

SIX MONTHS FOLLOW-UP STUDY ON COGNITIVE PERFORMANCES IN PATIENTS WITH ISCHEMIC VASCULAR EVENTS

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REZUMAT

Obiectiv: Principalul obiectiv al studiului nostru a fost evaluarea profilului cognitiv la pacienții care au suferit un prim accident vascular cerebral ischemic constituit sau un accident ischemic tranzitor. **Material și metodă:** Am luat în studiu un grup de 74 pacienți spitalizați în Clinica de Neurologie Craiova pentru un prim accident vascular cerebral ischemic constituit sau un accident ischemic tranzitor și un grup control compus din 80 de subiecți care nu prezentau semne de boală cardiovasculară dar cu factori de risc cardiovascular prezenți. Pentru evaluarea cognitivă am folosit Mini Mental State Examination (MMSE) și Montreal Cognitive Assessment (MoCA). Evaluările cognitive au fost făcute la intrarea în studiu, după 3 luni și după 6 luni. Ambelor grupuri li s-a efectuat computer tomografie craniană. **Rezultate:** La începutul studiului, pacienții aveau un scor mediu la MMSE de 27,6 și scor MoCA de 27,8. Grupul control avea scorul mediu MMSE de 28,9 și scor MoCA de 29. După 6 luni, în grupul de pacienți s-a obținut un MMSE scor de 25,6 și un scor MoCA de 20,1. În grupul control s-au obținut după cele 6 luni de studiu un scor mediu MMSE de 26,9 și un scor MoCA de 24,2. **Concluzii:** Pacienții cu boală cerebrovasculară au prezentat un declin cognitiv mai mare comparativ cu subiecții din grupul control. La pacienții cu accident vascular cerebral ischemic constituit am observat o afectare cognitivă mai accentuată comparativ cu pacienții spitalizați pentru accident ischemic tranzitor. Subiecții care prezentau factori de risc cerebrovascular aveau alterare cognitivă premergătoare semnelor clinice evidente.

Cuvinte cheie: accident vascular cerebral ischemic, tranzitor, declin cognitiv, MoCA, MMSE.

ABSTRACT

Objective: The main aim of our study was to assess the cognitive state in patients after first ever stroke/transient ischemic attack (TIA). **Material and methods:** We studied a group composed of 74 patients admitted to Clinic of Neurology from Craiova for first ever stroke or TIA and also a group composed of 80 control subjects without signs of cerebrovascular disease (CVD) but with vascular risk factors present. To assess the cognitive state we tested the patients using Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment Scale (MoCA) at baseline, and after three and six months of follow-up. In both groups we performed brain computed tomography for a correct diagnosis. **Results:** At baseline the patient group showed a mean MMSE score 27.6 and a mean MoCA score 27.8. The control subjects showed a mean MMSE score 28.9 and a mean MoCA score 29. After six months the patient group showed a mean MMSE score 25.6 and MoCA score 20.1. The control subjects showed a mean MMSE score 26.9 and MoCA score 24.2. **Conclusions:** The patients with CVD showed a greater cognitive impairment than control subjects. In patients with stroke we observed a greater cognitive impairment than in the patients with TIA. In subjects with cerebrovascular risk factors there were signs of cognitive impairment even before the CVD became clinically evident.

Key Words: cognitive impairment, stroke, TIA, MoCA, MMSE

INTRODUCTION

Stroke is the second most common cause of cognitive impairment and dementia. Evaluation of cognitive impairment is important, because it can enable early medical management in order to prevent severe dementia.

The risk of vascular cognitive impairment and the rate of cognitive decline in cerebro-vascular disease (CVD) is dependent upon the control of the risk factors for stroke.¹ The risk of developing cognitive impairment after stroke is greatest in those persons with vascular risk factors, such as hyperlipidemia, arterial hypertension, homocysteinemia, diabetes mellitus, heart disease, obesity, smoking, alcohol, coagulopathies, prior stroke, atherosclerotic vessel disease. Besides vascular risk, the vascular cognitive decline has other risk factors, such as demographic (e.g., age, education), genetic (e.g., family history and specific genetic features) and ischemic lesion-related variables (e.g., type of cerebrovascular disease, site and size of stroke).^{2,3} Hypoxic ischemic events (congestive heart failure, myocardial infarction, seizure, pneumonia) giving rise to global cerebrovascular insufficiency are

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important risk factors for incident dementia in patients with stroke.⁴ Increasing evidence also suggests that reducing the burden of vascular risk decreases the prevalence of dementia.⁵⁻⁷

The most common types of cognitive deficits arising from stroke are disturbance of attention, language, executive dysfunction affecting the ability to analyze, interpret, organize, plan and execute complex information.⁸⁻¹¹ The assessment of cognitive decline uses various neuropsychological scales. Mini Mental State Evaluation (MMSE) is still most widely used in assessment of patients with memory complaints, although it lacks sensitivity in detecting mild cognitive impairment or early stages of dementia.¹²⁻¹⁴ Montreal Cognitive Assessment (MoCA) is an easily to administer and brief screening tool with high sensitivity and specificity for mild cognitive impairment.¹⁵

While MMSE is superior for more advanced stages of cognitive impairment, MoCA is useful for the mild stages of cognitive decline and for distinguishing patients with MCI from cognitively intact patients, which makes it a practical tool for first line physicians.¹⁵ In our study we used both MMSE and MoCA to compare the incidence and severity of cognitive decline in patients with first clinical signs of CVD and in subjects with one or more cerebrovascular risk factors, with no clinical signs of cognitive impairment.

The simplicity of evaluation procedures will gain even more importance in the future, due to the increase in the proportion of elderly persons in the population.¹⁶

MATERIAL AND METHODS

We studied a group composed of 74 patients (mean age 61.02 ± 6.12 years) and mean level of education of 10.90 ± 2.10 years admitted to Clinic of Neurology Craiova during the year 2007, for first ever ischemic stroke or transient ischemic attack (TIA) and also a group composed of 80 control subjects without clinical signs of CVD but with vascular risk factors present. The control subjects had a mean age of 60.20 ± 5.30 years and a mean level of education of 10.30 ± 2.70 years. None of study subjects had any subjective or objective memory complaints prior to enrolment. In all patients we performed a CT scan for a correct diagnosis. In all control group subjects brain CT scan results were normal, free from any signs of CVD.

In all subjects data on conventional vascular risk factors were recorded, including age, arterial hypertension, diabetes, hyperlipoproteinemia, smoking, alcohol and obesity, coronary disease and atrial fibrillation. Upon giving an informative consent, both groups (patients and controls) were tested using MMSE and MoCA.

MMSE requires 10 minutes for administration and it is composed of items assessing orientation, immediate and delayed recall of three words, naming, phrase repetition, the ability to follow simple commands, writing, visuospatial function, attention and mental control. Total MMSE score of 25-30 points is considered normal, while scores below 24 points indicate dementia.

MoCA was designed as a rapid screening instrument for mild cognitive impairment. It assesses different cognitive domains: attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, orientation. The short term memory recall task (5 points) involves two learning trials of five nouns and delayed recall after approximately 5 minutes. Visuospatial abilities are assessed using a clock drawing task (3 points) and three-dimensional cube copy (1 point). Multiple aspects of executive functions are assessed using an alteration task adapted from the Trial Making B task (1 point), a phonemic fluency task (1 point), and a two item verbal abstraction task (2 points). Attention, concentration and working memory are evaluated using a sustained alteration task (target detection using tapping, 1 point), serial subtraction task (3 points) and digits forward and backward (1 point each). Language is assessed using a three-item confrontation naming task with low-familiarity animals (3 points), repetition of two syntactically complex sentences (2 points) and the above mentioned fluency task. The orientation to time and place is evaluated with 6 points. A previous study indicated that the subjects with 12 years of education or less had worse performance on MoCA, so 1 point was added to total MoCA score (if total score was <30 points). The total possible score is 30 points; a score of 26 or above is considered normal.

Our evaluations were made in the beginning of the study then after 3 and respectively 6 months. The results were analyzed by the Student Test.

RESULTS

Study populations

There were 53 ischemic acute stroke patients (71.62%) and 21 TIA patients (28.38%) enrolled in the patients group versus 80 control group subjects with no clinical evidence of CVD but with the presence of one or more risk factors. TIA was diagnosed according to redefined diagnostic criteria of the TIA Working Group.¹⁷ There was no statistically significant difference between groups concerning the age and the level of education. The demographic data are summarized in Table 1. In the control group arterial hypertension was

the most frequent risk factor (n= 66; 67.50%), followed by hyperlipoproteinemia (n=49; 61.20%) and diabetes mellitus (n=41; 51.25%). In stroke patients subgroup the arterial hypertension (n=50; 94.34%) was most commonly recorded, followed by smoking (n=37; 69.81%) and hyperlipoproteinemia (n=35; 66.09%). In TIA patients subgroup hyperlipoproteinemia (n=19; 90.47%) was most commonly recorded, followed by arterial hypertension (n=15; 71.42%) and atrial fibrillation (n=13; 61.90%). Also multiple risk factors were present in 30 (58.42%) stroke patients versus 12 (57.25%) TIA patients. (Table 2)

Table 1. Study subjects demographics

	Number of patients (n)	Age (years)	Education (years)
Patients group	74	61.02±6.02	10.90±2.10
Stroke group	53	59.03±61.2	10.52±2.41
TIA group	21	64.17±5.05	11.28±3.50
Control group	80	60.21±5.30	10.30±2.70

Table 2. Vascular risk factors in transient ischemic attack subgroup, stroke subgroup and control group.

	Transient ischemic attack subgroup (N=21) n%	Stroke subgroup (N=53) n%	Control group (N=80) n%
Arterial hypertension	15 (71.42%)	50 (94.34%)	66 (67.50%)
Hiperlipoproteinaemia	19 (90.47%)	35 (66.09%)	49 (61.20%)
Diabetes mellitus	9 (42.85%)	20 (37.72%)	41 (51.25%)
Smoking	11 (52.33%)	37 (69.81%)	30 (37.51%)
Atrial fibrillation	13 (61.90%)	15 (28.30%)	24 (30.00%)
Obesity	10 (47.63%)	16 (30.18%)	19 (23.75%)
Multiple risk factors	12 (57.25%)	30 (58.42%)	40 (50.00%)

Cognitive evaluation by MMSE and MoCA

The cognitive results using MMSE scale

In patients group we found at baseline a mean score 27.6; the mean score was 26.6 after three months and 25.6 after six months. The control group obtained at baseline a mean MMSE score of 28.9; the score was 27.9 after three months and 26.9 at the end of study. The values are represented in Figure 1.

The cognitive results using MoCA test

In patients group we found at baseline a mean score 27.8; after three months the mean score was 23.7 while six months later it was 20.1. In the control group the baseline mean score was 29; after three months it was 26.1 and at the end of study 24.2. The values are represented in Figure 2.

As shown in the two figures, cognitive performance on MMSE for both groups fell within the normal range throughout the study period and the administration of MoCA revealed early cognitive abnormalities (under 26 points): after three months in the patients group and after six months in both groups (patients and controls).

We have also observed by using MoCA scale assessment that the patients group showed a greater cognitive impairment in comparison to control group (p< 0.05) after six months. When we used MoCA scale, we observed that the patients stroke subgroup who had multiple vascular risk factors (n=30; 58.42%) and a statistically significant cognitive decline after six months (mean MoCA score 17.85) in comparison to TIA patients subgroup (n=12; 57.25%) with a mean MoCA score 24.40 points.

As shown in Figure 3, in control group the greatest cognitive decline at six months was recorded in the subgroup of subjects with arterial hypertension (mean MoCA 22.35) and multiple vascular risk factors (mean MoCA 19.27).

DISCUSSIONS AND CONCLUSIONS

Given the increased number of elderly population, dementia of any type represents a common illness today, and efforts are made to enable early diagnosis and treatment as soon as possible.

Our results indicated that first measurable signs of cognitive malfunction appear even before the disease itself had become clinically evident in patients with cerebrovascular disease. Cognitive follow up using MoCA during a six months period in both groups (patients and controls) showed a step-wise reduction of cognitive performances in both groups, with a more pronounced and more rapid decline in the patients group. (Fig. 2)

Discrete cognitive changes were also present in

asymptomatic controls, especially in subjects with arterial hypertension or multiple risk factors who had the most pronounced decline after six months. It appears that the concurrent presence of multiple vascular risk factors additionally increases the risk of subtle cognitive decline through possible cumulative action of risk factors even in subjects without evident clinical signs of cognitive impairment.

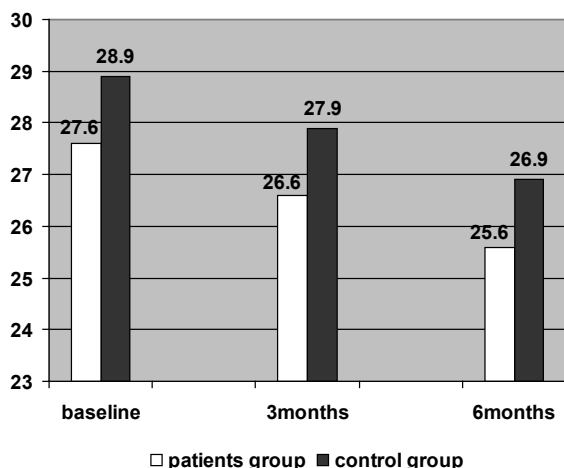


Figure 1. Mean MMSE score in patients group and control group at baseline, after 3 months and after 6 months.

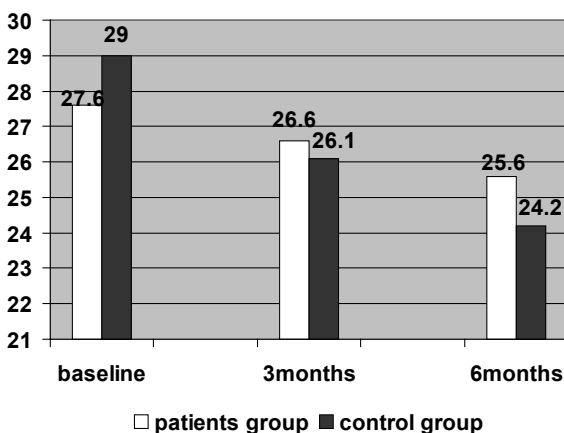


Figure 2. Mean MoCA score in patients group and control group at baseline, after 3 months and after 6 months.

This finding could be explained by small vessel disease, which is likely to be present in these individuals due to persistent damage to the small terminal vasculature of subcortical cerebrum caused by different vascular risk factors. Small vessel disease is closely linked to hypertension.¹⁸ This observation could suggest that in the elderly cerebral small vessel disease contributes to cognitive decline by affecting information processing speed and executive function.¹⁹ In patients with vascular impairment we observed a relatively mild memory loss but they

usually have presented early executive dysfunction. Executive function is mediated by series of parallel cortico-subcortical circuits connecting the prefrontal cortex, the striatum-pallidum and the thalamus, with thalamo-cortical projections closing the loop. Vascular lesions may interrupt these pathways with the end-result leading to a subcortical form of dementia.²⁰

Cerebrovascular disease is a common symptom of the aging process and several studies have suggested that cerebrovascular risk factors are strongly associated with dementia.^{21,22} Dementias were previously classified on the basis of the presence or absence of cerebrovascular disease with positive associations between stroke risk factors and vascular dementia and negative associations between stroke and Alzheimer disease.²³ The recent epidemiological and experimental studies showed that there are many reasons to consider the role of vascular factors in the initiation and progression of Alzheimer disease. According to these studies, common risk factors for Alzheimer disease and vascular dementia are now recognized such as age, previous TIA or stroke, arterial hypertension, diabetes mellitus, smoking, coronary heart disease and hiperlipoproteinaemia.²² As vascular pathology appears to be a common characteristic of both vascular dementia and Alzheimer disease, we think that is very important to early diagnose mild cognitive impairment, especially in the patients to whom strict medical control of risk factors could prevent clinically evident dementia of any type. Nasreddine et al showed MoCA to have excellent sensitivity in detecting mild cognitive impairment (90%) and higher sensitivity than MMSE.¹⁵

We have also observed in our study that MoCA can detect discrete cognitive changes in symptom free subjects with no cognitive complaints but with one or more cerebrovascular risk factors. (Fig. 2) The patients group showed a greater cognitive decline after six months in comparison to baseline and three months follow-up period. Also using MoCA test we have found that the ischemic stroke patients subgroup showed a greater cognitive impairment than TIA patients subgroup. Using MMSE for the cognitive assessment, we observed initial signs of cognitive impairment in patients after six months, while no abnormalities were have found in control group.

The features of MoCA design which probably explain its sensitivity compared to MMSE are memory testing which involves more words, fewer learning trials, and longer delay before recall than MMSE.¹⁵ Also the visuospatial processing, executive functions and language abilities are tested by MoCA with more numerous tasks in comparison to MMSE. Our results

are in concordance with other studies that showed MMSE could not be used alone to diagnose mild cognitive decline or dementia. We demonstrate that utilization of MoCA test for cognitive assessment is very useful for the early recognition of subtle cognitive impairment in apparently mentally healthy individuals. Thus, we recommend MoCA test to be used in patients with normal range score on MMSE scale in order to detect the subjects in presymptomatic stage earlier, which is essential in the prevention of severe dementia.

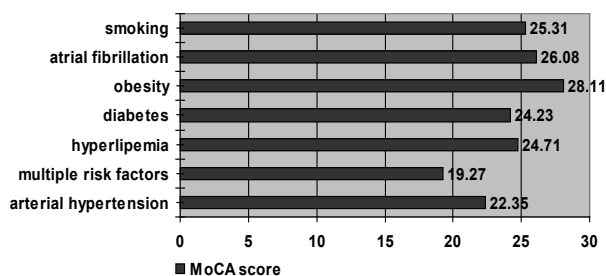


Figure 3. Mean MoCA scores in control group according to risk factors at 6 months.

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