

Impact of COVID-19 on Acute Myocardial Infarction Care



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KEYWORDS

- COVID-19 • Myocardial infarction • STEMI • NSTEMI • Percutaneous coronary intervention
- Fibrinolytic therapy

KEY POINTS

- COVID-19 has negatively impacted the overall care of patients with acute myocardial infarction (MI).
- Globally, there have been significant reductions in hospital admissions, cardiac catheterization laboratory activations, and percutaneous coronary interventions for acute MI, attributed to both patient- and system-related factors.
- Symptom onset to revascularization time increased significantly during the pandemic for both STEMI and NSTEMI, resulting in worse in-hospital outcomes, including all-cause death, cardiogenic shock, and heart failure.
- Although several studies have reported short-term outcomes, future research should focus on examining the long-term effects of the pandemic on this particularly vulnerable patient population.

INTRODUCTION

The coronavirus disease 2019 (COVID-19) outbreak, caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first reported in December 2019 in Wuhan, Hubei Province, China, and has quickly spread to the rest of the world causing a global health crisis. On March 11, 2020, the World Health Organization declared COVID-19 a pandemic. As of November 2021, a total of over 250 million cases have been reported worldwide with over 5 million deaths with a case fatality rate of about 2% (CDC, US Department of Health and Human Services). As of November 2021, the United States has recorded over 46 million confirmed cases of COVID-19 and

over 750,000 deaths. Most patients infected with the SARS-CoV-2 virus are either asymptomatic or minimally symptomatic, which likely underestimates the true prevalence of COVID-19.

This outbreak has quickly overwhelmed health care systems around the world consuming and shifting resources to care for these patients, resulting in deferral or avoidance of care for many non-covid patients, placing those with other health conditions at risk because of limited access to high-quality medical care. Similarly, patients with cardiovascular diseases have been greatly affected as a result. At the beginning of the pandemic, many elective cardiac procedures were canceled to minimize exposure to cardiac

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catheterization laboratory personnel and nursing staff with priority given only to the management of ST-segment elevation myocardial infarction (STEMI) and critically ill non-ST-segment elevation myocardial infarction (NSTEMI) patients.

Despite a declining trend in overall incidence, acute myocardial infarction (MI) continues to remain a condition with high morbidity and mortality, with an incidence of 805,000 cases annually.¹ Timely coronary revascularization, achieved by primary percutaneous coronary intervention (PPCI), remains the mainstay of management for acute MI. Data from around the world during the pandemic suggested significantly lower rates of hospitalizations for acute MI, both STEMI and NSTEMI, either due to lower referral rates, patients' hesitancy to seek health care in fear of contracting COVID-19 at the hospitals, or even misdiagnosis.²⁻⁸ We discuss the impact of COVID-19 on the treatment of the important aspects of acute MI.

Impact of COVID-19 on ST-Segment Elevation Myocardial Infarction Care

The COVID-19 pandemic has had a dramatic negative impact on the overall care of STEMI patients (Fig. 1).²⁻⁸ The areas most impacted by COVID-19 include:

- Reduction in STEMI activations
- Prolonged symptom-to-first medical contact time

- Prolonged door-to-balloon times
- A shift from PPCI to pharmacologic reperfusion (ie, fibrinolytic therapy)
- Reduction in patients undergoing invasive angiography and PPCI
- Worsening clinical outcomes

ST-segment elevation myocardial infarction activations and hospital admissions

Compared with the pre-pandemic years, STEMI activations were reduced significantly during the early months of the pandemic. This decrease in STEMI admissions was seen irrespective of age, gender, underlying comorbidities, and geographic region. In the first 3 months of the pandemic between January 2020 and March 2020, a 38% reduction in STEMI activations was noted in the United States compared with the same period the previous year.² An expanded and extended analysis of the United States that included 18 large health care systems showed a drop in STEMI activations of about 29%.⁹ Interestingly, this drop in STEMI activations affected all geographic regions irrespective of COVID-19 incidence or stay-at-home orders.⁹ A similar trend has been reported around the world (Fig. 2).^{5,8,10} This decrease in STEMI activations coincided with a significant increase in out-of-hospital cardiac arrests, which raised concerns about patients with cardiovascular emergencies foregoing medical care during the pandemic.¹¹ An increase in mechanical complications of STEMI was also noted.¹²

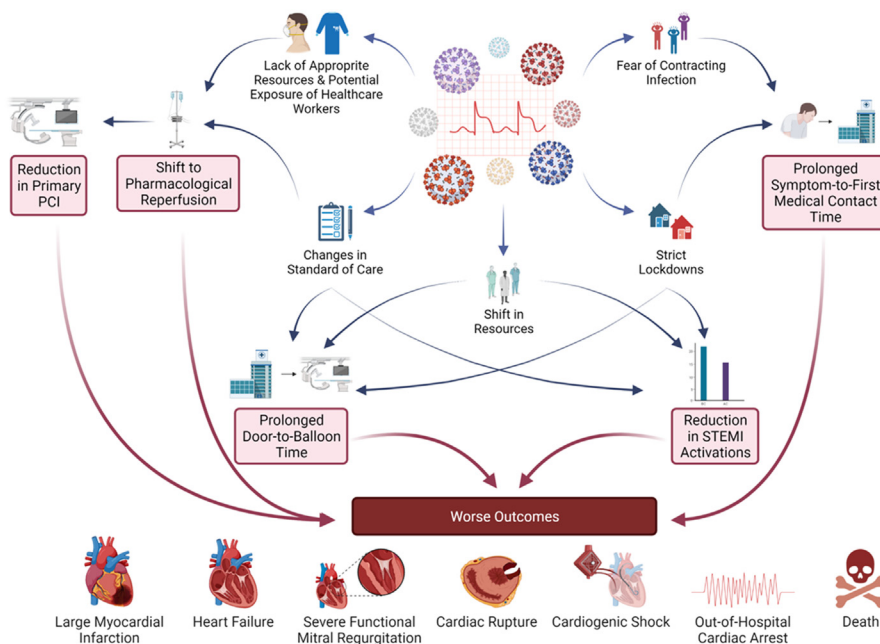


Fig. 1. Impact of COVID-19 on STEMI care (created with BioRender).

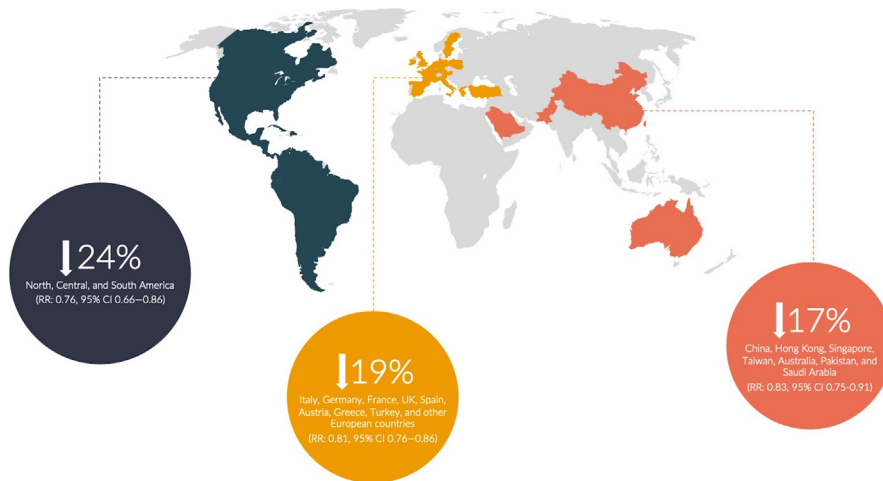


Fig. 2. Reductions in STEMI hospitalizations during the COVID-19 pandemic.⁴⁶

Using data from a National Patient Care database from January 2019 to May 2020, a 23% reduction in weekly STEMI admission rates was reported in the United Kingdom between mid-February and the end of March 2020 compared with the weekly average admissions in 2019.⁶ This decline was partially reversed in April and May 2020 to a weekly reduction of 16% by the end of the study period. Similarly, data from Italy showed in March 2020 there was a 26.5% reduction in STEMI admissions compared with the same period the year before.⁵ Interestingly, the reduction in admissions was higher among women compared with men (41.2% vs 17.8%), which could represent gender disparity in the management of STEMI during the pandemic.

In addition to the reluctance to seek medical attention by patients out of fear of contracting COVID-19, other potential explanations for the lower rate of STEMI activations during the pandemic include a shift to pharmacologic reperfusion to minimize operator exposure, misdiagnosis of STEMI, and changes in standard of care, including personal protective equipment, emergency medical services (EMSs), rapid testing and hospital beds, and a shift in resources to care for COVID-19 patients. It is unlikely that the reduction in STEMI represents reduced MI incidence related to less physical and work-related stress. The increased numbers of cardiac arrests and late complications of STEMI would suggest otherwise.

Symptom-to-first medical contact and door-to-balloon times

Although evidence suggests that reduced door-to-balloon times have significantly improved outcomes in STEMI,^{13,14} patient-related delay (symptom to

first medical contact) remains a significant challenge. The total ischemic time, defined as symptom onset to revascularization, is a major determinant of outcomes in STEMI.^{15–17} During the current pandemic, this important metric was significantly longer compared with that in the pre-COVID era as demonstrated by Abdelaziz and colleagues.¹⁰ In this study, once the patient presented to the hospital, the door-to-balloon time was similar between the 2 groups, but troponin levels were significantly higher in the COVID era patients (2739 [932–10,480] ng/L vs 1245 [327–2789] ng/L), demonstrating the probable consequences of delayed presentation.

In Italy, De Rosa and colleagues⁵ reported a 39.2% increase in symptom-to-coronary angiography time and a 31.5% increase in time from first medical contact to coronary revascularization, which signifies a substantial increase in both patient- and system-related delays. Analysis from the European International Study on Acute Coronary Syndromes-STEMI (ISACS-STEMI) COVID-19 registry demonstrated that the total ischemic time was significantly longer during the pandemic (181 [120–301] min in 2019 vs 200 [127–357] min in 2020; $P = .004$) as was the door-to-balloon time (34 [21–36] min in 2019 vs 36 [24–60] min in 2020; $P = .007$).¹⁸ Delayed presentations beyond 12 hours of ischemic time were also more common during the pandemic (9.1% in 2019 vs 11.7% in 2020; $P < .001$).

The prospective Magnetic Resonance Imaging in Acute ST-Elevation Myocardial Infarction (MARINA-STEMI) evaluated STEMI patients with cardiac magnetic resonance imaging (cMRI) during times of public health restrictions versus no restrictions and provided a mechanistic link between

patient delays and poor outcomes. MARINA-STEMI revealed that patients treated during lockdowns had larger infarct sizes (22 [IQR 12–29]% vs 14 [IQR 6–23]%, $P < .01$), more microvascular obstruction (77% vs 52%, $P < .01$) and a higher rate of intramyocardial hemorrhage (56% vs 34%, $P = .02$).¹⁹

Both patient- and system-related factors appear to have contributed to delay in symptom-to-first medical contact and door-to-balloon times during the pandemic, which limits the substantial benefit provided by primary PCI in STEMI. Fear of contracting COVID-19 infection at the hospital or the physician's office often seems to have led patients to delay seeking appropriate care for chest pain. Early in the pandemic, health care systems were stressed, which impacted the timely management of STEMI patients. Multiple countries implemented strict lockdowns to prevent the spread of COVID-19 with both hospital and EMSs redirected to critically ill COVID-19 patients. Longer EMS response times and shortages of experienced EMS personnel contributed to delays in cardiac catheterization laboratory activations from the field. These differences were more pronounced in countries that entered the pandemic with limited health care resources in infrastructure and personnel. In a systematic review, Chew and colleagues²⁰ demonstrated that low-income countries reported a larger increase in door-to-balloon times compared with high-income countries (19.64 minutes vs 4.52 minutes).

A shift to pharmacologic reperfusion

Over the past 2 decades, there has been a decline in the use of fibrinolytic therapy for STEMI as extensive data demonstrated superior outcomes with PPCI compared with lytic therapy.²¹ In the contemporary era, fibrinolytic therapy for STEMI is primarily used only for patients who initially present to a non-PCI-capable hospital with a transfer time to a PCI-capable center of greater than 2 hours. At the beginning of the pandemic, a shift to fibrinolytic therapy was more strongly considered for the management of STEMI even in PPCI-capable hospitals as health care organizations were severely overwhelmed with lack of appropriate resources, anticipated delays in primary PCI, and potential exposure of health care workers.^{8,22–24}

In a small case series by Wang and colleagues,²⁴ 17 STEMI patients who received fibrinolytics were compared with 20 who underwent primary PCI. This study showed comparable in-hospital and 30-day MACE, and mortality rates with no increase in major bleeding risk. By following a modified STEMI care protocol,

where-in fibrinolysis was the preferred treatment of choice for patients with unconfirmed COVID-19 status, intended as an infectious control measure in China at the beginning of the pandemic, Xiang and colleagues⁸ reported a dramatic increase in the probability of fibrinolysis as the treatment of choice for STEMI (odds ratio 1.66 [1.50–1.84]), which paralleled a similar decrease in primary PCI rates.

However, this approach has been associated with higher mortality, reinfarction, stroke, and major bleeding.^{25,26} Moreover, the benefit of fibrinolytic therapy was negated if there was a considerable delay in presentation, which could result in the formation of a more organized clot that may be resistant to lysis. Although large-scale randomized studies comparing the 2 strategies in the pandemic era are lacking, the rationale for changing the standard of care from PPCI to fibrinolytic therapy has not been clearly established. In addition, the Chinese experience has demonstrated more adverse events with this approach, including death and heart failure, and therefore this shift from mechanical to pharmacologic reperfusion cannot be recommended. Consistent with existing guidelines, a pharmacoinvasive approach can be considered for patients presenting initially to non-PCI-capable hospital when timely transfer to a PCI-capable hospital is not available.¹⁴

Primary PCI for ST-segment elevation myocardial infarction

Primary percutaneous coronary intervention (PCI), when available and performed by an experienced team in a timely manner, is the preferred reperfusion strategy for treating STEMI to improve survival and reduce rates of recurrent MI and hemorrhagic stroke relative to lytic therapy.^{13,21,25} During the pandemic there have been significant reductions in primary PCI rates for STEMI, which paralleled reductions in hospital admissions for STEMI. In The United Kingdom, an 18% reduction in weekly primary PCI rates for STEMI was observed during the first few months of the pandemic compared with the previous year.¹⁸ Similarly, data from the European ISACS-STEMI COVID-19 registry showed a 19% reduction in primary PCI rates between March and April 2020 compared with the same period the previous year.¹⁸ This reduction in procedures was independent of the number of COVID-19 patients.

Despite a significant reduction in overall STEMI admissions in Italy, De Rosa and colleagues⁵ noted similar rates of coronary angiography in 2020 compared to 2019 (94.9% vs 94.5%) among

those who presented to the hospital with a diagnosis of STEMI, which suggest that the principal barrier to PPCI during the pandemic may be a desire to avoid the health care system during the pandemic, in particular during lockdowns.

Clinical outcomes of ST-segment elevation myocardial infarction patients during the pandemic

Delayed reperfusion in STEMI is associated with larger myocardial scar size, increased risk of heart failure and shock, ventricular arrhythmias, and mortality.²⁷ There has been an increased risk of mortality and worse outcomes in STEMI patients during the pandemic. STEMI case fatality rate in Italy was 13.7% during the pandemic compared with 4.1% the previous year, a 3-fold increase in mortality.⁵ In addition, there was a higher prevalence of major complications (cardiogenic shock, life-threatening arrhythmias, cardiac rupture/ventricular septal defect, and severe functional mitral regurgitation) in these patients during the study period, an increase from 10.4% to 18.8%. In addition, Chew and colleagues²⁰ demonstrated that there was a higher proportion of patients with post-PCI fibrinolysis in MI thrombolysis in myocardial infarction (TIMI) flow grade less than 3 during the pandemic compared with the prepandemic era indicating suboptimal reperfusion.

In the European ISACS-STEMI COVID-19 registry, the overall in-hospital mortality rate in STEMI patients was significantly higher at 6.8% during the pandemic compared with 4.9% the prior year.¹⁸ This association between the COVID-19 pandemic and higher in-hospital mortality rates persisted even after adjusting for longer total ischemic and door-to-balloon times. There were more late STEMI presentations during the pandemic. Although the true incidence of post-STEMI mechanical complications during the pandemic is currently unknown,¹² Araiza-Garaygordobil and colleagues²⁸ demonstrated an incidence of 1.98% compared with 0.98% in the prepandemic era in one multinational study, despite similar GRACE risk scores. The increase in short-term complications may lead to prolonged admission to critical care units, which could, in turn, exacerbate a serious shortage in already sparse resources.

Potential causes for worse outcomes in STEMI include prolonged symptom-to-coronary angiography time due to need to test patients for COVID before transport to the CV laboratory, late presentations, reduced rates of primary PCI, and a switch from mechanical to pharmacologic reperfusion. Patients presenting initially to non-PCI hospitals may experience transfer delays or even refusal to

transfer due to COVID-19–related health care demands and resource limitations. At the beginning of the pandemic, cardiac catheterization laboratories in some hospitals were suspended to limit exposure until specific hospital-wide protocols were initiated to maintain the safety of personnel and minimize exposure.¹⁴ Also, STEMI protocols were altered during the pandemic to allow for screening and triaging of COVID-19 patients in the emergency department, which could have led to further delays in reperfusion and worse outcomes.¹⁴

COVID-19 and Non-ST-Segment Elevation Myocardial Infarction

Similar to STEMI, a significant reduction in hospital admissions for NSTEMI has been reported during the pandemic.^{3–5} In fact, reductions in hospital admissions and PCI rates for NSTEMI were more pronounced than that seen for STEMI.⁶ Compared with a 23% reduction in weekly STEMI admissions, Mafham and colleagues⁶ reported a 42% reduction in NSTEMI admissions. Data from Italy showed a 65.4% reduction in hospital admissions for NSTEMI.⁵ This was significantly higher compared with a 26.5% reduction in STEMI admissions during the same study period. Solomon and colleagues⁴ demonstrated a similar weekly reduction of NSTEMI-related hospital admissions at the beginning of the pandemic in the United States. One possible explanation for this observation is that STEMI patients who present with more severe symptoms tend to seek help more often than patients with NSTEMI.

In a small single-center study, Aldujeli and colleagues²⁹ reported a significantly longer chest pain-to-door (1885 [880–5732] min vs 606 [388–944] min) and door-to-reperfusion (332 [182–581] min vs 194 [92–329] min) times in NSTEMI patients during the pandemic compared with the prepandemic year. However, clinical outcomes were similar between the groups. Although symptom-to-revascularization time is less frequently studied in patients with NSTEMI/UA, studies have demonstrated worse outcomes in high-risk patients when revascularization is delayed.³⁰

A change in revascularization modalities has also occurred during the pandemic. Mafham and colleagues⁶ observed that NSTEMI patients were more likely to undergo PCI rather than coronary artery bypass graft surgery (CABG) surgery (up to 80% reduction in CABG surgery), which was in line with the recommendations from the British Cardiovascular Intervention Society to minimize utilization of intensive care unit beds. Moreover, there was also a paucity of mechanical ventilators

because of the diversion of resources to critically ill COVID-19 patients. Interestingly, these patients received PCI more often on the day of admission resulting in a shorter length of hospital stays, to minimize exposure and make beds available for sicker COVID-19 patients. Despite this shift away from CABG surgery, there was a 37% reduction in weekly PCI rates for NSTEMI during the pandemic compared with the year prior.

In addition to reduced hospitalizations and prolonged symptom-to-revascularization times, the rate of major complications (cardiogenic shock, life-threatening arrhythmias, cardiac rupture/ventricular septal defect, and severe functional mitral regurgitation) was reported to have increased from 5.1% to 10.7% in NSTEMI in one study.⁵

Acute Myocardial Infarction Care in COVID-19 Patients

Myocardial injury, defined as an elevation in troponin levels above the 99th percentile, is common in hospitalized patients with COVID-19 infection with an incidence ranging between 8% and 36% (see Laura De Michieli and colleagues' article, "Use and Prognostic Implications of Cardiac Troponin in COVID-19," in this issue).^{31,32} The incidence of myocardial injury parallels the severity of COVID-19 infection with a 13-fold increase in risk among patients in intensive care units.³¹ Troponin elevation in COVID-19 is independently associated with increased risk of mortality, especially for those with underlying history of cardiovascular disease.^{33,34} Differential diagnoses for elevated troponin in COVID-19 include acute MI, microvascular thrombosis, acute heart failure, myocarditis, stress-induced cardiomyopathy, supply-demand mismatch, disseminated intravascular coagulation, cytokine storm, and lastly acute pulmonary embolism.³⁵

COVID-19 may increase the risk of acute MI with a reported incidence between 1.1% and 8.9%.^{36,37} The risk is higher in the first 2 weeks after infection with Modin and colleagues³⁸ showing an approximately 5-fold increased risk. A large population-based study of all COVID-19 patients in Sweden reported that the risk of acute MI in these patients is significantly higher in the first 1 week after exposure and subsequently decreases by weeks 2 and 3.³⁹ The pathophysiology of acute MI in COVID-19 includes (1) increased risk of plaque rupture and thrombosis (type 1 AMI) or (2) myocardial oxygen imbalance due to supply-demand mismatch (type 2 AMI). This is attributed to the intense systemic inflammatory response and a relative prothrombotic state caused by the SARS-CoV-2 virus.⁴⁰

The diagnosis of acute MI become more challenging for clinicians around the world during these unprecedented times. In COVID-19 patients, it is crucial to differentiate ACS and myocardial injury as treatment varies significantly. Although the same criteria can be used to diagnose STEMI in COVID-19 patients compared with the general population, the diagnosis of NSTEMI can be particularly challenging as troponin elevation is commonly seen in these patients. COVID-19 patients presenting with acute MI may have complex coronary anatomy with higher thrombus burden, lesion haziness, ulcerative lesions, and prevalence of multivessel CAD.⁴¹ The prothrombotic state associated with COVID-19 infection could possibly play a role in a higher thrombus burden in acute MI patients.

Early in the pandemic, De Rosa and colleagues⁵ reported that among all STEMI patients, 10.7% were COVID+ with a case fatality rate of 28.6% compared with 11% in COVID patients. Similarly, in-hospital mortality from STEMI in COVID-19 patients was 29% in the European ISACS-STEMI COVID-19 registry.¹⁸ The North American COVID-19 Myocardial Infarction (NACMI) registry, a prospective, multicenter, observational registry of hospitalized STEMI patients with confirmed COVID-19 infection comprehensively evaluated patient characteristics in this high-risk population.⁴² This important registry has shown that 1 in 5 COVID-19 patients with STEMI did not undergo invasive coronary angiogram and among those who did about 1 in 4 had normal coronary arteries. In addition, the study demonstrated that despite having a high-risk presentation with more cardiogenic shock, COVID-19 patients were less likely to undergo PCI (71% vs 100%), had significantly longer door-to-balloon times (79 min vs 66 min), and significantly higher in-hospital mortality (33% vs 4%) compared with age- and sex-matched historical controls. Despite this, primary PCI remained the preferred revascularization strategy in these patients with a 48% mortality among those who did not undergo coronary angiogram compared with 28% among those who did. This highlights the feasibility of primary PCI in COVID-19 patients, which remains the recommended modality of revascularization in STEMI.¹³

The European Association for Cardiovascular Imaging (EACVI) and the American Association of Cardiology (ACC) have highlighted recommendations to help guide clinicians in making appropriate decisions with regard to caring for patients suspected or diagnosed to have COVID-related acute myocardial injury.^{14,43} Acute MI care in COVID-19 patients is discussed in detail in Thomas A. Kite and colleagues' article, "The Direct and Indirect

Effects of COVID-19 on Acute Coronary Syndromes,” in this issue.

Initiatives to Improve Acute Myocardial Infarction Care and Future Directions

It is clear that the COVID-19 pandemic continues to have a negative impact on acute MI care. Conceptually, the COVID-19 pandemic has had direct (increased arterial and venous thrombogenicity, troponin elevation, microthrombi, respiratory failure, in-hospital presentation) and indirect effects (lockdowns, cancellation of services, restrictive visitation policies, delayed presentations) on acute MI care, which collectively have resulted in increased morbidity and mortality.^{44,45}

A thorough understanding of the barriers to seeking and providing cardiovascular care in acute MI during this pandemic is crucial to improving outcomes. Primary PCI continues to be the preferred treatment of choice in STEMI patients and studies have demonstrated worse outcomes in those who did not receive primary PCI during the pandemic.²² COVID-19 may remain in the community for the foreseeable future, especially in light of mutations creating newer variants of the SARS-CoV-2 virus with a higher infectivity rate and complications. As vaccines have become available, clinical presentations of vaccinated COVID-19 patients may differ from the unvaccinated. Campaigns such as SCAI’s Seconds Still Count have reversed early declines in STEMI presentations and should be expanded.⁹ The use of social and other media to bring awareness about the importance of timely reperfusion should be emphasized. It is clear that restrictive lockdowns are detrimental to health care delivery and more circumspect approaches are needed.⁴⁴ For effective results, such campaigns should be able to cross cultural, socioeconomic, and psychosocial barriers. Strategies for emergency network reorganization, including rapid screening of acute MI patients and appropriate allocation of resources for critically ill non-COVID patients, are also needed. System-wide standardized protocols need to be implemented by health care organizations to ensure rapid, and safe access to health care in a timely manner for improved outcomes in acute MI while ensuring the safety of the health care personnel.

Interruptions in critical health care services have been reported during prior epidemics/pandemics. The American Heart Association issued temporary emergency guidance on STEMI care that included improving awareness among the general public about the symptoms and signs of “heart attack,” screening patients for COVID symptoms,

identifying STEMI mimics before catheterization laboratory activation, and minimizing delays to primary PCI for clear STEMI while testing for COVID-19.⁴⁶ PCI was recommended as the preferred primary reperfusion strategy in these patients irrespective of their COVID status. The Society for Cardiovascular Angiography and Interventions (SCAI), the American College of Cardiology (ACC), and the American College of Emergency Physicians (ACEP) advocate that those patients needing emergency cardiac catheterization should be treated as possible COVID-19 and treated accordingly pending testing.¹⁴ Cardiovascular societies and health care organizations need to continue to work together to formulate pragmatic guidelines and protocols with the goal of delivering the best possible care for acute MI patients while maintaining the safety of hospital personnel in these troubled times.

SUMMARY

The COVID-19 pandemic has resulted in restricted access to clinical services and worse clinical outcomes for patients with acute MI. The mechanisms are multifactorial and include avoidance of medical care during lockdowns, late presentations, reorganization of treatment pathways—including deviations from standard of care protocols during COVID surges—, and a shift from mechanical to pharmacologic reperfusion. Many of these trends have the potential to undo 3 decades of progress in STEMI care and therefore must be reversed in a timely manner. Educational campaigns such as SCAI’s Seconds Still Count have reversed early declines in STEMI presentations and should be replicated and expanded.

CLINICS CARE POINTS

- Timely primary percutaneous coronary intervention remains the dominant revascularization modality for STEMI patients during the pandemic.

DISCLOSURE

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