



Factors associated with fall-related fractures in Parkinson's disease



Kuei-Yueh Cheng^a, Wei-Che Lin^b, Wen-Neng Chang^c, Tzu-Kong Lin^c, Nai-Wen Tsai^c, Chih-Cheng Huang^c, Hung-Chen Wang^d, Yung-Cheng Huang^e, Hsueh-Wen Chang^f, Yu-Jun Lin^{d,f}, Lian-Hui Lee^d, Ben-Chung Cheng^{f,g}, Chia-Te Kung^h, Ya-Ting Chang^c, Chih-Min Su^{f,h}, Yi-Fang Chiang^c, Yu-Jih Su^{f,g,1}, Cheng-Hsien Lu^{c,f,*,1}

^a Department of Nursing, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

^b Department of Radiology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

^c Department of Neurology, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

^d Department of Neurosurgery, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

^e Department of Nuclear Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

^f Department of Biological Science, National Sun Yat-Sen University, Kaohsiung, Taiwan

^g Department of Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

^h Department of Emergency Medicine, Chang Gung Memorial Hospital-Kaohsiung Medical Center, Chang Gung University College of Medicine, Kaohsiung, Taiwan

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ABSTRACT

Purpose: Fall-related fracture is one of the most disabling features of idiopathic Parkinson's disease (PD). A better understanding of the associated factors is needed to predict PD patients who will require treatment.

Methods: This prospective study enrolled 100 adult idiopathic PD patients. Stepwise logistic regressions were used to evaluate the relationships between clinical factors and fall-related fracture.

Results: Falls occurred in 56 PD patients, including 32 with fall-related fractures. The rate of falls in the study period was 2.2 ± 1.4 per 18 months. The percentage of osteoporosis was 34% (19/56) and 11% in PD patients with and without falls, respectively. Risk factors associated with fall-related fracture were sex, underlying knee osteoarthritis, mean Unified Parkinson's Disease Rating Scale score, mean Morse fall scale, mean Hoehn and Yahr stage, and exercise habit. By stepwise logistic regression, sex and mean Morse fall scale were independently associated with fall-related fracture. Females had an odds ratio of 3.8 compared to males and the cut-off value of the Morse fall scale for predicting fall-related fracture was 72.5 (sensitivity 72% and specificity 70%).

Discussion: Higher mean Morse fall scales (>72.5) and female sex are associated with higher risk of fall-related fractures. Preventing falls in the high-risk PD group is an important safety issue and highly relevant for their quality of life.

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1. Introduction

After Alzheimer's disease, Parkinson's disease (PD) is the second most common neuro-degenerative disorder in the world [1]. One of its most disabling features is fall injury, estimated to be as high as 70–87% in patients who survive for 20 years after disease onset

[2,3]. The risk of fall-related fracture is also five-fold higher in patients with PD than in age- and sex-matched controls [4].

Falls have multiple causes. Factors independently associated with increased risk of falling are longer PD duration, limitations in activities of daily living, more severe motor symptoms, abnormal posture, freezing of gait, frontal impairment, impaired balance, and reduced knee extensor strength [5–8]. Furthermore, osteoporosis and osteopenia are very common findings in patients with PD. Several mechanisms are implicated in the development of osteoporosis in PD, including reduced mobility, endocrine problems (i.e., vitamin D deficiency), nutritional and iatrogenic factors, female sex, disease duration and severity (Hoehn and Yahr stages III and IV),

* Corresponding author. Department of Neurology, Chang Gung Memorial Hospital, 123, Ta Pei Road, Niao Sung District, Kaohsiung, Taiwan. Tel.: ? 7 7317123x2283.

E-mail address: chlu99@ms44.url.com.tw (C.-H. Lu).

¹ Drs. Cheng-Hsien Lu and Yu-Jih Su contributed equally to this work.

Table 1
Fall scale scoring system modified from the Morse Fall Scale score [11].

Item	Score
History of falling	
Yes	25
No	0
Secondary diagnosis (more than one diagnosis)	
Yes	15
No	0
Ambulatory aid	
Furniture	30
Crutches, cane(s), walker	15
None	0
Gait/transferring	
Impaired (unsteady, difficulty rising to stand)	20
Weak (uses touch for balance)	10
Normal	0
Mental status	
Forgets limitation	15
Oriented to own ability	0

old age, and low body mass index [9]. Because PD usually occurs late in life, postural instability and unsteady gait contribute to fall-related fractures.

This hospital-based study aimed to provide accurate information on the relative frequency of fracture locations, the severity and duration of PD, the daily dose of anti-parkinsonian agents, and functional outcome. Because of possible benefits, appropriate primary or secondary prophylactic treatment should be routinely recommended, with emphasis on regular physical activity to reduce the risk of falls and on vitamin D, calcium, and bisphosphonate supplementation as treatment for the established osteoporosis. Nonetheless, a better delineation of potential prognostic factors in PD patients who should receive preventive intervention is warranted.

This study aimed to analyze the clinical features, imaging findings, scientific clinical scores, and measurements to determine potential risk factors associated with fall-related fracture in PD patients.

2. Materials and methods

2.1. Study design

This single-center prospective, case–control study was conducted at Chang Gung Memorial Hospital–Kaohsiung, a tertiary medical center and the main referral hospital serving a population of 3 million in southern Taiwan.

2.2. Inclusion and exclusion criteria

This study evaluated 120 patients with a definitive diagnosis of idiopathic PD [10] who were followed-up at the Neurology Out-Patient Clinic for more than six months after titration of their daily anti-parkinsonian agents to a steady dose in accordance with their clinical symptoms [11]. Patients were excluded if they had (1) newly diagnosed PD or were on follow-up for less than six months since their daily dose of anti-parkinsonian agents was still under adjustment; (2) other pyramidal signs, severe sensorial impairment, or ataxia; (3) impaired consciousness or higher brain dysfunction that precluded following instructions; and (4) motor weakness caused by disuse of the lower limbs, or visual problems severe enough to interfere with balance. Only 100 patients were finally included in the analysis.

The hospital's Institutional Review Committees on Human Research approved the study protocol and all of the patients or their relatives provided written informed consent.

2.3. Clinical data collection

The clinical features recorded were age at disease onset (or age at the time of the first reported symptom attributable to the disease), disease duration (time from onset until follow-up), falls, and bone fracture (confirmed radiologically). In this study, exercise habituation was defined as patients engaged in physical activity of at least 30 min of moderate-intensity physical exercise more than twice per week. Data on falls and fall-related fracture were prospectively collected from either the clinical records starting at enrollment or the patient's information during the study period.

The Morse fall scale assessed the risk of falling for hospital in-patients or those in long-term care, and included things like whether or not they are on intravenous therapy [11]. Since all of the patients were enrolled from the Neurology Out-patient Clinic, the scale was slightly modified and the item "intravenous therapy or not" was deleted (Table 1).

An experienced neurology nurse specialist (K.-Y. C) who was blinded to the patients' clinical and biochemical data was trained to measure these functional scores at the time of enrollment. An experienced radiologist (W.-C. L.) blinded to the patients' clinical data interpreted the bone fracture images at the end of the study.

The severity of PD was graded according to the scores of the Unified Parkinson's Disease Rating Scale (UPDRS) and the Hoehn and Yahr staging [12,13]. The daily dose of anti-parkinsonian agents was converted into the equivalent dose of levodopa [14]. In fluctuating patients, the UPDRS and Hoehn and Yahr scales were administered in off situation (8–10 h after patients stopped their usual anti-parkinsonian treatment) to evaluate the possible influence of disease severity. All of the patients underwent cranial magnetic resonance imaging (MRI) scan, ^{99m}Tc-TRODAT-1 SPECT/CT and Region of Interest Analysis, and Bone densitometry study according to previously published methods [15,16].

2.3.1. Neuro-imaging studies

Cranial MRI was performed on a 3.0 Tesla MRI scanner (GE Signa Excite HD, GE Healthcare, Milwaukee, WI, USA) with routine protocol, including T1- and T2-weighted imaging, diffusion weight imaging, and MR angiogram, to exclude any organic intra-cranial or vascular lesions. Aside from the different degrees of brain atrophy, there was no active intra-cranial lesion found in the subjects.

2.3.2. ^{99m}Tc-TRODAT-1 SPECT/CT and region of interest analysis

The participants were intravenously injected with a single bolus dose of ^{99m}Tc-TRODAT-1 ([2]([2-[[[3-(4-chlorophenyl)-8-methyl-8-azabicyclo [1-3]-oct-2-yl]-methyl]([2-mercaptoethyl)amino]ethyl]amino]ethanethiolato(3-)-N2,N2',S2,S2] oxo-[1R-exo-exo]))-^{99m}Tc-technetium). Four hours after the injection, images were acquired using a dual-head SPECT/CT equipped with low-energy high-resolution collimators (Symbia T, Siemens Medical Solutions, Erlangen, Germany). With the help of anatomic co-registration CT images, the regions of interest (ROIs) of the bilateral striata (including its sub-regions of caudate and putamen) were defined on composite images of the six highest striatum activity slices. The occipital cortex was drawn in the same way and served as background area. The ROIs' radio-activities were then counted.

Striatal dopamine transporter uptake ratios (Trodate ratio) were calculated as the quotient of the mean counts per pixel in the each striatum divided by the mean counts per pixel in the occipital cortex. All images were reviewed by an experienced nuclear physician who was blinded to the patients' data.

2.3.3. Bone densitometry study

Osteoporosis was diagnosed using bone mineral density (BMD) in the spine and femoral neck as measured by dual energy x-ray absorptiometry (Hologic Delphi A, Florida, United States). Osteoporosis was defined as spinal BMD >2.5 SD below the average value in a young person, i.e. a T-score ≤ -2.5 SD [14].

The follow-up period in each patient was a minimum of 18-months (everybody was followed up for between 18 months and two years) and was terminated either by death or by the end of the study. Two separate statistical analyses were performed. First, the risk factors for fall-related fracture were determined after a minimum of 18 months follow-up. The effects of individual variables, including sex, underlying diseases, levodopa equivalent dose, and mean functional score on fracture were analyzed by univariate logistic regression. Stepwise logistic regression was then used to evaluate the relationships between baseline clinical factors and the presence of fall-related fracture, with adjustments made for other potential confounding factors. The receiver operating characteristic (ROC) curves were generated for significant predictor variables of fall-related fractures. All statistical analyses were conducted using the SAS software package, version 9.1 (2002, SAS Statistical Institute, Cary, North Carolina).

3. Results

The 100 patients with idiopathic PD included 49 males (age range, 32–85 years; mean age, 68.9 years) and 51 females (age range, 49–82 years; mean age, 68.3 years) (Table 2). Except for one who died of aspiration pneumonia, the remaining 99 returned to the Neurology Out-patient Clinic every three months and completed the minimum 18-month follow-up. The rate of falls in the study period was 2.2 ± 1.4 per 18 months. Thirty-two patients had fall-related fractures.

Of the 100 patients, 56 experienced falling, while 44 did not. The percentage of osteoporosis among PD patients with and without falls were 34% (19/56) and 11%, respectively ($p = 0.009$). In terms of frequency, 25 had one, 12 had two, and 19 had more than three falls

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