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EXPERIENCE OF STENTING OF THE EXTRACRANIAL PART OF THE INTERNAL CAROTID ARTERY IN PATIENTS WITH ACUTE ISCHEMIC STROKE

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Aim. To present the experience of stenting of the extracranial internal carotid artery (ICA) in case of tandem steno-occlusive carotid lesion in the most acute phase of ischemic stroke.
Materials and methods. From December 2018 to December 2021, 29 patients with acute ischemic stroke, because of tandem steno-occlusive lesions of the ICA and intracranial arteries, underwent endovascular surgery to restore cerebral blood flow.
Results. Successful restoration of cerebral blood flow (according to the mTICI 2b–3 scale) achieved in 22 (75.9 %) patients. Four (13.8 %) patients had stent thrombosis in the early postoperative period. The incidence of symptomatic hemorrhagic transformation observed in 2 (6.9 %) patients. The frequency of a favorable functional outcome (Rankine 0–2) on the 30th day was 20.7 %, mortality – 24.1 %.
Conclusion. Stenting of the extracranial ICA in patients with acute ischemic stroke improves the efficiency of restoration of cerebral blood flow. The use of low doses of glycoprotein receptor blockers prevents stent thrombosis in the early period after implantation and does not increase the incidence of symptomatic hemorrhagic complications.

Keywords: acute ischemic stroke, glycoprotein receptor blockers, carotid artery stenting

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INTRODUCTION

In patients with acute ischemic stroke undergoing intraarterial methods of restoring cerebral blood flow, the incidence of carotid tandem steno-occlusive lesion is 25–30 % [1]. The natural course of the disease is characterized by a poor functional outcome and high mortality rate. Literature is extremely controversial on the efficacy of endovascular surgical methods of reperfusion therapy in this patient population [2].

The aim is to present the experience of performing stenting of the extracranial internal carotid artery (ICA) in case of tandem steno-occlusive lesion in the carotid system in the most acute phase of ischemic stroke.

MATERIALS AND METHODS

From December 2018 to December 2021, in the Interregional Clinical Diagnostic Center (Kazan city), 29 patients with acute ischemic stroke, which occurred against the background of tandem steno-occlusive lesions of the ICA and intracranial arteries, underwent endovascular surgery to restore cerebral blood flow (Table 1).

All patients upon admission underwent a set of examinations according to the recommended patient management protocol for acute ischemic stroke. X-ray surgical interventions were performed on an Innova 3100 (GE) angiography system. Mean time from disease onset to hospitalization was 152 minutes. Nineteen interventions were performed under local anesthesia, and ten under general intubation anesthesia. to minimize the risk of distal embolism, blood flow in the carotid artery was blocked in every case by a large-diameter (9F) occlusive guiding catheter. Balloon angioplasty of the ICA was performed with a balloon catheter of at most 5.5 mm in diameter. The method of thrombectomy from the intracranial system (aspiration, stent retriever-assisted, or combination technique) was chosen depending on the surgeon's preferences and the anatomical features of the patient's extracranial and intracranial arteries. The efficacy of restoration of cerebral blood

Table 1. *Characteristics of the operated patients and performed interventions*

Characteristic	Value
Total number of patients, *n* (%)	29 (100)
Average age, years	66 ± 12.6
Sex, *n* (%): male female	 20 (69.0) 9 (31.0)
NIHSS score at hospitalization, points	20 (15–27)
Time from disease onset to hospitalization, min	152 (60–334)
Time from hospitalization to puncture, min	95 (45–145)
Time from puncture to completion of intervention, min	55 (35–85)
Performed intervention, *n* (%): Intravenous thrombolytic therapy Segmental occlusion of the extracranial ICA part Prolonged occlusion of the extra- and intra-cranial ICA parts Occlusion of the extracranial ICA part in combination with MCA embolism Mechanical thrombectomy using stent retriever Mechanical thrombectomy using aspiration catheter Mechanical thrombectomy using combination techniques	 2 (6.9) 2 (6.9) 5 (17.2) 22 (75.9) 19 (65.5) 3 (10.3) 4 (13.8)

Note. *NIHSS – National Institutes of Health Stroke Scale; ICA – internal carotid artery; MCA – middle cerebral artery.*

flow after the X-ray surgical intervention was assessed using the mTICI (modified Treatment In Cerebral Ischemia) scale. Effective restoration of cerebral blood flow was considered to be mTICI 2b–3. In 25 patients, stent implantation was performed after the intracranial blood flow was restored (Fig. 1), and in 4 patients, before performing mechanical thrombectomy from the intracranial arteries (Fig. 2).

Before stent implantation, the patients were injected with glycoprotein receptor blockers (GPRB) (GPRB administration protocol approved by the decision of the medical commission, Protocol 134 of 12 November 2018). The bolus and infusion doses were calculated based on the patient's body weight and amounted to half the manufacturer-recommended dose. Infusion with GPRB was continued for 4 hours. After the intervention was completed, the patients were transferred to the intensive care ward of the neurology department and administered a loading dose of aspirin (300 mg). In the postoperative period, all patients received comprehensive therapy according to the up-to-date recommendations on patient management for acute ischemic stroke [3]. Twelve hours later, a control cerebral computed tomography was performed. In the absence of hemorrhagic transformation, clopidogrel (75 mg) was administered. From then on, dual disaggregation therapy was administered (aspirin 100 mg, clopidogrel 75 mg). If there were any signs of type 2 hemorrhagic transformation, only aspirin was administered, which was discontinued if type 1 or 2 parenchymal hematoma was detected.

RESULTS

Successful restoration of cerebral blood flow (according to the mTICI 2b–3 scale) was achieved in 22 (75.9 %) patients. The incidence of distal embolism in the previously occluded vascular system was 31 %, and 17.2 % (5 patients) – in the previously unaffected vascular system. Four (13.8 %) patients had stent thrombosis in the early postoperative period (48 hours). The incidence of hemorrhagic transformations 37.9 % (11 patients), of which symptomatic hemorrhagic transformation was observed only in 2 (6.9 %) patients, while 1 (3.4 %) patient developed a malignant cerebral edema. The frequency of a favorable functional outcome (modified Rankine 0–2) on the 30th day was 20.7 %, mortality – 24.1 %. The results of endovascular surgical interventions are presented in Table 2.

DISCUSSION

Mechanical thrombectomy performed within the 24-hour therapeutic window is becoming standard treatment for patients with acute ischemic stroke, which occurred because of large cerebral artery occlusion [3]. Data are controversial on the efficacy of endovascular interventions in patients with carotid tandem steno-occlusive lesion, therefore the present-day recommendations list their proven level of efficacy as 2B. The problem yet to be solved is choosing the treatment method for extracranial occlusion. Performing isolated thrombectomy is rarely sufficient to ensure patency of the ICA, since occlusion occurs at the site of a complicated atherosclerotic plaque in a vast majority of the cases, and it requires balloon angioplasty and/or stenting to restore patency of the ICA [1]. A number of authors have demonstrated ICA stenting to be an independent predictor for restoring cerebral blood flow successfully and improving the functional outcome in this patient population [4, 5]. The results of TITAN, a major trial comprising 482 patients, have shown a reliable advantage of extracranial ICA stenting in terms of both frequency of successful restoration of cerebral blood flow and functional outcome [6]. Our clinic has been using stent implantation in the most acute phase of ischemic stroke in the presence of carotid tandem steno-occlusive lesion.

The phasing of restoration of cerebral blood flow in cases of tandem lesions in the carotid system is still debated. Retrograde access presumes that initial thrombectomy is performed from the intracranial system, while antegrade access assumes that extracranial blood flow is restored with subsequent thrombectomy performed from the intracranial arteries. Each method has its advantages and disadvantages. Initial thrombectomy from the intracranial system allows for a faster restoration of the intracranial blood flow because of the presence of anastomoses in the cerebral arterial circle

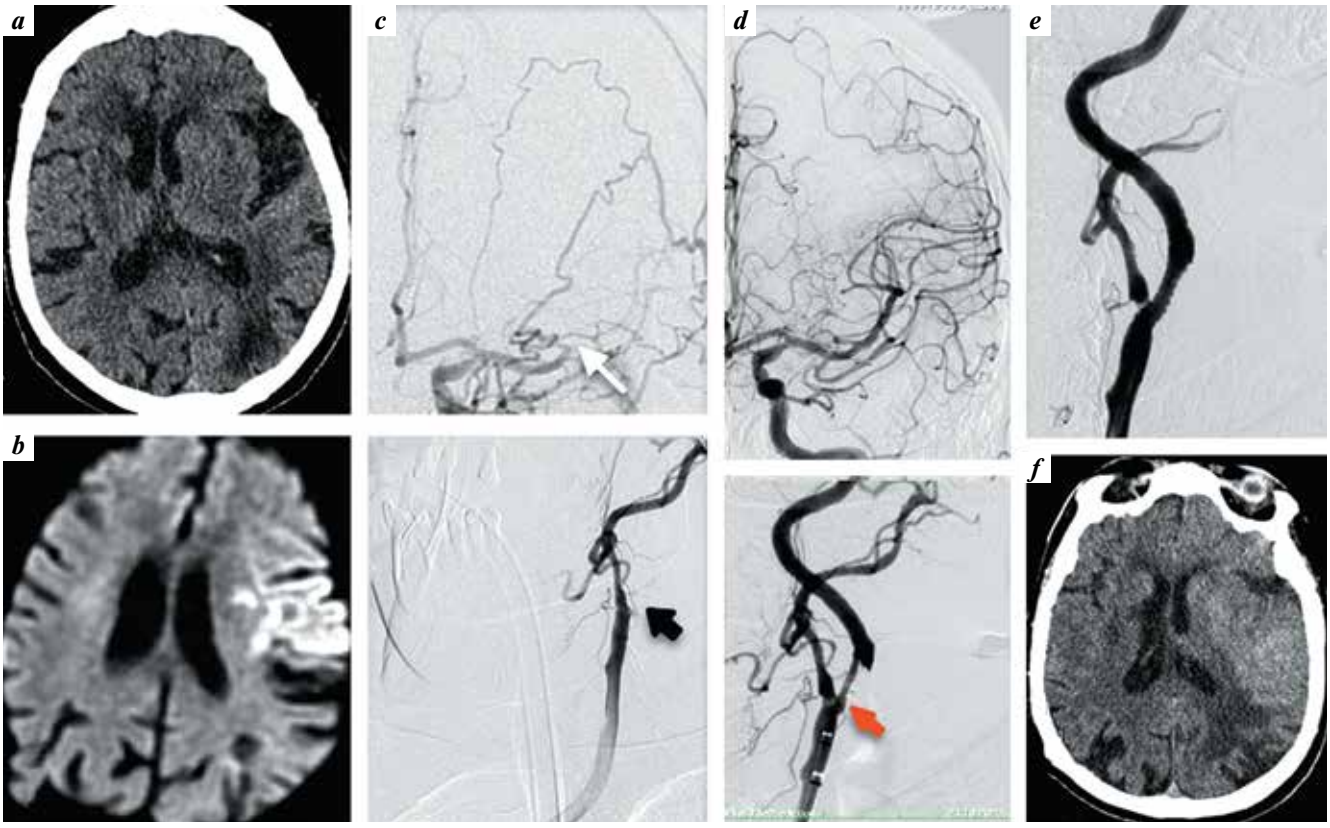

Fig. 1. *Data from computed tomography (CT), magnetic resonance imaging (MRI) and cerebral digital subtraction angiography of an 83-year-old patient hospitalized with an acute ischemic stroke symptoms in 320 minutes after the onset of the disease: a – CT scan at admission; b – MRI (DWI mode) at admission: hyperdense zone in the left temporal lobe; c – left carotid cerebral angiography at admission: occlusion of the extracranial internal carotid artery (ICA) (dark arrow), contrasting of the supraclinoid segment of the ICA due to extra-intracranial collaterals, and occlusion of the distal middle cerebral artery (MCA) (white arrow); d – left carotid cerebral angiography after ICA balloon angioplasty and MCA thrombectomy using a stent retriever. The blood flow through the intracranial arteries restored (mTICI –3). Residual stenosis of the extracranial ICA up to 85 % (red arrow); e – cerebral angiography of the ICA after stenting; f – CT scan of the patient in 12 hours after surgery: without signs of hemorrhagic transformation*

system, but retains the potential risk of recurrent embolism when extracranial revascularization is performed. The disadvantage of initially performing antegrade access is the absence of antegrade blood flow, increasing the risk of repeat thrombosis. In the observations presented, we preferred antegrade access in most patients, performing ICA stenting after the intracranial blood flow was restored successfully.

The antiaggregant and anticoagulant therapy regimen under stent implantation during the acute phase of ischemic stroke is still debated [7]. In this patient population, administration of heparin after carotid artery stenting is not pharmacologically justified; besides, the previously published works demonstrate a reliable increase in the incidence of symptomatic hemorrhagic transformations when heparin was used at >3,000 IU [8]. The scope of using oral P2Y12 receptor blockers in the most acute phase of ischemic stroke is limited by the time of achieving therapeutic concentration for an effective suppression of platelet aggregation. On the other hand, when this medication group is used and hemorrhagic complications develop, the aggregation capacity of platelets is extremely hard to restore, increasing the risk of severe complications. Thus, GPRB are becoming the medications of choice for patients with acute ischemic stroke when stent implantation is necessary [9, 10]. The advantage here is the swift suppression of the aggregation capacity of platelets. According to S.R. Steinhubl et al., ten minutes of intravenous infusion of eptifibatide or tirofiban lead to the aggregation activity of platelets being suppressed in 99 and 95 % patients respectively, which allows for an immediate stent implantation with a minimum risk of its thrombosis. Because of their low molecular mass, these medications have a weak bond with platelet receptors, thus 50 % of platelets restore their aggregation capacity in as early as two hours after the infusion is discontinued [11].

A. Jost et al. examined the experience of administering low doses of eptifibatide to treat 58 patients in the acute phase of stroke with occlusive lesion in the carotid system. The authors demonstrated that cerebral blood flow was successfully restored in 96 % of the patients, a favorable functional outcome in 72 %, and the incidence of developing symptomatic hemorrhagic transformations was 2 % [12]. In our work, we used GPRB (eptifibatide, tirofiban) at half the manufacturer-recommended dose. Successful restoration of cerebral blood flow was achieved in 75.9 %

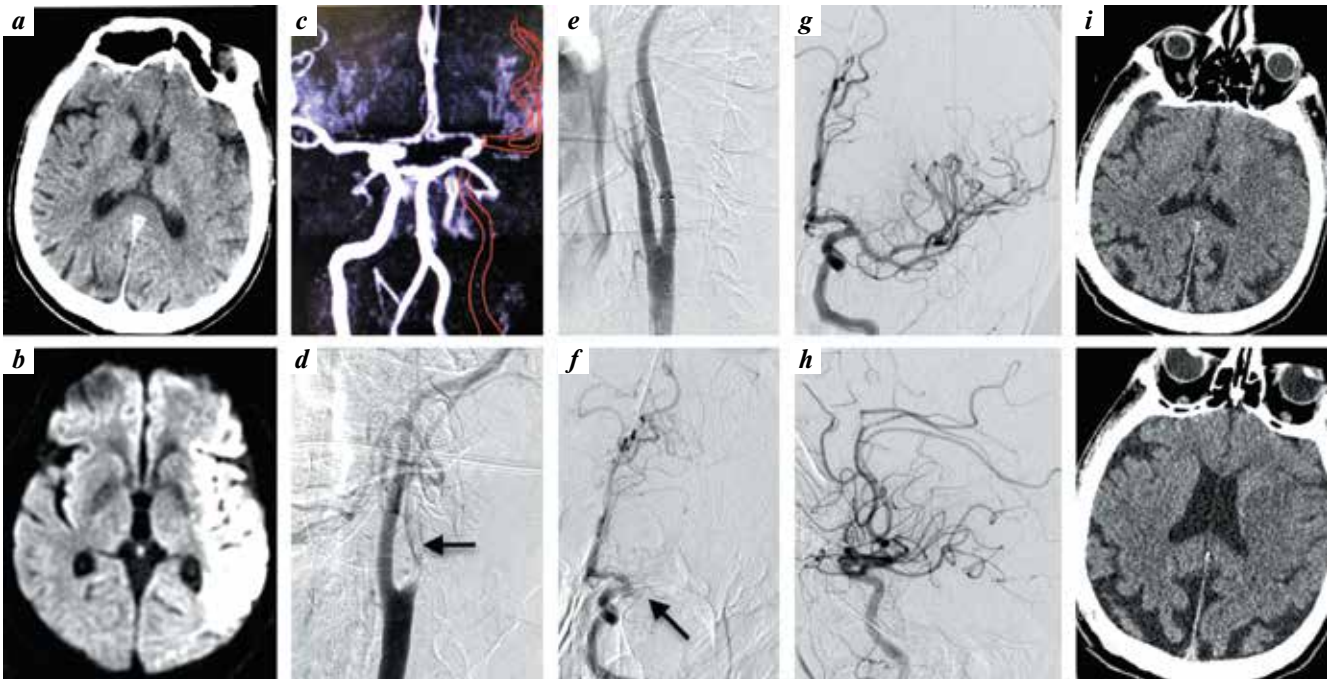

Fig. 2. *Data from computed tomography (CT), magnetic resonance imaging (MRI) and cerebral digital subtraction angiography of a 53-year-old patient hospitalized with an acute ischemic stroke symptoms in 65 minutes after the onset of the disease: a – CT scan at admission; b – MRI (DWI mode) on admission: extensive hypergingival zone in the left temporal lobe; c – MRI (2D TOF mode): occlusion of the internal carotid artery (ICA) and proximal middle cerebral artery (MCA) (shown by red lines); d – cerebral angiography of the extracranial part of the left ICA, occlusion of the left ICA with signs of a filling defect (thrombus); e – cerebral angiography after stent implantation, restoration of blood flow in the extracranial ICA; f – cerebral angiography of the intracranial basin on the left, occlusion of the proximal MCA; g, h – cerebral angiography of the left carotid basin after MCA aspiration with complete restoration of blood flow (mTICI – 3), frontal and lateral views; i – CT scan of the patient after 12 hours: without signs of hemorrhagic transformations*

Table 2. *Outcomes of using endovascular surgical interventions*

Result of intervention	Number of patients, *n* (%)
Effective restoration of cerebral blood flow (mTICI 2b–3)	22 (75.9)
Embolism in the previously occluded vascular system	9 (31.0)
Embolism in the previously unaffected vascular system	5 (17.2)
Stent thrombosis in the first 2 days	4 (13.8)
Hemorrhagic transformation	11 (37.9)
Asymptomatic hemorrhagic transformation	9 (31.0)
Symptomatic hemorrhagic transformation	2 (6.9)
Symptomatic cerebral edema	1 (3.4)
Favorable functional outcome on day 30 (mRs – 0–2)	6 (20.7)
Unfavorable functional outcome on day 30 (mRs – 3–5)	16 (55.2)
Death	7 (24.1)

Note. *mTICI – modified Treatment In Cerebral Ischemia; mRs – modified Rankin Scale.*

patients. The frequency of symptomatic hemorrhagic transformations was low, 6.9 %.

Early works mentioned that disaggregates increased the risk of symptomatic hemorrhagic transformations to 20 %. More recent research demonstrates that the frequency of their development in this patient population is not increased [6, 12]. According to the protocol in our clinic, dual disaggregate therapy was only prescribed after a control computed tomography was performed in 12 hours, and disaggregates were discontinued if there were signs of pronounced hemorrhagic transformation.

According to various authors, the incidence of stent thrombosis implanted during the acute phase of ischemic stroke varies between 1.3 and 17 %, reaching 52 % in certain observations [13, 14]. As reported by A. Jost et al., when GPRB was administered, stent thrombosis was observed in 7 % of the patients over the first 48 hours [12]. In our series of observations, stent thrombosis over the first 48 hours was observed in 4 (13.8 %) patients. In 2 patients, thrombosis could be explained by the onset of vomiting after taking a saturation dose of aspirin, which may well have been why aspirin had no therapeutic effect. In the series of observations presented, the infusion of GPRB never lasted over 4 hours, which could have led to the increase in the incidence of stent thrombosis in the early period. Further research is necessary to assess a safe and effective duration of GPRB administration.

When performing mechanical thrombectomy, distal embolism is an ominous complication that substantially decreases the clinical efficacy of the surgical intervention or renders it useless at all. Our works published earlier demonstrated that blocking the cerebral blood flow by means of an occlusive guiding catheter reliably decreases the risk of this complication [15]. The series of observations presented features the incidence of distal embolism in the previously affected vascular system at 31 %, and 17.2 % in the previously unaffected one. We routinely made use of large-diameter (9F) occlusive guiding catheters in order to ensure the guiding of instruments through its lumen.

CONCLUSION

Stenting of the extracranial ICA in tandem steno-occlusive lesions in patients with acute ischemic stroke helps improve the efficiency of restoration of cerebral blood flow. The use of low doses of GPRB prevents stent thrombosis in the early period after implantation and does not increase the incidence of symptomatic hemorrhagic complications.

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Authors contribution
M.Y. Volodukhin: data collection and analysis, article writing;
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D.R. Khasanova: research design development;
R.N. Khairullin: interpretation of data, final approval of the article.

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