Risk Factors for Falls in Patients with de novo Parkinson's Disease: A Focus on Motor and Non-Motor Symptoms

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ABSTRACT

Objective We aimed to identify risk factors for falls in patients with de novo Parkinson's disease (PD).

Methods Forty-six patients with de novo PD were retrospectively included in the study. We assessed details on the patients' motor symptoms as well as non-motor symptoms using several representative scales for global cognition, depression, fatigue, and dysautonomia. Fallers and non-fallers were identified according to their history of falls during the preceding year.

Results Twenty-two patients (45.8%) with de novo PD had a history of falls. Compared with the non-faller group, the faller group exhibited higher scores for postural instability/gait difficulty (PIGD), anxiety, fatigue, total dysautonomia, gastrointestinal dysfunction, and thermoregulatory dysfunction. Moreover, logistic regression analysis showed that falling was positively correlated with anxiety and gastrointestinal symptoms but negatively associated with the tremor scores.

Conclusion Our findings suggest that falling in patients with de novo PD is significantly associated with PIGD/non-tremor symptoms, anxiety, and gastrointestinal dysfunction.

Key Words Fall; Risk factor; De novo; Parkinson's disease; Motor; Non-motor.
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When each patient was initially admitted to our movement disorder clinic, his or her history of falls within the last year was recorded. A meta-analysis revealed that previous falls over a period of 12 months were recorded in the majority (50%) of studies in PD patients, although the length of the period varied across studies (i.e., 3, 6, and 12 mo). A fall event was defined as a person unexpectedly lost his or her balance and inadver-ently rested on the ground, floor, or other low surface. We recorded the number of falls that each patient experienced during the preceding year. If a patient with PD answered ‘no,’ the patient was categorized as a non-faller. If any patient with PD reported experiencing one or more falls, then the patient was categorized as a faller for this study.7 The baseline demographic and clinical characteristics, including motor and non-motor symptoms, were assessed. The total motor score was defined as the sum of the part III scores for the Unified Parkinson’s Disease Rating Scale (UPDRS). In addition, we calculated the subscores for tremor (the sum of the scores for UPDRS part III, items 3–9), rigidity (the sum of the scores for UPDRS part III, items 10–14), bradykinesia (the sum of the scores for UPDRS part III, items 15–22 and 27), and postural instability/gait difficulty (PIGD; the sum of the scores for UPDRS part II, items 13–15 and UPDRS part III items 25 and 26).8,9 In addition, the Hoehn and Yahr (HY) stages were also assessed. Non-motor symptoms were evaluated by the Korean version of the Montreal Cognitive Assessment (MoCA-K),10 the Korean version of the Beck Depression Inventory (BDI),12 the Korean version of the Beck Anxiety Inventory (BAI),13 the Parkinson’s Disease Fatigue Scale (PFS),14 and the Korean version of the Scale for Outcomes in Parkinson’s Disease-Autonomic Dysfunction (SCOPA-AUT).15

Statistical analysis

The fallers and non-fallers with de novo PD were compared using Student’s t-test for the numerical data and the chi-squared test for the categorical data. Univariable logistic regression analyses were used for the binary outcomes, and a subsequent multivariable logistic regression analysis was performed by backward stepwise selection. A p-value of < 0.05 was considered statistically significant. All statistical analyses in the study were performed using SPSS (version 20.0, IBM Corp., Armonk, NY, USA).

Table 1. Demographics and clinical characteristics of de novo Parkinsonian patients with and without falls

|                          | Non-faller (n = 26) | Faller (n = 22) | p value |
|--------------------------|---------------------|----------------|---------|
| Age, yr                  | 71.8 ± 7.3          | 71.3 ± 11.4    | 0.834   |
| Sex-male                 | 13 (50.0)           | 8 (36.4)       | 0.343   |
| Disease duration, yr     | 1.5 ± 1.1           | 1.3 ± 1.0      | 0.574   |
| BMI, kg/m²               | 23.1 ± 3.0          | 23.7 ± 3.1     | 0.462   |
| Level of education, yr   | 8.9 ± 5.2           | 9.0 ± 5.5      | 0.927   |
| UPDRS-III score (total motor) | 26.1 ± 8.4         | 25.3 ± 9.5     | 0.759   |
| Tremor score             | 3.7 ± 1.9           | 2.5 ± 2.5      | 0.076   |
| Rigidity score           | 6.0 ± 2.5           | 4.9 ± 3.1      | 0.188   |
| Bradykinesia score       | 11.4 ± 4.1          | 12.2 ± 4.6     | 0.545   |
| PIGD score               | 2.4 ± 1.6           | 4.3 ± 3.7      | 0.040*  |
| Hoehn and Yahr stage     | 2.2 ± 0.3           | 2.1 ± 0.4      | 0.150   |
| MoCA-K (global cognition)| 21.2 ± 4.7          | 20.8 ± 6.4     | 0.795   |
| BDI (depression)         | 9.9 ± 7.4           | 11.3 ± 7.1     | 0.498   |
| BAI (anxiety)            | 5.4 ± 4.5           | 9.5 ± 7.9      | 0.029*  |
| PFS (fatigue)            | 38.0 ± 16.4         | 48.8 ± 13.8    | 0.019*  |
| SCOPA-AUT (total dysautonomia) | 11.4 ± 5.9         | 16.8 ± 9.4     | 0.024*  |
| Gastrointestinal         | 2.9 ± 2.6           | 5.3 ± 4.1      | 0.020*  |
| Urinary                  | 6.1 ± 4.0           | 8.2 ± 4.8      | 0.107   |
| Cardiovascular           | 0.6 ± 1.2           | 1.1 ± 1.7      | 0.194   |
| Thermoregulatory         | 0.5 ± 0.8           | 1.1 ± 1.1      | 0.047*  |
| Pupillomotor             | 0.2 ± 0.6           | 0.4 ± 1.3      | 0.465   |
| Sexual                   | 4.1 ± 1.9           | 2.6 ± 2.8      | 0.236   |

Data are n (%) or mean ± standard deviation values. *p < 0.05. BAI: Beck Anxiety Inventory. BDI: Beck Depression Inventory. BMI: body-mass index. MoCA-K: Korean version of Montreal Cognitive Assessment. PD: Parkinson’s disease. PFS: Parkinson’s Disease Fatigue Scale. PIGD: postural instability and gait difficulty. SCOPA-AUT: Scales for Outcomes in Parkinson’s Disease-Autonomic Dysfunction. UPDRS-III: Unified Parkinson’s Disease Rating Scale part III.
Ethical standards
All procedures in the studies involving human participants were performed in accordance with the ethical standards of the institutional and/or national research committee and with the 1975 Helsinki declaration and its later amendments or comparable ethical standards. The need to obtain informed consent was waived by the IRB of our institution since this study is a retrospective study.

RESULTS
Comparison of clinical features between fallers and non-fallers with de novo PD
A total of 26 non-fallers and 22 fallers with de novo PD, who were grouped according to their histories of falls, were included in the study. The demographic and clinical characteristics, including motor and non-motor symptoms, between fallers and non-fallers with de novo PD are displayed in Table 1. Compared to the non-fallers with de novo PD, the fallers with de novo PD showed higher scores for PIGD (p = 0.040), anxiety (p = 0.029), fatigue (p = 0.019), and total dysautonomia (p = 0.024), as well as gastrointestinal and thermoregulatory subscores for dysautonomia (p = 0.020 and p = 0.047, respectively).

Risk factors for falls in patients with de novo PD
To identify the risk factors for falls in patients with de novo PD, we performed univariable and multivariable logistic regression analyses, as presented in Table 2. In the right column in Table 2, adjusted odds ratios (adj ORs) and 95% confidence intervals (95% CIs) are shown for the variables with significant results. We found that lower tremor scores were associated with the non-falling group of de novo PD patients (adj OR = 0.656, 95% CI = 0.459–0.938), whereas higher scores for anxiety and gastrointestinal symptoms correlated with the falling group of de novo PD patients (adj OR = 1.286, 95% CI = 1.026–1.613, respectively).

DISCUSSION
In this study, we found a high rate of falls (48.5%) during the preceding year in patients with de novo PD. Previously, a few studies have reported that 23% to 42% of patients with early PD experienced falls. Moreover, a meta-analysis also revealed that fall frequency followed an inverted U-shaped curve in PD pa-
tients. Collectively, our results suggest that patients with very early stages of PD may commonly experience falls. Therefore, clinicians need to be concerned for not only patients with advanced stages of PD but also patients with early stages of PD.

We evaluated the differences in the clinical characteristics between the falling and non-falling groups of drug-naïve patients with de novo PD. For the motor symptoms, the fallers with de novo PD showed higher PIGD scores than did the non-fallers with de novo PD (Table 1), whereas lower tremor scores were negatively associated with falling in patients with de novo PD (Table 2). Consistent with our results, Pelicioni et al. showed that the PIGD subtype was related to falls compared to the non-PIGD subtype in PD patients. These findings suggest that patients with non-tremor-dominant PD might be at risk for falls. However, several non-motor symptoms, including anxiety, fatigue, total dysautonomia, gastrointestinal dysfunction, and thermoregulatory dysfunction, were associated with falls in patients with de novo PD (Table 1). Intriguingly, the logistic regression analyses revealed that only anxiety and gastrointestinal dysfunction were significantly related to falls in patients with de novo PD (Table 2). To the best of our knowledge, this is the first report showing a relation between both anxiety and gastrointestinal dysfunction and falling in PD patients. However, the pathomechanisms of how anxiety or constipation might be associated with falls in patients with de novo PD remain unknown. Moreover, our results should be interpreted with caution since this study has a relatively small sample size. Accordingly, more well-designed studies with larger sample sizes need to be conducted to address this issue.

In summary, the present study showed that falling is related to PIGD/less tremors, anxiety, and gastrointestinal dysfunction in patients with de novo PD. Clinicians need to pay attention to patients at a high risk for falls in the very early stages of PD.

Conflicts of Interest

The authors have no financial conflicts of interest.

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Author Contributions

Conceptualization: Kyum-Yil Kwon. Data curation: Hyunjin Ju, Mina Lee, and Kayeong Im. Data analysis: all authors. Funding acquisition: Kyum-Yil Kwon. Investigation: all authors. Methodology: Hyunjin Ju, Mina Lee, and Kayeong Im. Project administration: Kyum-Yil Kwon. Resources: Kyum-Yil Kwon. Supervision: Kyum-Yil Kwon. Validation: Kyum-Yil Kwon. Data visualization: all authors. Writing—original draft: Kyum-Yil Kwon. Writing—review & editing: all authors.

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