

Prediction of the functional outcome of acute recurrent cerebral ischemic hemispheric stroke

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The aim of the work is to develop criteria for predicting the functional outcome of the acute period of recurrent cerebral ischemic hemispheric stroke (RCIHS) based on a comprehensive clinical and paraclinical examinations.

Materials and methods. An open, comparative, prospective, cohort study of 111 patients (49 (44.1 %) women and 62 (55.9 %) men, age 72.0 (64.0; 77.0) years) with acute RCIHS was performed. All patients underwent a detailed clinical and neurological examination using National Institutes of Health Stroke Scale, mRS (modified Rankin scale), computed tomography of the brain, hematological and biochemical investigation.

Results. Based on a univariate logistic regression analysis, it was found that the functional outcome of the acute RCIHS is influenced by the following parameters: age of patient (OR 1.06, 95 % CI 1.00–1.11, $P = 0.0284$), contralateral localization of RCIHS (OR 2.86 95 % CI 1.05–7.79, $P = 0.0391$), the baseline NIHSS score (OR 1.76, 95 % CI 1.38–2.26; $P < 0.0001$), the infarct volume (OR 1.03, 95 % CI 1.00–1.05, $P = 0.0221$). It was determined that localization of RCIHS in the contralateral hemisphere was associated with the unfavorable functional outcome on the 21st day of the disease ($\chi^2 = 4.44$, $P = 0.0352$). The independent influence of the initial level of glycemia on the functional outcome of the acute period of RCIHS in patients without diabetes (OR 2.39 95 % CI 1.32–4.33, $P = 0.0042$) was revealed.

Conclusions. The independent predictor of the unfavorable functional outcome of the acute period of the RCIHS (mRS ≥ 3 at 21st day of disease) was score by NIHSS >10 at baseline (sensitivity 73.3 %, specificity 90.5 %). The mathematical model, which included the baseline levels of neurological deficit was developed and it could determine the prognosis of the functional outcome of the acute period of RCIHS with an accuracy of 87.5 % (AUC = 0.92, $P < 0.05$).

Ключові слова:

гострий інсульт, прогноз.

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Прогнозування функціонального результату гострого періоду повторного мозкового ішемічного півкульового інсульту

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Мета роботи – розроблення критеріїв прогнозування функціонального результату гострого періоду повторного мозкового ішемічного півкульового інсульту (ПМІПІ) на підставі комплексного клініко-параклінічного дослідження.

Матеріали та методи. Виконали відкрите, порівняльне, проспективне, когортне дослідження 111 хворих (49 (44,1 %) жінок і 62 (55,9 %) чоловіки віком 72,0 (64,0; 77,0) року) в гострому періоді ПМІПІ. Усім пацієнтам провели детальне клініко-неврологічне обстеження з використанням National Institutes of Health Stroke Scale, mRS (modified Rankin scale), виконали комп'ютерну томографію головного мозку, а також гематологічне та біохімічне дослідження.

Результати. На підставі уніваріантного логістичного регресійного аналізу встановлено, що на функціональний результат гострого періоду ПМІПІ впливали вік хворих (ВШ 1,06 95 % ДІ 1,00–1,11, $p = 0,0284$), контралатеральна локалізація ПМІПІ (ВШ 2,86 95 % ДІ 1,05–7,79, $p = 0,0391$), значення сумарного бала за NIHSS на 1 добу (ВШ 1,76 95 % ДІ 1,38–2,26, $p < 0,0001$), об'єм осередку ураження (ВШ 1,03 95 % ДІ 1,00–1,05, $p = 0,0221$). Встановлено, що локалізація ПМІПІ у контралатеральній півкулі асоційована з гіршим функціональним відновленням на 21 добу захворювання ($\chi^2 = 4,44$, $p = 0,0352$). Виявили незалежний вплив ініціального рівня глікемії на функціональний результат гострого періоду ПМІПІ у пацієнтів без цукрового діабету (ВШ 2,39 95 % ДІ 1,32–4,33, $p = 0,0042$).

Висновки. Незалежним предиктором несприятливого функціонального результату гострого періоду ПМІПІ (mRS ≥ 3 на 21 добу) є значення сумарного бала за NIHSS >10 на 1 добу захворювання (чутливість 73,3 %, специфічність 90,5 %). Розробили математичну модель, котра враховує ініціальні рівні неврологічного дефіциту та глікемії і дає змогу визначати прогноз функціонального результату гострого періоду ПМІПІ з точністю до 87,5 % (AUC = 0,92, $p < 0,05$).

Ключевые слова:

острый инсульт, прогноз.

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Прогнозирование функционального исхода острого периода повторного мозгового ишемического полушарного инсульта

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Цель работы – разработка критериев прогнозирования функционального исхода острого периода повторного мозгового ишемического полушарного инсульта (ПМИПИ) на основании комплексного клинико-параклинического исследования

Материалы и методы. Проведено открытое, сравнительное, проспективное, когортное исследование 111 больных (49 (44,1 %) женщин и 62 (55,9 %) мужчины, возраст – 72,0 (64,0; 77,0) года) в остром периоде ПМИПИ. Всем пациентам проведено детальное клинико-неврологическое обследование с использованием National Institutes of Health Stroke Scale, mRS (modified Rankin scale), выполнена компьютерная томография головного мозга, а также гематологическое и биохимическое исследования.

Результаты. На основании унивариантного логистического регрессионного анализа установлено, что на функциональный исход острого периода ПМИПИ влияли возраст больных (ОШ 1,06, 95 % ДИ 1,00–1,11, $p = 0,0284$), контралатеральная локализация ПМИПИ (ОШ 2,86 95% ДИ 1,05–7,79, $p = 0,0391$), значение суммарного балла по NIHSS на 1 сутки (ОШ 1,76, 95 % ДИ 1,38–2,26; $p < 0,0001$), объем очага поражения (ОШ 1,03, 95 % ДИ 1,00–1,05, $p = 0,0221$). Установлено, что локализация ПМИПИ в контралатеральном полушарии ассоциировалась с худшим функциональным исходом на 21 сутки заболевания ($\chi^2 = 4,44$, $p = 0,0352$). Установлено независимое влияние инициального уровня гликемии на функциональный исход острого периода ПМИПИ у пациентов без сахарного диабета (ОШ 2,39, 95 % ДИ 1,32–4,33, $p = 0,0042$).

Выводы. Независимый предиктор неблагоприятного функционального исхода острого периода ПМИПИ (mRS ≥ 3 на 21 сутки) – значение суммарного балла по NIHSS >10 на 1 сутки заболевания (чувствительность 73,3 %, специфичность 90,5 %). Разработана математическая модель, учитывающая инициальные уровни неврологического дефицита и гликемии и позволяющая определять прогноз функционального исхода острого периода ПМИПИ с точностью до 87,5 % (AUC = 0,92, $p < 0,05$).

Cerebrovascular diseases, particularly cerebral ischemic stroke (IS) is the leading reason of disability and mortality throughout the world. It has been shown that the risk of recurrent acute cerebrovascular events among people who have had stroke in the past is 6–9 times higher than among people of the same age and sex without history of stroke. During the first year, every fourth person has a recurrent stroke [1–3], while the indicators of the 5th and 10th year cumulative risk of recurrent stroke reach 16.6 % and 43.0 % respectively. It has been revealed that recurrent IS is characterized by more severe course, accompanied by higher level of neurological deficiency and it is the common reason of severe cognitive impairments, which makes this problem extremely relevant in the medical, social and economic aspects [1–4]. Development of differentiated approach, which includes individual prognosis, is the optimal management strategy for increase the effectiveness of treatment patients with IS [5]. Numerous studies have found that the leading factors which influence the stroke outcome are: the age of the patient, the initial level of neurological deficits, infarct volume, the severity of the dislocation syndrome, and the presence of decompensated somatic pathology [6,7].

Accumulated certain information as for negative influence of stress hyperglycemia, hypercoagulation and proinflammatory activation on the course and IS outcome [8,9]. However, the issue of predicting the functional outcome of the acute period of recurrent IS stays unclear, so that justifies the necessity of our investigation, which dedicated to develop criteria for predicting the functional outcome of the acute period of recurrent cerebral ischemic hemispheric stroke (RCIHS) based on a comprehensive clinical and paraclinical investigations.

Materials and methods

Prospective, cohort and comparative hospital-based study which enrolled 111 patients (49 women and 62 men, age 72.0 (64.0; 77.0) years) with acute RCIHS was conducted. The inclusion of patients in the study was carried out according to the following criteria:

1. Men and women aged from 45 to 85 years.
2. Verified IS in the past.

3. Clinical and neuroimaging confirmations of RCIHS.
4. Atherothrombotic or cardiomyolic subtypes of IS according to TOAST classification.

5. Hospitalization in the first 24 hours from RCIHS onset.

6. Signed informed consent of the patient participation in the study.

The criteria for exclusion from the study were:

1. The presence of two or more focuses of lesion.
2. Hemorrhagic transformation of ischemic focus.
3. Combined cerebral stroke.
4. Baseline NIHSS score ≥ 20 .
5. Admission mRS score ≥ 3 (after primary stroke).
6. Lethal outcome of acute period of RCIHS.
7. Presence of oncological and/or decompensated somatic pathology.
8. Anamnestic data about alcohol abuse, craniocerebral trauma.
9. Psychopathological syndrome.

The baseline assessment of stroke severity was conducted using the National Institute of Health Stroke Scale (NIHSS). The functional outcome of the acute period of RCIHS was evaluated by Modified Rankin Scale (mRS) on the 21st day after stroke onset. Depending on mRS score all patients were divided into two groups. Thus the value of mRS score ≥ 3 was considered as an unfavorable functional outcome, whereas mRS score ≤ 3 was considered as a favorable one.

In order to verify the diagnosis of RCIHS and to assess the structural changes in the brain, all patients underwent brain computer tomography (CT) which was performed using Siemens Somatom Spirit (Germany). The localization, the infarct volume, the presence and severity of the dislocation process, the size and localization of the cyst (a sign of a previously ischemic stroke) were determined during CT. The infarct volume (IV) was evaluated by the following formula: $IV = (abc\pi)/6$, where a, b, c – the linear dimensions of the lesion center according to the computer tomography (cm).

The baseline laboratory investigations included hematological and biochemical samples, which were taken from a cubital vein. The levels of absolute white blood cells and their subpopulations, glucose levels,

the prothrombin index, and the content of fibrinogen in plasma were determined during laboratory assessment. The neutrophil-to-lymphocytic ratio (NLC) was considered as a marker of proinflammatory activation.

Statistical processing of the obtained results was carried out using the software Statistica 13.0 (StatSoft Inc., USA, serial number JPZ8041382130ARCN10J). Since the distribution of most of the studied indicators (according to the Shapiro–Wilk criterion) was different from normal, descriptive statistics was presented as median and interquartile intervals. The presence of intergroup differences in quantitative parameters was determined using the Mann–Whitney criterion. The Pearson χ^2 criterion was used to assess the correlations between qualitative indicators. In order to detect the dependent and independent risk factors of the unfavorable functional outcome of the acute period of RCIHS, univariate and multivariate regression analysis was conducted. The predictive value of the indicators was evaluated using ROC analysis with the calculation of sensitivity and specificity. Statistical significance of results was defined at the P value <0.05.

Results

Unfavorable functional outcome (UFO) was detected in 90 (81.1 %) patients, while 21 (18.9 %) patients had favorable functional outcome (FFO). Patients did not differ in gender structure (48 (53.3 %) males and 42 (46.7 %) females with NFU versus 14 (66.7 %) and 7 (33.3 %) respectively with FFO ($\chi^2 = 1.23$, $P = 0.2679$). The median of the time interval between first-ever stroke and recurrent one among patients with FFO was 24.0 (9.0; 48.0) months, that was not significantly different from patients with UFO, which had RCIHS in 20.5 (11.0; 36.0) months ($P = 0.269$). The patients with UFO were older than patients with FFO (74.0 (65.0; 79.0) years versus 66.0 (60.0; 74.0) years, $P = 0.0127$).

The frequency of right-hemisphere localization of RCIHS in patients with UFO was significantly higher than in patients with FFO (46.7 % versus 19.1 %, $\chi^2 = 5.30$, $P = 0.0213$). Difference in lateralization of RCIHS regarding to first-ever stroke lesion was found: localization of RCIHS in the ipsilateral hemisphere was more frequent among patients with FFO (66.7 % versus 41.4 %, $\chi^2 = 4.44$, $P = 0.0352$). At the same time, the frequency

of UFO in case of contralateral RCIHS localization consisted 88.3 %, which was 1.22 times higher than in case of ipsilateral RCIHS.

Diabetes mellitus was diagnosed in 20 (22.2 %) patients with UFO and in 3 patients (14.3 %) with FFO ($\chi^2 = 0.95$, $P = 0.3922$), atrial fibrillation in 35 (38.9 %) and 8 (38.1 %) patients respectively ($\chi^2 = 0.005$, $P = 0.974$).

Clinical and paraclinical characteristics of the general cohort patients as well as results of comparative analysis of neurological, computer-tomographic, biochemical and hematological parameters in comparison with the functional outcome of the acute period of RCIHS are presented in *Table 1*.

As shown in *Table 1*, patients with UFO at baseline assessment had significantly difference in: NIHSS score (12.0 (10.0; 14.0) points versus 8.0 (6.0; 10.0) points, $P < 0.0001$), infarct volume (36.5 (23.4; 65.3) ml versus 18.6 (11.6; 28.8) ml, $P = 0.0053$) and in glucose serum level (6.1 (5.0; 7.7) mmol/l versus 5.1 (4.8; 5.3) mmol/l, $P = 0.0034$). At the same time, no significant intergroup differences in levels of hematocrit, fibrinogen, prothrombin index, hematologic markers of proinflammatory activation were detected.

Univariate logistic regression analysis showed that age of patients (OR 1.06 95 % CI 1.00–1.11, $P = 0.0284$), contralateral localization of RCIHS (OR 2.86 95 % CI 1.05–7.79, $P = 0.0391$), baseline NIHSS score (OR 1.76 95 % CI 1.38–2.26, $P < 0.0001$), the infarct volume (OR 1.03 95 % CI 1.00–1.05, $P = 0.0221$) were the factors associated with stroke outcome.

According to multivariate logistic regression analysis the independent influence of the baseline NIHSS score on functional outcome of RCIHS (OR 1.74 95 % CI 1.36–2.23, $P < 0.0001$) was proved. Based on ROC-analysis it was found that baseline NIHSS score >10 was predictor of UFO of the acute period of RCIHS (AUC = 0.86, $P < 0.05$) with an optimal ratio of sensitivity (73.3 %) and specificity (90.5 %).

At the second stage of the study, the prognostic value of clinical neurological, computed tomography, biochemical and hematological parameters was determined among 88 patients without diabetes mellitus.

Unfavorable functional outcome of the acute period of RCIHS was determined in 70 (79.5 %) patients (38 men and 32 women), FFO – in 18 (20.5 %) persons (5 men

Table 1. Clinical and paraclinical characteristics of general cohort of patients with recurrent cerebral hemispheric ischemic stroke and comparative analysis of clinical neurological, computed tomography, biochemical and hematological parameters in comparison with the functional outcome of acute period of disease

Parameters, units	Total cohort (n = 111)	mRS <3 on the 21 st day (n = 21)	mRS ≥3 on the 21 st day (n = 90)	P
NIHSS score at baseline, points	12.0 (10.0; 13.0)	8.0 (6.0; 10.0)	12.0 (10.0; 14.0)	<0.0001
Infarct volume, ml	32.4 (17.9; 56.9)	19.8 (12.3; 28.8)	35.8 (23.0; 61.9)	0.0035
The volume of the post-stroke cyst, ml	8.3 (2.1; 18.4)	7.9 (2.3; 17.4)	8.7 (2.1; 19.0)	0.9169
Glucose serum level, mmol/l	5.9 (5.0; 7.2)	5.1 (4.8; 5.3)	6.1 (5.0; 7.7)	0.0034
Fibrinogen, g/l	3.5 (2.9; 4.4)	3.5 (2.7; 4.4)	3.5 (2.9; 4.4)	0.9969
Prothrombin index, %	90.0 (86.0; 96.0)	88.0 (86.0; 96.0)	91.0 (85.5; 96.0)	0.5801
Hematocrit, %	41.0 (37.5; 45.0)	41.0 (37.0; 43.0)	42.0 (37.8; 46.0)	0.3506
White blood cells (WBC), G/l	7.6 (6.3; 9.5)	6.8 (5.7; 10.1)	7.7 (6.4; 9.4)	0.1718
Absolute neutrophils count (ANC), G/l	5.5 (4.3; 7.6)	5.2 (3.8; 7.9)	5.8 (4.5; 7.3)	0.2833
Absolute lymphocyte count (ALC), G/l	1.3 (0.9; 1.9)	1.1 (1.0; 1.7)	1.4 (0.8; 1.9)	0.7433
Absolute monocyte count, G/l	0.4 (0.3; 0.6)	0.3 (0.2; 0.3)	0.4 (0.3; 0.6)	0.6299
NLC	4.4 (2.8; 7.0)	3.9 (2.9; 5.4)	4.6 (2.2; 7.3)	0.7206

Table 2. Clinical and paraclinical characteristics of general cohort of patients with recurrent cerebral hemispheric ischemic stroke without diabetes mellitus and comparative analysis of clinical neurological, computed tomography, biochemical and hematological parameters in comparison with the functional outcome of acute period of disease

Parameters, units	Total cohort (n = 88)	mRS <3 on the 21 st day (n = 18)	mRS ≥3 on the 21 st day (n = 70)	P
NIHSS score at baseline, points	12.0 (10.0; 14.0)	8.0 (6.0; 10.0)	12.0 (10.0; 14.0)	0.001
Infarct volume, ml	32.4 (17.9; 56.9)	18.6 (11.6; 28.8)	36.5 (23.4; 65.3)	0.0053
The volume of the post-stroke cyst, ml	6.9 (1.9; 16.5)	4.0 (0.9; 14.4)	6.9 (1.9; 16.5)	0.4438
Glucose serum level, mmol/l	5.5 (5.0; 7.2)	5.0 (4.6; 5.2)	6.0 (5.0; 7.7)	0.0118
Fibrinogen, g/l	91.0 (85.5; 96.0)	90.5 (85.0; 96.0)	91.0 (86.0; 96.0)	0.8526
Prothrombin index, %	3.4 (2.9; 4.6)	3.7 (2.7; 4.9)	3.4 (2.9; 4.4)	0.9070
Hematocrit, %	42.0 (37.8; 46.0)	41.5 (37.0; 44.0)	42.0 (38.0; 46.0)	0.3350
White blood cells (WBC), G/l	7.6 (6.3; 9.5)	6.8 (5.7; 10.1)	7.7 (6.4; 9.4)	0.1657
Absolute neutrophils count (ANC), G/l	5.4 (4.3; 7.2)	5.5 (4.5; 7.1)	4.9 (3.8; 7.9)	0.2797
Absolute lymphocyte count (ALC), G/l	1.4 (0.9; 1.9)	1.5 (0.8; 2.0)	1.2 (1.0; 1.7)	0.7289
Absolute monocyte count, G/l	0.4 (0.3; 0.6)	0.4 (0.2; 0.6)	0.4 (0.3; 0.6)	0.4690
NLC	4.1 (2.6; 6.6)	4.2 (2.4; 7.1)	3.7 (2.9; 5.4)	0.8280

and 13 women). No significant intergroup differences in gender structure were detected ($\chi^2 = 1.87$, $P = 0.1716$), however the patients with FFO were significantly younger (66.0 (59.0; 74.0) years versus 73.0 (65.0; 77.0) years, $P = 0.0245$). The frequency of left-stroke localization (77.8 % compared with 50.0 %, $\chi^2 = 4.43$; $P = 0.0354$) was significantly higher in patients who had FFO of RCIHS without diabetes mellitus. It was found that the lesion of contralateral hemisphere (61.4 % compared with 27.8 %, $\chi^2 = 6.46$; $P = 0.0110$) was significantly higher among patients with FFO without diabetes mellitus. No significant differences in median of time interval between first-ever stroke and recurrent one was detected (24.0 (9.0; 48.0) months in patients with FFO versus 21.0 (11.0; 32.0) months in patients with UFO, $P = 0.6894$).

Atrial fibrillation was diagnosed among 27 (38.6 %) patients with FFO and among 7 (38.9 %) patients with UFO ($\chi^2 = 0.0006$, $P = 0.9803$).

Comparative analysis of clinical neurological, computed tomography, biochemical and hematological parameters among patients without diabetes mellitus revealed the presence of significant intergroup differences by following indicators: baseline NIHSS score (8.0 (6.0; 10.0) points in patients with FFO versus 12.0 (10.0; 14.0) points in patients with UFO, $P = 0.001$), the infarct volume (18.6 (11.6; 28.8) ml versus 36.5 (23.4; 65.3), $P = 0.0053$), glucose serum level (5.0 (4.6; 5.2) mmol/l versus 6.0 (5.0; 7.7) mmol/l, $P = 0.0118$). According to other indicators significant intergroup differences were not found (Table 2).

Based on univariate logistic regression analysis it was found that contralateral stroke localization (OR 4.14 95 % CI 1.33–12.92, $P = 0.0144$), baseline NIHSS score (OR 1.83 95 % CI 1.38–2.42, $P < 0.0001$), the infarct volume (OR 1.03; 95 % CI 1.00–1.06, $P = 0.0266$), glucose serum level (OR 2.39 95 % CI 1.32–4.33, $P = 0.0042$) had association with functional outcome among patients without diabetes mellitus. Taking into account the results of multivariate regression analysis it was proved that functional outcome of RCIHS was independently associated not only with baseline NIHSS score (OR 1.77, 95 %, CI 1.32–2.38, $P = 0.001$) but with glucose serum level as well (OR 2.69, 95 %, CI 1.15–6.28, $P = 0.0220$). These indicators have been integrated into a prediction model of the following form: $\beta = 0.57 \cdot P_1 + 0.99 \cdot P_2 - 9.63$, where P_1 – baseline NIHSS score, P_2 – baseline glucose serum level.

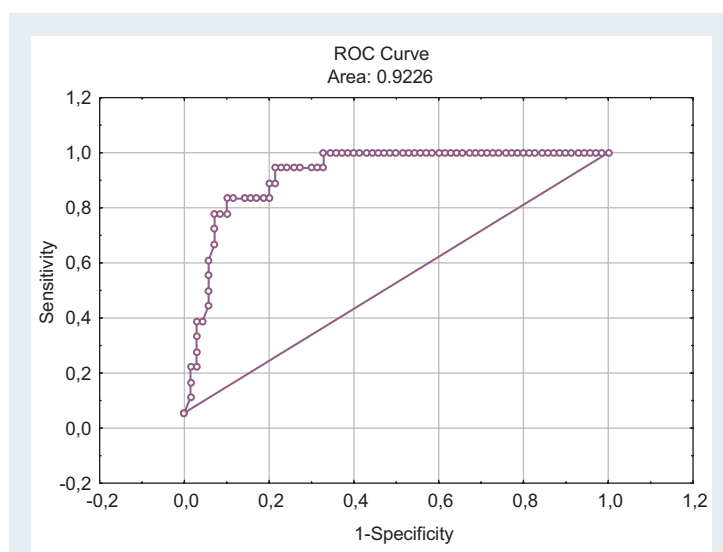


Fig. 1. ROC-curve for the developed mathematical model.

Based on ROC-analysis it was found that $\beta > 0.82$ is the integral predictor of UFO of the acute period RCIHS (AUC = 0.92, $P < 0.05$) with high sensitivity (90.0 %) and specificity (83.3 %) (Fig. 1).

The prediction accuracy of the developed mathematical model was 87.5 %.

Discussion

Based on our investigation, it was found that age of patient, localization of recurrent cerebral ischemic hemispheric stroke in the contralateral hemisphere, initial level of neurological deficiency and the infarct volume are the most important factors that negatively affect the functional outcome of the acute period of disease. The obtained results are in agreement with the results of other studies. Thus, in numerous studies it has been defined that younger patients have better stroke outcome and they have higher abilities for recovering than older people. In our opinion, it may be explained by the decrease in neuronal plasticity of the brain as a result of aging in conjunction with an increase in the frequency of comorbidity pathology, which worsens the recovery of the patient.

In our study we found out that the frequency of UFO among patients with contralateral localization of recurrent cerebral ischemic hemispheric stroke consisted 88.3%. It was 1.22 times higher than in patients with localization of recurrent cerebral ischemic hemispheric stroke in the ipsilateral hemisphere ($P = 0.0352$). These data coincide with the results of clinical and experimental studies [6, 10]. Thus, in the Copenhagen Stroke Study it was revealed, that patients who had recurrent stroke in the contralateral hemisphere regarding to the first-ever stroke, demonstrated worse functional outcome in comparison with patients with localization of RCIHS in the ipsilateral hemisphere [11]. Data from an experimental study by C. Fan et al. (2017) where the effect of recurrent cerebral ischemic hemispheric stroke lateralization on the level of α -mRNA tumor necrosis factor α was studied, also indicate that the severity of the brain injury following by second ischemic event would be alleviated when the second stroke located in the ipsilateral hemisphere [12].

The frequency of RCIHS localization in the right hemisphere in patients with UFO was significantly higher than in patients with FFO (46.7 % compared with 19.1 %, $\chi^2 = 5.30$, $P = 0.0213$). In accordance with the data of S. Laredo et al. (2018) patients with left and right hemisphere localization of stroke had no difference in the level of neurological deficiency [13], while in the study of V. S. Hedna et al. (2015), with the involvement of 2.673 patients with CHIS it was found that infarctions in the right hemisphere are characterized by more severe neurological deficiency [14]. On the one hand, our findings can be explained by the negative influence of the spatial neglect syndrome, which significantly impairs the functional recovery and is specific for right hemisphere damage. On the other hand, we support the idea that right hemisphere plays a crucial role in the cardiovascular regulation due to autonomic nervous system lateralization so that sympathetic functioning used to be more affected by right hemisphere stroke, which more often accompanies increase norepinephrine levels as well as elevations of blood pressure [15].

The obtained results concerning the influence of the infarct volume on functional outcome completely coincided with the data of other studies [16, 17].

Multivariate logistic regression analysis proved that baseline NIHSS score, was an independent factor associated with functional outcome of RCIHS. It also is in agreement with numerous studies that have proven a significant influence of the initial level of neurological deficiency on the functional outcome of cerebral ischemic hemispheric stroke [7, 18].

Based on the ROC analysis it was found that baseline NIHSS score >10 was a predictor of unfavorable functional outcome of the acute period of the RCIHS and was optimum for the ratio of sensitivity (73.3 %) and specificity (90.5 %). It coincides with S. A. Raza et al (2017) study where it was proved that total NIHSS score >10 is a predictor of severe disability [19]. However, in studies by M. E. Reznik et al. (2018) [20] and V. Inoa et al. (2014) [7] in which first-time CHIS patients were involved, the NIHSS total score for determining the risk of UFO was slightly lower: ≥ 6 and ≥ 8 respectively.

Our study did not reveal intergroup differences in levels of hematocrit, prothrombin index, fibrinogen and

hematological parameters among patients with different functional outcomes of the acute period of RCIHS. The obtained data dissociated with the results of a few studies, which described the association between the neutrophil-lymphocyte ratio [21] and the level of fibrinogen in plasma [22] with the functional outcome of cerebral ischemic hemispheric stroke. All mentioned above suggests that clinical neuroimaging methods have greater predictive value than the laboratory parameters.

Univariate logistic regression analysis which was performed among patients without diabetes mellitus, revealed an independent association of glucose serum levels and functional outcome of the acute period RCIHS (OR 2.69 95 % CI 1.15–6.28, $P = 0.0220$). Patients with UFO significantly differed in higher level of glycemia at baseline (6.0 (5.0; 7.7) mmol/l compared with 5.0 (4.6; 5.2) mmol/l, $P = 0.0118$). The obtained data are consistent with numerous studies, in which negatively influence of increased serum glucose level on the functional stroke outcome was proved [8, 23]. Thus, GLIAS (Glycemia in Acute Stroke) multicentre study described a high predictive value of an initial glucose serum levels in patients with ischemic stroke [23]. According to the study by J. Sung et al. (2017), serum glucose concentration during hospitalization of a patient with IS is a highly informative indicator for the determination of functional prognosis [24].

In order to cumulate the predictive value of the baseline NIHSS score and glucose serum level were integrated into the mathematical model that allows to determine the functional outcome of the acute period of RCIHS among patients without diabetes mellitus with an accuracy of 87.5 % (AUC = 0.92, $P < 0.05$).

The ROC analysis determined the value of β , which is an integral predictor of UFO of the acute period of RCIHS among patients without diabetes mellitus (sensitivity 90.0 %, specificity 83.3 %). It is expedient to use the developed mathematical model in routine clinical practice for improving the accuracy of prediction of functional outcome in patients.

Conclusions

1. Initial level of neurological deficiency (OR 1.74 95 % CI 1.36–2.23, $P < 0.0001$) and glucose serum level at baseline (OR 2.39 95 % CI 1.32–4.33, $P = 0.0042$) (in the absence of diabetes mellitus) had the most significant influence on the functional outcome of the acute recurrent cerebral ischemic hemispheric stroke.
2. Localization of recurrent cerebral ischemic hemispheric stroke in the contralateral hemisphere regarding first-ever stroke was associated with a unfavorable functional outcome on the 21st day of the disease. ($\chi^2 = 4.44$, $P = 0.0352$).
3. Baseline NIHSS score >10 was an independent predictor of unfavourable functional outcome which was determined by the mRS score ≥ 3 (sensitivity 73.3 %, specificity 90.5 %).
4. The mathematical model which included the level of initial neurological deficit and glucose serum level could predict the functional outcome of recurrent cerebral ischemic hemispheric stroke in patients without

diabetes mellitus with accuracy of 87.5 % (AUC = 0.92, $P < 0.05$).

Prospect of work is development of clinical and para-clinical criteria for vital prediction of the acute recurrent cerebral ischemic hemispheric stroke outcome.

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