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### Authors

Ahn, Sangwoo

Chung, Jae Woo

Crouter, Scott E

et al.



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# Gait and/or balance disturbances associated with Alzheimer's dementia among older adults with amnestic mild cognitive impairment: A longitudinal observational study

**Sangwoo Ahn**[1], **Jae Woo Chung**[2], **Scott E. Crouter**[3], **Jung-Ah Lee**[4], **Chung Eun Lee**[5], **Joel G. Anderson**[1]

[1]College of Nursing, University of Tennessee, Knoxville, Tennessee, USA

[2]Department of Neurology, University of Minnesota, Minneapolis, Minnesota, USA

[3]Department of Kinesiology, Recreation, and Sport Studies, University of Tennessee, Knoxville, Tennessee, USA

[4]Sue & Bill Gross School of Nursing, University of California, Irvine, Irvine, California, USA

[5]Paul H. Chook Department of Information Systems and Statistics, Baruch College, New York, New York, USA

## Abstract

**Aims:** To explore whether gait and/or balance disturbances are associated with the onset of Alzheimer's dementia (AD) among older adults with amnestic mild cognitive impairment (MCI).

**Design:** This study employed a longitudinal retrospective cohort design.

**Methods:** We obtained data from the National Alzheimer's Coordinating Center's Uniform Data Set collected from 35 National Institute on Aging Alzheimer's Disease Research Centers between September 2005 and December 2021. The mean age of participants ($n$ = 2692) was 74.5 years with women making up 47.2% of the sample. Risk of incident AD according to baseline gait and/or balance disturbances as measured using the Postural Instability and Gait Disturbance Score, a subscale of the Unified Parkinson's Disease Rating Scale Motor Score, was examined by the Cox proportional hazards regression models adjusting for baseline demographics, medical conditions and study sites. The mean follow-up duration was 4.0 years.

**Results:** Among all the participants, the presence or the severity of gait and/or balance disturbances was associated with an increased risk of AD. The presence or the severity of gait and/or balance disturbances was associated with a higher risk of Alzheimer's dementia among the subgroups of female and male participants.

**Correspondence** Jae Woo Chung, 717 Delaware St SE, R516, Minneapolis, MN 55414, USA. jwchung@umn.edu.

AUTHOR CONTRIBUTIONS

All the authors have agreed on the final version and meet at least one of the following criteria (recommended by the ICMJE*): 1. Substantial contributions to conception and design, acquisition of data or analysis and interpretation of data. 2. Drafting the article or revising it critically for important intellectual content. http://www.icmje.org/recommendations/.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

**Conclusion:** Gait and/or balance disturbances may increase the risk of developing AD, regardless of sex.

**Impact:** Gait and/or balance disturbances among community-dwelling older adults with amnestic MCI may need to be frequently assessed by nurses to identify potential risk factors for cognitive decline.

**No patient or public contribution:** Given the secondary analysis, patients, service users, caregivers or members of the public were not directly involved in this study.

### Keywords

Alzheimer's dementia; gait; Gerontological Nursing; mild cognitive impairment; older adults; posture balance

## 1 | INTRODUCTION

As global population ages, the prevalence of Alzheimer's dementia (AD) and other dementias increases. It is predicted that the number of people living with AD and other dementias worldwide will increase from 57.4 million in 2019 to 152.8 million in 2050 (Nichols et al., 2022). As of 2022, approximately 6.5 million adults in the United States are diagnosed with AD, which accounts for 60%–80% of all dementias. This number is expected to grow to 13.8 million by 2060. Accordingly, there is concern that the burden of AD and other dementias on society will continue to increase over time (Alzheimer's Association, 2022a; Nichols et al., 2022). Given there is no definitive cure for AD, the current best practice is to identify individuals at risk of AD and provide appropriate preventive strategies. Therefore, predicting the risk of AD is a research priority.

Physical frailty such as gait and/or balance disturbances is one of the fundamental characteristics of aging. Gait and/or balance are complex and controlled tasks that require physical (e.g., lower body muscle strength) and cognitive function (e.g., executive function for motor planning or body position) (Zhang et al., 2019). Gait disturbances are defined as any deviations from normal walking or gait. Balance disturbances are described as difficulties staying upright or moving confidently (Bahureksa et al., 2017; Zhang et al., 2019). Gait and/or balance disturbances in cognitively healthy older adults may represent a predictive marker of cognitive decline and/or AD because these disturbances reflect low-blood flow to skeletal muscle, low-physiologic reserve and/or high inflammation and oxidative stress (Nadkarni et al., 2017; Quan et al., 2017; Strandberg et al., 2013). Previous longitudinal cohort studies found that community-dwelling cognitively healthy older adults with gait or balance disturbances (mean age ranging from 65 to 93 years) were 1.2 to 2.5 times more likely to develop AD over 3 to 12 years (Bullain et al., 2016; Dumurgier et al., 2017; Kuate-Tegueu et al., 2017; Lee et al., 2018). Decreased lower extremity strength leading to gait and/or balance disturbances was associated with decreased global cognition and episodic memory scores among cognitively healthy older adults aged 69–80 years (Katsumata et al., 2011; Mielke et al., 2013; Tolea & Galvin, 2016).

### 1.1 | Background

Mild cognitive impairment (MCI) refers to a state in which people experience cognitive decline both subjectively and objectively but maintain the ability to perform most activities of daily living without major problems (Alzheimer's Association, 2022b; Roberts & Knopman, 2013). Although some people with MCI might revert to a cognitively normal state or will not progress to AD and other dementias over time, MCI is recognized as a stage between healthy cognition and AD and other dementias, with the rate for conversion from MCI to AD and other dementias being more than 10 times higher than that from a cognitively healthy state over 3–10 years (Mitchell & Shiri-Feshki, 2009). Based on symptoms, MCI is ategorized into amnestic (memory issues) and non-amnestic types and amnestic MCI (aMCI) was associated with a higher risk of progression to AD when compared with non-amnestic MCI (Cheng et al., 2017; Roberts & Knopman, 2013). Compared with cognitively healthy older adults, those with MCI are more likely to show some characteristics of physical frailty such as worse gait and balance parameters, for example, gait speed, stride length and anterior-posterior sway with small to moderate effect sizes (Bahureksa et al., 2017; Nyunt et al., 2017).

While several studies support the hypothesis that gait and/or balance disturbances may precede the diagnosis of AD in the pre-clinical Alzheimer's stage during which objective cognitive decline is not detected, the temporal relationship between gait and/or balance disturbances and AD occurrence has not been well characterized among people with aMCI. Therefore, research is needed to address the question of whether gait and/or balance disturbances would be an indicator of cognitive decline among older adults living with aMCI as well as cognitively healthy individuals.

## 2 | THE STUDY

### 2.1 | Aims

The purpose of this longitudinal observational study was to identify the association of gait and/or balance disturbances with the incidence of AD among older adults with aMCI. The hypothesis was that gait and/or balance disturbances at baseline would be associated with higher risk of the onset of AD.

### 2.2 | Design

Our study used a longitudinal retrospective cohort design.

### 2.3 | Data collection

Data for our study were from the National Alzheimer's Coordinating Center's Uniform Data Set (NACC–UDS). The NACC is located at the University of Washington (WA, USA, https://naccdata.org) and a detailed description of the NACC dataset can be found in a previous publication (Beekly et al., 2007). Since 2005, the National Institute on Aging Alzheimer's Disease Research Centers (NIA–ADRCs) across the United States have been assessing demographic and medical-related characteristics of participants with cognitive status ranging from normal cognition to MCI and dementias using standardized measures (UDS) about once a year and then provide de-identified data to the NACC. However,

because each center enrols its participants using its own protocol for research, research using the NACC–UDS is best regarded as a referral-based, not a population-based study. Regardless of whether they belong to ADRCs, researchers can request data from the NACC–UDS for secondary analyses based on their research questions. Our analyses included data from 35 ADRCs collected between September 2005 and December 2021.

### 2.4 | Ethical consideration

The authors' IRB did not require further review given that participants cannot be identified.

### 2.5 | Participants

Initially, the current study included English-speaking, community-dwelling individuals ($n$ = 3340) who were aged 60 years or over and diagnosed with either single- or multiple-domain aMCI using the Petersen criteria (Petersen, 2004) at baseline (i.e., at their first visit). We set age criteria because the presence of subjective cognitive decline, one of the key characteristics of MCI, for those aged 60 years or older is closely related to Alzheimer's pathophysiology (Jessen et al., 2014). To support the MCI diagnosis, participants should have a global score of 0.5 (questionable impairment) on the CDR® Dementia Staging Instrument at baseline (Hughes et al., 1982). Participants with baseline scores on the Mini-Mental State Exam (MMSE) <24 were excluded due to the likelihood of dementia ($n$ = 262) (Tombaugh & McIntyre, 1992). We excluded individuals diagnosed with Parkinson's disease (PD) at baseline ($n$ = 68). We further removed individuals who were severely underweight or obese at baseline using a body mass index (BMI) <16.5 ($n$ = 5) and ≥40 ($n$ = 44). Assuming data were missing at random using the missing value pattern in SPSS version 27 (IBM) (Bennett, 2001), we also removed those with incomplete data at baseline ($n$ = 269; alcohol use = 9, atrial fibrillation = 12, cigarette smoking history = 40, congestive heart failure = 18, diabetes mellitus = 24, hypercholesterolemia = 34, hypertension = 6, marital status = 25, stroke = 15, thyroid disease = 7, traumatic brain injury = 22, vitamin $B_{12}$ deficiency = 57), resulting in a total of 2692 participants used in our study.

A post hoc power analysis was done for the sample size justification using the Stata version 17.0 (StataCorp). The sample size of 2692 was adequate to achieve sufficient statistical power. Our adjusted hazard ratios (HRs; effect sizes) for gait and/or balance disturbances ranged from 1.24 to 1.53 in the final multivariate Cox proportional hazard regression models. With an alpha of 0.05, the effect size of 1.24 to 1.53, and a sample size of 2692, a statistical power of 0.96 to 1.00 was reached.

### 2.6 | Validity, reliability and/or rigour of measurements

The independent variable was gait and/or balance disturbances at baseline. The dependent variable was conversion to AD during follow-up visits among participants with aMCI at baseline. Covariates were demographic characteristics, medical conditions and study site. All the measures were evaluated by trained clinicians according to standardized criteria.

**2.6.1 | Gait and/or balance disturbances—**Gait and/or balance disturbances were determined using the validated Postural Instability and Gait Disturbance (PIGD) Score, the subscale of the Unified PD Rating Scale Motor Score. Construct validity was evaluated by

confirming correlations of the PIGD with other gait and/or balance assessment tools such as the activities-specific balance confidence scale, the berg balance scale and the timed up and go test ($r$=0.67–0.72) (Bloem et al., 2016). The total PIGD scores range from 0 to 8 with higher scores reflecting more severe symptoms (St. George et al., 2010). Scores are the sum of gait rated as 0 (normal), 1 (walks slowly), 2 (walks with difficulty), 3 (severe disturbance), or 4 (cannot walk at all) and balance rated as 0 (normal), 1 (minor, recovering unaided), 2 (absence of postural response), 3 (very unstable) or 4 (unable to stand). In addition to a numeric variable (severity; per 1-point increase), we considered gait and/or balance disturbances as a binary variable (absence [score = 0] versus presence [score ≥ 1]) in the absence of a threshold for dichotomous classification.

**2.6.2 | Outcome—**AD was ascertained based on either the National Institute of Neurological and Communicative Disorders and Stroke and the Alzheimer's Disease and Related Disorders Association criteria (McKhann et al., 1984) or the National Institute on Aging-Alzheimer's Association criteria (McKhann et al., 2011), the core characteristics of which are (1) objective cognitive impairment defined as performances falling greater than 1.5 standard deviations (SDs) outside the age- and education-adjusted normative mean in at least two cognitive domains including memory and executive function and (2) decreased activities of daily living directly related to cognitive impairment. The end point was AD at diagnosis for those who developed AD, other dementias at diagnosis for those who developed dementias other than AD, or at last follow-up for those who did not develop any form of dementia.

**2.6.3 | Covariates—**Demographic characteristics, medical conditions and study site were used as covariates (Ahn et al., 2020). Demographic characteristics included baseline age (years), sex (male, female), education (years), marital status (married, non-married [never married, widowed, divorced, and separated]), race (White, non-White) and ethnicity (Hispanic, non-Hispanic). Medical conditions were factors that could be related to cognitive health and included baseline MMSE score, cigarette smoking history (non-smoker, former smoker, current smoker), BMI (underweight, normal weight, overweight, obese) and the presence (yes, no) of atrial fibrillation, congestive heart failure, stroke, seizures, traumatic brain injury, diabetes mellitus, hypertension, hypercholesterolemia, vitamin $B_{12}$ deficiency, thyroid disease, alcohol or other substance use without information on the quantity, depressive symptoms and anxiety symptoms. The NACC–UDS has a nominal variable indicating study sites (ADRCs) where the data were collected.

## 2.7 | Data analysis

For descriptive statistics, means (SD) and frequencies (percentages) for baseline characteristics by follow-up status were compared using analysis of variance (ANOVA) for continuous variables and chi-square tests for categorical variables between participants with and without conversion to AD. We then examined associations of baseline gait and/or balance disturbances with incident AD using hierarchical Cox proportional hazards regression models that estimate HR with 95% confidence intervals (CIs), adjusting for covariates. The first model was a univariate, unadjusted model (Model 1). We included demographic characteristics in Model 2 and medical conditions in Model 3. Finally, to

control for any difference between study sites, we entered the ADRCs indicator into Model 4.

We ran the same models as sensitivity analyses after (1) excluding participants with reversion to normal cognition, (2) excluding participants with conversion to dementias other than AD and (3) excluding participants who met both conditions. We performed a subgroup analysis by sex to see the relationships between gait and/or balance disturbances and incident AD in male and female participants. Baseline gait or balance disturbances were treated as each independent variable for another subgroup analysis because our main analyses were based on gait and/or balance disturbances. The proportional hazards assumption was assessed and satisfied through the interaction between time and Schoenfeld residuals. Results were deemed statistically significant at $p < .05$. All the analyses were performed using SPSS version 27.

## 3 | RESULTS

### 3.1 | Participants' characteristics

The mean follow-up duration (SD) was 4.0 (3.0) years. Overall, 22.1% of the 2692 participants had gait and/or balance disturbances at baseline. The mean (SD) age was 74.5 (7.1) years (range: 60–89 years) with 47.2% being female, 84.1% White, 5.8% Hispanic and 70.4% married. The mean (SD) level of education was 15.5 (3.2) years and the mean MMSE score was 27.5 (1.7). In the terms of smoking history, 52.8% reported no lifetime smoking, 43.8% were former smokers, and 3.4% were current smokers. Based on BMI, 37.1% were normal weight ($18.5 \leq BMI < 25$), 1.3% were underweight ($BMI < 18.5$), 40.2% were overweight ($25 \leq BMI < 30$), and 21.4% were obese ($BMI \geq 30$). At baseline, atrial fibrillation (7.8%), congestive heart failure (2.2%), stroke (5.5%), seizures (2.4%), traumatic brain injury (11.3%), diabetes mellitus (13.3%), vitamin $B_{12}$ deficiency (4.7%), thyroid disease (19.0%) and alcohol (5.5%) or other substance use (1.4%) were present in a minority of the sample. The majority of the sample reported hypertension (54.4%) or hypercholesterolemia (58.5%). A third of the sample reported depressive symptoms (31.4%), while a quarter of the sample reported symptoms of anxiety (24.7%). When looking at gait or balance disturbances separately, 14.4% of participants ($n = 387$) had a gait disturbance and 14.7% ($n = 396$) had a balance disturbance at baseline.

There were 1223 (45.4%) participants who progressed to AD, which is comparable to the statistics that between 30% and 50% of individuals with aMCI develop AD over approximately 5–10 years (Liss et al., 2021). Baseline characteristics between participants with and without conversion to AD are compared in Table 1. Participants with conversion to AD were more likely to have gait and/or balance disturbances (27.6% vs. 17.4%, $p < .001$) and lower MMSE scores (27.1 [SD 1.7] vs. 27.8 [SD 1.7], $p < .001$), and were more likely to be older (75.7 [SD 6.8] vs. 73.5 [SD 7.2], $p < .001$), married (72.4% vs. 68.7%, $p = .033$), White (87.7% vs. 81.1%, $p < .001$) and normal weight (41.9% vs. 33.2%, $p < .001$) at baseline. They were less likely to have traumatic brain injury (9.1% vs. 13.1%, $p = .001$) and diabetes mellitus (11.4% vs. 14.8%, $p = .010$), consume alcohol (4.5% vs. 6.4%, $p = .032$) and other substance (0.8% vs. 2.0%, $p = .012$), and be Hispanic (4.3% vs. 6.9%, $p = .004$) at baseline.

### 3.2 | Association of baseline gait and/or balance disturbances with incident AD

Risk of AD by baseline gait and/or balance disturbances using Cox proportional hazard models is presented in Table 2. Based on HR (CI) from the independent variable treated as binary (presence) and numeric (severity), in the univariate-unadjusted models, participants with gait and/or balance disturbances had a 20% to 45% higher risk for developing AD (HR [CI]: 1.20 [1.13–1.27] to 1.45 [1.28–1.64]). Gait and/or balance disturbances were associated with a 14% to 29% higher risk of incident AD, when adjusting for demographic characteristics (Model 2, HR [CI]: 1.14 [1.07–1.22] to 1.29 [1.13–1.47]), 17% to 33% higher risk when adjusting for demographic characteristics and medical conditions (Model 3, HR [CI]: 1.17 [1.09–1.25] to 1.33 [1.16–1.52]) and 24% to 53% higher risk when adjusting for demographic characteristics, medical conditions and study sites (Model 4, HR [CI]: 1.24 [1.16–1.33] to 1.53 [1.33–1.77]), respectively.

Findings remained robust in sensitivity analyses based on follow-up status and HRs (CIs) for Models 1, 2, 3 and 4 are reported in Table 2. First, we performed sensitivity analyses by excluding individuals with reversion to normal cognition ($n = 225$). The final model indicated that gait and/or balance disturbances were associated with a 19% to 38% higher risk of incident AD. Second, we excluded participants with conversion to dementias other than AD (types not specified, $n = 28$). The final model indicated that gait and/or balance disturbances were associated with a 25%–55% higher risk for incident AD. Last, we removed individuals meeting both the first and second conditions. The final model indicated that gait and/or balance disturbances were associated with a 20%–40% higher risk for incident AD.

In addition, in subgroup analyses by sex, there were no noticeable changes compared with the original analyses. HRs (CIs) for Models 1, 2, 3 and 4 are reported in Table 3. The final model indicated that gait and/or balance disturbances were associated with a 29% to 73% higher risk of incident AD in males ($n = 1421$). The final model indicated that gait and/or balance disturbances were associated with a 26% to 44% higher risk of incident AD in females ($n = 1271$). In another subgroup analysis separating gait and balance disturbances, the final model indicated that those with gait disturbances had a 57% to 81% higher risk for incident AD while those with balance disturbances had a 23% to 32% higher risk. HRs (CIs) for Models 1, 2, 3 and 4 are reported in Table 4.

We further fitted interaction models based on the presence of disturbance and categorized participants into ones without gait or balance disturbances (gait−/balance−: 78.2%, $n = 2105$), those with gait disturbances only (gait+/balance−: 7.1%, $n = 191$), those with balance disturbances only (gait−/balance+: 7.4%, $n = 200$), or those with both gait and balance disturbances (gait+/balance+: 7.3%, $n = 196$). After adjusting for all covariates, compared with the gait−/balance− group, the gait+/balance− group was associated with a 88% higher risk of AD (HR: 1.88, CI: 1.51–2.33, $p < .001$) and the gait+/balance+ group with a 82% higher risk (HR: 1.82, CI: 1.47–2.24, $p < .001$). However, the gait−/balance+ group did not have a higher risk (HR: 1.14, CI: 0.92–1.43, $p = .233$). Compared with the gait+/balance− group, the gait+/balance+ group did not experience a difference in risk of AD, after adjusting for all covariates (HR: 0.97, CI: 0.74–1.26, $p = .814$). However, compared with the

gait−/balance+ group, the gait+/balance+ group had a 59% higher risk of AD, after adjusting for all covariates (HR: 1.59, CI: 1.20–2.10, $p = .001$).

## 4 | DISCUSSION

Because studies have rarely investigated the temporal associations of gait and/or balance disturbances with incident AD among individuals with aMCI, the aim of the current longitudinal observational study leveraging a well-characterized nationwide sample with aMCI was to test the hypothesis that gait and/or balance disturbances at baseline would be associated with higher risk for developing AD. Although there could be reasons why individuals have gait and/or balance disturbances that are not related to cognition, as hypothesized, gait and/or balance disturbances were associated with higher risk of AD after adjusting for demographic characteristics, medical conditions, and study sites. Findings remained robust in (1) sensitivity analyses excluding individuals with reversion to normal cognition and/or with conversion to types of dementia other than AD and (2) subgroup analyses by sex and by separating the gait or balance measure.

Although gait and balance disturbances were not previously examined simultaneously, our findings that gait and/or balance disturbances may predate the onset of AD are consistent with studies of cognitively healthy individuals who do not show objective cognitive decline. A decrease of gait speed was associated with increased risk of developing AD by 1.2–2.1 times (HRs: 1.2 to 2.1) over 4–12 years of follow-up periods among community-dwelling older adults aged 65–74 years (Dumurgier et al., 2017; Kuate-Tegueu et al., 2017; Lee et al., 2018). Other studies indicated that cognitively healthy older adults aged 80 years with fast or normal gait speed showed better global cognition (mean difference: 0.10–0.38) and episodic memory scores (mean difference: 1.38) when compared with those with slow gait (Katsumata et al., 2011; Mielke et al., 2013). Meanwhile, over the follow-up of 3 years, standing balance disturbances presented 1.9–2.5 times higher risk of AD and other dementias (HRs: 1.9–2.5) among the oldest-old population aged 93 years (Bullain et al., 2016). Better physical performance, including balance, decreased the risk of subsequent development of AD by 6% (HR: 0.94) over 5 years among cognitively healthy older adults aged 76 years (Wilkins et al., 2013). Decreased extremity strength in the lower body, leading to balance disturbances and/or falls, was associated with poorer global cognitive performance and higher chance of AD pathology among older adults aged 69–74 years (Stark et al., 2013; Tolea & Galvin, 2016). Thus, our findings are congruent with the extant literature and indicate gait and/or balance disturbances would be a marker of cognitive decline among older adults with aMCI as well as cognitively healthy individuals.

Mechanisms linking gait and/or balance disturbances and the onset of AD are not fully understood, but there could be several explanations. First, AD and physical frailty such as gait and/or balance disturbances would share common risk factors, for example, cardiovascular risk factors. Poor cardiovascular health could decrease blood flow to skeletal muscles and then gait and/or balance disturbances could occur (Strandberg et al., 2013). Second, gait and/or balance disturbances might be a strong indicator for decreased physiologic reserve, which makes the brain more vulnerable to the development of AD pathology (Nadkarni et al., 2017). Third, gait and/or balance disturbances may reflect

inflammation and oxidative stress, highly correlated with AD, would lead to muscle loss, especially of lower body muscles (Quan et al., 2017).

Based on the mechanisms described above, interventions exerting positive effects on cardioprotective, healthy physiological, anti-inflammatory and/or anti-oxidative stress mechanisms may be needed to mitigate gait and/or balance disturbances and further improve cognitive health for older adults with aMCI. These interventions could include healthy nutrition or physical activity including exercise (Chong et al., 2020; van den Brink et al., 2019). A higher adherence to the Mediterranean diet, consisting of olive oil, fish, nuts, vegetables and fruits, was associated with a 52% decreased risk of slow gait speed (OR: 0.48) among community-dwelling older adults aged 65 years (Talegawkar et al., 2012). Physical exercise that strengthens muscles, as well as aerobic exercise, is recommended by the recent physical activity guidelines for cognitive health of older adults with MCI (Chong et al., 2020). In line with these guidelines, systematic reviews indicate that strength and balance exercise combined with walking about 60 min a day, 2 to 3 times a week, appears to improve gait and/or balance among people with MCI or AD and other dementias (Lam et al., 2018; Zhang et al., 2019).

Some evidence suggests that single-modal physical activity (e.g., strengthening physical exercise) also could be considered for older adults with MCI or dementia. Physical activity that enhances lower body strength was found to improve balance and cognition among individuals with MCI or AD and other dementias (Bossers et al., 2015; Mavros et al., 2017). However, little is known about mechanisms by which strength training affects cognitive health when compared with neuroprotective and physiologically healthy aerobic training facilitating brain-derived neurotrophic growth factor, insulin-like growth factor and/or vascular endothelial growth factor. An experimental study for individuals with MCI indicates that strength training, including lower body muscle exercise, led to protection from degeneration or shrinkage in regions of the hippocampus, which is linked to AD pathology (Broadhouse et al., 2020). Further research is required to investigate how strength training, which may improve gait and/or balance disturbances, would mitigate AD pathology. To develop more interventions for cognitive health among individuals with aMCI who have gait and/or balance disturbances, more studies are needed to clarify the neurobiological mechanisms of the associations between gait and/or balance disturbances and risk of incident AD.

Our study suggests clinical implications. The findings highlight the importance of frequent measures of gait and/or balance by nurses and health care providers during the health assessment of older adults with aMCI. In addition, although improving gait and/or balance disturbances may not directly result in better cognitive health, options to mitigate these disturbances, such as healthy nutrition and physical activity, are clinical recommendations that can be provided. Education on various cooking techniques and recipes and modes of physical activity may help overcome barriers to these healthy behaviours (e.g., lack of knowledge on how to meet taste preferences or become physically active) (Chong et al., 2020; Timlin et al., 2021). Synchronous group videoconferencing educational sessions can be considered because these improve accessibility, provide supervision/feedback, and allow interactions with peer participants (Ahn et al., 2022; Ptomey et al., 2020). However,

older adults with aMCI are more prone to experience gait and/or balance disturbances, as well as falls, due to poorer physical function parameters compared with those with healthy cognition, leading to less activity and more sedentary behaviours (Bahureksa et al., 2017; Falcket al., 2017; Nyuntet al., 2017). Therefore, it is worth considering a gradual increase in doses (frequency, intensity and/or duration) for a sense of accomplishment to potentially improve compliance with physical activity sessions (Ahn et al., 2021).

Our study also suggests implications for future research. First, although we excluded patients with PD, the assessment tool for gait and/or balance disturbances in our study may be more sensitive and/or specific to PD. Thus, it may be necessary to conduct further research using more widely used tools for gait and/or balance disturbances, such as the timed up and go, walking speed, the berg balance scale, and/or the functional reach tests. Second, future research may need to differentiate diverse characteristics of gait and/or balance disturbances (gait: gait speed, step width, stance time and/or cadence; balance: standing and/or dynamic balance) to see which aspects of gait and/or balance disturbances are associated with the risk of developing AD among older adults with aMCI. Third, additional research that examines the association between changes in gait and/or balance disturbances over time and incidence of AD needs to be conducted because the scope of our study was to measure baseline physical assessment. Lastly, given that we found that gait and/or balance disturbances increased the risk of AD, it would be intriguing to see whether combined gait and balance disturbances would pose greater risk for AD than either gait or balance disturbances alone. We performed further interaction analyses to investigate this. We found that the combination of gait and balance disturbances predicted higher risk of AD when compared with balance disturbances alone but not with gait disturbances alone. This indicates that those with gait disturbances may be more at risk than balance disturbances. Further research that adopts different aspects of gait and/or balance disturbances is needed to confirm our findings.

### 4.1 | Limitations

Our study comprehensively investigated the associations of gait and/or balance disturbances with development of AD using a standardized nationwide dataset. However, this study is not without limitations. First, because this was not a population-based study, there would be a chance of participant selection bias. However, given that the adjusted HRs in the final Cox model include study sites (ADRC) as one of the covariates, we controlled for any difference between sites where the data were collected. Second, although we include a relatively large sample size and a power analysis indicates sufficient power of this study, there needs to be caution in interpretation of a post hoc power analysis with positive findings (Levine & Ensom, 2001). Third, this observational study provides information on the chronological, but not the causal, relationship between gait and/or balance disturbances and the onset of AD. Due to the data availability, we also could not rule out the possibility of residual confounders such as dietary patterns, physical activity behaviours, family history of AD and/or other fall risk factors, including visual impairment, neurological/skeletal muscle disorders, hospitalization, surgery, medication use (e.g., opioids), and delirium that underlie the associations of gait and/or balance disturbances with AD. Finally, our sample is not representative of all older adults with aMCI in the United States as the majority

of the sample was White (84%). Both nationwide and worldwide repetitive studies are necessary to enhance the generalizability of our findings by inviting participants from diverse backgrounds.

## 5 | CONCLUSION

Gait and/or balance disturbances were associated with incident AD among older adults with aMCI. A frequent assessment of gait and/or balance disturbances may be a more practical tool for nurses and health care providers to identify potential risk factors for cognitive decline.

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## DATA AVAILABILITY STATEMENT

This study was conducted using publicly available data from the National Alzheimer's Coordinating Center (https://naccdata.org).

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**TABLE 1**

Baseline characteristics of participants based on follow-up status ($n$ = 2692).

| Characteristics | All participants, $n$ = 2692 | Participants without AD, $n$ = 1469 | Participants with AD, $n$ = 1223 | $p$-value |
|---|---|---|---|---|
| Gait and/or balance disturbances[†], $n$ (%) | 594 (22.1%) | 256 (17.4%) | 338 (27.6%) | <.001*** |
| Age (years), mean (SD) | 74.5 (7.1) | 73.5 (7.2) | 75.7 (6.8) | <.001*** |
| Female, $n$ (%) | 1271 (47.2%) | 674 (45.9%) | 597 (48.8%) | .129 |
| Education (years), mean (SD) | 15.5 (3.2) | 15.5 (3.2) | 15.6 (3.1) | .193 |
| Married, $n$ (%) | 1895 (70.4%) | 1009 (68.7%) | 886 (72.4%) | .033* |
| White, $n$ (%) | 2265 (84.1%) | 1192 (81.1%) | 1073 (87.7%) | <.001*** |
| Hispanic, $n$ (%) | 155 (5.8%) | 102 (6.9%) | 53 (4.3%) | .004** |
| MMSE score, mean (SD) | 27.5 (1.7) | 27.8 (1.7) | 27.1 (1.7) | <.001*** |
| Smoking status, $n$ (%) | | | | |
| Never smoker | 1422 (52.8%) | 771 (52.5%) | 651 (53.2%) | .565 |
| Former smoker | 1180 (43.8%) | 644 (43.8%) | 536 (43.8%) | |
| Current smoker | 90 (3.4%) | 54 (3.7%) | 36 (3.0%) | |
| Body mass index, $n$ (%) | | | | |
| Normal weight | 1000 (37.1%) | 487 (33.2%) | 513 (41.9%) | <.001*** |
| Underweight | 36 (1.3%) | 18 (1.2%) | 18 (1.5%) | |
| Overweight | 1083 (40.2%) | 601 (40.9%) | 482 (39.4%) | |
| Obese | 573 (21.4%) | 363 (24.7%) | 210 (17.2%) | |
| Atrial fibrillation, $n$ (%) | 211 (7.8%) | 117 (8.0%) | 94 (7.7%) | .789 |
| Congestive heart failure, $n$ (%) | 59 (2.2%) | 38 (2.6%) | 21 (1.7%) | .125 |
| Stroke, $n$ (%) | 147 (5.5%) | 75 (5.1%) | 72 (5.9%) | .374 |
| Seizures, $n$ (%) | 64 (2.4%) | 41 (2.8%) | 23 (1.9%) | .123 |
| Traumatic brain injury, $n$ (%) | 303 (11.3%) | 192 (13.1%) | 111 (9.1%) | .001** |
| Diabetes mellitus, $n$ (%) | 358 (13.3%) | 218 (14.8%) | 140 (11.4%) | .010* |
| Hypertension, $n$ (%) | 1465 (54.4%) | 806 (54.9%) | 659 (53.9%) | .610 |
| Hypercholesterolemia, $n$ (%) | 1576 (58.5%) | 871 (59.3%) | 705 (57.6%) | .388 |
| Vitamin $B_{12}$ deficiency, $n$ (%) | 127 (4.7%) | 66 (4.5%) | 61 (5.0%) | .547 |

| Characteristics | All participants, *n* = 2692 | Participants without AD, *n* = 1469 | Participants with AD, *n* = 1223 | *p*-value |
|---|---|---|---|---|
| Thyroid disease, *n* (%) | 512 (19.0%) | 273 (18.6%) | 239 (19.5%) | .528 |
| Alcohol use, *n* (%) | 149 (5.5%) | 94 (6.4%) | 55 (4.5%) | .032* |
| Substance use, *n* (%) | 39 (1.4%) | 29 (2.0%) | 10 (0.8%) | .012* |
| Depressive symptoms, *n* (%) | 845 (31.4%) | 465 (31.7%) | 380 (31.1%) | .746 |
| Anxiety symptoms, *n* (%) | 666 (24.7%) | 362 (24.6%) | 304 (24.9%) | .898 |

Abbreviations: AD, Alzheimer's dementia; MMSE, Mini-Mental State Exam; SD, standard deviation.

†Based on the presence.

*$p < .05$

**$p < .01$

***$p < .001$.

**TABLE 2**

Risk of Alzheimer's dementia by baseline gait and/or balance disturbances ($n$ = 2692).

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** |
| Binary (reference: absence) | | | | | | | | |
| Gait and/or balance disturbances | 1.45 (1.28–1.64) | <.001*** | 1.29 (1.13–1.47) | <.001*** | 1.33 (1.16–1.52) | <.001*** | 1.53 (1.33–1.77) | <.001*** |
| Numeric (per 1-point increase) | | | | | | | | |
| Gait and/or balance disturbances | 1.20 (1.13–1.27) | <.001*** | 1.14 (1.07–1.22) | <.001*** | 1.17 (1.09–1.25) | <.001*** | 1.24 (1.16–1.33) | <.001*** |
| Sensitivity analyses: Binary (reference: absence) | | | | | | | | |
| Gait and/or balance disturbances ($n$ = 2467) – by excluding participants with healthy cognition at follow-up | 1.25 (1.10–1.42) | <.001*** | 1.16 (1.01–1.32) | .030* | 1.21 (1.06–1.38) | .005** | 1.38 (1.19–1.59) | <.001*** |
| Gait and/or balance disturbances ($n$ = 2664) – by excluding participants with dementias other than Alzheimer's dementia at follow-up | 1.45 (1.27–1.64) | <.001*** | 1.30 (1.14–1.48) | <.001*** | 1.34 (1.17–1.53) | <.001*** | 1.55 (1.35–1.79) | <.001*** |
| Gait and/or balance disturbances ($n$ = 2439) – by excluding participants who met both conditions | 1.25 (1.10–1.41) | .001** | 1.16 (1.02–1.32) | .025* | 1.22 (1.07–1.39) | .004** | 1.40 (1.21–1.61) | <.001*** |
| Sensitivity analyses: Numeric (per 1-point increase) | | | | | | | | |
| Gait and/or balance disturbances ($n$ = 2467) – by excluding participants with healthy cognition at follow-up | 1.13 (1.06–1.20) | <.001*** | 1.09 (1.02–1.17) | .008** | 1.12 (1.05–1.20) | .001** | 1.19 (1.11–1.28) | <.001*** |
| Gait and/or balance disturbances ($n$ = 2664) – by excluding participants with dementias other than Alzheimer's dementia at follow-up | 1.20 (1.13–1.27) | <.001*** | 1.15 (1.08–1.22) | <.001*** | 1.17 (1.10–1.25) | <.001*** | 1.25 (1.17–1.34) | <.001*** |
| Gait and/or balance disturbances ($n$ = 2439)—by excluding participants who met both conditions | 1.13 (1.06–1.20) | < .001*** | 1.10 (1.03–1.17) | .006** | 1.13 (1.05–1.21) | < .001*** | 1.20 (1.12–1.29) | <.001*** |

*Note*: Model 1 = HR was not adjusted, Model 2 = HR adjusted for demographic characteristics, Model 3 = HR adjusted for medical conditions and demographic characteristics, Model 4 = HR adjusted for study sites, demographic characteristics, and medical conditions. Binary = variable based on presence or absence, Numeric = variable based on score.

Demographic characteristics include baseline age, sex, education, marital status, race and ethnicity. Medical conditions include baseline Mini-Mental State Exam score, smoking history, body mass index, and the presence of atrial fibrillation, congestive heart failure, stroke, seizures, traumatic brain injury, diabetes mellitus, hypertension, hypercholesterolemia, vitamin $B_{12}$ deficiency, thyroid disease, alcohol or other substance use and depressive and anxiety symptoms.

Abbreviations: CI, 95% confidence interval; HR, hazard ratio.

* $p < .05$

** $p < .01$

*** $p < .001$.

**TABLE 3**

Risk of Alzheimer's dementia by baseline gait and/or balance disturbances by sex.

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** |
| Male | | | | | | | | |
| Binary (reference: absence) | | | | | | | | |
| Gait and/or balance disturbances | 1.60 (1.34–1.92) | <.001*** | 1.44 (1.20–1.73) | <.001*** | 1.47 (1.22–1.77) | <.001*** | 1.73 (1.41–2.11) | <.001*** |
| Numeric (per 1-point increase) | | | | | | | | |
| Gait and/or balance disturbances | 1.21 (1.11–1.32) | <.001*** | 1.16 (1.06–1.27) | .001** | 1.17 (1.07–1.29) | .001** | 1.29 (1.17–1.42) | <.001*** |
| Female | | | | | | | | |
| Binary (reference: absence) | | | | | | | | |
| Gait and/or balance disturbances | 1.28 (1.07–1.53) | .006** | 1.15 (0.95–1.38) | .159 | 1.18 (0.97–1.43) | .103 | 1.44 (1.16–1.79) | .001** |
| Numeric (per 1-point increase) | | | | | | | | |
| Gait and/or balance disturbances | 1.18 (1.08–1.28) | <.001*** | 1.11 (1.01–1.22) | .030* | 1.15 (1.04–1.27) | .006** | 1.26 (1.14–1.39) | <.001*** |

*Note*: Model 1 = HR was not adjusted, Model 2 = HR adjusted for demographic characteristics, Model 3 = HR adjusted for medical conditions as well as demographic characteristics, Model 4 = HR adjusted for study sites, demographic characteristics, and medical conditions. Binary = variable based on presence or absence, Numeric = variable based on score.

Demographic characteristics include baseline age, education, marital status, race and ethnicity. Medical conditions include baseline Mini-Mental State Exam score, smoking history, body mass index, and the presence of atrial fibrillation, congestive heart failure, stroke, seizures, traumatic brain injury, diabetes mellitus, hypertension, hypercholesterolemia, vitamin $B_{12}$ deficiency, thyroid disease, alcohol or other substance use and depressive and anxiety symptoms.

Abbreviations: CI, 95% confidence interval; HR, hazard ratio.

* $p < .05$

** $p < .01$

*** $p < .001$.

**TABLE 4**

Risk of Alzheimer's dementia by baseline gait or balance disturbances ($n$ = 2692).

| | Model 1 | | Model 2 | | Model 3 | | Model 4 | |
|---|---|---|---|---|---|---|---|---|
| **Characteristics** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** | **HR (CI)** | ***p*-value** |
| Binary (reference: absence) | | | | | | | | |
| Gait disturbances | 1.55 (1.34–1.78) | <.001*** | 1.39 (1.20–1.62) | <.001*** | 1.45 (1.24–1.69) | <.001*** | 1.81 (1.54–2.14) | <.001*** |
| Numeric (per 1-point increase) | | | | | | | | |
| Gait disturbances | 1.36 (1.22–1.51) | <.001*** | 1.28 (1.14–1.43) | <.001*** | 1.33 (1.18–1.49) | <.001*** | 1.57 (1.39–1.78) | <.001*** |
| Binary (reference: absence) | | | | | | | | |
| Balance disturbances | 1.38 (1.19–1.59) | <.001*** | 1.21 (1.04–1.40) | .012* | 1.22 (1.05–1.42) | .008** | 1.32 (1.12–1.54) | .001** |
| Numeric (per 1-point increase) | | | | | | | | |
| Balance disturbances | 1.27 (1.15–1.40) | <.001*** | 1.16 (1.04–1.29) | .006** | 1.18 (1.06–1.32) | .002** | 1.23 (1.10–1.38) | <.001*** |

*Note*: Model 1 = HR was not adjusted, Model 2 = HR adjusted for demographic characteristics, Model 3 = HR adjusted for medical conditions as well as demographic characteristics, Model 4 = HR adjusted for study sites, demographic characteristics, and medical conditions. Binary = variable based on presence or absence, Numeric = variable based on score.

Demographic characteristics include baseline age, sex, education, marital status, race, and ethnicity. Medical conditions include baseline Mini-Mental State Exam score, smoking history, body mass index, and the presence of atrial fibrillation, congestive heart failure, stroke, seizures, traumatic brain injury, diabetes mellitus, hypertension, hypercholesterolemia, vitamin $B_{12}$ deficiency, thyroid disease, alcohol or other substance use and depressive and anxiety symptoms.

Abbreviations: CI, 95% confidence interval; HR, hazard ratio.

* $p < .05$

** $p < .01$

*** $p < .001$.