

# Results of Carotid Endarterectomy Performed at Different Times During the Acute Period of Ischemic Stroke

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AIM OF STUDY To compare the results of carotid endarterectomy performed at different times (1st, 2nd and 3rd week) of the acute period of ischemic stroke.

MATERIAL AND METHODS In the acute period of ischemic stroke (1–21 days), 92 patients with symptomatic stenosis of the internal carotid artery of 50% or more were operated on using carotid endarterectomy. There were 66 men and 26 women. The average age was 65.7±8.4 years. All patients were divided into three groups depending on the timing of the operation: Group 1, where the operation was performed on the 1st week of stroke (n=48); Group 2, where the operation was performed on the 2nd week after stroke (n=28); Group 3, where carotid endarterectomy was performed on the 3rd week after stroke (n=16). In-hospital endpoints of the study in each group were ipsilateral ischemic stroke, any other stroke (contralateral ischemic or hemorrhagic), myocardial infarction, wound hemorrhagic complications requiring repeated operation and surgical hemostasis, death, and major adverse cardiovascular events (stroke + myocardial infarction + fatal outcome).

RESULTS There were no postoperative ipsilateral ischemic strokes, myocardial infarctions, or deaths in the study group (92 patients). In the overall group of patients (n = 92), the incidence of any postoperative stroke was 2.2% (2 patients): one hemorrhagic stroke on the side of carotid endarterectomy (group 3) and one contralateral ischemic stroke on the first postoperative day in a patient with bilateral critical stenosis of the internal carotid artery (group 1). Postoperative wound hematoma, which required revision and bleeding arrest in the early postoperative period, developed in one (1.1%) patient in Group 1. The overall incidence of major adverse cardiovascular events was 2.2% or 2 patients. In all three groups, a statistically significant and positive effect in regression of the initial neurological deficit was obtained at discharge. In patients operated in the first week after stroke, the neurological deficit at discharge according to the National Institutes of Health Stroke Scale (NIHSS) and the modified Rankin scale was the lowest. In general, 31.3%, 17.9% and 12.5% of patients in groups 1, 2 and 3 were discharged without neurological deficit (0 points according to the NIHSS scale), respectively.

CONCLUSIONS Carotid endarterectomy performed in the acute period of ischemic stroke is a safe surgical intervention in the prevention of recurrent ipsilateral ischemic events. The most positive neurological dynamics and the least neurological deficit at discharge were achieved after operations performed in the first week of ischemic stroke.

Keywords: ischemic stroke, acute period, carotid endarterectomy, early surgery

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CEA – carotid endarterectomy CT – computed tomography ICA – internal carotid artery MRI – magnetic resonance imaging

#### INTRODUCTION

One of the main causes of ischemic stroke is atherosclerotic lesions of the brachiocephalic arteries [1, 2]. Critical atherosclerotic stenosis of the internal carotid artery (ICA) can be a source of not only acute cerebrovascular accident and severe patient disability, but also lead to a significant decrease in cerebral perfusion, impairment of higher cognitive functions and the development of dementia [3–5]. Timely surgical prevention of ischemic stroke in the form of carotid endarterectomy (CEA) or ICA stenting allows for the effective prevention of acute ischemic cerebral events, as proven by numerous studies [6, 7–10].

In modern literature, the issue of optimal, safe and appropriate timing of CEA during the acute period of ischemic stroke, which, according to the domestic classification, is 28 days [11], i.e. contains four seven-day periods, is actively discussed.

According to domestic and foreign national recommendations, early CEA can be performed as soon as possible for patients with a "minor" non-disabling stroke. The appropriate time frame for performing surgery on symptomatic stenosis of the ICA is the first 14 days from the moment of stroke [12–14], i.e. the surgery can be performed both on the 1st and 14th day after the ischemic event.

As a rule, modern studies compare the results of "early" (the first 14 days after a stroke or the entire acute period of stroke) and delayed CEA (more than 14 days or outside the acute period of stroke) [5, 15–18]. There are few articles evaluating and comparing the results of CEA at different times within the acute period of ischemic stroke [19–21].

The aim of the work: to compare the clinical and neurological results of CEA performed at different times of the acute period of ischemic stroke - in the 1st, 2nd and 3rd week of the acute period.

#### **MATERIAL AND METHODS**

Study design: single-center and retrospective.

The work is based on the result of surgical treatment of 92 patients in the volume of CEA in the acute period of ischemic stroke (21 days). In the period from the 22nd to the 28th day of the acute period of stroke, 1 patient was operated, he was not included in the study.

The study included 66 men and 26 women. The average age was 65.7±8.4 years.

The indication for urgent surgical treatment was stenosis of the ICA on the side of the stroke of more than 50%. After the diagnosis of "symptomatic" stenosis of the ICA using ultrasound angioscanning, all 92 patients underwent computed tomographic (CT) angiography of the brachiocephalic arteries, according to which the stenosis of the carotid artery was finally assessed and the indications for surgery were determined.

All 92 patients were divided into three groups depending on the timing of CEA after ischemic stroke.

In the 1st group, there were 48 patients operated on in the 1st week.

In the 2nd group of patients, there were 28 who were operated on in the 2nd week.

In the 3rd group of patients, there were 16 who were operated on in the 3rd week.

The criteria for including a patient in the work were:

- 1. The presence of an ischemic focus (according to magnetic resonance imaging (MRI) or CT of the brain) in the middle cerebral artery basin.
- 2. Ipsilateral to ischemic stroke, ICA stenosis of 50% or more, diagnosed in all patients using CT with intravenous contrast enhancement.
- 3. Neurological deficit according to the modified *Rankin scale (mRs)* of no more than 4 points and neurological deficit according to the US National



Institutes of Health Stroke Scale (*NIHSS*) of no more than 12 points, which corresponds to a mild to moderate stroke.

- 4. The volume of ischemic damage to the cerebral hemisphere is less than 1/3 of the blood supply to the middle cerebral artery basin.
- 5. Timeframe for surgical treatment: from 1 to 21 days from the moment of stroke.

Patient exclusion criteria for the study:

- 1. Ipsilateral to ischemic stroke, ICA stenosis is less than 50%.
- 2. Neurological deficit according to the modified *Rankin scale* of more than 4 points and neurological deficit according to the *NIHSS scale* of more than 12 points.
- 3. The volume of ischemic damage to the cerebral hemisphere is more than 1/3 of the blood supply to the middle cerebral artery basin.
- 4. The patient has a heart rhythm disorder, primarily atrial fibrillation.
- 5. Hemorrhagic impregnation of the ischemic focus.
- 6. Severe cognitive impairment with the absence of the expected positive result from surgical treatment.
- 7. Absence of ischemic focus according to CT or MRI of the brain.
- 8. The presence of a concomitant disease (therapeutic, oncological or other), accompanied in the long term by a short life expectancy.

The study did not include patients with cardiac arrhythmias (primarily atrial fibrillation). All 92 patients underwent echocardiography before surgery to exclude cardiac defects, and, if necessary, Holter monitoring of the heart rhythm to identify other cardiac arrhythmias. This allows us to state with a high degree of certainty that in the study group of patients, ischemic stroke had an atherothrombotic subtype according to the TOAST (Trial of Org 10172 in Acute Stroke Treatment) classification [22].

Clinical data in the three groups are presented in Table 1.

Table 1
Comparative clinical data of patients operated in the acute stage of ischemic stroke

acute stage of ischemic stroke						
Sign	1st group (1–7 days) <i>n</i> =48	2nd group (8–14 days) n=28	3rd group (15–21 days) <i>n</i> =16	p		
Age, years	64±8.5	68±8.4	65±7.4	$p_{12} = 0.51$ $p_{13} = 0.66$ $p_{23} = 0.23$ p = 0.13		
Male/female, n (%)	39/9 (81/9)	14/4 (50/50)	13/3 (81/19)	$p_{12} = 0.01$ $p_{13} = 1$ $p_{23} = 0.08$ p = 0.01		
One ischemic focus, n (%)	24 (50)	11 (39)	9 (56)	$p_{12} = 0.51$ $p_{13} = 0.89$ $p_{23} = 0.44$ p = 0.51		
More than one ischemic focus, <i>n</i> (%)	24 (50)	17 (61)	7 (44)	$p_{12} = 0.51$ $p_{13} = 0.89$ $p_{23} = 0.44$ p = 0.51		
Neurological deficit according to NIHSS scale at admission, points	5.2±1.9	6.9±1.9	7.1±2.2	p <sub>12</sub> =0.0004 p <sub>13</sub> =0.005 p <sub>23</sub> =0.76 p=0.0002		
Degree of disability according to the <i>mRs scale</i> at admission, degree	3.6±0.4	3.6±0.5	3.9±0.1	$p_{12}=1$ $p_{13}<0.0001$ $p_{23}=0.0044$ p=0.029		
Patient mobility according to the Rivermead scale, score	1.5±0.6	1.5±0.7	1.1±0.1	$p_{12} = 1$ $p_{13} < 0.0001$ $p_{23} = 0.006$ p = 0.05		
Thrombolytic therapy administered on admission, n (%)	4 (8.3)	3 (10.7)	2 (12.5)	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 1$ $p = 0.87$		
Associated diseases						
Hypertension, n (%)	48 (100)	28 (100)	16 (100)	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 1$ $p = 1$		
Ischemic heart disease, n (%)	16 (33.3)	13 (46.4)	3 (18.8)	$\rho_{12} = 0.37$ $\rho_{13} = 0.43$ $\rho_{23} = 0.13$ $\rho = 0.17$		
History of myocardial infarction, <i>n</i> (%)	8 (16.7)	5 (17.9)	0 (0)	$p_{12} = 1$ $p_{13} = 0.19$ $p_{23} = 0.19$ p = 0.2		



Chronic heart failure, n (%)	3 (6.3)	10 (35.7)	3 (18.8)	$p_{12} = 0.003$ $p_{13} = 0.32$ $p_{23} = 0.4$ p = 0.005
History of stroke, <i>n</i> (%)	6 (12.5)	6 (21.4)	1 (6.3)	$p_{12} = 0.48$ $p_{13} = 0.82$ $p_{23} = 0.37$ p = 0.34
Chronic obstructive or non-specific pulmonary diseases, n (%)	4 (8.3)	2 (7.1)	2 (12.5)	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 0.96$ p = 0.83
Diabetes mellitus, n (%)	15 (31.3)	9 (32.1)	1 (6.3)	$p_{12} = 1$ $p_{13} = 0.1$ $p_{23} = 0.11$ $p = 0.12$
Chronic kidney disease, n (%)	6 (12.5)	3 (10.7)	4 (25)	$p_{12} = 1$ $p_{13} = 0.43$ $p_{23} = 0.41$ $p = 0.38$

Notes:  $p_{12}$  – for the difference between groups 1 and 2;  $p_{13}$  – for the difference between groups 1 and 3;  $p_{23}$  - for the difference between groups 2 and 3;  $p_{23}$  – for the difference between all three groups

As can be seen from the table, the three groups were comparable in most parameters. A statistically significant difference between the groups was obtained in the gender difference (there were statistically significantly more men in the 1st and 3rd groups), the degree of neurological deficit (in the 1st group, the initial deficit was statistically significantly lower than in the 2nd and 3rd groups) and the frequency of chronic heart failure (there were statistically significantly fewer such patients in the first group than in the 2nd and 3rd).

All 92 patients underwent CEA (classical, classical with patch or eversion technique) under regional (n = 67 or 72%) or general (n = 25 or 28%) anesthesia.

In the general anesthesia group, the tolerance of the cerebral hemisphere to compression of the carotid arteries was assessed based on the data of measuring retrograde pressure in the basin of the operated ICA (retrograde pressure of at least 30 mm Hg and with a characteristic pulse retrograde wave) and transcranial cerebro-oximetry figures (a decrease of no more than 25%).

In patients operated under regional anesthesia, in addition to the above-mentioned objective methods, after clamping, the patient's consciousness (clear/depressed), motor activity in the arm contralateral to the operation (maintaining initial

activity/appearance or increase in paresis) and speech (clear/worsening/aphasia) were assessed.

Each patient was additionally examined by a neurologist 24 hours after surgery, who also observed these patients throughout the hospitalization period. Neurological status was assessed by the *NIHSS* and modified *Rankin scale* for all patients at discharge.

The in-hospital endpoints of the study were:

- 1. Ipsilateral ischemic stroke.
- 2. Any other stroke (contralateral ischemic or hemorrhagic).
  - 3. Myocardial infarction.
- 4. Wound hemorrhagic complications requiring reoperation and surgical hemostasis.
  - 5. Fatal outcome.
- 6. Major adverse cardiovascular events (stroke + myocardial infarction + death).

A separate comparison of neurological deficits between groups at discharge was performed (*NIHSS scale* and modified *Rankin scale*, *mRs*).

Statistical analysis. The data obtained during the study were analyzed according to the basic principles of evidence-based medicine. Statistical processing of the clinical material was performed using Statistica 12 for Windows software (StatSoft Inc., USA). The analysis of the normality of data distribution was performed using the Kolmogorov-Smirnov and Shapiro-Wilk tests. To compare continuous variables with a normal distribution, Student's t-test for independent samples was used; for variables without a normal distribution, the Mann-Whitney U-test. Nominal data were compared using the Pearson Chi-square test. P values less than 0.05 were considered statistically significant. The data obtained during the study were analyzed according to the basic principles of evidence-based medicine.

## RESULTS

At the in-hospital stage, there were no postoperative ipsilateral ischemic strokes, myocardial infarctions, or deaths in the study group (92 patients).

In the general group of patients (n = 92), the incidence of any postoperative stroke was 2.2% (2 patients): one hemorrhagic stroke on the side



of the CEA in the area of cystic-gliotic changes in the cerebral hemisphere against the background of hyperperfusion (group 3) and one contralateral ischemic stroke on the 1st postoperative day in a patient with bilateral critical stenosis of the ICA (group 1).

A hematoma of the postoperative wound, which required revision and stopping of bleeding in the early postoperative period, developed in one patient (1.1%) in the 1st group.

The overall incidence of major adverse cardiovascular events was 2.2% or 2 patients.

The need for a temporary intraluminal shunt was 21.7% (20 patients out of 92). In the general anesthesia group, a shunt was used in 9 patients (36%), and in the regional anesthesia cohort in 11 observations (16.4%).

The main comparative results of surgical treatment in the three groups are presented in Table 2.

Table 2

Results of treatment of patients

Results of treatment of patients						
Result	1st group (1–7 days)	2nd group (8–14 days)	3rd group (15–21 days)	р		
Ipsilateral ischemic stroke, %	0	0	0	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 1$ $p = 1$		
Any other stroke, n (%)	1 (2.1)	0 (0)	1 (6.3)	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 0.77$ p = 0.39		
Myocardial infarction, %	0	0	0	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 1$ $p = 1$		
Wound hemorrhagic complications, n (%)	1 (2.1)	0 (0)	0 (0)	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 1$ $p = 1$		
Fatality rate, %	0	0	0	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 1$ $p = 1$		
Major adverse cardiovascular events, n (%)	1 (2.1)	0(0)	1 (6.3)	$p_{12} = 1$ $p_{13} = 1$ $p_{23} = 0.77$ p = 0.39		

Notes:  $p_{12}$  – for the difference between groups 1 and 2;  $p_{13}$  – for the difference between groups 1 and 3;  $p_{23}$  - for the difference between groups 2 and 3;  $p_{23}$  – for the difference between all three groups

All three groups demonstrated comparable efficacy and safety in terms of preventing recurrent ipsilateral ischemic events. All strokes that developed in the overall group were contralateral and hemorrhagic.

However, our main interest was in the comparative analysis of the neurological status upon admission and discharge, i.e. how the timing of CEA influenced the relief of motor, sensory, or other neurological disorders in the postoperative period.

Comparison of the dynamics of neurological status in the three groups upon admission and discharge is presented in Tables 3 and 4.

Table 3

Dynamics of neurological status according to NIHSS upon admission and discharge

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Groups	NIHSS scale, points		р	
	Admission	Extract		
1st group (1–7 days)	5.2±1.9	1.5±1.2	p <0.0001	
2nd group (8–14 days)	6.9±1.9	3.2±3.1	p <0.0001	
3rd group (15–21 days)	7.4±2.2	2.7±1.5	p <0.0001	

Table 4

Dynamics of neurological status according to mRs upon admission and discharge

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Groups	mRs scale,	р		
	Admission	Extract		
1st group (1-7 days)	3.6±0.4	1.1±0.7	p <0.0001	
2nd group (8-14 days)	3.6±0.4	1.8±1.3	p <0.0001	
3rd group (15–21 days)	3.9±0.1	1.9±0.3	p<0.0001	

As can be seen from these tables, in all three groups after CEA, a clear positive trend was noted in the relief of the initially existing neurological deficit, with the most positive trend noted in the earliest group (surgery in the first 7 days from the moment of stroke), which is demonstrated in Table 5.

Comparison of neurological status at discharge in the three groups is presented in Table 5.



Table 5
Neurological status upon discharge

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Neurological status	1st group (1st-7th day)	2nd group (8– 14 days)	3rd group (15–21 days)	р	
NIHSS scores	1.5±1.2	3.2±3.1	2.7±1.5	$p_{12} = 0.009$ $p_{13} = 0.008$ $p_{23} = 0.48$ p = 0.002	
Degree on the mRs scale	1.1±0.7	1.8±1.3	1.9±0.7	$p_{12} = 0.012$ $p_{13} = 0.0005$ $p_{23} = 0.074$ p = 0.001	
Patients with no neurological deficit at discharge (NIHSS score 0), n (%)	15 (31.3)	5 (17.9)	2 (12.5)	$p_{12} = 0.31$ $p_{13} = 0.25$ $p_{23} = 0.97$ $p = 0.21$	

As can be seen from Table 5, statistically significant better indicators for neurological status at discharge were obtained in the group of patients operated on in the first week of ischemic stroke. It is noteworthy that every third patient in this cohort was discharged without any neurological deficit at all (0 points on the *NIHSS scale*).

#### **DISCUSSION**

Timely surgical prevention of secondary ischemic stroke is one of the main tasks of modern vascular surgery, since ischemic stroke firmly occupies a leading place in the structure of mortality and disability of the population, together with acute cardiac events and oncological diseases [1, 11].

Operations in the acute period of ischemic stroke are actively used to prevent recurrent cerebrovascular accident. The main goals of early operations for symptomatic stenosis of the ICA in the acute period are: removal of the atherosclerotic plague as a possible source of recurrent atheroembolism of the cerebral arteries and restoration of adequate perfusion of the cerebral hemisphere in case of critical stenotic lesion of the ICA [23, 24]. However, taking into account the results of operations we obtained, especially in patients of the 1st group (1-7 days), we can add a third, no less important goal: reduction or relief of the initial neurological deficit. Regardless of the week (1st, 2nd or 3rd) in which the operation was performed, we noted a clear positive dynamics of the neurological status, up to complete recovery in 31.3%, 17.9% and 12.5% of patients in the 1st, 2nd and 3rd groups, respectively. The lowest neurological deficit or its complete absence at discharge in every third patient of the 1st group may be due to a statistically significantly better initial neurological status upon admission.

In the acute period of ischemic stroke, the entire spectrum of surgical interventions is used: CEA, endovascular operations and hybrid interventions [2, 8, 14, 25]. However, the main method of surgical treatment of "symptomatic" stenosis of the ICA in the acute period of ischemic stroke remains CEA, as it is accompanied by a statistically significantly lower incidence of stroke and death. This was demonstrated in a large study with an analysis of four randomized studies [26].

The optimal time for performing CEA after ischemic stroke is actively discussed in modern literature and has not been fully defined, varying from 1 to 28 days after an acute ischemic event [6, 7, 12, 14]. Nevertheless, the time frame of the first 2 weeks is currently recognized as appropriate for early operations in domestic and foreign recommendations [12, 13].

The incidence of postoperative stroke after "early" CEA ranges from 0.5 to 7.9%, and postoperative mortality can reach 3% [17, 20, 23, 27–29].

In a group of 92 patients, the overall incidence of any recurrent stroke was 2.2% (2 patients): one ipsilateral hemorrhagic stroke and one contralateral ischemic stroke. There were no recurrent postoperative strokes on the side of the intervention, clinically significant cardiac complications, or deaths.

It should be noted separately that, against the background of good results of "early" CEA, in a number of studies [18, 27, 30], according to recent large meta-analyses, conflicting results were obtained after operations in the acute period of stroke [5, 15, 31].

Y. Yuan et al. (2020) conducted a meta-analysis of 7 studies in which early CEA was defined as either surgery performed within the first 14 days or as an intervention within the first 30 days after stroke. In the cohort of patients operated within 30 days, compared with delayed surgeries, no statistically



significant differences in the incidence of stroke and postoperative mortality were obtained. However, in the case of CEA performed in the first 2 weeks, postoperative mortality was statistically significantly higher compared with delayed interventions. The authors conclude that early surgeries have a higher risk of postoperative mortality, and delayed interventions are safer in the treatment of symptomatic ICA stenosis [5]. A very recent Russian meta-analysis devoted to the assessment of the frequency of postoperative complications and mortality in the early (14 days or 28-30 days) and late periods after CEA showed comparable results regardless of the timing of the operation [15]. Finally, P. de Rango et al. (2015) in their meta-analysis compared the results of CEA and ICA stenting at different times after stroke (0-48 hours, 0-7 days, and 0-15 days). The authors indicated that the perioperative risk of stroke is comparable for CEA and ICA stenting within 15 days: less than 3.5% and 4.8%, respectively. And most importantly, carotid revascularization can be safely performed in the first week after stroke [31].

Some of the latest studies show the possibility of further reducing the time of CEA, which is confirmed by comparable results with later operations during the acute period of stroke [24]. For example, N. Angle et al. (2022) demonstrated a rate of only 0.5% of postoperative stroke after CEA in 194 patients, operated mainly in the acute phase of stroke (the first 72 hours) [27]. Other authors also point out the need to reduce the time of surgical intervention from 3 to 7 days [24]. The main argument in favor of reducing the time of intervention is the highest frequency of recurrent ischemic strokes in the 1-2nd week of the disease - from 19.5 to 26% [32], and according to S. Stromberg et al. (2012), the first week after an ischemic event is the riskiest in terms of recurrent stroke [33].

Another important result of the "early" operations in this work was the positive dynamics of neurological deficit: at discharge in the 1st, 2nd and 3rd groups, according to the *NIHSS scale*, it was 1.5±1.2; 3.2±3.1 and 2.7±1.5 points, respectively. The degree of neurological deficit was also significantly reduced according to the mRs scale. In our opinion, the result is important - 31.3% of patients in the 1st group were discharged without any neurological deficit at all (0 points on the *NIHSS scale*). In the 2nd and 3rd groups, there were 17.9% and 12.5% of such patients, respectively. In general, the results of operations performed in the first week of stroke demonstrated the most positive dynamics of deficit regression compared to the 2nd and 3rd groups.

The same data were obtained in the work of *G. Varetto et al.* (2017), where the authors compared the neurological status in patients operated on in the first 14 days after a stroke and after 14 days. A more significant improvement in the neurological status according to the *NIHSS scale* was achieved after earlier operations [18].

Thus, early CEA demonstrated satisfactory results in the acute period of ischemic stroke, both in terms of the main surgical indicators and in terms of the dynamics of the neurological status, especially after operations in the first week of stroke.

### CONCLUSION

Carotid endarterectomy performed in the acute period of ischemic stroke is a safe surgical intervention for preventing recurrent ipsilateral ischemic events. The most positive neurological dynamics and the least neurological deficit at discharge were achieved after operations performed in the first week of ischemic stroke. Additional studies are needed to determine the most optimal, safe and effective timing of carotid endarterectomy in the acute period of ischemic stroke.



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