Title: Comparing the Diagnostic Value of Four Dementia Tests in the Amnestic and Healthy Elderly

Running Title: Diagnostic Value of 4 Dementia Tests

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ABSTRACT

Objective: This study aimed to compare the diagnostic value of 4 questionnaires for the diagnosis of neurocognitive disorders (NCDs) in the elderly.

Methodology: In this project, people older than 60 years who lived in Tehran were investigated. A total of 99 literate persons were enrolled in the study, and 4 questionnaires of functional assessment staging tool (FAST), abbreviated mental test score (AMTS), mini-mental state examination (MMSE), and modified Persian test of Elderly for Assessment of Cognition and Executive function (PEACE) were completed for them. They were then referred to a neuropsychiatrist, and the status of their cognition and neurobehavior was determined. The specialists were blinded to the results of the tests.

Findings: Of the 99 participants studied, 39 were healthy, 8 had mild Alzheimer’s disease, 38 had amnesic MCI, 5 had secondary dementia, and 9 had mixed vascular dementia and Alzheimer’s disease. The area under the ROC curve for distinguishing the healthy group from the rest of the population was 0.692, 0.629, 0.734, and 0.751 for the FAST, AMTS, MMSE, and NBCSS questionnaires, respectively.

Conclusion: MMSE and NBCSS tests had better diagnostic power than the other two tests to distinguish the healthy group from the rest of the population.

Keywords: Alzheimer’s disease; Diagnosis; Mini-mental state examination; Abbreviated mental test score; Functional assessment staging tool.
Introduction

Alzheimer’s disease (AD) has multiple etiologies, which affect memory, cognitive abilities, and behavior, posing problems to the patients. Some of these problems are connected to driving ability, financial management ability, self-care ability, and independence\(^1\). AD can deeply affect the patient and their job, as well as their family, community, and society \(^2\).

The global prevalence of AD is on the rise, thereby necessitating active medical and social interventions and this demands more research on the elderly people\(^3,4\). Approximately, 47 million people worldwide were living with AD in 2015 which are estimated to reach 75 million by 2030 and 132 million by 2050\(^5\). A recent study estimated that there will be nearly 9.9 million new cases of dementia each year worldwide\(^4\).

The timely diagnosis of AD contributes to the provision of appropriate counseling, healthcare, and caregiving services\(^6-8\). Clinicians use various instruments to screen cognitive impairments. Despite their limitations, such as limited sensitivity to initial stages of cognitive impairment, these tests have been widely used in scientific areas and clinical studies\(^9,10\). The Mini-Mental State Examination (MMSE) is of the most widely used screening tests for the evaluation of cognitive impairments in the elderly\(^11\).

There is a substantial difference between some researchers, journals, a larger community of research physicians and physicians in screening healthy populations to predict the premature incidence of dementia and AD\(^12-15\). Here, premature refers to scenarios under which neither the patients nor their caregivers do not diagnose the symptoms, prove them, or recognize the need for clinical examination. The mild cognitive impairment refers to a transition state between the normal cognition of AD\(^16,17\). Nevertheless, the majority of screening tests can make only two-fold discriminations between normal cognition and AD, or between normal cognition and cognitive dysfunction.
There is no comprehensive screening test to evaluate other risk factors of AD, such as comorbidities, brain injury, and depression. Therefore, the screening programs should first review the current instruments to select the best one for wide utilization.

This study investigated four screening tests to find the best one as the first level of the screening process for AD.

METHODS

Participants

Ninety-nine people, including 42 men and 57 women, with a mean age of 69.8±7.4 years old, participated in the present study. The participants were selected from those who volunteered in a public announcement in Tehran. They had normal or normalized visual acuity, as well as sufficient hearing ability. There was no indication of psychiatric disorders irrelevant to their diagnosed disease. All participants completed the Geriatric Depression Scale (GDS)\textsuperscript{18}. The patients with symptoms of depression, GDS>5, were excluded from the study. All participants signed written informed consent.

Instruments

Four different instruments were used in this study, namely the Mini-Mental State Examination (MMSE)\textsuperscript{19}, Functional Assessment Staging Test (FAST)\textsuperscript{20}, abbreviated mental test score (AMTS)\textsuperscript{21}, and modified Persian test of Elderly for Assessment of Cognition and Executive function (PEACE)\textsuperscript{22}.

Gold Standard

All patients were examined by a neurologist and a psychiatrist. The specialists divided the participants into five groups (healthy, mild AD, amnesic mild cognitive impairment (MCI), secondary dementia (defined as a form of dementia that develops as a peripheral condition to
a pre-existing mental illness or physical condition), and mixed dementia (changes representing more than one type of dementia occur simultaneously in the brain, like vascular dementia and Alzheimer’s disease) using data from magnetic resonance imaging (MRI) results, medical examination, and interview.

**Statistical Analysis**

Data analysis was done with SPSS version 23 (IBM, USA). The significance level for all statistical tests was set at $p<0.05$. The Chi-square test was used to distinguish the groups in terms of the distribution of qualitative variables; in addition, the one-way ANOVA was employed to find between-group differences in quantitative variables. The Bonferroni posthoc test was utilized to evaluate the between-group differences. The Receiver operating characteristic (ROC) curves were created to illustrate specific characteristics of screening tests in terms of sensitivity in the classification of healthy people and patients with mild cognitive impairment, caused by dementia (healthy people versus patients with premature memory and cognitive impairment because of AD).
Results

In this study and from 99 literate participants, 39 patients were healthy, 8 patients had mild AD, 38 patients were with amnesic MCI, 5 patients had secondary dementia, and 9 patients suffered from mixed dementia. Table-1 presents a comparison between the five groups in terms of demographic variables and other characteristics. Table-2 presents a comparison between the five groups in terms of screening test scores. Table-3 presents a comparison of the area under the ROC curve between different groups and tests.

Discussion

The rapid and simple cognitive screening should be the first step in the assessment of the elderly susceptible to cognitive impairment. There are scant studies into the performance of these tests in diagnosing mild cognitive impairment. A systematic study reported a sensitivity of 88.3% and specificity of 86.2% for MMSE at the cutoff points of 23.24 or 25.24 for AD diagnosis. A meta-analytical of very heterogeneous studies reported the sensitivity of 81% (95% CI 78% to 84%) and specificity of 89% (95% CI 87% to 91%) for MMSE at the cutoff points of 23 or 24 for AD diagnosis; in addition, a sensitivity of 62% (95% CI 52% to 71%) and specificity of 87% (95% CI 80% to 92%) were reported for the diagnosis of mild cognitive impairment.

This study intended to determine a suitable screening test to distinguish between healthy people and patients with cognitive problems in a large population aged over 60 years old. As a result, the area under the ROC curve was selected for making the comparison.

In this study, the subjects were people diagnosed as healthy, or with mild AD, amnesic MCI, secondary dementia, or mixed dementia. The four tests used in the current study showed their ability to distinguish between these diagnoses. The lowest and best scores were obtained by
the AMTS and modified PEACE tests, respectively. The FAST test had moderate results and MMSE showed correct results in some cases and incorrect results in some other cases.

The tests acted best in distinguishing between the healthy people and individuals with amnesic MCI. Test results were more similar in amnesic MCI and healthy groups than other groups, thereby making it difficult to distinguish between the two former groups. The MMSE and, specifically, the modified PEACE tests produced different mean scores in the healthy and amnesic MCI groups.

Finally, the modified PEACE and MMSE performed best in distinguishing the healthy people from the patients, showing their broad screening applicability.

In a systematic review, various dementia screening tools were reviewed to find out which of them is the most suitable instrument in detecting dementia. Based on the findings of this review, the General Practitioner Assessment of Cognition (GPCOG), Mini-Cog, and Memory Impairment Screen (MIS) were chosen as the most suitable instruments for detecting dementia in the elderly in routine clinical care as they were reliable and easy to utilize. Another review showed that MMSE is the most frequently used instruments to evaluate cognitive impairment in clinical studies. Although other tests showed acceptable results in detecting dementia, the evidence regarding their use and reproducibility in primary health care is insufficient. On the contrary, another review showed that despite a high specificity, MMSE has a low sensitivity in comparison with memory section of the Cambridge Cognitive Examination (CAMCOG), Cognitive Capacity Screening Examination (CCSE), Chinese Abbreviated Mild Cognitive Impairment Test (CAMCI), and the Addenbrooke’s Cognitive Examination (ACE) or ACE-Revised (ACE-R). PEACE test has also proved to be a valid screening tool for dementia, particularly in low-middle income countries with high rates of illiteracy.
Study limitations

This study was performed in a single referral center and the results may not be generalized to the public. The small sample size of the study was the other limitation of our study. Moreover, exclusion of the illiterate individuals from this study reduces its generalizability.

Conclusion

In the present study, we found that NBCSS and MMSE performed best in distinguishing the healthy people from the patients, showing their applicability in screening programs. Further studies are required to determine the applicability of every individual test in detecting dementia in the elderly population.
References


**Table-1:** Baseline characteristics of the study groups based on their cognitive status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Mild AD</th>
<th>amnesic MCI</th>
<th>secondary dementia</th>
<th>mixed dementia</th>
<th>Healthy</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, year</td>
<td>76.1(5.8)</td>
<td>69.6 (7.2)</td>
<td>71.8 (7.6)</td>
<td>77.0 (8.8)</td>
<td>66.7 (5.5)</td>
<td>&lt;0.00</td>
</tr>
<tr>
<td>Male sex, %</td>
<td>50</td>
<td>35.9</td>
<td>60</td>
<td>33.3</td>
<td>47.4</td>
<td>0.702</td>
</tr>
<tr>
<td>Years of education</td>
<td>9.3 (4.7)</td>
<td>12.1 (5.2)</td>
<td>11.2 (7.7)</td>
<td>8.1 (4.9)</td>
<td>12.4 (3.9)</td>
<td>0.089</td>
</tr>
<tr>
<td>Married individuals, %</td>
<td>42.9</td>
<td>74.4</td>
<td>60</td>
<td>77.8</td>
<td>94.7</td>
<td>0.011</td>
</tr>
<tr>
<td>SBP, mmHg</td>
<td>131.4 (12.2)</td>
<td>133.7 (18.8)</td>
<td>122.2 (16.7)</td>
<td>143.1 (16.0)</td>
<td>134.4 (18.5)</td>
<td>0.329</td>
</tr>
<tr>
<td>DBP, mmHg</td>
<td>68.4 (5.0)</td>
<td>74.4 (8.3)</td>
<td>66.8 (6.9)</td>
<td>82.4 (7.5)</td>
<td>76 (9.2)</td>
<td>0.003</td>
</tr>
<tr>
<td>FBS, mg/dl</td>
<td>100.4 (11.0)</td>
<td>101.8 (20.2)</td>
<td>89.6 (7.0)</td>
<td>112.9 (47.1)</td>
<td>103.5 (19.2)</td>
<td>0.454</td>
</tr>
<tr>
<td>Family history of Alzheimer, %</td>
<td>12.5</td>
<td>28.2</td>
<td>20</td>
<td>11.1</td>
<td>31.6</td>
<td>0.63</td>
</tr>
<tr>
<td>Family history of Down syndrome, %</td>
<td>0</td>
<td>5.1</td>
<td>0</td>
<td>0</td>
<td>7.9</td>
<td>0.77</td>
</tr>
<tr>
<td>Family history of Parkinson, %</td>
<td>0</td>
<td>12.8</td>
<td>20</td>
<td>11.1</td>
<td>10.5</td>
<td>0.822</td>
</tr>
<tr>
<td>Family history of depression, %</td>
<td>0</td>
<td>7.7</td>
<td>40</td>
<td>11.1</td>
<td>15.8</td>
<td>0.202</td>
</tr>
<tr>
<td>Family history of seizure, %</td>
<td>0</td>
<td>10.3</td>
<td>40</td>
<td>0</td>
<td>5.3</td>
<td>0.061</td>
</tr>
<tr>
<td>GDS score</td>
<td>2.25 (1.91)</td>
<td>1.74 (1.45)</td>
<td>2.80 (1.64)</td>
<td>1.11 (1.45)</td>
<td>1.68 (1.54)</td>
<td>0.313</td>
</tr>
</tbody>
</table>

AD: Alzheimer's disease; DBP: Diastolic blood pressure; FBS: Fasting blood sugar; GDS: Geriatric depression scale; MCI: Mild cognitive impairment; SBP: Systolic blood pressure.

* Continuous variables are shown as mean (standard deviation) while categorical variables are shown as frequency (percentage).
† P<0.05 was considered as statistically significant.
**Table-2:** Comparing the cognitive test results between the study groups

<table>
<thead>
<tr>
<th>Characteristic*</th>
<th>Mild AD</th>
<th>amnesic MCI</th>
<th>secondary dementia</th>
<th>mixed dementia</th>
<th>Healthy</th>
<th>P-value †</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST score</td>
<td>2.37 (0.94)</td>
<td>2.72 (0.97)</td>
<td>3.63 (0.52)</td>
<td>3.40 (1.67)</td>
<td>4.33 (1.12)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>AMTS score</td>
<td>9.34 (0.88)</td>
<td>9.05 (1.5)</td>
<td>7.88 (0.99)</td>
<td>8.00 (1.58)</td>
<td>7.89 (2.71)</td>
<td>0.008</td>
</tr>
<tr>
<td>MMSE score</td>
<td>28.24 (2.1)</td>
<td>26.69 (2.82)</td>
<td>23.13 (3.4)</td>
<td>23.80</td>
<td>24.22</td>
<td>&lt;0.0</td>
</tr>
<tr>
<td>NBCSS score</td>
<td>45.55 (8.83)</td>
<td>40.67 (11.31)</td>
<td>30.63 (7.01)</td>
<td>30.60 (5.87)</td>
<td>25.44</td>
<td>&lt;0.0</td>
</tr>
</tbody>
</table>

AD: Alzheimer's disease; AMTS: Abbreviated Mental Test score; FAST: Functional Assessment Staging Test; MMSE: Mini-Mental State Examination; MCI: Mild cognitive impairment

* continuous variables are shown as mean (standard deviation)

† P<0.05 was considered as statistically significant.
<table>
<thead>
<tr>
<th>Test</th>
<th>The healthy group as compared to other people</th>
<th>Healthy and amnesic groups MCI as compared to amnesic MCI with Amnestic group</th>
<th>other people</th>
</tr>
</thead>
<tbody>
<tr>
<td>FAST</td>
<td>0.692</td>
<td>0.8</td>
<td>0.611</td>
</tr>
<tr>
<td>AMTS</td>
<td>0.629</td>
<td>0.548</td>
<td>0.732</td>
</tr>
<tr>
<td>MMSE</td>
<td>0.734</td>
<td>0.676</td>
<td>0.721</td>
</tr>
<tr>
<td>NBCSS</td>
<td>0.751</td>
<td>0.658</td>
<td>0.814</td>
</tr>
</tbody>
</table>

AMTS: ; FAST: Functional Assessment Staging Test; MMSE: Mini-Mental State Examination; MCI: Mild cognitive impairment