A comparison of the prevalence of Fear of Falling between older patients with Lewy body dementia, Alzheimer's Disease, and without dementia

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ABSTRACT

Background: The development of cognitive impairment and Fear of Falling (FoF) are strongly linked, but prevalence of FoF is not known in patients with different types of dementia. This study aims to evaluate and compare the prevalence and severity of FoF in patients' with dementia with Lewy bodies (DLB), Alzheimer Disease (AD), and non-dementia.

Methods: 46 participants with DLB, 86 participants with AD and participants without dementia (controls), underwent Comprehensive Geriatric Assessment (CGA). The Falls Efficacy Scale–International (FES-I) was used to determine and classify FoF. An overall score on the FES-I of 16-19, 20-27 and ≥28, was accepted as low, moderate, and high concern about FoF, respectively.

Results: Prevalence of high FoF was 86.9% in DLB, 36.0% in AD and 37.4% in controls. All CGA parameters were worse in the DLB and AD group than non-dementia group ($p<0.001$). The prevalence of high FoF/FES-scores was significantly higher in the DLB group than in the AD and non-dementia group ($p<0.001$), but was similar in AD and non-dementia groups ($p>0.05$). The significant relationship between DLB and FoF was maintained when adjusted for age, CGA parameters, and orthostatic hypotension (OR: 2.55, CI:1.03-6.25, $p=0.041$ comparison to AD; OR: 4.79, CI:2.10-10.92, $p<0.001$ comparison to non-dementia).

Conclusion: Eight out of ten elderly patients with DLB have high FoF, which is much higher than those with AD and without dementia. Therefore, clinicians should be aware of FoF and its related consequences in the management of DLB in older adults.

Keywords: Alzheimer's disease, dementia with Lewy bodies, Fear of Falling

INTRODUCTION

Fear of Falling (FoF) is defined as a person worrying about falling seriously enough to prevent them from carrying out daily activities. Avoiding such activities increases dependence and fall risk over time (Tinetti & Powell, 1993). FoF is associated with mental and physical disability development in the elderly (Tinetti & Powell, 1993). Approximately half of the community-living elderly experiences FoF, and nearly one-third of older adults develop FoF during a year (Murphy, Dubin, & Gill, 2003; Uemura et al., 2014). Moreover, 39.8% of geriatric outpatients have a high level of FoF (Arik et al., 2020). This high prevalence of FoF has resulted in a growing body of literature examining the factors that cause FoF development and the clinical reflections of FoF. Numerous factors such as visual impairment, balance and walking problems, female gender, experiencing a fall within the last year, low physical activity level, the presence of pain, arthritis and orthostatic hypotension, depression, and living alone have been found to be associated with the development of FoF (Austin, Devine, Dick, Prince, & Bruce, 2007; Kressig et al., 2001).

However, in recent years it has been suggested that cognitive decline and FoF development are strongly linked. For example, 1700 elderly people over 65 years old who did not have cognitive impairment and FoF were followed for 15 months, and it was shown that mild cognitive impairment (MCI) predicted new onset FoF (Uemura et al., 2015). In another study, MCI and global cognitive impairment were found to increase the prevalence of FoF (Uemura et al., 2014). Even though the FoF-cognitive dysfunction relationship is today known, the status of FoF in each dementia subtype has not been investigated yet. It has been reported that FoF and falls are higher only in patients with Alzheimer's disease (AD) compared to cognitively normal elderly people with subjective memory complaints (Borges, Radanovic, & Forlenza, 2015). However, factors that may increase the risk of FoF such as falls, impaired motor performance and autonomic dysfunction are more

common in dementia with Lewy bodies (DLB), the second most common neurodegenerative type of dementia in the elderly (Ballard, Shaw, Lowery, McKeith, & Kenny, 1999; Isik, Kocyigit, Smith, Aydin, & Soysal, 2019) (Fritz et al., 2016). Despite this, a comparison of FoF levels between DLB and AD has not been investigated to date.

Therefore, the present study aimed to evaluate and compare the presence and severity of FoF between people with DLB, AD and cognitively intact older adults.

METHOD:

Participants: A total of 498 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 (McKeith et al., 2017; McKhann et al., 2011). All patients underwent neuroimaging protocols such as cranial magnetic resonance imaging or computed tomography.

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 patients who did not agree to undergo the Comprehensive Geriatric Assessment (CGA) were excluded. Patients with MCI and patients with dementia except those with probable DLB or AD were also excluded. Patients with severe dementia (Clinical Dementia Rating 3) were also not

included, because the Falls Efficacy Scale–International has only been validated for patients with mild to moderate dementia, not severe dementia (Hauer et al., 2011).

Comprehensive Geriatric Assessment

All patients underwent CGA. Demographic characteristics (age, gender, and years of education) were recorded (Soysal, Isik, Buyukaydin, & Kazancioglu, 2014). Patients were questioned in terms of recurrent falls (≥1 falls/year) within the past year. Comorbid diseases of the patients were questioned. Laboratory data, which was performed routinely in geriatric population, was obtained. Basic and Instrumental Activities of Daily Living (ADL) were assessed by Barthel Index and Lawton-Brody Scale, respectively. Nutritional status was assessed using the Mini-Nutritional Assessment (MNA) score. Geriatric Depression scale was used to evaluate mood. Cognitive status was evaluated by Mini-Mental State Examination (MMSE). Gait and balance function was assessed by Tinetti Performance Oriented Mobility Assessment Scale (POMA) (Soysal et al., 2014).

Blood pressure was measured in the supine position, and after the patient stood up, and recorded at the 1st and 3rd minutes. For the measurement of blood pressure, a calibrated Omron M2 Compact (HEM 7102-E) device that meets the requirements of the international protocol was used. Orthostatic hypotension (OH) was defined as a decrease in systolic and / or diastolic blood pressure ≥20 mmHg and / or ≥10 mmHg, respectively, when an individual moved from the supine position to the upright position (Soysal, Aydin, Koc Okudur, & Isik, 2016).

The Falls Efficacy Scale–International (FES-I)

FES-I was used to determine and classify FoF. The scale consists of 16 questions and 1-4 points are assigned to each question. FoF was classified according to the total score given to the questions.

Total FES-I scores range from minimum 16 (no concern about falling) to maximum 64 (severe concern about falling). In addition, if the total score of the FES-I scale was 16-19, 20-27 and ≥28, it was assumed that there was no FoF, low, moderate, and high concern about falling, respectively (Delbaere, Smith, & Lord, 2011; Rivasi, Kenny, Ungar, & Romero-Ortuno, 2019). Previous studies showed that FES-I had very good reliability and validity to detect FoF in geriatric patients with and without cognitive impairment (Hauer et al., 2011; Kisvetrová et al., 2019) However, because the FES-I has only been validated for patients with mild to moderate dementia, not severe dementia, patients with severe dementia were excluded (Hauer et al., 2011).

Statistical Analyses

Data were analyzed using SPSS, version 22. The participants were divided into three groups: AD, DLB and controls and all statistical analyses were performed to compare three groups. Continuous variables were assessed as means and standard deviations and evaluated by Kolmogorov-Smirnov test for normal distribution. Normally distributed continuous variables were analyzed by paired sample t-test. In case of non-normal distribution, continuous variables were evaluated by Mann Whitney U test. Differences between categorical variables were evaluated by Chi-square and Fisher's exact Chi-square tests. A probability<0.05 was considered significant. All statistical analyses were carried out using SPSS 22.0 (SPSS Inc.). Binary logistic regression analysis was performed to assess covariate factors between binary groups (DLB and AD, AD and no dementia group, DLB and no dementia group).

RESULTS

Of 498 patients, 9.23% (46) had DLB, 17.26% (86) had AD and 73.51% (366) had no dementia. 48.6% of patients had low FoF, 9.6% had moderate FoF and 41.8% had high FoF. Prevalence of high FoF was 86.9% in DLB, 36.0% in AD and 37.4% in non-dementia group, while low FoF wa

6.5% in DLB, 53.5% in AD and 52.8% in non-dementia group ($p<0.001$). There were no significant differences between the two dementia groups in terms of age, education, gender, comorbidities except for coronary heart disease, number of drugs used, falls history and laboratory values ($p > 0.05$). All CGA parameters were worse in the DLB and AD group than no-dementia group ($p<0.001$). MMSE, BADL, IADL, MNA and POMA scores were worse in the DLB group than AD group. The presence of systolic OH, diastolic OH and OH were more common in the DLB than both AD and non-dementia group (<0.005). The comparison of participants characteristics is summarized in **Table 1.**

Insert table 1 here

While the prevalence of high FES-I scores were significantly higher in the DLB groups than in the AD and non-dementia group ($p < 0.001$, for both), they were similar in AD and non-dementia groups ($p>0.05$). The significant relationship between DLB and FoF was maintained when adjusted for age, POMA, ADLs, MNA, MMSE, presence of CHD and OH (OR: 2.55, CI: 1.03-6.25, $p=0.041$ comparison to AD; OR: 4.79, CI: 2.10-10.92, $p< 0.001$ comparison to non-dementia).

In addition, the prevalence of high FoF increased with CDR scale in patients with dementia (33.3% in CDR1; 52.15% in CDR2) ($p <0.001$). Both FoF scores and ratio of high FoF were higher in the DLB group than in the AD group for both CDR1 and CDR2 ($p<0.05$). In CDR1 patients, the prevalence of high FoF in DLB and AD was 86.3% and 65.0%, respectively, while in CDR2 patients, the frequency of high FoF was 87.5% in DLB and 61.5% in AD. **(figure 1 and 2).**

Insert figure 1

Insert figure 1

DISCUSSION

In this study, results showed that the severity and frequency of FoF is higher in DLB patients than both AD patients (approximately 2.5 times) and cognitively intact older adults (4.7 times). There were no significant differences between AD and non-demented patients in terms of FoF.

In our study, the prevalence of high FoF was found to be 41.8% in total, which is high compared to the results of previous studies. This may be due to the high average age or the high incidence of cognitive impairment in the present study (Arik et al., 2020; Rivasi et al., 2019). Although the relationship between FoF and cognitive impairment seems certain, not all longitudinal studies support this close association. Sakurai et al. found that the development of FoF and the change in the Montreal Cognitive Assessment total score were not associated at 1-year follow-up in 406 community-dwelling older adults (Sakurai et al., 2017). In another study, 4931 middle-age and older adults were followed for 4 years and no correlation was found between the emergence of FoF and cognitive decline assessed by MMSE (Peeters, Leahy, Kennelly, & Kenny, 2018). However, on the other hand, in a 3-year follow-up study evaluating FoF severity, as in the present study, it was found that being very fearful of falling increased the risk of cognitive decline in older adults (Noh, Roh, Song, & Park, 2019). Conversely, it has been reported that cognitive impairment can also predict FoF (Uemura et al., 2015). Interestingly, in our study, while FoF was not higher in AD patients compared to those without dementia, it was significantly higher in DLB. Therefore, the reason for the inconsistency of the study results mentioned above may be that the types of cognitive impairment (such as amnestic, non-amnestic) of the patients in these studies are different, because FoF is more related to inadequacy in some cognitive function domains (executive function and processing speed) (Peeters, Feeney, Carey, Kennelly, & Kenny, 2019).

In our study, for the first time in DLB patients it was found that almost 8 out of 10 patients had high FoF starting from the mild stage and even after adjustment for several covariates (age, cognition, functional dependence and balance-gait functions, orthostatic blood pressure changes), it was found that FoF developed in DLB patients approximately 2.5 times more than AD patients. There are several plausible pathways that help to explain this finding. First, common symptoms experienced by people with DLB, such as parkinsonism and postural instability findings, are known to increase fall risk, and are more severe in mild stages of DLB than what has been observed in patients with AD (Peeters et al., 2019). Moreover, in one study in which 51 AD and 27 DLB patients were included, risk factors for falling were investigated, and it was determined that parkinsonism was the most important factor for falling (Ehrlich, Hassan, & Stagg, 2019). However, extrapyramidal signs such as rigidity, bradykinesia, and postural impairment are also seen from the early stage of MCI and AD, and as AD progresses, the prevalence of parkinsonism also increases (Sasaki, 2018). On the other hand, not every DLB patient has parkinsonism (Zahirovic, Wattmo, Torisson, Minthon, & Londos, 2016). In our study, the reason for not finding a significant difference in falls between AD and DLB patients may be that there is no difference in parkinsonism in both types of dementia, but unfortunately, the relationship between FoF and parkinsonism could not be examined because parkinsonian symptoms or clinical features of DLB were not detailed in our study. Future studies should be designed accordingly. Second, oculo-visual changes such as visual hallucinations, color vision impairment, decreased occipital lobe activity, are common in DLB and also increase FoF (Flanigan, Khosravi, Leverenz, & Tousi, 2018; Peeters et al., 2019). Previous study has shown that elderly people with visual impairment avoid or restrict daily activities which consequently may increases ones risk of developing FoF (Ehrlich et al., 2019). The same scenario may be valid for DLB patients. The fact that many factors that may cause the development of FoF and falls, such as cognitive impairment, neuropsychiatric symptoms,

psychotropic drug use, and sleep disorders that may adversely affect attention, are more prevalent in DLB than AD may explain why FoF is more prevalent in DLB (Brønnick, Breitve, Rongve, & Aarsland, 2016; Hamilton et al., 2020).

However, future studies to identify potential mechanisms leading to higher levels of FoF in those with DLB are needed to further inform targeted interventions. Although it is known that one of the most important causes of FoF is the history of falling, in our study there was no difference between the DLB, AD and non-dementia groups in terms of falling frequency, although it was slightly higher in DLB. Falls are very common in the elderly even when dementia is not present (Dokuzlar, Koc Okudur, Smith, et al., 2020; Dokuzlar, Koc Okudur, Soysal, et al., 2020). Therefore, even though falls seem to be a distinguishing feature for DLB, this feature may lose its validity with advanced age. However, the frequency of FoF is higher in DLB patients from the mild stage. One of the reasons for the shorter survival of DLB patients compared to AD is falling and related complications, which are seen much earlier in DLB (Mueller et al., 2019; Shea et al., 2019). FoF is also an important cause of mortality, and FoF may also contribute to the reduced survival compared to AD in DLB patients (Lee, Lee, Lee, & Lee, 2020). They may become more scared of falling, therefore lower their habitual physical activity, therefore lose muscle strength, physical fitness, which leads to greater functional dependence (Delbaere, Close, Brodaty, Sachdev, & Lord, 2010).

The strengths of our study are that CGA was performed in all patients and that comorbid diseases, laboratory parameters and orthostatic blood pressure changes that may affect the development of FoF were simultaneously evaluated. Second, FoF has been evaluated with FES-I. The present study has some limitations. First, the design of the study is cross-sectional. Second, the number of patients with dementia, especially DLB patients, has a small sample size. Third, this study did not

neuropathologically confirm the dementia diagnosis. Last, parkinsonian symptoms (e.g. Unified Parkinson's Disease Rating Scale) or clinical features/domains of DLB were not detailed.

As a result, 8 out of 10 elderly patients with mild and moderate stage DLB have high FoF, which is much higher than those without AD and dementia. High prevalence of fear of falling are important for post-diagnostic consideration for DLB, as it can cause independence and death. Therefore, clinicians should be aware of FoF and its related consequences in the management of especially DLB in older adults. There is no difference in the frequency and severity of FoF between patients without AD and dementia.

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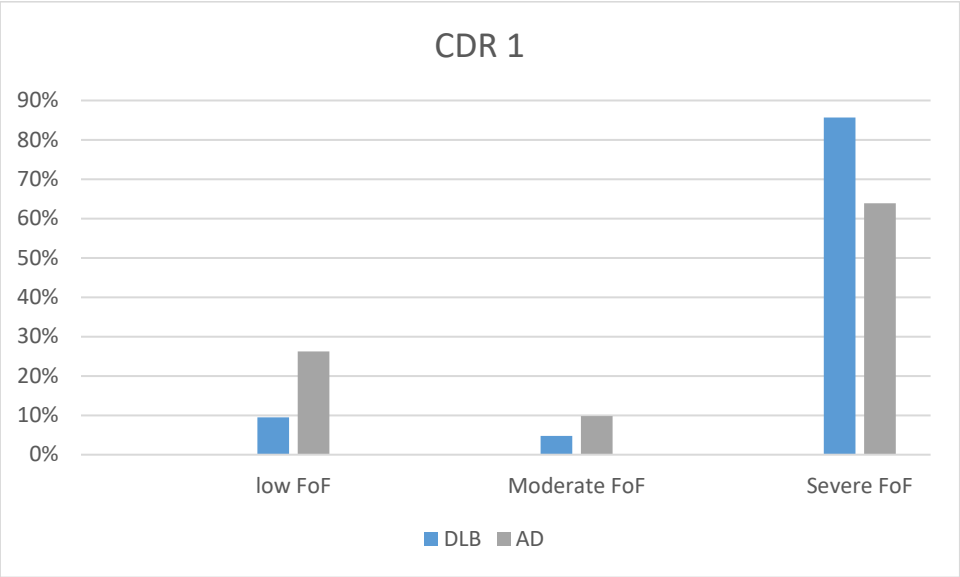
TABLES AND FIGURES

Table 1. Patients' characteristics

	DLB (46)	AD (86)	Non-Dementia (366)	p1	p2	p3
Age (years)	82.06 ±7.45	81.03±6.25	77.55±7.44	0.642	<0.001	<0.001
Female (%)	73.8	72.6	74.0	1.000	0.974	0.683
Recurrent Falls (%)	44.7	38.7	37.5	0.683	0.385	0.854
Number of drugs used	6.86 ±2.64	6.05 ±3.04	5.77 ±3.36	0.123	0.017	0.652
Comorbidities (%)						
Hypertension	62.2	57.3	69.5	0.686	0.270	0.022
Diabetes Mellitus	32.4	30.7	35.8	0.850	0.722	0.267
Coronary Heart Disease	32.4	12.0	18.2	0.019	0.048	0.154
Congestive heart failure	13.5	8.0	11.0	0.500	0.598	0.383
COPD	8.3	.3	10.2	0.680	0.691	0.164
Osteoarthritis	8.1	17.3	14.0	0.256	0.452	0.552
Laboratory values						
Hemoglobin (g/dL)	12.32±1.75	12.31±1.88	13.28±9.04	0.930	0.654	0.710
Vitamin B12 (pg/ml)	476.6.±205.2	581.87±466.9	491.6±372.5	0.963	0.317	0.474
Folic acid	7.29±5.32	8.03±4.60	9.18±2.73	0.242	0.144	0.921
Vitamin D (ng/ml)	20.74± 11.17	20.24±12.83	25.32±16.08	0.753	0.263	0.033
Comprehensive geriatric assessment						
MMSE	12.30±8.23	15.94±7.73	23.91±5.10	0.029	<0.001	<0.001
BADL	59.69±25.71	68.13±30.49	83.22±19.73	0.039	<0.001	<0.001
IADL	6.35±5.30	7.45±6.35	16.26±7.86	0.011	<0.001	<0.001
MNA	17.12±5.35	19.64±5.73	22.33±4.67	0.011	<0.001	<0.001
GDS	4.83±4.40	4.28±3.07	5.65±4.88	0.438	0.169	<0.001
POMA-Total	13.12±9.35	18.66±10.34	22.51±8.13	0.001	<0.001	<0.001
Orthostatic Blood Pressure Changes						
Systolic OH	46.2	27.1	23.3	0.132	0.010	0.395
Diastolic OH	61.5	32.2	35.9	0.017	0.010	0.664
OH	69.2	44.1	46.6	0.037	0.024	0.781
Fear of Falling						
FES-I score	45.46 ±13.44	28.00± 14.34	28.98±15.97	<0.001	<0.001	0.373
High FoF (%)	86.9	36.0	37.4	<0.001	<0.001	0.983
Moderate FoF (%)	6.5	10.5	9.8			
Low FoF (%)	6.5	53.5	52.8			

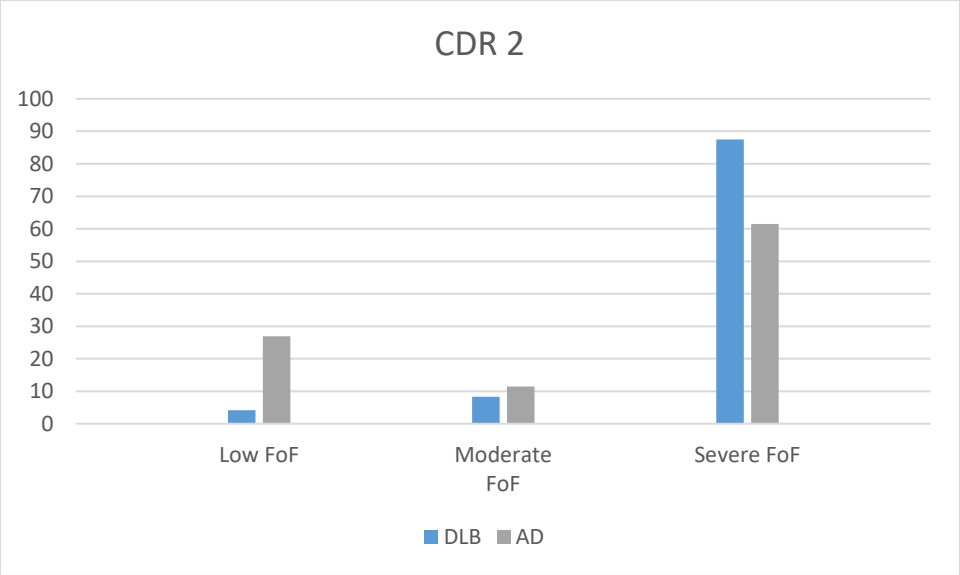
P1: comparisons between DLB and AD; P2: comparisons between DLB and non-dementia groups; P3: Comparisons between AD and non-dementia groups. BADL and IADL: Barthel and Instrumental Activities of Daily Living; COPD: Chronic obstructive pulmonary disease; GDS: Geriatric Depression Scale; FES-I: Falls Efficacy Scale–International; FoF: Fear of Falling; MMSE: Mini-Mental State Examination; MNA: Mini-Nutritional Assessment; OH: Orthostatic Hypotension; POMA: Tinetti Performance Oriented Mobility Assessment

Figure 1. Prevalence of the severity of Fear of Falling in patients with mild dementia



CDR: Clinical Dementia Rating, FoF: Fear of Falling

Figure 2. Prevalence of the severity of Fear of Falling in patients with moderate dementia



CDR: Clinical Dementia Rating, FoF: Fear of Falling