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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

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GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board since 1994. GMN carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

GMN is indexed in MEDLINE, SCOPUS, PubMed and VINITI Russian Academy of Sciences. The full text content is available through EBSCO databases.

GMN: Медицинские новости Грузии - ежемесячный рецензируемый научный журнал, издаётся Редакционной коллегией с 1994 года на русском и английском языках в целях поддержки медицинской науки и улучшения здравоохранения. В журнале публикуются оригинальные научные статьи в области медицины, биологии и фармации, статьи обзорного характера, научные сообщения, новости медицины и здравоохранения. Журнал индексируется в MEDLINE, отражён в базе данных SCOPUS, PubMed и ВИНИТИ РАН. Полнотекстовые статьи журнала доступны через БД EBSCO.

GMN: Georgian Medical News – საქართველოს სამედიცინო სიახლენი – არის ყოველთვიური სამეცნიერო სამედიცინო რეცენზირებადი ჟურნალი, გამოიცემა 1994 წლიდან, წარმოადგენს სარედაქციო კოლეგიისა და აშშ-ის მეცნიერების, განათლების, ინდუსტრიის, ხელოვნებისა და ბუნებისმეტყველების საერთაშორისო აკადემიის ერთობლივ გამოცემას. GMN-ში რუსულ და ინგლისურ ენებზე ქვეყნდება ექსპერიმენტული, თეორიული და პრაქტიკული ხასიათის ორიგინალური სამეცნიერო სტატიები მედიცინის, ბიოლოგიისა და ფარმაციის სფეროში, მიმოხილვითი ხასიათის სტატიები.

ჟურნალი ინდექსირებულია MEDLINE-ის საერთაშორისო სისტემაში, ასახულია SCOPUS-ის, PubMed-ის და ВИНИТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებიდან.

WEBSITE

www.geomednews.com

К СВЕДЕНИЮ АВТОРОВ!

При направлении статьи в редакцию необходимо соблюдать следующие правила:

1. Статья должна быть представлена в двух экземплярах, на русском или английском языках, напечатанная через **полтора интервала на одной стороне стандартного листа с шириной левого поля в три сантиметра**. Используемый компьютерный шрифт для текста на русском и английском языках - **Times New Roman** (**Кириллица**), для текста на грузинском языке следует использовать **AcadNusx.** Размер шрифта - **12**. К рукописи, напечатанной на компьютере, должен быть приложен CD со статьей.

2. Размер статьи должен быть не менее десяти и не более двадцати страниц машинописи, включая указатель литературы и резюме на английском, русском и грузинском языках.

3. В статье должны быть освещены актуальность данного материала, методы и результаты исследования и их обсуждение.

При представлении в печать научных экспериментальных работ авторы должны указывать вид и количество экспериментальных животных, применявшиеся методы обезболивания и усыпления (в ходе острых опытов).

4. К статье должны быть приложены краткое (на полстраницы) резюме на английском, русском и грузинском языках (включающее следующие разделы: цель исследования, материал и методы, результаты и заключение) и список ключевых слов (key words).

5. Таблицы необходимо представлять в печатной форме. Фотокопии не принимаются. **Все цифровые, итоговые и процентные данные в таблицах должны соответствовать таковым в тексте статьи**. Таблицы и графики должны быть озаглавлены.

6. Фотографии должны быть контрастными, фотокопии с рентгенограмм - в позитивном изображении. Рисунки, чертежи и диаграммы следует озаглавить, пронумеровать и вставить в соответствующее место текста **в tiff формате**.

В подписях к микрофотографиям следует указывать степень увеличения через окуляр или объектив и метод окраски или импрегнации срезов.

7. Фамилии отечественных авторов приводятся в оригинальной транскрипции.

8. При оформлении и направлении статей в журнал МНГ просим авторов соблюдать правила, изложенные в «Единых требованиях к рукописям, представляемым в биомедицинские журналы», принятых Международным комитетом редакторов медицинских журналов - http://www.spinesurgery.ru/files/publish.pdf и http://www.nlm.nih.gov/bsd/uniform_requirements.html
В конце каждой оригинальной статьи приводится библиографический список. В список литературы включаются все материалы, на которые имеются ссылки в тексте. Список составляется в алфавитном порядке и нумеруется. Литературный источник приводится на языке оригинала. В списке литературы сначала приводятся работы, написанные знаками грузинского алфавита, затем кириллицей и латиницей. Ссылки на цитируемые работы в тексте статьи даются в квадратных скобках в виде номера, соответствующего номеру данной работы в списке литературы. Большинство цитированных источников должны быть за последние 5-7 лет.

9. Для получения права на публикацию статья должна иметь от руководителя работы или учреждения визу и сопроводительное отношение, написанные или напечатанные на бланке и заверенные подписью и печатью.

10. В конце статьи должны быть подписи всех авторов, полностью приведены их фамилии, имена и отчества, указаны служебный и домашний номера телефонов и адреса или иные координаты. Количество авторов (соавторов) не должно превышать пяти человек.

11. Редакция оставляет за собой право сокращать и исправлять статьи. Корректура авторам не высылается, вся работа и сверка проводится по авторскому оригиналу.

12. Недопустимо направление в редакцию работ, представленных к печати в иных издательствах или опубликованных в других изданиях.

При нарушении указанных правил статьи не рассматриваются.

REQUIREMENTS

Please note, materials submitted to the Editorial Office Staff are supposed to meet the following requirements:

1. Articles must be provided with a double copy, in English or Russian languages and typed or compu-ter-printed on a single side of standard typing paper, with the left margin of **3** centimeters width, and **1.5** spacing between the lines, typeface - **Times New Roman** (**Cyrillic**), print size - **12** (referring to Georgian and Russian materials). With computer-printed texts please enclose a CD carrying the same file titled with Latin symbols.

2. Size of the article, including index and resume in English, Russian and Georgian languages must be at least 10 pages and not exceed the limit of 20 pages of typed or computer-printed text.

3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

5. Tables must be presented in an original typed or computer-printed form, instead of a photocopied version. **Numbers, totals, percentile data on the tables must coincide with those in the texts of the articles.** Tables and graphs must be headed.

6. Photographs are required to be contrasted and must be submitted with doubles. Please number each photograph with a pencil on its back, indicate author's name, title of the article (short version), and mark out its top and bottom parts. Drawings must be accurate, drafts and diagrams drawn in Indian ink (or black ink). Photocopies of the X-ray photographs must be presented in a positive image in **tiff format**.

Accurately numbered subtitles for each illustration must be listed on a separate sheet of paper. In the subtitles for the microphotographs please indicate the ocular and objective lens magnification power, method of coloring or impregnation of the microscopic sections (preparations).

7. Please indicate last names, first and middle initials of the native authors, present names and initials of the foreign authors in the transcription of the original language, enclose in parenthesis corresponding number under which the author is listed in the reference materials.

8. Please follow guidance offered to authors by The International Committee of Medical Journal Editors guidance in its Uniform Requirements for Manuscripts Submitted to Biomedical Journals publication available online at: http://www.nlm.nih.gov/bsd/uniform_requirements.html
http://www.icmje.org/urm_full.pdf
In GMN style for each work cited in the text, a bibliographic reference is given, and this is located at the end of the article under the title "References". All references cited in the text must be listed. The list of references should be arranged alphabetically and then numbered. References are numbered in the text [numbers in square brackets] and in the reference list and numbers are repeated throughout the text as needed. The bibliographic description is given in the language of publication (citations in Georgian script are followed by Cyrillic and Latin).

9. To obtain the rights of publication articles must be accompanied by a visa from the project instructor or the establishment, where the work has been performed, and a reference letter, both written or typed on a special signed form, certified by a stamp or a seal.

10. Articles must be signed by all of the authors at the end, and they must be provided with a list of full names, office and home phone numbers and addresses or other non-office locations where the authors could be reached. The number of the authors (co-authors) must not exceed the limit of 5 people.

11. Editorial Staff reserves the rights to cut down in size and correct the articles. Proof-sheets are not sent out to the authors. The entire editorial and collation work is performed according to the author's original text.

12. Sending in the works that have already been assigned to the press by other Editorial Staffs or have been printed by other publishers is not permissible.

Articles that Fail to Meet the Aforementioned Requirements are not Assigned to be Reviewed.

ავტორთა საყურადღებოდ!

რედაქციაში სტატიის წარმოდგენისას საჭიროა დავიცვათ შემდეგი წესები:

1. სტატია უნდა წარმოადგინოთ 2 ცალად, რუსულ ან ინგლისურ ენებზე,დაბეჭდილი სტანდარტული ფურცლის 1 გვერდზე, 3 სმ სიგანის მარცხენა ველისა და სტრიქონებს შორის 1,5 ინტერვალის დაცვით. გამოყენებული კომპიუტერული შრიფტი რუსულ და ინგლისურენოვან ტექსტებში - **Times New Roman (Кириллица)**, ხოლო ქართულენოვან ტექსტში საჭიროა გამოვიყენოთ **AcadNusx.** შრიფტის ზომა – 12. სტატიას თან უნდა ახლდეს CD სტატიით.

2. სტატიის მოცულობა არ უნდა შეადგენდეს 10 გვერდზე ნაკლებს და 20 გვერდზე მეტს ლიტერატურის სიის და რეზიუმეების (ინგლისურ, რუსულ და ქართულ ენებზე) ჩათვლით.

3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

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CEREBRAL OXIMETRY AS A PREDICTOR OF THE OUTCOME OF THE DISEASE IN PATIENTS WITH SECONDARY BRAIN LESIONS

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Abstract.

This study is devoted to the study of the prognostic value of cerebral oximetry of the brain and indicators of the outcome of brain damage.

The purpose of the study: To study the prognostic role of cerebral oximetry indicators as a predictor of mortality in vascular and traumatic brain injuries.

Materials and methods: A prospective cohort study involving 129 patients. Cerebral gas exchange and oxygenation, arteriovenous difference, neuron-specific markers (S100ß, NSE) and glucose, acid-base state and gas composition of arterial blood were studied during follow-up periods: at admission, on the 3rd, 5th and 7th days of patients' stay in the intensive care unit.

Results: The most significant risk factor for an unfavorable outcome is a marker with a threshold value or with a cut-off point rSO_2<45%. Statistically significant direct connections were determined between dependent rSO_2<45% with independent variables, such as: S100ß<0.6 mcg/l - OR is 4.22 (95%CI:10.76-1.66), p=0.0025; joining in a patient with a diagnosis of pneumonia - OR 6.21(95% CI:12.0-3.21), p<0.0001 and the patient's diagnosis was 8.13 (95% CI:25.59-2.59), p=0.0003. The measure of certainty of the obtained model was according to the criterion of pseudo R2 Nagelkerke -137.8; log Likelihood - 175.83.

The cut-off point of 97.1% had the best predictive value of the model, the area under the AuROC curve was 0.846; sensitivity - 68.47%; specificity - 90.16%; NPV - 61.11%; PPV - 92.68%. The quantitative indicator rSO_2 was obtained in relation to the independent variables GCS, ABP, NSE and pH and the quality characteristic of the model has: R2 = 16.7%; R2 (adjusted) = 15.5%; p <0.0001. This model can be used to predict the outcome in patients with acute cerebral pathology.

Key words. Strokes, traumatic brain injuries, cerebral oximetry, diagnostic and prognostic criteria, stroke outcome.

Introduction.

Currently, acute vascular and traumatic cerebral pathology continues to be one of the most frequent disabling diseases of the central nervous system. The most common causes of death are vascular in nature, and stroke is currently the second leading cause of death worldwide [1,2]. Coronary heart disease and stroke together caused 15.2 million deaths (15-15.6 million) in 2015 [2]. Many deaths occur before the patient arrives at the hospital or during treatment [3]. However, the continued violation of gas exchange in secondary brain injuries causes damage to molecular cells, changes in metabolism and cerebral blood flow, violation of axons and the blood-brain barrier, which can affect the development of a vegetative state in the separated period of cerebral injuries [4,5]. According to some authors, the role of the Glasgow assessment scale in assessing the severity, dynamics, and prognosis of neurological status outcomes in these patients is decreasing [6,7]. Also, the diagnostic value of computed tomography of the brain is low, due to low sensitivity and insufficient specificity [8,9]. Magnetic resonance examination makes it possible to assess the severity of neuroaxonal injuries, but its unavailability to some medical hospitals, a long study time, often severe patients who need to continue ventilator significantly limit its use [8,10]. In daily clinical practice, due to the invasiveness and the presence of certain indications, the control of intracranial pressure is also limited [10]. Therefore, more and more clinical, and experimental studies are aimed at studying the role of noninvasive methods in the diagnosis and prediction of outcomes of acute cerebral neuropathology [7].

Among the potential new markers, cerebral oximetry has a high specificity for neural networks associated with mortality and an unfavorable prognosis [9]. A number of researchers [11-13] suggested that cerebral oxygenation indicators can serve as an accurate indicator of the balance of oxygen delivery and consumption by the brain. Characteristic changes in cerebral oximetry indices were obtained in hypoxic and reperfusion changes in the brain after cardiac arrest and episodes of arterial hypotension. The coincidence in time and direction of changes in cerebral oximetry and hemoglobin oxygen saturation in cerebral blood during the act of respiration and episodes of hypoxic hypoxia was established [14,15]. Cerebral oximetry is especially useful in assessing tissue hypoxia in those clinical situations when pulse oximetry turns out to be uninformative, for example, with unstable hemodynamics and pronounced changes in peripheral microcirculation [16,17]. Studies have revealed the relationship between rSO_2 and cerebral blood flow in comatose patients. At the same time, a linear relationship between cerebral blood flow and gSO_2 was revealed. There was also evidence that changes in the central nervous system reacted to hypoxic episodes earlier than the analog electroencephalogram [18,19]. The brain uses only glucose for energy processing and usually does not accumulate energy, so continuous blood supply, stored in narrow circles, is necessary for brain functioning (90%) and cell viability (10%) [20]. At the time of admission from all patients, there is a connection of respiratory disorders with the development of coma of II-III degree, which coincides with the literature data [21,22]. The insufficiency of oxygen transport systems was manifested by a violation of the tissue component and an increase in the arteriovenous oxygen difference ($AVDO_2$), which, in turn, activates the noted pathological processes and begins a pathological cycle with the excretion of reactive oxygen species. The Oxygen Delivery and Consumption Index

($AVDO_2$) showed a significant number of cases of hypoxia, which, as studies have shown, is the only marker that can prevent secondary brain damage in patients with severe diseases. Borshchikova T.I., Antonov A.R. and the data obtained by the co-authors from the results of the study indicate a decrease in oxygen intake due to the development of hypodynamic blood circulation, pulmonary complications, and microcirculation disorders at an early stage of acute brain damage. Despite the growing interest of researchers in secondary brain injuries, the information related to the noninvasive assessment of the oxygen state of the brain is very contradictory and requires further study and refinement to optimize the timing of neuro-resuscitation correction and the adequacy of predicting long-term results [23-25]. The final results after the correction of secondary lesions are insufficiently studied and are mainly based on data on the survival and mortality of patients depending on the duration of treatment [26].

Thus, cerebral oximetry and brain metabolism with the determination of arteriovenous difference, with the state of systemic hemodynamics demonstrate their effectiveness in the diagnosis of secondary damaging processes in the brain in a number of clinical situations of vascular and traumatic genesis.

However, the exact place of these criteria in the complex of neuromonitoring methods, their value for the diagnosis of secondary cerebral ischemia, the possibility of correction of intensive therapy based on the information received, need further research.

Materials and Methods.

The study was performed in accordance with the standards of Good Clinical Practice, the principles of Declaration of Helsinki and in accordance with the principles of the Ethical Commission of the West Kazakhstan Medical University named after Marat Ospanov No. 12 dated 30.01.2018 [11]. Brain gas exchange studies determined the ratio of oxygen delivery/consumption in the cerebral cortex (rSO_2), which was carried out on the INVOS - 5100 device, SOMANETICS, USA, at admission and in dynamics was determined in 129 patients with vascular and traumatic brain diseases who were treated in intensive care units of stroke centers in Aktobe (Republic of Kazakhstan), for the period from 2020 to 2021.

Laboratory studies were carried out in dynamics by 1 (initial)-3-5-7 the days of the patient's stay in the hospital. Serum levels of NSE and S100 were determined using the human ELISA kit (DiaMetraSrl, cat. No.: DKO073, ZI Paciana, Italy) by a solid-phase, non-competitive method based on the use of two types of mononuclear antibodies specifically recognizing protein molecules. After written informed consent of the patient/relatives, 5.0 ml of venous blood was collected from v.mediana cubiti in a Vacutainer with BD separation gel. After taking a blood sample in a Vacutainer with gel, it was stirred by turning 5-6 times. 30 minutes after the formation of a blood clot, the Vacutainer was centrifuged at 1500 rpm for 10 minutes to separate the serum and shaped blood elements. Then the Vacutainer with blood serum was placed in a thermally insulated bag with dry ice and transferred by a specialized standard courier service to the in Vivo Medical Laboratory Center for analysis of biomarker levels. The analysis of all research indicators was carried out considering the range of normal reference values. Serum lactate dehydrogenase (LDH) levels were determined by kinetic method of selective inhibition of isoenzymes. For lactate and glucose indicators, ABS parameters (acid-base state) and arterial blood gas composition: pH (blood acidity index); pCO2; pO2, an EPOC analyzer (Canada) with a unique Smartcard technology (measuring cards with a built-in biosensor chip) was used, after the written informed consent of the patient / relatives.

The study included patients with hemorrhagic strokes (GS) - 80 patients (62,0%), ischemic strokes(IS) 29 (22,9%) and with acute closed craniocerebral injuries of moderate severity (TBI) - 20 (15.5%). The criteria for inclusion in the study of patients with hemorrhagic stroke were cases of intracerebral hemorrhages with a hematoma volume of more than 30 cm^3 (mainly hemispheric hemorrhages); patients with ischemic stroke – with the presence of cerebral infarction, confirmed by clinical and CT data; patients with severe traumatic brain injuries - moderate and severe brain contusions (Figure 1). Patients with intracerebral hemorrhages with a hematoma volume of more than 80 cm^3, with severe decompensated somatic diseases, with benign and malignant tumors of the brain, lungs and skin were excluded from the main group. According to the outcome of the disease, regardless of the diagnosis, patients were divided into groups: survivors – 63.5% (n=82) and deceased – 36.5% (n=47). To measure blood gases, lactate and glucose, samples were analyzed using an ABL 735 analyzer (Radiometer; Denmark).

To assess the severity of brain damage and predict the outcome of the clinical course of the disease of patients, the GCS (Glasgow Coma Scale) evaluation neurological scales were used. The distribution of patients in the groups by sex ($\chi2 = 0.0184$, $p = 0.8922$) and age ($\chi2 = 0.0183$, $p = 0.4288$), where all predictors were studied were comparable (Table 1).

Statistics.

The study of the statistical relationship between the qualitative feature and the clinical outcome was carried out using the analysis of conjugacy tables, with the calculation of the Pearson criterion $\chi2$. In case of non-fulfillment of the criterion applicability condition $\chi2$ (more than 25% of the cells in the conjugacy table have an expected frequency of less than 5), the analysis was carried out in pairs according to the two-sided Fisher exact criterion (2p(F)). In the case of insufficient statistical significance of the connection of two nominal features in the multipole conjugacy table, several gradations of the feature similar in meaning were combined into one, followed by the calculation of the Pearson criterion $\chi2$ with the achieved level of statistical significance (p) and the odds ratio (OR) with a 95% confidence interval (95% CI). The study of the relationship between the quantitative and qualitative feature was carried out using a one-factor logistic regression analysis with the calculation of statistics $\chi2$ Wald with the achieved level of statistical significance and OR with 95% CI.

Multiple linear regression analysis was performed to identify variables independently related to cerebral oximetry indicators. A step-by-step forward technique was used. The data are presented as an average value ± standard deviation or median and percentiles, p-values less than 0.05 were considered significant.

Table 1. *Clinical characteristics of deceased and surviving patients.*

Description,	**Cohort, % (N = 129)**	**survivors, % (N =82)**	**deceased, % (N =47)**	**p**
Basic score GCS Me [Q1; Q3]	11,07 (10,72; 11,43)	12,04	9,66	<0,0001[2]
Hyperglycemia	110	61 (47,29%)	49 (55,06%)	0,0231[1]
Arterial hypertension	50	38 (29,46%)	12 (13,48%)	0,0231[1]
Art. hypertension + coronary heart disease	27	17 (13,18%)	10 (11,24%)	0,0231[1]
Art. hypertension + diabetes mellitus	21	10 (7,75%)	11 (12,36%)	0,0231[1]
Other diseases	10	3 (2,33%)	7 (7,87%)	0,0231[1]
Pneumonia	94	22 (16,92%)	72 (80,90%)	<0,0001[1]
Notes: 1. 1- $\chi 2$ Pearson 2. 2- U-Mann-Whitney criterion				

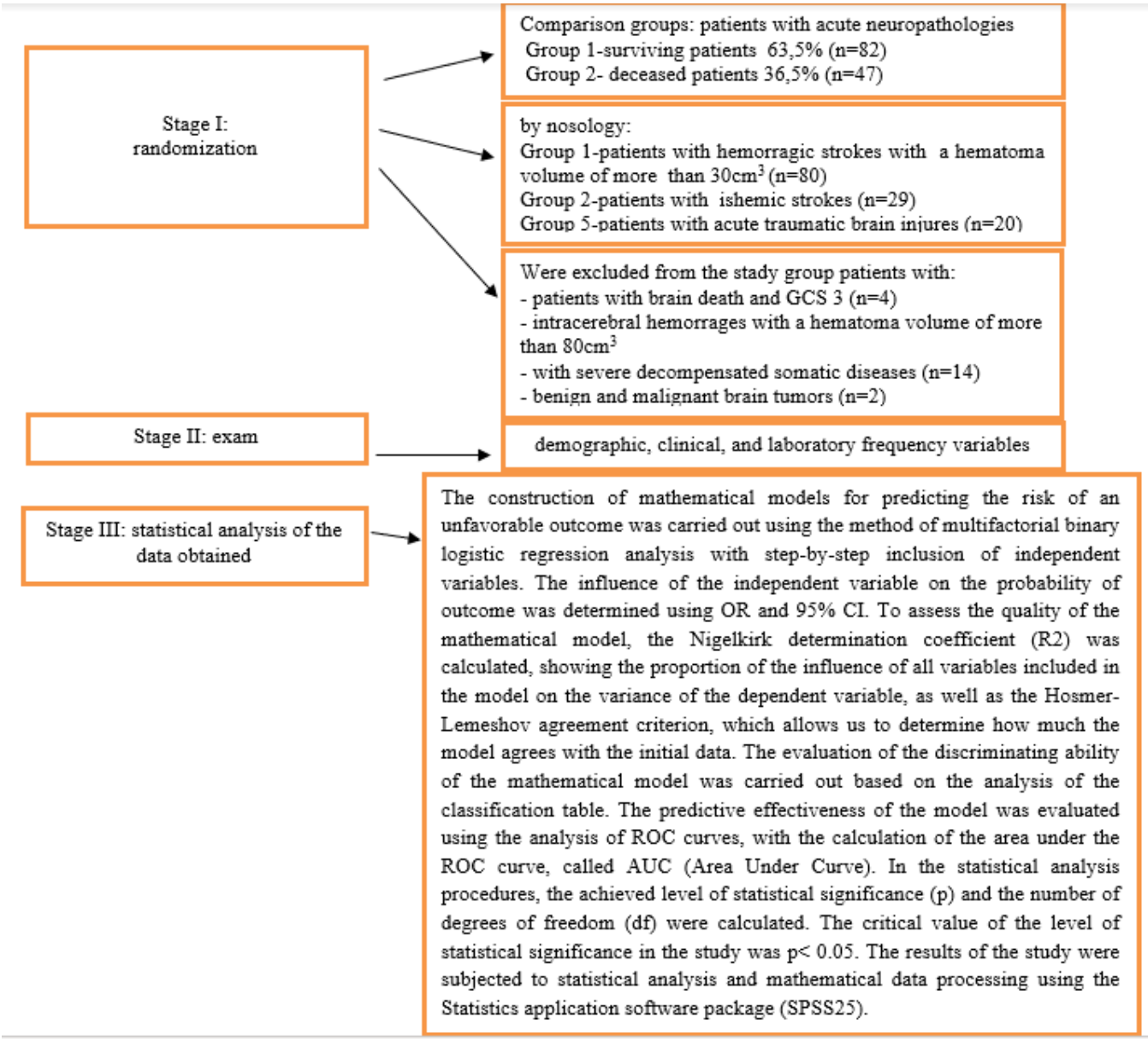


Figure 1. *Schematic flow diagram of patients included in the study.*

Results.

To determine the possibility of using rSO_2 indicators in predicting the outcome of vascular and traumatic brain injury, a statistical analysis was carried out. rSO_2 indicators at admission and in dynamics were determined by 129 patients from the general group. The distribution by sex ($\chi2 = 0.0184$, $p = 0.8922$) and age ($\chi2 = 0.0183$, $p = 0.4288$) in the group where rSO_2 was studied were comparable. The age group differs between the diagnosis groups, between GS (95%CI:57.01- 60.81) and IS (95%CI:66.00- 73.14) $p<0.0001$, and between IS (95%CI:66.00-73.14) and TBI (95% CI:45.01- 57.86) $p<0.0001$.

Upon further investigation of cerebral gas exchange, it was noted that the dynamics of the results of the ratio of oxygen supply/consumption by the brain (rSO_2) is insignificant compared to the initial values in all the studied groups of patients. The indicators of rSO_2 cerebral oximetry had the same direction of changes depending on the degree of impaired consciousness (correlation analysis with GCS) and the dynamics of its development, so we found that the data of groups of patients with GI and IS can be generalized. In these groups, there was a decrease in the average rSO_2: GI from 0.23% to 8.60%, but these results were not statistically significant. It should be noted that in most patients with TBI, rSO_2 indicators were unstable, had a large amplitude of fluctuations, varied by 2.14-5.93% during follow-up, and were also not statistically reliable.

The resulting arterial-venous difference $AVDO_2$ value between days is relatively small. On day 3, there is an increase in $AVDO_2$ indicators by 0.66% on the right (95% CI: 48.46-51.57), by 2.44% on the left (95% CI:49.42-52.23). On the 5th day, there is a decrease in the avdo2 index on the right-by 0.15% (95% CI: 47.77-51.45) and on the 7th day-by 1.22% (95% CI 46.90; 51.25). Note that for 72 hours on the left there was a negative dynamic of indicators, which is 2.44%, (95% CI: 49.42-52.23), on day 5 by 1.89% (95% CI: 48.74-52.37) and on day 7 by 0.15%, (95% CI: 47.54-51.85), but they did not show statistical significance.

In the IS group of patients, there was a decrease in the initial rSO_2 values for 72 hours -1.21% (95% CI: 45.90-51.07), on day 5 - by 5.18% (95% CI: 43.71-49.37), on day 5 left rSO_2 – by 6.42% (95% CI: 45.68-51.94), and on the 7th day -8.60% (95% CI: 43.88-51.47). $AVDO_2$ shows a bad forecast: 1.16% (95%CI: 46.76-52.00) for 72 hours on the right, 5.43% on the 5th day (95% CI: 48.36-54.55) and 6.76% on the 7th on the 1st day (95% CI:48.34-55.87) From the left side for 72 hours by 2.07% (95% CI: 44.19-49.16), on the 5th day it will increase by 7.57% (95%CI: 45.86-52.52) and on the 7th day by 10.22% (95% CI: 46.54-54.27). The dynamics of the arteriovenous difference in oxygen concentrations ($AVDO_2$) against the background of a decrease in the ratio of oxygen supply/consumption by the brain showed a direct negative relationship. Progressive hypoxemia leads to a decrease in oxygen transport and associated hypoxic vasoconstriction, inhibition of hypoxia as factors of secondary brain damage.

In the group of TBI patients, cerebral oximetry observed that the indicators of the initial rSO_2 values did not decrease but increased. This is explained by the fact that patients arrive in a serious condition, in the first hours of hospitalization can be explained by the fact that artificial ventilation with hyperventilation begins immediately according to the treatment protocol: for 72 hours by 3.37% (95% CI: 42.46-51.48), on the 5th day by 4.99% (95% CI: 42.94-52.46), on the 5th day changes are observed by 5.43% (95% CI: 44.38-54.02) and by 5.93% (95% CI: 43,59-55,28) on the 7th day. $AVDO_2$ indicators decrease positively after 72 hours -2.23% (95% CI: 46.82-55.38), on the 5th day -3.95% (95% CI: 45.62-54.78), on the 7th day -5.10% (95% CI: 43.92-55.28). Arteriovenous difference-a decrease in $AVDO_2$ indicators showed successful dynamics during treatment.

To determine the relationship between gas exchange indicators and the state of neurological status according to the Glasgow Scale (GCS), conducted with a correlation analysis, a positive relationship between GCS and cerebral oximetry was rSO_2 ($r=0.45$, $p<0.0001$) for all groups of patients and a negative difference between GCS and arteriovenosis was $AVDO_2$ ($r=-0.45$, $p<0.0001$ a relationship has been discovered, which we can see in Figure 2.

To assess the effectiveness of cerebral gas exchange indicators, the specificity and sensitivity of rSO_2 and $AVDO_2$ were evaluated as criteria for predicting the dynamics of the disease.

The ROC analysis study showed that rso_2 and $AVDO_2$ had the largest area of the ROC curve with a sensitivity of 93.9-95.12% and specificity of 86.05-86.82%, respectively, with cut-off points (0.91) and (0.88) (<45-48, $p<0.0001$) and (>54-52, $p<0.0001$). Taking into account the generally accepted ideas that the indicators of high sensitivity and specificity values range from 80 to 100%, it can be noted that in all samples of the examined patients, cerebral oximetry had high specificity and low sensitivity in 67.42% ($\chi2$-73.2528). A possible explanation for the low sensitivity during the first three days is that at these stages, the most severe patients may have an unfavorable outcome. It is obvious that disorders of brain oxygenation are often the result of deterioration of brain metabolism due to a variety of factors. Another possible explanation for the low sensitivity is that cerebral oximetry reflects local cerebral oxygenation of the cortical parts of the brain and does not reflect the nature of oxygenation of columnar structures.

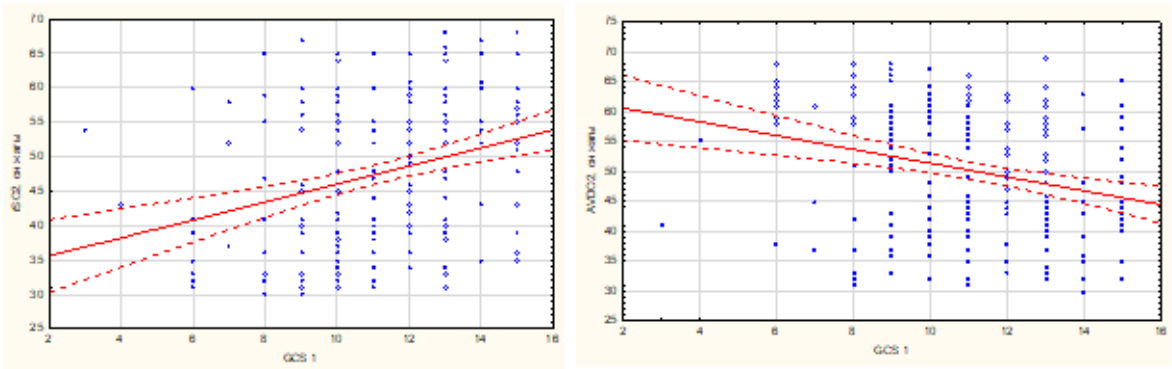
Later in the course of the study, we drew attention to the significance of statistical differences in indicators of cerebral metabolism and gas exchange and hemodynamics (Table 2).

As you can see, we observed the statistical significance of cerebral gas exchange indicators throughout the day.

A variance analysis was performed to determine a statistically significant difference in rSO_2 values. The maximum, minimum and average rSO_2 levels were evaluated for each group of outcomes. Figure 3 shows the distribution of the average rSO_2 value.

With this formation, the difference became even more statistically significant ($p<0.0001$). The threshold value or rSO_2 cut-off point for the formal division into a group of survivors and a group of deceased was $rSO_2<45\%$.

At the stage of multiple LRA, we studied the relationship of the risk of an increase in the level of the target variable $rSO_2<45\%$ with the indicators obtained during laboratory and instrumental examination methods. The results of the analyses are presented in Table 3.



a b

Figure 2. *Linear correlation between GCS (Glasgow coma scale) and markers of cerebral gas exchange in a group of patients. a- rSO_2 and GCS; b- GCS and $AVDO_2$*

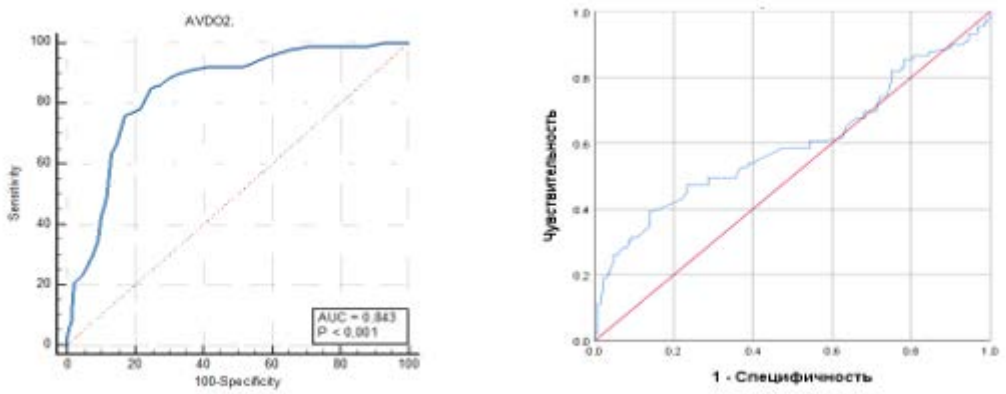


Figure 3. *Sensitivity and specificity of the cerebral gas exchange marker ($AVDO_2$ and rSO_2).*

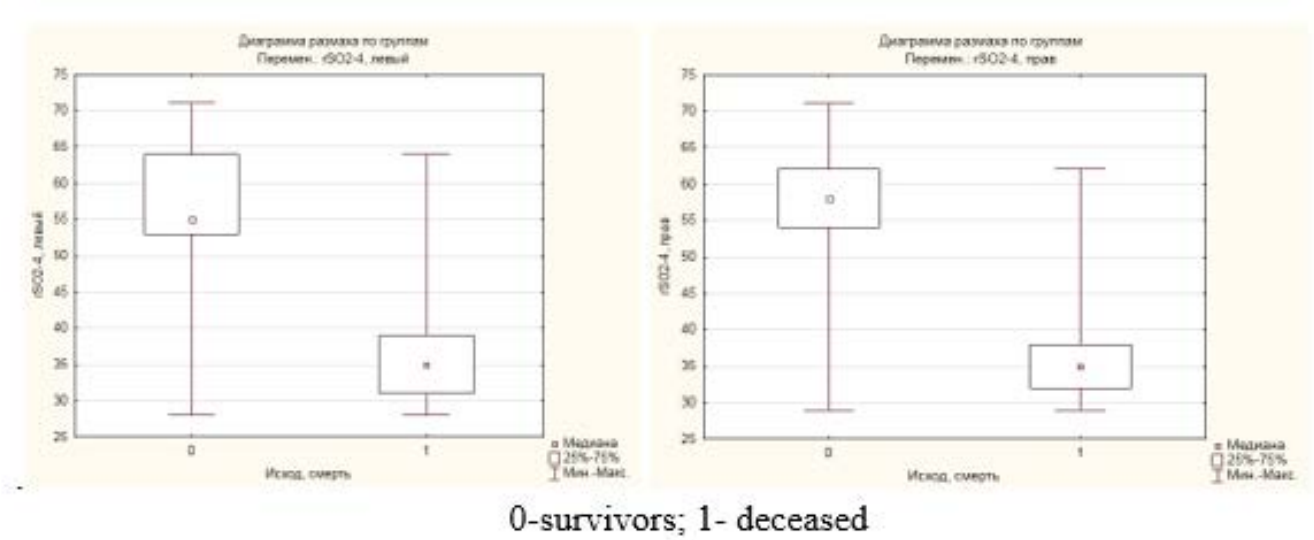


Figure 4. *Span diagram by rSO_2 groups.*

Table 3. *Forecasting the risk of an increase in rSO_2.*

Factor	AuROC	Stand error	odds ratio	95% CI OR		χ^2	Regression coefficient	p
				верхний	нижний			
Constant		0,4875				13,2960	-1,7777	
S100β[1] <0,6	0,766	0,4769	4,22	1,66	10,76	9,1280	1,4410	0,0025
Pneumonia	0,791	0,3364	6,21	3,21	12,00	29,4531	1,8255	<0,0001
Diagnosis	0,846	0,5848	8,13	2,59	25,59	12,8465	2,0960	0,0003
Notes: 1. S100ß is a calcium-binding protein								

Table 4. *Extended regression analysis results.*

Factor	R-square (corrected)	R-squared change	Correlation with the target	B-coefficient.	Stand error	p
Constant					6,4851	<0,0001
GCS[1]	9,3%	13,13%	0,30	4,4989	0,2782	0,0004
ABP[2]	14,0%	3,87%	-0,28	-0,0372	0,0261	0,0009
NSE[3]	14,8%	-0,82%	-0,16	-0,0503	0,0425	0,0823
pH[4]	15,5%	-1,66%	-0,11	-1,0586	0,1999	0,0976
Notes: 1. GCS- Glasgow com Scale 2. ABP- average blood pressure 3. NSE- neuron-specific enolase 4. pH is the concentration level of hydrogen ions in plasma, represented as a negative decimal logarithm						

The results of the analysis indicate the presence of a statistically significant direct relationship between rSO_2<45% and S100ß <0.6 compared to other variables by 4.22 times more often; if there is pneumonia almost 6 times; with ischemic stroke, it was documented more than 8 times more often. The measure of certainty of the obtained model according to the criterion of pseudo R2 Nagelkerke is 137.8; logLikelihood is 175.83.

The logistic regression equation of the model has the following form:

P = 1 / (1 + Exp(-(-1,778 + 1,441*S 100β <0 + 1,825*Pneumonia + 2,096*Diagnosis)))

Where P is the probability of rSO_2 reduction risk<45 %

e is the base of the natural logarithm (e=2.72); -1.7777 is a constant.

The best predictive value of the model had a cut-off point of 97.1%, AuROC-0.846; Se-68.47%; Sp-90.16%; NPV-61.11%; PPV-92.68.

Regression consisting of 3 factors relative risk reduction of rSO_2 - 2.17 (95% CI: 1.66 - 2.84); Se-75.69%, Sp-73.33%, χ2-48.9689, AuROC-0.84.

When predicting the quantitative indicator rSO_2, we used multiple regression analysis with a dependent variable rSO_2<45% and independent variables GCS, ABP, NSE and pH. All variables indicated in the table predicted the quantitative value of this marker. The extended results of the regression analysis of the prediction of the quantitative indicator rSO_2<45% are shown in Table 4.

A quantitative indicator of rSO_2 in relation to independent variables was obtained.

The logistic regression equation of the model has the following form:

rSO = 6.47 + 1.05*GCS - 0.09*ABP - 0.08*NSE - 0.34*pH,

where 6.468 is a constant. The results of the regression analysis showed that the quantitative indicator rSO_2 in relation to the independent variables GCS, ABP, NSE and pH and the quality characteristic of the model has: R2 = 16.7%; R2 (adjusted) = 15.5%; p <0.0001. The data we obtained showed that lower rSO_2 values significantly correlated with worse neurological outcomes, and in patients with higher values, outcomes were better. Next, we constructed Kaplan-Meier survival curves for rSO_2<45% and rSO_2>45%, Figures 4 and 5.

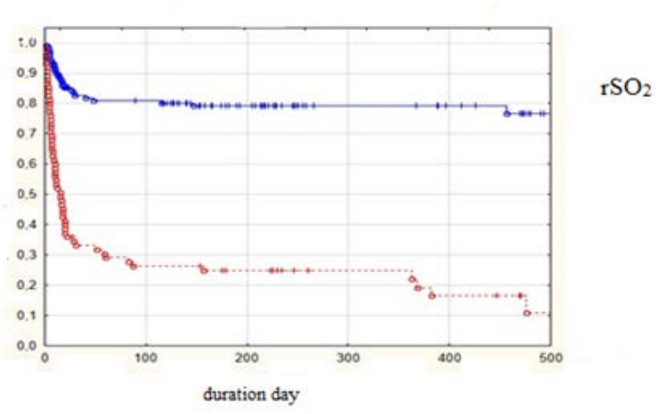


Figure 5. *Кривые выживаемости Kaplan-Meier для для rSO_2.*

As can be seen from the figure, the cumulative rate of cases of a bad outcome in the group with rSO_2 level >45% began to diverge already in the first days of observation. The achieved level of significance according to the log Rank criterion (Mantel Cox) <0.0001 differences in the studied groups are significant.

The dynamics of the data on the ratio of brain oxygen delivery/consumption (rSO_2) compared to the initial values were insignificant, had the same orientation depending on the degree of impaired consciousness (correlation analysis with GCS), and therefore we found it possible to generalize the data of groups

of patients with GI and IS. They had a decrease in the value of rSO_2: from GI - by 0.23%; IS – by 8.60%, but the results were statistically unreliable. It should be noted that the rSO_2 indicators in most patients with TBI were unstable, had a large amplitude of fluctuations, changing during the follow-up by 2.14% - 5.93% and also statistically not reliable. The developed hypoxemia leads to a decrease in oxygen transport and the associated inhibition of hypoxic vasoconstriction, hypoxia, as factors of secondary brain damage. There were no such changes in the group of patients with TBI, the indicators of the initial values did not decrease, but on the contrary, increased. This may be due to the fact that patients are admitted in a serious condition and in the first hours of hospitalization, ventilation begins in hyperventilation mode. To determine the relationship between gas exchange indicators and the state of neurological status according to GCS, the correlation analysis revealed a positive relationship between GCS and rSO_2 ($r=0.45$, $p<0.0001$) and similar changes were noted for the outcome of rSO_2 disease (42.72 (95% CI: 41.18-44.26), $p<0.0001$). Evaluation of the effectiveness of cerebral gas exchange indicators as criteria for disease prognosis according to the ROC analysis study showed that rSO_2 and had the largest area under the ROC curve (0.91) with a cut-off point (<45-48, $p<0.0001$). Sensitivity was 93.9%, specificity 86.05%, respectively. Taking into account the generally accepted ideas that the indicators of high sensitivity and specificity values range from 80 to 100%, it can be noted that, in general, in the entire sample of examined patients. Only on 1-3 days of follow-up, cerebral oximetry had high specificity and low sensitivity of 67.42% ($\chi 2$ - 73.2528). A possible explanation for the low sensitivity is that mainly during these periods, an unfavorable outcome may occur in the most severe patients. It is obvious that a violation of brain oxygenation is most often not the cause, but the result of deterioration of cerebral metabolism due to the influence of many factors. Another possible explanation for the low sensitivity is the following: cerebral oximetry reflects local cerebral oxygenation mainly of the cortical parts of the brain and does not reflect the nature of oxygenation of stem structures.

The results obtained by us and the study of these predictors of hypoxia allow us to expand the existing understanding of the pathogenetic processes of hypoxic brain damage in the acute period with acute vascular and traumatic injuries, which undoubtedly has a certain scientific value and can be used as markers of cerebral damage.

Discussion.

Mortality rates from traumatic and vascular lesions differ according to several studies. Some studies also use different time methods and parameters to analyze this mortality. The mortality rate ranges from 13 to 22% [27]. It has been established that after the primary injury, secondary brain damage develops from the first minutes, which can continue in subsequent periods for several years due to excessive metabolic, cellular, and molecular activity of inflammation [28]. Our data coincide with the opinions of many researchers, including (Gandee R, Miller C. 2017), who claim that hypoxia is an aggressive and damaging factor for patients, leading to functional disorders and damage to brain cells. In the future, this condition may be aggravated by the addition of secondary ischemic brain damage.

The brain oximeter (rSO_2) is a non-invasive method for determining brain oxygenation. At the heart of the core lies the perception of light, which does not pass as it has the pulse oximeter method and the reflected method. Therefore, there are topographic limitations when there is some uncertainty in the installation of sensors and the depth of penetration of the patient, there are soft tissues and bones of the skull [29]. The data obtained by us that lower rSO_2 values significantly correlated with worse neurological outcomes, and in patients with higher values, outcomes were better, consistent with the studies of Rivera-Lara L, Geocadin R., et.al .

As the results of studies have shown, with a decrease in rSO_2 <45%, the relative risk of an unfavorable outcome on the 1st day of the disease in patients increases by 4.54 times (95% CI: 2.01- 10.24), $p<0.0001$. Also, patients with rSO_2 values below 45% have a high probability of death or persistent vegetative state. Therefore, it can be said that lower rSO_2 values indicating cerebral ischemia are a marker of unfavorable neurological outcomes.

Limitations and further study.

This study had limitations. The study with a small number of patients was single center, which limits its validity. Secondly, there were certain difficulties in the process of work associated with the refusal of patients or their relatives from further participation in this study; there was no dynamic long-term follow-up of the studied patients.

This study provides the basis on which further multicenter studies should be built in order to establish generalizability and increase the validity of the results obtained.

Conclusions.

1. The levels of the dependent variable (rSO_2) and independent variables (S100ß<0.6 mcg/l, the addition of the diagnosis of pneumonia in the patient and the diagnosis) can be used as multimodal predictors of predicting the neurological outcome in patients with acute cerebral pathology.

2. The proposed mathematical model, which includes the dependent variable (rSO_2) and independent variables (rSO_2) as predictors of a bad outcome, had a cut-off point of 97.1%, the area under the AuROC curve was 0.846; sensitivity - 68.47%; specificity - 90.16%; predictive value of a negative result (NPV) - 61.11%; predictive value of a positive the result (PPV) is 92.68%, which corresponds to the excellent quality of the predictive ability of the mathematical model. The model can be used in everyday practice to identify and reduce the likelihood of a high risk of adverse clinical outcome in patients with acute cerebral pathology.

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