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The impact of non-motor symptoms on the Health-Related Quality of Life of Parkinson's disease patients from Southwest China

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ABSTRACT

Background: The impact of non-motor symptoms (NMS) on the Health-Related Quality of Life (HRQoL) of patients with Parkinson's disease (PD) in the Chinese population are largely unknown.
Objectives: To study the impact of NMS on the HRQoL in Chinese PD patients.
Methods: A total of 693 PD patients from Southwest China were included in the study. NMS of patients were evaluated by non-motor symptoms scale (NMSS) and Parkinson's disease questionnaire-39 item version (PDQ-39) was used to evaluate the HRQoL of PD.
Results: The mean total score of NMSS was 37.2 ± 33.0 and the most prevalent NMS domain was sleep/fatigue (79.8%). There was a significant strong positive correlation between total NMSS score ($r_s = 0.71$, $P < 0.01$), sleep/fatigue domain ($r_s = 0.60$, $P < 0.01$) and PDQ-39 SI. Mood/apathy ($r_s = 0.55$, $P < 0.01$), attention/memory ($r_s = 0.42$, $P < 0.01$), gastrointestinal ($r_s = 0.44$, $P < 0.01$) and Miscellany domains ($r_s = 0.46$, $P < 0.01$) moderately correlated with PDQ-39 SI. A strong correlation was found between PDQ-39 SI ($r_s = 0.71$, $P < 0.01$), emotional well-being ($r_s = 0.62$, $P < 0.01$), cognitions ($r_s = 0.62$, $P < 0.01$), and the total score of NMSS. Moderate correlation was found between mobility ($r_s = 0.45$, $P < 0.01$), activities of daily living ($r_s = 0.43$, $P < 0.01$), stigma ($r_s = 0.42$, $P < 0.01$), communication ($r_s = 0.47$, $P < 0.01$), bodily discomfort ($r_s = 0.46$, $P < 0.01$) and the total score of NMSS. Female, H–Y stage, UPDRS-III and NMSS total score were the potential determinants of worse HRQoL of PD patients.
Conclusions: NMS have close association with various aspects of the HRQoL. Severe NMS may be related to dramatic decline of the HRQoL of PD patients.

1. Introduction

Parkinson's disease (PD) is a progressive neurodegenerative disorder characterized by cardinal motor symptoms including tremor, rigidity, bradykinesia and postural instability. PD affects approximately 1.7% population aged 65 years and over in mainland China [1]. Recently, increasing evidence suggests that PD has numerous non-motor symptoms (NMS) which include: neuropsychiatric symptoms, sleep disorders, autonomic and sensory symptoms [2]. NMS have been found not only in the advanced stage but also in the early stage of the disease, and may precede the onset of motor symptoms by several years [3]. NMS are often under-recognized and poorly managed in clinical practice [4]. NMS also impair quality of life of PD patients and leads to institutionalization, which imposes a considerable economic burden on PD patients' families and society [2,5,6].

Health-Related Quality of Life (HRQoL) may be defined as the perception and self-evaluation by patients of the disease's impact on their life and its consequences [7]. The evaluation of HRQoL is important in patients with PD, as the information gained from it can lead to a better understanding of the disease's consequences and suggest optimum treatment. In the past 20 years, the impact of motor symptoms such as rigidity, bradykinesia, tremor, gait and impaired balance on the decline of HRQoL has been well understood [8–11]. Recently, the impact of NMS on the HRQoL of PD patients has attracted substantial attention. Many studies from the West have reported that NMS play a more important role in the decline of HRQoL than motor symptoms [12–15]. The correlation between NMS and HRQoL in PD may differ among populations of different ethnic, economic, cultural and educational background. There are two studies on the correlation between NMS and HRQoL of PD in the Chinese populations of Beijing and Guangzhou, which demonstrated that mood, sleep/fatigue, gastrointestinal and

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urinary symptoms played a key role in the impact on HRQoL [5,16]; however, the sample sizes of these two studies were small. Therefore, we performed a study that included 693 PD patients from Southwest China to analyze the association between NMS and HRQoL of PD in a large sample.

2. Patients and methods

This cross-sectional and observational study included 693 PD patients consecutively admitted to hospital or seen in the outpatient clinic in the Department of Neurology, West China Hospital of SiChuan University between January 2009 and March 2013. All the patients met the UK PD Brain Bank criteria for PD [17]. The clinical information including age, age at onset, gender and anti-Parkinson medication were collected by neurologists during face-to face interviews. The Unified Parkinson's Disease Rating Scale part III (UPDRS-III) was used to assess PD motor symptoms and Hoehn &Yahr staging (H–Y stage) was used to assess the severity of PD. UPDRS-lV was used to evaluate motor fluctuations and dyskinesia. NMS were assessed using the non-motor symptoms scale (NMSS) which has been confirmed as an acceptable, reproducible, valid and precise assessment instrument for NMS in both international and Chinese studies [18,19]. The NMSS comprises 30 items in 9 domains: cardiovascular (2 items), sleep/fatigue (4 items), mood/apathy (6 items), perceptual problems/hallucinations (3 items), attention/memory (3 items), gastrointestinal tract (3 items), urinary (3 items), and sexual function (2 items), and miscellaneous (4 items of pain, taste or smell, weight change and excessive sweating). Each item is scored as a multiple of severity (0–3) and frequency (1–4), and the maximum NMS score is 360. The HRQoL of PD patients was evaluated using the Chinese version of PD Questionnaire-39 item version (PDQ-39) which has been validated as a tool for measuring of HRQoL in Chinese PD patients [20]. The PDQ-39 contains 8 domains of mobility, activities of daily living (ADL), emotional well-being, stigma, social support, cognitions, communication and bodily discomfort. Summary index was calculated for both the total PDQ-39 scale (PDQ-39 SI) and the subscales of 8 domains, and the higher numerical values (maximal score of 100) indicated the worse level of HRQoL. Patients who were unable to cooperate with the clinical assessments (NMSS and HRQoL) were excluded. The local ethics committee approved the study. All subjects signed written informed consent.

3. Statistical analysis

The continuous variables including age, onset age, UPDRS-III, score of NMSS and PDQ-39 SI are presented as mean ± standard deviation (SD). H–Y staging is presented as median and interquartile range, while the categorical variables such as gender and prevalence of NMS are shown as a percentage. As the total score and scores of each domain of NMSS, scores of each domain of PDQ-39 SI were not distributed normally using Kolmogorov–Smirnov and Shapiro–Wilk tests, Spearman's correlation test was used to analyze the associations between domains of NMSS and PDQ-39 SI. Spearman rank relational coefficient (r_s) ≥0.8 was considered to be a very strong correlation, r_s = 0.60–0.79 a strong correlation, r_s = 0.4–0.59 a moderate correlation, r_s = 0.20–0.39 a weak correlation, and r_s ≤0.19 a negligible correlation [21]. In order to explore the potential determinants of HRQoL, we found that the independent variables had interaction and co-linearity and most of the variables were not normally distributed, so the multiple linear regression model was unsuitable. We used a Binary forward Logistic regression model to test the determinants of worse HRQoL. The PDQ-39 SI was employed as a dependent variable and divided into 2 strata, the highest quartile was considered as worse HRQoL and all other scores were considered as reference. Gender, age, age at onset, disease duration, H–Y stage, UPDRS-III and NMSS total score were included as independent variables. All the data analysis was performed using SPSS 19.0. A *P* value of less than 0.05 was considered statistically significant.

4. Results

Of the 693 PD patients, 386 were male and 307 were female. The mean age was 61.5 ± 11.4 years and the mean age of onset was 57.1 ± 11.4 years. The mean disease duration was 4.4 ± 4.2 years. The mean score of UPDRS-III was 30.2 ± 13.4 and the median H–Y stage was 2.5 (1.0). A total of 185 patients (26.7%) presented with motor fluctuation and 40 patients (5.8%) presented with dyskinesia. The mean daily dose of levodopa was 209.0 ± 229.6 mg. The proportion of patients receiving treatment of dopamine agonists (DAs) was 39.7%, amantadine was 27.3%, trihexyphenidyl was 13.4% and catechol-O-methyltransferase (COMT) inhibitors was 6.6%.

The mean total score of NMSS was 37.2 ± 33.0. The prevalence of each domain of NMSS is listed in Table 1 and the score of each domain of NMSS is listed in Table 2. The most prevalent NMS domain was sleep/fatigue (79.8%), followed by attention/memory (69.8%), mood/apathy (65.7%), and miscellaneous (64.9%). The most prevalent NMS were "forget things or events" (60.6%), "feelings of sadness" (52.2%), "difficulty falling asleep" (48.3%), and "difficulty experiencing pleasure" (42.9%). The mean total score of PDQ-39 SI

Table 1
Prevalence of non-motor symptoms of all PD patients.

Non-motor domains	*N*	Percent (%)
Domain 1: cardiovascular	185	26.7
1. Light-headedness	174	25.1
2. Falls due to fainting	27	3.9
Domain 2: sleep/fatigue	553	79.8
3. Daytime sleepiness	305	44.0
4. Fatigue	306	44.2
5. Difficulty falling sleep	335	48.3
6. Restless legs	222	32.0
Domain 3: mood/apathy	455	65.7
7. Loss of interest in surroundings	270	39.0
8. Lack of motivation	275	39.7
9. Feeling of nervousness	209	30.2
10. Feeling of sadness	362	52.2
11. Flat affect	163	23.5
12. Difficulty experiencing pleasure	297	42.9
Domain 4: perceptual problems	122	17.6
13. Hallucination	50	7.2
14. Delusions	38	5.5
15. Double vision	86	12.4
Domain 5: attention/memory	484	69.8
16. Concentration	192	27.7
17. Forgetting things or events	420	60.6
18. Forgetting to do things	223	32.2
Domain 6: gastrointestinal	390	56.3
19. Drooling saliva	152	21.9
20. Difficulty swallowing	130	18.8
21. Constipation	272	39.2
Domain7: urinary	342	49.4
22. Urgency	197	28.4
23. Frequency	185	26.7
24. Nocturia	272	39.2
Domain 8: sexual function	198	28.6
25. Interest in sex	168	24.2
26. Problems having sex	94	13.6
Domain 9: miscellaneous	450	64.9
27. Pain	275	39.7
28. Taste or smell	220	31.7
29. Weight change	60	8.7
30. Excessive sweating	190	27.4

PD: Parkinson's disease.