Patients with PD had increased risk of postoperative pulmonary embolism (OR 2.72, 95% CI 1.45–5.10), stroke (OR 1.77, 95% CI 1.53–2.05), pneumonia (OR 1.98, 95% CI 1.70–2.31), urinary tract infection (OR 1.52, 95% CI 1.35–1.70), septicemia (OR 1.54, 95% CI 1.37–1.73), acute renal failure (OR 1.36, 95% CI 1.07–1.73), and mortality (OR 1.45, 95% CI 1.06–1.98). The association between preoperative PD and postoperative adverse events was significant in both sexes and every age group. Low income, ≥65 years of age, surgery not in medical center, highest quartile of PD medication users, and more medical conditions worsened the risk of postoperative adverse events in patients with PD.

This study showed increased postoperative complications and mortality in patients with PD. Our findings suggest that revision of postoperative care protocols for this population is urgently needed.
program started in March 1995, and now covers more than 99% of 22.6 million Taiwan residents. Taiwan’s National Health Research Institutes established the NHIRD to record all beneficiaries’ inpatient and outpatient medical services. Information in the database includes patient demographics, primary and secondary disease diagnoses, procedures, prescriptions, and medical expenditures. The validity of this database has been favorably evaluated, and research articles based on it have been accepted in prominent scientific journals worldwide.12–18

Ethical Approval

Insurance reimbursement claims used in this study were from Taiwan’s NHIRD. This study was conducted in accordance with the Helsinki Declaration. To protect personal privacy, the electronic database was decoded with patient identifications scrambled for further academic access for research. According to National Health Research Institutes regulations, informed consent is not required because of the use of decoded and scrambled patient identifications.12–17 However, this study was evaluated and approved by Taiwan’s NHIRD-103–121 and the Institutional Review Board of Taipei Medical University (TMU-JIRB-201404070).

Study Design

We examined medical claims and identified 6455 patients aged ≥60 years with preoperative PD (at least 3 visits of medical care with physician’s primary diagnosis of PD and PD medications) from 2,023,346 patients who underwent major inpatient surgeries between 2008 and 2012 in Taiwan. These surgeries required general, epidural, or spinal anesthesia and hospitalization for more than 1 day. To identify patients with PD, we required at least 1 visit for outpatient or inpatient medical services, with a neurological physician’s diagnosis of PD within the 24-month preoperative period. We matched each surgical patient with PD with 2 randomly selected surgical patients without PD by sex, age, type of surgery, type of anesthesia, coexisting medical conditions, operation in teaching hospital or not, and low income or not, and conducted the analysis with a propensity score-matched pair procedure (case-control ratio = 1:2). The complications, length of hospital stay, medical expenditure, admission to intensive care unit, and mortality within postoperative 30-day period were compared between surgical patients with and without preoperative PD.

Measures and Definitions

We identified income status by defining low-income patients as those qualifying for waived medical copayment, because this status is verified by the Bureau of National Health Insurance. Whether the surgery was performed in a medical center, the time of surgery and the types of surgery and anesthesia were also recorded. We used the “International Classification of Diseases, Ninth Revision, Clinical Modification” (ICD-9-CM) to define preoperative medical diseases and postoperative complications. Preoperative PD (ICD-9-CM 332) was defined as the major exposure. Preexisting medical conditions that were determined from medical claims for the 24-month preoperative period included mental disorders (ICD-9-CM 290–319), hypertension (ICD-9-CM 401–405), diabetes (ICD-9-CM 250), chronic obstructive pulmonary disease (ICD-9-CM 490–496), hyperlipidemia (ICD-9-CM 272.0, 272.1, and 272.2), liver cirrhosis (ICD-9-CM 571), congestive heart failure (ICD-9-CM 428), and atrial fibrillation (427.3). Renal dialysis was defined by administration code (D8, D9). Inhospital 30-day mortality after the index surgery was considered the study’s primary outcome. Nine major surgical postoperative complications were noted, including pulmonary embolism (ICD-9-CM 415), stroke (ICD-9-CM 430–438), pneumonia (ICD-9-CM 480–486), urinary tract infection (ICD-9-CM 599.0), sepsis (ICD-9-CM 038, 998.5), acute renal failure (ICD-9-CM 584), postoperative bleeding (ICD-9-CM 998.0, 998.1 and 998.2), acute myocardial infarction (ICD-9-CM 410), and deep wound infection (ICD-9-CM 958.3) after the index surgery. Admission to intensive care unit, length of hospital stay, and medical expenditure after index surgery were analyzed as secondary outcomes.

Statistical Analysis

To reduce confounding errors,12,13,16 this study used a propensity score-matched pair procedure to balance the covariates between surgical patients with and without PD. We developed a nonparsimonious multivariable logistic regression model to estimate a propensity score for preoperative PD. Clinical significance guided the initial choice of covariates in this model: sex, age, operation in medical center or not, low-income status, mental disorders, hypertension, diabetes, chronic obstructive pulmonary disease, hyperlipidemia, renal dialysis, liver cirrhosis, congestive heart failure, atrial fibrillation, types of surgery and anesthesia, and time of surgery. A structured iterative approach was used to refine this model with the goal of achieving covariate balance within the matched pairs. We used chi-square tests to measure covariate balance, and P < 0.05 was suggested to represent meaningful covariate imbalance. We matched patients with PD to non-PD patients using a greedy-matching algorithm with a caliper width of 0.2 SD of the log odds of the estimated propensity score. This method could remove 98% of the bias from measured covariates.12,13,16

Adjusted odds ratios (ORs) with 95% confidence intervals (CIs) for 30-day postoperative complications and mortality between patients with and without PD were analyzed with multivariate logistic regression models by controlling for age, sex, operation in medical center, low-income status, mental disorders, hypertension, diabetes, chronic obstructive pulmonary disease, hyperlipidemia, renal dialysis, liver cirrhosis, congestive heart failure, atrial fibrillation, types of surgery and anesthesia, and time of surgery. We also performed stratification analysis by age, sex, and coexisting medical conditions for associations between preoperative PD and postoperative adverse events (including 30-day inhospital mortality, pulmonary embolism, stroke, pneumonia, urinary tract infection, and sepsis). The multivariate logistic regression analyses were applied to investigate 30-day postoperative adverse events associated with characteristics of PD after controlling for age, sex, operation in medical center or not, low-income status, mental disorders, hypertension, diabetes, chronic obstructive pulmonary disease, hyperlipidemia, renal dialysis, liver cirrhosis, congestive heart failure, atrial fibrillation, types of surgery and anesthesia, and time of surgery. SAS version 9.1 (SAS Institute Inc., Cary, NC) statistical software was used for data analyses; 2-sided P < 0.05 indicated significant differences.

RESULTS

Table 1 shows demographic characteristics of patients with and without preoperative PD who underwent major surgeries. After propensity score matching, there were no significant differences in perioperative characteristics between surgical
TABLE 1. Characteristics of Surgical Patients With and Without Parkinson Disease

| No PD (n = 12910)  | PD (n = 6455)  | n (%) | n (%) | P    |
|--------------------|---------------|-------|-------|------|
| Age, years         |               |       |       |      |
| 60–64              | 1238 (9.6)    | 619 (9.6) |       | 1.0000 |
| 65–69              | 2158 (16.7)   | 1079 (16.7) |       |      |
| 70–74              | 3996 (31.0)   | 1998 (31.0) |       |      |
| 75–79              | 5518 (42.7)   | 2759 (42.7) |       |      |
| Mean ± SD          | 72.8 ± 5.1    | 73.0 ± 5.1 | 0.0340 |      |
| Sex                |               |       |       |      |
| Female             | 6674 (51.7)   | 3337 (51.7) |       | 1.0000 |
| Male               | 6236 (48.3)   | 3118 (48.3) |       |      |
| Low income         | 192 (1.5)     | 96 (1.5) |       | 1.0000 |
| Operation in medical center | 4268 (33.1) | 2134 (33.1) |       | 1.0000 |
| Coexisting medical conditions |  |       |       |      |
| Mental disorders   | 5420 (42.0)   | 2710 (42.0) |       | 1.0000 |
| Hypertension       | 5928 (45.9)   | 2964 (45.9) |       | 1.0000 |
| Diabetes           | 3584 (27.8)   | 1792 (27.8) |       | 1.0000 |
| COPD               | 2108 (16.3)   | 1054 (16.3) |       | 1.0000 |
| Hyperlipidemia     | 654 (5.1)     | 327 (5.1) |       | 1.0000 |
| Renal dialysis     | 362 (2.8)     | 181 (2.8) |       | 1.0000 |
| Liver cirrhosis    | 286 (2.2)     | 143 (2.2) |       | 1.0000 |
| Congestive heart failure | 342 (2.7)  | 171 (2.7) |       | 1.0000 |
| Atrial fibrillation | 42 (0.3)     | 21 (0.3) |       | 1.0000 |
| Types of surgery   |               |       |       |      |
| Skin               | 170 (1.3)     | 85 (1.3) |       | 1.0000 |
| Breast             | 100 (0.8)     | 50 (0.8) |       | 1.0000 |
| Musculoskeletal     | 5932 (46.0)   | 2966 (46.0) |       |      |
| Respiratory        | 436 (3.4)     | 218 (3.4) |       | 1.0000 |
| Cardiovascular     | 578 (4.5)     | 289 (4.5) |       | 1.0000 |
| Digestive          | 3172 (24.6)   | 1586 (24.6) |       |      |
| Kidney, ureter, bladder | 1176 (9.1)  | 588 (9.1) |       |      |
| Eye                | 136 (1.1)     | 68 (1.1) |       | 1.0000 |
| Others             | 1210 (9.4)    | 605 (9.4) |       | 1.0000 |
| Types of anesthesia |           |       |       |      |
| General            | 8228 (63.7)   | 4114 (63.7) |       | 1.0000 |
| Epidural or spinal | 4682 (36.3)   | 2341 (36.3) |       |      |
| Time of anesthesia, minutes |  |       |       | 1.0000 |
| ≤120               | 6742 (52.2)   | 3371 (52.2) |       |      |
| 121–240            | 2460 (19.1)   | 1230 (19.1) |       |      |
| 241–300            | 960 (7.4)     | 480 (7.4) |       | 1.0000 |
| ≥301               | 2748 (21.3)   | 1374 (21.3) |       |      |
| Mean ± SD          | 225.6 ± 199.7 | 225.4 ± 197.0 | 0.9493 |      |

PD = Parkinson disease.

In this large-scale nationwide population-based study, patients with PD undergoing non-neurological surgery had higher 30-day postoperative mortality compared with those without PD. Higher incidence of postoperative complications in patients with PD included pulmonary embolism, pneumonia, stroke, urinary tract infection, and septicemia after multivariate adjustment. Increased risk of admission to intensive care unit, prolonged length of hospital stay, and increased medical expenditure were also found in surgical patients with PD. Departing from previous studies,6–11 our novel findings were that advanced age, medical conditions, and heavy PD medication were associated with postoperative adverse events in patients with PD.

Greater age,19 low-income status,20 and level of hospital21 were determinants of perioperative adverse outcomes. To avoid bias when investigating postoperative adverse outcomes in patients with PD, we used multivariate regression models to adjust these sociodemographic characteristics as potential confounding factors. As revealed by our database, previous studies from our database have that diabetes,3,12 stroke,13 heart failure,22 atrial fibrillation,23 liver cirrhosis,14 renal dialysis,24 chronic obstructive conditions such as diabetes (OR 2.00, 95% CI 1.78–2.25), chronic obstructive pulmonary disease (OR 1.76, 95% CI 1.51–2.04), and mental disorders (OR 1.70, 95% CI 1.53–1.89) worsen the risk of postoperative adverse events in PD patients compared with those without PD.

DISCUSSION

In this large-scale nationwide population-based study, patients with PD undergoing non-neurological surgery had higher 30-day inhospital mortality compared with those without PD. Higher incidence of postoperative complications in patients with PD included pulmonary embolism, pneumonia, stroke, urinary tract infection, and septicemia after multivariate adjustment. Increased risk of admission to intensive care unit, prolonged length of hospital stay, and increased medical expenditure were also found in surgical patients with PD. Departing from previous studies,6–11 our novel findings were that advanced age, medical conditions, and heavy PD medication were associated with postoperative adverse events in patients with PD.

Greater age,19 low-income status,20 and level of hospital21 were determinants of perioperative adverse outcomes. To avoid bias when investigating postoperative adverse outcomes in patients with PD, we used multivariate regression models to adjust these sociodemographic characteristics as potential confounding factors. Previous studies from our database have revealed that diabetes,3,12 stroke,13 heart failure,22 atrial fibrillation,23 liver cirrhosis,14 renal dialysis,24 chronic obstructive
TABLE 2. Risk of Postoperative Complications and Mortality for Surgical Patients with Preoperative Parkinson Disease

| Postoperative Outcomes | No PD (n = 12910) | PD (n = 6455) | Risk of Outcome |
|------------------------|-------------------|--------------|-----------------|
|                        | Events | %   | Event | %   | OR (95% CI) |                        |
| 30-day inhospital mortality | 99     | 0.77 | 71    | 1.10 | 1.45 (1.06–1.98) |
| Postoperative complications |       |      |       |      |            |                        |
| Pulmonary embolism      | 17     | 0.13 | 23    | 0.36 | 2.72 (1.45–5.10) |
| Stroke                  | 411    | 3.18 | 354   | 5.48 | 1.77 (1.53–2.05) |
| Pneumonia               | 377    | 2.92 | 353   | 5.47 | 1.98 (1.70–2.31) |
| Urinary tract infection | 781    | 6.05 | 6.05  | 8.78 | 1.52 (1.35–1.70) |
| Septicemia              | 732    | 5.67 | 538   | 8.33 | 1.54 (1.37–1.73) |
| Acute renal failure     | 175    | 1.36 | 117   | 1.81 | 1.36 (1.07–1.73) |
| Postoperative bleeding  | 88     | 0.68 | 39    | 0.60 | 0.89 (0.61–1.29) |
| Acute myocardial infection | 78   | 0.60 | 45    | 0.70 | 1.17 (0.80–1.70) |
| Deep wound infection    | 69     | 0.53 | 32    | 0.50 | 0.93 (0.61–1.41) |
| Adverse events          | 2093   | 16.21| 1544  | 23.92| 1.66 (1.54–1.80) |
| ICU stay                | 3753   | 29.07| 2075  | 32.15| 1.19 (1.11–1.28) |
| Medical expenditure, USD | 2788 ± 4024 | 3010 ± 4632 | P = 0.0010 |
| Length of hospital stay, days | 8.4 ± 12.5 | 9.5 ± 14.9 | P < 0.0001 |

CI = confidence interval, ICU = intensive care unit, OR = odds ratio, PD = Parkinson disease, USD = United States dollars.

* Adjusted for age, sex, low income, operation in medical center, types of anesthesia, types of surgery, coexisting medical conditions, and time of anesthesia.

† Adverse events after non-neurological surgery included 30-day inhospital mortality, pulmonary embolism, stroke, pneumonia, urinary tract infection, and septicemia.

TABLE 3. Stratification Analysis of Associations Between Parkinson Disease and Postoperative Adverse Events

| Adverse Events | No PD | PD | Risk of outcomes† |
|---------------|------|----|-------------------|
|               | n    | Events | %     | n    | Events | %     | OR (95% CI) |                |
| Female        | 6674 | 971   | 14.55 | 3337 | 697   | 20.89 | 1.59 (1.43–1.78) |
| Male          | 6236 | 1122  | 17.99 | 3118 | 847   | 27.16 | 1.74 (1.57–1.93) |
| 60–64 years   | 1238 | 136   | 10.99 | 619  | 111   | 17.93 | 1.83 (1.38–2.41) |
| 65–69 years   | 2158 | 263   | 12.19 | 1079 | 228   | 21.13 | 2.00 (1.64–2.45) |
| 70–74 years   | 3996 | 646   | 16.17 | 1998 | 478   | 23.92 | 2.00 (1.64–2.45) |
| 75–79 years   | 5518 | 1048  | 18.99 | 2759 | 727   | 26.35 | 1.56 (1.39–1.74) |
| No mental disorders | 7490 | 1219  | 16.28 | 3745 | 909   | 24.27 | 1.69 (1.53–1.87) |
| Mental disorders | 5420 | 874   | 16.13 | 2710 | 635   | 23.53 | 1.62 (1.45–1.83) |
| No hypertension | 6982 | 1145  | 16.40 | 3491 | 828   | 23.72 | 1.63 (1.47–1.80) |
| Hypertension   | 5928 | 948   | 15.99 | 2964 | 716   | 24.16 | 1.72 (1.53–1.92) |
| No diabetes    | 9326 | 1426  | 15.29 | 4663 | 1064  | 22.82 | 1.68 (1.53–1.84) |
| Diabetes       | 3584 | 667   | 18.61 | 1792 | 480   | 26.79 | 1.64 (1.43–1.88) |
| No COPD        | 10802 | 1698 | 15.72 | 5401 | 1269  | 23.50 | 1.69 (1.55–1.84) |
| COPD           | 2108 | 395   | 18.74 | 1054 | 275   | 26.09 | 1.57 (1.31–1.88) |
| No hyperlipidemia | 12256 | 2019 | 16.47 | 6128 | 1487  | 24.27 | 1.66 (1.54–1.80) |
| Hyperlipidemia | 654  | 74    | 11.31 | 327  | 57    | 17.43 | 1.70 (1.16–2.51) |
| No renal dialysis | 12548 | 1998 | 15.92 | 6274 | 1493  | 23.80 | 1.67 (1.54–1.80) |
| Renal dialysis  | 362  | 95    | 26.24 | 181  | 51    | 28.18 | 1.11 (0.73–1.68) |
| No liver cirrhosis | 12624 | 2057 | 16.29 | 6312 | 1510  | 23.92 | 1.65 (1.53–1.79) |
| Liver cirrhosis | 286  | 36    | 12.59 | 143  | 34    | 23.78 | 2.32 (1.35–4.00) |
| No CHF         | 12568 | 2000 | 15.91 | 6284 | 1505  | 23.95 | 1.68 (1.56–1.81) |
| CHF            | 342  | 93    | 27.19 | 171  | 39    | 22.81 | 0.78 (0.50–1.21) |
| No atrial fibrillation | 12868 | 2087 | 16.22 | 6434 | 1538  | 23.90 | 1.64 (1.52–1.76) |
| Atrial fibrillation | 42   | 6     | 14.29 | 21   | 6     | 28.57 | 3.16 (0.70–14.3) |

CHF = congestive heart failure, CI = confidence interval, COPD = chronic obstructive pulmonary disease, OR = odds ratio, PD = Parkinson disease.

* Adverse events after non-neurological surgery including 30-day inhospital mortality, pulmonary embolism, stroke, pneumonia, urinary tract infection, and septicemia.

† Multivariate adjustment.
pulmonary disease,25 and mental disorders15 were noted as risk factors of perioperative complications and mortality. Some of these coexisting medical conditions were also considered as comorbidities for patients with PD.26,27 By adjusting for the potential confounding factors, this study found increased postoperative adverse events in patients with PD.

Increased postoperative pneumonia and urinary tract infection in patients with PD had been reported in previous studies,6,7 and this phenomenon was also found in this study. In patients with advanced PD, dysphagia and poor control of the respiratory musculature can result in atelectasis, reduced cough, and saliva accumulation.28,29 Restrictive changes in lungs mainly secondary to chest wall rigidity and upper airway obstruction may present in patients with PD.30 It is plausible that these patients are at increased risk for pneumonia after operations.31 Preoperative assessment of respiratory function and postoperative

### TABLE 4. Preoperative Characteristics of Patients With Parkinson’s Disease and Risk of 30-Day Postoperative Adverse Events

| Preoperative Characteristics of PD Within 24 Months | n     | Events | Incidence, % | OR (95% CI) |
|----------------------------------------------------|-------|--------|--------------|-------------|
| Non-PD controls                                    | 12910 | 2093   | 16.21        | 1.00 (reference) |
| PD patients                                        |       |        |              |             |
| Age ≥65 years                                      | 5836  | 1433   | 24.55        | 1.72 (1.59–1.86) |
| Low-income status                                  | 96    | 33     | 34.38        | 3.45 (2.23–5.32) |
| Surgery not in medical center                      | 2134  | 481    | 22.54        | 1.52 (1.36–1.71) |
| With diabetes                                      | 1792  | 480    | 26.79        | 2.00 (1.78–2.25) |
| With COPD                                          | 1054  | 275    | 26.09        | 1.76 (1.51–2.04) |
| With mental disorders                              | 2710  | 635    | 23.43        | 1.70 (1.53–1.89) |
| Preoperative rehabilitation for PD                 |       |        |              |             |
| No rehabilitation                                  | 6132  | 1448   | 23.61        | 1.64 (1.52–1.77) |
| Simple rehabilitation                              | 139   | 35     | 25.18        | 1.66 (1.11–2.47) |
| Intensive rehabilitation                           | 184   | 61     | 33.15        | 2.60 (1.89–3.58) |
| Use of PD medications†                              |       |        |              |             |
| Low                                                | 1613  | 350    | 21.70        | 1.47 (1.29–1.68) |
| Moderate                                           | 1614  | 356    | 22.06        | 1.47 (1.29–1.67) |
| High                                               | 1615  | 425    | 26.32        | 1.88 (1.66–2.13) |
| Very high                                          | 1613  | 413    | 25.60        | 1.86 (1.64–2.10) |
| Expenditure on PD medications‡                     |       |        |              |             |
| Low                                                | 1613  | 340    | 21.08        | 1.39 (1.22–1.58) |
| Moderate                                           | 1614  | 354    | 21.93        | 1.49 (1.31–1.70) |
| High                                               | 1614  | 432    | 26.77        | 1.93 (1.70–2.18) |
| Very high                                          | 1614  | 418    | 25.90        | 1.89 (1.67–2.14) |
| Use of PD medications†                              |       |        |              |             |
| One type of PD medication                          | 108   | 30     | 27.78        | 2.10 (1.36–3.25) |
| ≥2 types of PD medications                         | 6347  | 1514   | 23.85        | 1.66 (1.54–1.79) |
| Preoperative medical expenditure                   |       |        |              |             |
| Low                                                | 1614  | 311    | 19.27        | 1.38 (1.20–1.58) |
| Moderate                                           | 1614  | 347    | 21.50        | 1.51 (1.32–1.72) |
| High                                               | 1614  | 394    | 24.41        | 1.71 (1.51–1.94) |
| Very high                                          | 1613  | 492    | 30.50        | 2.06 (1.83–2.33) |
| Preoperative emergency care                        |       |        |              |             |
| 0                                                  | 1988  | 379    | 19.06        | 1.34 (1.18–1.52) |
| 1                                                  | 1420  | 317    | 22.32        | 1.57 (1.37–1.80) |
| 2                                                  | 982   | 239    | 24.34        | 1.73 (1.48–2.02) |
| ≥3                                                 | 2065  | 609    | 29.49        | 2.02 (1.81–2.25) |
| Preoperative inpatient care                        |       |        |              |             |
| 0                                                  | 2221  | 447    | 20.13        | 1.46 (1.30–1.64) |
| 1                                                  | 1697  | 365    | 21.51        | 1.51 (1.33–1.72) |
| 2                                                  | 983   | 232    | 23.60        | 1.56 (1.33–1.83) |
| ≥3                                                 | 1554  | 500    | 32.18        | 2.20 (1.95–2.48) |

CI = confidence interval, COPD = chronic obstructive pulmonary disease, OR = odds ratio, PD = Parkinson disease.

†Adverse events include: 30-day inhospital mortality, pulmonary embolism, stroke, septicemia, pneumonia, acute renal failure, and urinary tract infection.

†Adjusted for age, sex, low income, operation in medical center, types of anesthesia, types of surgery, coexisting medical conditions, and time of anesthesia.

†Medications were calculated by mg/days and categorized into quartiles; expenditures were calculated by dollars/days and categorized into quartiles.
chest physiotherapy may be warranted to reduce the incidence of pneumonia. Minimizing the interruption of oral anti-Parkinsonism medication during the perioperative period could help to improve respiratory function.\textsuperscript{32} Urinary tract infection—another infectious complication—can be attributed to PD-related bladder dysfunction that can cause multiple urinary symptoms including urgency, frequency, nocturia, and urinary retention.\textsuperscript{33} Frequent bladder scans to check for retention and higher vigilance in monitoring for urinary infection may be useful to avoid urinary tract infection and treat it as promptly as possible.

In this investigation, we found significant increases in postoperative pulmonary embolism and stroke in patients with PD to our knowledge, these findings have never been documented in previous studies. After surgery, the musculoskeletal problems involved in PD make these patients more vulnerable to reduced mobility than the non-PD population.\textsuperscript{34} Since immobilization is a major risk factor for pulmonary embolism, it is reasonable to postulate that this increased risk in PD patients may relate to prolonged bed rest. Autonomic dysfunction is a common nonmotor symptom of PD\textsuperscript{35} that may present as orthostatic hypotension and cause fluctuations in blood pressure because of impaired baroreceptor activity during the perioperative period.\textsuperscript{29} Both of these conditions may lead to more possibility of acute stroke in surgical patients with PD. Because neuropsychiatric disturbances such as cognitive impairment and depression are also frequent nonmotor symptoms in PD,\textsuperscript{35,36} neurological deficits resulting from stroke may be easily missed by healthcare providers. Frequent blood pressure checks and early recognition of stroke symptoms could be encouraged to better avoid and manage this devastating postoperative complication.

In terms of increased 30-day inhospital mortality, length of hospital stay, and medical expenditure, there are several possible explanations why patients with PD had worse outcomes. First, anti-Parkinsonism oral medication schedules are difficult to maintain during the perioperative period, so exacerbation of PD symptoms is likely.\textsuperscript{29} The aggravating condition of PD may lead to immobility, which can accompany many fatal outcomes such as pulmonary embolism,\textsuperscript{37} infection,\textsuperscript{34} and pressure ulcer.\textsuperscript{16} Second, neuropsychiatric disturbances, including cognitive impairment, depression, and hallucinations, are not uncommon in patients with PD.\textsuperscript{35,36} These complex clinical problems can delay recovery during acute care services and increase postoperative complications.\textsuperscript{15,17}

Third, the increased risk of major adverse events such as stroke and pneumonia noted in this study can predispose patients with PD to higher mortality rates. To improve surgical outcomes in patients with PD, healthcare teams should optimize perioperative care by managing these specific issues according to updated guidelines.

In the subgroup analysis, the ORs of 30-day inhospital adverse events in PD patients with some coexisting medical conditions were lower than those without such comorbidities as renal dialysis and heart failure. This can be attributed to the harmful effects of those comorbidities, which decreased the influence on postoperative adverse events from PD itself. The association between PD and risk of postoperative adverse event was similar in patients with and without diabetes in this study. Although the potential link between PD and diabetes remains controversial, recent studies have demonstrated these 2 chronic diseases share similarly dysregulated molecular pathways.\textsuperscript{18}

Further analysis in patients with PD revealed that preoperative intensive rehabilitation and higher intake of and expenditure on PD medication were associated with higher risks of postoperative adverse events. These findings might indirectly reflect the detrimental effects from disease severity, since it was shown that disease severity was correlated with patient expenditure.\textsuperscript{39} In addition, the present study found that postoperative adverse events increased in PD patients with higher preoperative medical expenditure, more preoperative emergency visits, or more inpatient care. These 3 medical characteristics might be considered indicators of poor general physical or medical status that lead to increased postoperative adverse events.

Although the present study has strengths of large sample size, adjustment for potential confounding factors, analyzing all types of non-neurological surgery, and not being restricted by specific patient groups, there are some limitations common to research based on secondary data. First, detailed information on sociodemographic factors and lifestyles correlating with the postoperative complications or PD was not available from reimbursement claims data. Nor did the database contain patients’ records from physical and laboratory examinations. Second, severity and disability levels of PD could not be obtained in the administrative data for stratification of perioperative risks. Third, even though the accuracy of major diagnosis codes from the NHIRD has been accepted by peer reviewers of scientific journals,\textsuperscript{12,13,15–18} the validity of PD, comorbidity, and complication codes employed in this study might still be a concern. To reduce the possibility of misdiagnosis or miscoding, we used the inclusion criteria of at least 3 visits for medical care with physician’s primary diagnosis of PD.

In conclusion, this nationwide population-based study showed that patients with PD undergoing non-neurological surgery have higher 30-day mortality and more common postoperative major complications, including pulmonary embolism, stroke, pneumonia, sepsis, acute renal failure, and urinary tract infection. These findings can improve our understanding of these perioperative issues, and also can help healthcare providers to develop specific protocols to minimize complications and hospital stays in surgical patients with PD.

\textbf{REFERENCES}

1. Nussbaum RL, Ellis CE. Alzheimer’s disease and Parkinson’s disease. \textit{N Engl J Med.} 2003;348:1356–1364.
2. De Lau LM, Breteler MM. Epidemiology of Parkinson’s disease. \textit{Lancet Neurol.} 2006;5:525–535.
3. Okun MS. Deep-brain stimulation for Parkinson’s disease. \textit{Lancet Neurol.} 2006;5:525–535.
4. Jamsen E, Puolakka T, Peltola M, et al. Surgical outcomes of revision surgery are increased in patients with Parkinson’s disease: a nationwide registry-based case-controlled study. \textit{Bone Joint J.} 2014;96-B:486–491.
5. Jamsen E, Puolakka T, Peltola M, et al. Surgical outcomes of primary hip and knee replacements in patients with Parkinson’s disease: a nationwide registry-based case-controlled study. \textit{Bone Joint J.} 2014;96-B:486–491.
6. Karadoseh MS, Weaver M, Rodriguez K, et al. Mortality and revision surgery are increased in patients with Parkinson’s disease and fractures of the femoral neck. \textit{Clin Orthop Relat Res.} 2015;473:3272–3279.
10. Mehta S, Vankeulen JP, Booth RE, et al. Total knee arthroplasty in patients with Parkinson’s disease: impact of early postoperative neurologic intervention. *Am J Orthop.* 2008;37:513–516.

11. Weber M, Cabanela ME, Sim FH, et al. Total hip replacement in patients with Parkinson’s disease. *Int Orthop.* 2002;26:66–68.

12. Yeh CC, Liao CC, Chang YC, et al. Adverse outcomes after noncardiac surgery in patients with diabetes: a nationwide population-based retrospective cohort study. *Diabetes Care.* 2013;36:3216–3221.

13. Liao CC, Chang PY, Yeh CC, et al. Outcomes after surgery in patients with previous stroke. *Br J Surg.* 2014;101:1616–1622.

14. Lin CS, Lin SY, Chang CC, et al. Postoperative adverse outcomes after non-hepatic surgery in patients with liver cirrhosis. *Br J Surg.* 2013;100:1784–1790.

15. Liao CC, Shen WW, Chang CC, et al. Surgical adverse outcomes in patients with schizophrenia: a population-based study. *Ann Surg.* 2013;257:433–438.

16. Chou CL, Lee WR, Yeh CC, et al. Adverse outcomes after major surgery in patients with pressure ulcer: a nationwide population-based retrospective cohort study. *PLoS One.* 2015;10:e0127731.

17. Hu CJ, Liao CC, Chang CC, et al. Postoperative adverse outcomes in surgical patients with dementia: a retrospective cohort study. *World J Surg.* 2012;36:2051–2058.

18. Cheng CL, Kao YH, Lin SJ, et al. Validation of the National Health Insurance Research Database with ischemic stroke cases in Taiwan. *Pharmacoepidemiol Drug Saf.* 2011;20:236–242.

19. Afshar AH, Virk N, Porhomayon J, et al. The validity of the VA surgical risk tool in predicting postoperative mortality among octogenarians. *Am J Surg.* 2015;209:274–279.

20. Dik VK, Aarts MJ, Van Grevenstein WM, et al. Association between socioeconomic status, surgical treatment and mortality in patients with colorectal cancer. *Br J Surg.* 2014;101:1173–1182.

21. Leonard D, Penninckx F, Kartheuser A, et al. Effect of hospital volume on quality of care and outcome after rectal cancer surgery. *Br J Surg.* 2014;101:1475–1482.

22. Malje MD, Engoren MC, Tremper KK, et al. Worsening preoperative heart failure is associated with mortality and noncardiac complications, but not myocardial infarction after noncardiac surgery: a retrospective cohort study. *Anesth Analg.* 2014;119:522–532.

23. Attaran S, Shaw M, Bond L, et al. A comparison of outcome in patients with preoperative atrial fibrillation and patients in sinus rhythm. *Ann Thorac Surg.* 2011;92:1391–1395.

24. Gajdos C, Hawn MT, Kile D, et al. Risk of major nonemergent inpatient general surgical procedures in patients on long-term dialysis. *JAMA Surg.* 2013;148:137–143.

25. Gupta H, Ramanan B, Gupta PK, et al. Impact of COPD on postoperative outcomes: results from a national database. *Chest.* 2013;143:1599–1606.

26. Leibson CL, Maragane DM, Bower JH, et al. Comorbid conditions associated with Parkinson’s disease: a population-based study. *Mov Disord.* 2006;21:446–455.

27. Bhattacharjee S, Sambamoorthi U. Co-occurring chronic conditions and health care expenditures associated with Parkinson’s disease: a propensity score matched analysis. *Parkinsonism Relat Disord.* 2013;19:746–750.

28. Mu L, Sobotka S, Chen J, et al. Altered pharyngeal muscles in Parkinson disease. *J Neuroophathol Exp Neurol.* 2012;71:520–530.

29. Katus L, Shiltibans A. Perioperative management of patients with Parkinson’s disease. *Am J Med.* 2014;127:275–280.

30. Shill H, Stacy M. Respiratory function in Parkinson’s disease. *Clin Neurol.* 1998;5:131–135.

31. Easdown LJ, Tessler MJ, Minuk J. Upper airway involvement in Parkinson’s disease resulting in postoperative respiratory failure. *Can J Anaesth.* 1995;42:344–347.

32. Monteiro L, Souza-Machado A, Valderramas S, et al. The effect of levodopa on pulmonary function in Parkinson’s disease: a systematic review and meta-analysis. *Clin Ther.* 2012;34:1049–1055.

33. Yeo L, Singh R, Gundeti M, et al. Urinary tract dysfunction in Parkinson’s disease: a review. *Int Urol Nephrol.* 2012;44:415–424.

34. Gerlach OH, Broen MP, van Domburg PH, et al. Deterioration of Parkinson’s disease during hospitalization: survey of 684 patients *BMC Neurol.* 2012;12:13.

35. Lyons KE, Pahwa R. The impact and management of nonmotor symptoms of Parkinson’s disease. *Am J Manag Care.* 2011;17:S308–S314.

36. Hsu YT, Liao CC, Chang SN, et al. Increased risk of depression in patients with Parkinson disease: a nationwide cohort study. *Am J Geriatr Psychiatry.* 2015;23:934–940.

37. Trujillo-Santos J, Gussoni G, Gadella T, et al. Influence of recent immobilization or surgery on mortality in cancer patients with venous thromboembolism. *Thromb Res.* 2014;133:S29–S34.

38. Santiago JA, Potashkin JA. System-based approaches to decode the molecular links in Parkinson’s disease and diabetes. *Neurobiol Dis.* 2014;72:84–91.

39. Winter Y, Balzer-Geldsetzer M, Spottke A, et al. Longitudinal study of the socioeconomic burden of Parkinson’s disease in Germany. *Eur J Neurol.* 2010;17:1156–1163.