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Clinical Trajectories at the End of Life in Autopsy-Confirmed Dementia Patients With Alzheimer Disease and Lewy Bodies Pathologies

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Study Question

Does the disease trajectory in the years before death differ among patients with pure Alzheimer disease (AD), pure dementia with Lewy bodies (DLB), or mixed (AD and DLB) pathologies?

What Is Known and What This Paper Adds

Inconsistent findings have been reported regarding the disease course of the 2 most common types of dementia: AD and DLB. In this longitudinal study, we found that among patients with dementia, those with Lewy body pathology experienced faster cognitive and functional decline than those with pure AD pathology in the last few years of life.

Methods

The retrospective longitudinal study included 62 participants with autopsy-confirmed diagnoses of pure AD (n = 34), mixed AD and DLB (AD + DLB; n = 17), or pure DLB (n = 11) from the Predictors 2 Cohort Study, a prospective, clinic-based cohort of patients with dementia recruited at 3 sites: Columbia University, Johns Hopkins University, and Massachusetts General Hospital. Generalized estimating equation models were used to examine the trajectory of cognition (Folstein Mini-Mental State Examination [MMSE]), function (activities of daily living [ADL]), and dependence (dependence scale [DS]) among patients with different autopsy-confirmed diagnoses, adjusted for age, sex, education, and baseline features including extrapyramidal signs, MMSE, ADL, and DS.

Results

At time of recruitment, the participants were 73.5 ± 7.9 (mean ± SD) years old, had 15 ± 2.9 years of education, and scored 20.8 ± 4.3 on MMSE, 4.68 ± 3.0 on ADL, and 4.48 ± 2.6 on DS. Half of the participants were female, 36% had extrapyramidal signs, and 42% had psychotic symptoms. The participants on average received 9.4 ± 4.6 assessments at 6-month intervals. At baseline, cognition and function were highly correlated among patients with AD + DLB but not in patients with pure AD or pure DLB. All patients declined in both cognition and function. For patients with pure AD, MMSE declined 0.61 (SE 0.19; $p = 0.002$), ADL increased 0.55 (SE 0.15; $p < 0.0001$), and DS increased 0.40 (SE 0.09; $p < 0.0001$) points per year. Compared with the pure AD group, the pure DLB group had a faster decline in MMSE (b [SE] −1.02 [0.39]; $p = 0.010$) and faster deterioration in DS (0.41 [0.17]; $p = 0.015$); the AD + DLB group experienced a faster deterioration in ADL (0.48 [0.21]; $p = 0.026$) (Table). In other words, compared to the pure AD group, the pure DLB group experienced approximately double the rate in both cognitive and functional decline, and the AD + DLB group showed double the rate in ADL decline.

Table Disease Trajectory in Patients With Dementia

	B	SE	*p* Value
MMSE			
Time	−0.608	0.193	0.002
DLB*time	−1.020	0.394	0.010
Mixed*time	−0.339	0.420	0.420
ADL			
Time	0.552	0.153	<0.0001
DLB*time	0.446	0.254	0.079
Mixed*time	0.478	0.215	0.026
DS			
Time	0.400	0.094	<0.0001
DLB*time	0.408	0.167	0.015
Mixed*time	0.259	0.161	0.109

Abbreviation: DLB = dementia with Lewy bodies.
The Alzheimer disease (AD) group was treated as the reference group in all models. Models were adjusted for age, sex, education, baseline extrapyramidal signs, and all 3 clinical measures (Mini-Mental State Examination [MMSE], activities of daily living [ADL], and dependence scale [DS]) at baseline.

The study has some limitations. The study participants were predominantly White and well-educated, limiting the generalizability of the findings. The study has an overrepresentation of *APOE* ε4 allele carriers, which could indicate a potential selection bias.

Study Funding and Competing Interests

This research was funded by the National Institute on Aging (AG07370). The authors report no competing interests. Go to Neurology.org/N for details.

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