



## Diagnostic accuracy of Timed Up and Go test in patients with Parkinson's disease who had freezing of gait

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### Abstract

**Background:** Freezing of gait (FOG) is a disabling clinical phenomenon in patients with Parkinson's disease (PD), which is characterised by short episodes of inability to step and affect about 38.2 % of these patients. Abrupt FOG may disturb the balance and, thus, it is considered as a common cause of falls in PD. This study was designed to evaluate the fall diagnostic accuracy of the Timed Up and Go Test (TUG), a reliable and valid clinical test to assess mobility and risk of falls, in patients with PD who had FOG.

**Methods:** In this cross-sectional study, 80 subjects with a diagnosis of idiopathic PD who had FOG by mean  $\pm$  SD age of 63.63 $\pm$ 9.76 years and mean  $\pm$  SD disease duration of 7.82 $\pm$ 5.76 years were enrolled by simple non-probability sampling method. They were divided into two faller and non-faller groups based on the history of fall during the past six months. Sensitivity, specificity, negative and positive likelihood ratios, and receiver operator characteristic curve was calculated for TUG.

**Results:** The TUG score indicated significant differences between faller PD patients who had FOG and non-faller PD patients who had FOG ( $p=0.003$ ). The best cut-off point for discriminating faller and non-faller PD patients who had FOG was 11.85 seconds (sensitivity= 68.97% and specificity= 86%).

**Conclusion:** TUG demonstrated moderate sensitivity and specificity to fall status in patients with PD who had FOG, suggesting its use in conjunction with other tests for screening those who may need intervention for decreasing falls.

**Keywords:** Movement disorders, Parkinson's disease, Accidental falls, Balance, Sensitivity and specificity

**Conflicts of Interest:** The authors have no conflict of interest in this study.

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### Introduction

Parkinson's disease (PD) is a chronic progressive neurodegenerative disease characterized by a combination of motor and non-motor symptoms and signs [1]. Gait and balance impairments are disabling consequences of PD, with different contributing factors including the freezing of gait (FOG) [2]. This phenomenon is defined as a brief and unpredictable episode of inability to do effective forward stepping [3] with a prevalence rate of about 38.2% [4].

FOG occurs usually during gait initiation, turning while doing a simultaneous activity (i.e. dual-tasks), or crossing narrow spaces [5]. Sudden FOG may disturb the balance and, thus, it is considered as a common cause of falls in PD [6]. Fall, especially frequent falls, is the main cause of disability in PD [7], leading to decreased balance confidence, enhanced fear of future falls and finally restricted physical activities, as well as reduced social participation and quality

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#### ↑What is "already known" in this topic:

Although the diagnostic accuracy of TUG, a reliable and valid clinical test to assess mobility and risk of falls, has been investigated in different populations (e.g. stroke survivors, subjects with multiple sclerosis, etc.), its diagnostic accuracy has not yet been investigated in patients with PD who had FOG.

#### →What this article adds:

The results of this study showed the moderate sensitivity and specificity of TUG to fall status in these patients, suggesting its use in conjunction with other tests for screening falls in patients with PD who had FOG.

of life in these patients [7]. Approximately 65% and 50% of patients with PD experience at least one fall per year and frequent falls, respectively [8]. The severity of the FOG and the number of falls increases with increasing PD severity [3, 9].

It has been suggested that 30% to 40% of falls can be prevented if subjects at risk for falls are identified and given proper interventions [10]. Considering the high prevalence rate of FOG and falls in patients with PD and close relation between FOG and falls, identifying PD patients with FOG (PD+FOG) who had at risk of falls is important in order to refer them for receiving appropriate fall-related interventions and preventing future falls and its above-mentioned destructive consequences. In order to do this, clinical tests that provide accurate screening are required. Although various balance tests are currently being used in clinical settings, the Berg Balance Scale (BBS) is considered as a reference standard for balance evaluation. However, it has been shown that BBS has a ceiling effect in patients with PD and other populations [11-13]. Therefore, a patient may obtain perfect score on the BBS while still has balance impairments that should be addressed [14]. Timed Up and Go test (TUG) is one of the most common measures used to evaluate functional mobility and dynamic balance in patients with PD, which has been recently listed as "recommended measure" for use in these patients by the Movement Disorders Society (MDS)-commissioned task force [15]. The British Society of Gerontology Guidelines/American Geriatrics Society also recommended the TUG as a screening test for falls risk [16]. TUG needs both static and dynamic balance and is highly correlated with falls, gait speed, and functional mobility in older adults [17]. Higher TUG score in patients with PD is associated with reduced mobility and may more precisely predict falls compared with the total score of the UPDRS [18]. Administration of TUG is easy and not time-consuming and high validity and reliability have been reported for it in patients with PD [19]. Therefore, the aim of this study was to investigate the diagnostic accuracy of TUG for fall risk in patients with PD who had FOG.

### Methods

#### Participants

In this cross-sectional study, 80 patients with idiopathic PD who had FOG were enrolled using the simple non-probability method from Movement Disorders Clinics of the Iran University of Medical Sciences. The following inclusion criteria were considered: 1. Diagnosis of idiopathic PD by a neurologist, 2. Being in Hoehn & Yahr (H & Y) stage of I-III [20], 3. presence of FOG (i.e. score  $\geq 1$  on the item 3 of FOG questionnaire) [21], 4. Acceptable level of cognitive function (i.e. score  $\geq 24$  on the Montreal Cognitive Assessment (MoCA)) [22], 5. Ability to walk independently for at least 10 meters, and 6. Not having other neurologic disorders than PD (e.g. stroke), orthopedic disorders or any other comorbidity likely to affect balance and mobility. Before the enrolment of participants, approval for the study protocol was given from the Ethics Committee of Iran University of Medical Sciences (IR.IUMS.REC1396.9511355009). All participants signed

a written informed consent form before study commencement.

#### Procedure

The following information was recorded during the individual interview section of the examination: age, gender, height, weight, duration of PD diagnosis, the severity of motor impairments based on the motor subsection of Unified Parkinson's Disease Rating Scale (UPDRS-III), and fall history. An accident that leads to unintentionally come to rest on the ground or other low surfaces was considered as a fall in the present study [23]. Participants were classified as fallers if their self-reported falls were  $\geq 2$  during the previous 6 months [14].

Following the individual interview, participants were assessed by the TUG, in which the time taken to rise from a chair, walk forward for three meters, turn around, walk back, and sit down on the chair is recorded by a stopwatch. During the test, participants were allowed to use assistive devices, which they would normally use [24]. The participants performed one practice trial and then three trials of the TUG were conducted and their average value was considered as the final TUG score. High test-retest reliability and inter-rater reliability of the TUG has also been reported in patients with PD [25]. All assessments were performed in on-medication state of patients with PD (i.e. 1-2 h after taking the antiparkinsonian medications) by an expert occupational therapist with enough training to conduct the tests.

#### Statistical Analysis

Statistical analysis was done using SPSS for Windows (version 13) and Med Calc Statistical software (version 13.0.6). The normal distribution of data was confirmed by the results of the Kolmogorov-Smirnov test. Descriptive statistics were determined for general and clinical characteristics of the participants and comparison of faller and non-faller groups regarding these variables was performed using independent sample t-tests for quantitative variables and Chi-square test for qualitative variables. We used standard definitions of sensitivity (i.e.  $\frac{\text{true positive}}{(\text{true positive} + \text{false negative})} \times 100$ ) and specificity ( $\frac{\text{true negative}}{(\text{true negative} + \text{false positive})} \times 100$ ) to determine how accurately patients with PD+FOG were classified by TUG as fallers and non-fallers. Negative predictive value (NPV), and positive predictive value (PPV) are true negative and true positive results of a test, which calculated by the following formulae, respectively: true negative/ (true negative + false negative), and true positive/ (true positive + false positive). The positive likelihood ratio (PLR) and negative likelihood ratio (NLR) were calculated as sensitivity/ (1-specificity) and (1-Sensitivity)/ Specificity, respectively.

#### Results

Eighty patients with PD+FOG (28 females and 52 males) by mean  $\pm$  SD age of 63.63 $\pm$ 9.76 years, mean  $\pm$  SD duration of PD diagnosis of 7.82 $\pm$ 5.76 years, and mean  $\pm$  SD UPDRS-III score of 22.74 $\pm$ 10.15 participated in the current

study. According to the fall history during the previous 6 months, 29 participants (36.30%, 10 females and 19 males) were classified as fallers, while 51 participants (63.80 %, 18 females and 33males) were classified as non-fallers. The general and clinical characteristics of the participants are presented in Table 1. A comparison of faller and non-faller groups revealed that there was not a significant difference between groups, with the exception of UPDRS-III score ( $p=0.000$ ) (Table 1). The results also indicated a significant correlation between the TUG score and UPDRS-III score ( $r=0.49$ ,  $p=0.001$ ).

The mean  $\pm$  SD of the TUG score was  $19.77\pm 16.90$  and

$9.67\pm 3.19$  seconds in the faller and non-faller groups (Table 2), respectively, which was significantly higher in the faller group ( $p=0.003$ ). The best cut-off score of TUG for discriminating faller and non-faller PD+FOG patients was 11.85 seconds (sensitivity=68.97, specificity=88.24, AUC=79%, 95%CI=67-88%,  $p<0.0001$ , PPV=39.4, NPV=96.2, NLR= 0.35, and PLR=5.86) (Table 3, Figure. 1). With a TUG score equal to or greater than 11.85 seconds, 39.4 % of PD+FOG patients were correctly classified in the faller group.

## Discussion

Recently, different clinical tests including TUG have

Table 1. General and clinical characteristics of the participants

Variable	Non-faller group (n= 51)	Faller group (n= 29)	t	df	p
Age (year)	62.29 $\pm$ 11.14	65.97 $\pm$ 6.16	1.64	78	0.11
Height (cm)	166.71 $\pm$ 9.38	166.00 $\pm$ 7.91	0.34	78	0.73
Weight (kg)	72.50 $\pm$ 11.71	70.26 $\pm$ 10.73	0.85	78	0.40
BMI (kg/m <sup>2</sup> )	26.19 $\pm$ 4.05	25.46 $\pm$ 4.13	0.77	78	0.44
PD duration (year)	7.48 $\pm$ 6.14	8.41 $\pm$ 5.07	0.70	78	0.49
UPDRS-III (score)	18.50 $\pm$ 8.57	29.00 $\pm$ 9.14	4.01	78	0.000

Abbreviations: BMI, Body Mass Index; UPDRS-III, the motor subsection of Unified Parkinson's disease rating scale

Table 2. TUG score in patients with PD who had FOG with regards to the history of fall

TUG score	Non-faller	Faller
5-5.99	4	0
6-6.99	5	0
7-7.99	7	1
8-8.99	6	5
9-9.99	9	2
10-10.99	8	1
11-11.99	6	1
12-12.99	1	2
13-13.99	1	1
14-14.99	2	3
15-15.99	0	1
16-16.99	0	1
17-17.99	0	1
18-18.99	0	0
19-19.99	1	2
20-20.99	0	0
$\geq 21$	1	8
Total	51	29
Mean $\pm$ SD	9.67 $\pm$ 3.19	19.77 $\pm$ 16.90

Table 3. Sensitivity (%), Specificity (%), Positive Likelihood Ratio (PLR), Negative Likelihood Ratio (NLR), Positive Predictive Value (PPV) and Negative Predictive Value (NPV) for TUG cut-off score in patients with PD who had FOG

Cut-off score	Sensitivity	Specificity	PLR	NLR	PPV	NPV
10.86	68.97	76.47	2.93	0.41	24.6	95.7
11	68.97	78.43	3.20	0.40	26.2	95.8
11.39	68.97	80.39	3.52	0.39	28.1	95.9
11.40	68.97	82.35	3.91	0.38	30.3	96.0
11.56	68.97	84.31	4.40	0.37	32.8	96.1
11.69	68.97	86.27	5.02	0.36	35.8	96.2
11.85	68.97	88.24	5.86	0.35	39.4	96.2
11.98	65.52	88.24	5.57	0.39	38.2	95.8
12.30	62.07	88.24	5.28	0.43	37.0	95.4
12.35	62.07	90.20	6.33	0.42	41.3	95.5
12.70	58.62	90.20	5.98	0.46	39.9	95.1
13.13	55.17	90.20	5.63	0.50	38.5	94.8
13.99	55.17	92.16	7.03	0.49	43.9	94.9
14.05	51.72	92.16	6.59	0.52	42.3	94.5
14.16	48.28	92.16	6.16	0.56	40.6	94.1
14.19	48.28	94.12	8.21	0.55	47.7	94.2
14.54	48.28	96.08	12.31	0.54	57.8	94.4
14.66	44.83	96.08	11.43	0.57	55.9	94.0
15.66	41.38	96.08	10.55	0.61	54.0	93.7

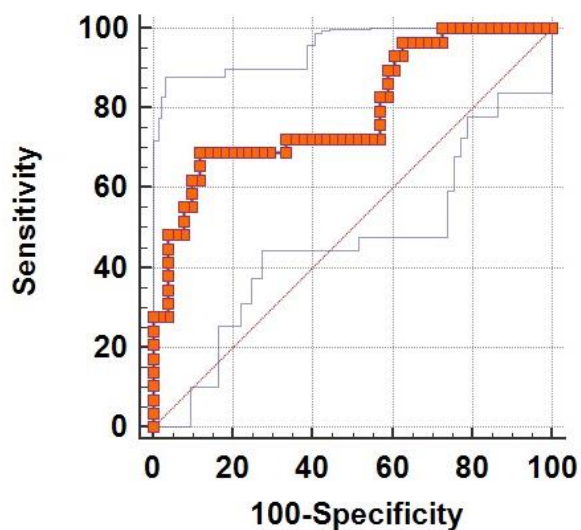


Fig. 1. Receiver operating characteristic (ROC) curve for TUG score in patients with PD+FOG

been listed as “recommended measures” by MDC-commissioned task force for assessing functional mobility, balance, and risk of falls in patients with PD. However, despite the high prevalence of both FOG and falls and their close relation in these patients, no attempt has yet been made to investigate the diagnostic accuracy of these tests for the risk of falls in patients with PD+FOG. The results of the current study provide the first evidence about the diagnostic accuracy of TUG for the risk of falls in patients with PD who had FOG.

We used the following descriptive terms to help the interpretation of the sensitivity and specificity results: high,  $\geq 90\%$ ; moderately high,  $\geq 80\%$  and  $< 90\%$ ; moderate,  $\geq 70\%$  and  $\leq 80\%$ ; moderately low,  $\geq 60\%$  and  $< 70\%$ ; and low,  $< 60\%$ . The results of this study showed that the best cut-off score for TUG in patients with PD+FOG was 11.85 seconds (with moderately low sensitivity (68.97%) and moderately high specificity (88.24%)) to discriminate between fallers and non-fallers. Different cut-off scores of TUG have reported in previous studies for screening falls, which may be due to different fall definitions, sample sizes or study designs. Dibble et al. (2006) used the TUG cut-off score of 13.5 seconds in patients with PD and found low sensitivity (39%) and moderately high specificity (87%). The results of their study showed increased sensitivity (93%) and decreased specificity (30%) by decreasing the cut-off score to 7.5 seconds. Nocera et al (2013) proposed a cut-off score of 11.5 s with moderately low sensitivity (66%) and specificity (62%) for discriminating faller and non-faller PD participants [24]. A recent systematic review and meta-analysis also reported an overall low sensitivity (31%) and moderate specificity (74%) using a cut-off score of  $\geq 13.5$  seconds for fall screening in older adults [26].

The results of the current study indicated a PPV of 39.4%, NPV of 96.2%, PLR of 5.68, and NLR of 0.35 for the best TUG cut-off score. The PPV of 39.4% showed that 39.4% of PD+FOG patients with a positive score (i.e. TUG

score  $\geq 11.85$  seconds) were correctly classified as fallers. The NPV of 96.2% revealed that 96.2% of participants with a negative test (i.e. TUG score  $< 11.85$ ) were classified as non-fallers. Thus, the misclassification rate for non-fallers was less than fallers (i.e. clinicians might be more confident about identifying non-fallers PD+FOG patients compared to fallers PD+FOG patients according to the TUG scores). These results did not support the use of TUG in isolation for assessing fall risk in patients with PD+FOG.

The results of this study found that faller PD+FOG patients had significantly greater TUG scores than non-fallers. This result is in accordance with the results of Vance et al. study (2015), which showed greater TUG score in the faller PD patients (i.e. PD patients who had a history of  $\geq 2$  falls in the preceding 6 months) as compared to the non-faller PD group [27]. The previous study on older adults, also showed that fallers took a longer time than non-fallers to complete the TUG [28].

Furthermore, we found that the faller PD+FOG group had significantly greater UPDRS-III score compared with the non-faller PD+FOG group. This finding was in line with the Bohnen et al. study (2009) who reported greater UPDRS scores in faller PD patients compared with non-fallers [29]. Lieberman et al. (2016) also found a significantly worse UPDRS-III score in recurrent faller PD patients (i.e. those who had  $\geq 2$  falls during the last year) than the non-faller PD patients [30].

There may be some possible limitations in this study. First, only community-dwelling PD patients who had FOG, were in the Hoeh & Yahr stages I-III and were free from cognitive impairments were enrolled in this study, which limits the generalizability of the results to the entire PD population. Second, using the self-reported history of falls may potentially cause bias in the results. However, a self-report history of falls has been commonly used in previous studies, which is suggested to be validated by a spouse and/or caregiver in future studies. Third, we performed the assessments only in the on-medication state of patients with PD because it is the common condition in which patients with PD usually ambulate and encounter the risk of falls, however, investigation of TUG diagnostic accuracy for falls during off-medication state may provide further information.

## Conclusion

The results of this study indicated that TUG has a moderate discriminative ability for falls screening in patients with PD who have FOG. The optimal cut-off score for discriminating faller PD+FOG patients and non-faller PD+FOG patients was 11.85 with moderately low sensitivity and moderately high specificity, indicating that TUG should be used in conjunction with other tests for the purpose of falls screening in clinical practice.

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## Implication to practice

The results of this study suggested that clinicians should

use TUG in conjunction with other tests in their routine examinations of patients with PD as a fall risk screening measure in order to identify faller PD+FOG patients and refer them for fall-specific interventions to reduce their risk of falls and disabling fall-related consequences.

### Conflict of Interests

The authors declare that they have no competing interests.

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## دقت تشخیصی آزمون برخاستن و راه رفتن زمان دار در بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن

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### چکیده

**مقدمه:** قفل شدن حین راه رفتن یک نشانه بالینی ناتوان‌کننده در بیماران مبتلا به پارکینسون است که با اپیزودهای کوتاه ناتوانی در قدم برداشتن مشخص می‌شود و تقریباً 38/2% این بیماران را تحت تاثیر قرار می‌دهد. قفل شدن حین راه رفتن ناگهانی ممکن است تعادل را مختل کند و بنابراین به عنوان علت رایج افتادن در بیماری پارکینسون در نظر گرفته می‌شود. این مطالعه برای ارزیابی دقت تشخیص افتادن آزمون برخاستن و راه رفتن زمان دار، آزمون روا و پایا برای ارزیابی تحرک و ریسک افتادن، در بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن بود.

**روش‌ها:** در این مطالعه مقطعی، 80 فرد مبتلا به پارکینسون ایدیوپاتیک که قفل شدن حین راه رفتن داشتند با میانگین  $\pm$  انحراف معیار سن  $63/63 \pm 9/76$  سال و میانگین  $\pm$  انحراف معیار مدت زمان بیماری  $7/82 \pm 5/76$  سال با روش نمونه‌گیری غیرتصادفی ساده شرکت کردند و بر اساس سابقه افتادن طی 6 ماه گذشته به دو گروه دارای سابقه افتادن و بدون سابقه افتادن تقسیم شدند. حساسیت، ویژگی، نسبت درست‌نمایی منفی و مثبت و منحنی مشخصه ی عملکرد (ROC) برای آزمون برخاستن و راه رفتن زمان دار محاسبه شد.

**یافته‌ها:** نمره آزمون برخاستن و راه رفتن زمان دار بین بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن با سابقه افتادن و بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن بدون سابقه افتادن تفاوت معناداری داشت ( $p=0/003$ ). بهترین نقطه برش برای تمایز بین بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن با سابقه افتادن و بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن بدون سابقه افتادن  $11/85$  ثانیه (حساسیت = 68/97% و ویژگی = 86%) بود.

**نتیجه‌گیری:** آزمون برخاستن و راه رفتن زمان دار حساسیت و ویژگی متوسطی برای وضعیت افتادن در بیماران مبتلا به پارکینسون دارای قفل شدن حین راه رفتن دارد که نشان می‌دهد این آزمون باید همراه با سایر آزمون‌ها برای غربالگری افراد نیازمند مداخله برای کاهش افتادن استفاده شود.

**کلیدواژه‌ها:** اختلالات حرکتی، بیماری پارکینسون، افتادن تصادفی، تعادل، حساسیت و ویژگی

## TUG in PD patients with FOG

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