A preliminary study of the Six-Item Screener in detecting cognitive impairment

Mei-Rong CHEN¹, Qi-Hao GUO², Xin-Yi CAO³, Zhen HONG², Xiao-Hong LIU¹

¹Department of Neurology, People's Hospital of Putuo District, Shanghai 200060, China

²Department of Neurology, Huashan Hospital, Fudan University, Shanghai 200040, China

³Shanghai Mental Health Center, Shanghai Jiao Tong University School of Medicine, Shanghai 200030, China

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Abstract: Objective The present retrospective study was to explore the clinical value of Six-Item Screener (SIS), which is constituted by 6 items from mini-mental status examination (MMSE), to identify cognitive impairment. **Methods** A total number of 1976 patients aged over 50 years, from the Memory Clinic of Huashan Hospital were employed in a battery of neuropsychological tests including MMSE. Subjects with severe conditions, unable to cooperate, or having been previously enrolled, were excluded from this study. The employed subjects were divided into 3 groups: subjective memory complaints (SMCs) (475 cases), patients with mild cognitive impairment (MCI) (440 cases), and patients with Alzheimer's disease (AD) (1061 cases, including 555 mild, 339 moderate, and 167 severe). A total score of MMSE and a score of SIS composed of date, month, year, three-word delayed recall from MMSE were calculated. Data were analyzed based on educational background. **Results** The cut-off of SIS score was ≤ 2 for illiterate, ≤ 3 for elementary, and ≤ 4 for junior high school or above. The sensitivity and specificity of SIS for detecting mild AD were 88.5% and 78.3%, respectively, with an overall accuracy of 83.8%, while for detecting MCI, the sensitivity and specificity were 34.3% and 90.1%, respectively, with an overall accuracy of 63.2%. **Conclusion** SIS is an effective and reliable instrument for dementia detection in outpatient department. However, it has limited value for MCI identification.

Keywords: cognitive impairment; dementia; Six-Item Screener; mini-mental status examination

1 Introduction

Alzheimer's disease (AD) is the most dominant type of dementia, which is a common chronic illness syndrome characterized by a gradual cognitive decline, and it affects daily life and social functions. With the increase in the number of the elderly and the improvement in living conditions,

dementia, especially AD, has become more prevalent in China. In outpatient clinic or emergency department, early detection of cognitive impairment in a rapid and effective way is especially important. Although neuropsychological tests are useful for recognizing cognitive impairment, they are complex and time-consuming. Even mini-mental status examination (MMSE), the most popular method in the world, costs 10-15 min, and calculating the score on scripts is not brief enough for quick detection^[1]. The present study was aimed to explore the validity of Six-Item Screener (SIS) for quick clinical detection of cognitive impairment in China.

Corresponding author: Qi-Hao GUO
Tel: +86-21-52888162; Fax: +86-21-62481930
E-mail: dr.guoqihao@126.com
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2 Materials and methods

2.1 Subjects A total number of 1976 subjects (862 male and 1114 female) aged (71.87 ± 8.71) years (63.16-80.58 years), from Memory Clinic of Huashan Hospital during April 2003 to April 2008, were employed in this study. They were divided into 3 groups: subjective memory complaints (SMCs) with subjective memory or other cognitive complaints but showing no objective cognitive impairment (475 cases), patients with mild cognitive impairment (MCI) (440 cases), and patients with AD (1061 cases, including 555 mild, 339 moderate, and 167 severe).

The educational level was classified into illiterate (142 cases, 7.2%), literacy class or elementary school level (educated for 1-6 years) (324 cases, 16.4%), and junior high school level or above (1510 cases, 76.3%). There was no significant difference ($P > 0.05$) in age, sex or educational level among SMC, MCI and AD groups.

2.2 Recruitment criteria All the subjects finished a medical workup consisting of a detailed medical history, a thorough physical examination, MMSE, evaluations of anxiety, depression and other mental disorders, and neuroimaging (computed tomography or magnetic resonance imaging). Besides, most of them took laboratory tests in hematological vitamin B₁₂, folic acid (FA), and thyroid function, together with a rapid plasma reagin (RPR) circle card test, Treponema Pallidum Particle Assay (TP-PA), and genotyping of apolipoprotein E (APOE). Patients ≥ 50 years old willing to finish the tests were recruited. None of the recruited subjects showed any neurological conditions, such as cerebrovascular disease, encephalitis, brain tumor or other severe organic brain disease, or anxiety and depression that could cause cognitive impairment. Subjects with a higher educational level (educated for over 6 years) and a MMSE score ≥ 20 were introduced to a battery of neuropsychological tests.

2.3 Diagnostic criteria for MCI Based on the Diagnostic Criteria of the International Working Group on MCI^[2], MCI was identified according to the following operational criteria: (1) Patients show subjective memory or other cognitive complaints; (2) Neuropsychological tests reveal objective evidence of cognitive decline, with a score ≤ -1.5 SD below age- and education-adjusted norms; (3) Patients show pre-

served basic activity of daily life (ADL) and subtle deficit of instrumental ADL; (4) Non-AD, not meeting Diagnostic and Statistical Manual of Mental Disorders (DSM-IV)^[3] diagnostic criteria for dementia. Diagnostic criteria for AD refer to DSM-IV. The subjects meeting all the above criteria were diagnosed with MCI.

2.4 Study methods All the patients were scanned by Chinese version of MMSE^[4] and the subjects with relatively good performance on MMSE were introduced to a battery of neuropsychological tests, including Auditory Verbal Learning Test (AVLT), Logical Memory Test (LM), Rey-Osterrieth Complex Figure Test (CFT), Verbal Fluency Test (VFT), Boston Naming Test (BNT), Clock Drawing Test (CDT), Trail Making Test A and B (TMT A & B), Stroop Colour-Word Test (SCWT), Clinical Dementia Rating scale, *etc.* Then the correct number of items (year, month, date, three-item recall) from MMSE was calculated as the score of SIS.

2.5 Data analysis Data were analyzed by SPSS for windows 13.0 version through Chi-square test, Variance test and correlation analysis.

3 Results

3.1 Correlation of SIS score with age, sex, educational level, three objective recall, and the total score of MMSE For the SMC group, SIS score was positively correlated with the educational level ($r=0.092$, $P \leq 0.05$) and the MMSE total score ($r=0.461$, $P \leq 0.05$), but negatively with age ($r=-0.181$, $P \leq 0.01$). Besides, there was no significant difference between male and female groups.

For all the subjects, the score of year, month, date, or three-item recall was significantly correlated with SIS total score ($r=0.749$, 0.738 , 0.707 and 0.871 , respectively; $P \leq 0.01$).

3.2 There are significant differences in the total scores of SIS and MMSE among the 5 groups As shown in Table 1, there were significant differences in the total scores of SIS and MMSE among normal, MCI, mild AD, moderate AD and severe AD groups. Since education may influence one's cognitive performance, the Receiver Operating Curves (ROCs) of MMSE and SIS were constructed according to different levels of education (Table 2). For each educational level, the appropriate cut-off scores were acquired for detecting AD or

Table 1. Comparison of SIS and MMSE scores among normal, MCI, mild AD, moderate AD and severe AD groups

Variable	Normal <i>n</i> =475	MCI <i>n</i> =440	Mild AD <i>n</i> =555	Moderate AD <i>n</i> =339	Severe AD <i>n</i> =167	F(P)	multiple comparison (<i>P</i> value)
SIS score	5.41±0.80	4.63±1.11	2.75±1.51	1.22±1.24	0.32±0.63	1096.53**	0.000**
MMSE score	27.83±2.02	26.04±2.28	19.50±2.91	12.03±2.57	4.55±2.34	4345.12**	0.000**

***P*<0.01 among the 5 groups.

Table 2. Cut-off scores for SIS and MMSE to detect mild AD

Variable	Cut-off scores	Sensitivity	Specificity
SIS	Illiterate ≤ 2	83.6%	95.0%
	Elementary ≤ 3	85.3%	89.4%
	Junior high school or above ≤ 4	90.7%	77.1%
	≤ Cut-off	88.5%	78.3%
MMSE	Illiterate ≤ 17	94.3%	95.0%
	Elementary school ≤ 21	96.9%	90.9%
	Junior high school or above ≤ 24	96.9%	98.4%
	≤ Cut-off	96.6%	97.8%

Table 3. Cut-off score for SIS to detect MCI

	MCI group (<i>n</i>)	SMC group (<i>n</i>)	Total number
≤ Cut-off (MCI positive)	151	47	198
> Cut-off (MCI negative)	289	426	715
Total	440	473*	913

Sensitivity: 151/440=34.3%, Specificity: 426/473=90.1%, Accuracy: (151+426)/913=63.2%. *Two SMC subjects without exact education information were excluded when analyzed according to the educational level.

MCI with different effectiveness. The sensitivity and specificity of SIS to detect AD were 88.5% and 78.3%, respectively, with 83.8% diagnosis accuracy (Table 2), while the sensitivity and specificity of SIS to detect MCI were 34.3% and 90.1%, respectively, with 63.2% diagnosis accuracy (Table 3). Besides, the sensitivity, specificity and accuracy of AD detection by SIS were lower than that by MMSE. The area under the ROC of SIS for AD detection was 0.921 (*P*=0.000, 95%CI=0.907-0.935) in the group of junior high school level or above; 0.932 (*P*=0.000, 95%CI=0.903-0.961) in the group of elementary school educational level, and 0.932 (*P*=

0.000, 95%CI=0.878-0.986) in the group of illiterate. The areas under the ROCs of SIS and MMSE for detecting MCI were 0.706 (*P*=0.000, 95%CI=0.671-0.741) and 0.753 (*P*=0.000, 95%CI=0.720-0.784), respectively.

4 Discussion

The SIS method has several advantages. Firstly, it is a simple and time-saving tool that costs 1-2 min. SIS is paper- and tool-free, and its scoring can be easily performed by a simple summation of right items. Secondly, patients can complete the test independently of their function of spatial structure and praxis. These characteristics make SIS a valuable tool for preliminary identification of cognitive impairment during the triage process in large sample studies or during the emergency department visit. SIS can be conducted by telephone or face-to-face interview^[1]. Although the deficits in episodic memory predominate in early stages of AD^[5], the deficit in orientation to place usually occurs later than the deficit in orientation to time. Thus the SIS composed of orientation to time and the 3-word recall task was selected for early detection of MCI or AD. Carcaillon has also reported that subscores of orientation to time and the 3-word recall task are well correlated with Free and Cued Selective Reminding Test (FCSRT) scores that reflect episodic memory function, and the summation of these 2 subscores is more closely associated with dementia and AD than is the total MMSE score^[6].

Since well-educated patients with the MMSE score in the normal range may actually have significant cognitive impairment or even dementia^[7] and the sample used here was very big, we analyzed the ROC according to different educational levels. As a result, SIS scores of 2, 3 and 4 fit the levels of illiterate, elementary, and junior high school or above,

respectively, with the total sensitivity of 88.5%, specificity of 78.3% and accuracy of 83.8% for detecting AD. Callahan^[1] has also reported that using a cut-off of three or more errors, the sensitivity and specificity of SIS to detect dementia are 88.7% and 88.0%, respectively. In the present study, SIS performed much worse as a tool for MCI detection than for AD detection, with the accuracy of 63.2%, and the sensitivity and specificity were 34.3% and 90.1%, respectively. Besides, the sensitivity and specificity of SIS for detecting cognitive impairment (defined by MMSE score ≤ 23) that were revealed by a multicenter study of Wilber were smaller than those reported by the previous research in 2005 (63% vs 94%, and 81% vs 86%)^[8,9]. The difference between our research and theirs may be attributed to the sample source and the criteria for cognitive impairment. In the present study, the subjects were recruited from memory clinic, and the diagnosis was based upon both clinic and a battery of neuropsychological tests. Callahan^[1] has demonstrated that although SIS performs worse than MMSE when screening dementia in a population with a high incidence, its diagnostic properties are comparable to the full MMSE in community or in primary hospital.

Klein LE^[10] has reported that as an initial screener for cognitive impairment, three-item recall has excellent sensitivity (97%) but poor specificity (43%), which makes it useful as an initial screener to identify those subjects without cognitive impairment. Although Lachs *et al.* have suggested using three-item recall as an initial screener to detect cognitive impairment followed by MMSE for those patients unable to recall all 3 items^[11], Kuslansky reports that three-item recall does not have excellent sensitivity (65%) or specificity (85%) for detecting AD^[12]. Thus, three-item recall, combined with orientation to time, can be used initially in outpatient clinic or emergency department to ensure the accuracy of diagnosis. Galasko has revealed that MMSE and the score summing tests of recall and orientation for place have similar sensitivities^[13]. Besides, adding a verbal fluency test to the MMSE could reduce the error rate by improving the accuracy of diagnosis of patients with AD scoring in the nondemented range. Scanlan *et al.* combined scores on the three-item recall task and the clock drawing task (CDT-CERAD version)

to create an optimal algorithm^[14]. A brief tool named quick cognitive screening test (QCST) for detecting MCI has been conducted in Chinese population, and has shown good sensitivity and specificity for MCI detection, which warrants its further clinical application. However, it may still take 15-30 min^[15]. Therefore, it is hard to find a perfect screener for detecting cognitive impairment in the outpatient clinic or emergency department.

In conclusion, the present study suggests that SIS is an efficient and reliable method for fast identifying AD, especially moderate or severe AD, but its value of identifying MCI is limited.

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六分法快速识别认知损害的初步研究

陈美蓉¹, 郭起浩², 曹歆轶³, 洪震², 刘晓红¹

¹上海市普陀区人民医院神经内科, 上海 200060

²上海市复旦大学附属华山医院神经内科, 上海 200040

³上海市交通大学医学院附属精神卫生中心, 上海 200030

摘要: **目的** 评价简易精神状态检查表(mini-mental status examination, MMSE)中时间定向与词语延迟回忆得分组成的六分法(Six-Item Screener, SIS)在识别认知损害中的价值。**方法** 在华山医院神经内科记忆障碍门诊部的1976例就诊者中,根据轻度认知损害(mild cognitive impairment, MCI)和痴呆的诊断标准分为认知功能正常的主观抱怨者(475例)、MCI患者(440例)和阿尔茨海默病(Alzheimer's disease, AD)患者(共1061例,其中轻度AD 555例、中度AD 339例、重度AD 167例)。所有就诊者完成包括MMSE在内的全套神经心理测验。分析MMSE中年份、月份、日期以及三个词语延迟回忆(简称三词)的总得分(共6分)在区分不同程度的认知障碍中的作用。**结果** SIS总分以文盲组≤2分、小学组≤3分、初中及以上组≤4分作为划界分,其识别轻度AD的敏感性为88.5%、特异性为78.3%、准确性为83.8%,识别MCI的敏感性为34.3%、特异性为90.1%、准确性为63.2%。**结论** 六分法对于门诊快速识别痴呆具有一定的价值,但不适用于识别MCI。

关键词: 认知损害; 痴呆; 六分法; 简易精神状态检查表