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Degree of cognitive impairment in patients with carotid stenosis in relation to cerebral ischemic lesions

Stepen kognitivnog oštećenja u odnosu na cerebralne ishemijske lezije kod bolesnika sa karotidnom stenozom

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Abstract

Background/Aim. Carotid stenosis is a risk factor for cognitive impairment. The aim of the 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 carotid stenosis, 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 on admission showed ischemic lesions in the left hemisphere in 13.3% of patients in the asymptomatic group and in 41% of those in the symptomatic group. In the right hemisphere, lesions were registered in 10% of the asymptomatic patients and in 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 Addenbrooke's Cognitive Examination Revised (ACE-R), was significantly different between the 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.

Key words:
cognition disorders; carotid stenosis; diagnosis; magnetic resonance imaging; severity of illness index; risk factors; x-ray computed tomography.

Apstrakt

Uvod/Cilj. Karotidna stenoza je faktor rizika od razvoja poremećaja kognitivnih funkcija. Cilj ovog istraživanja je bio da ispita stepen kognitivnog poremećaja kod bolesnika sa asimptomatskom i simptomatskom karotidnom stenozom i njegove povezanosti sa postojanjem, lokacijom i veličinom cerebralnih ishemijskih lezija. **Metode.** Prospektivnom analizom obuhvaćeno je 180 bolesnika starosti od 50 do 70 godina, podeljenih u tri grupe (asimptomatska i simptomatska karotidna stenoza i osobe bez stenoze karotnih aterija – kontrolna grupa). Procenjivane su demografske karakteristike i vaskularni faktori rizika, izvršeni su ultrazvučni pregled karotidnih arterija, kompjuterizovana tomografija (KT), magnetna rezonanca (MR) mozga, kao i neuropsihološko testiranje. **Rezultati.** Nalazi KT mozga na prijemu pokazali su lezije u levoj hemisferi kod 13,3% asimptomatskih bolesnika i 41% bolesnika u simptomatskoj grupi. U desnoj hemisferi registrovane su lezije kod 10% bolesnika u asimptomatskoj i 46,7% bolesnika u simptomatskoj grupi. Razlika između grupa bila je statistički značajna. Zapremina lezija, merena metodama KT i MR, statistički značajno se razlikovala ($p < 0,001$) između grupa sa asimptomatskom i simptomatskom karotidnom stenozom. Stepen kognitivnih oštećenja, meren Adenbrukovim revidiranim testom kognitivne procene (ACE-R), bio je značajno različit između grupa ($p < 0,05$) sa najizraženijim deficitom u simptomatskoj grupi. **Zaključak.** Naše istraživanje je pokazalo da je kognitivno oštećenje kod bolesnika sa simptomatskom karotidnom stenozom značajno višeg stepena od onog kod bolesnika sa asimptomatskom karotidnom stenozom.

Ključne reči:
saznanje, poremećaji; aa. carotis, stenoza; dijagnoza; magnetska rezonanca, snimanje; bolest, indeks težine; faktori rizika; tomografija, kompjuterizovana, rendgenska.

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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 (MRI), connected with microangiopathy and vascular risk factors [4].

The aim of our study was to evaluate the degree of cognitive impairment in asymptomatic and symptomatic carotid stenosis patients, and correlate it with the presence, location, and extent of cerebral ischemic lesions.

Methods

A prospective analysis included 180 patients aged 50–70 years, divided into three groups: asymptomatic patients with carotid stenosis, without transient ischemic attack (TIA)/stroke; symptomatic patients, with carotid stenosis and TIA/stroke; and a control group of patients with headache/vertigo and normal carotid arteries on a computed tomography (CT) scan. Written consent was obtained from the patients/their families and the study was approved by the local Ethics Committee.

Exclusion criteria were: aphasia, intracerebral hemorrhage, vascular malformations, tumors, multiple sclerosis, or other diseases on neuroimaging, severe stroke with the National Institutes of Health Stroke Scale (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 7.5 MHz probe according to the Atherosclerosis Risk in Communities (ARIC) protocol [5]. The patients were stratified according to the degree of stenosis as follows: no stenosis; low (0–49%); moderate (50–69%); and a high degree of stenosis (≥ 70%) [6]. Cognitive functions were evaluated using the Addenbrooke's Cognitive Examination Revised (ACE-R) score [7]. We analyzed temporal and spatial orientation, attention, calculation, speech, memory, and 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 in the control group. CT of the brain was performed on admission and at 24 h to 72 h thereafter, analyzing the size and location of acute ischemic lesions. MRI of the brain was performed within six months after the initial examination of all patients. The severity of stroke was estimated using the 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 using STATISTICA 7.1 and SPSS 17.0 statistical software.

Results

On admission, CT of the brain showed no structural lesions in 60% of patients in the asymptomatic group, 10% of patients in the symptomatic group, and 100% of patients in the control group. The difference between asymptomatic carotid stenosis (ACS) and symptomatic carotid stenosis (SCS) patients was statistically significant ($p < 0.001$). On the control CT, structural lesions were seen in 40% of ACS patients and in all SCS ones.

In the CT findings on admission, lesions in the left hemisphere were registered in 13.3% of ACS patients, and in 41% of SCS patients. The difference between the two groups was statistically significant ($p < 0.001$).

In the CT findings on admission, lesions in the right hemisphere were registered in 10.0% of ACS patients, and in 46.7% of SCS patients. 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 ACS patients and SCS patients (Figure 1).

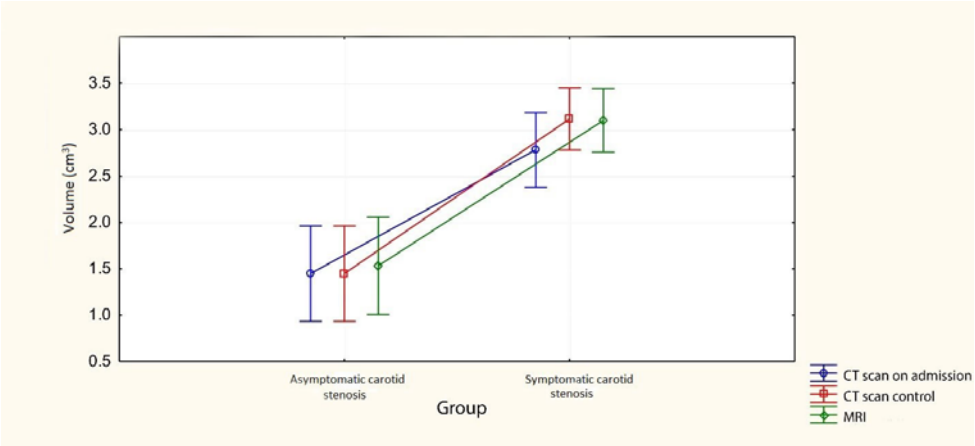

Fig. 1 – Ischemic lesion volumes (cm^3) in the asymptomatic carotid stenosis group and in the symptomatic carotid stenosis group.
CT – computed tomography; MRI – magnetic resonance imaging.

Ischemic brain lesions were registered on the follow-up MRI examination in 60% of ACS patients and in all SCS patients. Control subjects had no ischemic brain lesions on MRI.

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

Table 1

Location of structural brain lesions according to CT scan on admission and control CT and MRI scans

Location of lesion	ACS patients n (%)	SCS patients n (%)
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)

Note: CT of the brain was performed on admission and at 24 h to 72 h thereafter; MRI of the brain was performed within six months after the initial examination of all patients.

CT – computed tomography; MRI – magnetic resonance imaging; ACS – asymptomatic carotid stenosis; SCS – symptomatic carotid stenosis.

Impairment of temporal and spatial orientation was registered in 16.7% of patients in the SCS group ($p < 0.05$). Impairment of attention was recorded in 48.3% of ACS patients, 71.7% of SCS patients, and 25.0% of control subjects. There was a statistically significant difference regarding ACS patients compared to SCS patients and the control subjects ($p = 0.01$, $p = 0.009$, respectively). Impairment of calculation abilities was registered in 43.3% of ACS patients, 78.3% of SCS patients, and 13.3% of control subjects. The difference was statistically significant regarding SCS patients compared to the ACS patients and the control group, respectively ($p < 0.001$). Language impairment was seen in 3.3% of ACS patients, 58.3% of SCS patients, and in none in the control group. The difference between ACS patients and SCS patients was significant ($p < 0.001$), and nonsignificant between ACS patients and the controls ($p > 0.05$). Memory impairment was recorded in 75% of ACS patients, 91.7% of SCS patients, and in 28.3% of patients in the control group. The differences between ACS patients, SCS patients, and controls were significant ($p = 0.02$, $p < 0.001$, respectively).

The average ACE-R scores were 78.7 ± 4.6 in ACS patients, 65.6 ± 3.9 in SCS patients, and 96.5 ± 2.9 in the control subjects (Figure 2). Analysis of variance showed the statistically significant differences in the average scores in the three groups ($p < 0.001$). The *post hoc* Tukey HSD test showed a statistically significant difference between ACS patients, SCS patients, and the 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 examinations in ACS patients and SCS patients is shown in Tables 2, 3, and 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 ($p > 0.05$).

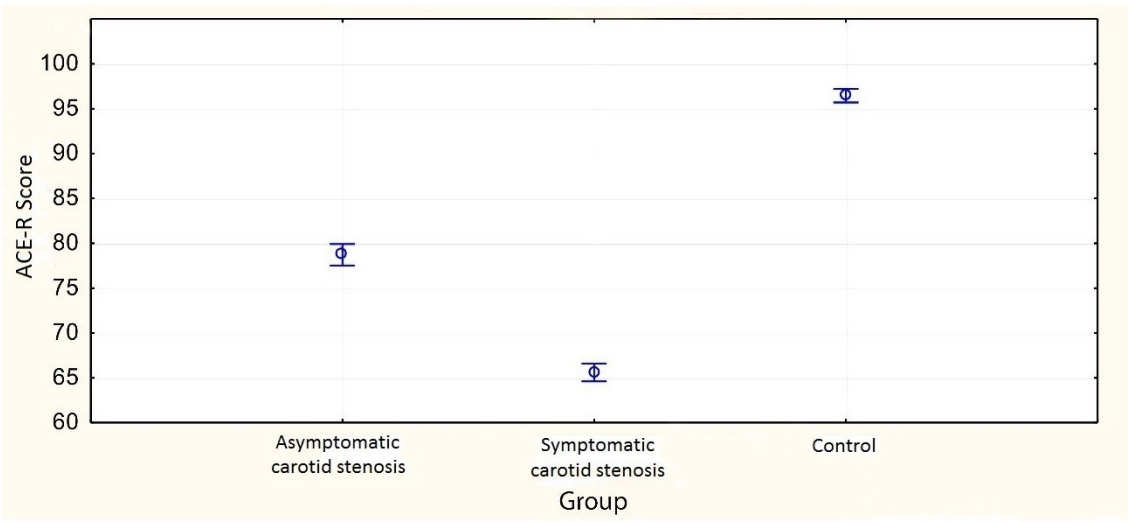

Fig. 2 – Average ACE-R score in the asymptomatic carotid stenosis group, the symptomatic carotid stenosis group, and the control group.
ACE-R – Addenbrooke's Cognitive Examination Revised.

Table 2

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

Location of lesion	Asymptomatic carotid stenosis			Total	Symptomatic carotid stenosis			Total
	mild CI	moderate CI	severe CI		mild CI	moderate CI	severe CI	
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

CT – computed tomography.

Table 3

Number of patients according to the location of lesions on control CT scans (24-72 h after initial examination) and the degree of cognitive impairment (CI)

Location of lesion	Asymptomatic carotid stenosis			Total	Symptomatic carotid stenosis			Total
	mild CI	moderate CI	severe CI		mild CI	moderate CI	severe CI	
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

CT – computed tomography.

Table 4

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

Location of lesion	Asymptomatic carotid stenosis			Total	Symptomatic carotid stenosis			Total
	mild CI	moderate CI	severe CI		mild CI	moderate CI	severe CI	
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

MRI – magnetic resonance imaging.

Discussion

The results of our study are in accordance with the data found in the literature. The study by Moreau et al. [9] directly compared the sensitivity of CT and MRI scans in patients with TIA and/or mild strokes with acute ischemic lesions. CT and MRI were performed within 24 h after symptom onset. Acute ischemic lesions were compared on CT and MRI, while the acute lesion volume was measured on MRI. The study showed that MRI exhibited 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 on 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 by Forster et al. [10] where the percentage of acute strokes proven on MRI after negative CT scans was greater than 33%. This difference is mostly the consequence of the size, i.e. the volume of the stroke because the sensitivity of 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 performed 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 with time, this fact goes potentially in favor of the MRI diagnostics [9]. The percentage of visualized lesions on MRI was higher in the asymptomatic carotid stenosis group.

A study by Tomlinson et al. [12] suggests that the volume of stroke is correlated to the appearance and development of cognitive impairment. Stroke can cause vascular dementia when the volume of stroke is greater than 100 mL [12]. A survey by Zekry et al. [13] suggests that the total volume of stroke can explain only a small portion of cognitive impairment in stroke patients. It finds that strokes in strategic areas play an important role in the cognitive disorder mechanism, and that they are connected with the severity of

dementia. These strategic regions are: cortical limbic regions, frontal cortex, and white mass. There are limitations due to the fact that many patients who have brain damage, usually have motor difficulties that adversely affect their performance on the test (eg. drawing), and often have a language difficulty [14, 15]. In our study too, there was no statistically significant correlation between the lesion location on admission and in control CT and 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 chose 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 possibly, with proper cognitive rehabilitation [15], delay cognitive impairment development. The study by Lees et al. [15] examined the usefulness of the ACE-R test in detecting cognitive impairment after stroke. The test yields data for the patient's cognitive profile, and as a screening method it can speed up the cognitive deficit diagnostic procedure after stroke [14]. It was shown that the ACE-R has a significant connection with other neuropsychological tests that examine only a certain domain. Assessment of memory by ACE-III is associated with two classic neuropsychological memory tests – Free and Cued Selective Reminding Test and the Rey Auditory Verbal Learning Test [14, 15]. Speech and verbal fluency, which were tested using ACE-R, were in correlation with the tests that assess attention and executive functions (the trail making test, memory span, Stroop test) [15]. In the study by Al-Qazzaz et al. [16], 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 [16]. This research showed 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, the results of the study confirmed that cognitive impairment was more severe in the patients with stroke and SCS compared to the patients with ACS.

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