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Spinal Surgery after Bilateral Subthalamic Stimulation for Patients with Parkinson's Disease: A Retrospective Outcome Analysis of Pain and Functional Control

Michiari UMAKOSHI,[1] Takao YASUHARA,[1] Jun MORIMOTO,[1] Satoshi MURAI,[1] Tatsuya SASAKI,[1] Masahiro KAMEDA,[1] Kyohei KIN,[1] Yasuyuki MIYOSHI,[2] and Isao DATE[1]

[1]*Department of Neurological Surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, Okayama, Okayama, Japan*
[2]*Department of Neurosurgery, Kawasaki Medical School General Medical Center, Okayama, Okayama, Japan*

Abstract

Parkinson's disease (PD) patients often suffer from spinal diseases requiring surgeries, although the risk of complications is high. There are few reports on outcomes after spinal surgery for PD patients with deep brain stimulation (DBS). The objective of this study was to explore the data on spinal surgery for PD patients with precedent DBS. We evaluated 24 consecutive PD patients with 28 spinal surgeries from 2007 to 2017 who received at least a 2-year follow-up. The characteristics and outcomes of PD patients after spinal surgery were compared to those of 156 non-PD patients with degenerative spinal diseases treated in 2013–2017. Then, the characteristics, outcomes, and spinal alignment of PD patients receiving DBS were analyzed in degenerative spinal/lumbar diseases. The mean age at the time of spinal surgery was 68 years. The Hoehn and Yahr score regarding PD was stage 1 for 8 patients, stage 2 for 2 patients, stage 3 for 8 patients, stage 4 for 10 patients, and stage 5 for 0 patient. The median preoperative L-DOPA equivalent daily dose was 410 mg. Thirteen patients (46%) received precedent subthalamic nucleus (STN) DBS. Lumbar lesions with pain were common, and operation and anesthesia times were long in PD patients. Pain and functional improvement of PD patients persisted for 2 years after surgery with a higher complication rate than for non-PD patients. PD patients with STN DBS maintained better lumbar lordosis for 2 years after spinal surgery. STN DBS significantly maintained spinal alignment with subsequent pain and functional amelioration 2 years after surgery. The outcomes of spinal surgery for PD patients might be favorably affected by thorough treatment for PD including DBS.

Keywords: abnormal posture, lumbago, neuromodulation, pain, spinal alignment

Introduction

Parkinson's disease (PD) is a neurodegenerative disorder related to the dysfunction of nigrostriatal dopaminergic neurons. PD is now the second most common degenerative neurological disorder in the elderly population.[1)] PD patients usually experience exacerbated clinical symptoms, including reduced mobility, shuffling gait, rigidity, balance disorder, abnormal posture, or pain.[2,3)] PD patients are also known to suffer from comorbidities such as degenerative disorders of the whole-body joints and spine.[4,5)] These degenerative conditions can further impair the quality of life of such patients.[4)] Several studies have reported poor outcomes of PD patients who have undergone spinal surgery and increased complications, implant failures, or revision surgeries, yet possible contributing or predictive factors for the postoperative outcomes of PD patients have not been well explored. On the other hand, neuromodulation including deep brain stimulation (DBS) might potentially improve abnormal posture and

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spinal deformities associated with PD.[6,7] DBS has been an established treatment modality for PD patients to improve their symptoms, including rigidity and tremors. However, there are few previous reports focusing on whether DBS can affect the postoperative outcomes of spinal surgery in PD patients.

In this study, we first conducted a cohort study to compare the characteristics and outcomes of spinal surgeries for PD and non-PD patients. Second, the characteristics, outcomes, and spinal alignment of PD patients with precedent subthalamic nucleus (STN) DBS were evaluated and compared to those of patients without DBS. Third, to minimize the heterogeneity of the patients, patients with degenerative lumbar diseases were evaluated.

Methods

This is a retrospective study approved by the Institutional Review Board of Okayama University Hospital (IRB#1904-034).

Study 1: Characteristics and outcomes of PD patients after spinal surgery

We first conducted a case–control study comparing the PD and non-PD patients in terms of degenerative spinal diseases to describe the characteristics and outcomes of PD patients. We included 24 consecutive PD patients with 28 spinal surgeries from 2007 to 2017 and 156 consecutive non-PD patients with spinal surgeries from 2013 to 2017. All the patients included in this study had symptomatic degenerative spinal disease or vertebral fracture with at least a 2-year follow-up after surgery. The characteristics of patients evaluated in this study were following: 1) Background: age; gender; previous history of hypertension or diabetes; body mass index (BMI); history of vertebral fracture, hip joint, or spinal surgery; administration of parathyroid hormone (PTH); previous neuromodulation; the duration after the diagnosis of PD; PD severity (Hoehn and Yahr scale); the preoperative L-DOPA equivalent daily dose for PD patients; location of the lesion; and preoperative symptoms; 2) operative information: types of surgery, operation and anesthesia times, and blood loss; 3) outcomes: The Japanese Orthopedic Association (JOA) score, the numerical rating scale (NRS) score, the duration of hospitalization, and complications. All of these data were collected and analyzed, and we then compared the parameters in the 3 categories for PD and non-PD patients.

Study 2: Characteristics and outcomes of PD patients receiving precedent STN DBS after spinal surgery

Second, we also compared the parameters in the 3 categories described earlier between PD patients with and without precedent STN DBS (n = 13 and 15). In addition to the analyses described earlier, spinal alignment was measured and evaluated before and at 2 years after surgery. The measured parameters were as follows: C7 sagittal vertical axis (C7SVA), Cobb angle, thoracic kyphosis (TK; T5-T12), lumbar lordosis (LL; T12-L5), pelvic incidence (PI), PI-LL, pelvic tilt (PT), and sacral slope (SS).

Study 3: The subgroup analyses of patients with lumbar degenerative diseases

To minimize the heterogeneity of patients, we then conducted subgroup analyses of lumbar degenerative disease patients like study 1 and 2 as referred to earlier. We included 19 consecutive PD patients (10 patients with STN DBS and 9 patients without DBS) who underwent lumbar surgery between 2007 and 2017, and 55 consecutive non-PD patients who underwent lumbar surgery.

Definition of the outcome measurements

For the neurological and neuroradiological evaluations, the blinded examiner collected the data. In terms of neurological investigations, the JOA improvement rate was defined as (postoperative JOA score – preoperative JOA score)/(17 – preoperative JOA score) × 100 (%) for cervical lesions and (postoperative JOA score – preoperative JOA score)/(29 – preoperative JOA score) × 100 (%) for thoracic and lumbar lesions. We also defined the JOA improvement rate at 2 years as (JOA score at 2 years – preoperative JOA score)/(17 – preoperative JOA score) × 100 (%) for cervical lesions and the JOA improvement rate at 2 years as (JOA score at 2 years – preoperative JOA score)/(29 – preoperative JOA score) × 100 (%) for thoracic and lumbar lesions. Similarly, the NRS reduction ratio was defined as (postoperative NRS – preoperative NRS)/preoperative NRS × 100 (%). The NRS reduction ratio at 2 years was also defined as (NRS at 2 years – preoperative NRS)/preoperative NRS × 100 (%). Categorical outcomes were utilized, and subjects were grouped based on percentage of functional recovery and pain relief: functional recovery in JOA and pain reduction in NRS of less than 30% and 50%, equal to or greater than 30% and 50% and less than 50% and 70%, and equal to or greater than 50% and 70%.[8] NRS and JOA scores were evaluated before, 3 months after, and 2 years after the surgery. In neuroradiological investigations, all

the parameters for spinal alignment were calculated using the OsiriX DICOM viewer (Pixmeo Sàrl, Bernex, Switzerland). The diagnosis of postoperative implant failure, including pedicle screw loosening, rod fracture, cage migration, and postoperative fracture, were conducted by the blinded examiner. If the results were inconclusive, the diagnosis of each case was discussed with radiologists. Postoperative complications were defined as infection, delirium, fall, and other complications. Implant failure and reoperation were also evaluated.

Statistical analyses

Descriptive statistics were performed using mean with standard deviation or median with interquartile range for continuous variables, as appropriate, and number with percentage for categorical variables. The cutoff points for JOA and NRS improvement rates were calculated using a receiver operating characteristic curve. The groups were compared using Student's t-test or Wilcoxon rank-sum test for continuous variables, and Pearson's chi-squared test or Fisher's exact test for categorical variables, as appropriate. We were unable to conduct multivariable analysis because of the small sample size. We used JMP 14 software (SAS Institute, Cary, NC, USA), and the statistical difference was set as $p < 0.05$.

Results

Study 1: Characteristics and outcomes of PD patients after spinal surgery

Patient characteristics: PD vs. non-PD groups

Patient characteristics are summarized in Table 1. There were significant differences between the PD (n = 28) and non-PD (n = 156) groups in terms of female sex (54% vs. 29%, p = 0.01), history of hypertension (29% vs. 58%, p = 0.004), history of vertebral fracture (21% vs. 3%, p = 0.002), PTH (14% vs. 2%, p = 0.011), cervical lesion (32% vs. 61%, p = 0.0047), lumbar lesion (68% vs. 35%, p = 0.0012), the presence of local pain (64% vs. 33%, p = 0.002), motor disability (57% vs. 87%, p <0.001), and numbness (61% vs. 89%, p <0.001). On the other hand, no significant differences were observed in terms of the mean age at surgery, history of diabetes, mean BMI, and history of hip joint surgery, spinal surgery, thoracic lesion, or limb pain. For the PD group, the mean duration after the diagnosis of PD at the initial surgery was 10 years. The Hoehn and Yahr score was stage 1 for 8 cases (29%), stage 2 for 2 (7%), stage 3 for 8 (29%), stage 4 for 10 (36%), and stage 5 for 0. The median preoperative L-DOPA equivalent daily dose was 410 mg (range 200–660 mg). Thirteen cases (46%) had undergone previous STN DBS and 2 (7%) had undergone spinal cord stimulation (SCS). All PD patients with DBS received bilateral STN DBS in this study. The median duration between precedent STN DBS and spinal surgery was 48 months (4–137 months). Two patients received SCS because of lumbago after DBS. One received SCS 26 months before spinal surgery and the other 20 months after spinal surgery with subsequent mild–moderate reduction of lumbago. Both patients with SCS had relatively good spinal alignment and SCS did not affect the spinal alignment.

Operative information: PD vs. non-PD groups

Operative characteristics are summarized in supplementary Table 1 (All supplementary tables are available Online). There were significant differences between the PD and non-PD groups in terms of laminoplasty (32% vs. 54%, p = 0.034), the mean duration of anesthesia (390 vs. 330 min, p = 0.035), the mean duration of operation (310 vs. 230 min, p = 0.0023), and median blood loss (120 vs. 100 ml, p = 0.03). There were no significant differences between the groups in terms of decompression, fusion, or multilevel surgery. In the PD group, 2 and 1 patients underwent 1 and 2 additional surgeries, respectively. All the cases with additional surgeries had undergone lumbar surgery as the initial surgery. The first patient underwent decompression and fusion (2-level posterior lumbar interbody fusion [PLIF] for L3/4, 4/5) for restenosis at 6 years after the initial surgery (L4/5 PLIF). The second patient underwent long fusion with vertebral column resection for a vertebral fracture after a fall at 2 years after the initial surgery. The third patient required 2 additional operations including spinal fusion in 3 years.

Outcomes: PD vs. non-PD groups

The functional amelioration and pain reduction were recognized in all the patients involved in this study, although the degree of symptom improvement varied by case. Comparative data for postoperative outcomes are summarized in Table 2. With respect to JOA score, the improvement rate was preserved at 2 years after the surgery (PD group: 48% vs. non-PD group: 40%) as well as at 3 months (PD group: 47% vs. non-PD group: 40%) with no significant difference between the 2 groups. Regarding NRS score, significant differences were observed in median NRS before and at 2 years after surgery (PD group: 8 and 3 vs. non-PD group: 6 and 2, p = 0.001 and p = 0.083, respectively). The NRS reduction rate of the PD group (71%, p = 0.051) was nearly significantly larger than that of the non-PD group

Table 1 Characteristics of the PD and non-PD groups

Factor	PD group (n = 28)	Non-PD group (n = 156)	p value
Age at spinal surgery, years	68.3 ± 7.7	68.5 ± 10.2	0.90
Age at spinal surgery over 75 (%)	6 (21.4)	44 (28.2)	0.46
Female sex (%)	15 (53.6)	45 (28.8)	0.01
Comorbidities			
HT (%)	8 (28.6)	91 (58.3)	0.004
DM (%)	9 (32.1)	39 (25.0)	0.43
BMI, kg/m^2	24.6 ± 3.1	24.6 ± 3.6	0.98
BMI ≥25 (%)	13 (46.4)	69 (44.2)	0.83
History of vertebral fracture (%)	6 (21.4)	5 (3.2)	0.002
History of hip joint surgery (%)	1 (3.6)	0 (0.0)	0.15
History of spinal surgery (%)	9 (32.1)	34 (21.8)	0.23
PTH administration (%)	4 (14.3)	3 (1.9)	0.011
History of SCS (%)	2 (7.1)	0 (0.0)	1
History of DBS (%)	13 (46.4)	0 (0.0)	1
PD			
Duration of PD, years	10.4 ± 7.5	-	
Hoehn and Yahr score (%)			
1	8 (28.6)	-	
2	2 (7.1)	-	
3	8 (28.6)	-	
4	10 (35.7)	-	
Over 3	18 (64.3)	-	
Preoperative L-DOPA dose, mg	410 (IQR: 200–656)		
Location			
Cervical (%)	9 (32.1)	95 (60.9)	0.0047
Thoracic (%)	0 (0.0)	12 (7.7)	0.22
Lumbar (%)	19 (67.9)	55 (35.3)	0.0012
Symptoms			
Limb pain (%)	17 (60.7)	95 (60.9)	0.99
Local pain (%)	18 (64.3)	52 (33.3)	0.002
Motor disability (%)	16 (57.1)	135 (86.5)	<0.001
Numbness (%)	17 (60.7)	138 (88.5)	<0.001

BMI: body-mass index, DBS: deep brain stimulation, DM: diabetes mellitus, HT: hypertension, IQR: interquartile range, local pain: lumbago and neck pain, PD: Parkinson's disease, PTH: parathyroid hormone, SCS: spinal cord stimulation.

(50%) after surgery. The mean duration of the hospitalization showed no significant difference between the groups. Regarding complications, the overall complication rate was significantly higher in the PD group (36%, p <0.001) than in the non-PD group (4%). The PD group showed a significantly higher rate of infection (11% vs. 1%, p = 0.01), delirium (25% vs. 2%, p <0.001), fall (7% vs. 0%, p = 0.022), implant failure (7% vs. 0%, p = 0.022), and reoperation (14% vs. 4%, p = 0.047). There was no case with complications requiring reoperation in 6 months.

Study 2: Characteristics, outcomes, and spinal alignment of PD patients receiving DBS after spinal surgery

Patient characteristics: DBS vs. non-DBS groups

Characteristics of PD patients with (n = 13) and without precedent STN DBS (n = 15) are presented

Table 2 Outcomes of the PD and non-PD groups

Factor	PD group (n = 28)	Non-PD group (n = 156)	p value
JOA			
JOA before surgery (IQR)	8 (5–11)	9 (7–11)	0.23
JOA after surgery (IQR)	19.5 (10–22.3)	13 (11–21)	0.19
JOA at 2 years (IQR)	18 (10–22.8)	13 (10–22)	0.61
JOA improvement rate after surgery, % (IQR)	46.5 (33.3–67.2)	40 (25–57.1)	0.17
<30 after surgery (%)	4 (14.3)	51 (32.7)	0.075
30–50 after surgery (%)	12 (42.9)	40 (25.6)	
50≤ after surgery (%)	12 (42.9)	65 (41.7)	
JOA improvement rate at 2 years, % (IQR)	48.1 (22.9–74)	40 (20.6–71)	0.74
<30 at 2 years (%)	7 (26.9)	57 (37.3)	0.55
30–50 at 2 years (%)	6 (23.1)	26 (17.0)	
50≤ at 2 years (%)	13 (50.0)	70 (45.8)	
NRS			
NRS before surgery (IQR)	8 (5.8–10)	6 (4–8)	0.001
NRS after surgery (IQR)	2 (2–3.3)	3 (2–3)	0.11
NRS at 2 years (IQR)	3 (2–4)	2 (1–3)	0.083
NRS reduction rate after surgery, % (IQR)	71.4 (15–80)	50 (25–63.6)	0.051
<50 after surgery (%)	10 (35.7)	73 (46.8)	<0.001
50–70 after surgery (%)	2 (7.1)	53 (34.0)	
70≤ after surgery (%)	16 (57.1)	30 (19.2)	
NRS reduction rate at 2 years, % (IQR)	52.7 (0–80)	57.1 (33.3–77.8)	0.54
<50 at 2 years (%)	13 (50.0)	56 (36.6)	0.09
50–70 at 2 years (%)	2 (7.7)	42 (27.8)	
70≤ at 2 years (%)	11 (42.3)	55 (36.0)	
Hospitalization			
Duration of hospitalization, days	25.0 ± 11.4	22.8 ± 8.4	0.22
Duration of hospitalization ≥30 days (%)	6 (21.4)	26 (16.8)	0.55
Complications			
All complications (%)	10 (35.7)	6 (3.8)	<0.001
Infection (%)	3 (10.7)	1 (0.6)	0.012
Delirium (%)	7 (25.0)	3 (1.9)	<0.001
Fall (%)	2 (7.1)	0 (0.0)	0.022
Other complications (%)	4 (14.3)	3 (1.9)	0.011
Implant failure (%)	2 (7.1)	0 (0.0)	0.022
Reoperation (%)	4 (14.3)	6 (3.8)	0.047

IQR: interquartile range, JOA: The Japanese Orthopedic Association, NRS: numerical rating scale, PD: Parkinson's disease, SCS: spinal cord stimulation.

in Table 3. The DBS group showed a significantly younger mean age at the surgery (65 vs. 72 years, p = 0.011) and a higher percentage of PTH administration (31% vs. 0%, p = 0.035). The DBS group also showed a significantly longer mean duration of PD (14 vs. 8 years, p = 0.037). Additionally, the DBS group showed a significantly higher percentage of patients with Hoehn and Yahr scores over 3 (100% vs. 33%, p <0.001) and a higher preoperative L-DOPA equivalent daily dose (640 vs. 200 mg, p <0.001).

Table 3 Characteristics of the DBS and non-DBS groups

Factor	DBS group (n = 13)	Non-DBS group (n = 15)	p value
Age at spinal surgery, years	64.5 ± 7.9	71.6 ± 5.9	0.011
Age at spinal surgery over 75 (%)	4 (30.8)	12 (80.0)	0.009
Female sex (%)	8 (61.5)	7 (46.7)	0.43
Comorbidities			
HT (%)	3 (23.1)	5 (33.3)	0.69
DM (%)	6 (46.2)	3 (20.0)	0.23
BMI, kg/m^2	24.9 ± 3.0	24.4 ± 3.3	0.71
BMI ≥25 (%)	6 (46.2)	7 (46.7)	0.98
History of vertebral fracture (%)	5 (38.5)	1 (6.7)	0.069
History of hip joint surgery (%)	1 (7.7)	0 (0.0)	0.46
History of spinal surgery (%)	5 (38.5)	4 (26.7)	0.69
PTH administration (%)	4 (30.8)	0 (0.0)	0.035
History of SCS (%)	2 (15.4)	0 (0.0)	0.21
PD			
Duration of PD, years	13.5 ± 2.9	7.7 ± 9.1	0.037
Hoehn and Yahr score (%)			
1	0 (0.0)	8 (53.3)	<0.001
2	0 (0.0)	2 (13.3)	
3	3 (23.1)	5 (33.3)	
4	10 (76.9)	0 (0.0)	
Over 3 (%)	13 (100.0)	5 (33.3)	<0.001
Preoperative L-DOPA dose, mg	640 (IQR: 525–700)	200 (IQR: 100–375)	<0.001
Lesion			
Cervical (%)	3 (23.1)	6 (40.0)	0.44
Thoracic (%)	0 (0.0)	0 (0.0)	-
Lumbar (%)	10 (76.9)	9 (60.0)	0.43
Symptoms			
Limb pain (%)	9 (69.2)	8 (53.3)	0.46
Local pain (%)	10 (76.9)	8 (53.3)	0.25
Motor disability (%)	7 (53.8)	9 (60.0)	0.74
Numbness (%)	8 (61.5)	9 (60.0)	0.93

BMI: body mass index, DBS: deep brain stimulation, DM: diabetes mellitus, HT: hypertension, IQR: interquartile range, PD: Parkinson's disease, PTH: parathyroid hormone, SCS: spinal cord stimulation.

Operative information: DBS vs. non-DBS groups

Operative characteristics for DBS and non-DBS groups are summarized in supplementary Table 2. There were no significant differences in the groups for any surgical procedure. The mean duration of anesthesia or operation time and the median blood loss also showed no significant differences between the groups.

Outcomes: DBS vs. non-DBS groups

The comparative data of outcomes in the DBS vs. non-DBS groups are summarized in Table 4. With respect to JOA score, the improvement rate was preserved at 2 years after the surgery (DBS group: 40% vs. non-DBS group: 52%) as well as at 3 months (DBS group: 47% vs. non-DBS group: 40%) with no significant difference between the 2 groups. Regarding the NRS, the DBS group showed a significantly higher NRS score before surgery (10 vs. 7, p = 0.002). The improvement rate was preserved at 2 years after the surgery (DBS group: 75% vs. non-DBS group: 42%) as well as at 3 months (DBS group: 78% vs. non-DBS group: 71%) with no significant difference between the 2 groups. The mean duration of the

Table 4 Outcomes of the DBS and non-DBS groups

Factor	DBS group (n = 13)	Non-DBS group (n = 15)	p value
JOA			
JOA before surgery (IQR)	8 (4–10)	9 (6.5–12.5)	0.41
JOA after surgery (IQR)	18 (11–23)	20 (10–21)	0.64
JOA at 2 years (IQR)	18 (10.8–23.3)	17.5 (10–22)	0.72
JOA improvement rate after surgery, % (IQR)	46.7 (33.3–76.2)	40 (33.3–63.6)	0.7
<30 after surgery (%)	1 (7.7)	3 (20.0)	0.47
30–50 after surgery (%)	7 (53.9)	5 (33.3)	
50≤ after surgery (%)	5 (38.5)	7 (46.7)	
JOA improvement rate at 2 years, % (IQR)	39.8 (25.8–81)	51.7 (18.1–61.9)	0.66
<30 at 2 years (%)	3 (25.0)	4 (28.6)	0.51
30–50 at 2 years (%)	4 (33.3)	2 (14.3)	
50≤ at 2 years (%)	5 (41.7)	8 (57.1)	
NRS			
NRS before surgery (IQR)	10 (9–10)	7 (5–8)	0.002
NRS after surgery (IQR)	2 (2–4)	2 (2–3)	0.67
NRS at 2 years (IQR)	2.5 (2.0–4.5)	3 (2–3.8)	0.96
NRS reduction rate after surgery, % (IQR)	77.8 (18.8–84.5)	71.4 (0–77.8)	0.36
<50 after surgery (%)	4 (30.8)	6 (40.0)	0.88
50–70 after surgery (%)	1 (7.7)	1 (6.7)	
70≤ after surgery (%)	8 (61.5)	8 (53.3)	
NRS reduction rate at 2 years, % (IQR)	75.0 (10–80]	41.5 (0–78.1)	0.38
<50 at 2 years (%)	5 (41.7)	8 (57.1)	0.19
50–70 at 2 years (%)	0 (0.0)	2 (14.3)	
70≤ at 2 years (%)	7 (58.3)	4 (28.6)	
Hospitalization			
Duration of hospitalization, days	26.9 ± 11.5	23.4 ± 11.5	0.43
Duration of hospitalization ≥30 days (%)	5 (38.5)	1 (6.7)	0.069
Complications			
All complications (%)	3 (23.1)	7 (46.7)	0.25
Infection (%)	1 (7.7)	2 (13.3)	1
Delirium (%)	2 (15.4)	5 (33.3)	0.4
Fall (%)	0 (0.0)	2 (13.3)	0.48
Other complications (%)	0 (0.0)	4 (26.7)	0.1
Implant failure (%)	1 (7.7)	1 (6.7)	1
Reoperation (%)	2 (15.4)	2 (13.3)	1

DBS: deep brain stimulation, IQR: interquartile range, JOA: The Japanese Orthopedic Association, NRS: numerical rating scale, PD: Parkinson's disease.

hospitalization also showed no significant difference between the groups (DBS group: 27 days vs. non-DBS group: 23 days). There were also no significant differences in terms of complications. In supplementary Table 3, the outcomes of lumbar lesions (n = 19) in the DBS and non-DBS groups are compared. Similar to the data of all patients, the DBS group with lumbar lesions showed a significantly higher NRS score before surgery (10 vs. 8, p = 0.001). The complication rate of the DBS group with lumbar lesions tended to be smaller (30%) than that of the non-DBS group (66.7%, p = 0.17).

Table 5 Spinal alignment before and at 2 years after surgery (DBS vs. non-DBS)

Factor	DBS group (n = 13)	Non-DBS group (n = 15)	p value
C7SVA before surgery	83.6 (50.6)	133.5 (85.0)	0.19
C7SVA at 2 years	129.8 (69.0)	199.0 (24.6)	0.12
Cobb before surgery	18.0 (15.0)	15.7 (9.1)	0.80
Cobb at 2 years	17.0 (9.7)	15.3 (12.9)	0.81
TK before surgery	23.0 (13.9)	25.0 (10.8)	0.82
TK at 2 years	24.4 (14.4)	25.7 (11.0)	0.89
LL before surgery	28.5 (20.7)	24.0 (14.7)	0.73
LL at 2 years	30.3 (18.0)	5.0 (1.7)	0.04
PI before surgery	54.6 (13.0)	54.3 (2.3)	0.97
PI at 2 years	56.2 (9.7)	51.0 (6.6)	0.40
PI-LL before surgery	30.6 (17.7)	32.7 (15.5)	0.86
PI-LL at 2 years	27.1 (12.5)	46.0 (5.3)	0.03
PT before surgery	33.6 (11.9)	32.0 (6.2)	0.83
PT at 2 years	30.8 (11.5)	35.0 (6.2)	0.55
SS before surgery	20.9 (14.8)	22.3 (4.9)	0.88
SS at 2 years	25.3 (14.0)	16.0 (4.0)	0.29

All data are shown as mean (SD).
DBS: deep brain stimulation, C7SVA: C7 sagittal vertical axis (mm), Cobb: Cobb angle (degrees), LL: lumbar lordosis (T12-L5, degrees), PI: pelvic incidence (degrees), PT: pelvic tilt (degrees), SD: standard deviation, SS: sacral slope (degrees), TK: thoracic kyphosis (T5-T12, degrees).

Spinal alignment: DBS vs. non-DBS groups

The data on spinal alignment of the DBS and non-DBS groups are shown in Table 5. LL measured at 2 years after spinal surgery in the DBS group (30 degrees) was significantly larger than that in the non-DBS group (5 degrees). Similarly, PI-LL at 2 years in the DBS group (27 degrees, p = 0.03) was significantly smaller than that in the non-DBS group (46 degrees). C7SVA at 2 years in the DBS group (130 mm, p = 0.12) was smaller than that in the non-DBS group (199 mm) although preoperative C7SVA of the DBS group (84 mm, p = 0.19) was smaller than that in the non-DBS group (134 mm). Thus, DBS might favorably affect spinal alignment for PD patients. Other than the parameters described earlier, there were no significant differences between the 2 groups in terms of Cobb angle, TK, PI, PT, or SS. In 19 patients with lumbar lesion, LL in the DBS group (28 degrees) was significantly larger than that in the non-DBS group (4 degrees).

Study 3: The subgroup analyses on lumbar degenerative disease patients with or without PD

Patient characteristics: PD vs. non-PD groups

There were significant differences between the PD (n = 19) and non-PD (n = 55) groups in history of hypertension (26% vs. 66%, p = 0.006), history of vertebral fracture (31% vs. 9%, p = 0.027), limb pain (74% vs. 93%, p = 0.04), lumbago (95% vs. 67%, p = 0.03), motor disability (37% vs. 71%, p = 0.013), and numbness (42% vs. 73%, p = 0.025). For the PD group, the mean time after PD diagnosis at the initial surgery was 11.6 years. The Hoehn and Yahr score was stage 1 for 4 cases (21%), stage 2 for 0, stage 3 for 8 (42%), stage 4 for 7 (37%), and stage 5 for 0. The median preoperative LEDD was 525 mg (range 300–688 mg). Ten cases (53%) had undergone previous DBS and 2 (11%) had undergone SCS. The information on SCS is described in *Study 1* section.

Operative information: PD vs. non-PD groups

There were significant differences between the PD and non-PD groups in terms of the mean duration of anesthesia (441 vs. 328 min, p = 0.03), the mean duration of operation (343 vs. 234 min, p = 0.023), and median blood loss (200 vs. 50 ml, p = 0.002).

Outcomes: PD vs. non-PD groups

With respect to the JOA score, the improvement rate was preserved at 2 years after the surgery in 56% of the PD patients vs. 75% of the non-PD patients (p = 0.035). Regarding the NRS score,

significant differences were observed in median NRS score before and at 2 years after surgery (PD group: 8 and 3 vs. non-PD group: 6 and 2, p = 0.015 and p = 0.022, respectively). The NRS reduction rate of the PD group (78%) was significantly larger than that of the non-PD group (67%) after surgery (p = 0.027), although the difference was not found at 2 years after surgery (PD group: 73%, non-PD group: 85%, p = 0.13). Regarding complications, the overall complication rate was significantly higher in the PD group (47%), than in the non-PD group (5.5%, p <0.001). The PD group showed a significantly higher rate of surgical site infection (15.8% vs. 1.8%, p = 0.05) and delirium (32% vs. 1.8%, p = 0.001).

Patient characteristics: DBS vs. non-DBS groups

The DBS group (n = 10) showed a significantly younger mean age at the surgery (50 vs. 62 years) than the non-DBS group (n = 9, p = 0.018). The DBS group showed a significantly higher percentage of patients with Hoehn and Yahr scores ≥3 (100% vs. 56%, p = 0.002) and a higher preoperative LEDD (588 vs. 300 mg, p = 0.014).

Operative information: DBS vs. non-DBS groups

There were no significant differences between the groups for any surgical procedure and other operative parameters.

Outcomes: DBS vs. non-DBS groups

With respect to the JOA score, the improvement rate was preserved at 3 months (DBS group: 47% vs. non-DBS group: 40%), as well as at 2 years after the surgery (DBS group: 40% vs. non-DBS group: 52%) with no significant differences between the 2 groups. Regarding the NRS score, the DBS group showed a significantly higher NRS score before surgery (10 vs. 8, p = 0.001). The improvement rate was preserved at 3 months (DBS group: 78% vs. non-DBS group: 71%), as well as at 2 years after the surgery (DBS group: 75% vs. non-DBS group: 42%) with no significant differences between the 2 groups. The mean duration of the hospitalization also showed no significant difference between the 2 groups (DBS group: 29 days vs. non-DBS group: 26 days). There were 2 cases with postoperative pneumonia, 1 case with urinary tract infection and 1 malnutrition case in the non-DBS group. The systemic complications were found only in the non-DBS group but not in the DBS group. STN DBS might ameliorate the systemic conditions with subsequent suppression of the perioperative complications after lumbar surgery.

Spinal alignment: DBS vs. non-DBS groups

LL measured at 2 years after lumbar surgery in the DBS group (27 degrees) was almost significantly larger than that in the non-DBS group (5 degrees, p = 0.052). Similarly, PI-LL at 2 years in the DBS group (29 degrees) was almost significantly smaller than that in the non-DBS group (46 degrees, p = 0.064). C7SVA at 2 years in the DBS group (138 mm) was smaller than that in the non-DBS group (199 mm, p = 0.17) although preoperative C7SVA of the DBS group (80 mm) was smaller than that in the non-DBS group (134 mm, p = 0.14). Thus, STN DBS might favorably affect spinal alignment for PD patients. Other than the parameters described earlier, there were no significant differences between the 2 groups.

Discussion

In this study, characteristics and outcomes after spinal surgery of PD patients with and without precedent STN DBS were explored. Before surgery, PD patients often suffered from pain due to lumbar lesions. The improvement of NRS in the PD group was greater than that in the non-PD group at 2 years after surgery, and PD patients receiving STN DBS preserved LL at 2 years after spinal surgeries. There were no significant differences in the DBS and non-DBS groups regarding functional recovery and pain reduction, although the severity of PD in the DBS group was significantly worse than that in the non-DBS group. STN DBS might favorably affect the results of spinal surgery for PD patients. By subgroup analyses on lumbar degenerative disease patients, the followings were shown. JOA score and improvement rate at 2 years in the non-PD group were significantly greater than those in the PD group. NRS score before surgery in the PD group was significantly greater than that in the non-PD group. NRS score reduction was greater in the PD group at 3 months after surgery, but not at 2 years after surgery. The complication rate was greater in the PD group. PD patients receiving DBS were more likely to preserve LL at 2 years after lumbar surgery (p = 0.052). There were no significant differences between the DBS and non-DBS groups regarding functional recovery and pain reduction, in spite of the worse PD severity in the DBS group with worse NRS score. Postoperative systemic complications including pneumonia, urinary tract infection, and hyponutrition were recognized only in the non-DBS group, but not in the DBS group (p = 0.033). Thus, STN DBS might favorably affect the results of lumbar surgery for PD patients.

Previous reports on spinal surgery for PD patients

Previous studies reported a higher complication rate following spinal surgery for PD patients. It was reported that 86% of spinal surgeries for PD patients required 1 or more additional surgeries.[9] In another study, the complication and revision surgery rates were 52% and 33%, respectively.[4] A study of 96 PD patients with spinal surgery showed that 21% of patients received revision surgeries and that a Hoehn and Yahr score over 3, diabetes mellitus, osteoporosis, and a combined anterior and posterior approach were risk factors for revision surgeries.[10] The incidence of complications at an early stage after surgery, such as infection and ruptured wounds, was reported to be nearly 20%. Other reports also showed that PD patients have an increased risk of poor postoperative outcomes following spinal surgery compared to non-PD patients.[4,9–16]A Hoehn and Yahr score over 3 in advanced PD patients was reported as a significant risk factor for requiring additional surgical intervention including revision surgeries.[10,12,17] Severe PD patients with spinal diseases are not usually considered appropriate candidates for surgical intervention.[10]

In our study, 10 cases (36%) experienced perioperative complications and 3 patients underwent reoperations (14%) although there were no reoperations at 6 months after surgery. Our data are preferable to the results of previous reports, largely because we preferred to choose less invasive surgeries for PD patients. For PD patients with lumbar spinal stenosis, we usually chose decompression surgery with a unilateral approach, which might minimize damage to the paraspinal, supra/interspinous muscles and preserve the facet joints with a subsequent reduction in postoperative iatrogenic instability. Postoperative delirium was reported to be more common in PD patients compared to the general population.[18] Similarly, in this study, the rate of postoperative delirium of PD patients was almost 8 times that of non-PD patients. It might therefore be important to control the perioperative complications after surgery for PD patients. The perioperative management of a multidisciplinary team and the partnership between neurosurgeons and neurologists are essential for perioperative care, and early intervention against adverse events is desirable.[14,19]

Neuromodulation and spinal surgery for PD patients

In our study, PD patients in the DBS group had a longer duration of PD at an advanced stage and an increased intake of L-DOPA. However, there were no significant differences in terms of surgery and outcomes after surgery, in spite of the preoperative worsened NRS. Advanced PD is thought to be a risk factor for spinal disease,[10] so DBS might favorably affect the outcomes. Interestingly, the LL of the DBS group was maintained at 2 years after spinal surgery compared to that of the non-DBS group. The maintenance of spinal alignment might contribute to pain control. In PD patients, chronic back pain is quite common.[20] Painful sensations in PD patients are classified into several categories: musculoskeletal pain, neuritic or radicular pain, dystonia-associated pain, primary or central pain, and akathisia-like discomfort.[21] DBS is reported to be effective for refractory low back pain in PD patients.[22] Although the mechanism of pain relief brought about by DBS remains unclear, 3 possibilities are considered: decreased muscle tonus, decreased sensitivity to pain/increased tolerance, and improved motor function.[23] Regarding spinal malalignment, a treatment algorithm was presented for abnormal posture in PD patients.[7] DBS and SCS are considered options for the treatment of some spinal deformities or postural abnormality associated with PD in selected patients.[6,24,25] We believe that shortening the off-period by DBS might result in excellent long-term outcomes. In several papers on DBS for PD and spinal alignment,[26–28] important data were revealed. DBS might be effective for spinal malalignment including camptocormia, although it is still controversial.[26] Longer duration of camptocormia might lead to poor prognosis after DBS. In cases of DBS-ineffective camptocormia, spinal surgery might be the resolution. Long fusion surgery for PD patients with spinal malalignment might be favorable after DBS.[27] In a review paper, it was described that preoperative optimization of motor control with medication and DBS might be needed for spinal surgery in PD patients.[28] In our study, the preservation of LL of PD patients with precedent STN DBS at 2 years after spinal surgery is first shown. The objective data on this issue might be critically important to think of spinal surgery for PD patients in the future.

Limitations of this study and unavoidable PD progression

There are several limitations to this study. First, since it is a retrospective study with a small sample size and heterogeneous spinal lesions, there is the natural possibility that it contains associated biases. Selection bias would not be excluded due to the difference of the indications for PD patients. As preoperative JOA and NRS scores showed, only the cases with severe impairment received spinal surgery in our study. We were able to limit long fusion surgeries to the minimum necessary. It has been

reported that long-range fixation to the pelvis might maintain LL with subsequent reduction of reoperations.[4,12] However, spinal deformities usually become exacerbated as PD progresses.[29] The main cause of postural disorder lies in the PD pathology itself. Nowadays, biotechnology is rapidly advancing, but it is still difficult to completely maintain the spinal balance in accordance with the progression of PD through existing therapeutic options.[30] It is important to evaluate the pathology for each PD patient and to determine the optimal treatment strategy by considering various treatment options.

Conclusion

In this study, we explored the characteristics, operative information, and outcomes after spinal surgery for PD patients and compared them with those for non-PD patients, with a particular focus on DBS. The pain relief persisted at 2 years after spinal surgery for PD patients, and precedent STN DBS maintained the spinal alignment with subsequent pain and functional amelioration at 2 years after surgery. By the subgroup analyses of lumbar degenerative disease patients, some significant differences were lost, but LL of patients with STN DBS was preserved at 2 years after surgery compared to that of patients without STN DBS ($p = 0.052$). Thus, the outcomes of spinal surgery for PD patients might be favorably affected by thorough treatment for PD including STN DBS.

Conflicts of Interest Disclosure

The authors have no conflicts of interest to be declared related to this study.

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Corresponding author: Takao Yasuhara, MD
Department of Neurological Surgery, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences, 2-5-1 Shikatacho, Kita-ku, Okayama, Okayama 700-8558, Japan.
email: tyasu37@cc.okayama-u.ac.jp