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Clinical Studies

A comparison of in-hospital outcomes after elective anterior cervical discectomy and fusion in cases with and without Parkinson's Disease

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ABSTRACT

Background: Following orthopedic surgery, patients with Parkinson's disease (PD) have been shown to have high rates of surgical complications, and some studies suggest that PD may be associated with greater risk for postoperative medical complications. As complication rates are critical to consider for elective surgery planning, the current study aimed to describe the association of PD with medical complications following anterior cervical discectomy and fusion (ACDF), the most commonly performed procedure to treat cervical degenerative pathology.
Methods: The 2008-2018 National Inpatient Sample database was queried for cases involving elective ACDF. Demographics and comorbidities were extracted using ICD codes. Cases were propensity matched based on demographic and comorbidity burden, and logistic regression was used to compare in-hospital complications between patients with and without PD.
Results: After weighting, a total of 1,273,437 elective ACDF cases were identified, of which 3948 (0.31%) involved cases with PD. After 1:1 propensity score matching by demographic and comorbidity variables, there were no differences between the PD and non-PD cohorts. Logistic regression models constructed for the matched and unmatched populations showed that PD cases have greater odds of in-hospital minor adverse events with no differences in odds of serious adverse events or mortality.
Conclusions: After matching for demographics and comorbidity burden, PD cases undergoing elective ACDF had slightly longer length of stay and greater risk for minor adverse events but had similar rates of serious adverse events and mortality. These findings are important for surgeons and patients to consider when making decisions about surgical intervention.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease after Alzheimer's disease, affecting 1% of the population over 60 years of age and 4% of the population over 85 years of age [1]. PD patients are known to be at higher risk of musculoskeletal problems due to rigidity and akathisia and have been shown to have increased rates of spinal pathology compared to the general population [2–7]. Thus, orthopedic surgery is an important consideration in patients with PD, and it is critical to understand the effects of PD on outcomes.

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Prior studies have investigated surgical and medical complications following orthopedic surgery in patients with PD [8–11]. Several studies assessed outcomes following thoracolumbar surgery and cervical decompression, finding that patients with PD had high rates of surgical complications and, compared to non-PD patients, had less symptom improvement and reduced improvement in quality of life [12,13]. Given these poorer outcomes, the risks of surgery must be weighed more heavily when considering surgical intervention. Some studies suggest an association of PD with postoperative medical complications. Following total hip arthroplasty, PD was associated with increased risk for postoperative delirium, altered mental status, urinary tract infection, and blood transfusion but not pneumonia, renal injury, or cardiovascular/thromboembolic events [11]. Following surgical treatment of cervical myelopathy, pulmonary, circulatory, and hematological complications were more common in patients with PD, but there was no difference in neurological or infectious issues [14].

Given the literature demonstrating an association between PD and a variety of medical complications following orthopedic surgery, it is important to gain insight into the postoperative medical course of PD patients undergoing elective spine surgery, which has not been studied previously. The current study used national data to compare the rates of medical complications for matched cohorts of patients with and without PD who underwent elective single- or multi-level ACDF, the most commonly performed procedure to treat symptomatic degenerative cervical spine pathology.

Methods

Study population

The 2008-2018 National Inpatient Sample (NIS) database was queried for anterior cervical spine procedures and further refined for ACDF using International Classification of Diagnoses, 9th Revision and 10th Revision (ICD-9/10) procedure codes.

Cases involving concomitant posterior approaches were excluded, as were emergent cases. Cases with Parkinson's disease (PD) were then identified using an ICD-9 diagnostic code 332.0 and ICD-10 diagnostic code G20. Overall comorbidity burden of each case was approximated using Elixhauser Comorbidity Index (ECI) and grouped into the following bins: 0 comorbidities, 1-5 comorbidities, and greater than 6 comorbidities. Additional variables abstracted included case age, gender, and involvement of multiple operative levels.

Outcome variables

Outcome data was collected using ICD coding for the following complications: surgical site infection, pneumonia, urinary tract infection, sepsis, renal injury, venous thromboembolic events, cardiac arrest, myocardial infarction, and stroke. Complications were then classified as either minor adverse events or serious adverse events, based upon a well-established binning schema commonly utilized in orthopaedic surgery literature [15–27].

Minor adverse events (MAE) included the occurrence of pneumonia, post-operative renal failure, or urinary tract infection whereas serious adverse events (SAE) included the occurrence of any of the following complications: surgical site infection, sepsis, unplanned reintubation, venothrombolic event, cardiac arrest, myocardial infarction, or stroke. The occurrence of any adverse event (AAE) was defined as the occurrence of a MAE and/or a SAE.

Statistical analysis

Case demographic and comorbidity characteristics were compared using chi-squared analysis for categorical data and student's T-tests or ANOVA for continuous data. Multiple logistic analyses were used to assess the odds of adverse events in cases with PD as compared to those without PD.

Next, propensity score matching was used to define two new PD and non-PD cohorts that were matched for age, gender, BMI, and comorbidity burden. Propensity score matching addresses potential selection biases that may occur during the selection of cohorts, and is particularly useful when evaluating relatively rare conditions [28]. The PSMATCH2 algorithm was used to define a new non-PD cohort that was similar in demographic covariates (age, gender, body mass index (BMI), and comorbidity burden) to the PD cohort. Multiple logistic regression models were then used to assess the odds of adverse events of cases with PD as compared to matched cases without PD (analogous to the non-propensity matched comparisons).

Previously described best practices for analyzing NIS data were followed in research design, data interpretation, and data analysis [29]. The level of significance was set to 0.05 for all tests. All statistical analyses were performed using STATA version 16 (StataCorp LP, College Station, TX).

Results

Study population

After weighting, a total of 1,273,437 ACDF cases were identified which met the inclusion/exclusion criteria. Of these, 3948 (0.31%) involved cases with PD.

Comparisons of entire cohorts

Cases with PD were found to be older (mean age of 66.6 years compared with 54.8 years, $p < 0.001$), more commonly male (61.3% male compared with 47.1% male, $p < 0.001$), and more likely to have a higher Elixhauser Comorbidity Index than non-PD cases (38.0% greater than 1 comorbidity compared with 20.6%, $p < 0.001$) (Table 1).

Cases in the PD group were found to have had significantly longer LOS (median of 2 days compared to 1 days, $p < 0.001$; Table 3); the median length of hospital stay for all-comers was 1 day.

According to the multiple logistic regression analysis, PD cases were found to have an increased odds ratio for AAE (OR 2.24; 95% CI 1.65-3.04; p < 0.001) and MAE (OR 2.15; 95% CI 1.54-3.02); $p < 0.001$). However, there was no difference in odds of SAE or hospital mortality (Table 5, Fig. 1).

Comparisons of propensity matched cohorts

After 1:1 propensity score matching based on demographic and comorbidity variables was performed, there were 3915 cases in the PD and non-PD groups as a sufficiently proximal match was unable to be found for 33 cases. A comparison of these cohorts revealed no differences between in terms of age, gender, BMI, or Elixhauser Comorbidity Index (Table 2). The LOS remained higher in the propensity score matched PD cohort compared to the propensity score matched non-PD cohort (2 days compared with 1 day, $p = 0.002$), as shown in Table 4.

Following propensity matching, PD cases continued to have greater odds for AAE (OR 2.42; 95% CI 1.46 – 4.03; $p = 0.001$) and MAE (OR 1.99; 95% CI 1.16-3.39; $p = 0.012$). There continued to no difference in odds of SAE. There were insufficient events for analysis of odds of mortality (Table 5, Fig. 2).

Discussion

Parkinson's Disease (PD) is a progressive neurodegenerative disorder that has been estimated to affect 0.10% - 0.20% of the population, which translates to millions of people around the world [30]. Furthermore, it has been estimated that the number of patients with PD will double between 2005 and 2030 [31]. Patients with PD are known to

Table 1
Demographic and comorbid characteristics of patients with Parkinson's disease and without.

Total Patients = 1,273,437	1,269,489	99.69%	3,948	0.31%	
Age	Mean: 54.8 years		Mean: 66.6 years		**<0.001**
< 40	118,175	9.31%	≤10	≤0.36%	
40-49	315,176	24.83%	140	3.55%	
50-59	402,533	31.71%	726	18.39%	
60+	433,605	34.16%	3,056	77.42%	
Sex					**<0.001**
Male	597,369	47.06%	2,420	61.29%	
Female	672,247	52.95%	1,528	38.71%	
Number of operative levels					**<0.001**
1	924,388	72.82%	2,547	64.52%	
>1	345,101	27.18%	1,273	32.26%	
Elixhauser Comorbidity Index					**<0.001**
0	1,007,416	79.36%	2,420	61.29%	
1-5	256,598	20.21%	1,401	35.48%	
6-12	5,476	0.43%	101	2.55%	

*= Statistically significant at $p < 0.05$.

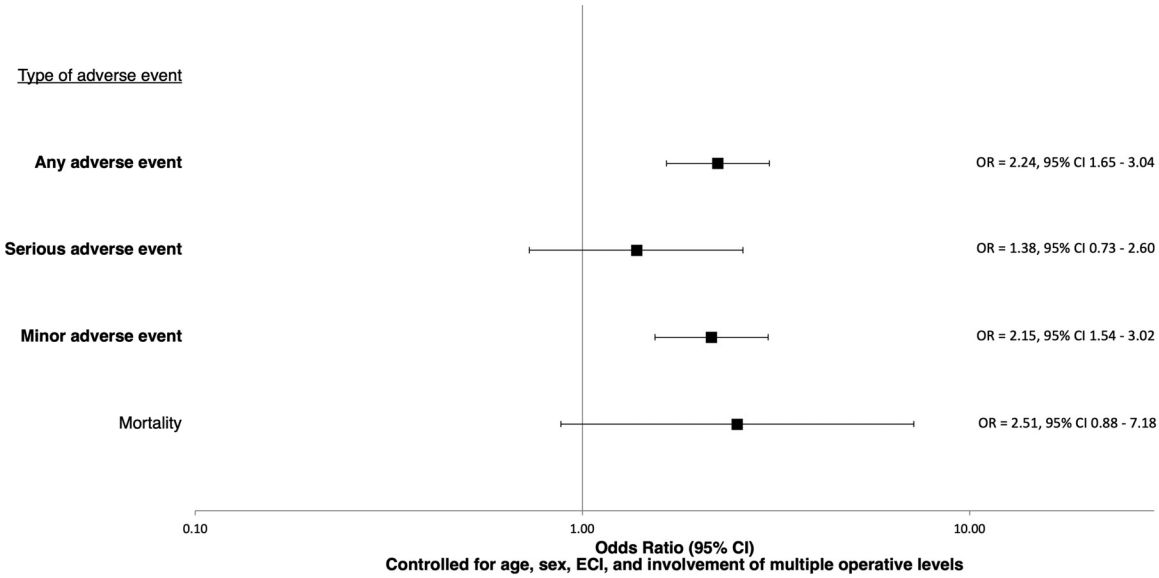

Fig. 1. is a forest plot showing the odds ratios and associated 95% confidence intervals for adverse events in Parkinson's disease cases undergoing ACDF, using the aggregate non-Parkinson's disease ACDF cohort as the referent. The logistic regression models generating these odds ratios controlled for age, sex, and cumulative Elixhauser Comorbidity Index.

Table 2
Demographic and comorbid characteristics of propensity score matched cohorts.

	Propensity Score Matched Non-PD Cohort§		Propensity Score Matched PD Cohort§		
	Number	Percent	Number	Percent	*p-value
Total Patients = 7,830	3,915	50.00%	3,915	50.00%	
Age	Mean: 64.4 years		Mean: 66.6 years		1.000
< 40	≤10	≤0.26%	≤10	≤0.26%	
40-49	146	3.72%	146	3.72%	
50-59	722	18.44%	722	18.44%	
60+	3,037	77.58%	3,037	77.58%	
Sex					1.000
Male	2,446	62.48%	2,446	62.48%	
Female	1,469	37.52%	1,469	37.52%	
Number of operative levels					0.963
1	2,584	66.00%	2,579	65.88%	
>1	1,331	34.00%	1,336	34.12%	
Elixhauser Comorbidity Index					1.000
0	2,469	63.08%	2,469	63.08%	
1-5	1,345	34.36%	1,346	34.38%	
6+	100	2.56%	99	2.53%	

* = Statistically significant at $p < 0.05$
§ Matched on age, sex, ECI, and involvement of multiple operative levels..

Table 3
Lengths of hospital stay by Parkinson's disease status.

	No Parkinson's disease (Non-PD)		Parkinson's disease (PD)		
Total Patients = 1,273,437	1,269,489	99.69%	3,948	0.31%	
	Median	IQR	Median	IQR	*p-value
Length of Stay (days)	1.0	1 - 2	2.0	1 - 3	**<0.001**

* Statistically significant at $p < 0.05$.

Table 4
Lengths of hospital stay in matched cohorts.

	No Parkinson's disease (Non-PD)		Parkinson's disease (PD)		
Total Patients = 7,830	3,915	50.00%	3,915	50.00%	
	Median	IQR	Median	IQR	*p-value
Length of Stay (days)	1.0	1-2	2.0	1-3	**0.002**

* Statistically significant at $p < 0.05$.§Matched on age, sex, ECI, multiple operative levels, and procedure approach.

Table 5
Adverse events, returns to operating room, readmissions and mortality by Parkinson's disease status.

Complication	No Parkinson's disease (Non-PD)		Parkinson's disease (PD)		Multivariable Odds Ratio		
					†Controlled for Preoperative Variables §Multivariate Propensity Matched Odds Ratio		
Total Patients = 1,273,437	1,269,489	99.69%	3,948	0.31%	OR	95% CI	p-value
Any Adverse Event (AAE)	22,540	1.78%	255	6.45%	**2.24**	**1.65-3.04**	**<0.001**
					§**2.42**	**1.46-4.03**	**0.001**
Serious Adverse Event (SAE)	5,476	0.43%	52	1.32%	1.38	0.73-2.60	0.319
					§2.18	0.75-6.31	0.150
Surgical site infection	103	0.01%	≤10	≤0.25%			
Sepsis	1,210	0.10%	≤10	≤0.25%			
Thromboembolic Events	1,910	0.15%	≤10	≤0.25%	‘		
Cardiac Arrest	1,070	0.08%	≤10	≤0.25%			
MI	1,210	0.10%	≤10	≤0.25%			
Stroke	611	0.05%	14	0.35%			
Minor Adverse Event (MAE)	18,847	1.48%	204	5.16%	**2.15**	**1.54-3.02**	**<0.001**
					§**1.99**	**1.16-3.39**	**0.012**
Pneumonia	4,966	0.39%	48	1.23%			
UTI	10,315	0.81%	120	3.03%			
Renal Failure	4,584	0.36%	45	1.13%			
In-hospital mortality	930	0.07%	19	0.48%	2.51	0.88-7.18	0.122
					§N/A	N/A	N/A

† Preoperative variables controlled for included age, sex, Elixhauser Comorbidity Index, and multiple operative levels.Bolding indicates statistical significance at $p < 0.05$

§ Propensity scores were generated based on age, sex, Elixhauser Comorbidity Index, and multiple operative levels.N/A indicates insufficient events for analysis

exhibit increased rates of spinal pathology when compared to the general population, but the risk profiles associated with performing spine surgery on this patient population has not yet been entirely elucidated [5,6]. The objective of the current study was to assess whether cases with PD had increased medical complications following elective ACDF surgery, which has not been previously studied.

After weighting and accounting for clustering and stratification, the present study found that approximately 3948 elective ACDF cases had a diagnosis of PD. This represented approximately 0.31% of all elective ACDF cases captured in the dataset after weighting. Prior studies by Martini et al and Miller et al investigating PD and cervical spine surgery have reported the percentage of overall cervical spine surgical cases with PD as 0.40% and 0.71% [14,32]. However, these studies were not limited to elective surgeries. Additionally, these prior studies included posterior and front-back approaches in addition to anterior approach procedures.

In both aggregate and propensity score matched comparisons, PD cases had a statistically significant increased length of hospital stay compared to non-PD cases. While this finding of increased length of stay is consistent with that of prior studies, the median lengths of stay for PD and non-PD cases were 2 days and 1 day, respectively. In contrast, Miller et al found median lengths of stay for PD and non-PD cases to be 3 days and 1 day, respectively. Martini et al found the mean lengths of stay for PD and non-PD cases to be 5.8 and 3.4 days, respectively. The findings of the present study suggest that the absolute difference in length of stay for PD cases is minimal when elective procedures are considered.

Prior to propensity score matching, PD cases were found to have higher rates of any and minor adverse events when undergoing ACDF. These findings are similar to those reported by Martini et al., who reported increased overall complication rates for PD patients who underwent a combination of cervical spine procedures. Notably, when comparing ACDF, PCDF and front-back procedures, Martini et al. found that only ACDFs in PD patients were associated with an increased incidence of overall complications when compared to the general population [14].

Multiple logistic regression assumes that input variables have a linear effect on the outcome of interest. Propensity score matching (PSM) is another method of controlling for preoperative covariate imbalances that does not make this assumption. In the present study, the findings of the PSM logistic regressions were concordant with those of the aggregate multiple logistic regression models. PSM logistic regressions did not find statistically significant differences in the odds of SAE and mortality between matched PD and non-PD cases.

Oichi et al used the Diagnosis Procedure Combination database, an inpatient database in Japan, to compare the outcomes of 1423 PD patients with 5498 matched controls who underwent spinal surgery [33].

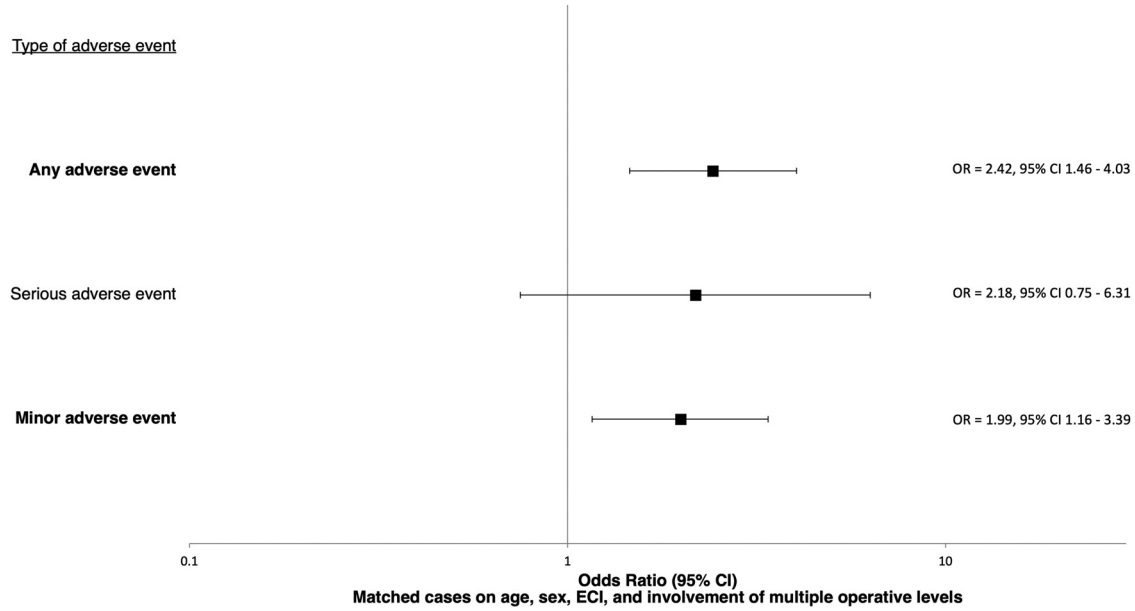

Fig. 2. is a forest plot showing the odds ratios and associated 95% confidence intervals for adverse events in Parkinson's disease cases undergoing ACDF, using a propensity score matched non-Parkinson's disease ACDF cohort as the referent. The referent non-PD cohort was matched to PD cases based on age, sex, and cumulative Elixhauser Comorbidity Index.

The authors determined that PD was a significant predictor of postoperative complications, but they did not separately analyze or adjust for surgical approach (anterior, posterior, front-back). Prior studies have suggested that the anterior approach is associated with shorter hospital LOS and less in-hospital morbidity compared to the posterior approach [34–36] which could have skewed the results of Oichi et al.

The current study certainly has limitations that should guide the interpretation of its results. One of these is the retrospective nature of the study with potential study group biases. The propensity matching and multiple logistic regression analyses were used in an attempt to control for these variables. This analysis is also subject to the inherent limitation of the administrative data derived from the National Inpatient Sample. Nevertheless, this type of data set was needed to achieve identify adequate numbers of cases to accomplish the study objectives. Finally, there is a lack of spine-specific and post-discharge outcomes reported in this database. Similarly, disease severity of the cervical pathology and PD also could not be ascertained.

In summary, the current study utilized the large NIS database to identify that 0.31% of inpatient ACDF procedures were performed on cases with PD. Matched logistic regressions showed that PD cases had increased odds of in-hospital minor adverse events, but no increased odds of serious adverse events and mortality in PD cases compared to non-PD cases. These findings may be used in preoperative counseling and in the informed consent process prior to surgery.

Declaration of Competing Interest

One or more of the authors declare financial or professional relationships on ICMJE-NASSJ disclosure forms.

Level of Evidence

III.

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IRB

Our institution's Human Investigations Committee deemed this study Not Human Research.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.xnsj.2022.100164.

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