Research Article
https://doi.org/10.23934/2223-9022-2021-10-3-484-492

Thrombectomy in patients with basilar artery thrombosis

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INTRODUCTION This article is devoted to the discussion of a life-threatening condition - basilar artery thrombosis (BAT). The article presents the results of a comparative analysis of two groups of patients with angiographically confirmed BAT: with and without reperfusion therapy.

RELEVANCE Basilar artery thrombosis is a life-threatening condition in which mortality can reach 95%, and severe neurological deficits and dependence in everyday life on others (modified Ran-kin Scale (mRS), score 4–5) are observed in 65% of surviving patients. Ischemic stroke (IS) due to BAT is diagnosed in 1–4% of patients with acute cerebrovascular event (ACVE). Currently, reperfusion therapy (RT) in the form of systemic thrombolytic therapy (sTLT) with rt-PA and/or thrombectomy (TE) is the only effective and safe method for treating patients with IS. In randomized trials, it was found that RT, whether it is sTLT, TE or a combination of these techniques, despite the best degree of functional recovery in patients by day 90 from the onset of the disease, does not lead to a statistically significant decrease in mortality. Nevertheless, the results of 10 prospective studies of the use of endovascular treatment in patients with IS in the posterior circulation system indicate that this type of therapy leads to a decrease in 90-day mortality from 95% to 16–47% in case of successful recanalization (mTICI (modified Thrombolysis in Cerebral Infarction), 2–b–3).

AIM OF STUDY To assess the safety and efficacy of TE in patients with BAT.

MATERIAL AND METHODS This study included 15 patients with IS, admitted within the 6-hour therapeutic window, and confirmed BAT by CT and/or MR-angiography. The baseline level of wakefulness was assessed using the Glasgow Coma Scale (GCS), and the severity of neurological deficit was assessed by the National Institutes of Health Stroke Scale (NIHSS).

RESULTS Basilar artery thrombectomy was performed in 7 patients (endovascular treatment group), 8 patients received no endovascular treatment (standard therapy group). Good clinical outcomes by day 90 from the onset of the disease (mRS, score 0–2) were observed in 57.1% of patients in the endovascular treatment group and in 12.5% of patients in the standard therapy group. However, these differences were not statistically significant ($p>0.05$). There were also no differences between the two groups in functional outcomes and Rivermead mobility index (RMI) by day 90 from the onset of the disease (Barthel Index of Activities of Daily Living (BI) score 97±5.0 and 100, RMI score 14.0±0.0 and 15 in the endovascular treatment group and standard therapy group, respectively). Mortality by day 90 in the endovascular treatment group was 42.9% (3 patients), in the standard therapy group — 87.5% (7 patients). In the subgroup of patients with GCS score at admission no more than score 8, there was a statistically significant strong two-way negative correlation between TE performance and mortality ($r=-1.0$; $p=0.000$), as well as a positive correlation between TE and a Rankine score by day 90 ($r=0.956$; $p=0.003$). Mortality was statistically significantly lower in the endovascular treatment group compared to the standard therapy group (0% versus 100%, respectively, $p=0.025$). Clinical outcomes of the disease by day 90 were statistically significantly better in the endovascular treatment group: mRS, score 0–2 in 100% of cases versus 0% in the standard treatment group ($p=0.028$).

CONCLUSION Currently, the only effective treatment for basilar artery thrombosis is thrombectomy. The possibility of performing thromboectomy in these cases should be considered in all patients, regardless of the severity of the stroke and the decrease in the level of wakefulness, since endovascular treatment in this case is a life-saving procedure. The symptom of a hyperdense basilar artery can be used as a diagnostic tool for suspected basilar artery thrombosis, but should not rule out angiography. In our series of observations, the mortality rate in patients who underwent thrombectomy was 42.9%. Good functional outcomes (mRS, score 0–2) and the absence mobility limitation (RMI, score 14) were observed in 57.1% of patients by day 90 after thrombectomy.

Keywords: systemic inflammatory response syndrome (SIRS), xenon, neutrophils

For citation Ramazanov GR, Kovaleva EA, Klychnikova EV, Kokov LS, Korigova KhV, Muslimov RSh, et al. Thrombectomy in patients with basilar artery thrombosis. *Russian Sklifosovsky Journal of Emergency Medical Care*. 2021;10(3):484–492. https://doi.org/10.23934/2223-9022-2021-10-3-484-492 (in Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study has no sponsorship

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BA – basilar artery
HT – hemorrhagic transformation
ALV – artificial ventilation of the lungs
IS – ischemic stroke
CT – computed tomography
MR angiography – magnetic resonance angiography
ACVA – acute cerebrovascular accident
RT – reperfusion therapy
sTLT – systemic thrombolytic therapy
BAT – basilar artery thrombosis
TE – thrombectomy
PE – pulmonary embolism
GCS – Glasgow Coma Scale
BI – Bartel's Daily Life Activity Index
ESUS – unidentified embolic stroke
mRS – modified Rankin scale
mTICI – modified scale of perfusion recovery in ischemic stroke
NIHSS – National Institutes of Health Stroke Scale
RMI – Rivermead mobility index
rt-PA – recombinant tissue plasminogen activator
TOAST – risk factors and mechanisms of stroke development in young people

INTRODUCTION

Basilar artery thrombosis (BAT) is a life-threatening condition in which mortality can reach 95% [1], and gross neurological deficit and dependence on others in everyday life (*modified Rankin Scale (mRS)*, 4–5 points) is observing in 65% of surviving patients [2]. Ischemic stroke (IS) due to BAT is diagnosed in 1–4% of patients with acute cerebrovascular accident (ACVI) [3]. Currently, reperfusion therapy (RT) in the form of systemic thrombolytic therapy (sTLT) with a recombinant tissue plasminogen activator (*rt-PA*) and / or thrombectomy (TE) is the only effective and safe method for treating patients with IS [4–12]. In randomized trials, it was found that RT, whether it is with sTLT, TE or a combination of these techniques, despite the best degree of functional recovery in patients by day 90 from the onset of the disease, does not lead to a statistically significant decrease in mortality. Moreover, the protocols of 6 studies on the use of endovascular treatment for IS did not envisage the inclusion of patients with IS due to BAT [6–11]. Only in the *THRACE* study (2016), the protocol allowed the inclusion of patients with BAT, however, the number of similar patients who underwent TE in this study did not exceed 1% (2 patients) [12]. The current recommendations for the diagnosis and treatment of patients with IS unambiguously regulate the implementation of TE only in patients with thrombosis of the internal carotid artery and / or M1 segment of the middle cerebral artery, and the advantages of performing TE in patients with thrombosis of other localization are not clear [13]. Nevertheless, the results of 10 prospective studies of the use of endovascular treatment in patients with IS in the posterior pool indicate that this type of therapy, provided that if successful recanalization is achieved (*mTICI (modified Thrombolysis in Cerebral Infarction)*, 2–*b*–3) leads to a decrease in 90-day mortality from 95% to 16-47% [14–23].

The aim of this study was to assess the safety and efficacy of TE in patients with BAT.

MATERIAL AND METHODS

This study included 15 patients with IS, admitted within the 6-hour therapeutic window, and confirmed by CT and / or MR-angiography TBA. The baseline level of wakefulness was assessed using the Glasgow Coma Scale (GCS), the severity of neurological deficit was assessed by the *National Institutes of Health Stroke Scale (NIHSS)*.

Therapy. The study compared two groups of patients: one (n = 7) underwent TE in the first 6 hours after the onset of the disease, the other (n = 8) – patients who were undergone to hospital care before introducing the TE technique, and therefore endovascular treatment did not carry out.

Main evaluation criteria. Primary endpoints were mortality, *NIHSS* severity of neurological deficit, Bartel's index (*BI*), *mRS*, and Rivermead mobility index (*RMI*) by day 90 of illness.

Clinical observation methods. All patients underwent computed tomography (CT) of the brain and CT / MR angiography of the extra- and intracranial arteries. The pathogenetic variants of IS were established in accordance with the *TOAST* criteria [24]. Cryptogenic IS was diagnosed based on eligibility *ESUS* criteria (unidentified embolic stroke) [25].

Subgroup analysis. 2 subgroup analyzes were planned, according to which stratification was carried out according to the baseline level of wakefulness according to the GCS (no more than 14 versus more than 14 points and no more than 8 versus more than 8 points).

Statistical analysis. We used the Mann – Whitney test for independent samples, which shows the likelihood that a patient randomly selected from the treatment group is better than a randomly selected patient from the reference group. Correlation was assessed using Pearson's method. The differences were considered statistically significant when $p<0,05$.

RESULTS

From January 2015 to November 2020 at the N.V. Sklifosovsky Research Institute for Emergency Medicine, 15 cases of acute cerebrovascular accident due to BAT were registered. BA thrombectomy was performed in 7 patients (endovascular treatment group), 8 patients did not receive endovascular treatment (standard therapy group). There were no significant differences between the groups in terms of demographic and clinical indicators (Table 1). All patients, in addition to TE in the endovascular treatment group, received standard ACVA therapy.

Table 1

Patient demographic and clinical characteristics

Indicator	Patient groups		Statistical significance of differences, *p*
	Endovascular treatment, *n*=7	Standard therapy, *n*=8	
Average age, years	66,14±9,84	50,38±22,07	>0,05
Gender, n (%): – male – female	 6 (85,7) 1 (14,3)	 6 (75,0) 2 (25,0)	>0,05
History of ACVA, *n* (%)	0	1 (12,5)	>0,05
History of myocardial infarction, *n* (%)	1 (14,3)	0	>0,05
Atrial fibrillation, *n* (%)	3 (42,9)	2 (25)	>0,05
Arterial hypertension, *n* (%)	7 (100)	5 (62,5)	>0,05
Diabetes, *n* (%)	0	1 (12,5)	>0,05
Obesity, *n* (%)	0	1 (12,5)	>0,05
Length of hospital stay, days	19,14+17,64	9,46+9,13	>0,05
GCS at admission, score	11,43+4,12	8,75+4,83	>0,05
NIHSS at admission, score	20,86+10,84 (*min* 9, *max* 34)	25,25+12,9 (*min* 1, *max* 34)	>0,05
Pathogenetic variant of ischemic stroke according to the criteria *TOAST*, *n* (%): – cardioembolic – unknown etiology	 3 (42,9) 4 (57,1)	 2 (25) 6 (75)	>0,05
Intrahospital stroke, *n* (%)	1 (14,3)	2 (25)	>0,05

Notes: ACVA – acute cerebrovascular accident; GCS – Glasgow Coma Scale; NIHSS – National Institutes of Health Stroke Scale; TOAST – risk factors and mechanisms of stroke development in young people

The average GCS score in the endovascular treatment group was 11 ± 4, in the standard therapy group - 9 ± 5 (p> 0.05). A decrease in the level of wakefulness at the onset of the disease was noted in 4 patients (66.7%) of the endovascular treatment group (in 2 patients - moderate coma (GCS, 6 points), in one patient - stupor (GCS, 10 points), in one patient - moderate stunning (GCS, 13 points)) and 7 patients (87.5%) in the standard therapy group: 3 patients had a deep coma (GCS, 3-5 points), 1 had a moderate coma (GCS, 6 points), one - stupor (GCS, 10 points), one has moderate stunning (GCS, 13 points).

The average *NIHSS* score in the endovascular treatment group was 21 ± 11 (min 9, max 34), in the standard therapy group - 25 ± 13 points (min 1, max 34). In patients of the endovascular treatment group on day 90, the average *NIHSS* score was 3 ± 2 points. In the surviving patient of the standard therapy group, by the 90th day, the neurological deficit completely regressed (*NIHSS* 0 points).

Good clinical outcomes by day 90 from the onset of the disease (*mRS*, 0–2 points) were observed in 57.1% of patients in the endovascular treatment group and in 12.5% of patients in the standard therapy group. However, these differences were not statistically significant. (p>0.05). Also, there were no statistically significant differences between the two groups in functional outcomes and *RMI* by day 90 from the onset of the disease (*BI* 97 ± 5.0 points and 100 points, *RMI* 14.0 ± 0.0 points and 15 points in the endovascular treatment and standard therapy group, respectively).

Systemic thrombolytic therapy with *rt-PA* at a dose of 0.9 mg / kg was performed in 2 patients (28.6%) in the endovascular treatment group. The average time to onset of sLT from the onset of the disease was 100 ± 40 minutes. The rest of the patients were contraindicated for sTLT. The reasons for not performing sTLT in patients of the endovascular treatment and standard therapy groups are given in Table. 2. In 2 patients (28.6%) of the endovascular treatment group, there were more than 1 contraindications for sTLT.

Table 2

Contraindications to systemic thrombolytic therapy

Indicator	Patient groups		Statistical significance of differences, p
	Endovascular treatment, n=7	Standard therapy, n=8	
More than 4.5 hours from the onset of the disease, *n* (%)	2 (28,6)	4 (50)	>0,05
NIHSS more than 25, *n* (%)	3 (14,3)	2 (25)	>0,05
Major surgery within the previous 10 days, *n* (%)	1 (14,3)	2 (25)	>0,05
Convulsions at the beginning of a stroke	1 (14,3)	0	>0,05

The TE procedure was performed in all cases under total multicomponent anesthesia. At control angiography, BA was passable in 6 patients (85.7%), the degree of recanalization (*mTICI*, 2b – 3), and the mean time from the onset of the disease to recanalization was 274 ± 112 minutes (*min* 125 min, *max* 380 min). In one case (14.3%) TE was unsuccessful - it was not possible to achieve recanalization (*mTICI*, 0). On the 2nd day after successful recanalization (*mTICI*, 3), one patient developed a clinical picture of BA retrombosis, confirmed by the results of transcranial Doppler scanning - blood flow was not located in BA, reverberating blood flow through the vertebral arteries, and there were no signs of collateralization of blood flow through the posterior communicating arteries.

At control CT of the brain (24 hours after TE), asymptomatic hemorrhagic transformation (HT) in the form of minimal saturation of the ischemic focus, not accompanied by an increase in neurological deficit, was detected in two patients (28.6%) who did not undergo sTLT. None of the cases of symptomatic HT was noted.

Mortality by day 90 in the endovascular treatment group was 42.9% (3 patients), in the standard therapy group - 87.5% (7 patients) (Table 3).

Table 3

Clinical indicators of the examined patients

Indicator ь	Patient groups		Statistical significance of differences, *p*
	Endovascular treatment, *n*=7	Standard therapy, *n*=8	
GCS no more than 14 points, *n* (%)	4 (57,1)	7 (87,5)	>0,05
ALV, *n* (%)	5 (71,4)	7 (87,5)	>0,05
Duration of mechanical ventilation, days	5,8 + 4,03	8,94 + 7,57	>0,05
Performing sTLT, *n* (%)	2 (28,6)	0	>0,05
Complete recanalization *mTICI*, 2*b*–3, *n* (%)	6 (85,7)	–	–
HT of the focus of ischemia, *n* (%)	2 (28,6)	0	>0,05
Symptomatic HT, *n* (%)	0	0	>0,05
BA retrombosis, *n* (%)	1 (14,3)	–	–
Complete independence (*mRS*, 0-1 point) by day 90, *n* (%)	3 (42,9)	1 (12,5)	>0,05
Mortality by the 7th day, *n* (%)	2 (28,6)	5 (62,5)	>0,05
Mortality by day 90, *n* (%)	3 (42,9)	7 (87,5)	>0,05

Notes: BA — basilar artery; HT — hemorrhagic transformation; ALV — artificial lung ventilation; sTLT — systemic thrombolytic therapy; GCS — Glasgow Coma Scale; mRS — modified Rankine scale; mTICI — modified treatment in cerebral ischemia score

Non-cerebral complications of stroke detected during hospitalization despite ongoing prophylaxis are presented in Table. 4. There were no statistically significant differences between the groups in the incidence of non-cerebral IS complications such as pneumonia, deep vein thrombosis (DVT), fatal pulmonary embolism (PE) and pressure ulcers.

Table 4

Non-cerebral complications of acute cerebrovascular event

Complication	Patient groups		Statistical significance of differences, *p*
	Endovascular treatment, *n*=7	Standard therapy, *n*=8	
Pneumonia, *n* (%)	3 (42,9)	3 (37,5)	>0,05
Deep vein thrombosis, *n* (%)	3 (42,9)	1 (12,5)	>0,05
Pulmonary embolism, *n* (%)	0	1 (12,5)	>0,05
Pressure ulcers	0	0	>0,05

Subgroup analysis. For a more detailed analysis, stratification was performed according to the decrease in the level of wakefulness - the GCS score on admission. In the subgroup of patients with GCS score at admission no more than 14 points, a statistically significant strong two-sided negative correlation was found between TE performance and mortality (r = -0.81; p = 0.003), as well as a positive correlation between TE and the Rankine score to 90 days (*r*=0,788; *p*=0,004). Mortality was statistically significantly lower in the endovascular treatment group than in the standard therapy group (25% versus 100%, respectively, *p* = 0.01). Clinical outcomes of the disease by day 90 were statistically significantly better in the endovascular treatment group: *mRS*, 0–2 points in 75% of cases versus 0% in the standard treatment group (*p* = 0.012).

In the subgroup of patients with GCS score at admission no more than 8 points, a statistically significant strong two-sided negative correlation was found between the performance of TE and mortality (r = -1.0; *p* = 0.000), as well as a positive correlation between TE and the Rankine score to day 90 (r = 0.956; *p* = 0.003).

Mortality was statistically significantly lower in the endovascular treatment group compared to the standard therapy group (0% versus 100%, respectively, p = 0.025). Clinical outcomes of the disease by day 90 were statistically significantly better in the endovascular treatment group: *mRS*, 0–2 points 100% versus 0% in the standard treatment group (p = 0.028).

DISCUSSION

Since the mortality in BAT reaches 95%, TE can be a life-saving procedure [1, 14–23]. Our series of observations included 15 cases of stroke in patients with angiographically confirmed BAT. Overall mortality in patients who underwent TE was 42.9% (3 patients out of 7), 7-day mortality was 28.6% (2 patients out of 7), and 90-day mortality was 42.9%, while as in the group of patients without TE, overall mortality was 87.5% (7 patients out of 8), 7-day mortality was 62.5% (5 patients out of 8), and 90-day mortality was 87.5% (p>0.05). In the group of endovascular treatment, in one deceased patient, TE was unsuccessful - recanalization was not achieved, in the second patient, after complete recanalization (*mTICI*, 3), BA rethrombosis developed on the 2nd day, in the third patient with severe concomitant pathology (3 myocardial infarctions in anamnesis). on the background of atherosclerosis of the coronary arteries) on the 3rd day after successful TE, acute repeated myocardial infarction developed, which was the direct cause of death. According to *S.H. Baik et al.* (2019) and *O.C. Singer et al*. (2015), 90-day mortality in endovascular treatment in patients with BAT was 21% and 35%, respectively [14, 15]. There are currently no data on the incidence of BA rethrombosis after TE.

Of the 15 patients, 5 (33.3%) had cardioembolic IS, and in 10 patients (66.7%) it was not possible to establish the pathogenetic variant of IS - the diagnosis was "Cryptogenic ischemic stroke". According to *D.H. Kang et al*. (2018), 47.6% of patients with BAT were diagnosed with cardioembolic IS, 38.7% with atherothrombotic IS, 11.8% failed to establish the pathogenetic variant of stroke, and 1.9% of patients had another cause of stroke [20]. No correlation was found between the pathogenetic variant of IS and the effectiveness of TE in our study.

Successful recanalization (*mTICI*, 2b–3) in TE was achieved in 6 patients (85.7%), the mean time from the onset of the disease to recanalization was 273.5±111.84 minutes (min 125 min, max 380 min), which corresponds to data from 10 large studies [14–23]. It should be noted that the patient, whose time from the onset of the disease to recanalization (*mTICI*, 3) was 380 min (the maximum time in our series of observations), survived, and by the 90th day, the mRS score was 2, which once again indicates that TE in BAT is a life-saving procedure.

A decrease in the level of wakefulness at the onset of the disease was observed in 4 patients (66.7%) of the endovascular treatment group and 7 patients (87.5%) of the standard therapy group, which corresponds to the literature data [26–31]. Of the 4 patients in the endovascular treatment group who were admitted with reduced levels of wakefulness, three survived. Restoration of BA patency (*mTICI*, 2b-3) in patients of the endovascular treatment group was associated with the restoration of wakefulness to clear consciousness in 100% of cases. The death in one patient after TE, who presented with a decrease in the level of wakefulness to deep stunning (*GCS*, 13 points), was associated with an unsuccessful attempt at recanalization. According to *S.H. Baik et al.* (2019), with BAT, recanalization cannot be achieved in 22% of patients [14].

The mean *NIHSS* score at the onset of the disease in the endovascular treatment group was 20.86±10.84 (min 9, max 34 min), in the standard therapy group it was 25.25±12.9 (min 1, max 34). 24 hours after TE, 4 patients (57.1%) showed a significant clinical improvement in the form of a decrease in the *NIHSS* score by 4 or more, which corresponded to successful recanalization. Good clinical outcomes of the disease (mRS, 0–2 points) by the 90th day of the disease were observed in 57.1% of patients after TE. The Rivermead mobility index at discharge from the hospital in the endovascular treatment group corresponded to 14 points, and BI by day 90 corresponded to complete independence in everyday life from others (from 90 to 100 points).

One of the main problems of reperfusion therapy is the development of symptomatic HT. The incidence of HT in our series of observations was 28.6% (2 patients). It should be noted that both cases of HT were asymptomatic, and BI in these patients by the 90th day corresponded to complete independence in daily life from others. *D.H. Kang* (2018) and *S.H. Baik et al.* (2019) found that symptomatic HT after TE was 1.9% and 6%, respectively [14, 20]. The incidence of asymptomatic hemorrhagic transformation does not exceed 24% [20]. However, there are currently no data on the incidence of HT after TE in BAT.

Native CT of the brain in 12 patients (80%) revealed an indirect sign of BAT — a symptom of hyperdense BA, which, according to *P.M. Heinrich et al.* (2011) are found in 65% of patients with BAT [32]. According to M. *Ernst et al.* (2015), the X-ray density of BA over 46.5 HU has 94% sensitivity and 81% specificity in relation to the detection of SBA [33]. In our study, no relationship was established between the presence of this symptom and the effectiveness of TE.

The present study did not reveal statistically significant differences between the groups in terms of the main assessed indicators. Subgroup analysis showed that in patients with a decrease in the level of wakefulness (*GCS*, no more than 14 points), TE from BA is accompanied by a statistically significant improvement in clinical outcomes and a decrease in mortality compared with that in the standard therapy group (*mRS*, 0-2 points to 90- m days in 75% of cases vs 0%, p=0.012; lethality 25% vs 100%, p=0.01, respectively). In patients with a decrease in the level of wakefulness at the onset of the disease to coma (GCS, no more than 8 points), TE from BA also leads to an improvement in clinical outcomes and a decrease in mortality compared with its value in the standard therapy group (*mRS*, 0–2 points to 90th day in 100% of cases vs. 0%, p=0.028; lethality 0% vs. 100%, p=0.025, respectively). Thus, it has been shown that TE in patients with SBA is a life-saving procedure and should be performed even in patients with a decrease in the level of wakefulness at the onset of the disease.

CONCLUSIONS

1. Currently, the only effective treatment for BAT is thrombectomy. The possibility of performing thrombectomy for thrombosis of the basilar artery should be considered in all patients, regardless of the severity of stroke and a decrease in the level of wakefulness, since endovascular treatment in this case is a life-saving procedure.

2. The symptom of a hyperdense basilar artery can be used as a diagnostic tool for suspected basilar artery thrombosis, but should not rule out angiography.

3. In our series of observations, mortality in patients who underwent thrombectomy was 42.9%.

4. Good functional outcomes (*mRS*, 0–2 points) and the absence of limitation of mobility (*RMI* 14 points) by day 90 after thrombectomy were observed in 57.1% of patients.

5. All patients with good clinical outcomes achieved complete recanalization (*mTICI*, 3).

6. The incidence of symptomatic hemorrhagic transformation was 0%, and that of asymptomatic hemorrhagic transformation - 28.6%.

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Received on 24.02.2021

Review completed on 14.05.2021

Accepted on 29.06.2021