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Correlation between depression and quality of life in patients with Parkinson's disease

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ABSTRACT

Objective: To understand the distribution of Parkinson's disease questionnaire-39 (PDQ-39) scores in Parkinson's disease (PD) patients with or without depression, and to analyze the factors that influence the quality of life of PD patients.

Materials and Methods: 300 PD patients were enrolled. Patients' general information and the results of assessments including UPDRS, H-Y, HAMD, HAMA, ADL and PDQ-39 were collected. They were divided into depression group and non-depression group according to HAMD score. The relationship between PD-related depression and quality of life and the factors that influence the quality of life of PD patients were analyzed based on PDQ-39 score.

Results: 111 patients with depression (37.0 %) and 189 patients without depression (63.0 %) were enrolled. The scores of PDQ-39 summary index (PDQ-39 SI) in the depression group were significantly higher than those in the non-depression group in all domains ($P < 0.05$). Patients in the depression group had a longer disease duration (6.89 ± 4.70 vs. 5.52 ± 4.12, $P < 0.038$), a higher UPDRS-III score (30.1 ± 13.55 vs. 25.2 ± 11.73, $P < 0.001$), and a higher H-Y stage level (2.41 ± 0.853 vs. 2.13 ± 0.707, $P < 0.001$), compared with patients in the non-depression group. All factors including age, disease duration, UPDRS-III, H-Y stage, HAMD score and HAMA score, may independently affected PDQ-39SI in PD patients, among which HAMD had the greatest effect. HAMD and HAMA were correlated with PDQ-39 in its all eight domains.

Conclusion: PD patients with psychological problems such as anxiety and depression may lead to a significant decline in the quality of life of patients in all domains.

1. Background

Parkinson's disease (PD) is one of the common degenerative diseases. With the aging of population, it is estimated that there will be up to 5 million PD patients by 2050 in China. The pathogenesis of PD is still unknown, and the pathology is characterized by degeneration and necrosis of dopaminergic neurons in the substantia nigra. Clinically, in addition to typical motor-related symptoms, PD patients are suffered from non-motor symptoms such as depression, cognitive impairment, olfactory disorders and autonomic nerve symptoms. Among them, the incidence of depression is the highest (40–70 %), and most antidepressants have limited efficacy on it [1–3], suggesting that the mechanism may be different from that of general depression.

The role of 5-hydroxytryptamine and norepinephrine in general depression is clear [4,5], and in some PD patients, in addition to the degeneration or loss of nigrostriatal dopaminergic neurons in substantia nigra, the autopsy also reveals a loss of 5-hydroxytryptamine dopaminergic nerve cells in the raphe nucleus, accumulation of Lewy bodies, and extensive loss of 5-hydroxytryptamine dopaminergic nerve fibers from the nucleus to the cortex and under cortex [6]. These changes help to explain depression in PD patients. It is found by Remy et al. [7] that there is a loss of limbic system neurons containing catecholamines in PD

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patients with depression, suggesting that the specific loss of dopamine and noradrenergic neurons in the limbic system may be associated with depression and anxiety in patients with Parkinson's disease.

PD-related depression may occur throughout the disease duration. In a 3-year study of PD non-motor symptoms, the incidence of depression was high at both baseline and at the end of 3-year follow-up, suggesting that early psychological stress to PD may increase the incidence of depressive symptoms and thus affect the overall quality of life of patients. Karlsen et al. [8] found that the quality of life of PD patients decreased significantly compared to the healthy elder population of the same age, and that depression was the main cause of the decline in their quality of life. Another study has shown that the effects of depression on the quality of life of PD patients are even more pronounced than the motor symptoms. A recent study from Taiwan confirmed that depression and anxiety have the greatest impact on patients' quality of life in non-motor symptoms of PD, resulting in more burdens to families and society [9,10]. Therefore, it is urgent to further understand the impact of PD depression on the quality of life in Chinese patients.

Most previous studies have focused on the motor symptoms and quality of life. This study was designed to investigate the relationship between the motor symptoms, mental and psychological conditions, such as depression and anxiety, and the quality of life in PD patients, and to further analyze the influencing factors for PDQ-39 in eight domains.

2. Methods and materials

2.1. Participants

PD patients who met the UK PD Society Brain Bank Clinical Diagnostic Criteria were enrolled. Exclusion criteria include atypical Parkinson's syndrome; postoperative DBS; medication of antipsychotic drugs in progress; patients with cognitive impairment (MMSE < 24); and severe liver and kidney disease.

2.2. Process of study

After ethical committee approval, medical records of 300 patients were retrospectively collected, including a well-established Unified Parkinson's Disease Rating Scale (UPDRS)score, Hoehn-Yahr (H-Y) stage, Hamilton Anxiety Scale (HAMA), Hamilton Depression Scale-24 (HAMD), and the Parkinson's disease questionnaire-39 (PDQ-39) score, to establish an electronic database of relevant patients. All the scales were tested by doctors in Parkinson's disease team in Beijing hospital, included resident, attending and neurology expert. All the scales were in Chinese version.

PDQ-39 which is formed of 39 items (ranged from 0 = never to 4 = always) that are grouped into eight domains. These domains include mobility (1–10, 10 items), ADL (11–16, 6 items), emotional well-being (17–22, 6 items), stigma (23–26, 4 items), social support (27–29, 3 items), cognition (30–33, 4 items), communication (34–36, 3 items), and bodily discomfort (37–39, 3 items). Following answering the questionnaire, a summary index for each domain (subscales) was calculated by dividing the sum of included items by the maximum possible score then multiplying by 100. Then, the total score [PDQ-39 summary index (PDQ-39 SI)] was calculated by summation of the eight domains' scores divided by 8. Consequently, lower scores reflect better Health-related quality of life (HRQOL). The frequency of impairment of each domain to any degree (score > 0) was also estimated.

2.3. Statistical methods

All data were processed using the statistical analysis software SPSS 19.0. The measurement results were expressed as mean ± standard deviation, and the statistical test significance level was set to bilateral $\alpha = 0.05$.

For comparison of baseline data and clinical scores between the depression group and the non-depression group, such as age, gender, disease duration, PDQ-39, UPDRS, H-Y stage, HAMA and levodopa equivalent dose, an independent sample *t*-test is used if the homogeneity test of variance is passed; a non-parametric test is used if the homogeneity test of variance is not passed; and the $\chi 2$ test is used to compare the count data.

In exploring how the factors such as age, disease duration, motor symptoms (UPDRS-III), H-Y staging, depression and anxiety, respectively correlate with PDQ-39SI and its eight domains, Pearson correlation analysis is used when both variables satisfy the normal distribution; and Spearman rank correlation analysis is used when they the variables fail to satisfy the normal distribution. The effect of depression on the quality of life of PD patients is analyzed by stepwise multiple regression (linear regression), taking PDQ-39 as the dependent variable, and taking factors such as gender, age, disease duration, H-Y staging, motor symptoms, motor complications, depression and anxiety as the influencing factors.

3. Results

3.1. General information of PD patients

In the 300 PD patients, 153 (51.0 %) were male and 147 (49.0 %) were female, with a mean age of 68.8 ± 10.37 years, a mean disease duration of 6.0 ± 4.39 years, and an average LED of 270.5 ± 228.10. UPDRS-III was 27.0 ± 12.64. The average score of the HAMD scale for 300 PD patients was 8.9 ± 6.47, HAMA was 10.0 ± 6.15, and PDQ-39SI was 16.0 ± 12.05. (Table 1)

3.2. Clinical manifestations and the difference in quality of life between depression and non-depression PD patients

All PD patients were divided into depression group (HAMD ≥ 10) and non-depression group (HAMD ≤ 9). There were 189 patients without depressive symptoms (63 %), with an average HAMD score of 4.93 ± 2.7 and 111 patients with depressive symptoms (37 %), with an average HAMD score of 15.55 ± 5.37. There were no significant differences in age distribution between the depression group and the non-depression group. Female patients accounted for a larger proportion in depression group. Patients in the depression group had a longer disease duration (6.89 ± 4.70 vs. 5.52 ± 4.12, P < 0.038), a higher UPDRS-III

Table 1
General Information of PD Patients.

Characteristics	Mean (±SD) or n (%)	Range (min–max)
Age (years)	68.8 ± 10.37	32–90
Sex		
Male	153 (51 %)	
Female	147 (49 %)	
Onset age (years)	62.6 ± 11.16	17–87
Disease duration	6.0 ± 4.39	0–22
MMSE	28.2 ± 1.55	24–30
LED	270.5 ± 228.10	0–997.5
UPDRS-I	3.1 ± 2.18	0–12
UPDRS-II	12.6 ± 6.20	0–37
UPDRS-III	27.0 ± 12.64	3–65
UPDRS-IV	3.1 ± 2.97	0–13
H-Y stage		
1	34(11.3 %)	
1.5	47(15.7 %)	
2	80(26.7 %)	
2.5	61(20.3 %)	
3	59(19.7 %)	
4	19(6.3 %)	
HAMD	8.9 ± 6.47	0–35
HAMA	10.0 ± 6.15	0–28
PDQ-39SI	16.0 ± 12.05	0–59.79

score (30.1 ± 13.55 vs. 25.2 ± 11.73, P < 0.001), and a higher H-Y stage level (2.41 ± 0.853 vs. 2.13 ± 0.707, P < 0.001), compared with patients in the non-depression group.(Table 2) The PDQ-39SI score of depression patients was significantly higher than that of non-depression patients, and the scores of depression patients were higher than those of non-depression patients in all eight domains of PDQ-39 such as exercise, daily living ability, emotional health, stigma, social support, cognition, social interaction and physical discomfort (P < 0.05) (Fig. 1).

3.3. Factors influencing PDQ-39SI of PD patients

By using Spearman correlation analysis, it was found that PDQ-39SI was correlated with age, disease duration, UPDRS-III, HY stage, HAMD score and HAMA score, with a correlation coefficient of 0.156, 0.348, 0.515, 0.485, 0.624 and 0.530, all with statistically significant difference. (Table 3) Stepwise linear multiple regression analysis showed that HAMD score, UPDRS-III, HAMA score, H-Y stage and age all could independently affect PDQ-39SI in PD patients. The regression model can account for 57.1 % of the variation in PDQ-39SI. In assessing the impact of the influencing factors on PDQ39SI with the standard coefficient, it was found that the effect of depression was the greatest, followed by motor symptoms (Table 4).

3.4. Factors influencing eight domains of PDQ-39 scale

In further analysis on how the eight domains of the PDQ-39 scale correlate with age, disease duration, UPDRS-III, HAMA, HAMD and H-Y staging, it was found that HAMD and HAMA have correlations with all the eight domains of the PDQ-39 scale, while other variables such as UPDRS-III and H-Y staging only correlate with some of the eight domains (Table 5).

4. Discussion

As a neurodegenerative disease, PD seriously affects the physical, psychological and social health of patients. Non-motor symptoms are very common in PD patients, and the incidence of depression is very high among them. This study has found that the proportion of depression in PD patients was 37 %, and that the depression PD patients had longer disease duration and more severe motor symptoms than non-depression patients did.

In the previous diagnosis and treatment of PD patients, doctors paid more attention to the impact of motor symptoms on quality of life, but recently, they start to care about the impact of non-motor symptoms on quality of life [11]. A multicenter, prospective study from Norway in which the effects of non-motor symptoms and untreated motor symptoms on HRQOL in PD patients were compared had shown that non-motor symptoms had a more significant effect on HRQOL compared with motor symptoms, with fatigue, depression and sensory abnormalities ranking the top three [12]. In another 18-month follow-up study in which a potential growth curve model was used to explore the impact of apathy, depression and motor symptoms on the quality of life of PD patients, the baseline data analysis showed that the quality of life was most strongly associated with depressive symptoms, followed by motor symptoms, and the follow-up results showed that aggravation of depressive symptoms was an independent predictor for decline in quality of life [13]. A study on the effects of depression on HRQOL in PD patients at the early stage in China, in which 391 PD patients at the early stage were enrolled to assess the quality of life by the 36-item Short-Form Health Survey (SF-36), the results showed that compared with the non-depression group, the scores of SF-36 in the depression group were lower in all aspects, and that the depressive symptoms were the only variable with predictive value for total SF-36 score and scores of all sub-scales [14]. Another study in which a quality of life measurement scale used to assess patients' quality of life showed that depression was the main predictor for decline in quality of life in patients [15]. In addition, studies have shown that PD patients with depression are more likely to fall, with a higher number of visits to hospitals, a longer average length of hospital stay, a lower rate of treatment with DBS, and a significantly higher mortality rate etc. [16,17]. This may form an impact on the overall health-related quality of life of PD patients. PD patients with depressive symptoms are more difficult to deal with daily life, with significantly lower Activities of Daily Living (ADL) score and HRQOL score.

Currently, multiple depression scales could be used to screen PD depression symptoms [18]. HAMD is one of the commonly used physician rating scales, including 24-item, 21-item, 17-item and 6-item versions. The literatures report that its sensitivity is 75 %–100 %, specificity 71 %–99 %, with good validity and reliability, and it could be used for screening PD-associated depression and assessing the severity [19]. In this study, the HAMD-24 scale was used to assess depressive symptoms in PD patients. In a diagnostic trial involving 148 patients with idiopathic PD, the HAMD-24 scale was compared to the gold standard (DSM-IV), with the optimal cut-off value of 9/10 points, sensitivity of 88 %, specificity of 78 %, and area under the curve of 0.91 [20]. According to this study and two recent systematic reviews, the patients with a HAMD-24 score of ≧ 10 will be classified into the group with depression [18,19,21]. Our cross-sectional study showed that 37 % of PD patients were associated with depressive symptoms, consistent with the results of most studies at home and abroad.

The PDQ-39 scale is widely used for assessment of PD-specific health-related quality of life (HRQOL) [22]. It consists of 39 questions in 8 domains: mobility, activities of daily of living, emotional well-being, stigma, social support, cognition, communication, and bodily discomfort. Higher score indicates worse HRQOL [23]. In this study, we find that age, disease duration, motor symptoms, anxiety symptoms and depressive symptoms are independent factors that influence the quality of life, among which the effect of depressive symptoms on quality of life is the most significant, even exceeding the effect of motor symptoms on quality of life. This result is also consistent with results of most previous studies [24–27].

Further analysis found that in the eight domains of quality of life, the scores of the depression group were significantly higher than those of the non-depression group. Since the patients in the depression group are found with more severe motor symptoms and longer disease duration at the same time, it is not excluded that the course of the disease and the motor symptoms have an impact on the quality of life. Therefore, the correlation analysis was further conducted, and it is found finally that anxiety symptoms and depressive symptoms correlate with all eight domains of the quality of life, while other factors such as disease duration, age and motor symptoms only correlate with some domains of the quality of life. This is also consistent with the findings from many previous studies, suggesting that anxiety is also an important factor for the

Table 2
Analysis of Baseline and Clinical Scores of PD Patients with and without Depression.

	With depression (111)	Without depression (189)	Statistics	P
Sex			4.242*	P = 0.039
Male	48	105		
Female	63	84		
Age	68.14 ± 9.23	69.12 ± 10.98	0.784#	P = 0.434
Disease duration	6.89 ± 4.70	5.52 ± 4.12	−2.644#	P = 0.038
UPDRS-III	30.1 ± 13.55	25.2 ± 11.73	−3.295#	P < 0.001
H-Y stage	2.41 ± 0.853	2.13 ± 0.707	−2.685&	P<0.007

* chi-square test.
\# independent *t*-test.
& non-parametric test.

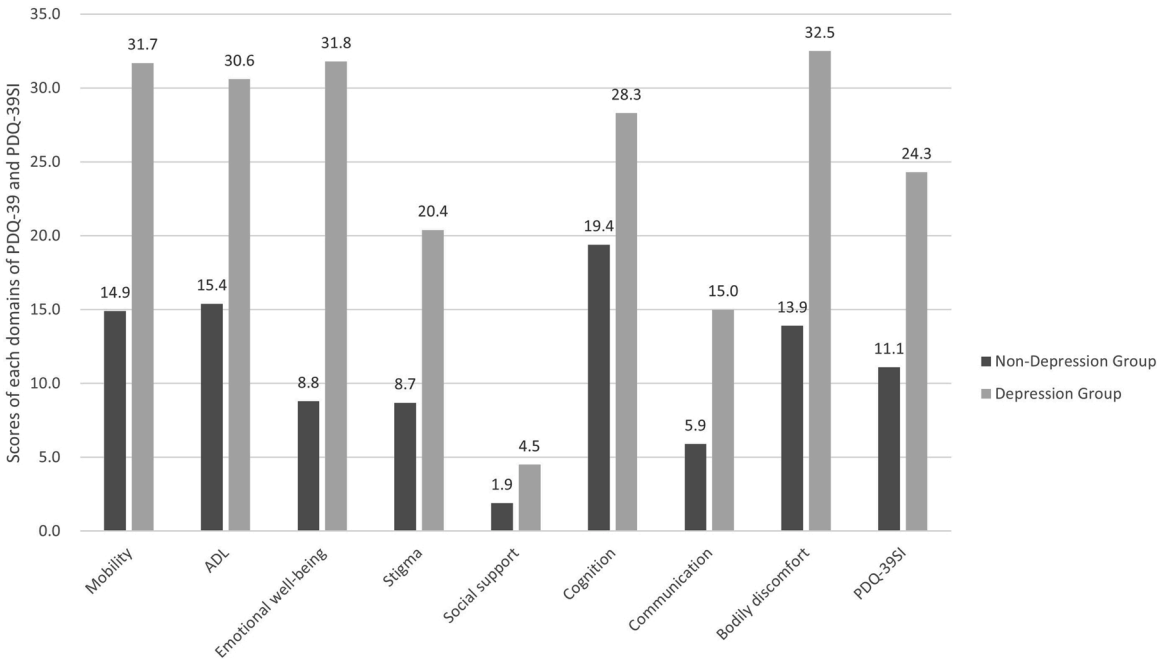

Fig. 1. The difference between two groups in PDQ-39SI and its 8 domains. Non-parametric tests were used to compare the quality of life between depression and non-depression patients. It was found that patients with depression had higher scores in PDQ-39SI.

Table 3
Analysis of Correlation between the Quality of Life and Depression in PD Patients.

Total PDQ-39 Score	Age	Disease duration	UPDRS-III Score	H-Y Stage	HAMD Score	HAMA Score
Correlation Coefficient (r)	0.156	0.348	0.515	0.485	**0.624**	0.530
P Value	0.007	<0.001	<0.001	<0.001	**<0.001**	<0.001

Note: The bold means the correlation coefficients is the highest in HAMD and Quality of Life and Depression in PD Patients.

quality of life of PD patients [28,29]. The above results also suggest that we need to pay more attention to the impact of mental and psychological problems on the quality of life of patients during the diagnosis and treatment of PD.

The shortcoming of this study is that it is a retrospective experimental design, and all patients are from a single center. A prospective cohort study, if possible, may be better to explain the factors that influence the quality of life. In this study, no in-depth analysis has been conducted for the severity of depression and anxiety. Additionally, this study fails to include all non-motor symptoms, such as sleep and fatigue.

Table 4
Stepwise Multiple Linear Regression Analysis of PDQ-39 in PD Patients.

Influencing factors	Non-standard coefficient	Standard coefficient (β)	R	R^2	t value	P value	Adjusted R^2
PDQ-39SI							
HAMD	0.664	0.364	0.637	0.406	6.687	<0.001	
UPDRS- III	0.209	0.222	0.717	0.515	4.537	<0.001	
HAMA	0.411	0.210	0.735	0.540	3.990	<0.001	
H-Y stage	2.684	0.187	0.751	0.564	3.880	<0.001	
Age	0.137	0.119	0.760	0.578	3.093	0.002	0.571

Note: The p-value cut-off for stepwise regression is 0.05.

Table 5
Analysis of Factors Correlated with Eight Domains of PDQ-39.

PDQ-39subscale	Age		Disease duration		UPDRS- III score		HAMA score		HAMD score		H-Y stage	
Mobility	0.342	**<0.001**	0.373	**<0.001**	0.508	**<0.001**	0.305	**<0.001**	0.417	**<0.001**	0.553	**<0.001**
ADL	0.217	**<0.001**	0.246	**<0.001**	0.547	**<0.001**	0.281	**<0.001**	0.339	**<0.001**	0.460	**<0.001**
Emotional well-being	−0.115	0.046	0.118	**0.042**	0.256	**<0.001**	0.600	**<0.001**	0.653	**<0.001**	0.214	**<0.001**
Stigma	−0.253	**<0.001**	0.045	0.437	0.093	0.108	0.266	**<0.001**	0.335	**<0.001**	0.056	0.334
Social support	−0.029	0.611	0.081	0.162	0.087	0.134	0.225	**<0.001**	0.173	**0.003**	0.088	0.130
Cognition	0.328	**<0.001**	0.254	**<0.001**	0.273	**<0.001**	0.276	**<0.001**	0.342	**<0.001**	0.254	**<0.001**
Communication	0.068	0.243	0.244	**<0.001**	0.376	**<0.001**	0.332	**<0.001**	0.382	**<0.001**	0.280	**<0.001**
Bodily discomfort	0.007	0.897	0.247	**<0.001**	0.224	**<0.001**	0.411	**<0.001**	0.457	**<0.001**	0.216	**<0.001**

Note: The bold means P < 0.05.

5. Conclusion

The age, disease duration, motor symptoms, anxiety and depression of PD patients are all the influencing factors of the quality of life, of which the depression have the greatest impact on the quality of life. Additionally, the depression and anxiety correlate with all domains of the quality of life.

CRediT authorship contribution statement

Wen Su: Conceptualization, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Writing - original draft. **Huijing Liu:** Data curation, Investigation, Methodology, Resources, Software, Writing - review & editing. **Yanyan Jiang:** Investigation, Methodology, Validation, Visualization, Writing - review & editing. **Shuhua Li:** Investigation, Methodology, Writing - review & editing. **Ying Jin:** Investigation, Methodology, Supervision, Writing - review & editing. **Chuanzhu Yan:** Data curation, Formal analysis, Investigation, Methodology, Writing - review & editing. **Haibo Chen:** Funding acquisition, Project administration, Resources, Writing - review & editing.

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