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Balance and mobility in patients with newly diagnosed Parkinson's disease – a five-year follow-up of a cohort in northern Sweden

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ABSTRACT

Background: The presence of early balance impairment in patients with Parkinson's disease has not been fully investigated.

Purpose: The purpose of this study was to examine balance and mobility, self-perceived unsteadiness, self-reported falls, and effects of medication on balance among patients at their first visit to a neurological clinic and during the ensuing five years.

Materials and methods: The participants were collected from a prospective longitudinal study. One hundred and forty-five patients with idiopathic Parkinson's disease and 31 healthy controls were included. The outcome measures were the Berg Balance Scale, the Timed Up and Go, the Postural Stability test and a questionnaire.

Results: At their first visit to the neurological clinic, the patients performed less well on the Berg Balance Scale ($p < 0.001$, $r = 0.36$), the Timed Up and Go ($p < 0.001$, $r = 0.32$), and the Postural Stability test ($p < 0.001$, $r = 0.35$) compared with the controls. In addition, a higher percentage of the patients reported self-perceived unsteadiness ($p < 0.001$, $phi = 0.47$). During the ensuing five years, balance and mobility worsened both with and without medication ($p < 0.01$, $r = 0.24$-0.37), although with small median differences.

Conclusions: Further studies are needed to confirm that minor balance impairments exist even at the time of diagnosis and worsen during the ensuing five years.

➤ IMPLICATIONS FOR REHABILITATION

- Impairments in balance and mobility may occur early in Parkinson's disease, especially in the elderly patients, and seem to worsen during the first five years.
- There is a need to use sensitive outcome measures and to ask the patients about unsteadiness and falls to detect balance impairment in this cohort.
- Parkinsonian medication has a limited effect on balance and may preferably be complemented with balance exercises to target balance impairment early in Parkinson's disease.

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Introduction

One of the cardinal motor features in Parkinson's disease (PD) is postural instability or balance impairment [1]. In literature on PD, the terms postural stability and balance are often used synonymously. Balance has been defined as control of the body's centre of mass over its base of support in order to achieve postural equilibrium and orientation [2]. Balance impairment in PD may be present in the early stage of the disease, even at diagnosis, but it becomes more prevalent and worsens with disease progression [3]. Balance impairment and resulting falls are major factors determining the quality of life, morbidity, and mortality in individuals with PD [4–7]. In a review of 22 studies, 60.5% of all patients reported at least one fall during the last year, with 39% reported recurrent falls [8]. The balance of persons with PD may be influenced by impairments such as rigidity affecting biomechanics, bradykinesia of postural responses and anticipatory postural adjustments, impaired kinaesthesia for sensory integration, and less automaticity of balance and gait [9]. Mobility, in terms of bradykinetic gait features such as reduced trunk rotation, decreased arm swing and slow turns may be present in newly diagnosed patients with PD, even when walking speed is normal. Mobility tasks such as sit to stand and stand to sit may also be affected by PD [10]. In addition, cognitive impairment such as altered attention may affect mobility and balance control [9,11–13].

Levodopa and dopamine agonists are the most common pharmacological treatments and strong evidence supports their use for motor symptoms at all stages of the disease [14]. Although most of the cardinal motor features respond well to dopaminergic treatment, the effect on balance impairment is fractional [15–17]. However, some studies show a positive effect on balance when measured with the Berg Balance Scale (BBS) [18–20]. For some people with PD, Deep Brain Stimulation may be required to improve motor symptoms of the disease [21], but the effect on balance is limited [21–23]. There is an increasing evidence that physiotherapy, especially highly challenging balance exercises, can improve balance in PD [24,25]. Balance exercises may also be effective in reducing falls in persons with PD [26]. However, the long-term effect of physiotherapy interventions needs to be explored given the progressive nature of PD [3,24,26,27].

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Balance impairment and the associated risk of falling have a huge impact on patients with PD, especially in later stages of the disease [3]. A few cohort studies have evaluated balance in patients with PD prospectively [28–32]. However, it has not been fully investigated to what extent balance is impaired at the very start of the disease. Furthermore, there are no studies that have prospectively investigated balance in PD from the first visit to a neurological clinic and during the ensuing five years. Hence, the main purpose of this study was to examine balance and mobility using clinical outcome measures among patients with idiopathic PD at their first visit to a neurological clinic and over-time during the ensuing five years. A second purpose was to examine self-perceived unsteadiness and self-reported falls at the first visit and at follow-ups. A third purpose was to study the effect of medication on balance and mobility in early PD.

Methods

Study design

This study is part of an ongoing longitudinal prospective research study, called the NYPUM study. NYPUM stands for New Parkinson in Umeå and investigates etiological, diagnostic and clinical aspects of Parkinsonism and PD [33].

Setting

All patients suspected to have Parkinsonism or PD and who were referred to the neurological clinic at the University Hospital of Umeå, Sweden, were assessed for possible inclusion in the NYPUM study. The local catchment area of Umeå's healthcare services serves a population of 142 000. The inclusion period was from 1 January 2004 to 30 April 2009. The patients were referred by physicians at primary healthcare centres and physicians at eldercare homes. After referral, the patients were assessed by two neurologists who were specialists in movement disorders. One neurologist examined the patient and the other neurologist assessed the patient by watching a video of the examination according to the Unified Parkinson's Disease Rating Scale (UPDRS) [34].

Participants

The inclusion criterion was the presence of Parkinsonism according to the definition of the United Kingdom Parkinson's Disease Society Brain Bank [35]. The exclusion criteria were secondary Parkinsonism (e.g., history of current use of neuroleptics or other drugs with extrapyramidal side-effects and vascular Parkinsonism) and impaired cognitive function (a Mini-Mental State Examination score of less than 24 of maximum 30 points [36]. A total of 493 referrals with suspected idiopathic Parkinsonism were assessed for inclusion in the NYPUM study, 186 of whom fulfilled the inclusion criterion. On the basis of the age and sex of the first 50 included patients, 31 controls, matched for age and sex, were recruited through advertisements in a local newspaper. They were medically examined to verify the absence of neurological disease and other major illnesses and they underwent the same evaluation procedures as the patients. The present study included 145 patients who fulfilled the United Kingdom Parkinson's Disease Society Brain Bank criteria for PD [35]. Severity of the disease was described according to the Hoehn and Yahr scale [37], where the first stage indicates mild impairment (unilateral involvement only, usually with minimal or functional impairment) and the fifth stage indicates severe impairments (confinement to bed or wheelchair unless aided). The NYPUM study is still ongoing and only patients who at the latest follow-up in June 2016 were diagnosed with PD were included in the present study (Figure 1). The NYPUM study was approved by the Regional Ethical Review Board in Umeå (Reg. No. 20031125; 03-387). All patients received oral and written information according to the Helsinki declaration and gave their written consent.

Measurements

The Berg Balance Scale (BBS) was used in this study to assess balance. The BBS is a well-established generic scale, the use of which is recommended for patients with PD [38,39]. It is an ordinal scale, with each item scored from 0–4 with a maximum score of 56. Higher scores represent better balance [40]. For both Parkinsonism and PD, the BBS has shown high test-retest reliability [41,42]. Furthermore, the BBS has shown high criteria validity for PD [43]. In our study, the BBS was assessed according to the version of the manual that had been translated into Swedish [44].

The Timed Up and Go (TUG) test was used to measure functional mobility such as standing up, initiating gait, walking, turning, and finally sitting down [45]. The time of performance was measured in seconds. The TUG has shown good intra-rater reliability for Parkinsonism [41] and for PD [39]. The interrater reliability is good for PD [46]. In a recent review, the TUG has been recommended for use with patients with PD with satisfactory clinometric properties [38].

The Postural Stability test (i.e., the Pull test), which is included as item 30 in the third part of the UPDRS, was used. The item can be scored from 0–4 where 0 is considered as normal, 1 as retropulsion but recovers unaided, 2 as absence of postural response (would fall if not caught by the examiner), 3 as very unstable, tends to lose balance spontaneously, and 4 as unable to stand without assistance [34] . The Postural Stability test is widely used as a tool to assess postural reactions although it has shown some limitations in sensitivity and interrater correlations [47].

The participants completed a questionnaire that aimed to capture self-perceived unsteadiness and self-reported falls. The questionnaire included 14 questions and was developed specifically for the NYPUM study. For the present study, two questions were selected for analysis: (1) "Have you perceived unsteadiness during the last year?" and (2) "Have you fallen anytime during the last year?" The response alternatives were yes and no.

Measurement procedure and conditions

The selected measurements were used at baseline and at one-year, three-year and five-year follow-up. The Postural Stability test was assessed by a neurologist while the BBS and the TUG were assessed by a physiotherapist. The questions about unsteadiness and falls were asked verbally by the physiotherapist after the assessments. The patients also received information about the importance of physical exercise and were given instructions for different exercises, including balance exercises. At baseline (i.e., at the first visit to the neurological clinic), none of the included patients were taking any parkinsonian medication. On the following test occasions, the BBS and the TUG were performed with and without medication. When performing the tests without medication, the patients were told to be without their L-dopa medication for at least 12 h and without their dopamine agonists for three days. The time between the two test occasions, with or without medication, was usually 1–2 weeks. The Postural Stability test was assessed only with medication at the follow-ups.

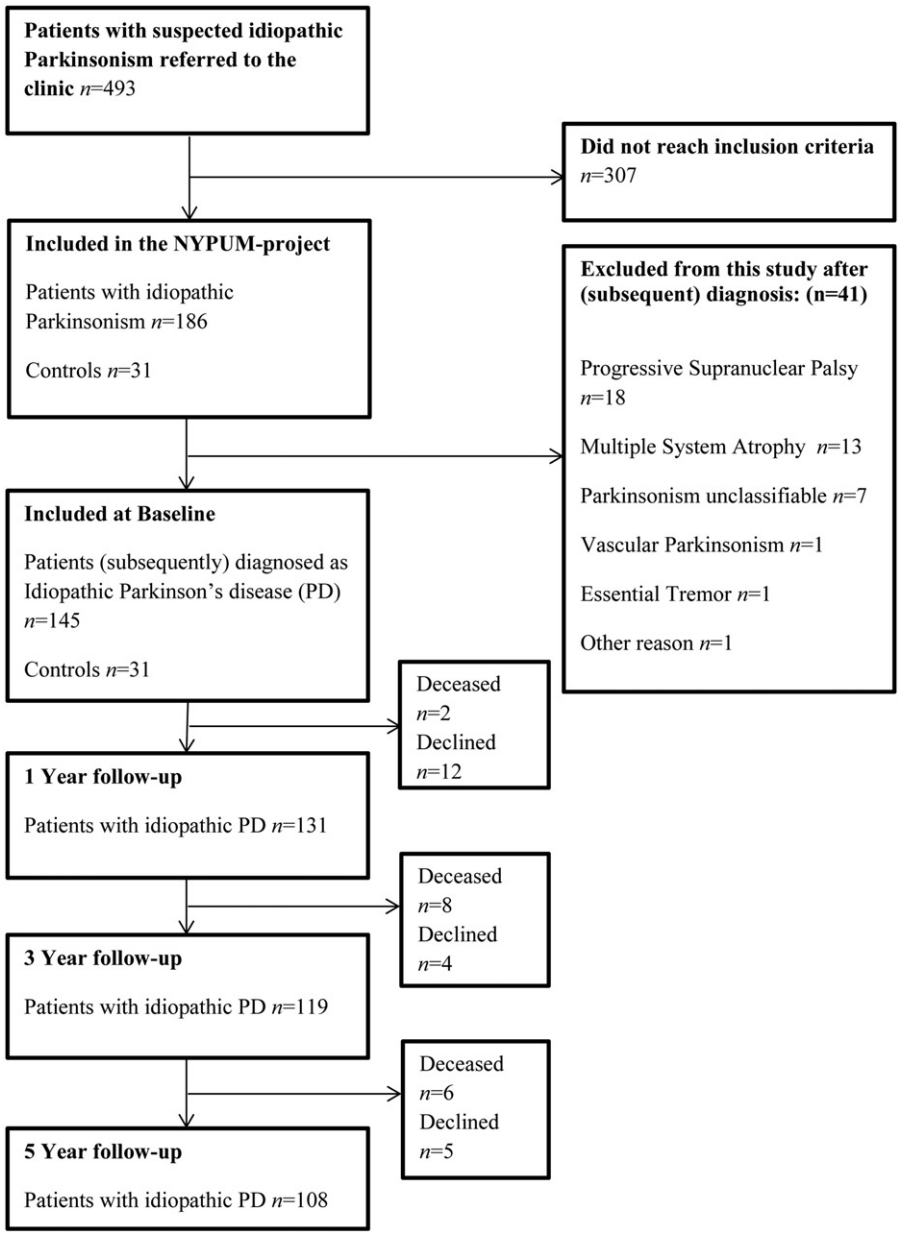

Figure 1. Flowchart of the included patients and controls in the study, at baseline and follow-ups. Note that declined refers to patients who canceled their participation at follow-ups.

Statistical methods

The statistical analysis was performed in the IBM SPSS (Statistical Package for Social Sciences, 23.0). Descriptive statistics were gathered for each group and tested for normality by using the Kolmogorov-Smirnov test. Comparisons between groups were conducted using the independent samples *t*-test, the Mann–Whitney *U*-test or the Pearson chi-square test, depending on the data distribution and type of data. Median difference (95% confidence interval) between groups and at different points in time was calculated using the Hodges-Lehman estimator. An approximate effect size *r* was calculated using the mathematical formula $r = z/\sqrt{N}$ where N = total number of cases. To estimate the effect size, the Cohen (1988) criteria were used and *r* was interpreted as 0.1 = small effect, 0.3 = medium effect and 0.5 = large effect [48]. The Spearman's Rho was used to calculate correlations between measurements. For all the statistical tests at baseline, the limit for statistical significance was set at $p < 0.05$.

For repeated measures analysis, the Friedman's test was calculated for the BBS, the TUG and the Postural Stability test, and the Cochran's Q was calculated for self-perceived unsteadiness and self-reported falls. After showing statistical significance across the four test occasions, *post-hoc* analyses of the Friedman's test and the Cochran's Q-test were done using the Wilcoxon Signed Rank Test for individual comparisons between the four test occasions. The Kruskal–Wallis test was calculated for between-group analysis of variance for three age groups. After showing statistical significance, a *post-hoc* analysis was done with the Mann–Whitney *U*-test. To check for Type 1 error at multiple comparisons *post-hoc*, a Bonferroni adjusted alpha value was set at $p < 0.017$. A drop-out analysis was computed based on patients who had dropped out by the five-year follow-up (BBS).

Results

Baseline population characteristics

Demographic and clinical characteristics of patients with PD and healthy controls at baseline are presented in Table 1.

The patients performed less well for all three outcome measures, the BBS, the TUG, and the Postural Stability test, compared with the controls ($r = 0.32–0.36$, indicating medium effect sizes) as shown in Table 2. Among patients, there was a correlation between the TUG and the Postural Stability test ($rho = 0.38$, $p < 0.001$), the BBS and the Postural Stability test ($rho = -0.44$, $p < 0.001$), and the BBS and the TUG ($rho = -0.77$, $p < 0.001$).

Seventy-eight percent (97 of 125) of the patients and 21% (6 of 29) of the controls reported self-perceived unsteadiness. The group difference in self-perceived unsteadiness was significant ($p < 0.001$, $phi = 0.47$). Thirty-one percent of the patients and 24% of the controls reported at least one fall, a difference which was not significant.

Comparisons between age groups showed that the youngest patients (<65 years) had the best balance (higher BBS scores) and the best mobility (fastest time on the TUG) both when compared with the patients aged 65–75 years and when compared with the oldest group (>75 years). The most adequate postural reactions (lower Postural Stability scores) were seen in the youngest group when compared with the oldest group (Table 3).

Changes over time

After one year with medication, the patients performed better on the BBS, the TUG and the Postural Stability test ($r = 0.16–0.24$, indicating small effect sizes) as shown in Table 4. From baseline to the five-year follow-up, there was a significant deterioration for the BBS and the TUG when tested both with and without medication ($r = 0.24–0.37$, indicating small to medium effect sizes).

The 35 patients who completed the questions about self-perceived unsteadiness and self-reported falls on all four occasions are shown in Figure 2. Pairwise comparisons showed a difference between how many patients who reported falls at baseline compared with the five-year follow-up ($p = 0.02$, $r = 0.20$). All other pairwise comparisons about self-perceived unsteadiness and self-reported falls between baseline and follow-ups were not significant.

Comparisons between tests with and without medication showed that medication improved the performance on the TUG

Table 1. Demographic and clinical characteristics of patients with Parkinson's disease and healthy controls at baseline.

	PD ($n = 145$)	HC ($n = 31$)
Male/female (%)	86/59 (59/41)	17/14 (55/45)
Age at first visit Mean (SD)	71 (10)	68 (7)
Age at first noted symptoms Mean (SD)	69 (10)	
MMSE score Median (IQR)	29 (28–30)	29 (28–30)
UPDRS part III total score Median (IQR)	26 (19–35)	
H&Y-stage Median (IQR)	2 (2–3)	

PD: Parkinson's Disease; HC: Healthy controls; SD: Standard deviation; IQR: Interquartile ranges (25th–75th percentiles); MMSE: Mini Mental State Examination Score; UPDRS: Unified Parkinson's Disease Rating Scale; H&Y: Hoehn and Yahr.

Table 2. Balance and mobility characteristics for patients with Parkinson's disease and healthy controls at baseline.

	PD	HC	Median difference in change (95% CI)	Effect Size *r*	*p* Value
BBS	$n = 131$	$n = 31$	−2 (−3 to −1)	0.36	<0.001*
Median (IQR)	54 (49–55)	56 (54–56)			
TUG	$n = 126$	$n = 30$	2 (1 to 3)	0.32	<0.001*
Median (IQR)	8 (7–10)	7 (6–8)			
Postural stability	$n = 145$	$n = 31$	0 (0 to 1)	0.35	<0.001*
Median (IQR)	0 (0–2)	0 (0–0)			

PD: Parkinson's Disease; HC: Healthy controls; BBS: Berg Balance Scale; TUG: the Timed Up and Go-test; IQR: Interquartile ranges (25th–75th percentile). *Significance level $p < 0.05$.

Table 3. *Post-hoc*. Comparisons by age groups at baseline.

	PD <65 year	PD 65–75 years	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS	$n = 43$	$n = 37$	2 (1 to 4)	0.51	<0.001*
Median (IQR)	56 (54–56)	53 (50–55)			
TUG	$n = 42$	$n = 35$	−2 (−3 to −1)	0.46	<0.001*
Median (IQR)	6.5 (6–8)	9 (7–11)			
Postural stability	$n = 43$	$n = 37$	0 (0 to 0)		0.06
Median (IQR)	0 (0–1)	0 (0–1)			
	PD 65–75 years	PD >75 year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS	$n = 37$	$n = 51$	2 (0 to 4)		0.029
Median (IQR)	53 (50–55)	50 (46–54)			
TUG	$n = 35$	$n = 49$	−1 (−2 to 0)		0.064
Median (IQR)	9 (7–11)	9 (8–13)			
Postural stability	$n = 37$	$n = 65$	0 (−1 to −0)		0.018
Median (IQR)	0 (0–1)	1 (0–2)			
	PD <65 year	PD >75 year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS	$n = 43$	$n = 51$	5 (3 to 7)	0.63	<0.001*
Median (IQR)	56 (54–56)	50 (46–54)			
TUG	$n = 42$	$n = 49$	−3 (−4 to −2)	0.60	<0.001*
Median (IQR)	6.5 (6–8)	9 (8–13)			
Postural stability	$n = 43$	$n = 65$	−1 (−1 to 0)	0.38	<0.001*
Median (IQR)	0 (0–1)	1 (0–2)			

BBS: Berg Balance Scale; TUG: the Timed Up and Go test; IQR: Interquartile ranges (25th–75th percentile). Corrected significance level $p < 0.017$.

Table 4. *Post-hoc*. Individual pairwise analysis between baseline and follow-ups, with and without medication. The number (*n*) of patients with Parkinson's disease who participated at both baseline and follow-up is given.

	Baseline	1-year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS med-on Median (IQR)	*n* = 88 54 (51–55)	*n* = 88 54.5 (52–56)	0.5 (0 to 1)	0.18	0.015*
BBS med-off Median (IQR)	*n* = 88 54 (51–56)	*n* = 88 54 (51–56)	0 (0 to 0.5)		0.398
TUG med-on Median (IQR)	*n* = 85 8 (7–10)	*n* = 85 7 (6–9)	−0.5 (−1 to 0)	0.24	0.001*
TUG med-off Median (IQR)	*n* = 88 8 (7–10)	*n* = 88 7 (6–9)	−0.5 (−0.5 to 0)		0.173
Postural stability med-on Median (IQR)	*n* = 131 0 (0–1)	*n* = 131 0 (0–1)	0 (0 to 0)	0.16	0.011*
	Baseline	3-year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS med-on Median (IQR)	*n* = 81 54 (52–56)	*n* = 81 54 (52–56)	0 (−0.5 to 0.5)		0.310
BBS med-off Median (IQR)	*n* = 68 55 (52–56)	*n* = 68 54.5 (51–56)	−0.5 (−1.5 to 0)		0.034
TUG med-on Median (IQR)	*n* = 74 8 (6–9)	*n* = 74 7 (7–9)	0 (−0.5 to 0)		0.341
TUG med-off Median (IQR)	*n* = 63 8 (6–9)	*n* = 63 7 (7–9)	0 (−0.5 to 0.5)		0.748
Postural stability med-on Median (IQR)	*n* = 119 0 (0–1)	*n* = 119 0 (0–1)	0 (0 to 0)		0.725
	Baseline	5-year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS med-on Median (IQR)	*n* = 61 55 (53–56)	*n* = 61 54 (51–56)	−1 (−2 to 0)	0.24	0.008*
BBS med-off Median (IQR)	*n* = 53 55 (52–56)	*n* = 53 53 (49–56)	−1.5 (−3 to −1)	0.37	<0.001*
TUG med-on Median (IQR)	*n* = 57 7 (6-9)	*n* = 57 8 (7–9)	1 (0.5 to 1.5)	0.27	0.004*
TUG med-off Median (IQR)	*n* = 46 7 (6–9)	*n*=46 8 (7–10)	0.5 (0 to 1)	0.30	0.004*
Postural stability med-on Median (IQR)	*n* = 108 0 (0–0)	*n* = 108 0 (0–0)	0 (0 to 0)		0.431

BBS: Berg Balance Scale; TUG: the Timed Up and Go test; IQR: Interquartile ranges (25th–75th percentile); med-on, with medication; med-off, without medication. *Corrected significance level $p < 0.017$.

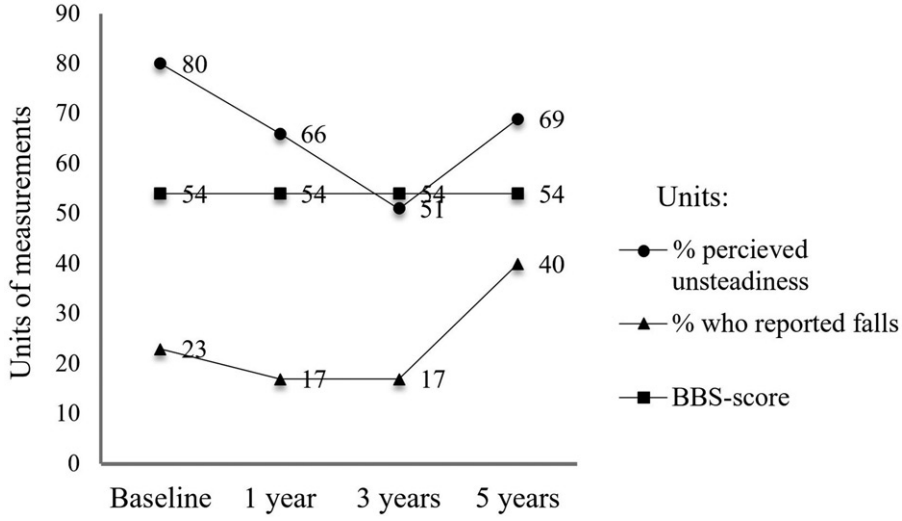

Figure 2. Percentage of 35 patients who completed the questions on all four occasions regarding perceived unsteadiness and reported at least one fall during the last year and their median score of the Bergs Balance Scale (BBS) at follow-ups.

at the three-year follow-up (small effect size) and on the BBS at the five-year follow-up (medium effect size), as shown in Table 5.

At the five-year follow-up, the oldest group (>75) showed a poorer result for all three outcome measures compared with the youngest group (<65 years), as presented in Table 6.

Drop-out analysis

The drop-outs were nine-years older than the group who participated at the five-year follow-up (75 years and 66 years, respectively, $p < 0.001$, $r = -1.15$). The drop-outs had more symptoms according

Table 5. Comparisons between measurements of patients with Parkinson's disease performed with and without medication at follow-ups.

1-year	Med-on	Med-off	Median difference in change (95% CI)	Effect size *r*	*p* Value 1-year
BBS Median (IQR)	*n* = 75 55 (52–56)	*n* = 75 54 (52–56)	0 (–0.5 to 0)		0.287
TUG Median (IQR)	*n* = 78 7 (6–9)	*n* = 78 7 (6–9)	0.5 (0 to 0.5)		0.074
3-year	Med-on	Med-off	Median difference in change (95% CI)	Effect size *r*	*p* Value 3-year
BBS Median (IQR)	*n*=65 54 (52–56)	*n*=65 54 (51–56)	–0.5 (–1 to 0)		0.079
TUG Median (IQR)	*n*=60 7 (6–9)	*n*=60 7 (7–9)	0.5 (0 to1)	0.26	0.005*
5-year	Med-on	Med-off	Median difference in change (95% CI)	Effect size *r*	*p* Value 5 years
BBS Median (IQR)	*n* = 51 54 (51–56)	*n* = 51 53 (49–56)	–1 (–1.5 to –0.5)	0.31	0.001*
TUG Median (IQR)	*n* = 46 7.5 (6–9)	*n* = 46 8 (7–10)	0.5 (0 to 0.5)		0.085

BBS: Berg Balance Scale; TUG: the Timed Up and Go test; med-on: with medication; med-off: without medication; IQR: Interquartile ranges (25th–75th percentile). *Significance level $p < 0.05$.

Table 6. *Post-hoc*. Comparisons by age groups at the five-year follow-up.

	PD <65 year	PD 65–75 year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS Median (IQR)	*n* = 33 55 (54–56)	*n* = 19 53 (50–54)	2 (0 to 3)		0.018
TUG Median (IQR)	*n* = 33 7 (6–8)	*n* = 19 8 (7–13)	–2 (–3 to –1)	0.38	0.006*
Postural stability Median (IQR)	*n* = 43 0 (0–0)	*n* = 32 0 (0–0)	0 (0 to 0)		0.134
	PD 65–75 year	PD >75 year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS Median (IQR)	*n* = 19 53 (50–54)	*n* = 10 47.5 (40–55)	5 (–1 to 10)		0.134
TUG Median (IQR)	*n* = 19 8 (7–13)	*n* = 9 9 (8–10)	0 (–2 to 2)		0.654
Postural stability Median (IQR)	*n* = 32 0 (0–0)	*n* = 33 1 (0–2)	–1 (–2 to 0)	0.44	<0.001*
	PD <65 year	PD >75 year	Median difference in change (95% CI)	Effect size *r*	*p* Value
BBS Median (IQR)	*n* = 33 55 (54–56)	*n* = 10 47.5 (40–55)	7 (1 to 11)	0.44	0.004*
TUG Median (IQR)	*n* = 33 7 (6–8)	*n* = 9 9 (8–10)	–2 (–3 to –1)	0.43	0.006*
Postural stability Median (IQR)	*n* = 43 0 (0–0)	*n* = 33 1 (0–2)	–1 (–2 to 0)	0.57	<0.001*

BBS: Berg Balance Scale; TUG: the Timed Up and Go test; IQR: Interquartile ranges (25th–75th percentile) *Corrected significance level $p < 0.017$.

to the Hoehn and Yahr scale than those who participated (2.5 and 2 median scores, respectively; $p = 0.002$, $r = 0.25$). The drop-outs performed significantly less well for the BBS at baseline (median 51; $p < 0.001$, $r = 0.39$). At the five-year follow-up, 21 of 145 patients had declined and 16 had decreased (Figure 1).

Discussion

Interestingly, the patients in our study already had minor balance impairment at their first visit to the neurological clinic. The patients performed less well on the BBS, the TUG, and the Postural Stability test compared with the controls. Despite statistical significance, the median differences were generally small and in the case of the Postural Stability test, the results were the same for both patients and controls. However, among the patients, especially those aged over 75, the results differed widely. The results confirm the heterogeneity of the disease and that increasing age has a negative impact on balance and mobility. The picture of impaired balance already at baseline was also confirmed by a higher percentage of patients who reported self-perceived unsteadiness compared with the control group. This finding shows that even though balance and mobility impairments were relatively small according to the three clinical outcome measures, the patients felt unsteady.

To our knowledge, no other study has presented data on self-reported falls in patients with PD at their first visit to a neurological clinic. However, in one cohort study of newly diagnosed patients, recruited within 4 months of receiving their PD diagnosis, 20.7% reported previous falls. In the following 12 months, the patients who reported falls increased to 36.9% [32]. The occurrence of at least one fall in the past year is a strong predictor of future falls and it is therefore of great importance to ask the patients about unsteadiness and falls [49,50]. Similar results to those of our control group members have been reported among persons aged 70 years [51].

The differences in median between patients and controls in both the BBS and the TUG were very small. Normative data on the BBS score and the TUG on healthy individuals gave rather similar

results to those of both the patients and the controls in our study [52–54]. The age groups analysis indicated clearly that age at the first visit to the neurological clinic had a huge impact on balance and mobility. The youngest patients had the best balance (BBS), fastest mobility (TUG) and the most accurate postural responses. Notably, the patients in the oldest group (>75 years) had a larger interquartile range in the performance time of the TUG compared with the younger groups. It could be useful to consider the minimal detectable change which has been calculated to be 3.5 s [55] up to 11 s [41] for patients with PD, which demonstrates the variety of the TUG performance in patients with PD.

The Postural Stability test in the UPDRS III is widely used to evaluate the typical loss of postural reflexes and it is a key component of the neurological examination in PD [56,57]. As expected, none of the controls in this study had balance impairment according to the Postural Stability test. Among patients, the median score was 0 on the Postural Stability test but with a wider interquartile range (0–2) compared with the controls. The fact that a few patients had quite severe postural responses could be because some patients may have had the disease for several years before being diagnosed. The case-finding strategy in this study included contacts or visits to institutional homes, aiming at complete case ascertainment of previously undiagnosed PD patients.

The pairwise comparisons showed that the time to perform the TUG was slightly improved after one year with medication ($p = 0.001$, $r = 0.24$). The patients had not started their antiparkinsonian medication at baseline and at the one-year follow-up, the parkinsonian medication is likely to have had an impact on bradykinesia in general [58]. The improved BBS result after one year may also be an effect of medication. The result of the Postural Stability test had also improved at one-year follow-up which is somewhat surprising because levodopa is not expected to have an effect on postural responses [17]. However, the effect sizes were generally small for all measurements ($r = 0.16$–0.24). At five-year, the balance and mobility had worsened (lower BBS scores and slower TUG time) which was expected due to the progression of the disease.

The result of the Postural Stability test was preserved after five years, which must be considered as unexpected given the progressive nature of the disease. However, the reduced sensitivity of the test was probably a contributing factor to the result.

To sum up, there were generally small but still statistically significant deteriorations on the BBS and the TUG and maintained postural responses on the Postural Stability test during the first five years, although with substantial individual differences. One plausible explanation of the small differences is that the drop-out rate was more pronounced in the oldest patients at all follow-ups, i.e., the group with the most severe balance impairments. Thus, balance impairment in PD is probably more pronounced during the first five years than this study has indicated.

Comparisons between measures with and without medication showed that there were only improvements in two out of six comparisons; TUG at the three-year follow-up and BBS at the five-year follow-up, where the result was better with parkinsonian medication (levodopa or dopamine agonists). The medication is expected to have an impact on bradykinesia [58], and therefore it was somewhat surprising that the improvement was only seen in one occasion (the three-year follow-up) for the TUG. For the BBS, there was only an improvement at the five-year follow-up with medication. Previous studies that have evaluated balance in patients with PD with and without medication have shown improvements in mean BBS scores from 52 to 53.5 [19], 53 to 54 [20], and 31.7 to 42.7 [18]. Other studies have not shown effects on balance postural adjustments with levodopa [15,17,59]. In summary, our results confirm the findings of the above-mentioned studies that levodopa has only limited effect on balance impairment.

Self-reported falls increased after five years which was expected as falling is a major problem for patients in the middle and late phases of the disease [60,61]. There were no significant changes between baseline and the one-year and three-year follow-ups, which may have to do with a large number of dropouts.

Limitations

One limitation of this study is the drop-out rate which makes it difficult to generalise and assume the results apply to the whole PD population. However, in a prospective study on a population with a mean age of 71 years, who suffer a neurodegenerative disease, drop-outs are expected and difficult to avoid. The drop-outs were about nine years older, performed significantly worse on the BBS and were at a later stage of the disease according to the Hoehn and Yahr scale. Hence, the oldest and the most impaired patients did not participate in the follow-ups. Another aspect is that the patients at baseline were receiving information about the importance of physical exercise and were given instructions on how to do various balance exercises. These kinds of interventions may have resulted in a better balance over-time. However, we did not check to what extent the patients exercised.

The BBS has a limitation in detecting small balance impairment, a ceiling effect [62–64]. Perhaps there would have been larger balance differences between the patients and controls at baseline and larger differences over-time with a more sensitive outcome measure. The Mini-BESTest has not shown the same ceiling effect and is better for distinguishing between those with and without postural response deficits in early PD [62,63,65,66]. The Postural Stability test (pull-test) has shown limitations in sensitivity and the test is not correlated with fall-history (like the BBS and TUG) [67]. An alternative and better test of postural responses is the Push and Release test which provides higher sensitivity and correlates better with self-reported falls [47]. The Postural Stability test in this study was based on the version of the UPDRS that existed at the time when the NYPUM study was initiated [34]. In particular, Items 2 and 3 have been changed in the new version [68]. Another limitation at baseline was that the control group was relatively small. Furthermore, when tested without medication, the patients in our study may still have been influenced by their medication despite not taking any levodopa for at least 12 h and dopamine agonists for three days. A longer period of time without medication may be needed to achieve a true off-medication result. Finally, the use of the non-parametric method of the repeated measures analysis of variance (the Friedman's test) limits the use of any covariates to be potentially controlled for.

The largest strength of the present study is its design. It is unique to have data collected from a community-based study population at the initial visit to the neurological clinic and to follow the patients for several years. The prospective design of the study has high scientific relevance and provides new knowledge about balance in PD during the first years of the disease. Another strength is that the same assessors, with a few exceptions, carried out all of the assessments during the five-year period.

Conclusion

This study showed that a majority of the patients with PD felt unsteady at their first visit to a neurological clinic although their

clinical outcome measures indicated minor balance and mobility impairments. Balance (measured with the BBS) and functional mobility (measured with the TUG) worsened during the first five years after diagnosis, both when tested with and without medication. The largest impairments were seen in the oldest patients. A significant drop-out rate, especially in the elderly group, affected the result and may indicate that balance impairment in early PD is probably more pronounced in the population as a whole. Further studies will be needed to confirm that there are already balance impairments at diagnosis. Our study is in line with other studies that parkinsonian medication has a limited effect on balance.

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