

Original Article



Cognitive Impairment Screening Test in Korea as a Screening Tool for Dementia: The Correlation Study of Subtest Scores With Korean Version of the Mini Mental State Examination 2nd Edition

Minseong Kim ,¹ Doyun Heo ,¹ Seonkyeong Kim ,¹ Yunjin Lee ,¹
Yong Sung Kim ,² Wonjae Sung ,² Hee-Jin Kim ²

¹Department of Neurology, College of Medicine, Hanyang University, Seoul, Korea

²Department of Neurology, Hanyang University Seoul Hospital, College of Medicine, Hanyang University, Seoul, Korea



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Correspondence to

Hee-Jin Kim

Department of Neurology, Hanyang University
Seoul Hospital, College of Medicine, Hanyang
University, 222 Wangsimni-ro, Seongdong-gu,
Seoul 04763, Korea.

Email: hyumcbrain@hanyang.ac.kr

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cited.

ORCID iDs

Minseong Kim

<https://orcid.org/0009-0003-6867-6373>

Doyun Heo

<https://orcid.org/0009-0002-8532-0451>

Seonkyeong Kim

<https://orcid.org/0009-0008-6308-2337>

Yunjin Lee

<https://orcid.org/0009-0009-3665-3269>

Yong Sung Kim

<https://orcid.org/0000-0002-6062-0821>

ABSTRACT

Background and Purpose: The Cognitive Impairment Screening Test in Korea (CIST-K) was designed to detect cognitive decline. Developed independently and widely used in Korea, it is yet to be validated with other screening tests. This study aimed to introduce normative data to the CIST-K and assess its clinical usefulness through correlation analysis with the Korean version of the Mini-Mental State Examination, 2nd edition (K-MMSE-2).

Methods: We enrolled 85 participants from a tertiary university hospital in Korea, including patients diagnosed with mild cognitive impairment and Alzheimer's disease by experienced neurologists. Both the CIST-K and K-MMSE-2 were administered to assess the cognitive function of the participants, with scores from each subtest of the neuropsychological tests compared.

Results: Multivariate correlation analysis, which was adjusted for age, sex, and education level, revealed a significant correlation between the two tests in orientation, memory, and attention. However, no significant correlation was found between the two tests in visuospatial and language functions.

Conclusions: In conclusion, this study demonstrates that some subtests in the CIST-K align with corresponding scores on the K-MMSE-2. However, caution is advised when interpreting visuospatial and language test scores from the CIST-K. Further validity studies are necessary to enhance the sensitivity of each subtest.

Keywords: Cognitive Impairment Screening Test in Korea; Cognitive Assessment Screening Instrument; Korean Version of the Mini Mental State Examination 2nd Edition

INTRODUCTION

Humans' prolonged life expectancy has led to an increase in the prevalence of dementia.¹ Although fatalities due to cardiovascular diseases have declined, the number of deaths caused by Alzheimer's disease (AD) has surged by approximately 1.5 times since 2000. Therefore,

Wonjae Sung 
<https://orcid.org/0000-0002-4637-5890>
 Hee-Jin Kim 
<https://orcid.org/0000-0001-7880-690X>

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Conflict of Interest

The authors have no potential conflicts of interest.

Author Contributions

Conceptualization: Kim YS, Sung WJ, Kim HJ; Data curation: Kim MS, Heo DY, Lee YJ, Kim SK, Kim HJ; Formal analysis: Kim MS; Methodology: Kim MS, Heo DY, Kim HJ; Project administration: Kim YS, Sung WJ, Kim HJ; Resources: Kim MS, Heo DY, Kim HJ; Supervision: Kim HJ; Writing - original draft: Kim MS; Writing - review & editing: Kim MS, Heo DY, Lee YJ, Kim SK, Kim YS, Sung WJ, Kim HJ.

highlighting the significance of early dementia diagnosis is crucial.² Therefore, early detection of individuals with dementia is essential for implementing effective prevention and timely interventions to diminish the impact of AD on patients.

Cognitive function tests are mainly used clinically to measure the progression of cognitive decline in neurodegenerative disorders such as dementia. Neuropsychological testing assesses the presence and severity of dementia, assigns differential diagnoses, and monitors disease progression and drug effects in patients with dementia.³ The test items include orientation, memory, attention, execution, language, and visuospatial functions.⁴ The Korean version of the Mini-Mental State Examination 2nd edition (K-MMSE-2)⁵ has mainly been used in Korea as a screening tool; however, a new screening test has been developed by the Ministry of Health and Welfare, the Cognitive Impairment Screening Test in Korea (CIST-K), which reflects the current situation of the country.⁶

Since repeated use of the same test tool on a single patient reduces accuracy, multiple test tools have been employed instead.⁷ To validate changes in a patient's condition, the outcomes of different tests must be compared. However, only a few studies have delved into the correlation between these tests. Additionally, although a previous comparative study between the K-MMSE-2 and CIST-K has been conducted, it focused solely on stroke patients, which limited the scope of the study.⁸ Therefore, we conducted a study on the relationship between these two tests in assessing patients with AD.

Our study initially aimed to introduce the degree of distribution of test scores. Subsequently, we investigated its clinical relevance in distinguishing patients with mild cognitive impairment (MCI) or AD from those cognitively unimpaired (CU).

METHODS

Participant enrollments

We collected data from the medical records of the neurology department at a tertiary university hospital from January 1, 2022, to September 1, 2023. The dataset comprised 371 patients who underwent K-MMSE-2 testing. Among these patients, 160 were selected based on the criterion that the CIST-K could be performed within one year from the last K-MMSE-2 test. The following exclusion criteria were applied to the 160 participants: 1) patients experiencing a rapid decline in cognitive function⁹, as assessed by K-MMSE-2⁵; 2) patients with a Clinical Dementia Rating (CDR)¹⁰ score of 2 or higher; and 3) patients who refused to participate in the test. After applying these exclusion criteria, 85 participants were included in the final analysis. Participants were categorized as follows: clinically probable AD patients based on the National Institute of Neurological and Communicative Diseases and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS-ADRDA) criteria¹¹ and patients with MCI according to Petersen et al.'s¹² criteria. The CU group included both healthy individuals and those with subjective cognitive decline (SCD) as recommended by Molinuevo et al.¹³ Finally, 14 patients were assigned to the CU group, 54 to the MCI group, and 17 to the AD group (Fig. 1).

CIST-K

The CIST-K was developed by the Ministry of Health and Welfare to address issues on the prolonged and repeated use of neuropsychological tests. The test reflects the current

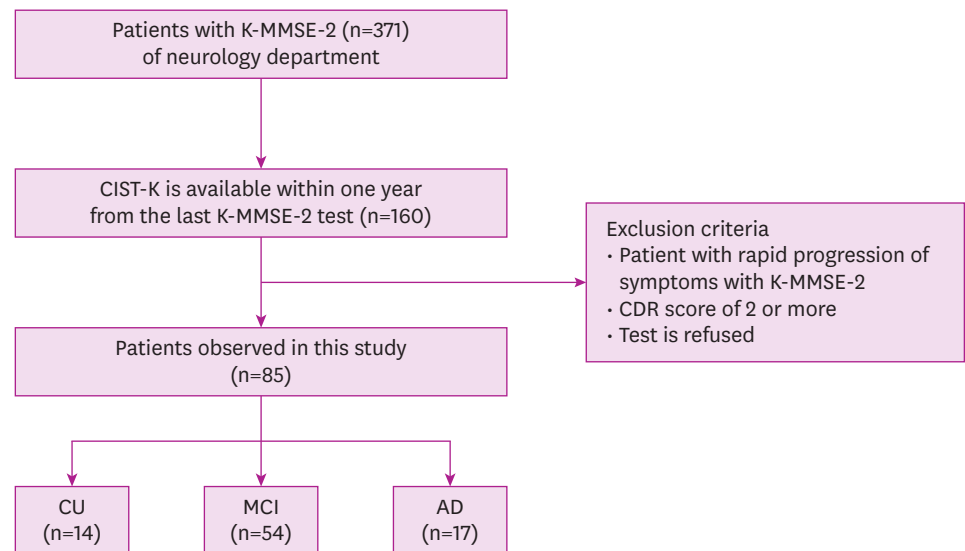


Fig. 1. Participant selection: a total of 371 patients who underwent K-MMSE-2 testing were enrolled from the neurology department's historical patient records at a tertiary university hospital. From these, 160 patients who could undergo CIST-K testing within one year after their last K-MMSE-2 test were selected. Ultimately, 85 patients were included in the study, excluding cases where symptoms progressed rapidly, the CDR score was 2 or higher, or the test was refused. We categorized the participants into three groups: CU, MCI, and AD. K-MMSE-2: Korean version of the Mini-Mental State Examination 2nd edition, CIST-K: Cognitive Impairment Screening Test in Korea, CDR: Clinical Dementia Rating, CU: cognitively unimpaired, MCI: mild cognitive impairment, AD: Alzheimer's disease.

situation in South Korea and provides solutions to overcome existing problems, which allows for the efficient screening of cognitive impairment within a relatively short timeframe. The CIST-K is conducted in a question-and-answer format involving both the participant and the examiner. It comprises 13 items across 6 domains (memory, attention, visuospatial function, executive function, orientation, and language). The total score is calculated by summing the scores of each item, with a minimum score of 0 and a maximum score of 30. The interpretation of the results includes an individual's sex, age, and education.⁶ The form of the examination paper is presented in **Supplementary Data 1**.

K-MMSE-2

The K-MMSE-2⁵ is a standardized Korean version of the Mini-Mental State Examination (MMSE) developed by Folstein et al.¹⁴ It is a convenient tool used for screening cognitive impairment. K-MMSE-2 included abbreviated, standard, and expanded versions. This study used a standard version consisting of 11 items across 7 domains (memory registration, attention and calculation, recall, language, drawing, time orientation, and place orientation). The total score is the sum of the scores for each item, with a minimum score of 0 and a maximum score of 30. The results were interpreted by comparing the total score to the expected level based on the individual's sex, age, and educational background. The reliability of the K-MMSE-2 standard version was reported with a test-retest reliability of 0.69 and an inter-rater reliability of 0.99.⁵

Statistical analysis

To identify the distribution of scores on the individual tests, we conducted a frequency analysis. In the validation study, Kruskal-Wallis and Pearson's χ^2 test were used to analyze the demographic characteristics and test scores of the three patient groups. We conducted

receiver operating characteristic (ROC) curve analyses and determined the sensitivity and specificity of the CIST-K to confirm its ability to differentiate patients with MCI and AD from those who are CU. Concurrent validity was assessed using a partial correlation analysis with the Spearman method between the CIST-K individual test scores and the subtests of the K-MMSE-2 described above, considering age, sex, and educational level as confounding factors. Statistical analyses were carried out using R Statistical software (version 3.1.2, R Foundation for Statistical Computing, Vienna, Austria), and differences were considered statistically significant at $p < 0.05$.

RESULTS

The baseline characteristics and total scores of the CIST-K and K-MMSE-2 tests for the study participants are presented in **Table 1**. 85 participants comprised 14 CU individuals, 54 patients with MCI, and 17 patients with AD. The Kruskal–Wallis test revealed significant age differences across the three groups, but not their years of education. In the *post-hoc* analysis, participants in the CU or MCI group were significantly younger than those in the AD group, while no significant difference was found between the CU and MCI groups. The Pearson's χ^2 test didn't show a significant difference in sex. The mean interval between the CIST-K and K-MMSE-2 tests was 166 days, with a standard deviation of 101 days and a median of 162 days. The mean CIST-K score was 22.02 ± 5.91 (CU, 26.36 ± 1.10 ; MCI, 22.81 ± 1.45 ; AD, 15.94 ± 2.41), and the mean score of the K-MMSE-2 was 26.06 ± 3.30 (CU, 27.29 ± 1.45 ; MCI, 26.74 ± 0.75 ; AD, 22.88 ± 1.89). A variance analysis revealed significant differences in the CIST-K score between the three groups. *Post-hoc* analysis revealed that both the CU and MCI groups scored significantly higher than the AD group, while there was no significant difference between the CU and MCI groups. A significant difference in the K-MMSE-2 was also observed. In *post-hoc* analysis, the CU and MCI groups scored higher than the AD group, and the MCI group performed comparably to the CU group. **Fig. 2** shows a box plot representing the distribution of the total CIST-K and K-MMSE-2 scores.

The CIST-K subtest scores of the different groups are shown in **Fig. 3** and **Table 2**. Tests on attention, visuospatial, and language function did not reveal any significant differences among the three groups; however, significant differences were found in the areas of orientation, execution, and memory. In the *post hoc* analysis for these items, the AD group scored the lowest compared to the MCI and CU groups, and no significant difference was found between the other two groups.

Table 1. Clinical and demographic data of participants

Variables	Group			p-value	Post hoc
	CU (n=14)	MCI (n=54)	AD (n=17)		
Age (yr)	69.50±5.04	72.15±2.12	78.82±2.38	0.001	CU=MCI<AD
Years of education	8.14±2.70	10.28±1.38	11.06±2.68	0.253	
Sex (male/female)	6/8	17/37	6/11	0.721	
K-MMSE-2	27.29±1.45	26.74±0.75	22.88±1.89	<0.001	CU=MCI>AD
CIST-K	26.36±1.10	22.81±1.45	15.94±2.41	<0.001	CU=MCI>AD

Sex data is the number of male/female. Compared with Pearson's χ^2 test.

Other data are means \pm SD. Compared with Kruskal–Wallis test.

Post hoc tests were performed using Bonferroni's method (<0.05).

CU: cognitively unimpaired, MCI: mild cognitive impairment, AD: Alzheimer's disease, K-MMSE-2: Korean-Mini Mental State Examination 2nd version, CIST-K: Cognivie Impairment Screening Test in Korea.

Comparison Study Between K-MMSE-2 and CIST-K

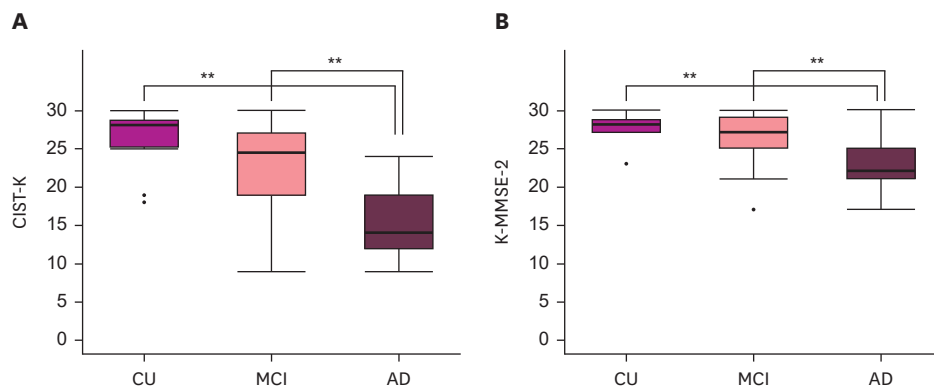


Fig. 2. Comparison of total scores of (A) CIST-K, (B) K-MMSE-2 in the AD, MCI, and CU groups using the Kruskal-Wallis test. AD patients had significantly lower score of each subtest than CU and MCI patients, and there was no significant difference between the MCI group and the CU group.

CIST-K: Cognitive Impairment Screening Test in Korea, K-MMSE-2: Korean version of the Mini-Mental State Examination 2nd edition, AD: Alzheimer's disease, CU: cognitively unimpaired, MCI: mild cognitive impairment.

* $p < 0.05$, ** $p < 0.01$.

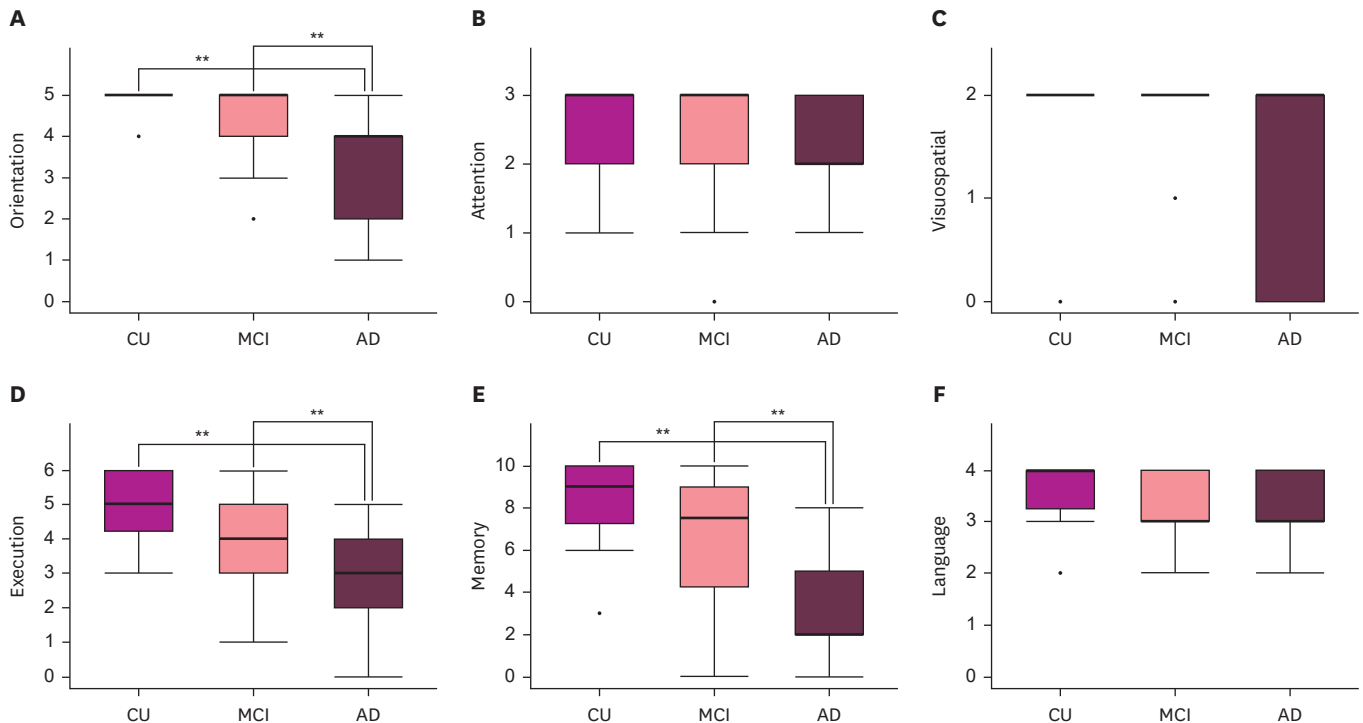


Fig. 3. Comparison of scores of each cognitive domain in CIST-K. (A) Orientation (B) attention (C) visuospatial function (D) execution (E) memory (F) language function in AD, MCI, and CU group using the Kruskal-Wallis test. (A, D, E) AD patients had significantly lower scores of each subtest than CU and MCI patients. There was no significant difference between the MCI group and the CU group. (B, C, F) There was no difference between the three groups in each subtest score.

CIST-K: Cognitive Impairment Screening Test in Korea, AD: Alzheimer's disease, CU: cognitively unimpaired, MCI: mild cognitive impairment.

* $p < 0.05$, ** $p < 0.01$.

We performed ROC curve analysis and calculated the area under the curve (AUC) to determine the power of the CIST-K score in differentiating the MCI and AD group from the CU group. The CIST-K had a sensitivity of 0.620 and a specificity of 0.857, with a cut-off total score of 24.5. The AUC of the CIST-K was 0.764, while the AUC value for the K-MMSE-2 was 0.621 (Fig. 4A). The AUC of the CIST-K total score for discriminating the MCI group from the CU group was 0.705, in contrast to the K-MMSE-2, which had an AUC value of 0.555. The CIST-K total score had a sensitivity of 0.796 and a specificity of 0.571 when a cut-off score of 27.5

Comparison Study Between K-MMSE-2 and CIST-K

Table 2. CIST-K subtest scores in the three groups

Variables	Group			p-value	Post hoc
	CU (n=14)	MCI (n=54)	AD (n=17)		
Orientation	4.86±0.11	4.50±0.22	3.35±0.68	<0.001	CU=MCI>AD
Attention	2.57±0.37	2.41±0.22	2.29±0.35	0.485	
Visuospatial	1.86±0.31	1.80±0.15	1.41±0.48	0.165	
Execution	5.00±0.55	4.17±0.38	2.65±0.81	<0.001	CU=MCI>AD
Memory	8.43±1.19	6.52±0.82	3.00±1.21	<0.001	CU=MCI>AD
Language	3.64±0.37	3.43±0.16	3.24±0.28	0.105	

Data are means ± SD. Compared with Kruskal-Wallis test.

Post hoc tests were performed using Bonferroni's method (<0.05).

CU: cognitively unimpaired, MCI: mild cognitive impairment, AD: Alzheimer's disease, K-MMSE-2: Korean-Mini Mental State Examination 2nd version, CIST-K: Cognitive Impairment Screening Test in Korea.

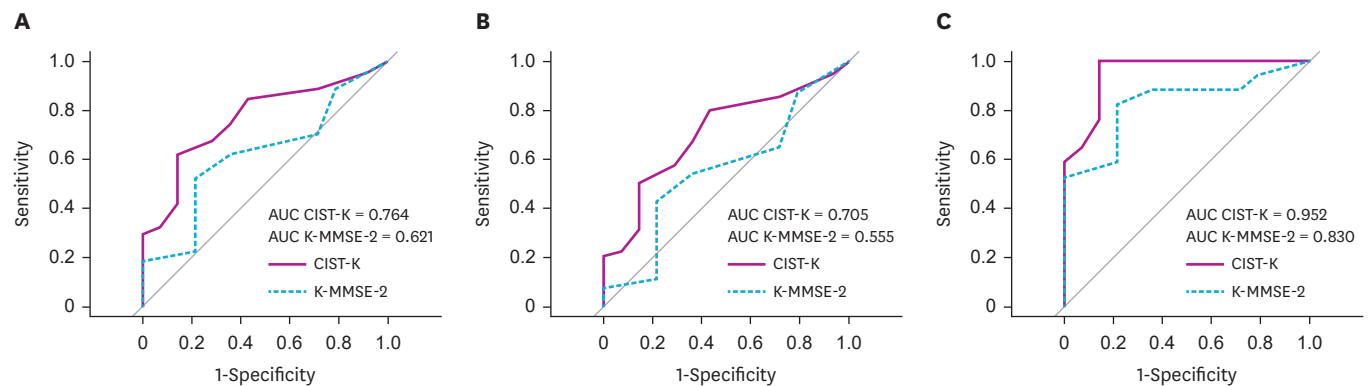


Fig. 4. ROC curves for the CIST-K and K-MMSE-2 total score. (A) When comparing the CU group and cognitively impaired group (MCI + AD), CIST-K showed an AUC value of 0.764, whereas K-MMSE demonstrated an AUC value of 0.621. (B) In the comparison between CU and MCI, CIST-K produced an AUC value of 0.705, while K-MMSE-2 showed an AUC value of 0.555. (C) When comparing the CU group and the AD group, the AUC value of CIST-K was 0.952. In contrast, K-MMSE-2 demonstrated an AUC value of 0.830.

ROC: receiver operating characteristic, CIST-K: Cognitive Impairment Screening Test in Korea, K-MMSE-2: Korean version of the Mini-Mental State Examination 2nd edition, CU: cognitively unimpaired, MCI: mild cognitive impairment, AD: Alzheimer's disease.

was applied (**Fig. 4B**). A cut-off score of 24.5 produced an AUC of 0.952 for the CIST-K total score when the AD group was compared with the CU group, with a sensitivity of 1.000 and a specificity of 0.857. The K-MMSE-2 had an AUC value of 0.830 (**Fig. 4C**).

To examine concurrent validity, a partial correlation analysis was conducted between the CIST-K and K-MMSE-2, with the results presented in **Table 3**. The correlations between the same cognitive function subtests without visuospatial and language functions were significant. The correlation coefficient was not significant at -0.027 and at 0.142 in visuospatial and language function, respectively. The orientation score of the CIST-K showed

Table 3. Correlations between CIST-K and K-MMSE-2's sub scores

Variables	K-MMSE-2						
	Time orientation	Spatial orientation	Memory recall	Attention calculation	Language	Visuospatial	Total
CIST-K							
Orientation	0.466**	0.370**	0.363**	0.175	0.191	0.079	0.438**
Attention	0.182	0.110	-0.078	0.326**	0.279**	0.022	0.194
Visuospatial	0.083	0.180	0.100	-0.026	-0.233**	-0.027	0.029
Execution	0.267**	0.126	0.366**	0.392**	0.054	0.069	0.420**
Memory	0.417**	0.279**	0.448**	0.139	0.234**	0.113	0.483**
Language	0.212	0.172	0.104	0.277**	0.142	-0.064	0.222**
Total	0.490**	0.314**	0.452**	0.310**	0.242**	0.095	0.559**

Test was conducted in partial correlation analysis with spearman method.

CIST-K: Cognitive Impairment Screening Test in Korea, K-MMSE-2: Korean-Mini Mental State Examination 2nd edition.

* $p < 0.05$; ** $p < 0.01$.

correlation coefficients of 0.466 for time and 0.370 for place with the K-MMSE-2. Memory has a correlation coefficient of 0.448, whereas attention has a correlation coefficient of 0.326. The correlation coefficient between the total scores of the two tests was the highest at 0.559.

DISCUSSION

This study introduced the distribution and characteristics of the data and investigated their reliability, validity, and correlation with the CIST-K test. The main results were as follows: ROC curve analysis showed significant sensitivity and specificity with cutoff values of 24.5, 27.5, and 24.5 for distinguishing MCI and AD from CU, MCI from CU, and AD from CU, respectively. When distinguishing between the CU and MCI groups, the CIST-K showed the largest difference in AUC values compared to the K-MMSE-2. This suggests that the CIST-K is quite sensitive in distinguishing between patients with MCI and CU individuals and is effective in screening tests in the early stages of neurodegenerative diseases. In the multivariate correlation analysis, which accounted for age, sex, and educational level, a notable correlation was observed between the two tests in the domains of orientation, memory, and attention. However, no significant correlation was found between the two tests in terms of visuospatial or language function.

Several correlation studies on CIST-K have been conducted.⁸ However, these studies did not include age, sex, and years of education as confounding factors and targeted only stroke patient groups. We selected groups according to the differences in cognitive function and investigated the correlations among confounding factors in the CU, MCI, and AD groups.

In the ROC analysis, the ability to distinguish between the CU and MCI groups was observed; however, a *post hoc* Kruskal-Wallis test revealed no significant difference in the CIST-K score between the two (**Fig. 2A**). Therefore, the test requires further modification to increase its ability to distinguish between the CU and MCI groups.

Although both subtest items assessed the same cognitive functions, the results showed a lower correlation coefficient due to differences in testing methods. In the K-MMSE-2, attention was evaluated through mental arithmetic, whereas in the CIST-K, participants were assessed based on their ability to repeat numbers provided by the examiner. Regarding executive function, the K-MMSE-2 did not include specific assessment items,⁵ whereas the CIST-K introduced a new measure, which revealed a significant difference in scores among the three groups. The visuospatial function was assessed in the CIST-K by presenting a figure composed of connected points, instructing participants to replicate it by connecting the points. For memory function, the K-MMSE-2 did not include a recognition test, while the CIST-K utilized a recognition test for items that were not recalled. Additionally, the K-MMSE-2 used unrelated words as memory stimuli, whereas the CIST-K employed a narrative format. Since narrative memory assessments evaluate not only memory retention but also attention and learning capabilities,³ it can be inferred that the primary focus of the K-MMSE-2 is on assessing memory function.

Most subtests analyzed in the CIST-K showed significant correlations with the corresponding items of the K-MMSE-2 after adjusting for age, sex, and education level. However, tests for visuospatial and language functions did not show any significant correlations. This may be attributed to the different difficulty levels of each task. As shown

in **Fig. 3**, Among 85 participants, 94.1% scored either 0 or 2 on the visuospatial test, and 95.3% scored either 3 or 4 on the language test. This indicates a concentration of scores at these specific points, suggesting that cognitive function is being assessed in a binary manner. Consequently, this makes it challenging to observe continuous changes in patients' cognitive function. To perform a naming test judging language function, a difference in the degree of familiarity with the words of the presented objects is necessary.¹⁵ The CIST-K should also improve discrimination through changes in the presented objects. Furthermore, future research should conduct a validation study on patients diagnosed with clinically impaired function.

This study had several limitations. First, the sample size was relatively small to validate the general applicability of the CIST-K test. Second, we performed a correlation study across CU individuals and patients with MCI and AD rather than separate studies. Further research should classify the causes of dementia and conduct an analysis with stratifications ranging from normal to dementia status. Finally, the time difference between the CIST-K and K-MMSE-2 scores may have affected the test results. In this study, the time difference between the two tests was set within one year, but cognitive decline may have occurred during this period. Nevertheless, the strengths of our study lie in the direct comparison between each subtest in the CIST-K and K-MMSE-2 across the three groups with different degrees of cognitive impairment, after adjusting for confounding factors.

This study demonstrated through ROC curve analysis that the CIST-K is superior to the K-MMSE-2 in diagnosing early cognitive impairment, making it a reliable diagnostic tool. However, when examining specific cognitive function domains, correlation analysis revealed instances where the same cognitive function domains did not show significant correlations between the CIST-K and K-MMSE-2. This indicates the need for caution when comparing cognitive function domains between the two tests in clinical practice. Further validation studies are required to clarify the correlations between the two tests and to develop a score conversion system that can map scores from one test to the other. This system would enable the integration of scores from various screening tests used for a single patient, allowing for continuous tracking of the patient's cognitive function status.

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SUPPLEMENTARY MATERIAL

Supplementary Data 1

The form of the Cognitive Impairment Screening Test

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