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Long-Term Outcomes of Bilateral Subthalamic Nucleus Deep Brain Stimulation for Patients With Parkinson's Disease: 10 Years and Beyond

BACKGROUND: Deep brain stimulation (DBS) of the subthalamic nucleus (STN) represents an effective treatment for severe Parkinson's disease (PD), but little is known about the long-term benefit.

OBJECTIVE: To investigate the survival rate and long-term outcome of DBS.

METHODS: We investigated all 81 patients including 37 males and 44 females who underwent bilateral STN DBS from March 2005 to March 2008 at a single institution. The current survival status of the patients was investigated. Preoperative and postoperative follow-up assessments were analyzed.

RESULTS: The mean age at the time of surgery was 62 (range 27-82) years, and the median clinical follow-up duration was 145 months. Thirty-five patients (43%) died during the follow-up period. The mean duration from DBS surgery to death was 110.46 ± 40.8 (range 0-155) months. The cumulative survival rate is as follows: 98.8 ± 1.2% (1 year), 95.1 ± 2.4% (5 years), and 79.0 ± 4.5% (10 years). Of the 81 patients, 33 (40%) were ambulatory up to more than 11 years. The Unified Parkinson's Disease Rating Scale (UPDRS) score was significantly improved until 5 years after surgery although it showed a tendency to increase again after 10 years. The patient group with both electrodes located within the STN showed a higher rate of survival and maintained ambulation.

CONCLUSION: STN DBS is a safe and effective treatment for patients with advanced PD. This study based on the long-term follow-up of large patient populations can be used to elucidate the long-term fate of patients who underwent bilateral STN DBS for PD.

KEY WORDS: Parkinson's disease, Deep brain stimulation, Treatment outcome, Subthalamic nucleus

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Deep brain stimulation (DBS) of the subthalamic nucleus (STN) for Parkinson's disease (PD) has been accepted as an effective treatment for patients manifesting medication-related side effects.[1-5] The motor improvement induced by STN stimulation is sustained for up to 5 to 8 years after surgery although some of the initial benefits diminish eventually, mainly because of worsening of axial signs.[1,2] Despite reports of long-term efficacy and safety after DBS surgery for PD, the fate of all patients is unclear. We performed a follow-up of all patients who underwent STN DBS surgery for PD more than 10 years ago and assessed the survival rate and long-term outcome of DBS.

ABBREVIATIONS: ANOVA, analysis of variance; **BPnd,** binding potentials; **DAT,** dopamine transporter; **LEDD,** levodopa-equivalent daily dose; **MER,** microelectrode recording; **PD,** Parkinson's disease; **SPECT,** single-photon emission computed tomography; **STN,** subthalamic nucleus; **UPDRS,** Unified Parkinson's Disease Rating Scale.

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METHODS

Patient Population

Consecutive 81 patients with advanced PD who received bilateral STN DBS implantation between March 2005 and December 2008 at single institution were enrolled in this study. As previously reported by our group, all patients were recruited according to defined inclusion/exclusion criteria and protocol.[6,7] This retrospective study was approved by the Institutional Review

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Board of our institution (IRB No. 1904-015-1022) and conformed to the principles of the Declaration of Helsinki. No written informed consent was needed because of the retrospective study design. We reviewed the medical records and follow-up data of all patients. We contacted the patients' caregivers who discontinued follow-up to identify survival and current status.

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Surgical Procedure

All patients underwent surgery using Leksell frame (Elekta AB), SurgiPlan with microelectrode recording, and macrostimulation under local anesthesia, as described previously.[8] The electrode was then connected to an implantable pulse generator placed in the subclavicular area under general anesthesia on the same day. Fusion with preoperative MRI and postoperative 3-dimensional stereotactic computed tomography scan was performed to confirm the lead location using a mutual information technique proposed by Wells et al and developed by Lucion (Cybermed).[9-14] This method enabled us to measure the statistical dependence or information redundancy between the image intensities of corresponding voxels in both images, which is assumed to be maximal if the images are geometrically aligned.[9] Using this method, we identified the three-dimensional location of the leads and of each contact in relation to the STN and indirectly plotted the location of 8 contacts onto the human brain atlas of Schaltenbrand[15] and Wahren for practical purposes. Based on the identified electrode location, the stimulation settings and medication were adjusted individually to maintain optimal clinical status. The stimulation parameter on the side where the electrode is accurately inserted into the target was more actively controlled and used for treatment. Revision surgery was decided when the lead was placed improperly and the simulation parameter adjustment was not effective. For the analysis regarding electrode location in this study, the location of the active contact was used.

Perioperative Evaluation

Preoperative and postoperative evaluation was performed according to our previously described protocol.[6,7] This study evaluated the patients' status immediately after surgery and at 1, 5, and 10 years after surgery. Patients who visited the outpatient clinic were evaluated clinically including assessment with UPDRS. The current status of patients who were unable to visit the hospital was confirmed through a telephone call with a main caregiver. In the case of patients who died, information about the time and cause of death was obtained.

The decline in dopamine transporter (DAT) level after DBS was evaluated using single-photon emission computed tomography (SPECT) performed 7 and 10 years after DBS surgery. The nondisplaceable binding potentials (BPnd) for the DAT were evaluated for patients who were investigated up to 10 years after DBS. When DBS surgery was first initiated at our center, no routine SPECT was performed. Because this study included patients who underwent surgery in the early period, it was impossible to compare preoperative and postoperative BPnd values of the same patient group. Instead, reference data from 83 patients who underwent SPECT before surgery were used for comparison. The demographic findings of the patients used as a control group are presented in **Supplementary Table 1**, http://links.lww.com/NEU/D309.

Data Availability

The data that support the findings of this study are available on request from the corresponding authors, SH Paek and B Jeon. The data are not publicly available because of their containing information that could compromise the privacy of research participants.

Statistical Analysis

All analyses were performed using SPSS 25.0 (SPSS Inc.). We presented the preoperative and postoperative absolute scores of UPDRS as the means ± SD and treated preoperative and follow-up UPDRS and functional disability scores as repeated measures using generalized estimating equations. For comparing the percentage of improvement of unmatched samples between preoperative and postoperative conditions, the Mann–Whitney *U* test was used. A *P* value of .05 or lower was considered statistically significant. A Kaplan–Meier analysis of the patients with PD was compared with that of the standard population.[16]

RESULTS

Patient Characteristics

A total of 81 patients including 37 males (45.7%) and 44 females (54.3%) were included in this study. The mean age was 61.7 ± 9.7 (range 27-82) years, and the mean age at onset was 48.3 ± 10.0 (range 11-66) years. The mean disease duration before surgery was 11.3 ± 4.8 (range 5-30) years, and levodopa-equivalent daily dose (LEDD) was 1063 ± 445.7 (range 375-2100) mg/D at the time of surgery.

Overall Progress

Revision surgery was required for repositioning of the electrodes in 12 of 81 patients (14.8%). During the follow-up period of more than 10 years, 35 patients (43%) died and 46 patients (57%) survived. Among them, 36 patients (45%) were under regular follow-up at the outpatient clinic, but 10 patients (12%) refused hospital visit and further follow-up, and their current condition was assessed through telephone interview with their caregivers. Clinical effects of stimulation persisted in 34 (42%) patients, and 33 (40%) were ambulatory up to more than 11 years. One patient was able to lead a completely independent life with a Barthel Activities of Daily Living score of 100, whereas 23 showed moderate dependency with a score of 61 to 90, 11 patients showed severe dependency with a

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TABLE 1. Comparison of Baseline Characteristics Between the 3 Groups According to the Clinical Outcome: A Group of Patients Alive and Under Follow-Up (n = 36), a Group of Patients Alive Who Discontinued With Follow-Up (n = 10), and a Group of Dead Patients (n = 35)

	Alive (n = 46)			
Baseline characteristics	Under follow-up (n = 36)	Follow-up discontinuation (n = 10)	Deaths (n = 35)	*P*
Male/female, number (%)	18 (50%)/18 (50%)	3 (30%)/7 (70%)	16 (45.7%)/19 (54.3%)	.523
Age at the time of surgery (y)	58.9 ± 11.1	64.1 ± 7.8	63.9 ± 7.8	.146
Age at disease onset (y)	45.6 ± 9.9	50.0 ± 8.9	50.5 ± 9.8	.042
Disease duration (y)	11.8 ± 4.9	11.9 ± 6.3	10.6 ± 4.1	.692
BMI (kg/m^2)	22.8 ± 3.7	23.7 ± 3.5	22.4 ± 2.7	.584
Dose of levodopa-equivalent medication (mg/D)	1010.5 ± 452.4	1138.4 ± 474.8	1095.5 ± 464.6	.507

BMI, body mass index.

score of 21 to 60, and 1 patient was totally dependent. In the cognitive function evaluation, 22 patients (27%) showed a final mini-mental state examination score of 24, and 14 (17%) experienced rapid eye movement (REM) sleep disturbance. None of the survivors for more than 10 years experienced any long-term stimulation-related complications.

We divided 81 patients into 3 groups according to the clinical outcome: alive and under follow-up (group A, n = 36), alive but discontinued follow-up (group B, n = 10), and dead patients (group C, n = 35). When comparing preoperative conditions between the 3 groups, the age at the time of surgery was the only significant factor varying between the 3 groups: patients alive and under follow-up were relatively young (Table 1).

Excluding 12 patients who underwent revision, the preoperative UPDRS scale of the remaining patients was analyzed (Table 2). Axial symptoms and gait were the only features that were significantly different among the 3 groups. Other axial symptoms were 5.0 ± 2.5 (group A), 8.0 ± 3.6 (group B), and 6.7 ± 3.9 (group C) in patients undergoing medication, showing a significant difference with a *P*-value of .009. Gait also showed a significant difference with a *P*-value of .001: 0.6 ± 0.5 (group A), 1.3 ± 0.9 (group B), and 0.9 ± 0.7 (group C).

TABLE 2. Comparison of the Preoperative UPDRS Scores Between the 3 Groups According to the Clinical Outcome: A Group of Patients Alive and Under Follow-Up (n = 36), a Group of Patients Alive Who Discontinued With Follow-Up (n = 10), and a Group of Dead Patients (n = 35)

	Medication on				Medication off			
	Alive (n = 46)				Alive (n = 46)			
Evaluation items	Under follow-up (n = 36)	Follow-up discontinuation (n = 10)	Death (n = 35)	*P*	Under follow-up (n = 36)	Follow-up discontinuation (n = 10)	Death (n = 35)	*P*
UPDRS III	17.9 ± 10.0	25.9 ± 17.2	21.8 ± 12.2	.429	39.1 ± 14.8	50.2 ± 17.5	39.1 ± 13.9	.182
Tremor	1.2 ± 1.7	1.1 ± 1.9	0.8 ± 1.3	.744	2.0 ± 2.3	2.0 ± 2.2	2.1 ± 3.3	.967
Rigidity	3.6 ± 2.9	4.8 ± 4.1	3.2 ± 2.7	.571	7.2 ± 2.6	8.4 ± 4.7	5.8 ± 3.1	.078
Bradykinesia	0.8 ± 0.5	1.4 ± 0.8	1.0 ± 0.8	.063	2.2 ± 1.1	3.1 ± 0.8	2.3 ± 0.9	.056
Speech	0.9 ± 0.8	1.4 ± 0.8	1.2 ± 0.8	.067	1.3 ± 0.7	1.7 ± 0.7	1.5 ± 0.7	.178
Other axial	5.0 ± 2.5	8.0 ± 3.6	6.7 ± 3.9	.009	11.2 ± 5.2	15.0 ± 5.4	12.3 ± 4.4	.095
Postural instability	0.8 ± 0.7	1.3 ± 0.9	1.1 ± 0.9	.152	1.6 ± 1.1	1.9 ± 0.7	1.9 ± 0.9	.334
Gait	0.6 ± 0.5	1.3 ± 0.9	0.9 ± 0.7	.001	1.7 ± 1.0	2.3 ± 0.8	1.9 ± 0.9	.224
UPDRS II	8.0 ± 6.7	6.5 ± 5.4	11.6 ± 8.2	.066	20.9 ± 8.8	23.6 ± 8.5	24.6 ± 6.8	.123
Freezing	0.6 ± 0.8	0.6 ± 1.1	0.8 ± 1.0	.549	1.9 ± 1.2	2.5 ± 1.6	2.4 ± 1.1	.136
UPDRS IV								
Dyskinesia duration	1.5 ± 1.0	1.6 ± 0.7	1.5 ± 0.9	.921				
Dyskinesia disability	2.1 ± 1.2	2.8 ± 1.2	2.5 ± 1.4	.223				
Off duration	1.7 ± 0.8	1.6 ± 0.7	1.9 ± 0.9	.513				

UPDRS, Unified Parkinson's Disease Rating Scale.

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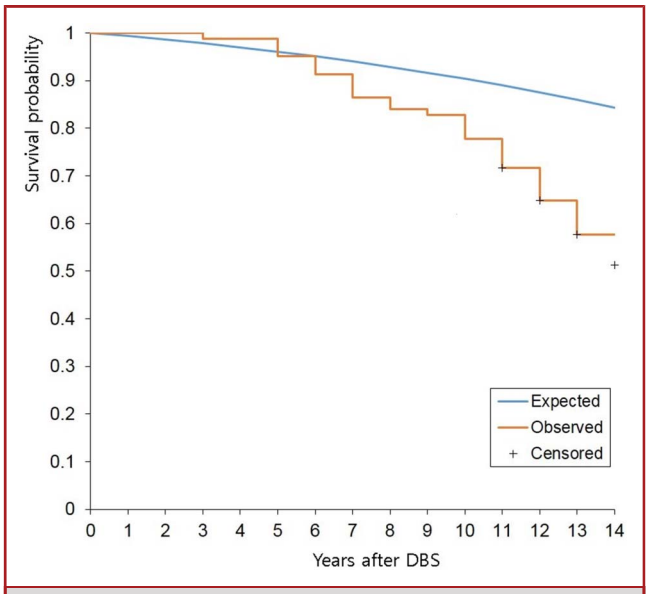

FIGURE 1. *Kaplan–Meier curve shows the survival probability of patients with PD after subthalamic nucleus DBS compared with the standard population. The blue line termed "Expected" represents the survival of the standard population, whereas the orange line termed "Observed" is the survival of the patients with PD. The log-rank P value is 1.6 × 10^{-16}. DBS, deep brain stimulation; PD, Parkinson's disease.*

A follow-up of 12 patients who underwent revision surgery to correct electrode location revealed that revision surgery was successful in 9 patients, whereas it failed in 3 patients. Of the 9 patients who underwent successful revision surgery, 6 patients (66.7%) survived with regular follow-up, whereas 3 patients (33.3%) died. All 3 patients who failed revision surgery were alive at the time of the study, but were not followed up.

Survival After STN DBS

The Kaplan–Meier curve in Figure 1 shows the survival probability of patients with PD after STN DBS. Overall, the cumulative survival rate was 95% at 5 years and 79% at 10 years after DBS surgery, implying that 64 (79%) of 81 PD patients with advanced disease survived more than 10 years after bilateral STN DBS.

Thirty-five of 81 patients (43%) died during the 11-year follow-up including 16 (45.7%) males and 19 (54.3%) females. Nonsurvivors lived on average for 110.46 ± 40.8 months after DBS surgery (range 0-166 months). The cause of death in a patient who died less than a month after surgery was suicide. The most common causes of death were PD progression (n = 13, 37.1%) and pneumonia (n = 11, 31.4%). The next most common cause of death was unknown (n = 4, 11.4%), followed by cancer (n = 2, 5.7%), whereas heart disease, drowning, suicide, sepsis, and peptic ulcer perforation were diagnosed in single cases (2.8%).

Of the survivors, 10 patients refused to visit hospital for follow-up, which was an average of 45 ± 33.1 (range 6-84) months. Follow-up was discontinued because of movement difficulty because of bedridden state (n = 5, 50%) or economical problem (n = 5, 50%).

Long-Term Motor Effects

The UPDRS-III score was significantly improved compared with baseline scores until a 5-year follow-up although it tended to reincrease at 10 years after bilateral STN DBS. Drug-related motor complications improved (Table 3). Dyskinesia duration, dyskinesia disability, and off duration were reduced up to 10 years after STN DBS. The mean preoperative LEDD decreased by 58% at 1 year and 45% at 10 years.

Electrode Location Analysis

Patients were divided into 3 groups based on the electrode position to determine the correlation between clinical outcomes (Table 4): group I, both electrodes within STN (n = 54); group II, 1 electrode within STN and the other outside (n = 20); and group III, both electrodes outside STN (n = 27). Group III showed significantly higher rates of revision (group I, 3.7% vs group II, 25% vs group III, 71.4%, $P = .0001$). Patients belonging to the group in which both electrodes were within STN showed higher rates of survival and continued follow-up, despite lack of statistical significance (group I, 51.9% vs group II, 35% vs group III, 14.3%, $P = .085$). In addition, patients belonging to the group in which both electrodes were within STN showed the optimal ambulatory survival outcomes.

Adverse Effects

The most common adverse effect was weight gain higher than 10 kg (n = 8, 9.8%), followed by transient confusion or decreased consciousness (n = 3, 3.7%), dysarthria (n = 2, 2.5%), track hemorrhage (n = 1, 1.2%), implantable pulse generator pocket abscess (n = 1, 1.2%), apraxia of eyelid opening (n = 1, 1.2%), severe depression requiring medication (n = 1, 1.2%), and abulia (n = 1, 1.2%). Among 8 patients with a weight gain of 10 kg or more, 5 patients gained weight at 1 year after surgery, 1 patient at 3 years later, and 2 patients at 5 years later. All 3 patients who showed postoperative confusion and decreased consciousness improved spontaneously within 3 days. In addition, other complications of dysarthria, abscess, and apraxia of eyelid opening improved within the first 3 months. However, 1 patient who experienced persistent abulia died at 3 years after surgery and the other patient with severe depression required medication until death for 7 years after surgery.

Difference in DAT BPnd

The DAT BPnd values were compared across 3 groups: before DBS (n = 83), 7 years after DBS (n = 8), and 10 years after DBS (n = 26). One-way analysis of variance (ANOVA) followed by Tukey's multiple comparison test was performed to evaluate the difference in DAT BPnd values between the groups. There was a significant difference in one-way ANOVA between the groups ($P < .0001$). After 7 and 10 years, a significantly lower DAT BPnd compared with pre-DBS was observed ($P < .05$, $P < .05$, respectively). However, there was no difference in DAT BPnd values between 7 and 10 years (Figure 2A). No significant difference in preoperative DAT BPnd was found between the group that

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TABLE 3. The UPDRS Scores at the Time of Surgery and 1, 5, and 10 Years After Surgery, Excluding 12 Patients Who Underwent Revision Surgery

	Medication on					Medication off				
Evaluation items	Baseline (n = 69)	S+ 1 y (n = 58)	S+ 5 y (n = 44)	S+ 10 y (n = 38)	*P*	Baseline (n = 69)	S+ 1 y (n = 63)	S+ 5 y (n = 54)	S+ 10 y (n = 46)	*P*
UPDRS III	20.1 ± 12.7	15.3 ± 8.6	22.2 ± 11.0	28.3 ± 12.7	.026	39.8 ± 14.6	20.1 ± 9.7	27.1 ± 12.5	29.5 ± 10.8	.000
Tremor	1.0 ± 1.6	0.3 ± 1.0	0.5 ± 0.7	0.7 ± 0.9	.004	1.9 ± 2.2	0.5 ± 1.3	1.1 ± 0.9	0.9 ± 0.9	.000
Rigidity	3.3 ± 3.1	1.8 ± 2.3	2.1 ± 2.0	2.9 ± 3.5	.015	6.6 ± 3.4	2.7 ± 2.8	3.1 ± 2.2	3.2 ± 3.4	.000
Bradykinesia	1.0 ± 0.8	1.0 ± 0.7	1.4 ± 1.0	1.2 ± 1.2	.012	2.4 ± 1.0	1.4 ± 0.7	1.6 ± 1.0	1.2 ± 1.1	.000
Speech	1.1 ± 0.8	1.3 ± 0.8	1.6 ± 0.9	1.8 ± 0.8	.041	1.4 ± 0.7	1.3 ± 0.7	1.8 ± 0.9	1.8 ± 0.8	.021
Other axial	5.9 ± 3.7	5.8 ± 3.1	8.7 ± 5.3	8.7 ± 5.8	.004	12.1 ± 5.1	7.3 ± 3.7	9.6 ± 5.6	9.0 ± 5.0	.000
Postural instability	0.9 ± 0.9	0.7 ± 0.8	1.4 ± 1.2	1.2 ± 1.0	.029	1.7 ± 1.0	0.9 ± 0.8	1.5 ± 1.2	1.3 ± 1.0	.000
Gait	0.8 ± 0.7	0.9 ± 0.7	1.5 ± 1.0	1.0 ± 1.0	.002	1.9 ± 0.9	1.2 ± 0.8	1.6 ± 1.1	1.1 ± 0.9	.000

	Baseline	S− 1 y (n = 54)	S− 5 y (n = 39)	S− 10 y (n = 31)	*P*	Baseline	S− 1 y (n = 54)	S− 5 y (n = 39)	S− 10 y (n = 31)	*P*
UPDRS III	–	27.9 ± 14.0	35.6 ± 14.0	41.2 ± 17.1	.010	–	34.7 ± 13.8	42.5 ± 13.4	46.2 ± 12.8	.006

	Medication on					Medication off				
	Baseline (n = 69)	S+ 1 y (n = 58)	S+ 5 y (n = 44)	S+ 10 y (n = 38)	*P*	Baseline (n = 69)	S+ 1 y (n = 63)	S+ 5 y (n = 54)	S+ 10 y (n = 46)	*P*
UPDRS II	9.3 ± 7.8	10.4 ± 6.5	16.2 ± 8.6	16.8 ± 8.1	.000	22.3 ± 8.1	15.3 ± 7.4	21.7 ± 8.4	22.6 ± 8.9	.000
Freezing	0.7 ± 1.0	1.0 ± 1.0	1.3 ± 1.2	1.3 ± 1.2	.012	2.1 ± 1.3	1.5 ± 1.1	2.0 ± 1.2	2.2 ± 1.3	.012
UPDRS IV										
Dyskinesia duration	1.5 ± 1.0	0.4 ± 0.8	0.4 ± 0.8	0.3 ± 0.5	.000					
Dyskinesia disability	2.2 ± 1.4	0.6 ± 1.2	0.7 ± 1.2	0.7 ± 1.3	.000					
Off duration	1.7 ± 0.8	1.1 ± 1.1	1.3 ± 1.2	1.5 ± 1.3	.000					
LEDD	1084.2 ± 455.3	439.0 ± 325.7	735.3 ± 540.5	621.6 ± 381.6	.000					

LEDD, levodopa-equivalent daily dose; S+, stimulation on; S−, stimulation off; UPDRS, Unified Parkinson's Disease Rating Scale.

underwent DBS surgery within 10 years of PD diagnosis and the group that underwent surgery after 10 years (Figure 2B).

DISCUSSION

The life expectancy of patients with PD is shorter than that of the general population.[17] The role of DBS in extending the life expectancy of patients with PD is disputed, and most studies are limited by the small sample size of patients or lack of a control group.[13-15,18-20]

In this study, the patients' mean age was 62 years. In male patients (n = 37), 5-year and 10-year survival rates were 91.9% and 75.7%, and in female patients (n = 44), 5-year and 10-year survival rates were 95.5% and 81.8%. In the Korean life table, the probability of survival of 62-year-old patients between 2005 and 2008 is as follows: male, 93.2% (5 years) and 83.1% (10 years)

TABLE 4. Analysis of Electrode Location According to the Clinical Outcome

Evaluation items	Group I (n = 54)	Group II (n = 20)	Group III (n = 7)	*P* value
Description	Both within STN	Only 1 within STN	Both outside STN	
Revision required	2 (3.7%)	5 (25%)	5 (71.4%)	.0001
Clinical outcome				.085
Survival and under follow-up	28 (51.9%)	7 (35%)	1 (14.3%)	
Survival and follow-up discontinuation	5 (9.3%)	3 (15%)	2 (28.6%)	
Death	21 (38.9%)	10 (50%)	4 (57.1%)	.6209
Disease progression	7 (33.33%)	3 (30%)	1 (25%)	
Other medical cause	14 (66.67%)	7 (70%)	3 (75%)	

STN, subthalamic nucleus.

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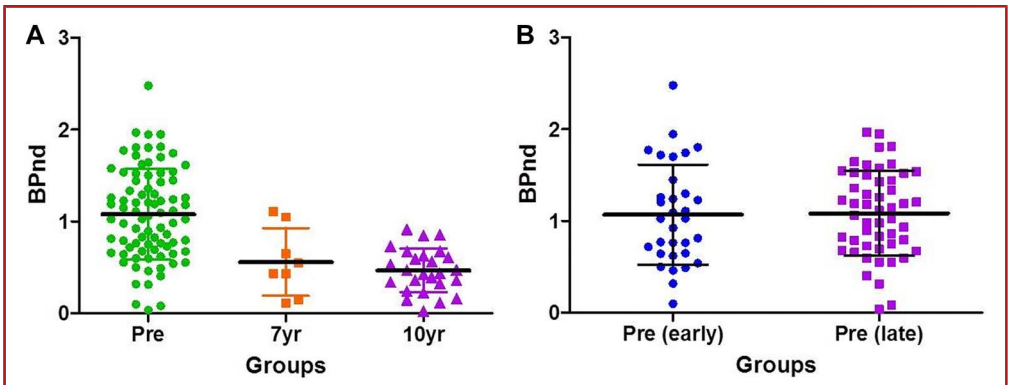

FIGURE 2. *Difference in DAT BPnd measured by SPECT. The DAT BPnd value was evaluated in patients who underwent SPECT until 10 years after DBS.* **A**, *DAT BPnd values were compared across 3 groups of patients 7 and 10 years after DBS in the current cohort group and a different preoperative reference group before DBS. Because the patients included in this study did not undergo preoperative SPECT, data from the preoperative SPECT group were used for preoperative and postoperative comparison. There was no difference in DAT BPnd values between the groups at 7 and 10 years although they were significantly lower than those in the other preoperative reference group.* **B**, *There was no significant difference in preoperative DAT BPnd between the current cohort group undergoing DBS surgery within 10 years of PD diagnosis and the current cohort group that underwent surgery after 10 years. BPnd, binding potentials; DAT, dopamine transporter; SPECT, single-photon emission computed tomography.*

and female, 97.4% (5 years) and 93.0% (10 years). Because this is not compared with the group of patients with PD treated medically, it is not known whether DBS surgery prolongs the life expectancy of patients with PD.

Compared with the preoperative group, the DAT BPnd was significantly lower in the patient group 7 and 10 years after surgery, suggesting degenerative changes because of continuous loss of cell bodies in the dopaminergic neurons of the substantia nigra even after DBS. In addition, there was no significant difference between the groups of patients who underwent surgery within and after 10 years, so it does not provide evidence to support the need for early DBS. This may refute the evidence of neuroprotective effects of DBS.[21,22] However, because this study was not compared with the group of patients undergoing medical management who had progressed during the same period without surgery, it does not suggest that surgery is not effective in preventing the progressive degeneration.[16-18]

TABLE 5. Previous Studies Reporting Long-Term Prognosis of More Than 5 Years After Subthalamic Nucleus Deep Brain Stimulation in Patients With Parkinson's Disease

Evaluation items	Patients (n)	Follow-up (mo)	Age (y)	Duration of PD (y)	Change in UPDRS score			Decrease Daily off time
					UPDRS II	UPDRS III	LEDD	
Krack et al[25]	49	60	55.0 ± 7.5	14.6 ± 5.0	66.1%	65.9%	58.5%	71%
Schüpbach et al[26]	37	60	54.9 ± 9.1	15.2 ± 5.3	40%	54%	58%	NR
Wider et al[27]	50	60	64.6 ± 7.6	14.4 ± 4.9	NR	47.7%	56.9%	NR
Romito et al[28]	20	60	56.4 ± 6.9	14.3 ± 6.2	NR	54.2%	61.9%	NR
Gervais-Bernard et al[29]	23	60	55.1 ± 7.2	12.9 ± 3.2	38%	55%	54.4%	NR
Moro et al[1]	35	60-72	59.6 ± 1.6	13.5 ± 1.1	NR	45.4%	29.7%	NR
Castrioto et al[30]	18	120	52.9 ± 7.9	13.4 ± 4.8	162.7%	144.7%	36.3%	38.1%
Aviles-Olmos et al[31]	12	96	52.8 ± 10.1	12.3 ± 4	126%	114%	48.6%	NR
Janssen et al[32]	26	120	58.0 ± 6.9	12.7 ± 5.1	94.4%	71.2%	31.8%	NR
Rizzone et al[33]	26	132	NR	NR	188.5%	91.8	32.2%	NR
Li et al[34]	195	60	58.2 ± 10.0	6.8 ± 4.2	54%	60%	26%	NR
Lezcano et al[35]	54	60	61.1 ± 7.6	13.0 ± 5.3	71.4%	73.2%	23.9%	46%
Bove et al[36]	51	204	51.03 ± 8.53	11.35 ± 3.77	138%	303%	50.6%	58.7%
This study (2021)	81/69[a]	145	61.7 ± 9.7	11.3 ± 4.8	105.8%	21.3%	45.1%	12%

LEDD, levodopa-equivalent daily dose; PD, Parkinson's disease; UPDRS, Unified Parkinson's Disease Rating Scale.
[a]Clinical outcomes of 69 patients, excluding 12 who underwent revision surgery, were analyzed.

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In patients with the electrode positioned precisely within the STN, long-term survival might have improved by DBS-related neuroprotective or disease-modifying treatment.[23] In our study, when at least 1 of the electrodes was located outside the STN, the clinical improvement was poor, and in some cases, relocation surgery was required. We hypothesize that the reasons for the increased survival of patients with both electrodes well-located in the STN are as follows: Patients with both electrodes well-located in the STN have a higher rate of maintaining better daily activity. In consideration of their ages, they experience various diseases common to old ages, and the resulting sequelae (pneumonia, pressure sores, urinary tract infection, etc) mostly lead to death. Patients with well-preserved daily activity tend to overcome these sequelae well, which could lead to increased survival. With the recent development of imaging and emerging new technologies, accurate positioning of the electrode within the STN may be helpful, and a better prognosis is expected in the future.[24]

It is noteworthy that the UPDRS-II scores in previous studies that were followed for more than 120 months listed in Table 5[1-13,25-36] returned to the same level as at the time of the surgery. However, UPDRS-III, LEDD, and daily off time are still maintained in an improved state. It can be used as a clue to guess how much effect that patients can expect when more than 10 years have passed since DBS. Recently, the Moro group published the results of a 15-year follow-up study of patients with PD, which shows maintained improvement in motor complication and reduction in LEDD.[36]

Limitations and Strengths of this Study

This study has several limitations. This is a retrospective study performed at a single center, and there is no control group of patients treated with medications alone. Another limitation is the lack of a neuropsychological outcome. However, this study is the longest follow-up study with a prospective follow-up protocol and the largest cohort without follow-up loss after bilateral STN DBS involving patients with advanced PD. We tried to present realistic results based on an analysis of the current status of patients who were lost to follow-up through telephone interview with their caregivers. In addition, 1 of the advantages is that the correlation between the precise position of the electrode within the STN and the current status after long-term follow-up was analyzed.

CONCLUSION

Bilateral STN DBS is a safe and effective treatment for advanced PD and may influence the progression of PD. The survival probability of patients with PD undergoing STN DBS is similar to that of the general population by at least 5 years. Patients carrying both electrodes within the STN showed a low probability of death and were likely to survive enough to visit the outpatient clinic. This study was based on a long-term follow-up of large-scale patients and elucidates the long-term outcomes of patients who underwent bilateral STN DBS for PD.

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Disclosures

The authors have no personal, financial, or institutional interest in any of the drugs, materials, or devices described in this article. Dr Im is the Chief Scientific Officer of Portai and a consultant of CellBion.

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Supplementary Table 1. Demographic characteristics of patients who underwent SPECT before deep brain stimulation vs the control group.

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