



## Original Article

# Quality of life in patients with Parkinson's disease after subthalamic stimulation: An observational cohort study for outcome prediction

Jiin-Ling Jiang<sup>a</sup>, Shin-Yuan Chen<sup>b,c</sup>, Sheng-Tzung Tsai<sup>b,c\*</sup>

<sup>a</sup>Department of Nursing, Tzu Chi University, Hualien, Taiwan,

<sup>b</sup>Department of Neurosurgery, Buddhist Tzu Chi General Hospital, Hualien, Taiwan,

<sup>c</sup>School of Medicine, Tzu Chi University, Hualien, Taiwan

## ABSTRACT

**Objective:** The objective of this study was to investigate the changes in health-related quality of life (HRQoL) and motor and depressive symptoms in patients with Parkinson's disease (PD) from baseline to 12 months following subthalamic nucleus deep brain stimulation (STN-DBS). **Materials and Methods:** The study utilized a prospective observational cohort design. Thirty-three PD patients with a good levodopa response but drug-related morbidity were included. PD Questionnaire-39 (PDQ-39) scores, unified PD rating scale (UPDRS) scores, Hoehn and Yahr stages, Beck Depression Inventory-II scores, and levodopa equivalent daily doses (LEDD) were obtained at baseline and 1 year after surgery. **Results:** The enrolled patients showed a significant HRQoL improvement of 21.43% at 12 months after STN-DBS as assessed by the PDQ-39 total score. There was a 34.92% improvement in UPDRS scores after STN-DBS at 1 year follow-up. Subitem analysis revealed significant improvement in UPDRS part II, III, and IV scores. The LEDD was significantly reduced by up to 27.36% 12 months after surgery. The preoperative PDQ-39 total score and LEDD predicted postoperative HRQoL in PD following STN-DBS. **Conclusions:** The current study demonstrated that STN-DBS surgery significantly improved HRQoL and motor outcomes of patients with PD. The preoperative PDQ-39 score and LEDD were predictors of the efficacy of postoperative HRQoL following surgery.

**KEYWORDS:** Deep brain stimulation, Parkinson's disease, Quality of life, Subthalamic nucleus

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## INTRODUCTION

Parkinson's disease (PD) is a chronic neurodegenerative disease that places a substantial burden on patients, their families, and their caregivers, as well as on society as a whole. The progressive decline in motor function and the comorbidities associated with PD negatively affect health-related quality of life (HRQoL) [1]. Subthalamic nucleus deep brain stimulation (STN-DBS) is the most common surgical procedure for PD. HRQoL significantly improved in the majority of patients who underwent STN-DBS [2], but not in all items of HRQoL [3]. However, when using patient-based self-assessment scales, the clinical benefits imparted by STN-DBS were more subtle: physical components related to HRQoL significantly improved, whereas the mental components of HRQoL, such as emotional well-being, social support, and communication, did not show consistently remarkable improvement [4]. Clinical evaluation of PD typically encompasses a variety of functional and mental assessments, in addition to data gathered during patient examinations. The Core Assessment Program for Surgical

Interventional Therapy (CAPSIT) protocol [5] recommends that patients complete questionnaires assessing HRQoL before starting preoperative evaluations and at 6 months, 1 year, and 2 years postsurgery, and once a year thereafter if evaluation is continued.

PD patients are particularly vulnerable to deterioration of HRQoL resulting from both motor disability and nonmotor symptoms. Motor improvement in PD patients by STN-DBS is sustained for up to 5–8 years after surgery [6,7]. Lyons and Pahwa found that while some early improvements in motor disability deteriorated over time [8], significant improvements in HRQoL following STN-DBS were strongly correlated with improvement in motor function [9]. On the contrary, some studies showed that the psychiatric symptoms following STN-DBS were not correlated with improvement

\*Address for correspondence:

Dr. Sheng-Tzung Tsai,  
Department of Neurosurgery, Buddhist Tzu Chi General Hospital,  
707, Section 3, Chung-Yang Road, Hualien, Taiwan.  
E-mail: flydream.tsai@gmail.com

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in HRQoL [10-12]. Another randomized trial documented that amelioration in mood symptoms, such as anxiety, paralleled the improvement in HRQoL [13]. Owing to the lack of consensus regarding correlation between changes in HRQoL and symptoms following STN-DBS, further investigation is needed [14]. Moreover, self-assessed health status may provide a more referable predictor of outcome than many objective measures of health. Improvements in HRQoL are usually reported as a summary score in clinical trials for PD [15,16]. It is necessary to improve our understanding of which components of HRQoL and clinical symptoms are affected by treatment. There are few reports regarding HRQoL and motor and depressive symptoms following STN-DBS, particularly in Asian patients, who have different cultural backgrounds, perceptions, and needs than Western patients. In the current study, we aimed to compare each domain of HRQoL and motor and depressive symptoms in patients with PD at baseline and 1 year after STN-DBS surgery and identify significant factors that impact quality of life following surgery.

## MATERIALS AND METHODS

### Participants

The current study utilized a prospective, observational cohort design to evaluate changes in HRQoL and in motor and depressive symptoms of PD patients from baseline through 1 year after bilateral STN-DBS surgery. This study was conducted at a medical center in Taiwan. From July 2011 to June 2014, 33 Taiwanese PD patients who underwent STN-DBS surgery were enrolled in our study. PD was diagnosed according to the United Kingdom PD Society Brain Bank criteria [17]. As described in detail previously [8], the inclusion criteria were as follows: (1) idiopathic PD; (2) a good levodopa response on the Unified PD rating scale (UPDRS) Part III (>28% improvement in Part III scores); and (3) the presence of drug-related complications (e.g. dyskinesia, “on-off” phenomenon, or psychiatric symptoms), even under optimal anti-parkinsonian medication adjustments. The exclusion criteria were as follows: (1) dementia, as defined by a mini-mental state examination score <24; (2) structural lesions in the brain identified by magnetic resonance imaging (MRI) or computerized tomography (CT); and (3) contraindications for surgery.

### Ethical considerations

The current study was approved by the Tzu Chi Hospital Ethical Committee (IRB097-32). The enrolled patients can understand the benefits and risks of STN-DBS before undergoing surgery, and the decision to pursue surgery was reached by consensus with the clinical team and patient. All patients provided written informed consent before data collection.

### Surgical procedure

Before the operation, cranial images were obtained with a 1.5-Tesla MRI machine (General Electric, Rahway, NJ, USA). The standard settings included T1-weighted axial images at a 0.75-mm thickness, T2-weighted axial images at a 2-mm thickness, and T1-weighted images with contrast (delineation of vasculature in cases of injury). Each of these sequences

was performed in contiguous axial slices. The images were transferred to a Stealth neuronavigation workstation (Medtronic, Minneapolis, MN, USA). The image fusion software fused all three sets of MR images. The surgical target coordinates for the tip of the permanent implantable electrode were set at the center of the STN by direct visualization from brain MRI (direct targeting) and adjusted according to the relative position of the anterior commissure–posterior commissure line and red nucleus (indirect targeting). On the morning of the operation, a Leksell G-frame (Elekta Instrument Inc., Norcross, GA, USA) was applied under local anesthesia with the patient sitting in a chair. Patients were then given CT examinations. The CT images were fused on the preoperative MRI to determine target coordinates. During neurophysiological mapping, neural firings obtained from the tip of the microelectrode (FHC, Bowdoin, ME, USA) were sent to the intraoperative microelectrode recording system (Leadpoint; Medtronic) where they were magnified and displayed. The selection of the final trajectory for electrode implantation (Medtronic 3389 DBS leads) depended on adequate length of STN hyperactivity neuronal firing and the presence of movement-related firing pattern changes. Brain CT imaging was obtained immediately after the operation to exclude intracranial hemorrhage and to localize the postoperative electrode. A pulse generator was usually implanted 1 week after electrode implantation. A postoperative active stimulation test was performed to identify the maximal effectiveness of contact and related adverse effects. Detailed surgical procedures have been described in a previous report [18].

### Study instruments

The HRQoL survey was assessed according to the PD questionnaire-39 (PDQ-39) score, which is a disease-specific measurement instrument for patients with PD. A higher score signifies a poorer quality of life [19]. The Chinese version of the PDQ-39 has been shown to be a reliable instrument [20]. This self-assessment was performed before surgery and at 1 year after STN-DBS surgery.

The UPDRS was used to follow the longitudinal course of PD. A nursing specialist scored patients on a scale from 0 to 199. A higher score indicates worse function [21]. The presurgery UPDRS Part III motor evaluation was performed for each patient after they achieved an off-medication condition, which was the withdrawal of dopaminergic medication for at least 12 h, as defined by the CAPSIT protocol for PD [5]. The same assessments were performed postoperatively under off-medication conditions with bilateral STN-DBS on. UPDRS Part III motor scores were separately assessed for tremor items 20–21, rigidity item 22, bradykinesia items 23–26 and 31, posture-gait items 28–29, and axial items 18 and 27–30.

The Hoehn and Yahr (H and Y) stage classifies patients with PD into one of the five different stages according to their bodily distributions of symptoms and level of dependency [22]. While the original scale included stages 1 through 5, in the 1990s, 0.5 increments were introduced for some clinical trials [23].

The Beck Depression Inventory-II (BDI-II) is one of the most widely used instruments for measuring the severity of depression. A previous cluster analysis demonstrated that

the BDI is a valid instrument for quantifying depression in PD patients [24]. The BDI-II contains 21 questions, and each answer is scored on a scale of 0–3. Scores of 0–13 indicate minimal depression; 14–19, mild depression; 20–28, moderate depression; and 29–63, severe depression [25]. The total levodopa equivalent daily dose (LEDD) was calculated according to the accepted equivalence between different dopaminergic drugs [26].

**Statistical analysis**

All descriptive data are presented as the median ± standard deviation (SD). Because normality could not be observed for the relatively small group of patients, nonparametric testing was used. The Wilcoxon matched-pairs signed-rank test was used to compare the variables measured at baseline and 1 year after surgery; these variables included the UPDRS score, H and Y stage, BDI-II score, LEDD, and PDQ-39 score. *P* < 0.05 was considered statistically significant. The relative magnitude of changes in HRQoL was standardized to percentages by applying the following formula: magnitude of the change (%) = (final value – baseline value) × 100/baseline value. A generalized linear model was used to predict the postoperative HRQoL from each preoperative characteristic.

**RESULTS**

Thirty-three patients with PD were included and completed the follow-up in the study. Details of the baseline characteristics of patients are given in Table 1. Women participants reported more problematic HRQoL and had more motor difficulties in daily living and experienced significantly more stigma than men.

**Effects of health-related quality of life after subthalamic nucleus deep brain stimulation**

One year after STN-DBS surgery, there was a significant overall improvement in HRQoL (21.43%). Among the PDQ-39 individual domains, significant improvements were found for mobility, ADL, emotional well-being, and bodily discomfort, but not for stigma, social support, cognition, or communication [Table 2].

**Clinical features and depressive symptoms after subthalamic nucleus deep brain stimulation**

In terms of clinical effectiveness, the patients showed a 34.92% improvement in PD status, as measured by UPDRS total scores and a 30.56% improvement in UPDRS Part III scores after STN-DBS [Table 3]. There were significant improvements in the UPDRS Part II (38.46%) and IV (44.16%) scores under off-medication/on-stimulation conditions at the 1-year follow-up, while no significant improvements were found in UPDRS Part I. Some individual variables of UPDRS Part III also showed significant improvements 1 year postsurgery, including tremor (48.77%), rigidity (41.44%), bradykinesia (10.50%), posture-gait symptoms (26.62%), and axial symptoms (14.94%). Significant improvements were also observed in the H and Y stage. In terms of depressive symptoms, patients had BDI-II scores of 16.2 ± 9.44 (median ± SD) at baseline and 13.58 ± 10.25 at 1 year, with no statistically significant changes between assessments. Significant reductions in medication of up to 27.36% were observed in LEDD values at 1 year postsurgery compared with preoperatively.

**Table 1: Preoperative data for Parkinson’s disease patients (n=33)**

	Female	Male	Total	P
Subject	17	16	33	
Age at PD onset (year)	50.47±7.73	50.88±10.49	50.67±9.03	0.900
PD duration (year)	10.18±3.34	9.88±4.47	10.03±3.87	0.827
LEDD (mg)	794.78±334.18	904.49±414.87	847.97±373.66	0.408
UPDRS total (0-199)	73.82±15.80	66.25±23.88	70.15±20.17	0.288
Part I (0-16)	4.24±1.79	4.00±2.16	4.12±1.95	0.735
Part II (0-52)	20.24±5.78	18.56±9.23	19.42±7.58	0.535
Part III (0-108)	42.24±10.36	37.69±12.18	40.03±11.34	0.256
Part IV (0-23)	7.12±2.69	6.00±3.92	6.58±3.34	0.344
H and Y stage (0-5)	3.21±0.66	3.16±0.89	3.18±0.77	0.856
MMSE (0-30)	26.06±3.85	27.44±1.90	26.73±3.10	0.206
BDI-II (0-63)	14.53±7.06	17.81±11.44	16.12±9.44	0.326
PDQ-39 total (0-156)	60.18±25.07	46.19±21.83	53.39±24.25	0.098
Mobility (0-40)	22.12±9.30	15.81±9.86	19.06±9.95	0.068
ADL (0-24)	8.65±5.50	5.81±4.48	7.27±5.16	0.116
Emotional well-being (0-24)	7.94±6.01	6.69±4.54	7.33±5.30	0.506
Stigma (0-16)	6.12±4.77	3.19±3.19	4.70±4.28	0.048*
Social support (0-12)	1.71±2.26	1.81±2.14	1.76±2.17	0.890
Cognition (0-16)	6.24±2.93	4.63±3.24	5.45±3.14	0.144
Communication (0-12)	2.59±3.18	3.94±2.21	3.24±2.80	0.169
Bodily discomfort (0-12)	5.41±2.94	4.31±2.50	4.88±2.75	0.257

\**P*<0.05 was considered statistically significant. Numbers in parentheses indicate range of scores. Data are presented as *n* or median±SD. PD: Parkinson’s disease, LEDD: Levodopa equivalent daily dose, UPDRS: Unified Parkinson’s disease rating scale, H and Y stage: Hohen and Yahr stage, BDI-II: Beck depression inventory-second edition, MMSE: Mini-mental state examination, PDQ: Parkinson’s disease questionnaire, ADL: Activities of daily living, SD: Standard deviation

**Factors associated with postoperative health-related quality of life**

We performed generalized linear model analysis to clearly illustrate that preoperative factors might influence postoperative HRQoL after STN-DBS. Of the clinical parameters examined, the preoperative PDQ-39 total score and LEDD at baseline were significantly correlated with the postoperative PDQ-39 score (*R*<sup>2</sup> = 0.519) [Table 4]. The positive standardized beta values show that patients with worse preoperative HRQoL (higher PDQ-39 total scores) and higher levodopa doses had worse HRQoL outcomes 1 year after STN-DBS.

**DISCUSSION**

Our study aimed to explore the impact of surgery on both motor and depressive symptoms and indicate the potential influence of some of these clinical features or factors on postoperative HRQoL. There was significant improvement in overall quality of life at 1 year after surgery, similar to other reports concerning PDQ-39 score changes after STN-DBS

**Table 2: Parkinson’s disease questionnaire-39 at baseline and 12 months after surgery (n=33)**

Item	Preoperative	Postoperative 12 months	Difference	P
PDQ-39 total	53.39±24.25	42.73±24.41	-10.67±24.27	0.011*
Mobility	19.06±9.95	14.58±11.08	-4.49±9.86	0.014*
ADL	7.27±5.16	5.33±4.41	-1.94±5.78	0.038*
Emotional well-being	7.33±5.30	5.70±4.34	-1.64±4.81	0.024*
Stigma	4.70±4.28	3.12±3.07	-1.58±4.10	0.057
Social support	1.76±2.17	1.73±1.93	-0.03±2.52	0.970
Cognition	5.45±3.14	5.52±3.71	0.06±2.86	0.954
Communication	3.24±2.80	3.24±2.68	0.00±2.80	0.942
Bodily discomfort	4.88±2.75	3.52±2.51	-1.36±2.76	0.006*

\*P<0.05 was considered statistically significant. PDQ: Parkinson’s disease questionnaire, ADL: Activities of daily living

**Table 3: Clinical features at baseline and 12 months after surgery (n=33)**

Item	Preoperative	Preoperative 12 months	Difference	P
UPDRS total	70.15±20.17	48.39±12.59	-21.76±22.18	<0.001*
Part I	4.12±1.95	3.45±1.68	-0.67±2.07	0.069
Part II	19.42±7.58	13.18±5.21	-6.24±8.54	<0.001*
Part III	40.03±11.34	27.76±7.12	-12.27±12.34	<0.001*
Tremor	4.45±4.24	2.09±2.71	-2.36±3.32	<0.001*
Rigidity	8.06±3.47	4.03±2.22	-4.03±3.89	<0.001*
Bradykinesia	17.21±5.10	13.94±3.45	-3.27±5.94	0.005*
Posture-gait symptoms	3.94±1.68	2.61±1.32	-1.33±1.59	<0.001*
Axial symptoms	8.48±3.36	6.55±2.64	-1.94±3.44	0.002*
Part IV	6.58±3.34	4.00±2.37	-2.58±4.24	0.002*
H and Y stage	3.18±0.77	2.71±0.38	-0.47±0.84	0.004*
BDI-II	16.12±9.44	13.58±10.25	-2.55±8.49	0.095
LEDD (mg)	847.97±373.66	616.40±331.57	-231.57±341.78	0.001*

\*P<0.05 was considered statistically significant. Values are median±SD. UPDRS: Unified Parkinson’s disease rating scale, H and Y: Hohen and Yahr stage, BDI-II: Beck depression inventory-second edition, LEDD: levodopa equivalent daily dose, SD: Standard deviation

surgery [14,27-29]. Nonetheless, when we analyzed PDQ-39 domains separately, the benefits with respect to baseline improved for only mobility (30.77%), activities of daily living (42.11%), emotional well-being (33.33%), and bodily discomfort (33.33%), but not for the domains of stigma, social support, cognition, and communication. These findings are consistent with the previous studies of STN-DBS for PD that included PDQ-39 subscale data [30-32].

These results may have arisen because the patients were aware that STN-DBS was not curative and that their underlying disease would continue to progress [33,34]. Stereotypes, misunderstandings, shame, isolation, discrimination, and stigmatization are silent and partly invisible phenomena, which must be considered. The absence of significant improvements in social support likely reflects the static natures of the patients’ social networks following surgery. PD negatively influences the social domain of HRQoL, which partially arises due to

embarrassment associated with PD symptoms and difficulties in communication and coping with stigma.

Our study showed a reduction of 10.67 ± 24.27 points in the PDQ-39 total score from baseline to 12 months postsurgery. This was in accordance with previous studies evaluating HRQoL after STN-DBS surgery [9,31]. Compared with the extent of HRQoL improvement in DBS reported by Witt *et al.* [35], our study showed a lower median reduction in the total PDQ-39 score and this difference may have been associated with our small sample size and more variations in PDQ-39 scores obtained after surgery.

The findings that the preoperative PDQ-39 total score and LEDD predicted postoperative HRQoL in PD following STN-DBS are consistent with a previous report [36]. No significant correlations were found between preoperative UPDRS scores, H and Y stage, BDI-II scores, and postoperative PDQ-39 scores in PD patients following STN-DBS. In the current study, 10 (30.3%) patients showed improvements in disease status and severity, but there was deterioration in the HRQoL score after 1 year. This discrepancy may have resulted because the operation outcomes did not meet the patients’ expectations of returning to a normal life; such disappointment may affect self-perception and HRQoL [4]. In addition, HRQoL improved less than the clinical measures of impairment and disability. Based on a previous report by Schrag *et al.* [37], we reasoned that this might be due to the difference between the impacts on objective motor impairment as measured by the UPDRS versus the subjectively evaluated HRQoL. The preoperative LEDD was significantly associated with postoperative HRQoL after STN-DBS surgery. It seemed reasonable that a higher preoperative LEDD had a negative influence on the postoperative HRQoL. A higher LEDD is associated with a higher risk of levodopa-related motor complications.

Previous studies have shown that a diagnosis of depression is a significant prognostic factor in the improvement of quality of life after DBS [38,39]. There was no remarkable change in BDI-II scores after STN-DBS in our study, which might have resulted from the low BDI-II scores in recruited patients. Another study showed that the prevalence of moderate or severe depression might reach 52% in PD patients [40]. The results of this study highlight the need to identify and treat depression in PD, especially for those who are considering STN-DBS. This will maximize the benefits of surgery. Health-care professionals should be aware of not only motor dysfunction but also nonmotor problems affecting the lives of individuals with PD.

The complexity of HRQoL as a whole is the main limitation of this study, as HRQoL is potentially affected by many different variables, including individual coping strategies, experience of spouses and caregivers, and socioeconomic status, which are not measured in the PDQ-39 [41]. Furthermore, we did not include a control group of patients with PD who did not undergo surgery. The information gained from our study and others will enable health-care professionals to become more attuned to the visible and invisible manifestations of PD that are associated with motor and psychiatric symptoms through

**Table 4: Factors associated with postoperative Parkinson's disease questionnaire-39 score (n=33)**

Item	$\beta$	95% CI	P
Intercept	-11.19	-61.99-39.62	0.654
Age	-0.13	-1.05-0.79	0.768
Gender	-	-	-
Female	-3.55	-21.15-14.05	0.681
Male	References		
Preoperative PDQ-39	0.54	0.10-0.98	0.019*
Preoperative UPDRS II	0.69	-0.88-2.26	0.371
Preoperative UPDRS III	0.19	-0.89-1.26	0.723
Preoperative UPDRS IV	-1.81	-4.32-0.70	0.150
Preoperative BDI-II	-0.06	-1.28-1.16	0.915
Preoperative LEDD	0.03	0.01-0.05	0.011*

\*P<0.05 was considered statistically significant. Data are presented as n or median±SD. PDQ: Parkinson's disease questionnaire, UPDRS: Unified Parkinson's disease rating scale, BDI-II: Beck depression inventory second edition, LEDD: Levodopa equivalent daily dose, CI: Confidence interval, SD: Standard deviation

the incorporation of multidisciplinary assessments to identify the needs of individuals living with this disease. HRQoL assessment should be an integral component of the clinical protocol used for patients with PD who consider STN-DBS.

**CONCLUSIONS**

Bilateral STN-DBS surgery successfully improved global HRQoL as well as reduced motor impairment, disease severity, and medication dosage at 12 months after surgery. Worse preoperative PDQ-39 scores and higher LEDD predicted worse HRQoL at 1 year after surgery.

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**Conflicts of interest**

There are no conflicts of interest.

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