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Title: Predictors of Quality of Life in Patients with Parkinson's Disease: A Multicenter Case-Control Study

Running Title: Predictors of Quality of Life in Parkinson

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Abstract

Background: Parkinson's disease (PD) is a common neurodegenerative disease whose motor and non-motor complication greatly affect a person's quality of life (QoL). This study aims to investigate the QoL of these patients using the PDQ-39 questionnaire and identify the prognostic factors associated with their QoL.

Method: In the current case-control study, the QoL of two groups (211 controls and 211 cases) was investigated and compared using the PDQ-39 questionnaire. Prognostic factors associated with QoL were determined using multivariate logistic regression analysis.

Results: A number of 422 patients with the mean age of 59.8 ± 13.7 years were included in the study. The mean score of PDQ-39 in the case group was significantly higher in all subscales except Social support compared to the control group. The mean score of PDQ-39 was significantly higher in the patients with non-DBS (53.9 ± 21.1) than those with DBS (42.22 ± 18.1), especially in the sub-scales of Mobility, Activities of daily living, Cognition, and Communication. As the stage of the disease increases, the mean score of PDQ-39 in these patients increases significantly. The results of multivariate analysis showed that gender, patient age, smoking, education level, duration of disease, patient stage, and intervention with DBS were significantly related to patients' QoL ($P < 0.05$).

Conclusion: In conclusion, this study highlights the significant impact of DBS on PD patients' QoL, especially in sub-scales of mobility, daily activities, emotional well-being, and cognition. Moreover, identifying the main prognostic factors in QoL (gender, age, smoking status, educational level, disease duration, and stage) can lead to avenues for improving these patients' lives.

Keywords: Parkinson, Quality of life, PDQ-39 questionnaire, Prognostic factors.

Introduction

Parkinson's disease (PD) is the second most common neurodegenerative disease, with rapidly increasing prevalence among other neurological diseases (de Lau & Breteler, 2006; Feigin et al., 2017). More than 4 million people suffer from this incurable disease, which is predicted to double by 2030 (Dorsey et al., 2007). The disease is characterized by the progressive degeneration of dopaminergic neurons in the Substantia Nigra region of the brain, leading to the typical motor symptoms of tremors, bradykinesia (slowness of movement), rigidity, and postural instability. However, PD is not limited to motor symptoms; it also has substantial non-motor manifestations that greatly impact affected individuals' quality of life (QoL) (Garcia-Ruiz et al., 2014; Wirdefeldt et al., 2011). By identifying and addressing the prognostic factors associated with QoL, healthcare professionals can improve the patient's overall well-being and ultimately help them to live a more fulfilling life (Morris et al., 2009). The low QoL in the idiopathic PD patients seems to be associated with fear of fall in PD patients, which is demonstrative of mobility and activities of daily living (Mehdizadeh et al., 2016). On the other hand, there has been growing concern regarding the non-motor symptoms, including dementia, sexual dysfunction, mood disturbance, and insomnia, as they are thought to have an even more detrimental effect on the QoL than classic motor deficits (Chaudhuri et al., 2006; Forsaa et al., 2008; Weintraub et al., 2004).

The WHO defines QoL as "an individual's perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns" (Group, 1995). Assessing QoL in PD requires reliable and validated measurement tools. One widely used instrument is the PD Questionnaire (PDQ-39). The PDQ-39 is a self-administered questionnaire to assess health-related QoL in individuals with PD. It consists of eight domains or sub-scales: mobility, activities of daily living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort (Jenkinson et al., 1997; Peto et al., 1995). By evaluating these domains, the PDQ-39 comprehensively assesses the disease's impact on different aspects of QoL. A poorer QoL in PD patients has been linked to several demographic parameters, including age (Sarah K Hendred & Erin R Foster, 2016), gender (Valeikienė et al., 2008), education (Cubo et al., 2002), and several clinical characteristics of the disease, such as its duration and stage (Dogan et al., 2015). In this case-control study, we aim to assess the QoL in patients with PD using the PDQ-39 questionnaire and identify the prognostic factors associated with their QoL.

Methods

The present observational (case-control) study was carried out in a multicenter manner after approval by the ethics committee of the Iran University of Medical Sciences (code: IR.IUMS.FMD.REC.1402.141). The cases included 211 patients with Parkinson's who had been referred to the neurology clinic of Taleghani and Rasoul Akram hospitals affiliated with Shahid Beheshti University of Medical Sciences and Iran University of Medical Sciences (2019-2022).

The sampling method of patients in two centers was done as available and among the patients who met the criteria for inclusion in the study. To control confounding variables in two groups, cases and controls were matched in terms of demographic characteristics, including age, gender, physical profile, and comorbidity, using the frequency matching method.

Eligibility criteria

Inclusion criteria: Definitive diagnosis of PD based on clinical findings and examination by a neurologist mainly based on UK Parkinson's disease society Brain Bank diagnostic criteria (Clarke et al., 2016), being alive at the time of follow-up, under intervention with DBS, at least six months have passed since the surgery, completeness of the file and informed cooperation of the patients to participate in the study and complete the QoL questionnaire.

Exclusion criteria: cancer, drug and alcohol addiction, patients with untreated severe depression or other neuropsychiatric diseases including MS and Alzheimer's, patients with a chronic viral infection such as viral hepatitis or HIV, and death Patients.

Data Gathering

The study was conducted in two retrospective (collecting demographic, clinical, and radiographic information using patients' files) and prospective (completion of QoL questionnaire) formats. Data was collected using a two-part checklist after visiting the archive department and accessing the patients' files. The first part included the patient's demographic information form (age, gender, body mass index, education, number of morbidities, and smoking history). The second part included clinical information (age of onset, duration, disease severity, and DBS surgery). The severity of PD was classified into four stages based on the index of Hoehn and Yahr et al., (Bhidayasiri & Tarsy, 2012). A higher stage means a more severe disease.

To evaluate the QoL, the Parkinson's QoL questionnaire (PDQ-39) was used. This questionnaire has eight separate dimensions: 1) Movement (10 questions), 2) Daily life activities (6 questions), 3) Feeling good (6 questions), 4) Stigma (4 questions), 5) Social support (3 questions), 6) recognition (4 questions), 7) communication (3 questions), and 8) physical discomfort (3 questions). Each questionnaire question has five options on the Likert scale; only one option is marked. The first option is the sign of the best situation (score 0), and the fifth option is the sign of the worst situation (score 4). The range of scores for each dimension is reported from 0 to 100, where zero means no problem and 100 indicates the worst health condition. The score of each dimension is calculated as follows: the sum of the raw scores of each dimension divided by the sum of the maximum possible raw score of that dimension, multiplied by 100. The average scores of these dimensions have created a single index called Parkinson's disease summary index (PDSI). The range of PDSI is also reported between 0 and 100. The validity and reliability of the Persian version of this questionnaire for Iranian patients have been confirmed by A Dehghan et al. (Dehghan et al., 2016). The same questionnaire was used to evaluate the QoL in the control group. After obtaining consent from the patients to participate in the study, the patients or the researcher

completed the quality of life questionnaire in person (in cases where the patients were unable to complete the questionnaire).

Statistical analysis

The data was analyzed using SPSS version 22 statistical software. Descriptive statistics (frequency and %) were used to report qualitative variables. Quantitative variables were reported using mean and standard deviation. The normality of the distribution of quantitative variables was evaluated using the Shapiro-Wilk test. The chi-square test was used to compare qualitative variables in two groups. To compare the quantitative variables in two groups, t-test was used in case of normal distribution of the quantitative variables and Mann-Whitney test was used if the assumption of normality was not applied. Analysis of single variables in more than two groups was done with a one-way variance test. Then, to control the confounding variables, all variables with a P value less than 0.05 in the univariate analysis were entered into the logistic regression multivariate analysis with the backward model. The effect size index was reported with the adjusted odds ratio in the 95% confidence interval. Multivariate logistic regression analysis was used to estimate predictor variables of quality of life in patients with PD. A p-value less than 0.05 was considered the statistical significance level.

Results

Demographic data

Four hundred twenty-two participants (211 cases and 211 controls) were included in the study. The average age of the patients was 59.8 ± 13.7 years. The median age was 60 years. One hundred twenty-eight patients (60.8%) were male. Regarding disease severity based on the H and Y stage index, most patients were in stages 2 and 3. The average duration of the disease since its onset was 4.28 ± 3.85 years. 86 (40.8%) patients underwent DBS intervention. No statistically significant difference was observed for the demographic variables in the two groups (Table 1)

Comparing QoL of patients with PD compared to the control group

The mean score of PDQ-39 in the case group was significantly higher than the control group ($p=0.001$). The average score of the PDQ-39 score in all subscales, except for Social support, was significantly lower in the control group than in the case group ($p<0.001$). The highest and lowest mean scores in patients with PD were 60.33 ± 12.1 and 31.26 ± 20.5 , respectively, for Mobility and Social support subscales (Table 2).

Comparing QoL of patients with PD based on DBS or non-DBS

The mean score of PDQ-39 in the group of patients with DBS and non-DBS was 42.22 ± 18.1 and 53.9 ± 21.1 , respectively, and this difference was statistically significant ($P<0.001$). The mean score of QoL in the sub-scales of Mobility, Activities of daily living, Cognition, and Communication in the intervention group was significantly better than the non-intervention group ($P<0.05$). Although the mean score of QoL in the sub-scales of Emotional well-being, Stigma, Social support, and Bodily discomfort was better in the intervention group, this difference was not statistically significant ($p>0.05$) (Table 3).

Comparing QoL of patients with PD based on the stage of the disease

The comparison of the mean score of QoL and sub-scales showed that QoL was significantly different in stages of the disease ($p < 0.05$) (Table 4).

Prognostic factors associated with their QoL in patients with PD.

The results of multivariate analysis showed that gender, patient age, smoking, education level, duration of disease, patient stage, and intervention with DBS were significantly related to patients' QoL ($p < 0.05$) (Table 5).

Discussion

The present study aimed to assess the QoL in patients with PD using the PDQ-39 questionnaire and identify the prognostic factors associated with their QoL. Aside from various motor dysfunctions, at a neuroscience level PD is found to be associated with neuropsychological dysfunctions such as sleep disturbance, depression, fatigue and cognitive disorders, which all can adversely affect QoL (Zhao et al., 2021). In this study, the assessment of QoL using the PDQ-39 questionnaire showed that the overall and sub-scale scores, except for social support, were significantly higher in the case group than in the control group. The factors most strongly associated with lower QoL in PD patients, ranked in order of importance, were mobility, stigma, communication, bodily discomfort, activities of daily living, cognition, and emotional well-being. These findings are consistent with most previous research highlighting PD's negative impact on overall QoL. (Hariz & Forsgren, 2011; Paolucci et al., 2018; Park et al., 2020; Schrag et al., 2000a; Vossius et al., 2009). Similar to our study, Shin Ying Chu et al. identified mobility as one of the dimensions with the highest impact on QoL in PD patients, and social support did not differ significantly between case and control groups (Chu & Tan, 2018). In contrast to our study, HJ Park et al. stated that PD patients had significantly lower QoL in all dimensions of the PDQ-39 compared to healthy controls, except for bodily discomfort (Park et al., 2014). This difference could be due to the lower mean age of PD patients in our study compared to HJ Park. With advancing age, even healthy individuals experience general physical decline, increasing the likelihood of lower QoL due to bodily discomfort (Lep lege & Hunt, 1997). Comparing QoL outcomes between PD patients with and without DBS intervention, we observed a significant difference in the PDQ-39 summary index scores. Patients who underwent DBS intervention exhibited a significantly better QoL, as indicated by a lower PDQ-39 summary index score, than those without DBS. This finding suggests that DBS positively impacts the overall QoL of PD patients. Consistent with numerous previous studies (Bohlega et al., 2016; Bratsos et al., 2018; Nijhuis et al., 2021; Perestelo-P rez et al., 2014), our findings showed DBS recipient PD patients presented better QoL (lower PDQ-39 score). In our study, generally, all the aspects of QoL after DBS. Since DBS improves the motor circuits in speech and language in PD patients, it is unsurprising to see enhancements in indicators such as mobility, daily activities, and communication (Bratsos et al., 2018; Follett et al., 2010; Krack et al., 2003; Weaver et al., 2012; Xie et al., 2016). Our study results support this improvement, consistent with previous research

(Baudouin et al., 2023; Follett et al., 2010; Perestelo-Pérez et al., 2014; Weaver et al., 2012; Laura B. Zahodne et al., 2009). In our study, social support scores, emotional well-being, and stigma did not significantly differ between the two groups. In terms of these criteria, the results can vary across studies due to different cultural contexts. For example, receiving DBS may be perceived as a form of electric shock therapy in a country, which could increase stigma levels. In contrast to our study, some findings have demonstrated that DBS can improve bodily discomfort due to pain alleviation (Follett et al., 2010; Weaver et al., 2012; Xie et al., 2016; Laura B Zahodne et al., 2009). The discrepancy may be attributed to several factors, including differences in study populations (variations in disease severity, duration of PD, and comorbidities) and variations in the surgical technique, target location, and stimulation parameters used in DBS procedures. Our findings align with previous studies (Koplas et al., 1999; Park et al., 2014; Schrag et al., 2000b), indicating a clear association between PD stage and QoL. As PD progressed from stage I to stage IV, we observed a gradual decline in QoL. The QoL was lowest in mobility followed by stigma sub-scales is all stages of disease. However, in some studies, the deteriorating trend has yet to be observed in all aspects of QoL (Fitzpatrick et al., 1997; Schrag et al., 2000b). The potential explanation for this discrepancy could lie in the healthcare system differences, such as variances in geriatric medicine and palliative care practices. According to the multiple regression results, female gender, older age, non-smoking status, lower educational level, longer disease duration, and advanced disease stage are the main prognostic factors associated with lower QoL. Among the factors considered, gender had the second strongest relationship with QoL. Similar to previous studies (Balzer-Geldsetzer et al., 2018; Dluzen & McDermott, 2000; Kuopio et al., 2000; Meng et al., 2022), our results indicated that females experience a lower QoL. The reason behind this difference could be found in older age of onset of PD among women due to estrogen neuroprotective effect before menopause (Haaxma et al., 2007). Our study, in contrast to findings by Hendred et al., in USA population (S. K. Hendred & E. R. Foster, 2016), showed a negative association between age and QoL. Our findings could be explained by the differences in retirement support and healthcare coverage in developing countries (Sarah K Hendred & Erin R Foster, 2016; Huang et al., 2020; Netuveli & Blane, 2008). The positive association between educational level and QoL can be explained by the crucial role of this prognostic factor in providing individuals with access to economic resources, employment opportunities, and stable supporting social relationships (Cubo et al., 2002; Sarah K Hendred & Erin R Foster, 2016; Ross & Van Willigen, 1997).

Conclusion

In conclusion, this study highlights the significant impact of DBS on PD patients' QoL, especially in sub-scales of mobility, daily activities, emotional well-being, and cognition. Moreover, identifying the main prognostic factors in QoL (gender, age, smoking status, educational level, disease duration, and stage) can lead to avenues for improving these patients' lives.

Authors Contributions

Conception and design: SAH, MB, AM, SM and AS. Analysis and interpretation of data: MB, SM. Data collection: SS, MB, NM, NH, MV and AS. SAH, NH, MB, AS, SM, MV and NM edited and read the manuscript. All authors read and approved the final manuscript.

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Data availability statement

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Research materials availability statement

Materials available on request from the authors.

Pre-registration statement

Not applicable

Funding statement

We have no funding resource for this study.

Conflict of interest disclosure

The authors declare that they have no competing interests.

Ethics approval statement

This study was approved in ethic committee of Iran University of Medical Sciences, Tehran, Iran (ethical code: IR.IUMS.REC. 1402.141). The research team of this study adhered to the ethical principles of the Helsinki Convention regarding clinical studies in all stages of the present study. consent was obtained from all subjects and/or their legal guardian(s) in case of minors (below 16 years of age). Due to the fact that no interventions are performed on patients, the condition for the confidentiality of patient information is not a moral restriction by the Ethics Committee.

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Not applicable

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Table 1: Demographic characteristics and number of comorbidities

Variable	Case group (n=211)	Control group (n=211)	P value*
Age (year)	58.2±16.1	61.4±11.3	0.45
Gender			
Female	83 (39.3)	88 (41.7)	0.28
Male	128 (60.7)	123 (58.3)	
Marriage status			
Married	161(76.4)	172 (81.5)	0.44
Single	11 (5.1)	10 (4.7)	
Divorced	8 (3.8)	9 (4.3)	
Widowed	31 (14.7)	20 (9.5)	
Educational status			
Illiterate	20 (9.5)	30 (14.3)	0.24
Under diploma	58 (27.5)	48 (22.7)	
Diploma	51 (24.2)	56 (26.5)	
College education	82 (38.8)	77 (36.5)	
Smoking history			
Positive	89 (42.1)	61 (28.9)	0.073
Negative	122 (57.9)	150 (71.1)	
BMI (kg/m²)	23.2±2.88	24.6±3.11	0.098
Number of comorbidities			
0	88 (41.7)	81 (38.4)	0.14
1	101 (47.9)	102 (48.3)	
2	18 (8.5)	21 (10)	
>2	4 (1.9)	7 (3.3)	
Onset of disease	60.88±3.11	-	-
Disease duration (Year)	4.28±3.85	-	-
H and Y stage			
I	37(17.5%)	-	-
II	74(35.1%)	-	-
III	65(30.8%)	-	-
IV	35(16.6%)	-	-
Medication information			
Drug Naïve	38(18%)	-	-
Dopamine agonists	121(57.3%)	-	-
Levodopa Equivalent Daily Dose; (mg)	300 (150,450)	-	-
DBS			
Yes	86(40.8%)	-	-
No	125(59.2%)	-	-

*Data are demonstrated as mean ± SD or number (%). P value of less than 0.05 is considered significant. **BMI:** body mass index, **DBS:** deep brain stimulation

Table 2: Comparison of the PDQ-39 questionnaire total and sub-scales' score.

Sub-scale	Case group (n=211)	Control group (n=211)	P value*
Mobility	60.33 ± 12.1	27.5±7.8	0.001
Activities of daily living	36.2 ± 19.5	26.7±8.2	0.001
Emotional well-being	33.4 ± 14.5	28.65±8.3	0.021
Stigma	50.5 ± 20.16	25.2±7.68	0.001
Social support	31.26 ± 20.5	29.33±8.5	0.24
Cognition	34.5± 21.6	20.1±7.2	0.006
Communication	43.56 ± 20.2	22.01±9.1	0.006
Bodily discomfort	40.1 ± 20.1	26.08±9.2	0.001
PDQ-39 summary index	47.3 ± 16.2	25.25±8.25	0.001

*p value less than 0.05 is considered significant.

Table 3: Comparison of the PDQ-39 Questionnaire total and sub-scales' score between the Patients with and without DBS.

Sub-scale	(DBS=86)	(Non-DBS=125)	P value*
Mobility	50.2 ± 18.3	67.4 ± 15.6	0.001
Activities of daily living	28.5 ± 13.6	43.5 ± 14.4	0.001
Emotional well-being	30.21 ± 19.5	36.1 ± 23.4	0.056
Stigma	47.5 ± 19.11	54.3 ± 24.5	0.11
Social support	24.3 ± 21.3	27.4 ± 15.8	0.16
Cognition	25.36± 19.6	45.2 ± 23.1	0.001
Communication	28.1 ± 19.66	53.6 ± 20.22	0.006
Bodily discomfort	48.4 ± 21.65	43.6 ± 20.2	0.11
PDQ-39 summary index	42.22 ± 18.1	53.9 ± 21.1	0.023

* p value fewer than 0.05 is considered significant, , **DBS:** deep brain stimulation.

Table 4: Comparison of the PDQ-39 Questionnaire total and sub-scales' score base on stage

Sub-scale	Stage I (n=37)	Stage II (n=74)	Stage III (n=65)	Stage IV (n=35)	P value*
Mobility	28.6 ± 17.3	56.2 ± 17.3	60.11 ± 22.1	62.4 ± 20.1	0.001
Activities of daily living	18.6 ± 19.5	30.11 ± 20.3	34.2 ± 19.5	40.6 ± 19.5	0.001
Emotional well-being	26.11 ± 14.	31.22 ± 13.2	33.4 ± 14.5	40.11 ± 14.5	0.001
Stigma	28.33 ± 22.6	47.3 ± 16.8	51.2 ± 18.3	62.2 ± 22.3	0.001
Social support	13.56 ± 23.5	25.4 ± 21.2	28.1 ± 16.5	40.11 ± 25.3	0.001
Cognition	15.3± 25.3	32.12± 18.5	35.6± 19.5	46.3± 21.6	0.001
Communication	23.33 ± 22.3	39.7 ± 19.6	44.2 ± 21.5	53.6 ± 22.3	0.001
Bodily discomfort	22.3 ± 24.1	37.6 ± 25.3	42.8 ± 18.6	53.2 ± 18.3	0.001
PDQ-39 summary index	25.33 ± 20.35	38.9 ± 18.6	47.11 ± 20.58	56.3 ± 16.2	0.001

Table 5: The multiple regression model showing the influence of patient-associated factors on health related QoL.

Variable	OR Adj	Lower (95% CI)	Upper (95% CI)	P value
Sex*	2.11	1.12	3.12	0.001
Age	1.09	1.02	1.18	0.013
Smoking **	0.89	0.79	0.98	0.013
Educational level ***	0.78	0.65	0.92	0.033
Disease duration	1.11	1.02	1.22	0.025
Stage of disease****	2.18	1.09	3.28	0.001
DBS**	0.48	0.31	0.65	0.001

*(Female Vs male), **(Yes vs No), ***(>Diploma Vs <Diploma), **** (>II vs <I)

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