Original Research Article

Frailty in Older Adults with Mild Dementia: Dementia with Lewy Bodies and Alzheimer's Disease

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Abstract

Introduction: The aim of the study is to describe the frequency of frailty in people with a new diagnosis of mild dementia due to Alzheimer's disease (AD) and dementia with Lewy bodies (DLB). **Methods:** This is a secondary analysis of the Dementia Study of Western Norway (Demvest). For this study, we analysed a sample of 186 patients, 116 with AD and 70 with DLB. Subjects were included at a time in which mild dementia was diagnosed according to consensus criteria after comprehensive standardized assessment. Frailty was evaluated retrospectively using a frailty index generated from existing data. The cut-off value used to classify an older adult as frail was 0.25. **Results:** The prevalence of frailty was 25.81% (n = 48). In the DLB group, 37.14% (n = 26) were classified as frail, compared to 18.97% (n = 22) of those with AD (p < 0.001). The adjusted multivariate analysis revealed an OR of 2.45 (1.15–5.23) for being frail in those with DLB when using AD as the reference group. **Conclusion:** Frailty was higher than expected in both types of dementia. The prevalence of frailty was higher in those with DLB compared to AD. This new finding underscores the need for a multi-systems approach in both dementias, with a particular focus on DLB.

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Introduction

Frailty leads to increased vulnerability toward stressors in older adults and is a known predictor for several adverse outcomes in this age group [1]. The most popular criteria used in order to operationalize frailty are the so-called frailty phenotype and the Frailty Index (FI) [2–4]. Studies suggest that around 9–17% of community-dwelling older adults over the age of 60 are frail [5, 6]. However, estimates vary depending on the criteria used for defining said condition [6].

With demographic transition, the number of older adults is increasing, and with it the prevalence of chronic conditions. Dementia is considered one of these [7], known for its terminal and disabling nature, high costs for healthcare systems, and serious consequences for both patients and caregivers [7–9]. This condition has traditionally been considered to be independent from purely physical domains. However, there is enough evidence to infer that both frailty and dementia are main drivers of disability related to aging, as well as for increased mortality [10, 11]. Dementia affects several systems and leads to many manifestations beyond cognition. For instance, it has been associated with geriatric syndromes [12]. Frailty and dementia are multifactorial in origin and share common etiological pathways [12]. Thus, both have been conceptualized as converging conditions resulting from cumulative exposure over time [13].

Previous studies have examined the relationship between frailty and cognitive impairment with a special focus on Alzheimer's disease (AD) [14], but none have studied other highly disabling and frequent dementias such as DLB (Dementia with Lewy Bodies). DLB is the second most common neurodegenerative dementia and is characterized by a tetrad consisting of signs and symptoms beyond cognitive impairment [15]. DLB patients have poor prognosis on a variety of key outcomes, including frequency and duration of hospital admissions, the need for specialized care, under-diagnosis, institutionalization, geriatric syndromes, autonomic impairment, behavioral disturbances, decreased quality of life, and increased caregiver burden [16–18].

The aim of this study is to describe the frequency of frailty in subjects with newly diagnosed mild DLB and mild AD. Given the lack of knowledge on frailty in DLB, it is important to estimate the frequency of said condition in this population, since understanding this association has the potential for better management and better outcomes.

Materials and Methods

Setting and Participants

We analyzed data from the Dementia Study of Western Norway (Demvest). This is a longitudinal cohort study with annual assessment of patients referred to dementia clinics in Hordaland and Rogaland counties [19]. Only baseline data were included in this study. The centers were contacted by certified mail prior to the beginning of the study and invited to refer all patients with suspected dementia. All dementia diagnostic units in the region recruited patients to the study. The same National Insurance Scheme with restricted copayments covered all residents of the region. Thus, it was possible to adequately represent dementia in the general population. After the main inclusion period, which took place between 2005 and 2007, we continued to selectively recruit patients with DLB dementia in order to enhance the number of patients in this group.

Exclusion criteria were the absence of dementia, having moderate or severe dementia, delirium, previous bipolar or psychotic disorder, terminal illness, or recently diagnosed major somatic illness, which might significantly impact on cognition, function, or study participation. After screening 657 patients, 234 were included at baseline. The sample included 116 subjects with AD, 70 with DLB, 12 with Parkinson's disease, 20 had mixed vascular and AD

and 16 participants had other types of dementia (frontotemporal dementia n = 4, vascular dementia n = 9, and alcohol-related dementia n = 3) [19]. For the purposes of our study, we included subjects living with AD and DLB, yielding a total of 186 participants. The youngest subject was 50 years old and the oldest was 92 years of age.

Clinical Assessments

The diagnosis of dementia was made according to DSM-IV criteria. It was further classified as AD dementia when complying with The National Institute of Neurological and Communicative Disorders and Stroke-AD and Related Disorders Association guidelines [20] and as DLB according to the revised consensus criteria [21]. Two of the study authors independently applied the diagnostic criteria. In cases of disagreement, and in patients fulfilling more than one set of operationalized diagnostic criteria, the final ascertainment was made through consensus. In addition, based on the same evaluation, the consensus criteria for a clinical diagnosis of probable DLB were also applied, and ultimately the proportion fulfilling the 2 sets of criteria for DLB were compared [19]. Mild dementia was defined as a Mini-Mental Status Examination (MMSE) score [22] of at least 20 or a CDR global score = 1. A pathological diagnosis was available for 56 patients in the Demvest cohort, proving diagnostic accuracy above 80% for both AD and DLB [19, 23].

Patients were evaluated through structured and detailed assessments; in addition, relevant information regarding past medical history was taken from medical records in order to obtain complete and detailed information about the medical background and comorbidities for each subject. Routine blood and CSF analyses, as well as brain imaging through magnetic resonance imaging were also performed. Dopamine transporter SPECT scans were available for most patients with suspected DLB [19].

Classification of Frailty

Collected information was employed to estimate frailty through the FI, which was blinded for clinical diagnosis. Our FI included 35 deficits:

(1) Inability to cook for themselves, (2) Inability to keep personal hygiene (shaving, hair combing, and dental hygiene), (3) Inability to go to the bathroom by themselves, (4) Inability to use the phone, (5) Inability to go shopping, (6) Inability to manage their finances, (7) Inability to take own medicines, (8) Inability to manage financial responsibilities (pay taxes), (9) Upper gastrointestinal complaints, (10) Lower gastrointestinal complaints, (11) Urinary system deficits, (12) Osteomuscular complaints, (13) Renal problems, (14) Low serum albumin, (15) Hypoglycemia, (16) Cardiac diseases (Arrhythmias, Myocardial infarction, Congestive heart failure), (17) Hypertension, (18) Diabetes Mellitus, (19) COPD, (20) Hypothyroidism, (21) Epilepsy, (22) Stroke or Transient Ischemic Attack, (23) Gait disturbances, (24) Tremor, (25) Smoking, (26) Glaucoma or other ophthalmologic diseases, (27) Delirium, (28) Hearing problems, (29) Aphasia, (30) Arthropathies, (31) Agitation or aggression, (32) Depression, (33) Anxiety, (34) Apathy, and (35) Falls.

Each item was rated as 0 (if no deficit was present) or 1 (if a real deficit was present), deficits from 1 to 13 had intermediate scores such as 0, 0.33, 0.66, and 1 according to severity. The score for each item was added and then divided by 35 in order to obtain a global score for the index. The cutoff value used to define frailty was established at >0.25 [4].

Statistical Analysis

Descriptive analyses are presented through frequencies and percentages for categorical variables, while SDs and means are used for continuous variables. For bivariate comparative analyses, χ^2-tests or Student t tests were used as appropriate, depending on the distribution

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Table 1. Descriptive and bivariate analysis

	Non-frail	Frail	p value	Total
	n (%) or mean ± SD	n (%) or mean ± SD		n (100%) or mean ± SD
Age, years	75.01±7.95	79.21±5.40	0.0009	76.10±7.59
≤69	96.55 (28)	3.45 (1)	0.003	29
70–79	75.86 (66)	24.14 (21)		87
≥80	64.18 (43)	35.82 (24)		67
Gender			0.5196	
Male	47 (68.12)	22 (31.88)		69
Female	91 (77.78)	26 (22.22)		117
MMSE	23.81±2.61	22.93±2.62	0.0458	23.59±2.63
AD	94 (81.03)	22 (18.97)	0.006	116
DLB	44 (62.86)	26 (37.14)		70
Total	138 (74.19)	48 (25.81%)		186
FI	0.15±0.079	0.21±0.01	<0.001	0.18±0.094

MMSE, Mini-Mental Status Examination; FI, frailty index; AD, Alzheimer's disease; DLB, dementia with lewy bodies.

of each variable. Multivariate logistic regression models were fitted in order to obtain an OR with 95% CI for the association between frailty and the independent variable (AD or DLB). The results were then adjusted for sex, age, and MMSE. The level of statistical significance was set at $p < 0.05$. All data were analyzed using STATA 15.

This study was approved by the regional Ethics Committee (2010/633) and the Norwegian authorities for the collection of medical data. All data were handled in accordance with national health and data privacy protocols. All participants signed an informed consent form before inclusion in the study.

Results

The cohort included 186 patients with mean age 76.10 ± 7.59, 116 with AD and 70 with DLB. Demographic and clinical characteristics for frail DLB and AD patients are shown in Table 1. Frailty was associated with higher age (79.21 ± 5.40 vs. 75.01 ± 7.95, p value ≤0.001), male gender (31.88% vs. women 22.22%, p value = 0.51 and lower MMSE scores (22.93 ± 2.62 vs. 23.81 ± 2.61, p value = 0.045; Table 1).

The global frequency of frailty was 25.81% (n = 48). In DLB, 37.14% (n = 26) of the subjects were frail, compared to 18.97% (n = 22) of those with AD (p = 0.006; Table 1 and Fig. 1). The adjusted multivariate analysis revealed an OR of 2.45 (1.15–5.23) for frailty in subjects with DLB when taking AD as the reference group. This association was statistically significant (p value 0.020; Table 2).

Discussion

We found a high general prevalence of frailty within the sample, with an even greater prevalence in those living with DLB. The odds for being frail were more than 2 times higher in DLB patients when compared with subjects with AD.
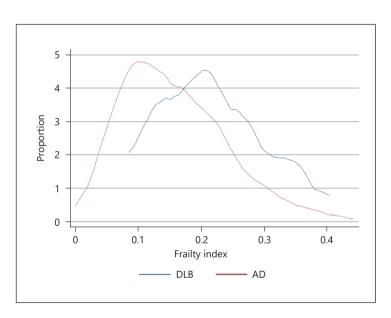
Table 2. Multivariate analysis

	Unadjusted		Adjusted	
	OR (95% CI)	*p* value	OR (95% CI)	*p* value
AD	Ref.		Ref.	
DLB	2.52 (1.29–4.94)	0.007	2.45 (1.15–5.23)	0.020
Age, years	–		1.11 (1.04–1.18)	0.001
Gender	–		0.61 (0.28–1.31)	0.211
MMSE	–		0.94 (0.82–1.07)	0.381

Model adjusted by sex, age and score in the MMSE.
AD, Alzheimer's disease; DLB, dementia with lewy bodies; MMSE, Mini-Mental Status Examination.

Fig. 1. Distribution of people with AD and DLB according to the FI. DLB, dementia with Lewy bodies; AD, Alzheimer's disease; FI, frailty index.

The trajectories of frailty and dementia share multiple etiologies, features, and related factors. However, in contrast with AD, DLB patients are more prone to be frail due to the symptoms of the disease per se. (i.e., executive function impairment, decreased mobility, motor and non-motor symptoms, psychiatric and autonomous symptoms) and due to the consequences of these manifestations (poor adherence and adverse effects to medications, polypharmacy, worsening of comorbidities, need for care, falls, geriatric syndromes, among others) [24]. Our research group has previously reported high mortality in DLB, which we can now infer, may be associated with the high prevalence of frailty [25].

For the purpose of this study, we used the FI because in this context it reflects the biological nature of frailty more than other approaches based mainly on physical variables and measurements, which can be biased by the illness itself. Furthermore, dementias in general have been long seen as diseases that are limited to the brain, focusing on cognitive and mental symptoms. However, and more importantly in DLB, other systemic manifestations and their consequences are very relevant and are usually under-detected or considered to be normal age-related changes [24]. All of these factors could lead to a greater and faster fragilization process.

It is also relevant to mention that people living with frailty are more likely to develop dementia due to several factors including inflammation and endothelial damage [26–28]. Thus, targeting frailty as a potentially modifiable factor in the early trajectory of dementia seems imperative. The prevalence of frailty found in our study is similar to previous reports on AD [29]. A recent systematic review reported the prevalence of frailty within people with AD ranging from 11.1 to 50%, with a pooled prevalence of 31.9% in mild and moderate stages [14]. However, the association between cognitive impairment and frailty had only been reported in AD.

It is important to highlight that people included in this analysis had been recently diagnosed with mild dementia, which leads us to conclude that in many cases the frailty process starts much before the onset of dementia, and efforts should be made toward prodromal or early detection of both neurodegenerative diseases and frailty.

Our study is at risk for potential recruitment bias because of referrals by primary care physicians, which may have led to an increased number of patients with complicated dementia or neuropsychiatric symptoms. However, referral centers were invited to refer any patients with suspected dementia, and patients were included from psychiatric, neurologic, and geriatric clinics. MMSE is language and memory dominant and thus less sensitive to the earliest changes in DLB patients, although the sensitivity of MMSE is comparable to other screening instruments when approaching moderate dementia levels [30]. In addition, we also used the CDR to compare dementia severity, which is independent of the cognitive impairment profile. Also, healthy controls were not included for comparison. Strengths of the study include careful and rigorous diagnostic procedures, assessment through structured instruments, longitudinal design, and high postmortem accuracy in the 56 cases with neuropathological diagnosis [19, 23]. To the best of our knowledge, this is the first study of its kind to address the association between frailty and DLB.

Conclusion

The prevalence of frailty at the time of diagnosis of dementia is high. Clinicians, particularly primary care practitioners, are thus encouraged to identify dementia earlier in its trajectory for timely and prompt interventions. Understanding frailty in DLB may guide management and improve prognosis. Nonetheless, better tools are required in order to allow early or prodromal detection of disease and prevent or stop the fragilization process, particularly in diseases such as DLB where frailty has shown to be prevalent and has been unexplored.

Statement of Ethics

This study was approved by the regional Ethics Committee (2010/633) and the Norwegian authorities for the collection of medical data, and received financial support from the regional health authorities of Western Norway, Helse Vest. All data were handled and kept in accordance with national health and data privacy protocols. All participants signed an informed consent form before inclusion in the study.

Disclosure Statement

The authors have no potential conflicts of interest to declare regarding research, authorship, and/or publication of this article.

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Author Contributions

M.G.B., H.S.: Conception and design, analysis and interpretation of data, manuscript preparation, final approval of the version to be published. C.E.: Conception and design, manuscript preparation, final approval of the version to be published. M.U.P-.Z.: Conception and design, analysis and interpretation of data, final approval of the version to be published. D.A.: Conception and design, analysis and interpretation of data, manuscript preparation, final approval of the version to be published, DEM-VEST study PI.

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