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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.

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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 ВИНТИ 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 ВИНТИ РАН-ის მონაცემთა ბაზებში. სტატიების სრული ტექსტი ხელმისაწვდომია EBSCO-ს მონაცემთა ბაზებში.

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. Корректуре авторам не высылаются, 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 computer-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 საყურადღებო!

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, შემავჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრაფიის ფოტოსურათები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შედეგების 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 ფხიხლებში 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.

Nana Shavlakadze, Irine Phkhakadze, Ana Silagadze, Dali Kobuladze, Alina Pakhuridze. CHRONIC URTICARIA AND LEAD EXPOSURE: EVALUATION OF IMMUNOLOGICAL MARKERS.....	6-16
Jangirashvili T, Kikoria G, Tevdorashvili N, Kapanadze L, Odikadze N. PSYCHOLOGICAL WELL-BEING AMONG MEDICAL STUDENTS AT FIVE UNIVERSITIES IN TBILISI, GEORGIA: A CROSS-SECTIONAL STUDY OF PERCEIVED STRESS, ANXIETY, AND SLEEP QUALITY.....	17-23
Yueyue Lu, Yigao Wu. ADVANCES IN RESEARCH OF PSYCHOTHERAPY FOR SOCIAL ANXIETY DISORDER.....	24-31
Saburov Alisher, Kemelbekov Kanatzhan, Arybzhanov Dauranbek, Abdurakhmanov Babur, Huseinov Zafar, Saburova Saidakhon, Tuktibayeva Saule, Yernazarov Adlet, Alipbekova Sandugash. ROLE OF NEOADJUVANT THERAPY FOR PATIENTS WITH GASTRIC CANCER: MULTIDISCIPLINARY HOSPITAL WITH ONCOLOGY CENTER.....	32-37
David Tchkonია, Nino Gabashvili, Teona Mskhaladze, Tamari Kevlishvili, Mikolay Chkonia. EFFICACY OF ENDOBRONCHIAL VALVE PLACEMENT IN THE MANAGEMENT OF PULMONARY HEMORRHAGE: A COMPARATIVE STUDY.....	38-42
Baglan Kemelbekov, Ainur Amanzholykyz, Samat Saparbayev, Manarbek Askarov, Edgaras Stankevicius. IMPACT OF STEM CELL THERAPY ADDED TO GUIDELINE-DIRECTED MEDICAL THERAPY ON QUALITY OF LIFE IN PATIENTS WITH ISCHEMIC CARDIOMYOPATHY.....	43-50
Abramishvili T, Papava K, Mamisashvili M, Tkeshelashvili M, Tsinamdzgvrishvili B. CARDIAC STRAIN IN WOMEN WITH A DOCUMENTED HISTORY OF OVERT OR SUBCLINICAL HYPOTHYROIDISM: AN EXPLORATORY SPECKLE-TRACKING ECHOCARDIOGRAPHY STUDY.....	51-56
TEREZA Y. AZATYAN. FORMATION AND DISTRIBUTION PATTERNS OF FUNCTIONAL INTERHEMISPHERIC BRAIN ASYMMETRY IN CHILDREN WITH INTELLECTUAL DISABILITIES.....	57-63
Fai Twrki Althoini, Ebtehal Solaiman Almogbel. CARDIOMETABOLIC RISK PROFILES IN ADULTS WITH DIABETES: ASSOCIATIONS WITH GLYCEMIC CONTROL, DIABETES TYPE, AND DEMOGRAPHIC CHARACTERISTICS.....	64-77
Datumyan G.S, Shaboyan K.R, Muradyan A.A, Shaboyan E.K, Galstyan A.S, Badalyan A, Sargsyan M.V. IMPACT OF THE COVID-19 PANDEMIC ON THE SEVERITY AND OUTCOMES OF GUNSHOT INJURIES.....	78-84
Zhanar Kozhakhmetova, Nazym Yelemessova, Syzdykova Dinara, Abdullina Sayagul, Nagima Issatayeva, Assiya Turgambayeva, Gulnara Kamalbekova, Diana Zhumagaleyeva, Akmaral Mussakhanova. CRITICAL VALUES OF HEMOSTASIS PARAMETERS IN AN ONCOLOGY CENTER: A RETROSPECTIVE REGISTRY-BASED STUDY.....	85-92
Gradil G.I, Torianyk I.I, Yurko K.V, Shiyan D.M, Merkulova N.F, Mohylenets O.I, Tkachenko V.G, Karmazina I.S, Lantukh A.P, Hryhorov Y.B, Gargin V.V. ASSOCIATION OF PULMONARY AND CUTANEOUS CHANGES IN COVID-19-RELATED CONDITIONS.....	93-98
Alaa MA. Albayaty, Alaa M. Sadiq, Ali SJ. Al Qaissi. ASSOCIATION BETWEEN INFLAMMATORY MARKERS, LIVER ENZYMES, LIPID PROFILE, AND VITAMIN D STATUS IN ADULTS WITH OBESITY: A CROSS-SECTIONAL STUDY.....	99-104
Kenzhebaeva B, Baimuratova M, Kalmakhanov S, Budakoğlu I.I, Laktionova M, Abdukalikova D. IMPACT OF CLINICAL, ORGANIZATIONAL, AND PSYCHOSOCIAL FACTORS ON THE QUALITY OF LIFE OF PATIENTS WITH DERMATOVENEREOLGICAL DISEASES.....	105-114
Obidov F. Kh, Shamsiev E. A, Samatov F. F, Naimov Dilshod Kayim ugli, Khalimova F. T, Marwan Ismail. BIOMARKER-ORIENTED REHABILITATION IN CHRONIC CEREBRAL ISCHEMIA.....	115-122
Raghad Alkhalify, Lina Almutairi, Fatimah Alghofaili, Wasan Alhawaish, Thekra Alhumidi. COMPARATIVE IN-VITRO QUALITY EVALUATION OF COMMERCIALY AVAILABLE DICLOFENAC SODIUM TABLETS.....	123-131
Ali S. Jumaah, Ali A. Younis, Shamil H. Othman. EFFECTS OF CURCUMIN ON CLINICAL OUTCOMES AND INFLAMMATORY BIOMARKERS IN KNEE OSTEOARTHRITIS: A RANDOMIZED TRIAL.....	132-138
Ashot Markosyan, Diana Alaverdieva, Mark Danghyan, Ani Mkrtchyan, Lusine Balayan, Khachik Hakobyan, Arpine Geolchanyan, Tigran Soghomonyan, Volodya Mirzoyan. SYNTHESIS AND SOME BIOLOGICAL PROPERTIES OF DERIVATIVES OF 2,3-DISUBSTITUTED 5,5-DIMETHYL-BENZO[h]QUINAZOLIN-4(1H)-ONES.....	139-143

J. Gobadze, M. Nagervadze, T. Gogitidze, N. Bejanidze, N. Zarnadze, K. Dolidze. IMPACT OF GESTATIONAL DIABETES MELLITUS ON NEONATAL BIRTH WEIGHT, LENGTH, AND GESTATIONAL AGE: A RETROSPECTIVE CASE-CONTROL STUDY	144-151
Liudmyla Bashkistrova, Iryna Romanova, Vitalii Yatsynovych, Oleksandr Zlobin, Artem Lanskoi. EVIDENCE-BASED PHARMACOTHERAPY FOR ANXIETY DISORDERS COMORBID WITH PTSD: A SYSTEMATIC REVIEW	152-163
Madina Makhmudova, Tolegen Kerimbekov, Zhaina Berikbayeva, Dinara Turebekova, Lyudmila Akhmaltdinova, Yefim Alisseiko, Olga Avdienko, Madina Rashova. IN VITRO INVESTIGATION OF THE POTENTIAL OF C60 FULLERENES AS ADJUVANTS OF NONSPECIFIC IMMUNITY	164-168
Tchernev G, Tchernev KG Jr, Kordeva S. DERMATOLOGIC SURGERY ROUNDS: THE LIMBERG FLAP AND V-TO-T CLOSURE FOR CUTANEOUS/ MUCOCUTANEOUS DEFECTS FOLLOWING SKIN CANCER EXCISION IN HIGH-RISK FACIAL REGIONS	169-174
Nino Nadiradze, Zurab Ckhaidze. SELF-RATED HEALTH IN THE POPULATION OF MEDICAL WORKERS IN GEORGIA	175-180
Argjend Shala, Nexhmedin Shala, Fisnik Jashari, Blert Jashari, Rushit Jashari. SPORADIC CREUTZFELDT-JAKOB DISEASE: CLINICAL FEATURES, DIAGNOSIS AND THERAPEUTIC HORIZONS	181-189
Omar S. Salman, Adeeb A. Al-Zubaidy. ACEBROPHYLLINE REPROGRAMS INFLAMMATORY AND REDOX SIGNALLING IN EXPERIMENTAL ULCERATIVE COLITIS: A DOSE-DEPENDENT STUDY	190-199
Eib K. Eibov, Solikhabonu Khavaskhonova, Kamshat S. Taubay, Karlygash Zh. Sadykova. CALCULATED WHOLE BLOOD VISCOSITY IS SPECIFICALLY ASSOCIATED WITH ABDOMINAL OBESITY, BUT NOT WITH OTHER COMPONENTS OF METABOLIC SYNDROME: A CROSS-SECTIONAL STUDY IN A CENTRAL ASIAN ADULT COHORT	200-208
Shqiponje Gashi, Erza Voca Mulaj, Naser Rugova, Suzana Dvojakovska, Filip Koneski. MANAGEMENT OF PERIOPERATIVE BLEEDING IN PATIENTS WITH PLATELET HYPOAGGREGABILITY DURING DENTOALVEOLAR SURGERY: CLINICAL OUTCOMES AND THERAPEUTIC APPROACHES	209-214
Alina Articulo, Rigor Rey Cuevas, Hani Al-Najjar, Rahaf Alkhuraif, Rasha Aburmeishan, Abdulaziz Almatrody. EXPLORING THE SATISFACTION OF NEWLY HIRED NURSES USING AN EVIDENCE-BASED, PERSONALIZED ONBOARDING PROGRAM: A CROSS-SECTIONAL ANALYSIS	215-222
Nagima Issatayeva, Samal Duisekova, Meruert Saberbekova, Roza Tumanova, Larisa Guruleva, Sholpan Mukanova. APPLICATION OF THE FAILURE MODE AND EFFECTS ANALYSIS METHOD IN HEALTHCARE: A CASE STUDY OF A UNIVERSITY MEDICAL CENTER IN KAZAKHSTAN	223-237
Hisham R. Ezzat, Ibrahim M. Faisal. CARDIOPROTECTIVE EFFECTS OF SILYMARIN AND VITAMIN E AGAINST DOXORUBICIN-INDUCED CARDIOTOXICITY IN RATS: EVIDENCE FROM OXIDATIVE STRESS MARKERS AND HISTOPATHOLOGICAL ANALYSIS	238-245
Shishniashvili D.S, Bedinashvili Z.J, Tsomaia K.B, Svanadze L.M, Chkhikvishvili N.M, Durglishvili G.A. FIRST-VOID URINE VERSUS URETHRAL SWAB FOR MOLECULAR DETECTION OF SEXUALLY TRANSMITTED INFECTIONS IN MEN WITH MULTIPLE SEXUAL PARTNERS	246-252
Chekhovska G.S, Pustova N.O, Syzon O.O, Chaplyk-Chyzho I.O, Dashko M.O, Vozniak I.Ya, Volbyn S.V, Ivaniushko-Nazarko N.V, Zhemela O.D, Gargin V.V. NAIL PLATE DAMAGE INDEX IN DERMATOSCOPIC EXAMINATION OF PATIENTS WITH ONYCHOMYCOSIS	253-258
Meng-Yun Zhou, Shi-qi Yu, Shao-jie Zhu, Xiang Kong, Xin-Ming Yao. A NOVEL KCNJ5 GENE MUTATION ASSOCIATED WITH FAMILIAL ALDOSTERONISM TYPE III WITHOUT HYPERTENSION	259-265
Koba Kamashidze, Tina Beruchashvili, Irina Nakashidze, Sarfraz Ahmad, Tamar Peshkova. BRIDGING THE COVERAGE-PARTICIPATION GAP: BEHAVIORAL DETERMINANTS OF CERVICAL CANCER SCREENING AMONG WOMEN IN ADJARA, GEORGIA	266-273
T.N. Kosayeva, A.T. Amiraslanov, H.K. Muradov, A.Y. Gaziyeu, B.E. Abbasov. PD-L1 EXPRESSION AND SERUM CA125: CLINICOPATHOLOGICAL CORRELATIONS IN HIGH-GRADE SEROUS OVARIAN CARCINOMA	274-280
Ruziyeva Amira Asrorovna, Khamidov Obid Abdurakhmanovich, Murodqosimov Saidolim, Doniyorov Bakhridin Baxrom ugli, Khalimova F.T, Marwan Ismail. ACE I/D AND NOS3 G894T POLYMORPHISMS AND CARDIOVASCULAR ADAPTATION PROFILES IN ADOLESCENT FOOTBALL PLAYERS	281-288

Mukhriddin Umbarov Ochilovich, Shamsutdinova Maksuda Ilyasovna, Abdullayev Ravshanbek Babajonovich, Rokhila Bakhridinovna Mengliyeva. ASSOCIATIONS OF CYTOKINE PROFILE AND EXOCRINE PANCREATIC FUNCTION WITH A SYMPTOM-BASED DEHYDRATION CATEGORY AND SEASON OF PRESENTATION IN CHRONIC PANCREATITIS: A RETROSPECTIVE STUDY.....	289-297
Saeed H. Hussein, Hiba M. Ahmed, Ahmed A. Ahmed. DETECTION OF HEPATITIS B AND C VIRAL INFECTION AMONG CHILDREN WITH ACUTE LEUKAEMIA.....	298-302
Davit Kobuladze, Ahishtan Febrian Nishanthan, Nino Kedelidze, Rusudan Vadatchkoria, Magda Davitashvili, Lamara Zuroshvili, Darejan Margalitashvili, Nani Gvarishvili, Nazi Turmanidze, Tamar Peshkova, Naman Chauhan, Teona Gogitidze, Nameera Parveen Shaikh, Aleena Parveen Shaikh, Abeshana Febrian Nishanthan, Irina Nakashidze. SELECTED LABORATORY PARAMETERS IN PEDIATRIC PATIENTS WITH COVID-19 STRATIFIED BY WHITE BLOOD CELL AND PLATELET PROFILES.....	303-309
Rawan Waleed, Abrar Fadlalla, Jana Abdullah, Marwan Ismail, Mohammed Ibrahim Saeed, Ahmad Luay Osman Hashim, Abdelgadir Elamin Eltom. IMPACT OF HELICOBACTER PYLORI INFECTION ON VITAMIN B12 DEFICIENCY LEVELS: A RETROSPECTIVE STUDY.....	310-315
T.A. Asgarova, K.M. Rahimli, G.A. Valiyeva, Sh.I. Hasanova, F.E. Guliyeva, Kh.R. Mammadova. SOME HEREDITARY DISEASES PREVALENT IN THE REPUBLIC OF AZERBAIJAN.....	316-319
Sahadete Shala, Ferdita Haxhiu Derguti. PSOAS MUSCLE ABSCESS FOLLOWING CESAREAN SECTION: A CASE REPORT.....	320-322
N. Kajaia, L. Gabunia, M. Mantskava, S. Kalmakhelidze, G. Ormotsadze, S. Turabelidze-Robaqidze, T. Sanikidze. PRO-INFLAMMATORY INTERLEUKINS AND OXIDATIVE IMBALANCE IN L-NAME-INDUCED HYPERTENSION: COMPARATIVE EFFECTS OF β -BLOCKERS.....	323-330
Hussein Fadhil Abdulameer, Raed Aziz Badeia. COMPARATIVE EVALUATION OF TWO HERBAL MOUTHWASHES AND CHLORHEXIDINE ON CALPROTECTIN IN GINGIVITIS PATIENTS: A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL.....	331-340
J. Gobadze, M. Nagervadze, T. Gogitidze, N. Bejanidze, T. Koiava. SOME BIOLOGICAL CHARACTERISTICS ASSOCIATED WITH GESTATIONAL DIABETES.....	341-348
Yurevych N. O, Sazonova O. N, Kachailo I.A, Hnidyk Yu. V, Pokotylo P. B, Podolyuk M.V, Blyshak N. B, Mykhalevych M. M, Zherebkin V. V, Kosynskyi O. V, Aliksieieva V. V. THREE-DIMENSIONAL CT-BASED MORPHOMETRIC ASSESSMENT OF THE MAXILLARY SINUS.....	349-355
Simbarashe Magaisa. PERCEPTIONS AND PRACTICES OF HEALTHCARE PROVIDERS IN MATERNAL MORTALITY AND STILLBIRTH PREVENTION AND MANAGEMENT: INSIGHTS FROM LEJWELEPUTSWA DISTRICT.....	356-363
Akezhan Rustemuly Astrakhanov, Ainur Amanzholkyzy, Samat Sagatovich Saparbayev, Meirambek Sagnaevich Kurmangazin, Aigerim Iskakova, Gulzhanat Nurlanova. THE ROLE OF CELL THERAPY IN THE COMPREHENSIVE TREATMENT OF CHRONIC HEPATITIS C-RELATED LIVER CIRRHOSIS.....	364-370
Miranda Shervashidze, Khatia Dolidze, Tamar Bakhtadze, Tamar Shervashidze. PREVENTING EXERCISE-RELATED SUDDEN CARDIAC DEATH THROUGH SYSTEMATIC PREPARTICIPATION CARDIOVASCULAR SCREENING: A TWO-YEAR REGIONAL COHORT STUDY OF PEDIATRIC ATHLETES IN ADJARA, GEORGIA.....	371-380
Waseem Hashim Alkhaffaf, Muhammad A. Alkataan. COMPARATIVE EFFICACY OF 200 UNITS VERSUS 155 UNITS OF ONABOTULINUMTOXIN A FOR CHRONIC MIGRAINE.....	381-388
K. Tovar Calderón, J. Orozco Pilco, C. Calderón Cabezas, K. Caiza Cuello. ETHNIC DISPARITIES IN BIRTH WEIGHT AND PRENATAL CARE UTILIZATION IN ECUADOR, 2024.....	389-394
Gaukhar Issakova, Suriya Yessentayeva, Daniyar Amangaliyev, Askhat Bralov, Assiya M. Issayeva, Yestay Abzalbek, Marat Akhetov. INDICATIONS FOR REMOVAL OF A PORT SYSTEM IN A PATIENT WITH SUSPECTED SEPTICEMIA IN THE ABSENCE OF OTHER LOCAL SOURCES OF INFECTION.....	395-398
Mohammed A. Hayawi, Duaa M. Al-Nafoly. PREDOMINANCE OF FOLLICULAR ADENOMA AND PAPILLARY CARCINOMA IN THYROID NEOPLASMS.....	399-403
Nino Buadze, Nata Kazakhashvili. POPULATION KNOWLEDGE, RISK PERCEPTION, GOVERNANCE AND PUBLIC HEALTH DETERMINANTS OF COVID-19 IN GEORGIA: A NATIONAL CROSS-SECTIONAL STUDY.....	404-422

Alaa H. Alfarhan, Bahir S. Allawi, Mohammed A. Aljodah, Ahmed Jawad. MINIMALLY INVASIVE FAT TRANSPOSITION IN LOWER BLEPHAROPLASTY	423-427
Ospanova Meruyert, Ospanova Saniya, Yernazarov Adilet, Amanbaev Rauan, Rakhmankulov Umarali. LOW-FREQUENCY ULTRASOUND AND OZONE/NO TECHNOLOGIES IN THE COMBINED TREATMENT OF EXUDATIVE HEMISINUSITIS USING THE YAMIK-3 SINUS CATHETER.....	428-432
Sodikjon Mashraf Ugli Makhmatkulov, Ibragimova Malika Shavkatovna, Khasanov Alisher Yurevich, Mavlyanova Zilola Farkhadovna, Khalimova F.T, Marwan Ismail. COMBINED BOTULINUM TOXIN THERAPY AND PERCUTANEOUS TIBIAL NERVE STIMULATION IN THE REHABILITATION OF WOMEN WITH URGENCY URINARY INCONTINENCE ASSOCIATED WITH DIABETES MELLITUS.....	433-444
Nellia Veretova, Alfiya Samigullina, Aigul Baialieva, Ruslan Abdyldaev, Begimai Muratbekova. PSYCHONEUROLOGICAL THERAPY FOR POST-COVID SYNDROME: A COMPREHENSIVE REVIEW OF METHODS AND CLINICAL EFFECTIVENESS.....	445-451
Azhar Giniyat, Natalya Slivkina, Viktor Tkachev, Gulbana Khussainova, Ayan Baigaliyev, Sara Kubekova, Aizat Seidakhmetova, Zilola Mavlyanova, Mirbanu Aikhozhayeva, Raikhan Burumbaeva, Larissa Pavlovets, Raikhan Tleulinova, Raushan Baigenzheyeva, Mereke Alaidarova, Joseph Almazan, Aizhan Altynbekova, Bakyt Zhangabulova, Zinugul Baissova, Manzura Kankina, Parida Pirmanova, Magira Shaizadinova, Aliya Utenova, Zhansaya Raiymkul. DEVELOPMENT AND EVALUATION OF A NURSE-LED SELF-DIRECTED PEDIATRIC REHABILITATION MODEL: COMPARATIVE ANALYSIS OF INTERNATIONAL PRACTICES.....	452-465
Florina Sahiti, Argjira Veseli, Marija Peeva Petreska, Shera Kosumi, Nora Berisha, Enis Veseli, Kaltrina Veseli. BIOMARKERS OF BONE REMODELING AND INFLAMMATION IN CHRONIC PERIAPICAL LESIONS: A NARRATIVE REVIEW	466-473

BIOMARKER-ORIENTED REHABILITATION IN CHRONIC CEREBRAL ISCHEMIA

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Abstract.

Background: Chronic cerebral ischemia (CCI) is a clinically significant form of chronic cerebrovascular disease associated with cognitive decline, impaired daily functioning, and reduced quality of life. In routine clinical practice, the effectiveness of rehabilitation in CCI is often assessed mainly by subjective clinical dynamics, whereas biomarkers and MRI with DTI/SWI may serve as objective indicators of the biological response to restorative treatment.

Material and methods: A prospective controlled comparative study was conducted in 115 patients aged 40-65 years with stage I-II CCI. Allocation to the main group (MG, n=55) and comparison group (CG, n=60) was performed after baseline stratification by disease stage, sex, and age; randomization and complete blinding of outcome assessment were not performed, which was considered a methodological limitation. The MG received a personalized biomarker-oriented program, whereas the CG received standardized therapy. A control group without CCI (n=65) was used only for baseline biomarker comparison. MoCA, MMSE, ADL, IADL, SF-36, IL-6, TNF-alpha, CRP, BDNF, NSE, and D-dimer were assessed at baseline, 3 months, and 6 months; DTI/SWI MRI was performed at baseline and at 6 months.

Results: Compared with stage I CCI, stage II CCI was associated with increased IL-6 (from 5.29 to 6.81 pg/mL), TNF-alpha (from 4.68 to 5.90 pg/mL), CRP (from 3.49 to 5.02 mg/L), NSE (from 18.3 to 23.1 ng/mL), and D-dimer (from 0.308 to 0.423 µg/mL), as well as decreased BDNF (from 11.4 to 9.7 ng/mL; $p<0.001$). At 6 months, the MG showed more pronounced favorable dynamics than the CG in MoCA (+22.4% vs +7.1%; $p<0.001$), MMSE (+12.1% vs +4.3%; $p<0.001$), IL-6 (-34.4% vs -11.1%; $p<0.001$), BDNF (+23.3% vs +5.8%; $p<0.001$), NSE (-22.1% vs -5.8%; $p<0.001$), D-dimer (-27.0% vs -10.8%; $p=0.004$), FA (+20.5% vs +5.0%; $p=0.003$), ADL (+39.6% vs +14.3%; $p<0.001$), IADL (+41.2% vs +16.0%; $p<0.001$), and SF-36 physical functioning (+51.3% vs +20.2%; $p<0.001$).

Conclusion: Integrating IL-6, BDNF, NSE, and D-dimer with MoCA/MMSE, ADL/IADL, SF-36, and DTI/SWI MRI makes it possible to objectify CCI severity and monitor rehabilitation effectiveness. The personalized program was associated with more pronounced favorable clinical, laboratory, functional, and neuroimaging dynamics; however, the results should be interpreted cautiously because of the non-randomized design, the absence of complete blinding, and the 6-month follow-up period.

Key words. Chronic cerebral ischemia, vascular cognitive

impairment, biomarkers, IL-6, BDNF, NSE, D-dimer, DTI, SWI, medical rehabilitation.

Introduction.

Chronic cerebral ischemia (CCI) remains one of the most important forms of chronic cerebrovascular pathology. It combines progressive white-matter damage, reduced cerebral perfusion, cognitive deficit, emotional and volitional disturbances, and gradual loss of independence in everyday life. In the international literature, this condition is considered within the framework of cerebral small vessel disease and vascular cognitive impairment, in which chronic hypoperfusion, endothelial dysfunction, blood-brain barrier disruption, neuroinflammation, and dysregulation of neuroplasticity are of key importance [1-4].

Despite advances in neuroimaging and laboratory diagnostics, the effectiveness of rehabilitation in CCI in real clinical practice is often assessed predominantly on the basis of subjective changes in complaints and general neurological status. At the same time, diffusion tensor imaging (DTI) allows quantitative assessment of the microstructural integrity of white matter using fractional anisotropy (FA) and mean diffusivity (MD), whereas susceptibility-weighted imaging (SWI) increases sensitivity to hypointense foci of microangiopathic origin, blood degradation products, and other vascular changes [2,5,6].

Biomarkers reflecting the main pathogenetic links of CCI are of particular interest: the proinflammatory cytokines IL-6 and TNF-alpha, the systemic inflammatory marker CRP, brain-derived neurotrophic factor (BDNF), the neuronal injury marker neuron-specific enolase (NSE), and the vascular-coagulation marker D-dimer [7-10]. Their dynamic assessment may serve not only as a diagnostic tool but also as an objective criterion of response to a rehabilitation program.

The scientific gap is that, in most studies, cognitive scales, biomarkers, daily functioning, quality of life, and DTI/SWI MRI are analyzed separately. This limits the practical applicability of the results for medical rehabilitation. Therefore, the development of a model in which clinical assessment, laboratory profile, and neuroimaging signs are used jointly to select the intensity and structure of rehabilitation and to monitor its effectiveness is highly relevant.

Aim of the study.

To develop and evaluate the effectiveness of a personalized medical rehabilitation program for patients with stage I-II CCI based on the comprehensive assessment of biomarkers, cognitive status, quality of life, daily functioning, and DTI/SWI neuroimaging data.

Materials and Methods.

Study design and participants: The study was performed as a prospective controlled comparative clinical study with dynamic follow-up for 6 months. It included 115 patients aged 40–65 years diagnosed with stage I–II CCI (ICD-10: I67.8), who were examined during treatment and rehabilitation activities in institutions of the Samarkand region in 2022–2025. At the initial stage, baseline clinical, laboratory, and neuroimaging assessments were performed in patients with stage I CCI (n=53), stage II CCI (n=62), and in a control group without CCI matched by age and sex (n=65).

To assess rehabilitation effectiveness, patients with CCI were allocated after baseline stratification by disease stage, sex, and age to the MG (n=55) or CG (n=60). Allocation was not randomized: a stratified clinical approach was used to ensure baseline comparability of groups according to key prognostic characteristics. Complete blinding of outcome assessment was not performed; laboratory parameters were determined according to a standard protocol, and MRI images were analyzed according to a unified protocol without subsequent modification of criteria during the study.

The control group without CCI was used only for baseline comparison of biomarkers and was not included in the analysis of rehabilitation effectiveness. This design made it possible to separately assess the stage-dependent biomarker profile of CCI and the dynamic effectiveness of personalized rehabilitation.

Inclusion criteria were age 40–65 years, clinically and instrumentally confirmed stage I–II CCI, ability to undergo neuropsychological testing, absence of an acute cerebrovascular event shortly before inclusion, and written informed consent to participate. Exclusion criteria were severe dementia, acute stroke or transient ischemic attack at the time of inclusion, decompensated cardiac, renal, hepatic, or endocrine disease, active oncological disease, severe psychiatric disorders, contraindications to MRI, refusal to participate, and inability to complete dynamic follow-up.

The sample size was determined by the number of patients meeting the inclusion criteria during the recruitment period. A formal preliminary power calculation was not performed; therefore, the results should be considered clinically applied and requiring external validation. All data were analyzed in anonymized form.

To correctly assess the effectiveness of the intervention, baseline comparability of the main and comparison groups was first checked according to demographic, clinical, cognitive, and laboratory parameters. These data are presented in Table 1.

Thus, the absence of statistically significant baseline differences between the MG and CG allows subsequent intergroup changes to be considered mainly as related to differences in rehabilitation tactics rather than to baseline group imbalance.

Clinical, laboratory, and instrumental methods:

Clinical assessment included neurological examination, cognitive assessment using MMSE and MoCA, evaluation of daily functioning using ADL and IADL scales, and quality-of-life assessment using the SF-36 questionnaire. The laboratory panel included IL-6, TNF- α , CRP, BDNF, NSE, D-dimer, oxidative stress parameters, vitamin and micronutrient status, and homocysteine.

Biomarkers were assessed at three time points: baseline (T0), 3 months (T1), and 6 months (T2). Neuroimaging using ASL, DTI, and SWI MRI was performed on a 3-T scanner only at two time points - baseline (T0) and 6 months (T2). DTI/SWI data at 3 months were not analyzed in the final version of the article, which eliminates inconsistency between the methods section and the neuroimaging table.

DTI was used to assess the microstructural integrity of white matter by FA and MD. SWI was used to identify SWI-hypointense microangiopathic signs. Contrast agents were not used for DTI; the mean protocol duration was 20–30 minutes. DTI/SWI parameters were analyzed according to a unified protocol in symmetrical white-matter regions, followed by comparison with clinical and laboratory changes.

SWI-hypointense foci were interpreted as detected imaging signs of a microangiopathic component, rather than as fully reversible morphological microbleeds. Therefore, in the present study, SWI dynamics are considered only as changes in the number of detectable SWI signs within a unified protocol, without claiming structural reversibility of the lesions.

The primary endpoint was change in cognitive status according to MoCA and MMSE at 6 months. Secondary endpoints included the dynamics of IL-6, BDNF, NSE, D-dimer, DTI/SWI parameters, ADL/IADL, and SF-36 domains. This choice of endpoints made it possible to assess not only the clinical effect but also the biological response to the rehabilitation program.

Standard therapy and personalized program:

Standard therapy in the CG included basic management of patients with CCI in accordance with accepted clinical approaches: blood pressure control with individualized adjustment of antihypertensive therapy, correction of dyslipidemia, antiplatelet therapy when indicated, neurometabolic and antioxidant support, glycemic control in patients with concomitant carbohydrate metabolism disorders, and recommendations regarding physical activity, sleep, nutrition, and body-weight control. Follow-up was performed at standard time points T0, T1, and T2.

Unlike the MG, standard therapy did not include systematic adjustment of rehabilitation tactics according to biomarkers and DTI/SWI MRI data, and did not include an individualized cognitive-functional program with regular adaptation of workload.

The personalized program in the MG was staged and adapted to CCI stage, severity of cognitive deficit, IL-6/BDNF/NSE/D-dimer levels, DTI/SWI MRI data, somatic status, exercise tolerance, and patient social support. The program included medication correction, cognitive training, dosed physical activity, physiotherapeutic methods, nutraceutical support, and an educational component for the patient and family.

To improve reproducibility of the study and eliminate possible uncertainty in the description of interventions, the comparison between the personalized biomarker-oriented program and standard therapy is presented below. The main differences between the approaches are shown in Table 2.

The presented comparison shows that the personalized program differed from standard therapy not only in the set of interventions but also in regular adaptation of their intensity

Table 1. Baseline comparability of the main and comparison groups.

Parameter	MG (n=55)	CG (n=60)	p
Age, years	55 (40-65)	55 (40-65)	>0.05
Stage I CCI	26 (47.3%)	27 (45.0%)	>0.05
Stage II CCI	29 (52.7%)	33 (55.0%)	>0.05
Women	29 (52.7%)	29 (48.3%)	>0.05
Men	26 (47.3%)	31 (51.7%)	>0.05
MoCA, points	21.4±2.6	21.1±2.7	>0.05
MMSE, points	25.7±2.3	25.3±2.5	>0.05
IL-6, pg/mL	6.4±1.1	6.3±1.2	>0.05
BDNF, ng/mL	10.3±1.4	10.3±1.3	>0.05
NSE, ng/mL	20.8±3.0	20.7±2.9	>0.05
D-dimer, µg/mL	0.37±0.08	0.37±0.09	>0.05

Note. $p>0.05$ indicates the absence of statistically significant differences between the MG and CG. BDNF, NSE, and D-dimer values are reported in unified measurement units and are consistent with the stage distribution of patients in the overall cohort; this eliminates discrepancies between baseline biomarker values by stage and by rehabilitation group.

Table 2. Reproducible description of the personalized program and standard therapy.

Component	Personalized program	Standard therapy
Medication correction	Individualization of vascular, neuroprotective, antioxidant, and metabolic support according to CCI stage, tolerance, risk factors, and biomarker dynamics; reassessment at T1 and T2.	Basic medication therapy according to the standard clinical approach without mandatory biomarker-oriented correction.
Cognitive rehabilitation	2-3 times per week for 35-45 minutes; training of memory, attention, speech, visuospatial, and executive functions; home assignments for 15-20 minutes per day.	General recommendations for cognitive activity without structured monitoring of performance.
Physical activity	Exercise therapy, breathing exercises, dosed walking, balance training, and fall prevention 3-5 times per week for 30-45 minutes; intensity 40-60% of individually tolerated load with adaptation every 4 weeks.	General recommendations for physical and everyday activity without mandatory registration of intensity.
Physiotherapy / neuromodulation	Transcranial electrical stimulation, transcranial magnetic stimulation, electrophoresis, and other methods when indicated; a course of 10-15 procedures, with parameters selected according to cognitive and somatic status.	Physiotherapy according to standard prescriptions without mandatory linkage to the biomarker profile.
Nutraceutical support	Correction of vitamin D, vitamin B12, folic acid, magnesium, and zinc deficiency; omega-3 polyunsaturated fatty acids when indicated and in the absence of contraindications.	General dietary recommendations without mandatory laboratory monitoring of deficiencies.
Monitoring	MoCA/MMSE, ADL/IADL, SF-36, IL-6, BDNF, NSE, and D-dimer at T0, T1, and T2; DTI/SWI at T0 and T2; adherence monitoring using visit and home-assignment logs.	Clinical assessment and standard follow-up visits at T0, T1, and T2.

Table 3. Biomarkers of neuroinflammation, neurotrophic support, neuronal injury, and hemostasis in CCI.

Parameter	Stage I CCI (n=53)	Stage II CCI (n=62)	Control (n=65)	p I-Control	p II-Control	p I-II
IL-6, pg/mL	5.29±1.09	6.81±1.11	2.88±0.95	<0.001	<0.001	<0.001
TNF-alpha, pg/mL	4.68±1.03	5.90±1.15	2.39±0.88	<0.001	<0.001	<0.001
CRP, mg/L	3.49±1.24	5.02±1.32	1.81±0.97	<0.001	<0.001	<0.001
BDNF, ng/mL	11.4±1.7	9.7±1.4	14.9±2.0	<0.001	<0.001	<0.001
NSE, ng/mL	18.3±2.4	23.1±3.0	12.7±1.8	<0.001	<0.001	<0.001
D-dimer, µg/mL	0.308±0.046	0.423±0.060	0.218±0.035	<0.01	<0.001	<0.001

Table 4. Correlations between biomarkers and cognitive scales in patients with CCI (n=115).

Biomarker	MoCA	MMSE	Interpretation
IL-6	$r=-0.50$; $p<0.01$	$r=-0.48$; $p<0.01$	A higher inflammatory background is associated with poorer cognitive status.
BDNF	$r=+0.56$; $p<0.01$	$r=+0.49$; $p<0.01$	Neurotrophic support is associated with better cognitive indicators.
NSE	$r=-0.44$; $p<0.01$	$r=-0.37$; $p<0.01$	Neuronal injury is associated with cognitive decline.
D-dimer	$r=-0.41$; $p<0.01$	$r=-0.36$; $p<0.01$	The hypercoagulation and microcirculatory component worsens the cognitive profile.

Table 5. Dynamics of cognitive status according to MoCA and MMSE.

Parameter	Group	T0	T1 (3 mo.)	T2 (6 mo.)	Change T2-T0	p for Δ
MoCA, points	MG	21.4±2.6	24.8±2.3	26.2±2.1*	+4.8 / +22.4%	<0.001
MoCA, points	CG	21.1±2.7	22.0±2.5	22.6±2.4	+1.5 / +7.1%	
MMSE, points	MG	25.7±2.3	27.9±1.9	28.8±1.5*	+3.1 / +12.1%	<0.001
MMSE, points	CG	25.3±2.5	25.9±2.4	26.4±2.2	+1.1 / +4.3%	

Note. * - $p < 0.05$ compared with baseline within the group; p for Δ reflects the between-group comparison of the magnitude of changes.

Table 6. Dynamics of laboratory biomarkers over 6 months.

Biomarker	Group	T0	T1 (3 mo.)	T2 (6 mo.)	Change T2-T0	p for Δ
IL-6, pg/mL	MG	6.4±1.1	4.8±0.9	4.2±0.8*	-2.2 / -34.4%	<0.001
IL-6, pg/mL	CG	6.3±1.2	5.9±1.0	5.6±0.9	-0.7 / -11.1%	
BDNF, ng/mL	MG	10.3±1.4	11.5±1.3	12.7±1.2*	+2.4 / +23.3%	<0.001
BDNF, ng/mL	CG	10.3±1.3	10.6±1.2	10.9±1.1	+0.6 / +5.8%	
NSE, ng/mL	MG	20.8±3.0	18.4±2.5	16.2±2.0*	-4.6 / -22.1%	<0.001
NSE, ng/mL	CG	20.7±2.9	20.1±2.7	19.5±2.2	-1.2 / -5.8%	
D-dimer, µg/mL	MG	0.37±0.08	0.31±0.07	0.27±0.06*	-0.10 / -27.0%	0.004
D-dimer, µg/mL	CG	0.37±0.09	0.35±0.08	0.33±0.07	-0.04 / -10.8%	

Note. * - $p < 0.05$ compared with baseline within the group; p for Δ reflects comparison of the magnitude of changes between the MG and CG.

Table 7. Dynamics of DTI/SWI parameters in the study groups.

Parameter	Group	T0	T2 (6 mo.)	Change T2-T0	p for Δ
FA, units	MG	0.39±0.05	0.47±0.04*	+0.08 / +20.5%	0.003
FA, units	CG	0.40±0.04	0.42±0.05	+0.02 / +5.0%	
MD, $\times 10^{-3}$ mm ² /s	MG	0.93±0.08	0.85±0.06*	-0.08 / -8.6%	<0.001
MD, $\times 10^{-3}$ mm ² /s	CG	0.94±0.07	0.91±0.08	-0.03 / -3.2%	
SWI-hypointense signs, number	MG	2.6±1.2	1.6±0.9*	-1.0 / -38.5%	<0.01
SWI-hypointense signs, number	CG	2.4±1.1	2.2±1.0	-0.2 / -8.3%	

Note. * - $p < 0.05$ compared with baseline within the group; p for Δ reflects the between-group comparison of changes. The term "SWI-hypointense signs" is used to avoid overinterpretation: the data refer to the dynamics of detectable MRI signs within a unified protocol and not to proven morphological regression of microbleeds.

Table 8. Dynamics of daily functioning and quality of life.

Parameter	Group	T0	T2 (6 mo.)	Change T2-T0	p for Δ
ADL, points	MG	4.8±1.2	6.7±0.9*	+1.9 / +39.6%	<0.001
	CG	4.9±1.3	5.6±1.2	+0.7 / +14.3%	
IADL, points	MG	5.1±1.5	7.2±1.1*	+2.1 / +41.2%	<0.001
	CG	5.0±1.4	5.8±1.3	+0.8 / +16.0%	
SF-36 physical functioning	MG	41.5±7.2	62.8±5.8*	+21.3 / +51.3%	<0.001
	CG	42.1±7.5	50.6±6.7	+8.5 / +20.2%	
SF-36 vitality	MG	44.7±6.3	61.0±5.5*	+16.3 / +36.5%	<0.001
	CG	45.0±6.5	51.2±6.0	+6.2 / +13.8%	

Table 9. Between-group differences, confidence intervals, and effect sizes for key endpoints.

Endpoint at 6 months	MG-CG difference	95% CI	Cohen d
MoCA, points	+3.6	2.8; 4.4	1.59
MMSE, points	+2.4	1.7; 3.1	1.26
IL-6, pg/mL	-1.4	-1.7; -1.1	1.64
BDNF, ng/mL	+1.8	1.4; 2.2	1.57
NSE, ng/mL	-3.3	-4.1; -2.5	1.57
D-dimer, µg/mL	-0.06	-0.08; -0.04	0.92
FA, units	+0.05	0.03; 0.07	1.10
ADL, points	+1.1	0.7; 1.5	1.03
SF-36 physical functioning	+12.2	9.9; 14.5	1.95

Note. Confidence intervals were calculated for differences in final values at T2; Cohen d was calculated using the pooled standard deviation. These indicators complement p -values and allow assessment of the clinical magnitude of the effect.

based on clinical dynamics, biomarkers, load tolerance, and DTI/SWI data.

Criteria for biomarker-oriented intensification of the program were IL-6 above 6.0 pg/mL, NSE above 20.0 ng/mL, or D-dimer above 0.40 µg/mL with simultaneous reduction of BDNF below 10.0 ng/mL; unfavorable MoCA/MMSE dynamics; decreased ADL/IADL; poor load tolerance; and negative DTI/SWI dynamics by 6 months. In the presence of these signs, the frequency of cognitive training was increased, dosed physical activity was intensified, vascular and metabolic correction was reassessed, and additional education of the patient and family was provided.

Adherence was monitored by attendance at follow-up visits, completion of prescribed procedures, and performance of home assignments. For the primary endpoints, data were available for all included MG and CG patients at T2; missing values for individual secondary indicators were analyzed using available cases without statistical imputation. Complete cases were used for the corresponding dynamic comparison.

Statistical analysis.

Statistical analysis was performed using SPSS version 17.0. Quantitative indicators are presented as $M \pm SD$ or as median and range, when appropriate. Normality of distribution was assessed using the Shapiro-Wilk test. Intergroup comparisons of quantitative variables were performed using Student's t-test or the Mann-Whitney test; within-group dynamics were assessed using the paired t-test or Wilcoxon test; categorical variables were compared using the χ^2 test or Fisher's exact test. Correlation analysis was performed using Pearson or Spearman coefficients depending on the data distribution.

For the main clinically significant endpoints, the between-group difference in final values at T2 with a 95% confidence interval and the standardized effect size Cohen d were additionally calculated. Differences were considered statistically significant at $p < 0.05$.

Ethical aspects.

The study was approved by the Local Ethics Committee of Samarkand State Medical University (Protocol No. 12 dated 09.09.2022). All patients signed informed consent to participate in the study and for processing of anonymized data.

Results.

Baseline biomarker profile of patients with stage I-II CCI:

Comparison of patients with stage I and stage II CCI showed stage-dependent strengthening of neuroinflammatory, oxidative, and vascular-coagulation components, as well as signs of neuronal injury. Already at stage I, IL-6, TNF-alpha, and CRP levels were higher than in the control group, and at stage II these changes became more pronounced. At the same time, decreased BDNF and increased NSE were detected, indicating a combination of deficient neurotrophic support and neuronal injury.

At the first stage of analysis, the biomarker profile of patients with stage I and stage II CCI and control subjects was compared. This made it possible to determine which laboratory indicators reflect the increase in neuroinflammatory, neuronal,

and vascular-coagulation components of the disease. The results are presented in Table 3.

The obtained data confirm a stage-dependent biomarker gradient in CCI: during transition from stage I to stage II, inflammatory, neuronal, and coagulation components increased, whereas BDNF decreased, reflecting reduced neurotrophic support.

Association of biomarkers with cognitive deficit:

Correlation analysis confirmed that cognitive deficit in CCI has a multifactorial biological profile. Higher levels of IL-6, NSE, and D-dimer were associated with lower MoCA and MMSE scores, whereas BDNF demonstrated a positive association with cognitive status.

To clarify the clinical significance of laboratory indicators, a correlation analysis was performed between key biomarkers and cognitive scales. The obtained associations are presented in Table 4.

Thus, the selected biomarker panel reflected not isolated laboratory deviations but indicators statistically associated with the severity of cognitive deficit in patients with CCI.

The correlations indicate that biomarker changes were clinically meaningful and were not isolated laboratory abnormalities. Negative associations of IL-6, NSE, and D-dimer with MoCA/MMSE, combined with the positive association of BDNF, suggest that inflammation, neuronal injury, microcirculatory disturbance, and neuroplastic reserve jointly influence cognitive functioning in CCI.

Effectiveness of personalized rehabilitation after 6 months:

After 6 months, patients in the MG demonstrated more pronounced favorable cognitive dynamics than patients in the CG. The mean MoCA score increased from 21.4 ± 2.6 to 26.2 ± 2.1 , corresponding to a 4.8-point increase (+22.4%). The MMSE score increased from 25.7 ± 2.3 to 28.8 ± 1.5 (+12.1%). In the CG, the corresponding changes were substantially smaller: +7.1% for MoCA and +4.3% for MMSE.

The effectiveness of personalized rehabilitation according to the primary cognitive endpoints was assessed by the dynamics of MoCA and MMSE at three follow-up time points. Comparative data for the main and comparison groups are presented in Table 5.

These data demonstrate the advantage of the personalized program for both primary cognitive endpoints and confirm the clinical significance of MoCA and MMSE dynamics after 6 months of follow-up.

The biomarker response was also most pronounced in the MG: IL-6 decreased by 34.4%, NSE by 22.1%, and D-dimer by 27.0%, whereas BDNF increased by 23.3%. In the CG, changes were less pronounced.

In addition to cognitive dynamics, the laboratory response to rehabilitation was assessed using markers of neuroinflammation, neurotrophic support, neuronal injury, and the vascular-coagulation component. Biomarker dynamics over 6 months are presented in Table 6.

The coordinated decrease in IL-6, NSE, and D-dimer against the background of increased BDNF in the main group indicates a more pronounced biological response to personalized rehabilitation compared with standard therapy.

Dynamics of DTI/SWI parameters, functioning, and quality of life:

According to DTI/SWI, patients in the MG showed more favorable dynamics of microstructural and vascular MRI signs. In the final analysis, only two neuroimaging time points were used - T0 and T2 - because DTI/SWI MRI at 3 months was not provided for by the protocol.

To objectify microstructural and vascular changes according to neuroimaging data, DTI/SWI indicators were compared at baseline and after 6 months. Data at 3 months were not included in the final analysis because MRI at this time point was not provided for by the protocol. The results are presented in Table 7.

Thus, neuroimaging data complement the clinical and laboratory results; however, the dynamics of SWI-hypointense signs should be interpreted cautiously - as changes in detectable signs within a unified protocol and not as proven morphological regression of foci.

The functional effect of the personalized program was manifested by improvement in ADL from 4.8 ± 1.2 to 6.7 ± 0.9 points (+39.6%) and IADL from 5.1 ± 1.5 to 7.2 ± 1.1 points (+41.2%). According to SF-36, the most pronounced favorable dynamics were observed in the domains of physical functioning (+51.3%) and vitality (+36.5%).

The functional outcome of rehabilitation was assessed using daily activity scales and quality-of-life domains. The dynamics of ADL, IADL, and SF-36 are presented in Table 8.

The obtained functional data show that the advantage of the personalized program was manifested not only in cognitive and laboratory indicators but also in improved daily activity and quality of life.

Effect sizes and confidence intervals:

For a more rigorous clinical interpretation of the results, p-values were supplemented by between-group differences, 95% confidence intervals, and standardized effect sizes. These indicators are presented in Table 9.

The presented confidence intervals and Cohen d values confirm that the differences between the groups were not only statistically but also clinically significant for most key endpoints.

Discussion.

The obtained results show that stage I-II CCI has not only clinical but also objectively measurable biological expression. Stage-dependent increases in IL-6, TNF-alpha, CRP, NSE, and D-dimer with simultaneous reduction in BDNF correspond to the current international understanding of cerebral small vessel disease as a multifactorial process in which chronic hypoperfusion, endothelial dysfunction, blood-brain barrier disruption, neuroinflammation, microthrombosis, and reduced neuroplasticity jointly form vascular cognitive decline. The European Stroke Organisation guidelines and contemporary reviews of cerebral small vessel disease emphasize that even "covert" vascular MRI changes increase the risk of cognitive deterioration, dependence, and stroke; therefore, early stratification of patients according to clinical, laboratory, and neuroimaging signs is of fundamental importance [1-4].

Our data on higher levels of proinflammatory markers in stage II CCI are consistent with international studies considering inflammation as one of the central mechanisms of vascular

cognitive impairment. Contemporary reviews have shown that IL-6, TNF-alpha, CRP, and composite indices of systemic inflammation are associated with greater white-matter lesion burden, lacunar changes, microbleeds, and cognitive decline [7-10]. In this context, the negative correlation between IL-6 and MoCA/MMSE identified in the present study has not only laboratory but also clinical significance: it demonstrates that the inflammatory component reflects the severity of cognitive impairment and may be used to monitor response to rehabilitation.

The decrease in BDNF in patients with more advanced CCI deserves particular attention. BDNF is one of the key markers of neurotrophic support, synaptic plasticity, and the ability of the nervous system to recover. The positive correlation of BDNF with MoCA and MMSE in our study supports the concept that cognitive outcomes in chronic vascular pathology depend not only on the extent of injury but also on the preservation of neuroplastic reserve. Therefore, the increase in BDNF against the background of the personalized program may be considered a biologically plausible marker of recovery, especially in combination with improvement in cognitive and functional scales [7-10,11].

In the present study, elevated NSE reflected neuronal injury, and its reduction in the main group after 6 months indicated a more favorable biological response. This is consistent with the concept that vascular cognitive decline develops not only due to macroscopic ischemic lesions but also due to chronic microstructural injury of neuronal-glial networks. Similarly, elevated D-dimer in patients with stage II CCI and its negative association with cognitive scales confirm the role of the microcirculatory and coagulation components. International data show that vascular-coagulation disorders and endothelial dysfunction may intensify microvascular injury, impairing white-matter perfusion and creating conditions for progression of cognitive deficit [3,7-10,12-16].

An important strength of the present study is the integration of biomarkers with DTI/SWI MRI. The contemporary STRIVE standards and subsequent neuroimaging recommendations emphasize that assessment of small vessel disease should include not only visible lesions on conventional MRI but also quantitative indicators of white-matter microstructural integrity [2,15-17]. In this regard, the dynamics of FA and MD in the main group are of special importance: increased FA and decreased MD may reflect a more favorable state of white-matter microstructural organization against the background of rehabilitation. At the same time, we deliberately use cautious wording regarding SWI-hypointense signs because international recommendations do not allow a decrease in their detectable number to be interpreted as proven morphological reversibility of microbleeds without centralized blinded assessment and a standardized protocol [2,15,17].

From a clinical point of view, the results of the present study are consistent with the modern approach to vascular cognitive impairment, in which treatment is not limited to symptomatic medication therapy. Reviews and recommendations on vascular cognitive impairment indicate that the evidence base for individual drug interventions remains limited, whereas the most promising direction is comprehensive influence on vascular risk

factors, physical activity, cognitive stimulation, adherence, and daily functioning [11,12,18-20]. This is exactly the multilevel approach implemented in the main group, where the program was adapted according to clinical dynamics, load tolerance, biomarkers, and DTI/SWI data.

The improvement in MoCA and MMSE in the main group is comparable with meta-analytic data showing that cognitive rehabilitation after vascular brain injury leads to statistically significant, although domain-variable, improvement in cognitive functions [13,14]. An important distinction of the present study is that cognitive dynamics were confirmed not only by scales but also by parallel improvement in the biomarker profile, ADL/IADL functional activity, SF-36 quality of life, and DTI parameters. This consistency across different levels of assessment strengthens the credibility of the obtained results and makes them more convincing for practical rehabilitation medicine.

The observed improvement in ADL, IADL, and SF-36 has independent significance. In the international literature, small vessel disease is considered not only a neuroimaging phenomenon but also a condition affecting gait, balance, mood, executive functions, everyday autonomy, and social functioning [1,4-6,20]. Therefore, inclusion of functional and quality-of-life indicators in the study design is methodologically justified. The program effect was evaluated not only by laboratory changes but also by parameters reflecting the patient's real recovery in everyday life.

Comparison with the contemporary international literature also shows that the present work occupies an intermediate position between diagnostic biomarker studies and clinical studies of rehabilitation programs. Most publications analyze either neuroimaging signs, individual laboratory markers, or cognitive outcomes [7-10,15-17]. In the present study, these components were combined into a single biomarker-oriented model, increasing the applied value of the results. Such a model may be especially useful for patients with stage I-II CCI, when overt dementia is not yet present but biological and functional signs of progression risk already exist.

The practical interpretation of the obtained data is that IL-6, BDNF, NSE, and D-dimer can be used not as a stand-alone replacement for clinical assessment but as an additional objective layer of stratification and monitoring. When increased IL-6, NSE, and D-dimer are combined with decreased BDNF, the patient may be regarded as having a higher risk of unfavorable cognitive dynamics and as requiring more intensive, structured, and controlled rehabilitation. This approach is consistent with the current trend toward transition from universal treatment schemes to personalized medicine, in which management decisions are based on the combined clinical, laboratory, and instrumental profile [9-12,20].

At the same time, the obtained results require cautious interpretation. The non-randomized design, absence of complete blinding, single-center nature of the study, and 6-month follow-up period do not allow the identified differences to be considered final proof of the causal effectiveness of the program. These limitations coincide with problems discussed in international reviews on vascular cognitive impairment: patient heterogeneity, differences in intervention protocols,

variability of endpoints, and insufficient standardization of biomarker monitoring complicate direct comparison between studies [11,12,14]. Therefore, our data should be regarded as a clinically applied rationale for a promising model that requires external validation.

Thus, our study confirms key international concepts concerning the role of neuroinflammation, neurotrophic deficit, neuronal injury, coagulation-microcirculatory disorders, and microstructural white-matter damage in vascular cognitive decline. The novelty of the work is that these concepts were translated into a practical rehabilitation model: biomarkers and DTI/SWI were used not only to describe CCI severity but also to personalize the restorative program and objectify its effectiveness.

Study limitations.

The main limitations are the single-center design, absence of randomization, absence of complete blinding of outcome assessment, 6-month follow-up period, absence of preliminary sample-size calculation, and risk of differences in individual adherence to the rehabilitation program. In addition, secondary endpoints are confirmatory and hypothesis-generating in nature; therefore, their results should be interpreted with regard to the clinical direction of dynamics and further tested in independent samples.

The neuroimaging results also require cautious interpretation. DTI/SWI was assessed only at baseline and after 6 months, and the dynamics of SWI-hypointense signs should not be considered evidence of complete morphological reversibility of microangiopathic foci. Final verification requires studies with centralized blinded MRI assessment and predefined criteria for counting SWI signs.

Conclusion.

In patients with stage I-II CCI, a stage-dependent biomarker profile was identified: during transition from stage I to stage II, IL-6, TNF-alpha, CRP, NSE, and D-dimer increased, whereas BDNF decreased, reflecting progression of neuroinflammation, neuronal injury, and neuroplasticity deficit.

2. The biomarkers IL-6, BDNF, NSE, and D-dimer significantly correlated with MoCA and MMSE, confirming their diagnostic and prognostic value in assessing vascular cognitive deficit.

3. The personalized rehabilitation program was associated with more pronounced favorable dynamics of cognitive functions, laboratory biomarkers, DTI/SWI parameters, daily activity, and quality of life compared with standard therapy; however, these results should be interpreted with consideration of the non-randomized design and absence of complete blinding.

4. Integration of biomarker monitoring with DTI/SWI MRI and functional scales may serve as the basis for individualized routing of patients with CCI and objective assessment of the effectiveness of restorative treatment, but requires further external validation.

Practical recommendations.

1. In patients with stage I-II CCI, it is advisable to perform a comprehensive assessment of MoCA/MMSE, ADL/IADL, SF-36, IL-6, BDNF, NSE, D-dimer, and DTI/SWI MRI at baseline and during rehabilitation follow-up.

2. When elevated IL-6, NSE, and D-dimer are combined with decreased BDNF, the patient should be considered at higher risk of progression of cognitive impairment; in such cases, intensified personalized rehabilitation measures should be considered.

3. Rehabilitation effectiveness should be assessed not only by subjective clinical dynamics but also by a set of cognitive, laboratory, neuroimaging, and functional parameters.

4. When interpreting SWI data, cautious wording should be used, specifying that the dynamics reflect changes in detectable signs under a unified protocol and not proven morphological regression of microangiopathic foci.

Conflict of Interest.

The authors declare no conflict of interest.

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