BY 4.0

DOI: 10.20514/2226-6704-2024-14-4-298-311
УДК 616.1/.9-002.2-06:616.9:578.834.1-036
EDN: YEAFRC

А.А. Карасева, А.Д. Афанасьева, Е.В. Гарбузова, А.А. Кузнецов, Ю.Ю. Палехина, Ю.В. Щепина, В.С. Шрамко, И.И. Логвиненко, Ю.И. Рагино

Научно-исследовательский институт терапии и профилактической медицины — филиал Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, Россия

СТЕПЕНИ ТЯЖЕСТИ ПОСТКОВИДНОГО СИНДРОМА У РЕКОНВАЛЕСЦЕНТОВ COVID-19 И ИХ АССОЦИАЦИИ С ОСНОВНЫМИ ФАКТОРАМИ РИСКА ХРОНИЧЕСКИХ НЕИНФЕКЦИОННЫХ ЗАБОЛЕВАНИЙ

A.A. Karaseva, A.D. Afanaseva, E.V. Garbuzova, A.A. Kuznetsov, Yu.Y. Palekhina, Yu.V. Shchepina, V.S. Shramko, I.I. Logvinenko, Yu.I. Ragino

Research Institute of Internal and Preventive Medicine — Branch of the Institute of Cytology and Genetics, Siberian Branch of Russian Academy of Sciences" (IIPM — Branch of IC&G SB RAS), Novosibirsk, Russian Federation

Severity of Postcovid Syndrome in Convalescent Covid-19 and Their Association with the Main Risk Factors for Chronic Non-Communicable Diseases

Резюме

Цель исследования: оценить влияние основных факторов риска (ФР) хронических неинфекционных заболеваний (ХНИЗ) на степень тяжести постковидного синдрома (ПКС) у реконвалесцентов COVID-19. **Материалы и методы:** в обсервационное одномоментное исследование было включено 270 человек (из них 48,1% мужчин, средний возраст 53,2±13,2 года), являющихся реконвалесцентами COVID-19. Пациенты были разделены на 3 группы в соответствии со степенью тяжести ПКС. В группу 1 вошли 79 человек с отсутствием ПКС, в группу 2 — 97 пациентов с легкой степенью тяжести ПКС, в группу 3 — 94 пациента со средней степенью тяжести ПКС. Всем пациентам было проведено стандартное общеклиническое и лабораторное обследование, антропометрия, эхокардиография (ЭхоКГ), оценивались данные анамнеза. Лица без ПКС были моложе, чем пациенты, страдающие ПКС (p=0,003). У пациентов, имеющих ПКС, в сравнении с лицами, у которых ПКС не развился, статистически значимо был выше уровень глюкозы и IgG в сыворотке крови, значения систолического артериального давления (САД) и диастолического артериального давления (ДАД), показатели индекса массы тела (ИМТ), окружности талии (ОТ) и индексов- триглицеридглюкозного индекса (ТГИ)/ОТ, ТГИ /ИМТ, индекса накопления липидов (LAP), индекса висцерального ожирения (VAI), количество пациентов, страдающих ожирением, и лиц, имеющих диастолическую дисфункцию левого желудочка (ДД ЛЖ). Пациенты со средней степенью тяжести ПКС чаще имели сердечно-сосудистые заболевания (ССЗ) до развития новой коронавирусной инфекции (НКИ). **Результаты:** Показатели объема форсированного выдоха за 1 первую секунду ($ОФВ_1$), форсированной жизненной емкости легких (ФЖЭЛ) были ниже при легкой и средней степени тяжести ПКС, по сравнению с лицами без него. Обнаружена прямая связь между наличием ПКС и уровнем глюкозы (r =3,138, p=0,000), ДД ЛЖ (r =2,876, p=0,008) в общей группе. У женщин данная ассоциация была выявлена только с наличием ДД ЛЖ (r=4,457, p=0,008), а у мужчин — с уровнем глюкозы (r =4,343, p=0,000), ОТ (r =1,068, p=0,060) и наличием ДД ЛЖ (r =3,377, p=0,033). Шанс наличия ПКС средней степени тяжести у мужчин и женщин был ассоциирован с уровнем глюкозы (r =1,537, p=0,001), VAI (r =1,256, p=0,005), САД (r =0,977, p=0,027), ССЗ до COVID-19 (r =0,465, p=0,036). А в группе мужчин данная ассоциация сохранялась только с уровнем глюкозы (r =2,357, p=0,004), индексом VAI (r =1,430, p=0,020) и наличием предшествующих ССЗ (r =0,160, p=0,014). **Заключение:** наличие ПКС у реконвалесцентов COVID-19 независимо от других факторов связано с уровнем глюкозы и наличием ДД ЛЖ. ПКС средней степени тяжести ассоциирован с повышением уровня глюкозы, САД, индекса VAI и наличием ССЗ до заболевания НКИ, при этом у мужчин ПКС средней степени тяжести в большей степени ассоциирован с кардиометаболическими факторами риска (ФР).

Ключевые слова: *COVID-19, постковидный синдром, степень тяжести постковидного синдрома, реконвалесценты COVID-19, новая коронавирусная инфекция, ожирение*

Конфликт интересов
Авторы заявляют, что данная работа, её тема, предмет и содержание не затрагивают конкурирующих интересов

Источники финансирования
Исследование выполнено в рамках Бюджетной темы No 122031700115-7, при поддержке стипендии Президента РФ NoСП-2974.2022.4 и гранта правительства Новосибирской области, заявка № 39423 (2024 год)

Соответствие принципам этики
Все пациенты дали свое информированное согласие на участие в исследовании. Исследование одобрено Этическим комитетом НИИТПМ — филиал ИЦиГ СО РАН, г. Новосибирска (Протокол № 71 от 10.11.2020 г.)

Статья получена 28.02.2024 г.
Одобрена рецензентом 20.06.2024 г.
Принята к публикации 15.07.2024 г.

Для цитирования: Карасева А.А., Худякова А.Д., Гарбузова Е.В. и др. СТЕПЕНИ ТЯЖЕСТИ ПОСТКОВИДНОГО СИНДРОМА У РЕКОНВАЛЕСЦЕНТОВ COVID-19 И ИХ АССОЦИАЦИИ С ОСНОВНЫМИ ФАКТОРАМИ РИСКА ХРОНИЧЕСКИХ НЕИНФЕКЦИОННЫХ ЗАБОЛЕВАНИЙ. Архивъ внутренней медицины. 2024; 14(4): 298-311. DOI: 10.20514/2226-6704-2024-14-4-298-311. EDN: YEAFRC

Abstract
The purpose of the study is to assess the impact of the main risk factors (RF) of chronic non-communicable diseases on the severity of the post-COVID-19 syndrome (PCS) in COVID-19 convalescents. **Materials and methods:** 270 persons (48.1% of them men, mean age 53.2±13.2 years) were included in the one-time observational study and are COVID-19 convalescents. The patients were divided into three groups according to the severity of the PCS. Group 1 included 79 people with no PCS, group 2 included 97 patients with light PCS, group 3 included 94 patients with moderate PCS. All patients were given standard general clinical and laboratory examination, anthropometry, echocardiography, and anamnesis data were evaluated. Persons without PCS were younger than patients with PCS (p=0,003). In patients with PCS compared to persons who did not develop PCS, statistically significantly higher levels of glucose and IgG in the blood serum, systolic blood pressure and diastolic blood pressure, body mass index (BMI) waist circumference (WC) and indexes: triglyceride-glucose index (TyG /WC), TyG /BMI, lipid accumulation product (LAP), visceral adiposity index (VAI), number of obese patients and persons with diastolic left ventricular dysfunction. Patients with moderate PCS were more likely to have cardiovascular disease before developing a new coronavirus infection. **Results:** The forced expiratory volume in 1 s (FEV1), forced vital lung capacity (FVC) scores were lower for mild to moderate PCS compared to persons without PCS. There is a direct relationship between the presence of PCS and glucose level (r =3,138, p=0,000), diastolic left ventricular dysfunction (r =2,876, p=0,008) in the general group. In women, this association was detected only with the presence of diastolic left ventricular dysfunction (r=4,457, p=0,008). In men with glucose (r =4,343, p=0,000), WC (r =1,068, p=0,060) и diastolic left ventricular dysfunction (r =3,377, p=0,033). The chance of having a moderate PCS in men and women was associated with glucose level (r =1.537, p=0.001), VAI (r =1.256, p=0.005), САД (r =0.977, p=0.027), CVD before COVID-19 (r=0.460.036). In the group of men this association was preserved only with the level of glucose (r =2,357, p=0,004), the index VAI (r =1,430, p=0,020) and the presence of preceding CVD (r =0,160, p=0,014). **Conclusion:** the presence of PCS in convalescents COVID-19 independently of other factors is due to the level of glucose and the presence of diastolic left ventricular dysfunction. PCS of moderate severity is associated with an increase in glucose, systolic blood pressure, VAI index, and the presence of CVD prior to COVID disease, with PCS of moderate severity more associated with cardio-metabolic risk factors in men.

Key words: *COVID-19, post-COVID-19 syndrome, severity of the post-COVID-19 syndrome, convalescents COVID-19, new coronavirus infection, obesity*

Conflict of interests
The authors declare no conflict of interests

Sources of funding
The study was carried out within the framework of Budget Topic No. 122031700115-7, with the support of the scholarship of the President of the Russian Federation NoSP-2974.2022.4 and a grant from the government of the Novosibirsk region, application No. 39423 (2024)

Conformity with the principles of ethics
All patients gave their informed consent to participate in the study. The study was approved by the Ethics Committee of Research Institute of Therapy and Preventive Medicine — branch of the Federal State Budgetary Scientific Institution «Federal Research Center Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Sciences», Novosibirsk (protocol No. 71 of November 10, 2020)

Article received on 28.02.2024
Reviewer approved 20.06.2024
Accepted for publication on 15.07.2024

For citation: Karaseva A.A., Afanaseva A.D., Garbuzova E.V. et al. Severity of Postcovid Syndrome in Convalescent Covid-19 and Their Association with the Main Risk Factors for Chronic Non-Communicable Diseases. The Russian Archives of Internal Medicine. 2024; 14(4): 298-311. DOI: 10.20514/2226-6704-2024-14-4-298-311. EDN: YEAFRC

AH — arterial hypertension, WHO — World Health Organisation, DBP — diastolic blood pressure, LV DD — left ventricle diastolic dysfunction, IHD — ischaemic heart disease, BMI —body mass index, IRI — insulin resistance index, NCVI — novel coronavirus infection, TC — thigh circumference, WC — waist circumference, FEV_1 — forced expiratory volume per 1 second, PCS — post-COVID syndrome, PCR — polymerase chain reaction, RNA — ribonucleic acid, SBP — systolic blood pressure, GFR — glomerular filtration rate, CVD — cardiovascular disease, TGI — triglyceride glucose index, TG — triglycerides, FVC — forced vital capacity, RF — risk factors, CNCD — chronic non-communicable diseases, HDL cholesterol — high density lipoprotein cholesterol, echoCG — echocardiography, AIP — Atherogenic Index of Plasma, COVID-19 — Coronavirus Disease 2019, HADS — Hospital Anxiety and Depression Scale, LAP — lipid accumulation product, MFI-20 — Multidimensional Fatigue Inventory, SARS-CoV-2 — Severe Acute Respiratory Syndrome-related Coronavirus 2, VAI — visceral adiposity index

Introduction

Currently, the medical community has to deal with the consequences of the novel coronavirus infection (NCVI) more often. The main focus is on the condition of patients with persisting symptoms, which last for a long period of time and significantly worsen the quality of patients' life, reducing their capacity to work. This condition is called post-COVID syndrome (PCS). According to the World Health Organisation (WHO), PCS affects patients with a history of suspected or confirmed severe acute respiratory syndrome-related coronavirus 2 (SARS-CoV-2), usually 3 months after the onset, with development of symptoms, which last for at least two months and cannot be attributed to any other alternative diagnosis [1]. The relevance of the studies of PCS is due to significantly growing numbers of patients with this condition all over the world. At the moment, it is quite challenging to accurately determine the incidence of PCS because of the lack of standardised diagnostic criteria. The global incidence of PCS varies from 4.7 % to 80 % [2]. There are no official statistical data on the incidence of PCS in Russia. A wide array of manifestations of PCS in post-COVID patients [3, 4] necessitates more thorough and comprehensive studies of this problem. Despite the growing number of studies in this area [5, 6], there are still uncertainties about the factors affecting the severity of PCS (age, gender-related differences, comorbidities, etc.); also, of interest is finding causes of newly developed diseases or aggravation of existing symptoms during this period, identification of groups of a high risk of more severe PCS.

Given that chronic non-communicable diseases (CNCD) are the main cause of disability and premature mortality [7], the study of the main risk factors (RF) of their development (high blood pressure, hypercholesterolaemia, hyperglycaemia, smoking, overweight or obesity) as part of PCS studies is essential for resolution of problems and consequences of PCS.

Materials and Methods

This is a cross-sectional, observational study. The study was conducted at the Scientific Research Institute of Therapy and Preventive Medicine, a branch of the Federal Budgetary Scientific Institution Federal Research Center Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Science. The study enrolled 270 subjects (48.1 % were male subjects) aged 18 to 84 years old (53.00 [43.00;64.00]), who were COVID-19 convalescents. Inclusion criteria: COVID-19 confirmed with a positive test for SARS-CoV-2 RNA by polymerase chain reaction (PCR) during the disease and/or presence of anti-SARS-CoV-2 IgG antibodies and at least two months after NCVI recovery. Exclusion criteria were acute infectious diseases and decompensated chronic diseases.

All patients provided their informed consent for participation in the study. The study was conducted as part of the budget section, Reg. No. 122031700115-7, and with a grant from the President of Russia and a grant from the Government of the Novosibirsk Region, Application No. 39423 (2024), approved by the Ethics Committee at the Federal Research Center Institute of Cytology and Genetics of the Siberian Branch of the Russian Academy of Science (Novosibirsk).

All patients were divided into three groups, depending on PCS severity, using certain criteria: presence of at least one sign, which developed during or after COVID-19 infection (verified by lab test results) and persisting over four weeks after onset of the disease; provided that it cannot be explained by any other causes [8]. Group 1 included 79 subjects without PCS; group 2 — 97 patients with mild PCS (non-life-threatening arrhythmias, development/aggravation of arterial hypertension (AH), changes in spirography without any impact on the quality of life, chronic cough, prediabetes, abdominal pain, mild neurological symptoms, subclinical anxiety/depression); group 3 — 94 patients with moderate PCS (ischaemic heart disease (IHD), atrial fibrillation, cardiac insufficiency, obstructive and interstitial lung disease, diabetes mellitus (DM), cerebrovascular event, anosmia, marked anxiety/depression, hair loss).

During the study, demographics (sex, age), medical history, chronic and newly diagnosed diseases (DM2, cardiovascular diseases (CVD), including IHD, AH, history of myocardial infarction, cerebrovascular event) were taken into account. Patients underwent anthropometry, including measurements of height, weight, waist circumference (WC) and thigh circumference (TC), and their blood pressure was measured. Body mass index (BMI) was calculated using the formula: BMI (kg/m2) = Weight (kg)/Height2 (m2); waist/thigh ratio (WC/TC) = WC (cm)/TC (cm). Fasting blood serum samples were taken after 8–14-hour night fasting. Thermo Fisher Scientific kits (Finland) and Konelab Prime 30i biochemical analyser (Thermo Fisher Scientific, Finland) were used to measure total cholesterol, triglycerides (TG) and high density lipoprotein cholesterol (HDL cholesterol) by direct enzymatic methods. Low density lipoprotein cholesterol levels were calculated using the Friedewald formula. Glomerular filtration rate (GFR) was calculated using the CKD-EPI (Chronic Kidney Disease Epidemiology

Collaboration, 2011 modification) formula. Since the subjects were of child-bearing age, data of the sex hormones (oestradiol, testosterone) were used to standardise the regression models.

Additionally, the atherogenic index of plasma (AIP) was calculated using the formula: logarithm to base 10 (LOG10) [fasting TG (mmol/L) / fasting HDL cholesterol (mmol/L)] [9]. AIP < 0.11 was a predictor of a low cardiovascular risk; AIP 0.11–0.21 predicted a moderate cardiovascular risk, while API > 0.21 was a predictor of a high cardiovascular risk [10]. Also, insulin resistance (IR) index was calculated: triglyceride glucose index (TGI) = Ln [TG (mg/dL) × fasting plasma glucose (mg/dL) / 2], its derivatives: TGI /WC = TGI multiplied by WC; TGI /BMI = TGI multiplied by BMI) [11-13]. Besides, the following indices were evaluated on the basis of lipid and anthropometric parameters: lipid accumulation product (LAP) — formula for men: (WC (cm) — 65) multiplied by TG (mmol/L); for women: (WC — 58) x TG); and visceral adiposity index (VAI) — visceral adiposity index (formula for men: [WC/(39.68 + 1.88 × BMI)] × (TG/1.03) × (1.31/ HDL cholesterol)]; for women [WC/(36.58 + 1.89 × BMI)] × (TG/0.81) × (1.52/ HDL cholesterol)], where TG and HDL cholesterol are in mmol/L)] [14]. Instrumental methods included echocardiography (echoCG) and spirometry. The left ventricle diastolic dysfunction (LV DD) status was evaluated using echoCG: grade I LV DD was diagnosed if the ratio between LV filling rate at early diastole and atrial systole (E/A) was ≤ 0.8, while LV filling rate at early diastole (E) was ≤50 cm/s; grade II LV DD was diagnosed if two criteria out of three were present: 1) the ratio between LV filling rate at early diastole and average rate of LV elevation at early diastole (E/e′ > 14), 2) indexed left atrial volume (> 34 mL/m2), 3) highest tricuspid regurgitation rate > 2.8 m/s [15]. Anxiety and depression were assessed using the Hospital Anxiety and Depression Scale (HADS) [16]. Pre-diabetes was diagnosed in accordance with the current clinical guidelines of the Russian Association of Endocrinologists (Type 2 Diabetes Mellitus in Adults, 2022). Cardiovascular pathologies were diagnosed in accordance with the current Russian guidelines. Asthenia was diagnosed on the basis of the Multidimensional Fatigue Inventory (MFI-20) results [17].

In the study subjects, CVDs (IHD, AH, chronic cardiac insufficiency) before NCVI were recorded in 161 subjects (59.6 %), bronchopulmonary disorders (chronic obstructive pulmonary disease, bronchial asthma) were diagnosed in 58 patients (21.5 %). The subjects did not demonstrate any significant differences in severity of the acute COVID-19 period and PCS manifestations; at the same time, all patients with severe acute COVID-19 period had PCS (Fig. 1).

The median age of the patients was 53.00 [43.00;64.00] (Table 1). All patients were divided into three groups, depending on PCS severity. Group 1 included 79 (29.3 %) subjects without PCS (45 (34.6 %) men, 34 (24.3 %) women); group 2 — 97 (49 (37.7 %) men, 48 (34.3 %) women) patients with mild PCS; group 3 — 94 patients with moderate PCS (36 (27.7 %) men, 58 (41.4 %) women). The characteristics of groups are presented in Table 1.

Statistical processing of results was performed in SPSS application package (v. 20.0). Statistical evaluations included a descriptive analysis of numerical characteristics. Normality of distribution was tested using the Kolmogorov–Smirnov test. Given that the distribution of a majority of data was other than normal, they were presented as median and quartiles (Me [Q1; Q3]).

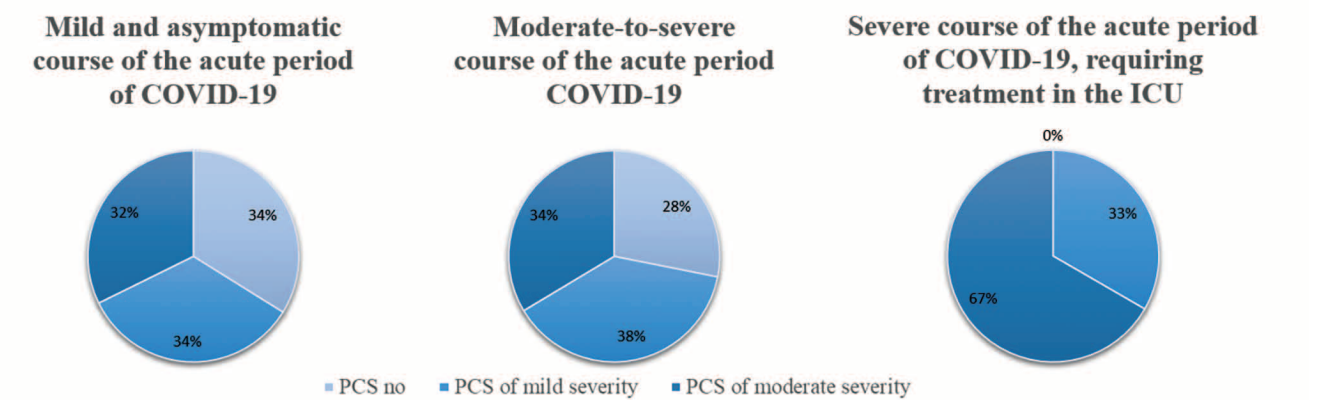

Figure 1. *Proportion of reported cases of PCS in COVID-19 convalescents, according to the course of the acute period of coronavirus infection*

Table 1. Characteristics of patients included in the study

Parameter	PCS no n=79 (29,3 %)	PCS of mild severity n=97 (35,9 %)	e PCS of moderate severity n=94 (34,8 %)	p
Age, years	46,0 [39,0;61,0]	56,0 [47,0;64,5]	55,5 [43,8;66,0]	**p — 0,003** **p_{1-2} — 0,002** p_{2-3} — 0,936 **p_{1-3} — 0,007**
Men, n (%)	45 (57,0 %)	49 (50,5 %)	36 (38,3 %)	p_{1-2} — 0,394 p_{2-3} — 0,089 **p_{1-3} — 0,014**
IgM, mg/dL	73,50 [37,25;256,25]	87,00 [44,75;297,25]	112,00 [40,25;180,00]	**p — 0,559** p_{1-2} — 0,302 p_{2-3} — 0,891 p_{1-3} — 0,398
IgM, mg/dL	1192,00 [367,00;1377,00]	1308,00 [773,00;1361,50]	1336,50 [1103,25;1390,25]	**p — 0,080** p_{1-2} — 0,402 p_{2-3} — 0,104 **p_{1-3} — 0,039**
SAD, mm Hg	121,25 [112,50;130,63]	128,00 [120,00;138,25]	125,00 [113,63;135,00]	**p — 0,005** **p_{1-2} — 0,001** **p_{2-3} — 0,024** p_{1-3} — 0,422
DAD, mm Hg	80,00 [70,75;85,00]	82,50 [79,75;88,00]	80,00 [70,75;87,13]	**p — 0,022** **p_{1-2} — 0,010** **p_{2-3} — 0,033** p_{1-3} — 0,734
WC, cm	92,00 [83,00;100,00]	101,00 [88,75;110,00]	100,00 [87,50;109,00]	**p — 0,002** **p_{1-2} — 0,001** p_{2-3} — 0,385 **p_{1-3} — 0,009**
BMI, kg/m	26,71 [23,75;30,53]	29,42 [25,85;34,66]	28,73 [24,76;32,36]	**p — 0,004** **p_{1-2} — 0,001** p_{2-3} — 0,169 **p_{1-3} — 0,043**

Note: SAD — systolic blood pressure, DAD — dyastolic blood pressure, WC — Waist circumference, BMI — body mass index

Standard characteristics for evaluation of statistical hypotheses were used: Mann–Whitney test for group comparison, univariate and multifactor logistic regression analysis for evaluation of the odds ratio. The Pearson's chi-squared test was used to compare frequencies in groups. The significance level for hypothesis testing was $p < 0.05$.

Results

52 (53.6 %) de novo cases of pre-diabetes were diagnosed in subjects with mild PCS, 12 (12.8 %) cases of pre-diabetes and 34 (36.2 %) cases of diabetes in patients with moderate PCS. Also, patients with moderate PCS had CVD, asthenia and hair loss de novo in 17 %, 37.2 % and 4.3 % of cases, respectively. The number of obese patients was statistically (2-fold) higher in the group of patients with mild PCS vs. patients without PCS. More patients with moderate PCS had CVD before COVID-19 vs. patients with mild PCS (Table 2).

No differences in lipid values were observed between the groups. In patients with mild PCS and moderate PCS, serum glucose levels were statistically higher (1.09 and 1.10 times higher, respectively) vs. patients without PCS (Table 3).

IR calculation showed that patients with mild and moderate PCS had higher values vs. patients without PCS: TGI (1.02 times higher), TGI/WC (1.13 and 1.10 times higher, respectively), TGI/BMI (1.09 and 1.05 times higher, respectively), and LAP (1.30 and 1.27 times higher, respectively) (Fig. 2). The visceral adiposity index (VAI) was statistically higher (1.15 times) in patients with moderate PCS vs. subjects without PCS ($p < 0.0001$). No statistically significant differences were observed in TG/HDL cholesterol ratio.

Table 2. *Incidence of risk factors for chronic non-communicable diseases in patients with PCS of various degrees of severity*

Parameter		PCS no n=79 (29,3 %)	PCS of mild severity n=97 (35,9 %)	PCS of moderate severity n=94 (34,8 %)	p
Smoking, *n (%)*		32 (40,5 %)	30 (30,9 %)	32 (34,0 %)	p_{1-2} — 0,186 p_{2-3} — 0,646 p_{1-3} — 0,380
Obesity, *n (%)*		22 (27,8 %)	46 (47,4 %)	36 (38,3 %)	**p_{1-2} — 0,008** p_{2-3} — 0,202 p_{1-3} — 0,148
CVD before COVID-19, *n (%)*		38 (48,1 %)	69 (71,1 %)	54 (57,4 %)	**p_{1-2} — 0,002** **p_{2-3} — 0,048** p_{1-3} — 0,220
Bronchopulmonary diseases before COVID-19, *n (%)*		9 (11,4 %)	10 (10,3 %)	9 (9,6 %)	p_{1-2} — 0,818 p_{2-3} — 0,865 p_{1-3} — 0,696
Hypertension, n (%)		38 (48,1 %)	73 (75,3 %)	56 (59,6 %)	**p_{1-2} — 0,0001** p_{2-3} — 0,605 **p_{1-3} — 0,004**
Prediabetes, *n (%)*			52 (53,6 %)	12 (12,8 %)	**p_{2-3} < 0,0001**
Anxiety disorder, *n (%)*	Subclinical stage	-	10 (10,3 %)	10 (10,6 %)	p_{2-3} — 0,808
	Severe stage	-	-	10 (10,6 %)	
Depression, *n (%)*	Subclinical stage	-	15 (15,5 %)	10 (10,6 %)	p_{2-3} — 0,457
	Severe stage	-	-	7 (7,4 %)	
Asthenia, *n (%)*		-	15 (15.5 %)	7 (7,4 %)	p_{2-3} — 0,083
Alopecia, *n (%)*		-	-	35 (37,5 %)	

Note: AH — arterial hypertension, PCS — postcovid syndrome, COVID-19 — Coronavirus Disease 2019, CVD — cardiovascular disease

As for the respiratory system, FEV_1 was lower in mild and moderate PCS vs. subjects without PCS (group 1 — 3.51 [2.71;4.20] L/s, group 2 — 3.03 [2.46;3.81] L/s, group 3 — 3.05 [2.50;3.62] L/s, p_{1-2} — 0.029 and p_{1-3} — 0.002 respectively). The same trend was observed for FVC (group 1 — 4.17 [3.48;5.22] L, group 2 — 3.76 [3.09;4.85] L, group 3 — 3.74 [2.98;4.48] L, p_{1-2} — 0.039, p_{1-3} — 0.002). No differences in the Tiffeneau index were observed. EchoCG results show that LV DD was statistically more often diagnosed in subjects with various degrees of PCS vs. subjects without PCS (group 1 — 24 (30.4 %), group 2 — 61 (62.9 %), group 3 — 59 (62.8 %), respectively, p_{1-2} — 0.000, p_{1-3} — 0.000); however, no statistically significant differences were recorded in LC ejection fraction and estimated pulmonary artery pressure.

Later, cardiometabolic parameters were included in the univariate logistic regression analysis, which demonstrated that the probability of PCS in COVID-19 convalescents was 0.97 higher if they had obesity; 0.96 times higher for an increase in WC by 1 cm; 3 times higher for an increase in glucose levels by 1 mmol/L; 0.92 times higher for an increase in BMI by 1 kg/m2; 0.97 times higher for an increase in DBP by 10 mm Hg; 2.5 times higher for diagnosed AH; and 3.5 times higher for diagnosed LV DD (Table 4). Besides, there was an association between PCS in COVID-19 convalescents with high IR index values (TGI, TGI/WC, TGI/BMI). When the multifactor logistic regression model includes such parameters as WC, glucose, TGI, DBP, DD, the probability of having PCS in COVID-19 convalescents is impacted by higher glucose levels (Exp (B) = 3.138; 95 % CI 1.797–5.478; p = 0.000) and LV DD (Exp (B) = 2.876; 95 % CI 1.315–6.292; p = 0.008).

The model of the multifactor logistic regression analysis of the probability of PCS in men and women (with age and sex hormone standardisation) included the following parameters: age, glucose, testosterone, oestradiol, DBP, TGI/BMI, WC, LV DD). In men, the probability of PCS was associated with higher glucose levels (Exp (B) = 4.343; 95 % CI 1.945–9.696; p = 0.000), WC (Exp (B) = 1.068; 95 % CI 0.997–1.143; p = 0.060) and LV DD (Exp (B) = 3.377; 95 % CI 1.106–10.313; p = 0.033). In women, this association was observed only with LV DD (Exp (B) = 4.457; 95 % CI 1.212–16.386; p = 0.024).

The unifactor logistic regression analysis demonstrated that the probability of moderate PCS was higher with higher glucose levels, VAI, SBP and was lower with

Table 3. *Clinical and biochemical values in patients with PCS*

Parameter	PCS no n=79 (29,3 %)	PCS of mild severity n=97 (35,9 %)	PCS of moderate severity n=94 (34,8 %)	p
ALT, Ed/*l*	20,00 [14,00;28,00]	23,00 [16,00;31,00]	20,00 [14,75;27,00]	p — 0,165 p_{1-2} — 0,106 p_{2-3} — 0,102 p_{1-3} — 0,902
AST, Ed/*l*	20,00 [17,00;26,00]	21,00 [18,00;28,00]	20,00 [16,00;24,25]	p — 0,381 p_{1-2} — 0,492 p_{2-3} — 0,155 p_{1-3} — 0,587
TC, mmol/l	196,80 [180,30;239,90]	209,70 [179,00;242,30]	204,85 [167,10;234,95]	p — 0,549 p_{1-2} — 0,825 p_{2-3} — 0,313 p_{1-3} — 0,402
Glucose, mmol/l	5,80 [5,40;6,10]	6,40 [5,70;6,90]	6,35 [5,70;7,60]	**p — 0,0001** **p_{1-2} — 0,0001** p_{2-3} — 0,346 **p_{1-3} — 0,0001**
TG, mmol/l	114,50 [74,50;170,30]	120,00 [90,20;172,95]	125,15 [80,23;219,08]	p — 0,383 p_{1-2} — 0,243 p_{2-3} — 0,760 p_{1-3} — 0,218
Uric acid, mmol/l	348,00 [281,00;410,00]	362,00 [282,00;418,00]	343,00 [294,25;415,50]	p — 0,857 p_{1-2} — 0,616 p_{2-3} — 0,675 p_{1-3} — 0,857
LDL-C, mmol/l	127,60 [104,50;159,85]	132,90 [100,55;159,27]	131,78 [90,35;157,44]	p — 0,860 p_{1-2} — 0,948 p_{2-3} — 0,634 p_{1-3} — 0,641
HDL-C, mmol/l	51,60 [39,80;63,70]	48,80 [41,25;63,80]	49,60 [36,97;56,52]	p — 0,163 p_{1-2} — 0,910 p_{2-3} — 0,108 p_{1-3} — 0,096
GFR, ml/min	84,00 [71,00;94,00]	78,00 [69,00;89,50]	78,50 [67,00;90,00]	p — 0,187 p_{1-2} — 0,106 p_{2-3} — 0,905 p_{1-3} — 0,110
Fibrinogen, g/l	3,77 [3,10;4,50]	3,55 [2,88;4,00]	3,55 [2,77;4,00]	p — 0,141 p_{1-2} — 0,055 p_{2-3} — 0,955 p_{1-3} — 0,108

Note: ALT — alanine aminotransferase, AST — aspartate aminotransferase, TG — triglycerides, LDL-C — Low-density lipoprotein cholesterol, HDL-C — high-density lipoprotein cholesterol, GFR — glomerular filtration rate

existing CVD (Table 5). This association persisted when the multifactorial logistic regression model included these parameters (glucose, VAI, CBP, CVD before COVID-19).

When the multifactor logistic regression analysis was performed in men, the probability of moderate PCS was 2.4 times higher with an increase in glucose levels by 1 mm, 1.4 times higher with an increase in VAI, and was 6.3 times lower in case CVD was diagnosed before COVID-19. In women, this analysis did not reveal any association with the above parameters (Table 6).

Discussion

The NCVI pandemic of 2021 established that it was necessary to make every effort to identify prognostic risk factors of complications and sequels of COVID-19, which have a direct impact on the long-term functional status and quality of patients' life.

One of the RF in question is visceral obesity, which impacts CVD development and anti-inflammatory status [18-20]. In this study, over a half (159 (58.9 %), men 43.4 %) of NCVI convalescents with PCS were obese.

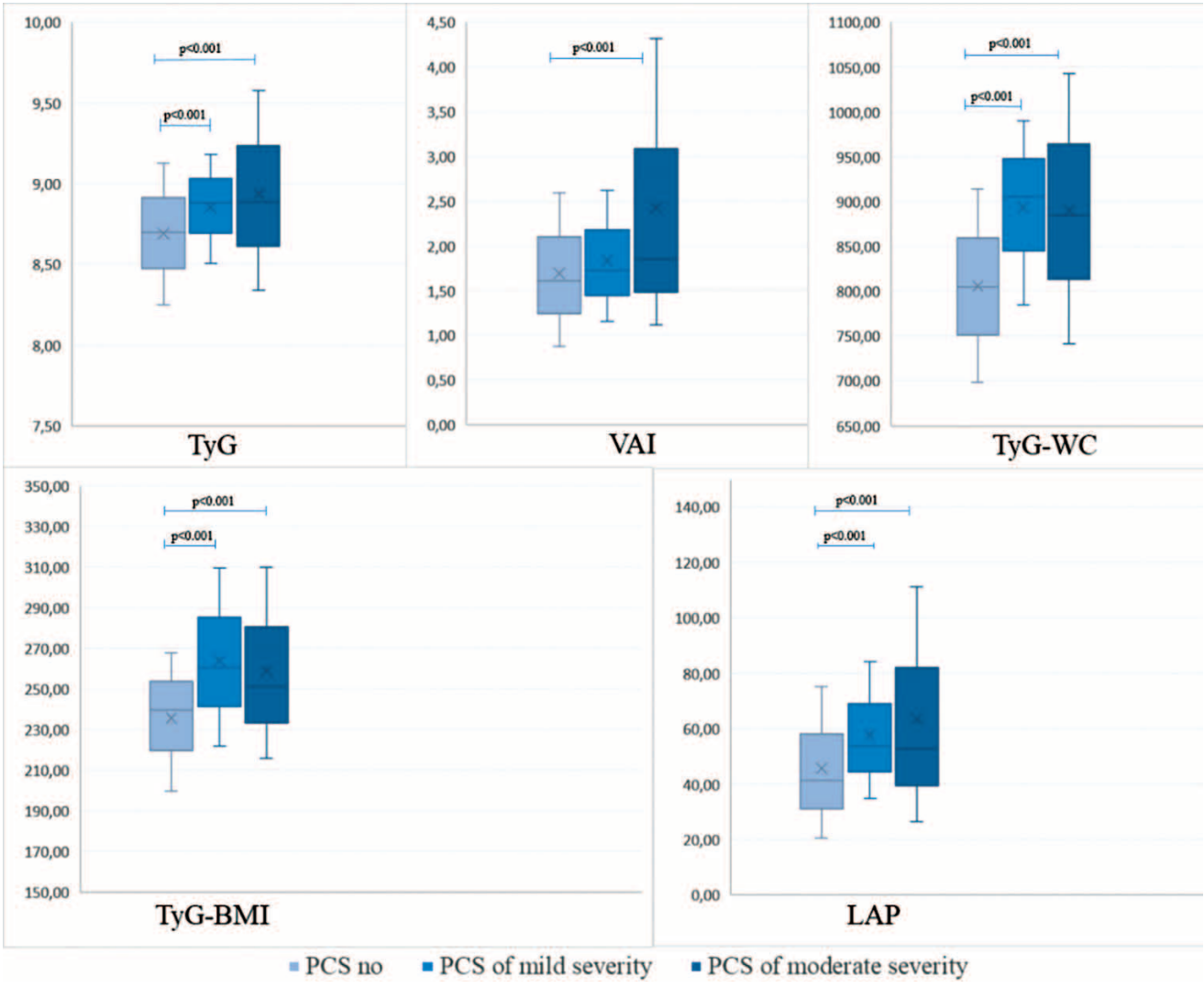

Figure 2. *Median and Quartiles of insulin resistance index in COVID-19 convalescents depending on the presence or absence of PCS of different severity*

Note: PCS — postcovid syndrome, TyG — triglycerides glucose index, TyG-WC — triglyceride glucose-waist circumference, TyG-BMI — triglyceride glucose-body mass index, LAP — lipid accumulation product, VAI — visceral adiposity index

Other authors provide similar information. According to the data from COVID-NET, a US surveillance network, 90 % of patients admitted to hospitals with confirmed NCVI had underlying conditions, and obesity accounted for 48.3 % of cases [21]. According to the AKTIV register, in 27.7 % of cases followed up for 6 months after hospitalisation, patients had obesity. The study results indicate that this risk factor is observed in patients with diseases de novo (AH, IHD, MI and DM) [22]. One of the mechanisms, of how obesity impacts the course and prognosis of NCVI, is detectable high levels of angiotensin converting enzyme-2 expression in visceral adipose tissue, which increases SARS-CoV-2 tropism to adipocytes and creates a virus depot in these cells [23]. Immunological and metabolic disorders typical for obese patients create conditions for chronic inflammation in the body, facilitating higher susceptibility to infections and defining the course of post-infectious changes [24]. In their study, S.H. Loosen et al. (2022) suggested that dyslipidemia, obesity and elderly age are a significant risk factor of PCS [25]. In this study, it was established that more severe PCS is directly associated with higher VAI values, which, in turn, are independently associated with new cases of IHD, type2 DM, AH [26,27]. It is worth mentioning that AKTIV and AKTIV 2 studies demonstrated that obesity in COVID-19 convalescents with PCS was associated with onset of such diseases as AH, DM1 and DM2, IHD, atrial fibrillation, arthritis, stroke, bronchial asthma, cancer, chronic cardiac insufficiency, myocardial infarction, chronic kidney disease, which aggravate PCS; during the three post-COVID months, obesity in patients over 60 years of age increased the probability of death (OR = 2.23; 95 % CI 1.05–4.72; p = 0.032) [28]. Therefore, the data obtained and the study results make

Table 4. Logistic regression analysis of the chance of availability PCS (standardized by age and gender)

Parameter	Univariate analysis			Multivariate analysis		
	Exp B	95,0 % C.I.	p	Exp B	95,0 % C.I.	p
Age	-	-	-	0,985	0,956-1,015	0,326
Gender	-	-	-	**3,602**	**1,735-7,478**	**0,001**
Obesity	**1,027**	**1,050-3,398**	**0,034**	-	-	-
WC	**1,042**	**1,020-1,065**	**0,0001**	1,019	0,992-1,048	0,171
Glucose	**3,038**	**1,924-4,798**	**0,0001**	**3,138**	**1,797-5,478**	**0,0001**
BMI	**1,088**	**1,031-1,148**	**0,002**	-	-	-
TyG	**1,663**	**1,042-2,655**	**0,033**	0,603	0,320-1,133	0,116
TyG/WS	**1,004**	**1,002-1,006**	**0,0001**	-	-	-
TyG/BMI	**1,009**	**1,004-1,014**	**0,001**	-	-	-
LAP	**1,007**	**1,001-1,014**	**0,033**	-	-	-
VAI	1,055	0,925-1,204	0,423	-	-	-
DAD	**1,033**	**1,002-1,064**	**0,034**	1,012	0,977-1,049	0,492
AH	**2,491**	**1,322-4,693**	**0,005**	-	-	-
DD LV	**3,538**	**1,778-7,041**	**0,0001**	**2,876**	**1,315-6,292**	**0,008**
CVD before COVID-19	1,435	0,773-2,663	0,252	-	-	-
FEV_1	0,952	0,636-1,424	0,812	-	-	-
FVC	1,017	0,727-1,424	0,919	-	-	-
Pulmonary pressure	1,007	0,964-1,053	0,749	-	-	-

Note: AH — arterial hypertension, DAD — diastolic blood pressure, DD LV — Left ventricular diastolic dysfunction, BMI — body mass index, WC — Waist circumference, TyG — triglycerides glucose index, TyG-BMI — triglyceride glucose-body mass index, TyG-WC — triglyceride glucose-waist circumference, FVC — forced vital capacity LAP — lipid accumulation product, VAI — visceral adiposity index

Table 5. Logistic regression analysis of the chance of availability PCS of moderate severity in persons with PCS (standardized by gender and age)

Parameter	Univariate analysis			Multivariate analysis		
	Exp B	95,0 % C.I.	p	Exp B	95,0 % C.I.	p
Age	-	-	-	0,995	0,966-1,025	0,733
Gender	-	-	-	**2,510**	**1,242-5,072**	**0,010**
Obesity	0,706	0,394-1,265	0,242	-	-	-
WS	0,999	0,979-1,020	0,917	-	-	-
Glucose	**1,537**	**1,183-1,998**	**0,001**	**1,736**	**1,268-2,378**	**0,001**
VAI	**1,256**	**1,070-1,474**	**0,005**	**1,224**	**1,015-1,475**	**0,034**
SAD	**0,977**	**0,956-0,997**	**0,027**	**0,975**	**0,951-0,999**	**0,043**
DAD	0,972	0,941-1,004	0,086	-	-	-
CVD before COVID-19	**0,465**	**0,227-0,951**	**0,036**	**0,365**	**0,157-0,846**	**0,019**

Note: DAD — diastolic blood pressure, WC — Waist circumference, SAD — systolic blood pressure , CVD — cardiovascular disease, VAI — visceral adiposity index

Table 6. Logistic regression analysis of the of the chance of availability PCS of moderate severity in men and women with PCS (standardized by age and sex hormones)

Parameter	Men			Women		
	Exp B	95,0 % C.I.	p	Exp B	95,0 % C.I.	p
Age	0,996	0,954-1,039	0,842	1,003	0,959-1,050	0,887
Glucose	**2,357**	**1,319-4,211**	**0,004**	1,443	0,916-2,241	0,115
Testosterone	1,002	0,959-1,047	0,926	-	-	-
Estradiol	-	-	-	1,332	0,202-8,786	0,776
SAD	0,995	0,950-1,041	0,823	0,970	0,939-1,003	0,073
VAI	**1,430**	**1,057-1,934**	**0,020**	1,085	0,871-1,351	0,467
CVD before COVID-19	**0,160**	**0,037-0,687**	**0,014**	0,506	0,165-1,555	0,235

Note: SAD — systolic blood pressure , CVD — cardiovascular disease, VAI — visceral adiposity index

it possible to suggest that the role of obesity in a higher probability of a poor outcome in NCVI convalescents with PCS is crucial.

Also, another risk factor of PCS is hyperglycaemia. It was established that PCS of a various degree of severity in COVID-19 convalescents is independently associated with glucose levels. Researchers report that higher glucose levels in the post-COVID period can smooth out or transform to DM, which can aggravate PCS [29,30]. It can be assumed that there are several causes of these findings: glucocorticosteroid therapy during the acute period and recovery; long-lasting pro-inflammatory status (including higher cytokine levels) after the infectious period; direct impact of SARS-CoV-2 and antivirals on β-cells of the pancreas and liver, impacting fasting glucose levels [31].

It is known that impaired diastolic functions of the myocardium usually precede a drop in the pumping ability of the LV and are a risk factor of a cardiac pathology [32]. According to Chistyakova MV et al. (2021), patients with moderate and severe NCVI develop LV diastolic impairment 98 [92;103] days after the diagnosis [33]. This study showed that LV DD was associated with PCS in COVID-19 convalescents irrespective of other factors. A systematic review by Ramadan M.S. et al. 3–6 months after the acute COVID-19 period showed a relatively high percent (40 %) of impaired LV diastolic function [34]. There are reports on various mechanisms of myocardial involvement in COVID-19: effects of the virus on cardiomyocytes via angiotensin converting enzyme-2 receptors with resulting fibrosis, that can manifest as impaired LV diastolic function [35-37], myocardial inflammation, vasculitis, thrombosis or sequels of hypoxia and haemodynamic instability [38]. LV DD is likely to be an early marker of intracardiac changes due to past NCVI; LV DD in COVID-19 convalescents can be a key to a comprehensive assessment of cardiac changes, which will help identify risks and develop a targeted approach to therapy.

Conclusion

PCS in COVID-19 convalescents is independently associated with glucose levels and LV DD. Moderate PCS is associated with higher glucose levels, SBP, VAI and pre-existing CVD. As far as gender differences are concerned, severe PCS in men is associated with cardiometabolic risk factors (visceral obesity, pre-existing CVD, glucose levels). No such associations were observed in women. Men with cardiometabolic risk factors, particularly with visceral obesity, are likely to be at high risk of moderate PCS.

Вклад авторов:

Все авторы внесли существенный вклад в подготовку работы, прочли и одобрили финальную версию статьи перед публикацией

Карасева А.А.: сбор, анализ, интерпретация данных, написание рукописи

Афанасьева А.Д.: разработка концепции и дизайна рукописи, проверка критически важного интеллектуального содержания

Гарбузова Е.В.: проверка критически важного интеллектуального содержания

Кузнецов А.А.: анализ и интерпретация данных функциональных методов исследования

Палехина Ю.Ю: проведение ультразвукового исследования, анализ и интерпретация полученных данных

Щепина Ю.В.: проведение ультразвукового исследования, анализ и интерпретация полученных данных

Шрамко В.С.: выполнение биохимических исследований, анализ и интерпретация данных исследования

Логвиненко И.И.: руководитель проекта

Рагино Ю.И.: окончательное утверждение рукописи для публикации

Author Contribution:

All the authors contributed significantly to the study and the article, read and approved the final version of the article before publication

Karaseva A.A.: data collection, analysis, interpretation, manuscript writing

Afanaseva A.D.: development of the concept and design of the manuscript, verification of critical intellectual conten

Garbuzova E.V.: verification of critical intellectual content

Kuznetsov A.A.: analysis and interpretation of data from functional research methods

Palekhina Yu.Y.: ultrasound examination, analysis and interpretation of the data obtained

Shchepina Yu.V.: ultrasound examination, analysis and interpretation of the data obtained

Shramko V.S.: performing biochemical studies, analysis and interpretation of research data

Logvinenko I.I.: Project Manager

Ragino Yu.I.: final approval for the publication of the manuscript

Список литературы/ References:

1. Soriano JB, Murthy S, Marshall JC, et al. WHO Clinical Case Definition Working Group on Post-COVID-19 Condition. A clinical case definition of post-COVID-19 condition by a Delphi consensus. Lancet Infect Dis. 2022; 22(4): e102-e107. doi: 10.1016/S1473-3099(21)00703-9.
2. Cabrera Martimbianco AL, Pacheco RL, Bagattini ÂM, et al. Frequency, signs and symptoms, and criteria adopted for long COVID-19: A systematic review. Int J Clin Pract. 2021; 75(10): e14357. doi: 10.1111/ijcp.14357.
3. Michelen M, Manoharan L, Elkheir N, et al. Characterising long COVID: a living systematic review. BMJ Glob Health. 2021; 6(9): e005427. doi: 10.1136/bmjgh-2021-005427.

4. Арутюнов Г.П., Тарловская Е.И., Арутюнов А.Г. и др. Клинические особенности постковидного периода. Результаты международного регистра «Анализ динамики коморбидных заболеваний у пациентов, перенесших инфицирование SARS-CoV-2 (АКТИВ SARS-CoV-2)» (12 месяцев наблюдения). Российский кардиологический журнал. 2023; 28(1): 5270. https://doi.org/10.15829/1560-4071-2023-5270
Arutyunov G.P., Tarlovskaya E.I., Arutyunov A.G., et al. Clinical features of post-COVID period. Results of an International Register "Dynamics Analysis of Comorbidities in SARS-CoV-2 Survivors (ACTIV SARS-CoV-2)" (12-month follow-up). Russian Journal of Cardiology. 2023;28(1):5270. https://doi.org/10.15829/1560-4071-2023-5270 [in Russian].
5. Погосова Н.В., Кучиев Д.Т., Попова А.Б., и др. Последствия COVID-19 на отдаленном этапе после госпитализации по данным клинико-инструментальных и лабораторных методов исследования. Кардиологический вестник. 2023;18(4):56–66. https://doi.org/10.17116/Cardiobulletin20231804156
Pogosova NV, Kuchiev DT, Popova AB, et al. Clinical, instrumental and laboratory data on consequences of COVID-19 in delayed period after admission. Russian Cardiology Bulletin. 2023;18(4):56–66. https://doi.org/10.17116/Cardiobulletin20231804156 [in Russian].
6. Волкова М.В., Кундер Е.В., Постковидный синдром: клинические проявления, терапевтические возможности. Рецепт. 2023; 158-168. doi: 10.34883/pi.2023.26.2.002
Volkova M.V., Kunder E.V. Postcovid Syndrome: Clinical Manifestations, Therapeutic Possibilities. Recipe. 2023; 26 (2): 158-168. doi: 10.34883/PI.2023.26.2.002 [in Russian].
7. Казаков С.Д., Каменских Е.М., Соколова Т.С. и др. Современная эпидемиология: вызовы общественного здравоохранения и возможности их решения (обзор литературы). Проблемы социальной гигиены, здравоохранения и истории медицины. 2023; 31(3): 368—378. doi: 10.32687/0869-866X-2023-31-3-368-378
Kazakov S.D., Kamenskikh E.M., Sokolova T.S., et al. The present-day epidemiology: challenges of public health and possibilities to settle them: publications review. Problemi socialnoi gigieni, zdravookhranenia i istorii meditsini. 2023; 31(3): 368–378. doi: http://dx.doi.org/10.32687/0869-866X-2023-31-3-368-378 [in Russian].
8. Карасева А.А., Худякова А.Д., Гарбузова Е.В. и др. Степени тяжести постковидного синдрома: систематический обзор. Архивъ внутренней медицины. 2023; 13(6): 422-435. doi: 10.20514/2226-6704-2023-13-6-422-435.
Karaseva A.A., Khudiakova A.D., Garbuzova E.V. et al. Severity of Postcovid Syndrome: A Systematic Review. The Russian Archives of Internal Medicine. 2023; 13(6): 422-435. DOI: 10.20514/2226-6704-2023-13-6-422-435. [in Russian].
9. Dobiasova M, Frohlich J. The plasma parameter log (TG/HDL-C) as an atherogenic index: correlation with lipoprotein particle size and esterification rate in apoB-lipoprotein-depleted plasma (FER(HDL)). Clinical biochemistry. 2001; 34(7): 583-8. doi: 10.1016/s0009-9120(01)00263-6.
10. Dobiasova M., Frohlich J., Sedova M. et al. Cholesterol esterification and atherogenic index of plasma correlate with lipoprotein size and findings on coronary angiography. Journal of lipid research, 2011; 52 (3): 566–571. doi: 10.1194/jlr.P011668
11. Simental-Mendía LE, Rodríguez-Morán M, Guerrero-Romero F. The product of fasting glucose and triglycerides as surrogate for identifying insulin resistance in apparently healthy subjects. Metabolic syndrome and related disorders. 2008;6(4):299-304. doi: 10.1089/met.2008.0034.
12. Zheng S, Shi S, Ren X, et al. Triglyceride glucose-waist circumference, a novel and effective predictor of diabetes in first-degree relatives of type 2 diabetes patients: cross-sectional and prospective cohort study. Journal of translational medicine. 2016 Sep 7; 14(1): 260. doi: 10.1186/s12967-016-1020-8.
13. Er LK, Wu S, Chou HH. et al. Triglyceride Glucose-Body Mass Index Is a Simple and Clinically Useful Surrogate Marker for Insulin Resistance in Nondiabetic Individuals. PLoS One. 20161;11(3):e0149731. doi: 10.1371/journal.pone.0149731.
14. Руяткина Л.А., Руяткин Д.С., Исхакова И.С. Возможности и варианты суррогатной оценки инсулинорезистентности. Ожирение и метаболизм. 2019; 16(1): 27-32. doi: 10.14341/omet10082
Ruyatkina LA, Ruyatkin DS, Iskhakova IS. Opportunities and options for surrogate assessment of insulin resistance. Obesity and metabolism. 2019; 16(1): 27-32. doi: 10.14341/omet10082 [in Russian].
15. Хроническая сердечная недостаточность. Клинические рекомендации 2020. Российский кардиологический журнал. 2020; 25(11): 4083.doi: 10.15829/1560-4071-2020-4083
Clinical practice guidelines for Chronic heart failure. Russian Journal of Cardiology. 2020;25(11):4083. https://doi.org/10.15829/1560-4071-2020-4083 [in Russian].
16. Zigmond A.S., Snaith R.P. The hospital anxiety and depression scale. Acta psychiatrica Scandinavica. 1983;67(6):361–370. doi: 10.1111/j.1600-0447.1983.tb09716.x.
17. Smets E.M., Garssen B., Bonke B., et al. The Multidimensional Fatigue Inventory (MFI) psychometric qualities of an instrument to assess fatigue. Journal of psychosomatic research. 1995; 39(3):315-25 https://doi.org/10.1016/0022-3999(94)00125-o
18. Fox, C. S., Massaro, J. M., Hoffmann, U. et al. Abdominal visceral and subcutaneous adipose tissue compartments: association with metabolic risk factors in the Framingham Heart Study. Circulation. 2007; 116(1): 39–48. doi: 10.1161/CIRCULATIONAHA.106.675355
19. Rabkin SW. The relationship between epicardial fat and indices of obesity and the metabolic syndrome: a systematic review and meta-analysis. Metab Syndr Relat Disord. 2014;12(1):31– 42. doi: 10.1089/met.2013.0107;
20. Pou KM, Massaro JM, Hoffmann U. et al. Visceral and subcutaneous adipose tissue volumes are cross-sectionally related to markers of inflammation and oxidative stress: the Framingham Heart Study. Circulation. 2007; 116(11): 1234–1241. doi: 10.1161/CIRCULATIONAHA.107.710509

21. Garg, S., Kim, L., Whitaker, M. et al. Hospitalization Rates and Characteristics of Patients Hospitalized with Laboratory-Confirmed Coronavirus Disease 2019 — COVID-NET, 14 States, March 1-30, 2020. MMWR. Morbidity and mortality weekly report, 2020; 69(15): 458-464. doi: 10.15585/mmwr.mm6915e3.
22. Арутюнов Г.П., Тарловская Е.И., Арутюнов А.Г. Клинические особенности постковидного периода. Результаты международного регистра «Анализ динамики коморбидных заболеваний у пациентов, перенесших инфицирование SARS-CoV-2 (АКТИВ SARS-CoV-2)». Предварительные данные (6 месяцев наблюдения). Российский кардиологический журнал. 2021; 26(10): 4708. doi: 10.15829/1560-407].
Arutyunov G.P., Tarlovskaya E.I., Arutyunov A.G. Clinical features of post-COVID-19 period. Results of the international register «Dynamic analysis of comorbidities in SARS-CoV-2 survivors (AKTIV SARS-CoV-2)». Data from 6-month follow-up. Russian Journal of Cardiology. 2021; 26(10): 4708. DOI: 10.15829/1560-4071-2021-4708. [in Russian].
23. Favre G, Legueult K, Pradier C, et al. Visceral fat is associated to the severity of COVID-19. Metabolism. 2021; 115: 154440. doi: 10.1016/j.metabol.2020.154440
24. Misumi I, Starmer J, Uchimura T. et al. Obesity Expands tinct Population of T Cells in Adipose Tissue and Increases Vulnerability to Infection. Cell Rep. 2019;27(2):514–524.e5. doi: 10.1016/j.celrep.2019.03.030
25. Loosen S.H., Jensen B.O., Tanislav C. et al. Obesity and lipid metabolism disorders determine the risk for development of long COVID syndrome: a cross-sectional study from 50,402 COVID-19 patients. Infection. 2022; 50(5): 1165–1170. doi: 10.1007/s15010-022-01784-0
26. Либис Р.А., Исаева Е.Н. Возможность применения индекса висцерального ожирения в диагностике метаболического синдрома и прогнозировании риска его осложнений. Российский кардиологический журнал. 2014; (9): 48-53. doi: 10.15829/1560-4071-2014-9-48-53
Libis R.A., Isaeva E.N. Opportunities for the use of visceral obesity index in metabolic syndrome diagnostics and prognosis of its complication risk. Russian Journal of Cardiology. 2014; (9): 48-53. https://doi.org/10.15829/1560-4071-2014-9-48-53 [in Russian].
27. Leite N.N., Cota B.C., Gotine AREM, et al. Visceral adiposity index is positively associated with blood pressure: A systematic review. Obesity research & clinical practice. 2021; 15(6): 546-556. doi: 10.1016/j.orcp.2021.10.001.
28. Арутюнов А.Г., Тарловская Е.И., Галстян Г.Р., и др. Влияние ИМТ на острый период COVID-19 и риски, формирующиеся в течение года после выписки. Находки субанализа регистров АКТИВ и АКТИВ 2. Проблемы Эндокринологии. 2022; 68(6): 89-109. https://doi.org/10.14341/probl13165
Arutyunov A.G., Tarlovskaya E.I., Galstyan G.R., et al. The impact of BMI on the course of the acute SARS-COV-2 infection and the risks that emerge during the first year after the hospital discharge. Subanalysis evidence of the AKTIV and AKTIV 2 registries. Problems of Endocrinology. 2022;68(6):89-109. https://doi.org/10.14341/probl13165 [in Russian].
29. Кононова А.А., Сурхаева А.А., Минаков А.А., и др. Характер нарушений углеводного обмена у пациентов, получавших лечение по поводу пневмонии, вызванной SARS-CoV-2. Известия Российской военно-медицинской академии. 2022; 41(S2): 215-221.
Kononova A.A., Surkhaeva A.A., Minakov A.A., et al. Risk factors for carbohydrate metabolism disorders in covid-19. Russian Military Medical Academy Reports.2022;41(S2):215–221. EDN XUANLT [in Russian].
30. Салухов В.В., Арутюнов Г.П., Тарловская Е.И. и др. Влияние нарушений углеводного обмена на ранние и отдаленные клинические исходы у пациентов с COVID-19 по данным регистров АКТИВ и АКТИВ 2. Проблемы Эндокринологии. 2023; 69(1): 36-49. https://doi.org/10.14341/probl13175
Salukhov V.V., Arutyunov G.P., Tarlovskaya E.I., et al. The impact of carbohydrate metabolism disorders on the early and long-term clinical outcomes of patients with COVID-19 according to the AKTIV and AKTIV 2 registries. Problems of Endocrinology. 2023; 69(1): 36-49. https://doi.org/10.14341/probl13175 [in Russian].
31. Ojo O., Wang X.H., Ojo O.O. et al. The Effects of COVID-19 Lockdown on Glycaemic Control and Lipid Profile in Patients with Type 2 Diabetes: A Systematic Review and Meta-Analysis. Int J Environ Res Public Health. 2022; 19(3): 1095. doi: 10.3390/ijerph19031095;
32. Brutsaert, D. L., Sys, S. U., Gillebert, T. C. Diastolic failure: Pathophysiology and therapeutic implications. Journal of the American College of Cardiology.1993;22(1):318–325. doi: 10.1016/0735-1097(93)90850-z.
33. Чистякова М.В., Зайцев Д.Н., Говорин А.В., и др. «Постковидный» синдром: морфо-функциональные изменения и нарушения ритма сердца. Российский кардиологический журнал. 2021; 26(7): 4485. doi: 10.15829/1560-4071-2021-4485
Chistyakova M.V., Zaitsev D.N., Govorin A.V., et al. Post-COVID-19 syndrome: morpho-functional abnormalities of the heart and arrhythmias. Russian Journal of Cardiology. 2021; 26(7): 4485. doi: 10.15829/1560-4071-2021-4485[in Russian].
34. Ramadan M.S., Bertolino L., Zampino R., et al. Monaldi Hospital Cardiovascular Infection Study Group. Cardiac sequelae after coronavirus disease 2019 recovery: a systematic review. Clinical microbiology and infection: the official publication of the European Society of Clinical Microbiology and Infectious Diseases. 2021; 27(9): 1250–1261. DOI: 10.1016/j.cmi.2021.06.015.
35. Chen, L., Li, X., Chen, M., et al. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovascular research, 116(6), 1097–1100. https://doi.org/10.1093/cvr/cvaa078
36. Потешкина Н.Г., Лысенко М.А., Ковалевская Е.А. и др. Кардиальное повреждение у пациентов с коронавирусной инфекцией COVID-19. Артериальная гипертензия. 2020;26(3):277-87. doi: 10.18705/1607-419X-2020-26-3-277-287
Poteshkina NG, Lysenko MA, Kovalevskaya EA, et al. Cardiac damage in patients with COVID-19 coronavirus infection. Arterial Hypertension. 2020;26(3):277-87 [in Russian].

37. Krishnamoorthy P, Croft LB, Ro R, et al. Biventricular strain by speckle tracking echocardiography in COVID-19: findings and possible prognostic implications. Future Cardiology. 2021 Jul; 17(4): 663-667. doi: 10.2217/fca-2020-0100. Epub 2020 Aug 4..
38. Akhmerov, A., & Marbán, E. (2020). COVID-19 and the Heart. Circulation research. 2020 May 8; 126(10): 1443-1455. doi: 10.1161/CIRCRESAHA.120.317055. Epub 2020 Apr 7.

Информация об авторах

Карасева Александра Александровна — Младший научный сотрудник лаборатории генетических и средовых детерминант жизненного цикла человека Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: Sas96@bk.ru, ORCID ID: https://orcid.org/0000-0002-0423-5021

Афанасьева Алёна Дмитриевна — к.м.н., зав. лабораторией генетических и средовых детерминант жизненного цикла человека Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: alene.elene@gmail.com, ORCID ID: https://orcid.org/0000-0001-7875-1566

Гарбузова Евгения Витальевна — к.м.н., Научный сотрудник лаборатории генетических и средовых детерминант жизненного цикла человека Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: stryukova.j@mail.ru, ORCID ID: https://orcid.org/0000-0001-5316-4664

Кузнецов Александр Александрович — д.м.н., ведущий научный сотрудник лаборатории молекулярно-генетических исследований терапевтических заболеваний Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: uznetsoviimed@gmail.com, ORCID ID: https://orcid.org/0000-0003-3502-7599

Палехина Юлия Юрьевна — Младший научный сотрудник Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: ukolova@hotmail.com, ORCID ID: https://orcid.org/0000-0002-9404-6987

Щепина Юлия Владимировна — Научный сотрудник Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: yulia@shchepin.ru, ORCID ID: https://orcid.org/0000-0003-3465-7572

Шрамко Виктория Сергеевна — к.м.н., професор, научный сотрудник, заведующая отделением клинико-биохимических и молекулярно-генетических методов исследований Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: nosova@211.ru, ORCID ID: https://orcid.org/0000-0002-0436-2549

Логвиненко Ирина Ивановна — д.м.н., профессор, главный научный сотрудник лаборатории профилактической медицины, заместитель руководителя по лечебной работе Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: 111157@mail.ru, ORCID ID: https://orcid.org/0000-0003-1348-0253

Рагино Юлия Игоревна — член-корреспондент РАН, д.м.н., профессор, руководитель НИИТПМ — филиал ИЦиГ СО РАН, главный научный сотрудник лаборатории клинических биохимических и гормональных исследований терапевтических заболеваний Научно-исследовательского института терапии и профилактической медицины — филиала Федерального государственного бюджетного научного учреждения «Федеральный исследовательский центр Институт цитологии и генетики СО РАН», Новосибирск, e-mail: ragino@mail.ru, ORCID ID: https://orcid.org/0000-0002-4936-8362

Information about the authors

Alexandra A. Karaseva — Junior Researcher of the Laboratory of Genetic and Environmental Determinants of the Human Life Cycle of the Research Institute of Therapy and Preventive Medicine — branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e-mail: Sas96@bk .ru, ORCID ID: https://orcid.org/0000-0002-0423-5021

Alena D. Afanaseva — candidate of medical sciences, head. Laboratory of Genetic and Environmental Determinants of the Human Life Cycle of the Research Institute of Therapy and Preventive Medicine — a branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e-mail: alene.elene@gmail.com, ORCID ID: https://orcid.org/0000-0001-7875-1566

Evgenia V. Garbuzova — Candidate of Medical Sciences, Researcher at the Laboratory of Genetic and Environmental Determinants of the Human Life Cycle of the Research Institute of Therapy and Preventive Medicine — a branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e-mail: stryukova.j@mail.ru, ORCID ID: https://orcid.org/0000-0001-5316-4664

Aleksandr A. Kuznetsov — Doctor of Medical Sciences, leading researcher at the Laboratory of Molecular Genetic Research of Therapeutic Diseases of the Research Institute of Therapy and Preventive Medicine — a branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e -mail: uznetsoviimed@gmail.com, ORCID ID: https://orcid.org/0000-0003-3502-7599

Yulia Yu. Palekhina — Junior Researcher of the Research Institute of Therapy and Preventive Medicine — branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e-mail: ukolova@hotmail.com, ORCID ID: https: //orcid.org/0000-0002-9404-6987

Yulia V. Shchepina — Researcher at the Research Institute of Therapy and Preventive Medicine — a branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e-mail: yulia@shchepin.ru, ORCID ID: https:/ /orcid.org/0000-0003-3465-7572

Victoria S. Shramko — Candidate of Medical Sciences, Professor, Researcher, Head of the Department of Clinical, Biochemical and Molecular Genetic Research Methods of the Research Institute of Therapy and Preventive Medicine — a branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SO" RAS", Novosibirsk, e-mail: nosova@211.ru, ORCID ID: https://orcid.org/0000-0002-0436-2549

Irina I. Logvinenko — Doctor of Medical Sciences, Professor, Chief Researcher of the Laboratory of Preventive Medicine, Deputy Head for Medical Work of the Research Institute of Therapy and Preventive Medicine — a branch of the Federal State Budgetary Scientific Institution "Federal Research Center Institute of Cytology and Genetics SB RAS" , Novosibirsk, e-mail: 111157@mail.ru, ORCID ID: https://orcid.org/0000-0003-1348-0253

Yulia I. Ragino — Corresponding Member of the Russian Academy of Sciences, Doctor of Medical Sciences, Professor, Head of NIITPM — branch of the Institute of Cytology and Genetics SB RAS, chief researcher of the laboratory of clinical biochemical and hormonal studies of therapeutic diseases of the Research Institute of Therapy and Preventive Medicine — branch of the Federal State Budgetary Scientific Research Institute institution "Federal Research Center Institute of Cytology and Genetics SB RAS", Novosibirsk, e-mail: ragino@mail.ru, ORCID ID: https://orcid.org/0000-0002-4936-8362

Автор, ответственный за переписку / Corresponding author