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IN-STENT THROMBOSIS AND RESTENOSIS OF THE CORONARY ARTERIES IN PATIENTS WITH CORONARY HEART DISEASE AFTER CORONAVIRUS INFECTION

Gulnara B. Batenova[1], https://orcid.org/0000-0003-3198-1860
Lyudmila M. Pivina[1], https://orcid.org/0000-0002-8035-4866
Yersin T. Sabitov[2], https://orcid.org/0000-0003-0937-5813
Evgeny I. Dedov[3], https://orcid.org/0000-0002-9118-3708
Diana G. Ygiyeva[1], https://orcid.org/0000-0001-8391-8842
Ulzhan S. Jamedinova[1], https://orcid.org/0000-0003-1671-289X
Galiya A. Alibayeva[2], https://orcid.org/0000-0002-1503-4663
Zhansaya T. Aukenova[1], https://orcid.org/0009-0001-3591-8175
Assylzhan M. Messova[1], https://orcid.org/0000-0001-5373-0523
Maksim R. Pivin[1], https://orcid.org/ 0000-0001-7206-8029
Zhanar M. Urazalina[1], https://orcid.org/0000-0002-4494-6565
Saltanat M. Adilgozhina[1], https://orcid.org/0000-0002-8408-7363
Alida Sh. Kaskabayeva[1], https://orcid.org/0000-0002-5184-214X
Zhanna Ye. Musdubayeva[1], https://orcid.org/0000-0002-9058-1878

[1] Semey Medical University, Semey, Republic of Kazakhstan;
[2] Emergency Hospital, Semey, Republic of Kazakhstan;
[3] Russian National Research Medical University named after. N.I. Pirogov, Moscow, Russian Federation.

Abstract

Introduction. Coronavirus infection (CVI) has made a significant contribution to the course of cardiovascular diseases in the population of almost all countries of the world. The peculiarities of this course during the COVID-19 pandemic were delayed medical care for patients with acute coronary syndrome and myocardial infarction due to insufficient resources for external care, hospital beds, shortage of ambulance crews, and means for resuscitative measures

The aim is to analyze the characteristics of in-stent thrombosis and restenosis of the coronary arteries in patients with coronary heart disease who suffered coronavirus infection.

Materials and methods. The study included 490 individuals who underwent repeated myocardial revascularization due to thrombosis of a previously implanted coronary artery stent or its restenosis. The main study group consisted of 181 patients who had a documented coronavirus infection. The control group included 309 patients of both sexes with revascularized coronary heart disease who had no history of coronavirus infection. The age of the patients is 34-87 years. The results obtained were analyzed using a specially created Register, which included all patients who underwent myocardial revascularization between March 2020 and 2023 after CVI

Results. People with acute coronary syndrome due to or after a coronavirus infection are significantly more likely to develop myocardial infarction compared to people who have not had an infection; among them, adverse outcomes in the form of death or transfer to other medical institutions due to the severity of the condition are statistically significantly more common. Among people in the main group, sub-acute thrombosis inside the stent was significantly more common.

Conclusion. It is necessary to carefully study the role of CVI in the development of coronary artery thrombosis in order to be prepared to provide timely and most effective medical care to patients.

Keywords: *acute coronary syndrome, in-stent thrombosis, stent restenosis, coronavirus infection, myocardial infarction.*

Резюме

ТРОМБОЗ И РЕСТЕНОЗ КОРОНАРНЫХ АРТЕРИЙ ВНУТРИ СТЕНТА У ПАЦИЕНТОВ С ИШЕМИЧЕСКОЙ БОЛЕЗНЬЮ СЕРДЦА, ПЕРЕНЕСШИХ КОРОНАВИРУСНУЮ ИНФЕКЦИЮ

Гульнара Б. Батенова[1], https://orcid.org/0000-0003-3198-1860
Людмила М. Пивина[1], https://orcid.org/0000-0002-8035-4866
Ерсин Т. Сабитов[2], https://orcid.org/0000-0003-0937-5813

Евгений И. Дедов[3], https://orcid.org/0000-0002-9118-3708
Диана Г. Ыгиева[1], https://orcid.org/0000-0001-8391-8842
Улжан С. Джамединова[1], https://orcid.org/0000-0003-1671-289X
Галия А. Алибаева[2], https://orcid.org/0000-0002-1503-4663
Жансая Т. Әукенова[1], https://orcid.org/0009-0001-3591-8175
Асылжан М. Месова[1], https://orcid.org/0000-0001-5373-0523
Максим Р. Пивин[1], https://orcid.org/ 0000-0001-7206-8029
Жанар М. Уразалина[1], https://orcid.org/0000-0002-4494-6565
Салтанат М. Адильгожина[1], https://orcid.org/0000-0002-8408-7363
Алида Ш. Каскабаева[1], https://orcid.org/0000-0002-5184-214X
Жанна Е. Муздубаева[1], https://orcid.org/0000-0002-9058-1878

[1] НАО «Медицинский университет Семей», г. Семей, Республика Казахстан;
[2] Больница скорой медицинской помощи города Семей, г. Семей, Республика Казахстан;
[3] Российский национальный исследовательский медицинский университет им. Н.И. Пирогова, г. Москва, Российская Федерация.

Введение. Коронавирусная инфекция внесла существенный вклад в течение заболеваний сердечно-сосудистой системы населения практически всех стран мира. Особенностями такого течения в период пандемии COVID-19 явились запоздалое оказание медицинской помощи пациентам с острым коронарным синдромом и инфарктом миокарда вследствие недостаточного количества ресурсов.

Целью исследования явился анализ особенностей тромбоза и рестеноза внутри стента коронарных артерий у пациентов с ишемической болезнью сердца, перенесших коронавирусную инфекцию.

Материалы и методы. В исследование были включены 490 лиц, перенесших повторную реваскуляризацию миокарда по поводу тромбоза предварительно имплантированного стента коронарной артерии или его рестеноза. Основную группу исследования составили 181 пациент, перенесших коронавирусную инфекцию, подтвержденную документально. В группу контроля вошли 309 пациентов обоих полов с реваскуляризированной ишемической болезнью сердца, не имеющие в анамнезе коронавирусной инфекции. Возраст пациентов – 34-87 лет. Анализ полученных результатов проводился с помощью специально созданного Регистра, который включил всех пациентов, прошедших реваскуляризацию миокарда в период с марта 2020 по 2023 гг. после перенесенной КВИ

Результаты. У лиц с острым коронарным синдромом на фоне или после перенесенной коронавирусной инфекции достоверно чаще развивается инфаркт миокарда в сравнении с лицами, не перенесшими инфекцию; среди них статистически значимо чаще наблюдаются неблагоприятные исходы в виде смерти или перевода в другие лечебные учреждения из-за тяжести состояния. Среди лиц основной группы существенно чаще встречался подострый тромбоз внутри стента.

Заключение. Необходимо тщательное изучение роли КВИ в развитии тромбозов коронарных артерий для того, чтобы быть готовыми к оказанию своевременной и максимально эффективной медицинской помощи больным.

***Ключевые слова**: острый коронарный синдром, тромбоз внутри стента, рестеноз стента, коронавирусная инфекция, инфаркт миокарда.*

Түйіндеме

КОРОНАВИРУСТЫҚ ИНФЕКЦИЯНЫ ӨТКЕРГЕН, ЖҮРЕК ИШЕМИЯЛЫҚ АУРУЫ БАР НАУҚАСТАРДЫҢ КОРОНАРЛЫҚ АРТЕРИЯЛАРЫНЫҢ ІШІНДЕГІ СТЕНТ ТРОМБОЗЫ МЕН РЕСТЕНОЗЫ.

Гульнара Б. Батенова[1], https://orcid.org/0000-0003-3198-1860
Людмила М. Пивина[1], https://orcid.org/0000-0002-8035-4866
Ерсин Т. Сабитов[2], https://orcid.org/0000-0003-0937-5813
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Максим Р. Пивин[1], https://orcid.org/ 0000-0001-7206-8029
Жанар М. Уразалина[1], https://orcid.org/0000-0002-4494-6565

Салтанат М. Адильгожина[1], https://orcid.org/0000-0002-8408-7363
Алида Ш. Каскабаева[1], https://orcid.org/0000-0002-5184-214X
Жанна Е. Муздубаева[1], https://orcid.org/0000-0002-9058-1878
[1] «Семей медицина университеті» КеАҚ, Семей қ., Қазақстан Республикасы;
[2] Семей қалалық жедел жәрдем ауруханасы, Семей қ., Қазақстан Республикасы;
[3] Ресей ұлттық ғылыми-зерттеу медицина университеті Н.И. Пирогов атындағы, Мәскеу қ., Ресей Федерациясы.

Кіріспе. Коронавирустық инфекция әлемнің барлық дерлік елдерінің жүрек-қан тамырлар ауруларының ағымына айтарлықтай үлес қосты. COVID-19 пандемиясы кезіндегі мұндай ағымның ерекшеліктері ресурстардың жеткіліксіз болуына байланысты жедел коронарлық синдромы және миокард инфарктісі бар науқастарға кеш медициналық көмек көрсету болды.

Зерттеудің мақсаты коронавирустық инфекцияны өткерген, жүрек ишемиялық ауруы бар науқастардың коронарлық артерияларының ішіндегі стент тромбозы мен рестенозының ерекшеліктерін талдау болды.

Материалдар мен әдістер. Зерттеуге алдын ала имплантацияланған коронарлық артерия стентінің тромбозы немесе оның рестенозы үшін миокард реваскуляризациясынан өткен 490 науқас қатысты. Зерттеудің негізгі тобы құжатпен расталған коронавирустық инфекциядан өткен 181 пациентті құрады. Бақылау тобына коронавирустық инфекция тарихы жоқ реваскуляризацияланған коронарлық артерия ауруы бар екі жыныстағы 309 пациент кірді. Науқастардың жасы-34-87 жас. Алынған нәтижелерді талдау 2020 жылдың наурызы мен 2023 жылдың наурызы аралығында миокард реваскуляризациясынан өткен барлық пациенттерді қамтитын арнайы құрылған Тізілім арқылы жүргізілді.

Нәтижелер. Коронавирустық инфекция фонында немесе одан кейін жедел коронарлық синдромы бар адамдарда инфекцияны жұқтырмаған адамдармен салыстырғанда миокард инфарктісі жиі дамиды; олардың арасында өлім немесе жағдайдың ауырлығына байланысты басқа емдеу мекемелеріне ауыстыру түріндегі қолайсыз нәтижелер статистикалық тұрғыдан айтарлықтай байқалады. Негізгі топтағы адамдар арасында стент ішіндегі субакуталық тромбоз жиі кездеседі.

Қорытынды. Науқастарға уақытылы және барынша тиімді медициналық көмек көрсетуге дайын болу үшін коронарлық артерия тромбоздарының дамуындағы КВИ рөлін мұқият зерделеу қажет.

Түйінді сөздер: *Жедел коронарлық синдром, стент ішіндегі тромбоз, стент рестенозы, коронавирустық инфекция, миокард инфарктісі.*

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Introduction

Coronavirus infection (CVI) has made a significant contribution to the course of cardiovascular diseases in the population of almost all countries of the world. The peculiarities of this course during the COVID-19 pandemic were delayed medical care for patients with acute coronary syndrome and myocardial infarction due to insufficient resources for external care, hospital beds, shortage of ambulance crews, and means for resuscitative measures [1,8,19]. In addition, patients with coronary events often refused to seek medical care due to fear of contracting coronavirus infection [17]. All these factors contributed to the fact that patients were admitted with severe complications in the form of cardiogenic shock, cardiac arrhythmias, low ejection fraction, etc. This significantly complicated the timely provision of medical care, leading to a significant increase in the need for invasive interventions, lengthening the length of stay in a hospital bed and ultimately to an increase in mortality rates from cardiovascular pathology [15].

Risk factors for coronary artery stent thrombosis include the following: 1) factors related to the lifestyle and health status of the patient (presence of comorbid diseases such as diabetes mellitus, arterial hypertension, chronic kidney disease or chronic renal failure, malignant neoplasms), smoking , obesity, ethnic characteristics, senility and old

age, genetic predisposition, taking antiplatelet and anticoagulant drugs); 2) factors associated with the characteristics of damage to the coronary vessels (localization of the stent, small diameter of the vessel, the presence of an aneurysm or erosion of the vessel, damage to the coronary artery over a long distance, thrombosis of several coronary arteries simultaneously, damage to the vessel beyond the boundaries of the stent, TIMI 0-1, damage to the type C artery; calcification of the coronary artery, leading to increased density and sclerosis); 3) risk factors associated with the type of stent (small stents, bare metal stents or sirolimus-eluting stents, presence of an inflammatory reaction in the stent); 4) factors associated with invasive intervention, which include the use of several stents, the lack of prior use of clopidogrel, bivalirudin or heparinization before the procedure, the need to use overlapping stents, when with a large extent of vessel damage it is necessary to use the technique of overlapping stents, the use of the wrong stent size or diameter, incomplete or excessive dilatation of the vessel during the procedure, malposition of the stent due to calcification of the vessel, or damage to the stent itself during implantation [13].

The role of coronavirus infection in the development of thrombosis and restenosis of stents in patients who have undergone percutaneous coronary intervention in the past is to enhance the pro-inflammatory environment due to activation of the complement system through binding to ACE2 receptors, which leads to a systemic inflammatory response with increased synthesis of adenosine phosphate, thromboxane with subsequent activation of calcium - dependent aggregation of platelets and the coagulation hemostasis system (fibrinogen-thrombin-fibrin), which ultimately leads to thrombus formation [4,5,6,9,10,11].

The purpose of our study was to analyze the characteristics of in-stent thrombosis and restenosis of the coronary arteries in patients with coronary heart disease who suffered coronavirus infection.

Materials and methods

Characteristics of the study groups

The study included 490 individuals who underwent repeated myocardial revascularization due to thrombosis of a previously implanted stent in a coronary artery or its restenosis. The main study group consisted of 181 patients who had coronavirus infection or COVID-associated pneumonia before or against the background of a cardiovascular event, which was documented. The control group included 309 patients. Criteria for inclusion in the control group of the study: patients of both sexes with revascularized coronary heart disease who do not have a history of coronavirus infection. The age of patients is 34-87 years; the median age in the main group is 63.7 years, in the control group - 64.1 years.

The exclusion criteria for the study were as follows:

- Patients in whom coronary artery stenting was performed for the first time;

- Patients with autoimmune systemic diseases, cancer, tuberculosis.

The sample was complete (all patients who underwent repeated vascularization for the period from 06/01/2020 to 05/05/2023 (the end date of the pandemic)). The study design was cross-sectional.

Characteristics of a specialized registry of patients with coronary artery disease who underwent repeated myocardial revascularization in the early or late stages after COVID-19.

The analysis of the results was carried out using a specially created Register, which included all patients who underwent myocardial revascularization in the period from March 2020 to 2023 after undergoing CVI.

The main register tabs were:

- ✓ socio-demographic data (age and sex characteristics, profession, work status, disease outcome);
- ✓ main diagnosis and concomitant diseases;
- ✓ information on myocardial revascularization (number of repeated revascularizations, date of last and previous revascularizations, presence of restenosis),
- ✓ laboratory data indicating a history of CVI (PCR test, IgM, IgG values),
- ✓ clinical data, data from instrumental examination of patients (coronary angiography, ECG, EchoCG)
- ✓ laboratory diagnostic data (leukocytes, lymphocytes, platelets, hemoglobin, APTT, fibrinogen, INR, d-dimer, troponin, ALT, AST, creatine phosphokinase, creatine phosphokinase of the cardiac fraction, glucose, urea, creatinine, CRP, lipid spectrum, LDH, ferritin).

The results described in this publication included the socio-demographic characteristics of the studied patients and clinical indicators characterizing myocardial revascularization.

Statistical analysis methods

During the study, descriptive statistics were carried out for each time period with the calculation of absolute and relative indicators. Pearson's goodness-of-fit test ($_X2$) was used to assess the statistical significance of differences between study groups. A p value <0.05 was accepted as statistically significant. Statistical data analysis was carried out using SPSS version 20.0 (IBM Ireland Product Distribution Limited, Ireland).

Results

According to the data presented in Table 1, in both the main and control groups, about a quarter of the studied individuals were women; the indicator did not have a statistically significant difference in the study groups; more than half of the patients in both groups were pensioners; only about one fifth of the patients in the main group and about a quarter of the patients in the control group had permanent jobs.

Statistically significant differences were found between study groups regarding disease outcomes. Thus, in the main group, 4.4% of patients died versus 3.6% of the control group. In the main group, five percent of patients were transferred after coronary artery stenting to covid hospitals due to COVID-associated pneumonia (p<0,001).

Of the concomitant diseases, arterial hypertension was observed in the vast majority of cases in both groups; type 2 diabetes was present in more than 20 percent in both study groups.

The majority of patients had the second blood group, Rh positive, the first and third blood groups were observed in almost the same number of patients in both study groups, only about 7% of the studied individuals had the fourth blood group. The absolute majority of people included in the study had Rh positive blood.

Table 1.

Social and demographic characteristics of the studied people.

Rates		Groups				p
		Main		Control		
		N	%	N	%	
sex	females	48	26.5	73	23.6	0.473
	males	133	73.5	236	76.4	
Job status	does not work	33	18.2	35	11.3	0.194
	disabled person	11	6.1	28	9.1	
	works	36	19.9	73	23.6	
	pensioner	100	55.2	172	55.7	
	other	1	0.6	1	0.3	
Outcome	discharged	164	90.6	298	96.4	0.001
	died	8	4.4	11	3.6	
	transferred	9	5.0	0	0.0	
Hypertension	Yes	175	96.7	305	98.7	0.127
	No	6	3.3	4	1.3	
Diabetes	Yes	41	22.7	59	19.1	0.346
	No	140	77.3	250	80.9	
Blood group	1	54	29.8	91	29.4	0.967
	2	64	35.4	116	37.5	
	3	50	27.6	81	26.2	
	4	13	7.2	21	6.8	
Rh factor	positive	168	92.8	297	96.1	0.109
	negative	13	7.2	12	3.9	
Median age (years)		63.7		64.1		0.735

Table 2 presents the characteristics of the clinical data of patients in the study groups in relation to myocardial revascularization. It was found that in the main group of people who had suffered coronavirus infection, the diagnosis of myocardial infarction predominated, while in the control group, unstable angina pectoris was statistically significantly more common (p=0,012).

Table 2.

Characteristics of clinical data in study groups.

Rates		Groups				p
		Main		Main		
		N	%	N	%	
Clinical diagnosis	Unstable angina	95	52.5	198	64.1	0.012
	Myocardial infarction	86	47.5	111	35.9	
Timing of previous revascularization	Acute	0	0.0	1	0.3	0.001
	Subacute	21	11.6	23	7.4	
	Late	43	23.8	130	42.1	
	Very late	117	64.6	155	50.2	
PCR test	negative	169	94.4	308	100.0	0.001
	positive	10	5.6	0	0.0	
Stents number	1	142	78.5	253	81.9	0.521
	2	28	15.5	45	14.6	
	3	9	5.0	10	3.2	
	4	2	1.1	1	0.3	
Stent location						
Marginal artery		2	1.1	5	1.6	0.644
Diagonal branch		3	1.7	5	1.6	0.947
Right coronary artery		63	34.8	111	35.9	0.803
Posterior descending artery		2	1.1	2	0.6	0.587
Left coronary artery		13	7.2	27	8.7	0.544
Circumflex artery		39	21.5	47	15.2	0.031
Left anterior descending artery		108	59.7	174	56.3	0.468

Of interest is the fact that in the main group of people who underwent CVI, subacute thrombosis of the coronary arteries (within one month from previous revascularization) was statistically significantly more common (p<0.001). In the control group, late restenosis (within one month to one year from previous revascularization) and very late

restenosis (more than one year from previous revascularization) predominated. It should be noted that late restenosis occurred significantly more often in both study groups.

The diagnosis of coronavirus infection preceding repeated myocardial revascularization was confirmed by anamnesis data, corresponding entries in extracts from medical histories and outpatient records, PCR analysis and analysis of immunoglobulins M and G. A positive PCR test was recorded in only 5.6% of people in the main group, which indicated that they had an acute infection at the time of diagnosis of acute coronary syndrome.

In the vast majority of cases, one stent was implanted in both study groups; their number reached four stents and did not have statistically significant differences between the subjects of the main and control groups.

The predominant location of implanted stents was the anterior interventricular branch of the left coronary artery (59.7% and 56.3% in the study groups, respectively). Statistically significant differences in the study groups were found only in relation to the circumflex artery (21.5% in the main group and 15.2% in the control group, p=0,031).

Discussion

It is known that during the COVID-19 pandemic, many hospitals were retrained as centers for the treatment of patients with CVI. This led to the need to cancel or postpone planned operations, including for patients with coronary artery disease. However, despite the coronavirus infection, it was necessary to perform emergency operations on patients with emergency conditions, such as acute myocardial infarction or unstable angina. Therefore, it was necessary to select correctly patients who had undergone stenting in the past and who needed coronary artery revascularization based on the clinical presentation, risk factors and possible consequences [2, 16].

In our study, the majority of patients subject to repeated revascularization were men aged 63-64 years, which is fully consistent with world statistics [20]. Certainly, CVI has contributed to poor outcomes in patients requiring re-invasive intervention for acute coronary syndrome, especially in cases of acute infection at the time of hospitalization, confirmed by PCR or the presence of IgM. These data are confirmed by the results of studies conducted in various countries, indicating that the course of myocardial infarction against the background of CVI differs in severity, when patients in a large number of cases require resuscitation measures, transfer to mechanical ventilation or ECMO [3,18].

The severity of the condition is also due to the presence of comorbid pathology, primarily diabetes mellitus, which was observed in every fifth patient in both study groups, as well as arterial hypertension in almost all patients. Treatment with ACE inhibitors could play a certain role in this case, which, as shown in some studies, helps trigger the mechanism of activation of thrombus formation in patients with coronavirus infection [11,12,14]. A more severe course of acute coronary syndrome against the background of CVI led to a more frequent development of myocardial infarction in the main study group compared to patients without CVI.

Taking into account the pathogenetic mechanisms of interaction of coronavirus infection with thrombus formation, it becomes clear that sub-acute coronary artery stent thrombosis predominated in the main group of the study. In the control group, the need for repeated revascularization was associated largely with late and very late restenosis of the coronary arteries due to chronic inflammation and neoatherosclerosis as well as calcification of arteries.

Conclusion

The results of our study demonstrate that people with acute coronary syndrome after coronavirus infection are significantly more likely to develop myocardial infarction compared to people who have not had an infection; among them, adverse outcomes in the form of death or transfer to other medical institutions due to the severity of the condition are statistically significantly more common.

Of interest is the fact that among people in the main group, subacute thrombosis inside the stent was significantly more common, while in the control group of people without CVI, revascularization was caused mostly by late and very late stent damage. These data require continued research with a comprehensive and thorough assessment of various laboratory parameters and instrumental examination data characterizing both the severity of an acute coronary event and coronavirus infection. Despite the end of the COVID-19 pandemic declared by WHO, the incidence rates of this infection remain quite high in all countries of the world. Therefore, a thorough study of the role of CVI in the development of coronary artery thrombosis is necessary in order to be prepared to provide timely and most effective medical care.

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***Corresponding author:**
Pivina Lyudmila, candidate of Medical Sciences, Professor of the Department of Emergency Medicine, NCJSC “Semey Medical University”, Semey, Kazakhstan.
Postal address: Kazakhstan, 071400, Semey, Abay st. 103.
Email: semskluda@rambler.ru
Phone: +7(705)5227300