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# HEMODYNAMIC LOAD ON THE INTRACRANIAL ARTERIAL SYSTEM IN SUBJECTS WHO HAVE SUFFERED A HEMORRHAGIC STROKE AS A COMPLICATION OF ESSENTIAL ARTERIAL HYPERTENSION

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**Ключові слова:** *гіпертонічна хвороба, геморагічний інсульт, добове моніторування артеріального тиску, ультразвукове дослідження магістральних артерій шиї, гемодинамічне навантаження*
**Ключевые слова:** *гипертоническая болезнь, геморрагический инсульт, суточное мониторирование артериального давления, ультразвуковое исследование магистральных артерий шеи, гемодинамическая нагрузка*

**Abstract. Hemodynamic load on the intracranial arterial system in subjects who have suffered a hemorrhagic stroke as a complication of essential arterial hypertension. Netiazhenko V.Z., Tkachyshyn O.V.** *The aim of the investigation was to compare a hemodynamic load on the intracranial arterial system, assessed by the indices of 24-hours ambulatory blood pressure monitoring and ultrasonography of the main cervical arteries between the group of patients with essential arterial hypertension in ≥6 months after a hemorrhagic stroke and a group of patients with essential arterial hypertension without complications. The first one was the main group (n=94; age – 54.4±0.9 years), M±m), the second one – the comparison group (n=104; age – 53.7±0.9 years). The indices of 24-hours ambulatory blood pressure monitoring in the main group and the comparison group were the following: the mean daytime systolic blood pressure was 109.6±1.6 and 121.1±1.1 mm Hg, the minimal one was 74.4±2.0 mm Hg and 82.3±12.5 mm Hg, and the maximal one was 168.2±1.9 and 161.9±1.7 mm Hg, p<0.05. The daytime systolic blood pressure sigma (17.9±0.6) and the average real variability of systolic blood pressure (11.31±2.52 mm Hg) were bigger in the main group (p<0.01). The daytime index of hyperbaric load of systolic blood pressure was bigger in the main group: it was 403.6±25.9 against 231.7±12.1 mm Hg × h in the comparison group (p<0.01). The maximal pulse pressure for a 24-hours interval was 74.2±2.0 and 66.4±0.9 mm Hg, respectively (p<0.01). The indices of ultrasonography of the large cervical arteries in the right and left vessels of the main group were the following: the Gosling's pulsatility index was 1.578±0.059 and 1.552±0.042 for the common carotid artery, 1.210±0.044 and 1.102±0.037 for the internal carotid artery, 1.191±0.030 and 1.150±0.023 for the vertebral artery. The above-mentioned indices were bigger in the main group than in the comparison one (p<0.01). The diameters of all the large cervical arteries were bigger in the main group (p<0.01). Therefore, according to the above-mentioned indices which are associated with a bigger risk of cerebrovascular events, a bigger hemodynamic load on the intracranial arterial system was found in the main group than in the comparison one, despite the smaller mean systolic blood pressure indices.*

**Реферат. Гемодинамическая нагрузка на внутричерепное артериальное русло у больных после перенесенного геморрагического инсульта как осложнение гипертонической болезни. Нетяженко В.З., Ткачишин А.В.** *Целью исследования было сравнить гемодинамические нагрузки на внутричерепное артериальное русло, оцененное по показателям суточного мониторирования артериального давления и ультразвукового исследования магистральных артерий шеи, между группой больных гипертонической болезнью через ≥6 месяцев после перенесенного геморрагического инсульта и группой больных гипертонической болезнью без осложнений. Первая из вышеуказанных – основная группа (n=94; возраст – 54,4±0,9 года), вторая – группа сравнения (n=104; возраст – 53,7±0,9 года). Показатели суточного мониторирования артериального давления в основной группе и группе сравнения соответственно: среднее систолическое артериальное давление днем 109,6±1,6 и 121,1±1,1 мм рт. ст., минимальное – 74,4±2,0 и 82,3±12,5 мм рт. ст., максимальное –*

*168,2±1,9 и 161,9±1,7 мм рт. ст., p<0,05. Показатели сигмы систолического артериального давления днем (17,9±0,6) и средней реальной вариабельности систолического артериального давления (11,31±0,26 мм рт.ст.) были больше в основной группе (p<0,01). Показатель гипербарической нагрузки систолического артериального давления днем был больше в основной группе и составил 403,6±25,9 против 231,7±12,1 мм рт. ст. × ч. в группе сравнения (p<0,01). Максимальное пульсовое артериальное давление за 24-часовой интервал – 74,2±2,0 и 66,4±0,9 мм рт. ст. соответственно (p<0,01). Показатели ультразвукового исследования магистральных артерий шеи в основной группе в правых и левых сосудах соответственно: пульсационный индекс Гослинга общей сонной артерии – 1,578±0,059 и 1,552±0,042, внутренней сонной артерии – 1,210±0,044 и 1,102±0,037, позвоночной артерии – 1,191±0,030 и 1,150±0,023. Указанные показатели были больше в основной группе, чем в группе сравнения (p<0,01). Диаметры всех магистральных артерий шеи были больше у лиц основной группы (p<0,01). Таким образом, по указанным показателям, которые ассоциируются с большим риском развития цереброваскулярных событий, было установлено большие гемодинамические нагрузки на внутричерепное артериальное русло у лиц основной группы, чем у лиц группы сравнения, несмотря на меньшие средние показатели систолического артериального давления.*

Arterial hypertension (AH) plays a leading role in both intracerebral and subarachnoid hemorrhage [2], which are types of hemorrhagic stroke (HS) [13]. There is little information regarding the course of hypertension disease (HD) and what changes occur in the cardiovascular system after an early recovery period – ≥6 months from the past HS. At the same time, patients who suffered HS as a complication of HD have an increased risk of further complications and death [3], which necessitates the improvement of diagnostic measures for timely detection and correction of increased arterial pressure (AP) as a factor of such risk. Thus, work on the study of the peculiarities of the processes in the body, in particular in the cardiovascular system, in such individuals will become more important. Studying the results of ambulatory blood pressure monitoring (ABPM) and ultrasound (US) of the main cervical arteries (MCA) can provide valuable information about the course of AH and its potential hemodynamic effect on the compromised intracranial arterial bed.

The aim of the study was to compare the hemodynamic load on the intracranial arterial bed, assessed by ABPM and ultrasound of MCA, between a group of patients with HD in ≥6 months after past HS and a group of patients with HD without complications.

**MATERIALS AND METHODS OF RESEARCH**

A total of 198 people were involved in the study, which was divided into 2 groups: the main group and the comparison group. The main group included patients who suffered HS as a complication of HD ≥6 months before (n=94), and the comparison group – patients with HD, stage II, without HS (n=104).

While forming the main group there was carried out selection of patients who suffered HS ≥6 months before and were treated in the vascular neurosurgery clinic of the State Institution “Institute of Neurosurgery named after acad. A.P. Romodanov National Academy of Medical Sciences of Ukraine" in 2013-2017. Criteria for inclusion: HD stage II prior to the development of HS. Examination carried in ≥6 months after HS was due to the need for patients to be in a stable phase. There were selected 94 individuals who recovered neurologically to 50-100 points by the Bartel scale and had elevated BP pressure after HS. Characteristics of the studied groups are presented in Table 1.

*Table 1*

**Characteristics of the studied groups (M±m)**

| Indicator | Main group, n = 94 | Comparison group, n=104 |
|---|---|---|
| **Average age, years** | **54.4±0.9** | **53.7±0.9** |
| **Male patients, %** | **46.8** | **48.1** |
| **Body mass index, kg/m$^2$** | **28.7±0.5** | **29.0±0.4** |
| **Office SAP, mm Hg.** | **154.3±0.7** | **155.2±0.7** |
| **Office DAP, mm Hg.** | **97.6±0.5** | **98.2±0.5** |
| **Patients with diabetes mellitus, %** | **12.8** | **14.4** |

**Note**. * – statistically significant difference between corresponding indicators of the study groups, p<0.05.

Examinations of patients of the main group were performed once at different terms after stroke – from 6 to 51 (18.3±1.2) months.

Examination of all patients was performed on the clinical bases of the Department of Propaedeutics of Internal Medicine No. 1 of O.O. Bogomolets National Medical University from November 2016 to July 2018.

Ultrasound examination of MCA with Doppler was performed on an ultrasound apparatus "Vivid-7 Pro" ("General Electric", USA). Diameters of common carotid arteries (CCA), internal carotid arteries (ICA), vertebral arteries (VA), peak systolic (Vps) and maximum end-diastolic (Ved) blood flow velocity in all vessels were measured [6], CIM thickness [12] . The Purcelo peripheral resistance index (RI) and the Gosling pulsation index (PI) were determined [5].

ABPM was performed on a CardioSpy device (Labtech Ltd, Hungary), software version V4.04.RC24, recorder version V1.16. There were three recording periods: day (06:00-22:00), night (22:00-06:00) and during 24 hours. We determined the arithmetic mean ($AP_{mean}$), minimum ($AP_{min}$) and maximum ($AP_{max}$) AP, its standard deviation (sigma) during the recording period, the percentage of excess time (time index) and the index of pressure load (PLI) [7], the average real variability (ARV) of systolic arterial pressure (SAP) and diastolic arterial pressure (DAP) [11].

The results of the study are presented in the form M±m. Statistical processing of the obtained data was performed using IBM SPSS Statistics Base v.22 [9] (license agreement of O.O. Bogomolets National Medical University No. 138 dated 04.08.2016).

The difference between the compared parameters with the normal distribution of variants was evaluated by the Student's t-test, between those that had an abnormal distribution of variants – by the U-Mann-Whitney test. The analysis of the obtained results was performed in accordance with generally accepted recommendations [1]. The difference between the study groups was considered statistically significant at $p < 0.05$.

The clinical study was conducted in accordance with the Helsinki Declaration of the World Medical Association "Ethical principles of medical research with human participation as an object of study" (1964, updated in 2000). The patient or his/her legal representative filled in the Informed Consent (Expert conclusion of the Ethics Commission of O.O. Bogomolets National Medical University dated 26.10.2016, protocol No. 98).

**RESULTS AND DISCUSSION**

According to the data obtained, which are shown in Table 2, it was found that the diameters of all MCA were larger in the main group relative to the comparison group. $V_{ps}$ in all vessels, except VA, in the main group were lower relative to comparison group due to larger vessel diameters and lower $SAP_{mean}$ in ABPM (Table 3). The same was observed in the $V_{ed}$ indicators, except for the right VA: in it the $V_{ed}$ indicator did not show a statistically significant difference between the groups. This could be caused by the fact that in the main group there was a statistically significantly smaller value of the diameter of the right VA compared to the left.

In the main group, at lower $V_{ps}$ and $V_{ed}$, the load on the vascular wall and, accordingly, the intracranial arterial bed was larger, which is reflected in the larger values of RI and PI. The lack of a significant difference between the studied groups for RI in the left ICA and right VA is due to the fact that RI is considered less sensitive and accurate indicator than PI.

The data presented in Table 3 show that $SAP_{mean}$ and $SAP_{min}$ during the day, night and during 24 hours were statistically significantly lower in the main group in contrast to the comparison group. At the same time, $SAP_{max}$ was statistically significantly higher during the day, and at night $SAP_{max}$ was lower in the main group, which indicates a more characteristic hemodynamic load during the day in the main group. PLI SAP during the day was higher in the main group and was 403.6±25.9 against 231.7±12.1 mm Hg. × hours in the comparison group ($p<0.01$).

The study also calculated the ratio of $SAP_{max}$ to $SAP_{mean}$ over a 24-hour interval in both groups. According to the obtained results, in the main group the excess of $SAP_{max}$ over $SAP_{mean}$ for a 24-hour period was 54.4±31.1% in contrast to 38.5±9.3% in the comparison group ($p<0.05$). The obtained data indicate significant intragroup differences in the main group, which requires ABPM screening in this category of patients to identify individuals with a higher percentage of excess of $SAP_{max}$ over $SAP_{mean}$ during the day, and hence a higher risk of cardiovascular events.

Regarding DAP, despite statistically significantly lower average and minimum values in the main group in all three time intervals, as well as the absence of statistically significant difference in daily and a 24-hour $DAP_{max}$, the hyperbaric load on the cardiovascular system in the main group was higher than in the comparison group.

The values of average, minimum and maximum SAP and DAP at night were statistically significantly lower in the main group than in the comparison group. This may indicate more pro-

nounced vasopressor effects in this period of the day in the latter, which resulted in a greater tendency to stability in blood pressure, elevation as well as during the day.

*Table 2*

**USI indices in the study groups (M±m)**

| Index | Right MCA | | Left MCA | |
|---|---|---|---|---|
| | main group, n=94 | comparison group, n=104 | main group, n=94 | comparison group, n=104 |
| Diameter CCA, mm | 7.036±0.077@ | 6.149±0.079 | 7.115±0.087@ | 6.200±0.085 |
| Diameter ICA, mm | 5.436±0.050^ | 5.182±0.061 | 5.558±0.072^ | 5.260±0.072 |
| Diameter VA, mm | 3.827±0.051@ | 3.390±0.053 | 3.989±0.049@ | 3.371±0.057 |
| $V_{ps}$ CCA, cm/s | 64.062±1.925^ | 74.58±1.090 | 56.259±1.532^ | 77.67±1.530 |
| $V_{ps}$ ICA, cm/s | 54.281±2.122^ | 67.49±0.930 | 55.029±1.447^ | 69.60±1.059 |
| $V_{ps}$ VA, cm/s | 37.257±1.260 | 38.55±1.070 | 38.029±1.161 | 37.80±1.050 |
| $V_{ed}$ CCA, cm/s | 14.721±1.025^ | 24.58±0.830 | 13.301±1.004^ | 24.67±0.880 |
| $V_{ed}$ ICA, cm/s | 18.021±1.010^ | 29.45±0.960 | 20.088±0.928^ | 27.90±0.980 |
| $V_{ed}$ VA, cm/s | 13.745±0.664 | 14.98±0.570 | 11.847±0.434^ | 14.96±0.610 |
| RI CCA | 0.768±0.029^ | 0.667±0.019 | 0.765±0.027* | 0.690±0.023 |
| RI ICA | 0.667±0.022^ | 0.561±0.019 | 0.634±0.021 | 0.601±0.022 |
| RI VA | 0.633±0.025 | 0.609±0.020 | 0.690±0.017^ | 0.597±0.020 |
| PI CCA | 1.578±0.059^ | 1.21±0.050 | 1.552±0.042^ | 1.25±0.060 |
| PI ICA | 1.210±0.044^ | 0.900±0.038 | 1.102±0.037^ | 0.923±0.041 |
| PI VA | 1.191±0.030@ | 1.030±0.025 | 1.150±0.023^ | 1.020±0.026 |

**Notes:** * – statistically significant difference between corresponding indices of the study groups, $p<0.05$; ^ – statistically significant difference between corresponding indices of the study groups, $p<0.01$; @ – statistically significant difference between corresponding indices of the study groups, $p<0.001$.

As for PAP, it was found that during the day all 3 indicators of PAP – $PAP_{mean}$, $PAP_{min}$ and $PAP_{max}$ differed significantly between groups. Only $PAP_{max}$ was larger in the main group. Although the average daily value of PAP in the main group (39.5±0.9 mm Hg) and in the comparison group (41.1±0.5 mm Hg) did not exceed the optimal level of PAP but $PAP_{max}$ for a 24-hour interval in the main group – 74.2±2.0 mm Hg attracted attention, because the brain compromised by past HS is vulnerable to elevated PAP. It is known that the higher this figure, the worse the patient's prognosis.

The time index of SAP and DAP in all time intervals was nonparametric with a significant value of standard deviation, which can be explained by significant individual differences between patients in the duration of periods of elevated blood pressure. Probably, this is why when comparing these indicators between the groups no statistically significant differences were found.

The mean value of the differences between $SAP_{min}$ and $SAP_{max}$ (Δ) during the day was calculated. Thus, Δ SAP during the day in the main group and the comparison group was 93.1±3.6 and

79.5±1.9 mm Hg. respectively (p<0.01). Accordingly, in the daytime period in the main group a wider range of SAP fluctuations dominated.

The sigma index for SAP during the day, neither at night nor within 24 hours, also showed a statistically significantly higher value in the main group. These results indicate that patients of the main group, mainly during the day experience short-term elevations of SAP and with a greater amplitude, which may not be detected in the office measurement of blood pressure, conducted outside this "time window" of blood pressure elevation. As a result, there may be a wrong impression about the success over HD control.

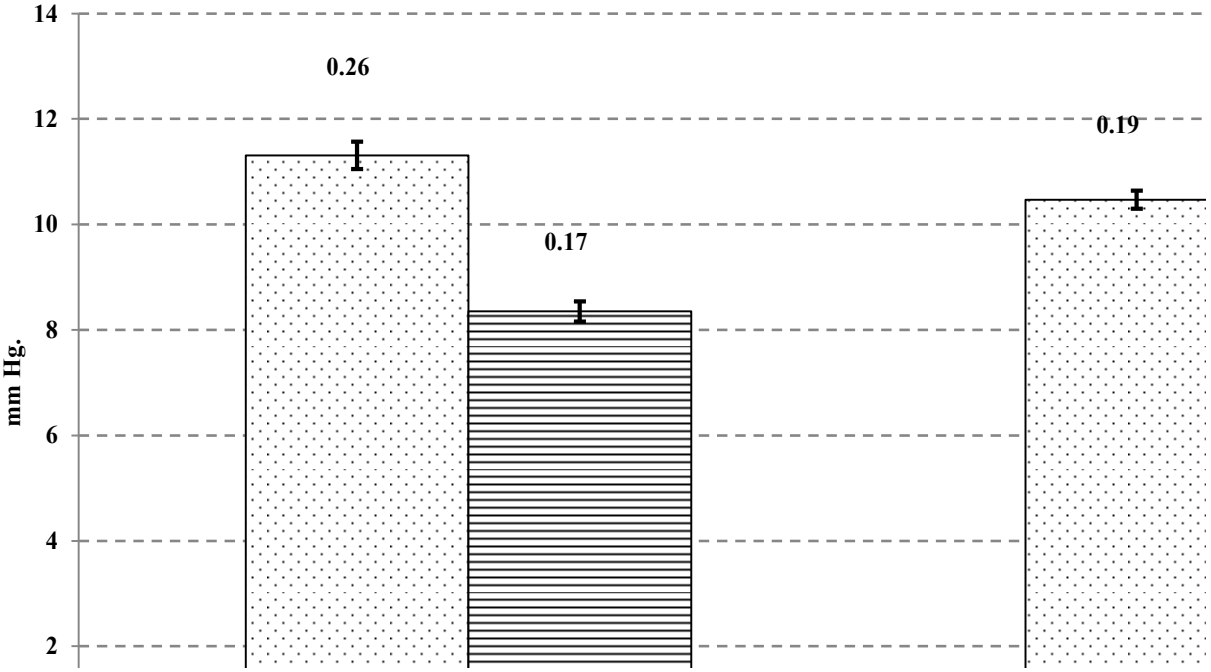
*Table 3*

**Values of ABPM in the main and comparison group (M±m)**

| Value | Day | | Night | | 24-hour period | |
|---|---|---|---|---|---|---|
| | main group, n=94 | comparison group, n=104 | main group, n=94 | comparison group, n=104 | main group, n=94 | comparison group, n=104 |
| $SAP_{mean}$, mm Hg. | 109.6±1.6@ | 121.1±1.1 | 101.9±1.8^ | 108.3±1.4 | 109.6±1.6@ | 118.1±1.0 |
| $SAP_{min}$, mm Hg. | 74.4±2.0^ | 82.3±1.2 | 79.7±1.7@ | 91.2±1.2 | 72.0±1.9^ | 80.1±1.3 |
| $SAP_{max}$, mm Hg. | 168.2±1.9* | 161.9±1.7 | 125.6±2.2@ | 137.1±1.8 | 168.3±1.9 | 164.5±1.7 |
| Sigma | 17.9±0.6^ | 15.1±0.3 | 13.5±0.5 | 12.1±0.4 | 17.8±0.5 | 16.5±0.4 |
| Time index, % | 10.7±1.5 | 14.3±1.5 | 21.0±2.8 | 25.3±2.6 | 14.3±1.7 | 16.6±1.4 |
| PLI, mm Hg.×hour | 403.6±25.9^ | 231.7±12.1 | 185.3±28.0 | 220.6±14.7 | 384.7±18.2^ | 256.5±9.5 |
| $DAP_{mean}$, mm Hg. | 71.1±1.0@ | 79.3±0.7 | 64.1±1.2* | 67.7±1.0 | 70.4±1.0@ | 76.6±0.7 |
| $DAP_{min}$, mm Hg. | 43.8±1.3^ | 55.5±1.3 | 50.5±1.3^ | 55.8±1.1 | 41.0±1.1^ | 51.9±1.1 |
| $DAP_{max}$, mm Hg. | 117.2±1.8 | 114.0±1.6 | 82.5±1.5^ | 87.5±1.0 | 117.9±1.8 | 114.1±1.6 |
| Sigma | 13.5±0.4^ | 10.5±0.2 | 9.1±0.3 | 8.7±0.2 | 13.6±0.3@ | 11.6±0.3 |
| Time index, % | 9.3±0.8 | 15.5±2.0 | 13.3±2.8 | 15.9±2.0 | 10.3±1.0 | 15.6±1.8 |
| PLI, mm Hg.×hour | 377.1±30.0^ | 221.3±12.5 | 132.8±18.4 | 139.0±10.9 | 376.4±30.1^ | 218.4±9.8 |
| $PAP_{mean}$, mm Hg. | 38.5±0.9^ | 41.4±0.5 | 39.2±1.1 | 40.2±0.7 | 39.5±0.9 | 41.1±0.5 |
| $PAP_{min}$, mm Hg. | 16.1±0.6^ | 18.8±0.4 | 26.8±1.1 | 27.7±0.6 | 14.8±0.5^ | 18.6±0.4 |
| $PAP_{max}$, mm Hg. | 72.3±2.1* | 65.0±1.0 | 52.2±1.3@ | 57.9±1.1 | 74.2±2.0^ | 66.4±0.9 |
| Sigma | 10.6±0.4 | 9.2±0.2 | 6.7±0.3 | 7.5±0.3 | 10.4±0.3^ | 9.3±0.2 |

**Notes:** * – statistically significant difference between corresponding values of the study groups, p<0.05; ^ – statistically significant difference between corresponding values of the study groups, p<0.01; @ – statistically significant difference between corresponding values of the study groups, p<0.001.

According to the Figure, ARV for SAP in the main group was statistically significantly higher than in the comparison group, which indicates a higher risk of cardiovascular disease for the former, because according to L.J. Mena et al., higher levels of ARV for SAP are associated with a higher risk of any cardiovascular event in hypertension and death [8]. Thus, despite the higher absolute $SAP_{mean}$ values in the comparison group, the change in SAP between successive measurements was smaller than in the main group. When comparing the groups with each other by ARV for DAP, no statistically significant difference was found.




^ – difference between corresponding values of the main and comparison group is statistically significant, p<0.01.

**Average real variability by systolic and diastolic blood pressure in the study groups**

It should be noted that, despite the lower $SAP_{mean}$ in the main group, the PLI during the day and a 24-hour period was statistically significantly higher than in the same comparison group at the appropriate time intervals. At the same time, as can be seen by PLI, short-term elevations of SAP made more load on the cardiovascular system than a more stable elevated SAP, which was more common in the comparison group. It is due to ABPM that such episodes are detected, which lead to higher risks of HD complications than stably elevated SAP.

Stéphane Laurent et al. note that the local pulsating load on the vascular wall plays a more important role than stable, because it leads to rupture of the supporting fibers of elastin in response to the fatigable effect of stable and pulsating compressive stress [10]. From the above, it can be concluded that periodic significant rises in blood pressure make it impossible to systematically remodel the arterial wall, which contributes to its rupture in weak places. In addition, it is known that in the recurrence of a hypertensive crisis, the failure of autoregulation is not diffuse in nature and occurs in the same segments of the arteries as in the first increase in BP [4]. The above better reveals the importance of a higher $PAP_{max}$ value in the main group, because it was clinically confirmed that in the middle-aged group, target organ damage in HD is associated with a 24-hour PAP> 50 mm Hg as compared to persons with a 24-hour PAP ≤50 mm Hg. [8].

Thus, it is possible to make a preliminary assumption that larger ARV of SAP, Δ SAP during the day, sigma SAT during the day, $PAP_{max}$ for a 24-hour interval, PLI of SAP have a significant fatigable effect on MVA with subsequent disintegration of the vascular wall scaffold, which is manifested by its dilatation. And although $V_{ps}$ and $V_{ed}$ in most MVA were smaller in the main group than in the comparison group, due to higher RI it led to a greater load of the pulse wave on the vascular wall of MVA and, accordingly, on the intracranial arterial bed.

Many above indicators of the main group belong to nonparametric and this testifies to the individual adaptive capacity of the organism as for HD course after HS in each case and requires screening ABPM to identify individuals with increased cardiovascular risk in comparison with the reference norms.

**CONCLUSIONS**

1. During ambulatory blood pressure monitoring in the main group, higher values of delta and sigma of systolic blood pressure during the day were

established, its average real variability during a 24-hour period, which testified to a greater variability in these individuals during the day.

2. In the main group there were established higher values of indicators which testify to the load on the cardiovascular system in general and on the intracranial arterial bed in particular: systolic blood pressure load index and maximum pulse blood pressure during the day and a 24-hour period, maximum systolic arterial pressure during a day, the percentage of excess of maximum systolic blood pressure over average one during a 24-hour period, higher Gosling pulsation indices in the main cervical arteries.

3. In the main group, larger diameters of all main cervical arteries were established with lower peak systolic and maximum end diastolic blood flow velocities in the common and internal carotid arteries, lower maximum end diastolic blood flow velocity in the left vertebral artery. This indicates a loss of elastic properties of blood vessels as a result of a greater impulse on their wall.

4. Summarizing and generalizing points 1-3, we note that the change in blood pressure on the reduced elasticity of the arterial wall was greater over a shorter period of time in individuals who suffered a hemorrhagic stroke. Thus, in the weak spot of the vascular wall, the risk of its rupture increases, and recurrent cerebrovascular events may occur.

5. In the main group, larger intragroup differences were found in terms of a 24-hour blood pressure monitoring: more indicators were nonparametric. This indicates that the individuals of the main group were more inherited with individual characteristics of the course of hypertension, which requires the creation of a screening program to identify patients at greater risk of further cerebrovascular events. These patients have such a risk from the whole cardiovascular system, in particular, for the cerebrovascular system, because it is inherent with autoregulation, which was impaired during the previous hemorrhagic stroke.

6. In the comparison group, higher mean systolic blood pressure was found during the day, night, during a 24-period, although the maximum systolic blood pressure during the day and pulse blood pressure per day were higher in the main group. This suggests that based only on office blood pressure measurement, there is a risk of insufficient or misleading blood pressure control in individuals after hemorrhagic stroke as a complication of hypertension, although the data suggest a greater risk of cerebrovascular events in them.

Conflict of interests. Authors declare no conflict of interests.

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