



Associations among falls, gait variability, and balance function in idiopathic normal pressure hydrocephalus

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ARTICLE INFO

Keywords:

Fall risk
Idiopathic normal pressure hydrocephalus
Gait variability
Balance function
Gait disturbance
Balance disturbance

ABSTRACT

Objectives: The factors influencing falls in idiopathic normal pressure hydrocephalus (iNPH) remain unclear, although iNPH-associated gait and balance disturbances can lead to an increased risk of falls. This study aimed to investigate the associations among fall status, gait variability, balance function in iNPH, and to identify fall-related factors in iNPH.

Patients and methods: Sixty-three patients with iNPH with a positive cerebrospinal fluid tap test result according to the iNPH diagnosis criteria participated in this prospective cross-sectional study. Patients were assessed using the 10-meter walk test (10MWT), the Functional Gait Assessment (FGA), the Berg Balance Scale (BBS), and the isometric quadriceps strength (QS). We also investigated each patient's history of falls in the past 6 months. Gait variability was measured using a triaxial accelerometer attached to the patient's torso at the L3 vertebra level during the 10MWT.

Results: Fall status correlated significantly with gait variability (measured as the coefficient of variation; CV) in step time and movement trajectory amplitude (*i.e.*, center of mass movement) in the medial/lateral (ML) and vertical (VT) directions, with balance function as assessed by FGA and BBS scores. In contrast, QS was not correlated with fall status. The independent variables associated with the risk of falling were step time CV, FGA score, and age.

Conclusion: The factors associated with the risk of falling in iNPH were aging and gait-balance instability, particularly temporal gait variability and dynamic balance dysfunction. Our results may enable physicians to identify the patients with iNPH who are at risk of falling and implement suitable prevention strategies.

1. Introduction

Idiopathic normal pressure hydrocephalus (iNPH) is a clinical syndrome characterized by gait and balance disturbances, cognitive impairment, and urinary incontinence in patients with enlarged brain ventricles and normal cerebrospinal (CSF) pressure [1]. Gait and balance disturbances are core symptoms in patients with iNPH and these disturbances lead to an increased risk of falling [2,3]. iNPH is a frontal higher-level gait disorder characterized by small step and disequilibrium gaits [4]. iNPH-associated balance disturbance is thought

to occur as a result of disequilibrium and peripheral and/or central vestibular dysfunction [5,6].

Increased gait variability is the result of inconsistent stepping patterns and reduced postural control during gait [7,8]. Neurological disorders characterized by movement dysfunction, including iNPH, involve a greater variability of gait cycle parameters [7,9,10], and falls occur frequently [4,11]. Indeed, several studies have reported that the fall rates of 60%–80% in patients with iNPH [3,10,12].

Several studies have reported that gait variability is associated with balance function and fall status in both healthy elderly adults and

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<https://doi.org/10.1016/j.clineuro.2019.105385>

Received 25 May 2019; Received in revised form 6 June 2019; Accepted 10 June 2019

Available online 10 June 2019

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patients with Parkinson's disease (PD) [13,14]. Considering that the characteristics of iNPH—namely a combination of gait and balance disturbances and disequilibrium—are likely to increase the risk of falls [2–4,6,10], it can be surmised that patients with iNPH will experience associated falls, gait variability, and balance dysfunction, especially dynamic balance dysfunction. However, no previous reports have attempted to evaluate the associations among fall status, gait variability, and balance function in patients with iNPH.

We hypothesized that in patients with iNPH, fall status will be strongly associated with both gait variability and dynamic balance functions, such as a postural control during gait, as opposed to static balance or lower limb muscle strength. The aims of this study were: 1) to investigate the associations among fall status, gait variability, balance function, and lower limb muscle strength in patients with iNPH, and 2) to identify fall-related factors in patients with iNPH.

2. Patients and methods

2.1. Participants

Eighty-seven patients with iNPH were recruited from the Clinical Department of Neurosurgery and Rehabilitation at Osaka Medical College Hospital. The patients had probable diagnoses with a positive CSF tap test (TT) result according to the iNPH diagnostic criteria [15].

The inclusion criteria for probable iNPH were the following clinical features proposed in the national iNPH guidelines [15]: (1) symptomatic onset at the age of 60 or older, (2) the presence of at least two of the following—gait disturbance, cognitive impairment, and urinary incontinence, (3) MRI-detected ventricular dilation (Evans Index > 0.3) accompanied by narrowing of the subarachnoid CSF space in the high convexity and interhemispheric fissure, (4) CSF pressure of 200 mmH₂O or less and normal CSF laboratory findings, (5) clinical symptoms not completely explained by other neurological or non-neurological conditions, (6) absence of other conditions associated with ventricular dilation, such as subarachnoid hemorrhage, meningitis, head injury, congenital hydrocephalus, or aqueductal stenosis, and (7) a positive clinical response to a CSF TT.

The exclusion criteria were: (1) negative TT according to the iNPH diagnostic criteria [15], (2) additional neurological or orthopedic disorders interfering with gait, and (3) an inability to walk unassisted for at least 15 m [10]. Based on these criteria, 24 patients were excluded in advance from this study. In total, 63 patients with iNPH (age [mean ± standard deviation], 77.9 ± 5.5 years, 42 men and 21 women) who met the inclusion criteria participated in this study. The study protocol was approved by the ethics committee at Osaka Medical College (No. 2341), and all patients provided informed consent.

2.2. Clinical assessments

Patients were assessed before the TT using the following tests: 1) the 10-meter walk test (10MWT) as a test of normal gait [10], 2) the Functional Gait Assessment (FGA) as a test of dynamic balance function during gait (*i.e.*, postural control during gait) [16], 3) the Berg Balance Scale (BBS) as a test of balance function, including static and dynamic balance in the standing position [17], and 4) the isometric quadriceps strength (QS) measured by a hand held dynamometer (HHD) as a test of representative muscle strength in the lower limb [18]. The patients performed right and left QS measured twice by an HHD (μ Tas F-1, Anima Corp, Tokyo, Japan), and the mean measurement values were normalized according to body mass (N/kg) [18]. Patients or their caregivers were interviewed regarding their history of falls in the past 6 months [3,19]. A fall was defined as any unintended contact with the ground or other lower surface [20]. Based on the answers, the number of falls for each patient was defined as one, two, three, four or more [19,20]. Each patient's cognitive function was assessed before performing the TT using the Mini-Mental State Examination (MMSE).

2.3. Gait variability assessment using an accelerometer

Gait variability assessment was performed during 10MWT using an accelerometer, as described previously [10]. Each patient had a triaxial accelerometer (MG-M1100-HW, LSI Medience, Tokyo, Japan, size 7.5 × 5 × 2 cm³, weight 120 g) attached to the lower torso at the L3 vertebra level with a belt [10,21]. The walkway was a 15-m straight path with 3-m acceleration and 2-m deceleration sections at the beginning and end, respectively [10]. Acceleration data were recorded at a sampling rate of 100 Hz. The patients undertook two walking trials at their comfortable speed without any assistance.

The data obtained from the 10-m section between the acceleration and deceleration zones were analyzed to calculate the mean valued velocity, and the length and time of one step [10,21]. The acceleration signals in the medial/lateral (ML) and vertical (VT) directions were integrated twice in the time domain and high-pass filtered with a moving-window mean to calculate spatial movement trajectory amplitudes reflecting the center of mass (COM) movement [10,21]. Gait variability was assessed as the percent coefficient of variation (CV = standard deviation/mean × 100) of step time and spatial movement trajectory amplitudes [10]. Each patient's CVs were calculated, based on acceleration data obtained from the 10-m section between the acceleration and deceleration sections [10]. All gait parameter variables were presented as the mean values of the two trials.

2.4. Data analysis

Statistical analyses were conducted with JMP Pro v. 14.0 (SAS Institute, Cary, NC). The clinical status and clinical assessments in the faller and non-faller groups were compared using a chi-square test and an independent t test, respectively. Additionally, to quantify the effect sizes, we calculated Cohen's *d*-based standardized mean differences (SMDs) and confidence intervals (CIs) comparing faller and non-faller data [22]. A Pearson's correlation coefficient analysis was conducted when associations were observed among the number of falls, gait parameter variables, balance assessment results, and QS for the entire study population and subgroups (*i.e.*, the fallers and the non-fallers). To identify the factors associated with the fall status, a multiple regression analysis was conducted using faller status as a dependent variable and the clinical status and clinical assessment of fallers as independent variables. We defined statistical significance as $p < 0.05$.

3. Results

3.1. Patients

Sixty-three patients with iNPH completed the clinical assessments according to our study protocol. The patients in this study had a fall rate of 71.4% (Table 1). All of the gait and balance assessments were significantly worse in fallers compared to non-fallers, whereas no significant differences were found between fallers and non-fallers for QS, MMSE, and clinical characteristics, including age, gender, height, and weight (Table 1).

3.2. Correlation analyses of gait parameters, balance function, and falls

In all patients ($n = 63$), the number of falls (18 non-fallers, 45 fallers [once; 25 patients, twice; 17 patients, three times; 3 patients, four times or more; no patients) correlated significantly with gait parameter variables and balance function, especially the step time CV and the FGA score, whereas the QS was not correlated with the number of falls. Similarly, in the total patient population, both the step time CV and the FGA score correlated significantly with the number of falls and the other variables, whereas the QS was not correlated with the number of falls (Table 2A). However, QS correlated significantly with gait velocity and step length in the total study population analysis (Table 2A).

Table 1
Clinical status and assessments in patients with iNPH.

	All patients (n = 63)	Non-fallers (n = 18)	Fallers (n = 45)	p-value	SMD (95% CI)
Age (years)	77.9 (5.5)	78.1 (5.8)	77.8 (5.4)	0.894 ^a	0.04 (−3.32, 2.90)
Gender (male / female)	41/22	12/6	29/16	0.867 ^b	N/A
Height (cm)	157.8 (8.0)	158.3 (8.5)	157.6 (7.9)	0.759 ^a	0.09 (−5.26, 3.84)
Weight (kg)	59.0 (11.4)	60.9 (12.1)	58.2 (11.2)	0.418 ^a	0.23 (−9.15, 3.79)
MMSE (score)	24.1 (4.0)	25.0 (4.0)	23.7 (4.0)	0.239 ^a	0.33 (−3.50, 0.87)
10MWT					
Gait velocity (cm/sec)	74.1 (25.4)	87.9 (25.3)	68.6 (23.4)	0.005^a	0.81 (−32.91, −5.79)
Step length (cm)	39.2 (13.2)	46.3 (13.8)	36.4 (11.8)	0.007^a	0.80 (−17.23, −2.67)
Step time CV (%)	11.01 (5.36)	6.71 (2.99)	12.73 (5.15)	< 0.001^a	1.29 (3.97, 8.05)
ML-CV (%)	11.19 (2.35)	9.36 (1.95)	11.92 (2.10)	< 0.001^a	1.24 (1.47, 3.65)
VT-CV (%)	24.51 (11.34)	17.61 (7.31)	27.28 (11.54)	< 0.001^a	0.92 (4.90, 14.44)
FGA (score)	14.2 (4.7)	18.6 (3.3)	12.4 (4.0)	< 0.001^a	1.62 (−8.15, −4.27)
BBS (score)	44.2 (5.9)	48.2 (4.3)	42.6 (5.8)	< 0.001^a	1.03 (−8.21, −2.97)
QS (N/kg)	3.76 (0.93)	3.49 (0.84)	3.86 (0.95)	0.124 ^a	0.41 (−0.10, 0.85)
Number of falls (n)					
0		18			
1			25		
2			17		
3			3		
4 [≥]			none		

p-values and SMDs indicate comparison between non-fallers and fallers.

Bold typed indicate statistically significant result (p < 0.05).

N/A = not applicable.

MMSE: Mini Mental State Examination, 10MWT: 10-m walk test.

CV: coefficient of variation.

ML-CV: coefficient of variation in the medial/lateral direction, VT-CV: coefficient of variation in the vertical direction.

FGA: Functional Gait Assessment, BBS: Berg Balance Scale, QS: isometric quadriceps muscle strength.

Values are mean (SD).

^a p-value of independent-t test.

^b p-value of Chi-Square test; SMD: standardized mean difference.

Table 2
A. Correlational matrix for all patients (n = 63).

	Number of falls	Gait velocity	Step length	Step time CV	ML-CV	VT-CV	FGA	BBS
Gait velocity	−0.354							
Step length	−0.357	0.963						
Step time CV	0.628	−0.591	−0.586					
ML-CV	0.442	−0.077	−0.089	0.377				
VT-CV	0.392	−0.721	−0.727	0.643	0.200			
FGA	−0.644	0.721	0.689	−0.664	−0.352	−0.629		
BBS	−0.444	0.629	0.592	−0.536	−0.232	−0.445	0.818	
QS	0.185	0.346	0.322	−0.058	0.167	−0.173	0.108	0.241

B. Correlational matrix for fallers group (n = 45).

	Number of falls	Gait velocity	Step length	Step time CV	ML-CV	VT-CV	FGA	BBS
Gait velocity	−0.165							
Step length	−0.181	0.963						
Step time CV	0.453	−0.677	−0.673					
ML-CV	0.107	0.121	0.117	0.155				
VT-CV	0.161	−0.731	−0.750	0.594	0.046			
FGA	−0.392	0.708	0.673	−0.635	−0.232	−0.624		
BBS	−0.209	0.589	0.541	−0.455	−0.110	−0.366	0.762	
QS	0.074	0.418	0.372	−0.184	0.029	−0.281	0.252	0.388

C. Correlational matrix for non-fallers group (n = 18).

	Gait velocity	Step length	Step time CV	ML-CV	VT-CV	FGA	BBS
Step length	0.950						
Step time CV	0.084	0.023					
ML-CV	0.106	0.062	0.234				
VT-CV	−0.555	−0.564	0.328	−0.150			
FGA	0.629	0.587	0.065	0.423	−0.126		
BBS	0.522	0.513	−0.146	0.286	−0.167	0.835	
QS	0.521	0.543	0.290	0.282	−0.228	0.359	0.253

Values are Pearson's rho (r).

Bold typed indicate statistically significant result (p < 0.05).

CV: coefficient of variation.

ML-CV: coefficient of variation in the medial/lateral direction, VT-CV: coefficient of variation in the vertical direction.

FGA: Functional Gait Assessment, BBS: Berg Balance Scale, QS: isometric quadriceps muscle strength.

Table 3
Multiple regression analysis for number of falls as dependent variable in all patients (n = 63).

Summery of fit	p-value	R ²	Adjusted R ²	RMSE
Independent variables	p-value	Logarithmic value	F- value	t- value
Age	0.022	1.668	5.641	-2.38
Gender	0.301	0.523	1.097	1.05
Height	0.695	0.158	0.155	-0.39
Weight	0.342	0.466	0.919	-0.96
MMSE	0.599	0.222	0.279	0.53
10MWT-				
Gait velocity	0.645	0.190	0.215	0.46
Step length	0.791	0.102	0.071	-0.27
Step time CV	0.004	2.468	9.476	3.08
ML-CV	0.375	0.426	0.802	0.90
VT-CV	0.226	0.646	1.504	-1.23
FGA	< 0.001	3.275	13.756	-3.71
BBS	0.140	0.855	2.256	1.50
QS	0.734	0.102	0.117	0.34

RMSE; Root mean squared error.

Bold typed indicate statistically significant result ($p < 0.05$).

MMSE: Mini Mental State Examination, 10MWT: 10-m walk test.

CV: coefficient of variation.

ML-CV: coefficient of variation in the medial/lateral direction, VT-CV: coefficient of variation in the vertical direction.

FGA: Functional Gait Assessment, BBS: Berg Balance Scale, QS: isometric quadriceps muscle strength.

In the faller group (n = 45), the number of falls correlated significantly with step time CV and FGA score, but not with the other variables (Table 2B). Both the step time CV and FGA score correlated significantly with the other gait and balance variables in the faller group, except for ML-CV (Table 2B). VT-CV correlated significantly with the other gait and balance variables, whereas ML-CV showed a relatively weak correlation or no correlation at all with the other variables in both, the all-patient analysis and the faller group analysis (Table 2A, 2B).

In the non-faller group (n = 18), the gait variability as measured by step time, the VT-CVs, and the ML-CVs did not correlate significantly with the balance function variables (Table 2C), whereas VT-CV and QS correlated significantly with both gait velocity and step length (Table 2C).

We observed strong correlations between gait velocity and step length, and between the FGA and BBS scores in all patients, as well as in the faller and non-faller subgroups (Table 2A-C).

3.3. Fall-related factors using a multiple regression analysis

Results of the multiple regression analysis are shown in Table 3. The coefficient of determination was measured by an adjusted R² value to assess goodness-of-fit (adjusted R²; 0.563, $P < 0.001$). The independent variables identified as fall-related factors were step time CV, FGA score, and age (Table 3).

4. Discussion

We aimed to investigate the associations among fall status, gait variability, balance ability, and lower limb muscle strength in patients with iNPH, and to identify the fall-related factors based on clinical characteristics and clinical assessments. Our results indicate that falls were strongly associated with temporal gait variability and dynamic balance function, but not static balance function or lower limb muscle strength. Moreover, we found that an increase in temporal gait variability in step time CV and a decline in dynamic balance function in the FGA were independent fall-related factors in patients with iNPH.

Gait parameters are reported to fluctuate minimally in healthy persons, which allows an individual to maintain repetitive and stable walking [7,8]. In contrast, several studies have reported more variable gaits in elderly persons and persons with neurological disorders, such as PD, iNPH, vestibular disorders, or cerebellar ataxia, which are related to risk of falls [7,10,13,23,24]. Studies have also reported that gait variability is associated with balance function and fall status in healthy elderly adults and patients with PD [13,14]. In the present study, the patients with iNPH who had experienced falls had greater spatio-temporal gait variability and worse balance function compared to the non-fallers. Furthermore, the correlation between spatiotemporal gait variability and balance function was stronger in the faller group than the non-faller group. Therefore, we suggest that iNPH-associated gait and balance disturbances may have resulted in deterioration in dynamic postural control and falls in patients with iNPH.

Muscle weakness is a well-known fall-related factor [25]. However, a previous study reported no significant difference in the isometric lower limb muscle strength between fallers and non-fallers in a cohort of healthy elderly adults; furthermore, isometric lower limb muscle strength could not predict falls in this group [26]. In the present study, the lower limb function of the faller group was comparable to that of the non-faller group, and there was no correlation between fall status and lower limb muscle strength in the faller group. Moreover, the lower limb muscle strength was not identified as a fall-related independent factor in the present study. Accordingly, we surmise that lower limb muscle strength does not influence the risk of falls in patients with iNPH.

The FGA can be used to assess dynamic balance functions, such as postural control during gait and it is a useful assessment in almost all neurological disorders, including vestibular dysfunction [16,27]. iNPH-associated balance disturbance and disequilibrium occur as a result of peripheral and/or central vestibular dysfunctions [5,6] and balance disturbances may lead to a wide-based gait pattern or trunk sway [9,10]. In the present study, we found that temporal gait variability and FGA score (representing dynamic postural control function) were independent fall-related factors in patients with iNPH, and the fall rate in our patients was high (71.4%). The variability of gait parameters is known to be useful for predicting falls [13]. Increased gait variability reflects a decrease in postural control during gait [7,8]. The FGA (reflecting dynamic balance function) is generally used to assess the risk of falls [27]. Accordingly, we surmise that a deterioration in dynamic balance function may result in an increase in temporal gait variability and an increased risk of falls in patients with iNPH.

One previous study reported that the degree of standing postural sway is useful for predicting falls in elderly persons [28]. However, our results show that dynamic balance function during gait, as indicated by FGA results rather BBS results that reflect static to dynamic balance function in a standing position, correlated with fall events in patients with iNPH. Similarly, our previous studies demonstrated that the characteristics of postural disturbance in patients with iNPH may be due to a deterioration in dynamic balance function with disequilibrium rather than static balance [2,12]. Taken together, these results suggest that falls in patients with iNPH may be caused by gait and balance disturbances due to iNPH-specific disequilibrium.

Another previous study reported that variability in ambulatory COM movement was greater in patients with iNPH compared to that in age-matched healthy adults [10]. In the present study, we found that the variability in ML and VT COM movements, which reflects spatial gait variability, was worse in fallers than in non-fallers. In addition, spatial gait variabilities correlated with balance function in the faller group, but not in the non-faller group. However, spatial gait variabilities were not independent fall-related factors in the present set of patients. In contrast, step time CV, which is indicative of temporal gait variability as measured by an acceleration amplitude, may be useful for identifying patients with iNPH at risk of falling.

Interestingly, in the faller group, variability in VT COM movements

showed a stronger correlation with other gait parameters and balance functions compared to ML COM movement variability. A previous study on patients with cerebellar ataxia and wide-based gait reported that variability in step length in the VT direction was greater than in healthy subjects; however, variability of step width in the ML direction did not differ [24]. Patients with iNPH exhibit a wide-based gait to compensate for the disturbances in dynamic equilibrium [9]. Therefore, it might be possible that the ML–CV values seen in this study were the result of patients employing a compensation strategy for iNPH-associated balance disturbance with disequilibrium.

It is well known that age is an independent fall-related factor [29]. Consistent with this, the present study also found that age was an independent factor associated with falls. Considering that iNPH is a disease associated with aging [15], these findings are not surprising. Importantly, falls were associated not only with age, but also with balance factors, such as temporal gait variability and dynamic balance function. The current study is the first report to identify the independent fall-related factors and our findings may allow physicians to predict falls in patients with iNPH. Moreover, to prevent falls in patients with iNPH, suppression of temporal gait variability by improving dynamic balance dysfunction may be effective. Future studies are needed to confirm the effectiveness of fall prevention strategies in rehabilitation therapy, the effectiveness of CSF shunting, or a combination of both.

This study had several limitations. First, the results of the present study cannot necessarily be generalized because there is potential selection bias in a hospital-based study; however, this also has advantages given that the present study was performed based on an accurate diagnosis with standardized iNPH criteria at one specialized institution. Second, the present findings did not clarify the causal associations among risk factors, such as fall, gait variability, and balance function because of the cross-sectional design of the study. Moreover, we did not provide postoperative data on the fall incidence of patients with iNPH in this study. A previous study has shown that the risk of falls increased in the first 6 months after CSF shunting [30]. Additional research is needed to investigate the causal associations among fall risk factors through a longitudinal research design.

Third, people with different disease conditions may show different movement behaviors and therefore our results should be interpreted with caution. Finally, the assessment of spatial gait variability as measured by COM movement variability using an accelerometer has potential methodological limitations because measurements are calculated as a relative displacement. However, such calculations have the advantage of improving the ease of clinical assessment.

In conclusion, the risk of falling in patients with iNPH was associated not only with aging, but also with gait-balance instability, particularly temporal gait variability and dynamic balance dysfunction. A patient with iNPH who presents with a combination of advanced age, significant temporal gait variability, and a deterioration of dynamic balance function is at a high risk of falling. Our results will enable physicians to predict the patients with iNPH who are at risk of falling and implement prevention strategies.

Conflict of interest statement

The authors declare that there are no conflicts of interest.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Authors' contributions

Study concept and design: YN, HU, Y Kajimoto, TA, Y Kawami, TI, KK, HO, and RS.

Acquisition of data: YN, Y Kajimoto, HU, NK, TH and KK.

Drafting of the manuscript or critical revision of the manuscript for important intellectual content: YN, HU, Y Kajimoto, TA, Y Okada, NK and RS.

Acknowledgements

We thank all persons who participated in this study. We would like to thank Yoshiyuki Ohta, Kouki Ninagawa and Ryu Hondo for their suggestions and advices on this study.

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