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Please cite this article **DEGREE OF COGNITIVE IMPAIRMENT IN PATIENTS WITH CAROTID STENOSIS IN RELATION TO CEREBRAL ISCHEMIC LESIONS**
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DEGREE OF COGNITIVE IMPAIRMENT IN PATIENTS WITH CAROTID STENOSIS IN RELATION TO CEREBRAL ISCHEMIC LESIONS

STEPEN KOGNITIVNOG OŠTEĆENJA KOD PACIJENATA SA KAROTIDNOM STENOZOM U ODNOSU NA CEREBRALNE ISHEMIJSKE LEZIJE

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Abstract

Background/Aim. The presence of carotid stenosis is a risk factor for cognitive impairment. The aim of our study was to evaluate the degree of cognitive impairment in patients with asymptomatic and symptomatic carotid stenosis and correlate it with the presence, location, and extent of cerebral ischemic lesions.

Material and methods. A prospective analysis of 180 patients aged 50-70years, divided into three groups (asymptomatic, symptomatic carotid stenosis and controls), was made. We assessed demographic characteristics, vascular risk factors, ultrasound examination of the carotid arteries, computerized tomography (CT), magnetic resonance imaging (MRI) of the brain, and neuropsychological testing.

Results. The brain CT findings at admission showed ischemic lesions in the left hemisphere in 13.3% patients of the asymptomatic and 41% in the symptomatic group. In the right hemisphere, lesions were registered in 10% of the asymptomatic and 46,7% of the symptomatic patients. The difference between groups was statistically significant. The lesion volumes measured on CT and MRI scans were significantly different ($p < 0.001$) between groups with asymptomatic and symptomatic carotid stenosis. The degree of cognitive impairment measured by the ACE-R test was significantly different between groups ($p<0.05$) with the most severe deficit in the symptomatic group.

Conclusion. Our study has shown that cognitive impairment was more severe in patients with symptomatic carotid stenosis, compared to the patients with asymptomatic carotid stenosis.

Keywords: asymptomatic carotid stenosis; symptomatic carotid stenosis; cognitive impairment; cerebral ischemic lesions

Sažetak

Uvod/Cilj. Postojanje karotidne stenoze predstavlja potencijalni faktor rizika za poremećaj kognitivnih funkcija. Cilj našeg istraživanja je ispitivanje stepena kognitivnog poremećaja kod pacijenata sa asimptomatskom i simptomatskom karotidnom stenozom i njegove povezanosti sa postojanjem, lokacijom i veličinom cerebralnih ishemijskih lezija.

Materijal i Metode. Sprovedena je prospektivna analiza 180 pacijenata starosti od 50 do 70 godina, podeljenih u tri grupe (asimptomatska, simptomatska karotidna stenoza i kontrolni subjekti). Procenjivali smo demografske karakteristike, vaskularne faktore rizika i

sprovedeni su ultrazvučni pregled karotdnih arterija, kompjuterizovana tomografija (KT), magnetna rezonanca (MR) mozga kao i neuropsihološko testiranje.
Rezultati. Nalazi na KT mozga na prijemu pokazali su lezije u levoj hemisferi u 13,3% asimptomatskih pacijenata i 41% pacijenata u simptomatskoj grupi. U desnoj hemisferi registrovane su lezije kod 10% pacijenata u asimptomatskoj i 46,7% pacijenata u simptomatskoj grupi. Razlika izmedju grupa bila je statistički značajna. Zapremina lezija merena neuroradiološkim metodama se statistički značajno razlikuje ($p < 0.001$) između grupa sa asimptomatskom i simptomatskom karotidnom stenozom. Stepen kognitivnih oštećenja meren ACE-R testom bio je značajno različit između grupa ($p<0,05$) sa najizraženijim deficitom u simptomatskoj grupi.
Zaključak. Naše istraživanje je pokazalo da je kognitivno oštećenje značajno većeg stepena kod pacijenata sa simptomatskom karotidnom stenozom, u poredjenju sa pacijenatima sa asimptomatskom karotidnom stenozom.

Ključne reči: asimptomatska karotidna stenoza; simptomatska karotidna stenoza; kognitivno oštećenje; moždane ishemičke lezije.

Introduction

The presence of carotid stenosis is a potential risk factor for cognitive impairment, which has been proven by several studies[1-4]. The underlying mechanisms are embolization and hypoperfusion that can cause lacunary or silent brain infarcts, associated with an increased risk of dementia. Cognitive impairment might also be present in asymptomatic high-grade carotid stenosis, without evidence of infarction on magnetic resonance imaging, connected with microangiopathy and vascular risk factors[4].
The aim of our study was to evaluate the degree of cognitive impairment in patients with asymptomatic and symptomatic carotid stenosis and correlate it with the presence, location, and extent of cerebral ischemic lesions.

Methods

A prospective analysis of 180 patients aged 50-70 years, divided into three groups: asymptomatic patients with carotid stenosis and without transient ischemic attack (TIA)/stroke, symptomatic patients, with carotid stenosis and TIA/stroke and control group

of patients with headache/vertigo and normal findings of the carotid arteries and CT scan. We have obtained written consent from the patients/their families. Exclusion criteria were: the presence of aphasia, intracerebral hemorrhage, vascular malformations, tumors, multiple sclerosis, or other diseases on neuroimaging, severe stroke with NIHSS score > 15.

We assessed demographic characteristics and vascular risk factors. Ultrasound examination of the carotid arteries was performed using B-mode ultrasonography with a probe of 7.5 MHZ according to the Atherosclerosis Risk in Communities (ARIC) protocol[5]. The patients were stratified according to the degree of stenosis as no stenosis, low (0-49%), moderate (50-69%), and a high degree of stenosis (≥70%)[6]. Cognitive functions were evaluated with Addenbrooke's cognitive examination (ACE-R) test[7]. We analyzed temporal and spatial orientation, attention, calculation, speech, memory, visuospatial abilities. The test was carried out six months after hospitalization in patients with symptomatic stenosis and six months after initial examination in patients with asymptomatic carotid stenosis and the control group. Computer tomography (CT) of the brain was performed at admission and 24 to 72 hours afterward, analyzing the size and location of acute ischemic lesions. Magnetic resonance imaging (MRI) of the brain was performed within six months after the initial examination of all patients. The severity of stroke was estimated by the National Institute of Health Stroke Scale (NIHSS), ranging from 0-30. Stroke was classified as mild (≤ 8), moderate (9 – 15), and severe (> 15)[8]. Patients with severe stroke (NIHSS > 15) were excluded from this study. Statistical analysis was performed with the statistical programs: STATISTICA 7.1; SPSS 17.0.

Results

In the brain CT findings at admission, structural lesions were absent in 60% of the patients in the asymptomatic group, 10% of the patients of the symptomatic group, and 100% of patients in the control group. The difference between the asymptomatic and symptomatic groups is statistically significant ($p<0.001$). On the control CT, structural lesions were seen in 40% of the asymptomatic group patients and all patients in the symptomatic group.

In the CT findings at admission, lesions in the left hemisphere were registered in 13.3% of patients in the asymptomatic group and 41% of the symptomatic group. The difference between the asymptomatic and symptomatic group was statistically significant ($p< 0.001$).

In the CT findings at admission, lesions in the right hemisphere were registered in 10.0% of patients in the asymptomatic group and 46.7% of patients of the symptomatic group while the difference was statistically significant ($p< 0.001$).

The ischemic lesion volumes (cm^3) measured on CT and MRI scans were significantly different ($p < 0.001$) between groups with asymptomatic and symptomatic carotid stenosis (Figure 1).

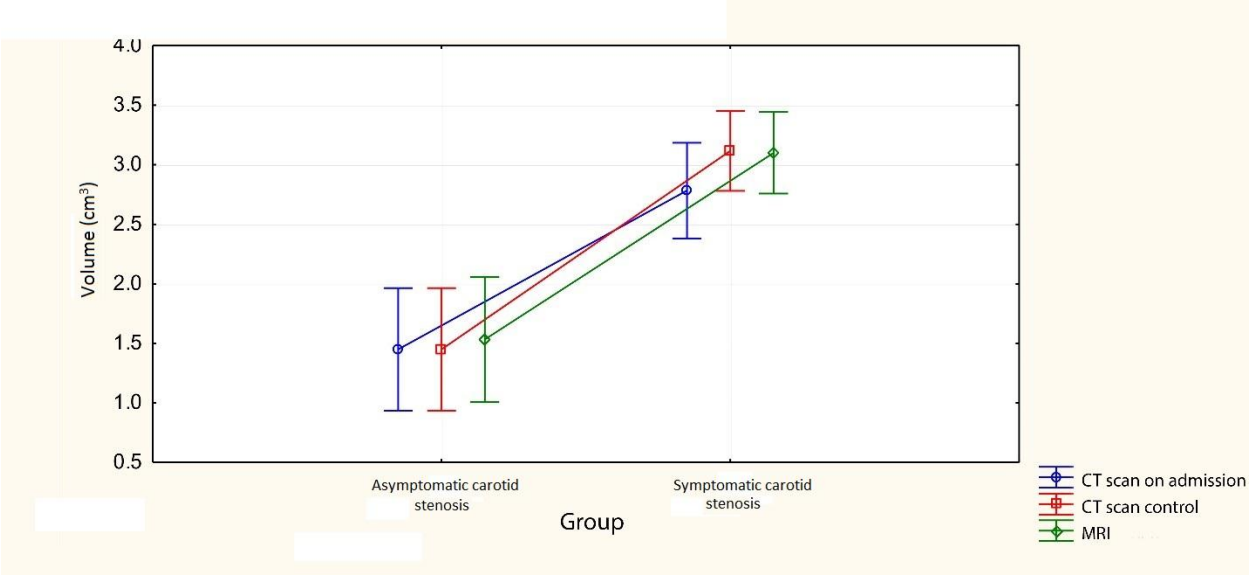

Figure 1. Ischemic lesion volumes (cm^3) in asymptomatic carotid stenosis group and symptomatic carotid stenosis group

Ischemic brain lesions were registered on the follow-up MRI examination in 60% of patients with asymptomatic carotid stenosis and all patients with symptomatic carotid stenosis. Control subjects had no ischemic brain lesions on MRI.

MRI examination showed lesions in the left hemisphere in 13.3% of patients in the asymptomatic group and 45% of the symptomatic group ($p< 0.001$), and lesions in the right hemisphere in 10% of patients in the asymptomatic group and 53.3% of the symptomatic group ($p< 0.001$). The locations of structural lesions on CT and MRI are shown in Table 1.

Table 1.

Location of structural lesions on admission and control CT and MRI scans

	ACS		***SCS***	
	No	%	No	%
CT scan on admission				
No lesion	36	60.0	6	10.0
Frontal	1	1.7	4	6.7
Parietal	6	10.0	19	31.7
Temporal	5	8.5	11	18.3
Occipital	1	1.7	8	13.3
Basal ganglia	11	18.3		
Control CT scan				
No lesion	36	60	0	
Frontal	1	1,7	4	6.7
Parietal	6	10.0	21	35.0
Temporal	5	8.5	13	21.7
Occipital	1	1.7	8	13.3
Basal ganglia	11	18.3	14	23.3
MRI				
No lesions	36	60	0	
Frontal	1	1,7	5	8.3
Parietal	6	10.0	20	33.3
Temporal	5	8.5	13	21.7
Occipital	1	1.7	8	13.3
Basal ganglia	11	18.3	14	23.3

Impairment of temporal and spatial orientation was registered in 16.7% of patients in the symptomatic carotid stenosis group ($p<0.05$). Impairment of attention was recorded in 48.3% in the asymptomatic group, 71,7% in the symptomatic group and 25.0% in the

control group. There was a statistically significant difference between the first group compared to the second and the control group, respectively (p = 0.01, p = 0.009). Impairment of calculation abilities was registered in 43.3% of the asymptomatic, 78.3% in the symptomatic, and 13.3% in the control group. The difference was statistically significant between the symptomatic compared to the asymptomatic and the control group, respectively (p< 0.001). Language impairment was seen in 3.3% in the asymptomatic, 58.3% in the symptomatic, and none in the control group. The difference between the asymptomatic and symptomatic group was significant (p< 0.001), and non-significant between the asymptomatic and control group (p<0.05). Memory impairment was recorded in 75% in the asymptomatic, 91,7% in the symptomatic, and 28,3% in the control group. The differences between the asymptomatic, symptomatic, and the control group were significant (p=0.02, p<0.001, respectively).

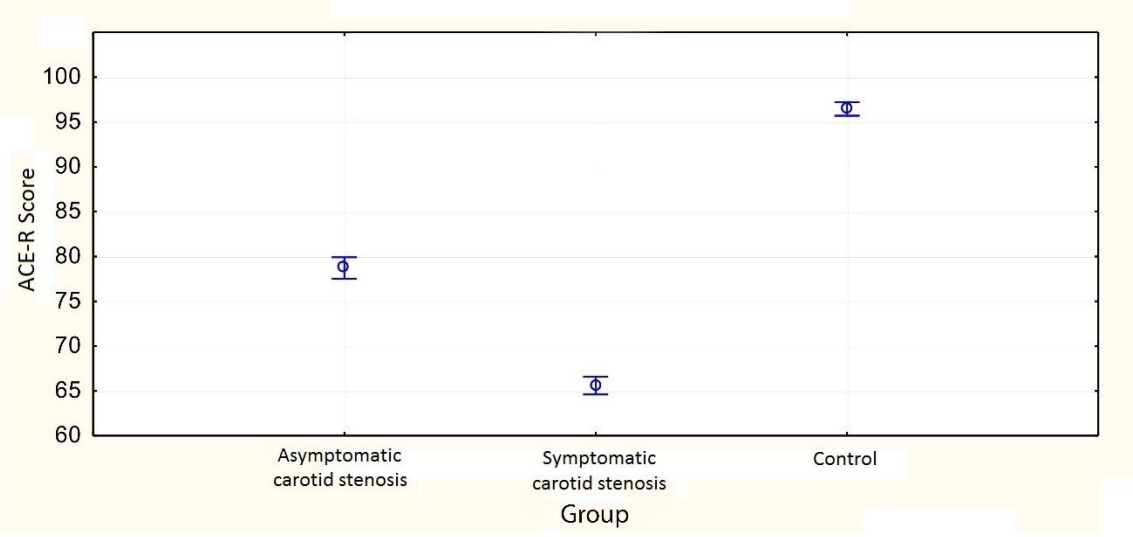

Figure 2. Average ACE-R score in asymptomatic carotid stenosis group, symptomatic carotid stenosis group, and control group

The average value of ACE-R scores was 78.7 ± 4.6in the asymptomatic group was 65.6 ± 3.9in the symptomatic group and 96.5 ± 2.9 in the control subject (Figure 2). According to Analysis of Variance, the difference between the average result values in the three groups was statistically significant (p< 0.001), The post hoc Tukey HSD test shows a statistically significant difference between the asymptomatic, symptomatic and control group (p< 0.001).

The relation between the degree of cognitive impairment and the location of lesions on the

initial CT, control CT, and MRI examination in the asymptomatic and symptomatic group are shown in Table. 2, Table 3, and Table 4, respectively. There was no statistically significant correlation between lesion location on admission, control scans and MRI findings and the level of cognitive impairment found on the ACE-R test ($p>0.05$).

Table 2.

Number of patients according to the location on CT scans on admission and degree of cognitive impairment (CI)

	Asymptomatic carotid stenosis				*Symptomatic carotid stenosis*			
	Mild CI	Moderate CI	Severe CI	Total	Mild CI	Moderate CI	Severe CI	Total
No lesions	35	13	0	48	0	5	1	6
Frontal lobe	0	0	0	0	0	3	1	4
Parietal lobe	1	0	0	1	0	9	10	19
Temporal lobe	1	2	0	3	0	7	4	11
Occipital lobe	1	0	0	1	0	5	3	8
Basal ganglia	3	4	0	7	0	7	5	12
Total	41	19	0	60	0	36	24	60

Table 3.

Number of patients according to the location on control CT scans and degree of cognitive impairment (CI)

	Asymptomatic carotid stenosis				*Symptomatic carotid stenosis*			
	Mild CI	Moderate CI	Severe CI	Total	Mild CI	Moderate CI	Severe CI	Total
No lesions	35	13	0	46	0	0	0	0
Frontal lobe	0	0	0	0	0	3	1	4
Parietal lobe	1	0	0	1	0	11	10	21
Temporal lobe	2	2	0	4	0	9	4	13
Occipital lobe	1	0	0	1	0	5	3	8
Basal ganglia	4	4	0	8	0	8	6	14
Total	41	19	0	60	0	36	24	60

Table 4.

Number of patients by the location of lesion registered on MRI scans and degree of cognitive impairment (CI)

	Asymptomatic carotid stenosis				*Symptomatic carotid stenosis*			
	Mild CI	Moderate CI	Severe CI	Total	Mild CI	Moderate CI	Severe CI	Total
No lesions	26	9	0	35	0	0	0	0
Frontal lobe	1	0	0	1	0	3	2	5
Parietal lobe	4	2	0	6	0	11	9	20
Temporal lobe	3	2	0	5	0	9	4	13
Occipital lobe	1	0	0	1	0	5	3	8
Basal ganglia	6	6	0	12	0	8	6	14
Total	41	19	0	60	0	36	24	60

Discussion

The results of our study are in accordance with the data found in the literature. The study of Moreau et al, aimed to directly compare the sensitivity of CT and MRI scans in patients with TIA and/or mild strokes with acute ischemic lesions[9]. CT and MRI were performed within 24 hours after symptom onset. Acute ischemic lesions were compared on CT and MRI, while the acute lesion volume was measured with MRI. The study showed that MRI had higher sensitivity compared to CT in identifying small acute ischemic lesions. MRI also showed lesions with smaller volumes that were missed on CT scans. In TIA or lacunar stroke patients, acute ischemic lesions were identified with MRI in 35-50% of the patients,

while the same lesions were found in only 10% when CT scans were performed. The same results were found in the study of Forster et al. where the percentage of acute strokes proven on MRI after negative CT scans were greater than 33%[10]. This difference is mostly a consequence of the size i.e. the volume of the stroke because the sensitivity of the CT in recognizing ischemic lesions smaller than 1 cm^3 is weak[11] . The limitation of our study is that CT and MRI scans were not done simultaneously, and the time between the symptom onset and MRI scans was longer compared to the timing of CT scans. As early ischemic changes become more prominent in time, this fact goes potentially in favor of the MRI diagnostics[12]. The percentage of visualized lesions on MRI was higher in the asymptomatic carotid stenosis group.

A study by Tomlinson et al., suggested that the volume of stroke is correlated to the appearance and development of cognitive impairment. Stroke can cause vascular dementia when the volume of a stroke is larger than 100 ml[13]. A survey by Zekry et al., suggested that the total volume of the stroke can explain only a small portion of the cognitive impairment in stroke patients, and discovered that strokes in strategic areas play an important role in the cognitive disorder mechanism and are connected with the severity of dementia[14]. These strategic regions are cortical limbic regions, frontal cortex, and white mass. There are limitations in the fact that many patients, who have brain damage, usually have motor difficulties that adversely affect the performance of the test (e.g. drawing) and often have a language difficulty[15,16]. In our study, there was no statistically significant correlation between the lesion location at admission and control CT scans, MRI scans in the examined groups of patients compared to the level of cognitive impairment seen on the ACE-R test. In our study, we have chosen neuropsychological testing which is necessary for the screening of patients with dementia after stroke or patients with carotid stenosis, without the anamnestic data for stroke and its identification in the early stages of the disease, which would enable early intervention and possible delay of the cognitive impairment development with proper cognitive rehabilitation[15]. The study of Lees et al., studied the usefulness of ACE-R test in detecting cognitive impairment after a stroke[16]. The test gives data for the patient's cognitive profile and as a screening method can speed up the cognitive deficit diagnostic process after stroke[15]. It was shown that the ACE – R has a significant connection with other neuropsychological teststhat examine only a certain domain. The memory that was assessed with ACE-III is associated with two classic

neuropsychological memory tests- Free and Cued Selective Reminding Test and the Rey Auditory Verbal Learning Test [15,16]. The speech and verbal fluency, which were tested with ACE-R, were in correlation with tests that assess attention and executive functions (the trail making test, memory span, Stroop test) [16]. In the study of Al-Qazzaz et al., it was found that stroke increases the risk of cognitive impairment, where 21% of the stroke survivors experienced cognitive function decline after the third month[17]. This research shows that demographic characteristics of stroke patients, including age and gender, are related to cognitive impairment and dementia. Cognitive impairment increased with age due to decreased cerebral flow.

Conclusion

We did not find a statistically significant connection between the locations of the cerebral ischemic lesions and the degree of cognitive impairment. However, we confirmed that cognitive impairment was more severe in patients with stroke and symptomatic carotid stenosis, compared to the patients with asymptomatic carotid stenosis.

Ethical consideration

Experiments were performed with the understanding and consent of each subject, with the approval of the local ethics committee.

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