



# Matched cohort analysis of peri-operative outcomes following total knee arthroplasty in patients with and without Parkinson's disease



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## ABSTRACT

**Background:** Increased complication rate has been reported in Parkinson's disease (PD) patients following total knee arthroplasty (TKA). However, this has not previously been studied on a national scale. The purpose of this study was to determine whether PD patients had increased cost, complication, mortality, and length of stay following TKA using a national database.

**Methods:** The HCUP Nationwide Inpatient Sample was evaluated for the years 2000 to 2012. PD patients were matched 1:10 with non-PD control patients for age, sex, Charlson Comorbidity Index (CCI), and year of admission utilizing a propensity score matching procedure. Univariable and multivariable logistic regression were used to determine the relationship between PD and surgical outcomes in the matched cohort.

**Results:** Before matching, TKA patients with PD were significantly older ( $p < 0.0001$ ), more frequently male ( $p < 0.0001$ ), and had a greater CCI ( $p = 0.3058$ ). In the matched cohort, PD was associated with significantly increased length of stay (3.92 vs 3.71 days,  $p < 0.0001$ ) and total hospital charges (\$41,523.52 vs \$40,657.00,  $p = 0.0037$ ). There was no significant difference in in-hospital complication rate (8.28% vs 8.04%,  $p = 0.4297$ ) or in-hospital mortality (0.164% vs 0.150%,  $p = 0.8465$ ) between PD patients and matched non-PD patients.

**Conclusions:** Matched cohort analysis demonstrated statistically significant but clinically minor increases in length and cost of hospitalization for TKA in PD patients. Complication rate and in-hospital mortality rate was not higher in PD patients, suggesting that this group may be safely considered for TKA.

Level of evidence: Prognostic – Level III.

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## 1. Introduction

Parkinson's disease (PD) is a progressive neuromuscular disease associated with bradykinesia, tremor, and postural instability. PD is the second most common neuromuscular disease, affecting one percent of the population over 65 [1]. The variable degrees

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of muscular rigidity and diminished bone quality that may be encountered in PD can present important challenges to the orthopedic surgeon [1,2]. Additionally, the non-motor sequelae, including depression and cognitive decline, further limit the long-term functional performance of these patients [2–5]. Rehabilitation difficulty has also been noted post-operatively, further limiting functional recovery [6,7].

While total knee arthroplasty (TKA) has been used to correct degenerative osteoarthritis in patients with PD, there may be an increased complication rate, higher rates of revision surgery, and worse functional outcomes in this patient population [2,5,8]. Orthopedic surgeons have noted increased intra-operative risk from anesthesia complications and implant malalignment due to flexion contracture [2,9,10]. Increased incidence of post-operative complications have also been noted in PD patients, including prolonged rehabilitation, higher rates of superficial and deep infection, and increased risk of DVT [11]. Long-term complications have also been reported, including accelerated rate of PD progression and diminished long-term functional outcome [11]. Because of these concerns, PD has historically been considered a relative contraindication to TKA, however, previous studies have lacked a matched analysis controlling for comorbidity.

The purpose of this study was to examine the Nationwide Inpatient Sample (NIS) to determine whether patients with PD had inferior in-hospital outcomes after elective TKA compared to a matched cohort of non-PD patients. We hypothesized that the peri-operative complication rate would be increased in PD patients when controlling for patient age and comorbidities.

## 2. Materials and methods

The Healthcare Cost and Utilization Project (HCUP) Nationwide Inpatient Sample (NIS) was used to collect U.S. inpatient data from 2000 to 2012. The NIS is the largest publicly available, all-payer database, containing over seven million de-identified inpatient records annually from 46 participating states [12]. The NIS estimates a 20% stratified sample of national hospital discharges, allowing for results to be generalized to the national population. Primary TKA patients were identified using International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9 CM) procedure codes (code 81.54). Patients with PD were identified using ICD-9 CM diagnosis codes (332.0). Patients with non-elective admission were excluded. Quasi-experimental design was achieved using a propensity score matching procedure as described by Parsons et al. to match each PD patient with 10 non-PD control patients [13]. The propensity score algorithm used a multivariable regression to match patients based on age, sex, Charlson Comorbidity Index (CCI), and year of admission. The CCI was developed to assess a patient's risk for peri-operative mortality based on a validated set of medical comorbidities [14,15]. Univariable and multivariable logistic regression were used to determine the relationship between PD and surgical outcomes in the matched cohort.

The primary outcome studied was in-hospital complication rate, defined using CSS multi-level diagnosis code “16.10: complications”. This represents a composite of device or implant malfunction, complications of surgical procedures, post-operative infection, and hemorrhage, in addition to medical complications including cardiac, respiratory, gastrointestinal, and urinary. Additional outcomes measured included mortality rate, length of stay (LOS), and total hospital charges.

Univariable and multivariable logistic regression were used to determine the relationship between PD and surgical outcomes in the matched cohort, including overall complication rate and in-hospital mortality. Adjusted odds ratios were calculated for demographic predictors of surgical complication. Linear regression was used to determine the relationship between PD and length of stay, and total hospital charges. Student's T-test was used to compare age and CCI between patients with and without PD in the overall total knee arthroplasty population and in the matched cohort. Chi-Square test was used to compare patient sex proportions between PD and non-PD patients. National estimates were calculated using NIS national discharge weights. Statistical analyses were performed utilizing SAS statistical software v.9.4 (SAS Institute, Inc. Cary, NC). Statistical significance was set at  $p < 0.05$ .

## 3. Results

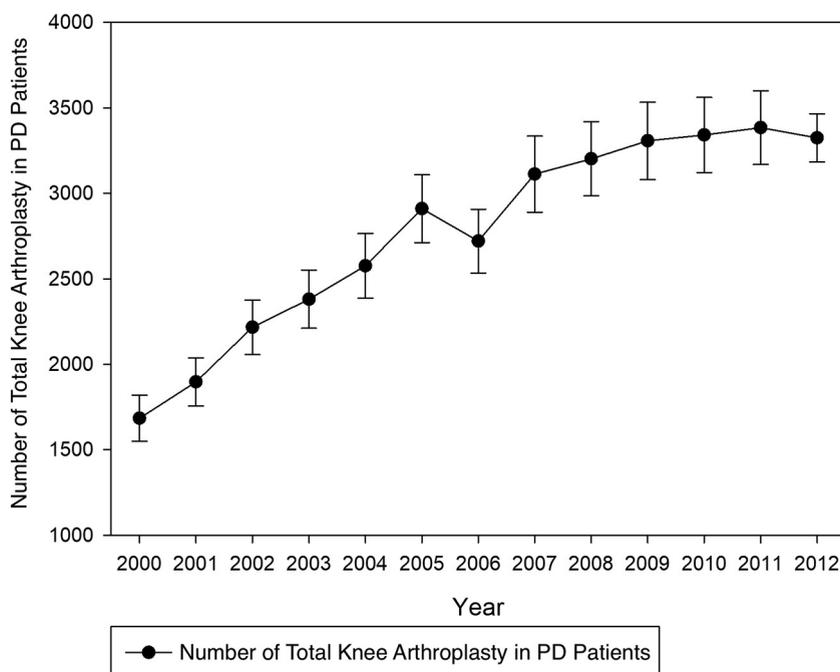
A total of 1,322,621 elective TKAs were performed between 2000 and 2012 and included for analysis. Of these patients, an estimated 7361 (0.56%) had PD. From 2000 to 2012, the estimated number of primary TKAs performed across the United States in patients with PD increased from 1684 in 2000 to 3324 in 2012 ( $p < 0.001$ ), representing a 2.0-fold increase (Figure 1). During this period, the estimated number of TKA performed nationwide increased as well, from 58,008 in 2000 to 126,253 in 2012 ( $p < 0.001$ ).

Before matching, TKA patients with PD were significantly older (72.0 vs 66.5 years old,  $p < 0.0001$ ) and were more likely to be male (48.6% vs 36.5%,  $p < 0.0001$ ), compared with non-PD patients (Table 1). CCI was not significantly different among TKA patients with PD (0.56 vs 0.55,  $p = 0.3058$ ).

The propensity score matching algorithm identified 73,610 non-PD control patients. After the propensity score matching procedure was applied, the demographics of TKA patients with and without PD were no longer different based on age (72.0 vs 72.1,  $p = 0.8921$ ) and sex (48.6% male vs 48.5%,  $p = 0.7495$ ). In the matched cohort, CCI was 0.56 in PD patients and 0.58 in the non-PD patients ( $p = 0.0476$ ) (Table 2).

In the matched cohort, in-hospital complication rate among patients with PD was not significantly increased compared with non-PD control patients (8.3% vs 8.0%,  $p = 0.4297$ ) (Table 3). On multivariable regression, the odds ratio for complication in PD patients was 1.036 (95% CL 0.949–1.130) (Figure 2). Complications were more likely in older patients ( $p < 0.001$ , OR 1.013 [95% CL 1.010–1.017]) and patients with increased CCI ( $p < 0.001$ , OR 1.179 [95% CL 1.149–1.209]). Female patients were less likely to experience complications ( $p < 0.001$ , OR 0.796 [95% CL 0.756–0.837]).

## Nationwide Number of Total Knee Arthroplasty in PD Patients



**Figure 1.** Number of total knee arthroplasty performed nationwide, by year.

Similarly, in-hospital mortality rate was similar in patients with PD (0.16% vs 0.15%,  $p = 0.8465$ ). In contrast, length of stay was significantly longer in patients with PD (3.9 vs 3.7 days,  $p < 0.0001$ ). Older age ( $p < 0.0001$ ) and increased CCI ( $p < 0.0001$ ) were also associated with longer length of stay. Patients with PD averaged total hospital charges of \$41,523, while matched non-PD patients averaged \$40,657 ( $p = 0.0037$ ).

## 4. Discussion

This study revealed that the annual number of TKAs performed on patients with PD has nearly doubled between 2000 and 2012, likely secondary to the increasing prevalence of PD. After matching, patients with PD who underwent TKA had slightly longer hospital lengths of stay and hospital charges; however, in-hospital complication and mortality rate among patients with PD was not significantly increased compared with non-PD control patients.

Peri-operative complications following TKA that have been associated with PD include pneumonia and thromboembolic disease [7,11,16]. It has been hypothesized that these risks are exacerbated by postural and neuromuscular changes associated with PD [16]. The literature regarding the association of PD with increased complications after TKA is controversial. Multiple case reports have reported hamstring flexion contractures in PD patients following total knee arthroplasty [6,9,10]. This increased risk may be linked to muscle rigidity associated with PD. Duffy and Trousdale reported the results of 24 PD who underwent TKA and reported TKA improves pain and function; however, they noted that in cases where PD progresses, functional outcomes are worse [17]. In contrast, Jansen et al. examined a large database that included over 53,000 TKAs to identify comorbid diseases that are associated with poor long-term survival [18]. They reported that neurodegenerative diseases that did not affect prosthesis survival.

Additionally, Jansen et al. compared infection and revision rates and one year mortality between 857 patients with PD who underwent either TKA or THA [19]. They reported no difference in infection and revision rates and one year mortality; however, in that study they reported that patients with PD had higher mortality at 10-year follow-up. They reported similar findings in TKA

**Table 1**

Mean age, sex, and CCI in TKA patients, overall population.

Demographic factor	Parkinson's disease (7361 patients)	Std error	Non-Parkinson's (1,315,260 patients)	Std error
Age ( $p < 0.0001$ )	72.1	0.09	66.5	0.01
Female Sex ( $p < 0.0001$ )	51.4%	0.6%	63.5%	0.1%
Charlson Comorbidity Index ( $p = 0.3058$ )	0.56	0.01	0.55	0.00

**Table 2**

Mean age, sex, and CCI in TKA patients, propensity score matched cohort.

Demographic factor	Parkinson's disease (7356 patients)	Std. error	Non-Parkinson's (73,560 patients)	Std. error
Age (p = 0.8921)	72.0	0.1	72.1	0.03
Female sex (p = 0.7495)	51.4%	0.6%	51.5%	0.2%
Charlson Comorbidity Index (p = 0.0476)	0.56	0.01	0.58	0.00

patients with comorbid Alzheimer's disease, finding no difference in the rate of infection, revision, or short-term mortality [20]. These results suggest that neurodegenerative disease is not an absolute contraindication to arthroplasty if careful patient selection and patient consenting is performed.

The current investigation has several potential limitations. First, the retrospective nature of the study is less optimal than a prospective study when attempting to interpret the relative risk of complications of TKA in PD patients. However, the high volume of surgeries accessible through the NIS database allows for a large, validated, and nationally representative population to be described. Given the multi-center nature of this database, our results and their interpretation are reliant upon accurate documentation and are subject to coding misclassification errors that may be present in this documentation. Additionally, the NIS database does not include long-term or functional outcome data, limiting the scope of our conclusions to peri-operative outcomes. As a result, 30-day rates of readmission and mortality could not be obtained using NIS data. Functional data is of particular interest in PD patients due to the challenges with post-surgical rehabilitation and long-term progressive degenerative nature of PD. To date, these results have only been explored in small case series. Lastly, the comorbidity burden of PD patients included in this study may not be representative of the entire PD population, as they were selected to undergo TKA. This suggests that clinical judgment is still necessary in identifying PD patients who can safely undergo TKA. Our data provide support for the perioperative safety of total knee arthroplasty in the setting of PD and shows that cost of care and length of stay are both slightly greater in PD patients.

The present investigation demonstrated that the number of TKA being performed nationwide in PD patients has steadily increased since 2000, demonstrating the importance of determining safety in this population. Overall inpatient complication burden and in-hospital mortality are not increased in PD patients. However, the matched cohort analysis found slightly increased length of stay and cost of care among PD patients. Further study is needed to determine the long-term outcomes of total knee arthroplasty among PD patients, as well as patient satisfaction and functional status. Based on the data in this study as well as the available body of literature, total knee arthroplasty may be safe to consider among PD patients in terms of in-hospital risk. However, careful patient selection is still recommended given the increased cost of care and rehabilitation challenges in this population.

### Declaration of competing statement

There has been no significant financial support for this work that could have influenced its outcome. The authors have the following potential conflicts of interest.

JK:

- None

JG:

- None

AE:

- Royalties, financial or material support from publishers: Springer; LWW

LR:

- DJ Orthopedics: Paid consultant
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AD:

- DePuy, A Johnson & Johnson Company: Paid consultant
- Globus Medical: Paid consultant

**Table 3**

Outcomes in the matched cohort.

Outcome	Parkinson's disease (7356 patients)	Std. error	Non-Parkinson's (73,560 patients)	Std. error	p-Value
Length of stay	3.9 days	0.2	3.7 days	0.0 days	<0.0001
Total charges	\$41,524	\$305	\$40,657	\$97	0.0037
Complication	8.3%	0.3%	8.0%	0.1%	0.4297
Mortality	0.16%	0.05%	0.15%	0.01%	0.8465

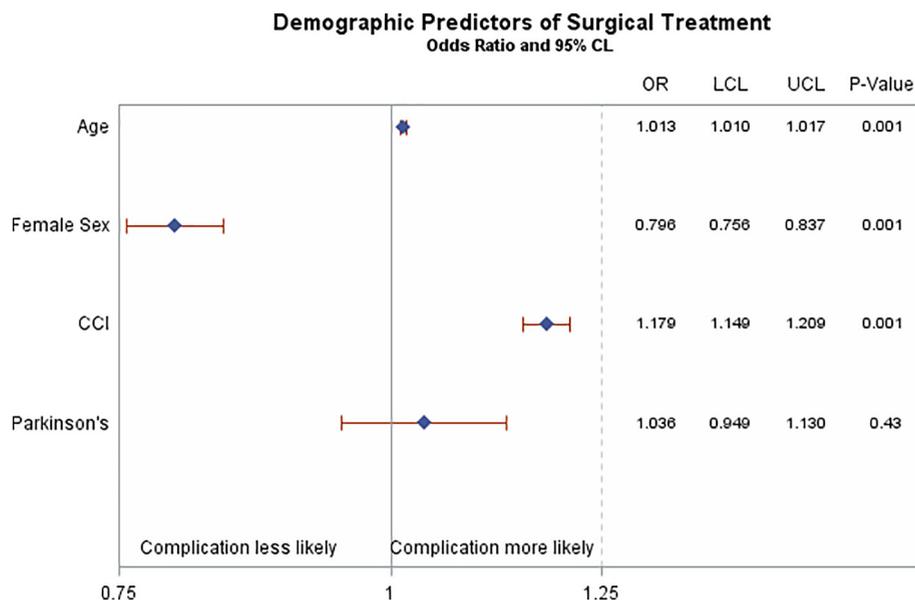


Figure 2. Demographic predictors of surgical treatment.

- Orthofix, Inc.: Paid consultant;
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