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To Evaluate the Results of Coronary Stent Implantation with Different Drug-Eluting Agents in Patients with Acute Myocardial Infarction, COVID-19, and Viral Pneumonia with Different In-Hospital Outcomes (Recovery or Death)

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ABSTRACT

Relevance: *After infection with the coronavirus disease 2018 (SARS - CoV -2), a person may be at increased risk for both acute non-ischemic myocardial injury and acute myocardial infarction, especially type 2. Timely interventional coronary artery revascularization after thrombosis does not always restore patency due to rethrombosis and inflammation. Several studies conducted in Europe and the United States involving coronary angiography and percutaneous coronary intervention (PCI) in patients with acute coronary syndrome (ACS) and COVID-19 confirm the validity of pathophysiologists' concepts regarding the nature of coronary and myocardial inflammatory and thrombotic injuries.*

The aim of the study: *To compare the frequency of use of coronary stents with different coatings in selected groups of patients with acute myocardial infarction, COVID-19 infection, and viral pneumonia, depending on the in-hospital outcome: hospital discharge or death from complications.*

Material and Methods: *In The study included 83 patients aged 45 to 85 years with a diagnosis of acute myocardial infarction (AMI) or unstable angina with viral pneumonia (or acute gas exchange disorders) and COVID-19, hospitalized for emergency indications. All patients with AMI underwent pulse oximetry, complete blood count (CBC), blood biochemistry, clinical (general) urinalysis (CUA), coagulation profile, multispiral computed tomography (MSCT) of the lungs, and COVID-19 virus infection diagnostics using polymerase chain reaction (PCR) in oropharyngeal and nasopharyngeal swabs. Renal nitrogen excretion function was assessed dynamically based on changes in serum creatinine concentrations. Clinical, electrocardiographic, angiographic (coronary angiography) and biochemical (enzyme) criteria for acute coronary syndrome and myocardial infarction with and without ST segment elevation were used. X-ray contrast coronary angiography (CAG) was performed on Artis Zee, Siemens, Healthinners (Germany) and Azurion 3 Philips (Netherlands) angiographs. CAG and transluminal balloon coronary angioplasty (TBCA) methodology Elchaninoff H. and co-authors [22], through radial, less often through femoral arterial access. Mechanical recanalization, balloon angioplasty and stenting of coronary arteries were performed using balloon dilation in 59 patients.*

Study Results: *In X-ray contrast coronary angiography of deceased patients with ACS and COVID-19, more severe atherosclerotic coronary lesions were diagnosed in the anterior descending coronary artery. The incidence of coronary occlusion was approximately similar in the two compared groups of deceased and surviving patients, averaging 58% and 46%, with acute forms predominating, accounting for 83-92% of all cases. Implantation of serolimus-eluting coronary stents during PCI was associated with a significantly*

higher mortality rate in the surviving group, by an average of 25.3%. Conversely, the use of zotarolimus-eluting stents showed a significant positive trend in the survival of patients with AMI and COVID-19 after coronary intervention.

Conclusions: *Analysis of the use of stents with various drug-based antiregeneration coatings in patients with AMI, COVID-19, and viral pneumonia during primary PCI revealed a link with unfavorable hospital outcomes when using sirolimus-coated stents and, conversely, a positive trend in patient survival after coronary revascularization with the installation of zotarolimus-coated stents.*

Keywords

Acute myocardial infarction, COVID-19, Pneumonia, Coronary stenting, Drug-eluting coating.

Relevance of the study

According to the existing concepts of pathophysiologists and cardiologists, after a person is infected with coronavirus-2 (SARS - CoV -2), he may have an increased risk of both acute non-ischemic myocardial injury and acute myocardial infarction, especially its type 2 variant, due to excessive inflammation, prothrombotic and procoagulant reactions, which are especially frequent in the development of severe acute respiratory syndrome, respiratory failure with hypoxia and hemodynamic instability in critically ill patients [1].

The proposed mechanisms of myocardial damage in COVID-19 are multifactorial and, according to data contained in a review by employees of the American and Bavishi Institute of Cardiovascular Diseases Ch, et al. (Providence, USA), [2] include:

1) acute inflammation and cytokine damage to the myocardium mediated by activated T cells and monocytes;
2) respiratory failure and hypoxia, which aggravate damage to cardiomyocytes;
3) imbalance in the regulation of angiotensin receptors (ACE_2 and sequential protective signaling pathways of cardiomyocytes;
4) coagulopathy and microvascular coronary thrombosis;
5) generalized damage to endothelial cells and endothelial inflammation in tissues, including the heart;
6) inflammation and/or stress, provoking rupture of atherosclerotic coronary plaque or leading to a mismatch between supply and demand in oxygen supply, causing ischemia/myocardial infarction [2].

In studies of the cardiovascular system of patients who died from complications of COVID-19, morphologists from the Monzino Cardiology Center (Milan, Italy) Pesce M, et al. [3] found that, in addition to atherosclerotic plaque rupture and thrombosis, other pathogenetic factors also contribute to the development of myocardial damage during the development of acute coronary syndrome (ACS). These factors were listed in the materials published by experts in cardiac cell biology of the European Society of Cardiology (ESC) Working Group, who believe that the main proven causes of cardiac damage in COVID-19 may be factors and mechanisms such as:

a. hypercoagulation with micro- (and, to a lesser extent, macro-) vascular occlusion;
b. viral infection of myocardial cells;
c. consequences of cytokine damage;
d. mechanisms provoking the development of coagulopathies [3].

A number of studies conducted in Europe and the United States involving coronary angiography and percutaneous coronary intervention (PCI) in patients with ACS and COVID-19 confirmed the validity of pathophysiologists' concepts regarding the nature of coronary and myocardial inflammatory and thrombotic damage. Thus, the presence of COVID-19 in patients with acute ST-segment elevation myocardial infarction (STEMI) and COVID-19 with acute heart failure and asystole that developed before the intervention, despite more intensive antiplatelet and anticoagulant treatment, were less likely to achieve optimal TIMI-3 response after PCI and increased the chances of undergoing coronary thrombectomy in the Polish study by Zajac P, et al., [4].

Similar to the results of the Polish study, a high frequency of cardiac complications and stent thrombosis in COVID-19-positive patients with STEMI was noted by authors from Baylor University Medical Center (Texas, USA) in a multicenter retrospective study of a series of cases in hospitals in 4 countries, in which stent thrombosis was diagnosed with a frequency of over 20% [5].

Significantly higher rates of stent thrombosis and post-first use of a modified thrombus removal device, followed by increased use of glycoprotein IIb/IIIa inhibitors and in-hospital thrombus aspiration, were observed in patients with STEMI and co-infection with COVID-19 in a UK study by authors from St Bartholomew's Hospital, London [6]. They concluded that patients with STEMI and co-infection with COVID-19 have a distinct hemostatic shift towards higher thrombotic burden and worse outcomes.

According to the journal's editor, H.L. Dauerman [7] from the University of Vermont (USA), there are specific considerations for PCI in patients with acute viral injury that require caution and additional techniques. He noted that a series of existing reports in patients with STEMI and COVID-19 have shown a sharp increase in coronary thromboembolism, and that primary PCI was technically more challenging in the setting of acute coronavirus infection [7].

The COVID-19 pandemic has significantly impacted care systems for patients with acute ST-elevation myocardial infarction (STEMI) worldwide, jeopardizing timely access to reperfusion therapy. For example, when comparing hospitalization rates across countries for more than 111,000 patients with STEMI, **a** study by Wu J, et al. from the University of Leeds (UK), it was shown that it decreased by 20% [8]. The lack of timely coronary artery revascularization

measures in patients with STEMI combined with COVID-19 can significantly worsen their life prognosis. According to the research group from the Cardiac Intensive Care Unit of Harvard Medical School in Boston (Massachusetts, USA) Bhatt AS, et al., when only half of the patients with MI and COVID-19 underwent coronary angiography and primary reperfusion, the incidence of in-hospital mortality, all-cause shock, cardiac arrest, acute heart failure and the need for renal replacement therapy sharply increased [9]. The issue of choosing the tactics and method of revascularization for the treatment of STEMI in patients with COVID-19 is widely discussed in the modern literature. However, according to American researchers from the Georgia Heart Institute (Gainesville, USA), primary PCI during the epidemic was the first-line reperfusion strategy for patients with STEMI in the United States, and the frequency of fibrinolysis-oriented reperfusion remained at a level of approximately 2-13% [10]. The PCI procedure (PPCI) for COVID-19 infection was technically feasible and remained the predominant strategy of coronary reperfusion, confirming the validity of existing national guidelines [11]. The results of transcatheter revascularization, as well as the prognosis of patients with ACS, can significantly depend on the properties of the coronary stents used, among which, in the pre-COVID period, designs with drug-eluting agents such as sirolimus, paclitaxel, and zotarolimus dominated [12,13]. Comparison of the safety and efficacy of their use in patients with coronary thrombosis and ACS did not yield reliable data on the advantages of one or another stent or balloon coating [13-15]. To further clarify the issues of the efficacy and safety of using various types of drug-eluting agents for coronary stents, a randomized clinical trial on this issue is planned and is being conducted by Mexican interventionalists in 2022-2025 [16]. However, in patients with ACS and COVID-19, such comparisons are still extremely rare or are not the subject of a separate analysis.

Purpose of the study

The aim of this study was to compare the frequency of use of coronary stents with different coatings in selected groups of patients with acute myocardial infarction, COVID-19 infection, and viral pneumonia, depending on the nature of the hospital outcome: discharge from hospital or death from complications of the disease.

Material and Methods

A total of 83 patients with a diagnosis of acute myocardial infarction or unstable angina with viral pneumonia (or acute gas exchange disorders) and COVID-19 were included in the study. To classify pneumonia variants, ICD-10 codes were used: U07.1 Coronavirus infection caused by COVID-19 virus, virus identified (confirmed by laboratory testing regardless of the severity of clinical signs or symptoms); J12.9 Community-acquired pneumonia. U07.2 Coronavirus infection caused by COVID-19 virus, virus not identified (COVID-19 is diagnosed clinically or epidemiologically, but laboratory tests are inconclusive or unavailable.

The patients were divided into 2 groups: Group 1 consisted of 45 deceased patients with AMI, COVID-19, and pneumonia, and Group 2 consisted of 38 patients discharged from the hospital after treatment (Table 1). The group of patients with a fatal outcome included 45 patients aged 53 to 87 years, including 25 men, with an average age of 71.1±9.2 years, and 20 women, with an average age of 76.4±6.5 years. The comparison group of patients with ACS who recovered and were discharged from the hospital included 38 patients aged 45 to 85 years, including 24 men, with an average age of 64.6±9.8 years, and 14 women, with an average age of

Table 1: Gender and age of patients with acute myocardial infarction examined in 2 groups who died in hospital (group 1) and were discharged (group 2).

Indicators	Group 1 (n=45)	Group 2 (n=38)	Difference in % Reliability, p1-2
The number of men and women examined, their age, and the diagnosis of acute myocardial infarction and COVID-19 according to ICD-X	Deceased patients with AMI, pneumonia and COVID-19 (n=45) Men 25, women 20 (ratio 1:0.8)	Discharged patients with AMI, pneumonia and COVID-19 (n=38) Men 24, women 14 (ratio 1:0.58)	-
Men average age, range of variations and % of the total number of patients	71.1+9.2 years From 53 to 87 years old n=25(55.5%)	64.6+9.8 years From 45 to 82 years old n=24(63.1%)	9.1% Nd
Women average age, range of variations and % of the total number of patients	76.4±6.5 From 65 to 86 years old n=20 (44.5%)	71.8+9.7 years From 46 to 85 years old n=14 (46.9%)	6.0 Nd
Diagnosis according to ICD-X - I 21 acute myocardial infarction, number of patients and % of the total	n=34(75.5%)	n=30(78.9%)	3.4% Nd
Diagnosis according to ICD-X - I 22 repeated myocardial infarction, number of patients and % of the total	n=11(24.5%)	n=8(21.1%)	3.4% Nd
Diagnosis according to ICD-X - U07.1 COVID-19, number of patients and % of the total	n=41 out of 45 (91.1%)	n=26 out of 38 (68.4%)	22.7% p1-2< 0.03
ICD-X diagnosis - U07.2 COVID-19, number of patients and % of the total	n=4 out of 45 (8.9%)	n=12 out of 38 (31.6%)	22.7% p1-2< 0.03

Notation - n= number of observations.

71.8±9.7 years (Group 2). In the sample of patients with ACS, men predominated by gender, with the ratio of men to women in the first group being 1:0.8 and in the second group being 1:0.56. The average age of patients, in both the male and female groups, was, on average, higher in those who died.

Data on the nature of pneumonia based on the results of instrumental diagnostics (MSCT and chest X-ray), gas exchange parameters upon admission to hospital, the severity of respiratory failure, the frequency of use of mechanical ventilation and tracheostomy surgery in the selected groups of patients are presented in Table 2.

The incidence of bilateral lung damage in patients of the first group, according to instrumental diagnostic data, was 93.3%, and in the group of discharged patients with AMI, it averaged 78.9%, which was 14.4% (p1-2> 0.1) lower than in the first group of deceased patients with COVID-19 with AMI. The incidence of unilateral lung damage did not exceed 8% in both groups. Non-pneumonia-related variants of acute hypoxia accounted for no more than 3% in the groups and were caused by pulmonary hypoventilation (rib fractures), aspiration, and decompensated heart failure. Artificial and assisted ventilation was used in 55.5% of patients, including 4.4% of patients with a performed tracheostomy. Multiple organ dysfunction syndrome (MODS) and sepsis complicated the course of the disease only in patients of the first group and were not detected in the second group of discharged patients. In terms of the degree of respiratory failure during the initial period of hospitalization, the most unfavorable indicators were in the group of patients who died: 48% of them had grade 3 respiratory failure, which exceeded the rate in group 2 by 44% (p1-2 < 0.001). Overall, the incidence of respiratory failure of varying severity was also significantly higher in the group of patients who died.

Table 2: The nature of lung pathology according to MSCT data and the frequency of gas exchange disorders according to clinical and laboratory data in hospital in patients in 2 groups of patients with acute coronary syndrome.

The nature of the lung pathology, the frequency of mechanical ventilation, the degree of respiratory failure and oxygen saturation indicators	Deceased patients with AMI, pneumonia and COVID-19 (n=45) Group 1	Discharged patients with acute myocardial infarction, pneumonia, and COVID-19 (n=38) Group 2	Difference in % Reliability
Bilateral pneumonia	n = 42 (93.3%)	n=30(78.9%)	14.4% Nd
Pneumonia with damage to one lung	n=3(6.7%)	n = 3 (7.9%)	1% Nd
Disorders of pulmonary ventilation without pneumonia: hypoventilation (rib fractures): CHF, congestive lungs:	n=2 (4.4%) n=0 n=2 (4.4%)	n=2(5.3%) n=0 n=2(5.3%)	0.9% Nd - 0.9% Nd
Tracheostomy	n=2(4.4%)	n=0	-
Artificial ventilation of the lungs (AVL)	n=25(55.5%)	n=1(2.6%)	52.9% p1-2< 0.001
Extracorporeal membrane oxygenation (ECMO)	n=1 (2.2%)	n=0	-
Acute respiratory failure	n=25 (55.5%)	n=1(2.6%)	52.9% p1-2< 0.001
Sepsis	n=1 (2.2%)	n=0	-
Multiple organ dysfunction syndrome (MODS)	n=14 (31.1%)	n=1(2.6%)	28.5% p1-2< 0.02
O_2 saturation levels:			
95% and above	n=18 (40 %)	n = 22(57.9%)	17.9% p1-2< 0.05
90-94%	n=14 (31.1 %)	n=12(31.6%)	1.2% Nd
75-89%	n=13 (28.9 %)	n=4(10.5%)	18.4% p1-2< 0.05
Less than 75%	n=1 (2.2%)	n=0	-
Degree of respiratory failure: DN O st.	n=0	n=15 (39.4%)	39.4%
DN 1 tbsp.	n=11 (24.4%)	n=4 (10.5%)	13.9% Nd
DN 2 tbsp.	n=7 (15.5%)	n=1(2.6%)	12.9% Nd
DN 3 tbsp.	n=18 (40%)	n=0	40%
Total with respiratory failure	n=36 (80%)	n=20(52.6%)	27.4% p< 0.02

In accordance with European international guidelines, clinical, electrocardiographic, angiographic (coronary angiography) and biochemical (enzyme) criteria of acute coronary syndrome (ACS) and myocardial infarction with and without ST segment elevation were used in the study [17,18]. The ratio of acute and recurrent MI cases was approximately equal in the group of deceased and discharged patients, amounting to 75.5 and 24.5% in the first group and 78.9 and 21.1% in the second. Macroscopic signs of myocardial necrosis, according to pathomorphological studies, were detected in 4 of 45 patients (8.9%) in the first group (Table 3). In 12 patients with ACS out of 83 (14.4%), surgical revascularization of the coronary arteries was not performed due to the long period from the onset of pain syndrome (in 3 out of 12) and the severity of the condition with respiratory failure and the use of mechanical ventilation (9 cases out of 12). All received dual antithrombotic therapy in dosages corresponding to European recommendations [19].

Research Methods

In hospital, all patients with AMI and in the comparison groups underwent mandatory laboratory and instrumental tests: pulse oximetry, complete blood count (CBC), blood biochemistry, clinical (general) urinalysis (CUA), coagulation profile, multispiral computed tomography (MSCT) of the lungs, COVID-19 virus infection diagnostics using polymerase chain reaction (PCR) in oropharyngeal and nasopharyngeal swabs, and assessment of renal nitrogen excretion function dynamics based on changes in serum creatinine concentrations, water excretion disorders, and the degree of diuresis reduction. Computed tomography (MSCT) of the chest organs was performed on Canon tomographs. Prime SP (produced by Russia: ArPn Canon Medical System LLC, Japan) and Toshiba Aqilion Prime (Canon Medical Systems Corporation, Japan). The data from the multislice computed tomography (MSCT) method of the lungs were assessed according to two classifications: by assessing the CT severity of pneumonia and by the area of the spread of lung damage. Echocardiography in patients with acute coronary syndrome was performed using Philips CX 50 (Germany) and Esaote mylab X8 (Italy) devices. "Acuson-128XP" by "Acuson Corporation" (USA) in two-dimensional and M-modality modes. X-ray contrast coronary angiography **(CAG)** was performed on Artis Zee, Siemens, Healthinners (Germany) and Azurion 3 Philips (Netherlands) angiographs according to the methods described in the manuals of domestic and North American interventionalists [20,21]. CAG and transluminal balloon coronary angioplasty

Table 3: Clinical assessment of the nature of acute myocardial infarction and methods of coronary artery revascularization in two groups of deceased (group 1) and discharged patients (group 2).

Indicators, frequency in %	Deceased patients with AMI, pneumonia and COVID-19 (n=45) Group 1	Discharged patients with acute myocardial infarction, pneumonia, and COVID-19 (n=38) Group 2	Degree of difference in %	Reliability of differences, p1-3
Intravital diagnosis of AMI	n=41(91.1%)	n=38(100%)	8.9%	Nd
Diagnosis of myocardial infarction after death based on autopsy data	n=4 (8.9%)	-	-	-
Transmural myocardial infarction	n=6 (13.3%)	n=2 (5.3%)	8.0%	Nd
AMI type 2	n=8 (17.8%)	n=2 (5.3%)	12.5%	Nd
ST- elevation myocardial infarction variant	n=7 (15.5%)	n=14 (36.8%)	21.3%	P1-2< 0.03
ST elevation myocardial infarction variant	n=1 (2.2%)	n=3 (7.9%)	5.7%	Nd
ST elevation myocardial infarction variant	n=7 (15.5%)	n=16 (42.1%)	26.6%	P1-2< 0.0 1
Clinical diagnosis of AMI without assessment of ST dynamics	n=26(57.8%)	n=5 (13.1%)	44.7%	P1-2<0.001
Unstable angina	n=1 (2.2%)	n=2(5.3%)	3.1%	Nd
Subendocardial AMI	P=0	n=1 (2.6%)	2.6%	Nd
Localization of IM:				
front incl. anterior-apical anterolateral	n=22(48.9%) n=1(4.5%) n=4 (18.2%)	n=14 (36.8%) n=0 n=1(7.1%)	12.1% - 11.1%	Nd - Nd
lower	n=11(24.4%)	n=9(23.7%)	0.7%	Nd
rear incl. posterolateral	n=9 (20%) n=4	n=2 (5.3%) n=0	14.7% -	Nd -
circular	n=1 (2.2%)	n=0	-	-
multiple localizationtions	n=2(4.4%)	n=0	-	-
The methods used for myocardial revascularization:				
PTCA, stenting	n=34(75.5%)	n=32(84.2%)	8.7%	Nd
AKSH , MKSH	n=2 (4.4%)	n=1 (2.6%)	1.8%	Nd
catheter attempt recanalization of coronary arteries	n=2 (4.4%)	n=1 (2.6%)	1.8%	Nd
thrombus extraction	n=2 (4.4%)	n=0	-	-

Notation - n= number of observations , ABCS - aortocoronary bypass surgery, mamara-coronary bypass surgery - MCBS.

(TBCA) were performed according to the method of Elchaninoff H, et al. [22], through radial, less often through femoral arterial access (3 cases). Mechanical recanalization, balloon angioplasty and stenting of the coronary artery were performed using balloon dilation according to the technique [22,23], using U-Pass 2 x 20, 17 atm 120 s devices - three dilations were performed at a pressure of 14, 17, 12 atm for 120 s and a Raptor 2.5 x 15, 18 atm, 120 s balloon, followed by stent placement. After mechanical recanalization and PTCA, the stenotic or thrombosed artery was stented, with subsequent optimization of the vessel lumen in the proximal and distal segments of the stent using a delivery balloon under a pressure of 12 atm for 120 s. Stents were most often used CALYPSO, MANUFACTURER OF ANGIOLINE (Russia). Diagnosis and assessment of the severity of acute kidney injury (AKI) were performed in accordance with the data on changes in the concentration of creatinine in the blood serum and the degree of decrease in diuresis, according to the KDIGO 2012 criteria [Classification of acute kidney injury according to KDIGO 2012. Clinical practice guideline for the evaluation and management of Chronic Kidney Disease. / Kidney International Supplements. 2013; 3 (1): 1-150. https://doi.org/10.1038]. Coagulogram parameters were studied on the automatic analyzer "ACL Elite Top", USA. Hemostasis parameters were assessed: prothrombin time according to Quick, prothrombin index and international normalized ratio - by calculation. Activated partial thromboplastin time was determined using a modified plasma recalcification reaction method. The fibrinogen level in blood plasma was analyzed using the ethanol method according to Breen F, Tullis J. In order to confirm the diagnosis of coronavirus infection and detect the genetic material (RNA) of the SARS-CoV-2 coronavirus in a biomaterial sample, PCR diagnostics were performed in all patients. The polymerase chain reaction was carried out using the reagents of the IMBIAN- SARS - COV -2 Ag ELISA test system (Imbian LLC) laboratory diagnostics » (Novosibirsk region, Koltsovo district, Russia).

In the first hours after the patient's admission to the hospital, the risk of myocardial necrosis, the dynamics of ECG changes, and the strategy and method of possible revascularization were assessed. During this period, angiographic examination of the coronary arteries was performed, and the timing of coronary procedures—thromboextraction, stenting, and coronary artery bypass grafting—was planned. After collecting the patient's medical history, the nature of the antithrombotic therapy administered during the outpatient phase was clarified, and if the patient was taking antiplatelet agents, acetylsalicylic acid (ThromboASS, Cardiomagnyl), clopidogrel (Plavix), or rivaroxaban (Xarelto), the doses of the prescribed antiplatelet and anticoagulants were adjusted. During the first 1-2 days, hemostasis parameters were monitored to monitor hemostasis and prevent antithrombotic overdose. Seven to 14 days after the coronary artery revascularization procedure, in-hospital outcomes were assessed, and groups of patients with fatal outcomes and those with recovery were identified. Within these groups, the frequency and nature of standard antiviral, antibacterial, hormonal, expectorant, gastroprotective, and antihypertensive therapy were compared, and their potential impact on outcome and the risk of complications, such as renal, hepatic, and multiple organ failure, were assessed.

Statistical processing of the obtained data was performed using the Stata/MP 13.0 for Mac software package. Distributions were tested using the Shapiro-Wilk W-test. Quantitative variables were described as M and SD (for a normal distribution) or as Me and IQR (for an asymmetric distribution). The significance of differences between the two groups for quantitative variables was assessed using the Mann-Whitney U-test. The significance of differences between mean values was determined using the Student's t-test. The chi-square test was used to compare the frequencies of qualitative variables between groups.

Research Results

According to the data of the X-ray contrast coronary angiography method, more severe coronary artery disease due to the atherosclerotic process was more often diagnosed in the anterior descending coronary artery in deceased patients with ACS and COVID-19. Thus, stenosis of high, hemodynamically significant grades was detected 22.3% more often than in the group of discharged patients, a significant difference ($p1\text{-}2<0.03$), Table 4. Signs of coronary occlusion were significantly more often detected in the right coronary artery territory in the group of discharged patients, on average by 19.6% ($p1\text{-}2 < 0.05$). The frequency of coronary occlusion was approximately similar in the two compared groups of deceased and surviving patients, amounting to 58 and 46% on average, with its acute forms dominating - 83-92% of all cases.

Surgical intervention on the coronary arteries for the purpose of revascularization and restoration of coronary blood flow was performed in 31 of 45 (68.9%) and 28 of 38 (72.7%) patients in the two analyzed groups (Table 4). Most often, the intervention was performed on the LAD (in 27-35%) and RCA (in 28-30%) arteries of patients. Rare complications of PTCA and stenting were coronary artery dissection - 2 cases (6.4%) and dislocation of the implanted stent - 1 case (2.3%).

Biolimus, zotoralimus, paclitaxel, sirolimus, and everolimus were used to coat the stents. The stents were implanted in the coronary arteries of patients with ACS and COVID-19 during PCI. (Figure 1) and only in two cases was the bare metal version without coating used (Table 6).

Biolimus, zotoralimus, paclitaxel, sirolimus, and everolimus were used to coat the stents. The stents were implanted in the coronary arteries of patients with ACS and COVID-19 during PCI. (Figure 1) and only in two cases was the bare metal version without coating used (Table 6).

Table 6 presents the analysis of the frequency of use of different types of coating in the groups of discharged and deceased patients. Coating with serolimus was associated with a higher incidence of fatal outcomes in the first group of patients, by an average of 25.3% (significant; $p1\text{-}2<0.02$).

Table 4: The nature of coronary circulation disorders in patients with COVID -19 with acute myocardial infarction according to X-ray contrast coronary angiography in groups of deceased patients and those discharged from hospital.

Name of the artery, type of lesion detected, nature of the complication during CAG (coronary angiography)	Deceased patients with AMI, pneumonia and COVID-19 (n = 31 of 45) Group 1 Frequency of defeat	Discharged patients with acute myocardial infarction, pneumonia and COVID-19 (n=28 out of 38) Group 2 Frequency of defeat	Difference in %	Reliability of differences; p1-2
Degree of coronary artery stenosis:				
1. LCA trunk:	n=13 out of 31 (41.9%)	n=13 out of 28 (46.4%)	4.5%	Nd
30-50%	n=8 out of 13 (61.5%)	n=7 out of 13 (53.8%)	7.7%	Nd
55-90%	n=5 out of 13 (38.5%)	n = 6 out of 13 (46.2%)	7.7%	Nd
2. DB 1-2 orders:	n=12 out of 31 (38.7%)	n=9 out of 28 (32.1%)	6.6%	Nd
50%	n=3 out of 12 (25%)	n=1 out of 9 (11.1%)	13.9%	Nd
55-95%	n=9 out of 12 (75%)	n=8 out of 9 (88.9%)	13.9%	Nd
3. OMB	n=10 out of 31 (32.2%)	n=8 out of 28 (28.6%)	3.6%	Nd
50%	n=1 out of 10 (10%)	n=2 out of 8 (25%)	15%	Nd
55-95%	n=9 out of 10 (90%)	n=6 out of 8 (75%)	15%	Nd
4. PLB	n=4 out of 31 (12.9%)	n=4 out of 28 (14.3%)	1.4%	Nd
50%	n=1 of 4	n=1 of 4	-	-
55-75%	n=3 out of 4	n=3 out of 4	-	-
5. PIVC	n=7 out of 31 (22.6%)	n=2 out of 28 (7.1%)	15.5%	p>0.1
50%	n=2 of 7	n=0	-	-
55-90%	n=5 out of 7	n=2 of 2	-	-
6. IA	n=1 out of 31 (3.2%)	n=1 of 28 (3.6%)	0.4%	Nd
50%	n=1 of 1	n=0	-	-
55-90%	n=0	n=1 of 1	-	-
7. OB	n=13 out of 31 (41.9%)	n=13 out of 28 (46.4%)	4.5%	Nd
40-50%	n=5 out of 13 (38.4%)	n=3 out of 13 (23.1%)	15.3%	-
55-90%	n=9 out of 13 (69.2%)	n=10 out of 13 (76.9%)	7.7%%	-
8. ShEB - sharp edge branch	n=1 out of 31 (3.2%)	n=0	-	-
50%	n=1 of 1	-	-	-
9. RCA	n=20 out of 31 (64.5%)	n=14 out of 28 (50%)	14.5%	Nd
30-50%	n=9 out of 20 (45%)	n=8 out of 14 (57.1%)	12.1%	Nd
55-99%:	n=14 out of 20 (55%)	n=8 out of 14 (57.1%)	12.1%	Nd
10. LAD	n=16 out of 31 (51.6%)	n=17 out of 28 (60.7%)	9.1%	Nd
30-50%	n=6 out of 16 (37.5%)	n=5 out of 17 (29.4%)	8.4%	Nd
55-99%	n=11 out of 16 (68.7%)	n=13 out of 17 (76.5%)	7.8%	Nd
11. ADB	n=9 out of 31 (29%)	n=9 out of 28 (32.1%)	3.1%	Nd
30-50%	n=3 out of 9 (33.3%)	n=6 out of 9 (66.7%)	33.4%	p< 0.01
55-95%	n=6 out of 9 (66.7%)	n=4 out of 9 (44.4;)	22.3%	p< 0.03
12. PDA	n=0	n=2 out of 28 (7.1%)	-	-
40-50%	-	n=2 of 2	-	-
13. Stent restenosis:	n=0	n=1 out of 28 (3.6%)	-	-
70%	-	n=1 of 1	-	-
14. Bifurcation stenosis:	n=0	n=1 out of 28 (3.6%)	-	-
80%	-	n=1 of 1	-	-
Detected occlusion of the coronary artery:	n=18 of 31 studies (58.1%)	n=13 out of 28 studies (46.4%)	11.7%	Nd
1. RCA	n=5 out of 18 (27.7%)	n=6 out of 13 (46.1%)	19.6%	p< 0.05
2. CB	n=3 out of 18 (16.6%)	n=3 out of 13 (23.1%)	6.5%	Nd
3. ADB	n=3 out of 18 (16.6%)	n=1 out of 13 (7.7%)	8.9%	Nd
4. OMB	n=2 out of 18 (11.1%)	n=0	-	-
5. PLB	n=2 out of 18 (11.1%)	n=0	-	-
6. LAD	n=2 out of 18 (11.1%)	n=1 out of 13 (7.7%)	3.4%	Nd
7. DB	n=1 out of 18 (5.5%)	n=0	-	-
8. PIVC	n=0	n=1 out of 13 (7.7%)	-	-
9. Stent occlusion	n=0	n=1 out of 13 (7.7%)	-	-
Acute occlusion	n=15 out of 18 (83.3%)	n=12 out of 13 (92.3%)	9.0%	Nd
Chronic occlusion	n=3 out of 18 (16.7%)	n=1 out of 13 (7.7%)	9.0%	Nd
Thrombosis of the coronary artery:	n=2 out of 31 (6.4%)	n=0 out of 28	-	-
1. PLB	n=1 of 2	-	-	-
2. PIVC	n=1 of 2	-	-	-
3. RCA	n=1 of 2	-	-	-
Calcification of the coronary artery	n=1 out of 31 (3.2%)	n=2 out of 28 (7.1%)	3.9%	Nd
Complications of CAG:				
radiation thrombosis	n=2 out of 31 (6.4%)	n=0 out of 28	-	-
arteries	n=2 of 2	-	-	-
Shuntography during coronary angiography	n=1 out of 31 (3.2%)	n=1 out of 28 (3.6%)	0.4%	Nd
Without CAG:				
patient refusal	n=5 out of 45 (11.1%)	n=2 out of 38 (5.3%)	5.8%	Nd
medical counter-	n=1 out of 5	n=1 of 2	-	-
testimony	n=4 out of 5	n=1 of 2	-	-

Legend: OMB - obtuse marginal branch, DB - diagonal branch, PIVC - posterior interventricular branch, CAG - coronary angiography, RCA - right coronary artery, OB - circumflex branch, LAD - anterior descending branch, PLB - posterolateral branch, LAD - anterior interventricular branch, LCA - left coronary artery.

Table 5: Data on the frequency and nature of stenting, percutaneous coronary intervention (PCI) and translumenal angioplasty (TLAP) in patients with CO VID -19 with acute myocardial infarction in groups of deceased and discharged patients.

Coronary artery subjected to intervention and PCI procedures and TLAP	Deceased patients with AMI, pneumonia and COVID-19 (n= 31 out of 45) Group 1 Frequency of defeat	Discharged patients with acute myocardial infarction, pneumonia, and COVID-19 (n=28 out of 38) Group 2 Frequency of defeat	Difference in %	Reliability of differences; p1-2
1. LCA trunk 2. OV 3. ZBV 4. ZMZHV PKA 5. LAD 6. In the LAD shunt 7. PCA 8. PNA 9. Into the existing stent	n=2 out of 42 (4.7%) n=6 out of 42 (14.3%) n=3 out of 42 (7.1%) n=1 out of 42 (2.4%) n=15 out of 42 (35.7%) n=1 out of 42 (2.4%) n=12 out of 42 (28.6%) n=2 out of 42 (4.7%) n=0	n=2 out of 43 (4.6%) n=6 out of 43 (13.9%) n=1 out of 43 (2.3%) n=1 out of 43 (2.3%) n=12 out of 43 (27.9%) n=0 n=13 out of 43 (30.2%) n=3 out of 43 (7%) n=1 out of 43 (2.3%)	0.1% 0.4% 4.8% 0.1% 7.8% - 1.6% 2.3% -	Nd Nd Nd Nd Nd - Nd Nd -
Complications during intervention: stent dislocation dissection: permanent resident LKA trunk	P=2 out of 31 (6.4%) n=0 n=2 out of 31 (6.4%) n=1 of 2 n=1 of 2	n=1 out of 43 (2.3%) n=1 out of 43 (2.3%) n=0 - -	- - - - -	- - - - -
Thrombectomy, aspiration	n=3 out of 31 (9.7%)	n=0	-	-
Attempt to perform PCI	n=2 out of 31 (6.4%)	n=1 out of 28 (3.6%)	2.8%	Nd
Thrombosis, restenosis of a previously installed stent	n=2 out of 31 (6.4%)	n=1 out of 28 (3.6%)	2.8%	Nd
CAG without PCI: without critical stenosis of the coronary artery	n=0	n=1 out of 28 (3.6%)	-	-

Table 6: Comparison of the number of coronary stents with different drug coatings (and without it) in two groups of deceased and discharged patients with acute myocardial infarction.

Name of the drug coating of the stent (or lack thereof) Types of stents	Deceased patients with AMI, pneumonia and COVID-19 (n=45) Group 1	Discharged patients with acute myocardial infarction, pneumonia, and COVID-19 (n=38) Group 2	Degree of difference in %	Reliability of differences, p1-2
Number of implanted stents with identified coating	n=48 for 31 patients (155%)	n=45 in 28 patients (161%)	6%	P>0.3
The drug sirolimus:	n = 25 out of 48 (52.1%)	n=12 out of 45 (26.7%)	25.3%	P<0.02
Stent types: Calypso, Alex, Superflex Crus	n=25	n=12		
The drug zotarolimus:	n= 8 and from 48 (16.7%)	n=15 out of 45 (33.3%)	16.6%	P=0.05
Types of stents: Resolute Integrity, Resolute Onyx	n=8	n=1 3		
The drug biolimus:	n=1 out of 48 (2.1%)	n=1 out of 45 (2.2%)	0.1%	P>0.5
Stent type: BMX	n=1	n=1		
The drug everolimus:	n=11 out of 48 (22.9%)	n=16 out of 45 (35.5%)	12.6%	P>0.2
Types of stents: Promus Premier, Promus Element, Xience, Orsiro	n = 7	n=13	14.3%	P>0.1
The drug paclitaxel:	n=2 out of 48 (4.2%)	n=0	-	-
Stent type: Stentonic	n=2	n=0	-	-
Uncoated stent	n=1 out of 48 (2.1%)	n=1 out of 45 (2.2%)	0.1%	P>0.5
Stent type: Nex Gen	n=1	n=1	-	-

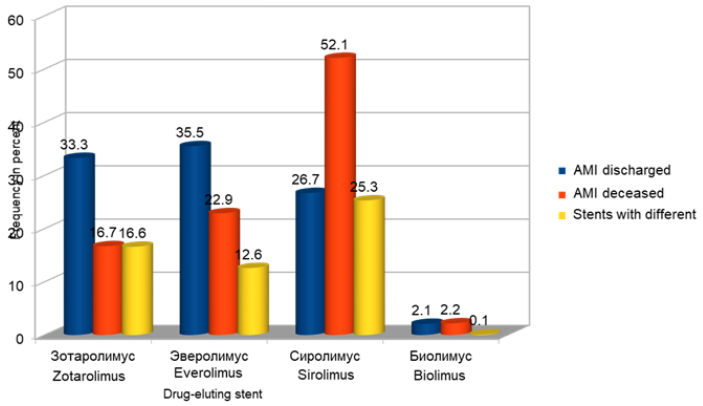

Figure 1: Frequency in percent of implantation of coronary stents with different drug coatings in 2 groups of patients with acute myocardial infarction and COVID-19 with different disease outcomes - recovery (AMI discharged) and death (AMI deceased).

In contrast, the use of zotarolimus-eluting stents demonstrated a significant positive trend in survival in patients with AMI and COVID-19 after coronary intervention. The difference from the discharged group was 16.6% (marginally significant; p1-2=0.05). Only a non-significant positive trend of this type was observed with everolimus-eluting stents. The use of everolimus-eluting stents in the surviving group exceeded the use in the first group of patients who died by 12.6% (non-significant, p1-2>0.2) (Table 6, Figure 1).

The differences in the frequency of cardiovascular pathology diagnosed by instrumental methods in the two groups of patients with ACS and COVID-19 were most significant for heart rhythm disturbances, such as paroxysmal atrial fibrillation - 64.7% more often diagnosed in the group of deceased patients (reliably (p1-2<0.001), and ventricular tachycardia by 17.4% (p1-2<0.05), significantly more often (Table 7).

In the group of deceased patients with ACS, signs of chronic heart failure of functional classes 2-3 were detected more often by 30.7% (p1-2<0.02), a decrease in the LV ejection fraction (LVEF) of the heart below 50%, acute and chronic left ventricular aneurysm was diagnosed more often by 18.5% (significant; p1-2<0.05). Signs of aortic atherosclerosis, when conducting transthoracic echocardiography, were also diagnosed 40.9% more often in the 1st group (the difference is significant; p1-2<0.001).

Discussion of Results

The first part of this study assessed the cardiovascular status after coronary revascularization procedures and coronary stent implantation in patients with ACS, COVID-19, and viral pneumonia. The analysis revealed that the PCI procedure itself Balloon angioplasty was minimally invasive and effective in restoring normal coronary blood flow. Complications such as arterial dissection occurred in 6.4% of patients (two in the group of deceased patients). Stent dislocation occurred in only one patient, who was subsequently discharged; it did not affect the outcome.

An analysis of in-hospital outcomes in patients, depending on the type of drug-eluting agent, revealed a possible association with adverse outcomes with the use of sirolimus-eluting stents and, conversely, a positive trend toward survival in patients with acute myocardial infarction and COVID-19 following coronary intervention with the placement of zotaralimus-eluting stents in stenotic coronary arteries. These data are difficult to interpret definitively, as we were unable to find studies in the available literature evaluating the feasibility and safety of using various types of coronary stents in patients with acute coronary syndrome

Table 7: The nature and frequency of identified cardiovascular pathology in 2 groups of patients with acute myocardial infarction according to instrumental (echocardiography, coronary angiography) and pathomorphological diagnostics.

Cardiovascular diseases (CVD)	Deceased patients with acute myocardial infarction, pneumonia, and COVID-19 (n=45) Group 1	Discharged patients with acute myocardial infarction, pneumonia, and COVID-19 (n=38) Group 2	Difference in % Reliability, p1-2
Aneurysm of the left ventricle	n=19 (42.2%)	n=9 (23.7%)	18.5% p<0.05
Atherosclerosis of the aorta	n=30 (66.7%)	n=6 (15.8%)	40.9% p<0.001
Venous thrombosis (VT) veins of the extremities	n=7 (15.5%)	n=0	15.5% p>0.1
Ventricular tachycardia	n=9 (20%)	n=1 (2.6%)	17.4% p<0.05
Atherosclerosis of the iliac and lower extremity arteries and stage 2-4 coronary heart disease.	n=11 (24.4%)	n=4 (10.5%)	13.9% p>0.1
Acute cardiovascular failure	n=14 (31.1%)	n=7 (18.4%)	12.7% p>0.2
Atrial fibrillation, paroxysms	n=12(85.7%)	n=8(21%)	64.7% p<0.001
LVEF 35-50%	n=17 (41.5%)	n=8 (23.6%)	17.9% p<0.05
Chronic heart failure 2-3 FC according to NYHA	n=15 (33.3%)	n=1 (2.6%)	30.7% p<0.02

and COVID-19, or the authors did not conduct a targeted analysis of these aspects.

In the available literature, we found numerous data on a comparative analysis of the efficacy and safety of bare metal stents and drug-eluting intracoronary devices, including sirolimus, paclitaxel, and zotarolimus, in patients with ACS in the pre-COVID period, including randomized trials, but with very contradictory results. Thus, Dutch cardiologists reported in 2004 that the incidence of angiographically confirmed stent thrombosis was virtually identical in the groups of patients implanted with bare metal and drug-eluting stents, ranging from 1.0 to 1.2% [2,4]. The advantages of sirolimus-eluting stents over paclitaxel-eluting stents (PES) are evidenced by the results of a meta-analysis conducted by German authors in 2007. According to their data, sirolimus-eluting stents (SES) were superior to PES in terms of significantly reducing the risk of re-intervention and stent thrombosis. The risk of patient death did not differ significantly between the two types of eluting stents (2 DES), but there was a trend towards a higher risk of myocardial infarction when using PES coating, especially after the first year after the stenting procedure [2,5]. In a meta-analysis of 5 randomized trials performed in 2010 by Chinese authors from Shanghai, it was noted in patients with diabetes that SES coating was superior to PES in reducing the incidence of restenosis and target lesion revascularization in patients with diabetes, with minor differences in cardiac death, myocardial infarction, and stent thrombosis [26].

A new type of zotarolimus-eluting stent (ZES) has shown promise in coronary angiology. A meta-analysis by authors from Chicago (USA) compared three types of drug-eluting coronary stents across seven randomized trials. ZES was not superior to PES (paclitaxel) and was inferior to SES (serolimus) in terms of angiographic results and clinically justified revascularization [14].

In the German study RESOLUTE, it was shown that the use of R-ZES coating appears to be equally safe for drug-eluting stents (DES) and non-drug-eluting stents (BMS), [12]. According to the data in a 2020 Chinese study, stent-associated thrombosis developed significantly less frequently with R-ZES stent implantation compared to PES (paclitaxel) [13].

The efficacy and safety of using different types of drug-eluting coronary stents is planned to be studied in a randomized Mexican study in 2022-2025 in patients with a high risk of bleeding who underwent elective percutaneous coronary intervention with a zotarolimus-eluting stent and a comparison with a sirolimus-eluting stent during short-term dual antiplatelet therapy [16].

According to the data of the cited studies, differences in the effectiveness and safety of drug-eluting coronary stents were associated with their thrombosis, the development of recurrent myocardial infarction, arterial restenosis, the need for repeated intervention, bleeding, and the timing of the development of fatal outcomes in patients undergoing surgery for ACS and myocardial infarction.

Our analysis of the frequency and nature of differences in cardiovascular pathology in these two patient groups revealed that hemodynamic changes and cardiac arrhythmias were the most significant factors and conditions for different in-hospital outcomes in the compared groups of stented patients. Thus, chronic heart failure with reduced ejection fraction and acute and chronic left ventricular aneurysm were significantly more frequently diagnosed in the groups of deceased patients with ACS. Ventricular tachycardia and paroxysmal atrial fibrillation were significantly more common cardiac arrhythmias. Our data suggest that the release of a cytostatic agent such as sirolimus into the coronary bloodstream from implanted stents may exacerbate existing hemodynamic disturbances in patients with ACS and COVID-19, have a negative cardiometabolic effect, and worsen the course of severe cardiac arrhythmias. On the contrary, when using zotoralimus-eluting stents in such patients, adverse changes in cardiac hemodynamics and rhythm disturbances develop less frequently and are less pronounced.

Conclusions

An analysis of the efficacy and safety of using sirolimus-coated intracoronary stents in patients with acute myocardial infarction, COVID-19, and viral pneumonia during primary PCI revealed a possible association with adverse in-hospital outcomes associated with the use of sirolimus-coated intracoronary stents and, conversely, a positive trend in patient survival after coronary revascularization with the installation of zotarolomus! coated stents. The use of these findings The data may be useful in choosing drug-eluting stents and balloons for PCI to perform coronary revascularization procedures in patients with heart failure and paroxysmal cardiac arrhythmias.

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