MSD Publications
Research is creating new knowledge

Research International Journal of Cardiology and Cardiovascular Medicine

Review Article

Does SARS-CoV-2 Cause Acute Myocardial Injury: A Literature Review

Javaria Tehzeeb[1], Mittal Savaliya[2], Hira Pervez[3]*, FNU Roshan[4] and Syed Muhammad Usama[4]

[1]Department of Internal Medicine, King Edward Medical University, Lahore, Karachi.

[2]Department of Internal Medicine, GMERS Hospital, India.

[3]Department of Internal Medicine, Dow University of Health Sciences, Karachi.

[4]Department of Internal Medicine, Jinnah Sindh Medical University, Karachi.

***Address for Correspondence:** Hira Pervez, Department of Internal Medicine, Dow University of Health Sciences, Karachi. E-mail: drhirapervez@gmail.com

Received: 16 June 2020; **Accepted:** 09 July 2020; **Published:** 11 July 2020

Citation of this article: Tehzeeb J, Savaliya M, Pervez H, Roshan FNU, Usama MS (2020) Does SARS-CoV-2 Cause Acute Myocardial Injury: A Literature Review. Rea Int J of Card and Cardio Med. 1(1): 001-004. DOI: 10.37179/rijccm.000001.

ABSTRACT

The Coronavirus disease (COVID-19) caused by Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2) has emerged as an era-defining pandemic. It has globally challenged all levels of healthcare systems. Previously, coronavirus was mentioned mostly in association with the common cold. However, COVID-19 has taken a much grimmer course now presenting as severe, and in some cases fatal, pneumonia. As the number of cases grows, we have learned that it affects not just the lungs but also other organs.

Till now, many studies have been highlighting the heart as the 2nd most common organ affected by this illness. The reports of acute myocardial injury caused by SARS-CoV2 warrant a special focus on the cardiovascular management of this infection. In our review, we have analyzed multiple studies that support the acute effect of COVID-19 on the heart by comparing various laboratory changes and imaging studies conducted on the patients.

Introduction and Background

The previous 6 months have seen their fair share of Nature turning against humans. The most recent example of this involves a novel strain of coronavirus. This virus has officially been named "Severe Acute Respiratory Syndrome coronavirus 2" (SARS-CoV-2) and the illness caused by this organism is called the "Coronavirus disease" (COVID-19) [1]. Coronavirus has been around for years, causing the usual common cold. However, this year, it has come forth as a highly infectious organism, threatening healthcare systems and economies around the world. By May 2020, the World Health Organization (WHO) has reported more than 5.7 million cases known to be infected with this virus globally and about 0.35 million deaths since Dec 2019.

The United States has the highest number of confirmed cases in the world, standing at a staggering 1,675,258 cases and 99,889 deaths attributed to COVID-19 as of May 29, 2020 [2]. Although lungs remain the primary target, the involvement of other organs by this virus has also attracted the attention of investigators.

The cardiovascular system has been observed as the second most commonly affected organ system [3]. Acute myocardial injury is emerging as an area of special concern in COVID-19. This finding demands a focus on protecting this vital organ to improve outcomes in such patients.

Review

It is common knowledge now that a novel coronavirus started an outbreak in Wuhan city of China in late December 2019, subsequently leading to what we now recognize as an era-defining pandemic.

Taxonomically, this pathogen is an enveloped beta coronavirus whose genome consists of positive-sense RNA [4].

Its official name is "Severe Acute Respiratory Syndrome coronavirus 2" (SARS-CoV-2), with the disease caused by this organism labeled as the "Coronavirus disease" (COVID-19) [1]. Lungs are the primary target of this disease.

However, the involvement of other organ systems by COVID-19 is increasingly being reported with the heart being mentioned frequently. In its pathogenicity, SARS-CoV-2 is related to the Middle East Respiratory Syndrome virus (MERS), another member of the coronavirus family. MERS has been known to cause myocarditis and worsen existing cardiac problems [5]. Hence the hypothesis that SARS-CoV-2 may also harbor similar potential.

Literature has reported the percentage of cardiac injury in COVID-19 patients to be as high as 12% [6]. This raises a query about COVID-19 preferentially victimizing the heart and the lungs. One of the reasons for this observation is that, microscopically, the navigator for attachment and entry of SARS-CoV-2 into the cell is the ACE-2 receptor, primarily found on the pneumocytes and cardiomyocytes [7].

Scientists believe that hypoxia and inflammatory proteins may also play a role in cardiac involvement [8]. Some experts have suggested that "cytokine storm" (i.e. massive release of inflammatory proteins) may be responsible for the multi-organ dysfunction seen in COVID-19 [6, 7].

Pathological changes seen on postmortem examination of the affected hearts might be due to either a direct viral infection or a harmful immune response [9].

Chinese experts have proclaimed that the direct effect is observed more commonly in neonates while the immune effect is seen more in adults [10]. Such myocardial injury can sometimes manifest as ischemia while some studies have linked COVID-19 to congestive heart failure (CHF) [11]. The following table summarizes some common cardiovascular manifestations of COVID-19 as reported in some recent studies (Table 1).

Table 1: Cardiovascular manifestations of COVID-19 [11].

Authors	Cardiovascular manifestations
Bansal [12]	• Acute myocardial injury defined by elevated troponin levels • Arrhythmias • Heart failure • Potential acute coronary syndrome • Left ventricular systolic dysfunction
Szekely et al. [13]	• Right ventricular dilation and dysfunction • Left ventricular diastolic and systolic dysfunction • Femoral vein thrombosis

Apart from these, complications related to hypercoagulability associated with the COVID-19 have also been seen. Many of the features of respiratory viral infections overlap with the symptoms of viral myocardial injury like shortness of breath, palpitations, and chest pain.

The common clinical manifestations of COVID-19 itself include fever, chest pain, dry cough, dyspnea, muscle pain, confusion, headache, sore throat, rhinorrhea, diarrhea, nausea, and vomiting [14].

This overlap in symptomology can lead to inadvertent misdiagnosis. This necessitates prompt utilization of laboratory data in detecting acute myocardial injury alongside the clinical presentation.

Hence, we studied several case reports and compared such laboratory studies that can reliably detect acute myocardial injury in COVID-19 patients. These included electrocardiograms (ECG), echocardiogram (with accepted normal ranges of left ventricular ejection fraction as 55-70% and Left Ventricular End Diastolic Diameter as <5.6cm), cardiac enzymes, and other biochemical markers like high sensitivity cardiac troponin I (hs-cTnI), etc (Tables 2, 3).

The findings listed in these tables suggest that COVID-19-induced myocardial injury has manifold presentations including, but not limited to, myocardial ischemia and rhythm abnormalities, heart failure, and other disturbances in ventricular function.

Stimulated by these findings, we delved a bit further into literature and found that myocardial injury that arises acutely without any pre-existing cardiac disease has been reported by many authors. Wuhan Jinyintan Hospital, China conducted a retrospective analysis on 101 patients who lost their lives to COVID-19 between Dec 30, 2019, and Feb 16, 2020 [3].

83 of these patients (82.18%) had abnormal myocardial enzymes on admission with average hs-cTnI 16.55 U/L (high in 24.07% patients), BNP 61.9 pg/mL (high in 16.67% patients), and CK-MB 17 U/L (high in 16.67% patients).

These values titrated uphill with an average hs-cTnI 361.35 U/L (high in 72.28% patients), BNP 501.80 pg/mL (high in 40.59% patients), CK-MB 32.50 U/L (high in 55.45% patients) just 48 hours before their deaths. These findings depict that the myocardial injury arose acutely in these patients, as their conditions worsened. This data also highlights that hs-cTnI has a strong positive correlation with the severity of the myocardial injury.

Five of the first 41 COVID-19 patients in Wuhan had elevated levels of Troponin-I (TnI) which is a highly sensitive indicator of myocardial injury [6]. A case series analyzing troponin levels in 187 COVID-19 patients at the Seventh Hospital of Wuhan City, China, 2020 found that 52 (27.8%) patients had elevated troponin levels [22].

The patients with high troponin also had remarkably high N-terminal pro-brain natriuretic peptide (NT-proBNP) levels and malignant arrhythmias, corresponding to myocardial injury. Similarly, Wang et al. reported significant acute elevation of cardiac-specific biomarkers in patients admitted to ICU with COVID-19 while such elevations were not seen in non-ICU patients [23].

The markers they measured included CK-MB (18 U/L vs 14 U/L, $P < 0.001$); and hs-cTnI (11.0 pg/mL vs 5.1 pg/mL, $P = 0.004$). Together, these findings suggest an association of COVID-19 with acute myocardial inflammation as these biomarkers are strongly associated with myocarditis.

Table 2: Cardiac markers at the time of presentation in index COVID-19 cases reported in the literature from March 2020- May 10, 2020.

Authors	Cases (Age, Gender)	Troponin* (Normal range: 0-0.034 ng/mL)	BNP* (Normal range: 0-125 pg/mL)	CK MB* (Normal range: 0-24 U/L or 0-4.9 ng/mL)	Myoglobin* (Normal range: 0-85 ng/mL)
He et al. [8]	70 years, Male	>0.034 ng/mL	24,245 pg/mL	72.6 U/L	
Zeng et al. [9]	63 years, Male	>10,000 ng/mL	22,600 pg/mL		390.97 ng/mL
Cui et al. [15]	55 days, Female	0.025 ng/mL		46 U/L	
Loghin et al. [16]	29 years, Male	<0.02 ng/ml		2034 U/L	55.0 ng/mL
Inciardi et al. [17]	53 years, Female	0.24 ng/mL	5647 pg/mL	20.3 ng/mL	
Hu et al. [18]	37 years, Male	>10 ng/mL	21,025 pg/mL	0.1129 ng/mL	
Kir et al. [19]	49 years, Male	<0.012 ng/mL	38.3 pg/mL		
Coyle et al. [20]	57 years, Male	0.02 to 7.33 ng/mL	859 pg/mL		
Dong et al. [21] (Labs from 3rd day of presentation)	11 years, Male	0.0486 ng/mL	250.4 pg/mL		
	38 years, Male	0.0095 ng/mL	2,085.7 pg/mL		
	57 years, Male	0.1435 ng/mL	8,222.1 pg/mL		
	67 years, Male	0.0712 ng/mL	4,450 pg/mL		

BNP= brain natriuretic peptide, CK-MB= creatine kinase- myocardial band.
*Some units have been altered using SI unit converter solely for the ease of the readers.

Table 3: Imaging studies in index COVID-19 cases reported in the literature between March 2020- May 10, 2020.

Authors	Cases (Age, Gender)	Electrocardiographic changes	Echocardiographic changes	Other cardiac imaging
He et al. [8]	66 years, Female	Sinus rhythm with first degree AV nodal block that progressed to sinus tachycardia, high degree AV block and S1Q3T3 pattern before recovery	Enlarged right atrium and ventricle with severe tricuspid regurgitation, Pulmonary hypertension (Pulmonary artery pressure>25 mmHg)	
	70 years, Male	Sinus tachycardia with incomplete RBBB followed by ST-segment elevations in the inferior and precordial leads	Diffuse hypokinesis of anterior and inferior walls	
Zeng et al. [9]	63 years, Asian Male	Sinus tachycardia	Enlarged LV, diffuse dyskinesia, LVEF 32% (normal range: 55-70%), pulmonary hypertension	
Loghin et al. [16]	29 years, Male	ST-segment elevation in lead II, III, aVF and V6, Sinus tachycardia, Right axis deviation	-	-
Inciardi et al. [17]	53 years, Female	Low voltage, diffuse ST elevation (especially in inferior and lateral leads), ST depression and T wave inversion (V1, aVR)	Diffuse hypokinesis, thickened interventricular septum, LVEF 40%, Circumferential pericardial effusion (maximum 11 mm)	Cardiac MRI: increased wall thickness, biventricular hypokinesis (especially apical), LVEF 35%
Hu et al. [18]	37 years, Male	ST-segment elevation (lead III, aVF)	Diffusely enlarged heart, LVEF 27%, trace pericardial effusion	Emergency CT coronary angiogram: no stenosis
Kir et al. [19]	49 years, Male	Intermittent high degree AV block with AV dissociation and bradycardia; HR <20 beats/min	No significant changes	
Coyle et al. [20]	57 years, Male	Sinus tachycardia	Diffuse hypokinesis with relative apical sparing and LVEF 35-40% on day 3	
Dong et al. [21]	11 years, Male	-	LVEF 22% with LVEDD: 5.5 cm	
	38 years, Male	-	LVEF 26% with LVEDD: 7.2 cm	
	57 years, Male	-	LVEF 22% with LVEDD: 10.8 cm	
	67 years, Male	-	LVEF 30% with LVEDD: 8.5 cm	

AV: atrioventricular, LV: Left Ventricle, MRI: Magnetic Resonance Imaging, TTE: transthoracic echocardiogram, LVEF: Left Ventricular Ejection Fraction, LVEDD: Left Ventricular End Diastolic Diameter.

Shaobo Shi et al. have reported cardiac injury in 12.7% of the 416 COVID-19 patients at Renmin Hospital of Wuhan University, as suggested by elevated cardiac markers like CK-MB (median 3.2 ng/mL vs 0.9 ng/mL in those without cardiac injury), myohemoglobin (median 128 vs 39 μg/L), hs-cTnI (median 0.19 vs <0.006 μg/L), NT-proBNP (median 1689 vs 139 pg/mL) [24].

Only 22 (26.8%) patients with cardiac injury had done ECG and 14 (63.6%) of these ECGs were abnormal with findings compatible with myocardial ischemia, such as T wave inversions, ST-segment depression, and the presence of Q waves.

Patients encountering acute myocardial injury appear to have a worse outcome than those who get just lung involvement. Zhou et al. described 191 patients from Jinyintan and Wuhan Pulmonary Hospitals in China suggesting that 46% of patients dying of COVID-19 had high hs-cTnI while only one percent of survivors had such elevations [25].

The fact that many other conditions may have falsely elevated cardiac biomarkers was pointed out by Wu et al. with high troponin levels seen in subarachnoid hemorrhage, pulmonary embolism, or kidney failure. Similarly, an elevated LDH may also be indicative

of tissue damage other than myocardial injury like renal, pulmonary or hepatic injury and sepsis, etc [26].

To avoid this floundering, researchers have establishing cut-off limits corresponding with high specificity for cardiac injury. For example, Zhang et al. have defined cardiac injury as hs-cTnI above the 99th percentile upper range of reference value chosen as 0.026 ug/L [27]. This criterion can drive more yield to the diagnostic utility of this test.

These authors also retrospectively analyzed 110 COVID-19 patients and found that 27.1 % of them had high levels of hs-cTnI and a high level of this biomarker at hospital admission was associated with high mortality (hazard ratio= 10.902, p=0.029).

The study reaffirms the above-mentioned observation that hs-cTnI is highly sensitive and specific for cardiac injury and the relatively common elevation of hs-cTnI in COVID-19 patients suggests its association with acute myocardial injury [28].

Lippi et al. reviewed 11 studies and found that 12% of patients show hs-cTnI value exceeding the 99th percentile in the upper limit of normal [29]. Given this observation and the clinical significance of hs-cTnI, the authors deemed it rational to suspect that SARS-COV-2 induced myocardial injury in these patients.

Mehra and Ruschitzka narrate in their article that, in elderly patients with coexisting heart disease, COVID-19 can cause stress cardiomyopathy or myocardial injury from fatally high levels of cytokines [30]. However, rarely, patients do present with fulminant myocarditis, which is the most severe form of acute myocardial injury leading to rapid decline and even fatality in most patients.

So, the spectrum of cardiac findings is COVID-19 patients is broad. The timelines of elevation of cardiac biomarkers and imaging findings do suggest that there is substantial evidence for the induction of acute myocardial injury by SARS-CoV-2.

From the studies that we have gathered, a suggestion arises that in order to make a baseline to follow the prognosis of COVID-19 patients, we should do an initial measurement of biomarkers of myocardial necrosis/injury such as hs-cTnI, CK-MB, NT proBNP, ECG, etc.

Following these biomarkers over time can then lead to early detection and management of acute cardiac injury. Further research should be done to define the need for imaging studies in such cases and to decide if adjunctive cardioprotective therapies may be advisable in patients with significantly elevated biomarkers supporting myocardial necrosis [31].

Conclusions

SARS-CoV-2 is seen to cause acute insult to almost every organ, including the cardiovascular system. Acute myocardial injury can affect the prognosis of COVID-19 patients adversely. However, symptom imbrication can further lead to an inadvertent increase in mortality due to misdiagnosis.

To avoid this issue, cardiac-specific biomarkers and radiologic utilities can be deployed in patients with SARS-CoV-2 infection from the time of their presentation in the emergency department until discharge irrespective of pre-existing cardiac conditions, deeming it important for medical management. Standard guidelines can also be established for every symptomatic patient.

We further suggest that similar measures to improve the prognosis of COVID-19 patients from other specific organ injuries should also be explored.

References

1. (2020) Naming the coronavirus disease (COVID-19) and the virus that causes it. Who.int. Link: https://bit.ly/3iw8MmK

2. (2020) Coronavirus disease (COVID-19) Situation Report – 130. WHO; Link: https://bit.ly/38sMcHb

3. Chen J, Fan H, Zhang L, Huang B, Zhu M, et al. (2020) Retrospective Analysis of Clinical Features in 101 Death Cases with COVID-19. medRxiv. Link: https://bit.ly/2NSDOr4

4. Lu R, Zhao X, Li J, Niu P, Yang B, et al. (2020) Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. The Lancet. 395: 565-574. Link: https://bit.ly/2VPZvMR

5. Alhogbani T (2016) Acute myocarditis associated with novel Middle East respiratory syndrome coronavirus. Ann Saudi Med 36: 78-80. Link: https://bit.ly/2ZIbqxa

6. Huang C, Wang Y, Li X, Ren L, Zhao J, et al. (2020) Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The Lancet. 395: 497-506. Link: https://bit.ly/2BG34hx

7. Zheng Y, Ma Y, Zhang J, Xie X. (2020) COVID-19 and the cardiovascular system. Nature Reviews Cardiology. 17: 259-260. Link: https://go.nature.com/31JPsfQ

8. He J, Wu B, Chen Y, Tang J, Liu Q, et al. (2020) Characteristic Electrocardiographic Manifestations in Patients With COVID-19. Can J Cardiol. 36: 966. Link: https://bit.ly/2DbqHiC

9. Zeng J, Liu Y, Yuan J, Wang F, Wu W, et al. (2020) First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. Infection. 10: 1-5 Link: https://bit.ly/2YZzNaq

10. Wang D, Li S, Jiang J, Yan J, Zhao C, et al. (2018) Chinese society of cardiology expert consensus statement on the diagnosis and treatment of adult fulminant myocarditis. Sci China Life Sci 62: 187-202. Link: https://bit.ly/2NVEXy1

11. Edwards S, Small J, Geratz J, Alexander L, Baric R (1992) An Experimental Model for Myocarditis and Congestive Heart Failure after Rabbit Coronavirus Infection. J Infect Dis. 165: 134-140. Link: https://bit.ly/2VL9QK0

12. Bansal M (2020) Cardiovascular disease and COVID-19. Diabetes & Metabolic Syndrome: Clinical Research & Reviews 14: 247-250. Link: https://bit.ly/3greqow

13. Szekely Y, Lichter Y, Taieb P, Banai A, Hochstadt A, et al. (2020) The Spectrum of Cardiac Manifestations in Coronavirus Disease 2019 (COVID-19)- a Systematic Echocardiographic Study. Circulation. Link: https://bit.ly/2C3ZON5

14. Chen N, Zhou M, Dong X, Qu J, Gong F, et al. (2020) Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. The Lancet 395: 507-513. Link: https://bit.ly/2YXW2O5

15. Cui Y, Tian M, Huang D, Wang X, Huang Y, et al. (2020) A 55-Day-Old Female Infant Infected With 2019 Novel Coronavirus Disease: Presenting With

Pneumonia, Liver Injury, and Heart Damage. The Journal of Infectious Diseases 221: 1775-1781. Link: https://bit.ly/31M16XR

16. Loghin C, Chauhan S, Lawless S (2020) Pseudo acute myocardial infarction in a young COVID-19 patient. JACC: Case Reports. Link: https://bit.ly/31SRF8K

17. Inciardi R, Lupi L, Zaccone G, Italia L, Raffo M, et al. (2020) Cardiac Involvement in a Patient With Coronavirus Disease 2019 (COVID-19). JAMA Cardiology. Link: https://bit.ly/2VLc108

18. Hu H, Ma F, Wei X, Fang Y (2020) European Heart Journal.

19. Kir D, Mohan C, Sancassani R (2020) Heart Brake: An Unusual Cardiac Manifestation of COVID-19. JACC: Case Reports. Link: https://bit.ly/3iEPlIA

20. Coyle J, Igbinomwanhia E, Sanchez-Nadales A, Danciu S, Chu C, et al. (2020) A Recovered Case of COVID-19 Myocarditis and ARDS Treated with Corticosteroids, Tocilizumab, and Experimental AT-001. JACC: Case Reports. Link: https://bit.ly/2ZbsBIF

21. Dong N, Cai J, Zhou Y, Liu J, Li F (2020) End-Stage Heart Failure With COVID-19. JACC: Heart Failure 8: 515-517. Link: https://bit.ly/38zqrWg

22. Guo T, Fan Y, Chen M, Wu X, Zhang L, et al. (2020) Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiology. Link: https://bit.ly/2ZJ5h3U

23. Wang D, Hu B, Hu C, Zhu F, Liu X, et al. (2020) Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus–Infected Pneumonia in Wuhan, China. JAMA 323: 1061. Link: https://bit.ly/2AFlcb5

24. Shi S, Qin M, Shen B, Cai Y, Liu T, et al. (2020) Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiology. Link: https://bit.ly/38CtBbG

25. Zhou F, Yu T, Du R, Fan G, Liu Y, et al. (2020) Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. The Lancet. 395: 1054-1062. Link: https://bit.ly/2Z6oWf8

26. Wu J, Zha P (2020) Association of COVID-19 Disease Severity with Transmission Routes and Suggested Changes to Community Guidelines. SSRN Electronic Journal. Link: https://bit.ly/2O6fwtC

27. Zhang F, Yang D, Li J, Gao P, Chen T, et al. (2020) Myocardial injury is associated with in-hospital mortality of confirmed or suspected COVID-19 in Wuhan, China: A single center retrospective cohort study. Link: https://bit.ly/2O4o6t5

28. Thygesen K (2019) 'Ten Commandments' for the Fourth Universal Definition of Myocardial Infarction 2018. European Heart Journal 40: 226-226. Link: https://bit.ly/3iFZaGi

29. Lippi G, Plebani M (2020) Laboratory abnormalities in patients with COVID-2019 infection. Clin Chem Lab Med 58: 1131-1134. Link: https://bit.ly/2VWywiF

30. Mehra M, Ruschitzka F (2020) COVID-19 Illness and Heart Failure. JACC: Heart Failure 8: 512-514. Link: https://bit.ly/3gDhYEm

31. Lippi G, Lavie C, Sanchis-Gomar F (2020) Cardiac troponin I in patients with coronavirus disease 2019 (COVID-19): Evidence from a meta-analysis. Progress in Cardiovascular Diseases. Link: https://bit.ly/2CfZZF7