A Combined Index Using the Mini-Mental State Examination and Lawton Index to Discriminate Between Clinical Dementia Rating Scores of 0.5 and 1:

A Development and Validation Study

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Abstract

Objective: To develop a combined index using cognitive function and instrumental activities of daily living (IADL) to discriminate between Clinical Dementia Rating (CDR) scores of 0.5 and 1 in the clinical setting, and to investigate its optimal cutoff values and internal and external validities.

Methods: We included outpatients aged 65–89 years with CDR scores of 0.5 or 1. The optimal cutoff values and internal validity were verified using Japanese memory clinic-based datasets between September 2010 and October 2021 [National Center for Geriatrics and Gerontology (NCGG) datasets]. Cognitive function and IADL were assessed using the Mini-Mental State Examination (MMSE) and Lawton Index (LI), respectively. The optimal cutoff values were defined using the Youden Index. To verify internal validity, sensitivity and specificity were calculated using stratified 5-fold cross-validation. To verify external validity, sensitivity and specificity of the optimal cutoff values were assessed in the Organized Registration for the Assessment of dementia on Nationwide General consortium toward Effective treatment (ORANGE) Registry dataset between July 2015 and March 2022, which has multicenter clinical data.

Results: A total of 800 (mean age, 77.53 years; men, 50.1%) and 1494 (mean age, 77.97 years; men, 43.3%) participants comprised the NCGG and ORANGE Registry datasets, respectively. The optimum cutoff values for men and women were determined as MMSE < 25 and LI < 5 and MMSE < 25 and LI < 8, respectively; such a combined index showed good discriminative performance in internal (sensitivity/specificity: men, 92.50/73.52; women, 88.57/65.65) and external validities (men, 81.43/77.62; women, 77.64/74.67).

Conclusion: The index developed is useful in discriminating between CDR scores of 0.5 and 1 and should be applicable to various settings, such as memory clinics and clinical research.

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People with dementia are estimated to account for 152.8 million worldwide in 2050—a clear indication that dementia is a growing global public health problem in an aging society.[1,2] Dementia is a condition characterized by the impairment of daily activity and social life due to at least one cognitive dysfunction.[3] Before the onset of dementia, many people experience mild cognitive impairment (MCI). MCI is a condition in which individuals have mild cognitive dysfunction while remaining mostly independent for daily activities and social life,[3,4] and such is considered a transitional state between normal cognition and dementia. Patients with MCI vary in clinical outcomes[5–7]: Some remain stable and some recover to normal cognition (reversion), while others develop dementia (conversion) at a rate of approximately 10%–15% per year in clinical-based populations.[8–10] Of these outcomes, conversion has been a major topic in recent dementia research, as evidence on pharmacologic and nonpharmacologic treatments for dementia prevention in patients with MCI has been gradually accumulating.[11,12] However, identifying the boundary between MCI and mild dementia is not easy,

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Clinical Points

- In an aging society, where the number of people with dementia is estimated to increase, there are few simple and accurate methods to identify the boundary between mild cognitive impairment and mild dementia.
- A combined index from the Mini-Mental State Examination and Lawton Index showed good discriminative performance in internal and external validities in discriminating between Clinical Dementia Rating (CDR) scores of 0.5 and 1.
- This index may be useful as a tool to assist in distinguishing CDR scores of 0.5 and 1 in various settings, such as memory clinics and clinical research.

and there is an increasing need for methods to accurately discriminate between MCI and mild dementia.

The Clinical Dementia Rating (CDR) is an international standard for the staging of dementia, which allows the severity of dementia to be determined by assessing community affairs, home function, and hobbies, in addition to cognitive functions.[13] In the staging of dementia, the overall score of 0.5 is generally considered to correspond to MCI and a score of 1 to mild dementia,[14] allowing the discrimination between MCI and mild dementia. However, the CDR is not readily available for use in clinical or research settings because it is time-consuming—it requires completing interviews not only with the patients but also with their caregivers. Thus, alternative screening tools to evaluate cognitive dysfunction, such as the Mini-Mental State Examination (MMSE) and Montreal Cognitive Assessment,[15,16] are often used to screen dementia. MMSE, one of the most used screening tools, can be easily used to assess global cognitive function, and older adults with an MMSE score <24 are suspected of having dementia (sensitivity, 81%; specificity, 89%).[17] In fact, the MMSE is reportedly consistently useful as a screening tool for cognitive dysfunction among community-dwelling older adults.[18] However, some studies have shown the low accuracy of MMSE in discriminating between MCI and dementia (sensitivity, 23%–76%; specificity, 40%–94%), suggesting that the use of MMSE alone for such goal is limited.[19] Therefore, we believed that combining MMSE with other indicators may more accurately discriminate MCI from mild dementia. Considering that MCI and dementia are distinguished based on the presence of impairments in daily activities and social life,[20] assessing the instrumental activities of daily living (IADL) may be useful. IADL indicates the activities of daily living (ADL) requiring a high level of skill in social life, such as managing finances, shopping, and cooking. Indeed, IADL begins to decline even before conversion to dementia, with significant impairments observed at the onset of dementia.[21,22] Thus, MCI and mild dementia may be accurately discriminated by evaluating both cognitive function and IADL. However, to the best of our knowledge, no simple and accurate discriminative tools or cutoff values currently exist.

In this study, we aimed to develop a combined index that allows the discrimination between CDR scores of 0.5 and 1 in some specialized clinical settings such as memory clinics using the MMSE for cognitive function and the Lawton Index (LI) for IADL and to evaluate its optimal cutoff values and internal and external validities.

METHODS

Study Population

To verify the optimal cutoff values of the tool and its internal validity, the study included outpatients who met the following criteria: (1) those who presented to the Memory Clinic at the National Center for Geriatrics and Gerontology (NCGG) of Japan between September 2010 and October 2021; (2) those aged 65–89 years at the time of examination and consultation; (3) those who had CDR scores of 0.5 or 1; (4) those who had no serious limitation in basic ADL [Barthel Index (BI) score ≥ 80]; and (5) those who completed CDR, MMSE, and LI assessments. At the Memory Clinic of the NCGG, approximately 1,000 patients visit for their first examination annually, and they are subsequently followed up as needed. MMSE, CDR, LI, and other assessments are performed at the time of the visit.

To verify its external validity, the study included patients who met the following criteria: (1) those registered with the Organized Registration for the Assessment of dementia on Nationwide General consortium toward Effective treatment in Japan (ORANGE Registry)[23] between July 2015 and March 2022; (2) those not registered with the NCGG; (3) those aged 65–89 years at registration; (4) those who had CDR scores of 0.5 or 1; (5) those who had no serious limitation in basic ADLs (BI score ≥ 80); and (6) those who had completed CDR, MMSE, and LI assessments. The ORANGE Registry is a clinical registry that has registered outpatients with MCI or early-stage dementia at 30 medical institutions nationwide since July 2015, and the medical information (including age, sex, years of education, ADL, and cognitive function) of more than 2,000 patients is currently registered.

This study was approved by the Ethics Committee of Human Research at NCGG, Japan (No. 1611). Patients were given the option to be excluded from the study using the opt-out approach.

Measurements

All patients underwent CDR, MMSE, LI, and BI assessments by trained clinical psychologists.

Clinical Dementia Rating Scale. MCI and mild dementia were defined employing the CDR as an international

standard for classifying dementia stage.[13] The CDR evaluates the patient's severity of impairment in 6 domains (memory, orientation, judgment and problem-solving, community affairs, home and hobbies, and personal care) and integrates such domains into 1 overall category of severity ranging from 0 to 3 (0 = no cognitive impairment; 0.5 = questionable dementia; 1 = mild dementia; 2 = moderate dementia; and 3 = severe dementia).[14] The CDR possesses good interrater and test-retest reliabilities[24,25] and has been validated against neuropathologic findings.[26–28]

Mini-Mental State Examination. The MMSE was developed to assess global cognitive function[15] and utilizes scores ranging from 0 to 30, with higher scores indicating better cognitive function.

Lawton Index. The LI is used to assess individuals' independence in IADL[29] in 8 domains, each of which scored 0 (dependent) or 1 (independent). Participants were assessed for IADL by their primary caregivers (eg, a family member living with the patient). Three items (preparing food, housecleaning, and laundry) were excluded when calculating total LI scores in men[29,30]; thus, the total scores ranged from 0 to 5 in men and 0 to 8 in women, with higher scores indicating greater independence in IADL. The LI possesses good interrater reliability.[30]

Other variables. Demographic variables including age, sex, and years of education were also assessed. The participants were assessed for their ability to perform basic ADL using the BI,[31] which consists of 10 items to assess the ability to perform basic self-care, with a total score ranging from 0 (complete dependence) to 100 (complete independence).

Statistical Analysis

To describe the characteristics of the participants in the NCGG and ORANGE Registries, the means ± SDs were calculated for their age, years of education, and MMSE, BI, and LI scores. A *t* test was conducted to compare the characteristics of participants with CDR scores ranging between 0.5 and 1. In addition, the *t* test and χ^2 test were performed to compare the characteristics of participants from the NCGG and ORANGE Registries and to compare the sex difference in the characteristics of participants from the ORANGE Registry.

To verify the optimal cutoff values, we initially created a 2 × 2 cross-tabulation table using the MMSE score and the combination of MMSE and LI scores as cutoff values in the range of MMSE scores between 21 and 27; this range was set as an MMSE score <24 is the cutoff to detect dementia.[15,17] Sensitivity, specificity, accuracy, positive predictive value (PPV), negative predictive value (NPV), and Youden Index (YI) were calculated for each cross-tabulation table. Optimal cutoff values were defined as the cutoff value with highest YI of those with a sensitivity greater than their specificity. In the development of a diagnostic tool, selecting statistically valid cutoff values is important after fulfilling its requirements for clinical use.[32] As the cutoff values validated in this study were assumed to detect the transition from a CDR score of 0.5–1 in clinical settings, priority was given to ensure a higher sensitivity over a higher specificity for determining cutoff values.

To verify internal validity, stratified 5-fold cross-validation (stratified 5CV) was employed. A k-fold cross-validation is a standard method for estimating the performance of cutoff values and can provide more reliable results than other validation datasets.[33,34] In the stratified 5CV, the entire dataset was divided into 5 folds with the same proportion of CDR scores of 0.5 and 1, and 5 datasets were created with no duplication in the training data (Figure 1). The stratified 5CV involved 2 steps: training and testing. In the training step, the optimal cutoff values in the training data were determined using cross-tabulation tables, the same method employed to determine the optimal cutoff values. In the testing step, the parameters (sensitivity, specificity, accuracy, PPV, and NPV) were calculated using the determined cutoff values. This process was performed on 5 datasets, with the mean ± SD calculated for each parameter. In the present study, we verified the internal validity by using the MMSE scores alone and by using the combined MMSE/LI scores.

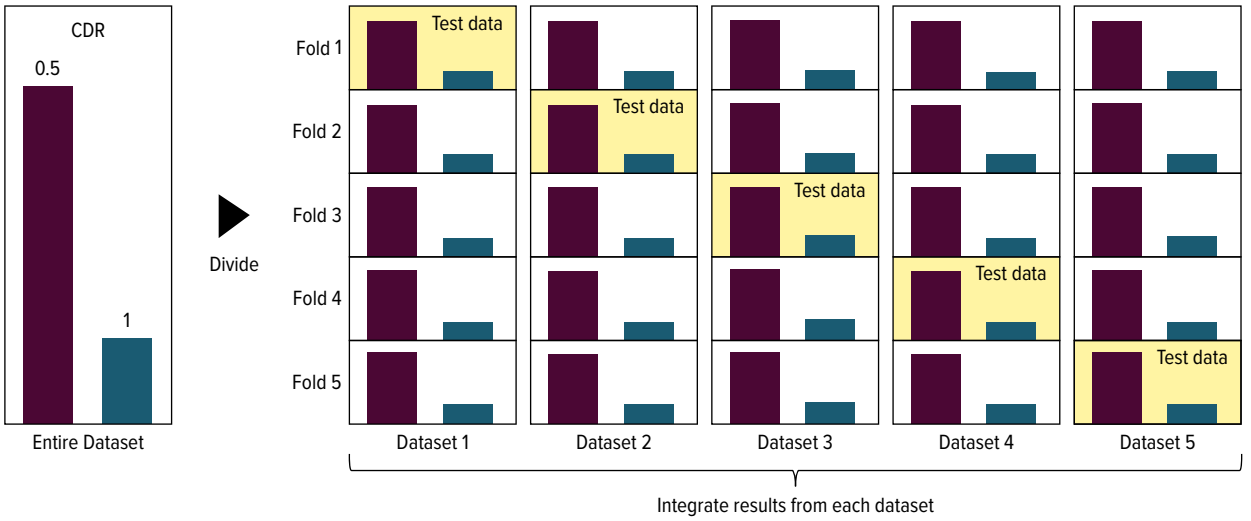
To verify external validity, the parameters (sensitivity, specificity, accuracy, PPV, and NPV) were calculated for the ORANGE Registry datasets using the optimal cutoff values obtained for the NCGG datasets. In the present study, we verified their external validity by using the MMSE scores alone and by using the combined MMSE/LI scores.

Furthermore, to confirm the accuracy of the cutoff value drawing on the combined MMSE/LI scores, the following method was used for sensitivity analysis: calculating composite scores drawing on a logistic regression model (LRM). Thus, this study also calculated the parameters (sensitivity, specificity, accuracy, PPV, and NPV) for the composite scores by LRM in the NCGG dataset and compared the discrimination performances of the 2 methods. Composite scores were calculated using the following formula (1):

$$\text{Composite score} = \beta 1 \times \text{MMSE score} + \beta 2 \times \text{LI score}. \quad (1)$$

Coefficients were calculated for MMSE (coefficients β1) and LI (coefficients β2) in an LRM with the CDR score as a dependent variable and the MMSE and LI scores as independent variables. The parameters were calculated by the stratified 5CV. The optimal cutoff values in the training data were evaluated using receiver operating characteristic curve analysis, and the parameters were calculated for the test data using the optimal cutoff values

Figure 1.
Stratified 5-Fold Cross-Validation[a]



[a]Blue bars indicate the proportion of a CDR score of 0.5, and red bars indicate the proportion of a CDR score of 1. The entire dataset was divided into 5 folds with the same proportion of CDR scores 0.5 and 1, and 5 datasets were created with no duplications in the training data. The optimal cutoff score was determined in 4 of the 5 folds (training data), and the parameters (sensitivity, specificity, accuracy, PPV, and NPV) were calculated in the other one (test data) using optimal cutoff score. This is performed for all 5 datasets, and the mean and SD of the parameters were calculated.
Abbreviations: CDR = Clinical Dementia Rating, NPV = negative predictive value, PPV = positive predictive value.

Table 1.
Characteristics of the Participants[a]

		Men (n = 401)			Women (n = 399)		
NCGG Registry participants	All participants (n = 800)	CDR score, 0.5 (n = 362)	CDR score, 1 (n = 39)	*P* value	CDR score, 0.5 (n = 329)	CDR score, 1 (n = 70)	*P* value
Age	77.53 ± 4.59	77.20 ± 4.63	76.67 ± 5.61	.689	77.71 ± 4.42	78.84 ± 4.27	.031
Years of education	11.44 ± 2.46	12.11 ± 2.79	11.82 ± 2.29	.462	10.84 ± 1.98	10.53 ± 1.70	.177
BI	98.75 ± 3.44	99.02 ± 2.75	95.13 ± 5.90	<.001	99.13 ± 3.06	97.57 ± 4.87	.012
MMSE	23.70 ± 4.34	25.16 ± 3.77	18.64 ± 4.04	<.001	23.68 ± 3.86	19.00 ± 4.00	<.001
LI in men	4.18 ± 1.08	4.35 ± 0.93	2.62 ± 1.11	<.001	-	-	-
LI in women	6.75 ± 1.41	-	-	-	7.06 ± 1.21	5.27 ± 1.34	<.001
		Men (n = 642)			Women (n = 852)		
ORANGE Registry participants	All participants (n = 1,494)	CDR score, 0.5 (n = 572)	CDR score, 1 (n = 70)	*P* value	CDR score, 0.5 (n = 691)	CDR score, 1 (n = 161)	*P* value
Age	77.97 ± 4.65	77.75 ± 4.64	79.10 ± 4.94	.033	77.89 ± 4.71	78.64 ± 4.19	.046
Years of education	12.21 ± 2.61	13.31 ± 2.87	12.17 ± 2.65	.019	11.56 ± 2.16	11.15 ± 1.93	.020
BI	98.66 ± 3.49	99.04 ± 2.81	96.50 ± 4.92	<.001	98.92 ± 3.17	97.17 ± 5.15	<.001
MMSE	24.53 ± 3.56	25.58 ± 3.09	21.41 ± 3.17	<.001	24.79 ± 3.23	21.03 ± 3.77	<.001
LI in men	4.06 ± 1.03	4.06 ± 1.03	2.79 ± 1.10	<.001	-	-	-
LI in women	6.62 ± 1.56	-	-	-	6.99 ± 1.28	5.07 ± 1.64	<.001

[a]Data were expressed as mean ± SD.
Abbreviations: BI = Barthel Index, CDR = Clinical Dementia Rating, LI = Lawton Index, MMSE = Mini-Mental State Examination, NCGG = National Center for Geriatrics and Gerontology, ORANGE = Organized Registration for the Assessment of dementia on Nationwide General consortium toward Effective treatment.

determined for the training data. This process was performed on each of the 5 datasets, with the mean ± SD calculated for each parameter.

All analyses were performed separately for men and women, given that the sum of the LI scores differed by sex.[29] The level of statistical significance was set at $P < .05$, and all analyses were conducted using R software (version 4.1.1 for Windows; R Foundation for Statistical Computing, Vienna, Austria).

Table 2.

Cutoff Values for CDR Scores 0.5 and 1 in Men[a]

MMSE	LI	Sensitivity	Specificity	Accuracy	PPV	NPV	YI
<21	-	64.10	86.46	84.29	33.78	95.72	50.57
	<3	23.08	98.07	90.77	56.25	92.21	21.14
	<4	51.28	94.75	90.52	51.28	94.75	46.03
	<5	61.54	90.33	87.53	40.68	95.61	51.87
<22	-	71.79	82.04	81.05	30.11	96.43	53.84
	<3	28.21	97.51	90.77	55.00	92.65	25.72
	<4	58.97	92.82	89.53	46.94	95.45	51.79
	<5	69.23	87.02	85.29	36.49	96.33	56.25
<23	-	82.05	75.14	75.81	26.23	97.49	57.19
	<3	33.33	96.69	90.52	52.00	93.09	30.02
	<4	66.67	91.16	88.78	44.83	96.21	57.83
	<5	79.49	81.77	81.55	31.96	97.37	61.26
<24	-	89.74	68.51	70.57	23.49	98.41	58.25
	<3	35.90	95.86	90.02	48.28	93.28	31.75
	<4	74.36	88.95	87.53	42.03	96.99	63.31
	<5	87.18	77.62	78.55	29.57	98.25	64.80
<25	-	94.87	61.60	64.84	21.02	99.11	56.47
	<3	38.46	95.86	90.27	50.00	93.53	34.32
	<4	79.49	88.12	87.28	41.89	97.55	67.61
	<5	**92.31**	**75.41**	**77.06**	**28.80**	**98.91**	**67.72**
<26	-	100.00	52.76	57.36	18.57	100.00	52.76
	<3	41.03	95.86	90.52	51.61	93.78	36.88
	<4	82.05	86.46	86.03	39.51	97.81	68.52
	<5	94.87	72.10	74.31	26.81	99.24	66.97
<27	-	100.00	42.82	48.38	15.85	100.00	42.82
	<3	41.03	95.86	90.52	51.61	93.78	36.88
	<4	82.05	85.36	85.04	37.65	97.78	67.41
	<5	94.87	68.51	71.07	24.50	99.20	63.38
<28	-	100.00	35.08	41.40	14.23	100.00	35.08
	<3	41.03	95.86	90.52	51.61	93.78	36.88
	<4	82.05	84.81	84.54	36.78	97.77	66.86
	<5	94.87	65.47	68.33	22.84	99.16	60.34

[a]Cutoff values in bold indicate optimal cutoff values using the combined MMSE/LI scores. Optimal cutoff values were defined as the cutoff value with highest YI of those with a sensitivity greater than their specificity.

Abbreviations: CDR = Clinical Dementia Rating, LI = Lawton Index, MMSE = Mini-Mental State Examination, NPV = negative predictive value, PPV = positive predictive value, YI = Youden Index.

Table 3.

Cutoff Values for CDR Scores 0.5 and 1 in Women[a]

MMSE	LI	Sensitivity	Specificity	Accuracy	PPV	NPV	YI
<21	-	60.00	77.20	74.19	35.90	90.07	37.20
	<6	30.00	94.83	83.46	55.26	86.43	24.83
	<7	44.29	90.27	82.21	49.21	88.39	34.56
	<8	57.14	86.63	81.45	47.62	90.48	43.77
<22	-	78.57	69.30	70.93	35.26	93.83	47.87
	<6	41.43	94.22	84.96	60.42	88.32	35.65
	<7	57.14	87.54	82.21	49.38	90.57	44.68
	<8	74.29	80.85	79.70	45.22	93.66	55.14
<23	-	85.71	59.88	64.41	31.25	95.17	45.59
	<6	48.57	92.71	84.96	58.62	89.44	41.28
	<7	64.29	84.50	80.95	46.88	91.75	48.78
	<8	81.43	74.47	75.69	40.43	94.96	55.90
<24	-	88.57	53.19	59.40	28.70	95.63	41.76
	<6	51.43	91.79	84.71	57.14	89.88	43.22
	<7	67.14	82.37	79.70	44.76	92.18	49.51
	<8	84.29	71.12	73.43	38.31	95.51	55.41
<25	-	95.71	42.55	51.88	26.17	97.90	38.27
	<6	58.57	90.58	84.96	56.94	91.13	49.15
	<7	74.29	79.03	78.20	42.98	93.53	53.31
	<8	**91.43**	**65.96**	**70.43**	**36.36**	**97.31**	**57.39**
<26	-	98.57	33.74	45.11	24.04	99.11	32.31
	<6	60.00	89.97	84.71	56.00	91.36	49.97
	<7	75.71	77.20	76.94	41.41	93.73	52.92
	<8	94.29	62.31	67.92	34.74	98.09	56.60
<27	-	98.57	26.44	39.10	22.19	98.86	25.02
	<6	60.00	89.36	84.21	54.55	91.30	49.36
	<7	75.71	75.68	75.69	39.85	93.61	51.40
	<8	94.29	59.57	65.66	33.17	98.00	53.86
<28	-	98.57	20.06	33.83	20.78	98.51	18.63
	<6	60.00	89.06	83.96	53.85	91.28	49.06
	<7	75.71	73.56	73.93	37.86	93.44	49.27
	<8	94.29	56.84	63.41	31.73	97.91	51.12

[a]Cutoff values in bold indicate optimal cutoff values using the combined MMSE/LI scores. Optimal cutoff values defined as the cutoff value with highest YI of those with a sensitivity greater than their specificity.

Abbreviations: CDR = Clinical Dementia Rating, LI = Lawton Index, MMSE = Mini-Mental State Examination, NPV = negative predictive value, PPV = positive predictive value, YI = Youden Index.

RESULTS

Characteristics of the Participants

Table 1 shows the characteristics of the participants from the NCGG and ORANGE Registries. The 800 participants from the NCGG Registry had a mean age of 77.53 ± 4.59 years (men, 401; 50.1%) and a mean MMSE score of 23.70 ± 4.34. Patients with a CDR score of 1 had lower BI, LI, and MMSE scores than those with a CDR score of 0.5. The 1,494 participants from the ORANGE Registry had a mean age of 77.97 ± 4.65 years (men, 642; 43.3%) and a mean MMSE score of 24.53 ± 3.56. Those with a CDR score of 1 were older, had fewer years of education, and had lower BI, LI, and MMSE scores than those with a CDR score of 0.5.

Supplementary Table 1 shows a comparison of the participant characteristics between the NCGG Registry and the ORANGE Registry. The participants from the ORANGE Registry had more years of education and higher MMSE scores than those from the NCGG Registry. No significant differences were found in other characteristics such as age and CDR, BI, and LI scores.

Supplementary Table 2 shows a comparison of the characteristics of men and women in the ORANGE Registry. The men had more years of education, higher MMSE scores, and a lower percentage of CDR score of 1 than the women.

Optimal Cutoff Values in Men and Women

Tables 2 and 3 show the parameters for each cutoff value obtained with the MMSE scores alone and with the combined MMSE/LI scores. For men, the optimal cutoff value obtained with the MMSE scores alone was MMSE < 24, and those with the combined MMSE/LI scores were MMSE < 25 and LI < 5. For women, the optimal cutoff value obtained with the MMSE scores

Table 4.
The Results of Verifying Internal Validity and External Validity[a]

	Sensitivity	Specificity	Accuracy	PPV	NPV
Internal validity					
Men					
MMSE	84.02 ± 16.26	69.02 ± 3.88	70.57 ± 2.56	22.33 ± 4.56	97.78 ± 2.10
MMSE and LI	92.50 ± 15.00	73.52 ± 3.88	75.31 ± 3.04	27.26 ± 6.87	99.02 ± 1.97
Women					
MMSE	78.57 ± 6.39	66.56 ± 9.84	68.67 ± 7.33	34.29 ± 4.70	93.68 ± 1.24
MMSE and LI	88.57 ± 3.50	65.65 ± 6.96	69.67 ± 5.34	36.11 ± 5.06	96.47 ± 0.91
External validity					
Men					
MMSE	78.57	74.83	75.23	27.64	96.61
MMSE and LI	81.43	77.62	78.04	30.81	97.16
Women					
MMSE	54.66	83.50	72.05	43.56	88.77
MMSE and LI	77.64	74.67	75.23	41.67	93.48

[a]Data were expressed as mean ± SD.
Abbreviations: LI = Lawton Index, MMSE = Mini-Mental State Examination, NPV = negative predictive value, PPV = positive predictive value.

alone was MMSE < 22, and those with the combined MMSE/LI scores were MMSE < 25 and LI < 8.

Verifying Internal and External Validities

Table 4 shows the results demonstrating the internal and external validities. Upon verification of the internal validity for both sexes, the use of combined MMSE/LI scores showed good discriminative performance, which was better than the one obtained with the use of MMSE scores alone [(sensitivity/specificity): men, combined MMSE/LI = (92.50 ± 15.00/73.52 ± 3.88) and MMSE alone = (84.02 ± 16.26/69.02 ± 3.88); women, combined MMSE/LI = (88.57 ± 3.50/65.65 ± 6.96) and MMSE alone = (78.57 ± 6.39/66.56 ± 9.84)].

To verify the external validity, the optimal combined MMSE/LI cutoff values obtained from the NCGG participants showed good discriminative performance in both sexes, as well as in the participants from the ORANGE Registry. Furthermore, the combined MMSE/LI cutoff values possessed a better discriminative performance than the MMSE alone cutoff values [men: combined MMSE/LI = (81.43/77.62) and MMSE alone = (78.57/74.83); women: combined MMSE/LI = (77.64/74.67) and MMSE alone = (54.66/83.50)].

Discrimination Performance of Composite Scores Drawing on a Logistic Regression Model and Cutoff Value Drawing on Combined MMSE/LI Scores

Supplementary Table 3 shows the discrimination performance when drawing on the LRM and combined MMSE/LI scores. The cutoff value drawing on the combined MMSE/LI scores was inferior in specificity but comparable in sensitivity to that drawing on an LRM for both men and women.

DISCUSSION

This study developed a tool to discriminate between CDR scores of 0.5 and 1 using combined MMSE/LI scores and investigated its optimal cutoff value and internal and external validities. Our results showed that combining the MMSE and LI scores had good discriminative performance in identifying CDR scores of 0.5 and 1, and its discrimination performance was better than when using MMSE alone. Furthermore, the following cutoff values were deemed optimal: MMSE < 25/LI < 5 for men and MMSE < 25/LI < 8 for women.

To the best of our knowledge, this is the first study to propose a tool and validate its cutoff values for discriminating the boundary between CDR scores of 0.5 and 1 using scales assessing cognitive function and IADL. Information regarding the presence of ADL impairment is essential for distinguishing MCI from mild dementia[20]; however, the accurate distinction based solely on the assessment of cognitive function is difficult. The cutoff values obtained in this study may be a simple and accurate tool that helps discriminate the borderline between CDR scores of 0.5 and 1, which are currently difficult to determine in clinical practice.

Although most screening tools focus solely on cognitive function, the Dementia Assessment Sheet for Community-based Integrated Care System 21-items (DASC-21) is a tool available for dementia screening that involves assessments of both cognitive and daily functions. The DASC-21 reportedly has sufficient

discriminative ability to distinguish between dementia (CDR 1≤) and nondementia (CDR 0 or 0.5; area under the curve = 0.804–0.895).[35] However, the DASC-21 is an instrument for detecting the presence of dementia, and its usefulness for discriminating between CDR scores of 0.5 and 1 and external validity remain unknown. The tool developed in this study has been externally validated in clinic-based patients and shown to have a good discriminative ability. The ORANGE Registry used for external validation in this study represents the largest MCI registry in Japan, enrolling patients from approximately 30 medical institutions,[23] suggesting that this tool should be generalizable to specialized clinical settings such as memory clinics where clinical psychologists are enrolled.

Other tools to assess both cognitive and daily functions include the Functional Assessment Staging of Alzheimer Disease (FAST)[36] and the Relevant Outcome Scale for Alzheimer Disease (ROSA).[37] Although the FAST is widely used to assess the progression of Alzheimer disease (AD), no cutoff value is available to accurately detect the boundary between CDR scores of 0.5 and 1. The ROSA is a tool available to assess the severity of AD; however, its ability to discriminate between CDR scores of 0.5 and 1 must still be validated. In this study, the cutoff values discriminating between CDR scores of 0.5 and 1 were calculated. Therefore, the use of the developed tool is not limited to any specific type of dementia and should be available for use in specialized clinical settings.

While measuring the external validity of the ORANGE Registry, the accuracy of the combined cutoff score was 78.04 for men and 75.23 for women. Although it has higher accuracy than the cutoff score of MMSE only, these accuracy levels are slightly below the desirable range. Further research is essential for an accurate and simple tool to distinguish the borderline between CDR scores of 0.5 and 1. In addition, there was a slight sex-related difference in accuracy. This might be caused by differences between men and women in characteristics, such as age and cognitive function, and evaluation item.

For the tool developed in this study, the MMSE < 25/LI < 5 and the MMSE < 25/LI < 8 were proposed as the optimal cutoff values for discriminating CDR scores of 0.5 and 1 in men and women, respectively. Without complex calculations, the developed cutoff values are obtained by simply combining the scores of the 2 measures in clinical settings. Additionally, the MMSE and LI are relatively easy to assess, and our tool could be available for dementia screening in primary care and nursing home settings, even in settings without specialized medical care for dementia. Another potential use could be its utilization as selection criteria in clinical research and trials.

The present study had some limitations. It included participants with a BI score ≥80, and the developed cutoff values were not applicable to older adults with more severe physical illnesses and an obvious decline in basic ADL. A comprehensive evaluation, including other assessments in addition to MMSE and LI, would be necessary for this population.

CONCLUSION

This study showed that combined MMSE/LI scores may be useful in discriminating between CDR scores of 0.5 and 1 in special clinical settings. The cutoff values developed should be applicable to various settings, such as memory clinics where clinical psychologists are enrolled and clinical research.

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Supplementary Material

Article Title: A Combined Index Using the Mini-Mental State Examination and Lawton Index to Discriminate Between Clinical Dementia Rating Scores of 0.5 and 1: A Development and Validation Study

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LIST OF SUPPLEMENTARY MATERIAL FOR THE ARTICLE

DISCLAIMER

Supplementary Table 1. Comparison of the characteristics of participants from the NCGG and the ORANGE Registry [a]

	Men			Women		
	NCGG (n = 401)	ORANGE Registry (n = 642)	*P* value	NCGG (n = 399)	ORANGE Registry (n = 852)	*P* value
Age	77.15 ± 4.73	77.30 ± 4.69	0.745	77.91 ± 4.41	78.03 ± 4.63	0.657
Years of education	12.08 ± 2.75	13.18 ± 2.87	< 0.001	10.79 ± 1.93	11.48 ± 2.12	< 0.001
CDR score			0.617			0.619
0.5	362 (90.27%)	572 (89.10%)		329 (82.46%)	691 (81.10%)	
1	39 (9.73%)	70 (10.90%)		70 (17.54%)	161 (18.90%)	
BI score	98.64 ± 3.39	98.76 ± 3.21	0.568	98.86 ± 3.49	98.59 ± 3.69	0.214
MMSE score	24.53 ± 4.26	25.13 ± 3.36	0.017	22.86 ± 4.27	24.08 ± 3.65	< 0.001

LI score	4.18 ± 1.08	4.06 ± 1.03	0.093	6.75 ± 1.41	6.63 ± 1.55	0.186

[a] Data were expressed as mean ± SD and n (%).

Abbreviations: NCGG, the National Center for Geriatrics and Gerontology; SD, standard deviation; CDR, Clinical Dementia Rating; BI, Barthel Index; MMSE, Mini-Mental State Examination; LI, Lawton Index

Supplementary Table 2. Comparison of characteristics of men and women in the ORANGE Registry [a, b]

	Men (n = 642)	Women (n = 852)	*P* value
Age	77.30 ± 4.69	78.03 ± 4.63	0.584
Years of education	13.18 ± 2.87	11.48 ± 2.12	<0.001
CDR score			<0.001
0.5	572 (89.10%)	691 (81.10%)	
1	70 (10.90%)	161 (18.90%)	
BI score	98.76 ± 3.21	98.59 ± 3.69	0.831
MMSE score	25.13 ± 3.36	24.08 ± 3.65	<0.001

[a] Data were expressed as mean ± SD and n (%).

[b] The comparison results of LI were not included because the full score of LI is differed for men and women.

Abbreviations: SD, standard deviation; CDR, Clinical Dementia Rating; BI, Barthel Index; MMSE, Mini-Mental State Examination; LI, Lawton Index

Supplementary Table 3. Discrimination performance of composite scores drawing on a logistic regression model and cut-off value drawing on combined MMSE/LI scores [a]

	Sensitivity	Specificity	Accuracy	PPV	NPV
Men					
composite scores drawing on a logistic regression model	92.82 ± 6.09	83.43 ± 2.69	84.29 ± 2.59	37.65 ± 6.62	99.01 ± 0.81
cut-off value drawing on combined MMSE/LI scores	92.50 ± 15.00	73.52 ± 3.88	75.31 ± 3.04	27.26 ± 6.87	99.02 ± 1.97
Women					
composite scores drawing on a logistic regression model	87.14 ± 10.50	75.08 ± 5.19	77.19 ± 3.50	43.04 ± 4.20	96.65 ± 2.66
cut-off value drawing on combined MMSE/LI scores	88.57 ± 3.50	65.65 ± 6.96	69.67 ± 5.34	36.11 ± 5.06	96.47 ± 0.91

[a] Data were expressed as mean ± SD.

Abbreviations: SD, standard deviation; MMSE, Mini-Mental State Examination; LI, Lawton Index; PPV, positive predictive value; NPV, negative predictive value