease; eGFR: estimated glomerular filtration rate; Cys-C: cystatin C; KDIGO: Kidney Disease Improving Global Outcomes; ICD-10-CM: international Classification of Diseases, 10th Revision, Clinical Modification; APACHE: the Acute Physiology and Chronic Health Evaluation; MDRD: the Modification of Diet in Renal Disease; CKD-EPI: the CKD Epidemiology Collaboration

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Introduction

Postoperative acute kidney injury (AKI) is a common and serious complication that is related to several adverse outcomes in critically ill patients [1]. The reported incidence of AKI after surgery is as high as 20%, depending on the patient population [1,2]. Patients who develop AKI after surgery often need continuous renal replacement therapy, which prolongs intensive care unit (ICU) stay and can exacerbate long-term morbidity [3]. Despite recent improvements in diagnosis and therapy, the mortality associated with AKI remains high, and those who survive have the additional burden of chronic kidney disease (CKD) [4].

One of the big challenges in preventing postsurgical AKI is to identify patients with high risk. Although the very elderly population is widely accepted to be more prone to AKI than younger populations either due to kidney senility or because of the high prevalence of comorbidities present, the exact incidence of postsurgical AKI among those patients is unclear [5–7]. Meanwhile, determining which patients will develop AKI after surgery remains very challenging [8]. New

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Supplemental data for this article can be accessed here.

biomarkers are widely used in the clinical setting to monitor the occurrence and progress of postsurgical AKI. For example, neutrophil gelatinase-associated lipocalin, which is expressed by renal tubular cells as the earliest induced proteins after ischemic AKI, has been shown to be an early predictor of AKI [9]. However, limited data have been obtained on the use of these biomarkers in elderly populations, which have unique characteristics and poor representation in clinical trials [10]. In addition, these new biomarkers are not always available in developing countries.

The estimated glomerular filtration rate (eGFR) is widely used to detect CKD because of the difficulty of measuring the actual glomerular filtration rate. In surgical populations, the eGFR is thought to reflect preoperative renal function and is used to guide postoperative fluid management to prevent postoperative AKI [11]. But, the rate of decline of eGFR with age varies widely among individuals, which may restrict the use of this parameter. As the elderly population continues to grow at an unprecedented rate worldwide, appropriate care for the elderly has attracted increasing attention. The usefulness of eGFR in predicting postsurgical AKI has not been fully elucidated; the aim of this study was to investigate the incidence of postsurgical AKI and the clinical utility of eGFR prior to surgery (eGFRpreSurg) for AKI prediction in very elderly patients.

Materials and methods

Setting

This single-center retrospective study was conducted in the Department of Critical Care Medicine, West China Hospital, Sichuan, China. The clinical research ethics boards of the West China Hospital approved the study and waived the need for participants' informed consent because of the study's retrospective, anonymous, and non-interventional nature (ethic committee's approval number: 2018-S-87). All methods were performed in accordance with the relevant guidelines and regulations.

Study population

All records of patients aged $\geq$80 years at admission who have undergone a surgery of any type and discharged from the ICU during the observation period (from 1 January 2017 to 31 December 2018) were considered for study inclusion. The following exclusion criteria were used: (a) non-postsurgical ICU admission, (b) ICU stay $<$24 h, (c) insufficient data for analysis, (d) occurrence of AKI prior to surgery and e) established of CKD before ICU admission. CKD was defined as a clear diagnosis prior to ICU admission, from both previous inpatient and outpatient records. Records of patients readmitted to the ICU during the observation period were discarded and only the records of the first ICU visit were kept.

The the primary aim of the study is to assess the association between eGFRpreSurg and post-op AKI. A twostep strategy is adapted in our study. We first calculate eGFR with four equations: the Modification of Diet in Renal Disease (MDRD) study equation, the CKD Epidemiology Collaboration (CKD-EPI) creatinine equation, the CKD-EPI Cys-C equation and the CKD-EPI creatinine and Cys-C equation [12,13]. The eGFR from equation with the highest AUC in predicting the occurrence of AKI was used to reflect eGFRpreSurg to do further analysis. The secondary aim is to access the association between AKI events and mortality.

According to occurrence of AKI or not, we divided our cohort into AKI group and non-AKI group. AKI diagnosis and severity stage were based on serum creatinine, in accordance with the Kidney Disease Improving Global Outcomes (KDIGO) practice guidelines [14]. In simple terms, mean of outpatient values from the year prior to admission were used as baseline values; AKI was defined as an increase to at least 1.5 times baseline within 7 days after surgery or an increase of $\geq$0.3 mg/dL in serum creatinine from baseline within 48 h after surgery. The staging system for evaluating the severity of AKI was also in accordance with KDIGO practice guidelines: stage I, serum creatinine increase to 1.5–1.9 times baseline within 7 days after surgery or $\geq$0.3 mg/dL increase from baseline within 48 h after surgery; stage II, serum creatinine increase to 2.0–2.9 times baseline within 7 days after surgery; and stage III, serum creatinine increase to at least 3.0 times baseline within 7 days after surgery, $\geq$4 mg/dL increase from baseline within 48 h after surgery or initiation of renal replacement therapy during the postsurgical ICU stay. The eGFRpreSurg was calculated based the last time laboratory test before surgery.

Data collection

The following information was obtained from the hospital information system: underlying medical conditions, type of surgery and results of all biochemical testing. Biochemical testing included red blood cell count, hemoglobin, hematocrit, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, red blood cell distribution width, platelet count, white blood cell count, international normalized ratio, prothrombin time, activated partial thromboplastin time, fibrin and fibrinogen degradation products, fibrinogen, thrombin time, arterial oxygen partial pressure, arterial carbon dioxide partial pressure, base excess, anion gap, lactate, procalcitonin, total bilirubin, direct bilirubin, indirect bilirubin, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total protein, albumin, creatinine, glucose, creatine kinase, lactate dehydrogenase, Cys-C, gamma-glutamyl transferase, triglycerides, cholesterol, high-density lipoprotein cholesterol and low-density lipoprotein cholesterol. Coagulated and non-coagulated blood samples were collected after ICU admission. Underlying medical conditions were confirmed according to the codes of the International Classification of Diseases, 10th Revision, Clinical Modification (ICD-10-CM) from the inpatient and outpatient hospital information system. Additional information obtained from the critical care information system included: sex, age, date of ICU admission, date of ICU discharge, patient admission type, and the Acute Physiology and Chronic Health Evaluation (APACHE) II score on the day of ICU admission. Of notes, intraoperative hypotension was defined as usage of dopamine or noradrenaline or both during operation. Data were collected and integrated with Excel (Microsoft Corporation, Redmond, WA, USA), and were screened and monitored by two dedicated intensive care specialists for any missing information and to ensure data accuracy.

Statistical analyses

All statistical analyses were performed with SPSS Statistics 17 (SPSS Software, Chicago, IL, USA), GraphPad Prism (GraphPad Software, San Diego, CA, USA) and MedCalc statistical program package (MedCalc Software, Mariakerke, Belgium). The Kruskal–Wallis and/or Mann–Whitney U-test were used for comparisons of numerical variables between groups; the chi-square test was used for categorical variables. To identify the sensitivity and specificity of cutoff values in predicting AKI after surgery, receiver operator characteristic curve analysis was performed. The eGFRpreSurg was first used as a categorical variable to plot the sensitivity and specificity for identifying risk of AKI and the value as a categorical variable which has a maximize Youden's index among those would be selected as the cutoff. The logistic analysis was used to analyze the correlation between eGFRpreSurg levels and the occurrence of AKI by forward conditional selection. Covariates were chosen for Cox proportional hazards regression models with 95% confidence intervals with regards to mortality. A two-sided p values $<.05$ was considered statistically significant.

Results

Baseline characteristics of study participants

From 1 January 2017 to 31 December 2018, 668 very elderly patients were admitted to the ICU without a specific history of CKD. After excluding rehospitalisation records, those with insufficient data and those with established AKI before ICU admission, our analysis included 243 postoperative patients with an ICU stay longer than 24 h (Figure 1, Supplementary Material 1). The average age in the study cohort was 85.64 years and the average APACHE II score was 18.50 (Table 1). Most patients had undergone elective surgery, most commonly abdominal surgery. Hypertension was the most common underlying medical condition. The in-hospital mortality rate for the entire cohort was 7.41%.

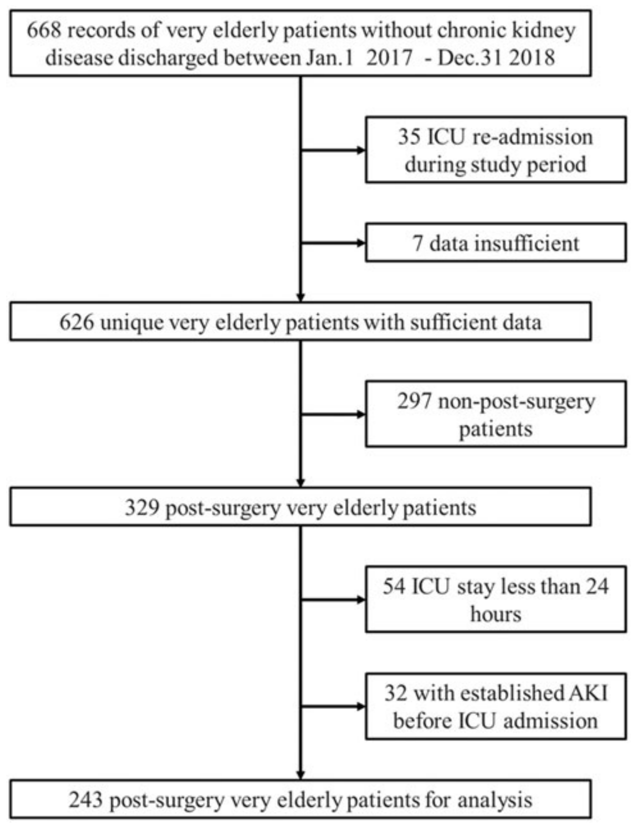

Figure 1. Flowchart of patients included in the study. The very elderly patients without chronic kidney disease discharged from ICU were scanned for occurrence of AKI according to the KDIGO definition. After excluding patients with re-admission, insufficient data, ICU stay <24 h and established AKI before surgery, 243 patients were enrolled for further analysis. ICU: intensive care unit; KDIGO: Kidney Disease Improving Global Outcomes.

Table 1. Characteristics of AKI patients and non-AKI patients.

Parameters	All patients ($n = 243$)	Non-AKI ($n = 195$)	AKI ($n = 48$)	p
Demographic Data				
Age (years)	84.64 ± 4.18	84.75 ± 4.41	84.19 ± 3.14	.407
Male (n)	131	108	23	.355
APACHEIIScore	18.50 ± 7.25	16.92 ± 6.36	24.71 ± 7.24	<.001
Underlying medical conditions				.782
Hypertension	143	118	25	
DM	89	73	16	
COPD	160	125	35	
Liver disease	31	25	6	
Patient admission type (n)				.424
Post emergency surgery	67	56	11	
Post selective surgery	176	139	37	
Types of surgery				<.001
Abdomen	141	126	15	
Bone	31	27	4	
Lung	24	15	9	
Breast	1	1	0	
Cardiac and vascular	24	13	11	
Brain	11	8	3	
Others	11	5	6	
eGFR prior to surgery[a]				
eGFR-MDRD	91.23 ± 26.29	91.75 ± 25.73	86.90 ± 21.50	.615
CKD-EPI Creatinine	78.78 ± 19.14	79.83 ± 19.20	69.59 ± 17.67	.103
CKD-EPI Cystatin C	85.36 ± 14.15	85.83 ± 13.88	81.49 ± 15.96	.140
CKD-EPI Creatinine–Cystatin C	72.07 ± 14.33	72.92 ± 13.96	64.99 ± 16.69	.117
Operation time (h)	3.01 ± 0.50	2.99 ± 0.49	3.10 ± 0.56	.282
Intraoperative hypotension (n)	114	96	18	.146
Postsurgical transfusion				
Red blood cell (U)	3.35 ± 2.77	2.69 ± 2.60	4.10 ± 2.82	.046
Plasma (ml)	846.25 ± 720.07	645.45 ± 494.47	1091.67 ± 878.37	.005
Platelet (U)	2.13 ± 1.55	2.00 ± 1.41	2.25 ± 1.89	.839
Postsurgical contract exposure (n)	18	10	8	.006
AKI (n)				–
Stage I	26	–	26	
Stage II	7	–	7	
Stage III	15	–	15	
Outcome				
Ventilation-free day (d)[b]	23.33 ± 5.99	24.51 ± 4.60	18.53 ± 8.25	<.001
Renal replacement therapy (n)	7	–	7	–
28-Day mortality (n)	15	3	12	<.001
In-hospital mortality (n)	18	4	14	<.001
ICU LOS (d)	7.73 ± 10.04	6.18 ± 7.38	14.02 ± 15.60	<.001

APACHE: Acute physiology and chronic health evaluation; AKI: acute kidney disease, DM: diabetes mellitus, COPD: chronic obstructive pulmonary disease, LOS: length of stay; IQR: interquartile range.
[a]Kidney function was calculated based on the last value of creatinine and cystatin C level prior to ICU admission.
[b]Within 28 days.

The mean eGFRpreSurg calculated with the four methods listed above were 91.23, 78.78, 85.36 and 72.07, respectively.

Association between eGFRpreSurg and postsurgical AKI

According to our definition, 48 patients experienced AKI while hospitalized in the ICU and 195 patients did not (Table 1). Among non-cardiac surgery patients, the incidence of postoperative AKI was 16.89% (Supplementary Material 2). The eGFR-MDRD was used to reflect eGFRpreSurg in order to distinguish patients with potential risk of AKI because it had the highest AUC in predicting the occurrence of AKI (AUC: 0.703, supplementary material 3). We then conducted sensitivity analysis to determine whether eGFRpreSurg was associated with a sharp increase in AKI risk. Although we saw a significant association between decreasing eGFRpreSurg and the increasing rate of postsurgical AKI, using eGFRpreSurg as a categorical variable and plotting the sensitivity and specificity for identifying increased risk of AKI revealed no high specificity or sensitivity cutoff values for predicting the occurrence of AKI (Supplementary Material 4). We chose to classify patients according to a threshold of 70 mL/min/1.73 m2 which has a maximize Youden's index among those categorical variables. The incidence of postoperative AKI was significantly higher among patients with lower eGFRpreSurg than among those with an eGFRpreSurg ≥70 mL/min/1.73 m2 (Table 2, $p < .05$). However, no difference was observed between the groups regarding AKI stage. In addition, eGFR calculated

Table 2. Characteristics of patients based on eGFRpreSurg stratification using cutoff 70 mL/min/1.73m^2.

Parameters	eGFRpreSurg > =70 (n = 137)	eGFRpreSurg < 70 (n = 106)	p
Demographic data			
Age (years)	83.54 ± 3.29	86.06 ± 4.77	.407
Male (n)	75	56	.767
APACHEIIscore	17.34 ± 6.47	19.94 ± 7.91	<.001
Underlying medical conditions			.724
Hypertension	80	63	
DM	48	41	
COPD	97	63	
Liver disease	17	14	
Patient admission type (n)			.050
Post emergency surgery	31	36	
Post selective surgery	106	70	
Types of surgery			.308
Abdomen	83	58	
Bone	17	14	
Lung	13	11	
Breast	0	1	
Cardiac and vascular	14	10	
Brain	5	6	
Others	5	6	
Kidney function[a]			
eGFR-MDRD	117.73 ± 23.81	66.99 ± 5.81	.015
CKD-EPI Creatinine	99.35 ± 17.31	65.19 ± 4.43	.003
CKD-EPI Cystatin C	94.73 ± 7.95	63.26 ± 2.83	.040
CKD-EPI Creatinine–Cystatin C	89.95 ± 12.46	68.97 ± 7.42	.017
AKI (n) cases	18	30	.003
AKI stage			.384
Stage I	10	16	
Stage II	4	3	
Stage III	4	11	
Outcome			
Ventilation-free day (d)[b]	24.15 ± 6.07	22.26 ± 5.73	.014
Renal replacement therapy (n)	0	7	<.001
28-day mortality (n)	3	12	.003
In-hospital mortality (n)	5	13	.011
ICU LOS (d)	6.18 ± 7.38	14.02 ± 15.60	.077

APACHE: Acute physiology and chronic health evaluation; AKI: acute kidney disease, LOS: length of stay; IQR: interquartile range.
[a]Kidney function was calculated based on the creatinine and cystatin C level prior to ICU admission.
[b]Within 28 days.

Table 3. Comparing AKI rate of patient cohort based on varied eGFR methods.

	eGFR-MDRD		CKD-EPI Creatinine		CKD-EPI Cystatin C		CKD-EPI Creatinine–Cystatin C	
Parameters	>=70 (n = 137)	<70 (n = 106)	>=70 (n = 153)	<70 (n = 90)	>=70 (n = 210)	<70 (n = 33)	>=70 (n = 137)	<70 (n = 106)
AKI (n) cases	18	30[a]	23	25[a]	34	14[a]	18	30[a]
AKI stage								
Stage I	10	16	14	12[a]	20	6[a]	10	16[a]
Stage II	4	3	4	3	6	1	4	3
Stage III	4	11	5	10	8	7	4	11
Outcome								
Ventilation-free day (d)[b]	24.15 ± 6.07	22.26 ± 5.73[a]	24.84 ± 6.14	22.46 ± 5.65	23.72 ± 5.71	20.85 ± 7.13[a]	24.15 ± 6.07	22.26 ± 5.73[a]
Renal Replacement Therapy (n)	0	7[a]	0	7[a]	0	7[a]	0	7[a]
28-day mortality (n)	3	12[a]	6	9	10	5[a]	3	12[a]
In-hospital mortality (n)	5	13[a]	8	10	12	6[a]	5	13[a]
ICU LOS (d)	6.18 ± 7.38	14.02 ± 15.60[a]	7.07 ± 11.53	8.85 ± 7.07	7.23 ± 9.99	10.90 ± 9.82[a]	6.73 ± 11.57	9.02 ± 7.45[a]

AKI: Acute Kidney disease, LOS: length of stay; IQR: interquartile range.
[a]$p < .05$ compared with other group using the same calculate method.
[b]Within 28 days.

with other methods using the same cutoff may also predict the occurrence of AKI (Table 3). Logistic analysis showed that eGFRpreSurg was a risk factor for postoperative AKI (Table 4, OR = 2.662, $p = .010$).

Association between AKI events and mortality

In the entire patient cohort, the APACHE II score was significantly higher in the AKI group than in the non-AKI group ($p < .001$, Table 1), along with other variables

(Supplementary material 5). Figure 2 shows the trends of creatinine, Cys-C and urea levels over time after ICU admission. The occurrence of AKI in very elderly patients after surgery was associated with longer ventilation times and higher mortality, regardless of the surgery type (Table 1, Supplementary Material 2, $p < .001$). The characteristics of the study patients stratified according to KDIGO AKI stage are shown in Supplementary material 6 and we saw a significant association between increasing AKI stage and 28-day mortality ($p < .05$ for all models, Table 5) after adjusting for age and other covariates.

Discussion

In this study, we observed that postoperative AKI is common after surgery in very elderly patients without CKD. The occurrence of AKI after surgery was associated with longer ventilation times and higher mortality. A lower eGFRpreSurg was related to increased risk of postoperative AKI. However, the level of eGFRpreSurg was not useful in predicting the severity of postsurgical AKI. Although the eGFR-MDRD and CKD-EPI equations have been shown to poorly estimate GFR in patients with muscle loss and resulting decreased creatinine levels [15], our study confirmed that eGFRpreSurg could be an index for risk stratification in very elderly patients before surgery. To our knowledge, this is the first study to investigate the AKI incidence and validate the role of eGFRpreSurg in predicting postsurgical AKI among very elderly patients.

AKI is a common complication of surgery. Previous studies have demonstrated that almost 18% of patients undergoing cardiac surgery experience at least one episode of AKI; approximately 6% require haemodialysis [16,17]. In non-cardiac surgery, the incidence of postsurgical AKI is relatively lower and most cases are mild [18]. In our study, 19.75% of patients experienced postoperative AKI, which is higher than the rates reported in other studies. In subgroup analysis, the incidence of AKI among non-cardiac surgical patients was as high as 16.89%. These data confirm that very elderly patients are prone to postsurgical AKI. There are several possible reasons for the relatively high incidence of AKI among very elderly patients. Although none of the patients in our study had CKD, they had many comorbidities over their lifetimes. Specific structural, functional and

Table 4. Multivariable logistical analysis of eGFR and other covariates associated with AKI events.

Variables	Odds Ratio	95% CI lower	95% CI upper	p value
APACHE IIscore at admission				
>=18.5	6.114	2.546	14.685	<.001
<18.5	1.000	–	–	–
eGFRpreSurg				
>=70	1.000	–	–	–
<70	2.662	1.264	5.608	.010
Postsurgical contract exposure				
No	1.000	–	–	–
Yes	3.703	1.117	11.655	.025

95% CI: 95% confidence interval.

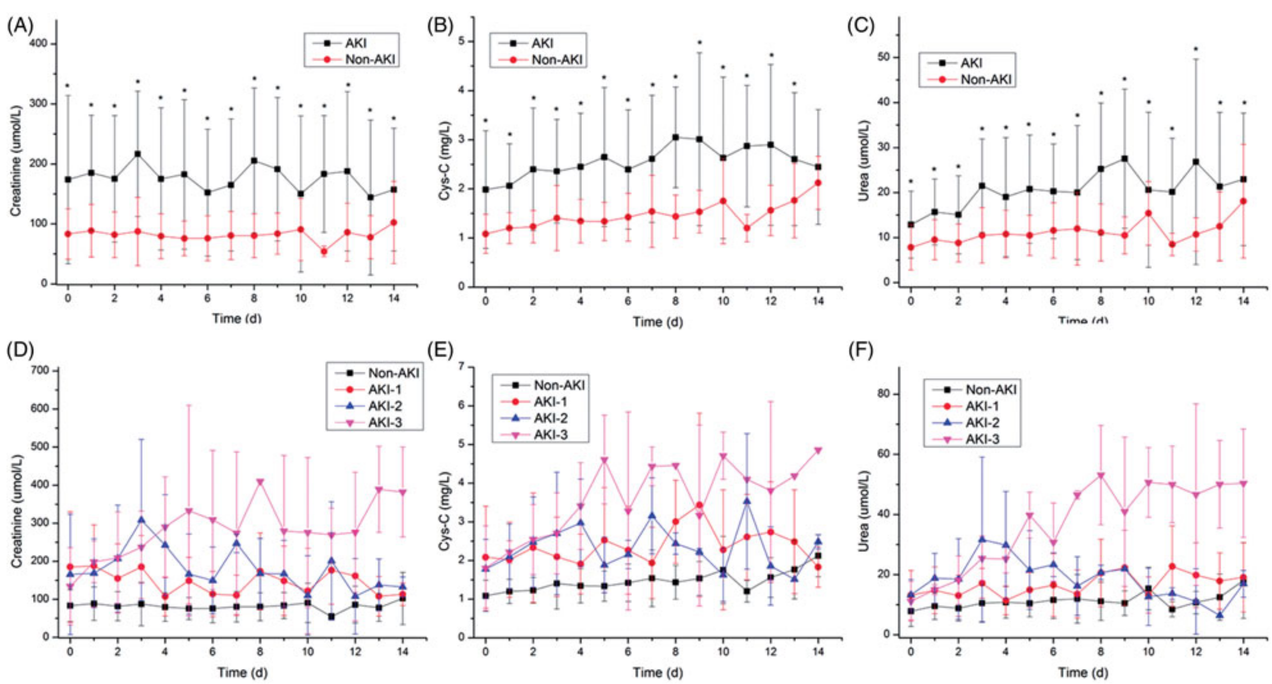

Figure 2. Plasma Crea, Cys-c and Urea values stratified according to AKI occurrence and AKI stage. Patients who experienced AKI during ICU stay had a significantly higher level in Crea, Cys-C and Urea ad admission and during the hospitalization. Crea, creatinine; Cys-c, Cystatin C. * indicated p values $<.05$ between groups.

Table 5. Outcomes of patients stratifying based on KDIGO AKI stage using cox proportional hazards regression models.

			Adjusted Hazard Ratio (95% CI)		
Parameters	Patient number	28 Days death	**Model 1**[a]	**Model 2**[b]	**Model 3**[c]
Non-AKI	195	3	1.00 (reference)	1.00 (reference)	1.00 (reference)
AKI-1	26	6	16.832 (4.187–67.664)	16.341 (4.085–65.366)	10.058 (2.346–42.785)
AKI-2	7	1	10.042 (1.039–97.082)	9.928 (1.016–96.968)	4.682 (0.446–49.172)
AKI-3	15	5	25.756 (6.804–130.129)	27.215 (6.462–114.626)	8.497 (1.465–49.301)
P for trend			<0.001	<0.001	0.018

[a]Adjusted for age.
[b]Adjusted for gender.
[c]Adjusted for APACHE II score.

molecular changes in the kidneys over time reduce kidney reserves and increase susceptibility to serious injury in the face of insults. Apart from surgical procedures and perioperative management, the physical decline in kidney function increases the susceptibility of very elderly patients to AKI.

Postoperative AKI, along with infection and bleeding, is known to be associated with mortality and morbidity after surgery [19]. In addition, postoperative ICU length of stay and total hospital stay are significantly longer in patients who develop AKI following cardiac surgery [20]. Results from our study confirm that these associations also exist among very elderly postsurgical patients, regardless of the type of surgery. In addition, trend analysis indicated a significant association between increasing AKI stage and 28-day mortality. Considering the high incidence of postsurgical AKI, the relationship between postoperative AKI and mortality and the aging trend globally, more studies on this subject are urgently needed.

Mathematically estimated GFR, or eGFR, is derived from a patient's serum creatinine or Cys-C level, age, sex and race. The MDRD equation and the CKD-EPI equation are the most widely used traceability equations for the estimation of GFR in patients 18 years of age and older [21]. Although the eGFR-MDRD equation underestimates high eGFR levels and the CKD-EPI equation is less accurate for patients with extreme muscle mass, both equations are widely used in clinical practice. Traditionally, the eGFR equation is only suitable for evaluating CKD and not AKI [22]. Besides, eGFR is not always sufficiently accurate for clinical decision making in very elderly patients because muscle mass and protein intake, which affect eGFR, are often abnormal in this population [23,24]. Indeed, both equations have been shown to provide risk stratification for AKI after surgery [25]. Our results indicate that although serum creatinine is unstable and eGFR may significantly change within days in very elderly patients, current eGFR equations remain useful for AKI risk stratification.

Using eGFR as a categorical variable, we found significantly differences in eGFRpreSurg between patients with versus without postsurgical AKI, regardless of surgery type. In addition, in non-cardiac surgical subgroup analysis, eGFRpreSurg was lower among patients who experienced postsurgical AKI. This suggests a closer association between preoperative conditions and postsurgical AKI in non-cardiac surgery, whereas surgical procedure and perioperative management are more important in avoiding postsurgical AKI in cardiac surgery patients.

We used 70 mL/min/1.73 m^2 as the cutoff to verify whether eGFRpreSurg was closely associated with the development of postsurgical AKI. In some previous literatures, 60 mL/min/1.73 m^2 is chosen as a cutoff point but in our study we choose the cutoff value 70 mL/min/1.73 m^2 instead the usual 60 mL/min/1.73 m^2 of for the following three reasons: 1) it has the highest Youden's index among all categorized eGFRpreSurg in our study, especially compared with 60 mL/min/1.73 m^2; 2) using an irregular number which has the highest Youden's index considering using 65.47 mL/min/1.73 m^2 treating eGFRpreSurg as continues variables is not conducive for clinical use; 3) the cut off 70 mL/min/1.73 m^2 although may overestimate risk compared with eGFRpreSurg as continues variables a little bit, it is acceptable since high mortality and extended ICU stay in patients who develop AKI [26]. Our study demonstrated that patients whose eGFRpreSurg was below 70 mL/min/1.73 m^2 were more likely than other patients to experience postsurgical AKI. Logistic analysis indicates that this association existed independent of underlying disease or surgery type. Results from our study indicate that eGFRpreSurg could be an index for assessing renal function in very elderly patients. Using a cutoff of 70 mL/min/1.73 m^2 allows identification of patients with a high risk of postsurgical AKI. However, we also found that eGFRpreSurg was not an index for predicting the severity of postsurgical AKI, suggesting that additional factors are involved in the deterioration of AKI.

We evaluated the performance of the eGFR-MDRD equation and the CKD-EPI equation based on creatinine or Cys-C or both. The eGFR-MDRD had the highest AUC in predicting the occurrence of AKI. However, the CKD-EPI equation was also able to identify patients at high risk of

AKI. Although, it has been suggested that serum Cys-C has better accuracy in predicting postsurgical AKI in adult cardiac surgery patients [27], our study demonstrated that eGFR-MDRD was more suitable in very elderly patients, not only from the predictive value but also from the costs. The recent introduction of novel biomarkers of AKI is resulting in a gradual replacement of serum creatinine in diagnosing AKI before elevated creatinine level can be detected several days after kidney injury [28]. Whether the new indicators are applicable in very elderly patients also needs to be verified in further studies, especially the costs regarding those new biomarkers.

Although body mass index, which reflects nutritional status, was not available for all the patients in our study, postoperative serum total protein and albumin were comparable in AKI and non-AKI patients, indicating that differences in eGFRpreSurg were not related to nutritional status. In addition, all patients enrolled in our study underwent surgery at a single center; most procedure-related factors as well as postoperative management parameters were likely controlled appropriately.

This study has limitations. First, although all patients who underwent surgery during the study period were included in the analysis to minimize selection bias, patient selection was inevitable because of the study's retrospective design. The lack of follow-up data prevents our analysis of out-of-hospital outcomes. Our study did not use urine output to determine AKI because urine volume data were not available in our hospital information system for most patients. This may have resulted in underestimation of the occurrence of AKI and caused a lack of increasing trends in AKI severity grades. We enrolled patients without CKD to avoid the bias from the inclusion of end-stage renal failure patients, according to both previous inpatient and outpatient records, some undiagnosed CKD patients have potential to be enrolled since CKD is not defined by previous eGFR or albuminuria data which is not available in our dataset. Although the eGFR calculated among very elderly patients without CKD in our study is comparable to other study [29], it still may have introduced selection bias, making our conclusions not universally applicable. We did not evaluate interactions between preoperative kidney function and intraoperative management. We did not calculate creatinine clearance with the Cockcroft–Gault equation because we did not have body weight for most patients. We compared the rate of renal replacement therapy between AKI and non-AKI patients, but we did not consider the reason for renal replacement therapy.

In conclusion, we found an increased risk of postoperative AKI in very elderly postsurgical patients and an association between AKI and mortality. Although eGFR is not an accurate reflection of renal function among very elderly patients, it can help in assessing the risk of postoperative AKI in very elderly patients. Regarding all the potential Equations which have been used for evaluation, the eGFR-MDRD has the best predictive value and may be considered to use in daily practice.

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Author contributions

QW and YK designed the whole study. HY and HB supervised the whole project and performed data analysis. HY, MF, XZ, GL and XJ supervised patient diagnosis and recruitment. QW, YX and ZH conducted data analyses and drafted the manuscript. HY and ZZ participated in the manuscript writing and contributed to protocol version development, on which this paper is based. All authors critically reviewed the article and approved the final manuscript.

Ethics approval and consent to participate

The clinical research ethics boards of the West China Hospital approved the study and waived the need for participants' informed consent because of the study's retrospective, anonymous, and non-interventional nature (ethic committee's approval number: 2018-S-87). All methods were performed in accordance with the relevant guidelines and regulations.

Disclosure statement

The authors declare that they have no competing interests.

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Availability of data and material

The datasets generated and analyzed in this article are not publicly available due to health privacy concerns. However, they are available from the corresponding author and will be obtainable by the public when the database construction is complete.

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