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О.А. Ефремова*, Е.В. Бондаренко, Л.А. Камышникова, Т.П. Голивец, И.И. Хамнагадаев

Белгородский государственный национальный исследовательский университет, Белгород, Россия

ДИНАМИКА ВОССТАНОВЛЕНИЯ ПАЦИЕНТОВ С ИШЕМИЧЕСКИМ ИНСУЛЬТОМ В ЗАВИСИМОСТИ ОТ ПОКАЗАТЕЛЕЙ АРТЕРИАЛЬНОГО ДАВЛЕНИЯ И ЕГО ВАРИАБЕЛЬНОСТИ

O.A. Efremova*, E.V. Bondarenko, L.A. Kamyshnikova, T.P. Golivets, I.I. Khamnagadaev

Belgorod State National Research University, Belgorod, Russia

Recovery Dynamics in Patients with Ischemic Stroke Depending on the Blood Pressure Indicators and Its Variability

Резюме

Цель — изучение неврологического и функционального восстановления у пациентов после ишемического инсульта в зависимости от показателей артериального давления (АД) и его вариабельности. **Материалы и методы**: обследовано 150 пациентов с ишемическим инсультом и артериальной гипертонией (АГ), которые находились на стационарном лечении в неврологическом отделении (76 (50,7 %) мужчин и 74 (49,3 %) женщин, средний возраст 67,4±7,3 лет). Всем пациентам проводили общепринятые физикальные и лабораторные исследования, измерение АД в динамике; для оценки тяжести неврологического дефицита на момент поступления в стационар, в динамике острого периода (до 21 суток) и на 21 сутки использовалась Шкала тяжести инсульта Национальных институтов здоровья США — NIHSS (National Institutes of Health Stroke Scale). **Результаты.** Установлено, что последствия острого периода инсульта зависят от уровня АД и его вариабельности в начале острого периода. Более чем 50–процентная вероятность снижения балла по NIHSS наполовину (от исходного) прогнозируется при наличии у пациента показателя стандартного отклонения (SD) систолического артериального давления (САД) на 1– 3 сутки менее 12,4 мм рт. ст. Кроме этого, SD САД на 1– 3 сутки и 1– 6 сутки, и SD диастолического артериального давления (ДАД) с 1 по 3 сутки являются наиболее значимыми при оценке связи со степенью функциональных нарушений в конце острого периода инсульта. **Заключение.** Уровень АД и его вариабельность в течение острого периода ишемического инсульта позволяют прогнозировать тяжесть неврологического дефицита и функциональные последствия инсульта в восстановительном периоде (до 21 суток).

Ключевые слова: *ишемический инсульт, артериальная гипертония, функциональный дефект, функциональное восстановление, вариабельность артериального давления*

Конфликт интересов

Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

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*Контакты: Ольга Алексеевна Ефремова, e-mail: efremova.bgu@gmail.com
*Contacts: Olga A. Efremova, e-mail: efremova.bgu@gmail.com
ORCID ID: https://orcid.org/0000-0002-6395-1626

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Abstract

The study aims to neurological and functional recovery in patients after ischemic stroke depending on blood pressure (BP) parameters and its variability. **Materials and methods**: We examined 150 patients with ischemic stroke and arterial hypertension (AH) who were hospitalized in the neurological department (76 (50,7 %) men and 74 (49,3 %) women, mean age 67,4±7,3 years). All patients underwent standard physical and laboratory examinations, measurement of blood pressure in dynamics; The National Institutes of Health Stroke Scale (NIHSS) was used to assess the severity of neurological deficits at the time of admission to the hospital, in the dynamics of the acute period (up to 21 days) and on the 21st day. **Results:** It was found that the consequences of the acute period of stroke depend on the level of blood pressure and its variability at the beginning of the acute period. A more than 50 percent probability of a decrease in the NIHSS score by half (from baseline) is predicted if the patient has a standard deviation (SD) systolic blood pressure (SBP) less than 12,4 mm Hg on days 1– 3. In addition, SD SBP on days 1– 3 and 1– 6 days, and SD diastolic blood pressure (DBP) from 1 to 3 days are the most significant in assessing the relationship with the degree of functional impairment at the end of the acute period of stroke. **Conclusion:** The level of blood pressure and its variability during the acute period of ischemic stroke makes it possible to predict the severity of the neurological deficit and the functional consequences of stroke in the recovery period (up to 21 days).

Key words: *ischemic stroke, arterial hypertension, functional defect, functional recovery, blood pressure variability*

Conflict of interests

The authors declare no conflict of interests

Sources of funding

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ADMV — average of daily mean value, AH — arterial hypertension, BI — Barthel index, BP — blood pressure, CT — computed tomography, DBP — diastolic blood pressure, ECG — electrocardiography, IS — ischemic stroke, MRI — magnetic resonance imaging, NIHSS — National Institutes of Health Stroke Scale, ROC — receiver operating characteristic, SBP — systolic blood pressure, SD — standard deviation, TCD — transcranial Doppler

Introduction

Severe social consequences of stroke and high costs of its management encourage the medical community to improve the measures for prevention and treatment of acute cerebrovascular accident [1, 2], rehabilitation approaches [3–5], and predicting the consequences of an acute cerebral accident [6–8]. High systolic blood pressure (SBP) is one of the main modified risk factors for stroke that determine its severity [9–11]. The problem of stroke with underlying arterial hypertension (AH) is very urgent in Russia, given the fact that according to the Ministry of Health of the Russian Federation, 4,303 thousand patients with cardiovascular diseases were registered in 2020 compared to 2000 when this value was 2,483 thousand of the entire population (according to the information of Federal State Statistics Service for 2020, https://rosstat.gov.ru/folder/13721).

Much attention is paid to the analysis of blood pressure (BP) levels and the parameters of neurological recovery after ischemic stroke (IS) [12–15]. It is thought that BP variability can be a predictor of IS consequences [16, 17], however, its correlation with the stroke characteristics in the acute period, the timing of BP measurement, and stroke outcome remains debatable [18, 19].

Hypertension is a key risk factor for vascular cognitive disorders, in particular, stroke [20], and stroke is one of the determining factors in the progression of vascular dementia [21–23]; its prevalence after the first IS increases to 23 % [24]. Meanwhile, the changes of functional disorders over time in the post-stroke period that depend on the stage of AH, indicators of cerebral atherosclerosis, BP variability, especially at the disease onset, remain unknown.

The **objective** of the study was to analyze the neurological and functional rehabilitation of patients after ischemic stroke depending on BP parameters and variability.

Materials and Methods

This study is based on the analysis of 24-hour BP variability and on the assessment of the severity of neurological deficit in 150 patients (76 (50.7 %) males and 74 (49.3 %) females, mean age (67.4 ± 7.3) years) with ischemic stroke and AH hospitalized into the Neurological Department of Borisov Central District Hospital at the period from 2018 to 2021. During this study, the course of IS associated with underlying essential AH within six months from stroke was analyzed in details.

Inclusion criteria: primary ischemic stroke (ICD-10I code 63.5), signing the voluntary informed consent form, hospitalization within 6 hours after stroke, history of essential (primary) hypertension, possibility of contact with the patient and their family during the entire follow-up period, obtaining information from medical records, interviews or emails.

Exclusion criteria: hemorrhagic stroke, recurrent ischemic stroke, ischemic stroke of unknown subtype, secondary (symptomatic) hypertension, coma.

Before the start of the examination of patients, informed consent was obtained for their participation in this study in accordance with the standards of the Declaration of Helsinki of the World Medical Association Ethical Principles for Conducting Medical Research Involving a Person as a Subject and the Rules of Clinical Practice in the Russian Federation approved by the Order of the Ministry of Health of the Russian Federation No. 266 dated June 19, 2003. Preliminary approval was obtained from the Committee on Bioethical Expertise and Research Ethics of the Medical Institute of the BelSU National Research University, record No. 56 dated February 12, 2019. In case of pronounced neurological deficit (paresis or plegia of upper limbs, impaired higher cortical functions, etc.), the informed consent was signed by patient's legal representatives — relatives or other legally authorized persons.

The patients were monitored during the admission and hospital stay, in the acute period of stroke on day 21 and within six months from the IS onset. Endpoints: BP level, severity of neurological deficit, Barthel index.

The ischemic stroke was diagnosed based on the results of clinical and neurological examination and confirmed by the results of a neuroimaging examination of brain according to the protocol for the management of patients with stroke of the National Standard of the Russian Federation, 2009 [25] and the Guidelines (Procedures) for the Provision of Emergency Medical Care in Acute Cerebrovascular Events [26].

AH was diagnosed according to the National Clinical Guidelines on Hypertension in Adults (2020) [27]. BP was registered using one standardized mechanical blood pressure monitor Gamma 700K. BP was measured according to the standard method in relaxed environment after a 5-minute rest [27]. BP was measured during hospitalization: repeated measurements were taken every 4 hours for 6 days after IS onset. BP variability was assessed using the following parameters: mean SBP, DBP, maximum SBP and DBP values, standard deviation (SD) estimated for SBP and DBP at each timepoint within 6 days and for the intervals of day 1–3, day 1–6, day 3–6.

On discharge from the hospital, each patient and their relatives were provided with detailed oral and written instructions on correct measuring blood pressure at home; their ability to master this skill was checked; it was suggested to keep a BP monitoring log as per the developed guidelines for BP measuring at home [27]. The patients were recommended to measure BP twice a day: in the morning (before taking medications) and in the evening (before meals). At the end of each month within six months after discharge from the hospital, information on the measured BP values was collected by phone.

To assess the severity of neurological deficit on admission and over time on day 21, the authors used the US National Institutes of Health Stroke Scale (NIHSS) — a validated and commonly used method for the standardized assessment of stroke severity [28–30].

To monitor functional recovery in the acute period and within six months after IS, Barthel index (BI) that assesses the activities of the daily living of patients was used [31, 32].

During their hospital stay, the patients received antihypertensive therapy prescribed after the consultation with a cardiologist in accordance with the corresponding domestic guidelines [27]. After discharge from the hospital, the recommended antihypertensive therapy continued under the supervision of a family physician.

All patients underwent standard laboratory tests and instrumental examinations that included standard 12-lead ECG, brain magnetic resonance imaging (MRI), ultrasound duplex of the vessels of head and neck, and transcranial Doppler (TCD).

Almost half of the examined patients (48.0 %) had cortical and subcortical lesions of brain, see Table 1.

In should be noted that 22 (14.7 %) patients had one lesion and 128 (85.3 %) patients had two lesions. Small (up to 15 mm in diameter), medium (15–30 mm) and large (more than 30 mm) lesions were diagnosed with the same statistical frequency, see Table 2.

Table 1. *Localization of the focus of ischemia in patients with hypertension*

Localization	Abs.	%
Cortical-subcortical	72	48,0
Subcortical	23	15,3
Basal ganglia	29	19,3
Stem-cerebellar	26	17,3

Table 2. *The size of the focus of ischemic stroke*

Size, mm	Abs.	%
More than 30	51	34,0
15-30	59	39,3
Under 15	40	26,7

Stage 1 AH was observed in 30 (20 %) patients, stage 2 AH — in 72 (48.0 %) patients, stage 3 AH — in 48 (32 %) patients, see Figure 1.

The patients were divided into groups according to AH duration: with the onset up to 5 years ago, 6 to 10 years ago and more than 10 years ago. 28 (18.7 %) patients reported of the duration of the disease up to 5 years, 67 (44.7 %) — 6 to 10 years, 55 (36.7 %) — more than 10 years.

Alongside with AH, the examined patients had other comorbidities. Coronary heart disease was found in 137 (91.33 %) patients, including CHD with atrial fibrillation — in 22 (14.67 %), type II diabetes mellitus — in 17 (11.33 %), past myocardial infarction — in 13 (8.67 %) patients, chronic diseases of gastrointestinal tract — in 97 (64.67 %), of lungs — in 37 (24.67 %), of kidneys — in 7 (4.67 %) patients.

On admission, the severity of neurological deficit according to the NIHSS scale ranged from 3 to 20 points, with average value of 12.5 (6.3–18.6) points. The distribution of patients with ischemic stroke according to NIHSS score is shown in Figure 2.

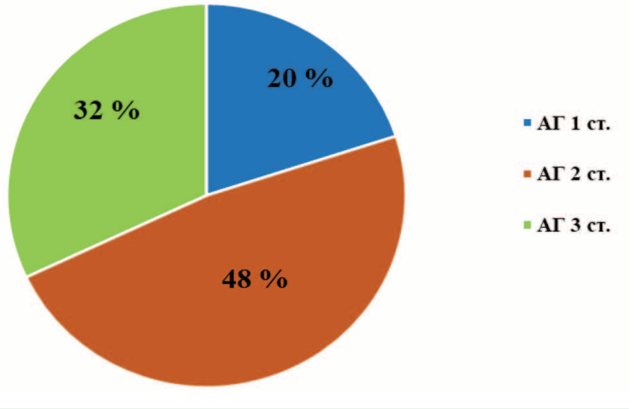

Figure 1. *Distribution of patients according to the degree of arterial hypertension, %*

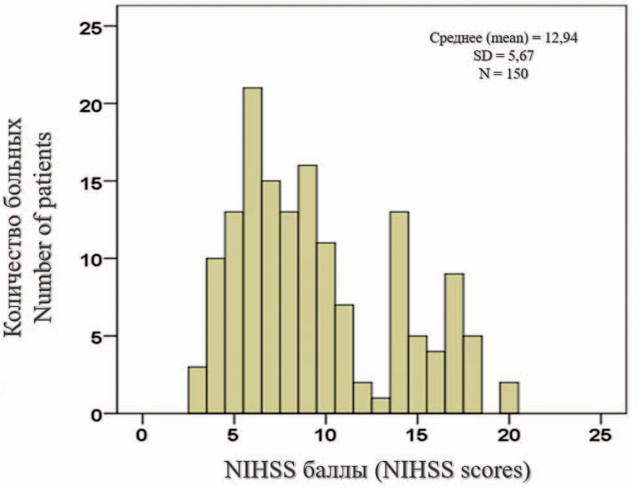

Figure 2. *Distribution of patients with ischemic stroke by NIHSS score*

Statistical processing of the obtained results was performed using IBM SPSS Statistics Base v.22 software for statistical analysis. Data for parameters with normal distribution are presented as arithmetic mean and standard deviation (M ± SD), and for parameters with non-normal distribution — as a median with interquartile range (Me (IQR)). Parametric methods were used for quantitative parameters with normal distribution; in other cases non-parametric methods were used. To assess qualitative parameters, parameters with non-normal distribution, and parameters with indeterminate distribution, Spearman's correlation coefficient was used. Pearson correlation coefficient was used to measure the degree of linear relationship between two variables in assessing quantitative parameters. For comparative analysis of samples with normal distribution, ANOVA analysis of variance and paired Student's t-test for independent and dependent samples were used. To compare three or more separate groups, the Kruskal — Wallis test and the median test were used. Independence test was performed using the chi-square test with Yates's correction for continuity and Fisher's exact test. For analysis of samples that did not correspond to the laws of normal distribution, the following non-parametric methods were used: paired Wilcoxon test for related samples and Mann — Whitney U test for independent samples.

The changes in the recovery of neurological deficit over time (decrease in NIHSS score in %) were calculated using the formula [29]:

$$\frac{100 \times (\text{NIHSS score on day 1} - \text{NIHSS score on day 21})}{\text{NIHSS score on day 1}}$$

To analyze BP variability in this study, we used standard deviation (SD). To assess the role of SBP SD parameters on days 1–3 as a predictor of stroke severity according to NIHSS at discharge, we used binary logistic regression analysis with the coefficient of determination (R^2).

Results and Discussion

During hospitalization in the Emergency Department, mean SBP was (163.17 ± 2.04) mm Hg, although according to the documents of emergency team, this parameter by the time of the first measurement after stroke development was significantly higher ($p = 0.001$) and amounted to (181.13 ± 2.02) mm Hg. This was probably the result of the use of medications at the prehospital stage.

After 8 hours, mean SBP was significantly higher than on admission: (177.8 ± 2.4) mm Hg, ($p = 0.001$). Subsequently, during the next 56 hours, there was a trend towards a decrease in mean BP and its stabilization at the level that was before stroke. Mean DBP values were characterized by the absence of significant fluctuations during the first 12 hours and by a smaller range of these fluctuations. At the same time, one should mention that in the acute period (first two days) a large range of individual daily fluctuations in the values of systolic and diastolic pressure remained: from 280 to 100 mm Hg and from 100 to 60 mm Hg, respectively (statistically significant differences on day 1 and day 2 compared to other days, $p < 0.05$), see Figure 3.

One of the objectives of this study was to determine the parameters that characterize AH course and are associated with the severity of neurological deficit in the presence of stroke on admission.

In strokes with neurological deficits of different severity, mean SBP values significantly differed at 8, 12, 16, and 20 hours. After 24 and 28 hours, significant differences remained only between mild and severe stroke in terms of mean systolic blood pressure values, see Table 3.

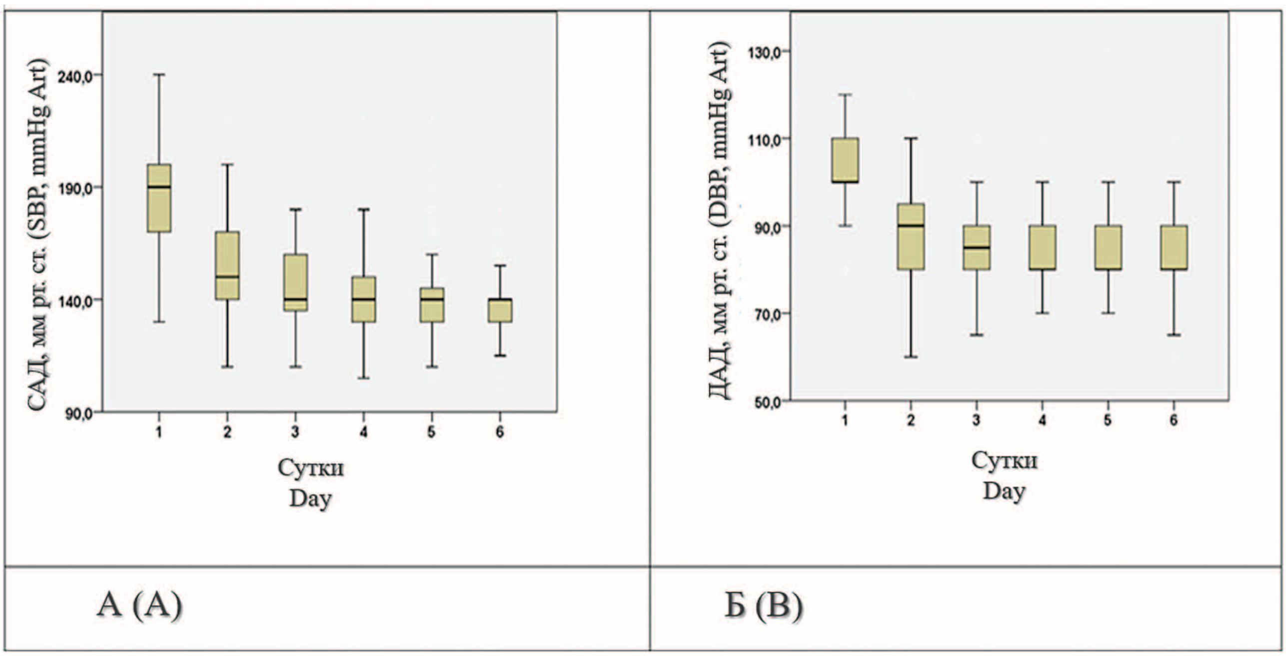

Figure 3. *Medians and quartiles of SBP (A) and DBP (B) values for the first six days of the acute period of stroke*

Note: SBP — systolic blood pressure, DBP — diastolic blood pressure (Days 1 and 2, SBP and DBP significantly differed from BP values on the following days, $p < 0.05$)

Table 3. *Mean SBP values in the first two days of stroke depending on the severity of neurological deficit according to NIHSS upon admission to the hospital (M±SD)*

Time after stroke, hour	The severity of the neurological deficit			p– value		
	Легкая/ Mild n=26	Средняя/ Medium n=86	Тяжелая/ Severe n=38	1vs 2	1 vs 3	2 vs 3
4	160,9±17,3	166,2±26,0	157,6±25,3	0,525	0,895	0,265
8	157,1±22,9	173,0±25,0	202,6±25,3	**0,003**	**0,001**	**0,001**
12	150,8±21,4	163,7±23,2	184,4±26,5	**0,012**	**0,001**	**0,001**
16	148,1±17,3	157,2±21,3	170,1±25,9	**0,035**	**0,001**	**0,007**
20	142,9±14,3	152,6±19,5	162,5±25,3	**0,021**	**0,001**	**0,006**
24	141,4±10,7	148,4±19,5	156,7±25,9	0,095	**0,006**	0,097
28	139,4±13,8	145,6±18,5	155,7±24,0	0,088	**0,005**	**0,036**
32	137,7±15,8	146,5±17,4	145,6±25,3	**0,035**	0,065	0,996
36	141,9±20,4	144,4±16,7	146,7±25,3	0,467	0,258	0,462
40	138,6±16,8	142,7±16,3	139,2±20,9	0,181	0,792	0,178
44	137,7±13,8	139,7±13,9	137,2±19,1	0,718	0,879	0,547
48	136,7±14,3	137,9±13,0	136,3±20,9	0,682	0,923	0,584

Note: p– values — significant differences between respective groups, SBP — systolic blood pressure

Mean DBP values (mm Hg) turned out to be less sensitive in indicating differences between different stroke severity and reliably demonstrated the difference between three stages only after 8 hours ((98.3 ± 12.2) mm Hg — mild neurological deficit, (101.3 ± 25.0) mm Hg — moderate, and (112.5 ± 28.7) mm Hg — severe neurological deficit, all p values < 0.05) and partly after 12 hours (significant difference was only between mild ((99.8 ± 16.3) mm Hg) and severe ((115.2 ± 22.2) mm Hg) stages of neurological deficit, p = 0.001) after acute cerebrovascular accident.

Considering the fact that in the acute period of stroke a significant range of individual 24-hour BP fluctuations is registered, a possible informative indicator of the progress of stroke (a prognostic factor) may be the 24-hour BP variability, calculated as a standard deviation from 24-hour average BP.

Analysis of SBP variability during 24 hours in the most acute period of stroke revealed the highest mean SD value on day 1 that was (18.7 ± 4.4) mm Hg, with fluctuations in individual SD values from 10.3 to 23.2 mm Hg. Mean SBP SD for the first three days ((18.9 ± 3.5) mm Hg) was also significantly higher compared to the values for days 2–6 ((9.6 ± 2.3) mm Hg), p = 0.001.

Maximal spread of individual values of SBP SD during 24 hours was observed on day 1 (Me 17.7, the second quartile — 11.6, the third quartile — 24.2), as well as in the period from day 1 to day 4, as evidenced by median and interquartile range, see Figure 4.

Mean SBP SD for the first three days was also reliably higher (19.4 (IQR: 12.2–23.1) mm Hg compared with the values for days 2–6 (10.35 (IQR: 5.9–14.3) mm Hg), p = 0.001.

Patients with IS of different severity demonstrated significant differences in terms of SBP SD per 24h on day 1 (p = 0.010). On day 2, there were differed significant differences in this value between mild and severe IS and between moderate and severe CIS, see Table 4.

It was found that the average values of daily mean SBP values during 24 hours in the acute period correlate with the severity of stroke (in points) at the time of discharge. There were significant correlations for day 1 (r = 0.396, p = 0.001), day 2 (r = 0.265, p = 0.001), within days 1–3 (r = 0.303, p = 0.001), and within days 1–6 (r = 0.239, p = 0.003) (Table 5). In patients with moderate and severe stroke, correlation coefficients of the standard deviation for daily mean SBP with the stroke severity increased to 0.725 (p = 0.001) on days 1–3 and to 0.695 (p = 0.001) on days 1–6. On discharge, there was moderate correlation between maximum DBP and NIHSS score (r = 0.472, p = 0.001) only on day 1. According to the data for days 1–3 of follow-up, DBP SD and NIHSS score on discharge also demonstrated moderate correlation (r = 0.550, p = 0.001) (Table 5). The table demonstrates that SBP SD and DBP SD turned out to be more informative indicators for correlation between the indicators of AH progress in the acute period and the regression of neurological deficit.

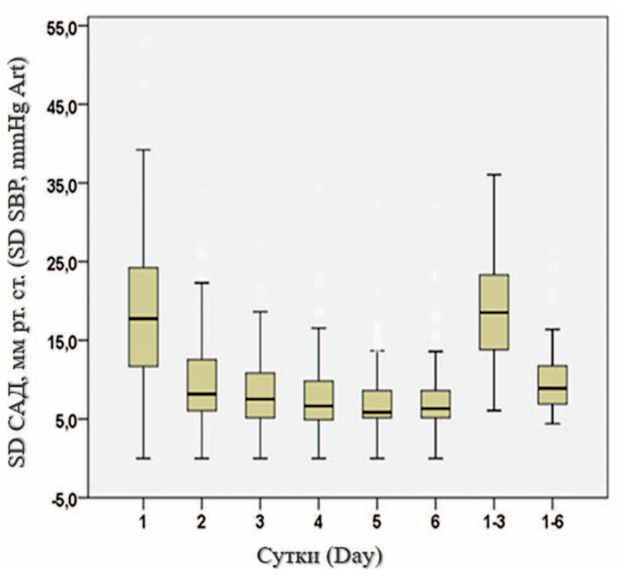

Figure 4. *Meaning of SD SBP medians and quartiles at different times from the onset of stroke*

Table 4. *Comparative assessment of SD SBP per day (Me(IQR)) depending on the severity of neurological deficit*

Time after stroke, day	The severity of the neurological deficit			p–value		
	Mild n=26	Medium n=86	Severe n=38	1vs 2	1 vs 3	2 vs 3
	SD	SD	SD	1/2	1/3	2/3
1	12,1(9,2-15,1)	18,6(15,8-21,4)	24,0(22,1-25,9)	**0,010**	**0,001**	**0,001**
2	7,3(6,4-8,2)	9,1(6,8-11,5)	12,1(8,9-15,1)	0,241	**0,015**	**0,014**
3	6,5(4,8-8,3)	7,3(6,2-8,5)	9,7(7,9-11,5)	0,338	0,040	0,059
4	5,5(3,6-7,4)	7,1(5,9-8,3)	8,0(5,9-10,2)	0,031	0,060	0,613
5	6,1(4,8-7,5)	7,0(5,4-8,6)	7,4(6,5-8,3)	0,145	0,902	0,108
6	7,5(4,7-10,3)	6,5(5,1-7,9)	8,3(6,9-9,8)	0,772	0,523	0,497
1-3	14,3(12,4-16,3)	18,2(16,5-19,9)	26,2(24,5-28,0)	**0,001**	**0,001**	**0,001**

Note: SBP — systolic blood pressure; SD — standard deviation; p– values — significant differences between respective groups

***Table 5.** Correlation Coefficients Between NIHSS Score at Discharge and BP Indicators*

Parameter	r	p		Parameter	r	p
AVADV SBP, 1 day	0,396	0,001		SD SBP, 1 day	**0,487**	0,001
AVADV SBP, 1– 3 days	0,303	0,001		SD SBP, 2 day	0,244	0,003
AVADV SBP, 1– 6 days	0,239	0,003		SD SBP, 3 day	0,194	0,018
SBP max, 1 day	0,383	0,001		SD SBP, 1– 3 days	**0,725**	0,001
SBP max, 2 day	0,265	0,001		SD SBP, 1– 6 days	**0,695**	0,001
AVADV DBP, 1 day	0,337	0,001		SD DBP, 1 day	0,330	0,001
AVADV DBP, 6 day	0,182	0,026		SD DBP, 4 day	0,172	0,035
AVADV DBP, 1 — 3 days	0,162	0,048		SD DBP, 1 — 3 days	**0,550**	0,001
DBP max, 1 day	**0,472**	0,001		SD DBP, 1 — 6 days	0,474	0,001
DBP max, 6 day	0,180	0,027		Duration of hypertension	**0,538**	0,001
Degree of hypertension	**0,481**	0,001				

Note: AVADV — the average value of the average daily value; SBP — systolic blood pressure; DBP — diastolic blood pressure; AH — arterial hypertension; SD — standard deviation; p– values — significant differences between respective groups

Univariate regression analysis revealed a significant dependence of stroke severity according to NIHSS on discharge on SBP SD on days 1–3, $R^2 = 0.526$, see Figure 5.

According to logistic regression analysis, there is a dependence between the decrease in NIHSS score on discharge and SBP SD on days 1–3. The final model has sensitivity of 93.9 %, specificity of 86.5 %, and diagnostic accuracy of 90.1 %, with ROC area of 0.957 (95 % CI: 0.94–0.99), p = 0.003, see Figure 6.

It was established that more than a 50 % chance of reducing the NIHSS score by half (from baseline) is predicted if a patient had SBP SD on days 1–3 less than 12.4 mm Hg, see Figure 7.

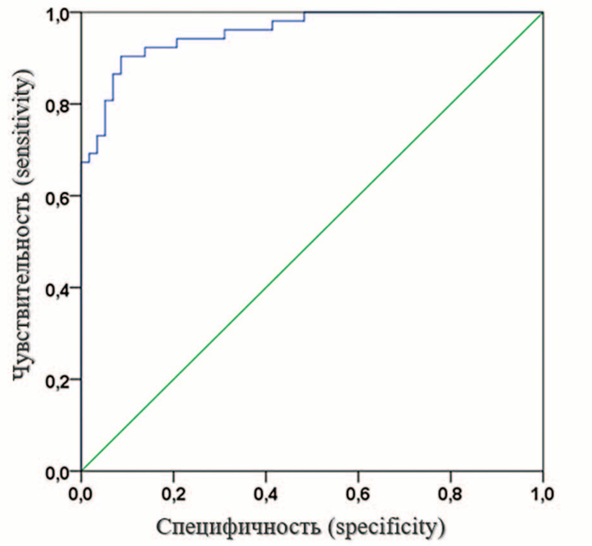

***Figure 6.** ROC-curve of the prognostic model of Barthel index recovery one month after cerebral ischemic stroke*

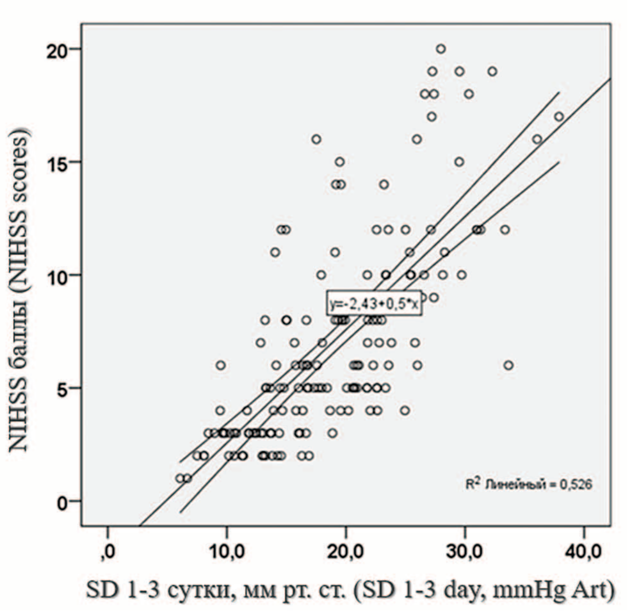

***Figure 5.** Scatter diagram (with a line of approximation) of SD SBP on days 1– 3 depending on the severity of stroke according to NIHSS on day 21.*

Note: NIHSS — National Institutes of Health Stroke Scale; SD SBP — standard deviation of systolic blood pressure during the day

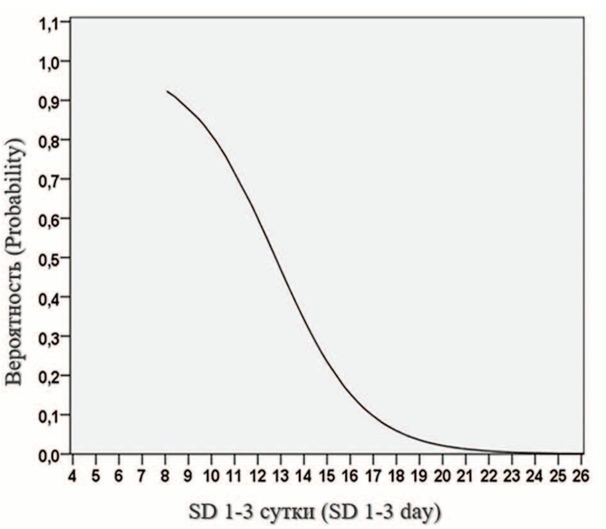

***Figure 7.** Probability of NIHSS score decrease by 50 % (from baseline) depending on SBP SD value for 1– 3 days*

Note: SD — standard deviation of systolic blood pressure during the day

Table 6. Correlation coefficients of the Bartel index for 21 days with blood pressure indicators

Parameter	r	p		Parameter	r	p
AVADV SBP, 1 day	– 0,232	0,004		SD SBP, 1 day	**– 0,427****	0,001
AVADV SBP, 2 day	– 0,072	0,379		SD SBP, 2 day	– 0,199	0,015
AVADV SBP, 1– 3 days	– 0,147	0,072		SD SBP, 3 day	– 0,144	0,078
AVADV SBP, 1– 6 days	– 0,109	0,186		SD SBP, 1– 3 days	**– 0,551****	0,001
SBP max, 1 day	– 0,289	0,001		SD SBP, 1– 6 days	**– 0,515****	0,001
SBP max, 2 day	– 0,132	0,107		SD DBP, 1 day	– 0,233**	0,004
AVADV DBP, 1 day	– 0,223	0,06		SD DBP, 2 day	– 0,108	0,190
AVADV DBP, 2 day	– 0,31	0,703		SD DBP, 1– 3 days	**– 0,550**	0,001
DBP max, 1 day	– 0,349	0,001		SD DBP, 1– 6 days	– 0,317	0,001
DBP max, 2 day	– 0,018	0,825				

Note: AVADV — the average value of the average daily value; SBP — systolic blood pressure; DBP — diastolic blood pressure; SD — standard deviation; p– values — significant differences between respective groups

Thus, BP variability during the acute period made it possible not only to reveal differences between mean values in the case of cerebral ischemic strokes of different severity over time, but also to trace individual fluctuations in systolic and diastolic pressure in terms of the maximum severity of cerebral disorders, as well as to demonstrate the effect of daily variability, in particular, of SBP SD, on the consequences of stroke with defining the most informative corresponding terms.

At the end of the acute period on day 21, mean Barthel score was 68.3 (53.2–83.4) (from 0 to 95). The relationship between the grade of functional recovery in the acute period and BP parameters was analyzed (Table 6), namely: average values of daily mean SBP and DBP, maximum SBP and DBP, BP variability.

Correlation coefficients between SBP SD and Barthel index on day 1, days 1–3 and days 1–6 were r = −0.427 (p = 0.001), r = −0.551 (p = 0.001), and r = −0.515 (p = 0.001), respectively; DBP SD significantly correlated only in the period from day 1 to 3 (r = −0.550, p = 0.001).

Using a one-way regression analysis, we searched for the dependence of the grade of functional deficiency in patients in the acute period on day 21 on the variability of SBP on days 1–3, see Figure 8.

It was found that the degree of functional deficiency in patients in the acute period on day 21 depended on the variability of systolic BP on days 1–3, R^2 = 0.304, see Figure 8.

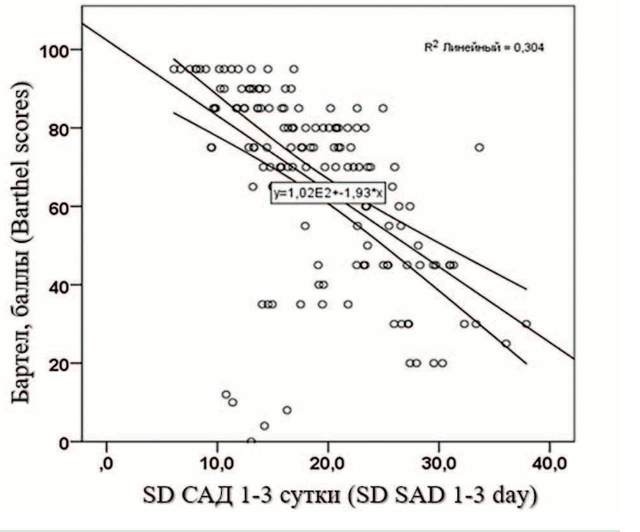

Figure 8. *Dependence of the degree of functional disorders in patients in the acute period of stroke on SD SBP on days 1– 3*

Note: SD SBP — standard deviation of systolic blood pressure during the day

Discussion

The results obtained demonstrate that BP variability during the acute period of stroke allows to identify the differences between mean systolic and diastolic blood pressure in stroke of different severity over time, and to demonstrate the significant role of BP variability in the functional consequences of stroke, defining the most informative corresponding terms.

Although hypertension has long been known to be a major vascular risk factor for cerebrovascular diseases and their clinical consequences, stroke, and dementia [13, 14, 16], randomized controlled trials (RCTs) and cohort studies provide ambiguous results as to whether high blood pressure (BP) and its management with antihypertensive agents contributes to the decrease in the risk of neurological deficits and functional impairment in stroke survivors. Inconsistent results increase the possibility that factors beyond absolute BP or target BP levels may be important in dealing with these issues.

Numerous empirical studies reveal that inter-measurement BP fluctuations, along with mean BP levels, have additional prognostic value for subclinical target organ damage, including brain [17, 18]. For example, A. E. Bennett et al. (2018) showed that increased blood pressure variability, as measured by standard deviation (SD), coefficient of variation (CV), and serial variation (SV), predicts worse neurological outcomes measured by modified Rankin scale in patients with ischemic stroke. SV is the strongest and most consistent predictor of worse outcomes across all time intervals [33].

Once considered to be a background "noise" or a measurement error, intra-individual BP variation known as BP variability is important for predicting incident and recurrent stroke [34]. Higher BP variability has indirect effect on brain, including impaired cerebral autoregulation and temporary hypoperfusion [35].

Accumulated evidence suggests that blood pressure variability can contribute to end-organ damage causing coronary heart disease, stroke, and kidney damage, regardless of blood pressure (BP) levels. In addition to stroke, blood pressure variability is associated with a higher risk of cognitive impairment and dementia [36].

Several meta-analyses on BP variability have reported an association with acute stroke and transient ischemic attack (TIA), headache, atrial fibrillation, left ventricular mass index, mortality, cardiovascular outcomes, and multiple endpoints including stroke, mortality, and cardiovascular outcomes. Other systematic reviews and guidelines have focused on the statistical methods and technical aspects of the quantitative evaluation of BP variability [37].

In our paper, we show that the consequences of the acute period of stroke depend on BP level and its variability at the beginning of the acute period. On the first day of stroke, significantly higher mean SBP and SBP SD were registered with an increase in the stage of neurological deficit (after 8, 12, 16, and 20 hours). According to our study, BP variability during the acute stroke period is most closely related to the NIHSS score at the end of the acute period, as evidenced by the following values: SBP SD for a period of day 1 through 3 ($r = 0.725$, $p = 0.001$) and DBP SD ($r = 0.550$, $p = 0.001$), duration of AH ($r = 0.538$, $p = 0.001$), SBP SD for day 1 ($r = 0.487$, $p = 0.001$). It was established that more than 50 % probability of halving a lower NIHSS score (compared to baseline) is predicted if a patient's SBP SD on days 1–3 is below 12.4 mm Hg.

Correlation coefficients between the Barthel index and SBP SD on days 1–3 and on days 1–6 were as follows: $r = -0.551$ ($p = 0.001$) and $r = -0.515$ ($p = 0.001$), respectively; DBP SD significantly correlated with the Barthel index only in the period between day 1 and day 3 ($r = -0.550$, $p = 0.001$).

Conclusion

BP level and its variability during the acute phase of ischemic stroke allows predicting the severity of neurological deficit and the functional consequences of stroke during the recovery period.

Вклад авторов:

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Ефремова О.А. (ORCID ID: https://orcid.org/0000-0002-6395-1626): разработка дизайна, ответственна за все аспекты работы, окончательное утверждение

Бондаренко Е.В. (ORCID ID: https://orcid.org/0000-0003-4515-7178): разработка концепции исследования, основной сбор, анализ, интерпретация данных, написание рукописи, ответственна за все аспекты работы

Камышникова Л.А. (ORCID ID: https://orcid.org/0000-0002-6129-0625): обзор литературы, анализ и интерпретация данных, участие в разработке дизайна

Голивец Т.П. (ORCID ID: https://orcid.org/0000-0002-5308-8072): создание критически важного интеллектуального содержания, готовность принять ответственность за все аспекты работы

Хамнагадаев И.И. (ORCID ID: https://orcid.org/0000-0001-8541-0364): математическая обработка и анализ результатов, готовность принять ответственность за все аспекты работы

Author Contribution

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Efremova O.A. (ORCID ID: https://orcid.org/0000-0002-6395-1626): design development, responsible for all aspects of the work, final approval

Bondarenko E.V. (ORCID ID: https://orcid.org/0000-0003-4515-7178): development of the research concept, main collection, analysis, interpretation of data, writing the manuscript, responsible for all aspects of the work

Kamyshnikova L.A. (ORCID ID: https://orcid.org/0000-0002-6129-0625): literature review, data analysis and interpretation, participation in design development

Golivets T.P. (ORCID ID: https://orcid.org/0000-0002-5308-8072): creation of critical intellectual content, willingness to take responsibility for all aspects of work

Khamnagadaev I.I. (ORCID ID: https://orcid.org/0000-0001-8541-0364): mathematical processing and analysis of results, willingness to take responsibility for all aspects of the work

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