

Application of total scores of CERAD neuropsychological battery in detecting MCI and dementia in a sample of Egyptian elderly

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Authors' contribution statements.

All authors contributed to the study conception and design. Material preparation, data collection and analysis were performed by Walaa Yusif. The first draft of the manuscript was written by Walaa Yusif and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

Abstract

Introduction: Consortium to Establish a Registry for Alzheimer's disease (CERAD) is an easy standardized and reliable neuropsychological assessment tool which can differentiate between normal cognition, mild cognitive impairment (MCI) and dementia.

Objective: to estimate the cut off points of the Arabic version of CERAD for detection of mild cognitive impairment (MCI) and dementia.

Methods: A case control study was conducted and included 150 elderly, 60 years and older, living in the community dwelling in Cairo recruited from geriatric memory and general clinics in Ain-Shams University Hospitals.

They were divided in to 3 equal groups; normal cognition, MCI and dementia according to Clinical Dementia Rating scale (CDR). Later, their CERAD test was applied, and the test scores were compared.

Results: To differentiate between normal and MCI groups, total score (TS I) cut off point ≤ 82 with 96% sensitivity and 80% specificity, total score (TS II) cut off point ≤ 90 with 82% sensitivity and 88% specificity. As regard differentiation between normal and dementia groups, TS I cut off point ≤ 69 with 90% sensitivity and 92% specificity and TS II cut off point ≤ 76 with 90% sensitivity and 92%

specificity, while to differentiate between MCI and dementia groups, TS I ≤ 69 with 90% sensitivity and 96% specificity and TS II ≤ 71 with 86% sensitivity and 98% specificity.

Conclusion: Cut off points of the Arabic version of CERAD were estimated to accurately differentiate normal cognition, mild cognitive impairment and dementia.

Keywords: Arabic, CERAD, dementia, mild cognitive impairment.

INTRODUCTION

The elderly population is expanding all over the world with subsequent increase in the number of dementia cases which increases with aging [1]. There are approximately 50 million people diagnosed with dementia worldwide and these numbers are expected to increase with an average rate of 10 million new cases diagnosed yearly [2].

Also, patients with mild cognitive impairment (MCI) are at risk for developing Alzheimer's disease (AD), and other subtypes of dementia. Studies reported a decline in one or more cognitive domains in elderly people 5–10 years before the clinical diagnosis of AD [3].

Consortium to Establish a Registry for Alzheimer's disease (CERAD) is a neuropsychological battery developed to provide a standardized assessment of cognition. It's composed of eight sub-tests: Mini-Mental State Examination (MMSE), Verbal Fluency, Modified Boston Naming Test, Word List Learning, Word List Recall, Word Recognition Discriminability, Constructional Praxis Copy, and Constructional Praxis Recall [4].

Many clinical and research settings have been using the CERAD neuropsychological assessment battery and it became popular because it's short, easy to perform and useful in differentiating between normal cognition, MCI and dementia [5].

The CERAD battery has been used to assess cognitive functions in patients with different types of dementia such as frontotemporal dementia [6] and dementia of Parkinson disease [7], not exclusively Alzheimer's disease.

Many scores of CERAD were developed. CERAD total score I (TS-I) was calculated by the sum of CERAD subtests, excluding the MMSE and the Constructional Praxis Recall (with a total score of 100) [8], while CERAD total score II (TS-II) was calculated by adding

the constructional recall score to the original total score (TS-I) [4].

CERAD total score has the advantage of being superior to any single CERAD subtest in discriminating between normal cognition and MCI [9], as well as being suitable for monitoring Alzheimer disease progression [10,11].

It was translated into various languages including Arabic [12]. with few studies conducted using the Arabic version mainly on the Egyptian and Omani populations [12,13], however, the available cut off scores are based on a United States normative study [14] which are not optimally sensitive and specific in the Egyptian population.

Many other cognitive tests have been translated and validated in Arabic such as MMSE [15], Addenbrooke's Cognitive Examination (ACE) [16], Mini Cog [17], Montreal Cognitive Assessment (MoCA) [18], Saint Louis University Mental Status exam (SLUMS) [19], however some of them are not suitable for illiterate and low educated patients and MMSE are not sensitive for MCI diagnosis.

OBJECTIVE

To estimate the cut off points of the Arabic version of CERAD to detect mild cognitive impairment and dementia.

MATERIALS AND METHODS

A case control study included 150 participants 60 years and older living in the community dwelling in Cairo recruited from geriatric memory and general clinics in Ain Shams University Hospitals from June 2020 till October 2021.

The sample size was calculated based on a previous similar study done by Bertolucci et al, 2001 [20]. Provisional sample size is 36 in each

group with a confidence level of 95%, power of 80%, 98% sensitivity and 75% specificity.

Those who refused to participate in the study were excluded, as well as participants with severe dementia who were unable to complete the tests, expressive and receptive aphasia unable to understand the tests, severe visual or hearing impairment, severe depression or delirium.

Informed consents were obtained from all participants or their proxies then all of them were divided into 3 equal groups using the Arabic version [21] of the clinical dementia rating scale (CDR) [22].

CDR assesses six domains of cognitive and functional performance which are memory, orientation, problem solving and judgment, community affairs, home and hobbies and personal care. Information was obtained through an interview of the patient and a reliable informant. An overall CDR global score was calculated based on a standard algorithm available online [23] that considers memory as the primary category and the other remaining categories as secondary; normal cognition (CDR 0), mild cognitive impairment (MCI) (CDR 0.5) and dementia (CDR \geq 1).

Patients were subjected to Comprehensive geriatric assessment including personal history, past medical history and drug history, assessment of mood in those with normal cognition and MCI using the Arabic version of Geriatric Depression Scale (GDS) [24] and the Arabic version of Cornell Scale for Depression in Dementia (CSDD) in those with dementia [25].

Then, participants of each group underwent cognitive assessment using the CERAD neuropsychological battery (verbal fluency with a maximum score of 24 [26], 15-items Modified Boston's Naming test with a maximum score of 15 [4], Mini-Mental State Examination with a maximum score of 30 [15], Word List Memory Task with a maximum score of 30 [27], constructional praxis with a maximum score of 11 [28], word list recall with a maximum score of 10, word list recognition with a maximum score of 10 [27] and constructional praxis recall with a maximum score of 11 [28].

The CERAD total score (TS-I) [8] was calculated by the sum of the previously

mentioned subtests, excluding the MMSE and the Constructional Praxis Recall while the CERAD total score (TS-II) [5] was calculated by adding the constructional recall score to the original total score TS-I. Later, CERAD scores were compared with CDR to estimate appropriate cut off points for MCI and dementia.

Statistical Analysis:

Data were collected, revised, coded and entered to the Statistical Package for Social Science (IBM SPSS) version 23. The quantitative data were presented as mean, standard deviations and ranges when parametric and median, inter-quartile range (IQR) when data found non-parametric. Also, qualitative variables were presented as number and percentages.

The comparison between groups regarding qualitative data was done by using *Chi-square test* and/or *Fisher exact test* when the expected count in any cell found less than 5.

The comparison between more than two groups regarding quantitative data and parametric distribution was done by using *One Way ANOVA test* followed by post hoc analysis using *LSD test* while with non-parametric distribution was done by using *Kruskal-Wallis test* followed by post hoc analysis using *Mann-Whitney test*.

Receiver operating characteristic curve (ROC) was used to assess the best cut off point with its sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) and area under curve (AUC) of the studied tool.

The confidence interval was set to 95% and the margin of error accepted was set to 5%. So, the p-value was considered significant as the following:

P-value > 0.05: Non significant (NS)

P-value < 0.05: Significant (S)

P-value < 0.01: Highly significant (HS).

RESULTS

The mean age of the participants was 66.67 ± 7.08 , 52.7% were females and 47.3% were males. Most of them were married with a percentage of 74%. As regard education, all of them were educated either below high school 39.3% or above high school 60.7%. Only 21.3%

had a positive family history of dementia. As regard comorbidities, 39.3% were diabetic, 48.7% were hypertensive, 18.7% had ischemic heart disease, 4.7% reported having AF, 22% had dyslipidemia, 10.7% had a history of

previous cerebrovascular stroke, 7.3% and 22% complained of hearing and visual impairment respectively. 18.7% were taking 5 or more medications (polypharmacy) and 17.3% were found to be depressed.

Table (1): Comparison between the three study groups as regard demographic data

		Normal group	MCI group	Dementia group	Test value	P-value	Sig.
		No. = 50	No. = 50	No. = 50			
Age	Mean ± SD	63.28 ± 3.77	64.42 ± 4.53	72.32 ± 8.26	35.298•	0.000	HS
	Range	60 – 74	60 – 77	60 – 92			
Gender	Male	21 (42.0%)	28 (56.0%)	22 (44.0%)	2.300*	0.317	NS
	Female	29 (58.0%)	22 (44.0%)	28 (56.0%)			
Marital Status	Single	1 (2.0%)	0 (0.0%)	2 (4.0%)	28.877*	0.000	HS
	Married	46 (92.0%)	41 (82.0%)	24 (48.0%)			
	Widow	3 (6.0%)	8 (16.0%)	21 (42.0%)			
	Divorced	0 (0.0%)	1 (2.0%)	3 (6.0%)			
Education	≤12 years	10 (20.0%)	18 (36.0%)	31 (62.0%)	18.830*	0.000	HS
	>12 years	40 (80.0%)	32 (64.0%)	19 (38.0%)			
Family History of dementia	Yes	7 (14.0%)	13 (26.0%)	12 (24.0%)	2.463*	0.292	NS
	No	43 (86.0%)	37 (74.0%)	38 (76.0%)			
Smoking	Non smoker	48 (96.0%)	42 (84.0%)	40 (80.0%)	6.000*	0.050	NS
	Smoker	2 (4.0%)	8 (16.0%)	10 (20.0%)			
Post hoc analysis							
		Normal Vs MCI		Normal Vs Dementia	MCI Vs Dementia		
Age		0.332		0.000	0.000		

*: Chi-square test; •: One Way ANOVA test

Post hoc analysis revealed age to be statistically significant between dementia group and both normal and MCI group, while there was no statistical significance between normal and MCI groups. Being widowed was of statistical

significance in the demented participants. Education was also found to be statistically significant as lower education levels were associated with worse cognition.

Table (2): Comparison between the three study groups as regard CERAD subtest scores

	Normal group	MCI group	Dementia group	Test value	P-value	Sig.
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		No. = 50	No. = 50	No. = 50			
Verbal Fluency	Median (IQR)	15.5 (12 – 17)	13 (12 – 16)	6 (3 – 11)	56.366	0.000	H S
	Range	8 – 24	10 – 20	0 – 23			
Modified Boston Naming	Median (IQR)	15 (15 – 15)	15 (15 – 15)	13 (9 – 15)	68.679	0.000	H S
	Range	12 – 15	12 – 15	6 – 15			
Mini-mental State Examination	Median (IQR)	30 (29 – 30)	29 (28 – 30)	19 (14 – 25)	100.676	0.000	H S
	Range	27 – 30	25 – 30	8 – 28			
First trial of word list learning	Median (IQR)	8.5 (7 – 10)	6 (5 – 7)	2.5 (2 – 4)	85.528	0.000	H S
	Range	4 – 10	3 – 10	0 – 9			
Second trial of word list learning	Median (IQR)	9 (8 – 10)	7 (7 – 8)	3.5 (2 – 5)	94.407	0.000	H S
	Range	6 – 10	4 – 9	0 – 9			
third trial of word list learning	Median (IQR)	10 (9 – 10)	8 (7 – 9)	3.5 (3 – 6)	95.652	0.000	H S
	Range	6 – 10	6 – 10	0 – 9			
Word List Memory Task	Median (IQR)	27 (25 – 29)	21 (20 – 23)	9.5 (7 – 15)	98.858	0.000	H S
	Range	17 – 30	15 – 28	0 – 27			
Constructional Praxis	Median (IQR)	11 (11 – 11)	11 (9 – 11)	5 (2 – 7)	76.448	0.000	H S
	Range	7 – 11	5 – 11	0 – 11			
Word List Recall	Median (IQR)	9 (8 – 10)	7 (6 – 8)	2 (1 – 5)	101.567	0.000	H S
	Range	5 – 10	5 – 9	0 – 8			
Word List Recognition	Median (IQR)	10 (10 – 10)	10 (9 – 10)	4 (1 – 8)	72.804	0.000	H S
	Range	5 – 10	7 – 10	0 – 10			
Constructional Praxis Recall	Median (IQR)	10.5 (8 – 11)	10 (7 – 11)	0.5 (0 – 5)	80.020	0.000	H S
	Range	5 – 11	4 – 11	0 – 11			
Total Score I	Median (IQR)	87 (84 – 90)	77 (74 – 79)	39.5 (26 – 58)	94.889	0.000	H S
	Range	60 – 96	60 – 85	10 – 89			

Total Score II	Median (IQR)	97 (92 – 100)	86 (83 – 90)	42.5 (26 – 62)	95.826	0.000	H S
	Range	65 – 107	66 – 96	10 – 97			

Table (2) shows different CERAD subtest scores of participants among the study groups. The CERAD total score (TS-I) was calculated by the sum of subtests, excluding the MMSE and the Constructional Praxis Recall while the CERAD total score (TS-II) was calculated by adding the constructional recall score to the original total score TS-I.

Post hoc analysis of CERAD subtests revealed that all subtests were found to be of statistical significance among the three groups except for modified Boston naming, word list recognition and constructional praxis recall which showed no statistical significance between normal and MCI groups.

Table (3): TS I and TS II cut off points and their sensitivity and specificity among the three study groups

	Normal vs MCI	Normal vs Dementia	MCI vs Dementia
TS I			
Cut off	≤ 82	≤ 69	≤ 69
AUC	0.899	0.948	0.897
sensitivity	96	90	90
specificity	80	92	96
PPV	82.8	91.8	95.7
NPV	95.2	90.2	90.6
TSII			
Cut off	≤ 90	≤ 76	≤ 71
AUC	0.887	0.958	0.898
sensitivity	82	90	86
specificity	88	92	98
PPV	87.2	91.8	97.7
NPV	83	90.2	87.5

Table (3) demonstrates different cut off points between the three study groups. To differentiate between normal and MCI groups, total score (TS I) cut off point ≤ 82 with 96% sensitivity and 80% specificity, total score (TS II) cut off point ≤ 90 with 82% sensitivity and 88% specificity. As regard differentiation between normal and dementia groups, TS I cut off point ≤ 69 with 90% sensitivity and 92% specificity and TS II cut off point ≤ 76 with 90% sensitivity and 92% specificity, while to differentiate between MCI

and dementia groups, TS I ≤ 69 with 90% sensitivity and 96% specificity and TS II ≤ 71 with 86% sensitivity and 98% specificity.

DISCUSSION

The current study aimed to estimate the cut off points of the Arabic version of CERAD.

The effect of demographic variables on the three study groups was observed with dementia patients are older in age. Post hoc analysis revealed age to be statistically significant between dementia group and both normal cognition and MCI groups. This is consistent with a study done by Wolters et al, 2020 which revealed that the incidence of dementia increases with age [29]. However, age had no statistical significance between normal and MCI groups. This finding is against a systematic review done by Gillis et al, 2019 which found that the incidence of MCI increases with age [30]. This is most probably because participants of both normal cognition and MCI groups had almost the same age.

Marital status was found to be of statistical significance as being widowed was significant in the dementia group. This is consistent with a study done in the United States by Liu et al, 2020 including almost 15379 participants, that found that unmarried participants including those who were widowed were more likely to develop dementia over the study period than their married counterparts [31] which might have been due to demographic differences as widowed participants were significantly older than the other participants. It can also be explained by financial and emotional stress, lack of social support, and loneliness which may increase the risk of depression.

Level of education was significantly lower in those with impaired cognition. This is consistent with many studies [32-34] that concluded that higher educational level may be associated with slower cognitive decline and is protective against the occurrence of dementia [32]. This can be explained by better cognitive reserve with higher educational level, higher financial status, sense of well-being with better access to healthcare services, promotion of healthy lifestyle and good attention to preventive care and increase participation in more cognitively demanding occupations requiring higher education.

As regard CERAD subtests, all of them were statistically significant between normal participants and demented ones. This is supported by a case-control study conducted in Finland by Karrasch et al, 2005 involving 22 controls, 17 MCI patients and 15 probable AD patients recruited from the community that concluded that all subtests were

significant except for constructional praxis recall which was found to be insignificant statistically [3].

On the other hand, modified Boston naming, word list recognition and constructional praxis recall were of no statistical significance between normal and MCI groups. Some studies had similar findings as regard modified Boston naming and word list recognition including a case-control study conducted in Thailand recruiting 63 participants of normal cognition and 60 participants with MCI from the community [33]. Other studies had contradictory findings, for example a study done by Paajanen and colleagues in the AddNeuroMed study in 2010, including more than 400 participants found that all CERAD subtests without exceptions were found to be statistically significant [9]. Another study conducted by Karrasch et al, showed that word list memory was the only test that distinguished MCI participants from those with normal cognition [3].

Various cut offs were proposed by many authors of other languages. A study done by Seo et al, 2010 that included 583 patients with dementia, 250 patients with MCI, and 1386 normal controls developed lower cut offs than ours. TS 1 and TS 2 cut offs were 59.5 and 66.5 respectively between normal and MCI groups, 49.5 and 53.5 between normal and dementia groups, 44.5 and 46.5 between MCI and dementia groups. This can be due to using a different tool to identify dementia and MCI, as well as the lower level of education of participants [5]. Other studies developed similar cut offs to ours including a study in done in Colombia [34] recruiting 1698 participants which concluded that the dementia diagnosis cut off point for the low education group was 54, and that for the high education group was 67, while the MCI diagnosis cut off point for the low education group was 66 and that for the high education group was 72. Another study done in the United States by Chandler et al, 2005 [8] found that TS 1 cut off was 85.1 between normal and MCI groups, 77 between normal and dementia groups, 68.5 between MCI and dementia groups. This is most probably due to the high level of education of participants.

Limitations of the study:

The sample size was relatively small, participants recruited from Cairo governorate only and were all educated, so these results may not be representative of illiterate population.

Further studies are needed to include larger sample size from different governorates to generalize these results to the Egyptian population. Also studies that include non-educated participants are encouraged.

Conclusion:

Cut off points of the Arabic version of CERAD were estimated to accurately differentiate normal cognition, mild cognitive impairment and dementia.

Statements and Declarations

Funding / Competing interests

The authors did not receive support from any organization for the submitted work.

The authors have no competing interests to declare that are relevant to the content of this article.

Compliance with Ethical Standards

This study was performed in line with the principles of the Declaration of Helsinki. Approval was granted by the Ethics Committee of Faculty of medicine at Ain Shams University.

Consent to participate

Informed consent was obtained from all participants and /or their legal guardian to participate in the study. Confidentiality of data of participants was assured and accessible only by the main researcher thus preserving patient anonymity.

Consent to publish

Not applicable.

Availability of data and materials section

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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