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The Clinical Utility of the Cognitive Impairment Screening Test (CIST)

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ABSTRACT

Background and Purpose: The Cognitive Impairment Screening Test (CIST) was developed for use at the Community Dementia Reassurance Center in South Korea. This study evaluated convergent and discriminant validity of CIST, as well as its clinical utility in identifying cognitive impairment and differentiating amyloid deposition.

Methods: We enrolled 252 participants from a hospital memory clinic (47 cognitively unimpaired [CU], 116 amnestic mild cognitive impairment, and 89 dementia). Participants completed CIST, K-MMSE-2, the Seoul Neuropsychological Screening Battery, 2nd edition (SNSB-II), and underwent amyloid positron emission tomography. To evaluate the convergent and discriminant validity of CIST, we conducted correlation analyses with SNSB-II. Receiver operating characteristic analyses were used to evaluate the ability to discriminate cognitive impairment and to distinguish amyloid positivity. Areas under the curve (AUCs) for CIST and K-MMSE-2 were compared using DeLong's test.

Results: The total score of CIST correlated significantly with all SNSB-II subtests, and the domain scores of CIST showed stronger associations with corresponding SNSB-II subtests than with unrelated ones. Both CIST and K-MMSE-2 effectively distinguished cognitively impaired individuals from CU, with CIST demonstrating superior discrimination (AUC=0.926 vs. 0.887, p=0.042). In the non-demented group, both CIST and K-MMSE-2 showed acceptable discrimination for amyloid positivity (AUC≈0.73), with high specificity but low sensitivity; however, there were no significant differences between the two tests.

Conclusions: The CIST demonstrated strong validity and discriminatory ability for detecting cognitive impairment. It also showed acceptable discrimination for amyloid positivity in non-demented participants, supporting its utility as a screening tool in both clinical and community settings.

Keywords: Cognitive Screening Test; Mild Cognitive Impairment; Dementia; Amyloid-Beta; CIST; SNSB-II

the convergent and discriminant validity of the CIST and assessed its ability to discriminate biomarker-positive (e.g., amyloid-positive) individuals at an early stage of cognitive impairment. Our results revealed significant correlations between the total and domain scores of the CIST and the corresponding subtests of the SNSB-II. While previous research has investigated correlations between the CIST and other cognitive screening tools, such as the K-MMSE-2,[11,13,14] to our knowledge, this is the first study to explore its associations with a comprehensive neuropsychological battery like the SNSB-II, which is well-established for domain-specific cognitive assessment in Korea. We observed moderate to strong correlations between each CIST domain and its corresponding SNSB-II subtests, while correlations for non-corresponding domains were weaker, supporting both convergent and discriminant validity. Notably, memory scores on the CIST showed the strongest association with the SVLT-E delayed recall, consistent with the CIST's weighting of memory items (maximum 10 points, one-third of total score). These findings underscore the CIST's strength in assessing memory impairment, a key early feature of Alzheimer's disease.

Group differences in CIST performance were found among the CU, aMCI, and dementia groups. The total CIST score and all domain scores showed significant differences between the groups. Notably, the domain scores for language, memory, and executive function differed significantly among three groups, with a stepwise decline observed from CU to dementia. In contrast, the orientation, attention, and visuospatial function domain scores did not significantly differ between the CU and aMCI groups. This may be attributed to the limited scoring range and ceiling effects associated with these tasks, which likely led to similarly high performance in both groups. A previous study also examined CIST performance across CU, MCI, and Alzheimer's disease dementia groups.[13] However, unlike our findings, that study did not identify significant group differences in attention, visuospatial function, and language domains, potentially due to its smaller sample size and reduced statistical power. Overall, our study extends previous research findings by demonstrating significant group differences across major cognitive domains in a larger sample. These findings provide robust evidence that the CIST can sensitively detect cognitive decline from normal aging to aMCI and dementia, thereby supporting its clinical utility as a screening tool in both community and clinical settings.

The utility of the CIST as a screening tool was demonstrated not only through group comparisons but also through ROC curve analyses. Notably, results from DeLong's test indicated that the CIST had significantly better discriminative ability than the K-MMSE-2 in distinguishing cognitively impaired individuals (i.e., aMCI and dementia) from CU. Since distinguishing cognitively impaired individuals from CU is a core function in primary care and the Community Dementia Reassurance Centers, our findings support the clinical validity of the CIST as a primary cognitive screening tool in these settings. The superior performance of the CIST as a screening test may be attributed to its item composition, which places greater emphasis on memory and executive function compared to the K-MMSE-2. The CIST includes a story recall task with five key words, and places significant emphasis on the memory domain, which is particularly sensitive to early Alzheimer's disease.[23,24] Story recall measures are well-established assessments of episodic memory. Recent biomarker-based studies have demonstrated that these measures have direct and robust associations with early pathological changes of Alzheimer's disease, even in CU adults.[25,26] Additionally, the CIST incorporates subtests assessing executive function, thereby providing a more comprehensive evaluation of the cognitive profile. These features indicate that the CIST may be more effective than the MMSE in identifying cognitive impairment due to various etiologies in community populations. Two prior studies also assessed the CIST's discriminative ability across CU, MCI, and AD dementia groups[13,14]; however, neither used statistical tests, such as DeLong's test, to compare AUCs. Additionally, Kang's study[14] focused on elderly participants with no formal education, which restricted the generalizability of the findings. Kim's study,[13] on the other hand, included relatively small sample sizes for each group, which limited the statistical power to compare the AUC values between the two screening tests. In addition, the AUC values for the CIST reported in Kim's study[13] were lower than those observed in our study, except for discrimination between CU and AD dementia. This discrepancy is likely attributed to our analysis controlling for demographic variables and APOE genotype, thereby enhancing the ability to differentiate between the groups.

Early detection of amyloid positivity in prodromal dementia—particularly in CU or aMCI—is essential for identifying candidates for disease-modifying treatments (e.g., lecanemab, donanemab) or non-pharmacological interventions. Although PET imaging and plasma biomarkers are commonly employed to assess amyloid and/or tau burden in the brain, cognitive screening tests often serve as the initial step in primary clinical settings for identifying individuals who may be positive for biomarkers. In our study, the AUC values for the CIST and the K-MMSE-2 were 0.733 and 0.732, respectively, for detecting amyloid positivity among non-demented individuals (i.e. CU and aMCI). These values indicate acceptable overall discrimination, reflecting each test's ability to differentiate between individuals with amyloid positivity and those with amyloid negativity. However, because the AUC represents performance across all possible thresholds, it does not directly capture a test's ability to identify amyloid-positive individuals at a specific cut-off. The relatively low sensitivity observed in both measures suggests that a substantial proportion of amyloid-positive individuals still perform within normative ranges on brief cognitive tests. Consequently, despite demonstrating discrimination comparable to the K-MMSE-2, the CIST may have limited practical utility as a standalone method for identifying amyloid positivity. Prior studies have reported modest associations between amyloid burden and performance on screening measures such as the MMSE and MoCA in non-demented populations.[20,27-29] However, recent evidence indicates that prediction models incorporating cognitive scores, demographic variables, and APOE genotype outperform cognitive tests alone, underscoring the need for multifactorial approaches when estimating amyloid positivity.[30]

In summary, the CIST demonstrated strong validity and practical utility as a cognitive screening tool. However, while it showed acceptable group-level discrimination for amyloid positivity, its limited sensitivity indicates restricted clinical utility for identifying individuals who are amyloid-positive. These findings suggest that the CIST may serve as a valuable screening tool not only in community-based settings but also in clinical settings. However, several limitations should be noted. The first limitation relates to the administration schedule of the cognitive assessments. In this study, the CIST, K-MMSE-2, and SNSB-II were all administered on the same day during a single testing session. Although this protocol reflects standard procedures commonly used in clinical settings, administering all cognitive measures within a relatively short 2–3-hour window without counterbalancing may introduce a same-session effect. This could inflate shared situational variance and slightly overestimate convergent validity. While this methodological approach is generally accepted in clinical research, future studies that employ separate testing sessions or counterbalanced administration orders would help further minimize this potential bias. The second limitation concerns the sample size. Although the sample size was larger than in previous studies, the number of participants with unimpaired cognition and those with dementia was insufficient, which limits the generalizability of the results. Additionally, this study focused solely on amyloid biomarkers and did not examine other biomarkers (e.g., tau), which may limit evaluation of the CIST's utility across diverse biomarker-defined pathologies. Furthermore, some participants were diagnosed with biomarker-confirmed Alzheimer's disease based on amyloid PET, while the specific clinical diagnoses of amyloid-negative participants, such as frontotemporal dementia or dementia with Lewy bodies, could not be verified. Future research should aim to replicate these findings with larger and more diverse samples and extend the investigation to include additional biomarkers, such as tauopathy, synucleinopathy, and vascular pathology. This work will help clarify whether the CIST can be effectively used as a practical screening tool for the early detection and differentiation of various neurodegenerative conditions.

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