Clinical research

Acute myocardial infarction in COVID-19 patients. A review of cases in the literature

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Abstract

Introduction: COVID-19 is an ongoing pandemic that has lasted more than a year. Patients with multiple comorbidities such as diabetes, hypertension, and smoking have been shown to be at increased risk of a more severe course and lethal outcome. Since the disease can also lead to a hypercoagulable state, several cases of acute myocardial infarction (AMI) have also been recorded.

Material and methods: We searched PubMed/Medline for case reports of AMI occurring in COVID-19 positive patients using "acute myocardial infarction", "COVID-19", and "SARS-CoV-2" as keywords.

Results: Thirty-three articles covering 37 patients were identified, among which 30 (81.1%) were male, and 7 (18.9%) were females. The mean age of these 37 patients was 52.8 ±15.6 years. Most cases were from the United States (17 cases, 45.9%). Several comorbidities such as hypertension (16 cases, 43.2%), diabetes (14 cases, 37.8%), smoking (8 cases, 21.6%), obesity (3 cases, 8.1%), morbid obesity (1 case, 2.7%), and elevated lipid levels (4 cases, 10.8%) were also identified. The most common symptom of AMI was chest tightness (22 cases, 59.5%), while the most common symptoms for COVID-19 were dyspnoea (25 cases, 67.6%) and fever (22 cases, 59.5%). The mortality rate was 35.1%.

Conclusions: Given the high mortality rate, physicians are encouraged to properly check for signs of cardiac dysfunction and possible AMI while treating COVID-19 positive patients with several comorbidities or previous history of AMI.

Key words: ECG changes, case reports, COVID-19, pandemic, acute myocardial infarction, risk factor.

Introduction

The first cases of coronavirus disease 2019 (COVID-19) occurred in December 2019. The virus continued to spread worldwide and became a pandemic on March 11th, 2020 [1]. The infection is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is a single-stranded RNA virus with an envelope that comes from the Coronaviridae family. This family also includes severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome-related

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coronavirus (MERS-CoV), which previously led to severe acute respiratory syndromes (SARS) and Middle East respiratory syndrome (MERS) respectively [1, 2].

The world slowly learned more about the virus, and found several risk factors such as diabetes, hypertension, advanced age, smoking, chronic obstructive pulmonary disease (COPD), asthma, and past history of cerebrovascular diseases that are believed to provoke worse outcomes of the infection [2–5]. Since COVID-19 is also associated with hypercoagulation and thrombosis, multiple early reports and questions were raised about the likely increased risk of acute myocardial infarction (AMI) developing in patients with risk factors [6]. The pandemic has also severely affected several health care systems and cardiovascular departments in several areas, which may cause a delay and hesitancy for patients with symptoms of AMI to seek appropriate care [7].

We, therefore, aim to perform a review of all cases of AMI published in the literature to identify the major risk factors and suggest possible changes in clinical care that can help improve the outcomes of patients.

Material and methods

We searched PubMed/Medline from inception to May 30th, 2021 for cases of AMI using the keywords "acute myocardial infarction", "COVID-19", and "SARS-CoV-2". Since several reports were rushed for publication during the early phase of the pandemic as letters, we limited our search criteria to case reports and letters published in English, French, Spanish, and Chinese. Our team was divided into two groups (PL/AL/NK and RV/KR) that independently searched and drafted their lists. The two groups then discussed their results, and all differences in choices were solved through thorough discussions.

Statistical analysis

Analyse-it software (Analyse-it Software Ltd, Leeds, UK, https://analyse-it.com/) and Microsoft Excel (https://www.microsoft.com/en-us/microsoft-365/excel) were used to evaluate the data obtained. We calculated the means with standard deviations of ages and presented several categorical values as percentages as appropriate.

Results

We found 147 results that fitted our initial search criteria. The authors read all full manuscripts and eventually retained 33 that contained reports from 37 patients (Table I) [8–40]. Thirty (81.1%) patients were male while 7 (18.9%) were females. The mean age was 52.8 years, with a standard deviation of 15.6. The youngest patient was 27 years of age, and the oldest was 86. Eight (21.6%) cases were reported within the age range of 27–39 years, 16 (43.2%) in the range 40–59, and 13 (35.1%) were 60 or older. Most cases were reported from the United States (17 cases, 45.9%). Other countries included France, Italy, Japan, South Korea, Pakistan, Qatar, Spain, and the United Kingdom with 2 cases each and Iran, Portugal, Saudi Arabia, and Switzerland with one case each.

Several comorbidities were also listed among the cases. Sixteen (43.2%) patients had a history of hypertension, 14 (37.8%) had diabetes, 8 (21.6%) were smokers, 3 (8.1%) were obese, 1 (2.7%) was morbidly obese, and 4 (10.8%) had elevated lipid levels. Six (16.2%) patients were also reported to have a previous history of MI, and 2 patients had a history of stroke in the past. The time of presentation and diagnosis of AMI relative to the symptoms or diagnosis of COVID-19 varied a lot. Some patients were diagnosed with COVID-19 only after they were admitted for symptoms of AMI, while some cases of AMI occurred during their admission for COVID-19. There were also some severe cases of COVID-19 in which a diagnosis was made as a routine check while the patient was sedated or on ventilation. Twenty-two (59.5%) patients reported symptoms of chest pain or tightness. Twenty-five (67.6%) patients had findings of dyspnoea. However, shortness of breath can be seen in both COVID-19 patients and in AMI patients. Among the main COVID-19 symptoms, 22 (59.5%) patients had fever, 20 (54.1%) had cough, 1 (2.7%) reported gastrointestinal symptoms, and 16 (43.2%) were entirely asymptomatic. All 38 cases had positive ECG changes, with 3 cases presenting with non-ST elevation myocardial infarction (NSTEMI), 29 with ST elevation myocardial infarction (STEMI), and 1 case presented initially with NSTEMI which turned into STEMI.

Unfortunately, 13 (35.1%) patients died during their hospitalization. The mean age of those who died was 54.9 years, with a standard deviation of 14.6 years. Eleven (84.6%) were male, and 2 (15.4%) were female. Seven (53.8%) of them had a history of hypertension, and 6 (46.2%) had diabetes. One of them (7.7%) had a previous history of MI, and 1 (7.7%) also had a stroke in the past. Three (23.1%) patients who died had a history of smoking. The majority of cases (5 cases, 38.5%) were from the United States.

Discussions

Our findings highlight several important points that can help address the care and prevention of AMI among patients with COVID-19. The higher incidence of cases of AMI in males compared to females has also been reported among non-

Table I. Clinical characteristics and risk factors in COVID-19 patients with acute myocardial infarction

Author name	Age [years]	Sex	Confirmed diagnosis of COVID-19? If yes, how many days after diagnosis did the patient have an MI?	Chest pain	Dyspnoea	Hypertension	Diabetes	Smoking	ECG changes seen	NSTEMI or STEMI	Died
Ali et al. [8]	59	M	Yes and developed MI after 12 days of symptoms, 3rd day of admission	Y	Y	N	Y	Y	Y	STEMI	N
Ali et al. [9]	27	M	Yes and developed MI during hospitalization	N	Y	N	N	N	Y	STEMI	Y
Alshoabi et al. [10]	42	M	Yes and developed MI after 9 days of diagnosis of COVID-19	Y	N	N	N	N	Y	STEMI	N
Bussmann et al. [11]	55	M	Yes and developed MI after 13 days of COVID-19 symptoms	N	Y	N	N	N	Y	STEMI	N
Capaccione et al. [12]	36	M	Yes and presented with MI	Y	Y	N	N	N	Y	NSTEMI	N
Cardenes Leon et al. [13]	74	M	Yes and diagnosed for COVID-19 after developing MI	Y	Y	Y	Y	N	Y	N/A	Y
Castagna et al. [14]	51	M	Yes and diagnosed for COVID-19 after developing MI	Y	N	Y	N	N	Y	STEMI	N
Darvishi et al. [15]	42	M	Yes and developed MI after 12 hours of hospitalization	Y	Y	N	N	N	Y	STEMI	Y
Fischer et al. [16]	63	M	Yes and developed MI after 6 days	N	Y	Y	Y	Y	Y	STEMI	Y
Fried et al. [17]	64	W	Yes and MI after 2 days of hospitalization	Y	N	Y	N	N	Y	STEMI	N/A
Fried et al. [17]	38	M	Yes and presented with MI	Y	Y	N	Y	N/A	Y	N/A	N
Genovese et al. [18]	60	M	Yes and presented with respiratory failure and developed MI overnight after admission	Y	Y	N	N	Y	Y	STEMI	Y
Harari et al. [19]	40	W	Yes and MI after 2 days of hospitalization	Y	Y	Y	Y	N	Y	STEMI	Y
Inam et al. [20]	51	M	Yes and presented with deep vein thrombosis and developed MI on 2nd day of hospitalization	N/A	N/A	N	Y	N	Y	STEMI	N
Juthani et al. [21]	29	M	Yes and diagnosed with COVID-19 during hospitalization and developed MI after 1 day of diagnosis	Y	N	N	N	N	Y	STEMI	N
Khalid et al. [22]	48	M	Yes and diagnosed during hospitalization after developing MI 1 week later	Y	Y	N	N	N/A	Y	N/A	N

Table I. Cont.

Author name	Age [years]	Sex	Confirmed diagnosis of COVID-19? If yes, how many days after diagnosis did the patient have an MI?	Chest pain	Dyspnoea	Hypertension	Diabetes	Smoking	ECG changes seen	NSTEMI or STEMI	Died
Khalid et al. [22]	34	W	Yes and was diagnosed COVID-19 positive after developing MI	Y	N	N	N	N	Y	N/A	N
Kim et al. [23]	60	M	Yes and developed MI during hospitalization	N	Y	Y	Y	N/A	Y	STEMI	Y
Nakamura et al. [24]	71	M	Yes and MI during hospitalization after 11 days	N	Y	Y	N	Y	Y	STEMI	y
Nakao et al. [25]	84	M	Yes and developed MI after 3 days during hospitalization	N	Y	N	N	Y	Y	STEMI	N
Ong et al. [26]	29	M	Yes and diagnosed for COVID-19 during hospitalization and developed MI after 14 hours of diagnosis	Y	N	N	N	N	Y	STEMI	N
Othman et al. [27]	53	M	Yes and presented with MI	N	Y	Y	Y	N	Y	NSTEMI	N
Pelle et al. [28]	86	W	Yes, COVID-19 positive on 26th March and developed MI on 8th May, had paraesthesia of her left arm	N	Y	Y	N	N	Y	STEMI	N
Proenca et al. [29]	62	W	Yes and developed MI after 11 days	Y	N	Y	Y	Y	Y	STEMI	N
Rahman et al. [30]	55	M	Yes and diagnosed after developing MI	Y	N	Y	Y	N	Y	STEMI	N
Ruiz-Ares et al. [31]	43	M	RT-PCR negative but serology for COVID-19 positive	N/A	N/A	N/A	N/A	Y	Y	STEMI	N
Saririan et al. [32]	61	M	Yes, and diagnosed COVID-19 positive on autopsy and developed MI on day 15 of admission	N	Y	Y	Y	N	Y	STEMI	Y
Saririan et al. [32]	59	W	Yes and dagnosed after developing MI	N/A	N/A	Y	N	N	Y	STEMI	N
Saririan et al. [32]	69	W	Yes, diagnosed with COVID-19 at 4th day of hospitalization after MI	Y	Y	N	N	N	Y	INITIALLY IT WAS NSTEMI THEN PROGRESSIVELY STEMI	Y

Table I. Cont.

Author name	Age [years]	Sex	Confirmed diagnosis of COVID-19? If yes, how many days after diagnosis did the patient have an MI?	Chest pain	Dyspnoea	Hypertension	Diabetes	Smoking	ECG changes seen	NSTEMI or STEMI	Died
Shams et al. [33]	28	M	Yes and MI after 9 days of hospitalization	Y	Y	N	N	N	Y	STEMI	N
Sheikh et al. [34]	36	M	Yes and developed MI on 10th day of hospitalization	N	Y	N	N	N	Y	STEMI	Y
Sheikh et al. [35]	56	M	Yes and developed MI during hospitalization	N	Y	Y	Y	N/A	Y	STEMI	N
Tedeschi et al. [36]	60	M	yes and MI after 7 days of hospitalization	Y	Y	N	N	N	Y	STEMI	Y
Ueki et al. [37]	82	M	Yes and after 7 days developed MI	N	Y	N/A	N/A	N/A	Y	STEMI	N
Yu et al. [38]	55	M	Yes and presented to hospital with paradoxical embolism causing MI	Y	Y	Y	Y	N	Y	NSTEMI	N
Zaher et al. [39]	51	M	Yes and MI during hospitalization	Y	Y	Y	Y	N	Y	STEMI	Y
Zendjebil et al. [40]	42	M	Yes, COVID-19 positive and had MI	Y	N	N	N	Y	Y	STEMI	N

M – male, F – female, Y – yes, N – no, n/a – not available, MI – myocardial infarction.

COVID-19 patients [41]. The incidence of hypertension, diabetes, and smoking was higher in the group of patients who died than in those who survived. Several theories have hypothesized that patients with COVID-19 may have a higher risk of thrombosis and thrombotic events or complications, and smoking, hypertension and diabetes may further worsen their prognosis [2, 4, 5, 42–46]. The infection can cause a rise in several cytokines and D-dimer level which leads to an elevated prothrombin time. It can also cause endothelial damage, which predisposes the patient to a hypercoagulable state [47]. Schoenhagen et al. also suggested that these changes may cause plaques to weaken and rupture, and thus cause coronary thrombosis [48]. The mortality rate observed in our study is lower than in the results reported by Bangalore et al. (72%) at their centre. However, we believe a larger sample size may help to provide greater predictive power eventually. Moreover, since antiplatelets and anticoagulation therapy might be helpful in preventing acute myocardial infarction, the role should be considered and further explored in at-risk patients such as those with multiple comorbid conditions but not already on therapy and admitted with severe COVID-19 [49]. In their analysis, Godino et al. suggested that the indications for such therapies should be evaluated based on the patient's clinical findings and also the severity of their disease [50]. The incidence of additional conditions related to COVID-19 such as findings of acute myocarditis, pulmonary embolism, and acute respiratory distress syndrome can also be studied and compared to understand the impact and protective role of such therapies in such scenarios [51–54].

Several changes in protocol and care can be encouraged to lower the occurrence and mortality among COVID-19 patients with an AMI episode. Patients who are at risk and have several comorbidities should have an ECG on admission, and it should be repeated as appropriate depending on their clinical findings. Our study also showed that while chest pain was very common, it can easily be missed in sedated patients. Thus, physicians should also include an ECG test and cardiac enzyme test in those groups of patients. Finally, since both COVID-19 and AMI patients may typically have shortness of breath or dyspnoea, further cardiac testing should be considered based on the presentation as well as the comorbidities of the patients. Cardiac imaging such as echo and spiral CT can also be helpful to rule out other possible cardiovascular complications in such at-risk patients. While these changes may be, at first, deemed challenging for several health care systems in developing countries, the proper pre-

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vention and early management and care may ultimately help to improve the survival rates and also the length of stays and burden.

There are some limitations to our study, and proper consideration should be taken when using the results obtained. The sample size was small as we used case reports from the literature, and researchers and physicians are encouraged to report the data from their centres in the future to further study and confirm our findings. Most studies did not provide adequate information on several laboratory values and the level of severity of COVID-19. It was thus not possible for us to subdivide and analyse the results based on the severity of COVID-19. The case reports also did not allow us to properly evaluate the levels of several markers such as D-dimers, and several past medical history or current medical findings may have been omitted by some of the authors. Finally, the case reports did not include any vaccination history of the patients (for COVID-19).

In conclusion, our study showed a high mortality rate among patients who suffer from acute myocardial infection during a positive infection of COVID-19. Males were more at risk than females, and several comorbidities such as hypertension, diabetes, and smoking may participate in the pathophysiology of these patients. We encourage further research to confirm our findings using larger samples from different centres.

Conflict of interest

The authors declare no conflict of interest.

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