RESEARCH ARTICLE

The Relationship Between Pain, and Freezing of Gait and Falls in Parkinson's Disease

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ABSTRACT

Introduction: To investigate the relationship between pain, freezing of gait (FOG) and falls in Parkinson's Disease (PD).

Methods: The study included 110 PD patients. The Unified PD Rating Scale (UPDRS) and Hoehn and Yahr Scale were used to evaluate disease severity. The patients self-reported occurrence of FOG and falls, and the FOG Questionnaire was administered to evaluate the severity of FOG. A visual analog scale (VAS) was used to measure the severity of pain and pain localization was self-reported by the patients.

Results: Fifty-eight of the patients had FOG and 43 experienced falls. Among the patients, 42 had no pain, whereas 35 had lower extremity pain. Higher UPDRS motor and FOG scores, and advanced-stage disease

were noted in significantly more of the patients with FOG and falls. VAS scores were not affected by the presence of FOG or falls. There was a positive correlation between the severity of FOG and VAS score in the male patients (r=0.308; p=0.010). More patients with falls had lower extremity pain than those without falls (r=0.308; p=0.010).

Discussion: Patients with FOG and falls had more severe motor findings. Pain is correlated with both FOG and falls. Further investigations should be done to understand the mechanism of this relationship to prevent the motor complications in advanced PD.

Keywords: Falls, freezing of gait, pain, Parkinson's disease

INTRODUCTION

Freezing of gait (FOG) and falls commonly occur in patients with Parkinson's disease (PD), as 75% of patients develop balance and gait problems (1). FOG, which is characterized by episodic brief temporary pauses at the onset of or while walking (2), leads to sudden and unexpected interruptions of movement. FOG increases the risk of falls and has a very negative effect on patient quality of life (QoL) (3).

PD patients report experiencing pain during all stages of the disease and pain is the symptom of PD most associated with disability. Pain in PD patients is often chronic and widespread (4). Pain also negatively affects patient QoL and leg pain is common in patients with PD (5).

Regarding the association between pain and motor functions, it was reported that PD patients with FOG experience pain more frequently than those without FOG (6). Although there are limited studies on this subject, it can be anticipated that patients with FOG have difficulty in initiating movement and the effort to do so can trigger pain. In addition, as the severity of pain increases so does the risk of falling. Inversely, pain can cause FOG and falls, especially when localized in the lower extremities. In the light of these findings the present study aimed to determine the relationship between pain (including localization and severity), and FOG and falls in idiopathic PD patients.

METHODS

The study included patients diagnosed as idiopathic PD according to the United Kingdom Brain Bank Clinical Diagnostic Criteria (7). Patients were examined during 'off' periods. 'Off' period was preferred because FOG usually presented during when the patient is without levodopa. The severity of motor functions was evaluated using the Unified Parkinson's Disease Rating Scale (UPDRS) (8). Hoehn and Yahr Scale (HYS) was used to determine the stage of the disease (9). Patients with neurological examination findings of pyramidal, cerebellar, and vertical gaze paralysis, head trauma, dementia, encephalitis, and cerebrovascular accident were excluded. The approvement from the ethical committee was obtained (number: 10840098–604.01.01-E. 47244). An informed consent was signed by all the participants.

Anti-PD drugs used by the patients were recorded and the levodopa equivalent dose was calculated for each (10). Patients' experiences of FOG (present/absent) and falls (present/absent) during the previous month were recorded. The FOG Questionnaire (11) was administered to evaluate the severity of FOG. The questionnaire's 6 items evaluate 1) walking, 2) gait and daily activities, 3) the presence of FOG 4) duration of FOG, 5) initiation of gait, and 6) duration of FOG during turns. The items are answered using a 5-point Likert-type scale; 0 (none) to 4 (severe). The FOG Questionnaire score ranges from 0–24; higher scores indicate greater severity of FOG.

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A visual analog scale (VAS) was used to assess the severity of pain during the previous month. Patients score the severity of pain on a scale of 0 (no pain) to 10 (severe pain). Patient reports of the localization of pain were categorized as upper extremity for neck and arm pain, lower extremity for back and leg pain, and multifocal for both upper and lower extremity pain.

Statistical Analysis

Statistical analysis was performed using of IBM SPSS Statistics for Windows v. 22.0 (IBM Corp., Armonk, NY). The Shapiro-Wilk test was used to compare continuous data with normal distribution. For data not normally distributed the Mann-Whitney U was used to compare categorical groups. The distribution of categorical variables in the groups was compared via the chi-square test. Correlations between continuous data were analyzed using Spearman's correlation test. The level of statistical significance was set at $p < 0.05$.

RESULTS

One hundred and ten PD patients (41 female, 69 male) participated the study. In all, 24 (21.8%) patients were HYS stage 1, 42 (38.2%) were HYS stage 2, 37 (33.6%) were HYS stage 3, and 7 (6.4%) were HYS stage 4. Patient characteristics, including FOG Questionnaire and VAS scores, are summarized in Table 1. In total, 58 (52.7%) patients had FOG, and 43 (39.1%) had falls. Among the patients, 42 (38.2%) did not have pain, versus 10 (9.1%) patients with upper extremity pain, 35 (31.8%) with

lower extremity pain, and 23 (20.9%) with multifocal pain. Patient sociodemographic and PD characteristics are summarized in Table 1.

The comparison of the sociodemographic and PD characteristics of the patients with and without FOG are presented in Table 2.

The UPDRS motor score and HYS were significantly higher in the patients with FOG than in those without FOG, whereas there weren't any significant differences in age, duration of disease, levodopa equivalent dose, or VAS score.

Pain localization did not differ significantly between the patients with and without FOG (Table 3). In addition, there wasn't a correlation between the FOG Questionnaire and VAS scores (r=0.149; p=0.121); however, there was a positive correlation between the FOG Questionnaire score and UPDRS motor score (p<0.001). Among the male patients there was a positive correlation between the FOG Questionnaire score and VAS score (r=0.308; p=0.010). The correlation between FOG Questionnaire, UPDRS motor, and VAS scores, according to gender, are presented in the Figures 1 and 2.

Table 1. Patient sociodemographic and PD characteristics

	Mean ± SD	Range
Age (years)	66.12±10.45	27–85
Duration of disease (years)	7.37±6.60	1–37
UPDRS motor score	18.55±8.67	1–41
Levodopa equivalent dose (mg)	683.10±490.66	0–2550
FOG Questionnaire score	9.27±8.02	0–24
VAS score	4.07±3.76	0–10

SD, standart deviation; UPDRS, unified Parkinson's disease rating scale; FOG, freezing of gait; VAS, visual analog scale.
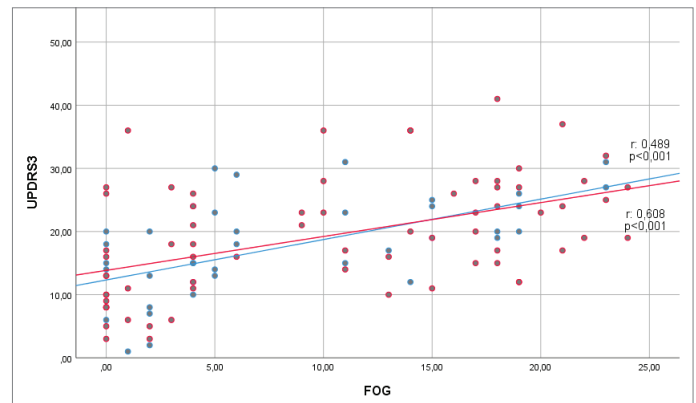

Figure 1. The correlation between FOG questionnaire and UPDRS motor scores according to gender (red line, male; blue line, female).

Table 2. Comparison of the patients with and without FOG

	Without FOG		With FOG		
	Mean ± SD	Range	Mean ± SD	Range	z; p
Age (years)	64.58±11.47	27–85	67.50±9.31	47–84	1.330; 0.183
Duration of disease (years)	6.83±7.12	1–37	7.86±6.11	1–35	1.750; 0.080
UPDRS motor score	14.33±7.72	1–30	22.34±7.71	6–41	4.767; <0.001
HYS	1.865±0.76	1–3	2.586±0.81	1–4	4.257; <0.001
Levodopa equivalent dose (mg)	579.27±311.59	100–1600	777.82±597.27	0–2550	1.454; 0.146
FOG Questionnaire score	2.77±3.82	0–18	15.10±6.06	1–24	7.973; <0.001
VAS score	3.79±3.85	0–10	4.33±3.70	0–10	0.716; 0.474

FOG, freezing of gait; SD, standart deviation; UPDRS, unified Parkinson's disease rating scale; HYS, Hoehn and Yahr scale.

Table 3. Comparison of pain localization between the patients with and without FOG

		Without FOG	With FOG	Total	Test value
		n (%)	n (%)	n (%)	x²; p
Pain Localization	No pain	22 (52.4)	20 (47.6)	42 (38.2)	2.533; 0.469
	Upper extremity	6 (60.0)	4 (40.0)	10 (9.1)	
	Lower extremity	13 (37.1)	22 (62.9)	35 (31.8)	
	Multifocal	11 (47.8)	12 (52.2)	23 (20.9)	

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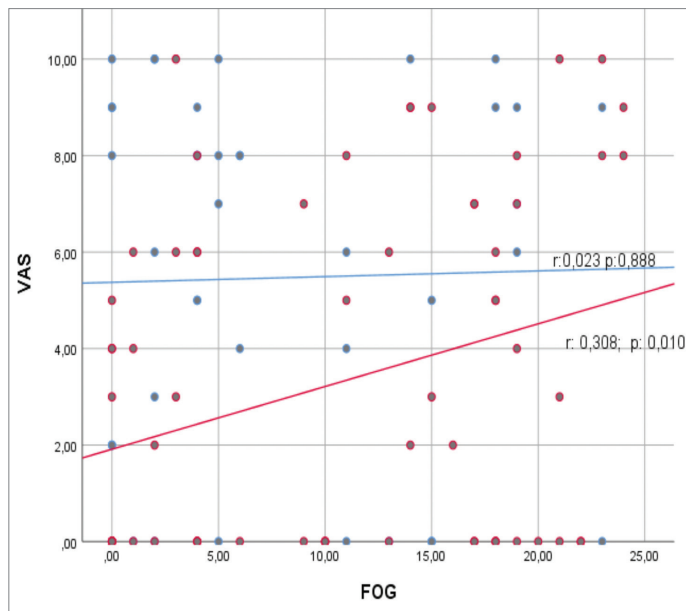
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Figure 2. The correlation between FOG questionnaire and VAS scores according to gender (red line, male; blue line, female).

The comparison of the sociodemographic and PD characteristics of the patients with and without falls are presented in Table 4.

Age, duration of disease, UPDRS motor score, HYS, and FOG Questionnaire score were higher in the patients with falls than in those without falls. More patients with falls had lower extremity pain, as compared to those without falls (Table 5).

DISCUSSION

In the present study the UPDRS motor score was higher in the PD patients with FOG (52% of patients), who also had higher HYS disease stage than those without FOG. In addition, there was a significant correlation between the UPDRS motor score and FOG Questionnaire score, regardless of gender. Moreover, there weren't any significant differences in age or disease duration between the groups with FOG and without FOG. Based on the present findings, we think the most important difference between PD patients with and without FOG is that those with FOG have more severe motor dysfunction and the severity of FOG increases as motor dysfunction becomes more severe. Earlier studies show that the occurrence of FOG is more common in PD patients that are elderly, those with longer disease duration, those with higher, and those with motor fluctuations (12–14). It was also reported that there isn't a significant difference in disease duration or stage between PD patients with and without FOG (15). These differences in findings might be related to differences in methodology between studies.

Levodopa is an effective treatment for FOG (14). FOG occurs primarily during the 'off' period, but in rare cases can occur during the 'on' period (16). Some researchers reported that the dose of levodopa is higher in PD patients with FOG than in those without FOG (12, 17), whereas others observed that there is no difference (18). In the present study there wasn't a difference in the levodopa equivalent dose between the PD patients with and without FOG.

PD patients commonly complain about pain and lower extremity pain (unilateral or bilateral) is most common (19). In the present study 60% of the PD patients experienced pain, of which approximately 50% had lower extremity pain. Although the frequency and severity of pain increase with disease stage, it is known that the severity of pain is greater in patients with postural instability gait disorder (20). To date, the literature includes only 1 study on the relationship between FOG and pain. Allen et al. (6) reported that FOG increases the frequency of pain, but has no effect on the severity of pain. In the present study FOG was not correlated with pain, as there wasn't a difference in the VAS pain score between the PD patients with and without FOG. Characteristics of PD patients with FOG include difficulty initiating walking, continuation of walking, and, most notably, turning while walking (21). The patient cannot move his lower extremities during seconds/minutes during FOG period. In the present study there wasn't a correlation between the presence of FOG and pain localization. Interestingly though, in the male patients there was a positive correlation between the FOG Questionnaire score and VAS pain score; the severity of pain increased as the severity of FOG increased. In

Table 4. Comparison of the patients with and without falls

	Without falls		With falls		
	Mean ± SD	Range	Mean ± SD	Range	z; p
Age (years)	63.81±10.87	27–85	69.72±8.71	50–84	3.008; 0.003
Duration of disease (years)	5.69±4.59	1–30	10.00±8.26	1–37	3.178; 0.001
UPDRS motor score	16.52±8.56	1–36	21.72±7.94	2–41	3.170; 0.002
HYS	1.91±0.733	1–3	2.767±0.812	1–4	4.987; <0.001
Levodopa equivalent dose (mg)	641.12±429.17	0–2550	750.07±574.62	0–2319	0.660; 0.509
FOG Questionnaire score	6.16±6.89	0–23	14.12±7.26	0–24	5.087; <0.001
VAS score	3.57±3.82	0–10	4.86±3.58	0–10	1.670; 0.095

SD, standart deviation; UPDRS, unified Parkinson's disease rating scale; HYS, Hoehn and Yahr scale; FOG, freezing of gait; VAS, visual analog scale.

Table 5. Comparison of pain localization between the patients with and without falls

		Without falls	With falls	Total	Test value
		n (%)	n (%)	n (%)	x^2; p
Pain Localization	No pain	30 (71.4)	12 (28.6)	42 (38.2)	
	Upper extremity	7 (70.0)	3 (30.0)	10 (9.1)	
	Lower extremity	13 (37.1)	22 (62.9)	35 (31.8)	12.236; **0.007**
	Multifocal	17 (73.9)	6 (26.1)	23 (20.9)	

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this case, it can be accepted that at the time of FOG, mechanically it is not only the legs but the whole body is forced and the pain can be felt in the whole body as the FOG severity increases.

Dopamine is known to modulate pain in the spinal cord, thalamus, periaqueductal gray matter, basal ganglia, and cingulate gyrus. Axons from these regions are projected to the mesocortical, mesolimbic, nigrostriatal, and tuberoinfundibular pathways. These pathways are responsible for the formation of various non-motor symptoms (sleep and pain) (22). In patients with PD neurodegeneration negatively affects not only the dopaminergic system, but also the noradrenergic, serotonergic, cholinergic, and peptidergic systems. Furthermore, connections between the pedunculopontine nucleus, and cerebellum, thalamus, and many regions of the frontal cortex decrease due to FOG in PD patients (23). In such cases, in addition to the presence of FOG the relationship between the brain regions related to FOG and pain might play a role in the severity of pain in male PD patients.

It was reported that falls commonly occur in PD patients (35%-90%) (24). In the present study 39% of the patients reported falls. In PD patients as the FOG Questionnaire score increases the risk of falls increases (especially falling forward) (25). PD patients that fall are generally older, have longer disease duration, have more advanced disease stage, and have a higher UPDRS motor score than those that do not fall (26–28), as was observed in the present study. In addition, the UPDRS motor score and FOG Questionnaire score were higher in the present study's PD patients with falls than in those without falls, whereas there wasn't a significant difference in the levodopa equivalent dose.

There wasn't a significant difference in VAS pain scores between the present study's PD patients with and without falls; however, more of the patients with falls had lower extremity pain. These findings might be related to 2 factors: (a.) Falling is associated with the presence of pain. Old patients have an increased risk of falling that is further increased in those with knee, back, and foot pain (29, 30). Furthermore, both the presence of PD and lower extremity pain increase the risk of falling. (b.) In addition, post-traumatic extremity injury is more common in the elderly (31); as such, the present study's PD patients with falls might have had more pain in their feet and legs, as compared to those without falls.

The prevention and treatment of FOG, falls, and pain are central to improving QoL in PD patients, and improving our understanding of the relationship between these 3 entities might yield better prevention and treatment strategies. The present study aimed to determine the relationship between pain, and FOG and falls; however, there were some limitations. 1) Psychiatric disorders and sleep disorders (non-motor findings) that play a role in the development of gait disorders and pain in PD were not examined, whereas investigating these could have provided important data; 2) Patients with HYS 4 were included; 3) The pain types were not considered.

In conclusion, the present findings are as follows: 1) As the severity of motor findings in PD patients increases, the presence of FOG and falls also increases; 2) The severity of FOG in male patients is positively correlated with pain; 3) Lower extremity pain is more common in PD patients with falls. Pain is correlated with both FOG and falls; additional functional imaging-based research conducted in balance laboratories might further delineate this correlation.

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