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INFLUENCE OF THE COURSE OF ACUTE COVID-19 INFECTION ON THE COURSE OF POST-COVID SYNDROME

Dobrynina M. A.[a],

Zurochka V. A. [a],

Zurochka A. V. [a]

[a] Federal Budgetary Institution of Science «Federal Scientific Research Institute of Viral Infections «Virome» Federal Service for Surveillance on Costumer Rights Protection and Human Wellbeing, Yekaterinburg.

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ВЛИЯНИЕ ТЕЧЕНИЯ ОСТРОЙ ИНФЕКЦИИ COVID-19 НА ТЕЧЕНИЕ ПОСТКОВИДНОГО СИНДРОМА

Добрынина М. А. [1],

Зурочка В. А. [1],

Зурочка А. В. [1]

[1] Федеральное бюджетное учреждение науки «Федеральный научно-исследовательский институт вирусных инфекций «Вирром» Роспотребнадзора, г. Екатеринбург.

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Abstract

The COVID-19 coronavirus pandemic caused by the SARS-CoV-2 virus has resulted in global morbidity and high mortality worldwide. According to case histories, for a long time (from six months to 2-3 years) after acute COVID-19 infection, patients experience severe fatigue, increased fatigue, an increase in the incidence of acute respiratory viral infections per year, an increase in the recurrence of skin diseases, allergies, exacerbation of pulmonary pathology, urinary tract diseases, an increase in the recurrence of chronic infectious diseases such as herpesvirus and papillomavirus infections, and an aggravation of chronic cardiovascular and other somatic diseases of various organs and systems. Patients were examined at least six months after recovery from acute COVID-19. Such persistent post-infectious consequences are known as post-COVID syndrome. When assessing post-COVID syndrome, it is necessary to identify the main clinical syndromes of multiorgan pathology characteristic of post-COVID patients. Endocrine and cardiac manifestations of post-COVID syndrome can be a consequence of direct damage by the virus, immunological and inflammatory damage, as well as iatrogenic complications.

Objective of the study: to assess the impact of the severity of acute COVID-19 on the course of post-COVID syndrome.

Research objectives:

1. To analyze the severity of clinical manifestations of the symptom complex of cardiovascular damage in post-COVID patients depending on the degree of lung damage in the acute period of COVID-19.

2. To analyze the severity of clinical manifestations of endocrine system pathology, including newly diagnosed, in post-COVID patients depending on the degree of lung damage in the acute period of COVID-19. Since no statistically significant differences by gender and age were found, all patients were divided into groups by the degree of lung damage in the acute period of COVID-19 according to clinical guidelines for the diagnosis and treatment of a new coronavirus infection:

This study showed that the clinical picture of post-COVID syndrome is characterized by a pronounced diversity of the formation of multiple organ pathology, both newly diagnosed and manifested in an increase in the frequency of exacerbations of chronic diseases.

Keywords: immune system, computed tomography, viral pneumonia, SARS-CoV-2 infection, post-COVID syndrome.

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Резюме

Пандемия коронавирусной инфекции COVID-19, вызванная вирусом SARS-CoV-2, привела к глобальной заболеваемости и высокой смертности во всем мире. По данным историй болезни, длительное время (от полугода до 2-3 лет) после перенесенной острой инфекции COVID-19 у пациентов отмечается выраженная усталость, повышенная утомляемость, учащение случаев заболеваний ОРВИ за год, учащение рецидивов кожных заболеваний, аллергопатологий, обострение легочной патологии, заболеваний мочевыводящих путей, учащение рецидивов хронических инфекционных заболеваний, таких как герпесвирусная и папилломавирусная инфекции, утяжеление течения хронических сердечно-сосудистых и других соматических заболеваний разных органов и систем. Обследование пациентов проводилось не менее чем через шесть месяцев после выздоровления от острого COVID-19. Подобные стойкие постинфекционные последствия известны как постковидный синдром. Оценивая постковидный синдром, необходимо раскрыть основные клинические синдромы полиорганной патологии, характерной для постковидных пациентов. Эндокринные и кардиальные проявления постковидного синдрома могут быть следствием прямого повреждения вирусом, иммунологического и воспалительного повреждения, а также ятрогенных осложнений

Цель исследования: оценить влияние тяжести течения острого COVID-19 на течение постковидного синдрома.

Задачи исследования:

1. Проанализировать выраженность клинических проявлений симптомокомлекса поражения сердечно-сосудистой системы у постковидных пациентов в зависимости от степени поражения легких в острый период COVID-19.

2. Проанализировать выраженность клинических проявлений патологии эндокринной системы, в том числе впервые выявленной, у постковидных пациентов в зависимости от степени поражения легких в острый период COVID-19.

Так как статистически значимых различий по полу и возрасту выявлено не было, то все пациенты были разделены на группы по степени поражения легких в острый период COVID-19 согласно клиническим рекомендациям по диагностике и лечению новой коронавирусной инфекции:

Данное исследование показало, что клиническая картина постковидного синдрома характеризуется выраженным разнообразием формирования полиорганной патологии, как впервые выявленной, так и проявляющейся в учащении обострений хронических заболеваний.

Выводы

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1. Согласно полученным данным, достоверные различия получены между группами КТ0 и КТ1-2, а также КТ0 и КТ3-4: частота обострений заболеваний сердечно-сосудистой системы в постковидном периоде достоверно выше в группах с поражением легких в острый период COVID-19 по сравнению с группой пациентов без поражения легких. Эти данные говорят о том, что поражения сердечно-сосудистой системы напрямую связаны с тяжестью течения COVID-19, вирусной нагрузкой и выявлялись наиболее часто (68 %) у постковидных пациентов, перенесших тяжелую коронавирусную инфекцию.

2. Согласно полученным данным, частота нарушений обмена глюкозы, в том числе. и впервые выявленных, достоверно возрастала в постковидный период у пациентов с поражением легких в острый период инфекции, тогда как по заболеваниям щитовидной железы, за исключение АИТ, достоверных различий не обнаружено. Возможно, эти нарушения также связаны, с одной стороны, с применением кортикостероидной терапии в острый период коронавирусной инфекции, а с другой стороны, с нарушением работы регуляторных механизмов эндокринной и иммунной систем под воздействием вируса SARS-CoV-2, что еще раз подтверждает наши предположения о формировании полиорганной патологии у постковидных пациентов.

Ключевые слова: иммунная система, компьютерная томография, вирусная пневмония, инфекция SARS-CoV-2, постковидный синдром.

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1 Introduction

The COVID-19 coronavirus pandemic caused by the SARS-CoV-2 virus has led to mass morbidity and high mortality on the planet. According to a survey of those who have recovered from acute COVID-19, for a long time (from six months to 2-3 years), patients experience significant asthenia, decreased performance, an increase in the incidence of acute respiratory viral infections per year, an increase in the frequency and severity of relapses of diseases of various organs and systems: skin, allergic, cardiovascular, endocrine, chronic injection and others. The examination of patients was carried out at least six months after recovery from acute COVID-19. Such persistent post-infectious consequences are known as post-COVID syndrome [14]. When assessing post-COVID syndrome, it is necessary to reveal the main clinical manifestations of multiorgan pathology characteristic of post-COVID patients according to the literature [1]. For example, out of 410 participants in a Swiss study, 7-9 months after diagnosis with COVID-19, 39.0% of patients reported long-term fatigue (20.7%), loss of taste or smell (16.8%), shortness of breath (11.7%), and headache (10.0%), including among young, previously healthy individuals [13]. In China, 1,733 patients were examined 6 months after acute COVID-19; prolonged tachycardia was recorded in 9% and chest pain in 5% of patients [9]. During autopsy of 39 people who died from COVID-19, the SARS-CoV-2 virus was detected in the heart in 62.5% of cases [1, 10]. The inflammatory response it induced often leads to the death of cardiomyocytes and fibro-fatty replacement of desmosomal proteins important for intercellular adhesion [17]. In patients recovered from COVID-19, the cardiac metabolic demand may be persistently increased, which has been observed in the long term [20]. This may be due to decreased cardiac reserve, corticosteroid use, and dysregulation of the renin-angiotensin-aldosterone system. Fibrosis, myocardial scarring, and cardiomyopathy that occur after a viral infection often lead to cardiac arrhythmia via the re-entry mechanism [1, 7, 18]. COVID-19 can also exacerbate cardiac arrhythmia due to increased catecholamine influence as a result of the cytokines interleukin-6, interleukin-1, and TNF-α, which can prolong the ventricular action potential by modulating the expression of cardiomyocyte ion channels [11]. Autonomic dysfunction with adrenergic influences predominating after viral diseases, including COVID-19, leads to postural orthostatic tachycardia syndrome and non-physiological sinus tachycardia [5]. Diabetic ketoacidosis was observed in patients who did not previously have diabetes mellitus, weeks or months after the disappearance of COVID-19 symptoms [18]. Unfortunately, there is still insufficient information on how long after COVID-19 the severity of pre-existing diabetes mellitus worsens or a hereditary predisposition to diabetic ketoacidosis manifests itself, and this issue is addressed to the international CoviDiab registry [15]. Ruggeri R.M., et al. (2021) write about subacute thyroiditis with clinical manifestations of thyrotoxicosis weeks after the disappearance of respiratory symptoms [16]. Endocrine manifestations of post-COVID syndrome may be due to direct damage by the virus, immunological and inflammatory damage, and iatrogenic complications. Expression of ACE2 and transmembrane serine protease in

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pancreatic β-cells has been reported, but researchers believed that the primary insulin deficiency in COVID-19 is likely mediated by inflammation or response to infectious stress along with peripheral insulin resistance [8]. Autopsy studies of COVID-19 patients confirmed the possibility of SARS-CoV-2 infection and replication in human pancreatic β-cells, leading to their death or transdifferentiation, decreased insulin production and release [12, 19]. Thus, according to the conducted theoretical research, there are indications in the literature of various clinical pathological manifestations of post-covid syndrome, however, there is no systematization of these studies, there is insufficient data on the pathogenesis of the formation of clinical manifestations of post-covid syndrome, there is no data on the relationship between the course of post-covid syndrome and the severity of acute coronavirus infection in the anamnesis. All this served as the basis for this study.

Objective of the study: to assess the impact of the severity of acute COVID-19 on the course of post-COVID syndrome.

Research objectives:

1. To analyze the severity of clinical manifestations of the symptom complex of cardiovascular damage in post-COVID patients depending on the degree of lung damage in the acute period of COVID-19.

2. To analyze the severity of clinical manifestations of endocrine system pathology, including newly diagnosed, in post-COVID patients depending on the degree of lung damage in the acute period of COVID-19. Since no statistically significant differences by gender and age were found, all patients were divided into groups by the degree of lung damage in the acute period of COVID-19 according to clinical guidelines for the diagnosis and treatment of a new coronavirus infection:

2 Materials and methods of research

A total of 131 patients who had recovered from SARS-CoV-2 infection were examined. Of these, 48 were men aged 20 to 76 years (mean age 55.3 years) and 83 were women aged 21 to 79 years (mean age 53.4 years). The inclusion criteria in the study groups were: confirmed diagnosis of SARS-CoV-2 infection by polymerase chain reaction (PCR), the presence of IgA, M to the SARS-CoV-2 virus in the acute and post-acute periods of infection and IgG to the SARS-CoV-2 virus during the recovery period, computed tomography data of the lungs on the presence or absence of changes of the "ground glass" type. This study was conducted at least 6-12 months after the infection caused by SARS-CoV-2. All patients were preliminarily examined by a general practitioner and an immunologist-allergist in order to identify concomitant diseases, as well as by doctors of other specialties before COVID-19 to establish concomitant diagnoses. The groups were randomized by gender, age, concomitant diseases according to the $\chi 2$ criterion. All studies were approved by the Independent Local Ethics Committee at the State Autonomous Healthcare Institution of the Republic of Chelyabinsk "City Clinical Hospital No. 1" of Chelyabinsk (protocol No. 8 dated 04/11/2022), on the basis of which these studies were

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conducted, and by the Independent Local Ethics Committee at the Federal Research Institute of Virology and Infection "Virom" of Rospotrebnadzor of Yekaterinburg, protocol No. 1 dated 03/22/2024, on the basis of which these studies were conducted.

Clinical research methods:

- Identification of persons with post-COVID syndrome after examination by doctors: therapist, allergist-immunologist.
- Filling out the immunological examination card.
- Physical, laboratory and instrumental examinations for diagnosis.

Statistical research methods

Based on the study results, a database was created in Excel (MS Office 2007). Data processing and analysis were performed using R 3.1.1 12 (RFoundation for Statistical Computing, Vienna, Austria) and Microsoft Excel version 14.0. Student's t-tests were used for parametric data; differences were considered significant at $p<0.05$.

Equipment:

The following equipment was used: computers with software packages required for mathematical and statistical analysis of the results.

3 **Results of the study**

No statistically significant differences by gender and age were found, all patients were divided into groups by the degree of lung damage in the acute period of COVID-19, which is the determining criterion for assessing the severity of acute COVID-19 according to clinical guidelines for the diagnosis and treatment of a new coronavirus infection [2, 6]:

Group 1 - CT0 (without lung damage of the "ground glass" type according to CT data)

Group 2 - CT 1-2 (less than 50% lung damage of the "ground glass" type according to CT data)

Group 3 - CT 3-4 (more than 50% lung damage of the "ground glass" type according to CT data)

According to the questionnaire, the percentage of patients who had complaints of aggravation of symptoms of comorbid pathology already existing before the pandemic (increased relapses, worsening of the severity of the course), or of newly diagnosed somatic diseases was determined after COVID-19. This study presents data on cardiovascular and endocrine pathology.

According to these data, presented in Table 1, reliable differences were obtained between groups KT0 and KT1-2, as well as KT0 and KT3-4: the frequency of exacerbations of cardiovascular diseases in the post-COVID period is significantly higher in groups with lung damage in the acute period of COVID-19 compared to the group of patients without lung damage. These data indicate that cardiovascular damage is directly related to the severity of COVID-19, viral load and was detected most often (68%) in post-COVID patients who had a severe coronavirus infection..

10.46235/1028-7221-17286-IOT

According to the data presented in Table 2, the frequency of glucose metabolism disorders, including those newly identified, increased significantly in the post-COVID period in patients with lung damage during the acute period of infection, while no significant differences were found in thyroid diseases, with the exception of autoimmune thyroiditis.

Perhaps these disorders are also associated, on the one hand, with the use of corticosteroid therapy during the acute period of coronavirus infection, and on the other hand, with disruption of the regulatory mechanisms of the endocrine and immune systems under the influence of the SARS-CoV-2 virus, which once again confirms our assumptions about the formation of multiple organ pathology in post-COVID patients.

The results and their discussion

According to ICD-10 and ICD-11 [3, 4], the above-mentioned somatic diseases have, among other things, pathogenetically significant mechanisms of immune system disorders, as does COVID-19, the severe forms of which are also based on damage to the immune system. In this regard, the immune status of patients included in this clinical study was assessed.

Thus, the clinical picture of post-COVID syndrome is characterized by a pronounced diversity of the formation of multiple organ pathology, both newly identified and manifested in the exacerbation of chronic diseases.

4 **Conclusions**

1. According to the data obtained, reliable differences were obtained between groups KT0 and KT1-2, as well as KT0 and KT3-4: the frequency of exacerbations of cardiovascular diseases in the post-COVID period is significantly higher in groups with lung damage in the acute period of COVID-19 compared to the group of patients without lung damage. These data indicate that cardiovascular disorders are directly related to the severity of COVID-19, viral load, and were detected most frequently (68%) in post-COVID patients who had a severe coronavirus infection.

2. According to the data obtained, the frequency of glucose metabolism disorders, including those detected for the first time, significantly increased in the post-COVID period in patients with lung damage in the acute period of infection, while no significant differences were found in thyroid diseases, with the exception of AIT. Perhaps these disorders are also associated, on the one hand, with the use of corticosteroid therapy in the acute period of coronavirus infection, and on the other hand, with disruption of the regulatory mechanisms of the endocrine and immune systems under the influence of the SARS-CoV-2 virus, which once again confirms our assumptions about the formation of multiple organ pathology in post-COVID patients.

(The work is completed on the topic of State assignments FBIS Federal Scientific Research Institute of Viral Infections "VIROM" Federal Service for Supervision of Consumer Rights Protection and Human Consumption "Study of the mechanisms of chronic viral infection formation in patients with post-COVID syndrome and impaired immune system functions. Development of pathogenetic approaches to effective prevention and immunocorrection of identified disorders in

10.46235/1028-7221-17286-IOT
172 *patients with "post-COVID syndrome" No state registration 124031800093–5.)*

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ТАБЛИЦЫ

Table 1. Severity of clinical manifestations of a symptom complex of damage to the cardiovascular system in kidney-shaped patients, depending on the degree of lung damage in the acute period of COVID-19.

Diseases with increased recurrence or first identified after clinical recovery from acute COVID-19 infection/ degree of lung damage according to CT	**Total number of examined patients (n=131)**		**Group 1 CT0 (n=38)**		**Group 2 WHO-2 (n=68)**		**Group 3 CT3-4 (n=25)**	
	bs	**%**	**bs**	**%**	**bs**		**bs**	
Diseases of the cardiovascular system (hypertension, coronary heart disease, acute myocardial infarction, acute cerebrovascular accident)	9	7,4		13,2	7	9,7 P1-2 <0,05	7	8,0 P1-3<0,05 P2-3<0,05

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10.46235/1028-7221-17286-IOT

Table 2. Severity of clinical manifestations of endocrine system pathology, including those newly identified, in postmenopausal patients, depending on the degree of lung damage in the acute period of COVID-19.

Diseases with increased recurrence or first identified after clinical recovery from acute COVID-19 infection/ degree of lung damage according to CT	**Total number of examined patients (n=131)**		**Group 1 CT0 (n=38)**		**Group 2 WHO-2 (n=68)**		**Group 3 CT3-4 (n=25)**	
	abs	**%**	**abs**	**%**	**abs**		**abs**	
Glucose metabolism disorder	7	5,9		5,3	30	4,1 P1-2 <0,05	5	0,0 P1-3<0,05
Diseases of the thyroid gland, with the exception of autoimmune thyroiditis	5	6,7		18,4	19	7,9		6,0

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10.46235/1028-7221-17286-IOT

ТИТУЛЬНЫЙ ЛИСТ_МЕТАДАННЫЕ

Блок 1. Информация об авторе ответственном за переписку

Добрынина Мария Александровна, к.м.н., научный сотрудник лаборатории иммунопатофизиологии ФГБУН «Институт иммунологии и физиологии» Уральского отделения Российской академии наук**,** Екатеринбург; старший научный сотрудник лаборатории трансмиссивных вирусных инфекций ФБУН ФНИИВИ «ВИРОМ» Федеральной службы по надзору в сфере защиты прав потребителей и благополучия человека, Екатеринбург; доцент кафедры терапии Медико-биологического университета инноваций и непрерывного образования ФГБУ «Государственный научный центр Российской Федерации – Федеральный медицинский биофизический центр им. А.И. Бурназяна» Федеральногомедико-биологическогоагентства,Москва, Россия

e-mail: mzurochka@mail.ru

Dobrynina Maria Aleksandrovna, PhD, MD, Researcher, laboratory ofimmunopathophysiology, Institute of Immunology and Physiology of the Ural Branch of the Russian Academy of Sciences, Ekaterinburg; Senior Researcher, Laboratory of Transmissible Viral Diseases, FBISFederal Scientific Research Institute of Viral Infections "VIROM" Federal Service for Supervision of Consumer Rights Protection and Human Consumption, Yekaterinburg;assistant professor of the Department of Therapy of the University of Innovation and Continuing Education of the State Research Center –Burnazyan Federal Medical Biophysical Center of Federal Medical Biological Agency, Moscow, Russia

e-mail: mzurochka@mail.ru

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Блок 2. Информация об авторах

Зурочка Владимир Александрович, д.м.н., старший научный сотрудник лаборатории иммунопатофизиологииФГБУН «Институт иммунологии и физиологии» Екатеринбург;старший научный сотрудник лабораторииииммунобиотехнологии Российско-Китайского Центра Южно-Уральского Государственного Университета (НИУ),v_zurochka@mail.ru

Zurochka Vladimir Aleksandrovich, D.Sc. MD, senior researcher,laboratory ofimmunopathophysiology, Institute of Immunology and Physiology, Ural Branch of the Russian Academy of Sciences,Ekaterinburg; senior researcher, laboratory of immunobiotechnology, Russian-Chinese Center, South Ural State University (NRU),Chelyabinsk, Russia. v_zurochka@mail.ru

Зурочка Александр Владимирович, ЗДН РФ, д.м.н., профессор, ведущий научный сотрудник лабораторииимунопатофизиологииФГБУН «Институт иммунологии и физиологии» Екатеринбург;заведующий лабораторией иммунобиотехнологии Российско-Китайского Центра Южно-Уральского Государственного Университета (НИУ), Челябинск, Россия av_zurochka@mail.ru

Zurochka Aleksandr Vladimirovich, honored worker of science of the Russian Federation, D.Sc. MD, professor, leading researcher, laboratory of immunopathophysiology, Institute of Immunology and Physiology of the Ural Branch of the Russian Academy of Sciences, Ekaterinburg; head of laboratory of immunobiotechnology of the Russian-Chinese Center of South Ural State University (NRU),Chelyabinsk, Russia. av_zurochka@mail.ru

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Блок 3. Метаданные статьи

INFLUENCE OF THE COURSE OF ACUTE COVID-19 INFECTION ON THE COURSE OF POST-COVID SYNDROME

ВЛИЯНИЕ ТЕЧЕНИЯ ОСТРОЙ ИНФЕКЦИИ COVID-19 НА ТЕЧЕНИЕ ПОСТКОВИДНОГО СИНДРОМА

Сокращенное название статьи для верхнего колонтитула:

Keywords: immune system, computed tomography, viral pneumonia, SARS-CoV-2 infection, post-COVID syndrome.
Ключевые слова: иммунная система, компьютерная томография, вирусная пневмония, инфекция SARS-CoV-2, постковидный синдром.

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СПИСОК ЛИТЕРАТУРЫ

Порядковый номер ссылки	Авторы, название публикации и источника, где она опубликована, выходные данные	ФИО, название публикации и источника на английском	Полный интернет адрес или DOI
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