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Comparative Analysis of the Alzheimer's Questionnaire (AQ) with the CDR Sum of Boxes, MoCA, and MMSE

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Abstract

The Alzheimer's Questionnaire (AQ) has been established as a valid and accurate informant-based screening questionnaire for Alzheimer's disease (AD) and amnestic mild cognitive impairment (aMCI). Although the AQ's validity and diagnostic accuracy has been established, its performance in comparison to other instruments has not. 39 amnestic mild cognitive impairment (aMCI) cases and 34 Alzheimer's disease (AD) cases were matched on age, education, and gender to 73 cognitively normal individuals. The sample had a mean age of 82.54±7.77 and a mean education level of 14.61±2.61 years. The diagnostic accuracy of the CDR Sum of Boxes, Mini Mental State Exam (MMSE), Montreal Cognitive Assessment (MoCA), were compared to the AQ. The AQ correlated strongly with the CDR Sum of Boxes (r = .79) and demonstrated similar diagnostic accuracy with the MoCA and MMSE. These results suggest that the AQ is comparable to other established informant-based and patient-based measures.

Keywords

cognitive screening; mild cognitive impairment; neuropsychological tests; dementia screening

Introduction

The Alzheimer's Questionnaire (AQ) has been established as a valid and accurate informant-based screening questionnaire for both Alzheimer's disease (AD) and amnestic mild cognitive impairment (aMCI)[1]. It is similar in content and structure to other informant-based dementia screening questionnaires[2,3], but contains questions that probe several

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Conflicts of Interest:
The authors have no conflicts of interest to report.

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domains including memory, orientation, functional ability, visuospatial function, and language. Given the widespread use of measures such as the Clinical Dementia Rating (CDR)[4], Mini Mental State Exam (MMSE)[5] and the Montreal Cognitive Assessment (MoCA)[6], comparing the AQ's performance to them is important in order to further establish its validity. Since the AQ is purely an informant-based instrument, comparing it to patient-based assessments (MoCA and MMSE) and with the CDR, which uses both informant- and patient-based information, a broader assessment of the AQ's validity can be made from these comparisons.

Methods

Study Sample

Data from 146 individuals participating in a brain and body donation program[7] were utilized for this study. Participants in this program are recruited predominantly from the northwest region of the Phoenix, Arizona metropolitan area. Informed consent was obtained from all individuals prior to enrolling in the program. The sample for this study ranged in age from 57 to 97 years with a mean of 82.54±7.77 and had a mean education level of 14.61±2.61 years and included 82 females and 64 males. Of the 146 individuals, 73 were classified as cognitively normal (CN), 39 were classified as amnestic mild cognitive impairment (aMCI), and 34 were classified as Alzheimer's disease (AD). Demographic characteristics of the clinical groups are reported in Table 1. Each aMCI and AD individual was matched on age, education, and gender to a CN individual. Both single and multiple domain aMCI cases were categorized as aMCI and both possible and probable AD were categorized as AD. The AD cases met NINCDS-ADRDA[8] criteria for a clinical diagnosis of probable or possible Alzheimer's disease. Amnestic-MCI cases were diagnosed as such based on Petersen criteria[9]. The CN cases were defined as having no limitations of activities of daily living by informant report and were within normal limits on neuropsychological testing.

Consensus diagnosis with a neurologist, geriatric psychiatrist, and neuropsychologist was used to determine the clinical status of each individual. Consensus diagnoses were made based on neuropsychological testing results, neurological and physical exam, and interviews with an informant that assessed global cognitive status, functional status, and mood and behavioral status. The AQ was not utilized in making the consensus diagnosis.

Statistical Analysis

Diagnostic accuracy of the individual tests was assessed using ROC analysis through the use of area under the curve (AUC) values. The Shapiro-Wilk test was performed on the data to determine the normality of distribution for the continuous variables. Non-parametric tests for group comparisons and correlations were used as the data for all continuous variables were not normally distributed. The Kruskall-Wallis test was used to compare the AQ total score among participants when grouped by both clinical status (CN, aMCI, AD) and CDR Global Score (0; 0.5; 1,2,3). The Conover-Inman test was used to assess groupwise differences for the Kruskall-Wallis tests. A Bonferroni-adjusted p-value of 0.02 was used to determine statistical significance for the clinical group and CDR Global Score group comparisons. Cohen's *d* was used to assess the effect size for each group comparison.

Spearman correlation analysis was used to determine the degree of association between the AQ, CDR-SOB, MoCA, and MMSE. A false discovery rate[10] p-value of 0.008 was used to correct for multiple comparisons among the correlations. Statistical analyses were carried out using Systat 12.0 (Systat, Inc., Chicago, IL) and MedCalc 12.2 (MedCalc Software, Mariakerke, Belgium).

Results

The Shapiro-Wilk test found that age, education, AQ, MoCA, MMSE, and CDR-SOB were not normally distributed. The distribution of males and females between clinical groups was not statistically significant ($\chi^2 = 0.57$ (df = 2), p = 0.75) (Table 1). There were no significant differences in age (Kruskall-Wallis = 5.35 (df = 2), p = 0.07) or education level (Kruskall-Wallis = 0.54 (df = 2), p = 0.76) between the clinical groups (Table 1).

Table 2 displays the AUC values with 95% confidence intervals for each of the instruments for all clinical groups. The AQ, MoCA, and MMSE demonstrated comparable AUC values for both aMCI and AD while the CDR-SOB demonstrated greater discriminatory power for aMCI than the other instruments. Groupwise comparisons from the Kruskall-Wallis test demonstrated that all three clinical groups were significantly different from each other on AQ total score (Kruskall-Wallis = 79.55, (df = 2), p<0.001; all groupwise comparisons p<0.001). Effect sizes (Cohen's *d*) for AQ clinical group differences were as follows: CN vs. aMCI = 0.98, CN vs. AD = 3.51, aMCI vs. AD = 2.04. The AQ correlated strongly with the CDR-SOB (r = 0.79) and correlated moderately with the MMSE (r = −0.56) and MoCA (r = −0.46). The MoCA was moderately correlated with the MMSE (r = 0.63) and CDR-SOB (r = −0.62). The MMSE and CDR-SOB were strongly correlated (r = −0.76). All correlations yielded p-values that were p<0.001.

An additional analysis was carried out to characterize the AQ's performance when participants were grouped according to their Global Score on the CDR (CDR = 0 [n = 66]; CDR 0.5 [n = 49]; CDR 1, 2, 3 [n = 31]). Individuals with a CDR Global Score of 1, 2 and 3 were combined as these three subgroups were not significantly different from each other when compared separately on the AQ total score. A statistically significant difference for the AQ total score was noted between the three CDR Global Score groups (Kruskall-Wallis = 82.35 (df = 2) p<0.001; all groupwise comparisons p<0.001). Cohen's *d* was used to assess the effect sizes of these group differences and found the following: CDR 0 vs. CDR 0.5 = 1.27; CDR 0 vs CDR 1, 2, 3 = 3.70; CDR 0.5 vs. CDR 1, 2, 3 = 1.87.

Discussion

This study demonstrated that the AQ is comparable to other commonly used informant-based and patient-based measures in terms of its ability to differentiate aMCI and AD patients from those who are cognitively normal. When the study sample was grouped according to the CDR Global Score, there were very large differences between the dementia (AD), questionable dementia (aMCI), and no dementia (CN) groups on the AQ total score.

The AQ's AUC value for aMCI was much lower than previously reported[1] which is likely due to the smaller sample size of the current study. The validation study of the AQ[1] used a

larger sample (100 CN, 100 aMCI, 100 AD); however, its ability to differentiate aMCI in this study was similar to the MMSE and MoCA. The CDR-SOB yielded a higher AUC than the AQ, but this is likely because the CDR-SOB was used to make the consensus diagnoses, resulting in an inflated AUC value. Despite this weakness the inclusion of the CDR-SOB AUC value does provide some frame of reference to compare the other instruments with. The AQ correlated moderately with the MMSE and MoCA which is expected as the modalities of instrument administration (patient-based vs. informant-based) differ greatly.

One weakness of the study is that the sample was homogenous with respect to ethnicity as the majority of participants in this study were Caucasian. Therefore, it is unclear whether these results can be applied to a more ethnically diverse population. Another weakness is the relatively small sample size to assess diagnostic accuracy of the instruments used in the study. Despite these shortcomings, this study demonstrated that the AQ's performance is comparable to other widely-used informant-based and patient-based instruments.

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Table 1

Clinical Group Demographic Characteristics

	CN	*aMCI*	*AD*	*p-value*
Gender (M/F)	40/33	21/18	21/13	0.75
Age	82.59 (7.67)	80.54 (8.43)	84.74 (6.74)	0.07
Education	14.55 (2.41)	14.77 (2.53)	14.56 (3.15)	0.76

Table 2

Diagnostic Accuracy Comparison of AQ, CDR-SOB, MMSE, and MoCA

	CN ra aMCI	*CN ra AD*	*CN ra aMCI+AD*
AQ	0.74 (0.62, 0.83)	0.99 (0.91, 1.00)	0.81 (0.72, 0.87)
CDR-SOB *	0.87 (0.77, 0.94)	0.99 (0.92, 1.00)	0.89 (0.82, 0.94)
MMSE	0.76 (0.64, 0.85)	0.97 (0.87, 1.00)	0.80 (0.72, 0.87)
MoCA	0.71 (0.60, 0.81)	0.94 (0.82, 0.99)	0.78 (0.70, 0.85)

AUC (95% CI)

* CDR-SOB was used to make consensus diagnosis