

Original Article

The correlation between white matter hyperintensity and balance disorder and fall risk: An observational, prospective cohort study

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Abstract

Objective: The presence of an association between white matter hyperintensity (WMH) and the risk of falls in older people is uncertain, with little supporting prospective evidence available at present. We aimed to determine whether WMH was associated with dysfunctions of balance and gait, and other sensorimotor factors leading to falls, and the independent factors related to falls in older Chinese people. The protective effect of exercise against falls was also addressed.

Methods: In a representative sample of hospital-based individuals aged 50 years and older in China, the patients' history of falls, magnetic resonance imaging data, scores on the 9-item Berg Balance Scale (BBS-9) test and timed up-and-go test (TUGT), and sensorimotor measures of computerized dynamic posturography (CDP) were analyzed. Incident falls were recorded prospectively over a 12-month period. Using regression modeling, the association between the risk of falls and baseline WMH was estimated.

Results: Only individuals with severe WMH were at an increased risk of falls, and CDP was more sensitive than BBS-9 in detecting WMH-related balance and gait dysfunction. However, WMH was not an independent predictor of falls. Taller height and overweight or obese body habitus were identified as novel protective factors for falls. Female, fall history, and increased TUGT score were identified as independent risk factors for falls in older Chinese people.

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Conclusion: Although WMH was associated with an increased risk of falls, it was not an independent predictor.

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Keywords: White matter hyperintensity; Balance disorder; Gait disorder; Fall risk

Introduction

Leukoaraiosis is a condition that was first proposed by Hachinski et al¹ in 1987 and manifests as white matter hyperintensity (WMH) on T2-weighted magnetic resonance images (MRI) of the brain. The reported incidence ranges from 21 to 95%,² but it is a general finding in people older than 60 years of age. It is considered a sign of cerebral small vessel disease and has been associated with an increased risk of cognitive decline, balance and gait disorders, and voiding dysfunction, with age and hypertension consistently identified as the two main risk factors.³

Falls in the elderly population continue to be a major public health issue. Nearly one in three people older than 65 years have one or more accidental falls each year, with 10% of these falls causing serious injury.⁴ Falls can also lead to poor quality of life, loss of independence, and high levels of anxiety. It is reported that fall rates in the Chinese elderly population are approximately half that found in Caucasian populations,⁵ suggesting that there might be some differences in the fall risk profiles of Chinese older people. Therefore, it is very important to identify the preventable risk factors for falls, and develop and implement effective prevention strategies specific to particular populations.

Balance problems and falls are two major symptoms of patients with WMH. WMH may disrupt important cortical-subcortical connections that assist in motor control and balance, leading to a progressive decline in motor abilities.⁶ However, previous studies evaluating the correlation between the occurrence of falls and WMH have yielded conflicting results. Although several studies have shown an association between WMH and gait and balance disorders, direct evidence for this association is scarce. Asian patients, including Chinese patients, have been under-represented in these trials. The primary goal of this study was to analyze the strength of the correlation of gait and balance disturbances with the degree of WMH in a Chinese hospital-based cohort. We also prospectively investigated the relative contributions of WMH and other sensorimotor factors to the risk of falls.

Methods

Study population

Our study included 85 consecutive in- and out-patients who exhibited any degree of WMH on brain MRI in the Department of Neurology at Beijing Tiantan Hospital from March 2012 to March 2013. We also included another 21 control and volunteer subjects (20%). The Beijing Tiantan Hospital Human Research Ethics Committee approved the study and written informed consent was obtained from all participants.

Inclusion and exclusion criteria

Patients aged a minimum of 50 years exhibiting any degree of change in the cerebral white matter on MRI according to a revised version of the Fazekas scale (with three severity classes) were included in the study. Exclusion criteria for the study included (1) inability or refusal to undergo cerebral MRI; (2) a history of intracranial hemorrhage; (3) a modified Rankin Scale score ≥ 3 with inability to walk without assistance and follow directions to complete the balance and gait assessment; and (4) severe unrelated neurologic diseases (aphasia, dysarthria, dementia, epilepsy, or parkinsonism), severe psychiatric disorders, and likelihood of dropping out because of the presence of severe illnesses.

Baseline information

At baseline, a comprehensive questionnaire, structured in detail was administered by trained personnel to the patients. The self-reported history of smoking, drinking, hypertension, hypercholesterolemia, diabetes mellitus, ischemic stroke, coronary heart disease, and medication use was obtained. We also assessed physical activity, defined as at least 30 min of activity per day, at least 3 days per week,⁷ and patients were classified as physically “active” or “inactive” accordingly. The Beijing version of the Montreal Cognitive Assessment (MoCA) was used to evaluate patients' cognitive function. In addition to demographic data (age, gender, education, and living status), we

considered the following potential confounders: depression as measured using the Hamilton depression scale (HAMD), self-reported visual and hearing impairment, hip/knee pain, and joint arthritis. At baseline, we also measured height (cm), weight (kg), and calculated the body mass index (BMI).

MRI

Imaging was performed using a 3 T scanner (MAGNETOM Trio Tim; Siemens Medical Solutions, Erlangen, Germany). The protocol consisted of the following: slice thickness, 5 mm; slice gap, 1 mm; 250×250 field of view (FOV); 256×256 matrix size; the sequences included a T1-weighted spoiled gradient echo [repetition time/echo time (TR/TE) 2300/2.99 ms, inversion time (TI) 900 ms] and fluid-attenuated inversion recovery (TR/TE 5000/388 ms, TI 1800 ms). All scans were rated by the same analyst who was blinded to subjects' clinical information. The degree of WMH on MRI was rated using a modified version of the visual scale of Wahlund et al.⁸ that scores deep and subcortical white matter lesions in three categories of WMH grade 1, 2, and 3, and periventricular hyperintensity and deep white matter hyperintensity were graded separately, with scores ranging from 1 to 6. Subjects with no WMH were considered to have WMH grade 0.

Assessment of gait and balance

The semi-quantitative assessment consisted of a 9-item Berg Balance Scale (BBS-9), as well as a timed-up-and-go test (TUGT), and both were performed three times. The BBS-9 was designed on the basis of the original BBS. The 14 original aspects of balance function were reduced to 9 items, including sitting to standing, transferring, reaching forward with outstretched arms, retrieving an object from the floor, turning to look behind, turning 360° , placing alternate feet on a stool, standing with one foot in front, and standing on one foot.⁹

Participants also underwent computerized dynamic posturography (CDP) (NeuroCom Int., Inc., Clackamas, Oregon, USA). A trained physical therapist performed the sensory organization test (SOT) and motor control test (MCT) of the CDP using EquiTest equipment (NeuroCom Int., Inc., Clackamas, Oregon, USA). The therapist followed the standard EquiTest protocol for testing (version 8.0). The SOT evaluates the patient's ability to make effective use of visual, vestibular, and somatosensory inputs and suppress

inappropriate sensory information.¹⁰ Six different conditions were assessed during the SOT. Conditions 1–3 were performed on a fixed platform with eyes open, eyes closed, and vision sway-referenced. Conditions 4–6 were performed on a sway-referenced platform with eyes open, eyes closed, and vision sway-referenced. The composite equilibrium score that was automatically computed using the standard algorithm in the computer software from the six conditions was recorded for analysis. The possible equilibrium scores ranged from 0 to 100, and higher SOT scores indicated greater stability. During the MCT, patients were required to open their eyes and stand on a dynamic platform that could move in parallel, forwards or backwards, to stimulate the subjects' automatic postural response. The timing, strength, and symmetry of the force response to the stimulus were recorded. The MCT scores were compared with those from age-matched historic control subjects and were considered abnormal if they were below the 5th percentile.

Falls

A fall was defined as a slip or trip due to a loss of balance that caused the participant to land on the floor, ground, or lower level based on the standard definition provided by the Prevention of Falls Network Europe.¹¹ Participants who fell more than once were referred to as having multiple falls. A history of falls was defined as any fall in the preceding 12 months. Additionally, we recorded falls that occurred during the 12 months after enrollment. Participants were telephoned every 3 months to remind them to record falls.

Statistical analysis

Statistical analysis was performed using the SPSS 21.0 statistical package (SPSS Inc., Chicago, IL, USA). We used the χ^2 test or *t*-test to compare relevant characteristics between groups. Based on published data and for the purposes of multivariate Logistic analysis, measures of physical performance were dichotomized according to pre-specified cutoffs. The BBS-9 was dichotomized using a cutoff of 32,⁹ and TUGT was dichotomized using a cutoff of 12.3 s.¹² We performed multivariate Logistic regression analyses with BBS-9, TUGT, SOT, and MCT as dependent variables, and WMH severity, age, gender, and factors known to interfere with balance and gait as independent variables. Statistically significant variables ($P < 0.1$) in the univariate analysis were included in

the multivariate stepwise Logistic regression analysis to determine the independent risk factors of fall, with two-tailed $P < 0.05$ considered statistically significant.

Results

Sample characteristics

Five participants were excluded from further analyses because of their withdrawal from the study. The demographic characteristics, presence of comorbidities, and factors potentially interfering with gait and balance in the four WMH severity groups are listed in Table 1. The mean age was 61.8 years and 35.6% (36/101) of the participants were women. Comparison of the baseline information between groups revealed that patients with a higher degree of WMH were older ($P = 0.004$) and had lower MoCA scores ($P < 0.001$), lower BBS-9 scores ($P < 0.001$), longer TUGT ($P < 0.001$), lower SOT scores ($P < 0.001$), and longer time in the MCT ($P < 0.001$). At the end of the 1-year

follow-up, 11 patients had experienced one fall and one patient had two falls. The total incidence of falls was 11.9% (12/101). The falls incidence in the WMH-Fazekas grades 0–3 were 4.8%, 2.9%, 17.4%, and 26.1%, respectively ($P = 0.030$).

WMH and risk of falls

We found significant differences in the aggregated scores of the BBS-9 between the four categories of WMH ($P = 0.013$). After dichotomous categorization, 27 individuals had a “pathologic” BBS-9 score (i.e., score values of 32 and below). Univariate Logistic regression analysis with a pathologic BBS-9 score as the dependent variable showed a significant association with WMH grade 3 when compared with grade 0 [odds ratio (OR) = 4.64, 95% confidence interval (CI): 1.19–18.11, $P = 0.002$]. The difference was no longer apparent in the multivariate Logistic regression analysis ($OR = 1.29$, 95% CI : 0.17–9.58, $P = 0.889$) (Table 2).

Table 1
Characteristics of 101 participants with Fazekas grades 0–3.

Items	WMH-Fazekas grade ($n = 101$)				P
	Grade 0 ($n = 21$)	Grade 1 ($n = 34$)	Grade 2 ($n = 23$)	Grade 3 ($n = 23$)	
Age, years	54.7 ± 10.2	60.9 ± 10.2	64.0 ± 11.6	67.4 ± 14.2	0.004
Female, n (%)	5 (23.8)	12 (35.3)	11 (47.8)	8 (34.8)	0.427
Living alone, n (%)	0	1 (2.9)	3 (13)	0	0.137
Height, cm	167.8 ± 7.4	167.4 ± 7.8	166.7 ± 8.8	165.7 ± 8.2	0.823
Weight, kg	74.9 ± 10.3	67.6 ± 8.2	66.8 ± 11.5	67.7 ± 11.3	0.034
BMI, kg/m ²	26.5 ± 2.8	24.6 ± 2.4	24.0 ± 3.8	24.6 ± 3.1	0.037
Overweight or obesity, n (%)	17 (81.0)	22 (64.7)	8 (34.8)	9 (39.1)	0.004
History of falls, n (%)	3 (14.3)	3 (8.8)	6 (26.1)	7 (30.4)	0.139
Physical active, n (%)	9 (42.9)	17 (50)	12 (52.2)	5 (21.7)	0.126
Ever-smoking, n (%)	12 (57.1)	16 (47.1)	9 (39.1)	13 (56.5)	0.569
Ever-drinking, n (%)	7 (33.3)	14 (41.2)	8 (34.8)	9 (39.1)	0.930
Hypertension, n (%)	14 (66.7)	20 (58.8)	15 (65.2)	16 (69.6)	0.854
Diabetes, n (%)	8 (38.1)	15 (44.1)	11 (47.8)	8 (34.8)	0.801
Hypercholesterolemia, n (%)	12 (57.1)	20 (58.8)	14 (60.9)	13 (56.5)	0.991
Ischemic stroke, n (%)	13 (61.9)	22 (64.7)	11 (47.8)	22 (95.7)	0.005
Coronary artery disease, n (%)	3 (14.3)	6 (17.6)	2 (8.7)	5 (21.7)	0.659
Antiplatelet drugs, n (%)	14 (66.7)	18 (52.9)	11 (47.8)	18 (78.3)	0.126
Antihypertensive drugs, n (%)	9 (42.9)	11 (32.4)	7 (30.4)	11 (47.8)	0.537
Hypoglycemic drugs, n (%)	1 (4.8)	7 (20.6)	5 (21.7)	5 (21.7)	0.376
Lipid-lowering drugs, n (%)	14 (66.7)	17 (50)	13 (56.5)	14 (60.9)	0.655
Sedative-hypnotics, n (%)	3 (14.3)	5 (14.7)	5 (21.7)	2 (8.7)	0.669
Kinds of drugs, n	2.6 ± 1.3	2.2 ± 1.8	2.5 ± 1.9	3.2 ± 2.0	0.192
MoCA, scores	24.3 ± 2.2	23.0 ± 4.0	20.5 ± 4.4	16.1 ± 5.7	0.000
BBS-9, scores	34.9 ± 1.7	34.7 ± 1.8	34.2 ± 2.1	31.9 ± 4.2	0.000
TUGT, s	8.3 ± 2.2	10.3 ± 3.1	11.3 ± 3.2	14.3 ± 4.3	0.000
SOT, scores	76.0 ± 7.9	73.0 ± 5.0	69.0 ± 6.0	62.4 ± 6.8	0.000
MCT, ms	143.3 ± 15.4	147.9 ± 10.2	151.2 ± 8.9	166.1 ± 21.9	0.000
Falls during follow-up, n (%)	1 (4.8)	1 (2.9)	4 (17.4)	6 (26.1)	0.030

Values are presented as mean ± standard deviation, n or n (%).

WMH: white matter hyperintensity; BMI: body mass index; MoCA: Montreal Cognitive Assessment; BBS-9: 9-item Berg Balance Scale; TUGT: timed-up-and-go test; SOT: sensory organization test; MCT: motor control test.

Table 2
WMH and risk of falls.

Items	WMH-Fazekas grade (n = 101)				P
	Grade 0 (n = 21)	Grade 1 (n = 34)	Grade 2 (n = 23)	Grade 3 (n = 23)	
Fall					
n (%)	1 (4.8)	1 (2.9)	3 (13.0)	6 (26.1)	0.030
Crude model, OR (95% CI)	1	0.14 (0.02–1.30)	0.42 (0.10–1.77)	0.60 (0.14–2.48)	
Adjusted model, OR (95% CI)	1	0.34 (0.01–5.37)	0.35 (0.02–6.47)	0.14 (0.01–3.72)	
BBS-9 score ≤ 32					
n (%)	4 (19)	5 (14.7)	6 (26.1)	12 (52.2)	0.013
Crude model, OR (95% CI)	1	0.73 (0.17–3.11)	1.50 (0.36–6.29)	4.64 (1.19–18.11) ^a	
Adjusted model, OR (95% CI)	1	0.75 (0.08–6.89)	0.84 (0.09–8.02)	1.29 (0.17–9.58)	
TUGT ≥ 12.3 s					
n (%)	3 (14.3)	7 (20.6)	5 (21.7)	13 (56.5)	0.005
Crude model, OR (95% CI)	1	1.56 (0.35–8.03)	1.67 (0.35–8.04)	7.80 (1.79–34.07) ^a	
Adjusted model, OR (95% CI)	1	0.98 (0.10–9.85)	0.53 (0.05–5.48)	3.32 (0.40–27.38)	
Abnormal SOT score					
n (%)	3 (14.3)	5 (14.7)	8 (34.8)	12 (52.2)	0.007
Crude model, OR (95% CI)	1	1.03 (0.22–4.86)	3.20 (0.72–14.25)	6.55 (1.50–28.49) ^a	
Adjusted model, OR (95% CI)	1	0.44 (0.06–3.18)	2.45 (0.36–16.77)	5.38 (0.89–32.51)	
Abnormal MCT score					
n (%)	7 (33.3)	15 (44.1)	13 (56.5)	17 (73.9)	0.039
Crude model, OR (95% CI)	1	1.58 (0.51–4.90)	2.60 (0.76–8.86)	5.67 (1.55–20.79) ^a	
Adjusted model, OR (95% CI)	1	1.25 (0.32–4.92)	1.88 (0.41–8.70)	5.01 (1.12–22.44) ^b	

WMH: white matter hyperintensity; OR: odds ratio; CI: confidence interval; BBS-9: 9-item Berg Balance Scale; TUGT: timed-up-and-go test; SOT: sensory organization test; MCT: motor control test.

^a In univariate regression analysis, a significant association of pathologic gait and balance testing could be observed for the conditions of grade 3 vs. grade 0 WMH.

^b Adjusted for age, gender, living status, smoking, drinking, hypertension, hypercholesterolemia, diabetes, ischemic stroke, coronary artery disease, medications, physical activity and MoCA scores. Only the difference regarding MCT remained significant for the categories of grade 3 vs. grade 0 WMH in multivariate Logistic regression.

There were significant differences in the TUGT time between the four categories of WMH ($P = 0.005$). After dichotomous categorization, 28 individuals had a “pathologic” TUGT time (i.e., exceeding 12.3 s in the best of three trials). Univariate Logistic regression analysis using a pathologic TUGT time as the dependent variable showed a significant association with WMH grade 3 compared with grade 0 ($OR = 7.80$, 95% CI: 1.79–34.07, $P = 0.000$). The difference was no longer apparent in the multivariate Logistic regression analysis ($OR = 3.32$, 95% CI: 0.40–27.38, $P = 0.179$) (Table 2).

In the univariate Logistic regression with SOT and MCT as dependent variables, the differences between WMH grade 3 and 0 were statistically significant (SOT: $OR = 6.55$, 95% CI: 1.50–28.49, $P = 0.003$; MCT: $OR = 5.67$, 95% CI: 1.55–20.79, $P = 0.014$). After adjustment for multiple factors related to balance and gait disturbance, the differences were only significant in the MCT ($OR = 5.01$, 95% CI: 1.12–22.44, $P = 0.042$).

Predictors of falls

Univariate analysis showed that age, female, height, weight, overweight and obese body habitus, history of

falls, physical activity, WMH, MoCA scores, and balance and gait disorders (low BBS-9 score, prolonged TUGT, and abnormal SOT and MCT results) were factors significantly correlated with falls. Taller height, heavier weight, overweight or obese body habitus, and physical activity were observed to confer protection against the risk of fall, while the other factors were associated with an increased risk for falls. However, in the multiple Logistic regression models, only female, history of falls, and prolonged TUGT remained independent risk factors of falls (Tables 3 and 4). WMH was not identified as an independent predictor of falls.

Discussion

Limitations in mobility often lead to a fatal outcome or long-lasting dependence. This is a challenging problem for socioeconomic systems and will become a significant issue in the upcoming decades. Because mobility critically depends on balance and gait function and the compromise of either one may be sufficient to cause significant disability. Resultantly, we chose to use a composite measure of both motor scales

Table 3
Risk factors for falls in univariate regression analysis.

Risk factors	Non-fallers (n = 89)	Fallers (n = 12)	P
Age, years	60.9 ± 12.3	68.7 ± 9.0	0.037 ^a
Female, n (%)	28 (31.5)	8 (66.7)	0.039 ^a
Living alone, n (%)	3 (3.4)	1 (8.3)	0.402
Height, cm	167.6 ± 7.6	162.4 ± 9.7	0.035 ^a
Weight, kg	69.8 ± 10.5	62.5 ± 8.2	0.022 ^a
BMI, kg/m ²	25.0 ± 3.2	23.6 ± 1.8	0.146
Overweight or obesity, n (%)	53 (59.6)	3 (25.0)	0.024 ^a
History of falls, n (%)	13 (14.6)	6 (50.0)	0.011 ^a
Physical active, n (%)	41 (46.1)	2 (16.7)	0.053 ^a
Ever-smoking, n (%)	46 (51.7)	4 (33.3)	0.233
Ever-drinking, n (%)	35 (39.3)	3 (25.0)	0.519
Hypertension, n (%)	59 (66.3)	6 (50.0)	0.269
Diabetes, n (%)	37 (41.6)	5 (41.7)	0.995
Hypercholesterolemia, n (%)	53 (59.6)	6 (50.0)	0.269
Ischemic stroke, n (%)	59 (66.3)	9 (75.0)	0.783
Coronary artery disease, n (%)	15 (16.9)	1 (8.3)	0.416
Antiplatelet drugs, n (%)	54 (60.7)	7 (58.3)	1.000
Antihypertensive drugs, n (%)	34 (38.2)	4 (33.3)	0.992
Hypoglycemic drugs, n (%)	15 (16.9)	3 (25.0)	0.772
Lipid-lowering drugs, n (%)	51 (57.3)	7 (58.3)	0.946
Kinds of drugs	2.5 ± 1.8	2.8 ± 2.3	0.576
WMH-Fazekas, n (%)			0.030 ^a
Grade 0	20 (22.5)	1 (8.3)	
Grade 1	33 (37.1)	1 (8.3)	
Grade 2	19 (21.3)	4 (33.3)	
Grade 3	17 (20.3)	6 (50.0)	
MoCA, scores	21.7 ± 4.6	17.3 ± 7.2	0.005 ^a
BBS-9, scores	34.2 ± 2.8	32.3 ± 2.2	0.023 ^a
TUGT, s	10.6 ± 3.6	14.3 ± 4.0	0.001 ^a
SOT, scores	70.8 ± 8.1	66.5 ± 5.5	0.078 ^a
MCT, ms	150.5 ± 15.9	161.6 ± 18.1	0.028 ^a

Values are presented as mean ± standard deviation or n (%). ^aP < 0.1. BMI: body mass index; WMH: white matter hyperintensity; MoCA: Montreal Cognitive Assessment; BBS-9: 9-item Berg Balance Scale; TUGT: timed-up-and-go test; SOT: sensory organization test; MCT: motor control test.

Table 4
Risk factors for falls in multiple regression analysis.

Risk factors	OR (95% CI)	P
Female	4.21 (1.02–17.40)	0.047
History of falls	4.84 (1.15–20.46)	0.032
TUGT	1.18 (1.03–1.40)	0.046

OR: odds ratio; CI: confidence interval; TUGT: timed-up-and-go test.

and the CDP test. The results have revealed a clear dose-dependent effect of WMH on several measures of balance and gait.

Some studies^{13–15} demonstrated that compared with the original BBS, the modified BBS-9 with a cut-off score of 32 could moderately predict the risk of falls among community-dwelling participants in lesser time

(13–15 vs. 20–30 min) and more conveniently.^{13–15} TUGT has been widely used in the balance test with the cutoff point for risk of falls ranging from 11.0 to 12.3 s^{16–18}; however, its predictive power is highly limited to a high-functioning population.¹⁹ Regarding the CDP, the SOT protocol could be used to differentiate elderly non-fallers from fallers due to balance impairment,²⁰ and it appears to be more sensitive in identifying those at a high-risk of recurrent falls, compared with clinical tests, especially in condition 5 and 6.²¹ Whitney et al²² introduced a cutoff point for falls of less than 38 points, but there is another study found that the SOT result did not relate to the rate of self-reported falls in nursing home residents. A prolonged response time in the MCT might be indicative of biomechanical pathology or abnormalities of peripheral nerves, spinal pathways, or brain structures.

To our knowledge, there are no previous studies in which the BBS-9, SOT, and MCT have been used to study the balance and gait function of patients with WMH. We have provided evidence demonstrating that WMH increases the risk of incident falls in the general older population. With respect to the BBS-9, TUGT, SOT, and MCT, there were no significant differences between WMH grade 1–2 and 0, but the differences between WMH grade 3 and 0 were statistically significant, raising the possibility that there may be a threshold effect where only those with severe WMH (grade 3) are at increased risk of falls. After adjustment for multiple factors related to balance and gait disturbance, the differences were only significant with respect to the MCT. This may be because the balance and gait function of the patients included in this study was relatively good, and visual rating scales might display ceiling effects for high-functioning patients, while the CDP is more sensitive than visual scores in identifying balance and gait disturbances. Although WMH is associated with an increased risk of falls, it does not appear to be an independent predictor of falls. This may be because of a threshold effect or because our sample did not include enough patients with severe WMH. Additionally, we did not divide patients into periventricular hyperintensity and deep white matter hyperintensity groups; instead, we chose the most affected level as the measure of a patient's WMH severity, limiting the generalization of the results. Whether deep or subcortical WMH is associated with balance disorder and fall risk should be further investigated. WMH volumes calculated as a percentage of the intracranial volume might be a more accurate method to evaluate the WMH burden; using this measure, Callisaya²³ observed that a greater WMH

progression score could independently increase the risk of multiple falls.

Among the risk factors we found related to falls in the univariate analysis, shorter height has not been previously reported and we believed that this might be because the fallers were in general older. The fallers weighed less and included fewer overweight or obese individuals, contradicting the findings of a previous study. Jeon et al²⁴ observed that fall efficacy tends to be lower (more afraid of falling) when there are higher degrees of obesity, and they thought that the decreased mobility caused by obesity in older people might result in increased fear of falling. They also demonstrated that a lower BMI was correlated with a more serious injury after falling, especially in women. Mitchell et al²⁵ reported a 31% increase in the risk of falls in obese patients compared with non-obese control subjects, but obesity was irrelevant to the degree of injury after falling. However, in both two studies, compared with people of average weight, patients with obesity took more medications, experienced more pain and discomfort, and fewer of them exercised regularly. All these factors could weaken the accuracy of the results. Future research is required to verify this potential association.

Exercise might have a protective effect in delaying the transition to disability as it was associated with better gait and balance test results. This hypothesis is currently addressed in our study where it was shown that more non-fallers exercised regularly than fallers ($P = 0.053$), although the difference was not statistically significant. This supports the previously proposed conclusion that active exercise is a protective factor against falls,²⁶ and especially when combined with balance training, it can significantly reduce the risk of falls and motor impairments.^{27,28} This may be of particular therapeutic value. However, both patients' fear of falling and limited mobility could prevent them from developing this beneficial habit, and need to be addressed in future studies.

In addition to female, fall history, and gait abnormalities, we did not find any other independent factors or comorbidities related to falls in this cohort, while previous studies have found a number of risk factors in older people, especially those living alone, with cognitive impairment and/or depression, and so on. Possible reasons might be that the included population had no or only mild degree of related diseases or risk factors, so the above-mentioned risk factors for falls did not reach a significant level, thus the incidence of falls was also lower than that found in previous research.

The small sample size is certainly the main limitation of our study, and our study sample is not population based. Most subjects had comorbid ischemic stroke, which would undermine the strength of the conclusion. It was required that patients included should be non-disabled subjects who could walk independently, so the correlation between serious WMH and gait and balance disorders may be underestimated. Furthermore, there may exist nonlinear and possible ceiling effects, observable using a visual rating scale application to evaluate the severity of WMH, which has relatively poor sensitivity and accuracy compared with voxel-based morphometry. Therefore, all these issues require large sample, multi-center controlled studies for further confirmation.

Conclusions

Our study showed a clear dose-dependent effect of WMH on several measures of balance and gait, with only patients with severe WMH found to be at increased risk of falls. In addition, CDP was more sensitive than visual scores (BBS-9) in detecting WMH-related disturbances of balance and gait. Although WMH was associated with an increased risk of falls, it was not an independent predictor. Taller height and overweight or obese body habitus were newly identified protective factors against falls and the protective effect of exercise on falls was addressed in our cohort. Female, fall history, and increased TUGT were independent risk factors for falls in a population of Chinese older people. Future studies should further investigate whether fall prevention strategies that include slowing WMH progression may be more effective.

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