

# Risk factors for decline in Montreal Cognitive Assessment (MoCA) scores in patients with acute transient ischemic attack and minor stroke

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## Abstract

Cognitive impairment after stroke/transient ischemic attack (TIA) has a high prevalence. The authors aimed to explore the risk factors for declined cognitive function with Montreal Cognitive Assessment (MoCA)-Beijing in patients with stroke/TIA at acute phase. Total 2283 patients with acute stroke/TIA without a history of dementia were assessed at 2 weeks of onset. Patients were assessed by MoCA-Beijing on day 14 and at 3 months follow-ups. Cognitive impairment was defined as MoCA-Beijing  $\leq 22$ . Patients' cognitive status was considered as declined if there were a reduction of  $\geq 2$  points in MoCA-Beijing score and patients were considered to have improved if there were an increase of  $\geq 2$  points. The score of MoCA-Beijing was considered to be stable if there were an increase or decrease of 1 point. Most patients were in 60 s ( $60.96 \pm 10.75$  years old) with a median (interquartile range) National Institute of Health Stroke Scale score of 3.00 (4.00) and greater than primary school level of education, and 1657 participants (72.58%) were male. Cognitive evaluation was conducted in 2283 of 2625 patients (82.70%) with MoCA-Beijing at baseline. Total 292 (12.79%) patients have a cognitive decline at 3 months, 786 (34.42%) patients were stable and 1205 (52.78%) patients were improved. In the logistic regression, a history of hypertension was associated with cognitive deterioration from baseline to 3-month. Patients with a history of hypertension have a higher risk for cognitive deterioration from baseline to 3-month after stroke/TIA.

## KEYWORDS

cognitive impairment, mild stroke, Montreal Cognitive Assessment-Beijing, transient ischemic attack

## 1 | INTRODUCTION

Post-stroke cognitive impairment (PSCI) is a well-known consequence after a stroke/transient ischemic attack (TIA). Our previous study reported that approximately 58.82% of patients developed cognitive impairment after stroke in acute phase.<sup>1</sup> The prevalence of poststroke dementia varied from 7.4% in a population-based study of first-ever stroke to 41.3% in hospital-based cases of recurrent stroke.<sup>2</sup> The prognosis of PSCI is poor, it could affect activities of daily living, consequently prevent patients from returning to family and work and lead to higher mortality and disability compared to patients with no cognitive impairment.<sup>3</sup>

Both the minimal state examination (MMSE) and the Montreal cognitive assessment (MoCA) are widely used tools for screening for cognitive impairment. Previous studies have indicated that the MMSE is less sensitive than the MoCA for identifying cognitive impairment in patients with cerebrovascular disease, in part owing to lower detection of executive dysfunction.<sup>4</sup> Acute temporary cognitive deficits after minor stroke/TIA is common, and these deficits may recover to some extent (transient cognitive impairment [TCI]) over time.<sup>5</sup> One study showed that around 25% patients have TCI in the first few days after TIA or minor stroke.<sup>5</sup> The changes in screening test score may have tips significance in approximating deterioration in cognitive status. One study reported that the MoCA is sensitive to these changes, but the MMSE is not.<sup>6</sup> Longitudinal assessment of patients with minor stroke/TIA in acute phase demonstrated that the cognitive profile of poststroke varied among time. Part of patients with cognitive deficits detected with MoCA at baseline improved over time. Reperfusion therapies have a good impact on cognition. One recent study reported that endovascular treatment plus intravenous thrombolysis treatment in patients with anterior circulation ischemic stroke performed better in cognition than that with intravenous thrombolysis alone at 6 months.<sup>7</sup> However, others with cognitive impairment might have persisting impairment.<sup>6</sup> While older age and lower education level have consistently emerged as risk factors for PSCI, other risk factors (e.g., hypertension, atrial fibrillation) have been inconsistently reported.<sup>8</sup> However, the clinical determinants of cognitive deterioration after PSCI at acute phase remain incompletely understood. Therefore, our primary aim was to examine the risk factors of declining MoCA test scores from acute stroke phase to chronic stroke phase.

## 2 | METHODS

### 2.1 | Participants

Patients in this study are from The Third China National Stroke Registry (CNSR-III) database. CNSR-III is a national prospective registry that consecutively recruited acute ischemic stroke or TIA in-hospital patients within seven days after onset from 201 hospitals that cover 22 provinces and four municipalities in China.<sup>9</sup> There are 2625 patients from 40 hospitals recruited in the subgroup of impairment of cognition and sleep quality (ICONS) among 15,166 patients in CNSR-III. Among

the 2625 stroke patients enrolled in ICONS, 2283 patients from 25 hospitals perform the MoCA-Beijing at baseline (within 2 weeks of index cerebrovascular event) and at 3 months after stroke/TIA by trained research psychologists.

The inclusion criteria of ICONS for patients are age older than 18 years; in-hospital acute ischemic stroke or TIA patients within seven days after onset. The exclusion criteria included: patients who have prior diagnosis of cognitive impairment, schizophrenia or psychosis disease, illiteracy, severe aphasia defined as National Institutes of Health Stroke Scale (NIHSS) item 9 > 2 points, visual impairment, hearing loss, dyslexia, severe unilateral neglect or consciousness disorders that may impede cognitive assessments are excluded. Acute ischemic stroke and TIA were defined according to the WHO criteria and confirmed by brain magnetic resonance imaging (MRI) or computed tomography (CT). Cerebral infarction on MRI or CT without symptoms and signs were excluded.

The collection of data for ICONS was approved by the ethics committee of all participating hospitals. Written informed consent was obtained from all the patients or their legal representatives before data collection.

### 2.2 | Procedure

#### 2.2.1 | Demographics and clinical profile

Data on demographics and clinical characteristics were collected during hospitalization at baseline. Demographic information including sex, age, education level, cardiovascular risk factors as well as medical history was collected. Hypertension was defined as systolic blood pressure  $\geq 140$  mmHg or diastolic blood pressure  $\geq 90$  mmHg. A history of hypertension, diabetes, or hypercholesterolemia, was defined as self-reported disease history, medical recordings or a patient who was on related medication. In all patients, the blood pressure was measured in a seated position after 5-min rest using an automated sphygmomanometer (OMRON Model HEM-7071, Omron Co. Ltd.). Measurements were taken two times consecutively in the non-dominant arm, with 1-min interval. The blood pressure was recorded as the average of the two measurement at admission and 3-month visits. MRI was performed at baseline (hospitalization), including T1-weighted, T2-weighted, fluid-attenuated inversion recovery sequences, diffusion-weighted imaging and magnetic resonance angiography (MRA).

#### 2.2.2 | Assessment of cognitive function

The original MoCA is a 30-point scale with seven cognitive subtests: visuo-executive function, naming, attention, abstraction, language, delayed recall, and orientation. The MoCA-Beijing was developed with the following modifications: (i) Item 1 (Visuospatial/Executive function): Chinese characters (甲/乙/丙/丁/戊) replaced the English alphabet letters; (ii) Item 2 (Attention): Arabic numerals were used instead of English letters; (iii) Item 3 (Language-verbal

fluency): Animal fluency test replaced the phonemic letter fluency. If education is <12 years, we add 1 point to the total score.<sup>10</sup> Patients in this study with MoCA-Beijing  $\leq 22$  defined as cognitive impairment at 2 weeks after minor stroke/TIA. The norms used were based on the results which were derived from our previous study of 102 patients after minor stroke/TIA at 2 weeks in China with MoCA-Beijing test and a formal neuropsychological test battery.<sup>1</sup> Our previous data showed that the optimal cutoff point for MoCA-Beijing in discriminating patients with CI from those with no cognitive impairment (NCI) was 22/23 (sensitivity = 85%, specificity = 88%, PPV = 91%, NPV = 80%). Patients' cognitive status was considered as declined if there were a reduction of two points in MoCA-Beijing score; The score of MoCA-Beijing was considered to have improved if there were an increase of two points. The score of MoCA-Beijing was considered to be stable if there were an increase or decrease of one point. Patients were divided into two groups based on the changing of MoCA-Beijing: the "decline" group and the "non-decline" group. The non-decline group included stable performance and improvement.

### 2.2.3 | Functional assessment

Functional status was assessed by the Katz basic activities of daily living (basic ADL) scale<sup>11</sup> and Lawton and Brody instrumental activities of daily living (instrumental ADL) scale.<sup>11</sup> The mood of patients was assessed with the generalized anxiety disorder (GAD) and patients' health questionnaire-9(PHQ-9) at baseline and 3 months follow-ups.

### 2.3 | Statistical analysis

All analyses were conducted using SAS 9.4 (SAS Institute Inc, Cary, NC). Continuous variables, if they were normally distributed, were presented as means  $\pm$  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  $\chi^2$  test was used to determine the group differences for categorical variables. A two-sided  $p < .05$  was considered to be statistically significant. Logistic regressions were conducted to determine the factors that were associated with the diagnosis transitional status (decline vs. non-decline).

## 3 | RESULTS

Table 1 showed the comparison of demographic information between the "decline" group and the "non-decline" group. The "decline" group possessed more patients who had a history of hypertension and atrial fibrillation than the "non-decline" group ( $p < .05$ ). The "decline" group experienced a much higher proportion of depression than the "non-decline" group ( $p < .05$ ) at 3 months after minor stroke/TIA. There was no significant difference in the values of systolic blood pressure (SBP)-baseline ( $n = 2283$ ), SBP-3-month, diastolic blood pressure (DBP)-

baseline, DBP-3-month, duration of hypertension ( $n = 1432$ ), infarction type and distribution.

At baseline, there were 2283 patients with a mean age of  $60.96 \pm 10.75$  years, and education of  $7.7 \pm 4.3$  years. At 3 months after minor stroke/TIA, total of 2283 patients completed MoCA-Beijing, among these patients, total 112 patients have recurrent stroke at 3 months. The mean MoCA score is  $21.27 \pm 5.82$  scores (Table 2). Total 292 patients have a cognitive decline (decline  $\geq 2$  scores) at 3 months, 786 patients were stable ( $\pm 1$  score) and 1205 patients were improved (improve  $\geq 2$  scores). The overall variation tendency could see in Figure 1.

In the logistic regression of risk factors for cognitive deterioration, according to the results of univariate analysis, correction factors included age, sex, education, history of hypertension and atrial fibrillation. The results in Table 3 indicated that a history of hypertension was significantly correlated with the cognitive deterioration exhibited by MoCA-Beijing at 3 months after minor stroke/TIA.

## 4 | DISCUSSION

PSCI is one of the most common factors contributing to life disabilities after stroke. Acute cognitive deficits have been demonstrated early after major and minor stroke, and these deficits may recover to some extent. Several studies reported that post-stroke cognitive performance fluctuated between subacute and chronic stages. At 3 months, half of the patients (52.78%) have an improvement in global cognition, recall, abstraction, orientation, visuoexecutive function and naming.

This study found that a part of patients (12.79%) have persisting cognitive decline. Previous study suggested that the MoCA was sensitive and useful for monitoring cognition over time. A decline in MoCA score, defined as a reduction of  $\geq 2$  points from 2 weeks to 3 month, was practical and time-efficient to detect high-risk patients and customize early intervention and rehabilitation for those patients. To the best of our knowledge, this is the first study that has examined the risk factors for cognitive deterioration in stroke/TIA patients from acute phase to chronic disease.

Older age is consistently demonstrated to be related to the development of Alzheimer's disease or vascular dementia.<sup>12</sup> As for sex, a part of researches have identified that the oldest women (aged >80 years) in China were at higher risk of cognitive impairment compared with their male counterparts and this sex risk might be due to women's socioeconomic status. In this study, there was no difference in age and sex between the decline group and the non-decline group at baseline, just because there were confounding factors at acute phase, such as delirium, which may have an impact on cognition. Patients in this study have a mean age of  $60.96 \pm 10.75$  years, and there was no statistically significant sex difference in cognitive impairment because of wider social networks and frequent contact with people.<sup>13</sup>

Epidemiologic studies have reported a stronger association of hypertension in midlife with neurocognitive outcomes in late-life than hypertension in late-life, which a null or inverse association has been

**TABLE 1** Demographics and clinical characteristics of decline and non-decline groups

	Acute stroke/TIA (N = 2283)	Non-decline (N = 1991)	Decline (N = 292)	p-Value
<b>Demographic characteristics</b>				
Age(year)	60.96 ± 10.75	61.01 ± 10.71	60.67 ± 11.08	.61
Sex (Male, %)	1657 (72.58)	1454 (73.03)	203 (69.52)	.20
Education level				.13
Elementary or below	599 (26.24)	524 (26.32)	75 (25.68)	
Middle school	830 (36.36)	724 (36.36)	106 (36.30)	
High school or above	763 (33.42)	663 (33.30)	100 (34.25)	
Unknown	91 (3.99)	80 (4.02)	11 (3.77)	
Current smoker (n, %)	808 (35.39)	696 (34.96)	121 (38.36)	.26
Second and smoking (n, %)	387 (16.95)	338 (16.98)	49 (16.78)	.93
Heavy drinker (n, %)	370 (16.21)	315 (15.82)	55 (18.84)	.19
Previous stroke (n, %)	500 (21.90)	432 (21.70)	68 (23.70)	.54
Previous TIA (n, %)	75 (3.29)	62 (3.11)	13 (4.45)	.23
Hypertension (n, %)	1432 (62.72)	1231 (61.83)	201 (68.84)	<b>.0207*</b>
SBP(mm Hg, mean ± SD)	147.81 ± 21.55	147.50 ± 21.55	149.93 ± 21.49	.07
DBP(mm Hg, mean ± SD)	86.92 ± 12.83	86.83 ± 12.68	87.59 ± 13.84	.38
Duration of hypertension(year, median [IQR])	10.00 (4.00–15.00)	10.00 (4.00–15.00)	9.00 (4.00–15.00)	.53
Anti-hypertensive therapy (n, %)	1040 (45.55)	893 (44.85)	147 (50.34)	.08
SBP at 3-month (mm Hg, mean ± SD)	135.40 ± 14.07	135.18 ± 13.84	137.01 ± 15.56	.09
DBP at 3-month (mm Hg, mean ± SD)	81.96 ± 9.22	81.96 ± 9.10	81.96 ± 10.07	1.00
Diabetes (n, %)	521 (22.82)	442 (22.20)	79 (27.05)	.90
Hypercholesterolemia (n, %)	222 (9.72)	193 (9.69)	29 (9.69)	.90
Coronary heart disease (n, %)	259 (11.34)	232 (11.65)	27 (9.25)	.23
Heart failure (n, %)	7 (.31)	7 (.35)	0 (.00)	.31
Atrial fibrillation (n, %)	107 (4.69)	86 (4.32)	21 (7.19)	<b>.0301*</b>
Epilepsy (n, %)	7 (.31)	6 (.30)	1 (.34)	.92
TOAST classification (n, %)				.35
Large artery atherosclerosis	530 (23.22)	460 (23.10)	70 (23.97)	
Cardiogenic embolism	118 (5.17)	95 (4.77)	23 (7.88)	
Small artery occlusion	580 (25.41)	513 (25.77)	67 (22.95)	
Others	24 (1.05)	18 (.90)	6 (2.05)	
Unknown	1031 (45.16)	905 (45.45)	126 (43.15)	
Stroke onset to enrollment time (day)median (IQR)	1.00 (.00–2.00)	1.00 (.00–2.00)	1.00 (.00–2.00)	.91
Baseline neurological function (n, %)				.33
NIHSS = 0	380 (16.64)	333 (16.73)	47 (16.10)	
NIHSS = 1	353 (15.46)	305 (15.32)	48 (16.44)	
NIHSS = 2	403 (17.65)	343 (17.23)	60 (20.55)	
NIHSS = 3	301 (13.18)	258 (12.96)	43 (14.73)	
NIHSS > 3	846 (37.06)	752 (37.77)	94 (32.19)	
Affective symptoms, median (IQR)				
Day-14 GAD-7	1.00 (.00–3.00)	1.00 (.00–3.00)	1.00 (.00–3.00)	.83
Month-3 GAD-7	.00 (.00–2.00)	.00 (.00–2.00)	.00 (.00–3.00)	.15
Day-14 PHQ-9	2.00 (.00–5.00)	2.00 (.00–5.00)	2.00 (.00–5.00)	.77
Month-3 PHQ-9	1.00 (.00–4.00)	1.00 (.00–4.00)	2.00 (.00–5.00)	<b>.016*</b>

(Continues)

**TABLE 1** (Continued)

	Acute stroke/TIA (N = 2283)	Non-decline (N = 1991)	Decline (N = 292)	p-Value
<b>Demographic characteristics</b>				
Functional outcome, median (IQR)				
Baseline pre-mRS	1.00 (1.00–2.00)	1.00 (1.00–2.00)	1.00 (1.00–2.00)	.91
Day-14 mRS	1.00 (.00–1.00)	1.00 (.00–1.00)	1.00 (.00–1.00)	.77
Month-3 mRS	1.00 (.00–1.00)	1.00 (.00–1.00)	1.00 (.00–1.00)	.38
Recurrence of ischemic stroke at 3 months	107 (4.69)	87 (4.37)	20 (6.85)	.061

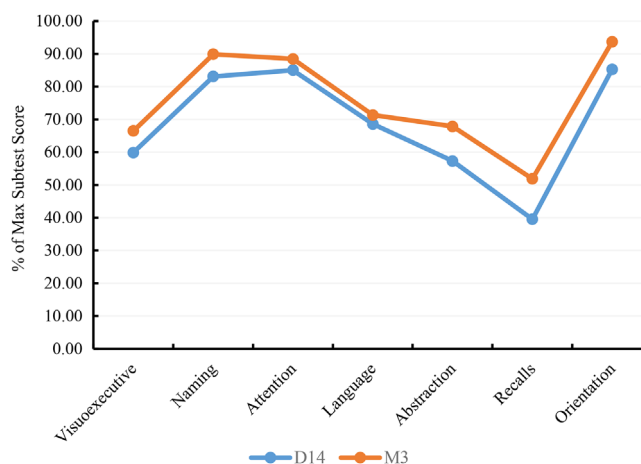
Abbreviations: DBP, diastolic blood pressure; SBP, systolic blood pressure; mRS, modified rankin scale; NIHSS, National Institutes of Health Stroke Scale.  
\* $p < .05$ .

**TABLE 2** MoCA subtest scores and mean percentage scores

Full score rate of MoCA subtests	Max subtest score		M3mean (SD)	Percentage	p-Value
	D14mean (SD)	Percentage			
Visuoexecutive/5	2.99 ± 1.64	59.89	3.33 ± 1.50	66.51	<.0001**
Naming/3	2.49 ± .89	83.12	2.70 ± .67	89.91	<.0001**
Attention/6	5.10 ± 1.32	85.02	5.31 ± 1.16	88.49	<.0001**
Language/3	2.06 ± .97	68.62	2.14 ± .91	71.32	<.0001**
Abstraction/2	1.15 ± .85	57.31	1.36 ± .78	67.85	<.0001**
Recalls/5	1.98 ± 1.74	39.54	2.59 ± 1.67	51.87	<.0001**
Orientation/6	5.12 ± 1.60	85.26	5.62 ± .85	93.69	<.0001**
Total/30	21.27 ± 5.82	70.89	23.54 ± 4.91	78.46	<.0001**

\* $p < .05$ .

reported in some studies.<sup>14</sup> Chronic hypertension is the major risk factor for ischemic and hemorrhagic stroke, which is associated with a three- to six-fold increase in cognitive impairment, especially when multiple strokes are involved (multi-infarct dementia).<sup>15</sup> Additional lesions associated with hypertension include microinfarcts and micro-hemorrhages, microscopic ischemic or hemorrhagic lesions most common in the cerebral cortex, which portend cognitive deficits.<sup>16</sup> Vascular oxidative stress and inflammation, leading to neurovascular trophic failure are potential contributing factors for cognitive impairment.<sup>17</sup> The most recent meta-analysis reported an association of blood pressure lowering with reduced risk of dementia.<sup>18</sup> Another meta-analysis included 14 randomized clinical trials showed that blood pressure lowering with antihypertensive agents compared with control was significantly associated with a lower risk of incident dementia or cognitive impairment.<sup>19</sup> However, other studies reported the effect of blood pressure lowering on cognitive impairment was modest and lower than the risk reduction for stroke.<sup>20</sup> There was no significant difference in antihypertensive therapy between “decline” and “non-decline” groups. In logistic regression, cognitive deterioration was related to hypertension. It implied that hypertension was a risk factor of cognitive impairment, and was also sensitive to cognitive deterioration.

**FIGURE 1** Changes of full score rate in each MoCA subset

There are some limitations in this study. Firstly, in this study, we recruit consecutive patients with ischemic stroke or TIA from several hospitals, but TIA patients possessed a relatively small part, the patients are unevenly distributed. Secondly, the blood pressure is likely to fluctuate as time flows, previous studies have reported that blood press variability was associated with poor outcome,<sup>21</sup> and a potential

**TABLE 3** Results of multivariate logistic regression analysis of the risk factors for decline in Montreal Cognitive Assessment (MoCA) scores in patients with acute transient ischemic attack and minor stroke

	OR (95% CI)	p-Value
Age	.99 (.980–1.00)	.99
Sex	.89 (.67–1.17)	.39
Education		
Elementary or below	Reference	—
Middle school	1.06 (.76–1.46)	.89
High school or above	1.05 (.75–1.46)	.78
Unknown	.90 (.54–1.78)	.76
Atrial fibrillation	1.43 (.70–2.89)	.32
Hypertension	1.32 (1.01–1.73)	.04*
Diabetes	1.28 (.96–1.70)	.09
TOAST classification	2.33 (.78–7.01)	.13
Large artery atherosclerosis	Reference	
Cardiogenic embolism	1.32 (.64–2.70)	.45
Small artery occlusion	.86 (.60–1.23)	.40
Others	2.14 (.81–5.63)	.12
Unknown	.92 (.67–1.27)	.62

\*\* $p < .001$ .

risk factor for cognitive decline. Yet, the CNSR-III is a registry study, and we recorded the blood pressure at three-time points: baseline, 3- and 12-months visits. We are unable to derive the relationship of blood pressure fluctuations and PSCI. We may do some in-depth research about blood pressure fluctuations and cognitive impairment in the future. Thirdly, the concurrent infections, or sedatives, as well as emotional disorders, may have affected cognitive performance at acute phase.

The results of this study indicate that a history of hypertension is a risk factor for cognitive deterioration for poststroke patients from acute phase to chronic phase. This result suggests that an overall evaluation of cognition in acute phase should be recommended. More attention can be paid to patients with hypertension after the diagnosis of PSC, and furtherly reduced the disease burden.

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#### COMPETING INTEREST

The authors have no competing interests.

#### AUTHOR CONTRIBUTIONS

Lijun Zuo: drafting/revising the manuscript, study concept or design, analysis or interpretation of data, accepts responsibility for conduct of

research and will give final approval, acquisition of data, statistical analysis. YanHong Dong: critical revision of the manuscript, assisted with study concept or design, accepts responsibility for conduct of research and will give final approval, verification of some data (neuropsychological test scoring). Xiaoling Liao: study concept or design, accepts responsibility for conduct of research and will give final approval, acquisition of data. Yuesong Pan: study concept or design, accepts responsibility for conduct of research and will give final approval, acquisition of data. Xianglong Xiang: study concept or design, accepts responsibility for conduct of research and will give final approval, acquisition of data. Xia Meng: study concept or design, accepts responsibility for conduct of research and will give final approval, acquisition of data. Hao Li: study concept or design, accepts responsibility for conduct of research and will give final approval, acquisition of data. Xingquan Zhao: assistance with early design, critical review of the analysis and manuscript. Yilong Wang: assistance with early design, critical review of the analysis and manuscript. Jiong Shi: assistance with early design, critical review of the analysis and manuscript. Yongjun Wang: study concept or design, analysis or interpretation of data, accepts responsibility for conduct of research and will give final approval, acquisition of data, statistical analysis, study supervision.

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