Journal of the Neurological Sciences 345 (2014) 56–60

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Freezing of gait in Chinese patients with Parkinson Disease

Ruwei Ou, Xiaoyan Guo, Wei Song, Bei Cao, Jing Yang, Qianqian Wei, Na Shao, Huifang Shang *

Department of Neurology, West China Hospital, Sichuan University, Chengdu, Sichuan, China

ARTICLE INFO

Article history:
Received 15 March 2014
Received in revised form 9 June 2014
Accepted 1 July 2014
Available online 8 July 2014

Keywords:
Parkinson disease
Gait disorder
Freezing of gait
Festination
Non-motor symptoms
Prevalence

ABSTRACT

A total of 474 Chinese Parkinson disease (PD) patients were evaluated to explore the prevalence and clinical correlates of freezing of gait (FOG) in this cross-sectional study. Two hundred and twenty-one PD patients (46.62%) reported FOG (freezers). FOG occurred more frequently in older patients and patients with low limbs as the site of onset, longer disease duration and higher Hoehn and Yahr (H&Y) stage ($P < 0.05$). After adjusting for confounding factors, the freezers had higher scores for the Unified PD Rating Scale (UPDRS) part III, Non-Motor Symptoms Scale (NMSS), PD Questionnaire 39 (PDQ-39), Hamilton Depression Scale (HAMD) and Hamilton Anxiety Scale (HAMA), and lower scores for the Mini-Mental status examination (MMSE), frontal assessment battery (FAB) and Montreal Cognitive Assessment (MoCA) compared with the non-freezers ($P < 0.05$). The binary logistic regression analysis indicated that festination, falls, a high daily dose of levodopa, the use of a dopamine receptor agonist, a high H&Y stage, the severity of urinary symptoms and a high HAMD score were associated with FOG. FOG is a relatively common disabling symptom in Chinese PD patients. Patients that were older, or reported a longer disease duration, low limbs as the site of onset and a more severe disability were more likely to experience FOG. Non-motor symptoms, especially urinary symptoms and depression, may also be related to FOG.

1. Introduction

Gait disorder, a core symptom of Parkinson disease (PD), can consist of a variety of symptoms, such as slowness, shuffle, festination, falls, and freezing of gait (FOG) [1]. FOG is defined as a brief, episodic absence of or marked reduction in the forward progression of the feet despite the intention to walk [2]. FOG not only affects gait in the form of start hesitation, when turning or approaching a destination, or when walking in an open walkway [3], but it can also affect speech and writing [4]. It is a relatively common symptom of PD. In a previous retrospective study on 100 PD patients, sixty of the patients (60%) reported FOG [5]. In another retrospective study on 172 advanced PD patients, 53% PD patients reported FOG [6]. It has been reported that FOG is a disabling symptom and a cause of falls in PD patients [7]. It is important to investigate FOG more thoroughly because of the impact that FOG has on motor function and the quality of life (QoL) of PD patients. Previous studies have already reported a partial clinical profile on FOG in PD. A study on an American population found that FOG can occur as a result of disease progression or as a side effect of levodopa treatment [8]. Another study on an Italian population, however, found that FOG is not affected by levodopa treatment but that it is associated with a longer PD duration and akinesia [5]. Other studies conducted on non-Asian populations found that there is a correlation between the severity of FOG and cognitive impairment [9,10]. The clinical symptoms of FOG in the Chinese PD population have yet to be reported. The aim of this study is to explore the prevalence and clinical correlates of FOG in a large cohort of Chinese PD patients.

2. Methods

This study was approved by the Ethics Committee of West China Hospital of Sichuan University. A total of 474 PD patients from the Department of Neurology, West China Hospital of Sichuan University were consecutively recruited between May 2011 and April 2014 for this observational study. All of the participating PD patients were diagnosed according to the Unified Kingdom PD Society Brain Bank Clinical Diagnostic Criteria for PD [11]. Patients with atypical and secondary Parkinsonism were excluded from this study. Clinical data including age, onset age, gender, disease duration, diagnosis delay, family history of PD, type of motor symptoms, site of initial motor symptoms, years of education, handedness, treatment regimen and motor complications were collected by neurologists majoring in PD through in person interviews. Early-onset PD (EOPD) was defined as an onset age of PD younger than 50 years, and late-onset PD (LOPD) was defined as older than 50 years. PD patients were grouped into three subtypes including tremor-dominant, akinetic-rigid and mixed based on the criteria described in a previous study [12]. Unified PD Rating Scale (UPDRS) part III [13] and Hoehn and Yahr (H&Y) stage [14] were used to evaluate

* Corresponding author at: Department of Neurology, West China Hospital, Sichuan University, 610041, Chengdu, Sichuan, China. Fax: +86 28 85423550.
E-mail address: hfshang2002@126.com (H. Shang).

http://dx.doi.org/10.1016/j.jns.2014.07.002
0022-510X/

the severity of the motor symptoms. The QoL of PD patients was evaluated using PD Questionnaire 39 (PDQ-39), which contains 8 domains [15]. Non-motor symptoms (NMS) were assessed using the Non-Motor Symptoms Scale (NMSS), which contains 9 domains [16]. Cognitive function was evaluated using the Mini-Mental status examination (MMSE) [17], frontal assessment battery (FAB) [18] and Montreal Cognitive Assessment (MoCA), which contains 7 domains [19]. The severities of depression and anxiety were assessed using the Hamilton Depression Rating Scale (HAMD) (24 items) [20] and Hamilton Anxiety Rating Scale (HAMA), respectively [21]. All of the assessments were conducted at "on" state.

Freezing episodes were observed by experienced neurologists during the visit and were reported by the patient, his or her family members or the caregiver when it occurred at home or anywhere outside of the hospital. Patients were identified as presented with FOG (freezers) based on the "yes" answer to the question "Do you feel that your feet get glued to the floor while walking, making a turn or when trying to initiate walking?", which is based on item 1.3 of the FOG Questionnaire [22]. If patients and their family members could not understand the definition of FOG, a description or imitation of all of the subtypes of FOG would be performed by neurologists during the visit. The answer obtained from the patients was confirmed by their relatives or caregivers and by the clinical records to ensure the accuracy of data.

3. Statistical analyses

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) version 19.0 for Windows. All of the continuous data, including age, age at onset, disease duration, diagnosis delay, years of education, daily levodopa dose, UPDRS part III score, the total scores and each domain score for the PDQ-39, NMSS and MoCA, and the total scores for the HAMD, HAMA, FAB and MMSE, are presented as the mean ± standard deviation (SD). The discontinuous data, including H&Y stage, is presented as the median value (quartile). Student's *T* test was used for the comparisons of the continuous data, including age, age at onset, disease duration, diagnosis delay and years of education, between the PD patients with and without FOG. The Chi-square test was used to evaluate the differences in the categorical variables between the PD patients with and without FOG. The Wilcoxon rank sum test was performed to compare the discontinuous data between the PD patients with and without FOG. Analyses of covariance (ANCOVA) adjusted for confounding factors were performed to compare the total scores from the UPDRS part III, PDQ-39, NMSS, FAB, MMSE, MoCA, HAMD and HAMA, as well as the scores of each domain from the PDQ-39, NMSS and MoCA between the PD patients with FOG and without FOG. A binary logistic regression model was used to explore potential factors related to FOG. The presence or absence of FOG was used as dependent variable. The parameters, including age, disease duration, onset age, low limbs as the site of onset, use of levodopa, dopamine receptor agonist or entacapone, daily dose of levodopa, H&Y stage, fluctuation, dyskinesia, festination, falls, as well as the scores for the sleep/fatigue, gastrointestinal, urinary, sexual dysfunction and miscellaneous subdomains in the NMSS, the scores for the visuospatial/executive abilities, naming, attention and orientation subdomains in the MoCA, and the total scores from the FAB, HAMD and HAMA, were used as covariables. All statistical tests were two-tailed, and *P* values < 0.05 were considered statistically significant (for multiple comparison of chi-square test, *P* values < 0.0125 were considered statistically significant).

4. Results

In the current study, 221 PD patients (46.62%) reported FOG. FOG was more frequent in patients older than 65 years than in patients younger than 65 years (53.55% vs. 41.06%, $P = 0.007$), in patients with lower limbs as the site of onset than in patients in which lower limbs were not the site of onset (52.17% vs. 43.32%, $P = 0.033$), and in patients with a disease duration greater than 5 years than in patients with a disease duration of less than 3 years or between 3 and 5 years ($P < 0.0125$) (Table 1). PD patients at a lower H&Y stage (1–2.5) demonstrated a significantly lower prevalence of FOG than patients at a higher H&Y stage (3 and 4–5) ($P < 0.0125$, Table 1). There was no significant difference in the prevalence of FOG between the male and female patients, between the EOPD and LOPD patients, between the patients with and without a family history of PD, or among the subtypes of PD patients (Table 1).

The demographic and clinical features of the PD patients are listed in Table 2. The mean age, age of onset, disease duration and median H&Y stage were significantly greater for the freezers than the non-freezers ($P < 0.05$). The percentages of patients receiving treatment of levodopa, dopamine receptor agonist and entacapone, as well as the frequencies of motor fluctuation, dyskinesia, falls and festination were higher in the freezers than the non-freezers ($P < 0.05$). After adjusting for age and disease duration, the freezers had a higher mean UPDRS part III score and were taking a higher daily dose of levodopa than the non-freezers ($P < 0.05$). The percentages of patients treated with amantadine and benzhexol were not different between freezers and non-freezers.

The PDQ-39 results for the PD patients with and without FOG are listed in Table 3. After adjusting for age, disease duration, H&Y stage and NMSS, the freezers had a significantly higher total score for the PDQ-39 and a higher score for the bodily discomfort subdomain compared with the non-freezers ($P < 0.05$). The NMSS results for the PD patients with and without FOG are listed in Table 4. After adjusting for age, disease duration and H&Y stage, the freezers had a significantly higher total score for the NMSS and higher scores for the sleep/fatigue, gastrointestinal, urinary, sexual dysfunction and miscellaneous domains compared with the non-freezers ($P < 0.05$). The cognitive function assessment results for the PD patients with and without FOG are presented in Table 5. After adjusting for age and disease duration, the freezers had lower total scores for the MMSE, FAB and MoCA, as well as lower scores for the visuospatial/executive abilities, naming, attention and orientation domains in the MoCA compared with the non-freezers ($P < 0.05$). No significant differences in the scores for the remaining domains of the PDQ-39, NMSS and MoCA were found between the freezers and non-freezers. The depression and anxiety severity results for the PD patients with and without FOG are listed in Table 6. After adjusting for age, disease duration and H&Y stage, the total scores for the HAMD and HAMA were significantly higher in the freezers compared with the non-freezers ($P < 0.05$).

The potential factors related to FOG are presented in Table 7. The binary logistic regression model indicated a high H&Y stage, festination, falls, high daily dose of levodopa, use of a dopamine receptor agonist, a high score for the urinary domain in the NMSS and a higher score for the HAMD were associated with FOG ($P < 0.005$). No significant correlations were found between the remaining clinical factors and FOG.

5. Discussion

To the best of our knowledge, this is the first study to investigate the prevalence of FOG and the clinical correlations between various factors and FOG in a large cohort of Chinese PD patients.

We found that FOG is very common in the Chinese PD population (46.62%), which is consistent with other previous studies on non-Asian populations (range from 32% to 72%) [5,6,8,23–25]. Our patients at higher H&Y stages were more likely to report experiencing FOG, which is consistent with a previous study on an Israeli population [6]. Our findings that the PD patients who were older or who had a longer disease duration or low limbs as the site of onset were more likely to experience FOG have never been previously systematically reported. Additionally, we also found that there was no difference in the