

# Pathological Changes in Microcirculation in the Early Recovery Period of Ischemic Stroke

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## Abstract

The rates of morbidity and mortality due to stroke among people of working age have been growing in recent years and have increased by more than 30% over the past 10 years. An important place among the complications of ischemic stroke is motor disorders, accompanied by persistent muscle hypertension and disorders of peripheral microcirculation. The purpose of the study: to reveal the features of microcirculatory disorders in patients in the early recovery period of ischemic stroke. Violations of peripheral hemodynamics are very typical for patients in the early recovery period of ischemic stroke. They are more pronounced on the side of the paresis. In the early recovery period, more severe forms of microcirculation disorder were observed more often on the paretic limb, accompanied by signs of a sharp decrease in blood flow, increased vascular tone with the phenomena of blood stagnation. The revealed disorders of the microcirculatory link allow the use of disaggregants, peripheral vasodilators, venotonics, massage, physiotherapy, reflex therapy, and physical therapy with the involvement of the patient and healthy limbs to be recommended to patients in the early recovery period after ischemic stroke. All this should contribute to improving the effectiveness of rehabilitation of this category of patients during the early recovery phase.

**Keywords:** Ischemic stroke; Early recovery period; Microcirculation; Vascular tone; Blood flow

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**Citation:** Hu B, Kulikov EV, Vatnikov YuA (2019) Pathological Changes in Microcirculation in the Early Recovery Period of Ischemic Stroke. *Prensa Med Argent*, Volume 105:2. 112. DOI: <https://doi.org/10.47275/0032-745X-112>.

**Received:** March 07, 2019; **Accepted:** March 25, 2019; **Published:** April 13, 2019

## Introduction

Currently, researchers are paying increasing attention to the issues of hemostasis and hemorheology in mammals [1,2] and in humans [3,4]. This is due to the fact that dysfunctions leading to the violation of these indicators can strongly limit life expectancy [5-7], determine the state of health of the organism [8-10] and its overall functional status [11-13]. This has been proved at various experimental [14-17] and clinical models [18-20]. This is clearly confirmed by the example of patients with vascular dysfunction [21,22], arterial hypertension [23,24] who underwent thrombotic events, including ischemic stroke [25]. Particularly close attention of modern medicine to the latter condition is due to the fact that cerebral stroke now occupies a leading position among the causes of disability and mortality of the population [26]. The rates of morbidity and mortality due to stroke among people of working age have been growing in recent years and have increased by more than 30% over the past 10 years. Stroke is very dangerous because about 30% of patients who have suffered from it constantly need outside help, another 20% cannot walk by them, and only 8% of surviving patients can later return to their previous work [27].

An important place among the complications of ischemic stroke is motor disorders, accompanied by persistent muscle hypertension and peripheral microcirculation disorders [28]. Currently, much attention is paid to secondary developmental disorders of microcirculation in

the paretic limb [29]. It is believed that its optimization in the process of complex multi-profile rehabilitation is a reserve for the recovery of post-stroke patients [30,31].

The detection of microcirculatory disorders in patients with ischemic stroke and their timely correction in the early stages of neuro-rehabilitation will improve the quality of life and enhance the effectiveness of early rehabilitation in this category of patients.

The purpose of the study: to reveal the features of microcirculatory disorders in patients in the early recovery period of ischemic stroke.

## Materials and Methods

The research was approved by the Ethics Committee of Peoples Friendship University of Russia (record №5 from 12.05.2014). A survey of 58 patients aged 43 to 75 years, of which 36 men and 22 women who underwent ischemic stroke were examined. All patients signed informed consent to participate in the study. The study was conducted in the early (after  $4.0 \pm 0.5$  months) recovery period after the ischemic stroke.

The diagnosis was verified with the help of anamnesis, clinical picture, laboratory indicators, CT scan of the brain, ultrasonic dopplerography of the vessels of the head and neck. All patients had a motor deficit from mild to moderate hemiparesis, due to the presence of a lesion of the brain, confirmed by the method of neuroimaging.



Data analysis with ultrasound Doppler scanning of the brachiocephalic arteries of patients showed the presence in half of patients of echographic signs of hypertensive angiopathy. In 34.5% of patients, stenosing arteriosclerosis of arteries of the carotid basin was visualized, 60% of them had moderate stenosis, and 40% had severe stenosis. 51.7% of patients had signs of non-stenosing atherosclerosis and only 13.8% of hemodynamically significant changes were not detected. Patients with hypertension could be included in the study. The study did not include patients with diabetes mellitus, with severe cardiac, hepatic or renal insufficiency. The control group is represented by 34 clinically healthy people aged 44 to 74 years, including 15 men and 19 women.

All the examined were carried out laser Doppler flowmetry (LDF) on the LAKK-04 instrument manufactured by Lazma (Russia). The study was carried out in the morning, at the same temperature in the room (about 21-24°C). Subjects during the study were in a sitting position. Before the study, the patients stayed calm for 15 minutes, did not smoke and did not eat or drink. The recording time was 6 minutes. The results were processed using a computer program (Table 1).

During the treatment of LDF-gram the following characteristics of microcirculation were determined: PM (microcirculation parameter), recorded in relative perfusion units (PE). Its value reflected the degree of perfusion, mainly the erythrocyte fraction, and the unit volume of tissue per unit time. The mean square deviation (RMS) of the detected Doppler signals from the mean value was taken into account. It characterized fluctuations in the flow of erythrocytes over time (or the level of the flask).

An amplitude-frequency analysis of hemodynamic rhythms of tissue blood flow oscillations was performed in the frequency range from 0.01 to 1.2 Hz. Among the considered fluctuations in blood flow reflected in the amplitude-frequency spectrum of the LDF-

gram, very low-frequency (0.01-0.03 Hz) oscillations (VLF) are most physiologically significant, characterizing the effect of humoral-metabolic factors on the state of microcirculation. Low frequency (0.05-0.15 Hz) oscillations (LF) were registered, which are caused by the spontaneous periodic activity of smooth myocytes in the arteriolar wall. A decrease in the amplitude of low-frequency fcomksmotion may indicate a spasm of the vessels of the microvasculature. High-frequency oscillations in the range of 0.2-0.4 Hz (HF-respiratory rhythms) were also taken into account. They are caused by changes in pressure in the venous section of the vascular bed. In addition, high frequency (1.0-1.2 Hz) pulse oscillations (CF) were recorded, which had a small fluctuation amplitude and caused changes in the rate of movement of erythrocytes in microvessels caused by changes in systolic and diastolic pressures.

In the course of the amplitude-frequency analysis of the LDF-gram, the contribution (P%) of various rhythmic components was considered, which was estimated from their power as a percentage of the total power of the spectrum of the flaxemias. An increase in the pulse wave amplitude means an increase in blood flow to the microcirculatory bed [32,33]. The ratio of active modulations of skin blood flow, caused by myogenic and neurogenic mechanisms, and passive modulations was calculated as the index of flaxemias:  $IFM = ALF / (ANF + ACF)$ . It is known that the index of fluctuations decreases with decreasing mechanisms of active modulation (with spasm of bringing arterioles), as well as with strengthening of passive modulation mechanisms caused by stagnation of blood in the venous bed, changes in the rate of movement of erythrocytes in micro-vessels. In the study, respiratory and occlusive samples were performed [34].

Statistical analysis of the results of the study was carried out using the software "Statistics 6.0" with the use of parametric and nonparametric methods (Student's criteria, Mann-Whitney). Critical significance level was assumed to be  $p < 0.05$ .

**Table 1.** Hemodynamic parameters in the early recovery period of ischemic stroke.

Parameters of LDF-gram	Early recovery period, M ± m, n=58		Control, M ± m, n=34
	Healthy limb	Paretic limb	
Parameter of microcirculation, perfusion units	8.4 ± 0.35	8.2 ± 0.63 p<0.05	8.6 ± 0.47
The level of the flask (mean square deviation), perfusion units	0.98 ± 0.033 p <sub>i</sub> <0.05	0.91 ± 0.023 p<0.05	1.04 ± 0.055
Index of flaxemias, conventional units	0.33 ± 0.011 p <sub>i</sub> <0.05	0.29 ± 0.20 p<0.05	0.34 ± 0.16
Very low frequency (VLF) oscillations, Hz	0.42 ± 0.015 p <sub>i</sub> <0.05	0.35 ± 0.019 p<0.05	0.43 ± 0.014
Low-frequency (LF) oscillations, Hz	0.27 ± 0.008 p <sub>i</sub> <0.05	0.24 ± 0.010 p<0.05	0.28 ± 0.009
High-frequency respiratory vibrations (HF), Hz	0.16 ± 0.005	0.13 ± 0.011 p<0.05	0.18 ± 0.006
High-frequency pulse (CF) oscillations, Hz	0.63 ± 0.007	0.56 ± 0.020 p<0.05	0.66 ± 0.012
%contribution VLF	26.8 ± 0.40 p <sub>i</sub> <0.05	23.1 ± 0.33 p<0.05	27.5 ± 0.59
%contribution LF	18.5 ± 0.14 p <sub>i</sub> <0.05	16.2 ± 0.16 p<0.05	19.2 ± 0.25
%contribution HF	12.0 ± 0.20 p <sub>i</sub> <0.05	10.0 ± 0.15 p<0.05	12.7 ± 0.12
%contribution CF	42.0 ± 0.10 p <sub>i</sub> <0.05	38.1 ± 0.17 p<0.05	42.3 ± 0.21
Vascular tone, units	3.9 ± 0.15 p <sub>i</sub> <0.05	4.2 ± 0.20 p<0.05	3.8 ± 0.16
Degree of decrease in blood flow in the respiratory sample,%	33.2 ± 0.26 p <sub>i</sub> <0.01	24.1 ± 0.16 p<0.01	40.0 ± 0.11
Reserve of capillary blood flow,%	147.0 ± 0.71 p <sub>i</sub> <0.01	132.2 ± 0.045 p<0.01	159.1 ± 0.25



## Results and Discussion

In the early recovery period, all patients had hemiparesis of moderate severity. Analysis of their microcirculation showed that 100% of the patients had a stasis form of microcirculation due to a sharp decrease in blood flow in the capillary part of the microcirculatory bed and increased aggregation of erythrocytes. The microcirculation index was variable, the flux was reduced. In the frequency-amplitude spectrum, the vasomotor waves of the LF rhythm were reduced; there was a moderate decrease in the amplitude and percentage contribution of the HF rhythm, as well as a decrease in the amplitude and percentage contribution of the CF rhythm, as well as a decrease in the index of floxemia. At the same time, small breaches of microcirculation were observed on the healthy limb.

All patients with ischemic stroke along with a disorder of central hemodynamics had peripheral microcirculatory disorders on paretic and on healthy limbs. At the same time, violations of central hemodynamics were revealed in the form of echographically confirmed hypertonic angiopathy, stenotic and non-stenosing atherosclerosis of the vessels of the carotid basin.

Thus, violations of peripheral hemodynamics are very typical for patients in the early recovery period of ischemic stroke. They are more pronounced on the side of the paresis. In the early recovery period, more severe forms of microcirculation disorder were observed more often on the paretic limb, accompanied by signs of a sharp decrease in blood flow, increased vascular tone with the phenomena of blood stagnation. The revealed disorders of the microcirculatory link allow the active use of disaggregants, peripheral vasodilators, venotonics, massage, physiotherapy, reflexotherapy [35], therapeutic physical training [36] involving patients and healthy limbs, to be recommended to patients in the early recovery period after ischemic stroke. All this should help improve the rheological properties of red blood cells [37-41] and increase the efficiency of rehabilitation of this category of patients during the early stage of recovery.

## Conclusion

In the early recovery period of ischemic stroke, violations of peripheral hemodynamics are noted. They are more pronounced on the side of the paresis. In the early recovery period, more severe forms of microcirculation disorder were observed more often on the paretic limb, accompanied by signs of a sharp decrease in blood flow, increased vascular tone with the phenomena of blood stagnation. The revealed disorders of the microcirculatory link allow recommending to patients in the early recovery period after ischemic stroke active use of medicamentous and non-medicamentous agents that can improve the rheological properties of red blood cells and improve the efficiency of rehabilitation of this category of patients during the early stage of recovery.

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