DOI: 10.20514/2226-6704-2025-15-1-42-56
УДК 616.248-036.11-085.234
EDN: NYAGOE

Г.Б. Батенова[1,2], Е.И. Дедов[2], А.Ю. Орехов[1], А.А. Дюсупов[1], Д.Г. Ыгиева[1], М.Р. Пивин[1], А.М. Манатова[3], Л.М. Пивина[1]

[1] — НАО «Медицинский университет Семей», Семей, Казахстан
[2] — ФГАОУ ВО РНИМУ им. Н.И. Пирогова МЗ РФ, Москва, Россия
[3] — Национальный научный онкологический центр, Астана, Казахстан

ОЦЕНКА ВЗАИМОСВЯЗИ КЛИНИЧЕСКИХ И ЛАБОРАТОРНЫХ ПОКАЗАТЕЛЕЙ С ПЕРЕНЕСЕННОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИЕЙ У ПАЦИЕНТОВ С РЕСТЕНОЗОМ КОРОНАРНЫХ АРТЕРИЙ

G.B. Batenova[1,2], E.I. Dedov[2], A.Yu. Orekhov[1], A.A. Dyussupov[1], D.G. Ygiyeva[1], M.R. Pivin[1], A.M. Manatova[3], L.M. Pivina[1]

[1] — Semey Medical University, Semey, Kazakhstan
[2] — Pirogov Russian National Research Medical University of the Ministry of Healthcare of the Russian Federation, Moscow, Russia
[3] — National Research Oncology Center, Astana, Kazakhstan

Assessment of the Association Between Clinical and Laboratory Parameters and Past Coronavirus Infection in Patients with Coronary Artery Restenosis

Резюме

Понимание факторов риска рестеноза стента коронарных артерий имеет особую важность в отношении лиц, перенесших коронавирусную инфекцию (КВИ). Такие пациенты требуют тщательного наблюдения, приоритетного лечения и профилактики. **Целью** нашего исследования явилась оценка связи клинических и лабораторных показателей с перенесенной коронавирусной инфекцией у пациентов с рестенозом коронарных артерий. **Материалы и методы.** Проведено поперечное исследование на сплошной выборке пациентов с ИБС (931 пациент), прошедших повторную реваскуляризацию миокарда в период с 2020 г. по 2023 г. 420 пациентов основной группы имели рестеноз стента коронарных артерий, из них 162 (38,5 %) пациентов перенесли в прошлом КВИ. В контрольную группу вошли 511 пациентов с повторной реваскуляризацией миокарда без рестеноза стента, из них 107 (20,9 %) перенесли КВИ. Лабораторные анализы включали тропонин I, D-димер, креатинкиназу (КК), креатинкиназу-МВ (КК-МВ), сывороточный креатинин и глюкозу, С-реактивный белок (СРБ), аланинаминотрансферазу (АЛТ), аспартатаминотрансферазу (АСТ) и фибриноген, антитела IgG и IgM к coronavirus и определение РНК методом полимеразной цепной реакции. Статистические расчеты проводились с использованием программного обеспечения SPSS версии 20.0. **Результаты**. Было установлено наличие статистически значимо более высоких показателей антител IgG к коронавирусу и С-реактивного протеина в основной группе исследования в сравнении с группой контроля. При делении групп исследования на подгруппы пациентов с перенесенной КВИ и без КВИ были установлены статистически значимые различия по уровню тропонина ($p<0,001$), в том числе в группе с рестенозом и КВИ в сравнении с группами без рестеноза с КВИ, с рестенозом без КВИ и в группах с реваскуляризацией без КВИ и с рестенозом без КВИ. Уровни D-димера, КФК, КФК-МВ, СРБ и АЧТВ имели статистически значимые различия в группах с перенесенным КВИ в сравнении с группами без КВИ. Результаты множественного регрессионного анализа свидетельствовали о наличии статистически значимой положительной взаимосвязи в группах исследования между развитием инфаркта миокарда и такими показателями, как СРБ, глюкоза крови, липопротеиды низкой плотности (ЛПНП), перенесенная КВИ, а также отрицательной взаимосвязи с фракцией выброса левого желудочка и липопротеидами высокой плотности (ЛПВП). Роль данных предикторов в развитии инфаркта миокарда была установлена с помощью ROC-анализа. **Заключение.** Результаты нашего исследования свидетельствуют о наличии взаимосвязи перенесенной коронавирусной инфекции с повышением риска развития рестеноза коронарных артерий у лиц с предшествующей реваскуляризацией миокарда.

Ключевые слова: *рестеноз коронарных артерий, коронавирусная инфекция, лабораторные показатели, отношения шансов, реваскуляризация миокарда*

Конфликт интересов

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

Источники финансирования

Исследование выполнено при финансовой поддержке Комитета науки Министерства образования и науки Республики Казахстан (грант № AP19677465 «Совершенствование системы оказания медицинской помощи лицам с предшествующей реваскуляризацией миокарда, перенесшим коронавирусную инфекцию»)

Соответствие принципам этики

Исследование одобрено локальным Этическим комитетом ФГАОУ ВО РНИМУ им. Н.И. Пирогова Минздрава России (выписка из протокола № 214 от 24 января 2022 г.). Также исследование одобрено локальным Этическим комитетом НАО «Медицинский Университет Семей», Казахстан (выписка из протокола № 7 от 16 марта 2022 г.).

Информированное согласие было получено от всех субъектов, участвовавших в исследовании. Письменное информированное согласие было также получено от пациентов для публикации этой статьи.

Статья получена 16.09.2024 г.
Одобрена рецензентом 04.11.2024 г.
Принята к публикации 23.12.2024 г.

Для цитирования: Батенова Г.Б., Дедов Е.И., Орехов А.Ю. и др. ОЦЕНКА ВЗАИМОСВЯЗИ КЛИНИЧЕСКИХ И ЛАБОРАТОРНЫХ ПОКАЗАТЕЛЕЙ С ПЕРЕНЕСЕННОЙ КОРОНАВИРУСНОЙ ИНФЕКЦИЕЙ У ПАЦИЕНТОВ С РЕСТЕНОЗОМ КОРОНАРНЫХ АРТЕРИЙ. Архивъ внутренней медицины. 2025; 15(1): 42-56. DOI: 10.20514/2226-6704-2025-15-1-42-56. EDN: NYAGOE

Abstract

Understanding the risk factors for coronary in-stent restenosis is particularly important in patients with coronavirus disease (COVID-19). Such patients require careful monitoring, priority treatment, and prevention. **The aim** of our study was to assess the association between clinical and laboratory parameters and previous coronavirus infection in patients with coronary artery restenosis. **Materials and methods.** A cross-sectional study was conducted on a continuous sample of patients with coronary artery disease who underwent repeated myocardial revascularization in the period from 2020 to 2023 (931 patients). 420 patients in the main group had coronary artery stent restenosis, of which 162 (38.5 %) had suffered from coronavirus infection (CVI). The control group included 511 patients with repeated myocardial revascularization without stent restenosis, of whom 107 (20.9 %) had undergone CVI. Laboratory tests included troponin I, D-dimer, creatine kinase (CK), creatine kinase-MB (CK-MB), serum creatinine and glucose, C-reactive protein (CRP), alanine aminotransferase (ALT), aspartate aminotransferase (AST) and fibrinogen, IgG and IgM antibodies to coronavirus and RNA detection by polymerase chain reaction. Statistical calculations were performed using SPSS version 20.0 software. **Results:** It was established that there were statistically significantly higher levels of IgG antibodies to coronavirus and C-reactive protein in the main study group compared to the control group. When dividing the study groups into subgroups of individuals with and without previous CVI, statistically significant differences in troponin levels were found ($p<0.001$): between the level in the group with restenosis and CVI compared to groups without restenosis with CVI, with restenosis without CVI, and in groups with revascularization without CVI and with restenosis without CVI. The levels of D-dimer, CPK, CPK-MB, CRP, and APTT had statistically significant differences in the groups with previous CVI compared to the groups without CVI. The results of multiple regression analysis indicated a statistically significant positive relationship in the study groups between the development of myocardial infarction and such indicators as CRP, blood glucose, low-density lipoproteins (LDL), previous CVI, as well as a negative relationship with left ventricular ejection fraction and high-density lipoproteins (HDL). The role of these predictors in the development of myocardial infarction was confirmed using ROC analysis. **Conclusion:** The results of our study indicated a relationship between previous coronavirus infection and an increased risk of coronary artery restenosis in patients with previous myocardial revascularization.

Keywords: *coronary artery restenosis, coronavirus infection, laboratory parameters, odds ratios, myocardial revascularization*

Conflict of interests

The authors declare no conflict of interests

Sources of funding

The study was carried out with the financial support of the Science Committee of the Ministry of Education and Science of the Republic of Kazakhstan (grant № AP19677465 «Improving the system of providing medical care to individuals with previous myocardial revascularization who have had coronavirus infection»)

Conformity with the principles of ethics

The study was approved by the Local Ethics Committee of the Pirogov Russian National Research Medical University of the Ministry of Health of the Russian Federation (extract from the protocol No. 214. January 24, 2022). The study was also approved by the Local Ethics Committee of Semey Medical University, Kazakhstan (extract from the protocol No. 7. March 16, 2022).

Informed consent was obtained from all subjects participating in the study. Written informed consent was also obtained from patients for the publication of this article.

Article received on 16.09.2024
Reviewer approved 04.11.2024
Accepted for publication on 23.12.2024

For citation: Batenova G.B., Dedov E.I., Orekhov A.Yu. et al. Assessment of the Association Between Clinical and Laboratory Parameters and Past Coronavirus Infection in Patients with Coronary Artery Restenosis. The Russian Archives of Internal Medicine. 2025; 15(1): 42-56. DOI: 10.20514/2226-6704-2025-15-1-42-56. EDN: NYAGOE

ALT — alanine aminotransferase; AST — aspartate aminotransferase; APTT — activated partial thromboplastin time; OMB — obtuse marginal branch; DB — diagonal branch; CHD — coronary artery disease; MI — myocardial infarction; CAG — coronary angiography; CVI — coronavirus infection; CK — creatine kinase; CK MB — creatine kinase MB; HDL — high-density lipoprotein; LDL — low-density lipoprotein; INR — International Normalized Ratio;

LC — left circumflex coronary artery; RCA — right coronary artery; LAD — left anterior interventricular branch of the coronary artery; PCR — polymerase chain reaction; RNA — ribonucleic acid; DM — diabetes mellitus; ESR — erythrocyte sedimentation rate; CRP — C-reactive protein; LVEF — left ventricular ejection fraction; HR — heart rate; PCI — percutaneous coronary intervention, EchoCG — echocardiography; COVID-19 — new coronavirus infection

Introduction

In recent decades, due to progress in the field of interventional cardiology, there has been a significant increase in cardiac surgery for coronary artery stenosis and thrombosis, which has led to an increase in life expectancy for patients with acute coronary syndrome and an improvement in their quality of life. Thanks to the development of new approaches to stenting and the emergence of new-generation drug-eluting stents, the number of complications of this intervention has been significantly reduced; however, due to numerous reasons, the risk of developing restenosis or thrombosis of the installed stent remains [1].

Restenosis can be defined as an angiographically confirmed narrowing of the lumen of a coronary artery by more than 50 %, localized in the area of a previously implanted stent [2,3]. Most often, restenosis develops within the first three months after previous revascularization. After six months, the risks of restenosis decrease, and the process remains, as a rule, stable, since during this period, stent endothelialization and remodeling of the coronary vessel wall are completed. However, when using drug-eluting stents, the endothelialization process can be delayed for up to 2 years [4]. The mechanism of early restenosis development is associated with trauma to the vascular wall during device implantation, leading to the development of an inflammatory reaction accompanied by the migration of neutrophils, monocytes, and platelets and the release of inflammatory mediators [5]. Subsequently, induction of smooth muscle cell migration into the vascular intima with their accumulation and proliferation of fibroblasts is observed. Increased synthesis of extracellular matrix causes thickening of neoadventitia and neointima, narrowing the lumen of the coronary vessel in the area of the previously implanted stent [6]. Thus, there is a direct relationship between inflammation, the formation of neointima, and the development of restenosis at the site of the implanted stent [7].

At the peak of the COVID-19 pandemic, due to the high burden on the healthcare system and the sharply increased need for resources, the activity of interventional cardiology worldwide significantly decreased, and the number of cardiac catheterization procedures decreased. At the same time, the need for repeated cardiac surgery for coronary restenosis due to coronavirus infection increased [8]. Understanding risk factors for stent thrombosis and restenosis is of particular importance for individuals at risk for adverse outcomes, especially elderly patients with previously revascularized myocardium and associated medical conditions who have had COVID-19. Such patients require close monitoring, priority treatment, and prophylaxis.

It has been established that coronavirus infection promotes thrombus formation in arterial and venous vessels and acts as a provoking factor in the development of acute coronary syndrome (myocardial infarction (MI) or unstable angina). Hypercoagulation risk can lead to the development of stent thrombosis, which progresses in the presence of other risk factors [4].

The aim of our study was to assess the interrelationship between clinical and laboratory parameters and previous coronavirus infection in patients with coronary artery restenosis.

Material and Methods

Characteristics of the study groups

We conducted our study on a continuous sample of patients with coronary artery disease who underwent repeat myocardial revascularization between May 2020 and May 2023. Design of the study is cross-sectional one. A total of 931 patients were included in the study. Inclusion criteria: patients with coronary artery stent restenosis aged 34 to 88 years with full information on clinical signs of myocardial ischemia, laboratory and instrumental examination data. 420 patients included in the main group had coronary artery stent restenosis requiring repeat revascularization, of which 162 (38.5 %) patients had a history of coronavirus infection for one year. The control group included 511 patients with repeated myocardial revascularization without stent restenosis. Of these, 107 (20.9 %) patients had coronavirus infection for the previous year.

The endpoints for the study were cardiovascular mortality, hospital discharge, and the incidence of coronary artery stent restenosis depending on the time of its development.

Exclusion criteria: individuals with autoimmune systemic diseases, oncological and hemato-oncological patients, patients with acute infectious and inflammatory diseases, coagulopathies, pregnancy and the postpartum period, mental illness, as well as individuals who refused to participate in the study.

After risk stratification, all patients underwent coronary angiography (CAG) followed by myocardial

Table 1. *Social-demographic characteristics of patients included in the study (N = 931)*

Indicators		Absolute number	%
Age (years)	<50 years	76	8.17
	51-70 years	592	63.58
	71>	263	28.25
Sex	male	700	75.18
	female	231	24.82
Job status	disabled person	76	8.17
	pensioner	508	54,56
	unemployed	133	14.28
	works	214	22.99
Have been vaccinated against COVID-19		504	54,1
Therapy received prior to hospitalization			
Dual antiplatelet therapy		738	79,2
Triple antiplatelet therapy		193	20,8
Beta Blockers		705	75,7
RAAS Blockers		814	87,4
Statins		837	89,9
Mineralocorticoid receptor antagonists		524	56,2
Arterial hypertension		911	97,9
Diabetes mellitus		191	20,5
Obesity I-III degree		217	23,3
Chronic kidney disease		248	26,6
Chronic heart failure		768	82,5

revascularization with stenting. A study participant card was created for each patient. Patients were informed that they were included in the study and that the results of the study would be published in a scientific journal with confidentiality of information. Written consent to participate in the study was obtained from each patient.

The average age of all patients included in the study was 64.31 ± 8.19 years. For women, this rate was 67.07 ± 10.48 years, for men — 63.39 ± 9.92 years. More than 60 % of patients were in the age stratum of 51-70 years, there was a predominance of males by more than three times. More than 70 % of patients were retired in accordance with age or disabled (Table 1). About half of the patients were vaccinated against COVID-19. The vast majority of patients had concomitant arterial hypertension and chronic heart failure, diabetes mellitus was established in 20.5 %, chronic kidney disease — in 26.6 %, obesity — in 23.3 % of patients.

Collection of clinical and laboratory parameters

Patient clinical data were collected from an electronic medical database, including demographics, clinical data, comorbidities, imaging results, laboratory tests, clinical outcomes, and information on previous myocardial revascularization and coronavirus infection. All registered events were reviewed from hospital electronic records and assessed by two cardiologists by consensus.

The study database included a description of the coronary angiography and coronary artery stenting procedure for each patient. Venous blood samples were collected from all patients within 10 minutes of admission. Laboratory tests included complete blood count, high-sensitivity troponin I, D-dimer, creatine kinase (CK), creatine kinase-MB (CK-MB), serum creatinine and glucose, ESR, C-reactive protein, alanine aminotransferase (ALT), aspartate aminotransferase

(AST), and fibrinogen. Evidence of previous coronavirus infection was provided by anamnesis data, as well as laboratory parameters — IgG and IgM antibodies to Coronavirus (SARS-CoV-2) and the determination of Coronavirus COVID-19 RNA by the polymerase chain reaction (PCR) method.

Methods of statistical analysis

Descriptive statistics were performed during the study. For all continuous variables, the mean value and corresponding confidence intervals were calculated depending on the type of data distribution. For variables with a distribution deviating from normal, the median and interquartile range were determined. Qualitative variables were analyzed by calculating absolute and relative indicators.

For categorical variables, data were presented as absolute and relative numbers. For qualitative data, the significance of differences in groups was determined by performing the Chi-square (χ 2) test. For quantitative data, central tendencies were measured.

Comparison of laboratory parameters between patient groups was performed using the nonparametric Mann-Whitney U test for samples with asymmetric distribution. Nominal variables were compared using the Pearson χ^2 goodness-of-fit test, and rank variables were analyzed using the Tau-s-Kendall test.

The relationship between clinical and laboratory parameters and the probability of MI development was studied using multiple linear regression analysis. Statistical significance was established at $p < 0.05$. ROC curve analysis was used to assess the diagnostic significance of quantitative features in predicting the outcome.

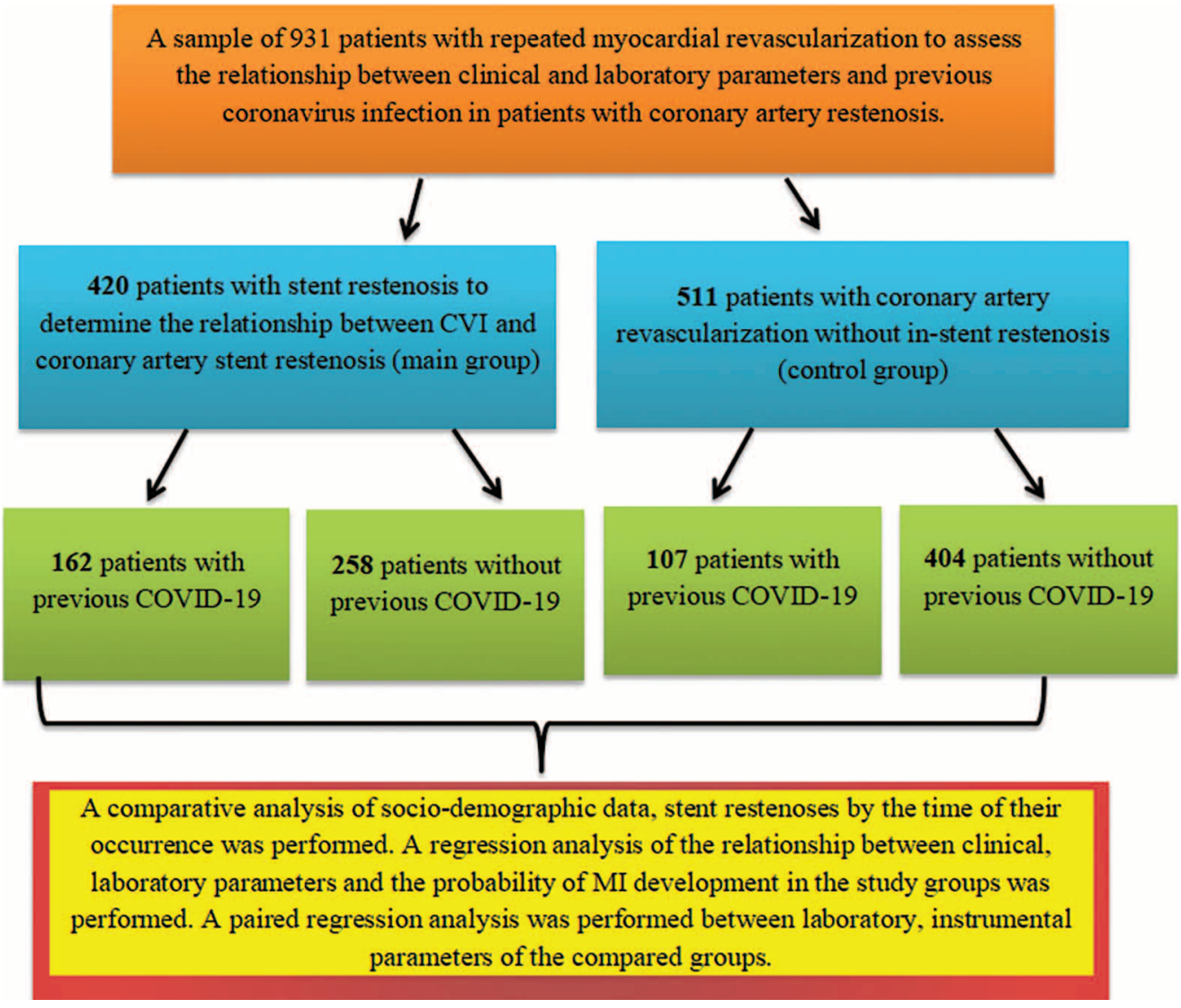

Figure 1. *Study design*
Note: CVI — coronavirus infection; MI — Myocardial infarction

The separating value of the quantitative feature at the cut-off point was determined by the highest value of the Youden index. Differences were considered statistically significant at $p < 0.05$. All statistical calculations were performed using SPSS version 20.0 software (IBM Ireland Product Distribution Limited, Ireland).

The study design is presented in Figure 1. The observation period was 1 year.

Results and discussion

In the main study group, the majority of patients were males — 315 (75 %) people; 25 % (105 people) were women. The control group included 385 (75.3 %) men and 126 (24.7 %) women. No statistically significant differences in gender and social status were found in the study groups. Arterial hypertension was present as a comorbid condition in the vast majority of patients in both study groups. Diabetes mellitus was diagnosed in approximately one-fifth of patients in both study groups, although no statistically significant differences were found between the study groups for these indicators. In the main study group, there were more deceased individuals compared to the control group — 19 (57.6 %) vs. 14 (42.4 %) patients, respectively, but the values did not have statistically significant differences ($\chi 2 = 3.597$; $p = 0.166$) (Table 2). At the same time, in the main group, among deceased individuals, coronavirus infection in the anamnesis was in 13 out of 19 individuals (68.4 %), and in the control group — in 7 patients out of 14 (50 %).

In the main group, at the time of inclusion in the study, more than half of the patients had very late stent restenosis (more than a year after previous stenting): 231 (55.0 %), 152 (36.2 %) patients had late stent restenosis (from one month to one year after stenting), 37 (8.8 %) had subacute stent restenosis (up to one month after previous stenting). In the control group, the structure of restenosis periods was identical; no statistically significant differences were found in the study groups (Table 3).

It was found that in more than half of the cases in both groups, interventions were performed on the anterior interventricular branch of the left coronary artery (LAD) (522 cases or 56.1 %), followed by the right coronary artery (RCA) (268 cases or 28.8 %), then the circumflex branch of the left coronary artery (LC) (121 cases or 12.9 %). No statistically significant differences in the study groups regarding stent localization were found (Table 4). In 326 (33.1 %) of the cases listed in the table, multivessel coronary vascular disease was observed, with two or more stents being implanted.

There were no statistically significant differences in the study groups concerning clinical parameters such as systolic and diastolic blood pressure, heart rate, and left ventricular ejection fraction according to echocardiographic examination. The median values of these parameters in both groups did not exceed normal values.

Analysis of laboratory parameters in patients included in the study groups demonstrated the presence of statistically significantly higher values of IgG antibodies to coronavirus and C-reactive protein in the main study group compared to the control group. No significant differences were found in other laboratory parameters in the study groups (Table 5). Non-zero values of antibodies to IgM and IgG in individuals in the control group can be explained by possible contact with patients with a history of coronavirus infection without any clinical manifestations of the disease or previous vaccination; it should be noted that the average values in the control group were within normal values (<10 for antibodies to IgG and <2 for antibodies to IgM).

It was of considerable interest to us to compare the results of clinical data and laboratory tests in the comparison groups depending on the presence of a history of coronavirus infection. For this purpose, we divided the main and control groups into subgroups of individuals with and without a history of COVID-19: group 1 — individuals with restenosis and COVID-19, group 2 — with restenosis without COVID-19, group 3 — with repeated myocardial revascularization without restenosis with COVID-19, and group 4 — with repeated myocardial revascularization without restenosis without COVID-19. No statistically significant differences were found for parameters such as age, gender, presence of comorbid diseases, and left ventricular ejection fraction according to echocardiography. Regarding laboratory parameters, statistically significant differences were found in troponin levels ($p < 0.001$), including by study group between the level in the group with restenosis and CVI compared with the groups without restenosis with CVI, with restenosis without CVI and in the groups with revascularization without CVI and with restenosis without CVI. The D-dimer level had statistically significant differences in the groups with previous CVI compared to the groups without CVI. The same trend was found for CPK, CPK-MB, and CRP (regarding this indicator, it should be noted that statistically significant differences were established even for the groups with restenosis without CVI compared to the group without restenosis and CVI) and APTT. For such parameters as fibrinogen and AST, statistically significant differences were found only in the main group between the subgroups with a history of CVI compared to patients without CVI. No statistically significant differences were found in the study groups for the other laboratory parameters (Table 6).

Multiple regression analysis was performed to assess the independent relationship between the development

of MI and in-stent restenosis of the infarction-related coronary artery. The results of the analysis are presented in Table 7. Adjusted odds ratios (AOR) indicated a statistically significant positive relationship between the risk of developing myocardial infarction in individuals with previous revascularization and such indicators as blood glucose, CRP, LDL, and previous CVI (1.114; 1.014; 1.199; 1.621, respectively). Left ventricular ejection fraction and HDL were statistically significantly negatively associated with the risk of MI (AOR 0.954; 0.638, respectively).

When assessing the probability of developing MI among the studied patients from the values of laboratory parameters using ROC analysis, the following curves were obtained (Figure 2). The area under the curve (AUC) for LDL was 0.542 (0.504-0.581, p=0.03), for CRP 0.6 (0.562-0.637, p=0.0001), blood glucose 0.649 (0.612-0.685, p=0.0001), and COVID-19 infection 0.558 (0.519-0.596, p=0.003). With an increase in the values of two variables — LVEF and HDL — a decrease in the risk of MI was shown. Thus, the AUC for LVEF was 0.343 (0.308-0.378, p=0.0001), for HDL — 0.46 (0.422-0.498, p=0.038).

It is known that stent restenosis remains a problem for patients with coronary artery disease who have undergone myocardial revascularization using stents, and the risk factors for its occurrence have not yet been fully studied. After stent implantation, restenosis develops mainly within the first three months [9]. Restenosis occurs due to intimal hyperplasia within the stent, which leads to myocardial ischemia. With the introduction of drug-eluting coronary stents, the incidence of restenosis and, consequently, re-interventions has been significantly reduced. The incidence of restenosis after bare metal coronary stent implantation is approximately 20-35 %, while the use of drug-eluting stents has further reduced the incidence of restenosis to 5 %-10 % [2].

Table 2. *Comparative characteristics of social and demographic data in the study groups*

Characteristics of study groups		Study groups				Statistical test for the significance of differences	
		Main group		Control groups			
		n	%	n	%	χ2	p
Outcome	discharged	392	93.3	491	96.1	3.597	0.166
	died	19	4.5	14	2.7		
	transferred	9	2.1	6	1.2		
Sex	male	315	75	385	75.3	0.014	0.904
	female	105	25	126	24.7		
Social status	invalid	30	7.1	46	9.0	3.765	0.288
	pensioner	238	56.7	270	52.8		
	unemployed	52	12.4	81	15.9		
	works	100	23.8	114	22.3		
Diabetes mellitus		91	21.7	100	19.6	0.622	0.430
Arterial hypertension		414	98.6	497	97.3	1.885	0.170

* Discharged after current hospitalization when stent restenosis was diagnosed

Table 3. *Characteristics of stent restenoses depending on the timing of their development*

Timing of restenosis	Studied groups				χ2	p
	Main		Control			
	n	%	n	%		
Subacute	37	8.8	48	9.4	0.187	0.911
Late	152	36.2	179	35.0		
Very late	231	55.0	284	55.6		
Total	420	46.1	511	53.9		

Table 4. *Characteristics of the localization and number of implanted stents*

Localization of stent	Total		n= 420 Main group		n= 511 Control group		p
	n	%	n	%	n	%	
OMB	8	0,9	2	0,5	6	1,2	
RCA	268	28,8	117	27,9	151	29,5	
DB	12	1,3	6	1,4	6	1,2	0,679
Cx	121	12,9	52	12,4	69	13,5	
LAD	522	56,1	243	57,9	279	54,6	
Number of implanted stents							
1	605	64,9	269	64,0	336	65,8	0,587
2 and>	326	33,1	151	36,0	175	34,2	

Note. OMB — obtuse marginal branch; RCA — right coronary artery; DB — diagonal branch; Cx — circumflex branch of the left coronary artery; LAD — left anterior interventricular branch of the left coronary artery

Table 5. *Characteristics of laboratory parameters in patients of study groups*

Rate	Main group		Control group		P
	Me	Q1-Q3	Me	Q1-Q3	
Troponin I mkg/l	0,10	0,1-0,26	0,10	0,1-0,28	0,831
D-dimer ng/ml	452,0	295,0-619,0	437,0	293,5-613,5	0,580
CPK (U/l)	190,0	117,75-289,0	186,0	109,1-304,5	0,816
CPK-MB (U/l)	18,95	15,0-32,78	19,0	15,0-34,4	0,796
Platelets 10^9/l	233,0	197,75-272,0	231,0	193,0-272,0	0,533
Antibodies IgG	8,6	6,5-67,3	6,9	5,4-9,31	0,001
Antibodies IgM	0,9	0,79-1,6	0,90	0,7-1,5	0,084
CRP mg/l	10,7	5,97-17,55	9,06	4,5-17,78	0,003
Fibrinogen g/l	3,18	2,61-3,81	3,20	2,60-3,95	0,661
APTT	29,0	25,4-33,7	29,4	25,42-33,8	0,609
Creatinine mkmol/l	82,25	72,0-102,0	87,0	72,0-102,1	0,794
Urea	5,85	4,8-7,4	5,7	4,75-7,26	0,546
ALT U/l	25,0	17,47-35,95	25,6	18,0-37,9	0,430
AST U/l	23,1	17,38-33,51	23,52	17,36-36,3	0,681
Leucocytes 10^9/l	8,0	6,5-10,11	8,20	6,7-10,68	0,199
Hemoglobin (g/l)	141,0	131,0-153,0	143,0	131,5-153,0	0,528
INR	1,0	0,92-1,09	1,0	0,92-1,10	0,401
Triglycerides mmol/l	1,67	1,17-2,38	1,60	1,12-2,36	0,677
HDL mmol/l	1,00	0,89-1,23	1,02	0,89-1,24	0,527
LDL mmol/l	2,78	2,19-3,45	2,78	2,17-3,49	0,882
Glucose mmol/l	6,10	5,42-7,66	6,01	5,4-7,5	0,583
Neutrophils * %	64,86± 10,61		65,98±10,38		0,106
Lymphocytes * %	25,85±9,33		25,11±9,34		0,229

Note. * The variable has a normal distribution (Cp [SD])
CRP — C-reactive protein; CPK — creatine phosphokinase; HDL — high-density lipoprotein; LDL — low-density lipoprotein; ALT — alanine aminotransferase; AST — aspartate aminotransferase; APTT — activated partial thromboplastin time, INR — International Normalized Ratio

Table 6. *Clinical and laboratory characteristics of patients in the main and control groups depending on the status of the transferred COVID-19*

Rate	Main group (Me, Q1-Q3)		Control group (Me, Q1-Q3)		p*
	CVI+ (group 1)	CVI- (group 2)	CVI+ (group 3)	CVI- (group 4)	
Age	64 (59-70)	63 (57-72.5)	65 (60-69)	64 (57-72)	0.992
Male gender	115 (71.4 %)	200 (77.2 %)	78 (73.6 %)	307 (76.0 %)	0.556
AH	158 (98.1 %)	256 (98.8 %)	105 (99.1 %)	391 (96.8)	0.241**
DM	39 (24.2 %)	52 (20.1 %)	28 (26.4 %)	72 (17.8 %)	0.142**
LVEF	51 (45.0-56.0)	53 (46.0-58.0)	52 (46.0-57.0)	51.5 (45.0-56.0)	0.354
Troponin I mcg/l	0.1 (0.1-3.39)	0.1 (0.1-0.12)	0.1 (0.1-0.62)	0.1 (0.1-0.22)	0.001 P3-1=0.001 P4-1=0.005 P3-2=0.037
d-dimer ng/ml	490.0 (350.6-719.0)	415.0 (287.5-574.0)	489.0 (346.75-694.0)	418.0 (283.75-597.25)	0.001 P2-1=0.005 P4-1=0.006 P3-2=0.02 P4-3=0.021
CPK (U/l)	199.0 (147.0-374.0)	183.0 (102-268.0)	196.5 (158.25-364.0)	183.2 (102.0-284.0)	0.001 P2-1=0.003 P4-1=0.005 P3-2=0.003 P4-3=0.005
CPK -MB (U/l)	22.6 (17.3-48.1)	17.8 (14.1-24.4)	23.65 (16.92-45.75)	18.25 (14.78-29.55)	0.001 P2-1=0.001 P4-1=0.001 P3-2=0.001 P4-2=0.002
Platelets 109/l	237.0 (201.0-272.0)	231.0 (194.0-272.0)	231.5 (195.5-271.0)	230.5 (193.0-272.0)	0.466
CRP mg/l	12.45 (4.8-19.3)	9.8 (4.79-28.3)	10.2 (4.9-21.7)	6.8 (3.5-11.0)	0.001 P2-1=0.001 P3-2<0.001 P4-2=0.001
Fibrinogen g/l	3.32 (2.75-4.18)	3.10 (2.5-3.73)	3.22 (2.71-4.12)	3.18 (2.6-3.8)	0.039 P2-1=0.039
APTT	31.3 (26.76-34.7)	28.0 (24.8-33.0)	31.2 (26.55-34.33)	29.0 (25.3-33.73)	0.001 P2-1=0.003 P3-2=0.026
Creatinine mkmol/l	83.5 (72-103)	86.0 (72-101.0)	79.85 (69.93-95.2)	88.0 (74.0-103.0)	0.055
ALT U/l	27.4 (18.99-37.2)	22.27 (17.0-34.15)	25.05 (17.21-34.0)	25.65 (18.0-38.0)	0.102
AST U/l	25.00 (18.3-39.0)	21.9 (17.0-32.0)	25.45 (18.5-40.5)	23.04 (17.27-35.0)	0.009 P2-1=0.021
Leucocytes 109/l	8.4 (6.5-10.9)	7.87 (6.5-9.9)	8.01 (6.37-9.93)	8.3 (6.73-10.86)	0.132
Hemoglobin (g/l)	141.0 (128.0-152.0)	142.0 (132.0-153.0)	140.0 (128.0-153.5)	143.0 (132.0-153.0)	0.394
INR	1.0 (0.91-1.1)	0.99 (0.92-1.08)	1.0 (0.9-1.13)	1.0 (0.93-1.1)	0.862
Triglycerides mmol/l	1.6 (1.12-2.2)	1.7 (1.2-2.45)	1.60 (1.11-2.40)	1.60 (1.12-2.34)	0.802
HDL mmol/l	0.98 (0.88-1.2)	1.02 (0.9-1.24)	1.0 (0.88-1.25)	1.02 (0.9-1.24)	0.783
Glucose mmol/l	6.18 (5.44-8.51)	6.1 (5.4-7.38)	6.35 (5.42-8.8)	6.01 (5.4-7.37)	0.078
Urea mmol/l	5.9 (4.8-7.5)	5.8 (4.8-7.3)	5.8 (4.7-6.88)	5.8 (4.79-7.3)	0.773
Neutrophils %	65.69 ± 11.1	64.35 ± 10.28	66.09 ± 11.06	65.96 ± 10.22	0.234***
Lymphocytes %	24.4 (19.4-33.3)	25.8 (20.7-31.6)	25.0 (17.55-32.05)	24.25 (19.68-31.6)	0.590
LDL mmol/l	2.85 (2.15-3.4)	2.74 (2.2-3.46)	3.0 (2.22-3.49)	2.7 (2.17-3.48)	0.658

Note. *Kruskal-Wallis test; **Pearson chi-square; ***Fisher F-test
AG — arterial hypertension, DM — diabetes mellitus; CRP — C-reactive protein; LVEF — left ventricular ejection fraction, CPK — creatine phosphokinase; HDL — high-density lipoproteins; LDL — low-density lipoproteins; ALT — alanine aminotransferase; AST — aspartate aminotransferase, APTT — activated partial thromboplastin time, INR — International Normalized Ratio

Table 7. *Characteristics of the relationship between model predictors and the probability of detecting MI*

Rate	Unadjusted indicator		Adjusted indicator	
	OR; 95 % CI	p	AOR; 95 % CI	p
LV ejection fraction, %	0.945; 0.93 –0.960	<0.001*	0.954; 0.938–0.969	<0.001*
Glucose, mmol/l	1.154; 1.099–1.212	<0.001*	1.114; 1.059–1.174	<0.001*
CRP, g/l	1.015; 1.009–1.021	<0.001*	1.014; 1.008–1.019	<0.001*
LDL, mmol/l	1.158; 1.009–1.328	0.036*	1.199; 1.034–1.392	0.017*
HDL, mmol/l	0.599; 0.401–0.896	0.013*	0.638; 0.411–0.989	0.045*
COVID-19	1.742; 1.305–2.326	<0.001*	1.621; 1.189–2.212	0.002*

Note. * — the influence of the predictor is statistically significant (p < 0,05); OR — odds ratio; AOR — adjusted odds ratio. CRP — C-reactive protein; HDL — high-density lipoproteins; LDL — low-density lipoproteins. COVID-19 — new coronavirus infection

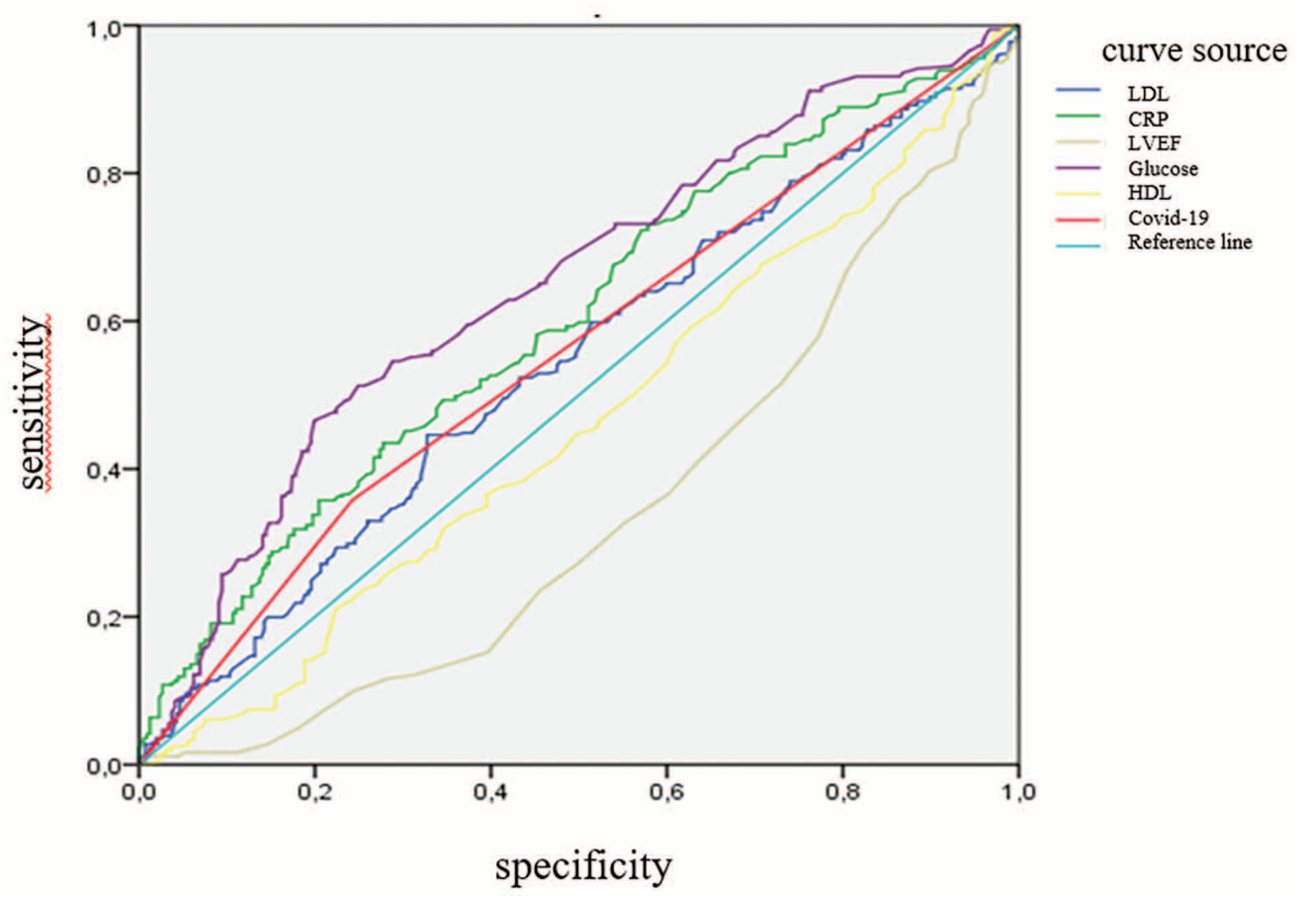

Figure 2. *Estimation of the probability of developing MI using ROC analysis*
Note. CRP — C-reactive protein; LVEF — left ventricular ejection fraction; LDL — low-density lipoproteins; COVID-19 — coronavirus infection

A comparative analysis of the results of our study with the data of other similar studies showed the comparability of the data. Thus, a retrospective study conducted in southern China to assess the incidence and risk factors of coronary artery restenosis included 341 patients with acute coronary syndrome who had previously been implanted with at least one stent. The follow-up was carried out for 3 years. It turned out that 18.2 % of such patients had in-stent restenosis throughout the monitoring period, which could form, on average, over a period of 32 months; the frequency of restenosis for the left main coronary artery, left anterior descending coronary artery, left circumflex coronary artery and the right coronary artery was 6.7 %, 20.9 %, 19.4 %, and 14.4 %, respectively); left ventricular ejection fraction, the number of stents, the type of stent, and antiplatelet therapy made a significant contribution to the development of coronary artery restenosis. Multivariate logistic analysis showed that left ventricular ejection fraction and the number of stents significantly correlated with the incidence of coronary artery restenosis [10]. In our study, very late in-stent restenosis was predominant in both study groups, its proportion was more than 50 %, about a third of patients had late restenosis, and only about 10 % of patients had subacute in-stent restenosis, no statistically significant differences were found in the study groups. In our study, the predominant stent location was also the left LAD, but the second place was the RCA, followed by the left LCA. Multiple coronary vessel lesions were observed in a third of cases. The results of our study similarly indicate the presence of an inverse statistically significant relationship with the risk of myocardial infarction in patients with previous revascularization.

The conducted studies show that patients with previous myocardial revascularization who have had coronavirus infection have a higher risk of developing severe complications [10, 11]. Thus, Polish scientists in their study came to the conclusion that stent thrombosis is more common in patients with multiple comorbidities and in patients with complex atherosclerotic lesions, diabetes mellitus, chronic kidney disease, diffuse and bifurcation lesions of small arteries requiring the installation of more than one stent [11]. During SARS-CoV-2 infection, a cytokine storm occurs 5-10 days after the onset of symptoms, leading to endothelial damage, platelet activation, and the coagulation cascade. The presence of a stent in the coronary artery should be considered a local stasis factor that completes Virchow's triad [11].

According to the results of the study by Giustino G et al., which included 305 patients with previous revascularization who had coronavirus infection, myocardial injury was observed in 190 patients (62.3 %). Compared with patients without myocardial injury, patients with myocardial injury had more electrocardiographic manifestations, higher inflammatory biomarkers, and an increased prevalence of major echocardiographic abnormalities, which included left ventricular wall motion abnormalities, global left ventricular dysfunction, left ventricular diastolic dysfunction and pericardial effusions [12].

Severe coronavirus infection is characterized by an increase in some biochemical parameters responsible for inflammatory reactions (ferritin, C-reactive protein), thrombus formation (D-dimer, fibrinogen, prolongation of PT), and damage to myocardial muscle tissue (troponin, creatine phosphokinase). Thus, serum ferritin levels are important for the immune response, which increases in severe cases of COVID-19, and elevated ferritin levels can cause a cytokine storm, exerting a direct immunosuppressive and proinflammatory effect [13].

According to current guidelines, determination of high-sensitivity troponin I is mandatory in the diagnosis of ischemic cardiac injury, since troponin I is a protein of the heart muscle [14]. The results obtained in our study indicate statistically significant differences in troponin levels ($p < 0.001$) in the study groups after dividing them depending on the previous coronavirus infection in both the main and control groups, whereas no such differences were found when comparing the main and control groups without taking into account the previous COVID-19. In a study conducted on a sample of patients with current COVID-19 in five hospitals in New York, an increase in cardiac troponin concentration was found in 36 % of patients. Troponin I levels in the range of 30–90 ng/L corresponded to an adjusted hazard ratio (HR) of 1.76 (95 % CI: 1.37–2.24), and troponin concentrations >90 ng/L increased the adjusted HR to 3.03 (CI: 2.42–3.80) [15]. However, some authors explain the increase in troponin I levels in COVID-19 not by ischemic injury, but by inflammatory changes in the myocardium [16].

After COVID-19, a common complication is a high prothrombotic status, which contributes to the development of thrombosis, heart attacks or strokes [14]. Elevated D-dimer levels are observed in thrombosis, thromboembolism, heart failure, coronavirus infection, etc. A high concentration of this laboratory indicator is a predictor of death [17]. Initial coagulopathy in patients with COVID-19 is manifested by an increased content of D-dimers. In the late period after coronavirus infection, an increase in prothrombin time and APTT, an increase in platelet and fibrinogen levels

are observed [17]. Assessment of the progression of COVID-19 is carried out, among other things, through regular monitoring of laboratory parameters, including D-dimer and fibrinogen [17]. Regarding the results of our study, it should be noted that statistically significant differences in the D-dimer level were found only when dividing the study groups into subgroups depending on the previous COVID-19, whereas a comparison of the indicator in the main and control groups did not show such differences.

C-reactive protein increases at the onset of COVID-19 [14,18]. There is a direct relationship between C-reactive protein concentration and adverse outcomes according to study results [18]. Patients with coronavirus infection with high levels of D-dimer and C-reactive protein have the highest risk of adverse outcomes [19]. The results of our study are consistent with these data: differences in C-reactive protein levels in the study groups remained statistically significant depending on both the presence of stent restenosis compared to patients with repeat myocardial revascularization without restenosis, and depending on the history of COVID-19.

The causes of elevated liver transaminases in inflammatory processes include impaired cell membrane permeability. In COVID-19 patients, liver lymphocyte infiltration, centrilobular sinusoidal dilation, and focal necrosis could be observed, and SARS-CoV-2 could directly bind to ACE2-expressing cholangiocytes [20,21]. Liver damage can also be drug-induced [22]. IL-6 is a potent cytokine that serves to transmit inflammatory signals. IL-6 production can occur from immune cells, fibroblasts, endothelial cells, and hepatocytes, which causes the acute phase of liver damage [23]. Increased AST and ALT activity are associated with a severe course and worse prognosis, the risk of death in patients with coronavirus infection. Thus, a systematic review with meta-analysis Wang Y et al., 2021 that included 1370 patients with COVID-19 showed a significant relationship between elevated AST levels and an increased risk of mortality in patients with COVID-19 (SMD = 0.75, 95 % CI: 0.33–1.17, p <0.001). The same relationship was found for ALT (SMD = 0.35, 95 % CI: 0.13–0.57, P = 0.002) [24]. The results of our study demonstrate statistically significant differences in the level of liver transaminases when dividing the study groups into subgroups depending on the previous COVID-19.

The results of a systematic review with meta-analysis conducted by Chinese scientists in 2023 showed an increased level of pro-inflammatory biomarkers (CRP, LDH, D-dimer, interleukin-6, leukocytes) for six months after COVID-19 [25], which may explain the results obtained in our study among patients who had COVID-19. A study conducted by Spanish scientists studying patients with myocardial revascularization (stenting) who had COVID-19 described cases of stent thrombosis associated with hypercoagulability due to the COVID-19 virus. In this study, there was an increase in D-dimer (more than 500 mg/l in 100 % of patients), an increase in C-reactive protein (more than 5 mg/l in 100 % of patients), an increase in ferritin (more than 400 ng/ml in 75 % of patients), lymphocytopenia (in 50 % of patients), an increase in troponin in 100 % of patients, and a decrease in the estimated glomerular filtration rate in 75 % of patients [26]. A group of American scientists examined 5,700 patients admitted to infectious disease departments with COVID-19. The following changes in the laboratory tests of patients were noted: lymphopenia (60 % of patients), an increase in D-dimer (56 %), ferritin (76 %), C-reactive protein (79 %), and lactate dehydrogenase (70 %) [27]. In a study from a hospital in Wuhan, China, 187 patients showed leukocytosis, increased neutrophils, and decreased lymphocytes with high troponin T levels [28].

The results of our work when comparing laboratory parameters in the study groups showed statistically significant differences in the C-reactive protein and IgG antibodies to coronavirus, which is probably due to the large proportion of patients who had coronavirus infection in the main group, even in the late period. Of considerable interest is the fact that after dividing the study groups by the presence of coronavirus infection in the anamnesis, statistically significantly higher values were found not only for the C-reactive protein indicator, but also for troponin, CPK, CPK-MB, D-dimer and APTT for individuals who had COVID-19. The results of multiple regression analysis indicate the presence of a statistically significant positive relationship between the likelihood of myocardial infarction in patients with previous revascularization and such laboratory parameters as CRP, blood glucose, LDL, and previous COVID-19.

Conclusions.

The results of our study allow us to conclude that there is a statistically significant positive association between the likelihood of myocardial infarction and previous coronavirus infection, increased levels of C-reactive protein, LDL and glucose in the blood, as well as a decrease in LVEF and HDL. These data allow us to judge the unfavorable role of previous coronavirus infection in the process of formation of coronary artery stent restenosis.

Вклад авторов:

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

Батенова Г.Б.: разработка дизайна исследования; организация набора материала, создание базы пациентов, написание текста рукописи и представление результатов

Дедов Е.И.: организация набора материала, редактирование текста рукописи

Орехов А.Ю.: разработка дизайна исследования, статистическая обработка, редактирование текста рукописи

Дюсупов А.А.: организация набора материала, редактирование текста рукописи

Ыгиева Д.Г.: создание базы пациентов, статистическая обработка

Пивин М.Р.: создание базы пациентов, обзор научной литературы

Манатова А.М.: создание базы пациентов, обзор научной литературы, редактирование рукописи

Пивина Л.М.: научная консультация, редактирование рукописи, обзор научной литературы

Author Contribution:

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

Batenova G.B.: development of study design; organization of data collection, creation of a patient database, writing the manuscript and presentation of results

Dedov E.I.: organization of data collection, editing the manuscript

Orekhov A.Yu.: development of study design, statistical processing, editing the manuscript

Dyusupov A.A.: organization of data collection, editing the manuscript

Ygyieva D.G.: creation of a patient database, statistical processing

Pivin M.R.: creation of a patient database, review of scientific literature

Manatova A.M.: creation of a patient database, review of scientific literature, editing the manuscript

Pivina L.M.: scientific consultation, editing the manuscript, review of scientific literature

Список литературы/ References:

1. Бабунашвили А.М., Иванов В.А., Дундуа Д.П. и др. Лечение коронарного атеросклероза: влияние массового применения стентов на ближайшие и отдаленные результаты коронарной ангиопластики. Архивъ внутренней медицины. 2011; (1): 35-43.
   Babunashvili A.M., Ivanov V.A., Dundua D.P., et al. Treatment of coronary atherosclerosis: the effect of mass use of stents on the immediate and remote results of coronary angioplasty. Archives of Internal Medicine. 2011; (1): 35-43 [In Russian].
2. Pleva L., Kukla P., Hlinomaz O. Treatment of coronary in-stent restenosis: a systematic review. J Geriatr Cardiol. 2018; 15(2): 173-184. doi: 10.11909/j.issn.1671-5411.2018.02.007.
3. Абдрахманова А.И., Цибулькин Н.А., Амиров Н.Б. и др. Безболевая ишемия миокарда у пациентов после проведенного чрескожного коронарного вмешательства. Архивъ внутренней медицины. 2022; 12(3): 165-174. doi: 10.20514/2226-6704-2022-12-3-165-174
   Abdrakhmanova A.I., Tsibulkin N.A., Amirov N.B., et al. Painless myocardial ischemia in patients after percutaneous coronary intervention. Archives of Internal Medicine. 2022; 12(3): 165-174 [In Russian]. doi: 10.20514/2226-6704-2022-12-3-165-174
4. Byrne R.A., Joner M., Kastrati A. Stent thrombosis and restenosis: what have we learned and where are we going? The Andreas Grüntzig Lecture ESC 2014. Eur Heart J. 2015;36(47):3320-31. doi: 10.1093/eurheartj/ehv511
5. Canfield J., Totary-Jain H. 40 Years of Percutaneous Coronary Intervention: History and Future Directions. J Pers Med. 2018;8(4):33. doi: 10.3390/jpm8040033.
6. Sun J., Yu H., Liu H., et al. Correlation of pre-operative circulating inflammatory cytokines with restenosis and rapid angiographic stenotic progression risk in coronary artery disease patients underwent percutaneous coronary intervention with drug-eluting stents. J Clin Lab Anal. 2020;34(3):e23108. doi: 10.1002/jcla.23108.
7. Cornelissen A., Vogt F.J. The effects of stenting on coronary endothelium from a molecular biological view: Time for improvement? J Cell Mol Med. 2019;23(1):39-46. doi: 10.1111/jcmm.13936.
8. Semenova Y., Pivina L., Khismetova Z., et al. Anticipating the Need for Healthcare Resources Following the Escalation of the COVID-19 Outbreak in the Republic of Kazakhstan. J Prev Med Public Health. 2020;53(6):387-396. doi: 10.3961/jpmph.20.395.
9. Алимов Д.А., Жалалов Б.З., Ганиев У.Ш. Рестеноз стента с точки зрения эндотелиальной дисфункции. Вестник экстренной медицины, 2017; 3: 109-112.
   Alimov D.A., Zhalalov B.Z., Ganiev U.Sh. Stent restenosis from the point of view of endothelial dysfunction. Bulletin of Emergency Medicine, 2017; 3: 109-112 [In Russian].
10. Li M., Hou J., Gu X., et al. Incidence and risk factors of in-stent restenosis after percutaneous coronary intervention in patients from southern China. Eur J Med Res. 2022;27(1):12. doi: 10.1186/s40001-022-00640-z.
11. Skorupski W.J., Grygier M., Lesiak M., et al. Coronary Stent Thrombosis in COVID-19 Patients: A Systematic Review of Cases Reported Worldwide. Viruses. 2022;14(2):260. doi: 10.3390/v14020260.
12. Giustino G., Croft L.B., Stefanini G.G., et al. Characterization of Myocardial Injury in Patients With COVID-19. J Am Coll Cardiol. 2020;76(18):2043-2055. doi: 10.1016/j.jacc.2020.08.069.
13. O'Shea P.M., Lee G.R., Griffin T.P., et al. COVID-19 in adults: test menu for hospital blood science laboratories.

Ir J Med Sci. 2020;189(4):1147-1152. doi: 10.1007/s11845-020-02252-0.
14. Neumann J.T., Twerenbold R., Weimann J., et al. Prognostic Value of Cardiovascular Biomarkers in the Population. JAMA. 2024;331(22):1898-1909. doi: 10.1001/jama.2024.5596.
15. Lala A., Johnson K.W., Russak A.J., et al. 2020. Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. Journal of the American College of Cardiology. 76(5):533-546. doi: 10.1016/j.jacc.2020.06.007.
16. Gupta A.K., Jneid H., Addison D., et al. 2020. Current perspectives on coronavirus disease 2019 and cardiovascular disease: A white paper by the JAHA editors. Journal of the American Heart Association, 9:e017013 doi: 10.1161.JAHA.120.017013.
17. Eljilany I., Elzouki A.N. D-Dimer, Fibrinogen, and IL-6 in COVID-19 Patients with Suspected Venous Thromboembolism: A Narrative Review. Vasc Health Risk Manag. 2020;16:455-462.
18. Pepys M.B. C-reactive protein predicts outcome in COVID-19: is it also a therapeutic target? Eur Heart J. 2021;42(23):2280-2283. doi: 10.1093/eurheartj/ehab169.
19. Smilowitz N.R., Kunichoff D., Garshick M., et al. C-reactive protein and clinical outcomes in patients with COVID-19. Eur Heart J. 2021;42(23):2270-2279. doi: 10.1093/eurheartj/ehaa1103.
20. Hanley B, Lucas SB, Youd E, et al. Autopsy in suspected COVID-19 cases. J Clin Pathol. 2020;73:239–242. doi: 10.1136/jclinpath-2020-206522.
21. Tian S, Xiong Y, Liu H, et al. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies. Mod Pathol 2020. 33:1007–14. doi: 10.1038/s41379-020-0536-x.
22. Zhang C, Shi L, Wang FS. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol. 2020;5:428–430. doi: 10.1016/S2468-1253(20)30057-1.
23. Hunter CA, Jones SA. IL-6 as a keystone cytokine in health and disease. Nat Immunol. 2015;16:448–457. doi: 10.1038/ni.3153.
24. Wang Y., Shi L., Wang Y., et al. An updated meta-analysis of AST and ALT levels and the mortality of COVID-19 patients. Am J Emerg Med. 2021;40:208-209. doi: 10.1016/j.ajem.2020.05.063.
25. Yong S.J., Halim A., Halim M., et al. Inflammatory and vascular biomarkers in post-COVID-19 syndrome: A systematic review and meta-analysis of over 20 biomarkers. Rev Med Virol. 2023;33(2):e2424. doi: 10.1002/rmv.2424.
26. Prieto-Lobato A., Ramos-Martínez R., Vallejo-Calcerrada N., et al. A Case Series of Stent Thrombosis During the COVID-19 Pandemic. JACC Case Rep. 2020;2(9):1291-1296. doi: 10.1016/j.jaccas.2020.05.024.
27. Richardson S., Hirsch J.S., Narasimhan M., et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020;323(20):2052-2059. doi: 10.1001/jama.2020.6775.
28. Guo T., Fan Y., Chen M., et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020;5(7):811-818. doi: 10.1001/jamacardio.2020.1017.

Информация об авторах

Батенова Гульнара Баяхметовна — ассистент кафедры неотложной медицины НАО «Медицинский университет Семей», кардиолог, Семей, Казахстан, e-mail: gulnara_batenova@mail.ru, ORCID ID: https://orcid.org/0000-0003-3198-1860

Дедов Евгений Иванович — д.м.н., профессор кафедры госпитальной терапии им. академика Г.И. Сторожакова, ревматолог, Москва, e-mail: dedov-e-i@yandex.ru, ORCID ID: https://orcid.org/0000-0002-9118-3708

Орехов Андрей Юрьевич — ассистент кафедры терапии НАО «Медицинский университет Семей», кардиолог, Семей, Казахстан, e-mail: andrey.orekhov@smu.edu.kz, ORCID ID: https://orcid.org/0000-0001-7201-1399

Дюсупов Алтай Ахметкалиевич — д.м.н., профессор, ректор НАО «Медицинский университет Семей», сосудистый хирург, Семей, Казахстан, e-mail: altay.dyusupov@smu.edu.kz, ORCID ID: https://orcid.org/0000-0003-0875-1020

Ыгиева Диана Габдыгалиевна — ассистент кафедры неотложной медицины НАО «Медицинский университет Семей», терапевт, Семей, Казахстан, e-mail: diana-dikosha@list.ru, ORCID ID: https://orcid.org/0000-0001-8391-8842

Пивин Максим Русланович — резидент НАО «Медицинский университет Семей», Семей, Казахстан, e-mail: pivin97@mail.ru, ORCID ID: https://orcid.org/0000-0001-7206-8029.

Манатова Альмира Манатовна — главный научный сотрудник Национальный научный онкологический центр, врач педиатр, Астана, Казахстан, e-mail: almira.baltakaeva@mail.ru, ORCID ID: https://orcid.org/0009-0007-6460-5606

Пивина Людмила Михайловна — к.м.н., профессор кафедры неотложной медицины НАО «Медицинский университет Семей», врач-терапевт, Семей, Казахстан, e-mail: semskluda@rambler.ru. ORCID ID: https://orcid.org/0000-0002-8035-4866

Author information

Gulnara B. Batenova — assistant of the Department of Emergency Medicine Semey Medical University, Semey, Kazakhstan, cardiologist, e-mail: gulnara_batenova@mail.ru, ORCID ID: https://orcid.org/0000-0003-3198-1860

Evgeniy I. Dedov — professor of the Department of Hospital Therapy named after Academician G.I. Storozhakov, rheumatologist, Moscow, e-mail: dedov-e-i@yandex.ru. ORCID ID: https://orcid.org/0000-0002-9118-3708

Andrey Yu. Orekhov — MD, PhD, assistant of the Department of Therapy of the Semey Medical University, cardiologist, Semey, Kazakhstan, e-mail: andrey.orekhov@smu.edu.kz, ORCID ID: https://orcid.org/0000-0001-7201-1399

Altay A. Dyussupov — MD, PhD, proofessor, Rector of Semey Medical University, angiologist, Semey, Kazakhstan, e-mail: altay.dyusupov@smu.edu.kz, ORCID ID: https://orcid.org/0000-0003-0875-1020

Diana G. Ygiyeva — assistant of the Department of Emergency Medicine of Semey Medical University, therapist, Semey, Kazakhstan, e-mail: diana-dikosha@list.ru, ORCID ID: https://orcid.org/0000-0001-8391-8842

Maxim R. Pivin — resident of Semey Medical University, Semey, Kazakhstan, e-mail: pivin97@mail.ru. ORCID ID: https://orcid.org/0000-0001-7206-8029.

Almira M. Manatova — PhD, chief Researcher of National Scientific Oncology Center, pediatrician, Astana, Kazakhstan, e-mail: almira.baltakaeva@mail.ru. ORCID ID: https://orcid.org/0009-0007-6460-5606

Lyudmila M. Pivina ✉ — MD, PhD, Professor of the Department of Emergency Medicine of the Semey Medical University, therapeutist, Semey, Kazakhstan, e-mail: semskluda@rambler.ru. ORCID ID: https://orcid.org/0000-0002-8035-4866

✉ — Автор, ответственный за переписку / Corresponding author