



## Which measures of physical function and motor impairment best predict quality of life in Parkinson's disease?

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### ABSTRACT

**Introduction:** Our objective was to compare the relative value of elements of the motor system in predicting the physical mobility domain of health related quality of life in patients with Parkinson's disease in order to specify targets for intervention.

**Methods:** In this cross-sectional study, the Parkinson's disease questionnaire-39 was administered to 263 subjects with Parkinson's disease to assess health related quality of life. Demographics, motor impairments and physical function were assessed using the Unified Parkinson disease rating scale, 10-m walk test, 6-min walk test, Freezing of gait questionnaire, Timed up & go, functional gait assessment, Berg balance test, functional reach and 9-hole peg test.

**Results:** The results revealed that demographic factors accounted for 19.7% of the variance in Parkinson disease questionnaire-39 mobility score. When motor impairments were added to the model, the bradykinesia composite score contributed a significant portion of the variance ( $R^2$  change = 0.12,  $p < 0.001$ ). The tremor and rigidity composite scores did not contribute significantly. The Freezing of gait questionnaire was the strongest predictor ( $R^2$  change = 0.23,  $p < 0.001$ ) of the physical function tests followed by Functional gait assessment ( $R^2$  change = 0.06,  $p < 0.001$ ) and 6-min walk test ( $R^2$  change = 0.01,  $p = 0.01$ ). Collectively, 61% of the variance in Parkinson disease questionnaire-39 mobility score and 41.5% of the Parkinson disease questionnaire-39<sub>total</sub> score was accounted for.

**Discussion:** These results suggest greater value of physical function tests, and not tests of motor impairments, in predicting health related quality of life.

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### 1. Introduction

Measures of health related quality of life (HRQOL) are increasingly used as outcome indicators in both research and clinical practice for patients with neurological disorders [1]. For individuals with Parkinson's disease (PD), the emphasis of treatment has shifted from one concerned primarily with ameliorating impairments of the motor system to one that also considers the impact of the disease state on HRQOL. Identifying predictors of HRQOL is necessary in order to target intervention most effectively.

Motor system impairments have long been the primary target of pharmacological interventions. However, an analysis from the DATATOP trial revealed that the Unified Parkinson disease rating scale (UPDRS) items reflecting severity of impairments of the motor system (e.g., bradykinesia, rigidity, tremor) were not significant predictors of decline in quality of life [2]. In contrast, other studies have identified an association between higher (worse) UPDRS postural instability gait disorder (PIGD) scores and poorer HRQOL [2–4]. This suggests a stronger relationship may exist between HRQOL and functional mobility (i.e., gait and postural control) than between HRQOL and motor impairments.

Given that the mobility items related to postural instability and gait limitations appear to be most related to HRQOL – other measures of mobility and physical function may provide additional predictive value and deserve consideration. Despite their common

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use and well-accepted clinical value, UPDRS items are limited in scope. PIGD items, for example, generally focus on the presence or absence of a gait limitation, freezing or a postural control response. These items do not consider other important functional considerations such as walking speed, endurance, obstacle negotiation or performance during other more complex walking and balance tasks.

Clinical physical function measures, in contrast, provide a relatively more comprehensive assessment of gait and balance limitations. Many valid and reliable tests of physical performance are available and include tests of walking (e.g., 6 min walk test, Freezing of gait questionnaire), postural control (e.g., Functional reach, functional gait assessment), transitional movements (e.g., Timed up & go) and upper extremity function (e.g., 9 hole peg test). Although these tests are commonly used by PD-focused researchers and clinicians, the extent to which they may provide value – either independently or in addition to the PIGD score – in predicting HRQOL has not been investigated.

The purpose of this study was to identify factors that strongly predict HRQOL in PD. Our specific objective was to expand on previous work by directly comparing three groups of relevant factors. The groups were: demographic factors, motor system impairments measured by the gold standard UPDRS, and physical function factors. In particular, we sought to compare the ability of each factor to predict the perception of HRQOL as reflected in the mobility domain of the PDQ-39 (PDQ-39<sub>mobility</sub>). The PDQ-39<sub>mobility</sub> was targeted in this study to hone in on the relationship between motor impairments, physical function limitations and perceived health related to the physical domain of HRQOL. Based on previous research [2–4], we hypothesized that measures of mobility would predict significantly greater portions of the variance in the PDQ-39<sub>mobility</sub> score compared to measures of motor impairment. In addition, we hypothesized that other measures of gait and balance – beyond the PIGD score – would significantly predict PDQ-39<sub>mobility</sub> score.

## 2. Methods

### 2.1. Study population

Subjects ( $N = 263$ ) were recruited from Movement Disorders clinics at Boston University ( $N = 77$ ), University of Utah ( $N = 36$ ), Washington University ( $N = 80$ ) and University of Alabama ( $N = 70$ ). Inclusion criteria included: a diagnosis of idiopathic PD according to the UK Brain Bank Criteria, modified Hoehn and Yahr (H&Y) stages 1–4, age  $\geq 40$  years and living in the community. Subjects were excluded if they had a diagnosis of atypical Parkinsonism or previous surgical management of their PD. This study was approved by the Institutional Review Boards of all institutions. All subjects provided informed consent.

### 2.2. Study design

A cross-sectional analysis was conducted using data from a larger longitudinal study. Subjects were examined in an outpatient clinic between July 2009 and July 2010 over a 2.5 h period and were tested on medication.

### 2.3. Training of evaluators

Measures were selected based on their common use in PD clinical settings and strong psychometric properties. Two to four evaluators per site were trained in the standardized implementation of each test. All testers were provided with a standard operating procedures manual that described the protocol for administering each test and an instructional video demonstrating the procedures on two patients with PD. Standardized scoring forms were used at all sites. Each evaluator rated both patients on the video on 2 occasions separated by one week. Intraclass correlation coefficients (ICC) were calculated to examine the consistency of the measurements among raters. Separate ICC (1,4) calculations were performed for each physical performance measures and these coefficients ranged from 0.64 to 0.89.

## 2.4. Measures

### 2.4.1. Parkinson's disease questionnaire-39 (PDQ-39)

The PDQ-39 is an HRQOL instrument that measures perceived health in terms of physical, mental and social functions [1,5,6]. The self-administered scale has 39 items made up of 8 domains. Scores range from 0 to 100 with higher scores reflecting a lower health related quality of life. The mobility domain (PDQ-39<sub>mobility</sub>) contains 10 items concerning the frequency in which patients have difficulty getting around the household and community and participating in chores and leisure activities. Adequate internal consistency and test–retest reliability have been demonstrated in both the total and motor subscale scores [7]. Given the emphasis in this study on predicting HRQOL related to the physical domain, the mobility subscale score of the PDQ-39 served as the primary dependent variable. Once significant predictors of the mobility subscale were identified, their value in predicting the PDQ-39<sub>total</sub> score was investigated.

**2.4.1.1. Demographic factors.** Demographic factors collected included age, gender and disease duration.

### 2.4.1.2. Motor impairment factors

**2.4.1.2.1. Unified Parkinson disease rating scale (UPDRS).** Part II (motor aspects of experiences of daily living) and Part III (motor examination) of the Movement Disorder Society (MDS) revised version of the UPDRS was administered by trained investigators [8]. For the analysis, composite scores for the following areas were established: 1) bradykinesia (left and right finger taps, hand movements, pronation–supination, heel-taps, leg agility and body bradykinesia), 2) rigidity (left and right arms, left and right legs, neck) and 3) tremor (left and right resting, postural, kinetic) [9].

### 2.4.1.3. Physical function factors

**2.4.1.3.1. Postural instability and gait (PIGD) items of the UPDRS.** The PIGD items of the MDS UPDRS consisted of the walking/balance and freezing items of part II and the gait, freezing of gait and postural instability items of part III [9].

**2.4.1.3.2. The 10 m walk test (10MWT).** The 10MWT is a test used to measure the time it takes for subjects to walk 10 m at maximum speed [10].

**2.4.1.3.3. The 6 min walk test: (6MWT).** The 6MWT is a test used to measure the distance subjects can walk in 6-min [11,12].

**2.4.1.3.4. The freezing of gait questionnaire (FOG-Q).** The FOG-Q is a self-administered 6-item survey tool used to assess the severity of freezing of gait in patients with PD [13]. Each item is rated on a 5-point ordinal scale. The total score ranges from 0 (absence of symptom) to 24 (most severe symptom).

**2.4.1.3.5. Functional gait assessment (FGA).** The FGA is a 10-item standardized test for assessing postural stability during various walking tasks. Items are scored using a 4-point ordinal scale. Scores range from 0 to 30 with lower scores indicating more impaired performance [14].

**2.4.1.3.6. Berg balance test (BBS).** The BBS is a 14-item scale that quantitatively assesses balance and risk for falls through direct observation of performance. The items are scored using a 5 point ordinal scale. Total scores range from 0 to 56 with higher scores indicating better balance [15].

**2.4.1.3.7. Functional reach test (FR).** The FR is a test used to measure the maximum distance subjects can reach in the forward direction while their base of support remains fixed [16]. The mean of these 3 trials was used in the analysis [12,16].

**2.4.1.3.8. Timed up & go (TUG).** The TUG is a test used to measure the time it takes for subjects to rise from a chair, walk 3 m, turn, walk back and sit down. Each subject performed 2 trials and the mean time was used in the analysis [10,17].

**2.4.1.3.9. Nine hole peg test (9HPT).** The 9HPT is a timed measure of fine dexterity and involves placing and removing nine pegs in a pegboard [18]. The mean time of 2 trials using the non-dominant hand was used in this analysis.

## 2.5. Statistical analysis

Means  $\pm$  standard deviations (SD) were calculated for all variables. Correlational analyses were conducted to examine the strength of association between the PDQ-39<sub>mobility</sub> and demographic variables, variables representing motor impairments and the physical function measures. Results were similar between Pearson and Spearman analyses; therefore only Pearson correlation coefficients are presented. Those variables found to correlate significantly ( $p < 0.05$ ) with the PDQ-39<sub>mobility</sub> were entered into a hierarchical regression model.

With the PDQ-39<sub>mobility</sub> score as the dependent variable, independent variables were entered systematically as three separate blocks into a hierarchical regression analysis. The order of block entry was determined according to the following clinical rationale: demographic variables (block 1) were entered first based on their non-modifiability; the motor impairment variables (block 2) were entered next based on their potential to respond to pharmacologic intervention; physical function variables (block 3), because of their potential to identify targets for rehabilitation intervention, were entered last to assess their predictive value above and beyond the preceding factors.

Within each block, variables were entered in stepwise fashion. Using an F test ( $\alpha = 0.05$ ), the significance of the  $R^2$  and  $R^2$  change values was examined to identify the strongest predictors of the PDQ-39<sub>mobility</sub> score. Those variables found to predict significant portions of the PDQ-39<sub>mobility</sub> score were then entered into a regression model with the PDQ-39<sub>total</sub> score as the dependent variable to further assess the predictive value of these mobility tests on overall quality of life. All data were analyzed using the statistical software program SPSS 16.0.

### 3. Results

Two-hundred and sixty-three subjects with PD participated in this study. Sample characteristics are presented in Table 1. Significant correlations were found between the PDQ-39<sub>mobility</sub> score and all independent variables with the exception of sex (Table 2). Older age and longer disease duration was significantly correlated with poorer PDQ-39<sub>mobility</sub> scores. Poorer scores on the tremor, rigidity and bradykinesia composite scores were significantly correlated to poorer PDQ-39<sub>mobility</sub> scores with magnitudes ranging from 0.19 to 0.49. A poorer performance on all physical function measures was significantly correlated to poorer PDQ-39<sub>mobility</sub> scores with magnitudes ranging from 0.30 to 0.72.

The results of the hierarchical regression analysis to predict PDQ-39<sub>mobility</sub> scores are presented in Table 3. Demographic factors (block 1) accounted for 19.7% of the variance in PDQ-39<sub>mobility</sub> score. Disease duration was the strongest predictor of the demographic variables ( $R^2 = 0.16$ ,  $p < 0.001$ ) followed by age ( $R^2$  change = 0.04,  $p < 0.001$ ) (Model 1). When the motor impairment factors (block 2) were added to the model, the bradykinesia composite score contributed a significant portion of the variance in PDQ-39<sub>mobility</sub> score ( $R^2$  change = 0.12,  $p < 0.001$ ) (Model 2). The tremor and rigidity composite scores did not contribute significantly to the model. Three of the nine physical function test scores (block 3) significantly contributed to the model (Model 3) with the FOG-Q score as the strongest predictor ( $R^2$  change = 0.23,  $p < 0.001$ ) followed by the FGA score ( $R^2$  change = 0.06,  $p < 0.001$ ) and the 6MWT distance ( $R^2$  change = 0.01,  $p = 0.01$ ). Collectively, those variables from each block that contributed significantly to the model accounted for 61% of the variance in PDQ-39<sub>mobility</sub> score and 41.5% of the more global PDQ-39<sub>total</sub> score.

### 4. Discussion

Our objective was to expand upon previous research by comparing the relative predictive value of various factors, both newly and previously identified, for predicting HRQOL in PD. Specifically, we sought to identify potential targets to optimize intervention geared toward improving HRQOL.

Our analysis was based on an *a priori* clinical rationale that recognized both the unmodifiability of demographic factors (e.g., age and duration of disease), the longstanding clinical focus on motor impairments (e.g., rigidity or tremor) as targets of pharmacological intervention and the potential importance of physical function factors in predicting HRQOL. Accordingly, the analysis revealed that demographic factors uniquely predicted 19.7% of the variance in mobility-related quality of life; UPDRS indicators of motor impairments uniquely predicted 11.8%, and physical function measures of mobility and postural control uniquely predicted a final 30%. Measures of physical function were stronger predictors

**Table 1**  
Subject characteristics.

Characteristic	Mean (SD)/Total # (%)	Range
Age (years)	67.7 (9.2)	40–88
Sex (males)	150 (57%)	–
Disease duration (years)	6.22 (4.8)	<1–25
Hoehn & Yahr stage	–	1–4
Stage 1	16 (6.1%)	
Stage 1.5	4 (1.5%)	
Stage 2	113 (43.1%)	
Stage 2.5	62 (23.7%)	
Stage 3	52 (19.8%)	
Stage 4	15 (5.7%)	
Tremor composite score	4.5 (4.5)	0–30
Rigidity composite score	7.1 (4.0)	0–18
Bradykinesia composite score	15.3 (8.0)	1–40
PIGD composite score	4.3 (3.6)	0–18
Freezing of Gait Questionnaire	6.0 (5.4)	0–20
9 Hole Peg Test (sec)	32.2 (12.4)	17.8–99.6
Berg Balance Test	50.2 (6.8)	14–56
Functional Reach (cm)	28.0 (8.5)	6.0–52.3
Functional Gait Assessment	20.5 (6.4)	0–30
Timed Up & Go (sec)	13.2 (18.5)	5.1–219.0
10 meter walk test (maximum speed)	6.9 (3.5)	3.1–50.0
6 minute walk test (meters)	383.1 (157.0)	29–744
PDQ-39 Mobility Subscale Score	24.2 (22.8)	0–92.5
PDQ-39 Total Score	21.3 (13.4)	0.52–63.1

of mobility-related quality of life compared to the motor impairment indicators, supporting our initial hypothesis.

Gait and balance function in our sample had a relatively strong relationship with HRQOL. Of the physical functional measures we included, those that reflected problems with freezing of gait (i.e., the FOG-Q) and postural control during walking (i.e., the FGA), appeared to be particularly valuable predictors of PDQ-39<sub>mobility</sub> score. Although the PIGD composite score did not significantly contribute to the variance in PDQ-39<sub>mobility</sub> score, the PIGD score was highly correlated with the FOG-Q score. A secondary analysis removing the FOG-Q variable from the analysis revealed that the PIGD score contributed significantly to the model (20% compared to 23% from the FOG-Q) with the FGA continuing as the second largest contributor. Use of the FOG-Q and the FGA may be advantageous as they distinguish the relative nature of the gait and balance limitation as compared to the PIGD, which generally establishes the presence or absence of a limitation. The FGA, in contrast, includes an assessment of walking speed, turning, changing directions and negotiating obstacles.

Our data were consistent with previous studies [2–4] suggesting that a weak relationship exists between motor impairments associated with PD and quality of life related to mobility. Our findings extend that idea by revealing that motor impairments appear to be substantially weaker predictors of mobility-related quality of life than either non-modifiable demographic factors or potentially modifiable aspects of physical function. Moreover, of the motor impairments we studied, only bradykinesia was identified as a significant contributor to quality of life. The latter result is consistent with previous research [3] but is not necessarily unequivocal [19]. Our use of the PDQ-39<sub>mobility</sub> score as the dependent variable, rather than a more global quality of life index, may have contributed to the finding.

Bradykinesia also was more strongly correlated than rigidity or tremor to physical function. Using structural equation modeling, Visser demonstrated that motor symptoms had only an indirect relationship on HRQOL [30]. It is likely that motor impairments

**Table 2**  
Bivariate correlation coefficients for PDQ-39<sub>mobility</sub> and demographic, motor impairment and physical function variables.

	PDQ-M	PDQ-T	Age	Gender	DD	Trem	Rig	Brady	PIGD	FOG	9HPT	FR	BBS	FGA	TUG	10MWT	6MWT
PDQ-M	—																
PDQ-T	0.81**	—															
Age	0.24**	0.21**	—														
Gender	0.03	0.02	–0.08	—													
DD	0.40**	0.32**	–0.06	—	—												
Tremor	0.19**	0.16*	–0.10	0.23**	—	—											
Rigidity	0.33**	0.30**	0.18**	0.22**	0.43**	—											
Brady	0.33**	0.30**	0.18**	0.22**	0.43**	—											
PIGD	0.72**	0.53**	0.26**	0.53**	—												
FOG	0.71**	0.57**	0.15*	0.79**	—												
9HPT	0.45**	0.37**	–0.20**	0.51**	0.41**	—											
FR	–0.40**	–0.33**	–0.25**	–0.40**	–0.40**	—											
BBS	–0.61**	–0.44**	–0.40**	–0.68**	–0.52**	0.51**	—										
FGA	–0.66**	–0.57**	–0.44**	–0.68**	–0.52**	0.51**	—										
TUG	0.30**	0.17*	0.12	0.50**	–0.37**	–0.39**	–0.39**	—									
10MWT	0.42**	0.27**	0.23*	0.50**	–0.30**	–0.30**	–0.30**	–0.30**	—								
6MWT	–0.46**	–0.35**	–0.38**	–0.44**	–0.30**	–0.30**	–0.30**	–0.30**	–0.30**	—							

\*\* = significance at  $p < 0.01$ ; \* = significance at  $p < 0.05$ ; PDQ-M = Parkinson disease questionnaire mobility score; PDQ-T = Parkinson disease questionnaire total score; DD = disease duration; tremor = tremor composite score; rigidity = rigidity composite score; brady = bradykinesia composite score; PI GD = postural instability gait disorder score; FOG = freezing of gait questionnaire; 9HPT = 9 hole peg test; FR = functional reach; BBS = Berg balance test; FGA = Functional gait assessment; TUG = Timed up & go; 10MWT = 10 m walk test; 6MWT = 6 min walk test.

serve as a precursor to restrictions in physical functioning but that the limitations in physical functioning have a more direct impact on HRQOL.

Shulman recently highlighted the pivotal role of gait and balance in daily function and suggested that difficulty with ambulation should be considered a clinical “red flag” that indicates emerging disability [20]. Although pharmacological treatment is generally effective in ameliorating the motor symptoms associated with PD, it is less effective in treating gait and postural control deficits. In contrast, there is evidence to support the effectiveness of physical therapy interventions in improving gait and postural control [21,22]. Treadmill training [23], external cues [24], strengthening exercises [25] and balance training [26] have been demonstrated to improve gait, balance, freezing and quality of life [27] in patients with PD and should be considered for those with mild to moderate disease severity. Our results suggest that interventions that address emerging and/or anticipated gait and postural control deficits, not only may help to delay disability, but also may be important for helping to slow decline in quality of life.

The study had several strengths. Its relatively large sample size and participation of subjects across four sites enhance the generalizability of the findings. The study was one of the few to investigate the relationship between several widely used measures of gait and balance and HRQOL. The results underscored those with the greatest predictive value helping to guide selection of outcome measures by clinicians and researchers. When considering the significant contributors within all three variable groups (i.e., demographics, motor impairment and physical function measures), the hierarchical model accounted for 61% of the variance in PDQ-39<sub>mobility</sub> score explaining the majority of significant mobility related HRQOL predictors in PD.

The study also had several limitations. Its cross-sectional design did not allow for us to make inferences about factors that predict changes in quality of life over time. In addition, 39% of the variance in the PDQ-39 score was unaccounted for, suggesting the importance of other relevant factors. Depression, anxiety and mood, for example, have been shown to impact overall HRQOL [28,29]. Other possible limitations included the potential overlap between measures of functional mobility and the items in the physical domain of the PDQ-39. For example, items # 4 and # 5 of the PDQ-39 physical mobility domain inquire about difficulties with walking ½ mile and 100 yards respectively. However, the strength of the correlations between the PDQ-39<sub>mobility</sub> score and items directly measuring walking (6MWT, 10MWT) were similar to the strength of the correlations between the PDQ-39<sub>mobility</sub> score and the upper extremity function (9HPT) and balance tests (BBS, FGA). In addition, only one walking measure (6MWT) was retained in the final model contributing less than 1% to the variability in the PDQ-39<sub>mobility</sub> score. It appeared that the more complex mobility tests measuring more than one construct – fluid walking while negotiating obstacles and maintaining postural control – more strongly impact the real-life mobility experiences of patients in the home and community.

In summary, performance on physical function tests of gait and postural control accounted for significant portions of the variance in both the PDQ-39<sub>mobility</sub> score and PDQ-39<sub>total</sub> score, supporting the value of physical function tests in predicting HRQOL. The FOG-Q and the FGA were the strongest predictors of the PDQ-39<sub>mobility</sub> score when compared to other tests of functional mobility. Motor impairments, in contrast, accounted for a relatively small portion of variance in quality of life, with only bradykinesia remaining in the final model. The results suggest that targeting mobility limitations, rather than motor impairments, may be an important consideration for optimizing quality of life for individuals with PD.

**Table 3**  
Hierarchical stepwise regression analysis.

	Model 1		Model 2		Model 3			
	Unstandardized Coefficients		Unstandardized Coefficients		Unstandardized Coefficients		Standardized Coefficients	
	B	P-value	B	P-value	B	Std Error	Beta	P-value
Block 1 ( $R^2 = 0.197$ )								
Disease Duration	1.8	<0.001	1.3	<0.001	0.38	0.21	0.08	0.07
Age	0.50	<0.001	0.27	0.05	−0.14	0.11	−1.2	0.22
Block 2 ( $R^2$ change = 0.118)								
Bradykinesia	–	–	1.1	<0.001	0.37	0.14	2.6	0.01
Block 3 ( $R^2$ change = 0.30)								
FOG	–	–	–	–	1.7	0.22	0.41	<0.001
FGA	–	–	–	–	−1.0	0.22	−0.30	<0.001
6MWT	–	–	–	–	−0.02	0.01	−0.14	0.01
$R^2$	0.197		0.31		0.61			

Variables listed include only those retained in the final models. FOG-Q = Freezing of gait questionnaire; FGA = Functional gait assessment; 6MWT = 6 min walk test; B = beta; Std Error = standard error.

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