

## ASSESSMENT OF SUBTLE COGNITIVE IMPAIRMENT IN STROKE-FREE PATIENTS WITH CAROTID DISEASE

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**SUMMARY** – Carotid disease is a known risk factor for stroke and stroke is a known risk factor for cognitive impairment, but relation between carotid artery stenosis and cognitive function in asymptomatic individuals is less clear. Most patients have only minor complaints of cognitive dysfunction and assessment with usual tests is not sensitive enough. The study included 26 stroke-free patients (15 male and 11 female), mean age  $66.3 \pm 8.7$  years, with advanced internal carotid artery stenosis or/and occlusion (ICAs/o). Left ICAs/o was present in 11, right ICAs/o in eight, and bilateral ICAs/o in seven patients. History was taken and assessment of risk factors, brain CT scan and neurologic examination were performed. Cognitive functions were tested by use of Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA). All patients were asymptomatic, except for two patients that presented with repeated transient ischemic attack (TIA). In all subjects median MMSE scores were within the normal range (27.5; IQ range 25–29), while mean MoCA scores were abnormal ( $22.6 \pm 3.4$ ). Patients with left ICAs/o scored slightly better on MoCA ( $22.9 \pm 3.3$ ) than patients with right ICAs/o ( $22.4 \pm 4.0$ ). Delayed recall MoCA subtest was impaired in 22/26 patients and visuospatial subtest in 23/26 patients; however, there was no statistically significant difference according to the side of ICAs/o. Patients with the presence of one or two risk factors scored lower on visuospatial/executive MoCA subtests ( $P=0.018$ ) as compared with patients with multiple risk factors. MoCA proved to be a sensitive tool for assessment of mild cognitive changes in stroke-free patients with advanced ICAs/o. Decline was most pronounced in visuospatial, executive and short-memory functions.

**Key words:** *Cerebrovascular disorders – etiology; Cerebrovascular circulation – physiology; Carotid stenosis – complications; Cognitive disorders – physiopathology*

### Introduction

The incidence of carotid disease increases with age. According to some studies, it is present in 75% of men and 62% of women aged  $\geq 65$ , with the prevalence of  $\geq 50\%$  stenosis in this population being 7% in men and 5% in women<sup>1</sup>. The most severe consequence of carotid occlusive disease is ischemic stroke, which is also recognized as a risk factor for dementia<sup>2,3</sup>. Stud-

ies report that up to 30% of all ischemic strokes occur due to the carotid occlusive disease<sup>4</sup>. On the other hand, the majority of carotid stenoses are classified as asymptomatic, implying the absence of stroke (retinal or focal cerebral dysfunction in the territory of the affected internal carotid artery) symptoms. However, patients with carotid stenoses often experience cognitive problems which are mostly subtle and not severe enough to interfere with daily activities. These subtle cognitive changes can eventually lead to mild cognitive decline as a premonitory state of dementia. The established risk factors such as arterial hypertension, hyperlipoproteinemia or diabetes mellitus are recog-

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nized to have measurable adverse effects in the etiology of cognitive impairment of vascular type<sup>5-13</sup>. The association of vascular risk factors and carotid artery disease is also well known, but when carotid stenosis or occlusion is categorized as symptomatic or asymptomatic, cognitive status of the patient is routinely not taken into consideration<sup>14</sup>. In addition, progressive cognitive decline in patients with cerebrovascular stenosis may be an even greater problem than the actual stroke, but it is still not a widely recognized symptom<sup>15</sup>.

Only a few studies of cognitive status, all of which included a small number of patients (less than 20) were conducted in patients with a advanced carotid stenosis or occlusion<sup>16-20</sup>. Patients with carotid stenoses have been shown to have significantly poorer scores on cognitive tests than matched control subjects. Some cognitive status analyses were performed regarding the side of carotid disease as well as hemispheric dominance, but common limitations of those studies were small numbers of patients included, variable definitions of internal carotid artery stenosis and inconsistent neuropsychological tests used<sup>16,20</sup>.

Previous studies mostly used the Mini Mental State Examination (MMSE) as a routine cognitive measure, whereas in others more complex neuropsychological test batteries were employed to analyze cognitive domains<sup>15,16,20,21</sup>. Neuropsychological testing with standardized tests often presents a problem for clinician due to its complicated and time-consuming nature. Although still the most widely used in the assessment of patients with memory complaints, MMSE lacks sensitivity in detecting subtle cognitive changes or early stages of dementia, especially of vascular type<sup>22</sup>. Most individuals meeting clinical criteria for mild cognitive impairment (MCI) score above 26 points on MMSE, which is also normal range for elderly individuals. Another problem with MMSE is that it is unable to distinguish between cognitive functions, so it is not suitable for deeper analysis<sup>23</sup>. The Montreal Cognitive Assessment (MoCA) developed by Nasreddine *et al.* is an easily administered and brief screening tool with high sensitivity and specificity for subtle cognitive decline<sup>24</sup>. While MMSE is superior for more advanced stages of cognitive decline, MoCA is useful for the mild stages of cognitive impairment and for distinguishing patients with MCI from cognitively intact patients, which makes it a practical tool

for first line physicians<sup>24</sup>. A growing number of recent studies support the use of MoCA as a valuable screening tool in the assessment of cognition in patients with different neurologic disorders<sup>25-28</sup>. Some of the MoCA subtests have also been proposed for routine use in a five-minute protocol aiming to assess cognitive decline in individuals with possible vascular cognitive impairment<sup>29</sup>.

In this pilot study, MMSE and MoCA were used to assess cognitive changes in stroke-free patients with advanced carotid stenosis or occlusion.

## Patients and Methods

Study participants were recruited from the University Department of Neurology, Sestre milosrdnice University Hospital in Zagreb. Twenty-seven consecutive patients who were referred to the Cerebrovascular Laboratory as outpatients for ultrasound assessment of carotid arteries were initially included in the study. All patients were diagnosed with advanced internal carotid artery (ICA) stenosis (more than 70%) or occlusion (ICAs/o). Such criteria were used for the known repercussions of ICAs/o on intracranial hemodynamics. All patients were asymptomatic except for two patients that presented with repeated transient ischemic attacks (TIA) and were enrolled in the study. Five out of 27 patients reported minor subjective cognitive problems, but others had no subjective or objective memory complaints prior to enrolment.

Our study was restricted to right-handed patients. Patients were selected as right-handed if they were observed to write with their right hand and if they reported using their right hand to throw a ball and to brush their teeth.

Color doppler flow imaging (CDFI) of carotid arteries was also performed in all subjects on admission. CDFI measurement was done on commercially available equipment (Aloka Prosound SSD-550 and Aloka Alfa 10) with linear 10-MHz transducer. Standard CDFI of both common carotid arteries (CCA), ICA and external carotid arteries (ECA) was performed according to the defined diagnostic protocol<sup>30</sup>. Advanced carotid stenosis or occlusion was assessed according to the predefined criteria and previously described procedure<sup>31</sup>. In all patients history was taken and data on conventional vascular risk factors were noted, including data on age and sex, arterial hyper-



tension, diabetes, hyperlipoproteinemia, previous or current cigarette smoking, and obesity (body mass index, BMI >25). As part of the neurologic diagnostic procedures, all patients underwent brain computed tomography (CT) scan within two weeks of enrolment, using Siemens-Sensation Multislice Computed Tomography scanner with 16-row detector layer, according to standard protocol (unenhanced scans with 1-mm slice thickness). Brain CT findings were classified as positive if the signs of ischemic stroke were present. One patient was diagnosed with ischemic stroke at the time of the study and was subsequently excluded. For the study, results in 26 patients (15 male and 11 female), mean age 66.3±8.7 (range 43–78) years, were analyzed. Of the 26 patients, 14 had left ICAs/o (12 with ICA stenosis and 2 with ICA occlusions), 8 had right ICAs/o (all stenosis) and 4 patients had bilateral ICAs/o (3 patients with left ICA stenosis also had the right ICA occlusion).

After giving their informed consent, all patients were tested using standard MMSE and Montreal Cognitive Assessment (MoCA)<sup>21,24</sup>. MMSE requires 5–10 minutes for administration. 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 is considered normal, while scores be-

low 24 points indicate dementia<sup>21</sup>. MoCA was translated to Croatian and was administered according to administration and scoring instructions given by the authors<sup>24</sup>. It is a 30-point test that takes approximately 30 minutes to administer. The short-term memory recall task (5 points) includes 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 a 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), a 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 (lion, camel, rhinoceros; 3 points), repetition of two syntactically complex sentences (2 points) and the aforementioned fluency task. Finally, orientation to time and place is evaluated (6 points)<sup>24</sup>. For MMSE, patients scoring ≤24 points were considered as cognitively impaired; cut-off score for MoCA was ≤26 points. In order to evaluate the pattern of cognitive impairment, besides total MoCA scores, subtest scores for different cognitive domains included

Table 1. Demographic data including risk factor profile

	All patients	ICA stenosis or occlusion		
		Left	Right	Bilateral
n	26	11	8	7
Age (yrs) (mean ± SD)	66.3±8.7	62.6±8.7	68.6±7.5	74.3±3.3
Female (n)	11	6	3	2
Arterial hypertension (n)	22	11	7	4
Hyperlipoproteinemia (total cholesterol >5.0 mmol/L or statin treatment) (n)	16	8	4	4
Diabetes mellitus (n)	13	6	5	2
Smokers (n)	7	3	3	1
Ex-smokers (n)	8	4	3	1
Obesity (BMI >25) (n)	2	1	1	0
Multiple RF (>2) (n)	16	9	4	3

BMI = body mass index; RF = risk factor

Table 2. Results of cognitive assessment by use of total Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA) scores

		MMSE	MoCA
		median (25-75 percentile, range)	mean $\pm$ SD
All patients (N=26)		27.5 (25-29)	22.6 $\pm$ 3.4
ICA stenosis or occlusion	Left (n=11)	28 (25.8-29)	22.9 $\pm$ 3.3
	Right (n=8)	27 (26-29.5)	22.4 $\pm$ 4.0
	Bilateral (n=7)	26 (25-27.5)	22.6 $\pm$ 3.3
	<i>P</i>	0.480*	0.946**

\*Kruskal-Wallis (ANOVA on ranks); \*\*One Way ANOVA

in the MoCA subtests were calculated separately for each patient.

Prior to any further analysis, all data sets were analyzed for normality using Kolmogorov-Smirnov test, and are presented as median  $\pm$  interquartile range (IQ) for data that were not normally distributed and mean  $\pm$  standard deviation for data that were normally distributed. Normally distributed data sets were analyzed using Student's t-test. Not-normally distributed data sets were analyzed using parametric One Way Analysis of Variance on Ranks (ANOVA on Ranks), Mann-Whitney Rank Sum Test, post hoc analysis was performed using all pair-wise multiple comparison procedures (Holm-Sidak method). Difference was considered to be statistically significant at  $P < 0.001$ . All statistical procedures were done using the SigmaStat 3.0, SPSS Inc. statistical software.

## Results

Basic demographic variables and vascular risk factor profile of patients with ICAs/o according to the International and National Stroke Association (NSA) Stroke Prevention Guidelines, along with recordings of multiple risk factors in patients with left, right and bilateral ICAs/o<sup>32</sup> are presented in Table 1.

According to the vascular risk profile, arterial hypertension (AH) was present in 22, hyperlipidemia in 16 and diabetes in 13 patients. Multiple vascular risk factors (>2) were noted in 16 patients. Risk factor profile was similar in subgroups of patients with right, left or bilateral ICA s/o.

### Cognitive results assessed by MMSE and MoCA.

For all patients with ICAs/o (median 27.5; IQ 25-29), as well as for subgroups of patients with left (median 28; IQ 25-29) or right (median 27; IQ 26-29.5) ICAs/o,

Table 3. Prevalence of cognition impairment as assessed by Mini Mental State Examination (MMSE) and Montreal Cognitive Assessment (MoCA), total and cognitive domains subtests scores

	All patients (N=26)	ICA stenosis or occlusion		
		Left (N=14)	Right (N=8)	Bilateral (N=4)
MMSE $\leq$ 24	9	5	2	2
MoCA $\leq$ 26	24	13	7	4
- visuospatial/executive (<5)	21	9	8	4
- naming (<3)	1	1	0	0
- attention (<6)	14	8	4	2
- language (<3)	22	13	6	3
- abstraction (<2)	17	10	5	2
- delayed recall (<5)	22	11	7	4
- orientation (<6)	3	1	1	1



Table 4. Cognitive scores assessed by Mini Mental State Examination (MMSE), Montreal Cognitive Assessment (MoCA) and MoCA cognitive domains subtests in patients with left, right and bilateral carotid stenosis or occlusion (one way ANOVA, Kruskal-Wallis ANOVA on ranks)

	Carotid stenosis or occlusion			P
	Left	Right	Bilateral	
n	11	8	7	–
F (n)	6	3	2	–
Age (yrs) <sup>1</sup>	62.8±8.6	68.6±7.5	69.0±9.4	0.229**
MMSE <sup>2</sup>	28 (25.8-29.0)	27 (26-29.5)	26 (25-27.5)	0.480*
MoCA <sub>tot</sub> <sup>1</sup>	22.9±3.3	22.4±4.0	22.6±3.3	0.946**
– visuospatial/executive <sup>2</sup>	3.5±1.5	3.0±1.0	3.3±1.4	0.690**
– naming <sup>2</sup>	3 (3-3)	3 (3-3)	3 (3-3)	0.506*
– attention <sup>2</sup>	5 (3.5-6)	5.5 (4-6)	6 (4-6)	0.836*
– language <sup>2</sup>	2 (2-2)	2 (2-2.5)	2 (2-2.8)	0.165*
– abstraction <sup>2</sup>	1 (1-1.8)	1 (1-2)	1 (1-2)	0.716*
– delayed recall <sup>2</sup>	2 (1.3-4.5)	0.5 (0-3.5)	0 (0-2.5)	0.246*
– orientation <sup>2</sup>	6 (6-6)	6 (6-6)	6 (6-6)	0.932*

<sup>1</sup>mean ± SD; <sup>2</sup>median (25-75 percentile, range); \*Kruskal-Wallis (ANOVA on ranks); \*\*One Way ANOVA

MMSE scores fell within the normal range. In patients with bilateral ICAs/o, the mean MMSE scores were slightly below the normal range (mean 25.5±2.6), although this subgroup of patients was represented with a small sample. The mean MoCA scores were below the normal range in all patients with ICAs/o. Patient subgroups with left, right or bilateral ICAs/o

also scored below the normal range on MoCA, with lowest score (mean 21.5±3.7) recorded in the subgroup of patients with bilateral ICAs/o. Neither MMSE nor MoCA results showed any statistically significant differences in cognitive scores among patient subgroups according to the side of ICAs/o. Total cognitive scores are presented in Table 2.

Table 5. Differences in cognitive testing scores in subgroups of patients with and without presence of multiple risk factors

	MRF (>2)	RF <sub>1-2</sub>	P
n	16	10	–
F	5	6	–
Age (yrs)**	62.3±9.3	67.9±7.8	0.461
MMSE*	28.5 (22-39)	26.5 (25-28)	0.155
MoCA**	23.25±3.5	21.7±3.2	0.266
– visuospatial/executive*	4 (3-5)	3 (2-3)	0.022***
– naming*	3 (3-3)	3 (3-3)	0.809
– attention*	6 (4-6)	5 (4-6)	0.316
– language*	2 (2-2)	2 (2-2)	0.353
– abstraction*	1 (1-1.5)	1.5 (1-2)	0.397
– delayed recall	2.13±2.0	1.5±1.7	0.427
– orientation*	6 (6-6)	6 (6-6)	0.979

MMSE = Mini Mental State Examination; MoCA = Montreal Cognitive Assessment; MRF = multiple risk factors; RF<sub>1-2</sub> = one or two risk factors; \*median ± interquartile range, Mann-Whitney Rank Sum Test; \*\*mean ± SD, t-test; \*\*\*statistically significant difference

Cognitive scores below normal range presented as MMSE and MoCA results and MoCA subtests scores are summarized in Table 3. MMSE was abnormal in 9 of 26 patients, while total MoCA score was below the normal range in all but two patients. When MoCA was used, most patients from all subgroups were found to have a cognitive decline (13 of 14 in patient subgroup with left ICAs/o; 7 of 8 in patient subgroup with right ICAs/o; and 2 of 4 in patient subgroup with bilateral ICAs/o). The most pronounced decline was found in delayed recall and language (22 of 26 patients) and visuospatial/executive functions (21 of 26 patients).

There were no statistically significant differences in cognitive domain scores among the subgroups of patients with right, left or bilateral ICAs/o when MoCA subtests were used for cognitive evaluation (Table 4).

**Cognitive testing scores and vascular risk factor profile.** In order to evaluate the possibility of the association between carotid stenosis or occlusion and cognitive performance to be modified by the presence of vascular risk factors, the risk factor profile was noted and subtest scores for cognitive domains were included in MoCA subtests calculated for all patients.

Cognitive testing scores in the subgroups of patients with more than 2 and with only 1 or 2 risk factors are summarized in Table 5. Comparison of MMSE and MoCA scores between patients with and without multiple risk factors (MRF) yielded no statistically significant differences between the subgroups, except for the visuospatial/executive subtest ( $P=0.022$ ).

Cognitive scores were also analyzed separately for subgroups of patients with only 1 or 2 risk factors, subgroups of patients with MRF including arterial hypertension, and subgroups of patients with MRF including arterial hypertension, hyperlipidemia and diabetes. There were no statistically significant differences among these groups, except for the visuospatial/executive subtest ( $P=0.018$ ) (Table 6).

## Discussion

Our results showed subtle cognitive impairment as assessed by MoCA in stroke-free patients with advanced carotid disease. Cognitive status of the patients with carotid disease has been observed in some previous studies, which mostly assessed

Table 6. Differences in cognitive testing scores in subgroups of patients without presence of multiple risk factors ( $RF \leq 2$ ), patients with multiple risk factors including arterial hypertension [MRF (+AH)] and patients with multiple risk factors including arterial hypertension, hyperlipidemia and diabetes [MRF (+AH, HLP, DM)]

	Risk factors			P
	RF $\leq$ 2	MRF (+AH)	MRF (+AH, HLP, DM)	
n	10	11	14	–
F	6	6	7	–
Age (yrs) <sup>1</sup>	67.9 $\pm$ 7.8	65.2 $\pm$ 9.9	66.9 $\pm$ 7.6	0.745**
MMSE	26.5(25-28) <sup>2</sup>	27.6 $\pm$ 2.4 <sup>1</sup>	27.0 $\pm$ 2.3 <sup>1</sup>	0.231*
MoCA <sup>1</sup>	21.7 $\pm$ 3.2	23.4 $\pm$ 3.1	22.5 $\pm$ 2.6	0.384**
– visuospatial/executive	2.6 $\pm$ 1.7 <sup>1</sup>	4(3-5) <sup>2</sup>	4(3-5) <sup>2</sup>	0.018* <sup>3</sup>
– naming <sup>2</sup>	3(3-3)	3(3-3)	3(3-3)	0.648*
– attention	4.6 $\pm$ 1.4 <sup>1</sup>	6(4-6) <sup>2</sup>	5(4-6) <sup>2</sup>	0.473*
– language <sup>2</sup>	2(2-2)	2(2-2)	2(1.3-2)	0.198*
– abstraction <sup>2</sup>	1.5(1-2)	1(1-2)	1(1-1)	0.434*
– delayed recall	1.5 $\pm$ 1.7 <sup>1</sup>	2(0-4) <sup>2</sup>	2(0-3) <sup>2</sup>	0.850*
– orientation <sup>2</sup>	6(6-6)	6(6-6)	6(6-6)	0.914*

<sup>1</sup>mean  $\pm$  SD; <sup>2</sup>median (25-75 percentile, range); <sup>3</sup>statistically significant difference; \*Kruskal-Wallis (ANOVA on ranks);

\*\*One Way ANOVA



cognitive decline in patients with symptomatic carotid disease (i.e. previous stroke or TIA) and/or in symptomatic ICA stenosis patients before scheduled carotid endarterectomy<sup>3,15,16,33-38</sup>. Cognitive assessment of asymptomatic patients with carotid disease has so far been investigated in a smaller number of studies<sup>16,18,20,36,39</sup>.

Whether carotid stenosis itself causes or contributes to cognitive impairment in patients that are otherwise asymptomatic has not yet been clarified<sup>20</sup>. Carotid artery disease is associated with underlying vascular risk factors. The same vascular risk factors are well known to increase the risk of ischemic injury to the brain independently of carotid disease<sup>32</sup>. Furthermore, several risk factors for vascular disease are strongly associated with cognitive impairment<sup>2,3,5-8</sup>.

In our study, MMSE scores showed no signs of cognitive impairment in patients with ICAs/o, either in the subgroup of patients with left ICAs/o or those with right ICAs/o. Slightly abnormal MMSE scores were only found in patients with bilateral ICAs/o (mean  $\pm$  SD: 25.5 $\pm$ 2.6), although this subgroup of patients was represented with a small sample. The mean MoCA scores were below the normal range in all patients with ICAs/o and in all subgroups of patients divided according to the side of stenosis. Patients with bilateral ICAs/o that were found to suffer from slight cognitive impairment when tested by MMSE, also had the lowest total MoCA score (mean  $\pm$  SD: 21.5 $\pm$ 3.7). This finding corroborates the superior ability of MoCA to detect very mild cognitive disturbances, as previously demonstrated elsewhere<sup>24,28</sup>. MMSE is still the most commonly applied cognitive screening tool. MoCA has been shown to be a rapid and reliable cognitive screening instrument that is sensitive enough to detect mild cognitive deficits<sup>24,29</sup>. Both tests are easy and convenient to administer, but MMSE is subject to criticism mostly because it fails to discriminate exactly between individuals with dementia and those that are non-demented, and has overly simple language items that reduce its sensitivity to mild linguistic deficits<sup>23,40</sup>.

The analysis of MoCA subtest scores for different cognitive domains revealed our patients with ICAs/o to have cognitive decline most often when tested for visuospatial/executive functions (21 of 26 patients) and for short-term memory and language functions as assessed by delayed recall task and verbal fluency

test (22 of 26 patients). Executive functions on MoCA are tested using Trial Making Test B and visuospatial abilities using clock drawing test and three dimensional cube copy, which all are known to be sensitive to frontal lobe dysfunction. In MoCA, short-term memory and language functions are assessed by delayed recall task and by verbal fluency test. Besides temporal lobe disturbances, these tests also assess involvement of the frontal lobe areas. A similar pattern of cognitive impairment with signs of frontal lobe dysfunction in patients with carotid stenosis was found in some previous studies, although some of them included larger patient samples. In a study of 83 patients with asymptomatic severe carotid stenosis, Silvestrini *et al.* found significantly lower performance at verbal fluency test in patients with left-sided disease as compared with controls and other groups of stenosis<sup>39</sup>. Rao showed impaired frontal lobe functions as assessed by verbal fluency test in patients with asymptomatic ICAs/o<sup>16</sup>, whereas Benke *et al.*, in a study of 20 patients with asymptomatic carotid stenosis found substantial deficits on verbal processing tasks, as well as on mental speed, learning, visuospatial abilities and deductive reasoning<sup>16,36</sup>. In a larger sample of 183 patients with different grades of carotid stenosis from the Tromsø study, Mathiesen *et al.* found attention, psychomotor speed and memory to be significantly lower when compared to controls without carotid stenosis<sup>18</sup>. The same pattern of cognitive impairment was recognized as typical for vascular cognitive impairment. It may include all cognitive domains, but there is likely to be a preponderance of executive dysfunction including working memory<sup>29</sup>. The most common problems when comparing study results are different sample size and inclusion/exclusion criteria. Non-uniformed neuropsychological testing protocols often present an additional problem.

We found no statistically significant differences in cognitive domain scores among patient subgroups with right, left or bilateral ICAs/o when MoCA subtests were used for cognitive evaluation. In a study that included a similar patient sample (32 patients, of which only 27 had unilateral stenosis), Johnston *et al.* found a higher prevalence of impaired cognition on modified MMSE in patients with severe stenosis of the left ICA as compared to the right ICA stenosis<sup>20</sup>. We believe that the size of our sample was probably insufficient to detect a difference in the laterality of stenosis. We



have previously shown an increased incidence of mild cognitive decline in symptom-free individuals with the presence of vascular risk factors<sup>28</sup>. Accordingly, the management of vascular risk factors and lifestyle adjustments may help prevent both Alzheimers disease (AD) and vascular dementia (VAD)<sup>42,43</sup>. In the present study, only visuospatial/executive subtests of MoCA yielded significant differences when patients with and without MRF were compared ( $P=0.022$ ). Comparison of subgroups of patients with MRF that included only arterial hypertension and subgroups of patients with MRF that included three most common risk factors (arterial hypertension, hyperlipidemia and diabetes) again revealed significant differences in visuospatial/executive subtests of MoCA ( $P=0.018$ ). Most of our patients had no subjective memory complaints, so our results agree with the aforementioned reports that have stressed the preponderance of executive dysfunction in the initial cognitive decline of vascular type<sup>29</sup>. Paradoxically, in our study patients with only one or two risk factors had lower cognitive scores than patients with MRF (Tables 5 and 6). This may have also been due to the small sample size or the lack of compliance in the management of vascular risk factors and lifestyle adjustments, which is often a problem in this patient group.

Our study had limitations since the overall number of patients was small, but statistical significance was achieved. There are no previous studies that investigated the ability of MoCA in patients with carotid disease. We did not speculate on the possible pathomechanisms of cognitive impairment in patients with severe carotid disease, which remain quite obscure. The mechanisms proposed include silent embolization and hypoperfusion, and Silvestrini *et al.* also consider altered cerebrovascular reactivity to be responsible for cognitive decline in patients with asymptomatic carotid stenosis<sup>23,39</sup>.

Although performed in a small patient sample, our study further implicates that the presence of multiple vascular risk factors could possibly aid to the cognitive decline in patients with severe carotid disease, especially considering executive and visuospatial domains. It also further stressed the importance of tight control of vascular risk factors in both symptomatic and asymptomatic patients with severe carotid disease<sup>28,43</sup>. Stroke-free patients with advanced carotid stenosis or occlusion express subtle cognitive impairment es-

pecially in visuospatial and executive domains. Such cognitive changes can be easily recognized if MoCA is used for assessment, while MMSE remains too rough to detect mild cognitive decline and fails to discriminate among affected cognitive domains more precisely. We found no differences in cognitive impairment according to the side of ICAs/o, but the initial cognitive impairment in visuospatial and executive domains was significantly related to the vascular risk factor profile.

In order to carefully evaluate cognitive changes in individuals with severe carotid disease and to reduce the risk of more severe cognitive decline, additional studies in a greater number of patients are needed.

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## Sažetak

## PROCJENA BLAGOG SPOZNAJNOG POREMEĆAJA KOD BOLESNIKA S KAROTIDNOM BOLEŠĆU BEZ MOŽDANOG UDARA

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Karotidna bolest je prepoznata kao čimbenik rizika za nastanak moždanog udara, a moždani udar kao čimbenik rizika za poremećaj spoznajnih funkcija, no povezanost stenoze karotidnih arterija i spoznajnih funkcija je manje jasna. Većina bolesnika navodi samo blaže spoznajne poteškoće za procjenu kojih uobičajeni testovi nisu dovoljno osjetljivi. Dvadesetšestero bolesnika s uznapredovalom stenozom i/ili okluzijom unutarnje karotidne arterije (ICA) je uključeno u ispitivanje (srednje dobi 66,3±8,7 godina, 15 muškaraca i 11 žena), jedanaestero s lijevostranom, 8 s desnostranom i 7 s obostranom stenozom i/ili okluzijom ICA. Uz anamnestičke podatke i neurološki pregled kod svih bolesnika zabilježeni su podaci o vaskularnim čimbenicima rizika i učinjen je CT mozga. Spoznajne funkcije su ispitane primjenom Mini Mental testa (MMSE) i Montrealske ljestvice kognitivne procjene (MoCA). Svi bolesnici su bili asimptomatski, osim dvoje bolesnika koji su imali ponovljene prolazne ishemijske atake (TIA). Kod svih bolesnika vrijednost medijana testa MMSE bila je u granicama normale (27,5; IQ raspon 25-29), dok su srednje vrijednosti testa MoCA bile snižene u odnosu na normalne vrijednosti (22,6±3,4). Bolesnici sa stenozom i/ili okluzijom lijeve ACI imali su nešto bolje rezultate na testu MoCA (22,9±3,3) u odnosu na bolesnike s desnostranom bolešću (22,4±4,0). Kod 22 od 26 bolesnika nađene su snižene vrijednosti na MoCA podtestu odgođenog prisjećanja, a kod 23 od 26 bolesnika snižene vrijednosti na MoCA podtestu ispitivanja vidno-prostornih funkcija, no nisu nađene statistički značajne razlike u odnosu na stranu stenoze i/ili okluzije ICA. Rezultati bolesnika s jednim ili dva vaskularna čimbenika rizika na MoCA podtestu za ispitivanje vidno-prostornih i izvršnih funkcija bili su su lošiji u odnosu na rezultate bolesnika s višestrukim čimbenicima rizika ( $P=0,018$ ). Test MoCA ima dovoljnu osjetljivost za procjenu blagog spoznajnog poremećaja kod bolesnika s uznapredovalom stenozom i/ili okluzijom karotidnih arterija, bez moždanog udara. Najizraženiji poremećaj zabilježen je u odnosu na vidno-prostorne funkcije te na kratkoročno pamćenje.

**Ključne riječi:** *Cerebrovaskularne bolesti – etiologija; Cerebrovaskularni krvotok – fiziologija; Karotidna stenoza – komplikacije; Spoznajni poremećaji – patofiziologija*