

Can Recurrent Falls be Predicted in Parkinson's Disease?

Parkinson Hastalığında Tekrarlayan Düşmeler Önceden Tahmin Edilebilir mi?

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Objective: To investigate the prevalence of recurrent falls in patients who are being followed up in Movement Disorder Outpatient Clinic, demographic and clinical characteristics of patients with recurrent falls, and relative accuracy of balance assessment for prediction of falls prospectively within 1 year.

Materials and Methods: The patients who were admitted to Movement Disorder Outpatient Clinic due to idiopathic Parkinson's disease were consecutively included in the study. Demographic data and disease characteristics of the patients were recorded. Berg Balance Scale, Functional Reach Test, Five Times Sit-To-Stand Test and Timed Up and Go Test were used for assessment of balance. Subsequently, the patients and/or their relatives were asked to fill out fall diaries for 1 year.

Results: At the end of one year, at least one fall was detected in 47 (46.1%) and recurrent falls were detected in 35 (34.3%) out of 102 patients. The patients who had recurrent falls had a longer duration of disease, were using higher doses of levodopa and had higher disease severity according to Hoehn & Yahr staging and Unified Parkinson's Disease Rating Scale. These patients obtained lower scores in Functional Reach Test, Five Times Sit-To-Stand Test, Timed Up and Go Test and Berg Balance Scale. According to Receiver Operating Characteristic analysis, Functional Reach Test had maximum specificity and sensitivity for prediction of falls followed by Berg Balance Scale, Timed Up and Go Test and Five Times Sit-To-Stand Test.

Conclusion: Recurrent falls have been found in approximately one-third of the patients with Parkinson's disease. Disease progression had a negative effect on falls. While the Functional Reach Test is the most appropriate test for prediction of fall risk, Berg Balance Scale, Timed Up and Go Test and Five Times Sit-To-Stand Test were also shown to be useful. Prediction of fall risk may positively influence quality of life through preventing complications.

Key Words: *Parkinson's Disease, Recurrent Falls, Balance Assessments*

Amaç: Hareket Bozuklukları Polikliniğinde takip edilen hastaların tekrarlayan düşme sıklığını, tekrarlayan düşmesi olan hastaların demografik ve klinik özelliklerini, son olarak da denge değerlendirmesinin prospektif olarak 1 yıllık süre içerisinde düşme tahmini için göreceli doğruluğunu araştırmaktır.

Gereç ve Yöntem: Hareket Bozuklukları Polikliniğine ardışık olarak başvuran idiyopatik Parkinson hastalığı olan hastalar çalışmaya dahil edildi. Hastaların demografik verileri ve hastalık özellikleri kaydedildi. Dengenin değerlendirilmesi için Berg Denge Ölçeği, Fonksiyonel Öne Uzanma Testi, 5 Kere Otur ve Kalk Testi ile Süreli Kalk ve Yürü Testi kullanıldı. Takiben hastalardan ve/veya yakınlarından prospektif olarak 1 yıl süreyle düşme günlüğü tutulması istendi.

Bulgular: Bir yıl sonra 102 hastanın 47'sinde (%46,1) en az bir kere, 35'inde (%34,3) ise tekrarlayan düşme tespit edildi. Tekrarlayan düşmesi olanlar daha uzun hastalık süresi ve levodopa dozları daha fazla olan, Hoehn & Yahr evrelemesi ve Birleşik Parkinson Hastalığı Değerlendirme Ölçeğine göre hastalık şiddeti artmış hastalardı. Aynı zamanda bu hastalar Fonksiyonel Uzanma Testinde, Süreli Kalk ve Yürü Testinde ve 5 Kere Otur ve Kalk Testinde daha kötü skorlar elde etti ve Berg Denge Ölçeğinde daha düşük puanlar elde ettiler. Alıcı İşletim Karakteristliği analizi sonuçlarına göre Fonksiyonel Uzanma Testi, düşmeleri öngören en yüksek sensitivite ve spesivite kombinasyonunu sağladı. Bunu sırasıyla Berg Denge Ölçeği, Süreli Kalk ve Yürü testi ve 5 Kere Otur ve Kalk testi izledi.

Sonuç: Parkinson hastalığı olan hastaların yaklaşık üçte birinde tekrarlayan düşmelere rastlanmaktadır. Hastalığın ilerlemesinin düşmeler üzerine olumsuz etkisi bulunmaktadır. Düşme riskini öngörmeye en uygun test Fonksiyonel Uzanma Testi olmakla birlikte, Berg Denge Ölçeği, Süreli Kalk ve Yürü Testi ve 5 Kere Otur ve Kalk Testinin de düşme riskini tahmin etmede faydalı olabileceği gösterilmiştir. Düşme riskinin öngörülmesi, komplikasyonların önlenmesi yoluyla yaşam kalitesini olumlu yönde etkileyebilir.

Anahtar Sözcükler: *Parkinson Hastalığı, Tekrarlayan Düşmeler, Denge Değerlendirmeleri*

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Parkinson's disease (PD) is a chronic, progressive neurodegenerative disease characterized by tremor, bradykinesia, rigidity, postural instability, and gait disorders. Posture and gait disorders, mainly postural instability, motor symptoms like freezing of gait are the main causes of recurrent falls in patients with PD (1). While prevalence of falls at least once varies between 35% and 90%, the prevalence of recurrent falls during the same time period is between 18% and 68% (2). Falls are among the main causes of disability and negatively affect both psychological and physical condition of the patients. Falls-related fractures and fracture-related complications are the main physical problems (3). Fear of falling poor quality of life and the patient's not going out unless required or in other words, reduced socializing are among the psychological problems (4,5). Both physical and psychological problems are related with significant economic costs (6). Timely detection of the patients susceptible to falls would enable early detection of the problems and application of the required interventions.

While fall prevalence is high among patients with PD, revealing accurate and useful methods for prediction of the patients susceptible to falls has great importance for the clinicians. Although history of two or more falls within the recent one year is the best predictor of falls in PD it loses its importance in the patients who did not have the history of falls (7).

While risk factors for falls include advanced age, cognitive disorders, hearing and visual disorders, osteoarthritis of the knee, medications (sedatives, hypnotics, neuroleptics, anti-psychotics and anti-depressants, non-steroidal anti-inflammatory drugs, anti-hypertensives), presence of any daily life difficulties, living conditions in general population, disease-specific symptoms are added to them in PD (8-11). Patients with PD who are at risk of falling may have problems with various areas of movement control, such as sensory integration, functioning with a narrow base of support, controlling their center-

of-mass movement within their base of support, and coordination of anticipatory postural control tasks (4,12) as well as comorbid conditions (eg, peripheral neuropathy) and medication side effects (eg, postural hypotension and dyskinesia) (13). Hence, standardized balance assessment tools have importance for detection of the patients susceptible to falls in order to achieve assessment goals. Benefits of different balance tests have been investigated in PD. The Tinetti Balance Scale, Berge Balance Scale, BESTest, Mini-BESTest, Dynamic Gait Index and Functional Gait Assessment require much time and thereby are not included in routine assessment tests in an outpatient setting (14).

It is required to reveal the effectiveness of easily applicable tests which can evaluate fall risk shortly in an outpatient setting. The main purpose of this study was to investigate the prevalence of recurrent falls in patients with PD who are being followed up in the Movement Disorder Outpatient Clinic, to reveal the demographic and clinical characteristics of patients with recurrent falls, and to assess the relative accuracy of balance assessment for prediction of falls prospectively within a year.

Material and Method

Participants

The patients who were 40 years and above, admitted to the Movement Disorders Outpatient Clinic of Physical Medicine and Rehabilitation Clinic, University of Health Sciences, Diskapi Yildirim Beyazit Training and Research Hospital between January and July 2014, whose diagnosis of PD was verified according to the United Kingdom Parkinson's Disease Association Brain Bank criteria. Mini-Mental State Examination (MMSE) score ≥ 20 (15,16) and Hoehn & Yahr (H&Y) stage ≤ 3 were consecutively included in the study. The patients who had significant visual and/or

hearing problems, chronic diseases which influence functional status, atypical PD, deep brain stimulation, who were using medications for psychiatric problems and who could not be mobilized independently were excluded from the study.

The study protocol was approved by the local ethics committee (18.02.2013, 07/42) and the study was conducted in accordance with the Helsinki Declaration. All patients were informed about the aim of the study and informed consent was obtained from all participants prior to the study.

Assessment of patients

The demographic and disease characteristics of the patients who agreed for participation have been recorded. Disease severity was evaluated with the H&Y staging (15), disease symptoms were evaluated with the Unified Parkinson's Disease Rating Scale (UPDRS) (16). PD has five stages according to the H&Y staging: stage 1, only unilateral involvement, usually with minimal or no functional disability; stage 2, bilateral or midline involvement without impairment of balance; stage 3, bilateral disease, mild to moderate disability with impaired postural reflexes, physically independent; stage 4, severely disabling disease, still able to walk or stand unassisted; and stage 5, confinement to bed or wheelchair unless aided. The UPDRS is composed of four sections including mental status, behavioral and psychological status (4 items, 0-16 points), activities of daily living (13 items, 0-52 points), motor examination (14 items, 0-56 points) and treatment complications (11 items). Higher scores indicate worse disability. We used the overall scores of the second and the third sections in the present study. Postural instability and gait disorders scores (overall score of items 27,28,29,30) obtained from the third section of UPDRS were also calculated.

Minimum 30 minutes walking and exercise in 3 days of the week was defined as "regular" walking and exercise (17).

Assessment of balance

Balance assessment was done by an educated physiatrist one hour after taking medication in "on" period.

Previously the Berg Balance Scale, Functional Reach Test, Five Times Sit-To-Stand Test and Timed Up and Go Test have been shown to be effective in PD for balance assessment (14). The latter three tests were applied three times and mean values were recorded in the current study.

The Berg Balance Scale is designed for assessment of balance and fall risk in the elderly. It is composed of 14 items toward direct observation of the individual's performance. Each item is scored between 0 (inability to perform the activity) and 4 (performing the activity independently) according to the performance for meeting the time and distance conditions of the test. Overall score varies between 0-56. Higher scores indicate better balance. The test is completed within 15-20 minutes.

The Functional Reach Test is used for assessment of antero-posterior stability. A patient is asked to take the dominant arm to 90 degrees flexion and keep it at shoulder level while standing with a constant support insole. Thereafter the patient is asked to reach forward as possible the arms so as to be parallel to floor. The distance between two positions is measured as cm through a measure placed on the wall.

The Timed Up and Go Test evaluates mobility, balance and walking skills. A standard chair which enables the patient's knees to stay at 90 degrees flexion and put his/her back on is used. The patient is asked to stand and walk 3 meters with standard steps, return back to the chair and sit. The time between standing and sitting is measured with a chronometer as seconds.

Five Times Sit-To-Stand Test is a measure of functional lower extremity power. A standard chair which enables the patient's knees to stay at 90 degrees flexion and put his/her back on is used.

The patient is asked to rapidly stand and sit the arms so as to be cross at the shoulders. The time between standing and put the back on is measured with a chronometer as seconds.

Assessment of falls

All patients and/or their relatives were asked to diarize falls during one year prospectively after clinical assessment of PD patients had been completed. Fall was defined as "an unexpected event which develops on a flat or mildly irregular surface as the result of carelessness without being due to an internal or external event" (18). Presence of falls and number of falls if present were recorded in three months follow ups. Two or more falls during one year was defined as "recurrent falls" (19).

Statistical Methods

Descriptive statistics are given as mean (standard deviation) and number (percent) for nominal variables. After the patients were divided into two groups according to presence of recurrent falls, the inter-group comparisons were made by the Chi-square test, Fisher's exact test, t-test or Mann-Whitney U test. Receiver operating characteristic (ROC) curves were formed for each balance assessment for analysis of the relationship between recurrent falls and balance tests. Area under the curve (AUC), cut-off point, sensitivity and specificity values, Youden index, positive and negative odds ratio (OR) were determined for each test (20). Higher AUC and positive LR and lower negative LR values indicate a stronger relationship between fall risk and balance tests. Statistical tests were done using MedCalc for Windows 17.0 version (MedCalc Software, Ostend, Belgium). A *p* level of <0.05 was taken as statistically significant.

Results

A total of 128 patients who were admitted to the Movement Disorders Outpatient Clinic during one year were evaluated. After 26 patients had been excluded (16

due to not coming for regular controls, 4 due to having <20 MMSE score, 6 due to history of DBS), 102 patients completed one year assessment and at least one fall was detected in 47 (46.1%) and recurrent falls were detected in 35 (34.3%). The number of falls varied between 2-24 and the mean number of falls was 7.2 (SD 6.8). The demographic characteristics and disease characteristics of the patients with or without recurrent falls are given and compared in Table 1.

Comparison of the patients with or without recurrent falls

When the patients with or without recurrent falls were compared, the ones with recurrent falls were detected to be older, have lower body mass index, diabetes mellitus and atherosclerotic heart disease prevalence were higher in these patients. These patients had poorer MMSE scores, lower ratio of regular walking and exercise. They also had longer duration of disease, using higher doses of levodopa and levodopa-equivalent doses, more severe disease according to H&Y staging and UPDRS. Although fluctuation was more frequent among the patients with recurrent falls, no difference was detected between the groups with regard to dyskinesia.

The patients with recurrent falls obtained poorer scores in the Functional Reach Test, Timed Up and Go Test and Five Times Sit-To-Stand Test and lower scores in the Berg Balance Scale (Table 1).

Receiver Operating Characteristic Analyses

Table 2 and Figure 1 show AUC analysis results for fall-related variables. AUC varied between 0,76 and 0,91 for clinical tests. The Functional Reach Test provided maximum sensitivity (74%) and specificity (90%) combination which predicts falls followed by the Berg Balance Scale (69% and 94%), Timed Up and Go Test (83% and 69%) and Five Times Sit-To-Stand Test (49% and 94%)

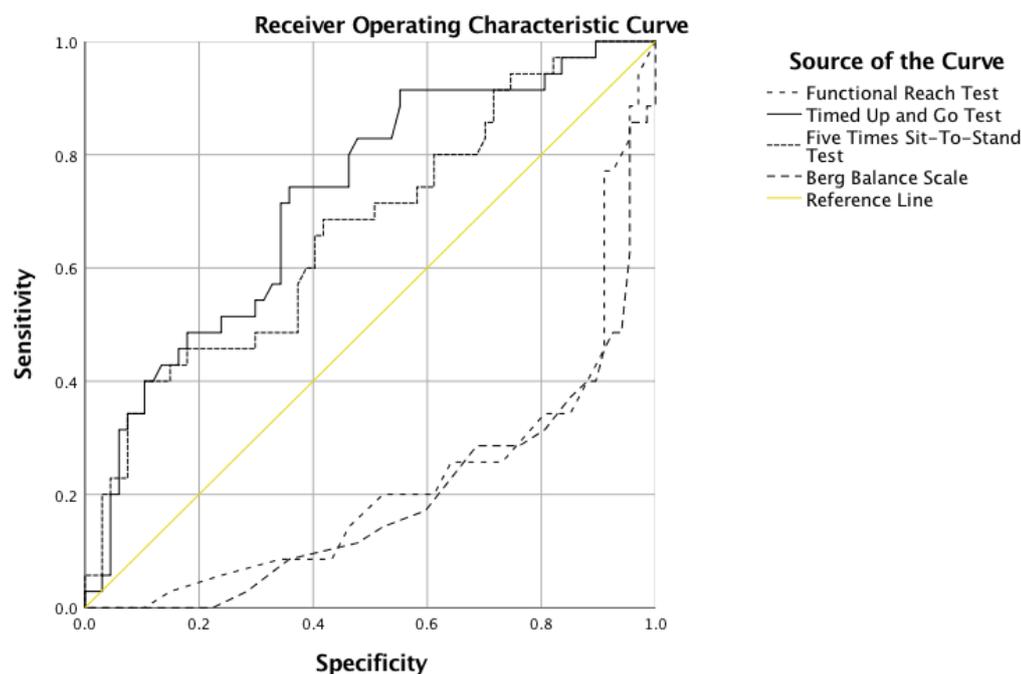


Figure1. Receiver operation curve characteristics of balance tests: Comparison of the patients with respect to overall accuracy of recurrent fall definition.

Table 1. Patient characteristics

Variables	All patients (n = 102)	Patients with recurrent falls (n = 35)	Patients without recurrent falls (n = 67)	Pvalue
Age (years) [mean (SD)]	67.1 (10.2)	72.4 (7.7)	64.4 (10.3)	<0.001*
Female (n, %)	58 (56.9)	20 (57.1)	38 (56.7)	0.967**
BMI [mean (SD)]	29.3 (4.9)	27.9 (4.9)	30.1 (4.8)	0.036***
Co-morbid conditions (n, %)				
DM	19 (18.6)	11 (31.4)	8 (11.9)	0.016**
ASHD	17 (16.7)	10 (28.6)	7 (10.4)	0.020**
Hypertension	40 (39.2)	15 (42.9)	25 (37.3)	0.586**
Hyperlipidemia	4 (3.9)	2 (5.7)	2 (3.0)	0.605**
Goitre	5 (4.9)	2 (5.7)	3 (4.5)	1.000****
Asthma	4 (3.9)	2 (5.7)	2 (3.0)	0.605**
Disease duration (months) [mean (SD)]	63.2 (53.1)	84.8 (59.8)	51.9 (45.7)	0.002*
Levodopa dose (mg) [mean (SD)]	364.0 (256.0)	481.4 (232.9)	302.6 (247.4)	<0.001*
Levodopa equivalent dose (mg) [mean (SD)]	588.3 (241.6)	712.8 (228.9)	536.3 (232.9)	<0.001*
MMSE score [mean (SD)]	25.1 (3.2)	23.2 (2.6)	26.1 (3.0)	<0.001*
Hoehn & Yahr [mean (SD)]	2.0 (0.7)	2.6 (0.5)	1.8 (0.6)	<0.001*
UPDRS II score [mean (SD)]	10.3 (6.3)	14.5 (7.0)	8.0 (4.6)	<0.001*
UPDRS III score [mean (SD)]	15.7 (8.5)	21.1 (8.5)	12.8 (7.1)	<0.001***
PIGD score [mean (SD)]	2.7 (2.4)	4.5 (2.6)	1.8 (1.6)	<0.001*
Dyskinesia (n, %)	16 (15.7)	8 (22.9)	8 (11.9)	0.150**
Motor fluctuation (n, %)	22 (21.6)	13 (37.1)	9 (13.4)	0.006**
Regular walking (n, %)	49 (48.0)	12 (34.3)	37 (55.2)	0.044**
Regular exercise (n, %)	25 (24.5)	5 (14.3)	20 (29.9)	0.083**
Regular walking (minute/day) [mean (SD)]	19.0 (23.1)	11.1 (16.4)	23.1 (25.1)	0.016*
Regular exercise (minute/day) [mean (SD)]	5.2 (10.0)	2.7 (7.1)	6.6 (11.0)	0.070*
Functional reach test (cm) [mean (SD)]	19.1 (7.3)	13.0 (5.9)	22.3 (5.7)	<0.001*
Timed Up and Go Test (second) [mean (SD)]	14.5 (7.2)	20.1 (8.9)	11.6 (3.8)	<0.001*
Five Times Sit-To-Stand Test (second) [mean (SD)]	19.7 (8.0)	25.1 (9.8)	16.9 (4.9)	<0.001*
Berg Balance Scale [mean (SD)]	45.7 (8.1)	37.9 (7.9)	49.7 (4.6)	<0.001*

* Mann-Whitney U test, ** Chi-square test, *** Independent samples t-test, **** Fisher's exact test

Abbreviations: BMI, body mass index; DM, Diabetes mellitus; ASHD, atherosclerotic heart disease; MMSE, Mini-Mental State Examination; UPDRS, Unified Parkinson's Disease Rating Scale; PIGD, postural instability and gait disorders

Table 2. Receiver operation characteristics (ROC) curves

Variables	AUC	Cut-off point	Sensitivity	Specificity	Youden Index	OR+	OR-
Functional Reach Test	0.87	≤14	0.74	0.90	0.64	7.11	0.29
Timed Up and Go Test	0.83	>12.56	0.83	0.69	0.52	2.64	0.25
Five Times Sit-To-Stand Test	0.76	>24.68	0.49	0.94	0.43	8.14	0.55
Berg Balance Scale	0.91	≤41	0.69	0.94	0.63	11.49	0.33

Abbreviations: AUC: Area under curve, OR: Odds ratio

With regard to the demographic and disease characteristics, sensitivity and specificity were 86% and 52% for age (AUC 0.73, cut-off point >65 year), 69% and 72% for disease duration (AUC 0.68, cut-off point >48 month), 54% and 81% for levodopa dose (AUC 0.71, cut-off point >450 mg), 58% and 80% for levodopa equivalent dose (AUC 0.73, cut-off point >661 mg), 83% and 76% for H&Y staging (AUC 0.84, cut-off point >2), 57% and 88% for UPDRS part 2 (AUC 0.78, cut-off point >13), 80% and 63% for UPDRS part 3 (AUC 0.77, cut-off point >15) and finally 80% and 73% for overall score of postural instability and gait disorders score (AUC 0.81, cut-off point >2).

Discussion

Different study designs are available in literature about fall and/or recurrent fall risk in PD. Duration of follow up varies between 3 months and 1 year. Another difference is retrospective or prospective design of the studies (2).

The present study aimed at investigating fall prevalence in PD patients and to reveal the differences in demographic and disease characteristics of the patients with recurrent falls and how can recurrent falls be predicted. We found a prevalence of at least once fall as 46.1% and at least two falls (recurrent falls) as 34.3% in PD patients followed up for a year. The prevalence of at least one fall was detected to be lower than detected by Dibble et al. (55%, (21)) and Landers et al. (51%, (22)) in retrospective studies, Wood et al. (68%, (18)) and Cole et al. (65%, (23)) in prospective studies, similar with the prospective study of Latt et al. (45%, (24)), higher than detected by Mak et al. (34%, (25)) and Duncan et al. (32%, (1)). The prevalence of recurrent falls was almost similar with that found by Almeida et al. (30%, (26)) in their retrospective study and lower than found by Cole et al. (43%, (23)) in their prospective study. These differences might arise from the study sample characteristics like disease severity.

A history of two or more falls within a year has been reported to be the most important predictor of future falls in patients with PD (7). However, this condition leads to an important disadvantage for assessment of fall risk in the patients who do not have the history of falls. Early detection of the patients who have high fall risk by the clinician and taking measures for prevention would have positive effects on the patients and the relatives. So, revealing fall risk through one or several simple tests has importance in the settings like outpatient clinic where a limited time can be spent for a patient. The Berg Balance Scale is known to be a useful structured tool for assessment of postural instability and fall risk not only in PD patients but also in all diseases which could influence balance in elderly (27). However, it is difficult to apply it to all patients as it takes 15-20 minutes to complete. So there is a clear need for easily applicable short tests to detect fall risk as accurate as the Berg Balance Scale. The present study has revealed that the Functional Reach Test ≤ 14 cm, Berg Balance Scale ≤ 41 , Timed Up and Go Test >12.6 seconds and 5 times Sit-to-Stand Test >24.7 seconds indicate higher fall risk.

Different studies have indicated that disease duration, levodopa equivalent dose, H&Y stage and UPDRS motor score are among the risk factors for falls (18,26,28). Similarly, in our study, the patients who had history of fall had higher levodopa doses, longer disease duration, higher disease stage and UPDRS scores. Although this study does not aim at investigating fall-related risk factors, PD patients who have recurrent falls usually have advanced disease stage. The higher disease stage and UPDRS score in addition to higher levodopa dose and higher disease duration are the indicators of advanced disease stage (29). More than 2 overall score of postural instability and walking difficulty have been detected to be important for fall risk. This condition suggests that falls may increase together with emergence of postural changes. Detecting that recurrent falls may increase in advanced stages of the disease does not mean that falls are not seen in

the early stages of PD. Because PD's emerging in older ages, coexisting with Diabetes mellitus which may lead to neuropathy or athero-sclerotic vascular diseases causing cardio-vascular imbalance may also be the risk factors for falls in patients with PD.

Although dyskinesia could be related to falls by leading to postural problems or increased postural swinging when trunk and feet are influenced (26,28,30,31,32), no difference was detected between the patients with or without recurrent falls with regard to dyskinesia prevalence in this study. On the contrary to this condition which may be related to sample characteristics, motor fluctuation a complication of PD was shown to be more frequent, consistent with the previous studies. Motor fluctuations have been reported to lead to reduced motor performance through causing dysfunction and walking difficulty and thereby may be associated with postural instability and fall risk in patients with PD (18,31,32).

There were several limitations of the present study. Because our study did not include a healthy control group, the prevalence of recurrent falls and fall characteristics were not compared in the two groups. Second, regular walking and exercise were roughly estimated in this study. The Physical Activity Scale could be used to assess physical activities of PD patients. And lastly, our study was a single-centered, so study results cannot be generalized to the Turkish PD population.

Conclusion

A history of recurrent falls has been found in approximately one-third of PD patients. Advanced disease has a negative effect on falls. While the Functional Reach Test is the most proper test for prediction of fall risk, the Berg Balance Scale, Stand-to-Walk and 5 times Sit-to-Stand test have also been shown to be useful. Prediction of fall risk by clinicians could improve quality of life of PD patients by preventing fall-related complications.

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