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Research Article
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Endovascular Treatment of Patients with Acute Ischemic Stroke Caused by Tandem Lesions of the internal Carotid Artery

A.G. Faybushevich[1], H.V. Galustyan[1] ✉, V.M. Sysoev[2], E.A. Gitelzon[1], M.V. Chernyaev[1]

Department of Hospital Surgery with a Course in Pediatric Surgery
[1] Patrice Lumumba Peoples' Friendship University of Russia
Miklukho-Maklaya Str. 6, Moscow, Russian Federation 117198
[2] S.S. Yudin City Clinical Hospital
Kolomensky proezd 4, Moscow, Russian Federation 115446

✉ **Contacts:** Hayk V. Galustyan, Postgraduate Student of the Department of Hospital Surgery with a course in pediatric surgery of the FSAEI HE Patrice Lumumba Peoples' Friendship University of Russia. Email: haykgalustyan@yandex.ru

ABSTRACT The incidence of tandem internal carotid artery (ICA) lesions, according to various sources, is 15–30% of all ischemic strokes (IS) caused by occlusion of a large intracranial artery. However, due to the lack of randomized clinical trials, the optimal revascularization strategy in this cohort of patients remains uncertain and requires further study.

AIM OF THE STUDY The aim of this study is to investigate the efficacy and safety of different endovascular approaches to the treatment of patients with acute ischemic stroke caused by tandem ICA lesions.

MATERIAL AND METHODS The study included 94 patients with acute ischemic stroke caused by tandem ICA lesions. After successful intracranial reperfusion (mTICI 2b-3), all patients were divided into two groups. In the study group (48 patients), after achieving successful intracranial reperfusion, patients were implanted with a stent in the area of the lesion of the extracranial ICA with the administration of loading doses of dual antiplatelet therapy. In the comparison group (46 patients), after achieving successful intracranial reperfusion, patients were prescribed optimal drug therapy in accordance with current international recommendations, including antiplatelet therapy (in this group, revascularization of the extracranial ICA was considered after achieving a favorable functional outcome; assessed using the modified Rankin scale 0–2). The statistical program Stattech was used to analyze the obtained data.

RESULTS The frequency of favorable functional outcome after 90 days (mRs 0–2) in the study and comparison groups were 64.6% and 41.3%, respectively (p=0.024), and there was also a statistically significant difference in the frequency of early patency of the extracranial ICA in the study and comparison groups — 89.6% and 67.4%, respectively (p=0.009). The frequency of symptomatic intracerebral hemorrhage in the groups was comparable: 6.2% and 4.3%, respectively (p=1.000). In the comparison group, death was observed more often, but the difference was not statistically significant — 19.6% and 10.4%, respectively (p=0.255). Patients with early patency of the extracranial ICA statistically significantly more often achieved a favorable functional outcome (p=0.019) and statistically significantly less often died within three months (p=0.032).

CONCLUSION This study showed that intravascular thromboembolectomy from an occluded large intracranial artery in combination with emergency stenting of the internal carotid artery is the most effective endovascular treatment for patients with acute ischemic stroke caused by its tandem lesion.

Keywords: ischemic stroke, internal carotid artery, tandem lesion, emergency stenting

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Affiliations

Aleksandr G. Faybushevich	Candidate of Medical Sciences, Associate Professor, Head of the Department of Hospital Surgery with a Course in Pediatric Surgery, Patrice Lumumba Peoples' Friendship University of Russia; https://orcid.org/0000-0001-7998-3051, faybushevich-ag@rudn.ru; 30%, concept development, quality control of the main sections of the research, project management
Hayk V. Galustyan	Postgraduate Student of the Department of Hospital Surgery with a Course in Pediatric Surgery, Patrice Lumumba Peoples' Friendship University of Russia; https://orcid.org/0009-0008-6321-4168, haykgalustyan@yandex.ru; 25%, concept development, methodology design, formal analysis, research, text preparation, visualization
Vitaly M. Sysoev	Candidate of Medical Sciences, Head of the Department of X-ray Surgical Diagnostic and Treatment Methods, S.S. Yudin City Clinical Hospital; https://orcid.org/0000-0001-8013-3580, vitally.sysoev@gmail.com; 25%, concept development, methodology design, data verification for correctness, quality control of the main sections of the study

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Ekaterina A. Gitelzon — Candidate of Medical Sciences, Assistant Professor at the Department of Hospital Surgery with a Course in Pediatric Surgery, Patrice Lumumba Peoples' Friendship University of Russia;
https://orcid.org/0000-0003-3871-5530, tarbaeva-ea@rudn.ru;
5%, control over the quality of the main sections of the study

Mikhail V. Chernyaev — Candidate of Medical Sciences, Assistant Professor at the Department of Hospital Surgery with a Course in Pediatric Surgery, Patrice Lumumba Peoples' Friendship University of Russia;
https://orcid.org/0000-0003-4925-7475, mikhailcherniaev@mail.ru;
5%, control over the quality of the main sections of the study

CI — confidence interval
CT — computed tomography
CT/MRI — computed tomography/magnetic resonance imaging
CVA — cerebrovascular accident
ICA — internal carotid artery
ICH — intracerebral hemorrhage
IS — ischemic stroke
IV TLT — intravenous thrombolytic therapy
IVTE — intravascular thromboembolectomy
MRI — magnetic resonance imaging
mRs — modified Rankin scale
NIHSS — National Institutes of Health Stroke Scale
OMT — optimal drug therapy
OR — odds ratio
RCTs — randomized clinical trials
sICH — symptomatic intracerebral hemorrhage

INTRODUCTION

Tandem lesion of the internal carotid artery (ICA) is defined as a combination of severe stenosis or occlusion of the extracranial ICA with occlusion of a large intracranial artery (intracranial segments of the ICA, M1 or M2 segments of the middle cerebral artery) [1]. The incidence of this pathology, according to various data, is 15–30% of all ischemic strokes (IS) caused by occlusion of a large intracranial artery [1–4].

In patients with tandem ICA lesions, optimal medical therapy (OMT), including intravenous thrombolytic therapy (IVT), is associated with poor outcomes [5]. Intravascular thromboembolectomy (IVTE) is currently the treatment of choice for large intracranial artery occlusion, but in the case of tandem ICA lesions, the optimal revascularization strategy remains uncertain due to the lack of randomized clinical trials (RCTs).

In three large RCTs (SWIFT PRIME, EXTEND-I A, THRACE) patients with tandem ICA lesions were not included [6–8]. The therapeutic effect of IST in patients with tandem ICA lesions was comparable to that in patients with isolated occlusion of a large intracranial artery in the Hermes Collaboration meta-analysis [2], however, the optimal revascularization strategy for extracranial lesions was not reported, and many patients with mild extracranial ICA stenosis (<70%) were included, especially in the MR CLEAN RCT [9].

Emergency stenting of the ICA in combination with mechanical thrombectomy from the occluded large intracranial artery is one of the endovascular approaches to revascularization of tandem ICA lesions. This approach has both advantages and disadvantages.

The advantages of emergency stenting include [10, 11]:

1. Plaque stabilization - stent stabilizes the plaque, reducing the risk of recurrent thromboembolic events, thereby reducing the risk of recurrent stroke.
2. Spontaneous lysis of intracranial thrombus in 20–25% of cases.
3. Improving cerebral perfusion.
4. Higher percentage of early ICA patency, which may contribute to early neurological improvement.

The disadvantages of emergency stenting include [12, 13]:

1. Increased risk of developing sICH due to possible cerebral hyperperfusion and the need to prescribe loading doses of dual antiplatelet therapy.
2. Increased risk of distal embolization during stent implantation despite the use of proximal and/or distal cerebral protection.
3. Risk of stent thrombosis.
4. Intraoperative risk of bradycardia and hypotension due to activation of carotid baroreceptors during stent implantation.

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Therefore, due to the lack of reliable data, the efficacy and safety of this approach remain unknown. The aim of this study is to investigate the efficacy and safety of different endovascular treatment approaches in patients with acute ischemic stroke due to tandem ICA lesions.

MATERIAL AND METHODS

A total of 94 patients with acute IS due to tandem ICA lesions were included in this study.

The inclusion criteria for the study were:

1. Atherosclerotic stenosis of the C1 segment of the ICA, narrowing the lumen of the artery by at least 70% according to NASCET, or atherothrombotic occlusion in combination with occlusion of a large intracranial artery.

2. Successful reperfusion of mTICI 2b-3 following IVTE.

3. Time from the onset of cerebrovascular accident (CVA) of the ischemic type to IVTE 0–6 hours (if the time is not known exactly, then from the moment when the patient did not have neurological disorders caused by the occlusion).

4. Stroke severity according to the NIHSS scale is not less than 6;

5. Age not less than 18 years;

6. Infarction size according to the ASPECTS scale is not less than 6;

The exclusion criteria for the study were:

1. CT/MRI signs of intracranial hemorrhage (computed tomography/magnetic resonance imaging).

2. Uncorrectable blood pressure over 185/100 mmHg.

3. Hypoglycemia less than 2.8 mmol/l, hyperglycemia more than 22.2 mmol/l.

4. SI in the affected artery basin in the previous 6 weeks.

5. Laboratory signs of a disorder of the blood coagulation system (platelet count less than 40×10^9/l, activated partial thromboplastin time more than 50 sec or international normalized ratio more than 3.0).

6. Contraindications to the use of contrast agents.

7. Unfavorable anatomy/associated lesions that prevent intravascular access to the affected intracranial artery.

All patients underwent standard clinical, instrumental and laboratory tests upon admission to the emergency department. After native computed tomography (CT) of the brain and exclusion of intracerebral hemorrhage (ICH) for the purpose of IV TLT, patients were started to receive Actilyse (in the absence of other contraindications) without delaying the CT angiography stage. After CT angiography of the head and neck vessels and detection of occlusion of a large intracranial artery, patients who were candidates for endovascular treatment were transported to the Department of X-ray Surgical Diagnostics and Treatment Methods for direct angiography followed by IVTE. The endovascular procedure was performed through a transfemoral approach. After direct angiography and confirmation of occlusion, the diagnostic catheter was changed to a guide catheter (in the vast majority of cases, a balloon guide catheter) for the subsequent intervention. The first stage involved crossing the affected area of the extracranial ICA (using balloon-assisted passage technique if necessary), followed by IVTE from the occluded large intracranial artery using contact aspiration, classical stent retriever thrombus extraction technique or combined IVTE techniques. After achieving successful intracranial reperfusion (mTICI 2b-3), patients were randomly divided into two groups. The comparison group included 46 patients who, after successful intracranial reperfusion (mTICI 2b-3), were prescribed OMT in accordance with current international recommendations [14], including antiplatelet therapy for the prevention of occlusion/reocclusion and/or repeated thromboembolic events:

— aspirin 300 mg (24 patients);

- aspirin 300 mg and clopidogrel 300 mg (22 patients).

The study group included 48 patients who underwent successful intracranial reperfusion (mTICI 2b-3) and underwent stent implantation in the extracranial segment of the ICA. During stent implantation, in addition to using distal cerebral protection (100% of cases), proximal protection (balloon guide catheter) was also used in most cases (90%). In this group, patients were prescribed a loading dose of dual antiplatelet therapy before stent implantation:

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— aspirin 300 mg and clopidogrel 300 mg (30 patients);

— aspirin 300 mg and ticagrelor 180 mg (18 patients).

After completion of the endovascular intervention , the patients were transferred to the neurological intensive care unit for further observation and treatment. Control neuroimaging was performed 24 hours after completion of the procedure. During the patient's stay in the hospital, the dynamics of the neurological status was assessed using the NIHSS (National Institutes of Health Stroke Scale) stroke severity scale, the functional status was assessed using the modified Rankin scale. Also during the hospital stay, the patients underwent ultrasound examination of the brachiocephalic arteries to determine patency. The presence of symptomatic hemorrhagic transformation was determined in accordance with the ECAS III criteria - any ICH detected during control neuroimaging (CT/MRI of the brain) in combination with an increase in neurological deficit by at least 4 points compared to the initial NIHSS level (or with the lowest NIHSS value during the improvement period) or death within 24 hours.

The functional outcome of patients was assessed after 3 months using the modified Rankin scale and by telephone call.

ANALYSIS OF VARIOUS INDICATORS IN THE STENTING AND CONSERVATIVE APPROACH GROUPS

When comparing the duration of surgery in the stenting and conservative approach groups, statistically significant differences were found ($p < 0.001$). When assessing the sum of points on the ASPECTS scale upon admission, age, the sum of points on the mRs before the last episode of stroke, the sum of points on the NIHSS stroke scale upon admission, the time from the onset of the first symptoms to reperfusion, no significant differences were found ($p = 0.943$, $p = 0.124$, $p = 0.330$, $p = 0.134$, $p = 0.220$, respectively) (Table 1).

All patients included in this study achieved successful intracranial reperfusion (mTICI 2b-3). In both groups, there were more men - 60.9% and 64.6%, respectively ($p = 0.71$), and in both groups, the vast majority of patients received IV TLT - 93.5% and 91.7%, respectively ($p = 1.0$) (Table 2).

Table 1

Analysis of quantitative indicators

Indicators	Group	M±SD / Me	95% CI / $Q_1 - Q_3$	n	p
Total ASPECTS score upon admission	Comparisons	8.00	7.25–9.00	46	0.943
	Stenting	8.00	7.75–9.00	48	
Age	Comparisons	67.3±6.1	65.5–69.1	46	0.124
	Stenting	65.6±4.8	64.2–66.9	48	
Modified Rankin Scale score (mRs) before the last episode of stroke	Comparisons	0,00	0.00–0.00	46	0.330
	Stenting	0,00	0.00–0.00	48	
NIHSS Stroke Scale Score upon admission	Comparisons	15.00	11.25–18.00	46	0.134
	Stenting	13.50	10.00–17.00	48	
Operation duration, min	Comparisons	67,00	64.25–69.75	46	<0.001*
	Stenting	93.50	90.75–97.00	48	
Time from onset of first symptoms before reperfusion, h	Comparisons	4.30	3.70–4.88	46	0.220
	Stenting	4.45	4.07–4.83	48	

Notes: * — differences in indicators are statistically significant ($p < 0.05$).
CI – confidence interval; CVA - cerebrovascular accident

Table 2

Analysis of categorical indicators

Indicators	Categories	Group		p
		Comparisons (n=46)	Stenting (n=48)	
Gender	Women	18 (39.1)	17 (35.4)	0.710
	Men	28 (60.9)	31 (64.6)	
IV TLT	IV TLT	43 (93.5)	44 (91.7)	1,000
Successful reperfusion rate of mTICI 2 b -3	Successful reperfusion	46 (100.0)	48 (100.0)	–

Note: IV TLT - intravenous thrombolytic therapy

RESEARCH RESULTS

Comparative analysis of the frequency of favorable outcome after 90 days depending on the selected approach of endovascular treatment revealed a statistically significant difference (the frequency of favorable functional outcome in the comparative group was 41.3%, in the study group - 64.6%, $p = 0.024$). Also, statistical analysis of the obtained results showed a significant difference in the early patency of the extracranial ICA depending on the selected strategy of endovascular treatment

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(in the comparison group, the frequency of early patency of the extracranial ICA was 67.4%, in the study group - 89.6%, p = 0.009). Comparative analysis of the frequency of death depending on the selected method of endovascular treatment did not show a statistically significant difference (in the comparative group, the frequency of death from all causes within 3 months was 19.6%, in the study group 10.4%; p = 0.255). The analysis also did not show a statistically significant difference in the incidence of symptomatic ICH (sICH) depending on the chosen endovascular treatment tactics (the incidence of sICH in the comparison group was 4.3%, in the stenting group - 6.2%; p = 1.000) (Table 3).

Table 3

Analysis of study results depending on randomization group

Indicators	Groups		p
	Comparisons(n=46)	Stenting (n=48)	
Frequency of sICH	2 (4.3%)	3 (6.2%)	1,000
Early patency rate of extracranial ICA	31 (67.4%)	43 (89.6%)	0.009*
Fatality within 90 days	9 (19.6%)	5 (10.4%)	0.255
Favorable functional outcome at 90 days (mRs0–2)	19 (41.3%)	31 (64.6%)	0.024*

Note: * — differences in indicators are statistically significant (p<0.05). ICA - internal carotid artery; sICH - symptomatic intracerebral hemorrhage; mRs—modified Rankin scale

In order to determine the patency of the extracranial ICA, all patients underwent ultrasound examination of the brachiocephalic arteries 24 hours after endovascular intervention and at discharge. In the comparison group, 15 patients (32.6%) had occlusion/reocclusion of the extracranial ICA, in 13 cases (86.7%) of 15, obstruction of the extracranial ICA was not accompanied by deterioration of the neurological status of patients. Only one patient (6.7%) of 15 had obstruction beyond 24 hours after endovascular intervention, in the remaining 14 patients (93.3%), obstruction of the extracranial ICA was noted within 24 hours after endovascular treatment. In the stenting group, acute stent thrombosis (within 24 hours) was noted in 5 patients (10.4%). 4 out of 5 cases were asymptomatic (not accompanied by early deterioration of the neurological status of patients).

Thus, in 19 cases (95%) out of 20, extracranial ICA obstruction was observed within the first 24 hours, and in 17 cases (85%) it was not accompanied by deterioration of the neurological status of patients. However, a comparative analysis of a favorable functional outcome depending on the early patency of the extracranial ICA revealed a statistically significant difference: the frequency of a favorable functional outcome among patients with early patency of the extracranial ICA was 59.5%, and among patients who had extracranial ICA obstruction - 30.0% (odds ratio (OR) = 3.422; 95% CI (confidence interval): 1.182–9.908; p = 0.019).

Also, statistical analysis of the obtained results revealed a significant difference in mortality depending on the early patency of the extracranial ICA: the incidence of mortality from all causes among patients with early patency of the extracranial ICA was 10.8%, and among patients who had obstruction of the extracranial ICA - 30.0% (OR = 0.283; 95% CI: 0.085–0.944; p = 0.032). Comparative analysis of the incidence of sICH depending on the early patency of the extracranial ICA did not reveal a statistically significant difference (among patients with early patency of the extracranial ICA, the incidence of sICH was 5.4%, and among patients with obstruction of the extracranial ICA - 5.0%; p = 1.000) (Table 4).

Table 4

Analysis of the results of the study depending on the early patency of the extracranial internal carotid artery

Indicators	Early patency rate extracranial ICA		p
	ICA obstruction (n = 20)	Passage ICA (n = 74)	
Frequency of sICH, n (%)	1 (5.0)	4 (5.4)	1,000
Fatality within 90 days, n (%)	6 (30.0)	8 (10.8)	0.032*
Favorable functional outcome at 90 days (mRs 0–2), n (%)	6 (30.0)	44 (59.5)	0.019*

Note: * — differences in indicators are statistically significant (p<0.05). ICA - internal carotid artery; sICH - symptomatic intracerebral hemorrhage; mRs—modified Rankin scale

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DISCUSSION

The present study demonstrated that in the stenting group, early patency of the extracranial ICA was statistically significantly more often achieved - 89.6% compared with patients randomized to the comparison group 67.4% (OR = 4.161; 95% CI: 1.368–12.658; p = 0.009). This can be explained by the fact that the stent, due to its high radial force, prevents elastic remodeling of the vessel, and the stent, by stabilizing the plaque, reduces the risk of repeated atherothrombotic occlusion and repeated thromboembolic events. Also, patients in the stenting group were statistically significantly more likely to achieve functional independence within 3 months - 64.6% compared to patients in the comparison group 41.3% (OR = 2.591; 95% CI: 1.126–5.962; p = 0.024), which can also be explained by the higher early patency of the extracranial ICA.

CONCLUSION

The study showed that intravascular thromboembolectomy in combination with stenting of the internal carotid artery (with intraoperative administration of loading doses of dual antiplatelet therapy) in patients with acute ischemic stroke is an effective and safe treatment method.

In our study, patients in the stenting group were statistically significantly more likely to achieve a favorable functional outcome within 3 months. Also, a higher percentage of survival was noted in the stenting group, but the difference was not statistically significant. Stenting and the administration of loading doses of dual antiplatelet therapy were not predictors of symptomatic intracerebral hemorrhage. This study also emphasizes the importance of early patency of the extracranial internal carotid artery. Patients who had obstruction of the extracranial internal carotid artery were statistically significantly less likely to achieve a favorable functional outcome and more often died within 90 days, despite the fact that in the overwhelming majority of cases, occlusion/reocclusion of the extracranial internal carotid artery and (or) stent thrombosis (implanted in the extracranial internal carotid artery) were not accompanied by early deterioration in the patient's neurological status (they were asymptomatic).

FINDINGS

1. In the stenting group, the frequency of early patency of the extracranial internal carotid artery was observed statistically significantly more often compared to the comparison group - 89.6% and 67.4%, respectively, (OR = 4.161; 95% CI: 1.368–12.658; p = 0.009), also in the stenting group, the frequency of favorable functional outcome after 90 days was observed statistically significantly more often - 64.6% and 41.3%, respectively, (OR = 2.591; 95% CI: 1.126–5.962; p = 0.024).

2. In the study and comparative groups, the difference in the incidence of systematic intracerebral hemorrhage was not statistically significant - 6.2% and 4.3%, respectively (OR = 1.467; 95% CI: 0.234–9.206; p = 0.863).

3. Intravascular thromboembolectomy from an occluded large intracranial artery in combination with emergency stenting of the extracranial internal carotid artery is an effective and safe endovascular method for treating patients with acute ischemic stroke caused by tandem lesions of the internal carotid artery.

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