UDC: 616.127-005.8:616.12-089.819:615.273:616.98:578.834.1

THE IMPACT OF COVID-19 INFECTION ON THE EFFICACY AND SAFETY OF REPERFUSION THERAPY IN ACUTE CORONARY SYNDROME WITH ST-SEGMENT ELEVATION: SHORT- AND LONG-TERM OUTCOMES

Khurshid G'ayratovich Fozilov *– Doctor of Medical Sciences (DSc), Director of Republican Specialized Scientific and Practical Medical Center of Cardiology (RSSPMCC).*

Baxtiyor Rajabboyevich Atamuratov *– Independent researcher, Department of Endovascular Treatment of Heart and Blood Vessels Interventional Cardiologist, Republican Specialized Scientific and Practical Medical Center of Cardiology.*

Abstract. *The study evaluated the impact of prior COVID-19 infection on the efficacy and safety of reperfusion therapy in patients with ST-segment elevation acute coronary syndrome (STEMI). COVID-19 positive patients exhibited a significantly higher incidence of MACE, while primary percutaneous coronary intervention (pPCI) provided a better long-term prognosis compared to thrombolytic therapy (TLT).*

Objective: *To investigate the impact of prior COVID-19 infection on the efficacy and safety of reperfusion therapy (thrombolytic therapy - TLT and primary percutaneous coronary intervention - pPCI) in patients with ST-segment elevation acute coronary syndrome (STE-ACS), as well as to evaluate short- and long-term (24-month) clinical outcomes, particularly the development of major adverse cardiovascular events (MACE).*

Materials and Methods*. From 2021 to 2024, 200 patients were followed for 24 months at the Republican Specialized Cardiology Center. Patients were divided according to COVID-19 history: COVID-positive (n=75) and COVID-negative (n=125). Each group was further stratified by reperfusion therapy type (TLT or pPCI). Clinical, laboratory, echocardiographic, and angiographic parameters, as well as MACE incidence, were analyzed using statistical methods.*

Conclusions. *STEMI patients with prior COVID-19 had a significantly higher incidence of cardiovascular death, repeat ischemia-related revascularization, and MACE. pPCI was more effective than TLT, improving long-term prognosis. Prior COVID-19 represents an independent adverse prognostic factor in STEMI patients.*

Keywords: *COVID-19, STEMI, reperfusion therapy, thrombolysis, pPCI, MACE.*

Annotatsiya. *Tadqiqot o'tkir koronar sindrom ST-segmenti ko'tarilishi (O'KS-ST) bilan kasallangan bemorlarda avval o'tkazilgan COVID-19 infeksiyasining reperfuziya terapiyasi samaradorligi va xavfsizligiga ta'sirini baholadi. COVID-musbat bemorlarda MACE hodisalari chastotasi sezilarli darajada yuqori bo'ldi, bTOKA TLTga nisbatan uzoq muddatli prognozni yaxshiladi.*

Materiallar va usullar*. 2021-2024 yillarda Respublika ixtisoslashtirilgan kardiologiya markazida 200 bemor 24 oy davomida kuzatildi. Bemorlar COVID-19 anamnezi bo'yicha COVID-musbat (n=75) va COVID-manfiy (n=125) guruhlarga ajratildi. Har bir guruhda reperfuziya terapiyasi turiga (TLT yoki bTOKA) qarab kichik guruhlar tashkil qilindi. Klinik, laborator, exokardiyografik va angiografik ko'rsatkichlar hamda MACE chastotasi statistik usullar bilan tahlil qilindi.*

Xulosa*. COVID-19 infeksiyasi anamnezi bo'lgan O'KS-ST bemorlarda yurak-qon tomir o'limi, qayta ishemiyaga bog'liq revaskulyarizatsiya va MACE hodisalari chastotasi sezilarli darajada yuqoriligi aniqlandi. bTOKA TLTga nisbatan samaraliroq bo'lib, uzoq muddatli*

prognozni yaxshiladi. COVID-19 infeksiyasi O'KS-ST bemorlarida mustaqil salbiy prognostik omil hisoblanadi.

***Kalit so'zlar**: COVID-19, O'KS-ST, reperfuziya terapiyasi, trombolizis, bTOKA, MACE.*

***Аннотация**. Исследование оценивало влияние перенесенной ранее COVID-19 на эффективность и безопасность реперфузионной терапии у пациентов с острым коронарным синдромом с подъемом сегмента ST (ОКСпST). У пациентов с COVID-19 частота MACE была значительно выше, при этом первичная чрескожная коронарная интервенция (пЧКВ) обеспечивала более благоприятный долгосрочный прогноз по сравнению с тромболитической терапией (ТЛТ).*

***Материалы и методы**. В 2021-2024 годах в Республиканском специализированном центре кардиологии было проведено наблюдение за 200 пациентами в течение 24 месяцев. Пациенты были разделены на группы в зависимости от анамнеза COVID-19: COVID-положительные (n=75) и COVID-отрицательные (n=125). Каждая группа дополнительно делилась в зависимости от вида реперфузионной терапии (ТЛТ или пЧКВ). Проводился статистический анализ клинических, лабораторных, эхокардиографических и ангиографических показателей, а также частоты MACE.*

***Выводы.** У пациентов с ОКС-ST и перенесенной COVID-19 наблюдалась значительная частота сердечно-сосудистой смерти, необходимости повторной ишемической ревскуляризации и MACE. пЧКВ была более эффективной по сравнению с ТЛТ, улучшая долгосрочный прогноз. Перенесенная COVID-19 является независимым неблагоприятным прогностическим фактором у пациентов с ОКС-ST.*

***Ключевые слова**: COVID-19, ОКСпST, реперфузионная терапия, тромболизис, пЧКВ, MACE.*

Introduction

Coronary artery disease (CAD) is one of the most prevalent cardiovascular conditions worldwide, currently affecting over 126 million people globally. Among the clinical manifestations of CAD, acute coronary syndrome (ACS), particularly the ST-segment elevation type, holds special clinical significance and accounts for approximately 15-18% of all CAD cases. According to statistics from the World Health Organization, annually 7-9 million people die due to complications of CAD, including acute myocardial infarction [1].

According to data from the European Society of Cardiology (ESC), sudden cardiac deaths caused by ACS exceed 1.8 million cases each year (ESC CardioMed, A. John Camm, European Society of Cardiology, 2018). In the United States, approximately 57% of sudden cardiac deaths are directly related to coronary artery disease [2]. In particular, ST-segment elevation myocardial infarction (STEMI) is one of the leading causes of death attributed to cardiovascular diseases [3].

In Russia, 161,300 cases of acute myocardial infarction were recorded in 2019, with an overall mortality rate of 36,8 per 100,000 population, and an average in-hospital mortality rate of 11,2% (6,4% in Moscow) [4]. In Uzbekistan, the mortality rate due to cardiovascular diseases in 2021 was 798 per 100,000 population, one of the highest rates globally, with a prevalence of cardiovascular diseases of 12,566 cases per 100,000 population [5].

In recent years, modern reperfusion therapy methods, particularly primary percutaneous coronary intervention (pPCI), have significantly improved the long-term survival prognosis of patients with ST-segment elevation acute coronary syndrome (STE-ACS) [6]. However, the COVID-19 pandemic, which began at the end of 2019, has profoundly affected global healthcare systems and clinical practices in the treatment of cardiovascular pathologies, including STE-ACS [7]. Delayed presentations of cardiovascular diseases during the pandemic, increased healthcare system burden, and the direct impact of COVID-19 infection on cardiac function may have negatively influenced patient outcomes.

COVID-19 (Coronavirus Disease 2019) is an infectious disease caused by the novel coronavirus Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2). The disease was first identified in Wuhan, Hubei Province, China, in December 2019, and was declared a global pandemic by the World Health Organization (WHO) on 11 March 2020. Clinically, COVID-19 presents with a wide spectrum of manifestations ranging from asymptomatic infection and mild upper respiratory tract illness to severe viral pneumonia, acute respiratory distress syndrome (ARDS), multiorgan failure, and death. The diagnosis is confirmed primarily through laboratory detection of SARS-CoV-2 RNA via reverse transcription polymerase chain reaction (RT-PCR) or other validated molecular or antigen-based diagnostic assays [8].

COVID-19 infection has been shown to affect the cardiovascular system through several mechanisms: direct viral myocardial injury, systemic inflammatory response, endothelial dysfunction, and hypercoagulability [9]. These factors may reduce the effectiveness of reperfusion therapy and worsen the long-term prognosis in patients with STE-ACS [10]. According to the European Society of Cardiology (ESC), hospital admissions for STE-ACS decreased by 22% during the pandemic, while in-hospital mortality rates increased [11]. Data from the ISACS-STEMI COVID-19 registry also indicated a 20% reduction in STE-ACS patient admissions during the pandemic accompanied by higher in-hospital mortality [12].

COVID-19 negative patients are individuals who, upon undergoing validated diagnostic testing for Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), demonstrate no molecular or antigenic evidence of active infection at the time of assessment. Diagnostic confirmation of a negative status is established through reverse transcription polymerase chain reaction (RT-PCR), nucleic acid amplification testing (NAAT), or rapid antigen assays, all of which must yield results below the detection threshold for SARS-CoV-2 viral RNA or antigen [13].

From an epidemiological and clinical standpoint, a COVID-19 negative result indicates the absence of detectable viral replication in the tested specimen, thereby suggesting the individual is not actively infected nor considered infectious at the time of testing. Nevertheless, this classification is inherently time-sensitive and may be influenced by factors such as the stage of infection, sampling technique, viral load dynamics, and assay sensitivity or specificity. Consequently, a negative diagnostic result should be interpreted within the broader context of clinical presentation, exposure history, and epidemiological risk factors, acknowledging the potential for false-negative outcomes [14].

To date, the long-term impact of COVID-19 on cardiovascular events in patients with STE-ACS remains insufficiently studied. Moreover, comparative long-term studies evaluating the efficacy and safety of different reperfusion therapies in patients with a history of COVID-19 are scarce [15, 16].

The aim of this study is to evaluate the efficacy and safety of reperfusion therapy (thrombolytic therapy and primary percutaneous coronary intervention) in patients with ST-segment elevation acute coronary syndrome (STE-ACS) who have previously had COVID-19 infection. Additionally, the study seeks to investigate the impact of these reperfusion therapies on major adverse cardiovascular events (MACE) during a 24-month follow-up period.

Study Objectives:

1. To investigate the impact of COVID-19 infection on the immediate and long-term outcomes of reperfusion therapy in patients with ST-segment elevation acute coronary syndrome.
2. To perform a comparative analysis of the immediate and long-term efficacy of primary percutaneous coronary intervention (pPCI) and thrombolytic therapy (TLT) in patients with STE-ACS with and without a history of COVID-19 infection.
3. To identify predictors of major adverse cardiovascular events (MACE) in

patients with STE-ACS with and without prior COVID-19 infection who underwent pPCI or TLT.

Materials and Methods: In accordance with the objectives and tasks of the study, a total of 200 patients diagnosed with ST-segment elevation acute coronary syndrome (STEMI) were selected. The patients were divided into two groups based on the presence or absence of a documented history of COVID-19 infection:

Group 1 ("COVID-Positive") – patients who had previously contracted COVID-19 (n = 75);

Group 2 ("COVID-Negative") – patients with no history of documented COVID-19 infection (n = 125).

The grouping was carried out based on the following diagnostic criteria:

Patients in the **"COVID-Positive" group** met one or more of the following criteria:

– laboratory-confirmed COVID-19 infection (positive PCR or antigen test result);

– detection of SARS-CoV-2-specific IgG/IgM antibodies through serological testing (if available);

– presence of clinical symptoms associated with COVID-19 in the medical history (fever, dry cough, shortness of breath, loss of smell or taste);

– documented COVID-19 diagnosis in electronic medical records (inpatient or outpatient).

Patients in the **"COVID-Negative" group** met all of the following criteria:

– absence of a documented COVID-19 test in medical records;

– no physician diagnosis or coding of COVID-19;

– no clinical symptoms characteristic of COVID-19 reported in the medical history;

– the patient either tested negative for COVID-19, has not reported of previous COVID-19 infection or was not tested due to lack of clinical indications.

– serological test results (if available) showed no detectable SARS-CoV-2 antibodies (IgG/IgM negative) or serology was not systematically performed;

We acknowledge the possibility of asymptomatic or undocumented infections in the COVID-19 group; however, this would likely bias our findings toward the null, making the observed differences conservative.

During the grouping process, possible chronological uncertainties and asymptomatic cases observed during the pandemic period were taken into account. Each patient's medical records were evaluated individually to ensure epidemiological accuracy and to minimize statistical error.

Patients in both groups were further subdivided into smaller groups according to the type of reperfusion therapy received (thrombolytic therapy and primary percutaneous coronary intervention) for additional analysis.

The study population comprised 200 patients, of whom 75 (37,5%) had a documented history of COVID-19 and 125 (62,5%) had no documented history of COVID-19 infection. The mean age of patients with prior COVID-19 was 60,2 ± 12,1 years, while those without documented infection had a mean age of 59,3 ± 11,6 years, indicating no substantial age difference between the groups. The proportion of male patients was slightly higher among individuals with a history of COVID-19 (81,3%) compared to those without (74,4%). The average body mass index (BMI) was comparable between the groups (28,6 ± 4,1 kg/m^2 vs. 28,3 ± 4,2 kg/m^2).

Table 1 presents the analysis of clinical-demographic and vaccination characteristics between patients with and without a history of COVID-19 in the study.

Table-1

Analysis of clinical-demographic and vaccination characteristics among patients with and without a history of documented COVID-19 (n=200)

№	Indicators	"COVID-Positive" n=75	"COVID-Negative" n=125
1	Common percentage (%)	37,5%	62,5%
2	Average age (M±SD)	60,2 ± 12,1	59,3 ± 11,6
3	Number of males (%)	61 (81,3%)	93 (74,4%)
4	BMI, kg/m^2 (M±SD)	28,6 ± 4,1	28,3 ± 4,2
5	Arterial hypertension (%)	47 (62,7%)	80 (64,0%)
6	Diabetus mellitus (2-type) (%)	16 (21,3%)	31 (24,8%)
7	Hypercholesterolemia (%)	32 (42,7%)	49 (39,2%)
8	Smoking (%)	28 (37,3%)	55 (44,0%)
9	Chronic obstructive pulmonary disease (%)	55 (73,3%)	39 (31,2%)
10	**Type of reperfusion therapy**		
	— TLT (%)	46,7%	47,2%
	— pPCI (%)	53,3%	52,8%
11	**Duration of stay in hospital (average days)**	8,6 ± 3,2	5,7 ± 2,4
12	**Vaccination status**		
	— Vaccinated before COVID-19 (%)	40,0%	52,0%
	— Vaccinated after COVID-19 (%)	35,0%	10,4%
	— Unvaccinated (%)	25,0%	37,6%
13	**Type of vaccine** *(only among vaccinated patients)*		
	— Moderna (%)	29,3%	27,2%
	— AstraZeneca (%)	20,0%	15,2%
	— Sputnik V (%)	22,7%	17,6%
	— Others / unknown (%)	8,0%	6,4%
14	**Vaccinated before myocardial infarction (%)**	100%	100%
15	**Reason unvaccinated** *(among non-vaccinated patients)*		
	— Refused by own will (%)	60,0%	58,3%
	— Afraid of side effects (%)	53,3%	44,7%
	— Not trusted because doubted efficacy (%)	40,0%	41,7%
	— Medical indication (allergy, medical advice) (%)	6,7%	10,0%

***Note:** M±SD – mean ± standard deviation; BMI – Body mass index; TLT – Thrombolysis therapy; pPCI – primary percutaneous coronary intervention;*

Among 200 STEMI patients, comorbidities were similar between groups: arterial

hypertension (62.7% vs. 64.0%), type 2 diabetes (21.3% vs. 24.8%), and hypercholesterolemia (42.7% vs. 39.2%) in COVID-Positive versus COVID-Negative patients. Smoking prevalence was slightly lower in COVID-Positive patients (37.3% vs. 44.0%), while COPD was markedly higher (73.3% vs. 31.2%). Reperfusion therapy distribution was nearly equal (TLT 46.7% vs. 47.2%; pPCI 53.3% vs. 52.8%), though hospital stay was longer for COVID-Positive patients (8.6 ± 3.2 vs. 5.7 ± 2.4 days). Vaccination patterns differed: 40% of COVID-Positive patients were vaccinated before infection, 35% after, and 25% unvaccinated; in COVID-Negative patients, 52% were vaccinated prior, 10.4% after, and 37.6% unvaccinated. Vaccine types were Moderna (29.3% vs. 27.2%), AstraZeneca (20.0% vs. 15.2%), Sputnik V (22.7% vs. 17.6%), and others/unknown (8.0% vs. 6.4%). All vaccinated patients received vaccines before myocardial infarction.

Among non-vaccinated patients, main reasons included personal refusal (60% vs. 58.3%), fear of side effects (53.3% vs. 44.7%), distrust in efficacy (40% vs. 41.7%), and medical contraindications (6.7% vs. 10%).

Results

Results of the impact of COVID-19 infection on short- and long-term outcomes of reperfusion therapy in patients with ST-segment elevation myocardial infarction (STEMI). The study included a total of 200 patients treated for acute coronary syndrome with ST-segment elevation (STEMI). Patients were divided into two groups: those with a history of COVID-19 infection (n=75) and those without prior infection (n=125). In both groups, the frequency of major adverse cardiovascular events (MACE) observed during hospitalization was analyzed, and differences between groups were compared using Fisher's exact test. MACE included cardiovascular death, recurrent myocardial infarction, and ischemia-related second-stage coronary revascularization. The results are presented in Table 2.

Table 2

Analysis of in-hospital MACE events, n=200

Indicators	"COVID-Positive" n=75	"COVID-Negative" n=125	Test statistics	p-value
Cardiovascular death, n (%)	3 (4,0)	1 (0,8)	Fisher's exact test	p=0,001
Recurrent MI, n (%)	1 (1,3)	0 (0)	Fisher's exact test	p=0,375
Stroke (ischemic/hemorrhagic), n (%)	0 (0)	1 (0,8)	Fisher's exact test	p=0,625
Ischemia-driven revascularization, n (%)	3 (4,0)	1 (0,8)	Fisher's exact test	p=0,001
Total MACE, n (%)	7 (9,3)	3 (2,4)	Fisher's exact test	p= 0,036

***Note:** p < 0,05 – statistically significant, MI – myocardial infarction, MACE – Major Adverse Cardiovascular Events.*

According to the obtained results, cardiovascular death (0.8% vs. 4.0%; p=0.001), second-stage revascularization of ischemic-related arteries (0.8% vs. 4.0%; p=0.001), and overall MACE incidence (2.4% vs. 9.3%; p=0.036) were statistically significantly higher in patients who had experienced COVID-19 infection compared to those who had not. No statistically significant difference was observed between the groups in terms of recurrent myocardial infarction and ischemic stroke (p>0.05). These results indicate a higher long-term risk of adverse

cardiovascular events in patients who had COVID-19 infection. MACE events occurring during the 12-month follow-up period of patients participating in the study were analyzed. Out of a total of 200 patients treated for ACS-ST, 188 patients (71 patients who had COVID-19 infection and 117 patients who had not) were fully followed for 12 months. During the follow-up, 4 patients from the COVID-19 group and 8 patients from the non-COVID-19 group could not be contacted and were therefore excluded from the final statistical analysis. Thus, the final analysis was conducted based on data from 188 patients.

The frequency of MACE events during the 12-month follow-up period between patients who had and had not experienced COVID-19 infection was compared in Table 3.

Table 3. Analysis of 12-month MACE events, n=188

Indicators	"COVID-Positive" n=71	"COVID-Negative" n=117	Test statistics	p-value
Cardiovascular death, n (%)	9 (12,7)	4 (3,4)	Fisher's exact test	p=0,017
Recurrent MI, n (%)	3 (4,2)	5 (4,3)	Fisher's exact test	p=0,853
Stroke (ischemic/hemorrhagic), n (%)	1 (1,4)	1 (0,9)	Fisher's exact test	p=0,721
Ischemia-driven revascularization, n (%)	7 (9,9)	3 (2,6)	Fisher's exact test	p=0,041
Total MACE, n (%)	20 (28,2)	13 (11,1)	χ^2=7,744	p=0,002

***Note:** p < 0,05 – statistically significant, MI – myocardial infarction, MACE – Major Adverse Cardiovascular Events.*

According to the follow-up results, cardiovascular death (12.7% vs. 3.4%; p=0.017), second-stage revascularization of ischemic-related arteries (9.9% vs. 2.6%; p=0.041), and overall MACE incidence (28.2% vs. 11.1%; χ^2=7.744; p=0.002) were statistically significantly higher in patients who had experienced COVID-19 infection compared to those who had not. No statistically significant difference was observed between the groups in terms of recurrent myocardial infarction and ischemic stroke (p>0.05). These results indicate a higher long-term risk of cardiovascular complications in patients who had COVID-19 infection.

The analysis of MACE events occurring during the 24-month follow-up period by groups of patients participating in the study is presented in Table 4. Out of a total of 200 patients initially included, 185 patients (70 patients who had COVID-19 and 115 patients who had not) were fully followed for 24 months. During the 12–24 month follow-up period, 1 patient from the COVID-19 group and 2 patients from the non-COVID-19 group could not be contacted and were therefore excluded from the final statistical analysis.

Table 4. Analysis of 24-month MACE events, n=185

Indicators	"COVID-Positive" n=70	"COVID-Negative" n=115	Test statistics	p-value
Cardiovascular death, n (%)	11 (15,7)	4 (3,5)	Fisher's exact test	p=0,005
Recurrent MI, n (%)	3 (4,3)	5 (4,3)	Fisher's exact test	p=0,987
Stroke (ischemic/hemorrhagic), n (%)	1 (1,4)	2 (1,7)	Fisher's exact test	p=0,863
Ischemia-driven revascularization, n (%)	7 (10,0)	4 (3,5)	Fisher's exact test	p=0,106
Total MACE, n (%)	22 (31,4)	15 (13,0)	χ^2=8,079	p=0,005

***Note:** p < 0,05 – statistically significant, MI – myocardial infarction, MACE – Major Adverse Cardiovascular Events.*

According to the 24-month follow-up results, cardiovascular death (15.7% vs. 3.5%; p=0,005) and overall MACE incidence (31.4% vs. 13.0%; χ^2=8.079; p=0,005) were statistically significantly higher in patients who had experienced COVID-19 infection compared to those who had not. No statistically significant difference was observed between the groups in terms of recurrent myocardial infarction, stroke, and second-stage revascularization of ischemic-related arteries (p>0.05). These results indicate a higher long-term risk of cardiovascular complications, particularly cardiovascular death and overall MACE, in patients who had COVID-19 infection. Comparative analysis of the immediate and long-term effectiveness of PCI and TLT in patients with ST-segment elevation ACS, with or without prior COVID-19 infection.

The frequency of MACE events during the in-hospital phase according to the type of reperfusion therapy in patients who had COVID-19 infection is shown in Table 5. Notably, patients receiving TLT experienced more cardiovascular complications. In patients who had not had COVID-19, MACE events were less frequent, and no significant differences were observed depending on the type of reperfusion therapy. These findings provide important information for clinical decision-making regarding patient monitoring and therapy selection during hospitalization.

Table 5. Analysis of in-hospital MACE events, n=200

Indicators	"COVID-Positive" TLT (n=35)	"COVID-Positive" pPCI (n=40)	"COVID-Negative" TLT (n=59)	"COVID-Negative" pPCI (n=66)	Test stics	p-value
Cardiovascular death, n (%)	2 (5,7%)	1 (2,5%)	1 (1,7%)	0 (0%)	N/A	p=0,274
Recurrent MI, n (%)	1 (2,9%)	0 (0%)	0 (0%)	0 (0%)	N/A	p=0,180
Stroke (ischemic/hemorrhagic), n (%)	0 (0%)	0 (0%)	1 (1,7%)	0 (0%)	N/A	p=0,500
Ischemia-driven revascularization, n (%)	2 (5,7%)	1 (2,5%)	0 (0%)	1 (1,5%)	N/A	p=0,290
Total MACE, n (%)	5 (14,3%)*	2 (5,0%)	2 (3,4%)	1(1,5%)*	N/A	p=0,041

***Note:** p < 0,05 – statistically significant, MI – myocardial infarction, N/A – Not Applicable, MACE – Major Adverse Cardiovascular Events.*

According to the results obtained, no statistically significant differences were found among the four groups in terms of cardiovascular death, recurrent myocardial infarction, ischemic stroke, and second-stage revascularization of ischemic-related arteries (p>0.05). However, the overall incidence of MACE differed significantly across the groups, with the highest rate observed in patients who had COVID-19 infection and received thrombolytic therapy (14.3%), and the lowest rate in patients who had not had COVID-19 and received PCI (1.5%) (p=0.041). These results suggest that COVID-19 infection and the type of reperfusion therapy may have a combined effect on the development of MACE.

Table 6 presents the analysis of 12-month MACE events according to the type of reperfusion therapy (TLT or PCI) in patients with and without COVID-19 infection. A total of

Table 6

Indicators	"COVID-Positive" TLT (n=32)	"COVID-Positive" pPCI (n=39)	"COVID-Negative" TLT (n=56)	"COVID-Negative" pPCI (n=61)	Test statis-tics	p-value
Cardiovascular death, n (%)	6 (18,8%)	3 (7,7%)	3 (5,4%)	1 (1,6%)	N/A (exact test)	p=0,020
Recurrent MI, n (%)	2 (6,3%)	1 (2,6%)	4 (7,1%)	1 (1,6%)	N/A (exact test)	p=0,440
Stroke (ischemic/hemorrhagic), n (%)	0 (0%)	1 (2,6%)	1 (1,8%)	0 (0%)	N/A (exact test)	p=0,560
Ischemia-driven revascularization, n (%)	6 (18,8%)	1 (2,6%)	2 (3,6%)	1 (1,6%)	N/A (exact test)	p=0,03
Total MACE, n (%)	14 (43,8%)	6 (15,4%)	10(17,8%)	3 (4,9%)	Chi-square test (χ^2 = 22,034)	P<0,01

Analysis of 12-month MACE events, n=188

188 patients were followed, but 3 patients from the COVID-19 TLT group, 1 patient from the COVID-19 PCI group, 3 patients from the non-COVID-19 TLT group, and 5 patients

from the non-COVID-19 PCI group could not be contacted and were therefore excluded from the analysis. The results allowed a comparison of MACE incidence according to the type of reperfusion therapy.

***Note:** p < 0,05 – statistically significant, MI – myocardial infarction, MACE – Major Adverse Cardiovascular Events.*

According to the 24-month follow-up results, MACE events differed significantly depending on the type of reperfusion therapy and COVID-19 infection status. The highest rates of cardiovascular death (18.8%; p=0.020), second-stage revascularization of ischemic-related arteries (18.8%; p=0.03), and overall MACE incidence (43.8%; χ^2=22.034; p<0.01) were observed in patients who had COVID-19 infection and received thrombolytic therapy. No statistically significant differences were observed between the groups in terms of recurrent myocardial infarction and ischemic stroke (p>0.05). These results indicate a higher long-term risk of cardiovascular complications, particularly when TLT is used, in patients who had COVID-19 infection.

Table 7 presents the analysis of 24-month MACE events according to the type of reperfusion therapy (TLT or PCI) in patients with and without COVID-19 infection. A total of 185 patients were followed; however, during the 12–24 month period, 1 patient from the COVID-19 TLT group, 1 patient from the non-COVID-19 TLT group, and 1 patient from the non-COVID-19 PCI group could not be contacted and were therefore excluded from the final analysis. Thus, the 24-month follow-up results allowed for a comparison of MACE incidence according to the type of reperfusion therapy.

Table 7

Analysis of 24-month MACE events, n=185

Indicators	"COVID-Positive" TLT (n=31)	"COVID-Positive" pPCI (n=39)	"COVID-Negative" TLT (n=55)	"COVID-Negative" pPCI (n=60)	Test statistics	p-value
Cardiovascular death, n (%)	7 (22,6%)	4 (10,3%)	3 (5,5%)	1 (1,7%)	N/A (exact test)	p= 0,005
Recurrent MI, n (%)	2 (6,5%)	1 (2,6%)	3 (5,5%)	2 (3,3%)	N/A (exact test)	p= 0,820
Stroke (ischemic/hemorrhagic), n (%)	0 (0%)	1 (2,6%)	1 (1,8%)	1 (1,7%)	N/A (exact test)	p= 0,870
Ischemia-driven revascularization, n (%)	6 (19,4%)	1 (2,6%)	3 (5,5%)	1 (1,7%)	N/A (exact test)	p= 0,005
Total MACE, n (%)	15 (48,4%)	7 (17,9%)	10 (18,2%)	5 (8,3%)	Chi-square test (χ^2=20,933)	p= 0,001

***Note:** p < 0,05 – statistically significant, MI – myocardial infarction, MACE – Major Adverse Cardiovascular Events.*

According to the 24-month follow-up results, the frequency of cardiovascular death and second-stage revascularization of ischemic-related arteries differed significantly between groups (p=0.005 for both), with the highest rates observed in patients who had COVID-19 infection and received thrombolytic therapy. No statistically significant differences were found between groups in terms of recurrent myocardial infarction and ischemic stroke (p>0.05). Overall MACE incidence was highest in the COVID-19 TLT group (48.4%), with significant differences observed across groups (χ^2=20.933; p=0.001). These results indicate a higher long-term risk of cardiovascular complications, especially when TLT is used, in patients who had COVID-19 infection.

The figure shows the 24-month MACE event frequencies according to COVID-19 infection status and treatment strategy (TLT or PCI), analyzed using Kaplan–Meier survival curves (Figure 1).

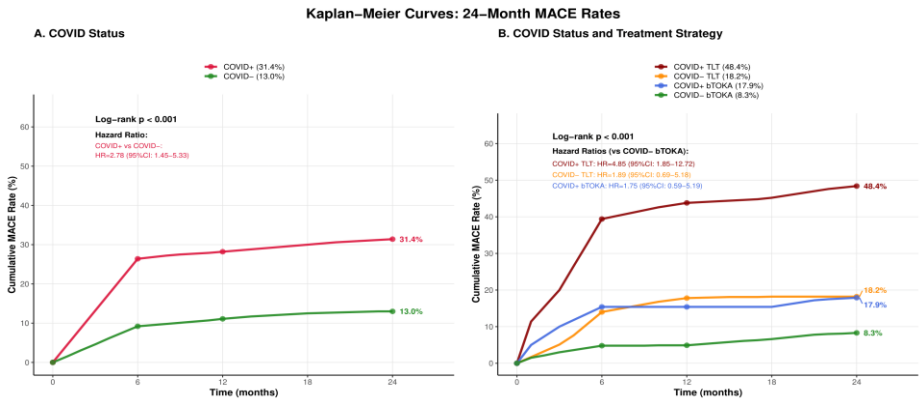


Figure 1. Kaplan-Meier analysis results:

Figure A shows a clear difference in MACE event frequencies between patients who had COVID-19 ($COVID^+$) and those who had not ($COVID^-$). During the 24-month follow-up, the MACE incidence was 31.4% in the $COVID^+$ group and 13.0% in the $COVID^-$ group. The difference was statistically significant by the log-rank test ($p < 0.001$). The hazard ratio (HR) was 2.78 (95% CI: 1.45–5.33), indicating a significantly higher risk of cardiovascular complications in patients who had COVID-19 infection.

Figure B presents the analysis of MACE event frequencies according to COVID-19 status and treatment strategy (TLT or PCI). The 24-month MACE incidence was 48.4% in the $COVID^+$ TLT group, 18.2% in the $COVID^-$ TLT group, 17.9% in the $COVID^+$ PCI group, and 8.3% in the $COVID^-$ PCI group. The differences between groups were statistically significant ($p < 0.001$).

Compared with the $COVID^-$ PCI group, the risk of MACE was as follows: $COVID^+$ TLT: HR = 4.85 (95% CI: 1.85–12.72), $COVID^-$ TLT: HR = 1.85 (95% CI: 0.65–5.18), $COVID^+$ PCI: HR = 1.75 (95% CI: 0.59–5.19).

These results indicate that COVID-19 infection, especially in patients receiving thrombolytic therapy (TLT), significantly increases the long-term risk of cardiovascular complications.

To identify predictors of MACE development in patients with ST-segment elevation ACS who had or had not had COVID-19 and received PCI or TLT, a univariable Cox regression analysis was performed in 200 patients with STEMI to assess factors influencing disease progression and complication development. The results are presented in Table 12.

Table 12

Univariable Cox regression analysis, n=200

Xavf omillari	HR	95% CI	Test statistics (Wald)	p-value
Demographic factors				
Age (every 10 years)	1,23	1,08-1,40	9,610	0,002**
Male	1,45	0,89-2,36	2,260	0,134
Body mass index >30 kg/m^2	1,28	0,81-2,03	1,120	0,291
COVID-19 status				
COVID-Positive	2,84	1,76-4,59	16,810	<0,001***
Treatment strategy				
TLT (relative to pPCI)	2,14	1,38-3,31	11,560	0,001**
Clinical indicators				
Killip class ≥ II	1,67	1,29-2,16	12,960	<0,001***
LVEF < 40%	2,41	1,48-3,92	11,560	<0,001***
GLS < -12%	1,89	1,21-2,95	7,840	0,005**
Comorbidities				
Arterial hypertension	1,56	0,94-2,59	2,960	0,087
Type 2 diabetes mellitus	1,78	1,12-2,83	5,920	0,015*
Hypercholesterolemia	1,43	0,89-2,31	2,210	0,142
Laboratory indicators				
Fibrinogen > 4.0 g/L	2,12	1,35-3,33	10,890	0,001**
Troponin I > 8.0 ng/mL	1,76	1,11-2,79	5,760	0,016*
Coronary angiographic characteristics				
Multivessel disease	1,94	1,21-3,12	7,290	0,006**
SYNTAX score > 22	1,67	1,04-2,68	4,530	0,033*

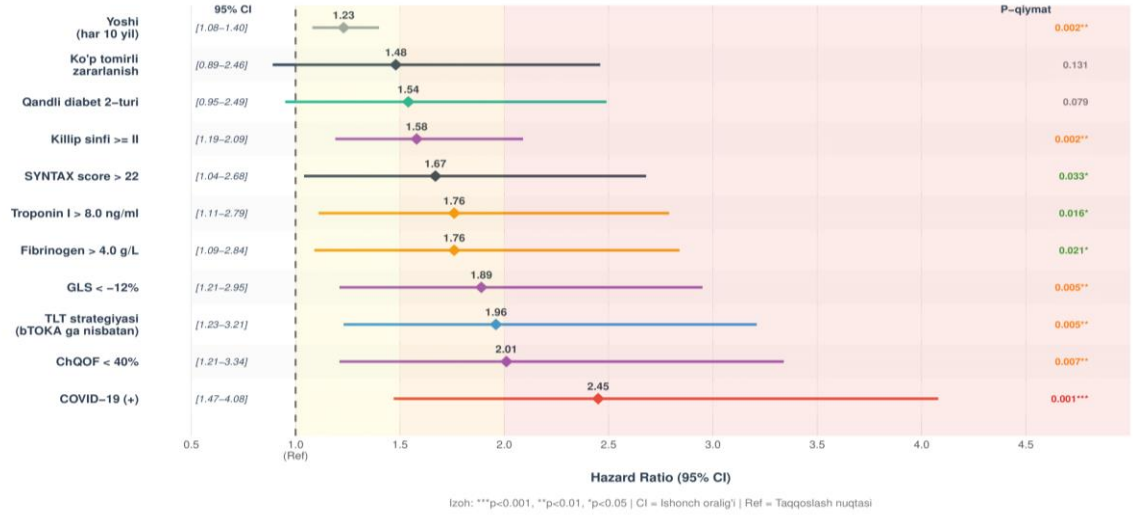
***Note:** p < 0,05 – statistically significant, HR (Hazard Ratio) – risk ratio, CI (Confidence Interval) – confidence interval.*

According to the multivariable analysis, the development of adverse cardiovascular outcomes in patients with ST-segment elevation acute coronary syndrome (STEMI) was associated with several independent risk factors. These included increasing age per 10 years, history of COVID-19 infection, thrombolytic therapy (compared to PCI), Killip class ≥ II, left ventricular ejection fraction < 40%, GLS < –12%, type 2 diabetes mellitus, fibrinogen > 4.0 g/L, troponin I > 8.0 ng/mL, multivessel coronary artery disease, and SYNTAX score > 22, all of which significantly increased the risk of adverse outcomes ($p < 0.05$). Male sex, body mass index > 30 kg/m^2, arterial hypertension, and hypercholesterolemia did not show independent prognostic significance. These findings highlight the need for comprehensive assessment of clinical, laboratory, and angiographic factors when stratifying risk in STEMI patients.

A multivariable Cox regression analysis was performed to evaluate the factors influencing the development of MACE in patients with STEMI (Figure 2). The graph presents the hazard ratio (HR), 95% confidence interval (CI), and p-values for each factor. Additionally, independent predictors of MACE development among patients who underwent reperfusion therapy were identified using a multivariable Cox regression model (n=200).

Figure 2

Identification of independent predictors of MACE development in patients undergoing reperfusion therapy using multivariable Cox regression analysis, n=200



According to the analysis, patients who had COVID-19 infection had a significantly higher risk of developing heart failure, with a hazard ratio (HR) of 2.45 [95% CI: 1.47–4.08], p = 0.001. Additionally, the following factors were identified as independent predictors of heart failure development: LVEF < 40% (HR = 2.01 [1.21–3.34], p = 0.007), TLT strategy (compared to PCI) (HR = 1.96 [1.23–3.21], p = 0.005), and GLS ≤ –12% (HR = 1.89 [1.21–2.95], p = 0.005).

Furthermore, fibrinogen > 4.0 g/L (HR = 1.76 [1.09–2.84], p = 0,021), troponin I > 8.0 ng/mL (HR = 1.76 [1.11–2.79], p = 0,016), SYNTAX score ≥ 22 (HR = 1.67 [1.04–2.68], p = 0,033), and Killip class ≥ II (HR = 1.58 [1.19–2.09], p = 0,002) were also statistically significant predictors. Other factors—age (per 10 years) (HR = 1.23 [1.08–1.40], p = 0,002), multivessel disease, and type 2 diabetes mellitus—showed notable trends but did not reach statistical significance (p > 0,05).

Discussion

According to the results of this study, COVID-19 infection significantly worsens long-term cardiovascular outcomes in patients with ST-segment elevation acute coronary syndrome (STEMI). The 24-month MACE rate in COVID-positive patients was 31,4%, which was two and a half times higher than in those in the COVID-Negative group (13,0%). Notably, cardiovascular mortality reached 15,7% in the COVID-Positive group, which was four times higher than in the COVID-Negative group (3,5%). Cox regression analysis showed that COVID-19 infection independently increased the risk of MACE development by 2.4 times. During reperfusion therapy, primary percutaneous coronary intervention (pPCI) showed superiority over thrombolysis regardless of COVID-19 status. The COVID-Positive thrombolysis group exhibited the highest risk level (48,4% MACE), whereas the COVID-Negative PCI group demonstrated the lowest rate (8,3% MACE). These findings align with data from the international ISACS-STEMI COVID-19 registry and the ESC EORP, confirming the long-term adverse impact of COVID-19 on the cardiovascular system.

Conclusion

1. The immediate effectiveness of reperfusion therapy was significantly lower in patients who had COVID-19. During the in-hospital phase, cardiovascular death occurred in 4.0% of patients in the COVID-19 group, compared to 0.8% in the non-COVID-19 group. Over the 24-month follow-up, MACE incidence reached 31.4% in the COVID-19 group and 13.0% in the non-COVID-19 group.
2. PCI demonstrated superiority over TLT across all groups. The lowest MACE

rate was observed in the non-COVID-19 PCI group (8.3%), whereas the highest rate was observed in the COVID-19 TLT group (48.4%).

3. The most important independent predictors of MACE development in patients with STEMI were identified as follows: COVID-19 infection (HR = 2.45), TLT strategy (HR = 1.96), LVEF < 40% (HR = 2.01), and fibrinogen > 4.0 g/L (HR = 2.76). Interaction analysis confirmed a synergistic negative effect of COVID-19 infection combined with TLT (HR = 2.12).

References

1. Khan, M. A. B., Hashim, M. J., Mustafa, H., et al. (2020). Global epidemiology of ischemic heart disease: Results from the Global Burden of Disease Study. Cureus, 12(7), e9349. https://doi.org/10.7759/cureus.9349.

2. Current trends in the classification of sudden cardiac death based on autopsy derived data: A review of investigations into the etiology of sudden cardiac death. Revista Española de Cardiologia (English Edition). Retrieved from https://www.revespcardiol.org/en-current-trends-in-classification-sudden-articulo-S1885585710000319.

3. Ibanez, B., James, S., Agewall, S., et al. (2018). 2017 ESC guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation. European Heart Journal, 39(2), 119–177.

4. Semenova, I. G., Sheglov, A. N., Semigolovskii, N. Yu., Ballyuzek, M. F., Mazurenko, S. O., Guslev, A. B., Kozaev, A. V., & Nikolskaya, E. M. (2024). Cardioprotection with levocarnitine intracoronary administration during percutaneous coronary interventions. Medical Council (Meditsinskiy sovet), 23, 50–59. https://doi.org/10.21518/ms2023-448.

5. World Population Review. (2025). Heart disease rates by country 2025 [Internet]. Walnut, CA: World Population Review. Retrieved January 16, 2025, from https://worldpopulationreview.com/country-rankings/heart-disease-rates-by-country.

6. Zeymer, U., Ludman, P., Danchin, N., et al. (2021). Reperfusion therapies and in-hospital outcomes for ST-elevation myocardial infarction in Europe: The ACVC-EAPCI EORP STEMI Registry of the European Society of Cardiology. European Heart Journal, 42(44), 4536–4549.

7. Pessoa-Amorim, G., Camm, C. F., Gajendragadkar, P., et al. (2020). Admission of patients with STEMI since the outbreak of the COVID-19 pandemic: A survey by the European Society of Cardiology. European Heart Journal - Quality of Care and Clinical Outcomes, 6(3), 210–216.

8. World Health Organization. Coronavirus disease (COVID-19): Situation Reports. WHO, 2020.

9. Garcia, S., Albaghdadi, M. S., Meraj, P. M., et al. (2020). Reduction in ST-segment elevation cardiac catheterization laboratory activations in the United States during COVID-19 pandemic. Journal of the American College of Cardiology, 75(22), 2871–2872.

10. Zheng, Y. Y., Ma, Y. T., Zhang, J. Y., & Xie, X. (2020). COVID-19 and the cardiovascular system. Nature Reviews Cardiology, 17(5), 259–260.

11. Libby, P., & Luscher, T. (2020). COVID-19 is, in the end, an endothelial disease. European Heart Journal, 41(32), 3038–3044.

12. Long, B., Brady, W. J., Koyfman, A., & Gottlieb, M. (2020). Cardiovascular complications in COVID-19. American Journal of Emergency Medicine, 38(7), 1504–1507.

13. Centers for Disease Control and Prevention [CDC], 2023; World Health Organization (WHO), 2020.

14. Arevalo-Rodriguez et al., 2020; Watson et al., 2020.
15. Mafham, M. M., Spata, E., Goldacre, R., et al. (2020). COVID-19 pandemic and admission rates for and management of acute coronary syndromes in England. The Lancet, 396(10248), 381–389.
16. Chew, N. W. S., Ow, Z. G. W., Teo, V. X. Y., et al. (2022). The global impact of the COVID-19 pandemic on STEMI care: A systematic review and meta-analysis. Canadian Journal of Cardiology, 38(11), 1657–1667.