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## Capabilities of perfusion ASPECTS in predicting the efficiency of intravenous thrombolytic therapy

Perfusion computed tomography (PCT) is increasingly used to diagnose ischemic stroke (IS), as well as to identify candidates for thrombolytic therapy (TLT). The feasibility of using this technique in all patients within the therapeutic window has not yet been established. **Objective:** To investigate cerebral blood flow according to PCT findings and its relationship to clinical and instrumental indicators and functional status of patients who received TLT in the acute period of IS.

**Patients and methods.** 62 patients with acute IS who had received TLT were examined. All the patients underwent clinical, laboratory, and instrumental examinations and PCT assessing cerebral blood volume (CBV), cerebral blood flow (CBF), and mean transit time (MTT) in 10 brain regions in accordance with the Alberta Stroke Program Early CT Score (ASPECTS). The total result of perfusion ASPECTS was calculated separately for CBV, CBF and MTT, as well as for combinations of these parameters. The penumbra size was calculated as CBV minus MTT (CBV – MTT) ASPECTS, the infarct core size was measured as CBV + MTT ASPECTS.

**Results.** There was an increase in MTT in most regions of interest of the affected hemisphere as compared to the intact one and a predominance of reversible perfusion disorders. The averaged penumbra size constituted three zones according to ASPECTS. No relationship was found between ASPECTS scores and the time from the onset of symptoms to hospital admission.

Perfusion parameters, particularly the penumbra size (CBV – MTT), were associated with the degree of stenosis in the contralateral common carotid artery, body mass index, and blood triglyceride level. Cerebral blood flow indices were also influenced by red blood cell counts and ejection fraction. The scores of the perfusion scales were correlated with those of the non-contrast scale. The data of the investigated ASPECTS variants correlated with the level of neurological deficit in patients, its course, and the functional outcome of acute IS.

**Conclusion.** The perfusion variants of ASPECTS have a high predictive value for patients' neurologic and functional status upon completion of the first treatment stage. The penumbra size (CBV – MTT ASPECTS) is a marker for the expected regression of neurological impairment during TLT. The infarct core size (CBV + MTT ASPECTS) determines the degree of neurologic deficit at a patient's discharge.

**Keywords:** stroke; thrombolysis; predictors; perfusion; ASPECTS.

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Intravenous thrombolytic therapy (TLT) is a world standard of brain reperfusion in ischemic stroke (IS). The TLT rate in Europe reaches 33% [1]. According to the Federal Register of Hospital Patient with Stroke in the period 2009–2013, more than 10 000 TLT procedures were performed in Russia, which corresponds to a 10-fold increase in the use of TLT after its introduction [2]. TLT has been used in Perm Region since 2014, and in 2016 TLT rate was 2.6%. In Perm Regional Vascular Center TLT rate increased from 1.6% in 2014 to 15% in 2016.

High efficiency of TLT determines the search for criteria for the expansion of indications for its use in order to improve functional outcome in the largest possible number of patients with IS. The main limitation for the wide use of TLT is the time window that is 4.5 hours in Russia. Nevertheless, the amount of data confirming that time is not a reliable criterion of irreversibility of brain damage in IS is growing, thus postulating the priority of perfusion pattern (mismatch) as the main indicator of brain damage. [3].

Perfusion computed tomography (PCT) is increasingly applied in the diagnosis of IS, which is confirmed by scientific research data and routine clinical practice. This method allows to identify reversible and irreversible brain damage and is characterized by rapid performance, quick interpretation of the results, absence of contraindications and high informativity [4]. The most popular neuroimaging technique for the assessment of early

ischemic brain changes in the middle cerebral artery territory is Alberta Stroke Program Early CT Score (ASPECTS), the result of which correlates with the final size of brain infarct [5,6]. Combined assessment of ASPECTS and perfusion parameters, particularly cerebral blood volume (CBV), has been highly informative in predicting both radiological and clinical outcomes of stroke [7]. Nevertheless, the advantages of the perfusion scale as compared to the non-enhanced scale are not fully convincing [8]. The expediency of taking into account the perfusion pattern in determining the indications and contraindications for reperfusion therapy has not been finally established. In DEFUSE, DEFUSE-2, EPITHET and EXTEND-IA trials the PCT allowed to identify candidates for delayed reperfusion therapy, whereas MR-RESCUE and DIAS-II trials did not demonstrate that benefit [9]. Nevertheless, the existing background for the effectiveness of the method stimulates further studies of its use in IS patients, including substantiating the need to analyze the diagnostic capabilities of PCT in real clinical practice.

**The aim** of this study is to evaluate the cerebral blood flow according to PCT scans and its interrelation with clinical and instrumental data and functional status of patients who underwent TLT in the acute period of IS.

**Patients and methods.** 62 patients with IS who received TLT were examined. All participants underwent clinical, laboratory and instrumental examination according to the existing stan-

# ORIGINAL INVESTIGATIONS AND METHODS

Table 1. *Clinical characteristics of patients*

Clinical characteristic	Premorbid status
<b>Premorbid status</b>	
mRS before admission $\geq 1$ , n (%)	17 (27)
Body mass index, kg/m <sup>2</sup>	26,3 (24,8–32,9)
Smoking, n (%)	20 (32)
Hypertension, n (%)	61 (98)
Ischemic heart disease, n (%)	30 (48)
Atrial fibrillation, n (%)	21 (34)
Diabetes mellitus, n (%)	13 (21)
Antiplatelets use before admission, n (%)	26 (42)
<b>Stroke characteristic</b>	
Recurrent stroke, n (%)	11 (18)
Time before admission, min	115 (85–150)
NIHSS on admission	8 (6–11)
Systolic blood pressure on admission, mm.Hg.	150 (160–170)
Brainstem infarction, n (%)	9 (15)
Large artery atherothrombotic stroke, n (%)	29 (47)
Cardioembolic stroke, n (%)	20 (32)
Lacunar stroke, n (%)	10 (16)
Stroke of unknown etiology, n (%)	3 (5)
<b>Outcome of acute phase of stroke</b>	
Mortality, n (%)	4 (7)
mRS 0–1, n %	30 (48)
NIHSS	2 (1–6)
Rivermead mobility index	12 (6–15)
Duration of treatment, days	12 (9–15)

dards. Indications for TLT were determined strictly in accordance with the «Clinical Guidelines for Thrombolytic Therapy for Ischemic Stroke 2015» [10]. All patients underwent neuroimaging procedures, including non-contrast CT and PCT; control non-contrast CT was performed 24 hours after the admission. CT examination was conducted using GE Optima CT660 (128 slices) in the mode of helical scanning, pitch factor 1.2, collimation of sections 2.5–5.0 mm with reconstruction 0.625 mm, kernel D30f. Parameters of the non-contrast CT: 140 kV, 320–360 mA. The scanning zone included the area from the base to the cranial vault. Primary non-contrast CT was used to assess the presence of early signs of the acute period of infarction. PCT was carried out using a scanning protocol (80 kV, 400 mA), the scan duration did not exceed 45 s; the width of the scanning zone was from 40 to 78 mm, and the scan area varied mainly within the supratentorial

Table 2. *CT on admission and after 24 hours*

CT	n (%)
<b>On admission:</b>	
hypodense lesion (acute infarction)	6 (10)
hypodense lesion (old infarction)	24 (39)
<b>After 24 hours:</b>	
Acute infarction on CT	29 (47)
Hemorrhagic transformation on CT	5 (8)
Hemorrhagic transformation types 1–2	3 (60)
Hemorrhagic transformation types 3–4	3 (40)

structures. In bolus-based contrast control, the total amount of non-ionic iodine-containing contrast medium (350–370 mg / ml) administered to each patient was 50 ml at a rate of 4 ml / s. The images obtained with the native CT were processed on Workstation Advanced 4.7 with the reconstruction of 3D- and multiplanar 2D (MPR)- reformation. The PCT data were processed using the 3D Perfusion program.

The following cerebral blood supply indicators – cerebral blood flow (CBF), cerebral blood volume (CBV), and mean transit time (MTT) were estimated in 10 brain regions in accordance with the ASPECTS scale [5]. This 10-point scale allows assessing the presence or absence of early ischemic changes in 10 brain regions, including 6 regions of the middle cerebral artery territory (M1–M6), caudate nucleus (C), insula (I), internal capsule (IC) and lenticular nucleus (L). In M1–M6 cerebral blood flow parameters were determined separately in cortical and subcortical brain matter. After evaluating absolute values of perfusion parameters, relative values (rCBV, rCBF, rMTT) were calculated by dividing the index in the area of the affected hemisphere by the index in the contralateral area. Total result of perfusion ASPECTS was calculated separately for CBV, CBF and MTT by subtracting 10 to 1 points for the presence of perfusion abnormalities at each measurement point. The following perfusion thresholds were used: rCBV  $\leq 40\%$ , rCBF  $< 40\%$  and rMTT  $> 145\%$  [11]. Since MTT and CBV reflect the zones of general hypoperfusion and the infarct core, respectively, ASPECTS mismatch was calculated as CBV ASPECTS minus MTT ASPECTS (CBV–MTT ASPECTS) [12]. The infarct core zone was also identified by a combination of rCBF  $< 40\%$  and rMTT  $> 145\%$  (CBF + MTT ASPECTS) [11]. In addition, the CBF–MTT ASPECTS was calculated. Due to the limitations of the reading frame, in some patients CT perfusion parameters were not assessed at all ASPECTS points. As a result, a complete analysis of the ASPECTS–10 scale data was obtained in 38 patients, whereas in all patients ASPECTS parameters were calculated at 7 points (M1–M3, C, IC, L, I, ASPECTS–7).

Assessment of pathogenetic subtypes of stroke was carried out with SSS–TOAST classification [13]. The severity of stroke was assessed using the NIHSS, the functional status at discharge – using the Rivermead mobility index (RMI) and the modified Rankin scale (mRS). Statistical analysis was performed with Statistica 8.0 software package. A quantitative comparative analysis of two independent groups was carried out with the Mann–Whitney criterion, qualitative analysis – with the  $\chi^2$  criterion. Spearman criterion was used for correlation analysis. The tables show the median and interquartile range.

**Results.** The age of the patients varied from 30 to 86 years (median 64.4  $\pm$  12.1 years). There were 32 men and 30 women. Clinical characteristics of TLT patients and patients of the comparison group are presented in Table. 1.

Table 3. *PCT data*

Area	Parameter	Hemisphere		Relative value (i/c), %	p
		ipsilateral	contralateral		
M <sub>1</sub> c	CBV, ml×100 g <sup>-1</sup>	1,9 (1,5–2,4)	2,1 (1,6–2,4)	93 (81–113)	0,26
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	18,5 (12–24,8)	19,4 (15,8–28,1)	89 (62–120)	0,030
	MTT, s	7,5 (5,7–11,0)	7,8 (5,3–9,5)	102 (75–150)	0,10
M <sub>1</sub> s	CBV, ml×100 g <sup>-1</sup>	1,0 (0,7–1,4)	1,0 (0,8–1,3)	100 (82–113)	0,41
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	7,7 (5,6–13,5)	8,8 (7,0–12,5)	86 (55–115)	0,31
	MTT, s	9,7 (8,4–11,9)	9,3 (7,6–10,4)	107 (91–129)	0,010
M <sub>2</sub> c	CBV, ml×100 g <sup>-1</sup>	2,3 (1,6–2,8)	2,1 (1,7–2,5)	106 (76–139)	0,70
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	17,7 (10,6–28,8)	21,8 (16,8–27,3)	81 (64–127)	0,16
	MTT, s	9,05 (7,0–12,3)	8,0 (6,6–9,4)	113 (83–172)	0,0004
M <sub>2</sub> s	CBV, ml×100 g <sup>-1</sup>	1,6 (1,2–2,0)	1,6 (1,2–2,0)	105 (75–138)	0,45
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	13,1 (8,8–18,4)	14,2 (10,0–19,5)	89 (55–137)	0,40
	MTT, s	10 (8,5–12,5)	9,4 (7,8–10,7)	109 (87–161)	0,002
M <sub>3</sub> c	CBV, ml×100 g <sup>-1</sup>	2,0 (1,6–2,4)	2,0 (1,5–2,4)	100 (86–122)	0,85
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	18,2 (14,2–23,8)	19,4 (13,4–24,6)	100 (71–149)	0,59
	MTT, s	8,9 (6,6–11,1)	8,4 (6,2–10,4)	104 (91–119)	0,28
M <sub>3</sub> s	CBV, ml×100 g <sup>-1</sup>	1,2 (0,9–1,4)	1,1 (0,8–1,4)	100 (82–129)	0,67
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	8,3 (6,3–11,3)	9,4 (7,6–11,3)	89 (71–119)	0,28
	MTT, s	10,6 (9,1–12,2)	10,2 (8,6–11,5)	104 (87–133)	0,072
I	CBV, ml×100 g <sup>-1</sup>	1,6 (1,2–2,1)	1,9 (1,2–2,3)	93 (69–125)	0,34
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	16,3 (9,2–25,4)	16,2 (12,7–23,6)	95 (59–146)	0,53
	MTT, s	9,15 (6,8–12,3)	7,7 (6,3–9,3)	111 (84–164)	0,002
L	CBV, ml×100 g <sup>-1</sup>	2,0 (1,4–2,7)	2,3 (1,7–2,9)	100 (79–110)	0,20
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	20,0 (14,5–26,1)	22,3 (16,4–32,8)	86 (61–115)	0,14
	MTT, s	8,15 (5,7–10,2)	6,3 (5,2–9,1)	110 (85–151)	0,031
C	CBV, ml×100 g <sup>-1</sup>	2,1 (1,6–2,5)	2,1 (1,7–2,5)	100 (89–110)	0,96
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	18,7 (13,5–27,0)	22,2 (17,0–27,5)	98 (71–120)	0,24
	MTT, s	7,3 (5,4–9,9)	6,8 (5,2–8,7)	104 (80–135)	0,17
IC	CBV, ml×100 g <sup>-1</sup>	1,4 (1,1–1,8)	1,4 (1,1–1,8)	100 (86–115)	0,55
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	12 (9,0–15,8)	12,8 (9,4–16,7)	90 (68–119)	0,46
	MTT, s	9,8 (7,7–11,8)	9,1 (7,6–10,2)	106 (87–139)	0,030
M <sub>4</sub> c	CBV, ml×100 g <sup>-1</sup>	1,7 (1,4–2,2)	1,85 (1,4–2,2)	98 (75–128)	0,89
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	17,7 (12,4–24,9)	21,5 (15,4–26,8)	98 (68–123)	0,25
	MTT, s	7,5 (6,3–9,4)	6,8 (5,6–8,1)	116 (77–148)	0,061
M <sub>4</sub> s	CBV, ml×100 g <sup>-1</sup>	0,9 (0,7–1,2)	0,9 (0,7–1,0)	108 (88–125)	0,35
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	7,5 (6,2–9,2)	8,0 (5,9–11,3)	87 (61–140)	0,41
	MTT, s	9 (7,9–11,5)	9,2 (7,7–10,7)	108 (87–145)	0,072
M <sub>5</sub> c	CBV, ml×100 g <sup>-1</sup>	1,75 (1,6–2,2)	1,8 (1,4–2,3)	103 (80–136)	0,65
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	16,5 (11,4–22,4)	20,0 (12,6–24,8)	85 (62–143)	0,27
	MTT, s	8,4 (7,4–12,4)	7,6 (6,0–9,8)	124 (83–163)	0,060
M <sub>5</sub> s	CBV, ml×100 g <sup>-1</sup>	1,0 (0,8–1,3)	1,0 (0,8–1,2)	104 (78–125)	0,81
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	8,5 (5,1–10,6)	9,8 (7,0–12,4)	88 (59–119)	0,12
	MTT, s	9,8 (8,3–12,8)	9,4 (8,0–10,8)	107 (81–160)	0,022
M <sub>6</sub> c	CBV, ml×100 g <sup>-1</sup>	1,9 (1,5–2,2)	1,9 (1,5–2,3)	100 (76–124)	0,64
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	15,8 (12,4–22,4)	18,6 (13,7–23,3)	90 (71–122)	0,033
	MTT, s	8,6 (6,8–11,4)	7,5 (6,2–9,1)	106 (86–151)	0,31
M <sub>6</sub> s	CBV, ml×100 g <sup>-1</sup>	1,0 (0,8–1,3)	1,0 (0,8–1,1)	109 (100–118)	0,30
	CBF, ml×100 g <sup>-1</sup> ×min <sup>-1</sup>	8,6 (6,4–11,5)	8,4 (6,1–14,4)	110 (90–137)	0,51
	MTT, s	10,4 (8,1–11,1)	10,1 (7,7–10,9)	103 (95–112)	0,28

Note. C – cortical area; S – subcortical area.

The examination showed that patients had an unfavorable metabolic status in the form of overweight and the presence of diabetes mellitus (DM) in every fifth observation. A third of

patients had a history of smoking. 27% of patients had functional limitations according to the mRS before admission to hospital. Recurrent stroke was observed in almost every fifth patient.

Table 4. *ASPECTS variants*

Variants	Maximal value	Estimated value
ASPECTS-10:		
CBV	10	10 (10–10)
CBF	10	9 (8–10)
MTT	10	7 (6–8)
CBV – MTT	–	3 (1–4)
CBF – MTT	–	2 (1–3)
ASPECTS-7:		
CBV	7	7 (7–7)
CBF	7	7 (6–7)
MTT	7	5 (4–6)
CBV – MTT	–	2 (1–3)
CBF – MTT	–	1 (1–2)
CBF + MTT	–	7 (6–7)
ASPECTS	10	10 (7–10)

Moderate neurological deficit (NIHSS scale) and significant prevalence of hemispheric infarctions were observed. In 47% of cases, there was large artery atherothrombotic stroke, in a third of cases – cardioembolic stroke. Mortality in the examined cohort was 7%, almost half of the patients completed the first stage of treatment with an excellent functional outcome. On average, the regression of the neurological deficit during treatment was 6 points NIHSS.

Signs of acute cerebral infarction were observed on CT at admission in one out of every 10 patients, while a significant proportion of patients (39%) had old infarctions. In a control study after 24 hours, the cerebral infarction was not formed in half of the patients undergoing TLT. Hemorrhagic transformation (asymptomatic variants) was observed in 8% of patients (Table 2). Quantitative analysis of PCT maps (Table 3) showed that patients had an increase in MTT (by 106–113%) in most areas of interest of the affected hemisphere in comparison with the intact hemisphere.

The averaged result of the non-enhanced ASPECTS corresponded to its maximum value, as well as the results of perfusion scales based on CBV and CBV/MTT ratio (Table 4). The majority of patients had no severe cerebral blood flow impairments corresponding to cerebral infarction. At the same time, there was a slight decrease in the CBF ASPECTS-10 and a more pronounced

decrease in the results of the MTT-ASPECTS, which indicates the prevalence of reversible perfusion abnormalities. The size of the penumbra, estimated by the ratio of the areas of significant CBV reduction and MTT elongation, averaged 3 points on the 10-point scale and 2 points on the 7-point scale, i.e., did not exceed one-third of the examined area of the brain.

There were no associations between the perfusion ASPECTS, as well as its non-enhanced version and such parameters as age, sex, concomitant pathology, the mRS before admission, the time from the development of symptoms to admission, systolic blood pressure at admission and pathogenetic variant of stroke.

An inverse correlation was found between the results of CBF ASPECTS-10, CBF ASPECTS-7 and the number of red blood cells ( $r=-0.42$ ,  $p=0.010$ ;  $r=-0.31$ ;  $p=0.016$ ). Negative correlations were observed between CBV-MTT ASPECTS-7 and body mass index ( $r=-0.25$ ,  $p=0.047$ ), as well as the concentration of triglycerides ( $r=-0.30$ ,  $p=0.028$ ). There was an association between the MTT ASPECTS-10, CBV-MTT ASPECTS-10, CBF-MTT ASPECTS-10 and percentage of stenosis of the contralateral common carotid artery ( $r=-0.36$ ,  $p=0.026$ ;  $r=0.34$ ;  $p=0.040$ ,  $r=0.35$ ,  $p=0.033$ ). In addition, the CBF ASPECTS-7 was associated with ejection fraction ( $r=0.31$ ,  $p=0.017$ ). The ASPECTS result was associated with glucose level at admission ( $r=0.28$ ,  $p=0.019$ ), the percentage of stenosis of the contralateral internal carotid artery ( $r=0.25$ ,  $p=0.034$ ), the ejection fraction of the heart ( $r=0.32$ ,  $p=0.008$ ), as well as the cerebral infarction size according to the subsequent magnetic resonance imaging (MRI) ( $r=-0.65$ ,  $p<0.001$ ). The results of almost all perfusion scales, except for CBV ASPECTS, are interrelated with non-enhanced ASPECTS ( $p<0.05$ ). In particular, a strong positive correlation was found between the results of CBV + MTT ASPECTS and non-enhanced scale ( $r=0.56$ ,  $p<0.001$ ).

In patients with developed cerebral infarction 24 hours after TLT there were lower MTT ASPECTS-7 (5 (3–6) versus 5 (4–7);  $p=0.031$ ) and non-enhanced ASPECTS (8.5 (5.5–10) versus 10 (9–10);  $p=0.002$ ) and higher CBV-MTT ASPECTS-7 (2 (1–3) versus 1 (0–3);  $p=0.043$ ). Table 5 demonstrates that the results of almost all variants of the ASPECTS (with the exception of CBV ASPECTS and CBF ASPECTS-7) are associated with the severity of stroke on admission to the hospital. However, the majority of perfusion parameters, except the size of the infarct core, were not associated with the final neurologic deficit in patients at discharge.

Table 5. *ASPECTS correlations with neurological and functional status*

Variant	NIHSS admission	NIHSS discharge	$\Delta$ NIHSS	RMI	mRS
ASPECTS-10:					
CBV	NS	NS	NS	NS	NS
CBF	$r=-0.48$ ; $p=0.003$	NS	$r=-0.36$ ; $p=0.027$	NS	NS
MTT	$r=-0.58$ ; $p<0.001$	NS	NS	NS	NS
CBV – MTT	$r=0.59$ ; $p<0.001$	NS	$r=0.32$ ; $p=0.056$	NS	NS
CBF – MTT	$r=0.37$ ; $p=0.021$	NS	NS	NS	$r=0.30$ ; $p=0.065$
ASPECTS-7:					
CBV	NS	NS	NS	NS	NS
CBF	NS	NS	NS	NS	NS
MTT	$r=-0.54$ ; $p<0.001$	NS	$r=-0.32$ ; $p=0.016$	NS	NS
CBV – MTT	$r=0.55$ ; $p<0.001$	NS	$r=0.37$ ; $p=0.004$	NS	$r=0.25$ ; $p=0.054$
CBF – MTT	$r=0.37$ ; $p=0.003$	NS	$r=0.31$ ; $p=0.016$	NS	NS
CBV + MTT	$r=-0.38$ ; $p=0.002$	$r=-0.28$ ; $p=0.036$	NS	NS	NS
ASPECTS	$r=-0.49$ ; $p<0.001$	$r=-0.38$ ; $p<0.001$	NS	$r=0.28$ ; $p=0.023$	$r=-0.24$ ; $p=0.044$

Note. NS – non-significant correlation.



At the same time, some variants of ASPECTS were predictors of the dynamics of neurological deficit. The marked positive dynamics of NIHSS was associated, in particular, with a greater prevalence of the penumbra. There was also a link between the low level of independence assessed by the mRS at discharge and a greater size of the penumbra. The result of NIHSS on admission and at discharge, the degree of mobility and functional independence of patients were associated with the result of the non-enhanced ASPECTS.

**Discussion.** The study allowed to characterize the cerebral blood flow according to PCT scans and its relationship with clinical and instrumental data and functional status of patients with IS who underwent TLT. The patients were characterized by an unfavorable cardiovascular and metabolic profile. The study showed a low mortality rate and a high frequency of excellent functional outcomes in these patients, which indicates the safety of TLT and its undoubted effectiveness in the acute period of stroke.

A significant proportion of patients (39%) had a history of cerebrovascular disease, including stroke (18%). This probably determined the presence of functional limitations before the development of index stroke in a third of the patients, which certainly reduces the expected effectiveness of reperfusion therapy. At the same time, the majority of patients (90%) did not have CT signs of acute infarction, which may be due to the admission in the first 2 hours after the onset of symptoms. A significant proportion of patients (32%) had cardioembolic stroke, which may also be due to the sampling of patients primarily on the principle of getting into the therapeutic window. The study noted a low incidence of hemorrhagic transformation (8%).

Quantitative analysis of PCT data revealed an increase in MTT in most areas of the affected hemisphere in comparison with the intact hemisphere. The study attempted to determine the optimal ASPECTS variant for predicting the neurological and functional outcome of an acute stroke. To that end, scales based on one of the perfusion parameters (CBV, CBF and MTT) and their combination characterizing the core of infarction and the mismatch zone were calculated and analyzed. The prevalence of potentially reversible perfusion changes was revealed, and this is quite natural, given the short period after the development of stroke. The average size of the penumbra was 3 points (zones) on the ASPECTS. We did not find any relationship between the results of the ASPECTS and the time from the development of symptoms to admission. This is consistent with the results of the study, which showed that, after adjustment for imaging variables, onset-to-treatment time was not significantly associated with disability-free life expectancy. [14].

The perfusion parameters, in particular the penumbra size, were associated with the degree of stenosis of the contralateral carotid artery, BMI and blood triglyceride level. Also, red blood cell count and the ejection fraction influenced the parameters of cerebral blood flow. The significance of stenosis of the contralateral carotid artery is probably due to compensatory mechanisms. Obviously, the contralateral carotid artery plays the most important role in compensating for the impaired blood flow in the affected hemisphere in the most acute period of stroke. Thus, a greater degree of stenosis is associated with an increase in perfusion mismatch.

The result of the non-enhanced ASPECTS was also associated with the given spectrum of parameters and correlated with the size of the formed infarction according to the MRI.

Perfusion scales data correlated with the result of the non-enhanced scale, which indicates its high sensitivity. A strong correlation between the infarct core size on the CBV + MTT ASPECTS and the result of the non-enhanced scale indicates a high significance of this combination as a marker of irreversible brain damage. It corresponds to the data of other authors on the equivalence of the volumetric parameters of PCT and the result of the non-enhanced scale [7]. In patients in whom TLT was ineffective and infarction was formed, there was an increase in MTT, an increase in the size of the penumbra and low result of the non-enhanced ASPECTS.

The studied ASPECTS variants were associated with the level of neurological deficit, its dynamics and functional outcome of the acute period of stroke, which is confirmed by previously published data on the relationship between perfusion parameters and clinical prognosis [15]. Thus, a greater severity of stroke is associated with a reduction in scores based on speed and time parameters, the combination of CBV and MTT, as well as CBF and MTT. The severity of neurological deficit before reperfusion therapy is directly proportional to the size of the penumbra and the infarct core. Only the size of the infarct core and the sum of the early ischemic signs were predictors of the neurologic deficit at discharge, which agrees with the results of the study by M. Padroni et al. [12]. At the same time, in contrast to the results of this study, which also shows a clear association of CBV ASPECTS, but not CBV-MTT ASPECTS, with the result of the mRS after 3 months, in our work it was the increase in the penumbra size that predicted the functional limitations. These differences are probably related to the discrepancy between the proportion of patients with effective recanalization and reperfusion, which is the decisive factor determining the prognostic value of penumbra measurement [16], and also to the time of evaluation of functional status. In the acute period of the disease in patients with ineffective TLT the size of the penumbra is a predictor of the final size of infarction. Perfusion parameters, in particular the penumbra size, are associated with the dynamics of neurological deficit: for example, a significant decrease in the NIHSS is characteristic of patients with a greater prevalence of the ischemic penumbra zone.

**Conclusion.** Both non-enhanced and perfusion ASPECTS have a high predictive value for the neurological and functional status of patients at the time of completion of the first stage of treatment and demonstrate a high degree of synergy. In this case, in contrast to non-enhanced ASPECTS, its perfusion variants, in particular, characterizing the size of the penumbra, are a marker of the expected regression of neurologic deficit against the background of TLT. In addition to the penumbra size, another informative perfusion parameter is the size of the infarct core, which determines the severity of the neurological deficit at discharge.

Despite the positive results of our study, it has a number of limitations: the absence of a control group, the absence of analysis of recanalization and reperfusion rate during TLT, the absence of direct measurement of the core and the penumbra zone. We performed only a single dynamic evaluation of CT data after 24 hours, and MRI was not performed in all patients. Limitations of the software allowed to present only relative, but not absolute threshold values of perfusion parameters. However, the importance of an individual approach in determining the indications / contraindications for the most effective and affordable treatment of IS demonstrates the relevance of the work performed and the prospects for further research

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