Functional loss and worsening geriatric assessment parameters are more common in dementia with Lewy Bodies than Alzheimer's disease

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Abstract

Background: The main aim of this study is to compare older patients with Alzheimer's disease (AD) to those with dementia with Lewy bodies (DLB) according to dependency on daily living activities and compherensive geriatric assessment (CGA) parameters.

Method: 227 AD patients and 123 DLB patients underwent CGA, including comorbidities, number of drug used, falls, urinary incontinence, handgrip muscle strength, Mini-Nutritional Assessment (MNA), Tinetti Performance Oriented Mobility Assessment Scale (POMA), Insomnia severity Index (ISI) and Epworth Daytime sleepiness (EDS). Basic and Instrumental Activities of Daily Living were assessed by Barthel Index and Lawton Scale, respectively.

Results: The mean age of participants was 83.4 years, and 73% were female. There was no statistically significant difference in age, gender, cognitive function, and comorbidities except for coronary artery disease in AD and DLB ($p<0.05$). The number of falls and drug used, ISI score and EDS score were higher in patients with DLB than patients with AD ($p<0.05$). DLB patients had lower MNA, POMA scores and handgrip muscle strength than AD patients. Dependency on basic ADL were higher in DLB than in AD ($p<0.05$), but there was no differences in dependency on instrumental ADL ($p>0.05$).

Conclusion: DLB patients are more dependent on their caregivers than AD patients. Nutritional deterioration, and sleep disorders, falls, balance and gait problems, decreased muscle strength and multiple drug use are more common in those with DLB compared to those with AD. The management of older patients with DLB may be more difficult than older patients with AD.

Keywords: dementia, Alzheimer's disease, Lewy bodies, activities of daily living, nutrition, sleep, falls, geriatric assessment

Introduction

Dementia is a common disorder that causes impairment, morbidity, and mortality, as well as increased caregiver burden. Alzheimer's disease (AD) is the most common cause of dementia, accounting for about 60-80% of cases[1] and dementia with Lewy bodies (DLB) is the second most common type of neurodegenerative dementia in the older adults, accounting for about 4-10% of all dementia cases.[2] There has been research showing that DLB has a worse prognosis than AD, as well as a greater burden on family caregivers, higher care costs, and higher admission rates to general hospitals and residential care facilities.[3] Among the reasons for this, autonomic dysfunction, extrapyramidal motor findings and neuropsychiatric symptoms, such as visual hallucinations, depression, daytime somnolence and delusions are more common in DLB than AD.[4,5] In addition, few studies have shown that the reasons mentioned may be more affected by dependence on activities of daily living in DLB than in AD.[6,7] However, how independence in basic and instrumental activities of daily living, which is already reduced in the older adults, is affected in both types of dementia has not been compared in detail.

Moreover, geriatric syndromes such as nutritional problems, sarcopenia, polypharmacy, fear of falling, balance and gait disturbances, falls, and sleep problems, which increase in frequency with aging, occur due to multifactorial causes.[8] These factors are indeed observed at a high rate in both older DLB and older AD patients from an early stage in disease progression, which is detrimental to both quality of life and life expectancy.[9] Moreover, such factors increase caregiver burden and complicated clinician treatment and follow-up. However, in the studies conducted so far, DLB and AD have been compared on neuropsychiatric symptoms, cognitive and functional decline, parkinsonism and caregiver burden.[6,7] When discussing the difficulties in the management of these patients, attention has often focused on these issues. However, from a geriatrician perspective, the two types of dementia have seldom been compared.

Patients with dementia are affected in activities of daily living at varying rates depending on the stage of the disease.[1] On the other hand, it can be predicted that a decreased in quality of life may be at the forefront in older dementia patients due to deterioration in activities of daily livings and geriatric syndromes. [1,3] Although the importance of these factors for dementia practice is well known, there are no previous studies comparing the most common dementia subtypes in older adults in terms of them.

Given this background, the aim of this study is to make a detailed comparison of DLB and AD, the two most common dementias in the older adults, with dependencies on basic and instrumental activities of daily living, and geriatric assessment parameters.

Method

Participants

A total of 1531 older adult outpatients who were admitted to a geriatric clinic based in Turkey for any reason and who had no exclusion criteria were included in this cross-sectional study. The investigation conformed to the Declaration of Helsinki and was approved by the local ethics committee (14/298). Informed consent was provided by each participant or a legal guardian before participating in the study.

Probable AD was diagnosed with National Institute on Aging-Alzheimer's Association workgroup's criteria and probable DLB was diagnosed with Fourth consensus report of the DLB Consortium.[10,11]

All patients underwent neuro-imaging protocols such as cranial magnetic resonance imaging or computed tomography to rule out other causes of cognitive impairment (such as intracranial hemorrhage, brain cancer). Patients who had severe illness that may impair their general health status, such as acute cerebrovascular event, sepsis, acute renal failure, acute coronary syndrome, and acute respiratory failure; and those who did not agree to undergo the Comprehensive Geriatric Assessment (CGA); those who have severe vision and hearing impairment that prevent communication and understanding commands during the examination were excluded. Except for those with probable DLB or AD, the patients with MCI were also excluded from the study. Moreover, other types of dementia were excluded such as vascular dementia, frontotemporal dementia and Parkinsons disease' dementia.

Finally, 350 patients with dementia (227 AD, and 123 DLB) were included.

Comprehensive geriatric assessment (CGA)[8]

A geriatrician, a psychologist, and a gerontologist interviewed family members or caregivers of each included patient, thereby obtaining information about the participants. Demographic characteristics (age, gender, and years of education) were recorded. Comorbid diseases including hypertension, diabetes mellitus, coronary artery disease, congestive heart failure, chronic obstructive pulmonary disease, cerebrovascular events, osteoarthritis, and peripheral

artery disease were reported. All the drugs and drug counts were recorded. The patients were also questioned in terms of recurrent falls (≥1 falls/year) within the past year. Urinary incontinence was considered as the involuntary leakage in the last 3 months except when urinary tract infection was present. Nutritional status was assessed using the Mini-Nutritional Assessment (MNA) score. Cognitive status was evaluated by Mini-Mental State Examination (MMSE)[12] or the Montreal Cognitive Assessment scale (MOCA)[13] according to the patients' education levels. The MOCA were used for the individuals who had 11 or more years of education. [13]

Gait and balance function was assessed by Tinetti Performance Oriented Mobility Assessment Scale (POMA). A hand dynamometer was used to determine muscle strength, and the highest of the 3 measurements of the dominant hand was accepted as the hand grip strength value. Insomnia Severity Index and Epworth Sleepiness Scale were used to detect insomnia and daytime sleepiness, respectively.[14]

Barthel Index for Basic Activities of Daily Living Scale (BADL) and Lawton for Instrumental Activities of Daily Living (IADL) Scale

Barthel Index measures the level of independence and functional status in daily activities like feeding, bathing, dressing, bowels/bladder control, using the toilet, and transfers (from bed to chair), mobility (on flat surfaces) and stair climbing. A score of 100 indicates complete independence, whereas a score of 0 indicates complette dependency on another person. Furthermore, the Barthel Index has been divided into five separate score ranges (100-91: fully independent; 99-91: mildly dependent; 62-90: moderately dependent; 61-21: highly dependent; 20-0: fully dependent.[15]

Disability levels and other factors in community-dwelling older adults individuals were first measured and evaluated by researchers Lawton and Brody in 1969 using the Lawton Instrumental Activities of Daily Living Scale (Lawton-IADL). In older people, the Lawton-IADL, the most commonly used assessment tool for instrumental activities of daily living, measures eight abilities, including ability to use telephone, shopping, food preparation, housekeeping, laundry, mode of transportation, responsibility of own medication, and ability to handle finances. Each activity is given a score ranging from 0 to 2-4. Low scores indicate a high degree of dependency, and the scale runs from 0 to 23. The total score is interpreted as follows: 0-8: dependent; 9-16: semi-dependent; 17-23: independent.[16,17]

Laboratory Findings

Laboratory tests, including complete blood count, kidney functions and cholesterol levels, were performed to evaluate the biochemical and metabolic status of the patients. Serum vitamin B12 level, folate levels and 25(OH)D was measured. All these biochemical tests were conducted using the Diagnostic Modular Systems auto analyzer (Roche E170 and P-800).

Statistical analyses

Data were analyzed using SPSS, version 22. The participants were divided into two groups: AD and DLB, and all the statistical analyses were performed to compare the two groups. Continuous variables were evaluated as mean and standard deviation, and for normal distribution by the Kolmogorov-Smirnov test. Normally distributed continuous variables were analyzed by paired sample t-test. In case of non-normal distribution, continuous variables were assessed by Mann Whitney U test. Differences between categorical variables were evaluated by Chi-square and Fisher's exact Chi-square tests. A probability $p<0.05$ was considered significant. All the statistical analyses were carried out using SPSS 22.0 (SPSS Inc.).

Results

The participants in this study included 350 individuals with a mean age of 83.4 years. There were 227 (65.3%) AD and 123 (34.7%) people with DLB. There was no statistically significant difference in the patients' ages, genders and MMSE/MOCA scores. Additionally, there was no statistically significant difference in comorbidities except for coronary artery disease ($p<0.05$).

BADL and IADL scores were lower in DLB than in AD ($p<0.05$). According to BADL scores, the rate of highly dependent patients in DLB was higher than AD ($p<0.05$). Grooming, bathing, dressing, feeding, toilet use, stairs, tranfer and mobility were significantly different between DLB and AD ($p<0.05$) (**Figure 1a and 2b**). Although total IADL scores were lower in DLB and dependency rates were higher in food preparation, shopping, housekeeping, and laundry, there was no difference in dependency rates determined by IADL scores (**Figure 1b and 2a**).

The patients with DLB had a higher rate of falls, number of drugs used, ISI score, and Epworth score than those with AD ($p<0.05$), whereas MNA, Tinetti and Handgrip strength scores were lower in DLB than in AD ($p<0.05$). It was determined that only serum albumin level was lower in those with DLB than in patients with AD ($p<0.05$), and all the other laboratory findings were not different between the two syndromes (**Table 1**).

DISCUSSION

When older DLB and AD patients who are similar in age, gender and cognitive status were compared, dependency in both basic and instrumental activities of daily living was higher in DLB patients. Falling, impaired gait and balance functions; number of drug use, insomnia and excessive daytime sleepiness, nutritional deterioration, and decrease in muscle strength were more common in older DLB patients compared to older AD patients.

Although the diagnosis of dementia is important for an older patient and his/her caregiver to aid in management, the dementia subtype is of equal importance for care management, because neuropsychiatric symptoms, neurocognitive domains affected, prognosis of the disease, caregiver burnout and survival times may differ in each dementia subtype. Therefore, the comparative studies of dementia subtypes have increased in recent years.[18,19,20] For example, the two most common dementia types in the older adults are AD and DLB, the latter with a high mortality (average survival time in DLB from diagnosis was 4.11 years and in AD 5.66 years, equating to a 1.60 years shorter survival in DLB.[3] In addition, caregiver burden in caregivers of DLB patients is higher than in caregivers of AD patients for two important reasons.[21] One of these reasons is the excess of neuropsychiatric symptoms in DLB, and the other is that the dependency in ADLs is much higher in DLB from the early stage of dementia.[7,21,22]

To date, comparative studies investigating how DLB and AD affect dependency in ADLs are few and their results are inconsistent. In our study, which included the patients with a mean age of 83, both BADL and IADL total scores were lower in DLB than AD, although they were similar in terms of age, gender, and cognitive status. Additionally, in our study, the DLB group had greater dependency on personal care, bathing, dressing, feeding, toilet use, stairs and mobilization (BADLs), as well asdependency on food preparation, cleaning, and laundry (IADLs). McKeith et al. compared both subtypes of dementia, showing that dependency on similar items of BADL and BADL was higher in DLB than in AD, as in the present study.[6] In the same study, a negative correlation was determined between extrapyramidal symptoms and neuropsychiatric symptoms, and dependency in BADLs.[6] Although IADL scores were lower in DLB in our study, there was no difference between AD and DLB in terms of dependency compared to IADL categories. The possible reason for this may be that the mean age of our patients was $\geq$ 80 years. Gill et al. demonstrated that the decrease in functionality was more pronounced in young dementia patients, but slower in older dementia patients, especially in IADLs.[7] Moreover, differences in patients with DLB and AD appear most pronounced early in the prognosis of the disease.[23] Since all the patients except

those severe with dementia were included in our study, a difference might not have been detected in dependencies compared to IADL.

Geriatric syndromes, which occur due to multifactorial reasons and cause many negative clinical outcomes in the older adults, reduce the quality of life and complicate the care of the patients.[8] Therefore, multiple syndromes in the same patient means that his/her care becomes more complicated to manage for both the clinician and the caregiver. Multiple drug use, nutritional problems, recurrent falls, gait and balance problems and sleep disorders are the leading ones of these syndromes.[8] There are several plausible pathways that help to explain such findings. Common symptoms experienced by people with DLB, such as Parkinsonism and signs of postural instability, are known to increase the risk of falling.[24] For example, in one study in which AD and DLB patients were included, risk factors for falling were investigated, and it was determined that parkinsonism was the most important factor for falling.[25] Additionaly, oculo-visual changes such as visual hallucinations, color vision impairment, decreased occipital lobe activity, are common in DLB and can also increase gait and balance function.[26] Moreover, the excess of drugs used in DLB, worsening of nutrition and higher sleep disorders detected in our study may also lead to higher falls, gait and balance problems in DLB.[27]

It is not surprising that the tendency to malnutrition is high in DLB, the reasons for which are prolonged duration of swallowing food and liquids, anorexia and constipation being more frequent in DLB than AD; extrapyramidal symptoms likely to cause eating and swallowing problems; decreased adequate energy intake due to the more frequent occurrence of neuropsychiatric symptoms such as hallucinations, delusions, depression, irritability, abnormal motor behavior and decreased social interaction in DLB as well as a reduction in energy consumption.[18,20] Among the laboratory parameters, the fact that albumin is lower in DLB than in AD also supports this finding.

Sleep-wake cycle are common features of neurodegenerative dementia. Although REM sleep Behavior Disorder is one of the core symptoms of DLB, sleep problems are also common in AD patients; however, there are only two tudies comparing older adults DLB and AD patients in terms of the two most common sleep disorders, insomnia and excessive daytime sleepiness (EDS).[28,29] In these studies, especially in which EDS was investigated further, it was indicated that the regions that affect the sleep cycle in DLB include locus coeruleus, raphe nucleus, tuberomamillary nucleus of the hypothalamus and the associated ascending reticular activating system.[30] Furthermore, the decrease in the level of the hypocretin hormone, which provides daytime wakefulness, in DLB may cause EDS to be seen more commonly than in AD.[31]

Although it is known that insomnia is common in neurodegenerative diseases, there is no study comparing it in DLB and AD. Decreased night sleep due to EDS in DLB or high RUDB and nutritional deficiencies in DLB may cause insomnia to be seen more frequently.[28,32]

Polypharmacy, one of the most important issues in geriatric practice, accelerates polypharmacy functional decline in both DLB and AD,[33] however, drug use was found to be higher in older adults DLB patients in our study. Prevalence of neuropsychiatric symptoms, sleep disorders and parkinsonism findings in DLB; having to add drugs to the treatment for each of them; and the fact that coronary artery disease was observed more commonly in DLB in our study, may cause the total number of drugs to be higher than AD.

Findings from this study must be interpreted in light of its limitations. First, the study was designed as cross-sectional. Second, a formal assessment of extrapyramidal symptoms, such as the Unified Parkinson's Disease Rating Scale, could not be performed or clinical features/domains of DLB were not detailed. Third, no actigraphy or polysomnography was used for sleep disorders; instead, validated scales were used and evaluations were made according to the information received from the caregivers. The strengths of the study include the adequate number of samples and the evaluation of many parameters important for geriatric practice. In this study we were to able to exclude all the factors affecting cognitive functions and geriatric assessment parameters, since laboratory parameters, such as vitamin levels, kidney functions were detailed.

In conclusion, older DLB patients are more dependent on activities of daily living than older AD patients. Moreover, multiple drug use, nutritional problems, recurrent falls, gait and balance problems, and sleep disorders are more common in DLB patients than in AD patients. Therefore, especially older DLB patients require special attention and follow-up. For this reason, it is important to follow up older adults dementia patients, especially DLB patients, with a multidisciplinary approach and from a geriatrician perspective.

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Table 1 Demographic and Clinical Characteristics of the Participants (n=350)

Characteristics	AD (n=227)	DLB (n=123)	P Value
Age (mean, SD)	82.3±5.5	82.9±7.2	0.163
Gender (Female) %	72.7	73.2	0.923
Marital Status %			
Married	39.7	29.4	0.097
Widowed	50.4	52.9	
Other	9.9	17.7	
Living Status %			**0.010**
Alone	8.7	4.9	
With Spouse	39.4	25.2	
With Children	42.9	54.5	
Other	9.1	15.4	
Number of drugs used (mean, SD)	6.3±3.1	7.03±3.02	**0.026**
Comorbities %			
HT	61.3	62.6	0.816
DM	32.9	31.7	0.822
CAD	16.5	27.9	0.012
COPD	5.8	7.4	0.553
CVE	7.6	5.7	0.517
CHF	9.9	13.0	0.371
OA	11.1	13.1	0.581
Geriatric Syndromes			
Falls %	38.5	59.5	**0.000**
The number of Falls in last year (mean,SD)	0.90±1.7	1.90±3	**0.000**
Urinery Incontinence %	58.6	58	0.918
Constipation %	41.3	45.9	0.434
MMSE/MoCA (mean, SD)	15.3±4.8	14.6±4.7	0.352
BADL score (mean, SD)	67.09±30.7	56.5±30.2	**0.000**
IADL score (mean, SD)	6.09±3.9	4.34±3.15	**0.005**
MNA (mean, SD)	19.13±5.8	18±5.28	**0.021**
Tinetti Balance (mean, SD)	10.52±5.8	7.56±5.9	**0.000**

Tinetti Gait (mean, SD)	8±4.3	6.4±4.62	**0.001**
Tinetti Total (mean, SD)	18.50±9.9	13.89±10.19	**0.000**
ISI (mean, SD)	9.81±9.57	14.61±9.9	**0.000**
Epworth (mean, SD)	7.29±6.47	9.23±6.9	**0.011**
Blood Analysis (mean, SD)			
GFR (ml/min/1.73 m^2)	57.0±20.12	54.3±20.9	0.321
Albumin (g/dL)	5.7±8.06	5.01±7.5	**0.015**
Trigliserid (mg/dL)	129±58.4	124.7±63.4	0.402
HDL (mg/dL)	56.7±20.4	54.07±17.8	0.307
LDL (mg/dL)	126.5±43.6	126.2±44.5	0.814
Vitamin B12 (pmol/L)	535.2±413.7	511.6±427.9	0.481
Vitamin D (ng/mL)	22.4±14.6	28.5±14.24	0.225
Folic acid (ng/mL)	18.8±9.2	17.98±7.4	0.795
Hemoglobin (g/dL)	12.7±3.7	12.7±3.2	0.578

Abbreviations. AD, Alzheimer's disease; BADL, Basic Activities of Daily Living; CAD, Coronary Artery Disease; CHF, Congestive Heart Failure; COPD, Chronic Obstructive Pulmonary Disease; CVE, Cerebrovascular events; DM, Diabetes Mellitus; GFR, Glomerular filtration rate; HDL, high-density lipoprotein; IADL, Instrumental Activities of Daily Living; ISI, Insomnia Severity Index; DLB, dementia with Lewy bodies; MMSE, Mini Mental State Examination; LDL, low-density lipoprotein; MNA, Mini-nutritional Assessment; MOCA, Montreal Cognitive Asssessment; OA, Osteoarthritis; PAD, Peripheral Artery Disease; SD, Standart deviation

The bold values show statistically significant results.

Figure Legends

Figure 1a. Comparison of Basic Activities of Daily Living between Alzheimer's Disease and Dementia with Lewy Bodies

Figure 1b. Comparison of Instrumental Activities of Daily Living between Alzheimer's Disease and Dementia with Lewy Bodies

Figure 2a. Dependency ratio of Instrumental Activities of Daily Living between Alzheimer's Disease and Dementia with Lewy Bodies.

Figure 2b. Dependency ratio of Basic Activities of Daily Living between Alzheimer's Disease and Dementia with Lewy Bodies

Figure 1.a

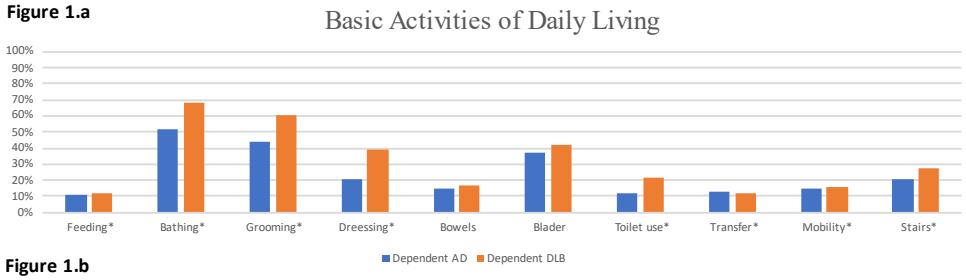
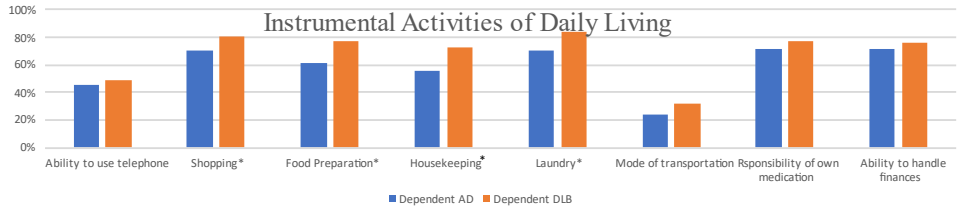


Figure 1.b



*: p<0.05

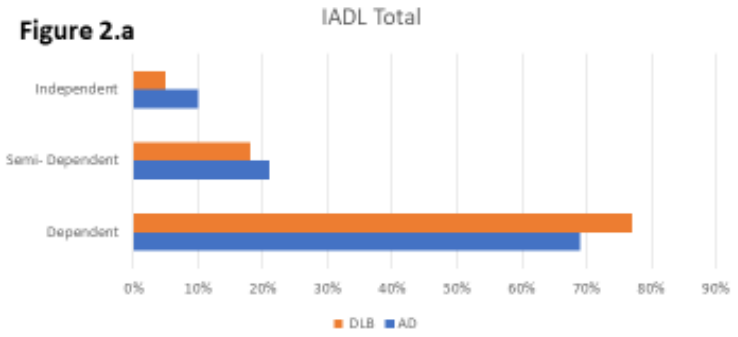
AD, Alzheimer's disease; LBD, dementia with Lewy bodies

1

2

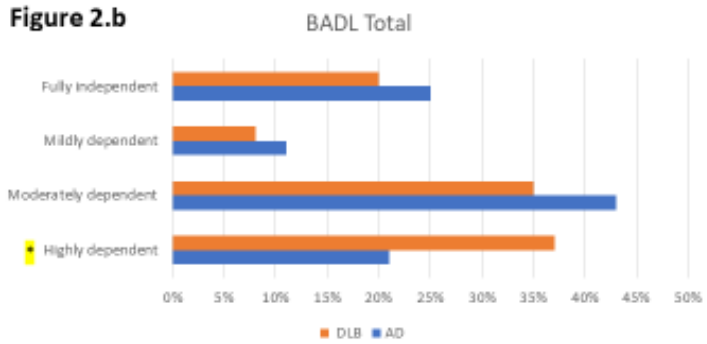
3

Figure 2.a



AD, Alzheimer's disease; DLB, dementia with Lewy bodies; IADL, Instrumental Activities of Daily Living.
p>0.05 for all.

Figure 2.b



AD, Alzheimer's disease; DLB, dementia with Lewy bodies BADL, Basic Activities of Daily Living.

*: p<0.05

4