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ORIGINAL RESEARCH

Adverse outcomes after non urological surgeries in patients with chronic kidney disease: a propensity-score-matched study

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Objective: To evaluate the complications, mortality, and medical expenditures after non-urological surgical procedures in patients with chronic kidney disease (CKD).

Methods: Using claims data of Taiwan's National Health Insurance, we conducted a matched cohort study of 35,643 patients with CKD who underwent nonurological surgeries in 2008–2013. By using a propensity-score matching procedure, 35,643 non-CKD patients were selected for comparison. Logistic regression was used to calculate the odds ratios (ORs) and the 95% confidence intervals (CIs) of postoperative complications and in-hospital mortality associated with CKD.

Results: The results showed that patients with CKD had higher risks of postoperative septicemia (OR: 1.78, 95% CI: 1.68–1.89), pneumonia (OR: 1.60, 95% CI: 1.48–1.73), stroke (OR: 1.34, 95% CI: 1.24–1.44), and in-hospital mortality (OR: 2.17, 95% CI: 1.90–2.47) compared with non-CKD patients. Longer hospital stays and higher medical expenditures after nonurological surgical procedures were noted in CKD patients. The association between CKD and postoperative adverse events was significant in both sexes, all of the age groups, and the other subgroups. Histories of myocardial infarction, epilepsy, and ages greater than 70 years were factors that were significantly associated with postoperative adverse events.

Conclusion: Compared with non-CKD patients, surgical patients with CKD exhibited more adverse events, with risks of in-hospital mortality that were approximately 2-fold higher after nonurinary surgery. These findings suggest an urgent need to revise the protocols for post-operative care in this population.

Keywords: chronic kidney disease, surgery, outcome

Introduction

Chronic kidney disease (CKD) is a global health problem, and its prevalence and incidence have gradually increased.[1,2] It has also been recognized as an independent risk factor for both cardiovascular complications and all-cause mortality in a wide spectrum of clinical scenarios.[2–7] The national prevalence of CKD for adults aged 20 years and older over the period from 1994 to 2006 in Taiwan was approximately 11.9%.[8] In the United States, the prevalence of CKD stages 1–5 during the 2011–2014 period reached 14.8%,[1] which was 1.23 times higher when compared with that in the 1988–1994 period.[1] Particularly, the largest increase was observed in stage 3 CKD (from 4.5% to approximately 6.5%), which has become the most prevalent stage.[1] Though the exact pathophysiology for postoperative morbidity and

mortality is still unknown, elevated levels of inflammatory mediators, plasma homocysteine, endothelial dysfunction, hypercoagulability, and arterial calcification may all serve important roles.[5,6,9–14]

Associated comorbidities, including diabetes mellitus, hypertension, hyperlipidemia, or cardiac diseases,[1,5,6,8] may complicate CKD, in terms of surgical outcomes.[5,15] In several widely used surgical risk indices, kidney dysfunction has often been listed as a major predictive factor.[5,16,17] In view of the potentially increased absolute number of CKD patients, these patients are more likely to undergo various surgical procedures.

Renal function impairment represents a wide variety of complex diseases[1,8,15] that may have differential impacts on postoperative adverse outcomes.[3–5,18] Although the perioperative outcomes of surgical risks in patients with CKD have been reported,[3–5,9] there were several limitations in the previous studies, such as small sample size,[3,9,19,20] inadequate adjustments for potential confounders,[9,19–22] and focus on a single surgical procedure or a specific population.[4,9,19–22] These previous studies indicated that the association between preoperative CKD and postoperative adverse events was not completely understood. By using Taiwan's National Health Insurance Research Database, we conducted a matched nationwide analysis to evaluate the global features of complications and mortality after various major surgeries in individuals with and without CKD.

Methods

Source of data

Taiwan's National Health Insurance program was implemented in March 1995, with a high coverage of more than 99% of Taiwan's 23 million residents. This study used reimbursement claims data from Taiwan's National Health Insurance Research Database that recorded all of the beneficiaries' medical services, including inpatient and outpatient demographic characteristics, the physicians' primary and secondary diagnoses, treatment procedures, prescriptions, and medical expenditures.

Ethical approval

To protect personal privacy, the electronic database was coded with patient identification scrambled for further public access for research. According to the National Health Research Institutes regulations, informed consent is not required because of the use of coded and scrambled patient identification. Our study was conducted in accordance with the Helsinki Declaration, and it was also approved by Taiwan's National Health Research Institutes and the institutional review board of Taipei Medical University (TMU-JIRB-201808012; TMU-JIRB-201509050).

Study design

We identified 35,643 patients with CKD, aged 20 years and older, who underwent major nonurological surgical procedures from January 1, 2008, through December 31, 2013. These procedures required general, epidural, or spinal anesthesia as well as hospitalization for at least 1 day. Each surgical patient with CKD was matched with 1 randomly selected, non-CKD surgical patient. We conducted the analysis by using a propensity-score-matched pair procedure and considered the following factors: age, sex, low income or not, whether the operation took place in a medical center, coexisting medical conditions, preoperative emergency care, preoperative inpatient care, types of nonurological surgeries, and types of anesthesia. To identify patients with CKD strictly, the present study required at least medical visits with a physician's primary diagnosis of CKD within the 24-month preoperative period. People without CKD were defined as those who had no medical visits with a physician's primary or secondary diagnosis of CKD within the 24-month preoperative period.

Measures and definitions

The patients' income statuses were identified from the Taiwan National Health Insurance Bureau, which defined low income as an economic status that qualified for waived medical copayments when receiving medical services. Whether the surgery was performed in a medical center and the types of nonurological surgeries and anesthesia were also recorded. The International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) was used to define the clinical diagnoses. Based on previous surgical studies, the medical conditions that were determined from the reimbursement claims for the 24-month preoperative period included mental disorders (ICD-9-CM 290–319), chronic obstructive pulmonary disease (ICD-9-CM 490–496), hypertension (ICD-9-CM 401–405), diabetes (ICD-9-CM 250), hyperlipidemia (ICD-9-CM 272.0, 272.1, and 272.2), ischemic heart disease (ICD-9-CM 410–414), epilepsy (ICD-9-CM 345), liver cirrhosis (ICD-9-CM 571), and heart failure (ICD-9-CM 428).

In-hospital mortality after the index surgery was considered to be the study's primary outcome. Nine major

postoperative complications were considered to be secondary outcomes and included septicemia (ICD-9-CM 038 and 998.5), stroke (ICD-9-CM 430–437) pneumonia (ICD-9-CM 480–486), urinary tract infection (ICD-9-CM 599.0), acute myocardial infarction (ICD-9-CM 410), postoperative bleeding (ICD-9-CM 998.0, 998.1, and 998.2), and pulmonary embolism (ICD-9-CM 415). The incidences of intensive care, lengths of hospital stay, and medical expenditures during the index surgical admission were also compared. In this study, surgical patients who had septicemia, stroke, pneumonia, urinary tract infection, acute myocardial infarction, surgical bleeding, and pulmonary embolism within preoperative 3 months were not considered as those had postoperative complications.

Statistical analyses

For the determination of the associations between CKD and the postoperative outcomes, we used a nonparsimonious multivariable logistic regression model to estimate a propensity score for each of the surgical patients with CKD or without CKD. Clinical significance guided the initial choice of the covariates in this model to include age, sex, low-income status, whether the operation took place in a medical center, types of surgery and anesthesia, hypertension, diabetes, cancer, mental disorders, peptic ulcer disease, chronic obstructive pulmonary disease, gout, anemia, atherosclerosis, pneumonia, asthma, osteoporosis, liver cirrhosis, angina, heart failure, venereal disease, Parkinson's disease, myocardial infarction, alcohol-related illness, peripheral vascular disease, atrial fibrillation, pulmonary tuberculosis, epilepsy, psoriasis, systemic lupus erythematosus, hypothyroidism, preoperative emergency care, and inpatient care.

We matched patients with CKD to non-CKD controls by using a greedy matching algorithm (without replacement) with a caliper width of 0.2 standard deviations of the log odds of the estimated propensity score. The categorical variables were summarized by using frequencies (percentages) and were compared between patients with and without CKD by using chi-square tests. The continuous variables were summarized by using means±standard deviations and were compared by using *t*-tests. Logistic regressions were used to calculate the adjusted odds ratios (ORs) and the 95% confidence intervals (CIs) of the postoperative outcomes that were associated with CKD. Additional analyses, which were stratified by age, sex, number of medical conditions, emergency visits, and hospitalizations, were also performed in order to examine the outcomes after nonurinary surgeries among patients with CKD within these strata.

Results

The baseline characteristics of the patients with and without CKD who underwent major surgeries are shown in Table 1. Under the propensity-score matching procedure (Table 2), there were no significant differences in age, sex, low-income status, types of hospitals, surgery or anesthesia types, hypertension, diabetes, cancer, mental disorders, peptic ulcer disease, chronic obstructive pulmonary disease, gout, anemia, atherosclerosis, pneumonia, asthma, osteoporosis, liver cirrhosis, angina, heart failure, venereal disease, Parkinson's disease, myocardial infarction, alcohol-related illness, peripheral vascular disease, atrial fibrillation, pulmonary tuberculosis, epilepsy, psoriasis, systemic lupus erythematosus, hypothyroidism, number of hospitalizations, and emergency care between the patients with CKD and those patients without CKD.

Compared with the non-CKD controls (Table 3), patients with CKD had higher risks of postoperative stroke (OR: 1.34, 95% CI: 1.24–1.44), pneumonia (OR: 1.60, 95% CI: 1.48–1.73), urinary tract infection (OR: 1.09, 95% CI: 1.01–1.17), septicemia (OR: 1.78, 95% CI: 1.68–1.89), admission to intensive care units (OR: 1.38, 95% CI: 1.32–1.43), and 30-day in-hospital mortality (OR: 2.17, 95% CI: 1.90–2.47). Longer lengths of stay (13.2 ±17.8 vs 11.0±16.5 days, respectively; $P<0.0001$) and higher medical expenditures (4,598±5,700 vs 3,938 ±5,195 US dollars, respectively; $P<0.0001$) were also noted in patients with CKD, compared to those patients without CKD.

Table 4 shows that the associations between CKD and increased postoperative adverse events were significant for women, men, every age group, and patients with lower than 3 medical conditions. Postoperative adverse event was associated with CKD in patients with hospitalization and emergency care or not.

After adjustments in the multivariate logistic regressions (Table S1), age (≥80 years; OR: 3.65, 95% CI: 2.28–5.83), the male sex (OR: 1.09, 95% CI: 1.03–1.15), and surgeries that did not occur in medical centers (OR: 1.13, 95% CI: 1.06–1.19), as well as incidences of neurosurgery (OR: 8.45, 95% CI: 5.16–13.8), general anesthesia (OR: 1.23, 95% CI: 1.14–1.33), myocardial infarction (OR: 2.17, 95% CI: 1.41–3.32), alcohol-related illness (OR: 1.88, 95% CI: 1.14–3.10), epilepsy (OR: 3.97, 95% CI: 1.77–8.92), Parkinson's disease (OR: 1.45, 95% CI: 1.08–1.94), diabetes (OR: 1.15, 95%

Table 1 Characteristics of patients received nonurological surgeries with and without chronic kidney disease

	No CKD (N=489,436)		CKD (N=122,359)		*P*
	n	(%)	n	(%)	
Age, years					<0.0001
20–29	4736	(1.0)	1184	(1.0)	
30–39	14,960	(3.1)	3740	(3.1)	
40–49	39,760	(8.1)	9940	(8.1)	
50–59	88,208	(18.0)	22,052	(18.0)	
60–69	115,976	(23.7)	28,994	(23.7)	
70–79	152,162	(31.1)	35,206	(28.8)	
≥80	73,634	(15.0)	21,243	(17.4)	
Sex					1.0000
Female	229,976	(47.0)	57,494	(47.0)	
Male	259,460	(53.0)	64,865	(53.0)	
Low income					<0.0001
No	479,230	(97.9)	115,838	(94.7)	
Yes	10,206	(2.1)	6521	(5.3)	
Operation in medical center					<0.0001
No	292,981	(59.9)	68,148	(55.7)	
Yes	196,455	(40.1)	54,211	(44.3)	
Types of surgery					<0.0001
Musculoskeletal	11,539	(2.4)	3661	(3.0)	
Digestive	8131	(1.7)	907	(0.7)	
Neurosurgery	176,298	(36.0)	34,909	(28.5)	
Cardiovascular	22,034	(4.5)	3577	(2.9)	
Respiratory	14,006	(2.9)	26,981	(22.1)	
Skin	126,124	(25.8)	25,499	(20.8)	
Eye	6525	(1.3)	313	(0.3)	
Breast	60,306	(12.3)	10,836	(8.9)	
Delivery, CS, abortion	6535	(1.3)	2325	(1.9)	
Others	57,938	(11.8)	13,351	(10.9)	
Types of anesthesia					<0.0001
General	350,831	(71.7)	97,402	(79.6)	
Epidural or spinal	138,605	(28.3)	24,957	(20.4)	
Coexisting medical conditions					
Hypertension	156,299	(31.9)	50,963	(41.7)	<0.0001
Diabetes	72,099	(14.7)	45,126	(36.9)	<0.0001
Anemia	21,626	(4.4)	30,086	(24.6)	<0.0001
Mental disorders	81,935	(16.7)	25,427	(20.8)	<0.0001
Peptic ulcer disease	54,820	(11.2)	23,675	(19.4)	<0.0001
COPD	61,406	(12.6)	17,760	(14.5)	<0.0001
Cancer	71,000	(14.5)	17,038	(13.9)	<0.0001
Atherosclerosis	23,342	(4.8)	15,708	(12.8)	<0.0001
Gout	25,172	(5.1)	14,300	(11.7)	<0.0001
Pneumonia	18,230	(3.7)	13,380	(10.9)	<0.0001
Heart failure	9213	(1.9)	12,342	(10.1)	<0.0001
Angina	15,391	(3.1)	7887	(6.5)	<0.0001
Asthma	27,408	(5.6)	7493	(6.1)	<0.0001
Liver cirrhosis	12,169	(2.5)	5406	(4.4)	<0.0001

(*Continued*)

Table 1 (Continued).

	No CKD (N=489,436)		CKD (N=122,359)		*P*
	n	(%)	n	(%)	
Myocardial infarction	4073	(0.8)	4502	(3.7)	<0.0001
Osteoporosis	17,870	(3.7)	4316	(3.5)	0.0383
Parkinson's disease	10,891	(2.2)	3608	(3.0)	<0.0001
Venereal disease	10,779	(2.2)	2785	(2.3)	0.1170
Peripheral vascular disease	4583	(0.9)	2742	(2.2)	<0.0001
Pulmonary tuberculosis	4671	(1.0)	2337	(1.9)	<0.0001
Alcohol-related illness	7233	(1.5)	2204	(1.8)	<0.0001
Atrial fibrillation	3834	(0.8)	1763	(1.4)	<0.0001
Epilepsy	3167	(0.7)	1563	(1.3)	<0.0001
Systemic lupus erythematosus	847	(0.2)	1521	(1.2)	<0.0001
Psoriasis	3331	(0.7)	1245	(1.0)	<0.0001
Hypothyroidism	2159	(0.4)	885	(0.7)	<0.0001
Number of hospitalizations					<0.0001
0	296,852	(60.7)	29,300	(24.0)	
1	105,368	(21.5)	24,751	(20.2)	
2	43,012	(8.8)	19,178	(15.7)	
≥3	44,204	(9.0)	49,130	(40.2)	
Number of emergency visits					<0.0001
0	258,654	(52.9)	27,654	(22.6)	
1	114,014	(23.3)	22,986	(18.8)	
2	54,457	(11.1)	18,017	(14.7)	
≥3	62,311	(12.7)	53,702	(43.9)	

Abbreviation: CKD, chronic kidney disease.

CI: 1.07–1.23), ≥3 preoperative hospitalizations (OR: 1.74, 95% CI: 1.58–1.91), and ≥3 emergency visits (OR: 1.47, 95% CI: 1.36–1.60), were significant factors that were associated with postoperative adverse events among surgical patients with CKD.

Discussion

By using a comprehensive study design that included matching by propensity score, a large sample size, a multivariate adjustment of confounders, and the inclusion of various types of surgery, we observed that patients with CKD had a nearly 2.5-fold higher postoperative 30-day in-hospital mortality and higher risk of complications, such as stroke, acute myocardial infarction, postoperative bleeding, pneumonia, urinary tract infection, and septicemia. In the CKD population, older age, low-income status, male sex, general anesthesia, and neurosurgery had relatively higher risks of postoperative mortality.

In this study, CKD is associated with postoperative mortality. A previous study suggested that the mortality in CKD patients is higher during hospitalization in other conditions as well especially in infections even without surgery.[23] The postoperative mortality in patients with CKD differed in the various types of surgeries,[3,4,9,19–22] and the corresponding complication rate was associated with both the preoperative stage of CKD and the estimated glomerular filtration rate (eGFR).[3,9,19,21,22] Our investigation focused on different types of surgical specialties, and the overall postoperative mortality was 2.6%. A previous meta-analysis suggested that most of the causes of postoperative death in CKD patients were due to cardiovascular adverse events, followed by septicemia.[4] Among previous studies, cardiovascular and infectious adverse events commonly occurred in patients with CKD, but there still existed inconsistencies in these events, either in mortality rate or complication incidence.[4,9,22] These observations can possibly be attributed to the different surgical procedures and varied severities of renal dysfunction.

Cardiovascular complications and associated death have been shown to be related to patients with renal function insufficiency.[1–3,6–8] In our investigation,

Table 2 Characteristics of patients received nonurological surgeries with and without chronic kidney disease

	No CKD (N=35,643)		CKD (N=35,643)		*P*
	n	**(%)**	**n**	**(%)**	
Age, years	n	(%)	n	(%)	1.0000
20–29	223	(0.6)	223	(0.6)	
30–39	848	(2.4)	848	(2.4)	
40–49	2789	(7.8)	2789	(7.8)	
50–59	6968	(19.6)	6968	(19.6)	
60–69	8816	(24.7)	8816	(24.7)	
70–79	10,966	(30.8)	10,966	(30.8)	
≥80	5033	(14.1)	5033	(14.1)	
Sex					1.0000
Female	16,851	(47.3)	16,851	(47.3)	
Male	18,792	(52.7)	18,792	(52.7)	
Low income					1.0000
No	35,286	(99.0)	35,286	(99.0)	
Yes	357	(1.0)	357	(1.0)	
Operation in medical center					1.0000
No	19,684	(55.2)	19,684	(55.2)	
Yes	15,959	(44.8)	15,959	(44.8)	
Types of surgery					1.0000
Musculoskeletal	12,196	(34.2)	12,196	(34.2)	
Digestive	9075	(25.5)	9075	(25.5)	
Neurosurgery	3971	(11.1)	3971	(11.1)	
Cardiovascular	2937	(8.2)	2937	(8.2)	
Respiratory	742	(2.1)	742	(2.1)	
Skin	480	(1.4)	480	(1.4)	
Eye	394	(1.1)	394	(1.1)	
Breast	263	(0.7)	263	(0.7)	
Delivery, CS, abortion	111	(0.3)	111	(0.3)	
Others	5474	(15.4)	5474	(15.4)	
Types of anesthesia					1.0000
General	27,580	(77.4)	27,580	(77.4)	
Epidural or spinal	8063	(22.6)	8063	(22.6)	
Coexisting medical conditions					
Hypertension	10,907	(30.6)	10,907	(30.6)	1.0000
Diabetes	7543	(21.2)	7543	(21.2)	1.0000
Cancer	4068	(11.4)	4068	(11.4)	1.0000
Mental disorders	3863	(10.8)	3863	(10.8)	1.0000
Peptic ulcer disease	2936	(8.2)	2936	(8.2)	1.0000
COPD	1858	(5.2)	1858	(5.2)	1.0000
Gout	1856	(5.2)	1856	(5.2)	1.0000
Anemia	1824	(5.1)	1824	(5.1)	1.0000
Atherosclerosis	903	(2.5)	903	(2.5)	1.0000
Pneumonia	602	(1.7)	602	(1.7)	1.0000
Asthma	554	(1.6)	554	(1.6)	1.0000
Osteoporosis	434	(1.2)	434	(1.2)	1.0000
Liver cirrhosis	353	(1.0)	353	(1.0)	1.0000
Angina	372	(1.0)	372	(1.0)	1.0000

(*Continued*)

Table 2 (Continued).

	No CKD (N=35,643)		CKD (N=35,643)		*P*
	n	(%)	n	(%)	
Heart failure	303	(0.9)	303	(0.9)	1.0000
Venereal disease	244	(0.7)	244	(0.7)	1.0000
Parkinson's disease	223	(0.6)	223	(0.6)	1.0000
Myocardial infarction	93	(0.3)	93	(0.3)	1.0000
Alcohol-related illness	96	(0.3)	96	(0.3)	1.0000
Peripheral vascular disease	67	(0.2)	67	(0.2)	1.0000
Atrial fibrillation	38	(0.1)	38	(0.1)	1.0000
Pulmonary tuberculosis	36	(0.1)	36	(0.1)	1.0000
Epilepsy	28	(0.1)	28	(0.1)	1.0000
Psoriasis	49	(0.1)	49	(0.1)	1.0000
SLE	27	(0.1)	27	(0.1)	1.0000
Hypothyroidism	30	(0.1)	30	(0.1)	1.0000
Number of hospitalizations					1.0000
0	18,344	(51.5)	18,344	(51.5)	
1	8903	(25.0)	8903	(25.0)	
2	3749	(10.5)	3749	(10.5)	
≥3	4647	(13.0)	4647	(13.0)	
Number of emergency visits					1.0000
0	15,573	(43.7)	15,573	(43.7)	
1	8719	(24.5)	8719	(24.5)	
2	4342	(12.2)	4342	(12.2)	
≥3	7009	(19.7)	7009	(19.7)	

Abbreviations: CKD, chronic kidney disease; SLE, systemic lupus erythematosus.

incidences of postoperative stroke and acute myocardial infarction were significantly higher in the CKD group. Although the exact mechanism for the development of postoperative cardiovascular events is still unknown, some hypotheses have been developed to explain the phenomena. For example, increased levels of inflammatory and prothrombotic markers, such as c-reactive protein, fibrinogen, albumin, hemoglobin, white blood cell counts, and coagulation factor VII, have been observed in cases of renal disease and decreased GFR.[24,25] Other factors contributing to the abnormal cardiovascular outcomes included accelerated atherogenesis, nutritional effects, endothelial dysfunction, metabolic changes, coronary artery calcification, and left ventricle abnormalities.[25]

Medical and surgical infections are common in patients with CKD.[26–29] In our investigation, pneumonia, septicemia, and urinary tract infection were remarkably major postoperative complications in patients with CKD. Although the probable pathophysiology for the association is still unclear, several potential mechanisms have been postulated. For example, more comorbid illnesses, declined vaccination responsiveness, increased inflammatory cytokine levels, higher serum c-reactive protein concentrations, albuminuria, degraded endothelial glycocalyx, and impaired host immunity were shown to be associated with different types of infectious adverse outcomes.[26,27,30] However, the results were inconsistent between systemic infections (pneumonia and septicemia) and local infections in our study. Deep wound infections in patients with CKD did not exhibit significant differences when compared with the non-CKD group. A prior investigation of coronary artery bypass surgery in CKD patients revealed that wound infection rates were doubled in the moderate CKD group and that there was a more than 5-fold increase in the severe CKD group.[29] Local wound infection was solely notably increased in advanced CKD,[27,29] and the discrepancies between our investigation and previous investigations are possibly due to the limitation of staging status in the presenting database. We suggested that the prevention of infection in CKD patients is crucial because it may lead to increased risk of cardiovascular events, end-stage kidney disease, and mortality.[31]

Table 3 Risk of postoperative complications and mortality for surgical patients with preoperative CKD

	No CKD (N=35,643)		CKD (N=35,643)		Risk of outcomes	
Postoperative outcomes	**Events**	**%**	**Event**	**%**	**OR**	**(95% CI)[a]**
30-day in-hospital mortality	346	1.0	733	2.1	2.17	(1.90–2.47)
Postoperative complications						
Septicemia	1818	5.1	3037	8.5	1.78	(1.68–1.89)
Stroke	1374	3.9	1785	5.0	1.34	(1.24–1.44)
Pneumonia	1141	3.2	1761	4.9	1.60	(1.48–1.73)
Urinary tract infection	1382	3.9	1497	4.2	1.09	(1.01–1.17)
Acute myocardial infarction	363	1.0	360	1.0	0.99	(0.85–1.15)
Postoperative bleeding	235	0.7	275	0.8	1.17	(0.98–1.40)
Pulmonary embolism	50	0.1	32	0.1	0.64	(0.41–1.00)
ICU stay	6301	17.7	7732	21.7	1.38	(1.32–1.43)
Medical expenditure, USD[b]	3938±5195		4598±5700		$p<0.0001$	
Length of hospital stay, days[b]	11.0±16.5		13.2±17.8		$p<0.0001$	

Note: [a]Adjusted for age, sex, low income, operation in medical center, types of anesthesia, types of surgery, and coexisting medical conditions. ‡Mean±SD.
Abbreviations: CI, confidence interval; CKD, chronic kidney disease; ICU, intensive care unit; OR, odds ratio.

In the nonoperative condition, individuals with CKD had greater chances of bleeding.[32] The possible mechanism was thought to be related to platelet dysfunction, an abnormal interaction between platelets and the vascular walls, anemia, or effects of certain drugs.[32–34] Nevertheless, the detailed risk for perioperative bleeding remains unclear. In our study, postoperative bleeding was significantly higher in patients with CKD than in the population without CKD. Our findings were similar with a previous meta-analysis, which revealed the increased risks of blood transfusion requirements and postoperative bleeding.[32] CKD was also considered to be an independent risk factor for blood transfusion predictions.[35] The postulated pathophysiology for the risk of postoperative bleeding is complicated and may be attributed to multiple defects in all of the steps of platelet aggregation.[32,33] Abnormal platelet adhesion has been observed to be due to the functional derangement of the interaction between von-Willebrand factors and glycoproteins IIb-IIIa as well as increased production of prostacyclin and nitric oxide, which makes platelet activation in CKD patients difficult.[34,36,37] Furthermore, inadequate platelet stores of adenosine diphosphate (ADP), as well as inadequate serotonin levels, cyclooxygenase defects, decreased thromboxane A_2 synthesis, and altered calcium mobilization, also appear to be associated with bleeding diathesis.[34,37]

There were some limitations that need to be addressed. First, we could not categorize the stage of CKD in this study because the information of glomerular filtration rate was not available in the database of Taiwan's National Health Insurance. The definition of CKD was based on physician's diagnosis during medical visits may cause misclassification because some people with mild CKD (such as stage 1 CKD) may not seek for medical care. This condition may lead to underestimation of the impact of CKD on perioperative outcome in this study because some mild CKD patients may exist in the non-CKD group in this study. Second, the administrative database lacked information on the individual characteristics of patients, such as socioeconomic condition, lifestyle, preoperative laboratory data, and pharmacological compliance. Third, the perioperative variables that were related to surgery and anesthesia were not adequately available in this research database, including factors such as changes in hemodynamic parameters, total volume of blood loss, transfusion details, use of prophylactic antibiotics or anticoagulants, duration of surgery, and postoperative meticulous care profiles. In addition, our study was of a retrospective nature, and a detailed randomization distribution could not be achieved between the groups, even though comprehensive matching and statistical adjustment were performed in this study. However, we assumed that the influence of all of the covariates was evenly distributed between the groups and that the bias would be reduced in this population-based, large-scale study. Finally, our study is based on

Table 4 Stratified analysis for the risk of postoperative adverse events in patients with and without CKD

		n	Postoperative adverse events[a]			
			Events	Incidence, %	OR	(95% CI)
Age 20–29 years	No CKD CKD	223 223	9 21	4.0 9.4	1.00 2.65	(reference) (1.15–6.11)
Age 30–39 years	No CKD CKD	848 848	26 67	3.1 7.9	1.00 3.02	(reference) (1.85–4.93)
Age 40–49 years	No CKD CKD	2789 2789	191 296	6.9 10.6	1.00 1.66	(reference) (1.37–2.02)
Age 50–59 years	No CKD CKD	6968 6968	571 930	8.2 13.4	1.00 1.77	(reference) (1.58–1.98)
Age 60–69 years	No CKD CKD	8816 8816	1034 1567	11.7 17.8	1.00 1.66	(reference) (1.52–1.81)
Age 70–79 years	No CKD CKD	10,966 10,966	1878 2530	17.1 23.1	1.00 1.48	(reference) (1.38–1.58)
Age ≥80 years	No CKD CKD	5033 5033	1231 1472	24.5 29.3	1.00 1.30	(reference) (1.18–1.42)
Female	No CKD CKD	16,851 16,851	2043 3001	12.1 17.8	1.00 1.62	(reference) (1.52–1.73)
Male	No CKD CKD	18,792 18,792	2897 3882	15.4 20.7	1.00 1.47	(reference) (1.39–1.55)
0 Medical condition	No CKD CKD	10,549 10,549	1195 1894	11.3 18.0	1.00 1.76	(reference) (1.62–1.90)
1 Medical condition	No CKD CKD	14,282 14,282	1951 2732	13.7 19.1	1.00 1.52	(reference) (1.42–1.62)
2 Medical conditions	No CKD CKD	8016 8016	1233 1610	15.4 20.1	1.00 1.40	(reference) (1.29–1.52)
3 Medical conditions	No CKD CKD	2276 2276	442 504	19.4 22.1	1.00 1.19	(reference) (1.03–1.38)
≥4 Medical conditions	No CKD CKD	520 520	119 143	22.9 27.5	1.00 1.30	(reference) (0.97–1.74)
0 Hospitalization	No CKD CKD	18,344 18,344	2101 2878	11.5 15.7	1.00 1.47	(reference) (1.38–1.57)
1 Hospitalization	No CKD CKD	8903 8903	1194 1756	13.4 19.7	1.00 1.63	(reference) (1.50–1.77)
2 Hospitalizations	No CKD CKD	3749 3749	596 883	15.9 23.6	1.00 1.67	(reference) (1.49–1.88)
≥3 Hospitalizations	No CKD CKD	4647 4647	1049 1366	22.6 29.4	1.00 1.46	(reference) (1.32–1.60)
0 Emergency visit	No CKD CKD	15,573 15,573	1674 2281	10.8 14.7	1.00 1.45	(reference) (1.36–1.56)

(*Continued*)

Table 4 (Continued).

		n	Postoperative adverse events[a]			
			Events	Incidence, %	OR	(95% CI)
1 Emergency visit	No CKD	8719	1222	14.0	1.00	(reference)
	CKD	8719	1713	19.7	1.54	(1.42–1.67)
2 Emergency visits	No CKD	4342	662	15.3	1.00	(reference)
	CKD	4342	979	22.6	1.67	(1.49–1.87)
≥3 Emergency visits	No CKD	7009	1382	19.7	1.00	(reference)
	CKD	7009	1910	27.3	1.56	(1.44–1.69)

Note: [a]Adverse events include stroke, pneumonia, urinary tract infection, septicemia, and 30-day in-hospital mortality.
Abbreviations: CI, confidence interval; CKD, chronic kidney disease; OR, odds ratio.

ICD-9-CM codes and very few coding errors could not be avoided.

In conclusion, CKD was an independent risk factor for postoperative mortality and complications, and adverse events after surgery could be observed in the various subgroups. The comprehensive preoperative assessment and optimal control of correctable risk factors should be effectively and efficiently implemented in advance to achieve better outcomes.

Abbreviations

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

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Disclosure

The authors report no conflicts of interest in this work.

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Supplementary material

Table S1 Factors associated with adverse events after nonurological surgeries in patients with chronic kidney disease (N=35643)[a]

		OR	(95% CI)
Age, years	20–29	1.00	(reference)
	30–39	0.83	(0.49–1.40)
	40–49	1.14	(0.70–1.84)
	50–59	1.35	(0.84–2.15)
	60–69	1.84	(1.16–2.94)
	70–79	2.55	(1.60–4.07)
	≥80	3.65	(2.28–5.83)
Sex	Female	1.00	(reference)
	Male	1.09	(1.03–1.15)
Operation in medical center	No	1.13	(1.06–1.19)
	Yes	1.00	(reference)
Types of surgery	Musculoskeletal	3.39	(2.07–5.54)
	Digestive	5.27	(3.22–8.62)
	Neurosurgery	8.45	(5.16–13.8)
	Cardiovascular	8.03	(4.89–13.2)
	Respiratory	6.19	(3.68–10.4)
	Skin	4.89	(2.85–8.39)
	Eye	1.00	(reference)
	Breast	3.02	(1.56–5.84)
	Delivery, CS, abortion	3.87	(1.58–9.52)
	Others	2.73	(1.66–4.50)
Types of anesthesia	Epidural or spinal	1.00	(reference)
	General	1.23	(1.14–1.33)
Myocardial infarction	Yes vs no	2.17	(1.41–3.32)
Alcohol-related illness	Yes vs no	1.88	(1.14–3.10)
Parkinson's disease	Yes vs no	1.45	(1.08–1.94)
Epilepsy	Yes vs no	3.97	(1.77–8.92)
Diabetes	Yes vs no	1.15	(1.07–1.23)
Number of hospitalizations	0	1.00	(reference)
	1	1.18	(1.10–1.26)
	2	1.38	(1.25–1.51)
	≥3	1.74	(1.58–1.91)
Number of emergency visits	0	1.00	(reference)
	1	1.27	(1.18–1.36)
	2	1.37	(1.25–1.50)
	≥3	1.47	(1.36–1.60)

Note: [a]Adverse events include stroke, pneumonia, urinary tract infection, septicemia, and 30-day in-hospital mortality.
Abbreviations: CI, confidence interval; OR, odds ratio.