ORIGINAL ARTICLE

BALANCE DISORDERS ASSOCIATED WITH ALZHEIMER'S DISEASE

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Abstract

Objective: The risk of falling dramatically increases in Alzheimer's disease. This study utilized static and dynamic balance tests to determine the stage of Alzheimer's disease at which balance impairment and fall risk become more pronounced.

Materials and Method: A total of 198 patients between 60 and 85 years of age were categorized into normal, mild cognitive impairment, mild dementia, moderate dementia, and advanced dementia based on the standardized Mini-Mental State Examination scores and the Reisberg Global Deterioration Scale. Static tests comprised the Romberg and Single-Leg Stance tests, and the 10-Step Tandem Gait Test was used as the dynamic test.

Results: Patients who failed the single-leg and Romberg tests had significantly lower Mini-Mental State Examination scores ($p<0.001$) and higher Reisberg Global Deterioration Scale scores ($p<0.001$). Similarly, failure in the 10-step tandem test correlated with lower Mini-Mental State Examination scores ($p<0.001$) and higher Reisberg Global Deterioration Scale scores ($p<0.001$). ROC analysis revealed a significant increase in the single-leg and tandem test failure rates when Mini-Mental State Examination scores dropped below 18.5, while positive Romberg results were significantly below 15.5. For Reisberg Global Deterioration Scale, failure rates rose above scores of 3.5 for the single-leg and tandem tests and above 4.5 for the Romberg test.

Conclusion: In patients with Alzheimer's disease, balance disorders begin in the early stages and increasing their risk of falls compared to the normal elderly population. Early environmental modifications are critical to prevent falls and injuries.

Keywords: Alzheimer Disease; Neuropsychological Tests; Accidental Falls.

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INTRODUCTION

Alzheimer's disease (AD) is a progressive neurodegenerative disease of the brain, characterized by a gradual loss in neurons' structure and function, ultimately leading to their death. It is the most common type of dementia in older adults, accounting for approximately 60-80% of all dementia patients (1). As a significant cause of dementia, Alzheimer's disease affects approximately 35 million people worldwide. The disease is most common in people over 65 years of age; however, approximately 5% of cases are classified as early-onset, developing in patients over 40 years of age (2). Its pathophysiology is marked by the accumulation of extracellular β-amyloid (B), the build-up of intracellular hyperphosphorylated tau (pTau), loss of neurons, and inflammation (3). The initial indication of the condition is typically a decline in recent memory. Early symptoms can encompass feelings of depression, anxiety, a tendency to socially isolation, and disruptions in sleep patterns. These symptoms are often distinguished from other neurodegenerative disorders by their early predominance of memory-related complaints and less frequent occurrence of motor dysfunction in the initial stages. As the disease advances, cognitive abilities further decline, resulting in significant memory impairment, neuropsychiatric issues such as hallucinations and delusions, and various behavioral challenges in the later stages. In addition, some patients may experience varying degrees of visual-spatial, language, executive, and motor dysfunctions (4).

AD is now recognized as a spectrum disease with the advent of clinical and biological tools, such as imaging techniques (PET and MRI scans) and biomarker analysis (amyloid-beta and tau levels in cerebrospinal fluid). The US National Institute on Aging-Alzheimer's Association (NIA-AA) group considered AD in 3 different spectra. The first is the preclinical stage, where there is no cognitive impairment, but biomarkers of Alzheimer's disease are detected. Stage 2 is mild cognitive impairment (MCI). This stage is characterized by evidence of impairment in memory or other cognitive domains, as well as biomarkers of AD on standard assessment. The final stage is dementia due to AD (5).

Falling is the foremost cause of trauma-related injuries, disabilities, and deaths in older adults. About 30% of older adults living in the community experience one or multiple falls each year. The consequences of falls range from fractures to severe morbidity (6). The incidence of falls in individuals with Alzheimer's disease is 60-80% higher than in elderly individuals with normal cognitive function . Injury after a fall is shown to be more common in patients with AD. The increased risk of falls among older adults with dementia and cognitive impairment can be linked to difficulties in navigating obstacles, balance issues, and problems with spatial awareness and vision. Effective fall prevention strategies are essential in reducing falls and their associated adverse consequences as well as the associated personal, societal, health, and economic costs (7). In this study, we utilized static and dynamic balance tests to determine the stage of AD at which the loss of balance first became pronounced and the risk of falls significantly increased.

MATERIALS AND METHOD

This study included patients aged 60-85 with mild cognitive impairment and AD, as well as healthy volunteers. The participants were recruited from a neurology outpatient clinic between December 2023 and November 2024. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. An authorized institution granted ethics committee approval with protocol number 18/12/2023-352, and informed consent was obtained from all participants.

In the patient and control groups, the Standardised Mini-Mental test (MMSE) and Reisberg

Global Deterioration Scale (RGDS) were evaluated by an experienced neurologist and clinical psychologist. MMSE scores were considered normal between 24 and 30, mild between 20 and 23, moderate between 10 and 19, and advanced dementia between 0-9 (8). RGDS stage 1 was considered as control group without cognitive impairment, RGDS stage 2 as cognitive loss due to normal aging, RGDS stage 3 as mild cognitive impairment (MCI), RGDS stage 4 as mild dementia, RGDS stage 5 as moderate dementia, and RGDS stage 6-7 as advanced dementia (9).

Two different neurologists assessed balance tests in both the patient and control groups at separate times, and any discrepancies in results led to a third evaluation. Participants underwent two static tests and one dynamic test to assess the balance and fall risk. The static tests included the single-leg stance and the Romberg test. Participants raised their dominant leg and bent the other leg at a 90-degree angle for the single-leg stance test, maintaining balance without external support. This test was conducted with the eyes open. Patients who failed to maintain their balance for 5 seconds during the test were deemed at risk for falling (10).

In the Romberg test, the patient was instructed to assume an upright position with the feet positioned at shoulder width and the arms held at the sides in a stationary position. All participants were instructed to wear flat footwear during the test. The subject was not provided with any assistance and was asked to maintain an upright stance with their eyes open and then closed. Measures were taken to prevent falling during the test. A positive Romberg sign indicated an abnormal deviation, or a step taken by an individual while standing with eyes open or closed for 10 seconds. A negative score indicated minimal or no deviation from the standing position (11).

The 10-step tandem gait test, performed as the dynamic assessment, is widely recognized for evaluating balance and coordination, particularly in populations at risk of falls (12). In this test, participants were asked to stand with their feet together and walk ten steps in a straight line, ensuring that the toe of one foot touched the heel of the other. The number of steps taken before the first misstep was noted. After completing the initial 10-step tandem gait test, the patient was instructed to turn around and repeat the test along the same line, with the steps counted similarly.

The higher score from the two attempts was considered in the evaluation. Participants were categorized into five subgroups based on the number of consecutive steps taken during the test: grade 0 (unable to walk), grade 1 (3 steps or fewer), grade 2 (fewer than 10 steps), grade 3 (10 steps but unstable, swaying side to side), and grade 4 (10 steps, normal). Patients who scored between grades 0 and 3 were considered to have failed. The dementia stages of the participants were determined using the MMSE and RGDS, and the results of the dynamic and static tests were compared.

The study excluded several patient groups including patients with a history of stroke and demyelinating diseases. Patients with central nervous system tumors or hydrocephalus observed on brain imaging were also excluded. In addition, patients with traumatic or inflammatory spinal cord conditions, any form of peripheral neuropathy (including diabetic, inflammatory, hereditary), and diabetes mellitus regardless of having diabetic polyneuropathy confirmed by standardized tests were also excluded. Furthermore, the study did not include patients with degenerative or inflammatory joint diseases that hindered walking and patients with severe visual impairment from any cause.

Statistical Analysis

Patient data collected within the scope of the study were analyzed with the IBM Statistical Package for the Social Sciences (SPSS) for Windows 26.0 (IBM Corp., Armonk, NY) package software. Categorical data were presented as frequency and percentage, and continuous data were described as mean and

standard deviation. The normality of the numerical variables was evaluated according to the skewness and kurtosis coefficients. Skewness measures the asymmetry of the data distribution, while kurtosis indicates the sharpness or flatness of the distribution compared to a normal distribution. The variables followed a normal distribution, as the coefficients were within the range of ±2. As a result, parametric statistical methods were used in the study. In addition, a receiver operating characteristic (ROC) curve analysis was performed to determine whether a specific numerical variable could effectively differentiate between various diagnostic categories. For comparisons between groups, the "Independent Sample T-test" was used for two groups, and the "Pearson Chi-Square Test" was used to compare categorical variables. The results were considered statistically significant when the p-value was less than 0.05.

RESULTS

A total of 198 patients were included in the study. The MMSE and RGDS tests were administered to all participants. The mean age was 75.16 ± 4.78 years, with 48% (n=95) female. This distribution closely reflected the general demographics of Alzheimer's disease, where prevalence tended to increase with age, and women were disproportionately affected due to their longer life expectancy. The mean MMSE score was 18.53 ± 5.61, while the average RGDS score was 3.52 ± 1.69.

According to the MMSE results, 5.6% (n=11) of the patients were classified as having advanced dementia, 50.5% (n=100) as having moderate dementia, 24.7% (n=49) as having mild dementia, and 19.2% (n=38) as having normal cognitive function. The RGDS results showed that 17.2% (n=34) of the patients were classified as having advanced dementia, 15.7% (n=31) as having moderate dementia, 16.2% (n=32) as having mild dementia, 19.2% (n=38) as having mild cognitive impairment, 16.7% (n=33) as having age-related cognitive impairment, and 15.2% (n=15) as being in the normal range.

Among the study participants, 54.5% (n=108) were unable to complete the single-leg test, 19.2% (n=38) failed the Romberg test, and 48% (n=95) could not complete the tandem test. These differences in failure rates may reflect the varying physical and cognitive demands of each

Table 1. Demographic Characteristics of Patients

(n=198)	Mean±SD
Age	75.16±4.78
MMSE	18.53±5.61
RGDS	3.52±1.69
	n(%)
Gender	
Woman	95(48.0)
Man	103(52.0)
MMSE	
Severe Dementia	11(5.6)
Moderate Dementia	100(50.5)
Mild Dementia	49(24.7)
Normal	38(19.2)
RGDS	
Normal	30(15.2)
Age-related cognitive impairment	33(16.7)
Mild Cognitive Impairment	38(19.2)
Mild Dementia	32(16.2)
Moderate Dementia	31(15.7)
Severe Dementia	34(17.2)
Single Leg	
Successful	90(45.5)
Failed	108(54.5)
Romberg	
Positive	38(19.2)
Negative	160(80.8)
Tandem	
Successful	103(52.0)
Failed	95(48.0)

SD: Standard Deviation, MMSE: Standardised Mini-Mental Test, RGDS: Reisberg Global Deterioration Scale

Table 2. Relationship of test results according to MMSE and RGDS

	MMSE			RGDS		
	Mean±SD	**t**	**p**	**Mean±SD**	**t**	**p**
Single Leg						
Successful	22.11±4.63	10.074	**<0.001**	2.43±1.36	-0.210	**<0.001**
Failed	15.55±4.51			4.43±1.38		
Romberg						
Positive	13.00±3.63	-9.535	**<0.001**	5.13±1.07	-9.326	**<0.001**
Negative	19.84±5.19			3.14±1.58		
Tandem						
Successful	21.66±4.62	10.029	**<0.001**	2.58±1.38	-9.963	**<0.001**
Failed	15.14±4.52			4.54±1.37		

SD: Standard Deviation, MMSE: Standardised Mini-Mental Test, RGDS: Reisberg Global Deterioration Scale, t: Independent Sample T-Test *: p<0.05

test. For example, the single-leg test focused on lower body strength and balance, while the Romberg test relied more on sensory input, such as proprioception and vision. The dynamic tandem test required coordination and spatial awareness, which may explain its intermediate failure rate (Table 1).

The MMSE and RGDS scores were analyzed using the Independent Sample T-Test to compare the means between two independent groups and determine statistically significant differences. The results showed that MMSE scores were significantly lower (22.11±4.63 vs. 15.55±4.51; t=10.074, p=0.000), whereas RGDS scores were significantly higher (2.43±1.36 vs. 4.43±1.38; t=-0.210, p=0.000). In addition, MMSE scores were also significantly lower (t=-9.535, p=0.000), and RGDS scores were significantly higher (t=-9.326, p=0.000). MMSE values were notably lower in patients who failed the Tandem Test (t=10.029, p=0.000), while RGDS scores were significantly higher (t=-9.963, p=0.000). These significant differences suggested that individuals with lower MMSE scores and higher RGDS scores had greater impairments in cognitive and functional domains, which may have impacted their inability to complete balance-related tasks successfully (Table 2).

A ROC analysis was performed to determine the best cut-off points for MMSE and RGDS values. This method is particularly suitable for evaluating the diagnostic ability of numerical variables, as it provides sensitivity and specificity values at various thresholds, enabling the identification of the optimal cut-off points. A notable rise in failure rates was observed in patients with MMSE scores below 18.5 for the single-leg and tandem Tests (sensitivity: 75.0%, specificity: 83.3%). These sensitivity and specificity values suggested that the tests were relatively reliable for identifying individuals at risk of balance issues, with a good balance between detecting true positives and minimizing false positives. A statistically significant positive rate was also identified in patients with MMSE scores below 15.5 for the Romberg Test (sensitivity: 80.0%, specificity: 81.6%). These cut-off points may guide clinicians in identifying patients at higher risk of falls, enabling early interventions such as balance training, physical therapy, or home safety modifications to mitigate these risks. For the single leg and tandem tests, a significant increase in failure rates was noted in patients with RGDS scores above 3.5 (sensitivity: 75.9%, specificity: 83.3%; sensitivity: 74.7%, specificity: 74.8%, respectively). Compared to MMSE cut-off values, which had similar pattern with scores below 18.5, the RGDS scores provided an additional perspective by focusing more on

global deterioration, complementing the cognitive emphasis of MMSE. Furthermore, a statistically significant positive rate was found in patients with RGDS scores above 4.5 (sensitivity: 78.8%, specificity: 81.6%) for the Romberg test. (Table 3, Figure 1, Figure 2).

Tablo-3. ROC Cut-Off Point for diagnosis in test results related to MMSE and RGDS Scores

Score	Test	Cut-Off Point	Sensitivity-Selectivity
MMSE	Single Leg	18.5	75.0%-83.3%
	Romberg	15.5	80.0%-81.6%
	Tandem	18.5	73.7%-74.8%
RGDS	Single Leg	3.5	75.9%-83.3%
	Romberg	4.5	78.8%-81.6%
	Tandem	3.5	74.7%-74.8%

ROC: Receiver Operating Characteristic, MMSE: Standardised Mini-Mental Test, RGDS: Reisberg Global Deterioration Scale

Figure 1. OC: Receiver Operating Characteristic, MMSE: Standardised Mini-Mental Test

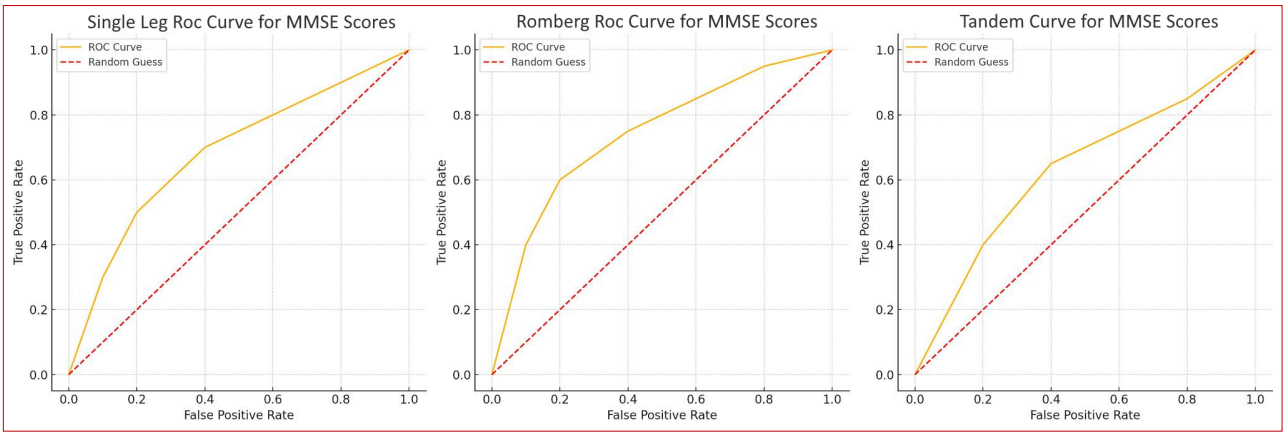
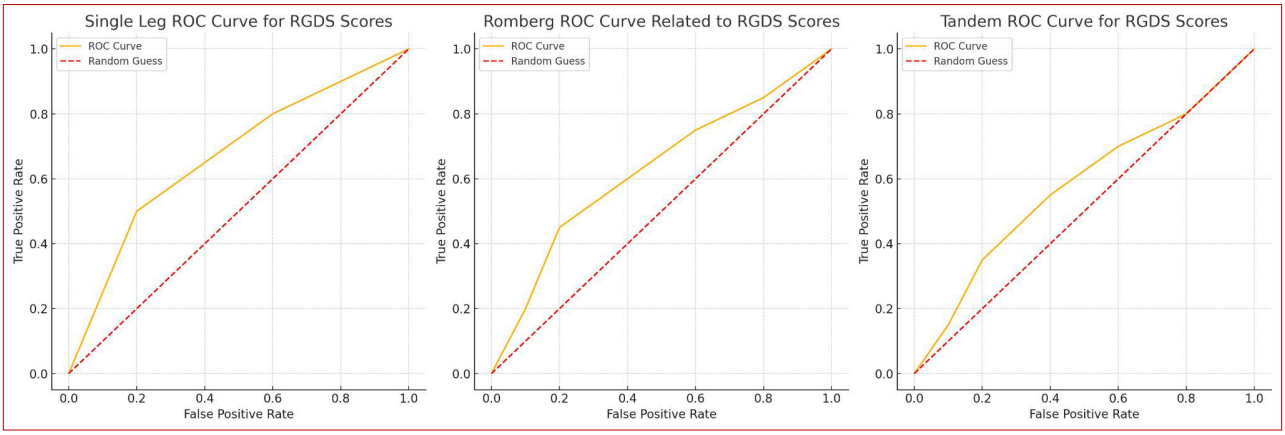


Figure 2. ROC: Receiver Operating Characteristic, RGDS: Reisberg Global Deterioration Scale



DISCUSSION

Looking at our findings, the decline in dynamic and static balance tests becomes pronounced at moderate dementia levels as measured by the MMSE and at mild cognitive impairment levels according to the RGDS. As the condition advances, deficits in balance tests become increasingly evident. We observed that the onset of deterioration in these balance tests occurred at similar stages of dementia. Some studies suggested that the severity of dementia assessed by the MMSE could differ from that evaluated using the RGDS. The MMSE assesses various cognitive functions, including short- and long-term memory, language skills, and orientation to time and place (13). However, it has been shown that MMSE scores are generally normal in patients with mild cognitive impairment at the initial stage of dementia (14). In our study, we hypothesize that the difference in balance tests at different stages of dementia determined according to various scales may be due to this reason.

Previous studies have found different results when using clinic-based and laboratory-based tests to investigate postural stability in AD. The most common clinic-based static balance tests are the tandem gait, Romberg, and single-leg stance tests (15). The tandem gait test and the functional reach test can be used in the clinic for dynamic balance (16). Functional performance tests also measure dynamic and static balance together. Among these tests, studies have assessed balance and coordination in AD using the Up and Go Test, the Berg Balance Scale, and the Parametric Rating Scale for Balance and Limb Coordination (17). The most popular tests in studies investigating balance loss in AD include the Computerized Dynamic Posturography Platform (EquiTest), the Force Platform, Stabilometry, and the NeuroCom Balance Master (18). The common feature of these studies is that static, dynamic, and functional tests deteriorate in early AD. Our study concluded that both dynamic and static tests revealed deteriorations in the early stages, similar to previous studies. Unlike other studies, instead of measuring the longest time patients could maintain balance in clinical tests, we classified patients according to their ability to complete the test within a certain time. This enabled us to assess patients' balance more quickly in an outpatient setting. In addition, unlike previous studies, we included a similar number of patients at similar ages at each stage from RGDS stage 1 to stage 6. We found that the deterioration in balance tests increased linearly.

Developing effective prevention strategies requires recognizing the multifaceted nature of falls among older adults. Understanding the underlying mechanisms of falls enables more accurate clinical assessments and analyses of the associated risks. The most common causes of falls are loss of balance and dizziness, followed by falling down stairs or steps (19). Multiple factors contribute to falls in AD, including cognitive, physical, sensory, psychological, medication-related, and environmental factors (20).

As cognitive impairment worsens, the likelihood of falls increases. Challenges such as impaired judgment, memory issues, difficulties with executive functions, attention deficits, and the inability to perform dual tasks can hinder a person's ability to navigate obstacles. This diminishes decision-making skills and heightens the risk of falling (21).

Impairments in cognitive processes affect functional mobility (gait and balance) and muscle strength through disruptions in motor planning, control, attention, and sensory integration. They may also affect motor function by disrupting neural networks fundamental to the planning and execution of various motor behaviors. Sensory deficits are also associated with gait and balance problems and an increased risk of falling. In particular, visual attention, perception, and peripheral sensory loss impairments are typical in AD (22).

In individuals with AD, psychological factors such as depression, anxiety, delirium, and sleep

disorders can lead to falls by reducing alertness. Side effects of medications prescribed to individuals with AD, including antidepressants, antipsychotics, and cholinesterase inhibitors, such as dizziness, imbalance, and weakness, may further increase the risk of falls (23).

More than 70% of falls in people with Alzheimer's disease occur at home, with approximately 10% occurring on stairs. Carrying heavy or bulky objects, slippery floors, and insufficient lighting are reported to be the most common environmental hazards associated with falls (24). Patterns on the floor or walls can also pose a potential danger by distorting or enhancing visual perception. Another significant risk factor is using poorly fitting or slippery footwear (25).

Our study had some limitations. Only clinic-based tests were used to assess patients' balance. Incorporating laboratory-based tests with clinic-based tests could enhance sensitivity. A second limitation was that we did not monitor changes in balance tests in individuals without cognitive impairment as they potentially developed dementia over time. As a result, we could not determine whether participants without dementia would face an increased risk of developing dementia in the future with impaired balance tests, based on MMSE and RGDS scores. Further studies with extended follow-up periods and multiple visits are needed to explore this potential association.

CONCLUSION

Balance impairment in AD begins in the early stages of the disease. Compared to the normal elderly population, individuals with AD face a significantly higher risk of falls due to impaired balance. Early intervention to address environmental factors is crucial, particularly in preventing potential falls and associated injuries.

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