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ORIGINAL ARTICLE

ST Segment Elevated Myocardial Infarction Associated with High Mortality and Thrombus Burden in Patients with COVID-19 Infection

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Abstract

Introduction: There is limited information regarding the clinical and angiographic characteristics and outcomes of patients with Coronavirus disease 2019 (COVID-19) presenting with ST segment elevation myocardial infarction (STEMI). The aim of this study was to describe the clinical and angiographic characteristics, as well as clinical outcomes, in COVID-19 positive patients with STEMI compared with COVID-19 negative STEMI patients.

Methods: This was a single-center observational study conducted between May 2020 and May 2021. The study population consisted of 35 patients who were followed with active COVID-19 and diagnosed with STEMI, and 35 STEMI patients without COVID-19 infection.

Results: Groups were similar in terms of gender, hypertension, obstructive airway disease, SYNTAX score, and localization of myocardial infarction (MI). Glucose levels, BUN, creatinine, and CRP levels were significantly higher in the COVID-19 group. LDL and hemoglobin levels were lower in the COVID-19 group ($p<0.05$). There was a positive correlation between in-hospital death and modified thrombus grade post-first device and a negative correlation between in-hospital death and post-procedural TIMI flow ($p=0.001$, $r=0.480$).

Discussion and Conclusion: Our results demonstrate that patients presenting with STEMI and concurrent COVID-19 infection have a higher post-procedural thrombus burden and worse Thrombolysis in Myocardial Infarction (TIMI) flow. STEMI patients with COVID-19 face procedural challenges and are associated with poorer clinical outcomes.

Keywords: Clinical outcomes; Coronavirus disease; Myocardial infarction; Thrombus burden.

Coronavirus disease 2019 (COVID-19) has been increasingly recognized to cause an overwhelming inflammatory response and cytokine storm, subsequently resulting in multi-systemic end organ damage[1]. Cardiac complications secondary to this infection are common and appear to be a source of significant morbidity and mortality in patients with COVID-19. COVID-19 is accepted as a multi-organ disease[2]. Myocardial infarction, which is a leading cause of death in the general population, has been seen more frequently in patients with COVID-19[3]. According to the fourth universal definition of acute MI, type 2 AMI incidences are expected to increase in COVID-19 infection because of oxygen demand-supply imbalance due to hypoxemia, high heart rate, and septic condition[4].

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Nevertheless, type 1 AMI also increased in COVID-19[5]. COVID-19 infections can cause AMI with multiple pathophysiological mechanisms, including inflammatory and increased shear stress causing plaque rupture leading to acute coronary events, aggravation of pre-existing coronary artery disease causing more severe cardiac injury, tendency of vessel thrombus, and other direct and indirect causes of myocardial injuries.

STEMI often occurs due to coronary occlusion from plaque rupture and thrombus formation. Treatment strategy in STEMI aims to recanalize the occluded coronary artery and provide good distal flow[6]. The keystones of treatment for STEMI are primary percutaneous coronary intervention (PCI) and anti-thrombotic drugs[6]. However, in COVID-19, previous studies showed that STEMI incidences increase. Clinical and angiographic features of STEMI in COVID-19 have not been adequately investigated.

In this study, we compared the clinical and angiographic characteristics, as well as clinical outcomes, including hospital mortality, between COVID-19 positive patients with STEMI and COVID-19 negative patients.

Materials and Methods

This study was performed in Kayseri City Education and Research Hospital. Patients presenting with STEMI from May 2020 to May 2021 were included in the study. The data were collected retrospectively. Thirty-five patients (age: 69.4±10.7, 25 male) who were followed with active COVID-19 were diagnosed with STEMI during this period. Additionally, 35 STEMI patients (age: 57.4±12.6, 27 male) without COVID-19 infection were enrolled in the study. Patients' demographic, clinical, and angiographic features were recorded. Treatment procedures and in-hospital outcomes were documented.

STEMI diagnosis was based on the Fourth Universal Definition of Myocardial Infarction[4]. Patients who had chest pain and ST segment elevation in two or more consecutive leads on an electrocardiogram were accepted as having STEMI. Patients who developed cardiac arrest at admission were not enrolled in the study. Additionally, patients who were treated 12 hours after initial chest pain were excluded from the study. The treatment protocol was performed according to ESC STEMI guidelines[6].

Table 1. Baseline Clinical, Demographic, and Laboratory Characteristics of All Patients.

	Covid (+), n=35	Covid (-), n=35	p
Age	69.4±10.7	57.4±12.6	0.001
Sex, male, n (%)	21 (59.9)	19 (54.2)	0.785
Diabetes Mellitus, n (%)	17 (48.5)	10 (28.5)	0.004
Hypertension, n (%)	17 (48.5)	16 (45.7)	0.0725
Coronary Artery Disease, n (%)	15 (42.8)	11 (31.4)	0.469
Obstructive Airways Disease, n (%)	3 (8.5)	5 (14.2)	0.710
SYNTAX score	15.9±8.9	17.4±8.4	0.471
Localization of MI			0.338
Anterior territory, n	17	19	NS
Inferior territory, n	18	16	NS
Glucose, mg/dL	196.2±98.1	123±99.0	0.021
BUN, mg/dl	26.4±15.3	15.3±6.1	0.001
Creatinine, mg/dL	1.05±0.61	0.85±0.50	0.020
Total cholesterol, mg/dL	154.8±47.2	186.3±40.1	0.004
LDL cholesterol, mg/dL	95.2±36.8	130.7±36.2	0.001
Triglyceride, mg/dL	146.8±68.0	140.9±70.7	0.725
HDL cholesterol, mg/dL	37.1±18.2	42.9±13.3	0.134
Na, mEq/L	135.1±4.4	137.6±2.7	0.007
K, mEq/L	4.60±0.52	4.34±0.46	0.063
CRP, mg/L	80.8±63.3	21.9±33.4	0.001
Troponin-T, ng/dL	882.6±1646	1720±2108	0.073
WBC, $mm^3 \times 10^3$	12.1±4,8	12.2±3,4	0.938
Hemoglobin, g/L	13.1±2.11	14.6±2.10	0.006
Platelet count, mm^3	269.8±98.9	269.7±70.0	0.994

BUN: Blood urea nitrogen; CRP: C-reactive protein; HDL: high-density lipoprotein; LDL: low-density lipoprotein; MI: Myocardial infarction; WBC: White blood cell.

Primary PCI was performed in all cases. TIMI flow scores and angiographic modified thrombus grades were determined before and after primary PCI[7,8]. The following classification was used for angiographic thrombus burden: Grade 0: no thrombus, Grade 1: possible thrombus, Grade 2: the thrombus' greatest dimension is <1/2 vessel diameter, Grade 3: greatest dimension >1/2 to <2 vessel diameters, Grade 4: greatest dimension >2 vessel diameters, Grade 5: total vessel occlusion due to thrombus[8].

COVID-19 diagnosis was confirmed with nasopharyngeal swab PCR test and thorax CT in all patients. COVID-19 patients were treated according to the Türkiye Republic Health Ministry COVID-19 treatment guidelines[9].

Post-PCI TIMI flow score, modified thrombus score, and cardiovascular death were used to determine outcomes. COVID-19 related deaths, such as acute respiratory distress syndrome, septic shock, and respiratory insufficiency, were denoted separately.

All study procedures were performed in line with the principles of the Declaration of Helsinki. Informed consent was not required since the study was retrospective. Ethics approval was confirmed by the local ethics committee (decision no: 188, date: 14.07.2021).

Statistical Analysis

Statistical analyses were performed using SPSS for Windows software (version 22.0; IBM Corp., Armonk, NY, USA). Continuous variables are expressed as means±standard deviations, and categorical variables as percentages. The distribution of continuous variables was assessed using the Kolmogorov–Smirnov test. Continuous variables were compared using Student's t-test and the Mann–Whitney U test. Categorical variables were compared using the chi-square test. Univariable and multivariable logistic regression analysis was used to determine the association between independent factors (such as diabetes, hypertension, and culprit vessel) and in-hospital mortality. P-values <0.05 were considered to be statistically significant.

Results

Baseline clinical, demographic, and laboratory characteristics are summarized in Table 1. Age was statistically higher in the COVID-19 (+) group (69.4±10.7 vs. 57.4±12.6, p=0.001). Risk factors, except for diabetes, were not statistically different between the groups. The presence of diabetes was higher in the COVID-19 (+) group (22 vs. 9, p=0.004).

Table 2. Procedural Characteristics All Patients Underwent Primary PCI Procedure.

	Covid (+), n=35	Covid (-), n=35	p
Culprit vessel			0.610
LAD, n	17	19	
LCX, n	11	11	
RCA, n	7	5	
Baseline TIMI flow grade			0.154
Grade 0	23	30	
Grade 1	8	4	
Grade 2	3	0	
Grade 3	1	1	
Post-procedural TIMI flow grade			0.018
Grade 0	4	1	
Grade 1	4	1	
Grade 2	8	2	
Grade 3	19	31	
Baseline thrombus grade (4–5)			0.792
Grade 4	11	9	
Grade 5	24	26	
Modified thrombus grade post first device			0.012
Grade 0	1		
Grade 1	14	25	
Grade 2	2	2	
Grade 3	7	5	
Grade 4	8	2	
Grade 5	3	1	
In-hospital death	10	1	0.001

LAD: Left anterior descending artery; CX: Circumflex artery; RCA: Right coronary artery; TIMI: Thrombolysis in myocardial infarction.

Glucose, creatinine, BUN, and CRP levels were higher in the COVID-19 group (196.2±98.1 vs. 123.0±99.0, 1.05±0.61 vs. 0.85±0.50, 26.4±15.3 vs. 15.3±6.1, 80.8±63.3 vs. 21.9±33.4, respectively). LDL, Na, and Hb levels were lower in the COVID-19 (+) group (95.2±36.8 vs. 130.7±36.2, 135.1±4.4 vs. 137.6±2.7, 13.1±2.11 vs. 12.2±3.4). Angiographic findings are shown in Table 2. Culprit vessels were not statistically different between the two groups (p=0.610). Baseline TIMI flow was not different between the two groups (p=0.154). The COVID-19 (+) group had a statistically significantly higher modified thrombus grade after PCI (p=0.012).

There was a positive correlation between in-hospital death and modified thrombus grade post-first device, CRP (p=0.002, r=-0.366; p=0.001, r=-0.525). Additionally, there was a negative correlation between in-hospital death and post-procedural TIMI flow (p=0.001, r=0.480).

Discussion

COVID-19 mainly affects the respiratory system and causes acute respiratory distress syndrome (ARDS). However, while mortality in COVID-19 is primarily related to ARDS, cardiovascular system (CVS) involvement also contributes to the increased mortality rate. STEMI, which is one of the manifestations of CVS involvement, is a significant cause of morbidity and mortality. Understanding the mechanisms and features of STEMI in COVID-19 is important for treatment strategy. In our study, we investigated the clinical and angiographic features of STEMI patients with COVID-19.

In this study, three main findings were observed: 1) Post-procedural thrombus burden was higher and post-procedural coronary flow was worse in the COVID-19 (+) group; 2) In-hospital death was higher in the COVID-19 (+) group; 3) A positive correlation between thrombus burden and in-hospital mortality was observed.

STEMI often occurs due to the acute occlusion of a coronary artery[6]. Restoration of coronary flow with primary PCI or thrombolysis is a life-saving treatment in STEMI. COVID-19 may cause other clinical conditions such as an imbalance of the myocardial oxygen demand-supply equation, myocarditis, pericarditis, pulmonary thromboembolism, or stress cardiomyopathy. Also, COVID-19 patients generally require significant oxygen therapy, so STEMI diagnosis and treatment may be delayed. Delayed primary PCI is associated with worse outcomes. In our study, impaired post-procedural flow, higher thrombus burden, and in-hospital death may be associated with delays in primary PCI.

Acute coronary events often occur due to atherosclerotic plaque rupture or erosion. Inflammatory cells (mostly T cells and macrophages) play critical roles in plaque progression, rupture, erosion, and thrombosis[10]. It has been shown that COVID-19 induces endothelitis. Leukocyte adhesion molecules, pro-inflammatory cytokines (IL-1, IL-6, TNF-α), and chemokines that prompt leukocyte aggregation increase in the endothelium in COVID-19 endotheliitis[11]. These changes are associated with inflammation and coagulopathy. In light of these data, STEMI incidences and thrombus burden can be expected to increase. In this study, we observed that the post-procedural thrombus burden was higher in COVID-19 patients. This result may be associated with increased inflammation and coagulopathy in COVID-19.

Another finding of the study is lower TIMI flow grade after primary PCI in the COVID-19 (+) group. Failure of normal perfusion after mechanical opening of the occluded artery in MI is defined as 'no-reflow'[12]. Because no-reflow causes delayed healing of the infarct area and adverse remodeling, it is associated with a high incidence of left ventricular malfunction and mortality[13]. In this study, failure to supply normal coronary flow after primary PCI was observed more frequently in the COVID-19 group. One of the reasons for this condition could be thrombotic microangiopathy, endotheliitis, and microvascular dysfunction caused by COVID-19[14]. An autopsy study showed fibrin-rich thrombi within capillaries and small blood vessels in COVID-19 patients[15]. This finding can explain the tendency to no-reflow in STEMI patients with COVID-19.

Higher in-hospital death was observed in the COVID-19 (+) group in our study. In Rodriguez-Leor et al.'s[16] study, stent thrombosis, cardiogenic shock, heart failure, and in-hospital mortality were higher in STEMI patients with COVID-19. Also, other studies that evaluated STEMI patients with COVID-19 found high mortality in COVID-19 patients[17,18]. However, in these studies, not all patients were treated with primary PCI[18]. In our study, all STEMI patients received primary PCI, yet mortality was higher in the COVID-19 (+) group.

Limitations

This study has several limitations. First, the single-center observational design and the relatively small sample size limit the generalizability of the findings. Second, our study lacked long-term follow-up. If we had followed patients long-term, we could have obtained additional information about the prognosis of STEMI patients with COVID-19. Because COVID-19 causes many clinical situations such as ARDS, sepsis, and pulmonary thromboembolism, determining the specific reason for death is not always possible. Third, cardiac imaging was not performed in any of the study patients during their illness.

Conclusion

The current study demonstrated that STEMI patients with COVID-19 who underwent primary PCI have a high post-procedural thrombus burden and worse TIMI flow. In-hospital death was significantly higher in STEMI patients with COVID-19.

Ethics Committee Approval: All study procedures were performed in line with the principles of the Declaration of Helsinki. Informed consent was not required since the study was retrospective. Ethics approval was confirmed by the local ethics committee (decision no: 188, date: 14.07.2021).

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