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Parkinsonian Signs are a Risk Factor for Falls

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Abstract

Background—Parkinsonian signs are common, non-specific findings in older adults and associated with increased rates of dementia and mortality. It is important to understand which motor outcomes are associated with parkinsonian signs.

Objectives—To determine the role of parkinsonian signs on fall rates among older adults.

Methods—We conducted a longitudinal study of primary care patients from the University of Pennsylvania Health System. Adults over 55 years were assessed at baseline through surveys and a neurological examination. We recorded falls over the following 2 years. Parkinsonian signs were defined as the presence of 2 of 4 cardinal signs. Incident falls were compared between subjects with and without parkinsonian signs, and modified Poisson regression used to adjust for potential confounders in the relationship between parkinsonian signs and falls.

Results—982 subjects with a mean age of 68 (s.d. 8.8) years participated. 29% of participants fell and 12% exhibited parkinsonian signs at baseline. The unadjusted RR for falls among individuals with parkinsonian signs was 1.36 (95% CI 1.05–1.76, $p=0.02$). After adjusting for age, cognitive function, urinary incontinence, depression, diabetes, stroke and arthritis, individuals with parkinsonian signs were still 38% more likely to fall than those without parkinsonian signs (RR 1.38, 95% CI 1.04–1.82; $p=0.03$). Falls among those with parkinsonian signs were more likely to lead to injury (53% vs 37%; $p=0.04$).

Conclusions—Parkinsonian signs are a significant, independent risk factor for falls. Early detection of this clinical state is important in order to implement fall prevention programs among primary care patients.

Keywords

parkinsonism; postural stability; cohort studies; outcome research

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Conflict of interest statement

The authors report no financial or personal conflicts of interest.

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Introduction

Parkinsonian signs are an indicator of basal ganglia dysfunction characterized by bradykinesia, rigidity, tremor and postural/gait changes. They are similar, but often milder signs than seen in idiopathic Parkinson's disease (PD) and without the supporting features of asymmetric onset and response to levodopa[1]. Parkinsonian signs (PS) are not only common among older adults with prevalence estimates that range from 15–40%[2, 3], but their importance as an early indicator of poor outcomes is growing. Studies show that these signs are progressive and predict a greater risk of dementia and mortality[2, 4]. While people with idiopathic Parkinson's disease (PD) and other parkinsonian syndromes (Progressive Supranuclear Palsy, Multiple System Atrophy, dementia with Lewy bodies) have a well-established increased risk of falls[5, 6], the relationship between PS and fall risk is less clear.

Falls in older adults are common and costly, yet often preventable[7]. Despite increasing recognition of the impact of falls, fall-related morbidity and mortality continue to rise[8]. Often no single etiology is identified for recurrent fallers. The multifactorial etiology of falls combined with their high prevalence, shared risk factors with other conditions of aging and associated high morbidity and mortality, have led to the categorization of falls as a geriatric syndrome[9]. However, disentangling the often over-lapping and synergistic etiologies of falls will help in the development of targeted preventive therapies and earlier implementation of fall reduction programs.

PS may be one such fall risk factor though it is not routinely assessed in a primary care setting. In cross-sectional analyses, mild parkinsonian signs are associated with subjective balance complaints, a greater need for assistive walking devices and impaired function on a variety of objective gait performance tasks[10–12]. Furthermore, Buracchio and colleagues found that worsening parkinsonian sign scores were associated with an increased odds of falling[13].

In this study we sought to estimate the risk of falls among a diverse sample of community-dwelling older adults without previously diagnosed Parkinson's disease or dementia, and determine the role of PS on fall risk.

Methods

Ethics statement

The study protocol was approved by the University of Pennsylvania Institutional Review Board. We obtained written informed consent from all participants.

Study design and Sample

This was a longitudinal study of primary care patients from the Philadelphia Healthy Brain Aging (PHBA) cohort at the University of Pennsylvania Health System. Subjects were recruited from primary care waiting rooms from January 2010 through December 2012. Follow-up data was collected every 6 months for the next two years. Subjects were all > 55 years of age and English-speaking. We excluded people with a prior diagnosis of

Parkinson's disease or dementia, and those with severe cognitive impairment, defined as a Montreal Cognitive Assessment (MoCA) score of ≤ 15 [14].

Data Collection

At the baseline visit, we collected demographics including age, gender, race and highest level of education completed. We obtained medical history both from self-report and review of the medical record. Lastly, we collected cognitive and functional measures including: Katz Activities of Daily Living Scale, MoCA, 5-item Geriatric Depression Scale (GDS) and Timed Up and Go (TUG).

Every 6 months for a period of 2 years, we assessed for falls by a standardized phone interview with participants and review of the medical record. Participants were also instructed to call the research team to report any fall. Falls were defined as unintentionally coming to rest on the ground or at some other lower level, not as a result of a major intrinsic event (e.g. stroke or syncope) or overwhelming hazard (i.e. hazard that would result in a fall in most young, healthy people)[7]. If a fall occurred, additional data regarding the fall characteristics were obtained.

Neurological examination

A standardized, modified 18-item version of the motor portion of the Unified Parkinson's Disease Rating Scale (UPDRS)[15] was performed by both a trained research coordinator and movement-disorders neurologist and videotaped. The 18 items of the UPDRS were facial expression, tremor at rest, finger taps (right and left), rapid alternating movements (right and left), leg agility (right and left), rigidity (neck, right and left arm, right and left leg), posture, body bradykinesia and gait (shuffling, arm swing and turning). Each item was scored from 0 (normal) to 4 (severely impaired).

The movement-disorders neurologist conducted the UPDRS on 35% (n=348) of the sample in-person, and assessed the remaining 65% (n=634) by videotape review. Video examinations of parkinsonism can detect Parkinson's disease with high sensitivity and specificity[16, 17]. Unfortunately, video examinations lack assessment of rigidity, one of the cardinal parkinsonian features. We measured the agreement between the trained research coordinator and neurologist assessment of rigidity for the 348 subjects that both evaluated. Since agreement was high (Kappa 0.56; 95% CI 0.47–0.65)[18], we imputed the coordinator's assessment of rigidity to determine the rigidity sign score for the 634 cases that were only assessed by the neurologist via video.

Case definition

There are several ways to quantify or categorize PS. As our primary analysis, we chose to categorize PS as present or absent based on previously established criteria that are more specific to parkinsonism[2]. Briefly, the 18-items of the UPDRS were grouped into the 4 cardinal Parkinsonian sign categories as follows: 1) bradykinesia – facial expression, body bradykinesia, finger taps, rapid alternating movements and leg ability; 2) rigidity – neck, arms and legs; 3) gait – posture, shuffling, arm swing and turning; 4) tremor – jaw, arms and legs. A total score for each cardinal sign category was calculated. A score of two or more

within the cardinal sign categories of bradykinesia, rigidity or gait, or a score of one within tremor was required to indicate the presence of that parkinsonian sign category. PS were then defined as the presence of two or more parkinsonian sign categories. In secondary sensitivity analyses we evaluated the relationship between falls and PS among: 1) participants with an in-person MD exam only; and 2) PS defined as the total score on the UPDRS (potential range 0–76)

Data Analysis

Participants with missing baseline UPDRS data were excluded. Chi squared, student t-tests and Wilcoxon rank sum tests were used to compare demographic and clinical characteristics between subjects with and without PS. A modified Poisson regression was used to analyze the relationship between PS and falls, and adjust for possible confounders in the relationship. Any variable with a p-value <0.25 in bivariate analysis or a previously established fall risk factor was included in the multivariate model. A p-value of <0.05 was used as a cut-off for significance.

Results

A total of 1100 subjects were recruited, and we analyzed data for 982 (89%; 8 lost to follow-up/withdrawn, 26 excluded due to PD or dementia, 84 missing or incomplete baseline data) of the participants. See Figure 1 for the flow of study participants.

The sample was 56.6% (n=554) women and 51.5% (n=506) African-American with a mean age of 68.2 years (s.d. 8.8). A total of 12.3% (n=121) of the cohort exhibited PS at baseline, and 28.5% (n=280) experienced a fall during the follow-up period. Only 13 subjects called in to report a fall (4.6%).

Individuals with PS were more likely to be older, African-American, completed fewer years of education and have a history of stroke, arthritis and urinary incontinence (Table 1). In addition, individuals with PS had lower cognitive scores, greater functional disability as measured by basic ADLs and longer timed up and go times.

The unadjusted RR for falls among individuals with PS was 1.36 (95% CI 1.05–1.76, p=0.02). After controlling for demographics and clinical fall risk factors such as prior stroke, diabetes, arthritis, urinary incontinence, cognitive impairment, depression, timed up and go and ADLs, individuals with PS were still 38% more likely to fall than those without PS (RR 1.38, 95%CI 1.04–1.82; p=0.03) (Table 2). Other factors associated with a higher risk of falls were female sex (RR 1.38, 95%CI 1.12–1.70; p<0.01), history of arthritis (HR 1.47, 95%CI 1.19–1.81; p<0.01), greater functional impairment by ADLs (HR 1.10, 95%CI 1.00–1.20; p=0.05) and slower TUG scores (RR 1.04, 95% CI 1.00–1.05; p=0.04).

In secondary analyses, when only including participants who were examined in person by the physician, the relationship between PS and falls remained similar (RR 1.41, 95%CI 0.91–2.16; p=0.12). When analyzed as a continuous measure, the median parkinsonian sign score was 1 (IQR 0–4). For every one point increase in parkinsonian sign score, there was a non-significant 4% increase in the risk of falls (RR 1.04, 95%CI 0.98–1.13; p=0.19). There

was no significant association between falls and the individual PS categories (bradykinesia, rigidity, tremor and gait).

Additionally, the fall characteristics differed between individuals with and without PS (Figure 2). Individuals with PS were just as likely to have fallen more than once than those without PS. However, they were significantly more likely to be injured during the fall (53% vs. 37%; $\chi^2 = 4.25$; $p=0.04$) and had greater utilization of emergency services related to the fall (ER visits 40% vs. 25%; $\chi^2 = 4.33$ $p=0.04$; PCP visits 56 vs. 43; $p=0.12$).

Discussion

While there are a number of etiologies for falls, PS may represent one of these underlying mechanisms. We found that individuals with PS had a significantly higher rate of falls even after controlling for standard measures of mobility that are often used to assess fall risk. Additionally, falls among individuals with PS led to higher rates of injury and emergency room visits which further emphasize the clinical import of PS. In the long term, understanding the underlying pathophysiology of PS will help guide targeted prevention and therapeutics of these signs themselves. In the short term, it is important to recognize PS as a predictor of falls in the clinical fall risk assessment.

An earlier study demonstrated that progression of parkinsonism over time was associated with falls in a cohort of even older adults (average age 80) from the Chicago-area[13]. Our findings corroborate this earlier study in a younger sample of older adults with just the presence of PS. In addition to falls, PS has been associated with functional disability both in our findings and prior studies[12, 19]. Given the high baseline prevalence of PS in the community, and the increasing prevalence with older age, it is increasingly important to assess for PS and PS-related morbidity in an older adult population.

Unfortunately, the identification of PS compared to signs of normal aging can be challenging[1, 20]. In-person physician examination has higher sensitivity and specificity to detect parkinsonism when compared to cheaper and more time-efficient assessments such as screening questionnaires[21]. However, alternative assessments may also be viable. Video-taped examinations based on the UPDRS that are reviewed and scored later by neurologists can also accurately measure parkinsonism at reduced cost and travel time for the physician[16, 17]. In addition, nurses' assessments of parkinsonism using the UPDRS is both reliable and accurate when compared to physician exam[22]. We demonstrate that a video assessment of a modified UPDRS with the aid of an on-site trained non-health professional captured PS as well.

One of the standard measures of the clinical fall risk assessment is the timed up and go test or variations of this test such as standing unassisted from a sitting position[23, 24]. However, the presence of PS contributed to fall risk in addition to their timed walk results. While increased PS scores have been associated with slower timed gait test[12], our results suggest that it is not just the slower speed of gait that contributes to falls in PS.

Understanding the mechanism through which PS leads to falls independent of slower gait speed is important for fall prevention. Some studies have found that targeting deficits

common in a specific clinical sub-population may reduce falls. As an example, donepezil has been found to reduce falls in Alzheimer's patients[25], while exercise reduces falls in early stage PD patients[26]. In a primary care population, where there is no single predominant factor contributing to falls, understanding the independent contributions of different risk factors will allow us to create targeted fall prevention programs unique to each patient. More immediately, our results suggest that including the assessment of PS in a fall risk assessment in the primary care setting is an opportunity to identify high-risk fallers earlier and enable earlier implementation of fall prevention interventions.

While fall prevention programs targeting balance and mobility may help reduce falls related to PS, PS has also been shown to be associated with a number of other adverse outcomes including higher mortality[2] and dementia[4]. Ideally the prevention of PS itself would reduce the rate of all of these adverse outcomes. Evidence suggests that the underlying pathology in PS is, in part, related to the sequelae of vascular disease, which may be preventable[27]. However, studies have also found an association between PS and both Lewy Bodies and neurofibrillary tangles which may indicate that PS are early signs of a neurodegenerative disease such as Parkinson's disease or Progressive Supranuclear Palsy[28, 29].

The study has several limitations to note. We collected fall data in 6-month intervals, which is subject to recall bias. An earlier report suggested that the recall of a fall in the past 12 months has very high specificity (91–95%) and high sensitivity (80–89%) when compared to more intensive methods of follow-up [30]. Nevertheless, missed cases of falls would attenuate the relationships between potential fall risk factors and falls, and bias our results towards the null. In addition, our method to assess PS took advantage of the more practical assessment of a video examination for the majority of individuals. This could lead to misclassification of some cases. To limit this bias, only a single, extensively trained research coordinator completed the UPDRS examination. Furthermore, even when only the 35% (n=348) of individuals who were examined in-person by the neurologist were evaluated, the results were the similar but underpowered. There were several additional fall risk factors that were not accounted for in the analysis (e.g. vision loss, polypharmacy). Lastly, the cohort consisted of older adults attending a primary care clinic, which may differ relative to the general population due to greater rates of co-morbidity. On the other hand, the primary care clinic is an ideal setting to implement interventions to reduce falls in older adults.

Interventions aimed at reducing the risk of falls from any cause have been tested, with varying levels of success[31] and can be both timely and costly[32]. As a result, targeting successful fall prevention programs to those at a greater risk of falling, such as those with PS, may yield the highest benefit. Ultimately, there is a pressing need for the development of treatments to reduce the risk of PS itself.

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Highlights

- The clinical importance of parkinsonian signs is growing
- 12% of our sample showed these signs
- Individuals who exhibited parkinsonian signs had a greater fall risk
- Falls among individuals with parkinsonian signs more often led to injury

Figure 1.
Flow of study participants

Figure 2.

Characteristics of falls between individuals with and without parkinsonian signs (PS)

* $p < 0.05$; ER = Emergency room; PCP = Primary care physician

Table 1

Demographic, clinical and functional characteristics of Philadelphia Healthy Brain Aging cohort by baseline parkinsonian sign (PS) status

<i>Variable</i>	<i>– PS at baseline (n= 861)</i>	<i>+ PS at baseline (n= 121)</i>	<i>p-value</i>
Mean age (sd)	67.3 (8.3)	74.5 (9.6)	<0.001
% Race			
<i>White</i>	47.0	35.5	
<i>African-American</i>	49.7	64.5	
<i>Other</i>	3.3	0	<0.01
% Sex			
<i>Female</i>	56.6	55.4	0.81
% Education			
<i>Less than High School</i>	10.2	30.6	
<i>High School</i>	27.1	32.2	
<i>Some college or more</i>	62.7	37.2	<0.001
% History of diabetes	28.2	28.9	0.87
% History of stroke	7.3	14.1	0.01
% History of arthritis	27.5	36.4	0.04
% Urinary incontinence ¹⁰	14.6	22.0	0.04
Median Activities of daily living (IQR) ¹⁰	0 (0–0)	0 (0–1)	<0.01
Mean MoCA score (sd)	25.7 (3.2)	23.6 (3.8)	<0.001
Median GDS score (IQR)	0 (0–1)	0 (0–2)	0.34
Median Timed up and Go, seconds (IQR) ³	8.1 (7.0–9.9)	10.7 (8.2–13.6)	<0.001

* Superscript indicates number of missing values for each variable

Table 2

Predictors of falls in univariate and multivariate analysis

<i>Covariate</i>	<i>Univariate</i>			<i>Multivariate^d</i>		
	<i>RR</i>	<i>95% CI</i>	<i>p</i>	<i>RR</i>	<i>95% CI</i>	<i>p</i>
Parkinsonian Signs	1.36	1.05–1.76	0.02	1.38	1.04–1.82	0.03
Age	1.00	0.99–1.01	0.58	1.00	0.99–1.01	0.90
Race						
<i>White (reference)</i>	--	--	--	--	--	--
<i>African-American</i>	0.85	0.69–1.03	0.11	0.88	0.69–1.13	0.31
<i>Other</i>	1.40	0.89–2.20	0.14	1.40	0.83–2.38	0.21
Female	1.39	1.13–1.71	<0.01	1.38	1.12–1.70	<0.01
Education						
<i>Less than high school (reference)</i>	--	--	--	--	--	--
<i>High school</i>	0.69	0.49–0.97	0.03	0.72	0.51–1.02	0.06
<i>Some college or more</i>	0.96	0.72–1.28	0.79	1.13	0.81–1.56	0.49
History of diabetes	0.96	0.77–1.20	0.72	0.92	0.73–1.16	0.53
History of stroke	1.11	0.79–1.56	0.16	1.13	0.81–1.59	0.49
History of arthritis	1.57	1.29–1.91	<0.01	1.47	1.19–1.81	<0.01
Urinary incontinence	1.43	1.13–1.80	<0.01	1.15	0.88–1.51	0.31
Activities of daily living	1.19	1.11–1.27	<0.01	1.10	1.00–1.20	0.05
MoCA score	1.01	0.98–1.04	0.52	1.03	0.99–1.07	0.12
GDS score	1.13	1.06–1.22	<0.01	1.08	1.00–1.18	0.06
Timed Up and Go	1.04	1.03–1.07	<0.01	1.03	1.00–1.05	0.04

^a All variables in the table were used as covariates in the multivariate model