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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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COURSE OF POST COVID-19 DISEASE IN HEART FAILURE PATIENTS WITH MODERATELY REDUCED LEFT VENTRICULAR EJECTION FRACTION

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Abstract.

Background: In this study, we assessed the impact of COVID-19 on the course of HFmrEF by determining the biomarkers furin and NT-proBNP, questionnaires (EQ-5D-5L), and cardiac ultrasound.

Methods: A comprehensive examination of 72 patients with HFmrEF (main group) and 18 apparently healthy individuals (control group). The main group was divided into two subgroups depending on the history of coronavirus disease. All patients gave their consent to participate in the study.

Results: In the group of patients with a history of coronavirus infection compared to the patients without a COVID-19 history were established: significantly higher concentrations of NT-proBNP (1002.79±215.94 pg/ml and 405.37±99.06 pg/ml, respectively, p-value 0.01), uric acid (429.08±27.01 mmol/l *vs.* 354.44±28.75 mmol/l, p-value 0.04) and a lower furin to NT-proBNP ratio (0.87± 0.26 and 1.38 ± 1.16, p-value 0.045) in blood serum; using the EQ-5D-5L questionnaire, a significant deterioration of quality of life indicators (64.21±3.04 points vs. 72.81±1.82 points by VAS, p-value 0.02); higher indicators of LVMMi (157.39±6.14 g/m^2 and 138.68±6.02 g/m^2, p-value 0.03), LA dimensions (43.74±0.95 mm and 41.12±0.85 mm, p-value 0.04) and RA dimensions (40.76±1.23 mm and 37.75±0.85 mm, p-value 0.04).

Conclusion: Coronavirus infection in patients with HFmrEF leads to disorders of intracardiac hemodynamics and persistent negative structural changes of the heart. The ratio of furin to NT-proBNP serum levels can be used to determine the impact of the HF syndrome itself on the patients' subjective assessment of their quality of life.

Key words. Heart failure, COVID-19, NT-proBNP, furin.

Introduction.

The presence of CHF in the context of COVID-19 leads to complications in the diagnosis, treatment, and prognosis of these diseases. Viral infections can exacerbate pre-existing CHF, with multiple studies showing an increase in readmissions due to HF during influenza-like disease seasons [1].

The mutually aggravating CHF course with concomitant COVID-19 is well-known. On the one hand, CHF increases the probability of acquiring COVID-19 and high severity of the infection, on the other hand – COVID 19 contributes to the development of HF exacerbation due to various mechanisms, including ischemia or myocardial infarction, increased oxygen dependence, increased pressure in the pulmonary artery or its thrombosis, myocarditis, stress cardiomyopathy or diffuse cytokine release [2].

According to various authors, the prevalence of CHF in patients with coronavirus infection varies significantly. Thus, in a study by Shi at al., 4.1 % (17 individuals) of the population of COVID-19 patients already had CHF syndrome [3]. In another Chinese cohort, CHF was present in 23 % of patients with COVID-19 [4].

Chronic heart diseases, including CHF syndrome, are the factors which can contribute to the severe phenotype of COVID-19, characterized by poorer prognosis and increased patient mortality [5].

The object of special attention are patients with HF with moderately reduced left ventricular ejection fraction (HFmrEF), which is due to the lack of a convincing evidence base regarding the tactics of follow-up and treatment of this patient category and significant "lability" of LVEF [6].

Considering the well-known mutually aggravating course of CHF under the conditions of COVID-19, questions arise what laboratory, hemodynamic, and structural changes should be expected among patients with HFmrEF who have suffered from COVID-19. The factors that affect the higher incidence of coronavirus disease in patients with HF and the predictors of the adverse course of CHF in patients having suffered from COVID-19 remain unknown.

From this point of view, it is interesting to study the activity of furin, which was identified in 2015 as a convertase of biologically inactive pro-BNP into bioactive BNP and inactive NT-proBNP, in patients with HFmrEF [7]. In addition, the relevance of the study is due to the proven significantly higher level of furin in patients with CHF [8,9] and the active involvement of furin in the process of penetration of the SARS-CoV-2 virus into a cell for replication [10].

With an aggressive COVID-19 infection, patients with HF have a significantly higher risk of exacerbations, many mechanisms may be responsible for initiating and intensifying this process. The acute infectious process leads to the release of pro-inflammatory cytokines and the involvement of pro-inflammatory macrophages and granulocytes, which is accompanied by a pronounced inflammatory storm that can increase the primary damage. All this contributes to the development of acute decompensation of chronic HF [11,12].

The study of the consequences of COVID-19 for the cardiovascular system of patients in the remote period continues, which will help to develop strategies for the effective treatment of such patients and the prevention of the development of cardiovascular complications in them.

Purpose. to evaluate the impact of coronavirus disease on the general condition, laboratory, and echocardiographic parameters in patients with HFmrEF, to investigate the activity of furin.

Materials and methods.

The research study was planned for 2021 and was initiated in January 2022. Completion of the study is scheduled for February 2024. This is a retrospective cohort research study.

This study was conducted in accordance with the requirements

of the Declaration of Helsinki of Human Rights (1964), the Council of Europe Convention for the Protection of Human Rights and Dignity of the Human Being with Regard to the Application of Biology and Medicine (Convention on Human Rights and Biomedicine) (ETS-164), including the additional protocol to the Convention on Human Rights and Biomedicine dated 25.01.2005, the International Conference on Harmonization of Good Clinical Practice (ICH GCP E6(R2), 2016) and the legislation of Ukraine. The study was reviewed and approved by the Committee on Ethics and Deontology at the State Institution "L.T. Malaia National Institute of Therapy of the National Academy of Sciences of Ukraine".

The sample size was calculated in advance so that it could guarantee the validity of the result. All patients who participated in the study were given information about the purpose and methods of the examination, benefits, and risks before initiation of the study procedures. The patients were informed that participation in the study was entirely voluntary, and emphasis was placed on the possibility to withdraw from the study at any time without loss of benefits. Each of the patients who agreed to participate in the study signed an informed consent.

A comprehensive examination of 72 patients with HFmrEF (main group), of whom 54 were men, 18 women, and 18 apparently healthy individuals (control group), which included anthropometric, laboratory, instrumental examinations, and surveys to assess the quality of life, was conducted at the clinical-diagnostic therapeutic department of the State Institution "L.T. Malaia National Institute of Therapy". The main group was divided into two subgroups depending on the history of coronavirus disease: 38 patients were included in the group of patients who had a history of COVID-19, and 34 patients were included in the group of those who had not suffered from COVID-19. One of the criteria for inclusion of patients in the study (the group of those who had COVID-19) was the course of coronavirus disease with confirmed mild to moderate pneumonia.

The average age of patients was 63.6±4.1 years. The study group mainly included patients with coronary heart disease (91.7 %) and essential hypertension (86.1 %).

Before starting the examination procedures, all patients completed the EQ-5D-5L Quality of Life questionnaire, which is one of the most commonly used general health questionnaires [13]. The EQ-5D-5L includes five parameters: mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. It also has a visual analog scale (EQ-VAS) that rates health on a scale of 0 to 100, with a higher score indicating better health. The validity of the obtained data of the EQ-5D-5L questionnaire has been psychometrically confirmed for a large number of diseases and conditions, including cardiovascular ones.

Anthropometric studies were conducted using conventional methods with the calculation of the body mass index (BMI) according to the formula:

BMI = (body weight (kg))/(height (m))^2.

Laboratory tests were carried out in the clinical and diagnostic laboratory with the bacteriological department and in the laboratory of immuno-biochemical and molecular genetic studies of the State Institution "L.T. Malaia National Institute of Therapy of the National Academy of Sciences of Ukraine". To study the laboratory parameters, blood sampling was performed in the morning under fasting conditions from the ulnar vein. Laboratory tests included clinical blood count, blood chemistry panel with measurements of AST, ALT, creatinine, glucose, lipid spectrum, potassium, sodium, and magnesium. Also, the blood levels of NT-proBNP and glycated hemoglobin were measured by enzyme-linked immunoassay (ELISA).

The furin level in blood serum was also determined by the ELISA method using the set of reagents "Human Fur (Furin) ELISA kit" manufactured by "Wuhan Fine Biotech Co., Ltd.", the detection range was 0-1000 pg/ml, the sensitivity was 9.375 pg/ml.

To assess the lipid spectrum, the levels of total cholesterol (TC), high-density lipoprotein cholesterol (HDL-C), triglycerides (TG), low-density lipoprotein cholesterol (LDL-C) were determined using the formula by W.T. Friedewald: LDL-C = TC – (HDL-C + TG/2.22).

Instrumental methods included electrocardiography (ECG) in standard leads and transthoracic Doppler echocardiography (EchoCG). ECG at rest was recorded in 12 standard leads. Echocardiography was performed according to the recommendations of standard approaches on a Toshiba Aplio 500 device with measurements of: end-diastolic dimension (EDD), end-diastolic volume (EDV), end-systolic dimension (ESD), end-systolic volume (ESV), stroke volume (SV), left ventricular ejection fraction (LVEF), interventricular septal thickness (IVST), left ventricular posterior wall thickness (LVPWT), left atrium (LA) size, LA volume, right heart chamber dimensions (right ventricle (RV) and right atrium (RA)) [14].

LV myocardial mass (LVMM) was calculated using the formula:

$LVMM = 0.8 \times [(IVST_d + EDD + LVPWT_d)^3 - EDD^3] + 0.6.$

Body surface area (BSA) was calculated using the formula:

$BSA = 0.007241 * \text{weight (kg)}^{0.725} * \text{height (cm)}^{0.425}$

LVMM index (LVMMi) was calculated using the formula:

LVMMi = LVMM / BSA

LA volume index (LAVi) was calculated using the formula:

LAVi = LA volume / BSA

LV diastolic function was assessed using the latest recommendations of the American Society of Echocardiography (2021).

The patients received conventional therapy.

Statistical processing of the obtained data was carried out using the SPSS v.19.0 statistical program package. The mean (M) and standard error of the mean (m) were calculated. The differences between the compared values were considered reliable if the value of the Student's t-test was greater than or equal to 95 % ($p<0.05$).

Results and Discussion.

The clinical characteristics of the patients included in the study are shown in Table 1.

The majority of the examined patients in both groups were men. Women make up 25 % of the total patient cohort. During comparison, no significant differences were found between

groups of patients in terms of such indicators as age, height, weight, BMI, BSA, systolic (SBP) and diastolic blood pressure (DBP), heart rate (HR).

Table 1. *Clinical characteristics of patients with HFmrEF depending on the history of coronavirus disease.*

	HFmrEF and a history of COVID-19 (n = 38)	**HFmrEF (n = 34)**	**p-value**
Age, years	64.68 ± 1.86	63.56 ± 2.11	0.39
Sex, % of women (n)	26.3 (10)	23.5 (8)	0.48
Height, cm	172.47±1.32	175.25±1.76	0.45
Body weight, kg	92.97±5.32	94.43±3.49	0.21
DM type 2, %	57.9	41.18	0.18
SBP, mm Hg	135.27±17.96	133.19±17.22	0.26
DBP, mm Hg	84.51±8.84	85.65±8.79	0.31
HR, bpm	79±11.45	73±12.06	0.09
BMI, g/m^2	31.10±1.53	30.74±1.11	0.18
BSA, m^2	2.05±0.06	2.09±0.07	0.27
EQ-5D-5L*	64.21±3.04	72.81±1.82	0.02

Interrogating of patients with HFmrEF using the EQ-5D-5L questionnaire demonstrated that the quality-of-life indicators were significantly worse in the group of patients who have suffered from the coronavirus disease compared to those without a history of COVID-19 (64.21±3.04 points vs. 72.81±1.82 points according to VAS, p-value 0.02). At the same time, there was no difference in terms of age and LVEF between the indicated groups of patients. The RECODE-HF study, conducted in 3778 patients with HF, has proven the reliability and validity of the EQ-5D-5L questionnaire with visual analogue scale (VAS) for the assessment of quality of life in patients with HF. According to the data of this study, patients with comorbid pathology and a higher NYHA class [15], had lower VAS scores, in other words, patients with a more severe course of the disease were characterized by worse quality of life indicators according to EQ-5D-5L.

It should be noted that in our study, in a certain proportion of patients, the deterioration of the quality of life was caused by the deterioration of the course of angina, and not by manifestations of HF decompensation. That is, a low VAS score indicates only the severity of the patient's condition without indicating the probable cause of its occurrence.

A comparison of the results of laboratory tests among groups of patients is shown in Table 2. It can be seen that the groups do not differ in terms of such parameters as furin, creatinine, glycated hemoglobin, AST, ALT, and clinical blood count indicators. A significant difference was noted in NT-proBNP, furin/NT-proBNP ratio and uric acid.

Our study demonstrates a significantly higher level of uric acid in the blood serum in the group of patients with HFmrEF and with a history of COVID-19 (429.08±27.01 mmol/l *vs.* 354.44±28.75 mmol/l, p-value 0.04). Similar results were obtained by Mohammed Ali Gameil et al. in their study looking for the delayed outcomes of the coronavirus disease [16]. Hyperuricemia is known to be associated with more pronounced hemodynamic disorders and is an independent predictor of all-cause mortality among patients with HF.

Table 2. *Results of laboratory tests in patients with HFmrEF depending on the history of coronavirus disease.*

	HFmrEF and a history of COVID-19 (n = 38)	**HFmrEF (n = 34)**	**p-value**
NT-proBNP, pg/ml	1002.79±215.94	405.37±99.06	0.01
Furin, pg/ml	426±57.81	382±81.66	0.33
Furin/NT-proBNP*	0.87±0.26	1.38±0.16	0.045
Creatinine, μmol/l	97.54±4.16	100.8±7.69	0.71
Glycated hemoglobin, %	6.64±0.43	6.04±0.26	0.24
Erythrocytes, x10^{12}/l	4.54±0.13	4.78±0.15	0.08
Hemoglobin, g/l	136.63±4.62	143.65±5.12	0.10
Leukocytes, x10^9/l	6.67±0.39	6.69±0.38	0.48
Platelets, x10^9/l	225.05±11.87	239.56±12.02	0.20
AST, U	29.26±2.33	30.18±3.18	0.40
ALT, U	29.21±1.98	31.01±2.54	0.34
Uric acid, mmol/l*	429.08±27.01	354.44±28.75	0.04
Total cholesterol, mmol/l	4.27±0.26	4.40±0.28	0.38

According to our results, the levels of furin in patients with HFmrEF were significantly higher than in the control group (412.43±49.71 pg/ml *vs.* 113.80±35.18 pg/ml, p 0.0001), while the ratio of furin to NT-proBNP was significantly lower (0.93±0.24 and 2.29±0.31, p-value 0.002). When comparing the furin levels in patients with HFmrEF and with a history of coronavirus disease with a group of patients with HFmrEF who did not suffer from COVID-19, no significant difference was found (426±57.81 pg/ml and 382±81.66 pg/ml, p-value 0.33). At the same time, a significantly lower ratio of furin to NT-proBNP (0.87 ± 0.26 and 1.38 ± 1.16, p-value 0.045) was established in the group of patients suffering from COVID-19.

The study of furin levels in blood serum was performed in order to determine its possible connection with the course of HFmrEF in patients after coronavirus disease in connection with its known involvement in the conversion of pro-BNP and in the process of the penetration of the SARS-CoV-2 virus into the cell for further replication [17]. Considering the possible pathogenetic relationship between furin and NT-proBNP, as the final product of pro-BNP conversion, we calculated their ratio as a possible more sensitive indicator of the severity of HF in patients after a past coronavirus infection.

When we examined the entire group of patients with HFmrEF, regardless of the history of coronavirus disease, a strong positive correlation was found between the indicators of the quality of life according to the EQ-5D-5L questionnaire and the ratio of furin to NTproBNP (r= 0.76, p < 0.001) (Figure 1), while the negative correlation between the indicators of the quality of life and the level of NT-proBNP in blood serum was weaker (r=-0.61, p <0.01). That is, the determination of the ratio of furin to NTproBNP in the blood serum of patients who filled out a fairly simple and quick EQ-5D-5L questionnaire would allow to determine the degree of influence of HF on their subjective assessment of the quality of life. In clinical practice, the serial measurement of the ratio of furin to NT-proBNP can allow timely identification of HF as the cause of the deterioration of the patient's condition, which will allow timely optimization of

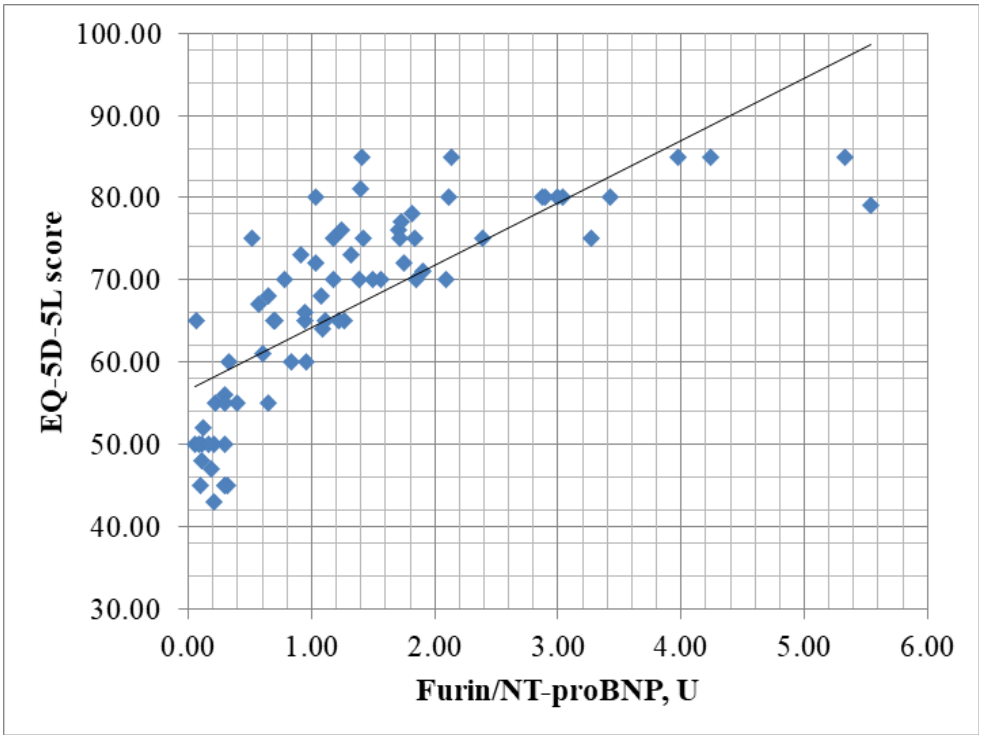

Figure 1. *Correlation between quality-of-life score and furin/NT-proBNP ratio.*

HF treatment, especially among patients with comorbidities. This statement requires further research.

Reddy et al. investigated the relationship of the quality of life in HF patients with preserved LVEF, with HF severity determined by physical capacity, amount of daily activity, functional class, echocardiography at rest, and plasma natriuretic peptide level. Quality of life was found to be the worst in young patients with obesity and diabetes and was not associated with NTproBNP or echocardiographic parameters [3].

According to our data, significantly higher concentrations of NT-proBNP in blood serum were established in the group of patients with HFmrEF and with a history of coronavirus disease (1002.79±215.94 pg/ml and 405.37±99.06 pg/ml, respectively, p-value 0.01) compared to patients with HFmrEF who did not suffer from COVID-19. Our data are consistent with the results of an analysis of 120 patients with COVID-19, which showed elevated levels of NTproBNP in 27.5 % of cases and high-sensitivity troponin cTnI in 10 % of deceased patients, respectively, indicating the presence of myocardial damage [18,19].

Similar results were obtained in another study conducted in Wuhan, China, which included 138 patients with COVID-19. It was shown that the levels of biomarkers of myocardial damage were significantly higher in patients who required intensive care unit treatment compared to those who did not require intensive care [20]. The authors argue that the monitoring of treatment efficacy in HF patients after recovery from COVID 19 should include a series of laboratory tests, including myocardial damage biomarkers.

The analysis of our data demonstrated that in the group of patients with HFmrEF who suffered from COVID-19, significantly more pronounced indicators of LVMMi (157.39±6.14 g/m^2 and 138.68±6.02 g/m^2, p-value 0.03), LA dimensions (43.74±0.95 mm and 41.12±0.85 mm, p-value 0.04) and RA dimensions (40.76±1.23 mm and 37.75±0.85 mm, p-value 0.04) were found, according to the transthoracic echocardioscopy results (Table 3). The groups of patients did not differ by other parameters. Pro-inflammatory cytokines, causing the development of cytokine storm syndrome, can damage cardiomyocytes and participate in pathological remodeling of heart cavities, as well as negatively affect myocardial inotropic function and metabolism [21,22].

Table 3. *Results of echocardioscopy examination among patients with HFmrEF, depending on the history of coronavirus disease.*

	HFmrEF and a history of COVID-19 (n = 38)	**HFmrEF (n = 34)**	**P-value**
LV EDD, mm	59.52±1.29	57.08±1.06	0.07
LV EDV, ml	181.21±8.48	165.31±7.18	0.08
LV ESD, mm	45.21±1.18	42.68±1.10	0.09
LV ESV, ml	99.54±5.68	90.13±5.01	0.11
LV EF, %	45.05±1.38	45.81±1.25	0.39
LV SV, ml	81.47±2.92	75.18±2.49	0.06
LV SVi, ml/m^2	39.69±1.68	36.12±1.59	0.06
LVMM, g	320.47±13.41	290.37±13.07	0.06
LVMMi, g/m^2	157.39±6.14	138.68±6.02	0.03
LA dimension, mm	43.74±0.95	41.12±0.85	0.04
LAVi, ml/m^2	34.85±1.10	34.09±0.99	0.61
RA dimension, mm	40.76±1.23	37.75±0.85	0.04
RV EDD, mm	30.63±1.09	29.43±0.94	0.41

Therefore, the data we have obtained demonstrate intracardiac hemodynamic disorders and persistent negative structural

changes of the heart, which are a consequence of the coronavirus disease in patients with HFmrEF.

Conclusion.

1. According to the results of interrogating the patients with HFmrEF using the EQ-5D-5L questionnaire, a significant deterioration of quality-of-life indicators was established in the group of patients with a history of coronavirus disease compared to those without a history of COVID-19 (64.21±3.04 points *vs.* 72.81±1.82 points by VAS, p-value 0.02). The indicated groups of patients did not differ by age and LVEF.

2. Significantly higher concentrations of NT-proBNP (1002.79±215.94 pg/ml and 405.37±99.06 pg/ml, respectively, p-value 0.01), uric acid (429.08±27.01 mmol/l *vs.* 354.44±28.75 mmol/l, p-value 0.04) and a lower furin to NT-proBNP ratio (0.87± 0.26 and 1.38 ± 1.16, p-value 0.045) in blood serum were established in the group of patients with a history of coronavirus infection compared to the patients without a COVID-19 history.

3. According to the results of transthoracic echocardioscopy, individuals with HFmrEF and a history of coronavirus infection showed higher indicators of LVMMi (157.39±6.14 g/m^2 and 138.68±6.02 g/m^2, p-value 0.03), LA dimensions (43.74±0.95 mm and 41.12±0.85 mm, p-value 0.04) and RA dimensions (40.76±1.23 mm and 37.75±0.85 mm, p-value 0.04) compared to patients who have not suffered from COVID-19, which indicates disorders of intracardiac hemodynamics and persistent negative structural changes of the heart as a consequence of the coronavirus disease in this category of patients.

4. The ratio of furin to NT-proBNP serum levels in patients with HFmrEF is significantly lower compared to the control group individuals, positively correlates with the quality-of-life indicators according to the EQ-5D-5L questionnaire and can be used to determine the impact of the HF syndrome itself on the patients' subjective assessment of their quality of life.

Disclosure.

The authors declare no conflict of interest.

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Течение болезни после COVID-19 у пациентов с сердечной недостаточностью с умеренно сниженной фракцией выброса левого желудочка.

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Резюме

Цель: оценить влияние COVID-19 на течение СНуснФВ путем определения биомаркеров фурина и NT-proBNP, анкетирования (EQ-5D-5L) и ЭхоКС.

Методы: комплексное обследование 72 пациентов с СНуснФВ (основная группа) и 18 практически здоровых лиц (контрольная группа). Основная группа была разделена на две подгруппы в зависимости от наличия коронавирусной болезни в анамнезе. Все пациенты дали согласие на участие в исследовании.

Результаты: В группе пациентов, перенесших коронавирусную болезнь, по сравнению с пациентами без COVID-19 в анамнезе были установлены: значительно более высокие концентрации NT-proBNP (1002,79±215. 94 пг/мл и 405,37±99,06 пг/мл, соответственно, p-0,01), мочевой кислоты (429,08±27,01 ммоль/л против 354,44±28,75 ммоль/л, p- 0,04) и более низкое соотношение фурина к NT-proBNP (0,87± 0,26 и 1,38 ± 1. 16, p- 0,045) в сыворотке крови; при использовании опросника EQ-5D-5L значительное ухудшение показателей качества жизни (64,21±3,04 балла против 72,81±1,82 балла по ВАШ, p-0,02); более высокие показатели индекса ММЛЖ (157,39±6,14 г/м2 и 138,68±6,02 г/м2, p- 0,03), размеров ЛП (43,74±0,95 мм и 41,12±0,85 мм, p-0,04) и ПП (40,76±1,23 мм и 37,75±0,85 мм, p-0,04).

Выводы. коронавирусная инфекция у пациентов с СНуснФВ приводит к нарушениям внутрисердечной гемодинамики и стойким негативным структурным изменениям сердца. Соотношение уровней фурина и NT-proBNP в сыворотке крови может быть использовано для определения влияния самого синдрома СН на субъективную оценку пациентами качества своей жизни.

Ключевые слова: сердечная недостаточность, COVID-19, NT-proBNP, фурин.

დაავადების მიმდინარეობა COVID-19-ის შემდეგ პაციენტებში გულის უკმარისობით მარცხენა პარკუჭის განდევნის ფრაქციით ზომიერად შემცირებული.

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მიზანი: COVID-19-ის გავლენის შეფასება HFrEF კურსზე ფურინის და NT-proBNP-ის ბიომარკერების, კითხვარის (EQ-5D-5L) და EchoCS-ის განსაზღვრით.

მეთოდები: 72 პაციენტის ყოვლისმომცველი გამოკვლევა HFrEF-ით (მთავარი ჯგუფი) და 18 აშკარად ჯანმრთელი ინდივიდი (საკონტროლო ჯგუფი). ძირითადი ჯგუფი დაიყო ორ ქვეჯგუფად კოროვირუსული დაავადების ისტორიის მიხედვით. ყველა პაციენტი დათანხმდა კვლევაში მონაწილეობაზე.

შედეგები: პაციენტების ჯგუფში, რომლებმაც გადაიტანეს კოროვირუსული დაავადება, COVID-19-ის ანამნეზის მქონე პაციენტებთან შედარებით, NT-proBNP-ის მნიშვნელოვნად მაღალი კონცენტრაცია (1002.79±215.94 pg/ml და 405.37±99.06 pg/ml, შესაბამისად, p-0.01). შარდმჟავა (429,08±27,01 მმოლ/ლ 354,44±28,75 მმოლ/ლ, p-0,04) და ფურინის უფრო დაბალი თანაფარდობა NT-proBNP-თან (0,87±0,26 და 1,38±1,16, p-0,045 სისხლის შრატში) EQ-5D-5L კითხვარის გამოყენებისას, ცხოვრების ხარისხის მაჩვენებლების მნიშვნელოვანი გაუარესება (64,21±3,04 ქულა VAS-ის მიხედვით 72,81±1,82 ქულა, p-0,02); უმაღლესი LVMM ინდექსი (157.39±6.14 გ/მ2 და 138.68±6.02 გ/მ2, p-0.03), LA ზომები (43.74±0.95 მმ და 41.12 ±0.85 მმ, p-0.04) და PP (40.73 მმ და 7±31). 0,85 მმ, p-0,04).

დასკვნები. კორონავირუსული ინფექცია პაციენტებში HFrEF იწვევს ინტრაკარდიული ჰემოდინამიკის დარღვევას და გულში მუდმივ უარყოფით სტრუქტურულ ცვლილებებს. სისხლის შრატში ფურინის და NT-proBNP დონის თანაფარდობა შეიძლება გამოყენებულ იქნას თვით HF სინდრომის გავლენის დასადგენად პაციენტების ცხოვრების ხარისხის სუბიექტურ შეფასებაზე.

საკვანძო სიტყვები: გულის უკმარისობა, COVID-19, NT-proBNP, ფურინი.