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A Review of ST-Elevation Myocardial Infarction in Patients with COVID-19



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KEYWORDS

• ST-Elevation myocardial infarction • COVID-19 • SARS-COV 2

KEY POINTS

- COVID-19 leads to a hyper-inflammatory response and increase in procoagulants and platelet activation predisposing to an acute myocardial infarction (AMI).
- Cardiogenic shock is more common in patients with COVID-19 who present with STEMI than those without COVID-19 but not cardiac arrest
- STEMI in patients with COVID-19 is associated with worse clinical outcomes compared with STEMI in patients without COVID-19.
- Primary PCI remains the first-line treatment approach in patients with COVID-19 who develop STEMI

INTRODUCTION

The Coronavirus disease 2019 (COVID-19) pandemic has led to a significant increase in worldwide morbidity and mortality. Patients with COVID-19 are at risk for developing a variety of cardiovascular conditions including acute coronary syndromes, stress-induced cardiomyopathy, and myocarditis. Patients with COVID-19 who develop ST-elevation myocardial infarction (STEMI) are at a higher risk of morbidity and mortality when compared with their age- and sex-matched STEMI patients without COVID-19.¹ We

review current knowledge on the pathophysiology of STEMI in patients with COVID-19, clinical presentation, outcomes, and the effect of the COVID-19 pandemic on overall STEMI care.

EPIDEMIOLOGY

Initial reports suggested a drop in the number of patients presenting with STEMI to hospitals in the few months following February–March 2020.^{2–11} However, some centers later witnessed a U-shaped phenomenon in STEMI incidence during the pandemic.^{12,13} This U-shaped phenomenon

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indicated a decline in STEMI incidence during the first few weeks of the pandemic followed by a rebound in the following weeks.

PATHOPHYSIOLOGY

COVID-19 is caused by SARS-CoV-2 and has been shown to predispose patients to a prothrombotic

state, involving both the venous and arterial circulations as well as both microvascular and macrovascular systems.^{14,15} This prothrombotic state has been shown to be associated with poor prognosis in patients with COVID-19 pneumonia.¹⁶ Several mechanisms are believed to play a role in this process including inflammation, endothelial dysfunction, and platelet activation (Fig. 1).¹⁷ SARS-CoV-

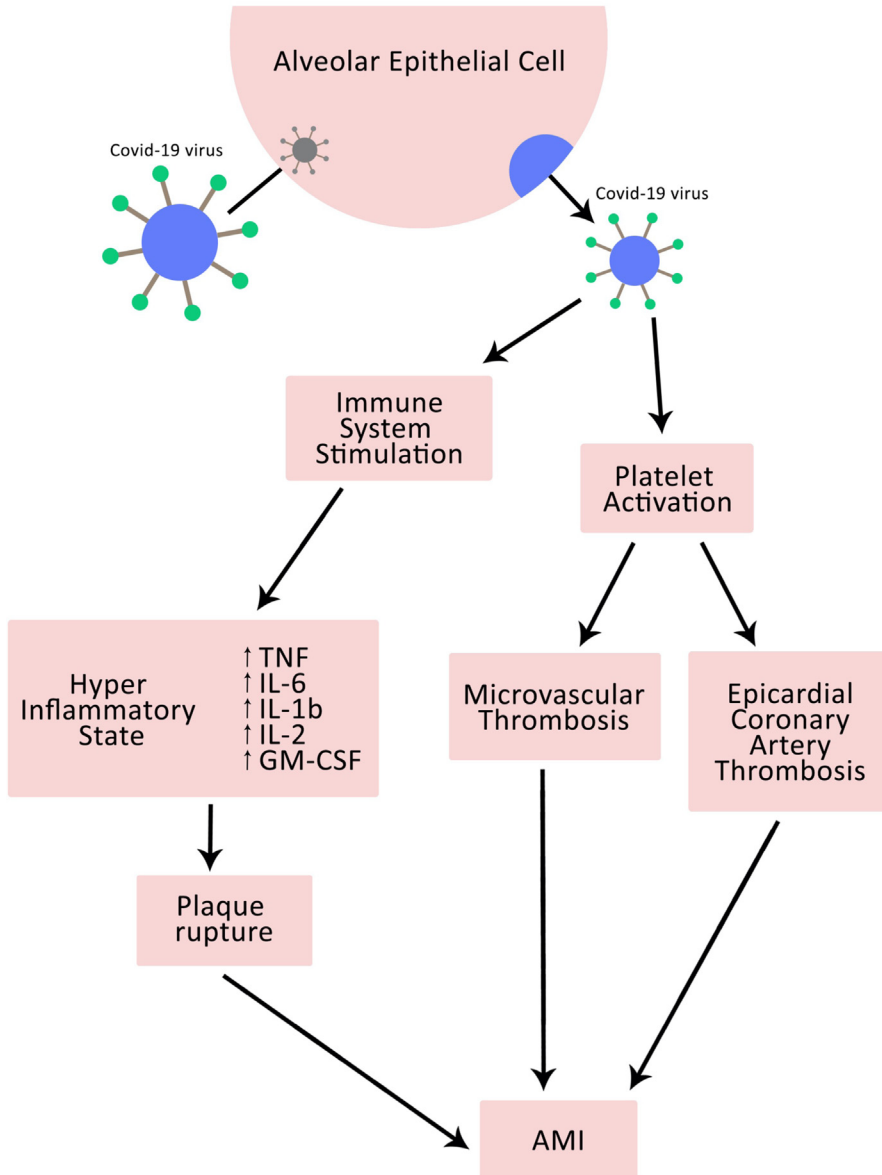


Fig. 1. Pathophysiology of STEMI in patients with COVID-19. COVID-19 induced hyperinflammatory state and thrombosis as mechanisms leading to acute myocardial infarction. COVID-19 enters alveolar epithelial cells via the angiotensin-converting enzyme-2 receptor. Once it gets replicated in these cells, then it exits the alveolar cells and stimulates a dysregulated immune response which leads to hyperinflammatory response with the elevation of multiple biomarkers such as TNF, Interleukin-1 beta (IL-1 β), Interleukin-6 (IL-6), interleukin-2 (IL-2), and granulocyte monocyte colony-stimulating factor (GM-CSF). Parallel to this, there is upregulation of procoagulants and increased platelet activation which leads to thrombosis. Hyperinflammatory response and thrombosis are the main mechanisms behind STEMI in patients with COVID-19.

2 infects epithelial respiratory cells by binding to the angiotensin-converting enzyme-2 receptor, viral shedding follows, which stimulates an inflammatory response leading in some cases to a cytokine storm mediated by proinflammatory cytokines such as interleukin 1- β (iL-1 β), iL-2, iL-6, tumor necrosis factor (TNF), and granulocyte macrophage colony-stimulating factor (GM-CSF). This cascade then leads to an overexpression of procoagulant factors such as tissue factor, factor VIII, p-selectin, Von Willebrand factor (vWF), fibrinogen, and down-regulation of anticoagulants which leads to thrombus formation.¹⁸

A pathologic analysis of 40 hearts from hospitalized patients in Italy who succumbed to COVID-19 showed that 35% of these patients had evidence of myocardial necrosis. The most common reason for myocardial necrosis was the presence of microthrombi, which were distinctly different in composition from thrombus aspirates from epicardial coronary arteries containing more fibrin and terminal complement.^{19,20}

PATIENT CHARACTERISTICS

Most of the patients with COVID-19 who presented with STEMI were male in both the Israeli and North American cohorts (**Table 1**).^{1,20} Their age ranged from 56 to 75 years.¹ Patients with COVID-19 who

presented with STEMI had a significantly lower risk factor burden compared with those who were admitted with STEMI before the COVID-19 pandemic.²⁰ Most of those patients belonged to racial minorities (23% Hispanics, 24% Blacks, 6% Asians). The most common presenting symptom was dyspnea and 46% of patients had the presence of pulmonary infiltrate on chest x ray.¹ An Italian cohort in Lombardy showed that 85.7% of patients with STEMI experienced myocardial infarction as the first manifestation of COVID-19 and a quarter of those patients reported dyspnea as the initial complaint.²¹ Cardiogenic shock is more frequent in patients with COVID-19.^{1,9,22}

PROCEDURAL CHARACTERISTICS

In the North American experience, about a quarter of patients with COVID-19 or suspected of having COVID-19 who presented with STEMI did not undergo emergent coronary angiography.¹ Door to balloon (D2B) time was reported in several studies to be significantly longer in patients with COVID-19 compared with historical controls. In a recent meta-analysis of 19 studies mainly across Asia, Europe, and Canada, the mean D2B time was reported to be 8.1 minutes longer in patients with COVID-19 compared with controls.²³ This difference was more noticeable in the North American

Table 1
Comparison of baseline characteristics reported in prior studies

	Garcia et al, ¹ 2021	De Luca et al, ⁹ 2021	Hamadeh et al. ³⁶	Fardman et al, ¹³ 2020	Controls Midwest STEMI Consortium
Median Age (y)	65	64	65	62	62
Male Sex (%)	71	73.7	63	81	71
Hypertension (%)	73	54.7	73	52	69
Dyslipidemia (%)	46	41.5	92	58	60
Diabetes mellitus (%)	46	21.8	27	31	28
Prior PCI (%)	13	12.6	—	—	26
Prior MI (%)	13	9.4	—	18	24
Prior CABG (%)	5	1.7	11	2.6	8
Smoking (%)	44	41	—	49	59
Prior stroke/TIA (%)	10	—	8	5.9	9
History of CAD (%)	24	—	78	—	31
Aspirin (%)	38	—	22	—	39
Statin (%)	39	—	42	—	35
Cardiogenic Shock (%)	18	7.7	—	—	10
Out of hospital cardiac arrest (%)	11	6.6	—	—	7

Abbreviations: CABG, coronary artery bypass grafting; MI, myocardial infarction; TIA, transient ischemic attack; PCI, percutaneous coronary intervention.

centers with a mean difference of 12 minutes.¹ Patients with COVID-19 presenting with STEMI were more likely to receive medical therapy alone compared with controls (20% vs 2%) and less likely to undergo primary PCI (71% vs 93%). These patients were more likely to have no identifiable culprit lesion on coronary angiography as compared with the control group (23% vs 1%).¹

In a meta-analysis of several studies, post-PCI thrombolysis-in-myocardial-infarction (TIMI) flow grade was 60% more likely to be suboptimal with TIMI flow less than 3 than the control group of patients from the prepandemic era.²³ Even though left ventricular ejection fraction (LVEF) following primary PCI was reported to be similar in the North American experience, several other studies have shown a significantly lower LVEF (−4.2%) following primary PCI in patients with COVID-19 compared with their counterparts (Table 2).²³

LENGTH OF HOSPITAL STAY

Patients with STEMI who underwent PCI during the pandemic had an overall longer duration of hospital stay as shown in several studies. In the North American experience, the average length of hospital stay was 4 days longer in patients with COVID-19 compared with patients without COVID-19.¹ Other studies have shown an increased length of ICU stay in patients with STEMI who were admitted during the pandemic era as compared with those admitted before the pandemic onset.²³

IN-HOSPITAL OUTCOMES

In the North American experience, the primary composite endpoint of in-hospital death, stroke, recurrent MI, or repeat revascularization was significantly higher in patients with COVID-19 compared with patients without COVID-19 (36% vs 5%, $P < .001$).¹ This was primarily due to markedly higher risk of in-hospital death in patients with COVID-19 as compared with controls (33% vs 4%, $P < .001$). The incidence of stroke was also statistically higher in patients with COVID-19 (3% vs 0%, $P = .017$). In a meta-analysis conducted by Chew and colleagues, the overall mortality of patients with STEMI was 27% higher during the pandemic as compared with prepandemic controls.²³ Similarly, the Israeli experience reported an overall higher composite endpoint of malignant arrhythmia, congestive heart failure, or in-hospital mortality in those admitted with STEMI in the pandemic era as compared with prepandemic controls (12% vs 8.6%, $P = .04$), Table 3.²⁰ In a large recent retrospective analysis of both out-of-hospital and in-hospital patients with STEMI with COVID-19, the mortality rate was significantly higher when compared with their COVID-19 negative propensity-matched counterparts (15.2% vs 11.2%). In this study, Saad and colleagues also compared the outcomes between in-hospital patients with STEMI with concomitant COVID-19 to in-hospital patients with STEMI without COVID-19 from prior years and reported a dramatically

Table 2
Comparison of procedural characteristics reported in prior studies

	Garcia et al, ¹ 2021	De Luca et al, ⁹ 2021	Fardman et al, ¹³ 2020	Controls from Midwestern STEMI Consortium
No angiography (%)	22	–	2	0
D2B time, min. Median (IQR)	79 (52–125)	34 (21–36)	52 (29–90)	66 (46–93)
D2B time <90 (%)	58	—	–	73
LV Ejection Fraction (%)	45	–	45	45
Primary PCI (%)	71	–	87	93
Presence of culprit lesion (%)				
Multiple culprits	16	–	6.4	–
No culprit	23	–	–	0
TIMI flow post-PCI (%)				
0–1	6	–	–	2
2–3	94	92.2	–	98
Length of hospital stay, days	6	–	4	2

Abbreviation: D2B, door to balloon time; LV, left ventricular; PCI, percutaneous coronary intervention; TIMI, thrombolysis-in-myocardial-infarction.

Table 3
Comparison of clinical outcomes reported in prior studies

	Garcia et al, ¹ 2021	De Luca et al, ⁹ 2021	Fardman et al, ¹³ 2020	Controls from Midwestern STEMI Consortium
In-hospital death (%)	33	29	18	5
Stroke (%)	3	–	1.2	0
Recurrent myocardial infarction (%)	2	–	3	0
Unplanned revascularization (%)	4	–	–	4

higher mortality rate of 76% as compared with 44% in those without COVID-19.²⁴

DISPARITIES IN ST-ELEVATION MYOCARDIAL INFARCTION MANAGEMENT IN THE COVID-19 ERA

Several studies have shown higher cardiovascular disease-related deaths in the COVID-19 era in racial and ethnic minorities including African Americans, Asians, and Hispanics compared with Whites.^{25,26} In a retrospective study of 73,746 patients admitted with AMI in the pandemic and prepandemic eras in the United Kingdom, there was a significantly higher odds ratio of AMI in ethnic minority groups as compared with Whites.²⁶ These patients, however, were more likely to be younger, male, with lower body mass index, and a higher prevalence of comorbidities. They were more likely to present with out of hospital cardiac arrest (7.6% vs 6.2%, $P = .04$) and cardiogenic shock (3.5% vs 2.4%, $P < .001$) as compared with Whites. There was a longer delay in reperfusion therapy in the minority group as compared with Whites with an absolute increase of 30 minutes in the D2B time.²⁶ The ethnic minorities were significantly less likely to be discharged on dual antiplatelet therapy compared with Whites (70% vs 73%, $P = .03$). Risk of in-hospital and 7-day mortality was significantly higher in the ethnic subgroup compared with Whites.²⁶

REPERFUSION STRATEGIES

Even though primary PCI has been the first-line reperfusion strategy for patients with STEMI in the United States, the rate of fibrinolysis-focused reperfusion strategy remains about 2%-13% nationally.²⁷ During the COVID-19 pandemic, longer delays were reported to reperfusion. Tim and colleagues reported longer delays of symptom onset to first medical contact (318 vs 82.5 minutes), D2B time (110 vs 84.5 minutes), and catheterization laboratory to balloon time (33 vs 20.5 minutes)

compared with the prepandemic era.²⁸ Delayed presentation, lack of adequate COVID-19 testing early on, potential hazard to staff members, longer assessment times in emergency departments resulting in longer D2B times and therefore, potentially loss of primary PCI benefit, led to suggestions for a fibrinolytic-first approach in a selected patients with STEMI.²⁹ However, given the higher rate of no culprit including microthrombi with slow flow, stress-induced cardiomyopathy, COVID-19 induced myocarditis, or pericarditis, fibrinolysis may not only provide no benefit, but confer additional bleeding risk. With the adoption of enhanced safety measures in cardiac catheterization laboratories, greater access to rapid testing, and wider availability of personal protective equipment for staff, a joint recommendation from the ACC, SCAI, and American College of Emergency Physicians (ACEP) later recommended primary PCI for all patients with definite STEMI regardless of COVID-19 diagnosis.³⁰ Thrombolysis was instead recommended for patients with STEMI with severe COVID-19 pneumonia or those for whom transfer to PCI-capable hospital is not possible within 120 minutes from first medical contact.^{30,31}

IMPACT OF COVID-19 PANDEMIC ON SYSTEMS OF CARE IN ST-ELEVATION MYOCARDIAL INFARCTION MANAGEMENT

The COVID-19 pandemic has impacted the delivery of health care in all its aspects around the globe. STEMI systems of care that require a synchronized network of referring hospitals, emergency departments, and PCI-capable cardiac catheterization laboratories have similarly been affected. During the initial phase of the pandemic, some studies suggested up to 31% reduction in cardiac catheterization laboratory activations with an estimated 18% to 20% reduction in primary PCI volume.¹¹ During the same period, a study by Garcia and colleagues showed an increase of 20% in D2B times as compared with before the pandemic.¹¹ Several

factors were reported to contribute to the increase in time to reperfusion during the pandemic including overwhelmed emergency rooms, COVID-19 testing requirement in the ED before transfer to catheterization laboratory, use of strict infection control measures, and increased use of imaging to triage these patients.³² Early in the pandemic, it was observed that the time from onset of symptoms to assessment in ED was significantly longer compared with prepandemic times.²³ Fear of exposure to COVID-19 in hospitals and concern for overburdening hospital systems were contributing factors.^{33,34} Furthermore, other key challenges in caring for these patients has been shortage of ICU beds and medical equipment such as ventilators, mechanical circulatory support devices, and lack of sufficient health human resources to care for these patients. With the adoption of protocols endorsed by cardiovascular societies and with wider access to COVID-19 testing, some of these challenges have been overcome. Furthermore, triage of patients with low-risk STEMI to non-ICU settings has been proposed to mitigate the challenge of ICU bed shortages. Risk scores such as CADILLAC and Zwolle have been validated in the non-COVID-19 setting to be useful in triage of patients with low-risk STEMI and theoretically were even more needed during the pandemic.³⁵

SUMMARY

The COVID-19 pandemic presented a profound international crisis that has altered the landscape of medicine. From disease pathophysiology to the disruption of health care resources, COVID-19 presents unique challenges in terms of the direct and indirect effects on patient care. The pandemic highlights critical stress points within the health care system forcing organizations to reassess resource allocation and management. Patients with STEMI are uniquely affected as this patient population shares special disease characteristics and requires the coordination of multidisciplinary teams involved in STEMI systems of care. We have highlighted these challenges and lessons learned in STEMI management in the face of this pandemic. Overall patients with STEMI with COVID-19 have been shown in several studies to have worse in-hospital outcomes as compared with their COVID-19 negative counterparts. Previously reported racial and ethnic disparities in cardiovascular outcomes are magnified in the face of the pandemic. Further research needs to be conducted to understand the effect of COVID-19 on long-term outcomes of patients with STEMI who survive hospital discharge.

CLINICS CARE POINTS

- Healthcare professionals should be aware that patients presenting with COVID-19 and STEMI have a different presentation profile and disease course in-hospital. Patients with STEMI and COVID-19 tend to have greater mortality rates, lengthier stays at the ICU, and ethnic minorities appear to be disproportionately affected as compared to those without COVID-19.
- Patients with STEMI are uniquely affected as this patient population shares special disease characteristics. More mechanistic studies including ECG and angiogram characteristics are required to better understand different outcomes in this patient population.
- STEMI care has been greatly impacted by COVID-19, with delayed presentation, lack of adequate COVID-19 testing early on, potential hazard to staff members, and longer assessment times in emergency departments resulting in longer D2B times. However, primary PCI should remain the primary focus in this patient population.

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DISCLOSURE

The authors have nothing to disclose.

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