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Carotid Endarterectomy in the Acute Period of Ischemic Stroke After Thrombolytic Therapy

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AIM OF STUDY To study the outcomes, complications and risk factors of CEA surgery in patients after thrombolytic therapy.

MATERIAL AND METHODS The results of treatment of patients after carotid endarterectomy in the acute period of ischemic acute cerebrovascular accident after thrombolytic therapy were assessed. The group of patients operated on with thrombolytic therapy included 43 patients (29 women and 14 men). The average age of the operated patients was 64±8.9 years. In 24 patients, the stroke was localized in the blood supply of the left middle cerebral artery, in 19 — in the right. A group of patients (n=50) with similar clinical characteristics was selected as a comparison group.

RESULTS Adverse events occurred in only two patients (4.6%) in the thrombolytic therapy group. One complication required active surgical tactics, the formation of a significant hematoma in the area of surgical intervention. No adverse events were noted in the control group. There were no lethal outcomes in both groups. There were no significant differences in long-term survival rates between groups (p>0.05).

DISCUSSION Numerous researchers have come to the conclusion that by observing clear criteria for selecting patients for surgical treatment, it is possible to minimize complications associated with the use of thrombolytic drugs in the preoperative period. Our study confirms these conclusions. Patients with previously performed thrombolytic therapy for stroke are in a group of special attention and require close monitoring in the short and long term.

CONCLUSION Carotid endarterectomy in the acute period of stroke during thrombolytic therapy is not associated with an increased risk of postoperative complications and does not compromise long-term treatment results. Further large studies are needed to clarify the results obtained.

Keywords: carotid artery stenosis, ischemic stroke, carotid endarterectomy, acute cerebrovascular accident, thrombolytic therapy
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AF — atrial fibrillation
ASP — atherosclerotic plaque
CABG — coronary artery bypass grafting
CEA — carotid endarterectomy
CT — computed tomography
COPD — Chronic Obstructive Pulmonary Disease
FC IHD — functional class of ischemic heart disease
ICA — internal carotid artery
ICS — pacemaker
IS — ischemic stroke
MCA — middle cerebral artery
PAD — peripheral artery disease
PICS — post-infarction cardiosclerosis
PTCA — percutaneous transluminal coronary angioplasty
TIS — temporary intraluminal shunt
TLT — thrombolytic therapy
VAS — visual analogue scale

INTRODUCTION

With the widespread implementation of the state program for the treatment of strokes, the number of patients undergoing thrombolytic therapy (TLT) is steadily increasing. According to the report of the chief neurologist of the Ministry of Health of the Russian Federation, Professor N.A. Shamalov, in 2022, TLT was performed in 26,449 patients with ischemic stroke (IS), the estimated need for this procedure is about 60,000 per year. Some patients who underwent TLT have an atherothrombotic subtype of IS according to *TOAST*. As a result, there is an increasing need for secondary surgical prevention of recurrent ischemic events in this category of patients.

Despite the large number of studies devoted to the safety and efficacy of CEA in the acute period of cerebrovascular accident, there are very few studies devoted to the surgical treatment of internal carotid artery (ICA) stenosis in the early stages after TLT, not only in Russian but also in world literature [1–3]. Current national guidelines for the treatment of patients with brachiocephalic artery disease prescribe performing CEA as early as possible after IS in the presence of ICA stenosis of 70–99%. In the absence of significant concomitant diseases and a severe condition of the patient, it is permissible to perform CEA even with moderate ICA stenosis (60–69%) [4, 5]. However, the question of the possibility and timing of CEA against the background of TLT in IS is still a subject of discussion [1].

Aim of study: to study the outcomes, complications and risk factors of CEA surgery in patients after TLT.

MATERIAL AND METHODS

For the analysis, data from 776 patients operated on in the acute period of ischemic stroke were taken, with subsequent assessment of adverse outcomes and factors of their occurrence in the early and late periods.

The group of patients operated on the background of TLT consisted of 43 patients, or 5.5% of the entire cohort of patients (29 women and 14 men). The average age of the operated patients was 64±8.9 years. In 24 patients, the stroke was localized in the left middle cerebral artery (MCA), and in 19 - in the right.

The group with similar clinical characteristics was selected (n=50) to assess the safety of CEA in the acute period of stroke without previously performed TLT (Table 1).

Table 1

Clinical characteristics of the selected groups

Factor	Main group, *n* (%)	Comparison group, *n* (%)	*p*
Severity of stroke Easy Average	 5 (11.6) 38 (88.4)	 11 (22) 39 (78)	0.2
Gender Male Female	 14 (32.6) 29 (67.4)	 15 (30) 35 (70)	0.8
Age, years	64±8.9	63±9.3	0.9
Days from stroke	14±3.5	12±4	0.8
Duration of hospital stay	5.3±2.0	6.1±1.8	0.9
Amaurosis fugax	0	0	1.0
Tortuosity of the target artery	6 (14)	7 (14)	1.0
Percentage of target artery stenosis, %	75.6±13.3	72.3±14.1	0.9
Contralateral ICA lesion	28 (65.1)	33 (66)	1.0
History of contralateral ICA surgery	0	0	1.0
Application of TIS	0	0	1.0
Classical CEA	21 (48.8)	23 (46)	0.8
Eversion CEA	22 (51.2)	27 (54)	0.8
ICA resection	6 (14)	7 (14)	1.0
ICA prosthetics	0	0	1.0
AF	5 (11.6)	5 (10)	1.0
PICS	6 (14)	7 (14)	1.0
PTCA	2 (4.7)	2 (4)	1.0
CABG	2 (4.7)	2 (4)	1.0
Mechanical prosthetic heart valve	0	0	1.0
PAD	6 (14)	4 (8)	0.4
Obesity	5 (11.6)	11 (22)	0.2
COPD	3 (7.0)	5 (10)	0.3
ICS	0	1 (5)	0.9
FC IHS 0 1 2	 7 (16.3) 19 (44.2) 17 (39.5)	 9 (18) 21 (42) 20 (40)	
Arterial hypertension	43 (100)	50 (100)	
Diabetes mellitus	8 (18.6)	7 (14)	0.9
Complicated ASP	40 (93%)	42 (84)	0.8

Notes: PAD — peripheral artery disease; CABG — coronary artery bypass grafting; ASB — atherosclerotic plaque; TIS — temporary intraluminal shunt; ICA — internal carotid artery; CEA — carotid endarterectomy, PICS — postinfarction cardiosclerosis, COPD — chronic obstructive pulmonary disease, FC IHD — functional class of coronary artery disease; AF —atrial fibrillation; PTCA — percutaneous transluminal coronary angioplasty; ICD — pacemaker

All patients took acetylsalicylic acid preparations at a dose of 100 mg orally once a day. Patients after TLT began taking acetylsalicylic acid 2 days after completion of the thrombolytic drug administration with normal coagulogram parameters.

Patients in the two groups did not have statistically significant differences in stroke severity assessed in points on the *NIHSS scale* and in the degree of independence limitation according to the criteria of the modified Rankin scale, *mRs* (Table 2).

Table 2

Stroke severity scores according to the modified Rankin Scale (mRs) and the National Institutes of Health Severity Scale (NIHSS)

	Main group		Comparison group	
	NIHSS	*mRs*	*NIHSS*	*mRs*
Upon admission for acute cerebrovascular accident	12.7±2.7	2.9±0.7	11.9±3.5	2.9±0.7
When transferred to the vascular surgery department	10.5±2.5	1.5±0.5	9.8±2.1	1.5±0.6
Upon discharge from the vascular surgery department	5.0±1.8	1.1±0.7	4.9±1.9	1.1±0.4

Notes: NIHSS — National Institutes of Health Severity Score; mRs — Modified Rankin Scale

RESULTS

As can be seen from the tables presented, the groups were comparable in terms of the main parameters. The stroke severity was assessed using the generally accepted scale of the National Institute of Health (*NIHSS*), less than score 6 - mild stroke, from 7 to 13 - moderate stroke. In patients of the main group, CEA was performed from 3 to 17 days after the development of ischemic stroke, on average on the 14th day, in the comparison group, the interventions were performed in the interval from the 3rd to 16th day, on average on the 12th day from the development of ischemic stroke.

When assessing the frequency of complications, adverse events occurred only in 2 patients (4.6%) in the TLT group. No adverse events were observed in the comparison group (Table 3).

Formation of postoperative hematoma, which required revision of the postoperative wound and active actions aimed at eliminating the source of bleeding, occurred in the first 5 hours after surgery in a patient operated on 12 days after suffering IS and performed TLT. During revision of the postoperative wound, the source of bleeding was a previously coagulated branch of the external carotid artery up to 1 mm in diameter. Hemostasis was achieved by ligation and suturing of the bleeding artery. When analyzing the coagulogram parameters, such as international normalized ratio, prothrombin time, activated partial thromboplastin time, the amount of fibrinogen, antithrombin III, all were within the reference values. Hyperperfusion syndrome developed on the 2nd day after surgery in a patient with critical stenosis of the left ICA, operated on the 10th day after the development of ischemic stroke and performed TLT, it was manifested by severe headache 7-8 points on the visual analogue scale (VAS) of pain and psychomotor agitation of the patient against the background of high blood pressure with a maximum recorded systolic pressure level of 190 mm Hg. The patient continued treatment in the intensive care unit, with a decrease and stabilization of systolic blood pressure at the level of 120-130 mm Hg. A day later, significant positive dynamics were noted in the form of a decrease in headache to 1-2 points on the VAS, the absence of psychomotor agitation. According to the computed tomography of the brain, no new changes were

Table 3

Adverse events

	Main group, *n* (%)	Group comparisons, *n* (%)	*p*
Hospital complications	2 (4.6)	0	1.0
Revision, hemostasis	1 (2.3)	0	1.0
Thrombosis of the reconstruction zone	0	0	1.0
Damage to the 12th pair of cranial nerves	0	0	1.0
Hemorrhagic transformation	0	0	1.0
Hyperperfusion syndrome	1 (2.3)	0	1.0
Acute myocardial infarction in hospital	0	0	1.0
Death in hospital	0	0	1.0
Remote complications	0	0	1.0
Acute cerebrovascular accidents in hospital	0	0	1.0
Lethal outcome in distant period	0	1	1.0

detected in the left MCA basin compared with the preoperative picture of ischemic stroke.

All patients after completion of the treatment stage in the vascular surgery department are referred to the medical rehabilitation department to continue treatment.

When analyzing the remote results more than 1 year after the operation, one fatal outcome was noted in the comparison group in a patient with significant damage to the contralateral ICA. The fatal outcome was not associated with the development of ischemic disorders of the brain. There were no statistically significant differences in survival rates in the remote period between the groups (p >0.05).

DISCUSSION

Current European guidelines define indications for CEA for patients with symptomatic ICA stenosis within 6 days after TLT. These include recovery of neurological deficit to 0–2 points on the modified Rankin scale after TLT, a lesion in the brain of the IS less than one third of the MCA blood supply zone, recanalization of previously occluded MCA according to computed tomography (CT) angiography, ipsilateral ICA stenosis from 50 to 99%, and the absence of signs of parenchymal hemorrhage or cerebral edema. Contraindications include severe persistent neurological deficit (*mRs of* 3 or more), high surgical risk of the operation, intracerebral hemorrhage detected by CT, previous neck surgery, or radiation therapy in the area of the proposed surgical intervention [6].

In a large study based on the National Intervention Sample (*NIS*) in the United States, it was found that the number of patients who received systemic thrombolysis before CEA was only 1.1% (1157/109784) of the total number of patients with IS [7]. Nevertheless, the issue of determining the indications for surgery, the optimal timing of surgical intervention after TLT remains important, since it is necessary to maintain a balance between not increasing the risk of perioperative intracranial hemorrhage due to too early intervention, and preventing recurrent IS due to delayed surgery [7].

A systematic review by *S.K. Kakkos et al.* analyzed 25 observational studies on revascularization procedures after systemic thrombolysis. The total number of patients was 147,810, of whom CEA was performed in 2,076 cases. As a result, after CEA, the overall incidence of perioperative stroke/death was 5.2% (95% CI [3.3–7.5]) and intracranial hemorrhage was 3.4% (95% CI [1.7–5.6]). When comparing the outcomes of CEA in patients who received TLT and those who did not, the incidence of perioperative stroke/death was higher after TLT (4.3% vs. 1.5%), the incidence of intracranial hematomas was significantly higher after TLT (2.2% vs. 0.12%), as was the incidence of hematomas on the neck in the area of surgery (3.6% vs. 2.26%). According to the study results, the incidence of perioperative stroke/death was 13.0% when CEA was performed 3 days after TLT, 10.6% when performed 4 days later, and when the operation was performed 6–7 days after systemic thrombolysis, this figure decreased to 6% [8].

A recent study *by A.K. Vellimana et al.*, including 551 patients who underwent CEA with and without TLT, showed a significantly higher incidence of postoperative hemorrhagic stroke in patients who underwent surgery <7 days after TLT compared to patients who did not undergo TLT. Comparisons of interventions with and without TLT on the risk of hemorrhagic stroke are balanced at day 7 after systemic thrombolysis (0.2%), and the risks of recurrent ischemic stroke are balanced at day 6 (1%) [9].

The obtained data cast doubt on the justification and effectiveness of urgent CEA (in the first 7 days) after systemic thrombolysis. In view of the high risk of hemorrhagic complications, a wait-and-see approach may be justified. However, this study did not take into account the initial neurological deficit and somatic status of the patient, which does not exclude the inclusion of patients with AF or transient ischemic attack in the comparison group.

Numerous researchers have concluded that by following clear criteria for selecting patients for surgical treatment, it is possible to mitigate complications associated with the use of thrombolytic drugs in the preoperative period. Of particular interest are patients requiring intervention on the ICA after previously performed thrombolytic therapy for acute ischemic stroke [10].

In the group of 46 patients operated by us, 2 developed complications, which amounted to 4.6%, one complication was associated with the development of cerebral hyperperfusion without the formation of hemorrhagic changes in the brain tissue, the second complication was characterized by the formation of a hematoma in the area of operative access, which required repeated intervention, evacuation of the hematoma and active surgical

hemostasis. No fatal outcomes were recorded. Risk factors for the development of complications and adverse events in the near and distant periods in this category of patients were not identified.

Many authors remain of the opinion about the very high risk of hemorrhagic complications after CEA performed in the first 48 hours after TLT. Most likely, this complication is associated with a significant systemic change in hemostasis after TLT. Indications for performing surgery in these periods are very limited and often conditional, which reduces the effectiveness and justification of urgent surgical intervention.

The lack of a comprehensive assessment of hemostasis after TLT in many patients also does not allow a full assessment of the potential risk of hemorrhagic complications in the perioperative period. A personalized approach to assessing the blood coagulation system, the appointment of adequate antiplatelet therapy after CEA are one of the main tasks in the treatment of this group of patients.

Based on our experience, it seems to us that the most significant factor in the occurrence of complications in the early postoperative period is high blood pressure, which is difficult to correct.

CONCLUSION

At present, a multidisciplinary approach to the treatment and prevention of recurrent acute cerebrovascular accident is extremely important in medical practice: joint work of a vascular surgeon, neurosurgeon, neurologist, cardiologist, and resuscitator.

The risk of hemorrhagic complications causes caution regarding the tactics of surgical treatment of patients with carotid artery stenosis who have undergone thrombolytic therapy. However, this group of patients still has a high risk of repeated acute cerebrovascular accident with a possible fatal outcome in case of untimely surgery.

We believe that it is possible to perform such surgical interventions in the acute period of stroke under the following conditions: stroke severity (mild or moderate), normalization of coagulogram parameters, the possibility of invasive monitoring of arterial pressure during surgery and in the first day after surgery, at least 3 days from the moment of completion of thrombolytic therapy for ischemic stroke. Our conclusions are based on the analysis of a relatively small group of patients, which necessitates further research aimed at determining clear criteria for their selection, determining indications and optimal timing of surgical treatment for this group of patients.

1. The study did not reveal any risk factors for performing carotid endarterectomy in the acute period of ischemic cerebrovascular accident after thrombolytic therapy. The degree of risk was comparable to the risk of surgical intervention in a similar group of patients without previous thrombolytic therapy ($p = 1.0$).

2. Carotid endarterectomy in the acute period of stroke against the background of thrombolytic therapy is not associated with an increased risk of postoperative complications and does not compromise the long-term results of treatment.

REFERENCES

1. Vinokurov IA, Yasnopolskaya NV, Gasanov EN, Mutaev OM, Ropova AI. Carotid endarterectomy in the early period after systemic thrombolysis for acute cerebrovascular accident. *Russian Journal of Cardiology and Cardiovascular Surgery.* 2021;14(5):370–375. (In Russ.). https://doi.org/10.17116/kardio202114051370
2. Bartoli MA, Squarcioni C, Nicoli F, Magnan PE, Malikov S, Berger L, et al. Early Carotid Endarterectomy after Intravenous Thrombolysis for Acute Ischemic Stroke. *Eur J Vasc Endovasc Surg* . 2009;37(5):512–518. PMID: 19231256 https://doi.org/10.1016/j.ejvs.2008.12.018
3. Van Dellen D, Tiivas CA, Jarvi K, Marshall C, Higman DJ, Imray CH. Transcranial Doppler ultrasonography-directed intravenous glycoprotein IIb/IIIa receptor antagonist therapy to control transient cerebral microemboli before and after carotid endarterectomy. B *r J Surg.* 2008;95(6):709–713. PMID: 18425794 https://doi.org/10.1002/bjs.6204
4. Chernyavsky MA, Irtyuga OB, Yanishevsky SN, Alieva AS, Samochernykh KA, Abramov KB, et al. Russian consensus statement on the diagnosis and treatment of patients with carotid stenosis. *Russian Journal of Cardiology* . 2022;27(11):5284. (In Russ.). https://doi.org/10.15829/1560-4071-2022-5284
5. Naylor R, Rantner B, Ancetti S, de Borst GJ, De Carlo M, Halliday A, et al. Editor's Choice – European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. *Eur J Vasc Endovasc Surg* . 2023;65(1):7–111. PMID: 35598721 https://doi.org/10.1016/j.ejvs.2022.04.011

6. Naylor R, Rantner B, Ancetti S, de Borst GJ, De Carlo M, Halliday A, et al. Editor's Choice - European Society for Vascular Surgery (ESVS) 2023 Clinical Practice Guidelines on the Management of Atherosclerotic Carotid and Vertebral Artery Disease. *Eur J Vasc Endovasc Surg* . 2023;65(1):7–111. PMID: 35598721 https://doi.org/10.1016/j.ejvs.2022.04.011
7. Emiru T, Adil MM, Suri MF, Qureshi AI. Thrombolytic treatment for in-hospital ischemic strokes in the United States. *J Vasc Interv Neurol* . 2014;7(5):28–34. PMID: 25566339
8. Kakkos SK, Vega de Ceniga M, Naylor R. A systematic review and meta-analysis of periprocedural outcomes in patients undergoing carotid interventions following thrombolysis. *Eur J Vasc Endovasc Surg.* 2021;62(3):340–349. PMID: 34266765 https://doi.org/10.1016/j.ejvs.2021.06.003
9. Vellimana AK, Washington CW, Yarbrough CK, Pilgram TK, Hoh BL, Derdeyn CP, et al. Thrombolysis is an independent risk factor for poor outcome after carotid revascularization. *Neurosurgery* . 2018;83(5):922–930. PMID: 29136204 https://doi.org/10.1093/neuros/nyx551
10. Krylov VV, Luk'yanchikov VA, Polunina NA. *Surgical revision of the head brain* . Moscow: PRIZ Publ.; 2023 (In Russ.)

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