Monitoring of Hematological Indices in Prediction of Outcomes in Critical Conditions in Neuroreresistance Patients

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ABSTRACT

The objects of the study were 50 patients with acute cerebral insufficiency (a complication of ischemic and hemorrhagic stroke, as well as traumatic brain injury) aged 32 to 65 years (mean age was 56,3 ± 3 years), in whom clinical (systemic indicators) were analyzed. hemodynamics and respiration, neurological status), instrumental (ECG, chest X-ray, MSCT examination of the brain) and laboratory data (leukoformula, IRNL). Comparison of clinical and laboratory parameters was carried out in three stages: the first stage - on admission, the second stage - the 3rd day, the third stage - the 7th day of intensive therapy. It has been established that a high rate of IRNL is a reliable indicator of the clinical deterioration of the condition of patients and a predictor of an unfavorable outcome of critical conditions caused by acute cerebral insufficiency.

Keywords: ischemic and hemorrhagic stroke, craniocerebral injury, immune system leukoformula.

Introduction: It is known that in neurocritical patients the systemic immune response has specific features and is characterized by leukocytosis in combination with relative lymphopenia, deficiency of the T-cell component of the immune system [4,9] and activation of the humoral immune response with an increase in the blood content of B-lymphocytes (SB19+ , SB20+), A , M, c and cytokines [1,4,20]. This fact allows us to say that the nature of changes in the immune status in acute disorders of cerebral circulation (ADCC) and traumatic brain injury (TBI) has the same vector of direction, so individual indicators of the immune status can be used to assess the prognosis of the course and functional outcome of the disease.

The normal functioning of the immune system is one of the determining conditions for an adequate state of the physiological systems of the body. The decrease in the immunological reactivity of the population determines the features of the formation, course and prognosis of diseases, including neurosurgical ones [8,13,22]. A decrease in the number of lymphocytes leads to a decrease in the body's

resistance to pathogenic microorganisms and is an important manifestation of immunodeficiency in critically ill patients [12,15]. Immunological monitoring will allow to distinguish between rapidly changing phases of progressive inflammation and severe immunosuppression, which will help improve the results of differentiated correction [3,24,25].

Today, clinical laboratory medicine has a huge number of methods for early and accurate diagnosis of a large number of diseases, dynamic control over the pathological process. Quantitative analysis of the leukocyte formula is an important research method that has diagnostic value in critical conditions. A thorough analysis of the leukoformula makes it possible to judge the course of the disease, the occurrence and severity of inflammatory manifestations, and the effectiveness of the therapy [2,26,27]. Along with modern methods of neuroimaging such as MSCT and MRI, successful therapy of critically ill patients with severe forms of acute cerebrovascular accident and TBI is based on laboratory parameters [7,28]. In order to objectify the assessment of these results, a number of indices have been proposed to judge the course of the pathological process in the body, including the severity of inflammatory manifestations and the effectiveness of the therapy [13,18]. According to a number of authors, one of these indicators is the index of the ratio of neutrophils to lymphocytes (IRNL) of blood [6,11,16].

Currently, research is underway to search for biomarkers in all areas of medicine, including in the field of cerebrovascular pathology and traumatic brain injury. Due to their epidemiological characteristics, strokes and TBIs undoubtedly seem to be an important object, since, in addition to high mortality, they are accompanied by a significant incidence of complications and disability, which ultimately result in significant economic costs, since it allows individualizing the approach to treatment and rehabilitation of patients [15,17,29].

In practice, procalcitonin (PCT), presepsin (PSP), C-reactive protein (CRP) are most often used. All of these markers can play a significant role in the diagnosis of infection, but none of them has absolute sensitivity and specificity. Therefore, the search for available reproducible and highly informative markers is still ongoing.

The use of inflammatory biomarkers is one of the routine tools in monitoring the postoperative period. Surgical interventions are closely associated with the development of a systemic inflammatory response of the body, characterized by metabolic and immunological changes [9,19,30]. During this period, there is an increase in the level of circulating neutrophils in the blood and a decrease in the level of lymphocytes, which leads to immunosuppression as one of the key aspects of the development of an infectious complication [10,31]. In this regard, the assessment of the level of neutrophil-lymphocyte ratio can serve as a simple and effective tool for identifying patients with a high risk of developing infectious complications [10,14,32].

Studies aimed at studying the prognostic significance of laboratory tests and their evaluation as biomarkers, due to the insufficiency and inconsistency of existing information, continue to be relevant and in demand. The discovered biomarkers will allow, as knowledge is accumulated, to refine the criteria for prescribing a particular type of therapy, to conduct timely preparation for possible complications, which will undoubtedly increase the effectiveness of treatment of patients with neurocritical care profile [5,21,33].

Based on all the listed literature data, it can be argued that autoimmune inflammation in acute brain injuries is one of the key factors that determine the further development and affect the outcome of the disease. All these characteristics of hematological indices are associated with their predictive significance in relation to the risk of an unfavorable outcome. The search for laboratory biomarkers that can be used to predict the outcome of the disease in patients with neuroresuscitation profile remains an urgent task[23].

Objective of the study: to determine the prognostic significance of IRNL in predicting the outcome of critical conditions caused by stroke.

Materials and methods of research: as an object of research, data of 50 patients who were treated in the Neuroresuscitation department of the Bukhara branch of the Republican Scientific Center for Emergency Medical Care during 2021-2022 were studied. According to nosology, 18 patients diagnosed with acute cerebrovascular accident of the ischemic type, 22 patients with closed craniocerebral injury, 10 patients with a diagnosis of acute cerebrovascular accident of the hemorrhagic type were treated. The collected data included the age of the patients, sex, time of disease development, assessment of neurostatus (level of impaired consciousness), neuroimaging data (MSCT), hemodynamic and respiratory parameters, clinical and laboratory parameters. The mean age of the patients (32 men and 28 women) was 56,3±3 years. The study database included the case histories of patients hospitalized in the first 2 hours after the onset of the disease. All patients underwent diagnostic studies and a treatment program according to the relevant standard.

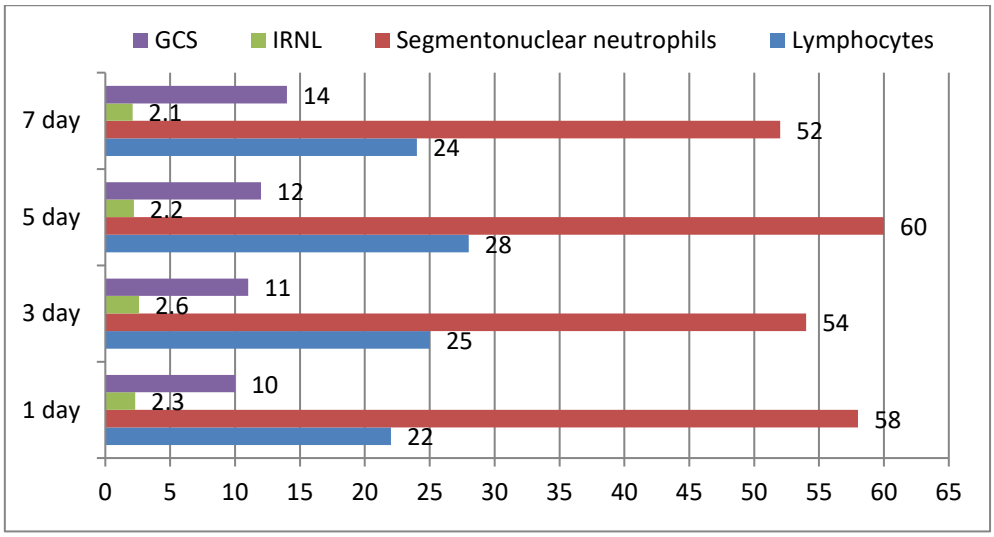
To assess the neurological status of patients, the Glasgow scale (GCS) and Glasgow-Pittsburgh (GCS-P) were used. The study mainly included patients with impairment of consciousness ranging from stupor to stupor (GCS score of 10 or more). In order to assess the state of the brain, all patients underwent a multispiral computed tomography study using a General Electric Revolution (USA) tomograph, which revealed hemorrhages in the brain parenchyma, ventricular system and under the membranes, localization and size of the hemorrhagic or ischemic focus, dislocations of median structures, zones of contusion and perifocal ischemia, the presence of neuroimaging signs of cerebral edema was assessed. Non-invasive monitoring of hemodynamic and respiratory parameters (blood pressure, saturation, heart rate, body temperature and respiratory rate) was performed using a Mindray heart monitor (China).

The control of laboratory parameters included a complete blood count and dynamic changes in the leukoformula, which were repeated upon admission of patients (before treatment) and on days 3, 5, 7 of the treatment process and were checked on a Mindray analyzer (China). Particular attention was paid to the change in the ratio of segmental neutrophils to lymphocytes (IRNL) depending on changes in the neurological status and clinical condition of patients, respectively.

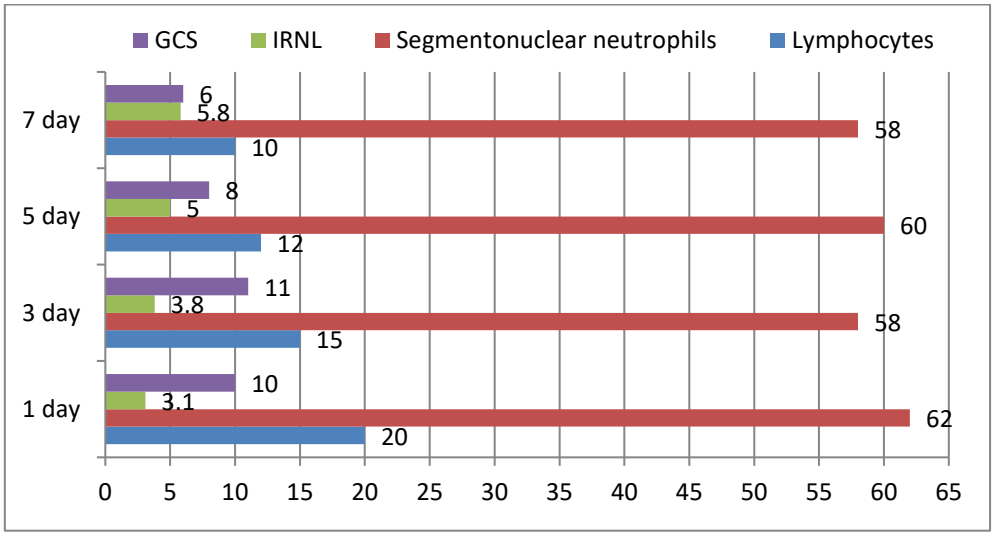
The studied patients, grouped according to nosological characteristics, were comparable to each other in all parameters. Based on the results of examinations of patients, therapeutic measures were carried out in accordance with the generally accepted standard of treatment. These treatments included decongestant, antibacterial, hemorheological, cerebroprotective, anticoagulant, hemostatic, antihypertensive, vasopressor, and symptomatic treatment, depending on the clinical condition of the patients. In a state of coma and with strong psychomotor agitation, patients were adapted to artificial lung ventilation devices with the help of sedatives, anticonvulsants, and maximally synchronous respiratory therapy was performed.

The results of the examination and their discussion: analysis of the parameters of patients treated with a diagnosis of "ischemic stroke" showed that during the initial MSCT examination, it was found that in 12 patients in the a.cerebri media pool, an ischemia focus began to form, and in 4 patients in the pool vertebrobasilar artery. In 2 patients, the ischemic zone was not visible during primary MSCT, but hemisyndrome was clearly manifested. Despite intensive therapeutic measures, the condition of 3 patients with ischemic foci formed in the cerebral hemispheres and 1 brain stem progressively worsened, which led to death. An analysis of the initial and dynamically repeated leukoformula of patients in this group showed

that there were specific changes in the leukoformula and the IRNL index, corresponding to positive changes in the neurological status and clinical condition. The patient's consciousness became clear, the total GCS score increased dynamically, the patients' lymphocytes were always above 20, and the IRNL score was below 3,5 (graph 1[a]). On the contrary, during dynamic observation, the number of neutrophils increased, the number of lymphocytes, respectively, decreased in patients in whom the IRNL index increased from 3,5, worsening of neurostatus, which was reflected in a progressive decrease in the total GCS score (Figure 1[b]), aggravation of the clinical picture and worsening of the general condition , death was noted.



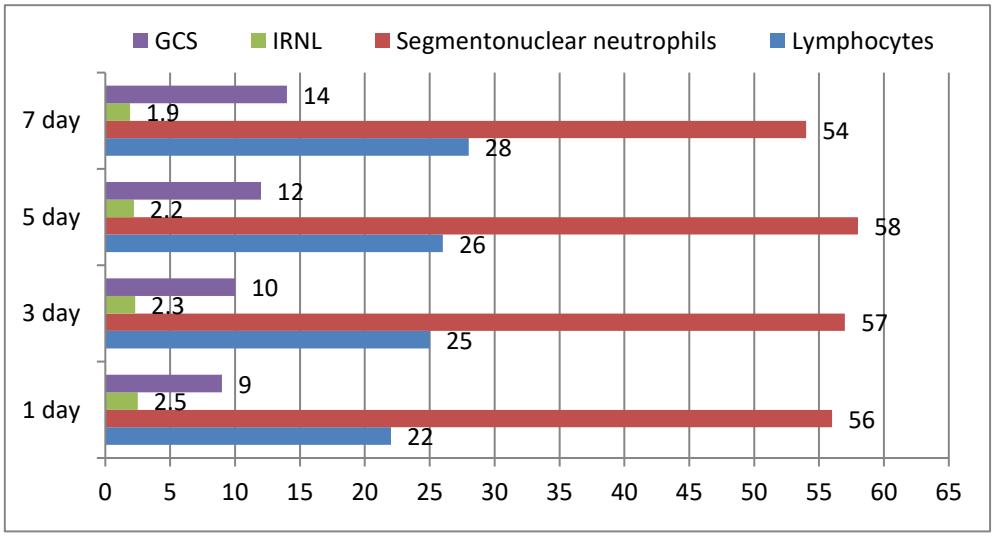
Graph 1[a]. Survivors rates for patients with ischemic stroke



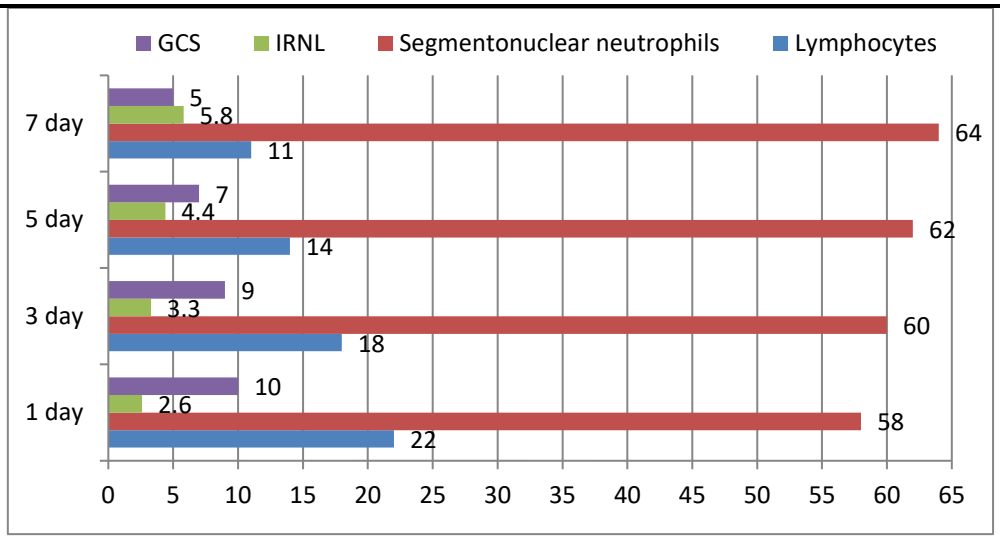
Graph 1[b]. Indicators of deceased patients with ischemic stroke

When analyzing the results of a neuroimaging examination of 10 patients included in the study and treated with a diagnosis of hemorrhagic stroke, with primary MSCT performed when patients came to the hospital, in 5 patients in the medial basin a. cerebri, in 1 patient in the anterior pool a. cerebri, in 2 patients inside the ventricles of the brain, in 2 patients hemorrhages were detected in the basin of the vertebrobasilar artery. Hemorrhage into the subarachnoid space was also observed in patients with hemorrhage into

the ventricles of the brain. The volume of stroke hematomas formed in the cerebral hemispheres was estimated from 12 cm^3 to 85 cm^3. Due to the size of the hematoma of more than 30 cm^3, located laterally, and cerebral edema in 2 patients who had a displacement of more than 6 mm in the opposite direction of the middle structures of the brain, but consciousness was not deeply impaired (grades 1 and 2 on the Hunt-Hess scale), a surgical intervention was performed for the removal of a hematoma stroke. Of the total number of patients, mechanical ventilation was performed in 8 patients, since their level of consciousness on arrival was below 10 points on the Glasgow scale. Against the background of intensive therapy, progressive deterioration of the general condition and death was observed in 1 patient with cerebral ventricular hemorrhage, 1 operated patient with removal of lateral hematomas, and 1 patient with brainstem hemorrhage. During the primary and repeated leukoformula analysis in this group of patients with a diagnosis of hemorrhagic stroke, it was revealed that the characteristic changes in the leukoformula and the ISNL index are noted as positive changes in the neurological status and clinical condition. As the consciousness of the patients improved (a progressive increase in the total score on the Glasgow scale), as they emerged from the coma and the positive dynamics of the general condition, the lymphocyte counts were above 22, the IRNL in the blood test of the patients was below 3,0 (graph 2[a]). Laboratory parameters of patients who were in a coma for a long time without positive dynamics of the general condition (a progressive decrease in the total score on the Glasgow scale) and who died during the observation period indicated a progressive increase in the number of segmented neutrophils, and the number of lymphocytes decreased below 10, respectively, an increase in the IRNL indicator was noted above 3,5 (graph 2[b]).



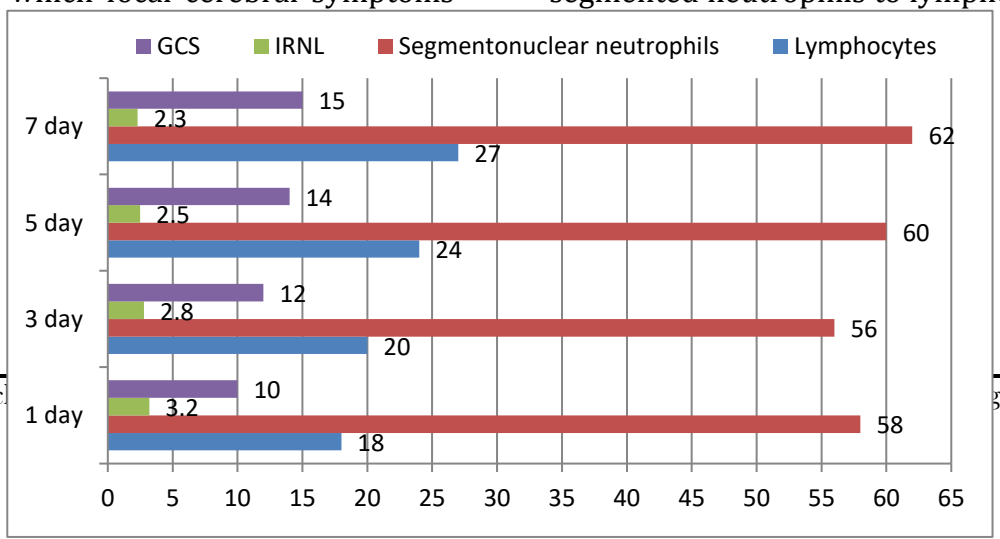
Graph 2[a]. Survivors rates for patients with hemorrhagic stroke



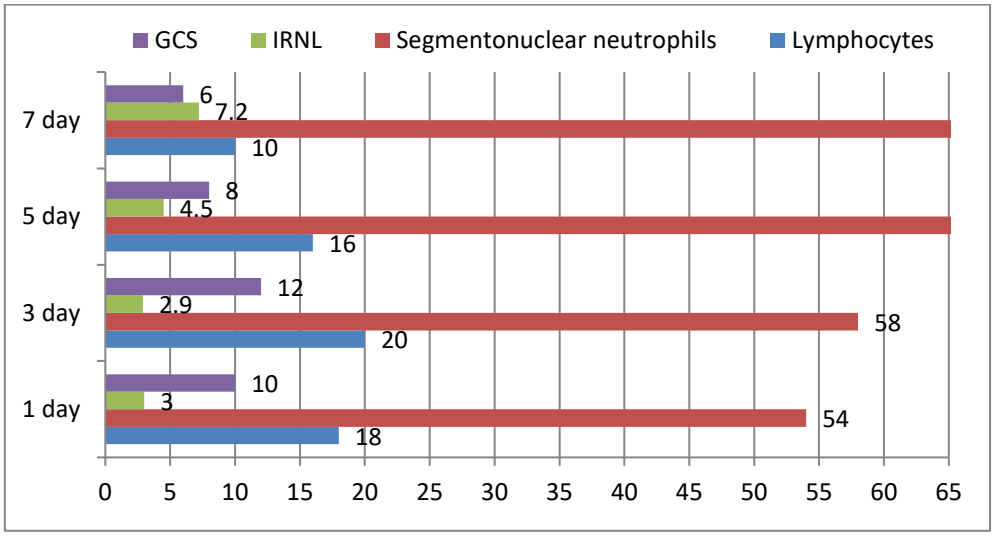
Graph 2[b]. Indicators of deceased patients with hemorrhagic stroke

The 22 traumatic brain injury patients analyzed as the source of the study were injured as a result of a traffic accident, violence, or natural disaster. Due to the possibility of data confounding, the study did not include patients with injuries of the musculoskeletal system and with damage to other organs. At the initial CT of the patients, it was found that 15 patients had subdural, 4 epidural and 3 intracerebral hematomas. In cases when a hematoma detected on CT scan led to dislocation of the median structures of the brain, the hematoma was surgically removed (n=18) - resection decompressive craniotomy was performed. At the time of admission to the hospital, the level of consciousness was assessed: in 4 patients - in a state of stupor (GCS 12-14 points), 8 patients - in stupor (GCS 10-11 points), 5 - in superficial coma (according to GCS 8-9 points, and 3 were regarded as a deep coma (below GCS score 7), 2 patients were treated in clear consciousness (GCS score 15).Clinical symptoms of brain contusion (amnesia, vomiting, psychomotor agitation...) in which focal cerebral symptoms were noted - anisocoria, hemisymptomatics.In patients who at the time of admission, consciousness was assessed below 10 points on the Glasgow scale and all patients treated surgically, mechanical ventilation was performed.The duration of mechanical ventilation ranged from 2 to 18 days.

When conducting laboratory tests together with the control of clinical and neurological changes in patients, quantitative changes in neutrophils and lymphocytes in the blood were observed in accordance with changes in the general condition of patients. The general condition of 19 patients changed in a positive direction against the background of intensive therapeutic measures carried out after the operation, which manifested itself in the form of a clarification of consciousness and an increase in the total GCS score. During dynamic MSCT examination, it was noted that the dislocation of the median structures of the brain in these patients was eliminated, the sizes of the basal cisterns and ventricles of the brain were normalized, there were no signs of impaired CSF circulation. The results of laboratory analysis showed that the ratio of segmented neutrophils to lymphocytes in these patients was below 3,2 (graph 3[a]).



Graph 3[a]. TBI Survivor Rates



Graph 3[b]. Indicators of deceased patients with TBI

Despite intensive therapy, in 3 patients included in the study, there was a progressive progression of cerebral edema and death. During dynamic monitoring of the deceased on MSCT, smoothing of the cerebral cortex, compression of the cerebral ventricles, zones of local and diffuse hypoperfusion around the contusion foci were noted, while a blood test showed changes in the number of segmented neutrophils inversely proportional to the number of lymphocytes. These patients showed characteristic undulating changes in the IRNL index. With a primary indicator of IRNL 3,0 in the initial period after the operation, there was a decrease in this indicator to 2,9 and an increase to 7,2 in the following days. We observe the same undulating changes in the patient's neurological status, first an increase and then a sharp decrease in the GCS score. These changes can be explained by the fact that although intracerebral hypertension due to epi-, subdural or parenchymal hematomas in the initial state was compensated as a result of decompressive trepanation (during this period, the GCS score increased, and the IRNL decreased to 2,9), in the dynamics there was a progressive an increase in cerebral edema, which coincided with a deepening of disorders of consciousness and a deterioration in the general condition (during this period, the GCS score decreased to 6 points and below, and the IRNL increased to 7,2) (graph 3[b]).

Thus, the dynamic increase in peripheral blood IRNL can serve as a predictor of an unfavorable prognosis in patients with a neuroresuscitation profile.

Conclusion. Based on the results obtained at the end of the study, it can be said that IRNL is an important indicator for predicting the course and outcome of acute brain diseases. Depending on the IRNL indicator, in accordance with the neurological status indicators and neuroimaging data, it will be possible to apply timely measures aimed at preventing negative changes in the course of brain diseases. This allows improving the outcomes of treatment of severe diseases, leading to brain catastrophe.

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