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Colorectal surgery in Parkinson's disease—outcomes and predictors of mortality

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Abstract

Purpose Although diseases of the lower gastrointestinal tract are common in patients with Parkinson's disease, there is a paucity of data regarding postoperative outcomes after colorectal surgery.

Methods The Nationwide Inpatient Sample database (2007–2011) was utilized to analyze outcomes in patients with Parkinson's disease (PD) undergoing colorectal surgery. Main outcomes were risk-adjusted inpatient morbidity, mortality, hospital charge, and length of hospital stay.

Results A total of 6490 patients were identified. Utilization of laparoscopic surgery in Parkinson's patients has progressively increased in frequency over the latest 5 years analyzed. The most common diagnoses were colorectal malignancy (39 %) and intestinal obstruction (20 %). Right hemicolectomy (37 %) and sigmoidectomy (30 %) were the most common operations. Laparoscopy was used in 18 % of Parkinson's patients and most commonly in the elective setting. 54.3 % of Parkinson's patients had emergency surgery compared to 38.6 % in non-Parkinson's. Overall morbidity and mortality

were significantly lower after laparoscopic surgery compared to open (20 vs. 25 % and 2.1 vs. 6.6 %, respectively). Length of stay was significantly shorter (OR -1.86; $p < 0.01$) for laparoscopic operations, but there were no significant differences in risk-adjusted outcomes between laparoscopic and open groups.

Conclusion PD patients have high rates of morbidity and mortality after colorectal surgery; this may be because more than half of all patients in this population undergo emergent surgery. The laparoscopic approach appears to have short-term benefits in this patient population.

Keywords Parkinson's disease · Colorectal surgery · Laparoscopy · Outcome

Introduction

Parkinson's disease (PD) is the second most common progressive neurodegenerative disorder worldwide and results in annual health care costs ranging from 2000 to \$20,000 per person [1]. Compared to patients without neurodegenerative disorders, patients with PD are hospitalized at rates ranging from 7 to 28 % per year, and are at a greater risk for morbidity and mortality, including sepsis [2–4]. Parkinson's has been shown to be an independent risk factor for increased length of stay and morbidity following elective surgery [5]. Parkinson's disease pathology has been identified in nerves of the colonic submucosa in early, untreated patients [6]. Gut motility disorders are common throughout the disease course and are likely due to central and peripheral autonomic dysregulation manifested as gastroparesis, constipation, colonic dysmotility, colonic inertia, obstruction, and ileus [7, 8].

Despite the relative frequency of this neurologic disorder, there is a paucity of literature examining perioperative

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morbidity and mortality of Parkinson's patients undergoing colorectal surgery. There are no studies to date investigating the prevalence of colorectal disease or colorectal surgeries in these patients. Therefore, the aim of this study was to investigate outcomes of colorectal surgery in patients with PD. A secondary aim of the study was to describe national trends in patients with PD undergoing colorectal operations as well as to evaluate the impact of minimally invasive techniques on postoperative outcomes.

Methods and methods

Database

The Healthcare Cost and Utilization Project's Nationwide Inpatient Sample (NIS) database is the largest all-payer inpatient care database in the United States, containing information from approximately 8 million hospital stays each year. The data set approximates a 20 % stratified sample of community hospitals nationwide, resulting in a sampling frame of nearly 95 % of all hospital discharges in the United States. Data elements are drawn from hospital discharge abstracts and raw numbers are weighted to reflect national averages. Approval for the use of the NIS was obtained from the institutional review board of the University of California, Irvine, School of Medicine and the Healthcare Cost and Utilization Project.

Patient selection and inclusion criteria

The NIS database was utilized to perform a retrospective analysis of patients with Parkinson's disease undergoing colorectal surgery between 2007 and 2011. Appropriate diagnosis and procedural codes were selected using the International Classification of Disease, 9th Edition, Clinical Modification (ICD-9-

CM). We first identified all patients with a primary or secondary diagnosis of Parkinson's disease (332.0 and 333.0). 98.5 % of all Parkinson's patients who underwent colorectal surgery were coded under ICD-9 code 332.0, and 1.5 % were coded under 333.0. Patients with one of the following admission diagnosis were then selected: colon cancer (153.0–153.9), rectal cancer (154.0, 154.1, 154.2, and 154.8), diverticulitis (562.10–562.13), colon benign tumors (211.3, 230.3, and V12.72), rectal benign tumors (211.4, 230.4, 230.5, and 569.0), intestinal obstruction (560.0, 560.1, 560.2, 560.3, 560.8, and 560.9), constipation (564.00, 564.01, 564.022, and 564.03), megacolon (564.7), neurogenic bowel (564.81 and 564.89), unspecified motility disorder (564.9), gastrointestinal malfunction arising from mental factors (306.4), Crohn's disease (555.1 and 555.9), vascular insufficiency of the large bowel (557.0 and 557.9), ulcerative colitis (556.9), rectal prolapse (569.1), and rectal bleeding including angiodysplasia (569.85). All elective, urgent, and emergent procedures were included. The ICD-9 procedural codes included open anterior resection, open and laparoscopic sigmoidectomy, laparoscopic and open right hemicolectomy, laparoscopic and open left hemicolectomy, laparoscopic and open transverse colectomy, laparoscopic and open cecectomy, laparoscopic and open total colectomy, fixation of large intestine to abdominal wall, laparoscopic robotic assisted procedures, and open rectopexy. Patients with missing "surgery type" data were excluded.

Outcome variables

Patient demographics (age, gender, and ethnicity), severity of illness (minor, moderate, major, and extreme based on APR-DRG [all patient refined DRG]), procedure type (laparoscopic versus open), and outcomes were recorded. Primary outcome measures were rate of in-hospital mortality and serious morbidity. The in-hospital mortality rate was defined as the

Fig. 1 Colorectal surgery in Parkinson's disease patients by year

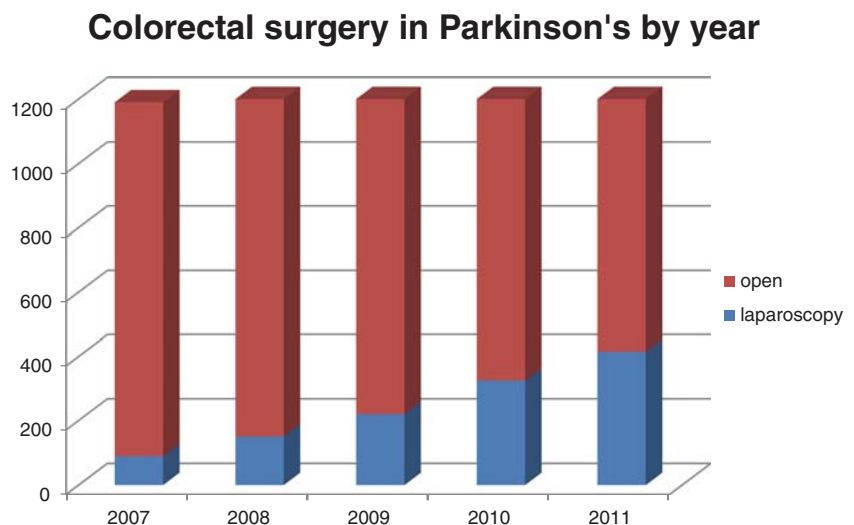


Table 1 Demographic characteristics of the selected sample

Demographic characteristics	CRS-Parkinson's study cases (%) (n=6490)
Age (years, mean±SD)	76.50±9.03
Gender	
Male	56.32 %
Female	43.68 %
Race	
White	72.65 %
Black	4.70 %
Hispanic	3.93 %
Asian or Pacific Islander	^a
Other	2.70 %
Missing	15.33 %
Severity (loss of function)	
No class specified	0.00 %
Minor	10.71 %
Moderate	31.90 %
Major	37.75 %
Extreme	19.65 %
Surgical method	
Laparoscopy	18.5 %
Open	79.4 %
Other	2.2 %
Setting	
Elective	46.4 %
Emergent	53.6 %
Diagnosis	
Colorectal benign neoplasm	11.32 %
Colorectal malignant neoplasm	39.37 %
Constipation	2.00 %
Inflammatory bowel disease (Crohn's and UC)	0.77 %
Diverticulitis	18.41 %
Intestinal obstruction	20.42 %
Neurogenic bowel/Megacolon/motility disorder	^a
Rectal prolapse	3.85 %
Vascular insufficiency (large bowel)	3.39 %

Continuous variables are reported as AVE±SD, and categorical variables are reported as proportions

^a Result omitted (due to very small number) in order to decrease risk of individual identification

percentage of patients who died during their hospital stay. Since the NIS database does not have information on deaths occurring after discharge, the 30-day mortality rate is unable to be analyzed. Serious morbidity was defined as anastomotic leak, intra-abdominal abscess, sepsis, wound infection, ileus, bowel obstruction, pneumonia, respiratory failure, acute renal failure, cardiac complications, CVA, DVT, postoperative

Table 2 Comparing rates of colorectal surgery

	Non-Parkinson's disease	Parkinson's disease patients
Colorectal surgery	1,262,270	6490
%	0.81	0.47

bleeding, and pulmonary embolism. Length of hospital stay and hospital charge were also evaluated. Postoperative outcomes were compared with laparoscopic and open surgery types.

Statistical analysis

Statistical analysis was performed using SAS version 9.3 (SAS, Cary, NC, USA) and the R statistical environment (version 3.0.3, Copyright © 2014 The R Foundation for Statistical Computing). Raw numbers were used to perform statistical analysis, and then weighted to reflect national averages. Binary outcomes were compared using chi-square tests with Yates correction and continuous variables were compared using two-sample *t* tests with unequal variance [9]. Multivariate logistic regression analysis was performed to compare risk-adjusted outcomes between laparoscopic and open surgery types [10]. Comparisons were considered statistically significant if the *p* value was <0.05 and all reported *p* values are two-sided.

Results

A total of 6490 patients with Parkinson's disease undergoing elective, urgent, and emergent colorectal surgery between 2007 and 2011 were identified using the NIS database. The mean age was 76 years and 56 % of patients were male. The frequency of laparoscopic cases utilized in Parkinson's patients increased over the last 5 years analyzed (Fig. 1). The most common severity illness score recorded was "major" (37 %) and 19 % of patients were categorized as "extreme". A complete demographic data of patients evaluated can be seen in Table 1. The most common admission diagnosis was colorectal cancer (39 %), followed by intestinal obstruction (20 %) and diverticulitis (18 %). Compared to non-PD patients, a significant portion of Parkinson's patients who underwent colorectal surgery did so in the emergency settings in 54.3 % of the time, vs. 38.6 % in non-PD (Tables 2, 3, and 4). The majority of PD patients underwent open procedures (81 %), with right hemicolectomy (37 %) and sigmoidectomy (30 %) being the most common surgical procedures (Table 3). The most common complications overall were ileus (19 %), acute renal failure (16 %), and anastomotic leak (15 %)

Table 3 Colorectal surgery by type

	Non-Parkinson's (%) (<i>n</i> =1,262,270)	Parkinson's (%) (<i>n</i> =6490)
Overall (%)	0.81 %	0.47 %
Surgery type		
Laparoscopic	22.88 %	18.49 %
Open	73.49 %	79.35 %
Missing	3.63 %	2.16 %
Conversion to open	2.90 %	2.08 %
In elective	47.70 %	20 %
In emergency	52.30 %	80 %
Procedure Type		
Abdominoperineal resection	2.00 %	1.54 %
Anterior resection laparoscopic	5.93 %	5.01 %
Anterior resection open	13.61 %	10.86 %
Fixation of large intestine to	0.02 %	^a
Laparoscopic robotic assisted	1.61 %	0.54 %
Left hemicolectomy laparoscopic	1.38 %	1.46 %
Left hemicolectomy open	7.49 %	6.93 %
Rectopexy open	0.81 %	1.23 %
Right hemicolectomy laparoscopic	7.09 %	6.70 %
Right hemicolectomy open	22.79 %	30.89 %
Sigmoidectomy laparoscopic	6.92 %	4.62 %
Sigmoidectomy open	22.70 %	25.42 %
Total colectomy laparoscopic	0.45 %	0.23 %
Total colectomy open	1.54 %	1.93 %
Transverse colectomy laparoscopic	0.46 %	0.46 %
Transverse colectomy open	2.43 %	2.08 %

^a Result omitted (due to very small number) in order to decrease risk of individual identification

(Table 5). Overall in-hospital morbidity and mortality rates were 25.34 and 6.60 %, respectively (Table 6).

Fewer patients in the Parkinson's group underwent laparoscopic surgery compared to the general population (Tables 3 and 4). However, a significant majority of Parkinson's patients had surgery in the emergent setting (54.3 %, *n*=3525)

(Table 4). In the emergent setting, 87.1 % of Parkinson's group had open surgery (*n*=3070) vs. 83.8 % in non-PD group (*n*=408,265) (Table 4). In the elective setting, laparoscopy was implemented in 25.9 % of PD patients (*n*=770) and 27.8 % of non-PD patients (*n*=215,350). Conversion to open surgery occurred in 2.08 % of the PD group and 2.90 % of the

Table 4 Elective vs. emergent surgery

Surgery type	Non-Parkinson's disease (%) (<i>n</i> =1,264,270)			Non-Parkinson's disease (%) (<i>n</i> =6,490)		
	Laparoscopic	Open	Total	Laparoscopic	Open	Total
Emergent	73,415	408,265	457,055 38.8 %	455	3070	3,525 54.3 %
Elective	215,350	519,365	775,215 61.4 %	770	2195	2,965 45.7 %
	288,765 22.9 %	927,630 73.5 %		1,225 18.9 %	5,265 81.1 %	

Table 5 Postoperative outcomes of the selected sample by surgery type. Variables reported as proportions

Postoperative outcomes in Parkinson's disease			
Variable (%)	Laparoscopic (%)	Open (%)	<i>p</i> value
Anastomotic leak	13.8	15.6	0.55
Intra-abdominal abscess	3.8	3.2	0.69
Sepsis	3.3	9.6	0.01
Wound infection	3.8	5.2	0.41
Ileus	21.7	18.7	0.32
Bowel obstruction	1.7	3.8	0.11
Urinary tract infection	7.9	13.3	0.02
Urinary retention	^a	0.7	0.99
Pneumonia	5.4	6.4	0.66
Respiratory failure	4.2	9.5	0.01
Acute renal failure	14.2	16.6	0.38
Cardiac complications	1.7	2.5	0.64
CVA	0	0.2	0.99
DVT	^a	0.8	0.99
Postoperative bleeding	5.4	5.4	0.99
Pulmonary embolism	0.8	1.0	0.99
In-hospital mortality	2.1	6.6	0.01
Serious morbidity	20.8	25.3	0.03
Length of stay (days)	8.94±7.85	11.39±7.96	0.01
Total hospital charge (\$)	64,720.51±54,711.62	77,114.19±72,588.56	0.01

^a Results omitted (due to very small number) in order to decrease risk of individual identification

non-PD group. A substantially higher portion of conversion in Parkinson's patients was in the emergent setting (80 % in PD vs. 52.3 % in non-PD). Outcomes for PD patients undergoing laparoscopic compared to open colorectal surgery can be seen in Table 5.

Parkinson's patients who underwent laparoscopic colorectal surgery had a significantly lower incidence of postoperative sepsis (3.3 % laparoscopic vs. 9.6 % open, $p=0.01$), urinary tract infection (7.9 % laparoscopic vs. 13.3 % open, $p=0.02$), and respiratory failure (4.2 % laparoscopic vs. 9.5 % open, $p=0.01$) (Table 5). The laparoscopic group also had a lower

incidence of in-hospital morbidity (20.8 vs. 25.34 %, $p=0.03$) and mortality (2.1 vs. 6.6 %, $p=0.01$; Table 6). Finally, a minimally invasive approach was associated with a 3-day shorter mean hospital stay as well as a \$12,400 lower mean hospital charge (\$64,720 laparoscopic vs. \$77,114 open, $p=0.01$)

On multivariate regression analysis, we found no significant differences in laparoscopic vs. open in-hospital mortality (OR 0.43; 95 % CI [0.17, 1.09]; $p=0.15$) or morbidity (OR 0.85; 95 % CI [0.59, 1.23], $p=0.39$) (Table 7). Risk-adjusted length of stay was significantly shorter after laparoscopic procedures (OR -1.86; 95 % CI [-3.00, -0.73], $p<0.01$). Total hospital charge trended toward significantly lower cost after laparoscopic surgery (OR -10,074; 95 % CI [-18,565, -15,836], $p=0.06$).

Table 6 Unadjusted endpoints of the selected sample by surgery type. Continuous variables are reported as AVE±SD, and categorical variables are reported as proportions

Variable	Laparoscopic (%)	Open (%)
In-hospital mortality		
Did not die	97.92 %	93.40 %
Died	2.08 %	6.60 %
Serious morbidity		
No	79.17 %	74.66 %
Yes	20.83 %	25.34 %
Length of stay (days)	8.94±7.85	11.39±7.96
Total hospital charge (\$)	64,720.51±54,711.62	77,114.19±72,588.56

Discussion

Postoperative morbidity and mortality rates after gastrointestinal (GI) surgery have historically been found to be higher in Parkinson's patients compared to those without neurodegenerative disorders. However, there is limited data evaluating outcomes of PD patients after abdominal surgery. In this study, we found that PD patients undergo fewer colorectal surgeries compared to non-PD patients (0.47 vs. 0.81 %, respectively; Table 2). This may be due to the shorter average

Table 7 Adjusted odds ratios (OR) or mean difference (MD) for each endpoint

Variable	Adjusted OR/MD (95 % CI)	Naive <i>p</i> value	Adjusted <i>p</i> value
In-hospital mortality			
Laparoscopic vs Open	0.43 (0.17, 1.09)	0.0767	0.1534
Morbidity (any of 12 complications)			
Laparoscopic vs. open	0.85 (0.59, 1.23)	0.39	0.39
Length of stay			
Laparoscopic vs. open	-1.86 (-3.00, -0.73)	0.0013	0.0052
Total hospital charge (\$)			
Laparoscopic vs. open	-10,074.73 (-18,565.81, -15,83.65)	0.0200	0.0601

life span of patients with Parkinson's disease [11]. Moreover, more than half of all colorectal operations in Parkinson's patients are performed in the emergency setting. Possible reasons for this may include delayed presentation or clinician recognition due to higher prevalence of chronic bowel complaints in this patient group, poorer awareness of symptoms, or atypical manifestations of serious underlying disease. Compared to non-PD patients, more Parkinson's patients not only underwent emergent surgery, but also were inclined to have open surgery in both elective and emergent settings, consistent with the impression that PD patients are generally higher risk patients going into surgery [5].

Our study also showed that the majority of colorectal operations PD patients undergo include low anterior resection, right hemicolectomy and sigmoidectomy, which is similar to frequencies seen in non-PD population. The majority of operations were for cancer (39 %), and not for colonic dysfunction (including constipation, neurogenic bowel, and megacolon) which only make up about 3 % of all Parkinson's patients undergoing colorectal surgery (Table 1). However, the 20 % categorized as bowel obstruction in Parkinson's patients may actually be a result of bowel dysfunction and be associated with autonomic dysfunction.

When comparing postoperative complication rates in Parkinson's with non-Parkinson's patients, our results show that patients with PD are at a higher risk of developing postoperative morbidity. A study group in Tokyo examining postoperative morbidity in PD after GI surgery found that morbidity rates in PD (77 %) were similar to patients with cerebrovascular disease (70 %) and higher than normal patients (33 %), with major postoperative complications including GI and pulmonary complications and delirium [12]. This study also showed that the PD group had longer postoperative hospital stay and higher operative and hospital mortality rates. The greatest risk factor for postoperative death in PD patients was pulmonary complications [12]. Particularly, respiratory dysfunction and dysphagia are common among PD patients, and are predisposing factors for pneumonia and respiratory failure. Overall, the most common cause of death in patients with PD includes respiratory complications, specifically

aspiration pneumonia [13]. Multiple causes of respiratory dysfunction have been proposed, including impaired central control of respiration, abnormal extrapyramidal control of respiratory muscles, excessive secretions, decreased chest wall compliance, and upper airway obstruction [14, 15]. Gastrointestinal motility is frequently affected in the PD patient population. Compounded with the stresses of GI surgery along with PD pathology, the likelihood of more GI complications such as postoperative ileus and bowel obstruction in the postoperative period is high, which is also reflected in our study (Table 5). The increased rate of UTI observed in this study is likely also secondary to autonomic dysfunction, cognitive and mobility impairment common among PD patients [12].

In both elective and emergent settings, Parkinson's patients are undergoing open surgery more frequently than laparoscopic surgery. 87.1 % of emergent cases in Parkinson's patients are open, and 83.8 % of emergent cases are open in non-PD. In elective cases, 74.0 % were open in PD and 67.0 % open in non-PD. In addition, about 1 in 48 laparoscopic cases (2.1 %) converted to open surgery in the Parkinson's group vs. 1 in 34 laparoscopic cases (3.0 %) in the non-PD group. This may be a reflection on various confounders such as surgeon bias and the perception of Parkinson's patients having higher surgical risk.

Predictably, the use of laparoscopy in Parkinson's patients has increased in frequency over the latest time period reviewed and mirrors trends observed in the general population. Improved outcomes have been demonstrated with the implementation of minimally invasive techniques in colorectal surgery. Laparoscopic colorectal surgery has shown clear clinical benefit and is very well established in the United States and worldwide. Laparoscopy is associated with shorter hospital stay, lower hospital costs, and lower mortality compared to open surgery [16–18]. Therefore, we examined outcomes of laparoscopic versus open outcomes in PD patients and found that PD patients have similar improvements in overall outcome and length of stay. Non-PD patients who underwent laparoscopy were discharged 1 to 3 days earlier than patients after open surgery [16, 19]. Similarly, our results show that

laparoscopy in PD patients shortened postoperative hospital stay by about 2 days, resulting in lower hospital costs, and potentially lower mortality when compared to open surgery in patients undergoing colorectal surgery (Table 7; OR -1.86; 95 % CI [-3.00, -0.73], $p < 0.01$). Laparoscopy was associated with significantly lower rate of sepsis, urinary tract infection, and respiratory failure compared to open surgery. Our results indicate that a laparoscopic approach may improve outcome and shorten hospital length of stay for patients in this population.

There were several limitations to this study. Due to the retrospective nature of the analysis, there was the potential for selection bias. There is also the potential for selection bias by the surgeon in determining which patients are candidates for laparoscopic surgery. We also were unable to distinguish outcomes based on comorbidities such as ASA classification in the NIS database. As a retrospective database study, we were also unable to stratify outcomes based on severity of Parkinson's as there are currently no ICD or CPT codes that can differentiate between early and advanced disease. Prior to 2008, we are aware that there is a lack of a dedicated ICD-9 procedure code for laparoscopic cases. However, when examining number of laparoscopic procedures by year in Parkinson's patients, only 7.5 % of all laparoscopic cases (90 cases) were performed before 2008. Furthermore, specific information on disease process, which would likely affect outcomes such as cancer stage and Hinchey scoring, is unavailable in the NIS and unidentifiable using ICD-9 codes. Other information not included in the NIS database including history of neoadjuvant and chemoradiation therapy in patients with malignancy, intraoperative information such as difficulty of the case, and complications following discharge or readmission. These limitations, however, are inherent to all database studies.

Conclusion

This is the first large study published to date evaluating postoperative complications of colorectal surgery in patients with Parkinson's disease. Our results demonstrate that PD patients generally are much more likely than non-PD patients to have emergency surgery. Also, PD patients have higher rates of postoperative complications compared to the general population. This population may also benefit from laparoscopic surgery, which appears to contribute to better postoperative outcomes. With life expectancy on the rise and increasing prevalence of PD worldwide, it is expected that more patients with PD will undergo surgical intervention in the future. Therefore, it is important to recognize and develop measures to improve postoperative results. The complications that we evaluated are

potentially preventable, and early detection and treatment may reduce perioperative and postoperative mortality and morbidity, and decrease the length of hospitalization. Consequently, we consider these results to be an important adjunct to surgical management of patients with PD. Further prospective trials are necessary to compare long-term functional outcomes after laparoscopic versus open colorectal surgery in PD patients.

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Conflict of interest The authors d no conflict of interest related to the content of the manuscript.

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