

Outcomes After Non-neurological Surgery in Patients With Parkinson's Disease

A Nationwide Matched Cohort Study

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Abstract: Patients with Parkinson disease (PD) were known to have increased risk of complications during hospitalization. The purpose of this study is to validate the global features of postoperative adverse outcomes for patients with PD.

Using reimbursement claims from Taiwan's National Health Insurance Research Database, we conducted a nationwide retrospective cohort study of 6455 patients with preoperative PD receiving major surgery during 2007 to 2012. With a propensity score matching procedure, 12,910 surgical patients without PD were selected for comparison. The adjusted odds ratios (ORs) and 95% confidence intervals (CIs) for 9 major postoperative complications and 30-day postoperative mortality associated with preoperative PD were calculated in the multivariate logistic regressions.

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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 worsen 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.

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Abbreviations: ICD-9-CM = International Classification of Diseases, 9th Revision, Clinical Modification, CI = confidence interval, OR = odds ratio, PD = Parkinson disease.

INTRODUCTION

Parkinson disease (PD) is the second-most common neurodegenerative disorder worldwide, and mainly affects those in the middle to older age groups.¹ Approximately 1% of the population aged more than 60 years has PD, which is expected to impose an increasing social and economic burden on societies as populations age.² The average annual US healthcare cost for patients with PD is more than twice that of people without PD.^{3,4} Common motor manifestations of PD include tremor at rest, stiffness (rigidity), slowness of movements (bradykinesia), shuffling steps, and difficulties with balance.⁵

Previous studies noted increased adverse events such as aspiration pneumonia and urinary tract infection after surgeries in patients with PD.^{6,7} However, these previous studies were limited by small sample size,^{6,8–11} focusing solely on specific types of surgery,^{7–11} lack of control group,^{10,11} inadequate adjustment for potential confounders,^{6,9–11} and lack of matching procedure.^{7,9–11} In addition, postoperative outcomes in patients with PD were not completely understood.

We conducted a nationwide population-based retrospective cohort study using Taiwan's National Health Insurance Research Database (NHIRD) to investigate the full spectrum of adverse postoperative outcomes, and to analyze the impact of PD severity for patients who underwent major non-neurological surgeries.

METHODS

Data Sources

This study used reimbursement claims data from Taiwan's National Health Insurance program. This universal insurance

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-IRB-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). In-hospital 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), septicemia (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 in-hospital mortality, pulmonary embolism, stroke, pneumonia, urinary tract infection, and septicemia). 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)		P
	n (%)	n (%)	
Age, years			1.0000
60–64	1238 (9.6)	619 (9.6)	
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			1.0000
Female	6674 (51.7)	3337 (51.7)	
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			1.0000
Skin	170 (1.3)	85 (1.3)	
Breast	100 (0.8)	50 (0.8)	
Musculoskeletal	5932 (46.0)	2966 (46.0)	
Respiratory	436 (3.4)	218 (3.4)	
Cardiovascular	578 (4.5)	289 (4.5)	
Digestive	3172 (24.6)	1586 (24.6)	
Kidney, ureter, bladder	1176 (9.1)	588 (9.1)	
Eye	136 (1.1)	68 (1.1)	
Others	1210 (9.4)	605 (9.4)	
Types of anesthesia			1.0000
General	8228 (63.7)	4114 (63.7)	
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)	
≥301	2748 (21.3)	1374 (21.3)	
Mean ± SD	225.6 ± 199.7	225.4 ± 197.0	0.9493

PD = Parkinson disease.

patients with and without PD, including 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. Patients with PD had higher mean age than non-PD group (73.0 ± 5.1 vs 72.8 ± 5.1 years; *P* = 0.0340).

Compared with surgical patients without PD (Table 2), patients with PD showed higher risks of postoperative

complications, including 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 any adverse events (OR 1.66, 95% CI 1.54–1.80). Preoperative PD was associated with a significant increase in 30-day postoperative mortality (OR 1.45, 95% CI 1.06–1.98). Patients with PD were more likely to be admitted to intensive care units after surgery than those without PD (OR 1.19, 95% CI 1.11–1.28). The means of medical expenditure (3010 ± 4632 vs 2788 ± 4024 US dollars; *P* = 0.0010) and length of hospital stay (9.5 ± 14.9 vs 8.4 ± 12.5 days; *P* < 0.0001) were greater in PD patients than in non-PD patients.

The stratification analysis (Table 3) shows that the association between preoperative PD and postoperative adverse events was significant in women (OR 1.59, 95% CI 1.43–1.78), men (OR 1.74, 95% CI 1.57–1.93), patients aged 60 to 64 (OR 1.83, 95% CI 1.38–2.41), 65 to 59 (OR 2.00, 95% CI 1.64–2.45), 70 to 74 (OR 1.67, 95% CI 1.45–1.91), and 75– to 79 (OR 1.56, 95% CI 1.39–1.74) years. Preoperative PD was associated with postoperative adverse events, whether surgical patients had or did not have mental disorders, hypertension, diabetes, chronic obstructive pulmonary disease, hyperlipidemia, or liver cirrhosis. The association between PD and postoperative adverse events was not significant only in surgical patients with renal dialysis, congestive heart failure, and atrial fibrillation.

Compared with patients without PD (Table 4), PD patients ≥65 years of age (OR 1.72, 95% CI 1.59–1.86), with low-income status (OR 3.45, 95% CI 2.23–5.32), with surgery not in medical center (OR 1.52, 95% CI 1.36–1.71), with high PD medications (OR 1.88, 95% CI 1.66–2.13), and with high expenditure for PD (OR 1.93, 95% CI 1.70–2.18) had increased risk of postoperative adverse events. Coexisting medical 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,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 infarction	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.

‡ Mean ± SD.

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	1.67 (1.45–1.91)
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	23.43	1.63 (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.

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	30-Day Postoperative Adverse Events*		
		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 in-hospital 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.

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

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.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.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.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 PD³⁵ that may present as orthostatic hypotension and cause fluctuations in blood pressure because of impaired baroreceptor activity during the perioperative period.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,^{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 in-hospital 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.²⁹ The aggravating condition of PD may lead to immobility, which can accompany many fatal outcomes such as pulmonary embolism,³⁷ infection,³⁴ and pressure ulcer.¹⁶ Second, neuropsychiatric disturbances, including cognitive impairment, depression, and hallucinations, are not uncommon in patients with PD.^{35,36} These complex clinical problems can delay recovery during acute care services and increase postoperative complications.^{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 in-hospital 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.³⁸

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.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,^{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, septicemia, 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.

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