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Acute Kidney Injury as an Independent Predicting Factor for Stage 3 or Higher Chronic Kidney Disease after Nephrectomy

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Abstract

Background: Acute kidney injury (AKI) during the perioperative period mainly causes the loss of renal function after nephrectomy, while accurate prognostic models in which AKI as an independent predicting variable are still absent.

Methods: A retrospective study of 528 patients with renal cell carcinoma who underwent nephrectomy between January 2013 and December 2016 was carried out. The endpoint was the time to the incident stage 3 or higher chronic kidney disease (CKD), or any claim for initiation of dialysis. Cox proportional hazards regression analysis was conducted to construct the final model. Internal validation was performed using 10-fold cross-validation. The model was evaluated in discrimination by c statistics and area under curve (AUC) values, and calibration by calibration plots.

Results: Among 528 admitted patients, 232 (43.9%) developed AKI, and stage 3 or higher CKD occurred in 8.9% of people during the follow-up time. AKI was significantly correlated with poor prognosis (HR=3.079, P<0.001), and after the adjustment of conventional predictors, AKI was still independently related to kidney function deterioration, and the correlation was influenced by the severity of AKI. Five variables were selected to establish the prognostic model, including age, surgery type, preoperative estimated glomerular filtration rate, preoperative blood urea nitrogen and AKI. The model had good discrimination, with a C-harrell statistic of 0.92 (95% CI 0.89 to 0.95), AUC values varied from 87.7 to 95.7 at different time points.

Conclusion: AKI during the perioperative period is an independent predicting factor of stage 3 or higher CKD after nephrectomy.

Keywords: Acute kidney injury; Nephrectomy; Risk model; Carcinoma, Renal cell; Kidney function tests

Abbreviations: ACEI: Angiotensin-Converting Enzyme; AKI: Acute Kidney Disease; ALT: Alanine Aminotransferase; ARB: Angiotensin-Receptor Blocker; AST: Aspertate Aminotransferase; AUC: Area Under Curve; BUN: Blood Urea Nitrogen; CI: Confidence Interval; CKD: Chronic Kidney Disease; DM: Diabetes Mellitus; Egfr: Estimated Glomerular Filtration Rate; ESRD: End Stage Renal Disease; GGT: Gamma-Glutamyl Transpeptidase; HR: Hazard Ratio; IPCW: Inverse Probability Censoring Weighted; KDIGO: Kidney Disease Improving Global Outcomes; MDRD: Modification Of Diet In Renal Disease; NPV: Negative Predictive Value; PPV: Positive Predictive Value; PN: Partial Nephrectomy; RCC: Renal Cell Carcinoma; RN: Radical Nephrectomy; ROC: Receiver Operator Characteristics; RRT: Renal Replacement Therapy; SCR: Serum Creatine; SD: Standard Deviation

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Introduction

Renal cell carcinoma (RCC) is a commonly diagnosed urological malignancy, with an estimated 68.3 thousands new cases and 18.7 thousands deaths in China during 2014 [1]. A number of management options are available for clinically localized renal masses, including surgery with partial nephrectomy (PN), radical nephrectomy (RN) and thermal ablation [2]. Patients accepted PN or RN due to renal cancer undergo perioperative nephron loss, which may result in *de novo* chronic kidney disease (CKD), or the advancement of pre-existing disease [3]. It is well established that CKD is independently associated with increased risks of kidney failure, cardiovascular events, and all-cause mortality [3]. Therefore, it is significant to identify risk factors of stage 3 or higher CKD after nephrectomy, which is of great important to manage preventive treatment to patients at high risk of CKD.

Recent studies revealed that perioperative acute kidney injury (AKI) is closely associated with an increased relative risk of all-cause mortality, need for dialysis, or CKD [4-6]. Currently, there are several studies on evaluating prognostic factors or building models to predict functional outcomes after nephrectomy [7-10]. Lower preoperative estimated glomerular filtration rate (eGFR), hypertension, diabetes, older age, gender, tumor size and longer ischemic interval were identified as predicting factors of poor renal functional outcomes. However, few of the studies included postoperative AKI as an independent predictive factor. Some studies evaluated the association between postoperative AKI and long-term renal outcomes, but the study population was limited to patients who underwent RN or PN [11,12]. These limitations of the existing models have given ties to some difficulties for their clinical application.

Thus, we aim to exam the AKI in both RN and PN population. The purpose of the present study was to explore whether postoperative AKI is an independent predictive factor of the renal functional outcomes of RCC patients who were treated with nephrectomy, thus building a predicting model to identify patients at high risk.

Materials and Methods

Study population

Patients with non-metastatic unilateral RCC treated with radical/non-radical nephrectomy from 2013 to 2016 in Shanghai Renji Hospital were retrospectively reviewed. The inclusion criteria are as follows: 1) aged at 18 or older; 2) follow-up time over 3 months; 3) first time to undergo nephrectomy due to unilateral RCC. Patients with confirmed End-Stage Renal Disease (ESRD) or other kidney disease such as glomerulonephritis, and those who have died or lacked renal function test during the perioperative period are excluded. Besides, patients with eGFR<60ml/min/1.73m² before surgery are also excluded.

Cancer-specific information

We extracted tumor-specific data from the HIS system of Shanghai Renji Hospital when available using the 2010 TNM staging system. Patients with metastatic kidney cancer (clinical T stage=4, N stage > 0, or M stage > 0) were excluded from the analytic cohort.

Endpoints

The endpoint was the time to the incident stage 3 or higher CKD (defined as eGFR decreasing to 60ml/min/1.73m²) or any claim for the initiation of dialysis [13].

Definitions

We used KDIGO definitions for CKD, ESRD [13] and AKI [14]. CKD is defined as the abnormalities of kidney structure or function, presenting for > 3 months, with implications for health. Based on GFR category, CKD is classified, suggesting that stage 3 or higher CKD requires GFR < 60ml/(min·1.73m²). ESRD is defined as the requirement of renal replacement therapy (RRT) that is dialysis and transplant. AKI is classified as stage 1 [1.5-1.9 times baseline OR ≥ 0.3 mg/dl (≥ 26.5 μmol/L) increase], stage 2 (2.0-2.9 times baseline), and stage 3 [3.0 times baseline OR Increase in serum creatine to ≥ 4.0 mg/dl (≥ 353.6 μmol/L) OR Initiation of renal replacement therapy]. The baseline serum creatine was tested before the nephrectomy surgery within 3 days. eGFR was calculated with modified MDRD equation for Chinese patients.

Statistical analysis

Baseline characteristics were retrospective collected through HIS system. The statistical analysis was completed with R studio, version 1.2.5033 and SPSS, version 26.0. Variables were summarized as frequency and percentage for categorical variables, means (standard deviation) for continuous variables emerging on normal distribution, and medians with 25th and 75th percentiles for continuous variables emerging on non-normal distribution. The chi-squared and Student's t-tests were carried out to compare the preoperative characteristics of AKI and non-AKI groups. Predictive accuracy of the model was measured at the cut-point of each receiver operator characteristics (ROC) curve by adopting Inverse Probability Censoring Weighted (IPCW) method. A time-dependent area under curve (AUC) curve was provided by the timeROC package with RStudio.

Variables selection

We developed a set of candidate variables for possible model inclusion. A univariable analysis with Cox proportional hazards regression was conducted with the candidate variables. Relevant variables were selected to improve the model even if they did not reach the threshold for significance ($P < 0.05$), and a standard multivariable regression analysis was performed at the 0.1 level of significance for variables from a univariable analysis [15,16]. Considerable attentions have been paid to the consistence of variables' clinical value and hazard ratio, and 5 variables were chose as the final variables from the multivariable regression analysis.

Model development and performance

5 final variables were entered into the Cox proportional hazards regression analysis and the assumption of proportional hazards was confirmed by the Standardized Schoenfeld residuals graph and P value [17]. The plots of the dfbeta exponent for each variable were given to check influential cases [18]. And the vif

value was calculated to rule out the multicollinearity [19].

The model was evaluated in discrimination and calibration. Discrimination was calculated with C-harrell statistic, ranging from 0.5 (no discrimination) to 1.0 (perfect discrimination). Discrimination was also assessed by ROC curves and AUC values at three different points of time, because the model performance may differ over time. Calibration was assessed with the calibration plots. Perfect calibration is implied by a 45° diagonal line, whereas relevant deviation above or below this line reflects under prediction or over prediction.

Internal validation was performed using 10-fold cross-validation, and participants were divided into 10 separate and equally-sized folds [20]. Overall performance was reported as the mean AUC and standard deviation over 10-fold cross-validation.

Results

Study population

528 patients were finally included in the study cohort **(Figure 1)**. The baseline characteristics of patients who did and those who did not develop AKI within 3 days after nephrectomy are displayed in **Table 1**. The median follow-up time was 38 months. Overall, stage 3 or higher CKD occurred in 8.9% of people during the follow-up time after surgery. Among 528 admitted patients, 232 (43.9%) developed AKI, and 216 were at stage 1 (93.1% of the patients developed AKI), 15 were at stage 2 (6.5%), only 1 was at stage 3 (0.4%). Patients who underwent RN had a higher risk of occuring AKI compared with patients who did PN, 73.4% vs. 16.2% ($P < 0.001$). There was no difference in blood and urine tests between patients with AKI and those without.

Prognosis of postoperative AKI

Patients experienced postoperative AKI had higher preoperative eGFR compared with patients without postoperative AKI (134.1 ml/min/1.73 m^{2}and 124.9 ml/min/1.73 m^2 respectively, P=0.02), indicating the better renal function before surgery. Patients with postoperative AKI had a higher morbidity of stage 3 or higher CKD than those in the No-AKI group, 14.2% vs. 4.7% ($P < 0.001$). The eGFR declined 42.7 ml/min/1.73 m^2 (31.8% of the preoperative eGFR) in 5 years in patients with postoperative AKI, compared wtih 15.4 ml/min/1.73 m^2 (12.3%) in patients without postoperative AKI, suggesting that the renal functional prognosis after nephrectomy was poorer in patients with AKI **(Figure 2)**.

AKI performance in detection of the novel CKD

The results of univariable and multivariable analysis were exhibited in **Table 2**. In the univariable regression analysis, 8 variables including postoperative AKI and the surgery type showed a significant correlation with stage 3 or higher CKD after nephrectomy ($P < 0.1$). Five variables remained in the final predictive model after simplification: age (HR=1.064, P=0.002), surgery type (HR=0.316, P=0.009), preoperative eGFR (HR=0.946, $P < 0.001$), preoperative blood urea nitrogen (BUN, HR=1.043, P=0.002) and postoperative AKI (HR=3.193, P=0.004). To explore the relationship between postoperative AKI and long-term renal

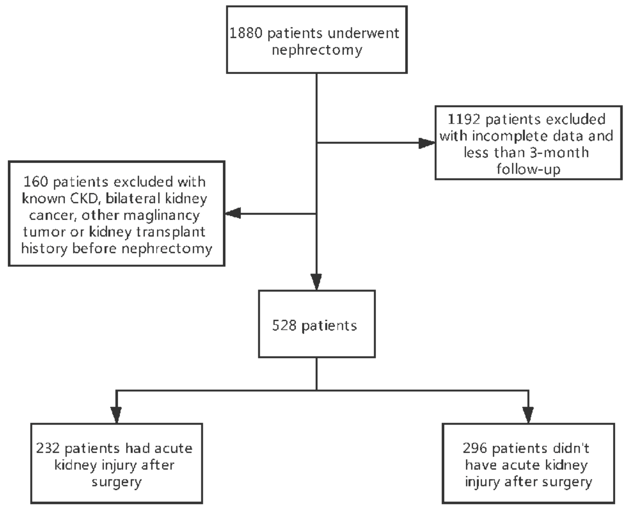


Figure 1 Enrollment and exclusion of RCC patients treated with nephrectomy.

Table 1 Baseline characteristics of patients underwent nephrectomy for renal cell carcinoma that did and did not develop AKI.

Characteristics	Overall (N = 528)	No AKI (N = 296)	AKI (N = 232)	*P-value*
Age (Year)	55.89 (11.56)	55.47 (11.86)	56.42 (11.18)	0.35
Gender				
Male	352 (66.7)	199 (67.2)	153 (65.9)	0.781
Female	176 (33.3)	97 (32.8)	79 (34.1)	
Surgery Type				
Radical Nephrectomy	256 (48.5)	68 (23.0)	188 (81.0)	<0.001
Non-Radical Nephrectomy	272 (51.5)	228 (77.0)	44 (19.0)	
Hypertension				
No	367 (69.5)	213 (72.0)	154 (66.4)	0.198
Yes	161 (30.5)	83 (28.0)	78 (33.6)	
Diabetes Mellitus				
No	483 (91.5)	270 (91.2)	213 (91.8)	0.932
Yes	45 (8.5)	26 (8.8)	19 (8.2)	
Use of ACEI and/or ARB				
No	471 (89.2)	266 (89.9)	205 (88.4)	0.681
Yes	57 (10.8)	30 (10.1)	27 (11.6)	
Albumin (g/L)	44.58 (4.81)	44.71 (4.88)	44.40 (4.72)	0.456
Globulin (g/L)	27.55 [25.20, 30.30]	27.50 [25.50, 30.30]	27.65 [24.82, 30.30]	0.843
ALT (U/L)	17.00 [12.00, 25.00]	17.00 [12.00, 25.00]	17.00 [13.00, 25.25]	0.257
AST (U/L)	18.00 [15.00, 22.00]	18.00 [15.00, 22.00]	18.00 [15.00, 22.00]	0.728
GGT (U/L)	23.70 [16.20, 39.52]	22.00 [15.50, 39.12]	25.75 [17.85, 40.42]	0.094

Characteristics	Overall (N = 528)	No AKI (N = 296)	AKI (N = 232)	*P-value*
Total Bilirubin (μmol/L)	9.75 [7.10, 13.22]	9.70 [7.18, 13.10]	9.80 [7.10, 13.33]	0.748
Direct Bilirubin (μmol/L)	3.40 [2.70, 4.40]	3.40 [2.70, 4.30]	3.40 [2.68, 4.40]	0.813
eGFR (MDRD)#	129.37 (31.96)	124.92 (28.89)	134.10 (35.22)	0.020
BUN (mmol/L)	5.20 [4.40, 6.10]	5.20 [4.40, 6.30]	5.20 [4.30, 5.90]	0.153
Uric Acid (μmol/L)	326.83 (87.61)	327.05 (89.32)	326.55 (85.58)	0.948
White Blood Cell Count (× 10^9/L)	6.08 [5.11, 7.23]	5.88 [5.05, 7.15]	6.27 [5.15, 7.35]	0.225
Hemoglobin (g/L)	137.90 (18.92)	138.20 (18.63)	137.53 (19.31)	0.686
Platelets (×10^{-9}/L)	216.69 (63.45)	215.50 (67.55)	218.20 (57.91)	0.628
Proteinuria				
No Proteinuria	389 (73.7)	218 (73.6)	171 (73.7)	0.796
0-30 mg/g	124 (23.5)	68 (23.0)	56 (24.1)	
30-300 mg/g	13 (2.5)	9 (3.0)	4 (1.7)	
>300 mg/g	2 (0.4)	1 (0.3)	1 (0.4)	
Leukocyturia※				
No	434 (82.2)	250 (84.5)	184 (79.3)	0.155
Yes	94 (17.8)	46 (15.5)	48 (20.7)	
Hematuria†				
No	432 (81.8)	238 (80.4)	194 (83.6)	0.403
Yes	96 (18.2)	58 (19.6)	38 (16.4)	

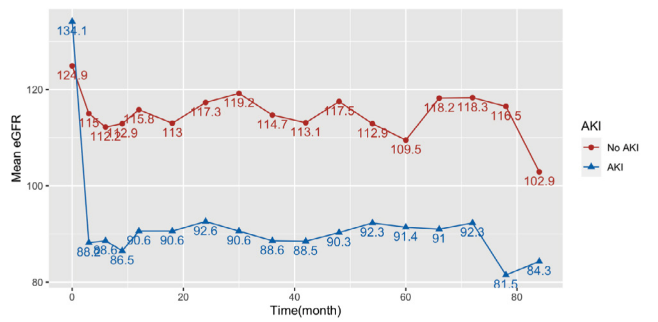
*Values are given as n (%), mean (SD) or median[25th-75th percentile]. AKI denotes acute kidney injury, ACEI angiotensin-converting enzyme, ARB angiotensin-receptor blocker, ALT, alanine aminotransferase, AST aspertate aminotransferase, GGT gamma-glutamyl transpeptidase, eGFR estimated glomerualr filtration rate and BUN blood urea nitrogen. #The estimated glomerular filtration rate as calculated by the Modification of Diet in Renal Disease equation for Chinese people.
※Leukocyturia is defined as white blood cell count >5/HP in the urine routine test
†Hematuria is defined as red blood cell count >4/HP in the urine routine test

function prognosis after nephrectomy, we illustrated the survival curve stratified by the AKI stages of patients, demonstrating that the risk of developing stage 3 or higher CKD is positive correlated with the severity of AKI **(Figure 3)**.

Model performance and validation

The final model had a C-index of 0.92 (0.89-0.95), suggesting the good ability to differentiate between patients with or without stage 3 or higher CKD after surgery. The mean C-harrell statistics was 0.9128 in the 10-fold cross-validation. ROC curves and AUC values (0.941, 0.936 and 0.924) were given at three different points of time: 2 years, 4 years and 6 years after nephrectomy **(Figure 4A)**.

The time-dependent AUC curve illustrated the AUC values of the predictive model varied from 0.88 to 0.96 through the follow-up



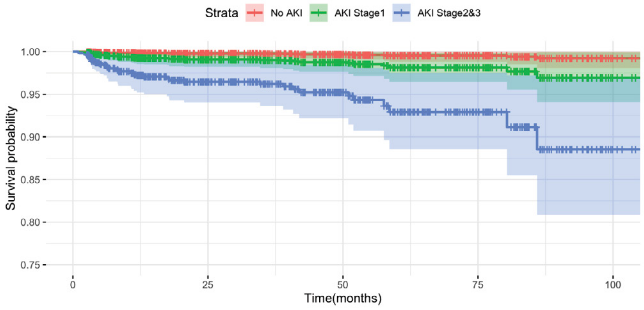
Red line represents patients who developed AKI after nephrectomy within 3 days, while blue line represents those who did not. The numbers below the lines represent the mean eGFR of all patients who had a renal function test at the corresponding time point on the x axis.

Figure 2 Line graph illustrating variation of eGFR after nephrectomy in patients with and without postoperative AKI.

Table 2 Predictors of renal function after nephrectomy in univariable and standard multivariable regression analysis.

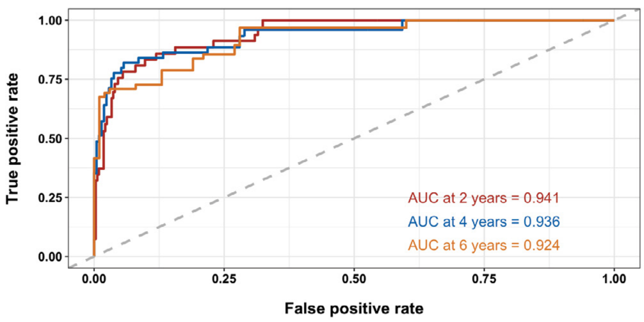
Predictors	Univariable HR	Univariable *P-value*	Multivariable HR	Multivariable *P-value*	CI
Age (year)	1.083	< 0.001	1.064	0.002	1.023-1.106
Gender (Male)	0.621	0.167			
Surgery Type (PN)	0.298	< 0.001	0.316	0.009	0.133-0.752
Hypertension	2.422	0.002	0.931	0.847	0.451-1.923
Diabetes Mellitus	0.557	0.419			
Use of ACEI or ARB	1.261	0.596			
eGFR (ml/min/1.73 m²)#	0.943	< 0.001	0.946	< 0.001	0.929-0.963
BUN (mmol/L)	1.040	< 0.001	1.043	0.002	1.015-1.072
Uric Acid (μmol/L)	1.007	< 0.001	1.003	0.043	1.000-1.007
Leukocyturia※	1.200	0.623			
Hematuria†	1.263	0.513			
Proteinuria					
No proteinuria	ref		ref		
0-30 mg	1.159	0.155	1.382	0.34	0.711-2.687
30-300 mg	4.232	0.018	2.259	0.225	0.606-19.564
>300 mg	12.930	0.012	1.356	0.823	0.094-19.564
AKI	3.079	< 0.001	3.193	0.004	1.463-6.970

* Variables with P smaller than 0.1 in a univariate cox regression model were further analysed in a multivariate cox regression model. HR denotes hazard ratio, CI confidence interval, PN partial nephrectomy, ACEI angiotensin-converting enzyme, ARB angiotensin-receptor blocker, eGFR estimated glomerualr filtration rate, BUN blood urea nitrogen and AKI acute kidney injury. #The estimated glomerular filtration rate as calculated by the Modification of Diet in Renal Disease equation for Chinese people. ※ Leukocyturia is defined as white blood cell count >5/HP in the urine routine test. † Hematuria is defined as red blood cell count > 4/HP in the urine routine test



Red line represents patients who developed AKI after nephrectomy within 3 days, while blue line represents those who did not. The numbers below the lines represent the mean eGFR of all patients who had a renal function test at the corresponding time point on the x axis.

Figure 3 Survival curves stratified by existence of AKI and the stage of AKI.



Red line represents patients who developed AKI after nephrectomy within 3 days, while blue line represents those who did not. The numbers below the lines represent the mean eGFR of all patients who had a renal function test at the corresponding time point on the x axis.

Figure 4A ROC curves of the predictive model at different time points.

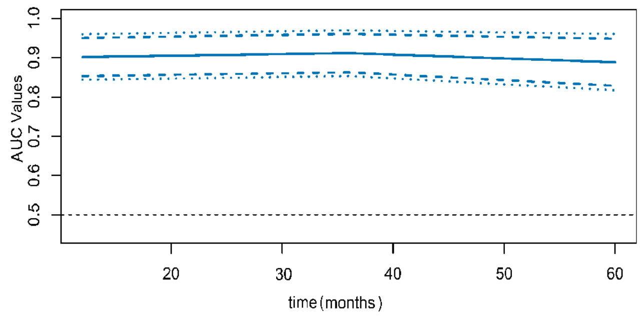
time, thus testifying the stable discrimination ability of the model **(Figure 4B)**.

The predictive accuracy of the model was measured at the cut point of each ROC curve **(Table 3)**. Calibration plots were nearly ideal, and there was a growing tendency to fit the 45° diagonal line with the follow-up time getting longer **(Figures 5A-5C)**.

Discussion

We demonstrated that postoperative AKI is an independent predictive factor with the surgery type for stage 3 or higher CKD in RCC patients who were treated with nephrectomy, along with age, preoperative eGFR, and preoperative BUN. The relationship between AKI and long-term renal function after nephrectomy is influenced by the severity of injury.

Nephrectomy induced chronic kidney disease is associated with increased risk of cardiovascular death and death from any cause in patients with RCC [21]. Previous studies proved that postoperative CKD occurs in a significant percentage of patients



The figure illustrates the discrimination stability (Figure 4B) of the predictive model. The red, blue and yellow ROC curves in Figure 4A representing the relationship between sensitivity and specificity at 2, 4 and 6 years after nephrectomy respectively. The solid line in Figure 4B shows that AUC values of the model vary from 0.88 to 0.96 during the follow-up time, and the two dotted lines represent the 95% CI.

Figure 4B Time-dependent AUC curve illustrating AUC values' variation.

Table 3 Predictive accuracy measures at cut-point estimated using IPCW.

Time Points	Sensitivity	Specificity	PPV	NPV
2 years	0.62	0.62	0.56	0.68
4 years	0.68	0.62	0.58	0.71
6 years	0.88	0.97	0.96	0.91

*IPCW denotes as inverse probability censoring weighted
PPV: Positive Predictive Value, NPV: Negative Predictive Value

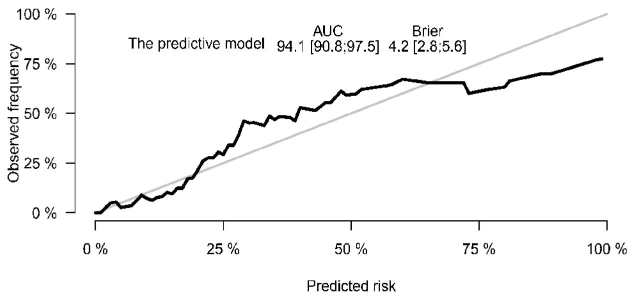


Figure 5A The calibration plot of the predictive model at 2 years after nephrectomy.

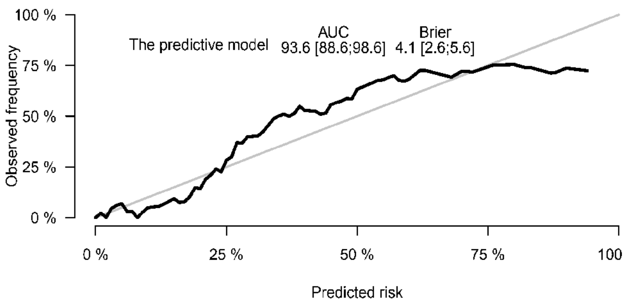
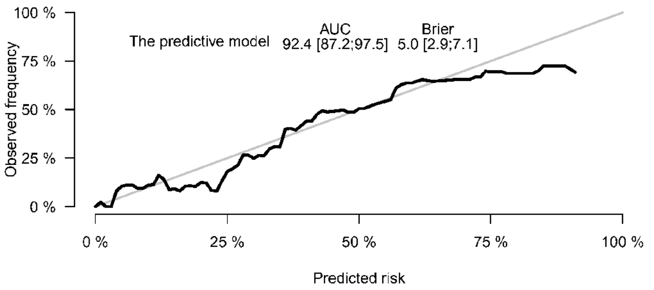


Figure 5B The calibration plot of the predictive model at 4 years after nephrectomy.



The grey 45° diagonal line represents models with perfect calibration. Figure 5A, 5B and 5C illustrate the relationship between predictive risk and observed frequency 2, 4, and 6 years after nephrectomy respectively, indicating the predictive model has good calibration, but tends to over-predict the risk for stage 3 or higher CKD among higher risk patients.

Figure 5C The calibration plot of the predictive model at 6 years after nephrectomy.

following nephrectomy due to inevitable nephron loss. 81 of 209 (38.8%) Japanese patients who underwent radical nephrectomy from 1994 to 2008 developed CKD within 3 years after RN, and 192 of 491 (39.1%) patients being treated with nephrectomy developed new onset stage 3 or higher CKD after surgery [22,23]. In the current study, a cohort of 528 RCC patients experienced nephrectomy has been assembled, of which 47 (8.9%) patients eventually developed stage 3 or higher CKD. Although the incidence rate of CKD after nephrectomy in patients with normal preoperative renal function declined over time, probably because of the progression of the surgical technique and the widely use of PN, postoperative CKD remained to be the main reason for unsatisfied life quality after surgery, and was required to be predicted and treated preventively [24].

Several studies have evaluated risk factors for poor renal functional outcomes after nephrectomy, and most of them regarded new onset CKD or declining of eGFR as the main endpoint. Previous researches revealed that lower preoperative eGFR, older age, preoperative proteinuria, presence of diabetes mellitus (DM) or hypertension, tumor size, and ischemia time predicted postoperative renal insufficiency [25,26]. PN presented better renal function preservation compared with RN that should be considered carefully when making clinical decisions [27]. Tumor size and ischemia time had been proved to be risk factors of new onset CKD after nephrectomy, and they both contribute to acute changes in serum creatine (Scr) level after surgery [28]. As a result, postoperative AKI should be taken into the variables pool when developing a predictive model for long-term renal outcome.

The present study proved that postoperative AKI is an independent predictor for poor renal function in patients underwent nephrectomy, after the adjustment of conventional predictors (surgery type, demographics characteristics and preoperative renal functional parameters). The survival curve illustrated that the severer the AKI condition is, the steeper the survival probability is decreased by time **(Figure 3)**. These results were confirmed by previous studies. Takagi et al. demonstrated that postoperative AKI was an independent predictor for decrease of eGFR>25% after PN, and a retrospective study enrolling 519 patients underwent RN showed that patients who experienced postoperative AKI had a 4.24-fold higher risk of new-onset CKD after multiple adjustments, and the median GFR decreased faster in AKI injury or failure group than that in AKI risk group [29,30]. However, these studies had some limitations, including small sample size and single surgical type (PN or RN). The combination of the above studies indicated postoperative AKI as an independent predictor of surgery type for poor long-term renal outcomes after nephrectomy. Therefore, the current study enrolled a cohort that includes RCC patients underwent all kinds of surgery types, and AKI together with age, surgery type, preoperative eGFR, and preoperative BUN were selected to be the predictive variables to build the prognostic model for stage 3 or higher CKD after nephrectomy.

The model discriminated very well in both full cohort (C statistic=0.92) and the internal validation (C statistic=0.91). However, the C statistics are high in this model in part because overall mortality is relatively low, except for some patients with very high risk characteristics, such as presentation with stage 2 or higher acute kidney injury in the perioperative period and presentation with old age, which also determines that the model tends to over-predict the risk of stage 3 or higher CKD after surgery, thus resulting in high NPV and relatively low PPV **(Table 3)**. With the extension of follow-up time, the number of censored patients has increased. Considering that patients with poor renal function after surgery may have a longer follow-up time, time extension indirectly caused the increase of mortality, thus resulting in the decrease of AUC value **(Figure 4B)**.

Our findings by providing information on the association between postoperative AKI and the incidence of stage 3 or higher CKD after nephrectomy may help surgeons and nephrologists early identify the high-risk patients and then make proper clinical choices. Knowing that AKI was an independent predictor for poor postoperative renal function, surgeons may take some preventive measurements before and during surgery, such as shortening surgical and clamping time, by using cold ischemia technique instead of warm ischemia and controlling preoperative hypertension. By increasing awareness of AKI, more accurate AKI biomarkers and early risk stratification before nephrectomy are warranted in further investigations.

Although this model represents an approach to predict the long-term renal function after nephrectomy, it should be considered in the context of some potential limitations. First, the study population was under-represented in the general population. There was only one contributing institution in the study population selection, which operation and perioperative management level may not be generalizable to all hospitals caring for nephrectomy patients. Recall bias was unavoidable in a retrospective study. Patients with missing data were deleted from the cohort instead of imputation, to some extent having caused loss of information. Second, the candidate variables were limited to those available in the routine perioperative examination. In particular, incorporating more information on patients presenting after the surgery, such as the length of hospital stay and postoperative medication, would be likely to create a more robust model. We evaluated the existence and the severity of postoperative AKI using serum creatine (SCR) levels within 24 hours after surgery, instead of the SCR levels at the next morning of nephrectomy. The stages of AKI were only stratified by the SCR category, and the study did not include data on urine output, which is a component of the current classification criteria for AKI. Third, the model has been validated using only the original study cohort and it has not been validated on an external dataset.

Conclusion

We have revealed that postoperative AKI is an independent predicting factor of stage 3 or higher CKD after nephrectomy, and the risk for the development of stage 3 or higher CKD is positively correlated with the severity of AKI.

Ethics Approval and Consent to Participate

Written informed consent was obtained from all subjects (patients) in this study. Institutional Review Board approval was obtained. All methods including enrollment of the study population and the statistical analysis were carried out in accordance with relevant guidelines and regulations.

Consent for Publication

Not applicable.

Availability of Data and Materials

The datasets generated and/or analyzed during the current study are not publicly available due further analysis is going to be done basing it.

Competing Interests

The authors declare that they have no competing interests.

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Authors' Contributions

All authors have contributed significantly: Designed research: Shan Mou, Wei Xue, Jin Zhang. Performed Research: Hang Zhou, Tianyi Zhang, Zhaohui Ni, Qin Wang, Qian Chen, Jiajia Wu, Ming Qiu, Yue Wang, Tingting Fu, Mingyu Ye, Jin Zhang, Wei Xue, Shan Mou. All authors and authors' institution have no potential conflicts of interest. All authors have contributed significantly, and that all authors are in agreement with the content of the manuscript. The authors claim that none of the material in the paper has been published or is under consideration for publication elsewhere.

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