ASSESSMENT OF THE PSYCHO-EMOTIONAL STATE OF PATIENTS AFTER COVID-19-ASSOCIATED PNEUMONIA IN RELATIONSHIP WITH LABORATORY INDICATORS

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ABSTRACT

The aim. *To study peculiarities and association of psychological and laboratory indicators in patients with cardiovascular diseases (CVD) who underwent COVID-19 to clarify the factors affecting the possibility of developing delayed psychological and cardiovascular adverse events.*

Materials and methods. *The study enrolled 350 patients with COVID-19. Group 1 consisted of 92 patients without CVD, Group 2 – of 258 patients with CVD. Indicators of laboratory and psychological parameters were assessed according to the data of psychological questionnaire using GAD-7 (General Anxiety Disorder-7), PHQ-9 (Patient Health Questionnaire-9), PSS (Perceived Stress Scale) screening scales and SF-36. Parameters of complete blood count and biochemical blood tests were measured during hospitalization and three months after discharge from the monohospital.*

Results. *After three months, in the general group of patients, signs of anxiety and depression were detected in more than 30 % of the examined patients, signs of stress – in 10.4 %. In the group with CVD, psycho-emotional disorders were identified in 1/4 of the patients, and severe stress – in 8 % of those included in the study. In addition, it was registered that the indicators of erythrocyte sedimentation rate, fibrinogen, high-sensitivity C-reactive protein (CRP), homocysteine and IL-6 remained at a higher level in the second group. Correlation analysis showed that the psychological component of health is interconnected with the level of neutrophils ($p = 0.044$) and fibrinogen ($p = 0.050$); the physical component of health is correlated with the level of erythrocytes ($p = 0.030$), hemoglobin ($p = 0.015$), CRP ($p = 0.002$), creatine phosphokinase ($p = 0.036$) and glucose ($p = 0.017$). Regression analysis revealed that in patients with CVD three months after hospitalization, an increased glucose index contributes to deterioration, and increased hematocrit and mean hemoglobin concentration improve the quality of life of patients.*

Conclusion. *Laboratory markers that maintain the duration of a prolonged vascular reaction, violation of the rheological and metabolic properties of blood, determine the nature of the development of both psychological and cardiovascular complications.*

Key words: *COVID-19, biomarkers, psychological status, cardiovascular disease*

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ОЦЕНКА ПСИХОЭМОЦИОНАЛЬНОГО СОСТОЯНИЯ ПАЦИЕНТОВ, ПЕРЕНЁСШИХ COVID-19-АССОЦИИРОВАННУЮ ПНЕВМОНИЮ, ВО ВЗАИМОСВЯЗИ С ЛАБОРАТОРНЫМИ ПОКАЗАТЕЛЯМИ

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РЕЗЮМЕ

Цель. *Исследовать особенности и ассоциацию психологических и лабораторных показателей у пациентов с сердечно-сосудистыми заболеваниями (ССЗ), перенёсших COVID-19-ассоциированную пневмонию, с целью уточнения факторов, влияющих на возможность развития отсроченных психологических и сердечно-сосудистых нежелательных явлений.*

Материалы и методы. *В исследование включены 350 пациентов, сформировано две группы исследования. Первая группа – 92 пациента без ССЗ, вторая – 258 пациентов с ССЗ. Оценивали параметры общего и биохимического анализов крови, психологические показатели по данным анкетирования с использованием скрининговых шкал GAD-7 (General Anxiety Disorder-7 – признаки тревоги), PHQ-9 (Patient Health Questionnaire-9 – признаки депрессии) и ШВС (шкала воспринимаемого стресса – признаки стресса) и опросника качества жизни (SF-36, Short Form 36) во время госпитализации и через 3 месяца после выписки из моногоспиталя.*

Результаты. *Через 3 месяца в общей группе пациентов признаки тревоги и депрессии выявлены более чем у 30 % обследованных пациентов, признаки стресса – у 10,4 %. В группе с наличием ССЗ нарушения психоэмоциональной сферы определены у 1/4 больных, а выраженный стресс – у 8 % включённых в исследование. Кроме этого, зарегистрировано, что показатели скорости оседания эритроцитов, фибриногена, высокочувствительного С-реактивного белка (СРБ), гомоцистеина и ИЛ-6 сохранились на более высоком уровне во второй группе. Корреляционный анализ показал, что психологический компонент здоровья взаимосвязан с уровнем нейтрофилов ($p = 0,044$) и фибриногена ($p = 0,050$); физический компонент здоровья взаимосвязан с уровнем эритроцитов ($p = 0,030$), гемоглобина ($p = 0,015$), СРБ ($p = 0,002$), креатинфосфокиназы ($p = 0,036$) и глюкозы ($p = 0,017$). Регрессионный анализ выявил, что у пациентов с ССЗ через 3 месяца после госпитализации повышенный показатель глюкозы способствует ухудшению, а повышенные показатели гематокрита и средней концентрации гемоглобина – улучшению качества жизни пациентов.*

Заключение. *Лабораторные маркеры, поддерживающие длительность пролонгированной сосудистой реакции, нарушение реологических и метаболических свойств крови, определяют характер развития как психологических, так и сердечно-сосудистых осложнений.*

Ключевые слова: *COVID-19, психологический статус, биомаркеры, сердечно-сосудистые заболевания*

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INTRODUCTION

The pandemic of coronavirus infection COVID-19 (COronaVIrus Disease-2019), which is caused by a new strain of coronavirus – SARS-CoV-2 (severe acute respiratory syndrome coronavirus-2), has caused a rapid increase in the number of cases and high mortality worldwide [1]. Despite the tropism of SARS-CoV-2 to the lungs, COVID-19 has a high risk of developing multiple organ failure (MOF), including due to cardiovascular system (CVS) diseases [1, 2]. The expression of receptors in the vascular wall, cardiomyocytes makes it possible to partially explain the pathogenetic basis of the occurrence and features of the course of cardiovascular diseases, and the effect of the virus on the central nervous system determines the development of neurological and psychological disorders [3, 4].

At the beginning of the pandemic, there was no information about the long-term consequences of this infectious disease, but as the course of the process was studied, more and more data appeared in the literature regarding an expanded spectrum of systemic, cardiovascular, neurological and psychosocial symptoms. The authors described symptoms of varying duration from 1.5 months to 1 year from the onset of the acute stage of the disease, and there was not always a correlation between the severity of COVID-19, the number and severity of delayed manifestations [5]. It is assumed that the mechanisms underlying the post-COVID syndrome include changes in the immune response and damage to the vascular bed with the development of hypercoagulable thrombotic complications [6]. The entry point into the central nervous system for the virus can be either indirect – through the bloodstream, or direct – through the lattice plate. Moreover, it is assumed that the infection can cause a general depression of the hypothalamus-pituitary axis, associated with the systemic effect of inflammation and hypoxia [7]. Post-treatment follow-up is necessary not only to understand the relationship between the manifestations of the post-COVID syndrome and the course of the disease caused by the SARS-CoV-2 virus, but also to justify the need to develop algorithms for effective prevention of post-covid complications, including programs for restoring psychological health.

THE AIM OF THE STUDY

To study peculiarities and association of laboratory and psychological indicators in patients with cardiovascular diseases who have underwent COVID-19 to optimize preventive measures against the development of delayed cardiovascular and psychological adverse events.

MATERIALS AND METHODS

Prospective study complying with the standards of Good Clinical Practice and the provisions of the Helsinki Declaration of the World Medical Association. Research protocol was approved by the Committee on Biomedical Ethics of the Tyumen Cardiology Research Center – Branch of the Tomsk National Research Medical Center of the Russian Academy of Sciences (Protocol No. 159 dated July 23, 2020). Prior to enrollment in the study, each of the study participants received written informed consent to use the survey results for scientific purposes. The study is registered in the clinical research database ClinicalTrials.gov (identifier: NCT04501822).

Patients were identified according to the data of the 1C medical information system of the monoinfective hospital on the basis of the Tyumen Regional Clinical Hospital in the period from April 10, 2020 till July 11, 2021. Data on diagnoses and examination results during the hospitalization of patients in the monohospital are taken from the extracts provided by patients from medical records and 1C system data. The inclusion criteria were: a documented diagnosis of COVID-19 associated pneumonia and the patient's desire to participate in the follow-up. Criteria for non-inclusion: chronic and systemic diseases in the acute stage; diseases accompanied by pneumofibrosis; oncological diseases detected less than 5 years ago. Exclusion criteria: pregnancy, refusal to participate in the study.

The study included 350 patients who agreed to follow-up. The patients were divided into two groups. The first group included 92 patients without cardiovascular diseases (CVD), the average age was 42.16 ± 11.18 years. The second group included 258 patients with CVD (arterial hypertension (AH) and coronary heart disease (CHD)), the average age was 56.30 ± 8.44 years. There were statistically significant differences in age, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), body mass index (BMI) with higher indicators in the second group ($p < 0.001$). The differences of the listed parameters between the groups did not affect the study of the parameters dynamics within the groups. There were no statistically significant differences by gender in the study groups ($p < 0.312$), women accounted for 56.5 % (52 patients) in the first group and 50.4 % (130 patients) in the second. According to the chest computed tomography data, initially in the first group the volume of lung lesion of more than 50 % was registered in 30.7 % of cases, in the second group – in 57.8 % of cases.

With respect to CVDs in the second group, 98 % of patients had hypertension, 20.5 % had coronary artery disease, 32.6 % had cardiac arrhythmias, etc. By the time of the control visit after 3 months, patients in the second group (with CVDs) in 22.4 % of cases were taking drugs of angiotensin-converting enzyme inhibitors (ACE inhibitors), in 48.2 % of cases – angiotensin receptor blockers (ARBs), in 46.6 % of cases – beta blockers, in 61.7 % of cases – statins, in 19.8 % – acetylsalicylic acid preparations, in 7.51 % – oral anticoagulants.

The study evaluated the data of laboratory tests of blood samples taken during hospitalization and at the point 3 months after discharge from the monohospital. The parameters of the Complete Blood Count (CBC) were determined by the impedance method with flow cytome-

try technologies on 5Diff analyzer "Mindrey BC 5800" (China); creatinine, liver enzymes, total cholesterol, fasting glucose, concentration of C-reactive protein (CRP) – "Cobas integra plus 400" (Italy), reagents of Mindrty were studied from biochemical parameters; highly sensitive CRP (hs-CRP) – solid-phase enzyme immunoassay, Vector Best reagents (Russia); interleukin-6 (IL-6) – solid-phase, chemiluminescent enzyme immunoassay, IMMULITE 1000 Systems SIEMENS Healthcare Diagnostics (Germany); and homocysteine – on the analyzer "IMMULITE 2000" (Siemens Diagnostics, USA), solid-phase, competitive, chemiluminescent enzyme immunoassay, reagents from SIEMENS Healthcare Diagnostics (Germany); coagulogram parameters – on Destiny Plus analyzer (Ireland), reagents from NPO Renam (Russia). The psycho-emotional sphere of patients was studied using the screening scales GAD-7 (General Anxiety Disorder-7 – signs of anxiety), PHQ-9 (Patient Health Questionnaire-9 – signs of depression) and SPS (scale of perceived stress – signs of stress). For anxiety and depression scales, the threshold value for the presence of signs of disorders was considered to be 5 scores, for signs of severe stress – 30 scores. The quality of life (QOL) was assessed using SF-36 questionnaire, which allows us to characterize this concept quantitatively according to 8 specific and 2 generalized scales showing psychological and physical health. The physical health includes Physical functioning, Role-based physical functioning, Pain intensity and overall health status scales. The psychological health consists of Mental health, Role-based emotional functioning and Vitality scales. In this paper, we relied on the indicators of generalized scales [8–10].

Statistical analysis was carried out using IBM SPSS Statistics 21 application software package (IBM Corp., USA). Depending on the distribution, when comparing the indicators in two independent groups, the Student's t-test or Mann – Whitney U test were used. With a normal distribution, the data were presented as mean (M) and standard deviation (SD), with a distribution other than normal, the data were presented as median (Me) and interquartile range [25 %; 75 %]. The dynamics between related groups was calculated using the paired Student t-test or the Wilcoxon test. Spearman and Pearson correlation analysis (depending on the type of data distribution) and linear regression with step-by-step inclusion of predictors in the model were used. The purpose of the regression analysis was to identify the predictors that have the greatest impact on the psycho-emotional state of patients with CVDs who have suffered COVID-19 pneumonia. The results were evaluated as statistically significant at the two-sided $p < 0.05$ level.

RESULTS

The analysis of the parameters of the complete blood count in the study groups of patients is given in Table 1.

Analysis of the table data showed that individual erythrocyte parameters, such as RDW-SD, RDW-CV and ESR, in the second group of patients exceeded the ones in the first group ($p < 0.001$, $p < 0.023$ and $p < 0.001$, respectively).

The remaining parameters varied in different directions in both groups, remaining within the reference values to the observation point "3 months after discharge from the hospital". The level of ESR decreased statistically significantly in the second group of patients ($p < 0.001$).

The characteristics of leukocyte parameters in the patients included in the study are given in Table 2.

The data show that at baseline there was a statistically significant increase in WBS, NLR and a decrease in the LYM/CRP ratio in patients of the second group ($p < 0.001$).

Three months after admission, there were statistically significant decreases in WBC, NEU, NLR ratio and increases in EOS, LYM/CRP in both groups and LYM in the second group of patients. However, the parameters of WBC, LYM, NEU, while remaining statistically significantly higher than in the first group, indirectly confirm the presence of a persistent prolonged inflammatory reaction in patients with CVDs caused by the coronavirus infection.

According to platelet counts, no statistically significant difference was found at the baseline of the study. Three months after discharge, a statistically significant decrease in the mean platelet volume (MPV) was registered: baseline in the first group – 11.20 [10.70; 11.9] fL, in dynamics – 8.40 [7.90; 8.90] fL, in the second group – 11.20 [10.50; 11.70] and 8.30 [7.70; 11.70] fL, respectively ($p < 0.001$ for both groups); platelet large cell count (PLCC): baseline in the first group – 35.00 [30.20; 41.60] %, in dynamics – 23.80 [19.30; 29.70] %, in the second group – 34.30 [28.80; 37.70] and 23.80 [19.30; 28.80] %, respectively ($p < 0.001$ for both groups); statistically significant increase in platelet count (PLT): baseline in the first group – 206.00 [152.00; 258.00], in dynamics – 226,00 [190,00; 261,00] $\times 10^9$/L, in the second group – 203.50 [156.50; 250.50] and 230,00 [200,00; 272,00] $\times 10^9$/L, respectively ($p < 0.001$).

Of the hemostasis parameters, patients in the second group had a statistically significant fibrinogen level increase at baseline compared to the first group (4.60 [3.60; 5.80] and 3.90 [3.60; 5.80] g/L, respectively; $p < 0.001$) with achievement of reference values in both patient groups in 3 months. In addition, increased fluctuations of these parameters of APTT and PTI were recorded in the second patient group.

At baseline, characterization of biochemical parameters in the groups showed an excess of fasting glucose in both groups (6.70 [6.22; 7.39] and 7.52 [6.79; 9.40] mmol/L, respectively) with a statistically significant decrease in the parameters after 3 months ($p < 0.001$, respectively, for the groups) and a statistically significant excess of HbA1c (6.70 [5.90; 8.00] in the second group); excess values of aspartate aminotransferase (AST) (32.80 [23.45; 50.80] U/L), alanine aminotransferase (ALT) (34.20 [22.90; 53.20] U/L) and total cholesterol (TCL) (4.11 [3.32; 4.84] mmol/L) in the second patient group. In addition, there was a statistically significant excess of baseline lactate dehydrogenase (LDH) values (361.14 ± 135.98 and 437.50 ± 212.85 U/L) and max CRP (29.8 [3.80; 24.60]

TABLE 1

COMPARATIVE CHARACTERISTICS OF ERYTHROCYTE PARAMETERS IN PATIENTS WITH THE ABSENCE AND PRESENCE OF CARDIOVASCULAR DISEASES WHO SUFFERED COVID-19 PNEUMONIA, AT BASELINE AND THREE MONTHS AFTER HOSPITAL ADMISSION

Parameters	Examination period	Without CVDs (*n* = 92)	With CVDs (*n* = 258)	*p*
RBC, 10^{12}/L (norm: male – 4.0–5.2; female – 3.9–4.7)	At baseline	4.79 ± 0.49	4.71 ± 0.54	0.200
	In 3 months	4.76 ± 0.43	4,90 ± 0,44	**0.003**
	p	0.151	**< 0.001**	
HGB, g/L (norm: male – 130–166; female – 117–140)	At baseline	137.50 [125.50; 146.50]	137.00 [127.00; 146.00]	0.770
	In 3 months	136.00 [127.00; 146.00]	142.00 [132.00; 149.00]	**0.008**
	p	0.852	**< 0.001**	
HCT, % (norm: male – 39–49; female – 35–43)	At baseline	40.20 [37.80; 43.10]	40.50 [37.50; 43.00]	0.968
	In 3 months	43.70 [40.80; 46.00]	45.40 [42.60; 48.10]	**< 0.001**
	p	**< 0.001**	**< 0.001**	
MCV, fL (norm: 80–95)	At baseline	85.10 [80.40; 87.20]	85.00 [82.20; 88.50]	0.095
	In 3 months	92.00 [88.00; 94.00]	92.00 [90.00; 95.00]	**0.039**
	p	**< 0.001**	**< 0.001**	
MCH, pg (norm: 27–31)	At baseline	28.90 [27.70; 29.70]	29.00 [27.90; 30.00]	0.272
	In 3 months	29.00 [28.00; 30.00]	29.00 [28.00; 30.00]	0.903
	p	**0.055**	0.876	
MCHC, g/dL (norm: 31–37)	At baseline	33.60 [33.10; 34.30]	33.80 [33.20; 34.50]	0.360
	In 3 months	32.00 [31.00; 32.00]	31.00 [31.00; 32.00]	**0.001**
	p	–	–	
RDW–SD, fL (norm: 35–56)	At baseline	39.50 [37.50; 40.90]	40.50 [38.80; 43.00]	**0.001**
	In 3 months	46.40 [44.30; 48.00]	48.50 [46.30; 51.30]	**< 0.001**
	p	**< 0.001**	**< 0.001**	
RDW–CV, % (norm: 11.5–14.5)	At baseline	13.00 [12.40; 13.60]	13.30 [12.80; 13.90]	**0.023**
	In 3 months	12.40 [12.00; 12.80]	12.90 [12.30; 13.60]	**< 0.001**
	p	**< 0.001**	**< 0.001**	
ESR, mm/h (norm: 0–15)	At baseline	12.50 [8.00; 16.00]	39.00 [24.00; 53.00]	**< 0.001**
	In 3 months	11.00 [7.00; 17.00]	12.00 [8.00; 19.00]	0.327
	p	0.600	**< 0.001**	

Note. RBC – red blood cells; HGB – hemoglobin (concentration); HCT – hematocrit; MCV – mean corpuscular/cell volume; MCH – mean corpuscular haemoglobin; MCHC – mean cell haemoglobin concentration; RDW-SD – red cell distribution width, standard deviation); RDW-CV – red cell distribution width, coefficient of variation/variation coefficient; ESR – erythrocyte sedimentation rate. *p* is the statistical significance of the differences in parameters: horizontally – between the first and second groups; vertically – within the group in dynamics – at baseline and 3 months after discharge from the hospital.

TABLE 2

COMPARATIVE CHARACTERISTICS OF LEUKOCYTE PARAMETERS IN PATIENTS WITH THE ABSENCE AND PRESENCE OF CARDIOVASCULAR DISEASES WHO SUFFERED FROM COVID-19 PNEUMONIA, AT BASELINE AND 3 MONTHS AFTER HOSPITAL ADMISSION

Parameters	Examination period	Without CVDs (*n* = 92)	With CVDs (*n* = 258)	*p*
WBS, 10^9/L (norm: 4.0–8.8)	At baseline	4.98 [3.88; 6.70]	6.53 [4.92; 8.13]	**< 0.001**
	In 3 months	4.56 [4.04; 5.72]	5.65 [4.81; 6.78]	**< 0.001**
	p	**0.050**	**< 0.001**	
LYM, 10^9/L (norm: 1,4–8)	At baseline	1.43 [1.01; 1.95]	1.23 [0.88; 1.67]	**0.035**
	In 3 months	1.58 [1.41; 1.90]	1.92 [1.61; 2.32]	**< 0.001**
	p	**0.011**	**< 0.001**	
NEU, 10^9/L (norm: 1.8–7.7)	At baseline	2.94 [2.02; 4.43]	4.37 [2.98; 6.29]	**< 0.001**
	In 3 months	2.52 [2.04; 3.16]	3.05 [2.38; 3.81]	**< 0.001**
	p	**0.010**	**< 0.001**	
EOS, 10^9/L (norm: 0–5)	At baseline	0.03 [0.01; 0.10]	0.02 [0.01; 0.06]	**0.025**
	In 3 months	0.10 [0.06; 0.16]	0.12 [0.08; 0.18]	**0.048**
	p	**< 0.001**	**< 0.001**	
NLR (norm: 1.6–1.8)	At baseline	1.96 [1.30; 3.09]	3.47 [2.03; 6.18]	**< 0.001**
	In 3 months	1.57 [1.17; 2.06]	1.57 [1.17; 2.00]	0.659
	p	**0.004**	**< 0.001**	
LYM/CRP	At baseline	0.11 [0.02; 0.38]	0.02 [0.01; 0.04]	**< 0.001**
	In 3 months	0.51 [0.32; 1.63]	0.39 [0.26; 0.74]	**0.005**
	p	**< 0.001**	**< 0.001**	

Note. WBS – white blood cells; LYM – the number of lymphocytes; NEU – the number of neutrophils; EOS – the number of eosinophils; NLR – the ratio of neutrophils to lymphocytes; LYM/CRP – the ratio of leukocytes to C-reactive protein. *p* is the statistical significance of the differences in parameters: horizontally – between the first and second groups; vertically – within the group in dynamics – at baseline and 3 months after discharge from the hospital.

and 65.10 [32.00; 128.00 mg/L]) in both groups with a decrease in the parameters after 3 months with a continued value excess in the second group ($p < 0.001$, respectively).

It is important to note that during the planned complex drug therapy performed 3 months after discharge, the second group showed increased levels of homocysteine, IL-6, and hs-CRP (14.36 ± 6.08 and 14.67 ± 6.69 mmol/L), (1.75 [1.30; 2.45] and 2.26 [1.60; 3.90] μg/ml), (2.13 ± 2.26 and 4.13 ± 3.92 mg/L), exceeding both the reference values and the indicators in the first group. The recorded parameters related to the planned complex drug therapy indicate the presence of increased vascular inflammatory potential for the development of possible adverse events in patients during the post-COVID period.

Simultaneously with blood sampling at the point "3 months after hospital discharge", a medical psychologist collected questionnaire details from all patients reflecting the psycho-emotional state of patients who had un-

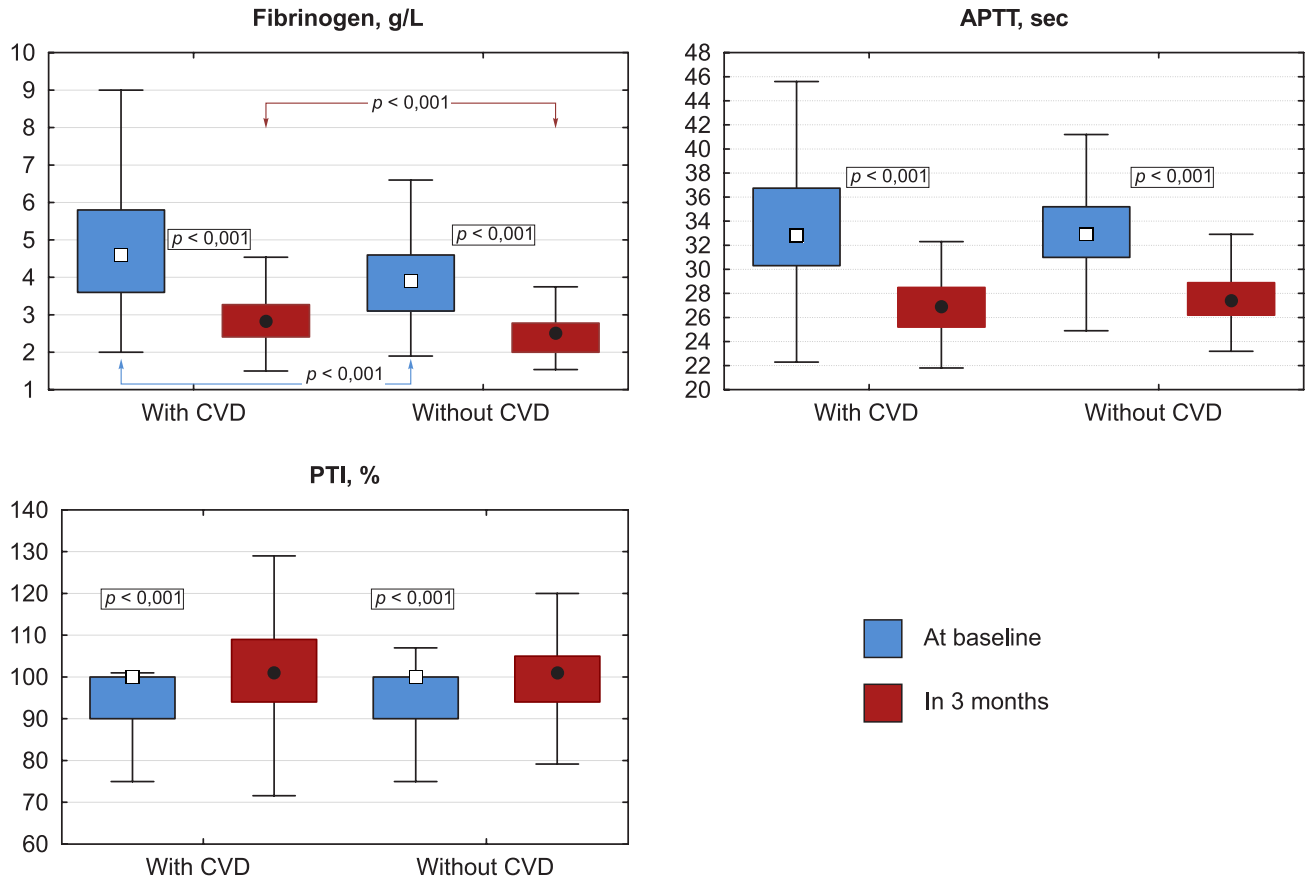

FIG. 1.

Hemostasis parameters in patients with and without cardiovascular disease who had COVID-19 pneumonia at baseline and three months after hospital admission

TABLE 3

COMPARATIVE CHARACTERISTICS OF THE SEVERITY OF DISORDERS OF THE PSYCHO-EMOTIONAL SPHERE AND QUALITY OF LIFE IN PATIENTS WITH THE ABSENCE AND PRESENCE OF CARDIOVASCULAR DISEASES WHO SUFFERED FROM COVID-19 PNEUMONIA, THREE MONTHS AFTER HOSPITAL ADMISSION

Parameters	Without CVD, Me [25%; 75%]	With CVD, Me [25%; 75%]	*p*
Signs of anxiety	3.00 [1.00; 6.00]	2.00 [1.00; 6.00]	0.770
Signs of depression	3.00 [1.00; 5.00]	3.00 [1.00; 6.00]	0.507
Signs of stress	20.00 [15.00; 25.00]	21.00 [15.00; 26.00]	0.300
The physical health	50.27 [47.31; 52.72]	46.88 [41.33; 50.88]	**0.000**
Psychological health	67.08 [57.17; 71.18]	65.55 [57.66; 72.01]	0.748

dergone COVID-19. Screening scales GAD-7 (signs of anxiety), PHQ-9 (signs of depression), SHVS (signs of stress) and SF-36 questionnaire were used to assess patients' quality of life. The data of general characterization of the psychological sphere of patients showed that in the general group of patients, signs of anxiety and depression were detected 3 months after hospital discharge in more than 30 % of the examined patients, signs of stress – in 10.4 %. In the group of patients with CVDs, disorders of the psycho-emotional sphere were found in 1/4 of the patients en-

TABLE 4

RESULTS OF REGRESSION ANALYSIS OF THE EFFECT OF BLOOD PARAMETERS IN PATIENTS WITH CARDIOVASCULAR DISEASES ON THE PSYCHO-EMOTIONAL STATE AND QUALITY OF LIFE THREE MONTHS AFTER HOSPITAL DISCHARGE

Parameters	Predictors	Non-standardized coefficient b	Standardized coefficient β	*p*
Severity of anxiety	Thrombocrit	17.855	0.226	0.014
	Fibrinogen	1.700	0.256	0.007
Severity of depression	LDH	0.030	0.226	0.015
	Ferritin	–0.008	–0.203	0.031
Severity of stress	Fibrinogen	3.002	0.265	0.003
	Glucose (acute period)	–0.727	–0.356	0.003
The physical health	Hematocrit	0.326	0.188	0.002
	Average hemoglobin concentration	1.068	0.148	0.017

rolled in the study. Severe stress is typical for 8 % of those included in the study.

When comparing the severity of disorders of the psycho-emotional sphere and generalized indicators of QOL (SF-36), the results of only the physical health differ statistically significantly between groups of patients with the absence and presence of CVD. The data is shown in Table 3.

The physical health was statistically significantly reduced in the group of CVD patients, which is consistent with the clinical data on the presence of an increase in the frequency of crisis states of hypertension, newly detected cases of coronary heart disease (6.1 %), chronic heart failure (8.7 %) and 1 case of diabetes mellitus in this group. There were no differences between the groups by categories of psycho-emotional state.

The relationship of the psychological state of CVD patients and hematological and biochemical blood parameters is shown by the results of correlation analysis. During admission, the psychological health is inversely correlated with the level of neutrophils ($r = –0.137$; $p = 0.044$) and directly correlates with the level of fibrinogen ($r = 1.135$; $p = 0.050$); the physical health is interrelated with the level of erythrocytes ($r = 0.140$; $p < 0.030$), hemoglobin ($r = 0.158$; $p = 0.015$), CRP ($r = –0,200$; $p = 0.002$), CPK ($r = 0.175$; $p = 0.036$) and glucose ($r = –0,182$; $p = 0.017$). In the post-COVID period (3 months after discharge), the psychological health was associated with the level of transforming growth beta factor ($r = 0.404$; $p = 0.030$); the physical health was associated with the level of erythrocytes ($r = 0.143$; $p = 0.023$), hemoglobin ($r = 1.222$; $p = 0.001$), hematocrit ($r = 0.187$; $p = 0.003$). During general data processing, it was recorded that the level of anxiety and depression was more related to hematological indicators, while the level of stress was more related to the level of inflammatory parameters. The results of the regression analysis aimed at determining blood biomarkers that affect the psycho-emotional state and CVD patients's quality of life are given in Table 4.

The results of the regression analysis indicate that an increase in the level of anxiety in patients with cardiovascular diseases is associated with an increase in the blood thrombocrit level. Depression scores increase statistically significantly with an increase in fibrinogen and LDH levels and a decrease in ferritin levels. The severity of stress is affected by changes in the level of fibrinogen.

In addition, the analysis showed that in patients with cardiovascular diseases, 3 months after hospital admission, the physical health has an inverse relationship with glucose levels in the acute period of the disease. Increased glucose levels contribute to a prolonged deterioration of the physical component of QOL, especially in patients with baseline elevated glucose levels. Increased hematocrit and average hemoglobin concentration after discharge add scores to the physical health component, which indicates an improvement in patients' quality of life.

DISCUSSION

Based on a number of studies, patients who have undergone COVID-19 often show altered parameters of lab-

oratory findings in the post-COVID period, the relationship between which and newly emerged clinical manifestations may indicate the presence of a latent prognostic potential in the development of delayed cardiovascular events [11–18].

Most of the published results have been confirmed in our works and our own data have been obtained, in particular, on the association of the volume of lung tissue lesion with the parameters of erythrocyte and leukocyte formulas, coagulation profile, liver enzymes at the initial stage of the disease, on the influence of inflammatory markers and hyperglycemia on the risk of adverse vascular complications of the disease [20]. Thus, lymphopenia and eosinopenia have prognostic significance in the detection of a severe course of the disease and hospital mortality [13, 14]. Registered microangiopathies and microthrombosis in hepatic sinusoids are associated with impaired hepatic enzyme levels, with elevated bilirubin levels and hyperglycemia associated with the persistent inflammatory process in hepatocytes and cholangiocytes [15–20].

The problem of psychological consequences of COVID-19 is the object of attention. Many authors have noted a significant degree of heterogeneity in terms of populations, sampling methods, and scales in such studies, which complicates data interpretation [21, 22]. Dozens of meta-analyses are devoted to physical and mental health. For example, in Europe, more than 3 million people participated in 692 primary studies where it was shown that the prevalence of psychological problems was closely related to the patients themselves, their environment and social support. The findings clearly indicate that social isolation is associated with a number of adverse consequences for physical and mental health [23–25].

The research results published by Chinese experts showed that 53.8 % of respondents who underwent COVID-19 assessed the registered individual psychological manifestations as protective factors. Anxiety is designed to perform an adaptive function in stressful circumstances, which in a pandemic are represented by social aspects of isolation and distancing, the use of antiseptics, as well as concern about health, future and material well-being. Functional level anxiety motivates a person to look for ways to solve problems, change habitual behavior, which allows patients to strengthen their faith in the competence of physicians and reports on successful recovery, having a mobilizing effect on a person. However, the presence of severe anxiety negatively affects cognitive functioning and coping behavior aimed at overcoming problematic situations [21].

The level of psychological stress is more often associated with a deterioration in social functioning: a decrease or lack of support, the detection of COVID-19 in relatives or the loss of ones due to infection, as well as the presence of a non-transmissible disease that significantly worsens somatic health. Overstress is often combined with symptoms of anxiety or depression, which seriously impairs a person's adaptive abilities.

According to the results of research by Russian scientists, severe deterioration in both physical and emotional health has been recorded in the post-reproductive-stage women after suffering a moderately severe form of COVID-19. The results suggest a potential link between COVID-19 and future risk of cognitive decline, persistent deterioration of health and quality of life [23].

Depressive states are often a response to changes in social status, marital status, and material well-being. After COVID-19, factors contributing to persistent mood declines include persistent physiological manifestations of the disease (prolonged loss of taste and smell, sleep disorders, increased heartbeat and fatigue), peculiarities of disease perception and behavior (frequent news viewing and isolation after hospital discharge) [22].

It is known that patients with cardiovascular diseases are characterized by high comorbidity with disorders of the anxiety and depressive spectrum, which not only worsens the severity of the course and prognosis of the disease, but also contributes to a decrease in the effectiveness of the therapy received by the patient. In this regard, it is recommended to influence psychosocial factors with the use of pharmacological therapy and psychological correction in this category of patients [26].

During the study, the data on the study of neuroimmunological processes and their association with proinflammatory cytokines in the pathogenesis of anxiety-depressive disorders were of particular interest to us [21, 27].

Intensely perceived stress leads to activation of the autonomic nervous system and hypothalamic-pituitary-adrenal axis, resulting in increased levels of cortisol, adrenaline, norepinephrine. This in turn enhances the inflammatory response by inhibiting humoral and cellular immunity, and changes the balance of pro-inflammatory cytokines. At the same time, SARS-CoV-2 infection leads to the production of IL-Ib and IL-6 [27]. The works of other authors confirm the relationship between fibrinogen and stress, which leads to the formation of endothelial dysfunction and deterioration of cardiovascular health [28]. It is also known that the presence of anxiety states is associated with increased levels of platelet counts [29]. The relationship between fibrinogen, depression and CVD has also been described, where researchers consider fibrinogen as the key factor in the formation of cardiovascular disorders, since this marker contributes to increased platelet aggregation and blood clotting, which increases plasma viscosity and thrombosis [30]. In addition, the literature describes the relationship of depressive states with ferritin, which is a biomarker of the iron amount in the blood. H.S. Lee et al. found a relationship between ferritin, depression, and overweight, which aggravates the course of CVD [31]. The effect of glucose and the consequences of the formation of excessive amounts of metabolically active free oxygen radicals in the acute period of COVID-19 on the deterioration of the physical aspect of QOL is of interest [32]. In addition, we should not forget about the possible mechanisms of drug-induced lesion processes of the target organs and systems, modifying both psychological and physical components of health [21, 25].

The decrease in the level of proinflammatory cytokines IL-1ß, tumor necrosis factor α, responsible for depressive-

like behavior recorded in animal models by antidepressants broadens the research horizons of possible prevention and complex therapy of patients with viral infections in the future [21].

Study limitations

In this paper, only generalized data on the psychological and physical components of health were studied. In the future, detailed characteristics of the studied data will be described, taking into account age, gender, and social characteristics.

CONCLUSION

Analysis of the literature data and our own research results suggest that the detected changes in biomarkers and the presence of their relationship with psychological manifestations allow us to consider the expectation of an increase in anxiety-depressive disorders in COVID-19 survivors justified, determining the relevance of the medical problem under study. The lack of data in terms of the common links in the pathogenesis of the investigated combined states allows, through the study of laboratory markers, to identify a range of parameters that together can both initiate and maintain the duration of a prolonged vascular reaction that determines the risk of developing both cardiovascular and neuropsychiatric complications.

Our findings indicate the need for dynamic follow-up of patients and the feasibility of developing preventive measures optimized by specialized specialists, both for the post-COVID period and for future waves of the pandemic and subsequent daily life.

Conflict of interest

The authors of this article declare the absence of a conflict of interest.

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