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Application of AD8 Questionnaire to Screen Very Mild Dementia in Taiwanese

Yuan-Han Yang, MD, MS[1,2,3], James E. Galvin, MD, MPH[4,5], John C. Morris, MD[6,7,8], Chiou-Lian Lai, MD, PhD[1,3], Mei-Chuan Chou, MD[9], and Ching-Kuan Liu, MD, PhD[1,2,10]

Abstract

The AD8 questionnaire developed by Washington University in St Louis is a screening tool with 8 questions to reliably differentiate nondemented from demented individuals even at the very mild stage. We recruited 239 participants, including 114 cognitively normal, 73 very mild dementia, and 52 mild dementia to validate its application in Taiwanese. The cut-off value of AD8 was 2 in discriminating cognitively normal from demented individuals with the area under curve (AUC) = 0.961, sensitivity = 97.6%, specificity = 78.1%, positive likelihood ratio (PLR) = 4.5, and negative likelihood ratio (NLR) = 0.03. The cut-off value also was 2 in discriminating nondemented from very mild dementia with the AUC = 0.948, sensitivity = 95.9%, specificity = 78.1%, PLR = 4.4, and NLR = 0.05. The Chinese AD8 is effective in discriminating individuals with dementia, even at its mildest stages from those without dementia with properties identical to the original English version. The cAD8 is a quick dementia screening tool that can be applied across cultures.

Keywords

AD8 questionnaire, very mild dementia, Taiwanese, Alzheimer's disease

Introduction

Dementing illnesses such as Alzheimer's disease (AD) are significant health problems and with increasing prevalence in the aging population, especially in Asia.[1] A major challenge in treating and slowing progression of the devastating effects of AD is how to best diagnose in its earliest stages,[2] because more advanced stages of disease are associated with greater pathologic burden[3] and poorer response to current therapies.[4] In Taiwan, a community-based study has found that 10.2% of population older than 65 years were at a prodromal stage of dementia, mild cognitive impairment (MCI).[5] Such high prevalence of MCI in general population highlights the necessity to early diagnosis and treatment because most of the MCI individuals will develop dementia in the coming years.[6] Unfortunately, this goal is not easily achieved. This is due, in part, to the lack of easy-to-administer sensitive clinical tools to measure early cognitive decline. Current criteria for AD diagnosis such as those developed by the Work Group of the National Institute of Neurological and Communication Disorders and Stroke/Alzheimer's Disease and Related Disorders Association (NINCDS/ADRDA)[7] require standard assessment of patients, which are not easily applied in community settings.

Currently, several cognitive tests are used extensively in Taiwan, but each have their limitations to reach this goal. The mini-mental state examination (MMSE)[8] has a ceiling effect that makes it insensitive to the early signs of dementia,[9] especially in highly educated individuals. The cognitive abilities screening instrument (CASI)[10] requires extensive training to administer and generally is too lengthy for use in general practice. The Clock-Drawing Task is limited to a single cognitive domain and may not be useful in detecting mild cases of dementia.[11,12]

Informant-based assessments such as clinical dementia rating (CDR) have been invaluable in the longitudinal studies characterizing AD, particularly in its earliest stages,[13-15] but the CDR interview takes 75 to 90 minutes. The Chinese version

[1] Department of and Master's Program in Neurology, Faculty of Medicine, Kaohsiung Medical University
[2] Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University
[3] Department of Neurology, Kaohsiung Medical University Hospital
[4] Center of Excellence on Brain Aging
[5] Departments of Neurology and Psychiatry, New York University Langone Medical Center, NY, USA
[6] Department of Neurology
[7] Pathology and Immunology
[8] Alzheimer Disease Research Center, Washington University School of Medicine, St Louis, MO, USA
[9] Kaohsiung Municipal Ta-Tung Hospital, Kaohsiung Medical University, Taiwan
[10] Department of Neurology, Kaohsiung Municipal Hsiaokang Hospital, Taiwan

Corresponding Author:
Ching-Kuan, Liu, Department of Neurology, Kaohsiung Medical University Hospital, No. 100, Tzyou 1 Rd, Kaohsiung City, Taiwan
Email: ckliu@kmu.edu.tw

Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE)[16] has published to screen dementia but it has not been validated for its capacity to screen very mild dementia. Therefore, a screening tool capable to screen dementia, even at its very mild stage, with some trade-off to clinicians, sacrificing sensitivity and specificity to make itself brief is necessary in Taiwan.

The AD8 screening questionnaire is a brief informant-based measure developed by Washington University in St Louis to reliably differentiate cognitively normal from demented individuals, even at its very mild stage, and is sensitive to the earliest signs of cognitive change as reported by an informant[17,18] and has been validated in a Korean population.[19] We have conducted this study to examine the application of AD8 in Taiwanese.

Material and Methods

Participants

All participants were recruited from the longitudinal project in the Neurological Department of Kaohsiung Medical University Hospital, a medical center in southern Taiwan. All participants have received a comprehensive medical evaluation, including clinical history, physical and neurological examinations, and blood chemistry examinations. The diagnosis of AD was based on the NINCDS-ADRDA criteria[7] referring to a series of comprehensive neuropsychological tests, including MMSE,[8] CASI,[10] CDR, and sum of CDR boxes (CDR-SB).[14] Patients with other conditions possibly contributing to the diagnosis of AD were excluded. Alzheimer's disease participants were treated at our clinic. The cogntively normal participants comprised spouses of the patients with AD and volunteers who agreed to enroll in our longitudinal study.

The CASI includes a neuropsychological test that can be administered to evaluate the 9 cognitive domains, including attention, concentration, orientation, short-term memory, long-term memory, language abilities, visual construction, category fluency and abstraction, and judgment. The maximum score for the various domains ranges from 8 to 18. The 9 domain scores add up to a total score of 100.[10]

The ascertainment of cognitive status (AD vs cognitively normal) and subsequent staging was made according to the assignment of a CDR by the examining clinician. A CDR score of 0 indicates no dementia, and 0.5, 1, 2, and 3 indicate very mild, mild, moderate, and severe dementia. Following the CDR evaluating and scoring rules, the clinical diagnosis of AD has confirmed pathologically in 93% of cases,[15,20] even when diagnosed at the CDR 0.5 level, the earliest symptomatic stage of AD.[20] Individuals who met *Diagnostic and Statistical Manual of Mental Disorders* (Fourth Edition; *DSM-IV*) criteria[21] for major depression were excluded.

Translation

The English-version AD8[17] was translated into traditional Chinese by 2 senior Chinese neurologists according to the guideline of cross-cultural adaptation of health-related quality of life measures.[22] In order to make sure the accuracy of translation, the Chinese-version AD8 (cAD8) was translated back into English by another neurologist who did not know AD8 before. After comparing both English versions, original and back-translation one, the back-translation version was the same to the original one.

Evaluation

All procedures were approved by the Kaohsiung Medical University Hospital Institutional Review Board (IRB), and written informed consent was obtained from all participants or their legal representative. For each recruited participant, a series of neuropsychological assessments, including MMSE and CASI, were administered. The CDR was rated by a senior neuropsychologist and an experienced physician based on the information from a knowledgeable collateral source (usually a spouse or adult child). The Chinese version of the AD8(c AD8) was independently administered.

Statistical Analysis

Data analysis was performed using SPSS (version 12.0.1 for Windows, SPSS Inc, Chicago, Illinois). All statistical tests were 2-tailed and an α of .05 was taken to indicate significance.

Chi-square test was conducted to compare the differences, if any, of gender and 1-way analysis of variance (one-way ANOVA) was used to compare the means of age, education, MMSE, CDR-SB, CASI, and CASI subitems among 3 groups: CDR = 0, CDR = 0.5, and CDR = 1 groups.

Pearson's product-moment correlation coefficient, r, was used to assess the relationship between the total score of cAD8 to each of the other measurements, MMSE, CDR-SB, CASI total score, and every score of each cognitive domain of CASI. Receiver operating characteristic (ROC) analysis was used to determine cAD8-appropriate threshold values by choosing the point on the ROC curve closest to point (0, 1) to discriminate nondemented from very mild demented and nondemented from demented status. The sensitivity, specificity, and PLR and NLR of the cAD8 were calculated.

Results

about a total of 239 participants including 114 CDR 0 no dementia, 73 CDR 0.5 very mild dementia, and 52 CDR 1.0 mild dementia participants were recruited. The mean age for the 3 groups were CDR0 (72.5 ± 5.7 y), CDR0.5 (75.1 ± 8.4 y), and CDR1.0 (75.4 ± 9.6 y). Detailed information for these 3 groups, including education, MMSE, CDR-SB, cAD8, and CASI, are presented in Table 1.

In the correlation analyses between cAD8 and other dementia ratings, we found that cAD8 was highly correlated with CDR-SB ($r = .834$, $P < .0001$), MMSE ($r = -.613$, $P < .0001$), and CASI total score ($r = -.605$, $P < .0001$; Table 2). Among the 9 subitems of CASI, we have found cAD8

Table 1. Clinical Characteristics of Recruited Individuals

Participants (N = 239)				
	Normal CDR = 0 (n = 114)	Very Mild Dementia CDR = 0.5 (n = 73)	Mild Dementia CDR = 1.0 (n = 52)	*P* Value
Female (n, %)	53, 46.5%	43, 58.9%	33, 63.5%	.075
Age (mean ± SD), years	72.5 ± 5.7	75.1 ± 8.4	75.4 ± 9.6	.020
Education (mean ± SD), years	10.8 ± 3.7	7.4 ± 5.1	5.6 ± 4.6	<.001
MMSE (mean ± SD)	26.1 ± 2.4	21.6 ± 4.6	16.5 ± 4.4	<.001
CDR-SB (mean ± SD)	0	2.8 ± 1.1	5.7 ± 1.3	<.001
cAD8 total score (mean ± SD)	0.9 ± 1.4	4.8 ± 1.6	6.6 ± 1.8	<.001
cAD8 range	0-8	1-8	2-8	
CASI total score (mean ± SD)	90.5 ± 4.7	74.3 ± 13.3	59.5 ± 14.9	<.001
CASI domains (mean ± SD)				
Long-term memory	10.0 ± 0.9	9.6 ± 0.9	8.8 ± 2.1	<.001
Orientation	17.8 ± 1.0	14.5 ± 3.5	11.2 ± 4.1	<.001
Attention	7.0 ± 1.0	6.4 ± 1.3	5.6 ± 1.8	<.001
Concentration	8.4 ± 1.6	6.8 ± 2.7	5.0 ± 3.1	<.001
Short-term memory	9.1 ± 1.9	4.9 ± 3.3	2.6 ± 2.1	<.001
Fluency	7.7 ± 1.9	6.4 ± 2.2	4.5 ± 2.3	<.001
Language	10.2 ± 1.3	8.8 ± 1.6	7.6 ± 2.1	<.001
Abstraction and judgment	10.6 ± 1.1	8.6 ± 2.1	7.3 ± 2.4	<.001
Visual construction	9.8 ± 1.2	8.4 ± 2.4	7.0 ± 2.9	<.001

Abbreviations: MMSE, mini-mental status examination; CASI, cognitive assessment screening instrument; CDR-SB, sum of boxes of clinical dementia rating scale; cAD8, Chinese version AD8.

Table 2. Correlations Between AD8 and Cognitive Measurements

	Pearson's Correlation Coefficient	*P* Value
MMSE	−.613	<.0001
CDR-SB	.834	<.0001
CASI total score	−.605	<.0001
CASI domains		
Long-term memory	−.237	<.0001
Orientation	−.572	<.0001
Attention	−.228	<.0001
Concentration	−.439	<.0001
Short-term memory	−.651	<.0001
Fluency	−.382	<.0001
Language	−.352	<.0001
Abstraction and judgment	−.423	<.0001
Visual construction	−.385	<.0001

Abbreviations: MMSE, mini-mental status examination; CASI, cognitive assessment screening instrument; CDR-SB, sum of boxes of clinical dementia rating scale.

was most highly correlated with short-term memory ($r = -.651$, $P < .0001$; Table 2).

The prevalence of informant endorsement of each question in the cAD8 varied among the 3 groups. In nondemented (CDR 0) group, Question 8: Consistent problems with thinking and/or memory was most frequently reported with its prevalence: 28.1%, and then followed the Question 2: Reduced interest in hobbies/activities with its prevalence: 18.4% (Table 3).

In demented group, including very mild (CDR 0.5) and mild (CDR 1) dementia groups, Question 8 also has the highest endorsement rate = 95.9% in very mild demented and 96.2% in mild demented groups, followed by Question 3: Repeats questions, stories, or statements (80.8% in very mild and 90.4 % in mild groups). Both the questions detected by AD8 questionnaire were consistently and frequently reported in demented participants regardless of the stage of dementia (Table 3).

The cut-off value of cAD8 to discriminate cognitively normal CDR 0 individual from demented participants (CDR > 0) was 2, with the AUC = 0.961, sensitivity = 97.6%, specificity = 78.1%, PLR = 4.5, and NLR = 0.03 (Figure 1). Similarly, the cut-off value of cAD8 to discriminate cognitively normal, CDR 0 participants from very mild dementia (CDR 0.5) also was 2 with AUC = 0.948, sensitivity = 95.9%, specificity = 78.1%, PLR = 4.4, and NLR = 0.05 (Figure 2).

Discussion

We have found the cut-off values of cAD8 to discriminate demented from cognitively normal participants, even in very mild dementia, was 2, which was the same as the original English version. The "Consistent problems with thinking and/or memory" and "Repeats questions, stories, or statements" were most frequently endorsed by informants when characterizing the cognitive change associated with the AD phenotype.

The same cut-off value to the original English version suggests that the cAD8 was not overly influenced by the different cultural backgrounds, similar to what was reported in the Korean version of the AD8.[19] This may be due in part to the informant-based nature of the cAD8, which is not likely to be influenced by age, education, or cultural background,[23-25] although there were different educational levels and age in our

Table 3. The Prevalence of Each AD8 Question in 3 Groups[a]

All Participants (N = 239)			
	CDR 0 (N = 114)	CDR 0.5 (N = 73)	CDR 1.0 (N = 52)
AD8-1, n (%)	3 (3.0%)	26 (35.6%)	42 (80.8%)
AD8-2, n (%)	21 (18.4%)	37 (50.7%)	31 (59.6%)
AD8-3, n (%)	17 (14.9%)	59 (80.8%)	47 (90.4%)
AD8-4, n (%)	3 (3.0%)	25 (34.2%)	35 (67.3%)
AD8-5, n (%)	5 (4.4%)	42 (57.5%)	44 (84.6%)
AD8-6, n (%)	4 (3.5%)	40 (54.8%)	46 (88.5%)
AD8-7, n (%)	15 (13.2%)	54 (74.0%)	47 (90.4%)
AD8-8, n (%)	32 (28.1%)	70 (95.9%)	50 (96.2%)

Abbreviation: CDR, clinical dementia rating scale.
[a] AD8-1, problems with judgment; AD8-2, reduced interest in hobbies/activities; AD8-3, repeats questions, stories, or statements; AD8-4, trouble learning how to use a tool, appliance, or gadget; AD8-5, forgets correct month or year; AD8-6, difficulty handling complicated financial affairs; AD8-7, difficulty remembering appointments; AD8-8, consistent problems with thinking and/or memory.

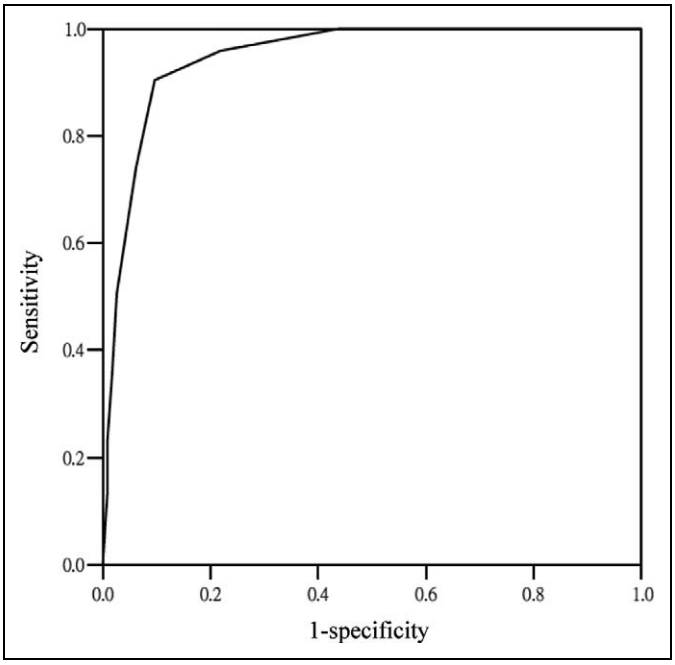

Figure 1. Receiver operating characteristic curve for cAD8 in discriminating nondementia from very mild dementia.

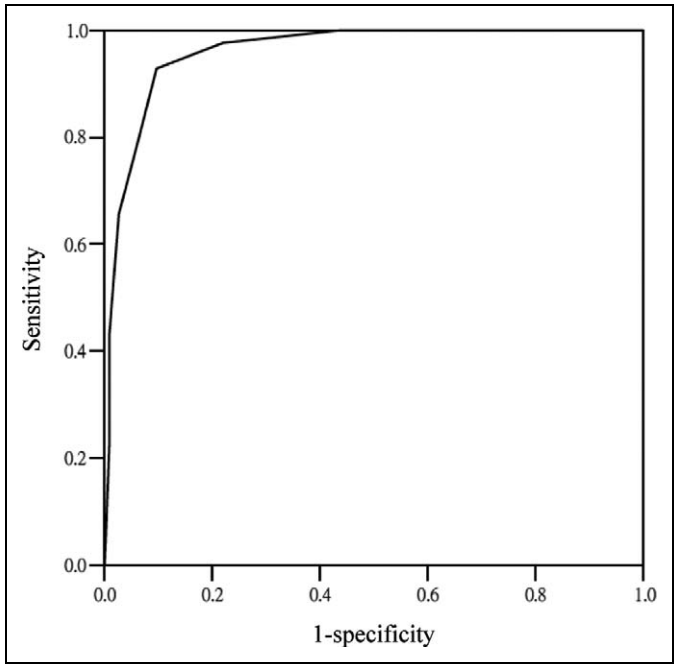

Figure 2. Receiver operating characteristic curve for cAD8 in discriminating nondementia from dementia.

3 groups These points also have been illustrated in our results that cAD8 was more highly correlated with CDR-SB than MMSE or CASI. Such correlation may result from the original development of AD8, which is based on an extensive review of the literature and the experience with semistructured informant interviews.[17,18] Compared to the original AD8, in discriminating CDR = 0 group from CDR = 0.5 group, the cAD8 has yielded relatively higher sensitivity (95.9% in cAD8 vs 74% in original AD8) and relatively lower specificity (78.1% in cAD8 vs 86% in original AD8). The differences may be related to the traditional Chinese cultural background, where Chinese people who were taught to be humble will report the problems mentioned in AD8 questionnaire when they were asked with less chance of denial or minimizing problems.

In the prevalence of each question in AD8 questionnaire in our 3 different groups, we have found that Question 8, consistent problems with thinking and/or memory, was the most commonly endorsed item in the demented groups, while reported in <30% of control individuals. Such findings also underlined the importance of recognizing the consistency of memory and/or thinking changes in the detection of cognitive impairment. In the nondemented CDR 0 group, Question 2, reduced interest in hobbies/activities, was the second most commonly endorsed item. Participants with major depression were excluded from this study. However, mild depressive symptoms are common in older adults[18] and these symptoms may precede any overt cognitive symptoms by several years to develop clinical AD.[26] It is possible that with longitudinal follow-up, these cognitively normal individuals will go on to develop cognitive impairment.

We have validated the AD8 questionnaire and examined its application in Taiwanese. Although informant-based screening tool such as AD8 has shown its potential in discriminating nondemented from demented individuals, even the very mild stage, reliable caregivers or informants may not always be available. However, AD8 can be used as a self-rating scale for those normal or very mild stage demented individuals.[18] One of the main goals of AD8, and moreover, with available informants, the advanced stage of dementia also can be screened by AD8. The demonstration of the effectiveness of the cAD8, along with previous demonstration of the validity of the Korean AD8,[19] supports efforts for cross-cultural comparisons.

Declaration of Conflicting Interests

The authors declared no potential conflicts of interests with respect to the authorship and/or publication of this article.

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