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# Single-center register of myocardial revascularization in patients with coronary artery disease and acute coronary syndrome in the context of COVID-19 pandemic

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**Aim.** To assess the short- and long-term outcomes of myocardial revascularization (MR) in patients with coronary artery disease (CAD) and acute coronary syndrome (ACS) in the context of coronavirus disease 2019 (COVID-19) pandemic.

**Material and methods.** In the period from April to August 2020, 550 patients with CAD and ACS were included in the register. Emergency percutaneous transluminal coronary angioplasty (n=499) and on-pump coronary artery bypass grafting (CABG) (n=51) were performed. The follow-up period lasted 6 months. The pattern of complications after MR and effects of COVID-19 were analyzed.

**Results.** The studied cohort is represented by patients with CAD >65 years old. ST segment elevation ACS was detected in 23%, acute myocardial infarction — in 59,1%, in other cases — unstable angina. During hospitalization after MR, atrial fibrillation prevailed among cardiovascular complications (4,7%). During this period, 29 (5,3%) patients was diagnosed with COVID-19. In the short-term period after MR, 3 (0,5%) people died due to COVID-19 complications. In the long-term period after MR, 4 (0,7%) cases of non-fatal stroke were registered, while repeated MR — in 7,1%. The all-cause mortality rate was 1,3% (n=7), of which 57,1% of patients died due to COVID-19 complications. In the subgroup of patients who underwent CABG, the greatest number of in-hospital complications was noted, where exudative pleurisy, atrial fibrillation and anemia prevailed. Of the patients with COVID-19, pneumonia in the short- and long-term postoperative periods was recorded in 48,3 and 61,3%, respectively. Pneumonia is associated with respiratory failure, cardiac dysfunction, and anemia. The risk of COVID-19 pneumonia during the entire follow-up period was higher in patients with ACS who underwent CABG (odds ratio, 19,4; confidence interval: 13,3-26,1; p<0,001). The overall survival rate was 98,7%.

**Conclusion.** COVID-19 infection in patients with ACS after MR effects pattern of postoperative complications. The proportion of COVID-19 pneumonia in patients with ACS in hospital, short- and long-term postoperative periods after MR significantly exceeds that in the general population. The leading factor associated with COVID-19 pneumonia in patients with ACS is on-pump CABG.

**Keywords:** acute coronary syndrome, myocardial revascularization, COVID-19.

**Relationships and Activities:** none.

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The pandemic of coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is a serious challenge for world medical science and practical healthcare [1]. The high-risk group for COVID-19 complications is made up of patients with coronary artery disease (CAD), especially patients with acute coronary syndrome (ACS) [2]. Regardless of the epidemiological situation, patients with ACS require urgent surgical care with the ineffectiveness of conservative therapy [3]. This requires the development of an optimal routing scheme for emergency myocardial revascularization (MR) and tactics for further management in order to prevent infection and its complications. Difficulties with early diagnosis and the variety of clinical types of COVID-19 complicate these tasks [3].

MR in ACS patients is aimed, first of all, at reducing the mortality rate both in hospital and in the long-term periods after surgery [4].

The COVID-19 pandemic, especially its onset, characterized by the restrictions in work of medical institutions and specialized hospitals, as well as compliance/non-compliance with self-isolation regime, could lead to an increase in various adverse events both in the immediate and long-term periods after MR in

patients with ACS [5]. In this regard, the study of this cohort of patients is currently the most urgent.

The aim was to assess the short- and long-term outcomes of MR in ACS patients in the context of COVID-19 pandemic.

## Material and methods

The study involved 550 patients with ACS who were admitted for emergency MR at the Meshalkin National Medical Research Center (Novosibirsk) for the period from April to August 2020 inclusive. The mean age of patients was 66,8±3,9 years. The study was carried out in accordance with the Declaration of Helsinki and Good Clinical Practice regulations. The study protocol was approved by the Ethics Committee. Written informed consent was obtained from all participants prior to enrollment.

At the prehospital stage, the studied patients with ACS received therapy with the following drug groups: antiplatelet agents, anticoagulants, thrombolytics, nitrates, β-blockers, calcium channel blockers, statins, symptomatic agents.

MR was performed using percutaneous transluminal coronary angioplasty (PTCA) or on-pump coronary artery bypass grafting (CABG). Indications for surgical treatment, as well as the type and technique of MR was carried out according to the 2018 ESC/EACTS guidelines on myocardial revascularization [6]. When deciding on MR method, the clinical status of patients was taken into account: age, comorbidities, mobility, left ventricular function, contraindications to dual antiplatelet therapy. Assessment of coronary artery (CA) segments was performed, including the total number of CA stenoses, the number of hemodynamically significant CA stenoses (⩾50%) and hemodynamically significant stenoses of main CA branches. The severity of CA tortuosity and calcification, anatomical features of CAs, and presence of shunt material, were taken into account. The Synergy Between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery (SYNTAX) score was estimated using an online calculator (http://www.syntaxscore.com). Time parameters were analyzed in all patients: pain duration before MR, door-to-balloon/CABG time. PTCA was performed using drug eluting stents. When performing CABG, the following were used as grafts: internal thoracic artery, radial artery, autogenous vein.

Acute myocardial infarction (MI) was diagnosed based on clinical data and diagnostic investigations, cardiac specific markers. All patients underwent coronary angiography to determine the localization and degree of coronary lesions.

During hospitalization, all patients with ACS underwent collection of epidemiological history, thermometry, rapid test for COVID-19, chest x-ray, and a complete blood count. The diagnosis of COVID-19 was confirmed by a polymerase chain reaction for SARS-CoV-2 using nasopharyngeal and oropharyngeal swabs.

The management and surgical treatment of patients with ACS was carried out in compliance with the anti-epidemic regime: a separate ward for a patient, an operation in an isolated room, the use of personal protective equipment. MR in patients with ACS was performed on the first day (hours) of hospitalization. In this regard, the results of COVID-19 test were obtained after the surgical treatment.

After verification of COVID-19, patients with ACS were transferred to an isolation unit and, when their condition stabilized, were sent to an infectious disease hospital with recommendations for cardiovascular therapy.

All patients received standard treatment according to the Temporary guidelines for Prevention, Diagnosis and Treatment of COVID-19 (version 4-7) of the Russian Ministry of Health [7]. Depending on the disease course, therapy included the following drug groups: antiviral, antibiotic, anticoagulants, anti-inflammatory, antipyretic.

For patients referred to a specialized infectious diseases facility, medical documentation was received via digital communication channels.

During the hospitalization, the following were recorded: postoperative complications, COVID-19 infection cases, COVID-19 pneumonia, mortality. The composite endpoint included the following outcomes: adverse cardiovascular events, repeated MR, any surgical interventions, bilateral multisegmental pneumonia caused by COVID-19, death after MR and within a further 6 months.

Statistical analysis was performed using Statistica 6.1 software (USA). We used parametric statistical methods with calculating the mean (M) ± standard deviation (SD) and nonparametric methods with calculating the median (Me) with an interquartile range (25 and 75 percentiles,%). To determine the risk factors for complications after MR, a univariate logistic regression model was used. Odds ratios (OR) and 95% confidence intervals (CIs) are indicated. Differences were considered significant at $p<0,05$.

## Results

The clinical and functional characteristics of CAD patients with ACS are shown in Table 1. The studied cohort is represented by patients aged >65 years, >50% of whom are males. ST segment elevation ACS was detected in 23% of patients; in other cases, according to electrocardiography, non-ST segment elevation ACS was recorded. The symptom onset-to-balloon/CABG time was 2 days on average. The door-to-ballon/CABG time did not exceed 7 hours on average. It should be noted that in 61% of cases the patients had prior MR mainly in the form of endovascular intervention (80,3%).

In the studied patients, acute myocardial infarction was registered in 59,1% of cases, while in other cases — unstable angina. Of the comorbidities, the largest percentage were obesity (>40%), while type 2 diabetes was observed in 25% of cases. Of the total cohort, PTCA was performed in 499 (90,7%) patients. In 51 (9,3%) patients, on-pump CABG was performed. The high CABG frequency is due to the following reasons: all patients had multivessel (⩾3) diffuse CAD with CA stenosis ⩾75%; in 50% of cases, CA occlusions were observed, while in 25% of cases — restenosis of previously stented CA segments and severe calcification. It should be emphasized that the Center provides high-tech cardiac surgery, including patients with ACS and varying severity of CAD. In this regard, the proportion of CABG can be higher than that in other clinics that mainly perform endovascular interventions.

Table 2 shows intra- and postoperative characteristics and complications in patients with ACS in 2

**Table 1**

Clinical and functional characteristics of CAD patients with ACS

| Parameter | (n=550) |
|---|---|
| Age, M±SD | 66,8±3,9 |
| Men, n (%) | 368 (66,9) |
| STEACS, n (%) | 127 (23,1) |
| NSTEACS, n (%) | 423 (76,9) |
| Unstable angina, n (%) | 225 (40,9) |
| Acute MI, n (%) | 325 (59,1) |
| SYNTAX score, M±SD | 14,8±4,5 |
| CA stenoses, total, M±SD | 3,8±0,6 |
| Hemodynamically significant stenoses, total, M±SD | 2,7±0,7 |
| Hemodynamically significant stenoses of main CA branches, M±SD | 2,0±0,6 |
| Symptom onset-to-balloon/CABG time (hours), M±SD | 48,9±13,2 |
| Door-to-ballon/CABG time (hours), M±SD | 6,9±2,5 |
| Hypertension, n (%) | 522 (94,9) |
| Type 2 diabetes, n (%) | 137 (24,9) |
| Obesity, n (%) | 235 (42,7) |
| AF, n (%) | 104 (18,9) |
| Chronic lower limb ischaemia, n (%) | 72 (13,1) |
| Chronic obstructive pulmonary disease, n (%) | 33 (6,0) |
| Chronic renal failure, n (%) | 93 (16,9) |
| Cancer, n (%) | 19 (3,5) |
| Peptic/duodenal ulcer disease, n (%) | 66 (12) |
| Prior MI, n (%) | 291 (52,9) |
| Prior stroke, n (%) | 58 (10,5) |
| Prior PTCA, n (%) | 269 (48,9) |
| Prior CABG, n (%) | 66 (12) |
| Smoking, n (%) | 126 (22,9) |
| LVEF (%), M±SD | 55,1±5,8 |
| RVFAC (%), M±SD σ | 43,2±2,4 |
| Age-adjusted Charlson Comorbidity Index, M±SD | 5,0±0,8 |

Note: STEACS — ST-segment elevation acute coronary syndrome, NSTEACS — non-ST-segment elevation acute coronary syndrome, LVEF — left ventricular ejection fraction, RVFAC — right ventricular fractional area change.

**Table 2**

Intra-, postoperative characteristics and complications in ACS patients with CAD

| | |
|---|---|
| CAD patients with ACS who underwent PTCA (n=499) | |
| Number of stents, M±SD | 1,2±0,4 |
| AF, n (%) | 12 (2,4) |
| Frequent premature ventricular contractions, n (%) | 7 (1,4) |
| Anemic syndrome, n (%) | 3 (0,6) |
| Red blood cell transfusion, n (%) | 1 (0,2) |
| COVID-19 pneumonia, n (%) | 2 (0,4) |
| Respiratory failure, n (%) | 2 (0,4) |
| Length of hospital stay (days), M±SD | 2,5±1,1 |
| In-hospital mortality, n (%) | 0 |
| CAD patients with ACS who underwent on-pump CABG (n=51) | |
| Number of stents, (Me, 25-75%) | 2 (1-3) |
| AF, n (%) | 14 (27,5) |
| Frequent premature ventricular contractions, n (%) | 4 (7,8) |
| Anemic syndrome, n (%) | 13 (25,5) |
| Red blood cell transfusion, n (%) | 4 (7,8) |
| Heart failure, n (%) | 8 (15,7) |
| Exudative pleurisy, n (%) | 29 (56,9) |
| Cardiopulmonary failure, n (%) | 4 (7,8) |
| Encephalopathy, n (%) | 6 (11,8) |
| Stroke, n (%) | 1 (2) |
| All neurological complications, n (%) | 7 (13,7) |
| Pacemaker implantation, n (%) | 4 (7,8) |
| Resternotomy, n (%) | 2 (3,9) |
| COVID-19 pneumonia, n (%) | 7 (13,7) |
| Respiratory failure, n (%) | 7 (13,7) |
| Mechanical ventilation (hours), (Me, 25-75%) | 6,0 (4,1-7,5) |
| Length of stay in intensive care unit (hours), (Me, 25-75%) | 46,0 (26,2-54,4) |
| Length of hospital sta (days), (Me, 25-75%) | 15,3 (10,3-19,1) |
| In-hospital mortality, n (%) | 0 |

following subgroups: 1) patients who underwent PTCA; 2) patients who underwent on-pump CABG.

The greatest number of in-hospital complications was found in patients who underwent on-pump CABG, of which exudative pleurisy, atrial fibrillation (AF), and anemia were the leading ones. Mortality for this period was not registered in both subgroups. During the early period after MR (30 days), mortality in the general cohort was recorded in 3 (0,5%) people. The cause of death in all cases was pulmonary heart failure due to a severe bilateral COVID-19 pneumonia. Of the number of infected patients, this amounted to 10,3%.

During hospitalization, a total of 29 (5,3%) cases of COVID-19 infection were detected. In the subgroup of patients with CABG, 9 (17,6%) COVID-19 cases were registered. Of these, 7 (77,8%) patients developed bilateral multisegmental pneumonia. In the subgroup of patients with PTCA, there were 20 (4%) COVID-19 cases, while pneumonia developed in 2 (10%) patients.

In the early period after MR (30 days), no new cases of COVID-19 infection were recorded in the studied patients. During the hospitalization and early postoperative periods, bilateral multisegmental pneumonia was recorded in 14 (48,3%) people. At the same time, 85,7% developed pneumonia after on-pump CABG. Moderate COVID-19 (without pneumonia) during this period were recorded in 11 (37,9%) patients, while the asymptomatic disease course — in 4 (13,8%).

Table 3 shows the relationship of bilateral multisegmental COVID-19 pneumonia with complications during hospitalization after MR in ACS patients.

According to univariate regression analysis, pneumonia that developed during hospitalization after MR against the background of COVID-19 is associated not only with respiratory failure, but also with impaired cardiac function and anemic syndrome.

**Table 3**

Interrelation of bilateral multisegmental COVID-19 pneumonia with complications during hospitalization after MR in CAD patients with ACS

| Complications | OR | 95% CI | p |
|---|---|---|---|
| Respiratory failure | 8,7 | 5,2-11,7 | <0,001 |
| AF | 7,6 | 4,1-13,4 | <0,001 |
| Heart failure | 4,1 | 2,4-8,5 | 0,001 |
| Anemic syndrome | 3,4 | 1,9-5,8 | 0,001 |

**Table 4**

Results of 6-month follow-up of CAD patients with ACS after MR

| Parameter | n=535 |
|---|---|
| MI, n (%) | 0 |
| Stroke, n (%) | 4 (0,7) |
| PTCA, n (%) | 35 (6,5) |
| On-pump CABG, n (%) | 3 (0,6) |
| Internal carotid artery revascularization, n (%) | 6 (1,1) |
| Peripheral vascular revascularization, n (%) | 2 (0,4) |
| Aortic valve replacement, n (%) | 2 (0,4) |
| Total number of surgical operations, n (%) | 48 (9) |
| Number of new COVID-19 cases, n (%) | 31 (5,8) |
| New COVID-19 pneumonia cases, n (%) | 19 (3,6) |
| Total number of COVID-19 cases (hospital, early postoperative and long-term periods), n (%) | 60 (11,2) |
| Total number of COVID-19 pneumonia cases (hospital, early postoperative and long-term periods), n (%) | 33 (6,2) |
| Long-term mortality, n (%) | 4 (0,7) |
| All-cause mortality, n (%) | 7 (1,3) |

Data on 6-month follow-up of CAD patients with ACS after MR are presented in Table 4.

Twelve people dropped out of the study group because they could not be contacted by phone. Of 38 patients who underwent repeated MR, in 22 (57,9%) cases, PTCA was performed as a staged revascularization. Six (15,8%) patients underwent PTCA due to restenosis/reocclusion of the stented CA segment, while in 2 (5,3%) patients — due to rethrombosis. Due to the progression of CA atherosclerosis, PTCA was performed in 5 patients, and on-pump CABG — in 3, which amounted to 21% of the total number of repeated MRs.

Over the entire follow-up period, the total mortality in the study cohort was 7 (1,3%) people. Among them, 4 (57,1%) people died from COVID-19 complications, 2 (28,6%) — from cancer, and 1 (14,3%) — from acute heart failure after aortic valve replacement. The overall survival rate was 98,7%.

In the long-term period after MR, new COVID-19 cases were detected in 31 (5,8%) patients with CAD. Among them, 61,3% developed bilateral multisegmental pneumonia, which required treatment in a specialized infectious diseases facility. Thus, over the entire follow-up period (hospital, early postoperative and long-term periods) in patients who underwent MR for ACS, 11,2% of COVID-19 cases were recorded. No repeated COVID-19 cases have been identified. It should be noted that the risk of COVID-19 pneumonia in the hospital, early postoperative and long-term periods after MR is significantly higher in patients with CAD who received emergency on-pump CABG (OR, 19,4; CI: 13,3-26,1 (p<0,001). Initially, this category of patients is characterized by a more severe diffuse coronary lesion with the presence of occlusions, calcification, which increases the risk of complications after MR.

## Discussion

Currently, for ACS, the preferred type of management is percutaneous coronary intervention as a minimally invasive method of surgical treatment [4]. After PTCA, the following specific complications most often occur: acute occlusion, coronary artery perforation, stent dislocation/migration, stent thrombosis/restenosis, etc. Complications associated with damage to other organs and systems (stroke, internal bleeding, renal failure) are much less common [8]. If PTCA can not be performed, patients with ACS receive on-pump CABG. This technique allows for a complete blood flow restoration in altered vessels, including diffuse coronary atherosclerosis. The structure of postoperative complications in this case changes significantly. This is due to the systemic body response to artificial circulation, which may be accompanied by dysfunction of various organs and systems [9].

Providing emergency care to ACS patients in the context of the COVID-19 pandemic entails additional risks associated with infection and its complications. This, in turn, can make significant adjustments to complication patterns after MR and increase the death risk [3].

In the present study, CAD patients with ACS during the hospital and early postoperative periods after MR developed bilateral COVID-19 pneumonia in 48,3%. In the long-term period after MR (after 6 months), this complication was recorded in 61,3% of patients among new COVID-19 cases. Patients who received emergency on-pump CABG significantly had higher risk of bilateral multisegmental COVID-19 pneumonia in the hospital, early postoperative and long-term periods after MR. In addition to respiratory failure, pneumonia has been associated with the development of AF, heart failure, and anemic syndrome after MR. All these factors complicate the postoperative period, prolonging the hospitalization. According to literary data, in the general population of various countries, the development of COVID-19 pneumonia was observed within 10-25% [10, 11].

A high percentage of bilateral COVID-19 pneumonia in the studied patients with ACS, who underwent on-pump CABG, is due to the adjacent pathophysiological mechanisms of the effect of cardiopulmonary bypass and COVID-19 on organs and systems. Against the background of disease progression in patients with CAD, open surgery aggravates disorders in the hemostatic system. Activation of the systemic inflammatory response as a result of blood passage through the surfaces of heart-lung machine and changes in microvascular tone lead to a reduction in capillary blood flow, disruption of systemic and regional tissue perfusion, and the development of tissue hypoxia [12]. In addition, COVID-19 aggravates the systemic inflammatory response, where, as in the first case, it is mediated by regulatory molecules — cytokines, which include a cascade of activation and synthesis of acute phase proteins and inflammatory mediators, adhesion molecules, cell proliferation and differentiation stimulators [13]. In this regard, in order to prevent severe complications and reduce mortality in CAD patients with ACS undergoing on-pump CABG, it is necessary to carry out an operation in an emergency-delayed manner after receiving the test results for COVID-19.

The overall mortality rate for the entire follow-up period in the study cohort of patients was 1,3%. Among them, 57,1% of patients died from COVID-19 complications. The immediate cause of death was pulmonary heart failure against the background of a severe bilateral multisegmental pneumonia.

**Study limitations.** In the studied cohort of patients with ACS in the long-term post-MR period, the actual number of new COVID-19 cases may exceed the presented data, since not all patients underwent tests. As a result, the proportion of patients with COVID-19 pneumonia among the total number of infected patients may slightly differ from the data presented in this study.

## Conclusion

One of the vulnerable groups of CAD patients in the context of COVID-19 pandemic are ACS patients in need of emergency MR.

COVID-19 infection in patients with ACS after MR effects pattern of postoperative complications. The proportion of COVID-19 pneumonia in patients with ACS in hospital, short- and long-term postoperative periods after MR significantly exceeds that in the general population. The leading factor associated with COVID-19 pneumonia in patients with ACS is on-pump CABG.

**Relationships and Activities:** none.

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