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THE OPTIONS FOR PROGNOSIS OF THE OUTCOME OF ISCHEMIC STROKE IN YOUNG PATIENTS

V.V. Gusev[1,2,3]*, O.A. Lvova[1,2], O.P. Kovtun[1], N.A. Shamalov[4], A.P. Sergeev[2,5], M.V. Sergeeva[5], D.A. Medvedeva[6]

[1] Ural State Medical University, Yekaterinburg,
[2] Ural Federal University Named After the First President of Russia B.N. Yeltsin, Yekaterinburg,
[3] Central City Clinical Hospital № 23, Yekaterinburg,
[4] Institute of Cerebrovascular Pathology and Stroke "Federal Brain and Neurotechnology Center", Moscow,
[5] Institute of Industrial Ecology of the Russian Academy of Sciences, Ural Department, Yekaterinburg,
[6] Children`s City Clinical Hospital № 9, Yekaterinburg, Russian Federation

ВАРИАНТЫ ПРОГНОЗИРОВАНИЯ ИСХОДОВ ИШЕМИЧЕСКОГО ИНСУЛЬТА У ЛИЦ МОЛОДОГО ВОЗРАСТА

В.В. Гусев[1,2,3]*, О.А. Львова[1,2], О.П. Ковтун[1], Н.А. Шамалов[4], А.П. Сергеев[2,5], М.В. Сергеева[5], Д.А. Медведева[6]

[1] Уральский государственный медицинский университет, г. Екатеринбург,
[2] Уральский государственный университет имени первого Президента России Б.Н. Ельцина, г. Екатеринбург,
[3] Центральная городская клиническая больница № 23, г. Екатеринбург,
[4] Институт цереброваскулярной патологии и инсульта Федерального центра мозга и нейротехнологий, г. Москва,
[5] Институт промышленной экологии Уральского отделения РАН, г. Екатеринбург,
[6] Детская городская клиническая больница № 9, г. Екатеринбург, Российская Федерация

tel. +7 912 284 18 25
e-mail: gusev_vadim@inbox.ru
[Gusev V.V. (*contact person) – Candidate of Medical Sciences, Associate Professor, ORCID: 0000-0003-2232-7074; Lvova O.A. – MD, PhD, Associate Professor, ORCID: 0000-0002-2280-3096; Kovtun O.P. – MD, PhD, Professor, Academician of the Russian Academy of Sciences, Rector, ORCID: 0000-0002-5250-7351; Shamalov N.A. – MD, PhD, Professor, ORCID: 0000-0001-6250-076; Sergeev A.P. – Candidate of Physical-Mathematical Sciences, Associate Professor, ORCID: 0000-0001-7883-6017; Sergeeva M.V. – Researcher, ORCID: 0000-0002-9782-5185; Medvedeva D.A. – Physician, ORCID: 0000-0001-8613-5982].

тел. +7 912 284 18 25
e-mail: gusev_vadim@inbox.ru
[Гусев В.В. (*контактное лицо) – кандидат медицинских наук, доцент, ORCID: 0000-0003-2232-7074; Львова О.А. – доктор медицинских наук, доцент, ORCID: 0000-0002-2280-3096; Ковтун О.П. – доктор медицинских наук, профессор, академик РАН, ORCID: 0000-0002-5250-7351; Шамалов Н.А. – доктор медицинских наук, профессор, ORCID: 0000-0001-6250-076; Сергеев А.П. – кандидат физико-математических наук, доцент, ORCID: 0000-0001-7883-6017; Сергеева М.В. – научный сотрудник, ORCID: 0000-0002-9782-5185; Медведева Д.А. – врач, ORCID: 0000-0001-8613-5982].

Objective. To develop criteria for prognosis of the outcome of ischemic stroke, taking into account age, dynamics of state assessment, the Rankin and NIHSS scales readings and the fact of disability in the long-term period. The universal reliable criteria, that allow to predict the outcome of ischemic stroke, have not been developed yet.
Material and methods. The study group consisted of 246 patients with ischemic stroke aged 18 to 44 who were observed from 2008 to 2021.
Results. It is impossible to predict disability in a long-term period of ischemic stroke reliably. Predicting the outcome of ischemic stroke using the Rankin and NIHSS scales is significant in the acute period and allows to predict the dynamics of recovery in mild and moderate cases.
Conclusion. The predictive value of the integrative indicators of the patient's condition, assessed by the Rankin and NIHSS scales, has been established.
Keywords. Stroke, young age, mRS, prognosis.

Цель. Разработка критериев прогнозирования исходов ишемического инсульта (включая инвалидность) с учётом возрастного аспекта, динамики оценки состояния, показателей шкал Рэнкина и NIHSS. В настоящее время не разработаны универсальные достоверные критерии, позволяющие с высокой точностью предсказать исход ишемического инсульта у конкретного пациента.
Материал и методы. В период с 2008 по 2021 г. наблюдали 246 пациентов в возрасте от 18 до 44 лет включительно, перенесших ишемический инсульт.
Результаты. Достоверно спрогнозировать инвалидность в отдаленном периоде ишемического инсульта не представляется возможным. Благоприятные исходы ишемического инсульта в виде высокого уровня самообслуживания, а также сохранения трудоспособности возможны по показателям шкал Рэнкина и NIHSS в остром периоде.
Выводы. Установлена прогностическая ценность интегративных показателей состояния пациента, оцениваемых по шкалам Рэнкина и NIHSS.
Ключевые слова. Инсульт, молодой возраст, mRS, прогнозирование.

INTRODUCTION

The social consequences of ischemic stroke are currently one of the significant problems of modern society. Although most cases of stroke are diagnosed in the elderly, approximately 10 % of all onsets of the disease occur at a young age (the so-called "young" strokes) [1–4].

Ischemic stroke in young people causes limitations in the quality of life and professional status [5–7]. According to various sources, from 50 to 70 % of young people after an ischemic stroke return to work, and the period of time ranges from a few days after the stroke to 40 months, an average of 8 months. However, about 25 % of them need adjustments (another job or part-time work) in their profession due to their inability to perform their previous activities after a stroke, so less than half of patients return to their previous job [4–7].

There are no well-known risk factors indicating the likelihood of disability in the outcome of ischemic stroke in young patients [4–7]. Our research group attempted to predict a decrease in the level of disability in patients who have suffered an ischemic stroke using a combination of available anamnestic, clinical and laboratory data, assessment of the condition according to the Rankin and NIHSS scales readings [8–9] in the acute and long-term periods of ischemic stroke.

The objective of the study is to develop criteria for prognosis of the outcome of ischemic stroke (including disability), taking into account age, dynamics of state assessment, the Rankin and NIHSS scales readings.

MATERIALS AND METHODS

In the period from 2008 to 2021, 246 patients aged 18 to 44 years inclusive who had suffered an ischemic stroke were observed. Ischemic stroke was confirmed clinically and by neuroimaging results. On average, patients were observed for 6.18 ± 2.1 years. An analysis of the recurrence rate of vascular events and the frequency of deaths in the study groups, Rankin scale readings, analysis of the results of laboratory and instrumental research methods, as well as RMIS (Regional Medical Information System) data, the presence of disability (medical and social assessment certificate, extract from the certificate of examination of a citizen recognized as disabled, issued by the Federal Government Institution Main Bureau of Medical and Social Expertise) was performed.

To process the data, the mathematical method of linear discriminant analysis was performed using the Statistica 10.0 program.

RESULTS AND DISCUSSION

The universal criterion for assessing the severity of a condition after a stroke is the Rankin scale score (Modified Rankin Scale – mRS). We have assessed the results of recovery of patients after ischemic stroke in the long-term period (from 2 to 11 years) using this criterion (table).

The overwhelming majority of surviving patients ($n = 187$, 77.6 %) could be characterized in the period of residual effects as having a fairly high degree of self-care and minimal limitations in life due to the disease (0–2 on the Rankin scale).

We have recorded obvious positive dynamics in assessing the condition of young adult patients: in the period of residual effects, according to the Rankin scale, the number of patients who had 3–5 scores in the acute period decreased by 5.3 times (191 and 36, respectively).

A total of 47 recurrent acute cerebrovascular events were recorded in the observed group, including 35 ischemic strokes (74.5 %), with 3 patients developing 2 recurrent ischemic strokes each, 2 patients having 3 strokes, and 14 patients having fatal recurrent ischemic strokes. Transient ischemic attacks were observed in 9 patients (17.2 %). Hemorrhagic strokes were recorded in 3 patients (6.4 %), 2 of them against the background of taking anticoagulants, and one against the background of antiplatelet therapy; 2 patients died. Other acute ischemic events were recorded in 14 patients, of which 9 developed myocardial infarction.

It should be noted that there were no fatal outcomes during the inpatient stay in the patients we studied. A total of 23 patients (9.0 %) died during the observation period. The causes of death in the main group were recurrent ischemic stroke in

Dynamics of the severity of patients' condition in the acute and late periods based on the results of the Rankin scale assessment

Group	Rankin Score						
	0	1	2	3	4	5	6
The main group in the acute period (n = 248), abs. (%)	3 (1.2)	10 (3.90)	44 (17.2)	96 (37.5)	59 (23.0)	36 (14.1)	0
Main group at outcome (n = 246), abs. (%)	61 (24.8) *	82 (33.3) *	44 (17.9) *	20 (8.1) *	13 (5.3) *	3 (1.2) *	23 (9.4) *

N o t e: * – $p < 0.05$ when comparing the Rankin scale score in patients over time.

14 cases (60.9 %), hemorrhagic stroke in 2 cases (8.7 %) (in one of these patients, hemorrhagic stroke developed against the background of Fabry disease). 2 patients (8.7 %) died as a result of myocardial infarction. In 5 cases (21.8 %), the causes of death were other reasons (oncological diseases, bleeding of internal organs, diabetes mellitus, etc.).

Disability was established in 23.4 % (n = 60) of patients: group I – in 11 (18.3 %), II – in 23 (38.3 %), and III – in 26 (43.3 %). It is worth noting that the basis for establishing disability was not always neurological causes; in three young adults diabetes mellitus was the cause, one patient had mental disorders, and two had cardiovascular pathology.

In most cases, factors that can be regarded as obvious predictors of persistent impairment of life activity and social interaction in patients after a stroke remain unknown. Thus, we were faced with the task of predicting disability based on a combination of available anamnestic and clinical laboratory data.

To solve this problem, the research group selected prognostically significant features that were significantly different in patients at an atypical age who had not formed and formed persistent impairment of life activity and social interaction with the establishment of disability after the end of the recovery period of the disease. The use of the mathematical method of linear discriminant analysis made it possible to identify a set of features that characterized each variant of the outcome of ischemic stroke (disability or its absence) and to obtain a decision rule (IPI – integrative prognostic index), allowing each patient to be assigned to a certain group, when it is not known in advance which of the groups he belongs to. If, as a result of substituting the data of a specific patient into the decision rule, the IPI value is less than 0, then the patient is assigned to the group without disability, if the IPI is greater than 0 – then to the group that has formed disability.

In total, 14 parameters characterizing the anamnesis, clinical picture and laboratory data of the acute period of ischemic stroke were included in the analysis: gender, age, Rankin scale score in the acute period upon admission, NIHSS score, presence of an infarction focus according to CT (MRI) results in the acute period, involved vascular bed, ultra-

sound data of the brachiocephalic arteries (percentage of stenosis), lateralization of clinical symptoms in the acute period, glucose, fibrinogen, platelets levels in the acute period, significant changes in the ECG, pathogenetic type of stroke according to the TOAST criteria and the fact of smoking.

Based on the available data, an integrative prognostic index (IPI, *Z*) was formed using logistic regression by the formula:

$$Z = b_0 + b7Var7 + b8Var8,$$

where b_0 – 3.488881; *b*7 0.5727652; b8 0.07390234; *Var*7 – Rankin scale score upon admission to hospital in the acute period; *Var*8 – NIHSS score upon admission to hospital in the acute period.

Mathematical processing of acute period data made it possible to predict such a parameter as the preservation of working capacity in young adults in the period of residual effects of ischemic stroke (specificity was 94.4 %), while, focusing on the sensitivity of the method (33.9 %), it is not possible to reliably predict disability in ischemic stroke.

Assessing the severity of the patient's condition using the Rankin scale is the most universal and generally accepted indicator that allows for an integrated characterization of the patient's condition at any stage after stroke, including the period of residual effects.

We conducted a mathematical analysis of the relationship between the Rankin scale score in the acute period of the disease and various aspects of prognosis in the long-term period of ischemic stroke. This was demonstrated in the above-described attempt to predict the remote consequences of ischemic stroke (disability) based on available anamnesis information, the course of the acute period of the disease, and clinical and laboratory data.

The registration of a combination of 3 or more scores on the Rankin scale and simultaneously 8 or more scores on the NIHSS scale in a patient in the acute period had a high prognostic potential in relation to an unfavorable outcome of ischemic stroke, assessed on the Rankin scale as 3 scores or more (OR = 17.5; CI 95 % 1.67–182.93; $p = 0.017$).

When assessing the risk of disability in the outcome of ischemic stroke in young patients, based only on the score of 3 points or more on the Rankin scale in the acute period of the disease, its prognostic value was also demonstrated (OR = 2.66; CI 95 % 1.13–4.32; $p = 0.0089$).

At the same time, another traditional indicator for assessing the severity of stroke – NIHSS – in isolation also had a reliable effect on the chance of developing disability as a result of the disease (OR = 5.76; CI 95 % 1.12–8.07; $p = 0.0001$).

It is known that the degree of loss of ability to work and independence in everyday life, assessed by the Rankin scale, does not always strictly correlate with the presence and degree of disability. In this regard, we decided to evaluate the prognostic significance of the Rankin scale in the dynamics of the disease.

It was shown that the presence of 3 scores or more on the Rankin scale in the acute period increases the chance of main-

taining a high score (3 or more) in the period of long-term effects (OR = 2.71; CI 95 % 1.95–3.95; $p = 0.0001$).

8 scores or more on the NIHSS scale in the acute period had the same prognostic value of high Rankin scale scores in the outcome (3 scores or more) (OR = 4.83; CI 95 % 1.97–6.37; $p = 0.0001$).

We also attempted to predict the outcome of ischemic stroke at a young age using the Rankin scale, taking into account the course of the acute period of the disease. The analysis included 14 parameters characterizing the anamnesis, clinical picture and laboratory data of the acute period of stroke: gender, age, Rankin scale score in the acute period upon admission, NIHSS score, the presence of an infarction focus according to CT (MRI) results in the acute period, the involved vascular pool, ultrasound data of the brachiocephalic arteries (percentage of stenosis), lateralization of clinical symptoms in the acute period, glucose, fibrinogen, platelets levels in the acute period, significant changes in the ECG, the pathogenetic type of stroke according to the TOAST criteria and the fact of smoking.

The problem was solved by the mathematical method of discriminant analysis using the Statistica 10.0 program and included the selection of prognostically significant features that definitely differ in patients at an atypical age, who survived and formed or did not form an outcome according to the Rankin scale of 0–2 scores versus 3–5 scores after the end of the disease recovery period.

If, as a result of substituting the data of a specific patient into the decision rule, the IPI value is less than 0, then the patient is assigned to the first group (according to 0–2 Rankin scores), if the IPI is greater than 0, then to the group that formed 3–5 Rankin scores.

Based on the available data, an integrative prognostic index (IPI, Z) was formed using logistic regression by the formula:

$$Z = b_0 + b3Var3,$$

where b_0 – 4.765466; $b3$ 1.023786; $Var3$ – Rankin scale score on admission to hospital in the acute period.

Mathematical processing of the acute period data did not show any significance for predicting the acute period parameters taken into account in the analysis, except for the Rankin scale score in the acute period. The ability to predict such a parameter as good recovery and a high level of self-care (0–2 Rankin scores) in young adults in the period of residual effects of ischemic stroke (specificity 95.2 %), with the impossibility of reliably predicting more severe outcomes according to the Rankin scale (3–5 scores) the sensitivity of the method was determined as 45.8 %.

We also attempted to predict a very good (so-called excellent) outcome of ischemic stroke at a young age according to the Rankin scale (0–1 scores) according to the parameters of the Rankin and NIHSS scales in the acute period of ischemic stroke.

If, as a result of substituting the data of a specific patient into the decision rule, the IPI value is less than 0, then the patient is assigned to the group of excellent outcomes (0–1 Rankin scores), if the IPI is greater

than 0, then to the group that formed 2 or more Rankin scores in the outcome period.

Based on the available data, an integrative prognostic index (IPI, *Z*) was formed using logistic regression by the formula:

$$Z = b_0 + b3Var3,$$

where b_0 – 3.688542; *b*3 1.011257; *Var*3 – Rankin scale score on admission to hospital in the acute period.

The ability to predict such a parameter as excellent recovery and a high level of self-care (0–1 Rankin scores) in young adults in the period of residual effects of ischemic stroke was demonstrated by specificity of 79.0 %, with the impossibility of reliably predicting more severe variants of outcomes according to the Rankin scale (more than 2 scores) the sensitivity of the method was 62.1 %.

The second version of the prognostic rule, taking into account both integrative indices, showed similar results:

$$Z = b_0 + b3Var3 + b8Var8,$$

where b_0 – 3.129286; *b*3 0.5767037; b8 0.1168231; *Var*3 – Rankin scale score on admission to hospital in the acute period; *Var*8 – NIHSS score on admission to hospital in the acute period.

The ability to predict such a parameter as excellent recovery and a high level of self-care (0–1 Rankin scores) in young adults in the period of residual effects of ischemic stroke based on the Rankin and NIHSS scales in the acute period demonstrated a specificity of 85.7 %, with the impossibility of reliably predicting more severe variants of outcomes according to the Rankin scale (more than 2 scores) the sensitivity of the method was 54.5 %.

In order to clarify the role of various indicators of the patient's condition with ischemic stroke in the acute period and the possibility of predicting outcome options using them in the long-term period, we applied the decision trees method. This method took into account both discrete and continuous values for variables denoting factors of the acute period of ischemic stroke.

In total, 14 parameters characterizing the anamnesis, clinical picture and laboratory data of the acute period of stroke were taken into analysis by this machine learning method. An attempt to build a forecast using a decision tree also showed the prognostic value of integrative assessments of patients' condition using the Rankin and NIHSS scales in the acute period of the disease (Figure).

It was shown that the first decision boundary was the NIHSS score of 6.5. The NIHSS score above 6.5 was the condition for moving to the right side of the tree. The second decision boundary was the Rankin scale score in the acute period of ischemic stroke, equal to 3.5. The attempt was successful in terms of specificity (83.2 %) and quite successful in terms of sensitivity (66.1 %). Thus, using another mathematical method of data processing, the prognostic value of only integrative indicators of the patient's condition, assessed by the Rankin and NIHSS scales, was demonstrated once again.

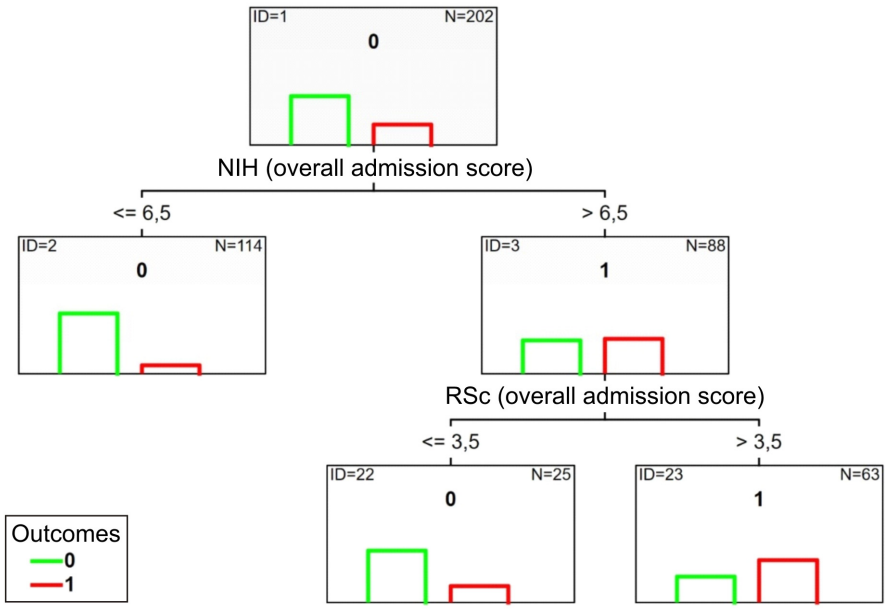

Fig. Decision tree for predicting the preservation of working capacity in the long-term period of IS in young patients: N is the number of patients, ID is the unique identifier of the tree node, NIH is the NIHSS score, RSc is the Rankin scale score in patients in the acute period

Thus, over the observation period (2–11 years), the recurrence rate was 18.3 % (n = 47), fatal outcomes were recorded in 23 young patients, disability was established in 23.4 % (n = 60), which characterizes ischemic stroke at a young age as a significant medical and social problem.

It is not possible to reliably predict disability as a result of ischemic stroke (specificity – 94.4 %, sensitivity – 33.9 %). At the same time, it remains possible to predict favorable outcomes, namely the absence of disability and the preservation of working capacity.

The study found that the Rankin and NIHSS scales have a significant prognostic value for the rate of recovery to mild and moderate status (specificity – 85.7 %, sensitivity of the method – 54.5 %). We also showed that the assessment of the patient's condition according to the NIHSS and Rankin scales in the acute period of ischemic stroke has a high prognostic value (OR 2.66–5.76) in relation to the formation of disability in the period of remote consequences.

Conclusions

The remote outcomes of ischemic stroke developed in young patients were analyzed. High prognostic value of integrative indicators of the patients' condition, assessed by the Rankin and NIHSS scales, was established. Using mathematical methods, a number of prognostic rules were identified for young patients who suffered an ischemic stroke, in terms of the absence of disability and a high level of self-care in the period of remote consequences.

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