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Review Article

Acute Myocardial Injury in COVID-19: Epidemiology, Aetiology and Management

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Abstract

The 2019 coronavirus pandemic (COVID-19), caused by SARS-CoV-2, has affected 5,701,337 individuals globally and accounted for 357,688 deaths as of May 2020. While much of the focus has been on systemic inflammation and pulmonary complications, including interstitial pneumonia and acute respiratory distress syndrome (ARDS), cardiovascular complications related to COVID-19 can also result in severe morbidity and mortality. Mortality for acute myocardial infarction in ARDS caused by SARS-CoV-2 accounts for 2.6%, with risk factors including older age, hypertension, diabetes mellitus and previous cardiovascular events. In approximately 5-25% of hospitalized COVID-19 cases, elevations in cardiac Troponin have been reported. This biomarker appears to correlate with disease severity and poorer prognosis. The pathophysiology behind acute myocardial injury is complex and includes variable degrees of type I and type II myocardial infarction, with a wide range of coronary artery appearances on angiography. This pandemic has disrupted several protocols of care for emergency cardiac conditions. This has led to clinicians relying on fibrinolysis to a much greater extent in the management of acute coronary syndrome, as opposed to primary Percutaneous Coronary Intervention (PCI).

Keywords: Acute myocardial injury; Acute myocardial infarction; Acute coronary syndrome; COVID-19; SARS-CoV-2; Troponin

Introduction

The 2019 coronavirus pandemic (COVID-19), caused by Severe Acute Respiratory Distress Syndrome Coronavirus 2 (SARS-CoV-2), has affected 5,701,337 individuals globally and accounted for 357,688 deaths as of May 2020. [1]. On 11 March 2020, The World Health Organization declared the pandemic status.

While much of the focus has been on systemic inflammation and pulmonary complications, including interstitial pneumonia and acute respiratory distress syndrome (ARDS) requiring invasive ventilation, cardiovascular complications related to COVID-19 can also result in severe morbidity and mortality [2].

Mortality for acute myocardial infarction in ARDS caused by SARS-CoV-2 accounts for 2.6% of all COVID-19 cases, with overall mortality rates at 6.6% [3]. Risk factors include older age, hypertension, diabetes mellitus and previous cardiovascular events [4].

Methods

A total of 34 articles were selected for inclusion. Authors searched PubMed database for articles using the following keywords: “acute myocardial injury”, “troponin”, “acute myocardial infarction”, “acute coronary syndrome”, “COVID-19” “SARS-CoV-2”. Authors included retrospective studies, prospective studies, systematic reviews and meta-analyses, narrative reviews, clinical guidelines and case reports on COVID-19 and acute myocardial injury. Pre-printed articles were also included. No language restrictions were applied.

Discussion

Epidemiology and Aetiology

The acute myocardial injury is defined as a rise and fall in cardiac troponin (cTn) with at least one value above the 99th percentile upper reference limit (URL), attributable to cardiovascular and non-cardiovascular causes [5].

The existing literature reports that 5-25% of patients hospitalized with COVID-19 had elevations in cTn, with a higher prevalence in those admitted to intensive care units (ICU), and those who died [6,7]. This biomarker appears to correlate with disease severity and higher levels were associated with a poorer prognosis [3]. Brain natriuretic peptide (BNP)/N-terminal proBNP (NT-proBNP) levels were also reported to be elevated in COVID-19 patients, particularly in those with a concomitant cTn elevation, and result from pre-existing cardiac disease and the acute haemodynamic stress caused by COVID-19 infection [3,8].

Cardiogenic shock (CS) of undetermined aetiology was also demonstrated in up to 12% of COVID-19 patients [9], perhaps as a combination of myocardial virus localization [10] and acute myocardial injury/type II myocardial infarction (MI) [11]. Clinical outcome in CS appears to be worse in COVID-19 patients (30–40% vs. 45–50% survival) [12].

The pathophysiological mechanisms underlying myocardial injury caused by SARS-CoV-2 are not fully characterized so far and more studies need to be completed to further delineate them. However, the majority of published literature reports the following hypotheses [2,12]: The “cytokine cascade” would destabilize the pre-existing atherosclerotic plaques

leading to microinfarction, type I MI. Severe hypoxaemia and myocardial oxygen demand supply mismatch, systemic inflammatory response, coronary vasospasm and microthrombi caused by the prothrombotic state result in myocyte injury and thus type II MI. Cases of myocarditis [10] and Takotsubo syndrome [13,14] have also been reported.

Troponin elevation appears to have a role in management strategy [12]. Mild elevations (e.g. <2-3 times the ULN) do not require work-up for type I MI (unless presenting with a strongly suggestive clinical picture and ECG changes), as these cases are generally explained by the pre-existing cardiac disease and the acute stress related to COVID-19. Marked elevations (e.g. >5 times the ULN) may indicate type I or type II MI, myocarditis and Takotsubo syndrome, triggered by COVID-19. ECG and echocardiographic parameters have to be integrated to target the most appropriate strategy [15,16], and the use of coronary angiography should be restricted to those in whom type I MI is suspected. Early reports indicate that in COVID-19 patients with ST-segment elevation myocardial infarction (STEMI), angiography revealed a variety of findings including classic obstructive coronary artery disease (CAD), non-obstructive CAD, angiographically normal epicardial coronary arteries, and/or left ventricular dysfunction due to myocarditis or stress-induced cardiomyopathy [17-19]. Hinterseer and colleagues reported a case of a coronary stent thrombosis in a 65 year old gentleman with acute myocardial infarction due to proximal occlusion of the previously stented left anterior descending artery [20].

Shi's analysis showed that among the 416 hospitalized patients with confirmed COVID-19, 19.7% had myocardial injury, manifested by elevated cTn. These patients, compared with those without myocardial injury, required non-invasive (46.3% vs 3.9%, p<0.001) or invasive mechanical ventilation (22% vs 4.2%, p<0.001) at a greater rate, and reported more complications, such as ARDS (58.5% vs 14.7%, p<0.001), AKI (8.5% vs 0.3%, p<0.001), electrolyte disturbance (15.9% vs 5.1%, p=0.003), and coagulation disorders (7.3% vs 1.8%, p=0.02). Finally, patients with myocardial injury had a significant higher in-hospital mortality rate (51.2% vs 4.5%) [3].

Guo et al also reported a cohort of 187 hospitalized with confirmed COVID-19 and a total of 27.8% had myocardial injury. Similarly, mortality was significantly higher in those with elevated cTn levels than those with normal cTn levels (59.6% vs. 8.9%, respectively; p < 0.001) [21].

Yang and co-workers analysed the clinical outcomes of 52 critically ill patients with COVID-19 admitted to the ICU (mean age 59.7 years) with a mortality rate of 61.5% by 28 days. Cardiac injury was reported in 23% of the population (15% of survivors and 28% of non-survivors) [22].

In Zhou's study, a series of 191 patients with laboratory-confirmed COVID-19 was analysed. Overall, 54 died and 137 survived. Non-survivors showed greater cTn elevation and higher rates of heart failure (52% vs 12%) and acute cardiac injury (59% vs 1%) than survivors [23].

Ruan's retrospective analysis of 150 patients with laboratory-confirmed COVID-19 evaluated the factors associated with mortality. Of the 68 deceased patients, 5 (7%) died of myocardial damage and circulatory failure, and 22 (33%) of cardiac and respiratory

causes. Higher levels of troponin, myoglobin, C-reactive protein, serum ferritin, and interleukin-6 were also noted in those who died [24].

Cosentino and colleagues reported significantly worse outcomes in STEMI patients admitted to ICCU (University Cardiology Centre in Milan, Italy) during the coronavirus pandemic, when compared with those of the same time interval in the previous year. In particular, the study analysed 119 patients, 76 of which belonging to the COVID-19 group. The two cohorts were similar in terms of age, rate of diabetes mellitus, and history of previous acute myocardial infarction. It revealed that the rate of cardiogenic shock and in-hospital cardiac mortality has tripled. However, it should be noted that the time taken from symptom onset to hospital presentation has doubled during the COVID-19 outbreak compared to 2019 [25].

De Rosa and collaborators conducted a multicentre nationwide survey (54 hospitals) to collect data on acute myocardial infarction (AMI) admissions at Italian CCUs over a one-week period during the COVID-19 outbreak, compared with the equivalent week in 2019. There was a 48.4% reduction in admissions for AMI compared with the equivalent week in 2019 (319 vs 618, P < 0.001), for both STEMI [STEMI; 26.5%, 95% confidence interval (CI) 21.7–32.3; P = 0.009] and non-STEMI (NSTEMI; 65.1%, 95% CI 60.3– 70.3; P < 0.001). A similar reduction in AMI admissions was registered in North Italy (52.1%), Central Italy (59.3%), and South Italy (52.1%). The STEMI case fatality rate during the pandemic was substantially increased compared with 2019 [risk ratio (RR) = 3.3, 95% CI 1.7–6.6; P < 0.001], and remained significantly higher than in 2019 even after excluding SARS-CoV2-positive patients (P=0.018). A parallel increase in complications was also registered (RR = 1.8, 95% CI 1.1–2.8; P = 0.009) [26].

Management

COVID-19 has disrupted several protocols of care for emergency cardiac conditions.

Although primary percutaneous coronary intervention (PCI) is the preferred reperfusion strategy when available, its success depends on rapidly achieving first-medical-contact-to-device times within 90-120 minutes [27]. This timeframe is clearly altered during the coronavirus pandemic for different contributing factors including delayed or refused transfers for bed capacity, lack of early cardiac catheterization laboratory activation, delays in preparation due to personal protective equipment, and COVID19- related misleading clinical presentations.

A study performed in Hong Kong showed long delays in seeking medical help in a small cohort of STEMI patients, with a median time of 318 min from onset of symptoms to first medical contact (before the epidemic, the median time was 82 minutes) [28].

Garcia's analysis on 9 high-volume hospitals in United States reported an estimated 38% reduction in cardiac catheterization laboratory STEMI activations, similar to the 40% reduction noticed in Spain [29,30].

In De Rosa's study, both patient and system related delays were substantially increased during the COVID-19 outbreak. The time from symptom onset to coronary angiography was increased by 39.2% in 2020 compared with the equivalent week in 2019, while the time from first medical contact to coronary revascularization rose by 31.5% [26].

Different treatment strategies for acute myocardial infarction have been proposed and applied. The Chest Pain Centre Committee, Medical Quality Control Centre of Cardiovascular Diseases in Liaoning province, China, received great attention from cardiologists [31]. This implies:

- All patients with chest pain should be first screened for COVID-19 and be classified into four categories: confirmed, suspected, ruled out, and cannot be ruled out at present (no epidemiological exposure history, no fever, 1–2 clinical manifestations of COVID-19, but insufficient for the suspected patients criteria).
- Lung CT scanning and COVID-19 nucleic acid testing should be performed as soon as possible.
- Third-grade protection for medical staff should be adopted during the whole medical process.
- STEMI (confirmed/suspected COVID-19): if symptom onset is within 12 h, thrombolysis may be the treatment of choice, if indicated. Percutaneous coronary intervention (PCI) is considered only for patients with contraindications or failed thrombolysis. For patients with symptom onset beyond 12 h, optimized medical treatment (OMT) in intensive care unit (ICU) quarantine wards is recommended.
- NSTEMI (confirmed/suspected COVID-19): if low or intermediate-risk, OMT in the quarantine wards and selective PCI to be performed after the termination of quarantine. If high or very high-risk (GRACE score >140), early (<24h) or immediate (<2h) PCI following OMT, respectively, in qualified cardiac catheter labs.

The Society for Cardiovascular Angiography and Interventions (SCAI), the American College of Cardiology (ACC), and the American College of Emergency Physicians (ACEP) stated that primary PCI should remain the default strategy in patients with clear evidence of a STEMI; if a primary PCI approach is not feasible, a pharmacoinvasive approach may be considered [32].

The European Society of Cardiology and the American College of Cardiology (ACC)/American Heart Association (AHA) STEMI Guidelines both recommend fibrinolytic therapy and pharmacoinvasive strategy if timely primary PCI cannot be achieved [27].

Aksit and colleagues focused on the inflammatory response elicited by SARS-CoV-2; 71.4% of non-survivors and 0.6% of survivors had disseminated intravascular coagulation (DIC) with the majority of non-survivors having raised D-dimer levels [33]. Therefore, the ADP inhibitor Ticagrelor should be considered in the treatment of patients with concomitant COVID-19 related pneumonia and acute myocardial infarction, as it contributes to patient survival [34].

Conclusion

The novel coronavirus SARS-CoV-2 is responsible for Coronavirus disease 2019 (COVID-19), an infectious disease first identified in Wuhan, China, in December 2019. Since then, it has spread rapidly worldwide, resulting in a publish health crisis.

Although SARS-CoV-2 pathogenesis was initially associated with the respiratory system, it has currently been acknowledged that it involves multiple organs, particularly the heart. Mortality for acute myocardial infarction in ARDS caused by SARS-CoV-2 accounts for 2.6%, with risk factors including older age, hypertension, diabetes mellitus and previous cardiovascular events.

Approximately 5-25% of patients hospitalized with COVID-19 reported elevations in cardiac Troponin, a biomarker which appears to correlate with disease severity and poorer prognosis.

The pathophysiology behind acute myocardial injury is complex and include variable degree of type I and type II myocardial infarction, with a wide range of coronary artery appearances on angiography.

This pandemic has disrupted several protocols of care for emergency cardiac conditions and fibrinolysis has gained a significant role over primary Percutaneous Coronary Intervention.

The COVID-19 pandemic has triggered an explosion of research, which is already providing key knowledge of the disease. Nevertheless, much remains unanswered and requires further analysis, particularly regarding the involvement of the cardiovascular system.

Limitations

There are some limitations inherent to the current literature evaluating the acute myocardial injury in COVID-19, which merit consideration. These include the significant heterogeneity in study design, patient selection and outcomes. Due to the current pandemic, a consistent amount of literature is published in a preprint form, prior to full peer review.

Disclosures

The authors report no conflict of interest.

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