

Original Article



Development and Validation of a Screening Questionnaire for Dementia With Lewy Bodies (DLB): the DLB Screening Questionnaire (DLBSQ)

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Conflict of Interest

The authors have no financial conflicts of interest.

Author Contributions

Conceptualization: Park M, Ye BS; Data curation: Park M, Ye BS; Formal analysis: Park M, Baik K; Investigation: Park M; Methodology: Park M, Baik K; Project administration: Ye BS;

ABSTRACT

Background and Purpose: Although dementia with Lewy bodies (DLB) is the second most common cause of neurodegenerative dementia, its clinical prevalence is low. We developed a short and easy-to-complete DLB screening questionnaire (DLBSQ) to raise diagnostic sensitivity in routine clinical settings.

Methods: A total of 501 participants were retrospectively enrolled, including 71 controls, 184 patients without DLB, and 246 patients with probable DLB. All patients underwent clinical evaluation, including core features of DLB, the DLBSQ, brain magnetic resonance imaging, and detailed neuropsychological assessments. The diagnostic performance of the DLBSQ for probable DLB was investigated using a receiver operating characteristic curve analysis.

Results: Total DLBSQ score was associated with visuospatial and frontal/executive dysfunction and the diagnosis of probable DLB. The area under the receiver operating characteristic curve for total DLBSQ score was 0.727. Youden's method revealed an optimal cutoff value of 3. The sensitivity and specificity of the DLBSQ were 68.7% and 62.4%, respectively. Its discriminating performance improved when cognitive test profiles were additionally considered (area under the curve: 0.822, sensitivity: 80.6%, and specificity: 70.4%).

Conclusions: The DLBSQ might be a useful screening tool for DLB in routine clinical practice with good sensitivity and specificity.

Keywords: Lewy Body Disease; Diagnosis; Questionnaire

INTRODUCTION

Dementia with Lewy bodies (DLB) is the second most common cause of neurodegenerative dementia, manifesting motor parkinsonism, rapid eye movement sleep behavior disorder (RBD), visual hallucinations, and cognitive fluctuation as core clinical features.¹ There have been several revisions to diagnostic criteria for DLB to improve diagnostic sensitivity and specificity in clinical practice. The prevalence of DLB has been reported to vary. A meta-analysis of epidemiological studies reported that DLB represented 7.5% of all dementia in secondary care settings and 4.2% of dementia in a community-based population.² However,

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the clinical prevalence varied largely among studies, ranging from 2.2% to 24%.³ Recently, a large nationwide study from the UK revealed that the clinical prevalence of DLB was 4.6% of all dementia cases.⁴ However, the neuropathological prevalence of DLB differs from the clinical prevalence in that DLB consists of up to 15%–20% of cases of dementia.⁵ Concomitant Alzheimer's disease and DLB pathology of varying severity might raise the neuropathological prevalence of DLB even higher. Markesbery et al.⁶ have reported that brains of 33 (23%) of 139 normal subjects have Lewy body pathology in various regions. The frequency of Lewy body pathology ranged from 1.1 to 24.7% in clinical and cohort settings.⁵ These discrepancies between pathological and clinical prevalence might be attributed to a low clinical detection rate of DLB. Probable diagnosis of DLB or prodromal DLB requires more than two core clinical features regardless of biomarkers or one core clinical feature plus one indicative biomarker.⁷ Indicative biomarkers of DLB include dopamine transporter imaging for the detection of nigrostriatal dopaminergic degeneration,^{1,3} iodine-metaiodobenzylguanidine myocardial scintigraphy for detecting degeneration of sympathetic innervation of the heart, and polysomnography for detecting RBD.⁷ However, investigating all indicative biomarkers in every patient with cognitive complaints would be unrealistic in routine clinical settings. Moreover, core clinical features can easily be neglected or misdiagnosed when investigated without high suspicion. Several methods can be used to assess these core features, including the Unified Parkinson's Disease Rating Scale (UPDRS) part III for motor parkinsonism,⁸ questionnaires and scales for visual hallucinations and psychosis,^{9,10} cognitive fluctuation,^{11,12} and RBD.^{13,14} However, each of these scales and questionnaires for core clinical features takes up to 10–20 minutes to complete. In addition, detailed neurological examination might not be feasible in a routine primary clinic. Therefore, administering all these questionnaires and examinations to every patient with cognitive complaints might be time-consuming and difficult to perform in real-world clinical circumstances. Thus, this study aimed to develop a questionnaire that would be quick and easy to apply in a routine clinical setting to increase the diagnostic sensitivity for DLB. We developed a brief questionnaire that included questions about clinical features of DLB administered by an informant or caregiver. We hypothesized that this questionnaire would be adequate for diagnosing and discriminating patients with DLB from controls and cognitively impaired patients without DLB.

METHODS

Patient enrollment

In this retrospective cohort study, 501 participants from a university-based memory clinic were enrolled between June 2017 and December 2021. All participants underwent 3T brain magnetic resonance imaging (MRI) and detailed neuropsychological tests (Seoul Neuropsychological Screening Battery, SNSB¹⁵) to investigate cognitive function. Core features of DLB regarding parkinsonism, RBD, visual hallucinations, and cognitive fluctuation were evaluated by careful history taking and investigation by clinicians. Dopamine transporter imaging was performed for all participants in the disease group. The severity of motor parkinsonism was assessed by scoring UPDRS part III. Global cognitive function was assessed using the Mini-Mental Status Examination (MMSE) and Clinical Dementia Rating scale-sum of boxes (CDR-SOB). Participants without evidence of underlying neurodegenerative disease on brain MRI regarding disproportionate cortical atrophy¹⁶ and those with preserved cognition not fulfilling the diagnostic criteria for mild cognitive impairment (MCI)¹⁷ in consecutive neuropsychological tests over five years were regarded as the control group. Participants with MCI or dementia during the follow-up period were classified as having DLB or prodromal

DLB (probable DLB) or not (non-DLB, encompassing Alzheimer's disease, frontotemporal dementia, primary progressive aphasia, suspected non-Alzheimer disease pathophysiology, and vascular cognitive impairment) according to the fourth consensus criteria for the clinical diagnosis of DLB and research criteria for prodromal DLB.^{7,18}

Exclusion criteria were as follows: 1) history of significant traumatic brain injury; 2) severely ill medical conditions (chronic renal failure, liver cirrhosis, and decompensated heart failure) and history of malignancies; 3) history of ischemic stroke and/or cortical/subcortical lesions suggestive of previous infarction; and 4) other causes sufficiently explaining cognitive impairment, including psychiatric disorders, normal pressure hydrocephalus, and brain structural lesions (e.g., tumor, large infarct, or hemorrhage).

This study was approved by the Institutional Review Board (IRB) of Yonsei University Severance Hospital (IRB No. 4-2015-0551). The need for informed consent was waived by the IRB due to the retrospective nature of this study.

Development of DLB screening questionnaire (DLBSQ)

The DLBSQ was originally developed in Korean by B.S. Ye, the corresponding author of this study. It was composed of several questions to investigate core and supportive clinical features of DLB according to the fourth consensus report of the DLB consortium.⁷ The DLBSQ comprised nine questions inquiring about hyposmia (DLBSQ1), RBD (DLBSQ2), orthostatic dizziness/loss of consciousness (DLBSQ3), constipation (DLBSQ4), restless legs syndrome (DLBSQ5), bradykinesia (DLBSQ6), masked face (DLBSQ7), visual hallucination (DLBSQ8), and cognitive fluctuation (DLBSQ9). The DLBSQ was completed by informants at the first visit to the office. It took 5–10 minutes to complete the questionnaire. Hyposmia, orthostatic dizziness/loss of consciousness, constipation, leg restlessness, bradykinesia, masked face, and RBD were responded qualitatively (yes=1, no=0), and visual hallucination and cognitive fluctuation were asked to respond semiquantitatively with scores ranging from 0 to 3 and 0 to 2, respectively. Total score ranged from 0 to 11, with a higher score indicating more clinical features of DLB. The authors (B.S.Y and M.P) translated the original version of the DLBSQ into an English version and a bilingual translator made a backward translation. B.S.Y and M.P then reviewed the consensus on forward and backward translation. Contents of the DLBSQ translated to English are presented in **Table 1**.

Neuropsychological test

All participants underwent a standardized neuropsychological battery called the SNSB,¹⁵ which contained the following scorable tests: digit span test (forward and backward), Korean version of the Boston naming test, Rey-Osterrieth complex figure test (RCFT; copying, immediate recall, 20 minutes delayed recall, and recognition), phonemic and semantic (animal and supermarket)-Controlled Oral Word Association Test (COWAT), and Stroop test (word and color reading). General cognitive function was evaluated using the Korean version of the MMSE¹⁹ and the CDR-SOB. The operational definition for the presence of cognitive dysfunction has been described previously.²⁰ Scales administered by caregivers for activities of daily living (ADL), including the Seoul Instrumental ADL²¹ and Korean-Instrumental ADL,²² were used to define the presence of dementia.

Statistical analysis

All statistical analyses were performed using Statistical Product and Service Solutions version 26.0 (IBM Corporation, Armonk, NY, USA). Significance level was set at 0.05. χ^2

The DLB Screening Questionnaire (DLBSQ)

Table 1. Dementia with Lewy bodies screening questionnaire

No.	Question	Response
1	The patient does not smell well, or does not smell as well as before.	Yes (1)/No (0)
2	The patient makes sound, mutters, or swings his/her hand in the air during sleep. The patient appears to “act out his/her dreams” while sleeping (e.g. punching, kicking, or flailing arms in the air).	Yes (1)/No (0)
3	The patient complains dizziness. Especially when standing up, the patient feels light-headedness, dizziness, or faintness. Or, he/she had lost his/her consciousness briefly.	Yes (1)/No (0)
4	The patient suffers from constipation.	Yes (1)/No (0)
5	When lying in the evening or before the bed, the patient has uncomfortable or unpleasant feeling in his/her feet or legs, or these uncomfortable or unpleasant sensation are relieved by movement of lower extremities.	Yes (1)/No (0)
6	The patient moves more slowly, compared to 10 years earlier. Specifically, it takes more time to get in or out of a car than it used to. The patient’s gait speed got slower and stride got shorter, patient walking in short and quick steps.	Yes (1)/No (0)
7	The patient become inexpressive and emotionless. The patient has been told that the patient looks like he/she is angry because of his/her blank face.	Yes (1)/No (0)
8	The patient sometimes insists that he/she have seen something that does not exist (visual hallucinations).	0 No, never. 1 Sometimes he/she mistakes or confuses objects with persons when he/she is waking up or falling asleep. 2 Sometimes he/she mistakes or confuses objects with persons when he/she is awake. 3 Sometimes he/she sees animal or insects with distinct color or shape.
9	The patient’s cognitive function fluctuates to such an extent that he/she may look like a completely different person (There are alternating periods of close-to normal functioning and deficits in daily functioning).	0 No, never. 1 Sometimes he/she looks vacantly staring into space or zoning out. 2 Sometimes he/she gets so confused or disorganized that he/she could barely communicate or engage in daily lives.

tests and analysis of variance (ANOVA) were used to compare demographics and baseline characteristics between control and disease groups. To compare responses to individual questions among the control, non-DLB patient, and DLB patient groups, chi-square tests were performed. Post hoc analysis was performed to investigate differences between groups. Effect of total DLBSQ score on cognitive test scores was assessed using a general linear model after controlling for age, sex, education, and MMSE score. Logistic regression analysis was performed to investigate effect of DLBSQ score on diagnosis of probable DLB. Model 1 included DLBSQ score as a predictor and Model 2 included cognitive function scores associated with probable DLB (digit span forward, SVLT delayed recall, RCFT delayed recall, animal COWAT, and Stroop color reading, see **Supplementary Table 1**) as additional predictors after controlling for age, sex, education, and MMSE score. Performance of the DLBSQ was investigated using sensitivity, specificity, and area under the receiver operating characteristic (ROC) curve. The optimal cutoff score for the DLBSQ was determined using Youden’s index.²³ Thereafter, we investigated whether considering cognitive test scores simultaneously with the DLBSQ score could improve the performance of the DLBSQ. Multiple statistical tests across neuropsychological tests were corrected using the false discovery rate method and a corrected Q value of less than 0.05 was considered significant.

RESULTS

Demographics and clinical characteristics

Demographic and clinical characteristics of study participants are summarized in **Table 2**. The probable DLB group was older than control and non-DLB groups. The non-DLB group was older than the control group. There were more male participants in the non-DLB group than in the control group. The probable DLB group had more participants with hypertension

Table 2. Baseline characteristics of study participants

Variables	Control	Non-DLB	Probable DLB	p-value
Number	71	184	246	
Age (yr)	68.0±7.5	73.1±8.4	76.4±7.3	<0.001*†‡
Sex, male	20 (28.2)	83 (45.1)	97 (39.4)	0.046*
Education (yr)	10.9±4.0	10.6±5.2	9.6±5.1	0.050
Hypertension	35 (49.3)	91 (49.5)	155 (63.0)	0.009‡
Diabetes mellitus	11 (15.5)	36 (19.6)	70 (28.5)	0.023
Dyslipidemia	33 (46.5)	63 (34.2)	98 (39.8)	0.175
Parkinsonism	0	54 (29.3)	222 (90.6)	<0.001*†‡
RBD	0	7 (3.8)	91 (37.0)	<0.001†‡
Visual hallucination	0	4 (2.2)	30 (12.2)	<0.001†‡
Fluctuation	0	8 (4.4)	93 (37.8)	<0.001†‡
MMSE	27.7±2.0	23.2±4.3	21.7±4.3	<0.001*†‡
CDR	0.5±0.3	0.6±0.2	0.7±0.4	<0.001†‡

Values are presented as number (%) or mean ± standard deviation.

DLB: dementia with Lewy bodies, RBD: rapid eye movement sleep behavior disorder, MMSE: Mini-Mental State Examination, CDR: clinical dementia rating scale.

*Significant difference between control group and non-DLB patient group.

†Significant difference between control group and DLB patient group.

‡Significant difference between non-DLB patient group and DLB patient group.

than the non-DLB group. All groups had comparable educational levels and histories of diabetes mellitus and dyslipidemia. Regarding clinical features of DLB, none of the controls had RBD, significant parkinsonism, visual hallucinations, or cognitive fluctuations. The probable DLB group had parkinsonism, RBD, visual hallucinations, and fluctuations more frequently than non-DLB and control groups. The non-DLB group had parkinsonism more frequently than the control group. The probable DLB group had lower MMSE scores but higher CDR scores than control and non-DLB groups, whereas the non-DLB group had lower MMSE scores than the control group.

Responses to the questionnaire among participant groups

The probable DLB group responded positively more frequently to every question except for DLBSQ5 than the non-DLB group (Table 3). The probable DLB group responded more frequently to DLBSQ2, DLBSQ4, DLBSQ6, DLBSQ7, DLBSQ8, and DLBSQ9 than the control group, but not to hyposmia, orthostatic dizziness, or restless legs syndrome. The non-DLB group responded positively more frequently only to bradykinesia than the control group. The total DLBSQ score was higher in the probable DLB group than in control and non-DLB groups. Total DLBSQ scores were comparable between control and non-DLB groups (Fig. 1).

Impact of total DLBSQ score on neuropsychological test scores

The impact of total DLBSQ score on neuropsychological test scores was investigated using GLM after controlling for age, sex, education, and MMSE score (Table 4). Higher total DLBSQ scores were associated with worse test scores for RCFT copy, supermarket, and phonemic COWAT and Stroop color reading after correction for multiple comparisons.

Neuropsychological tests associated with probable DLB

The association between cognitive test scores and the diagnosis of probable DLB was investigated using logistic regression after controlling for age, sex, education, and the MMSE score (Supplementary Table 1). Higher odds of probable DLB were associated with lower test scores for digit span forward, RCFT delayed recall, animal COWAT, and Stroop color reading tests and higher test scores for SVLT delayed recall.

Table 3. Responses to questionnaire among participant groups

Variables	Control	Non-DLB	Probable DLB	p-value
DLBSQ				
DLBSQ1	16 (22.5)	39 (21.2)	88 (35.8)	0.002 [‡]
DLBSQ2	6 (8.5)	28 (15.2)	98 (39.8)	<0.001 ^{†‡}
DLBSQ3	22 (31.0)	54 (29.3)	109 (44.3)	0.003 [‡]
DLBSQ4	7 (9.9)	28 (15.2)	81 (32.9)	<0.001 ^{†‡}
DLBSQ5	19 (26.8)	44 (23.9)	72 (29.3)	0.464
DLBSQ6	25 (35.2)	113 (61.4)	198 (80.5)	<0.001 ^{*†‡}
DLBSQ7	19 (26.8)	48 (26.1)	128 (52.0)	<0.001 ^{†‡}
DLBSQ8				<0.001 ^{†‡}
0	69 (97.2)	176 (95.7)	194 (78.9)	
1	1 (1.4)	1 (0.5)	30 (12.2)	
2	1 (1.4)	6 (3.3)	13 (5.3)	
3	0 (0)	1 (0.5)	9 (3.7)	
DLBSQ9				<0.001 ^{†‡}
0	63 (88.7)	137 (74.5)	133 (54.1)	
1	8 (11.3)	45 (24.5)	103 (41.9)	
2	0 (0)	2 (1.1)	10 (4.1)	
DLBSQ total	1.76±1.54	2.28±1.73	3.98±2.28	<0.001 ^{†‡}

Values are presented as number (%) or mean ± standard deviation.

DLB: dementia with Lewy bodies, DLBSQ: dementia with Lewy bodies screening questionnaire.

*Significant difference between control group and non-DLB patient group.

†Significant difference between control group and DLB patient group.

‡Significant difference between non-DLB patient group and DLB patient group.

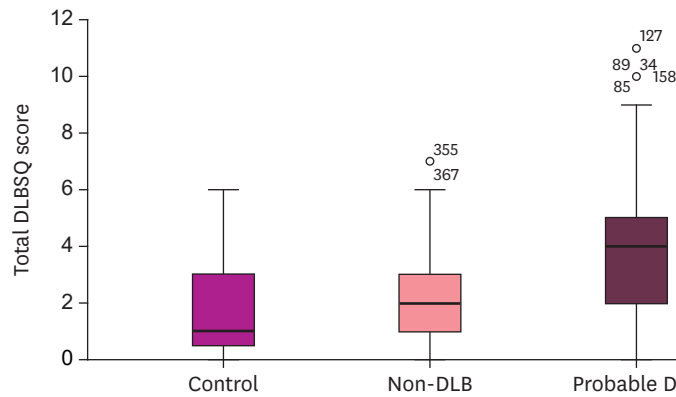


Fig. 1. Total DLBSQ scores of different participant groups. The probable DLB patient group showed a significantly higher total DLBSQ score than non-DLB group and control groups. Control and non-DLB groups had comparable DLBSQ scores.

DLBSQ: dementia with Lewy bodies screening questionnaire, DLB: dementia with Lewy bodies.

Table 4. Effect of DLBSQ score on cognitive function scores

Variables	B (SE)	p-value	Q-value
Digit span forward	-0.026 (0.021)	0.211	0.264
Digit span backward	-0.032 (0.022)	0.146	0.213
K-BNT	-0.025 (0.028)	0.358	0.398
RCFT copy	-0.125 (0.051)	0.014	0.040
SVLT delayed recall	0.031 (0.022)	0.149	0.213
RCFT delayed recall	-0.004 (0.018)	0.817	0.817
Animal COWAT	-0.042 (0.020)	0.036	0.072
Supermarket COWAT	-0.044 (0.018)	0.016	0.040
Phonemic COWAT	-0.085 (0.020)	<0.001	<0.001
Stroop color reading	-0.073 (0.026)	0.005	0.025

Results of general linear models using DLBSQ total score as a predictor after controlling for age, sex, education, and Mini-Mental State Examination score.

DLBSQ: dementia with Lewy bodies screening questionnaire, SE: standard error, K-BNT: Korean version of the Boston naming test, RCFT: Rey-Osterrieth complex figure test, SVLT: Seoul verbal learning test, COWAT: Controlled Oral Word Association Test.

Table 5. Effect of DLBSQ score on diagnosis of probable DLB

Variables	OR (95% CI)	p-value
Model 1		
DLBSQ score	1.47 (1.32–1.63)	<0.001
Model 2		
Digit span forward	0.81 (0.64–1.02)	0.063
SVLT delayed recall	1.37 (1.06–1.78)	0.016
RCFT delayed recall	0.58 (0.42–0.78)	<0.001
COWAT animal	0.61 (0.46–0.80)	<0.001
Stroop color reading	0.75 (0.61–0.91)	0.003
DLBSQ score	1.44 (1.28–1.62)	<0.001

Results of logistic regression using DLBSQ as a predictor after controlling for age, sex, education, and Mini-Mental State Examination score in Model 1. In Model 2, cognitive test scores were regarded as predictors in addition to those included in Model 1.

DLBSQ: dementia with Lewy body screening questionnaire, DLB: dementia with Lewy bodies, OR: odds ratio, CI: confidence interval, SVLT: Seoul verbal learning test, RCFT: Rey-Osterrieth complex figure test, COWAT: Controlled Oral Word Association Test.

Effect of DLBSQ score on the diagnosis of probable DLB

The association between the DLBSQ score and the diagnosis of probable DLB was analyzed in two models (Table 5). Higher DLBSQ scores were associated with higher odds of probable DLB. This association was significant when cognitive test scores were additionally regarded as predictors.

ROC curve analyses

ROC curve analyses showed that the DLBSQ had fair accuracy in diagnosing probable DLB (area under the curve [AUC]: 0.727, 95% confidence interval [CI]: 0.683–0.770, Fig. 2). The sensitivity and specificity of the DLBSQ were 68.7% and 62.4%, respectively, with an optimal cutoff value of 3. Combining the DLBSQ score and neuropsychological test scores,

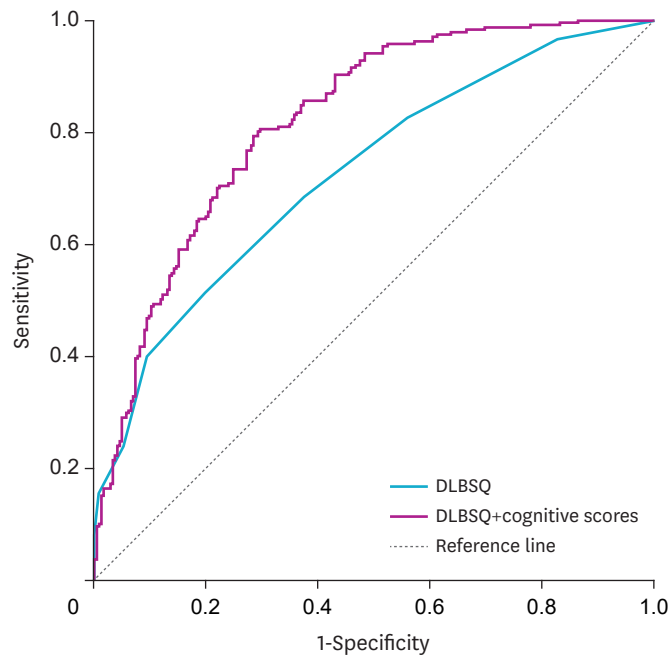


Fig. 2. ROC curve for DLBSQ. Blue line indicates ROC curve discriminating probable DLB using DLBSQ only. Red line indicates ROC curve discriminating participants with probable DLB using DLBSQ plus cognitive scores associated with the presence of DLB. DLBSQ: dementia with Lewy bodies screening questionnaire, ROC: receiver operating characteristic, DLB: dementia with Lewy bodies.

which were associated with probable DLB, increased the discriminative ability with a good performance (AUC: 0.822, 95% CI: 0.785–0.858, **Fig. 2**), showing a sensitivity of 80.6% and a specificity of 70.4%.

DISCUSSION

This study aimed to develop a short and easy-to-perform questionnaire for screening DLB in patients with cognitive complaints. The DLBSQ is composed of qualitative and semiquantitative questions regarding clinical features of DLB, including core clinical features such as bradykinesia, RBD, visual hallucinations, and cognitive fluctuations, as well as other clinical features such as hyposmia, orthostatic dizziness/loss of consciousness, restless legs syndrome, constipation, and a masked face. Our major findings are as follows. First, patients with probable DLB responded positively more frequently than controls and non-DLB patients to every question except for restless legs syndrome. Second, a higher DLBSQ score was associated with worse visuospatial function and executive function known to be characteristic cognitive impairment pattern in DLB. It was also associated with the diagnosis of probable DLB regardless of cognitive test scores. Third, the DLBSQ showed fair performance in discriminating patients with probable DLB from controls and non-DLB patients. Its performance was improved by additionally considering significant cognitive test scores. These results suggest that the DLBSQ could be a useful screening tool for diagnosing DLB, especially for those with characteristic cognitive impairment patterns.

Several scales and toolkits are available to enhance the detection rate of DLB in clinical circumstances.^{24,25} However, these tools are time-consuming. In addition, they are mainly administered by experienced clinicians. Moreover, to the best of our knowledge, there is no scale that can assess the diagnostic possibility of DLB performed by a caregiver or an informant. The DLBSQ can be administered by a caregiver or an informant. It consists of nine simple questions, taking 5–10 minutes to complete. In the setting of routine clinical care, the compliance and accessibility of an investigation are crucial factors affecting the usefulness of an assessment instrument. Therefore, the easy-to-administer and fast-to-complete nature of the DLBSQ might make it adequate for implementation in daily clinical settings.

As the DLBSQ comprised seven qualitative and two semiquantitative questions, Cronbach's alpha was not available to confirm the internal validity of the questionnaire. However, the present results suggest that the DLBSQ exhibits good convergent and divergent validity with neuropsychological test scores for DLB. DLBSQ positivity was associated with higher odds of significant parkinsonism, RBD, visual hallucinations, and cognitive fluctuations known to be core clinical features of DLB (data not shown). In addition, the total DLBSQ score was associated with RCFT copy, animal, supermarket, and phonemic COWAT and Stroop color reading test scores that could reflect characteristic cognitive impairment domains in DLB.^{26,27} These findings suggest that the DLBSQ is associated with clinical features and cognitive dysfunction of patients with DLB, reflecting its convergent and divergent validity.

ROC curve analysis was used to evaluate the sensitivity and specificity of the DLBSQ. When discriminating the probable DLB group with the DLBSQ alone, the analysis showed a cutoff score of 3, with a sensitivity of 68.7% and a specificity of 62.4%, indicating a fair performance of the DLBSQ. Moreover, when neuropsychological test scores associated with the diagnosis of DLB were simultaneously considered, its sensitivity and specificity for

diagnosing probable DLB were improved to 80.6% and 70.4%, respectively. The accuracy of indicative biomarkers for DLB revealed that abnormal dopamine transporter imaging showed a sensitivity of 77.7% and a specificity of 90.4% with an overall accuracy of 85.7%, whereas abnormal cardiac innervation scintigraphy had a sensitivity of 69% and a specificity of 87% with an overall accuracy of 78%.^{28,29} Our short- and easy-to-administer questionnaire showed fair discriminative performance. When it was combined with cognitive test scores, it showed comparable performance to those indicative biomarkers.

However, this study has some limitations. First, because this study was performed primarily in a referral-based clinic, selection bias might exist. This selection bias might explain the relatively high proportion of patients with probable DLB in the study population. Moreover, the probable DLB group showed lower MMSE but higher CDR scores than the non-DLB group. These findings suggest that there might be differences in the severity of underlying conditions between probable DLB and non-DLB groups. This discrepancy might have affected the accuracy of DLBSQ. Therefore, replicating the validity of the DLBSQ in other populations is warranted. Second, as quantification of response to the questionnaire was not available, an investigation of internal consistency was not possible for the DLBSQ. Moreover, because the DLBSQ is composed of simple questions about each clinical feature of DLB, it cannot be directly compared to other existing questionnaires or scales. However, the DLBSQ score was qualitatively associated with several clinical features and global cognitive function. Moreover, a higher DLBSQ score was associated with visuospatial and executive dysfunction known to be characteristic domains affected in DLB. These findings indirectly confirmed the validity of the DLBSQ. Third, the sensitivity and specificity of the DLBSQ were 68.7% and 62.4%, respectively, which were not excellent. However, the sensitivity and specificity for diagnosing probable DLB were increased to 80.6% and 70.4%, respectively, after considering neuropsychological test scores. Such sensitivity and specificity were adequate for a screening tool.

In conclusion, the DLBSQ takes a short time to administer. In addition, it is easy to administer by caregivers. Considering cognitive profiles together, the DLBSQ showed good accuracy in diagnosing probable DLB. Therefore, the DLBSQ might be a useful screening tool to increase the diagnostic rate of DLB in a routine clinical setting.

AVAILABILITY OF DATA AND MATERIALS

Data generated and analyzed in the present study are not publicly available, but are available from the corresponding author upon reasonable request.

SUPPLEMENTARY MATERIAL

Supplementary Table 1

Association between cognitive function scores and diagnosis of probable DLB

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