Research Article
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Thrombotic Occlusion in Patients with Acute Ischemic Stroke

E.A. Kovaleva*✉, *G.R. Ramazanov, L.S. Kokov, R.Sh. Muslimov, M.V. Parkhomenko, V.N. Stepanov, E.M. Bardina, K.R. Pushkareva, M.S. Solovtsova, A.O. Sherstyanikh, A.M. Izmailova

Neurological Department for Patients with Acute Cerebrovascular Accidents
N.V. Sklifosovsky Research Institute for Emergency Medicine of the Moscow Health Department
3, B. Sukharevskaya Sq., Moscow 129090, Russian Federation

✉ **Contacts:** Ella A. Kovaleva, Candidate of Medical Sciences, Senior Lecturer of the Educational Department, Neurologist of the Neurological Department for Patients with Acute Cerebrovascular Accidents with the Resuscitation and Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine. Email: kovalevaea@sklif.mos.ru

INTRODUCTION Currently, reperfusion therapy is the main method of treating patients with ischemic stroke (IS). The safety and efficacy of systemic thrombolytic therapy with a recombinant tissue plasminogen activator in patients with IS within 3 hours, and then 4.5 hours after the onset of symptoms of the disease was demonstrated in the NINDS (1995) and ECASS III (2008) studies. In 2018, based on the results of five studies, clear indications were formulated for performing thrombectomy (TE) in patients with IS, which involve the detection of thrombosis of a large stroke-associated artery. Given the continuous growth in the number of the adult population, which constitutes the bulk of patients with IS, information on the prevalence of patients with thrombotic occlusion of cerebral arteries, who are potential candidates for TE, may be important for regional vascular centers.

AIM OF STUDY To describe IS patients admitted within the 6-hour "therapeutic window".

MATERIAL AND METHODS The study included 145 patients with cerebral IS who were admitted within the first 6 hours after the onset of symptoms of the disease. All patients underwent computed tomographic (CT) angiography in order to verify the occlusion of the cerebral artery.

RESULTS In our study, a correlation was established between the NIHSS severity of IS and the likelihood of verification of stroke-related artery thrombosis by CT angiography, but in 32.6% of patients with severe stroke (NIHSS at least score 14), no thrombotic occlusion was detected, and in 13% of patients with a clinic of mild acute cerebrovascular accident (NIHSS no more than 6), on the contrary, thrombotic occlusion was detected. Mortality in patients with verified thrombotic occlusion of the cerebral artery was higher than in patients without it (38% versus 10.5%, p<0.001). Such a significant difference in the mortality rate was due to the initially more severe stroke (NIHSS at admission 17 [10; 23] versus 5 [2; 10], p<0.001) in patients with thrombotic occlusion of a stroke-related artery, as well as a higher incidence of severe swallowing disorders (30% versus 9.5%, p <0.002), which are a risk factor for pneumonia, as well as a higher frequency of such a comorbid background as chronic kidney disease and atrial fibrillation (30% versus 13.7%, p=0.018% and 58% versus 29.5%, p=0.001, respectively).

CONCLUSION 1. Thrombosis of the cerebral stroke-associated artery was detected in 34.5% of patients with ischemic stroke who were admitted within the first 6 hours from the onset of the disease. 2. The main reason for the failure to perform thrombectomy in patients with ischemic stroke admitted within the 6-hour therapeutic window is the lack of verification of stroke-related artery thrombosis using computed tomographic angiography. Due to thrombosis at a different location (other than thrombosis of the internal carotid artery and / or M1 segment of the middle cerebral artery), 10% of patients with verified thrombosis did not meet the currently existing selection criteria for thrombectomy.

Keywords: ischemic stroke, reperfusion therapy, cerebral artery thrombosis, cryptogenic stroke

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Affiliations

Ella A. Kovaleva	Candidate of Medical Sciences, Senior Lecturer of the Educational Department, Neurologist of the Neurological Department for Patients with Acute Cerebrovascular Accidents with the Resuscitation and Intensive Care Unit, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-8490-1417, kovalevaea@sklif.mos.ru; 20%, searching and analyzing literature data, collecting and analyzing materials, working with primary documentation, interpreting and processing of research results, preparing illustrations, summarizing, writing a working version of a manuscript, editing text material
Ganipa R. Ramazanov	Candidate of Medical Sciences, Head of the Scientific Department of Emergency Neurology and Rehabilitation Treatment, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0001-6824-4114, ramazanovgr@sklif.mos.ru; 16%, searching and analyzing literature data, collecting and analyzing materials, working with primary documentation, interpreting and processing of research results, preparing illustrations, summarizing, writing a working version of a manuscript, editing text material

Leonid S. Kokov	Doctor of Medical Sciences, Member of the Russian Academy of Sciences, Professor, Head of the Scientific Department of Diagnostic Radiology, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-3167-3692, kokovls@sklif.mos.ru; 10%, interpreting and processing of research results, preparation of illustrations, generalization of results, editing of text material
Rustam Sh. Muslimov	Candidate of Medical Sciences, Leading Researcher of the Department of Diagnostic Radiology, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-5430-8524, abaevr@mail.ru; 10%, interpreting and processing of research results, preparation of illustrations, generalization of results, editing of text material
Mstislav V. Parkhomenko	Head of the Department of X-ray Surgical Methods of Diagnosis and Treatment, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0001-5408-6880, parhomenkomv@sklif.mos.ru; 10%, interpreting and processing of research results, preparation of illustrations, generalization of results, editing of text material
Valentin N. Stepanov	Head of the X-ray Computed Tomography Department, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0003-0007-8054, stepanovvn@sklif.mos.ru; 10%, interpreting and processing of research results, preparation of illustrations, generalization of results, editing of text material
Elena M. Bardina	Clinical Resident, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0001-7556-4933, bardinaelena2011@mail.ru; 5%, collection and analysis of materials, work with primary documentation
Kristina R. Pushkareva	Clinical Resident, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0001-9088-0694, kristinka.pushkareva@gmail.com; 5%, collection and analysis of materials, work with primary documentation
Margarita S. Solovtsova	Clinical Resident, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0001-7698-5385, m.solo1995@yandex.ru; 5%, collection and analysis of materials, work with primary documentation
Alina O. Sherstyanikh	Clinical Resident, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-6508-2401, alina.sher125@gmail.com; 5%, collection and analysis of materials, work with primary documentation
Aza M. Izmailova	Junior Researcher, Scientific Department of Emergency Neurology and Rehabilitation Treatment, N.V. Sklifosovsky Research Institute for Emergency Medicine; https://orcid.org/0000-0002-5979-5667, azaizmailova@yandex.ru; 4%, interpretation of research results, their processing

ALT - alanine aminotransferase
AST - aspartate aminotransferase
aPTT - activated partial thromboplastin time
BA - the basilar artery
ICA - the internal carotid artery
HT - hemorrhagic transformation
PCA – the posterior cerebral artery
MV – mechanical ventilation
IS - ischemic stroke
КТ-ангиография — компьютерная томографическая ангиография
CT- angiography - computed tomographic angiography
INR - the international normalized ratio
AIS - acute ischemic stroke
ACA – the anterior cerebral artery
MCA - the middle cerebral artery
ESR - erythrocyte sedimentation rate

sTLT - systemic thrombolytic therapy
TE - thrombectomy
PE - pulmonary embolism
AF - atrial fibrillation
CKD - chronic kidney disease
CNS - central nervous system
GCS - Glasgow Coma Scale
BI - the Barthel Index for Activities of Daily Living
DWI - Diffusion-weighted imaging
mRS — the modified Rankin Scale
NIHSS — National Institutes of Health Stroke Scale
RMI – the Rivermead mobility index
ESUS — Embolic Stroke of Undetermined Source
TOAST— classification of pathogenic subtypes of ischemic stroke

INTRODUCTION

Reperfusion therapy is currently the main method of treating patients with ischemic stroke (IS) [1]. The safety and efficacy of systemic thrombolytic therapy (sTLT) using a recombinant tissue plasminogen activator in patients with IS within 3 hours, and subsequently (4.5 hours after symptom onset) was demonstrated in the NINDS (1995) and ECASS III (2008) trials [2, 3]. In 2018, based on the results of five studies, clear indications for performing thrombectomy (TE) in patients with IS which involve the detection of thrombosis of a large stroke-related artery were formulated [4—9]. Thus, TE is currently indicated in case of detection of thrombosis of a large stroke-related artery (M1 segment of the middle cerebral artery (MCA) and / or internal carotid artery (ICA)), provided that the following conditions are met: no more than 6 hours from the symptom onset, National Institutes of Health Stroke Scale (NIHSS) score at least 6, age at least 18 years, ASPECTS score at least 6, no more than 1 point on the modified Rankin scale (mRS) before the present stroke [1]. Despite the fact that the advantages of TE for patients with thrombosis of the M2 and M3 segments of the MCA, as well as the anterior cerebral (ACA), vertebral and basilar arteries (BA) are unclear, the American recommendations for the diagnosis and treatment of patients with IS allow this procedure to be performed in this kind of patients [1]. It should be noted that confirmation of cerebral artery thrombosis is not required in patients with IS prior to sTLT. Moreover, even in patients with severe stroke (NIHSS score of at least 14 points), thrombosis of a stroke-related artery cannot be detected in 30% of cases [10].

In the context of the continuously growing older adult population which constitutes the bulk of patients with IS, information on the prevalence of patients with thrombotic occlusion of cerebral arteries, who are potential candidates for TE, may be important for regional vascular centers. Currently, there is no reliable information on the prevalence of thrombotic occlusion of stroke-related arteries in patients with IS admitted within the 6-hour "therapeutic window". There are also no other characteristics of this patient group, as well as IS patients without thrombotic occlusion. The results of the present study can help in planning the work of regional vascular centers involved in reperfusion therapy for IS patients.

The aim of this study is to describe IS patients admitted within the 6-hour “therapeutic window”.

MATERIAL AND METHODS

The study included 145 patients with cerebral IS admitted within the first 6 hours after the symptom onset. In order to verify cerebral artery occlusion, all the patients underwent computed tomographic (CT) angiography. We attributed thrombosis at the level of the internal carotid artery (ICA) regardless of its segment, M1 – M3 segments of the MCA, A1 – A2 segments of the ACA, any segment of the vertebral artery, BA, as well as P1 – P2 segments of the posterior cerebral artery (PCA) to the large vessel proximal cerebral occlusions [1]. The diagnosis of IS was confirmed by diffusion-weighted imaging (DWI). The pathogenic variant of IS was established in accordance with the TOAST classification criteria, and cryptogenic IS - according to the ESUS criteria [11, 12]. The level of consciousness was assessed according to the Glasgow Coma Scale (GCS), and neurologic deficit severity - according to the NIHSS scale. According to the criteria of L.B. Goldstein et al., NIHSS score of les than 6 points was defined as mild stroke, from 7 to 13 points - as moderate stroke, over 14 points - as severe stroke [13]. Functional and clinical outcomes of the disease were assessed using the the Barthel Index for Activities of Daily Living (BI), mRS, and the degree of patient mobility limitation was assessed using the Rivermead Mobility Index (RMI).

STATISTICAL ANALYSIS

The Mann-Whitney test was used to compare differences between two independent samples. Correlation was assessed by the Pearson method. We also used multiple logistic regression analysis. Differences were considered statistically significant at $p < 0.05$. For a normally distributed variable the result was presented as the mean. In cases of skewed distributions, the median was used to characterize the central tendency.

RESULTS

From January 2019 to October 2020, 1426 patients with IS were admitted at the N.V. Sklifosovsky Research Institute for Emergency Medicine, 145 (10.2%) of them - within 6 hours from the onset of the disease. An analysis of patients admitted within the 6-hour "treatment window" will be presented later in the text. The mean patient age was 71 ± 13.4 years, women were 74 (51%), men - 71 (49%). The patient characteristics are presented in Table 1.

Table 1

Characteristics of examined patients (n=145)

Indicator	Value
Mean age, years	71±13,4
Gender, n (%) — male — female	 71 (49) 74 (51)
History of stroke, n (%)	37 (25,5)
History of transient ischemic attack, n (%)	3 (2,1)
History of myocardial infarction, n (%)	26 (17,9)
AF, n (%)	57 (39,3)
Arterial hypertension, n (%)	135 (93,1)
Diabetes, n (%)	38 (26,2)
CKD, n (%)	28 (19,3)
Oncological diseases, n (%)	25 (17,2)
Smoking, n (%)	27 (18,6)
Length of hospital stay, days	21,1±16,4
GCS severity upon admission, score, M [25; 75]	15 [15; 15]
NIHSS severity upon admission, score, M [25; 75]	7 [3; 16]
NIHSS severity on day 21, score, M [25; 75]	3 [1; 7]
Pathogenetic variant of IS according to TOAST criteria, n (%): — atherothrombotic — cardioembolic — lacunar — other established etiology — unknown etiology	 28 (19,3) 54 (37,2) 8 (5,5) 3 (2,1) 52 (35,9)
The number of patients who required MV during hospitalization, *n* (%)	39 (26,9)
mRS, day 21, point, M [25; 75]	2 [2; 5]
BI, day 21, point, M [25; 75]	85 [41; 100]
RMI, day 21, point, M [25; 75]	13 [8; 14]
Mortality, n (%)	29 (20)

Notes: MV — mechanical ventilation; IS — ischemic stroke; AF — atrial fibrillation; GCS — Glasgow Coma Scale; CKD — chronic kidney disease; mRS — modified Rankin scale; NIHSS — ischemic stroke severity scale; BI - the Barthel Index for Activities of Daily Living; RMI — Rivermead Mobility Index; TOAST — classification of pathogenetic subtypes of ischemic stroke

Out of 145 patients, 54 (37.2%) had cardioembolic IS; for 52 patients (35.9%) it was not possible to verify the pathogenetic variant of IS - a diagnosis of cryptogenic IS was established; in 28 cases (19.3%) atherothrombotic IS was detected, lacunar IS was diagnosed in 8 patients (5.5%); some other etiology of stroke was established in 3 patients (2.1%). The mortality rate was 20% (see Table 1).

According to CT angiography, thrombotic occlusion of a stroke-related artery was detected in 50 out of 145 examined patients (34.5%). In the vast majority of patients, arterial occlusion was localized in the carotid system (94%, 47 cases), while thrombosis in the vertebrobasilar system was diagnosed only in 3 patients (6%). MCA was the most frequent statistically significant site of occlusion (in 31 patients (90%)) ($p < 0.05$). ACA thrombosis was diagnosed in 2 patients (4%), PCA - in 2 (4%), BA - in 1 patient (2%). The patient characteristics of the two groups are presented in Table 2. Atrial fibrillation (AF) and chronic kidney disease (CKD) were found statistically significantly more often in patients with diagnosed thrombotic occlusion (58% versus 29.5%, $p = 0.001$ and 30% versus 13.7%, $p = 0.0018$, respectively). There were no other significant differences between the groups in terms of demographic indicators.

Table 2

Characteristics of patients with stroke-related artery occlusion and without stroke-related artery occlusion

Indicator	Patient groups		Statistical significance, p
	Patients with stroke-related artery thrombosis, *n*=50	Patients without cerebral artery thrombosis, *n*=95	
Mean age, years	71,6±12,4	70,8±14	>0,05
Gender, n (%) — male — female	 26 (52) 24 (48)	 48 (50,5) 47 (49,5)	>0,05
History of stroke, n (%)	13 (26)	24 (25,3)	>0,05
History of transient ischemic attack, n (%)	2 (4)	1 (1,1)	>0,05
History of myocardial infarction, n (%)	13 (26)	13 (13,7)	>0,05
AF, n (%)	29 (58)	28 (29,5)	0,001
Arterial hypertension, n (%)	48 (96)	87 (91,6)	>0,05
Diabetes, n (%)	11 (22)	27 (28,4)	>0,05
CKD, n (%)	15 (30)	13 (13,7)	0,018
Oncological diseases, n (%)	10 (20)	15 (15,8)	>0,05
Smoking, n (%)	8 (16)	19 (20)	>0,05
Time of admission: - less than 4.5 hours from the onset of the disease - 4.5-6 hours from the onset of the disease	 45 (90%) 5 (10%)	 79 (83,2%) 16 (16,8%)	 >0,05 >0,05

Notes:AF — atrial fibrillation; CKD — chronic kidney disease

The level of consciousness at the onset of the disease, as well as on the 2nd, 3rd, 5th and 7th days in patients diagnosed with thrombotic occlusion of a symptomatic artery was lower than in patients without it (Fig. 1).

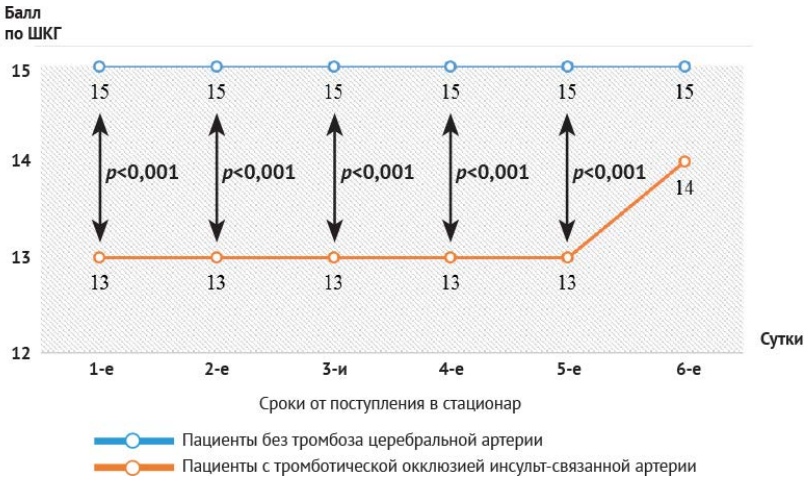

Fig. 1. Dynamics of the level of consciousness of examined patients

Note: GCS — Glasgow Coma Scale

The initial severity of neurologic deficit in patients with stroke-related artery thrombosis was statistically significantly higher than in the group without verified cerebral artery occlusion (NIHSS score 17 [10; 23] versus 5 [2; 10], p <0.001). These differences persisted on the 2nd, 3rd, 5th, 7th and 14th days of the disease (Fig. 2).

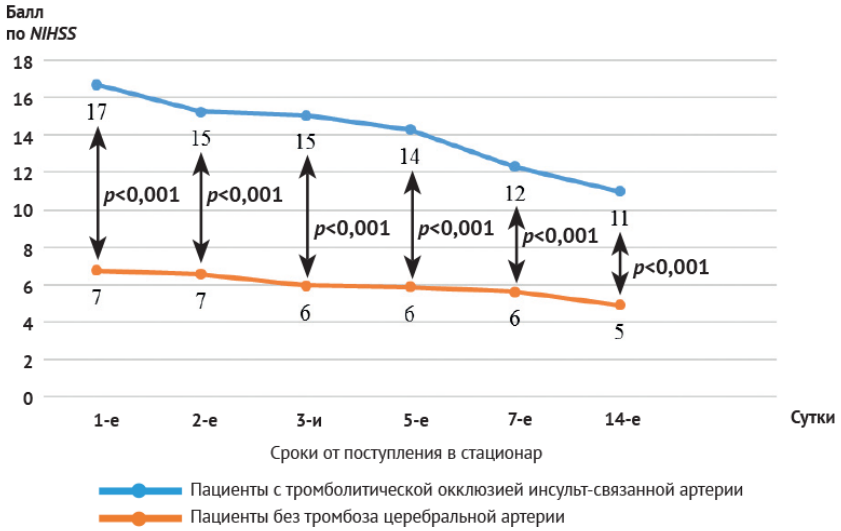

Fig. 2. Dynamics of the severity of neurological deficit in the examined patients

Note: NIYSS — National Institutes of Health Stroke Scale

A statistically significant mean two-way correlation was revealed between the presence of thrombosis of a stroke-related artery and the NIHSS score at the onset of the disease (r = 0.5; p <0.001). Depending on the neurologic deficit severity, the patients were divided into three subgroups: NIHSS score from 0 to 6 points, 7-13 points, and over 14 points (Fig. 3). Out of 95, 40 patients (42.1%) without verified cerebral artery occlusion had a NIHSS score of more than 7, which corresponded to moderate and severe stroke.

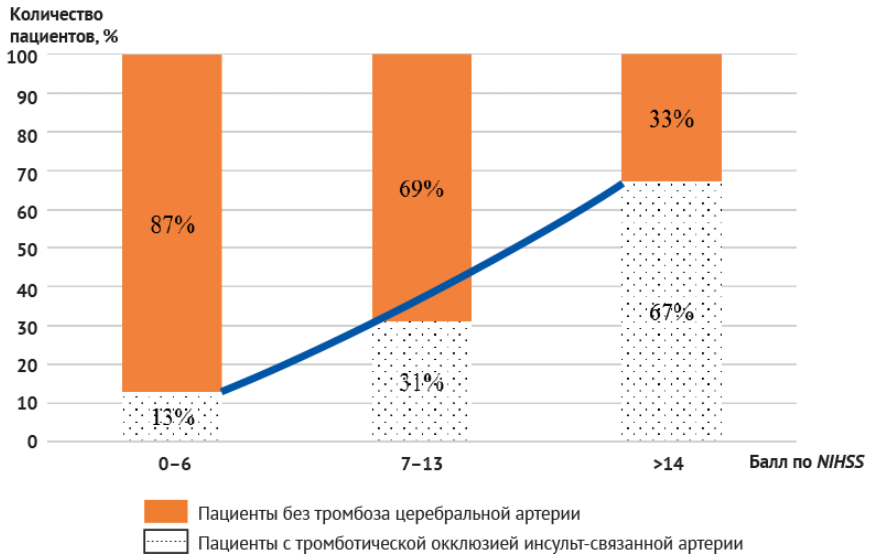

Fig. 3. Distribution of patients according to NIHSS — National Institutes of Health Store Scale — a scale for assessing the severity of ischemic stroke, neurological deficit. The number of patients with verified occlusion of a stroke-related artery was significantly higher in the subgroups with NIHSS score 7–13 and more than 14 ($p<0.05$)

Dysphagia and vocal cord paresis were statistically significantly more often detected in patients with symptomatic artery occlusion compared with patients without it (30% versus 9.5% ($p = 0.002$) and 32% versus 8.4% ($p <0.001$). There were no other significant differences between the groups in terms of clinical parameters (Table 3).

Table 3

Clinical indicators of examined patients

Indicator	Patient groups		Statistical significance, p
	Patients with stroke-related artery thrombosis, *n*=50	Patients without cerebral artery thrombosis, *n*=95	
Length of hospital stay, days	23,4±16,9	19,8±15,9	>0,05
GCS severity upon admission, score, M [25; 75]	14 [13; 15]	15 [15; 15]	<0,001
NIHSS severity upon admission, score, M [25; 75]	17 [10; 23]	5 [2; 10]	<0,001
Pathogenetic variant of IS according to TOAST criteria, n (%): – atherothrombotic – cardioembolic – lacunar – other established etiology – unknown etiology	 9 (18) 21 (42) 3 (6) 2 (4) 15 (30)	 19 (20) 33 (34,7) 5 (5,3) 1 (1,1) 37 (38,9)	 >0,05 >0,05 >0,05 >0,05 >0,05
Clinical deterioration on the 1st day, n (%)	3 (6)	10 (10,5)	>0,05
Dysphagia, n (%)	15 (30)	9 (9,5)	0,002
Vocal cord paresis, n (%)	16 (32)	8 (8,4)	<0,001
Reperfusion therapy, n (%) – sTLT – TE – sTLT + TE	48 (96) 3 (6) 28 (56) 17 (34)	20 (21,2) 20 (21,2) – –	

Notes: sTLT — systemic thrombolytic therapy; TE — thrombectomy; GCS — Glasgow Coma Scale; NIHSS — National Institutes of Health Stroke Scale

Reperfusion therapy was performed in 68 (46.9%) patients out of 145. At the same time, sTLT alone was performed in 23 patients (15.9%), TE alone - in 28 patients (19.3%), and sTLT followed by TE was performed in 17 patients (11.7%). The reasons for not performing sTLT are given in Table 4.

Table 4

Reasons for failure to perform systemic thrombolytic therapy

Indicator	Number of patients, n = 145
More than 4.5 hours from the onset of the disease,n (%)	21 (14,5)
Insignificant neurologic deficit severity, n (%)	34 (23,4)
NIHSS severity more than 25, n (%)	15 (10,3)
Rapid improvement of patient condition by the time of the sTLT start, n (%)	4 (2,8)
Effective anticoagulant treatment in the previous 48 hours, n (%)	5 (3,4)
Major surgery within the previous 10 days, n (%)	14 (9,7)
Early seizures after stroke onset, n (%)	3 (2,1)
Recurrent stroke in patients with diabetes mellitus, n (%)	9 (6,2)
Thrombocytopenia of less than 100,000 / μL, n (%)	3 (2,1)
Infective endocarditis, n (%)	2 (1,4)
Bleeding peptic ulcer within the last 3 months, n (%)	2 (1,4)
Blood pressure over 185/110 mm Hg, n (%)	6 (4,1)
History of neoplasms of the CNS, n (%)	2 (1,4)
Previous prolonged cardiopulmonary resuscitation, n (%)	2 (1,4)

Notes: sTLT — systemic thrombolytic therapy; CNS — central nervous system; NIHSS — International Institutes of Health Stroke Scale

5 (10%) out of 50 patients with verified cerebral artery thrombosis did not undergo thrombectomy: in one patient control digital subtraction angiography revealed complete recanalization on sTLT; 3 patients did not undergo TE due to low functional activity before IS (mRS score of at least 2 points); in one patient the occlusion was assessed as chronic.

Asymptomatic hemorrhagic transformation (HT) was detected in 9 patients after TE (20%) out of 45 who did not undergo sTLT and in 7 (41.2%) patients out of 17 who underwent sTLT, as well as in 1 patient (33.3%) out of 3with cerebral artery thrombosis after sTLT without TE. The development of symptomatic HT was not noted at all. Asymptomatic HT was also detected in 4 cases (20%) after sTLT in patients without verified stroke-related artery occlusion.

There were no significant differences between the groups in the length of stay in the intensive care unit ($p > 0.05$). The number of patients who required mechanical ventilation during hospitalization was statistically significantly higher in the group of patients with stroke-related artery thrombosis (42% versus 18.9%, $p = 0.003$). Patients with verified symptomatic artery occlusion statistically significantly more often than patients without this diagnosis underwent tracheostomy (32% versus 16.8%, $p = 0.037$), received vasopressor support (30% versus 13.7%, $p = 0.018$) and tube feeding (38% versus 14.7%, $p = 0.002$), and also had urinary (54% versus 27.4%, $p = 0.002$) and central venous catheters (32% versus 12.6%, $p = 0.005$) inserted (Table 5).

Table 5

Intensive therapy in the examined patients

Intensive therapy	Patient groups		Statistical significance, p
	Patients with stroke-related artery thrombosis, *n*=50	Patients without cerebral artery thrombosis, *n*=95	
Length of ICU stay, M [25; 75]	5 [3; 14,3]	4 [2; 10]	>0,05
The number of patients who required MV during hospitalization, n (%)	21 (42)	18 (18,9)	0,003
Tracheostomy, n (%)	16 (32)	16 (16,8)	0,037
Vasopressor support, n (%)	15 (30)	13 (13,7)	0,018
Tube feeding, n (%)	19 (38)	14 (14,7)	0,002
Transfusion of blood products, n (%)	4 (8)	4 (4,2)	>0,05
Urethral catheter insertion, n (%)	27 (54)	26 (27,4)	0,002
Central venous catheter insertion, n (%)	16 (32)	12 (12,6)	0,005

Note: MV — mechanical ventilation

There were no statistically significant differences in laboratory parameters between patients with stroke-related artery thrombosis and without the cerebral artery occlusion, except for the level of the international normalized ratio (INR) upon admission to the hospital, which was statistically significantly higher in patients with verified occlusion (1.3 ± 0.4 versus 1.2 ± 0.3, p <0.05) (Table 6).

Table 6

Laboratory indicators in the examined patients upon admission to the hospital

Indicator	Patient groups		Statistical significance, p
	Patients with stroke-related artery thrombosis, *n*=50	Patients without cerebral artery thrombosis, *n*=95	
Red blood cells, $x10^{12}$/L	4,0±0,6	4,4±0,6	>0,05
Hemoglobin, g / L	132,7±17,3	137,3±19,9	>0,05
White blood cells, $x10^{9}$/L	14,9±4,8	18,8±5,3	>0,05
Platelets, $x10^{9}$/L	208,1±79,2	224,5±99,7	>0,05
ESR, mm / h	7,2±2,8	7,1±2,7	>0,05
Creatinine, mmol / L	96,1±39,0	87,1±29,3	>0,05
Urea, mmol / L	6,9±4,4	6,5±4,1	>0,05
Total bilirubin, mmol / L	10,2±5,5	9,3±4,8	>0,05
Cholesterol, mmol / L	5,2±1,7	10,6±7,7	>0,05
ALT, U / l	21,7±15,4	21,2±17,8	>0,05
AST, U / l	28,6±14,0	25,8±19,7	>0,05
Glucose upon admission, mmol / L	6±3,4	5,5±2,9	>0,05
Glucose at discharge, mmol / L	5,3±2,0	5,2±1,9	>0,05
Glycated hemoglobin,%	5,1±1,5	4,9±1,3	>0,05
Potassium, mmol / L	4,5±0,8	4,5±0,9	>0,05
Sodium, mmol / L	141,9±9,6	141,7±9,5	>0,05
INR	1,3±0,4	1,2±0,3	<0,05
APTT, s	35,1±20,9	30,0±5,9	>0,05

Notes: ALT — alanine aminotransferase; AST — aspartate aminotransferase; APTT — activated partial thromboplastin time; INR — international normalized ratio; ESR — erythrocyte sedimentation rate

Non-cerebral complications of acute cerebrovascular accident (ACVA) identified during hospitalization despite ongoing prophylaxis are presented in Table 7. There were no statistically significant differences between the groups in the incidence of non-cerebral complications of IS such as fatal pulmonary embolism (PE) and pressure ulcers. Pneumonia, deep vein thrombosis, and other infectious complications developed statistically significantly more often in patients with verified stroke-related artery thrombosis.

Table 7

Non-cerebral complications of acute cerebrovascular accident in the examined patients

Complications	Patient groups		Statistical significance, p
	Patients with stroke-related artery thrombosis, *n*=50	Patients without cerebral artery thrombosis, *n*=95	
Pneumonia, n (%)	15 (30)	13 (13,7)	0,018
Deep vein thrombosis, n (%)	20 (40)	10 (10,5)	<0,001
PE, n (%)	6 (12)	8 (8,4)	>0,05
Other infectious complications, n (%)	13 (26)	9 (9,5)	0,009

Notes: PE — pulmonary embolism

Good clinical outcomes by day 21 from the onset of the disease (mRS score 0-2 points) were observed in 14% of patients with stroke-related artery occlusion and in 46.3% of those examined without thrombosis (p <0.001, statistically significant). The ability to walk by the 21st day from the onset of the disease was statistically significantly higher in patients without verified stroke-related artery occlusion compared to patients with cerebral artery thrombosis (RMI score 13 [8; 14] versus 12 [8; 14], p = 0.041). There were no significant differences in functional outcomes by day 21 of the disease between the groups (BI 90 [43; 100] points in patients with verified cerebral artery thrombosis versus 80 [40; 95] points in patients without it, p> 0.05) (Table 8).

Table 8

Functional and clinical outcomes of the disease on the 21st day

Indicator	Patient groups		Statistical significance, p
	Patients with stroke-related artery thrombosis, *n*=50	Patients without cerebral artery thrombosis, *n*=95	
mRS score 0-2 points, n (%)	7 (14)	44 (46,3)	<0,001
mRS score 3-4 points, n (%)	19 (38)	23 (24,2)	>0,05
mRS score 5 points, n (%)	5 (10)	18 (19)	>0,05
mRS score 6 points, n (%)	19 (38)	10 (10,5)	<0,001
BI, score, M [25; 75]	80 [40; 95]	90 [43; 100]	>0,05
RMI, score, M [25; 75	12 [8; 14]	13 [8; 14]	0,041

Notes: BI — The Barthel index; mRS — modified Rankin scale; RMI — Rivermead Mobility Index

Mortality in the group of patients with thrombotic occlusion of a stroke-related artery was higher than in the group of patients without thrombosis of the symptomatic artery (38% versus 10.5%, p <0.001).

According to multivariate logistic regression analysis stroke-related artery thrombosis was associated with baseline NIHSS severity and AF (odds ratio 3.3; 95% CI 1.62–6.75).

DISCUSSION

Currently, reperfusion therapy is the main method of treating patients with IS, however, its implementation is limited by the so-called therapeutic window, which for sTLT is 4.5 hours, and for endovascular TE - 6 hours from the onset of the disease [1]. The most common reasons for refusal to perform systemic thrombolysis in IS patients admitted within the first 4.5 hours are mild neurologic deficit, rapid improvement in the patient's condition by the time of sTLT initiation, blood pressure over 185/110 mm Hg,

and effective anticoagulant treatment in the previous 48 hours [14]. The published data on the reasons for refusing to perform TE in IS patients is currently insufficient, and our study showed that in 65.5% of patients admitted within the first 6 hours from the onset of the disease, the reason for not performing TE was the absence of verified thrombosis of a stroke-related artery. Moreover, the protocol unambiguously regulates the TE performance only in the case of verified thrombotic occlusion of the ICA and / or M1 segment of the MCA, and in our study, out of 50 patients with stroke-related artery thrombosis, thrombosis of such localization was found in 45 patients (90%), and in 5 (10%) patients - thrombosis was of a different localization.

The currently recommended patient selection protocol for TE implies performing cerebral CT angiography in patients with an NIHSS score of at least 6 [1]. Despite the fact that our study established a correlation between the NIHSS severity of IS and the likelihood of CT angiography verified stroke-related artery thrombosis, 32.6% of patients with severe stroke (NIHSS of at least 14 points) had no thrombotic occlusion, and in 13% of patients with mild AIS (NIHSS under 6 points), on the contrary, thrombotic occlusion was found. Consequently, in order to search for thrombotic occlusion of a stroke-related artery, CT angiography should be performed in all the patients admitted within the "therapeutic window", regardless of the NIHSS score.

Mortality in patients with verified thrombotic occlusion of the cerebral artery was statistically significantly higher than in patients without it (38% versus 10.5%, $p < 0.001$). Such a significant difference in the mortality rate was due to the initially more severe stroke (NIHSS severity at admission 17 [10; 23] versus 5 [2; 10] points, $p < 0.001$) in patients with thrombotic occlusion of a stroke-related artery, as well as a statistically significantly higher prevalence of gross swallowing disorders (30% versus 9.5% $p < 0.002$) which are risk factors for the development of pneumonia, and such a comorbid background as CKD and AF (30% versus 13.7%, $p = 0.018$ and 58% versus 29 , 5%, $p = 0.001$, respectively).

CONCLUSIONS

1. Thrombosis of the cerebral stroke-associated artery was detected in 34.5% of patients with ischemic stroke who were admitted within the first 6 hours from the onset of the disease.

2. The main reason for the refusal to perform thrombectomy in patients with ischemic stroke admitted within the 6-hour "therapeutic window" is the lack of verification of stroke-related artery thrombosis using CT angiography. Due to thrombosis of a different localization (other than thrombosis of the internal carotid artery and / or M1 segment of the middle cerebral artery), 10% of patients with verified thrombosis did not meet the currently existing selection criteria for thrombectomy.

3. Despite the fact that the detection of stroke-related artery thrombosis did correlate with the severity of stroke, in 32.6% of patients with severe stroke (NIHSS severity of at least 14 points), thrombotic occlusion of the cerebral artery was not detected, and in 13% of patients with mild IS, on the contrary, thrombotic occlusion was diagnosed.

4. In patients with thrombotic occlusion of a stroke-related artery, atrial fibrillation (58% versus 29.5%), chronic kidney disease (30% versus 13.7%), dysphagia (30 % versus 9.5%) and epiglottis paresis (32% versus 8.4%) were detected statistically significantly more often than in patients without it. The most frequent pathogenetic variant of ischemic stroke in patients with verified cerebral artery thrombosis was cardioembolic (42%).

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