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

Yih-Guien Cherng¹,²
Chuen-Chau Chang²,³,⁴
Chun-Chieh Yeh⁵,⁶
Yung-Ho Hsu⁷
Ta-Liang Chen⁸,⁹,*
Chien-Chang Liao¹⁰,¹¹,¹²

¹Department of Anesthesiology, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan; ²Department of Anesthesiology, School of Medicine, College of Medicine, Taipei Medical University, Taipei, Taiwan; ³Department of Anesthesiology, Taipei Medical University Hospital, Taipei, Taiwan; ⁴Anesthesiology and Health Policy Research Center, Taipei Medical University Hospital, Taipei, Taiwan; ⁵Department of Surgery, China Medical University Hospital, Taichung, Taiwan; ⁶Department of Surgery, University of Illinois, Chicago, USA; ⁷Department of Nephrology, Shuang Ho Hospital, Taipei Medical University, New Taipei City, Taiwan; ⁸Department of Anesthesiology, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan; ⁹School of Chinese Medicine, College of Chinese Medicine, China Medical University, Taichung, Taiwan; ¹⁰Research Center of Big Data and Meta-analysis, Wan Fang Hospital, Taipei Medical University, Taipei, Taiwan

*These authors contributed equally to this work

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 postoperative 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.\textsuperscript{5,6,9–14}

Associated comorbidities, including diabetes mellitus, hypertension, hyperlipidemia, or cardiac diseases,\textsuperscript{1,5,6,8} may complicate CKD, in terms of surgical outcomes.\textsuperscript{5,15}

In several widely used surgical risk indices, kidney dysfunction has often been listed as a major predictive factor.\textsuperscript{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\textsuperscript{1,8,15} that may have differential impacts on postoperative adverse outcomes.\textsuperscript{3–5,18} Although the perioperative outcomes of surgical risks in patients with CKD have been reported,\textsuperscript{3–5,9} there were several limitations in the previous studies, such as small sample size,\textsuperscript{3,9,19,20} inadequate adjustments for potential confounders,\textsuperscript{9,19–22} and focus on a single surgical procedure or a specific population.\textsuperscript{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 with 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, 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        | 6335 (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)
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. The postoperative mortality in patients with CKD differed in the various types of surgeries, and the corresponding complication rate was associated with both the preoperative stage of CKD and the estimated glomerular filtration rate (eGFR). 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. 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. 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. In our investigation,

|                      | 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                     | 296,852           | (60.7)          | 29,300| (24.0)          | <0.0001|
| 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.
Table 2 Characteristics of patients received nonurological surgeries with and without chronic kidney disease

| Category                              | No CKD (N=35,643) | CKD (N=35,643) | P  |
|---------------------------------------|-------------------|----------------|----|
|                                       | n (% )            | n (% )         |
| Age, years                            |                   |                |    |
| 20–29                                 | 223 (0.6)         | 223 (0.6)      | 1.0000 |
| 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)    |    |
| Cancer                                | 4068 (11.4)       | 4068 (11.4)    |    |
| Mental disorders                      | 3863 (10.8)       | 3863 (10.8)    |    |
| Peptic ulcer disease                  | 2936 (8.2)        | 2936 (8.2)     |    |
| COPD                                  | 1858 (5.2)        | 1858 (5.2)     |    |
| Gout                                  | 1856 (5.2)        | 1856 (5.2)     |    |
| Anemia                                | 1824 (5.1)        | 1824 (5.1)     |    |
| Atherosclerosis                       | 903 (2.5)         | 903 (2.5)      |    |
| Pneumonia                             | 602 (1.7)         | 602 (1.7)      |    |
| Asthma                                | 554 (1.6)         | 554 (1.6)      |    |
| Osteoporosis                          | 434 (1.2)         | 434 (1.2)      |    |
| Liver cirrhosis                       | 353 (1.0)         | 353 (1.0)      |    |
| Angina                                | 372 (1.0)         | 372 (1.0)      |    |

(Continued)
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.\(^\text{24,25}\) Other factors contributing to the abnormal cardiovascular outcomes included accelerated atherogenesis, nutritional effects, endothelial dysfunction, metabolic changes, coronary artery calcification, and left ventricle abnormalities.\(^\text{25}\)

Medical and surgical infections are common in patients with CKD.\(^\text{26-29}\) 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 glycoalyx, and impaired host immunity were shown to be associated with different types of infectious adverse outcomes.\(^\text{26,27,30}\) 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.\(^\text{29}\) Local wound infection was solely notably increased in advanced CKD,\(^\text{27,29}\) 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.\(^\text{31}\)

|                | No CKD (N=35,643) | CKD (N=35,643) | P     |
|----------------|-------------------|----------------|-------|
|                | n      | (%)  | n      | (%)  |       |
| Heart failure  | 303    | (0.9)| 303    | (0.9)| 1.0000|
| Venerreal 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 | 18,344 | (51.5)| 18,344 | (51.5)| 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 | 15,573 | (43.7)| 15,573 | (43.7)| 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.
In the nonoperative condition, individuals with CKD had greater chances of bleeding. 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. 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.

CKD was also considered to be an independent risk factor for blood transfusion predictions. 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. Abnormal platelet adhesion has been observed to be due to the functional derangement of the interaction between von-Willebrand factors and glycoproteins Ib-IIIa as well as increased production of prostacyclin and nitric oxide, which makes platelet activation in CKD patients difficult. Furthermore, inadequate platelet stores of adenosine diphosphate (ADP), as well as inadequate serotonin levels, cyclooxygenase defects, decreased thromboxane A2 synthesis, and altered calcium mobilization, also appear to be associated with bleeding diathesis.

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

| Postoperative outcomes                  | No CKD (N=35,643) | CKD (N=35,643) | Risk of outcomes |
|----------------------------------------|-------------------|----------------|-----------------|
| **Postoperative outcomes**             | Events           | %              | Event           | %              | OR (95% CI)*     |
| 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                | 3938±5195        |                | 4598±5700       |                | p<0.0001         |
| Length of hospital stay, days          | 11.0±16.5        |                | 13.2±17.8       |                | p<0.0001         |

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

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

(Continued)
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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Author contributors
All authors contributed to study design, data analysis, drafting or revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure
The authors report no conflicts of interest in this work.

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Note: *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.
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# Supplementary material

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

|                      | 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:** *Adverse events include stroke, pneumonia, urinary tract infection, septicemia, and 30-day in-hospital mortality.

**Abbreviations:** CI, confidence interval; OR, odds ratio.
