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Internal Carotid Artery Stenting: Predictive Screening of Cognitive Function

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Abstract—Carotid artery stenting is a common method of stroke prevention. The aim of this work was to examine the relationship between carotid angioplasty with stenting (CAS) of the internal carotid artery (ICA) and cognitive function (CF), based on two years of patient follow-up data (after stenting), including clinical assessment and neuroimaging using magnetic resonance imaging (MRI). This prospective study included 137 patients (64% men) aged 47 to 85 years (with a median age of 66 years), who had undergone CAS for atherosclerotic stenosis. The inclusion criterion was stenosis (symptomatic or asymptomatic) of the internal carotid artery, which was confirmed on ultrasound. The exclusion criteria were patients with stroke (whose neurological deficits included aphasia and/or neglect), severe cognitive and mental disorders, contraindications to antiplatelet drugs and statins, and patients with ICA restenosis after prior carotid endarterectomy. The Montreal Cognitive Assessment (MoCA) Test was used for cognitive function screening before stenting, and 6, 12, and 24 months after the vascular intervention. Diffusion-weighted MRI was used to assess the presence (before CAS and 24 hours after surgery) of focal cerebral changes, specifically intraoperative acute embolic lesions (AEL). Patients with previously identified AEL were re-examined using 3D-FLAIR MRI after 6 months. The number of patients with cognitive impairment, who had scored less than 26 points on the MoCA, was 23/137 (17%) prior to the CAS. When measured 6, 12 and 24 months after stenting, there was no statistically or clinically significant change in cognitive function in 125/137 (91%) patients, cognitive function improved in 12/137 (9%) (3 of whom had reduced CF before stenting), and there were no instances of deterioration. No association was found between asymptomatic foci due to intraoperative AEL, and postoperative cognitive abilities.

Keywords: carotid artery, stenosis, stenting, cognitive function

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INTRODUCTION

Cerebrovascular disease is the second most common cause of cognitive impairment (CI) [1]. Carotid artery stenosis (due to atherosclerotic plaques) can cause cerebral hypoperfusion and lead to cognitive dysfunction [2]. With greater use of vascular reconstructive methods to treat internal carotid artery (ICA) stenosis, assessment of cognitive function (CF) has become an important component in the efficacy and safety of surgical intervention. Data on cognitive function after endovascular surgery, such as carotid angioplasty with internal carotid artery stenting, are quite contradictory in the studies conducted to date [3]. The aim of this work was to examine the relationship between carotid angioplasty with stenting (CAS) of the internal carotid artery and cognitive function, based on two years of patient follow-up data.

SCOPE AND METHODS

Patients

This prospective study ran from May 2015 to May 2019 and included 137 patients (64% men), aged 47 to 80 years (with a median age of 66 years), with atherosclerotic stenosis of the carotid arteries, who underwent CAS at the Research Center of Neurology (Moscow). The inclusion criterion was the presence of atherosclerotic stenosis (symptomatic or asymptomatic) of carotid arteries as confirmed on ultrasound. The exclusion criteria were patients with stroke, whose neurological deficits included aphasia and/or neglect, severe cognitive disorders due to concomitant disease (severe heart, liver or kidney disease, malignant tumours), mental disorders, contraindications to antiplatelet drugs and statins, prolonged substance abuse, as well as patients with carotid stenosis due to restenosis after prior carotid endarterectomy.

Table 1. Characteristics of patients depending on their cognitive status before stenting

No.	Characteristics	All patients (n = 137)	Cognitive status	
			MoCA < 26 (n = 23), %	MoCA ≥ 26 (n = 114), %
	Gender:			
1	men, n (%)	88 (64)	20 (87)	68 (60)
	women, n (%)	49 (36)	3 (13)	46 (40)
2	Age, years, Me (range)	66 (47–85)	71 (52–85)	65 (47–81)
3	Body mass index, kg/m^2, M (range)	27.6 (19.8–35.5)	27.2 (20.3–35.4)	27.6 (19.8–35.5)
4	Symptomatic stenosis, n (%)	23 (17)	5 (22)	18 (15)
5	Asymptomatic stenosis, n (%)	114 (83)	18 (78)	96 (84)
6	Degree of stenosis, M (range):	77 (50–99)	78 (70–99)	77 (50–95)
	50–69%, n (%)	4 (3)	1 (4)	3 (3)
	70–89%, n (%)	115 (84)	19 (83)	96 (84)
	90–99%, n (%)	18 (13)	3 (13)	15 (13)
7	Occlusion of contralateral ICA, n (%)	17 (12)	2 (8)	15 (13)
8	Arterial hypertension, n (%)	130 (95)	23 (100)	107 (94)
9	Exertional angina, n (%)	34 (25)	8 (35)	26 (23)
10	Myocardial infarction before CAS, n (%)	22 (16)	0 (0)	22 (19)
11	Coronary artery surgery before CAS, n (%)	18 (13)	1 (4)	17 (15)
12	Diabetes mellitus, n (%)	36 (26)	6 (26)	30 (26)
13	Hyperlipidaemia, n (%)	111 (81)	15 (65)	96 (84)
14	Smoking, n (%)	80 (58)	12 (52)	68 (59)
15	Time from onset of symptoms to intervention, days, M (range)	123 (30–180)	144 (90–180)	138 (30–180)
16	Antihypertensive drugs, n (%)	111 (81)	17 (74)	94 (82)
17	Antiplatelet therapy, n (%)	105 (77)	17 (74)	88 (77)
18	Antidiabetic therapy, n (%)	25 (18)	3 (13)	22 (19)
19	Statin therapy, n (%)	92 (67)	15 (65)	77 (67)
20	LDL, mmol/L, M (range)	1.7 (0.6–6.1)	1,4 (0.7–2.5)	1,8 (0.8–6.1)
21	Total cholesterol, mmol/L, M (range)	5.1 (2.9–14)	4.8 (3.3–6.9)	5.1 (2.9–14)

LDL—low-density lipoproteins. Designation: n—number of patients, M—mean value, Me—median.

Ultrasound Examination

All patients underwent an ultrasound examination of the carotid arteries (Philips iE33, the Netherlands, with a linear sensor with a radiation frequency of 11 MHz) in the pre- and postoperative periods [4]. The diagnosis of atherosclerotic ICA stenosis was confirmed using the NASCET (North American Symptomatic Carotid Endarterectomy Trial) algorithm [5]. The stenosis was considered symptomatic if patients had experienced ipsilateral symptoms of retinal ischaemia, transient ischaemic attacks or ischaemic stroke in the last 6 months (prior to CAS) [6]. The stenosis was asymptomatic in most patients (according to information in the medical history and the results of the neurological examination). Nearly all patients had arterial hypertension, and every second patient had three or more risk factors for developing vascular disease. The baseline patient characteristics are shown in Table 1. The endovascular intervention was carried out in accordance with the SAPPHIRE (Stenting and Angioplasty with Protection in Patients at High Risk for Endarterectomy) criteria, in patients with symptomatic ≥50% stenosis of the ICA, and for asymptomatic >80% stenosis [7].

Assessment of cognitive function using the MoCA was performed on average 3 (1–10) days before stenting and 6, 12 and 24 months after it; a score below 26 points was considered to be evidence of cognitive impairment (according to the standard use of the MoCA test) [8]. The MoCA Test was used to evaluate CF due to its wide prevalence (compared to other neuropsychological tests), well-documented procedure for data collection and processing, and ease of use in screening studies [9].

The possible training effect due to task repetition was considered a kind of systematic bias that occurred

Table 2. Patient characteristics according to changes in their cognitive status, two years after stenting

No.	Characteristics	*n* (%), 137 in total	Cognitive status	
			unchanged, *n* (%), 125 (91) in total	improved, *n* (%), 12 (9) in total
	Gender:			
1	Men, *n* (%)	88 (64)	80 (64)	8 (67)
	Women, *n* (%)	49 (36)	45 (36)	4 (33)
2	Age, years, Me (range)	66 (47–85)	75 (60)	2 (17)
3	Body mass index, kg/m^2, M (range)	27.0 (20.0–35.5)	27.0 (20.0–35.5)	29.0 (26.0–35.5)
4	Symptomatic stenosis, *n* (%)	23 (17)	22 (18)	1 (8)
5	Asymptomatic stenosis, *n* (%)	114 (83)	103 (82)	11 (92)
6	Degree of stenosis, M (range):	77 (65–95)	77 (68–95)	80 (70–90)
	50–69%, *n* (%)	4 (3)	4 (3)	0
	70–89%, *n* (%)	115 (84)	106 (85)	9 (75)
	90–99%, *n* (%)	18 (13)	15 (12)	3 (25)
7	Occlusion of contralateral ICA, *n* (%)	17 (12)	17 (14)	0 (0)
8	Arterial hypertension, *n* (%)	130 (95)	118 (94)	12 (100)
9	Exertional angina, *n* (%)	34 (25)	31 (25)	3 (25)
10	Myocardial infarction before CAS, *n* (%)	22 (16)	19 (15)	3 (25)
11	Coronary artery surgery before CAS, *n* (%)	18 (13)	17 (14)	1 (8)
12	Diabetes mellitus, *n* (%)	36 (26)	35 (28)	1 (8)
13	Hyperlipidaemia, *n* (%)	111 (81)	99 (79)	12 (100)
14	Smoking, *n* (%)	80 (58)	68 (54)	12 (100)
15	Time from onset of symptoms to intervention, days, M (range)	123 (30–180)	115 (30–180)	105 (35–170)
16	Antihypertensive drugs, *n* (%)	111 (81)	103 (82)	8 (67)
17	Antihypertensive drugs, *n* (%)	105 (77)	94 (75)	11 (92)
18	Antiplatelet therapy, *n* (%)	25 (18)	24 (19)	1 (8)
19	Antidiabetic therapy, *n* (%)	92 (67)	83 (66)	9 (75)
20	LDL, mmol/L, M (range)	1.7 (0.6–6.1)	1.7 (0.6–6.1)	1.5 (0.8–3.1)
21	Total cholesterol, mmol/L, M (range)	5.1 (2.9–14.0)	5.1 (2.9–14.0)	4.5 (3.1–9.1)
22	Acute embolic lesions (on DW-MRI) 24 hours after surgery, *n* (%)	65 (47)	60 (48)	5 (42)

LDL—low-density lipoproteins. Designation: *n*—number of patients, M—mean value, Me—median.

equally for all patients. The set of monitored factors included demographic and medical (clinical, neuroimaging and laboratory) patient characteristics (Table 2).

The CAS Procedure

Five days before CAS, double antiplatelet therapy (acetylsalicylic acid 100 mg and clopidogrel 75 mg) was prescribed, as well antihypertensive and antidiabetic drugs, statins to correct the vascular risk factors; smoking cessation was advised. Double antiplatelet therapy continued for at least 3 months after CAS (acetylsalicylic acid was prescribed for life). All patients were given intravenous heparin with an individual dosage to increase the activated clotting time during surgery. All stenting procedures were performed on the Innova 3131 Biplane Angiographic System (General Electric, USA) under local anaesthesia (using percutaneous transfemoral access) by the same interventional neurology team of doctors. The stents and cerebral protection systems were chosen at the discretion of the interventional neurologist. The final result of the stenting was recorded angiographically. Patient adherence to medications recommended by the doctor after surgery was evaluated during the follow-up visits (after 6, 12, 24 months).

Neuroimaging

The patient underwent diffusion-weighted magnetic resonance imaging (DW-MRI) 1–3 days before and then 24 hours after CAS (using the Magnetom Verio, a 3T MRI system (Siemens Medical System, Germany)). Diffusion-weighted images were obtained using an isotropic echo-planar sequence [10, 11]. Axial images were obtained with automatic calculation of the apparent diffusion coefficient map. To determine whether the previously detected acute embolic lesions (AEL) led to persistent changes in cerebral tissue, subsequent examinations (after 6 months) in these patients included repeat MRI in 3D FLAIR mode.

Statistical Analysis

The SAS 9.4 statistical software package was used. The Mann-Whitney test was used to compare continuous variables in the groups, and Fisher's exact test was used for categorical variables.

RESULTS

In the postoperative period, one patient (out of 137) developed ischaemic stroke two months after stenting due to stent occlusion (the reason was diagnosed after surgery as thrombophilia). The patient's cognitive assessment during postoperative visits did not differ from the preoperative result. In the remaining patients, ultrasound examination of the ipsilateral carotid artery (immediately after surgery and during the two-year follow-up period) showed no evidence of restenosis or stent occlusion. None of the patients had any coronary complications after stenting.

Cognitive impairment was detected in 23 (17%) patients at the preoperative stage (<26 points on the MoCA). No relationship was found between these CI and the preoperative patient characteristics (Table 1).

Compared to the preoperative findings, 125 (91%) patients showed no change in CF 24 months after CAS, while the remaining 12 (9%) demonstrated an improvement in CF, and no statistically significant deterioration in CF was found in any of the patients (Table 2).

AEL were detected on DW-MRI in 65 (47%) patients 24 hours after stenting, with no clinical manifestations. The detected ischaemic lesions were located mostly in the ipsilateral cortex. The average lesion number and size were 3 (1–10) and 4 (2–15) mm, respectively, in the cortex, and 2 (1–3) and 3 (2–8) mm in the white matter.

The previously detected AEL remained in only 3 out of 65 (5%) patients when brain imaging was performed 6 months after stenting (3D-FLAIR MRI). No correlation was found between these asymptomatic, postoperative ischaemic brain lesions, and the state of and changes in CF after 2 years.

The two-year follow-up period in patients with postoperative lesions showed that there were no significant changes in CF in most patients (60 people) when compared to the pre-stenting level, while CF improved in 5 patients. Therefore, the absence of a statistically significant association between intraoperative acute embolic brain lesions (detected one day after stenting on DW-MRI) and CF (during 2 years of follow-up) is an important finding (Fisher's exact test, $p = 0.30$).

DISCUSSION

An important indicator of the effectiveness of endovascular surgery, along with a reduction in stroke risk, is the state of cognitive function [12–14].

According to the literature, the prevalence of cognitive impairment among patients scheduled for vascular surgery can reach 55% [15–17]. Several studies have shown an association between carotid atherosclerosis (accompanied by stenosis and/or increased carotid intima-media thickness), and low memory and attention measures [18, 19]. We previously demonstrated a link between low intensity of the ultrasound signal from fragments of a heterogeneous atherosclerotic plaque (ASP) and the development of ischaemic events (in the absence of pronounced stenosis) [4]. The heterogeneous composition of an atherosclerotic plaque (a risk for cerebral microembolism) can be considered a possible cause for cognitive decline (regardless of hypoperfusion), however, the significance of this was not reflected in our data. In a number of studies, neurocognitive impairment (appearing approximately 1 month after carotid intervention) was linked to intraoperative microembolism [20], however, studies on the persistence of this phenomenon have not produced definite conclusions [21–23]. In our study, AEL were detected on DW-MRI in 65 out of 137 (47%) subjects 24 hours after stenting, and were located mainly in the area of the cortex supplied by the stented artery, which is consistent with the data of other authors [24, 25].

An important aspect of this study was identifying a relationship between intraoperatively detected AEL and the patients' postoperative cognitive abilities; we did not find such a relationship (within the capabilities of the MoCA Test). There were also no cases of perioperative stroke. The absence of any persisting effect of AEL on cognitive ability may be due to their transient nature: 95% of the acute embolic brain lesions (detected one day after stenting) were no longer seen 6 months after the surgery (according to 3D-FLAIR MRI data). This may demonstrate the compensatory capabilities of the brain [26]. It is also possible that the ischaemic lesions were located in areas of the brain that are not vital for cognitive function.

Whether carotid revascularization affects cognitive function in patients with cerebrovascular disease remains an unanswered question in the literature [27–30]. The ambiguity of the described results may be due to various reasons, including methodological ones, namely: small sample sizes in studies, different duration of follow-up, lack of preoperative CF assessment, and the use of univariate instead of multivariate analysis. The Montreal Cognitive Assessment Test was used as the main screening measure of CF due to its sensitivity in detecting cognitive impairment in patients with cerebrovascular disease. This test, rather than other, time-consuming neuropsychological assessments, was used specifically to screen CF. Other neuropsychological and neurophysiological tests can be used in medical practice if necessary and if cognitive impairment is detected [31, 32].

In our study (based on the results of two years of follow-up), 125 out of 137 (91%) patients had no changes in CF (compared to the baseline level), while 12 out of 137 (9%) patients showed an improvement in CF. These results demonstrate that surgical intervention not only reduces the risk of stroke, but also can prevent cognitive deterioration to some extent.

CONCLUSIONS

Cognitive function screening in patients after carotid angioplasty with stenting revealed no cognitive changes. No association was found between changes in cognitive function and intraoperative embolic brain lesions.

LIST OF ABBREVIATIONS

ASP —atherosclerotic plaque
ICA —internal carotid artery
DW-MRI —diffusion-weighted magnetic resonance imaging
IHD —ischaemic heart disease
BMI —body mass index
CAS —carotid angioplasty with stenting
CF —cognitive function
CI —cognitive impairment
LDL —low-density lipoproteins
TC —total cholesterol
AEL —acute embolic lesions
MoCA —Montreal Cognitive Assessment Test

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CONFLICT OF INTEREST

The authors declare that there are no clear or potential conflicts of interest related to the publication of this article.

ETHICAL STANDARDS

All studies were conducted in accordance with the principles of biomedical ethics as formulated in the Declaration of Helsinki 1964 and its subsequent revisions, and approved by the Local Bioethics Committee of the Research Center of Neurology (minutes No. 11/14 dated 19 November 2014, Moscow).

INFORMED CONSENT

Each study participant provided their voluntary written informed consent, which they signed after receiving an explanation about the potential risks and benefits, as well as the nature of the upcoming study.

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