

# Complications and Mortality After Surgery in Patients with Chronic Kidney Disease: A Retrospective Cohort Study Based on a Multicenter Clinical Database

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**Objective:** To evaluate the postoperative complications and mortality among patients with chronic kidney disease.

**Methods:** Biochemical measurements, diagnosis codes for CKD and comorbid conditions for surgical patients aged  $\geq 20$  years were obtained from electronic medical records of three large hospitals in Taiwan in 2009–2017. We conducted this retrospective cohort study by using propensity score-matching methods to balance the baseline characteristics between CKD and non-CKD groups. The multiple logistic regression analysis was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) of risks of primary outcome (included postoperative mortality) and secondary outcome (included postoperative infectious complications and non-infectious complications) associated with CKD.

**Results:** Among 31950 eligible surgical patients, the adjusted OR of in-hospital mortality in patients with CKD was 5.49 (95% CI 3.42–8.81) compared with that in non-CKD controls. The adjusted ORs of postoperative septicemia, pneumonia and cellulitis in patients with CKD were 5.90 (95% CI 2.12–16.5), 5.39 (95% CI 1.37–21.16), and 4.42 (95% CI 1.57–12.4), respectively, when compared with the non-CKD patients. CKD was also associated with postoperative stroke (OR 2.21, 95% CI 1.47–3.31).

**Conclusion:** Patients with CKD are at increased risk of postoperative stroke, infectious complications, and mortality. Our study implicated that it is crucial to improve the levels of hemoglobin and K<sup>+</sup> in patients with CKD before surgery. Preventive strategies should be developed to improve clinical outcomes in these populations.

**Keywords:** complications, dental scaling, mortality, hospitalization, stroke

## Introduction

Chronic kidney disease (CKD) is currently defined as evidence of either (a) kidney damage or (b) an estimated glomerular filtration rate (eGFR) of  $<60$  mL/min/1.73 m<sup>2</sup> for 3 or more months.<sup>1</sup> CKD is a public health problem worldwide. In 2017, the prevalence of CKD in the world's population was estimated to be 9.1%.<sup>2</sup> In 2017, CKD resulted in 1.2 million deaths, and an additional 1.4 million deaths from cardiovascular disease were attributable to impaired kidney function.<sup>2</sup> The kidneys play an important role in the regulation of electrolytes and acid–base balance. With the

progressive decline of kidney function, abnormal electrolyte levels and acid-base imbalance may occur and lead to serious complications and poor patient outcomes.<sup>3</sup>

However, patients with kidney damage and/or a decreased eGFR might be asymptomatic and not be formally diagnosed. A previous study found that CKD was undiagnosed in 5.2% of the middle-aged general population by physical examination and medical claims data.<sup>4</sup> Especially in the perioperative setting, diagnosing CKD may be challenging because of the lack of longitudinal data and/or long-term follow-up in surgical patients.

Previous studies have found an association between CKD and postoperative mortality and morbidity. Lee et al showed that CKD was associated with an increased risk of acute myocardial infarction (AMI) in patients undergoing orthopedic surgery.<sup>5</sup> Blitz et al reported that preoperative renal insufficiency was associated with an increased risk of readmission and postoperative complications.<sup>6</sup> A recent population study demonstrated that surgical patients with CKD exhibited more adverse events and an approximately 2-fold mortality rate after nonurologic surgery when compared to those of non-CKD patients.<sup>7</sup> There is an important meta-analysis indicated that patients on chronic dialysis are at increased odds of both cardiovascular and infectious complications following elective surgery.<sup>8</sup> However, most of these studies were limited by small sample sizes, inadequate adjustments for confounders, or a focus on a single type of surgery.<sup>5-7,9</sup> The association of renal insufficiency and postoperative outcomes has not been clearly studied.

In this propensity score-matched cohort study, we investigated the risk of postoperative mortality and morbidity in patients with CKD.

## Methods

### Data Source and Study Population

The data used in this study were obtained from the Taipei Medical University Research Database,<sup>10,11</sup> which contains the electronic health records of more than 3.6 million patients from three hospitals: Taipei Medical University Hospital, Wan Fang Hospital, and Shuang Ho Hospital. Patient clinical information, including records of outpatient and emergency visits, admissions, laboratory tests, and prescriptions, has been collected since 1997. Informed consent was not required because patient's identity was removed in the clinical database. This study was approved by the Joint Institutional Review Board of Taipei Medical University (TMU-JIRB-201903005) in accordance with Declaration of Helsinki.

The study included patients who underwent elective surgery between January 1, 2009, and September 30, 2017. Patients were excluded if they met the following criteria: i) aged <20 years old and ii) a hospital length of stay (LOS) <1 day. All diagnosis codes were defined by the International Classification of Diseases, Ninth revision, Clinical Modification (ICD-9-CM). For investigating the influence of CKD on postoperative complications and mortality, patients who received AV shunt surgery and peritoneal dialysis catheter surgery were excluded from this study. In this study, surgical patients received elective or emergency surgery were both enrolled in the analysis.

### Exposure

The chronic kidney disease (CKD) group was defined as subjects with the following: i) two or more outpatient records indicating a CKD diagnosis (ICD-9-CM 581–586) within two years before the surgery date; ii) inpatient records indicating a CKD diagnosis within two years before the surgery date; iii) regular dialysis (present for >3 months) records within one year before the surgery date; iv) estimated glomerular filtration rates (eGFRs) <60 mL/min per 1.73 m<sup>2</sup> within one year before the surgery date; or v) a urine albumin-to-creatinine ratio (ACR) ≥ 30 mg/g within one year before the index surgery.

The estimated GFR in our laboratory was computed with the Modification of Diet in Renal Disease Formula.<sup>12</sup> The non-CKD group was defined as the study subjects without the abovementioned criteria for the CKD group, any records indicating a CKD diagnosis, or an eGFR <90 mL/min per 1.73 m<sup>2</sup> before the index surgery.

For comprehensively evaluating the postoperative outcomes in patients with CKD, we considered primary outcome (included postoperative mortality) and secondary outcome (included postoperative infectious complications and non-infectious complications) in this study. Outcomes during the hospitalization of the index surgery was analyzed, which included the following: i) in-hospital mortality; ii) noninfectious complications: acute kidney injury (ICD-9-CM 584),

acute myocardial infarction (ICD-9-CM 410), stroke (hemorrhagic, occlusion, transient cerebral ischemia) (ICD-9-CM 430–437), pulmonary embolism (ICD-9-CM 415), deep vein thrombosis (ICD-9-CM 451.11, 451.19, 451.2, 451.81, 451.9, 453.40–453.42, 453.8, 453.9), pneumonia (ICD-9-CM 480–486), and postoperative bleeding (ICD-9-CM 998.0–998.2); and iii) infectious complications: septicemia (ICD-9-CM 038, 998.5), urinary tract infection (ICD-9-CM 599.0), surgical site infection (ICD-9-CM 998.5, 996.6, 998.1, 998.3), deep wound infection (ICD-9-CM 958.3), cellulitis (ICD-9-CM 682, 681, 614.3, 614.4, 528.3, 478.21, 478.71, 376.01), fungal infection (ICD-9-CM 110–118), necrotizing fasciitis (ICD-9-CM 728.86), acute pyelonephritis (ICD-9-CM 590.1), infectious arthritis (ICD-9-CM 711.0, 711.4, 711.5, 711.6, 711.9), and osteomyelitis (ICD-9-CM 730). We excluded patients who had the above complications before the index surgery. Postoperative adverse events included at least one complication or in-hospital mortality. Furthermore, we calculated the rate of intensive care and length of hospital stay at admission.

## Covariates

The preoperative coexisting medical conditions within one year before the surgery date that were considered included the following: hypertension (ICD-9-CM 401–405); cardiac dysrhythmias (ICD-9-CM 427); ischemic heart disease (ICD-9-CM 410–414); heart failure (ICD-9-CM 428); mental disorders (ICD-9-CM 290–319); chronic obstructive pulmonary disease (ICD-9-CM 491, 492, 494); asthma (ICD-9-CM 493); diabetes (ICD-9-CM 250); hyperlipidemia (ICD-9-CM 272.0–272.2); liver cirrhosis (ICD-9-CM 571.2, 571.5); and Parkinson's disease (ICD-9-CM 332).

## Statistical Analysis

Risk estimates were computed via univariate analyses based on risk factors and multivariate analyses with additional adjustments for potential confounders for all variables of interest. The chi-square test and *t*-test were used for categorical variables and continuous variables, respectively. The Wilcoxon signed-rank test and Wilcoxon rank sum test were used for length of hospital stay.

The propensity score method is a good alternative method for reducing selection bias when analyzing nonrandomized observational data.<sup>13</sup> Each patient's probability of developing CKD was derived from a logistic regression model in which all of the abovementioned baseline covariates were included. Potential risk factors associated with postoperative adverse outcomes, including age, sex, low income, coexisting medical conditions, emergency surgery, type of surgery, duration of surgery and type of anesthesia (general, regional), were used for the propensity score method. For propensity score matching, a nearest neighbor, 1-to-1 pair matching within 0.1 standard deviations of the logit of the propensity score was used.<sup>14</sup> Standardized differences in covariates between the CKD and non-CKD groups denoted important residual imbalances between CKD and non-CKD patients. An absolute standardized difference of <0.1 usually suggests that baseline covariates are well balanced.<sup>15</sup>

Conditional logistic regression analysis was used to estimate the odds ratios (ORs) and 95% confidence intervals (CIs) in the risk of in-hospital mortality, postoperative complications, and the rate of intensive care for CKD. For subgroup analyses, the relative risk of outcomes in surgical patients was stratified by hemoglobin levels  $\leq 8.5$  g/dL and potassium levels  $>5.5$  mmol/L. All data management and analyses were performed using SAS software version 9.4 (SAS Institute, Cary, NC); a *p* value  $<0.05$  was considered statistically significant.

## Results

Of the 80,334 patients who underwent surgery from 2009 to 2017, 56.7% were females, and the mean age was 53.7 years; a total of 43.1% ( $n=34,632$ ) of the patients in our study had CKD and 56.9% ( $n=45,702$ ) did not have CKD. The mean  $\pm$  SD of age of the CKD and non-CKD groups were  $67.1 \pm 14.6$  years and  $43.6 \pm 14.9$  years, respectively (Table 1).

Propensity score matching created 15,975 distinct pairs. After matching, all baseline characteristics of the subjects were balanced (absolute standardized difference  $< 0.1$ ) between the CKD and non-CKD groups (Table 2). There was no significant difference in sex, low income, cardiac dysrhythmias, mental disorders, chronic obstructive pulmonary disease, asthma, diabetes, hyperlipidemia, liver cirrhosis, Parkinson's disease, duration of surgery, and type of anesthesia between patients with and without CKD.

**Table 1** Baseline Characteristics of Surgical Patients with and without CKD Before Matching

	No CKD (N=45,702)		CKD (N=34,632)		P
	n	(%)	n	(%)	
Age, years					<0.0001
20–29	8864	(19.4)	342	(1.0)	
30–39	12,700	(27.8)	1298	(3.7)	
40–49	9668	(21.2)	2846	(8.2)	
50–59	7501	(16.4)	5863	(16.9)	
60–69	4369	(9.6)	8426	(24.3)	
70–79	1854	(4.1)	8625	(24.9)	
≥80	746	(1.6)	7232	(20.9)	
Mean ± standard deviation	43.6	±14.9	67.1	±14.6	<0.0001
Sex					<0.0001
Male	16,031	(35.1)	18,718	(54.0)	
Female	29,671	(64.9)	15,914	(46.0)	
Low income	502	(1.1)	549	(1.6)	<0.0001
Comorbidities					
Hypertension	1680	(3.7)	6315	(18.2)	<0.0001
Cardiac dysrhythmias	80	(0.2)	656	(1.9)	<0.0001
Ischemic heart disease	118	(0.3)	1629	(4.7)	<0.0001
Heart failure	12	(0.0)	765	(2.2)	<0.0001
Mental disorders	256	(0.6)	559	(1.6)	<0.0001
COPD	34	(0.1)	120	(0.3)	<0.0001
Asthma	71	(0.2)	148	(0.4)	<0.0001
Diabetes	975	(2.1)	3966	(11.5)	<0.0001
Hyperlipidemia	30	(0.1)	83	(0.2)	<0.0001
Liver cirrhosis	42	(0.1)	225	(0.6)	<0.0001
Parkinson's disease	44	(0.1)	204	(0.6)	<0.0001
Emergency operation	5494	(12.0)	3776	(10.9)	<0.0001
Type of surgery					<0.0001
Skin	510	(1.1)	373	(1.1)	
Breast	1128	(2.5)	425	(1.2)	
Musculoskeletal	9299	(20.3)	6752	(19.5)	
Respiratory	2597	(5.7)	1256	(3.6)	
Cardiovascular	430	(0.9)	1902	(5.5)	
Digestive	8915	(19.5)	6440	(18.6)	
Kidney, ureter, bladder	1185	(2.6)	4587	(13.2)	
Delivery, caesarean section	4482	(9.8)	133	(0.4)	
Neurosurgery	4077	(8.9)	4569	(13.2)	
Eye	27	(0.1)	6	(0.0)	
Other	13,052	(28.6)	8189	(23.6)	
Duration of surgery, hours					<0.0001
<2	31,855	(69.7)	21,301	(61.5)	
2–4	10,868	(23.8)	8689	(25.1)	
>4	2979	(6.5)	4642	(13.4)	
Mean ± standard deviation	1.77±1.46		2.13±2.01		<0.0001
Type of anesthesia					<0.0001
General	32,865	(71.9)	24,338	(70.3)	
Regional	12,837	(28.1)	10,294	(29.7)	

**Abbreviations:** CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

**Table 2** Baseline Characteristics of Surgical Patients with and without CKD After Matching

	No CKD (N=15,975)		CKD (N=15,975)		ASD*	p-value
	n	(%)	n	(%)		
Age, years						<0.0001
20–29	309	(1.9)	341	(2.1)	0.01	
30–39	1219	(7.6)	1277	(8.0)	0.01	
40–49	2455	(15.4)	2518	(15.8)	0.01	
50–59	5029	(31.5)	4371	(27.4)	0.10	
60–69	4363	(27.3)	4262	(26.7)	0.02	
70–79	1854	(11.6)	2138	(13.4)	0.05	
≥80	746	(4.7)	1068	(6.7)	0.07	
Mean ± standard deviation	57.8±12.9		58.6±13.8		0.05	
Sex						1.0000
Male	7771	(48.6)	7771	(48.6)	0.00	
Female	8204	(51.4)	8204	(51.4)	0.00	
Low income	233	(1.5)	231	(1.4)	0.00	0.9255
Comorbidities						
Hypertension	1443	(9.0)	1594	(10.0)	0.03	0.0040
Cardiac dysrhythmias	61	(0.4)	81	(0.5)	0.01	0.0925
Ischemic heart disease	118	(0.7)	161	(1.0)	0.02	0.0097
Heart failure	12	(0.1)	30	(0.2)	0.01	0.0054
Mental disorders	149	(0.9)	168	(1.1)	0.01	0.2835
COPD	22	(0.1)	25	(0.2)	0.00	0.6614
Asthma	37	(0.2)	43	(0.3)	0.01	0.5018
Diabetes	820	(5.1)	868	(5.4)	0.01	0.2300
Hyperlipidemia	21	(0.1)	14	(0.1)	0.01	0.2365
Liver cirrhosis	41	(0.3)	38	(0.2)	0.00	0.7354
Parkinson's disease	41	(0.3)	44	(0.3)	0.00	0.7446
Emergency operation	1608	(10.1)	1596	(10.0)	0.00	0.8231
Type of surgery						0.0008
Skin	209	(1.3)	209	(1.3)	0.00	
Breast	311	(1.9)	319	(2.0)	0.00	
Musculoskeletal	3686	(23.1)	3504	(21.9)	0.03	
Respiratory	821	(5.1)	788	(4.9)	0.01	
Cardiovascular	358	(2.2)	386	(2.4)	0.01	
Digestive	3319	(20.8)	3251	(20.4)	0.01	
Kidney, ureter, bladder	1075	(6.7)	1276	(8.0)	0.05	
Delivery, caesarean section	119	(0.7)	133	(0.8)	0.00	
Neurosurgery	2379	(14.9)	2283	(14.3)	0.02	
Eye	8	(0.1)	5	(0.0)	0.01	
Other	3690	(23.1)	3821	(23.9)	0.02	
Duration of surgery, hours						0.7792
<2	9940	(62.2)	9937	(62.2)	0.00	
2–4	4309	(27.0)	4276	(26.8)	0.00	
>4	1726	(10.8)	1762	(11.0)	0.01	
Mean ± standard deviation	2.03±1.76		2.04±1.85		0.00	
Type of anesthesia						0.2561
General	11,871	(74.3)	11,782	(73.8)	0.01	
Regional	4104	(25.7)	4193	(26.2)	0.01	

**Note:** \*Absolute standardized difference >0.1 for imbalance.

**Abbreviations:** ASD, absolute standardized difference; CKD, chronic kidney disease; COPD, chronic obstructive pulmonary disease.

**Table 3** Risks of Postoperative Mortality and Complications

Postoperative outcomes	No CKD (n=15,975)		CKD (n=15,975)		Risk of Outcomes		
	Events	Rate, %	Events	Rate, %	OR	(95% CI)*	p-value
In-hospital mortality	63	(0.4)	342	(2.1)	5.49	(3.42–8.81)	<0.0001
Non-infectious complications							
Acute kidney injury	0	(0.0)	29	(0.2)	NA		-
Acute myocardial infarction	0	(0.0)	7	(0.0)	NA		-
Stroke	135	(0.8)	227	(1.4)	2.21	(1.47–3.31)	<0.0001
Pulmonary embolism	0	(0.0)	3	(0.0)	NA		
Infectious complications							
Septicemia	15	(0.1)	60	(0.4)	5.90	(2.12–16.5)	<0.0001
Urinary tract infection	31	(0.2)	47	(0.3)	1.29	(0.51–3.25)	0.2952
Pneumonia	14	(0.1)	43	(0.3)	5.39	(1.37–21.2)	<0.0001
Cellulitis	28	(0.2)	43	(0.3)	4.42	(1.57–12.4)	<0.0001
Necrotizing fasciitis	3	(0.0)	14	(0.1)	3.87	(0.47–31.9)	0.3199
Surgical site infection	5	(0.0)	10	(0.1)	21.1	(0.68–655)	0.2419
Osteomyelitis	3	(0.0)	4	(0.0)	7.93	(0.07–879)	0.2438
Deep wound infection	4	(0.0)	3	(0.0)	4.43	(0.04–448)	0.2458
Postoperative adverse events <sup>†</sup>	271	(1.7)	696	(4.4)	3.48	(2.66–4.55)	<0.0001
Intensive care	317	(2.0)	712	(4.5)	3.17	(2.45–4.09)	<0.0001
Length of stay, days	6.5±8.9		10.7±16.9		p-value <0.0001 <sup>‡</sup>		

**Notes:** \*Propensity-score matched and adjusted for all covariates listed in Table 1. <sup>†</sup>Having at least one of complications or mortality.

<sup>‡</sup>Beta coefficient = 0.29 (p-value <0.0001) for the association between CKD.

**Abbreviations:** CKD, chronic kidney disease; OR, odds ratio; NA, not available.

Table 3 shows that the rates of in-hospital mortality, noninfectious complications, and infectious complications of the patients with CKD after propensity score matching were 2.1% (n=342), 1.8% (n=287) and 1.1% (n=169), respectively. Compared with the controls, the patients with CKD had a higher risk of postoperative adverse events (adjusted OR 3.48, 95% CI 2.66–4.55). The patients with CKD had a higher risk of mortality, noninfectious complications, and infectious complications (adjusted ORs 5.49, 2.78, 3.59, respectively). The adjusted ORs of stroke, pneumonia, septicemia, cellulitis, and the rate of intensive care were 2.21 (95% CI 1.47–3.31), 5.39 (95% CI 1.37–21.16), 5.90 (95% CI 2.12–16.46), 4.42 (95% CI 1.57–12.41), and 3.17 (95% CI 2.45–4.09), respectively. A longer LOS was noted in patients with CKD than in patients without CKD (mean difference 4.2 days, p<0.0001).

In CKD patients with a hemoglobin level ≤ 8.5 g/dL, the risk of postoperative adverse events was higher than that in non-CKD patients, with an adjusted OR of 4.18. In CKD patients with a potassium level >5.5 mmol/L, the risk of postoperative adverse events was higher than that in non-CKD patients, with an adjusted OR of 17.93 (Table 4). The supplementary file (Table S1) showed the risk of post-operative adverse events in patients with chronic kidney disease by levels of GFR.

**Table 4** Risk of Postoperative Adverse Events in CKD Patients with Other Conditions

	Postoperative Adverse Events					
	n	Events	Rate, %	OR	(95% CI)*	p-value
No CKD	15,975	271	1.7	1.00	(references)	
CKD	15,975	696	4.4	3.48	(2.66–4.55)	<0.0001
CKD with hemoglobin > 8.5 g/dL	12,235	518	4.2	3.37	(2.49–4.56)	<0.0001
CKD with hemoglobin ≤ 8.5 g/dL	264	22	8.3	4.18	(1.71–10.2)	<0.0001
CKD with K+ ≤ 5.5 mmol/L	11,184	460	4.1	3.15	(2.31–4.28)	<0.0001
CKD with K+ > 5.5 mmol/L	461	120	26.0	17.9	(8.61–37.3)	<0.0001

**Note:** \*Adjusted for the propensity score.

**Abbreviations:** CKD, chronic kidney disease; OR, odds ratio.

## Discussion

In this study, we found that CKD was associated with an increased risk of in-hospital mortality and postoperative adverse outcomes, including stroke, pneumonia, septicemia and cellulitis. The rates of intensive care and the length of hospital stay were significantly increased in patients with CKD compared with those in the matched non-CKD group.

Patients with CKD often have various types of chronic conditions, such as hypertension, diabetes, cardiac dysrhythmias, and ischemic heart disease. These findings are consistent with previous research.<sup>16,17</sup> Many comorbid illnesses may contribute to postoperative adverse outcomes. To reduce the confounding effects of comorbidities on the risk calculation, we used a propensity score matching procedure to select the control group, which included patients without CKD. Potential confounding factors were then adjusted in multivariate logistic regression to calculate the risk of postoperative adverse outcomes in patients with CKD.

The previous study showed that the prevalence of CKD ranging from 17% to 27% among people undergoing surgery was higher than in the general population.<sup>18</sup> In this study, 23.6% of surgical patients had CKD and it was considered as reasonable because the prevalence of CKD varied considerably between the various laboratory-based definitions.<sup>19</sup>

Regarding the postoperative non-infectious complications in this study, we found that patients with CKD had a 2.2 times higher risk of postoperative stroke than matched non-CKD controls. A previous study reported that patients with CKD or ESRD had a nearly 1.5- to 2.5-fold risk of stroke, respectively, when compared with controls.<sup>20</sup> A meta-analysis of 21 studies showed that an eGFR less than 60 mL/min per 1.73 m<sup>2</sup> was associated with a 43% higher risk of incident stroke.<sup>21</sup> Although the mechanism of stroke in CKD remains unclear, we proposed some causes may further increase the risk of stroke in the perioperative settings. First, anesthetic agents may impair cerebral autoregulation. A previous study demonstrated that cerebral autoregulation was significantly influenced by inhaled agents such as desflurane and isoflurane.<sup>22</sup> Second, fasting and fluid limitation prior to surgery may lead to unstable hemodynamics in patients with CKD.<sup>23</sup> Intraoperative hypotension plays a role in the development of postoperative ischemic stroke, especially for mean blood pressure values that are decreased by more than 30% from baseline blood pressure.<sup>24</sup> Third, CKD patients have paradoxical hemostatic potential, with increased rates of bleeding, but they are also prone to thrombosis.<sup>25,26</sup> When undergoing surgery, more surgical bleeding might lead to perioperative hypotension and further increase the risk of ischemic stroke.

Regarding the postoperative infectious complications in this study, we found that patients with CKD demonstrated a 5.9-fold risk of postoperative septicemia and a 4.4-fold risk of postoperative cellulitis when compared with non-CKD patients. Previous studies have shown a strong association between the incidence of infection and decreased kidney function.<sup>27–29</sup> Numerous risk factors predispose patients with CKD to infection. Potential risk factors for infection among patients with CKD include a high burden of comorbidities, malnutrition, hypoalbuminemia and anemia.<sup>30</sup> Furthermore, the abnormalities in neutrophil and lymphocyte function that occur in patients with ESRD suggest that the impairment of immune function may contribute to infection susceptibility.<sup>31</sup> In the perioperative setting, several factors alter immune function. The surgical stress-induced release of hormones such as catecholamines, adrenocorticotropic hormone and cortisol mediates the inhibitory effects on immune functions.<sup>32</sup> Perioperative tissue damage exerts a dominant influence on altered perioperative immunity and is predominantly immunosuppressive in its nature.<sup>33</sup> Along with surgical stress, blood transfusion, hypothermia, hyperglycemia, and postoperative pain, anesthetics per se are associated with suppressed immunity during the perioperative period. A better understanding of the factors that affect the pathogenesis of infection could help us to develop more effective strategies for infection control, which are especially essential for patients with CKD.

Hyperkalemia is common in patients with CKD. In this study, we found that CKD patients with a potassium level > 5.5 mmol/L had a 17.9-fold risk of postoperative adverse outcomes when compared with non-CKD patients. Patients with CKD have a high risk for hyperkalemia due to the effects of renal dysfunction on potassium homeostasis.<sup>34</sup> Hyperkalemia increases the risk of cardiac arrhythmia and sudden death.<sup>35</sup> Symptoms of hyperkalemia may be nonspecific and therefore require attention to preoperative laboratory analysis to prevent the potentially lethal intraoperative consequences of hyperkalemia, such as ventricular fibrillation. Thus, preoperative analysis and the subtle control of potassium levels are essential for reducing the mortality rate in this population.

Previous studies have reported CKD to be an independent risk factor for postoperative mortality. There was a population-based study indicated that patients with CKD exhibited more adverse outcomes with risks of mortality that were nearly 2.2-fold higher after non-urinary surgery.<sup>7</sup> In a systematic review suggested that CKD as an independent risk factor for postoperative death and cardiovascular events after noncardiac surgery.<sup>36</sup> Our results were similar with previous studies showed that patients with CKD had increased postoperative mortality than patients without CKD.

## Strength and Limitations

This study has several strengths, including a large sample size and the use of propensity score methods to reduce the systematic differences in baseline characteristics between the CKD and non-CKD groups so that it mimicked some of the particular characteristics of a randomized controlled trial. This study also has some limitations. First, the inclusion criteria for patients with CKD in this study consisted of a physician's diagnosis of CKD, current dialysis records, or ever having an eGFR < 60 mL/min per 1.73 m<sup>2</sup>. Potential misclassification may have occurred and may have contributed to underestimating the risk of postoperative adverse events in patients with CKD. Second, detailed information about lifestyles, dietary habits, and sociodemographic factors was not available in the database. The association of the potential confounders and postoperative adverse outcomes could not be validated and adjusted. Third, patients with CKD often have many coexisting chronic conditions. Various severities of chronic conditions could have confounded the analysis of postoperative outcomes but could not be adjusted in this study. In addition, the use of immunosuppressive agents may influence the postoperative outcomes. However, due to the unavailable data and information of the current clinical research database, we could not consider the immunosuppressive agents in this study and this point is one of study limitations. Finally, using a physician's diagnosis and ICD-9-CM codes to identify AKI may not be a perfect procedure and could lead to misdiagnosis of AKI.

In conclusion, patients with CKD, particularly those with higher potassium levels and lower hemoglobin had increased risks of postoperative in-hospital mortality, stroke, and infectious complications than non-CKD patients. Preoperative potassium analysis and preventive strategies should be provided to improve clinical outcomes in these populations.

## Abbreviations

CI, confidence interval; CKD, chronic kidney disease; ICD-9-CM, International Classification of Diseases 9th Revision Clinical Modification; OR, odds ratio.

## Data Sharing Statement

Data are available from the Taipei Medical University Clinical Research Database, published by Taipei Medical University (TMU). Due to the Personal Information Protection Act in Taiwan, the data cannot be publicly available. However, the datasets collected and analyzed in this study are available from the corresponding author, Chao-Shun Lin, upon reasonable request.

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## Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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## Disclosure

The authors report no conflicts of interest in this work.

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