RESEARCH

ASSOCIATION OF NEURODEGENERATIVE DISEASES WITH SARCOPENIA AND OTHER GERIATRIC SYNDROMES

Turkish Journal of Geriatrics
DOI: 10.31086/tjgeri.2022.282
2022; 25(2): 246-253

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Abstract

Introduction: This study aimed to evaluate the association between two most common neurodegenerative diseases, Alzheimer's disease and Parkinson's disease, with sarcopenia and other common geriatric syndromes.

Materials and Method: In this retrospective cross-sectional study, patients admitted to the geriatrics outpatient clinic for the first time were included. Patients who were under 65 years of age and who presented a history of acute severe diseases that may impair the general health status or with malignancies (except being in full remission for at least 5 years) were excluded.

Results: A total of 339 (243 females) patients were included. The prevalence of geriatric syndromes among the participants was as follows: 225 (66.4%) patients had polypharmacy; 111 (32.7%) had sarcopenia; 100 (29.5%) had osteoporosis; 95 (28%) had depression; 83 (24.5%) had malnutrition; 62 (18.3%) had urinary incontinence; 31 (9.1%) had insomnia, and 30 (8.8%) had delirium. Sixty-four patients were diagnosed with Alzheimer's and 30 with Parkinson's disease. In multivariate logistic regression analysis, Alzheimer's disease was significantly associated with sarcopenia [p=0.036, odds ratio (OR)=2.048, 95% confidence interval (CI)=1.049–3.998] and delirium (p<0.001, OR=16.365, 95% CI=6.103–43.880). Parkinson's disease was significantly associated with sarcopenia (p=0.014, OR=2.744, 95% CI=1.231–6.116).

Conclusion: To our best knowledge, the present study is the first to evaluate the association between the two most common neurodegenerative diseases and multiple geriatric syndromes. Sarcopenia is the common independent factor for both Alzheimer's and Parkinson's disease. Therefore, screening for sarcopenia in patients with Alzheimer's and Parkinson's disease is important in routine practice.

Keywords: Sarcopenia; Alzheimer Ddisease; Delirium; Parkinson Disease.

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Received: Feb 23, 2022
Accepted: May 11, 2022

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INTRODUCTION

Geriatric syndromes are not isolated diseases and are often associated with complex clinical manifestations, with common risk factors in older adults (1). In clinical settings, cognitive impairment, delirium, urinary incontinence, malnutrition, depression, polypharmacy, sarcopenia, and sleep problems represent common geriatric syndromes (2). Geriatric syndromes are the leading causes of mortality, morbidity, and increased healthcare cost.

The rise in global elderly population and advances in geriatrics have promoted interest in geriatric syndromes, particularly sarcopenia. In 2019, the European Working Group on Sarcopenia in Older People (EWGSOP2) revised the definition of sarcopenia. According to EWGSOP2, low muscle strength is the primary component of sarcopenia, followed by muscle dysfunction. In cases with low muscle strength alone, sarcopenia is the probable diagnosis, and the definite diagnosis of sarcopenia is made when low muscle mass accompanies low muscle strength (3).

Aging is one of the most important risk factors for the occurrence and progression of neurodegenerative diseases. This is because the brain is primarily composed of post-mitotic cells, which are more vulnerable to DNA damage than proliferating cells (4). Elevation of pro-inflammatory mediators and increased oxidative stress, leading to the activation of microglia and, ultimately, chronic inflammation, are associated with age-related neurodegenerative diseases (5). In the elderly population, Alzheimer's disease (AD) and Parkinson's disease (PD) are the two most common neurodegenerative diseases, respectively.

Neurodegeneration in AD leads to progressive cognitive and functional decline. The prevalence of sporadic (late-onset) AD has been increasing. Specifically, in 2010, over 35 million people in the world had AD, and by 2050, the incidence is expected to triple (6). According to the amyloid cascade hypothesis, accumulation of beta-amyloid plaques outside and of tau tangles inside the neurons activates the immune system, and this chronic inflammation leads to cell loss, atrophy, or brain shrinkage (7). Although some promising anti-amyloid plaque agents exist, no treatment has been found to slow or stop neuronal damage in routine clinical practice (8).

PD is the second most common age-related neurodegenerative disorder. The cardinal motor symptoms include bradykinesia, tremor, rigidity, and postural instability. PD is characterized by the loss of dopaminergic neurons in the substantia nigra and intracellular accumulation of misfolded alpha-synuclein called Lewy bodies. The predicted prevalence of PD is 0.3% in the general population, 1.0% in people older than 60 years, and 3.0% in people older than 80 years in industrialized countries. The estimated incidence rate of PD ranges between 8 and 18 per 100,000 person-years (9). PD treatment is mainly based on dopamine replacement.

A limited number of studies in the literature have investigated the link between neurodegenerative diseases and geriatric syndromes. Therefore, the present study aimed to evaluate the association of the two most common neurodegenerative diseases, AD and PD, with the most common geriatric syndromes, including sarcopenia, malnutrition, polypharmacy, depression, delirium, osteoporosis, and urinary incontinence.

MATERIALS AND METHOD

The present retrospective cross-sectional study included patients admitted for the first time to a geriatrics outpatient clinic, between September 1, 2019, and September 1, 2020. Patients who were under 65 years of age and who presented a history of acute severe disease that may impair the general health status (cerebrovascular disease, acute coronary syndrome, gastrointestinal bleeding, acute respiratory failure, and/or sepsis) or with malignancies (except being in full remission for at least 5 years) were excluded from the study. In addition, patients with

non-Alzheimer's dementia (vascular dementia, frontotemporal dementia, lewy body dementia, Parkinson's disease dementia) were also excluded from the study. The study was approved by the ethics committee of Istanbul University-Cerrahpasa, Cerrahpasa Medical Faculty (2020-117344).

Turkish translations of the Mini Mental State Examination scale and Yesavage Geriatric Depression scale were used to determine the general cognitive status (according to the education level of the patients) and mood of patients, respectively (10,11). Diagnoses of probable AD and depression were made according to the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-V), criteria (12). Based on the evaluation of patients' past medical history, laboratory tests, and brain imaging, other potential causes of dementia were excluded. The nutritional status of patients was evaluated using the Mini Nutritional Assessment long form, and patients with a score below 17 out of 30 points were considered malnourished (13). Use of five or more drugs per day was defined as polypharmacy (14). Insomnia was evaluated by questioning the patients whether they experienced any difficulty in falling asleep and/or maintaining sleep (15). Urinary incontinence was defined as "complaint of any involuntary leakage of urine in the past 12 months" (16). Dual energy X-ray absorptiometry (DEXA) was used to measure bone mineral density for osteoporosis diagnosis. A T score below -2.5 standard deviation (SD) in the femoral (total or neck) or vertebral (total or at least two vertebrae) measurements was accepted as osteoporosis (17). PD diagnosis was based on the criteria of the United Kingdom Parkinson's Disease community (18). According to the EWGSOP2 diagnostic criteria, patients with low muscle strength and muscle mass were considered sarcopenic (3).

Statistics

Categorical variables were expressed as numbers and percentages. Continuous variables were presented as mean ± standard deviation. Chi-square test was used for categorical variables, and if this was not applicable, Fisher exact test was used. Student t-test was used for continuous variables. The relationship of AD and PD with geriatric syndromes was first analyzed with the univariate Logistic Regression (LR) method. After the univariate LR analysis, the gradual multivariate LR method was applied to the significant values. P value below 0.05 was considered significant. Analysis of the data was done in SPSS for Windows 22 package program.

RESULTS

A total of 339 patients were included in this study. Of these, 243 (71.7%) were females, and the mean patient age was 76.9±7.1 years. Of the 339, 225 (66.4%) patients presented polypharmacy, 111 (32.7%) presented sarcopenia, and 83 (24.5%) presented malnutrition. The general demographic characteristics of the patients and the frequency of neurodegenerative diseases and geriatric syndromes are presented in Table 1.

Table 1. The demographic data of the patients and frequency of neurodegenerative diseases and geriatric syndromes

Number of patients	339
Female/Male	243 (71.7%)/96 (28.3%)
Age (years)*	76.9±7.1
Alzheimer's disease	64 (18.9%)
Parkinson's disease	30 (8.8%)
Sarcopenia	111 (32.7%)
Polypharmacy	225 (66.4%)
Malnutrition	83 (24.5%)
Depression	95 (28%)
Delirium	30 (8.8%)
Insomnia	31 (9.1%)
Osteoporosis	100 (29.5%)
Urinary incontinence	62 (18.3%)

* Mean ± standard deviation (SD)

Table 2. Association of Alzheimer's Disease with Parkinson's Disease and Geriatric Syndromes

	Alzheimer's Disease	Others	*p* value
Number of patients	64	275	
Male / Female	15 (23%) / 49 (77%)	81 (30%) / 194 (70%)	0.336
Age (years)*	77.65±6.70	76.77±7.26	0.249
Parkinson's disease	11 (17%)	19 (7%)	**0.009**
Sarcopenia	33 (52%)	78 (28%)	**<0.001**
Polypharmacy	52 (81%)	173 (63%)	**0.005**
Malnutrition	22 (34%)	61 (22%)	**0.041**
Depression	30 (47%)	65 (24%)	**<0.001**
Delirium	23 (36%)	7 (3%)	**<0.001**
Insomnia	11 (17%)	20 (7%)	**0.013**
Osteoporosis	17 (26%)	83 (30%)	0.567
Urinary incontinence	19 (20%)	43 (16%)	**0.009**

*Data are shown as mean ± standard deviation (SD); Statistically significant p values are indicated as bold

Sixty-four (18.9%) of 339 patients presented with AS. The frequency of PD (p=0.009), sarcopenia (p<0.001), polypharmacy (p=0.041), malnutrition (p=0.005), depression (p<0.001), delirium (p<0.001), insomnia (p=0.013), and urinary incontinence (p=0.009) were significantly higher in patients with AD than in patients without AD (Table 2). Furthermore, regression analysis revealed that PD, sarcopenia, polypharmacy, malnutrition, depression, delirium, insomnia, and urinary incontinence were the independent variables associated with AD (dependent variable). In multivariate LR analy-

Table 3. Univariate and stepwise multivariate logistic regression analysis for factors associated with Alzheimer's disease

	Univariate LR		Multivariate LR	
	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p
Parkinson's disease	2.796 (1.257-6.219)	0.012	1.752 (0.686-4.474)	0.241
Sarcopenia	2.689 (1.542-4.688)	<0.001	2.048 (1.049-3.998)	0.036
Polypharmacy	2.555 (1.303-5.011)	0.006	1.340 (0.622-2.886)	0.454
Malnutrition	1.838 (1.020-3.312)	0.043	0.925 (0.440-1.944)	0.836
Depression	2.851 (1.621-5.012)	<0.001	1.754 (0.883-3.486)	0.109
Delirium	21.477 (8.665-53.231)	<0.001	16.365(6.103-43.880)	**<0.001**
Insomnia	2.646 (1.197-5.848)	0.016	2.087 (0.814-5.352)	0.126
Urinary incontinence	0.194 (1.217-4.266)	<0.001	1.021 (0.450-2.313)	0.961

Abbreviations LR, Logistic Regression; CI, Confidence interval
Statistically significant *p* values are indicated as bold

sis, AD was significantly correlated with sarcopenia [p=0.036, odds ratio (OR)=2.048, 95% confidence interval (CI)=1.049–3.998] and delirium (p<0.001, OR=16.365, 95% CI=6.103–43.880) (Table 3).

Of the 339, 30 patients (8.8%) presented with PD. The frequency of sarcopenia (p=0.001), polypharmacy (p=0.014), depression (p=0.017), and AD (p=0.009) were significantly higher in patients with PD than in patients without PD (Table 4). Moreover, in regression analysis, sarcopenia, polypharmacy, depression, and AD were the independent variables associated with PD (dependent variable). In multivariate LR analysis, PD was significantly correlated with sarcopenia (p=0.014, OR=2.744, 95% CI=1.231–6.116) (see Table 5).

DISCUSSION

The frequency of neurodegenerative diseases, including AD and PD, and geriatric syndromes increase with aging. Some previous studies have addressed the link between neurodegenerative diseases and an isolated geriatric syndrome. However, as far as we know, there is no study evaluating the relationship of these diseases with more than one geriatric syndrome and analyzing the independent variables with multivariate regression analysis. Therefore, the present study is the first to analyze the association of AD and PD with multiple geriatric syndromes.

In this study, sarcopenia was the only significant independent variable associated with both AD and PD in multivariate analysis. A few studies have reported on muscle strength and sarcopenia in AD. For instance, Shin et al. observed lower muscle strength in patients with dementia, although the authors did not evaluate muscle mass and physical performance (19). Likewise, Boyle et al. reported that decreased muscle strength was associated with an increased risk of cognitive decline and AD (20). In a study conducted in Austria, the incidence of sarcopenia was higher in patients with PD than in the general population (21). However, all these studies evaluated sarcopenia alone. Taken together, these

Table 4. Association of Parkinson's Disease with Alzheimer's Disease and Geriatric syndromes

	Parkinson's Disease	Others	*p* value
Number of patients	30	309	
Male / Female	13 (43%) / 17 (57%)	83 (27%) / 226 (73%)	0.056
Age (years)*	76.50±6.64	76.98±7.21	0.735
Alzheimer's disease	11 (37%)	53 (17%)	**0.009**
Sarcopenia	18 (60%)	93 (30%)	**0.001**
Polypharmacy	26 (87%)	199 (64%)	**0.014**
Malnutrition	11 (36%)	72 (23%)	0.105
Depression	14 (47%)	81 (26%)	**0.017**
Delirium	5 (17%)	25 (8%)	0.115
Insomnia	5 (17%)	26 (8%)	0.174
Osteoporosis	9 (30%)	91 (29%)	0.950
Urinary incontinence	8 (27%)	54 (18%)	0.135

*Data are shown as mean ± standard deviation (SD); Statistically significant P values are indicated as bold

Table 5. Univariate and stepwise multivariate logistic regression analysis for factors associated with Parkinson's disease

	Univariate LR		Multivariate LR	
	Odds Ratio (95% CI)	p	Odds Ratio (95% CI)	p
Sarcopenia	1.838 (1.020-3.312)	0.043	2.744 (1.231-6.116)	**0.014**
Depression	2.851 (1.621-5.012)	<0.001	1.754 (0.774-3.974)	0.178
Alzheimer's disease	21.477 (8.665-53.231)	<0.001	1.718 (0.722-4.088)	0.221
Polypharmacy	2.646 (1.197-5.848)	0.016	2.393 (0.781-7.337)	0.127

Abbreviations: LR, Logistic Regression; CI, Confidence interval
Statistically significant P values are indicated as bold

findings indicate that sarcopenia, AD, and PD share a common pathogenesis involving inflammation, autophagy, oxidative stress, and apoptosis (22).

In addition to sarcopenia, we found delirium as an independent variable associated with AD. In a systematic review by Fick et al. the prevalence of delirium in patients with AD ranged from 22 to 89% (*versus* 36% in the present study) (23). The presence of a number of common manifestations of delirium and dementia, such as inflammation, oxidative stress, neuronal dysfunction, and dementia acceleration, explain this frequency and association. Polypharmacy is a risk factor for hospitalization and length of stay. In the present study, polypharmacy was the most common geriatric syndrome. Likewise, in a study by Bulut et al., polypharmacy was the most common geriatric syndrome, and that study reported comparable prevalence rates of depression, dementia, and sarcopenia to those observed in the present study (1). Urinary incontinence is more frequent in patients with AD than in the general population (24). In the present study, the incidence of urinary incontinence was significantly higher in patients with AD.

Insomnia is a common symptom in many neurodegenerative diseases, such as AD and PD, and it has recently been identified as a risk factor for these conditions (25). In the present study, the incidence of insomnia and urinary incontinence were significantly higher in patients with AD. Although insomnia and urinary incontinence were more common in patients with PD, this trend was not statistically significant, perhaps due to the small number of patients with PD. One of the reasons for the lower prevalence of insomnia in PD patients in our study compared to the literature may be that the low number of PD patients made the prevalence assessment difficult. Another reason may be that geriatric patients see insomnia as a natural consequence of aging and have not reported it as a complaint.

CONCLUSION

This study is important as it is the first study to investigate the relationship of AD and PD with multiple geriatric syndromes. Sarcopenia was found to be the common independent factor for both AD and PD. Therefore, sarcopenia screening is warranted in patients with neurodegenerative diseases. In patients diagnosed with sarcopenia, the quality of life may be improved through appropriate exercise and protein-rich nutritional support.

Conflict of interest: The authors declare that there is no conflict of interest

Financial Disclosure: The authors declare this study to have received no financial support.

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