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ORIGINAL RESEARCH PAPER

Screening for cognitive impairment with the montreal cognitive assessment at six months after stroke and transient ischemic attack

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ABSTRACT

Objective: Cognitive impairment usually occurs in the acute phase after stroke, but most stroke survivors experience some form of long-term cognitive deficit. The aim of this study was to establish the cutoff point of the Montreal Cognitive Assessment (MoCA-Beijing) in screening for cognitive impairment (CI) at 6 months of ischemic stroke or transient ischemic attack (TIA).

Methods: A total of 301 stroke patients and 15 TIA patients were recruited. Patients were assessed at six months by the MoCA-Beijing and a formal neuropsychological battery. The 1.5 SD below the level of the norm on several tests indicated cognitive impairment (CI).

Results: Most stroke and TIA patients were in their 60s (61.23 ± 10.60 years old). The optimal cutoff point for MoCA-Beijing in discriminating patients with CI from those with no cognitive impairment (NCI) was 24/25 (sensitivity 63.28%, specificity 71.22%, PPV = 73.68%, NPV = 60.37%, classification accuracy = 66.72%). The predominant cognitive deficits were visuospatial ability (84.85%), and then attention/executive function (79.27%).

Conclusion: The MoCA-Beijing cutoff score for differentiating CI from NCI after stroke and TIA at six months was at 24/25, and it is important for routine clinical practice.

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KEYWORDS
Mild stroke; transient ischemic attack; cognitive impairment; montreal cognitive assessment-Beijing

Introduction

Cognitive impairment is a common complication after ischemic stroke and can affect all cognitive functions. It is observed in 21% to 70% of stroke survivors because of different evaluation time. China bears the biggest stroke burden in the world [1]. The age-standardized prevalence of stroke is 1114.8/100 000 people [2]. The prevalence of TIA is reported to be 2.27% [3]. TIA indicates a reversible disorder, but persistent cognitive impairment is found in nearly 30% of patients at 3 months. Post-stroke cognitive impairment (PSCI) carries a poor prognosis. It is a hidden cost if is not specifically managed. Neuropsychological testing is one of the most important diagnostic procedures for PSCI, which is used to determine the extent and type of cognitive impairment. However, neuropsychological testing is time-losing. Therefore, a screening test is required to improve the early recognition of PSCI.

The widely used screening tool is Mini-Mental State Examination (MMSE), which is more sensitive to detect Alzheimer's type of cognitive impairment with early language and memory dysfunction but has a low sensitivity for vascular cognitive impairment (VCI) [4–6] and ceiling effect for detecting VCI patients [7]. In contrast, MoCA includes executive function and attention tests (among many different cognitive domains) and has been recommended for screening for CI in patients with stroke or TIA [8]. Studies have demonstrated that MoCA was more suitable for detecting PSCI [9]. The Beijing version of the MoCA (MoCA-Beijing) is a Chinese version of MoCA that is modified from the original MoCA (English version) by the research team based on mainland cultural, linguistic, and population characteristics.

Most studies of cognitive screening are only conducted at acute or subacute phase after stroke. As we all known, incident delirium is common in acute stroke [10] and will impact on cognition. There are no big data on MoCA-Beijing screening for CI in Chinese stroke patients at six months. Therefore, the objective of this study is to validate the MoCA-Beijing determined by a 'gold' standard neuropsychological evaluation in stroke patients at six months.

Methods

Participants

Patients are from The Third China National Stroke Registry (CNSR-III) database, which consecutively recruits patients with ischemic stroke or TIA between

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August 2015 and March 2018 from 201 hospitals that covers 22 provinces and four municipalities in China. Among the 15,166 stroke patients enrolled in CNSR-III, a total of 2625 patients are recruited in the subgroup of impairment of cognition and sleep quality (ICONS) from 40 hospitals. In ICONS subgroup, 316 patients from 25 hospitals perform the MoCA-Beijing and the neuropsychological test battery at six months after ischemic stroke or TIA.

The inclusion criteria for patients are age of 18 years or older, with an ischemic stroke or TIA within 7 days. Patients' stroke/TIA is diagnosed according to World Health Organization criteria (acute onset of neurological deficit, persisting for >24 hours in case of stroke, or for <24 hours in case of TIA), and confirmed with brain CT or MRI. All patients in this study were asked to complete the MRI examinations during hospitalization. If the patient has evidence of associated acute focal infarction on imaging, he or she will be diagnosed as a stroke rather than a TIA, even if neurological deficit persisting for <24 hours [11,12]. During hospitalization, all stroke patients are invited to follow-up at the stroke clinic after their discharge. Patients who have stroke mimics (i.e., seizures, migraine), illiteracy, history of dementia, aphasia, hemispatial neglect, disturbance of consciousness or limb dyskinesia and any major mental conditions that may impede cognitive assessments are excluded. The 316 consecutive stroke patients comprise 301 patients with acute ischemic stroke and 15 patients with TIA. Patients with a severe cognitive disorder before stroke (diagnosed by the Informant Questionnaire on Cognitive decline in the Elderly (IQCODE)) were excluded.

This database was approved by the ethics committee of Beijing Tiantan Hospital. Written informed consent was obtained from all the patients or their representatives before data collection.

Procedure

Demographics and clinical profile

All patients were examined physically and neuropsychiatrically at baseline. Sociodemographic information including gender, age, educational background, cardiovascular risk factors as well as medical history, was collected. Stroke severity and disability measures by National Institutes of Health Stroke Scales (NIHSS) and the modified Rankin Scale (mRS) were collected within 24 hours after admission. MRI was performed at baseline (hospitalization). T1-weighted imaging, axial T2-weighted, fluid-attenuated inversion recovery sequences, diffusion-weighted imaging and 3-dimensional time-of-flight magnetic resonance angiography (MRA) were administrated to all patients.

Neuropsychological assessments

Neuropsychological assessments were administered by trained neurologists and were completed at six months after the ischemic stroke/TIA. A comprehensive battery of neuropsychological tests was designed to include tests of all cognitive domains, as recommended by the NINDS-CSN harmonization standards [8] (1) language using the Animal Fluency Test (AFT) [13] and the Boston Naming Test (BNT, 15-item) [14] (2) visuospatial ability using the Rey-Osterrieth Complex Figure Test (RCFT) copy; (3) memory using the Auditory Verbal Learning Test; (4) attention/executive function using the Trail Making Test (TMT)-B [15], Stroop Color-Word Test (CWT)-Color time and Symbol Digital Modalities Test (SDMT).

The original MoCA is a 30-point scale with seven cognitive subtests (i.e. visuospatial/executive function, naming, attention, abstraction, language, delayed recall, and orientation). The MoCA-Beijing was developed with the following modifications: (1) visuospatial/executive function: Chinese characters (甲/乙/丙/丁/戊) are used instead of the English alphabet letters which have the same sequential meaning as 'A/B/C/D/E'; (2) attention: English alphabet letters are replaced by numbers; (3) language: in the verbal fluency test, the phonemic fluency test that needs subjects to make words beginning with the letter F is taken placed by the animal fluency test. If education is <12 years, we add 1 point to the total score [16].

The MoCA-Beijing and neuropsychological tests were conducted at the same time, and the neuropsychological tests are completed by trained neurologists blinded to the MoCA scores.

Functional assessment

Functional status was assessed by the Katz basic activities of daily living (basic ADL) scale [17], with 6 basic items, and Lawton and Brody instrumental activities of daily living (instrumental ADL) scale [18], with 8 instrumental items.

Diagnosis of VCI

Cognitive impairment was made according to Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-4) criteria. PSCI was defined as a score of 1.5 standard deviations below the established norms of neuropsychological tests [19]. The norms used were based on a normative study of healthy cognitively normal community-dwelling older adults in China [15]. A patient with scores of all the individual neuropsychological tests within the normal range was considered to have no cognitive impairment (NCI).

Statistical analyses

All analyses were conducted with SAS 9.4 (SAS Institute Inc, Cary, NC). The discriminatory ability

of the MoCA-Beijing in detecting CI was analyzed using the receiver operating characteristic (ROC) curve. Continuous variables, if they were normally distributed, were presented as means ± standard deviations and compared by Student t-test. Continuous variables, if they were not normally distributed, were presented as median (quartile) and compared by nonparametric test. Pearson's χ^2 test was used to determine the group differences for gender, educational level as well as for each of the vascular risk factors. A two-sided p value <0.05 was considered to be statistically significant.

Results

Demographic and clinical characteristics

The average age of stroke patients is 61.12 ± 10.59 years with mostly men (70.25%). The median of NIHSS score in recruited patients is 2.00 point [interquartile range (IQR):3.00 point (s)]. Amongst the stroke patients, approximately half have atherothrombotic infarction (n = 194/301, 65.45%), followed by small-vessel occlusion (n = 91/301, 30.23%), cardiogenic embolism (n = 7/301, 2.33%), other type (n = 3/301, 1.00%) and undetermined (n = 6/301, 1.99%). More than half of the sample (55.48%) have cognitive impairment as determined by the neuropsychological tests (Table 1).

Demographic information shows that the NCI and CI groups are similar except for age, educational level, prevalence of current smoking, heavy drinker, coronary heart disease and the scores of instrumental ADL and basic ADL (Table 1). Logistic regression shows cognitive impairment is related to older age and lower education level (Table 2).

Comparison of cognitive function in different domains are presented in Table 3. The results show that all scores of MoCA-Beijing, AVLT-immediate recall, AVLT-long delayed recall, visual delayed recall, CFT, CWT-C correct, AFT, BNT and SDMT in the CI group are significantly lower than those in NCI group ($p< 0.0001$); The time for TMT-B and CWT-C in the CI group is prominently longer than that in NCI group ($p< 0.0001$) (Table 3).

Receiver operator characteristic curve analysis

A separate ROC analysis for the score of the MoCA-Beijing which includes only stroke patients with no or mild cognitive symptoms yields an AUC of 0.72 [95% CI: (0.67 ~ 0.78)] (Figure 1), suggesting that MoCA-Beijing has good ability to discriminate between impaired and nonimpaired cognitive status. The sensitivity, specificity, PPV and NPV of MoCA-Beijing for detection of cognitive impairment are provided in Table 4. The cutoff score is determined by the Youden index (calculated by sensitivity+specificity-1). Optimal cutoff points are determined using the maximum value of the Youden index. In this study, the optimal cutoff score of MoCA-Beijing≤24 is established to best discriminate CI from NCI (Table 4). The cutoff point determined using the Youden index (Table 4) provides suboptimal sensitivity (<0.7) for screening test (MoCA-Beijing) for diagnostic purposes.

Table 1. Clinical characteristics of patients with acute minor stroke or TIA within 6 months after onset.

Baseline variables	All patients n (%) n = 316	No cognitive impairment NCI n (%) n = 139	Cognitive impairment (CI) n (%) n = 177	*P* value
Gender (male, %)	222/316(70.25)	100/139 (71.94)	122/177 (68.93)	0.56
Average age (years)	61.12 ± 10.59	57.00 ± 10.76	64.36 ± 9.27	**<0.0001****
Education level				**<0.0001****
Elementary or below	82/316(25.95)	24/139 (17.27)	58/177(32.77)	
Middle school	114/316(36.08)	41/139 (29.50)	73/177(41.24)	
High school or above	111/316(35.13)	70/139(50.36)	41/177(23.16)	
Unknown	9/316(2.85)	4/139(2.88)	5/177(2.82)	
Current smoker	112/316(35.44)	61/139(43.88)	51/177(28.81)	**0.005****
Heavy drinker (>60 g/d)	18/316(5.70)	12/139(8.63)	6/177(3.39)	**0.046***
Medical History				
Diabetes	74/316(23.42)	34/139(24.46)	40/177(22.60)	0.70
Hypertension	207/316(65.51)	86/139(61.87)	121/177(68.36)	0.23
Lipid metabolism disorders	22/316(6.96)	9/139(6.47)	13/177(7.34)	0.76
Stroke History				
Cerebral infarction	57/316(18.04)	21/139(15.11)	36/177(20.34)	0.23
ICH	2/316(0.63)	1/139(0.72)	1/177(0.56)	1.00
Subarachnoid hemorrhage	1/316(0.32)	0/139(0.00)	1/177(0.56)	1.00
TIA	5/316(1.58)	2/139(1.44)	3/177(1.69)	1.00
Heart disease				
Coronary heart disease	28/316(8.86)	7/139(5.04)	21/177(11.86)	**0.034***
Atrial fibrillation	12/316(3.80)	4/139(2.88)	8/177(4.52)	0.45
Median NIHSS score (IQR)	2.00(1.00 ~ 4.00)	2.00(1.00 ~ 4.00)	3.00(1.00 ~ 5.00)	0.10
IADL	8.00(8.00–10.00)	8.00(8.00–8.00)	8.00(8.00–12.00)	**<0.001****
BADL	6.00(6.00–6.00)	6.00(6.00–6.00)	6.00(6.00–6.00)	**0.003****

Data show that the CI group has older age, lower education, higher rate of coronary heart disease and more scores of instrumental ADL and basic ADL but lower rate of current smoker and heavy drinker than NCI group.

ICH, intracerebral hemorrhage; TIA,transient ischemia attack; IADL, instrumental activities of daily living; BADL, basic activities of daily living. **: <0.01; *<0.05.

Table 2. Association of cognitive function after stroke/TIA at six months.

	Univariate	
Variable	OR(95% CI)	*P* value
Average age (years)	1.06(1.03 ~ 1.09)	**<0.001****
Education level		
Elementary or below	1(Refrence)	-
Middle school	0.92(0.48 ~ 1.78)	0.800
High school or above	0.30(0.16 ~ 0.59)	**0.0004****
Unknown	0.92(0.20 ~ 4.29)	0.920
Current smoker	0.79(0.45 ~ 1.36)	0.389
Heavy drinker (>60 g/d)	0.57(0.18 ~ 1.76)	0.327
Coronary heart disease	1.87(0.70 ~ 5.03)	0.213
IADL	1.13(0.99 ~ 1.30)	0.071
BADL	0.91(0.71 ~ 1.16)	0.431

IADL, instrumental activities of daily living; BADL, basic activities of daily living. Logistic regression is established, in which cognitive impairment is set as a dependent variable, whereas Average age, Education level, Current smoker, Heavy drinker, Coronary heart disease, IADL and BADL are set as independent variables: p < 0.01.

Characteristics of neuropsychological impairment

The predominantly impaired cognitive domain is visuospatial ability (84.85%), followed by executive function/attention (79.20%), language (34.24%) and memory (28.69%); For the memory, visual delayed-memory decline is more prevalent than verbal memory, and verbal delayed-memory (23.11%) is more impaired than verbal immediate-memory (16.67%) (Table 5).

Discussion

There is evidence -shows that secondary prevention of recurrence might reduce the heavy burden of

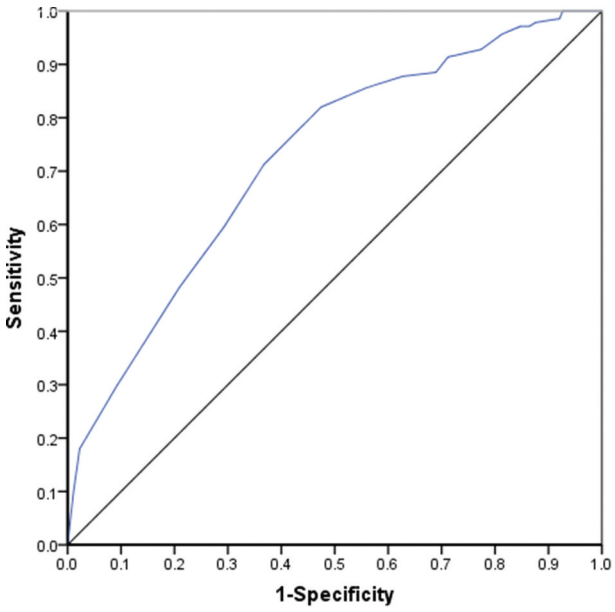

Figure 1. ROC curve.

PSCI. Therefore, early detection facilitates timely intervention, and lead to favourable outcomes. For the first time, our study is a multicentric study using the MoCA-Beijing to screen for cognitive impairment in Chinese patients with stroke or TIA at six months. The cutoff point of MoCA-Beijing at 24/25 provides favorable sensitivity (63.28%) and specificity (71.22%) (Table 4). Our data provide a useful reference point for Chinese patients at subacute stage.

Table 3. Comparison of scores of cognitive scales in two groups.

	No cognitive impairment (NCI)	Cognitive impairment (CI)	*P* value
	(n = 139)	(n = 177)	
Overall cognitive level			
MoCA-Beijing [scores, median (quartile)]	26.00 (24.00 ~ 28.00)	23.00 (19.00 ~ 26.00)	**<0.0001****
Cognitive domains			
Memory			
Verbal memory			
AVLT-immediate recall [scores, median (quartile)]	5.67 (4.67 ~ 7.33)	4.00 (3.00 ~ 5.33)	**<0.0001****
AVLT-long delayed recall [scores, median (quartile)]	6.00 (4.00 ~ 8.00)	4.00 (2.00 ~ 5.00)	**<0.0001****
Visual delayed recall			
CFT-delayed recall [scores, median (quartile)]	12.00 (5.00 ~ 20.00)	2.00 (0.00 ~ 6.00)	**<0.0001****
Visuospatial ability			
CFT [scores, median (quartile)]	28.50 (16.00 ~ 33.00)	10.00 (3.00 ~ 17.50)	**<0.0001****
Executive function/attention			
TMT-B time [seconds, median (quartile)]	118.00 (90.00 ~ 167.00)	196.00 (110.00 ~ 272.00)	**<0.0001****
CWT-C time [seconds, median (quartile)]	84.00 (61.00 ~ 105.00)	118.00 (90.00 ~ 167.00)	**<0.0001****
CWT-C correct [scores, median (quartile)]	46.00.00 (40.00 ~ 49.00)	41.00 (27.00 ~ 46.00)	**<0.0001****
SDMT(scores, mean ± SD)	33.77 ± 14.55	17.52 ± 16.52	**<0.0001****
Language			
AFT(scores, mean ± SD)	16.05 ± 4.57	11.75 ± 4.82	**<0.0001****
BNT[scores, median (quartile)]	26.00 (23.00 ~ 27.00)	21.00 (17.00 ~ 25.00)	**<0.0001****

The scores of MoCA-Beijing, AVLT-immediate recall, AVLT-long delayed recall, CFT-delayed recall, CFT, CWT-C correct, AFT, BNT and SDMT in the CI group are significantly lower than those in NCI group ($p< 0.0001$); The time for TMT-B and CWT-C in the CI group is prominently longer than that in NCI group ($p< 0.0001$).

AVLT, Auditory Verbal Learning Test; CFT, Rey-Osterrieth Complex Figure Test; TMT-B, Chinese modified version of Trail Making Test B; CWT-C, Stroop Color-Word Test-Chinese version (CWT)-Color; SDMT, Symbol Digit Modalities Test; AFT, Animal Fluency Test; BNT, Boston Naming Test.**: $p< 0.01$.

Table 4. Discriminant indices of Montreal Cognitive Assessment (MoCA)-Beijing in detecting cognitive impairment in patients with acute minor stroke and TIA within 6 months after onset.

MoCA-Beijing	Se,%	Sp,%	PPV, %	NPV, %	Correctly classified
20/21	31.07	88.49	77.46	50.20	56.32
21/22	37.29	87.77	79.52	52.36	59.49
22/23	44.07	85.61	79.59	54.59	62.34
23/24	52.54	82.01	78.81	57.58	65.51
24/25*	63.28	71.22	73.68	60.37	66.72
25/26	70.62	59.71	69.06	61.48	65.82
26/27	79.10	48.20	66.04	64.42	65.81
27/28	90.96	29.50	62.16	71.93	63.92
28/29	97.74	17.99	60.28	86.21	62.66
29/30	98.87	10.07	58.33	87.50	59.81

The Optimal cutoff score determined using the Youden index. The optimal cutoff score of MoCA-Beijing≤24 is established to best discriminate CI from NCI.

Table 5. Percentage of each impaired cognitive domain in total patients with acute minor stroke and TIA within 6 months after onset.

Cognitive domain	Percentage of patients with impaired cognitive domain (percentage %)
Global cognition	177/316(56.01)
Executive function/ attention	217/274(79.20)
Visuomotor speed	
Visuospatial ability	168/198(84.85)
Language	88/257(34.24)
Memory	70/244(28.69)
Visual delayed memory	117/231(50.65)
Verbal short memory	20/280(7.14)
Verbal delayed memory	58/250(23.2)

The MoCA-Beijing cutoff score (MoCA-Beijing≤24) in this study is lower than the commonly recommended cutoff point of 26, which may attribute to several reasons [19]. Recent studies show that using a cutoff score as high as 26 increases the risk of false positive results for those of older age and/or lower education [20]. The original MoCA study and our study recruit different patients (94 MCI or 93 AD patients vs. 316 patients with mild stroke/TIA), educational background (senior high school vs. junior high school), and different age (70s vs 60s). Another recent study [21] investigates the ability of the MoCA for screening for VCI in Chinese patients with a clinical lacunar stroke at least 3 months. The optimal sensitivity and specificity are 76.7% and 81.4%, respectively, for the detection of VCI patients with MoCA cutoff points of ≤24 in that study. These results are comparable to ours. The two studies have common clinical settings: patients with stable cerebral vascular diseases (TIA or stroke vs. subcortical ischemic vascular disease (SIVD)) and a comparable educational level (Secondary Education), they adopt similar neuropsychological tests and criteria (below 1.5 SD). Xu et al. recruit SIVD subjects, which include the same subcortical type, in contrast with both cortical and subcortical types in our study [22]. Pendlebury et al. investigate the capability of the MoCA for detecting mild cognitive impairment in patients at least 1 year after TIA and stroke [21]. They find that MoCA cutoff points of ≤24 have optimal sensitivity (77%) and specificity (83%) in screening for VCI patients in that study. Additionally, one meta-analysis reports that MoCA at its conventional cutoff point (<26/30) has excellent sensitivity (0.95) but low specificity (0.45) [23]. ROC curve analysis for MoCA demonstrates that mild cognitive impairment best detection can be achieved with a cut-off point of 24/25 (n = 9350, the sensitivity of 80.48% and specificity of 81.19%) [24]. By comparison, in this study, the adapted MoCA cutoff point (≤24/30) improves specificity (71.22%) while also maintains relatively optimal sensitivity (63.28%) but can not completely replace the neuropsychological test.

This study finds that PSCI is associated with older age and lower education. Age has also been shown to be an important predictor of the development of cognitive impairment or dementia in the chronic period after stroke [25]. Low level of education has consistently emerged as risk factors for PSCI [26]. In further study, data show that visuospatial ability is the most frequently impaired domain, followed by executive function/attention, language and memory in patients with stroke/TIA at six months. This is consistent with previous studies which report similar characteristics of neuropsychological impairment in patients with stroke. PSCI is also associated with visuospatial dysfunction [27]. Our previous study reports that the rate of visuospatial/executive dysfunction is 78/.91% [28]. Another study reports that visuospatial dysfunction is related to some dissociation for space-based information in frontal-subcortical systems [29].

However, our study still has some limitations. Firstly, the sample size is relatively small. We do not establish any cut-off of the MoCA stratified by age and education which have an impact on cognition. Secondly, we recruited consecutive patients with ischemic stroke or TIA from several central hospitals between August 2015 and March 2018, but TIA patients in this study are relatively less, the patients are unevenly distributed. Thirdly, although we hope to enroll patients consecutively, however, only patients who cooperatively perform cognition evaluation recruited in this study, and not all patients complete the neurological tests at six months because of failure to cooperate with inspection, to fulfil or loss to follow-up, which could incur biases. Future study should

include a larger and relatively balanced sample and develop age- and education-adjusted cutoff points for MoCA.

In conclusion, the MoCA is appropriate to screen for cognitive impairment in TIA/stroke patients, as it is more favorable to detect executive function and visual perception/construction. Further longitudinal studies with larger samples are needed to predict cognitive changes and progression from an early stage.

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Data sharing statement

No additional unpublished data are available.

Disclosure statement

The authors declare that no competing interests exist.

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