GEORGIAN MEDICAL NEWS

ISSN 1512-0112

NO 9 (354) Сентябрь 2024

ТБИЛИСИ - NEW YORK

ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

Медицинские новости Грузии

საქართველოს სამედიცინო სიახლენი

GEORGIAN MEDICAL NEWS

Monthly Georgia-US joint scientific journal published both in electronic and paper formats of the Agency of Medical Information of the Georgian Association of Business Press. Published since 1994. Distributed in NIS, EU and USA.

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.

GEORGIAN MEDICAL NEWS
No 7-8 (352-353) 2024

Содержание:

ASSESSMENT OF CHANGES IN HEART RATE VARIABILITY INDICES OF STUDENTS AFTER COVID-19 LOCKDOWN: A COHORT STUDY

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Abstract.

Introduction: The objective of this study was to investigate the heart rate variability indicators of students who had contracted COVID-19 after performing physical activity. The aim was to uncover the potential cardiac complications and dysregulations of the autonomic nervous system.

Material and Method: We explored about 11 heart rate variability indicators and their changes immediately after a 5-minute physical activity performed by using Proteus pes 3320 bicycle odometer. Furthermore, we conducted electrocardiographic recording using variational pulsometry. Recording and the analysis of ECG were carried out on a computer using special programs "Cardio reg" and "Cardio prog".

Results: The study revealed that the activity of the heart rhythm regulation indices among students infected by coronavirus was significantly elevated compared to the healthy controls ($p<0.05$). After the physical activity, the Tension Index, VBI, VRI and LF/HF indicators characterizing the sympathetic tone of HRV regulation were increased, while the coefficient of cardiointervals variation decreased among infected group students. Moreover, the ECG recording showed that after physical activity, the disturbances of cardiac functioning changed, accompanied by tachycardia.

Conclusion: The findings of this study demonstrate that short-term physical activity contributed to the transition of cardiovascular system indicators from the adaptive stress zone to the tense zone, which is likely due to the negative impact of COVID-19 on the capabilities of both the cardiovascular and nervous systems. Therefore, this study contributes to a deeper understanding of changes in HRV in the context of post-COVID-19 cardiovascular dysfunction among young adults.

Key words. Heart rate variability, COVID-19, SARS-CoV-2, post-COVID syndrome, electrocardiography.

Introduction.

SARS 2019 Coronavirus Disease (COVID-19), caused by coronavirus 2, is a pandemic that has led to considerable morbidity and death across the world. The clinical manifestation of COVID-19 could be specifically displayed in a wide spectrum and self-limiting [1]. Acute manifestations of COVID-19 were widely researched and published; however, long-term sequela of COVID-19 are unknown and still investigated [2,3]. While the virus mainly affects the respiratory system, it also causes acute myopericarditis, acute coronary syndrome, congestive heart failure, cardiogenic shock, and cardiac arrhythmias [4]. The host cell receptor for SARS CoV-2 is the biologically critical enzyme ACE2 (angiotensin-converting enzyme-2), which is generated by angiotensin 1-7 from ANG II (angiotensin II) in the intact human LV (left ventricle). The virus has an RBD (receptor binding domain) spike that enables contacting the extracellular region of ACE2. The binding of the spike protein RBD (receptor binding domain) to ACE2 brings the virion into proximity with the host cell surface membrane and induces conformational changes in the RBD that initiate the process of membrane fusion [5-7]. Along with that, there is the release of inflammatory mediators known as cytokine storm that causes diffuse alveolar damage, resulting in ARDS (Acute respiratory distress syndrome) [8,9].

The SARS 2019 Coronavirus Disease, also known as COVID-19, is a pandemic that has caused significant illness and death worldwide. While acute symptoms of COVID-19 have been widely researched and published, the long-term effects of the disease are still being investigated. Although the virus primarily affects the respiratory system, it can also cause cardiac problems such as acute myopericarditis, acute coronary syndrome, congestive heart failure, cardiogenic shock, and cardiac arrhythmias. A rat coronavirus model has shown that neutrophils produce cytokines and chemokines in response to alveolar epithelial cell infection with SARS-CoV-2, resulting in an inflammatory response that contributes to lung injury. In patients with cardiovascular disease, increased circulating ACE2 activity predicts adverse cardiovascular outcomes in patients with heart failure, coronary artery disease, and aortic stenosis [10].

Post-COVID-19 cardiovascular dysautonomia (PCCD) is a common condition that can be caused by direct damage from the SARS-CoV2 virus, cytokine storm-mediated dysregulation of the autonomic nervous system (ANS), or immune-mediated dysregulation of the ANS. This condition can be diagnosed using 12-lead electrocardiography (ECG) by measuring the time between two successive heartbeats. Heart rate variability (HRV) is a useful measure of ANS activity and can be measured using pulse oximetry or other devices. HRV can also be used to assess the course of the disease. In patients with COVID-19, cardiac complications can range from arrhythmias to ST-elevation myocardial infarction (STEMI) mimics, thrombus formation, and fulminant myocarditis. However, the arrhythmic risk related to COVID-19 is still being evaluated [11].

To better understand the cardiac complications associated with COVID-19, we aimed to assess the heart rate variability of young patients infected with the virus over the past 1.5 years. Our primary focus was to evaluate the heart's adaptive capabilities under physical exertion. This evaluation could help us identify potential cardiac disorders and develop strategies for treating post-COVID-19 complications related to cardiac dysfunction. Our study specifically examined the integral, histographical, and spectral indicators of heart rhythm regulation in students who had contracted COVID-19.

Methodology.

Forty-four female students aged 18-22 and with a mean age of 19.5 (SD = 1.09), from the Yerevan State University's Faculty of Biology were examined. Ten of them were not infected with COVID-19 and acted as the control group. The study group consisted of 34 students who had been infected with coronavirus in the last 1.5 years. The disease manifested in all treated students with various symptoms such as fever, cough, weakness, sweating, loss of smell and taste, nausea, vomiting, intestinal problems, muscle and joint pain, headaches, and in some cases pneumonia.

The portable device has been developed at the Laboratory of Integrative Biology of the Institute of Physiology after L. Orbeli. The indicators of HRV were assessed in both groups after a 5-minute physical load on a special exercise bicycle. In order to evaluate the functional capabilities of the cardiovascular system, ECG recording and analysis were carried out using the method of variational pulsometry after Baevsky [12]. For this purpose, a hardware-software complex was used, which combines a portable electrocardiograph of the model "Bio-Art 001" and a computer equipped with automatic ECG recording and heart rhythm variation pulse measurement analysis programs. Three 5-minute ECG segments were analyzed for students in each study group. Any student who was suspected of having any cardiac disorders or risks underwent Holter monitoring and was excluded from the study. The experimental design is represented in Figure 1.

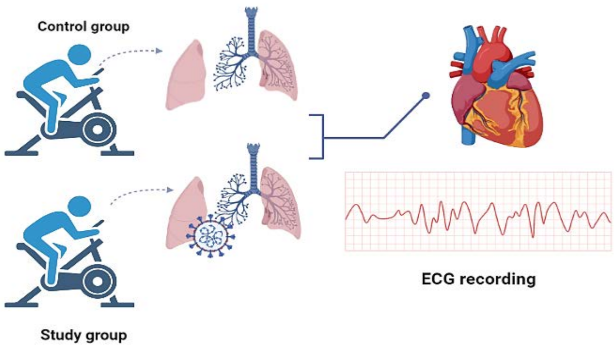

Figure 1. *Graphical representation of study design. All students from the control and study groups underwent a 5-minute bicycle load after which the ECG analysis has been performed for HRV assessment.*

The control group was selected based on clinical, laboratory, and physical examination data to exclude COVID-19 disease, any risk for cardiac, pulmonary, or related diseases, and comorbidities. ECG study and analysis programs were made according to the standards of the European Association of Cardiologists and the North American Association of Electrophysiology and Arrhythmology. To assess the adequacy of the heart rate regulation processes, the HRV assessment parameters proposed by Bayevsky and Mikhailov [12,13] were used. The following indicators were selected and studied for HRV assessment: histographic indicators - coefficient of variation of the examined mass of cardiointervals (CV), R-R(s). integral indicators: autonomic balance index (ABI): ABI = AMo/ΔX, to determine the ratio of sympathetic and parasympathetic regulation of the heart; autonomic rhythm index (ARI); ARI = 1/ (Mo*ΔX) - to assess the autonomic balance (the smaller the ARI, the more the autonomic balance is shifted towards the predominance of parasympathetic regulation); regulation adequacy index (indicator of the adequacy of the processes of regulation (RAI) = AMo/Mo, - to identify the correspondence between the level of functioning of the sinus node and sympathetic activity; strain index (SI) = AMo/(2ΔX*Mo), reflects the degree of centralization of heart rate control, and spectral indicators; power of the spectrum in the high-frequency range (HF, %) (0.15-0.4 Hz), which is related to the breathing act and reflects the level of activity of the parasympathetic nervous system in the process of heart rhythm regulation; law frequency (LF, %) - spectrum power in the medium frequency range (0.04-0.15Hz), is related to the arterial pressure and expresses the degree of activity of the sympathetic tone of heart rhythm regulation (although it has a mixed sympatho-parasympathetic origin); total power of spectrum (TP, ms^2) and spectrum power in the low frequency range (VLF, %) - (0.003-0.04 Hz); ratio of LF-to-HF power (LF/HF).

Statistical analysis.

Statistical analysis of research data is presented by mean and deviations (M±m). The significance between studied groups was determined using Student's t-test (paired) and the significance was considered as p<0.05.

Results.

A 5-minute pedometer workout (3rd degree of load) was accompanied by moderate changes in all heart rate measurements. This is probably related to reduced physical activity, which has become even more pronounced in the last years due to distance learning during pandemics. The changes in HRV indicators for healthy controls before and after 5min physical load are shown in Table 1.

Table 1. *Changes in HRV indicators of healthy students of the control group before and after 5 min physical activity.*

HRV indicators	Before physical activity	After physical activity
R-R (s)	0.75 ±0.06	0.61 ±0.07
CV (%)	7.83±0.85	6.17 ±0.68***
SI	140.90 ±17.59	218.40±22.50***
RAI	89.81 ±9.34	158.30±14.21***
ABI	232.91 ±29.8	299.40 ±28.2**
ARI	4.72 ±1.32	9.49 ±2.11***
TP (ms^2)	2351.0 ±335.4	1200.8 ±112.4**
VLF%	22.55 ±6.7	14.38 ±3.90
HF%	33.02 ±8.21	37.06 ±9.02
LF%	45.0±13.62	48.70±14.02
LF/HF	1.46 ±0.60	1.65 ±0.71*

** p < 0.05, ** p < 0.01, *** p < 0.001*

After bicycle load, moderate tension in the activity of the sympathetic mechanisms of processes regulating the heart rhythm was observed in healthy controls, which was expressed by an increase in SI by 55% (p<0.001). Furthermore, it was accompanied by a significant increase in the levels of other markers of the sympathetic tone, ABI, RAI and ARI by 28.5%, 76.2% and 101.0% respectively. Following the physical activity the TP has changed from 2351.0±335.4sm^2 to 1200.8±112.4sm^2 (49,0%, $p<0.001$), which was accompanied by a decrease in the middle- and high-frequency waves in the total spectrum (HF) with a weak increase in power by 3.68% and 4.0%, respectively, and a decrease in the spectrum of low-frequency (VLF) waves by 8.2%. As a result, the LF/HF indicator was increased by 13.0%.

The analysis of the neurovegetative regulation indicators among the students from the studied group showed that the HRV indicators of accompanied by a high functional tension of the heart. The results are shown in Table 2. The increase of SI (by 190%, $p<0.001$) along with the other indicators characterizing the high activity of the sympathetic tone, particularly RAI, ABI and ARI were increased by 94.1%, 123.3%, 124.3% respectively ($p<0.01$) in the COVID-19 infected group, in contrary of control group.

Table 2. *Changes in HRV indicators of students from experimental group before and after 5 min physical activity.*

HRV indicators	Before physical activity	After physical activity
R-R (s)	0.60 ±0.05	0.52 ±0.04***
CV (%)	7.74±0.30	5.26 ±0.36***
SI	201.70±77.31	586.10±86.42***
RAI	105.70 ±6.37	205.21±11.61***
ABI	239.18 ±28.1	534.2 ±45.8***
ARI	5.39 ±1.34	12.09 ±4.09**
TP (ms^2)	2131.0 ±305.0	618.82 ±93.4***
VLF%	20.87±6.7	32.21±6.0
HF%	20.89±3.26	15.96±3.02
LF%	58.40±6.69	50.15±6.02
LF/HF	2.16 ±0.80	4.25 ±0.79*

* $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$.

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Discussion.

During the physical activity, the students of the studied groups were considered to have tachysystole, arrhythmia, and cardiac output disturbances. The analysis of the cardiograms, rythmograms, histograms and scattergrams of the student from the control group is presented in Figure 2 (A, a-e). After the 5min physical load, the functional tension was expressed with activation of the cholinergic link of regulation, and the total effect of regulation was accompanied by tachycardia, moderate destruction of automation, and dysregulation of PNS activity.

This is probably because, in normal conditions, the heart rhythm and cardiac output intracardiac mechanisms usually work efficiently. However, in the post-infected period, the heart rhythm regulation function is disturbed due to damage to the central nervous system. Evidence of this consideration is the pronounced increase of SI, AMo, and IC, as well as the sympathetic/parasympathetic index and the spectrum of low-frequency waves in the process of heart rhythm regulation in the studied group of students. In the conditions of a strong signal flow from the central nervous system, the intracardiac homo- and heteromeric mechanisms of cardiac regulation are unable to cope with the increase in tension, and consequently

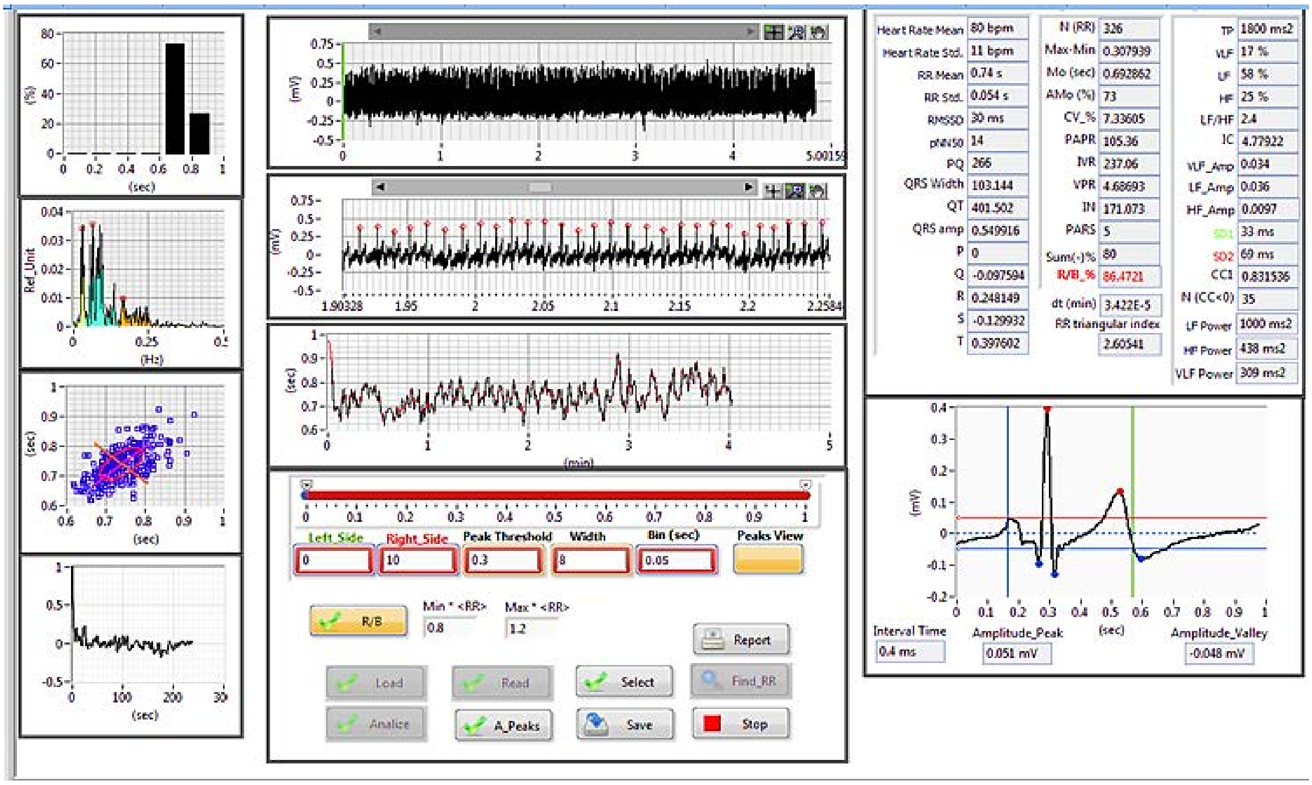

Figure 2. *Fragments of the original recordings of a cardiogram (a), scattergram (b), rhythmogram (c), histogram (d), and spectrogram (e) of the student from the control group after a 5min bicycle load.*

the imbalance in the frequency and strength of the heart contractions occurs. These changes cause the tension of vessel walls, arrhythmia, extrasystole, tachycardia, and other cardiac disorders. From Figure 2 it can be considered that in students from the healthy group, the vegetative homeostasis was preserved with sustainable regulation and normal activity of PNS.

While the student from the studied group was infected with coronavirus disease, there was observed a severe disturbance of automatism of the heart, tachycardia, and sinus arrhythmia. Although the vegetative homeostasis was preserved, the dysregulation with a predominance of subcortical nerve center activation and moderate weakening of the PNC activity has been recorded (Figure 3).

The severity of clinical manifestations of the heart depends on the degree of heart muscle damage. According to Mikhaylovskaya [14] elevated levels of troponin, myoglobin, C-reactive protein, serum ferritin, and interleukin-6 in deceased patients were revealed. This suggests the high inflammatory activity of COVID-19 and predicts an increase in cardiac lesions due to myocardial inflammation. Most likely, the coronavirus also has an effect on the students' organism that reduces muscle performance, helps to overcome physical load with the pronounced tension of the sympathetic systems, and increases the manifestation of sympathetic reactions, which is evidenced by the changes in the heart rate indicators that we observed. The effect of COVID-19 on lung tissue is weakened by the blockade of the renin-angiotensin system. This has been proven by experiments on rats. Under the influence of COVID-19, a decrease in systemic pressure is observed, which leads to an increase in the activity of the renin-angiotensin system. This in turn, causes an increase in systolic blood pressure (SBP), leading to an increase in heart contractions frequency (HCF), tachysystole, and arrhythmia [15,16]. Disorders of the cardiovascular system were also observed in children, in the post-COVID period, the disease was also manifested in the form of Kawasaki syndrome. Most of them did not have serious respiratory problems, but doctors prescribed forced ventilation to improve heart function and blood circulation [17].

Based on this body of basic and applied HRV research, we wish to urgently propose using HRV monitoring as an element of a larger framework of truly personalized health. HRV screening, analysis, and feedback can be applied immediately to the present COVID-19 pandemic [18]. Cardiovascular implications of Sars-COV-2 infection have been widely documented and associated with poor prognosis, which can be worsened by underlying cardiovascular diseases [19]. Accumulating evidence indicates that COVID-19 patients are burdened by a higher risk of malignant ventricular arrhythmias, with a potential contributing role of repurposed antiviral therapies [20]. The studies of post-acute COVID-19 sequelae across the spectrum of care settings of acute infection are also lacking. Addressing this knowledge gap will inform post-acute COVID-19 care strategies [21].

SARS-CoV-2 can also affect the cardiac system directly. The virus has been shown to potentially cause myocarditis (inflammation of the heart muscle), arrhythmias, and other

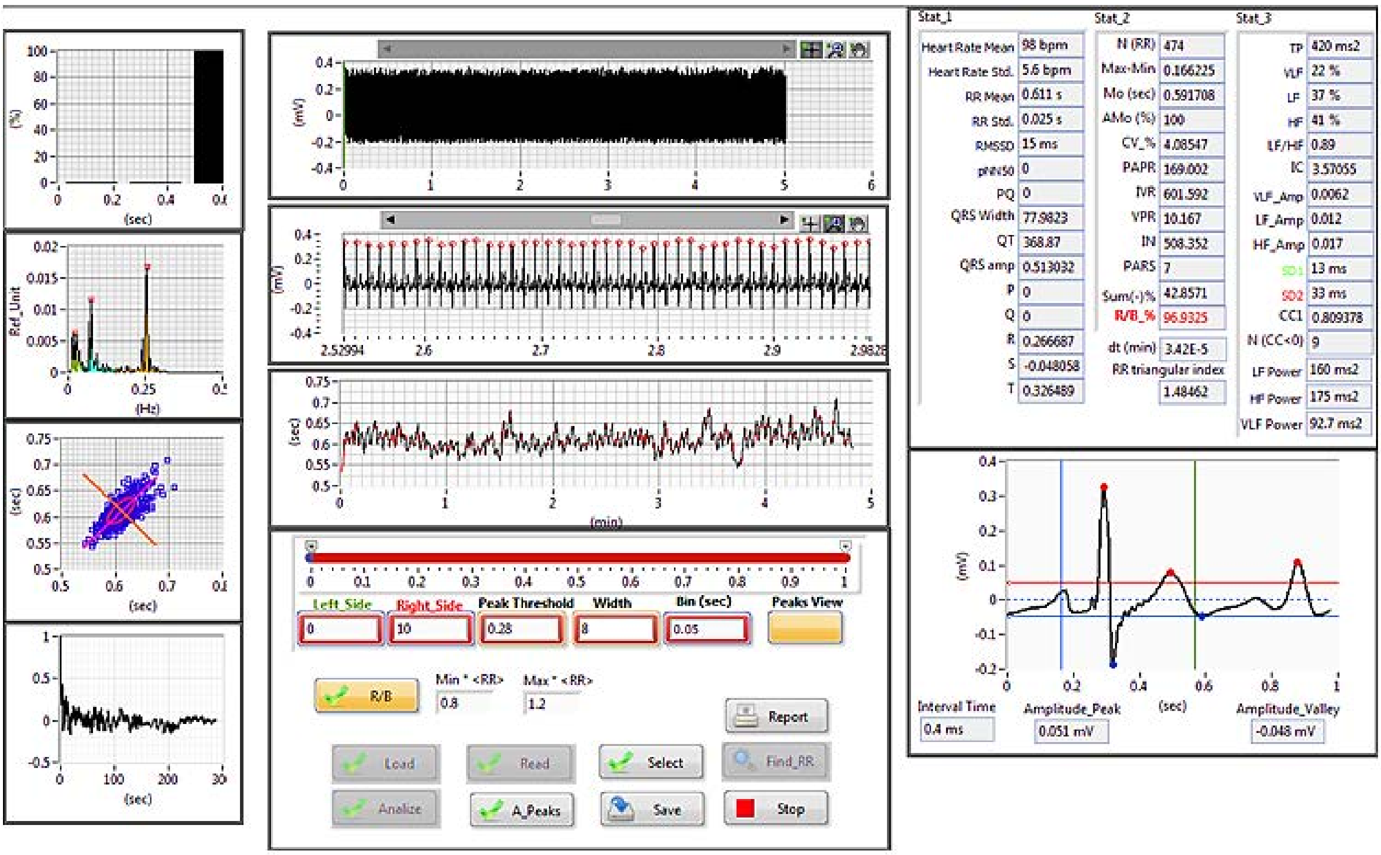

Figure 3. *Fragments of the original recordings of a cardiogram (a), scattergram (b), rhythmogram (c), histogram (d), and spectrogram (e) of the student from the studied group before (A) and after 5min bicycle load (B).*

cardiovascular complications, which can contribute to changes in HRV. Myocardial inflammation or damage could lead to altered electrical conduction in the heart, thereby reducing the variability in the intervals between heartbeats. In addition, COVID-19 can exacerbate pre-existing cardiovascular conditions, further impacting HRV [22].

SARS-CoV-2 infection has also been shown to significantly affect the autonomic nervous system, both during the acute phase of infection and in post-viral recovery (often referred to as "long COVID"). The virus can directly affect the CNS, particularly the brainstem, which is critical in regulating autonomic functions like heart rate. SARS-CoV-2 may interact with the autonomic centers in the brain, either directly through viral entry into neurons or indirectly through inflammation (cytokine storms and immune responses). This interaction may lead to an imbalance between the sympathetic and parasympathetic systems, resulting in altered HRV [23].

Limited understanding of the pathological mechanisms underlying post-COVID syndrome represents a critical challenge to effectively testing and treating this syndrome. Injury to the autonomic nervous system (ANS) has recently been suggested to be responsible for many of the aforementioned manifestations and may be key in the pathogenesis of post-COVID syndrome [24]. Therefore, our study reveals the HRV variability changed among students with COVID-19 and elucidated by various cardiac complications in post-infected period.

To summarize, the negative impact of COVID-19 on HRV is due to several factors. While SARS-CoV-2 can influence the cardiac system—especially through conditions like arrhythmias, the main reason for reduced HRV seems to be the virus's effect on the autonomic nervous system. This includes both direct and indirect influences on the CNS and increased systemic inflammation. In our study, we highlighted the significance of HRV as a non-invasive biomarker for assessing autonomic function. This can help guide potential interventions aimed at restoring balance in the autonomic nervous system, particularly for patients experiencing long COVID-19.

Moreover, we suggest that controlled breathing exercises (such as paced breathing, slow deep breathing, or diaphragmatic breathing) could be effective in promoting parasympathetic nervous system activity and help mitigate symptoms associated with autonomic dysfunction during and after the acute phase of the infection. Also, for the patients recovering from COVID-19 who exhibit low HRV (indicating autonomic imbalance or stress), we recommend a gradual introduction of physical activity. Moderate aerobic exercise, such as walking or cycling, has been shown to improve HRV by enhancing cardiovascular health and autonomic regulation. This intervention can be tailored to the individual's recovery status, starting with low-intensity exercises and progressing as tolerated.

Conclusion.

This study supports our understanding of heart rate variability changes and cardiac dysfunction among young people infected by COVID-19, which is crucial for diagnosing the post-infected complication of coronavirus. Elucidating the mechanisms of the impact of COVID-19 on the cardiovascular system will make it possible to provide timely and correct complex medical care to young and elderly patients.

Conflict of interest.

Authors declare about not having financial and personal interests.

Financial support.

The work was supported by the Science Committee of MESCS RA, in the frames of research project No 21T-1F316 and ANSEF Foundation based in New York, USA, research project No 24AN:NS-hubio-3092.

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АННОТАЦИЯ

Оценка изменений показателей вариабельности сердечного ритма у студентов после карантина COVID-19: когортное исследование

Введение: Целью данного исследования было изучение показателей вариабельности сердечного ритма у студентов, переболевших COVID-19, после выполнения физической нагрузки. Целью было выявление любых потенциальных кардиологических осложнений и нарушений регуляции автономной нервной системы.

Материал и методы: Вариабельность сердечного ритма и его изменения анализировались сразу после 5-минутной физической нагрузки, выполненной с использованием велоэргометра Proteus pes 3320. Регистрация и анализ ЭКГ осуществлялись на персональном компьютере с помощью специальных программ <<Cardio reg>> и <<Cardio prog>>.

Результаты: Анализ полученных данных показал, что активность показателей регуляции сердечного ритма у студентов, инфицированных коронавирусом, была значительно повышена по сравнению со здоровыми лицами ($p<0.05$). После физической нагрузки у студентов инфицированной группы увеличились показатели индекса напряжения, VBI, VRI и LF/HF, характеризующие симпатический тонус регуляции ВСР, понизился коэффициент вариации кардиоинтервалов. Последнее сопровождалось тахисистолией и аритмией.

Заключение: Результаты этого исследования демонстрируют, что временные физические нагрузки способствовали переходу показателей сердечно-сосудистой системы из состояния адаптивного напряжения в состояние напряжения, что, вероятно, связано с негативным воздействием COVID-19 на функции как сердечно-сосудистой, так и нервной системы. Таким образом, исследование помогает лучше понять изменения вариабельности сердечного ритма в контексте постковидной дисфункции сердечно-сосудистой системы у молодежи.