http://jmscr.igmpublication.org/home/
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v11i12.24

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

COVID-19 and Cardiovascular Diseases: A Literature Review from Pathogenesis to Diagnosis

Authors
Kashif Raza[1], Naushin Alam[2], Shahana[3], Makseena Khatoon[4], Mohd Arsalan[5], Bhawna[6]
[1]Faculty, Department of Paramedical Sciences, Jamia Hamdard, New Delhi, India
[2]Sun Pharmaceutical Industries Limited, HAHC Hospital, New Delhi, India
[3,4,5,6]Student, Department Of Paramedical Sciences, Jamia Hamdard, Delhi, India

Abstract
After the first case of COVID-19 emerged in China on December 8, 2019, the coronavirus disease 2019 (COVID-19) quickly spread throughout the world. Although the illness is typically thought to be a respiratory infection, cases of severe, perhaps fatal cardiac damage have been linked to this virus. By attaching themselves to the angiotensin-converting enzyme 2 (ACE-2) receptor, coronaviruses can harm cardiac myocytes. Among COVID-19-affected patients, myocardial infarction, myocarditis, heart failure, cardiac arrhythmias, and Takotsubo cardiomyopathy are common cardiac clinical symptoms.
It Is possible to observe certain heart abnormalities both during and after an infection. Myoglobin, troponin, creatine kinase-MB, lactate dehydrogenase (LDH), plasma interleukin-6, and N-terminal pro-b-type natriuretic peptide (NT-proBNP) have all been observed to be elevated in COVID-19-associated cardiac damage. Electrocardiography (ECG), cardiac magnetic resonance imaging (CMR), endomyocardial biopsies, echocardiography (Echo), and computerized tomography (CT-Scan) are the diagnostic modalities employed in cases of myocardial damage caused by COVID-19. This review of the literature will go into great detail about the etiology, clinical presentation, and diagnosis of COVID-19-related myocardial damage.
Keywords: *troponin, echocardiography, dysrhythmia, myocarditits, acute myocardial infection,sars-cov-2,COVID-19,cardiovascular insult,myocardial injuries.*

Introduction & Background

Severe Acute Respiratory Distress Syndrome-Coronavirus-2 (SARS-CoV-2) is the cause of coronavirus disease 2019 (COVID-19), which has emerged as one of the biggest threats to public health in recent years. The tremendous transmissibility of this virion, even in the asymptomatic phase, and its infectious nature have led to the global pandemicization of this disease. On December 8, 2019, a region in China named Hubei announced the first COVID-19 victim[1]. This infection became a worldwide pandemic within only three months, during which time it spread to 177 countries and territories[1]. COVID-19 has

infected millions of people to date, and as of right now, the virus is still spreading. As of January 8, 2023, the current COVID-19 outbreak's confirmed case count

COVID-19 has significant cardiovascular symptoms, such as arrhythmias, ischemic heart disease, and myocarditis. Palpitations and chest discomfort may be nonspecific symptoms that patients report with[5]. In addition to being frequent with COVID-19 infection, current research has revealed that certain mRNA COVID-19 vaccinations have also been linked to cardiac problems. These issues can range from cardiac inflammation to potentially fatal thrombosis and myocardial ischemia[6]. Depending on the severity of the cardiac insult, treatment choices can range from conservative measures to ICU hospitalizations. Improved knowledge of the pathophysiology of COVID-19 in producing cardiac clinical symptoms can aid in early diagnosis and effective treatment to minimize potential injury and lower cardiovascular death rates in COVID-19-affected persons. The goal of this paper is to present a thorough analysis of the etiology, clinical manifestations, and diagnosis of myocardial injuries due to COVID-19

Review

Pathogenesis of myocardial injuries among COVID-19 patients

Role of Angiotensin-Converting Enzyme 2 (ACE-2)

Cells of the respiratory system, heart myocytes, and other organ systems are known to express ACE-2 [7]. SARS-CoV-2's viral glycoprotein spike 1 interacts to ACE2 in the host cells[8]. It damages the heart, which leads to the downregulation of ACE2, the induction of an inflammatory cascade, the development of myocardial interstitial fibrosis, and the instability of the coronary plaque [9–10]. Angiotensin II is converted to the vasodilator molecule angiotensin 1 by ACE2. Angiotensin II, a pro-inflammatory substance linked to increased inflammatory cytokines in the systemic circulation and thought to be connected to extrapulmonary manifestations of coronavirus infection like cardiovascular disease, is elevated when the ACE2 enzyme is blocked[8].

Cytokine storm's role

Numerous investigations have revealed elevated concentrations of inflammatory markers and cytokines in COVID-19 patients, such as TNF alpha, IP-10, monocyte chemoattractant protein (MCP-1), interferon-gamma, and interleukin-1 beta (IL-1β)[11]. Direct and indirect impacts are the two ways in which cytokine storm may have contributed to myocardial injury in COVID-19 patients:

Direct result of cytokine storm: Following the start of COVID-19, there is a notable increase in MCP-1. It has a significant role in the recruitment of macrophages and monocytes[12]. The recruitment of macrophages surrounding the viral inclusions is a serious risk to the heart's ability to contract mechanically. Patients with COVID-19 myocarditis had a high number of lymphocytes and macrophages in their histopathology[13]. Another significant cytokine in COVID-19 patients is IL-1β. It thickens the heart layers and triggers the production of other cytokines, such as IL-21, IL-17, and IL-22, which eventually results in cardiomyopathy[13–14].

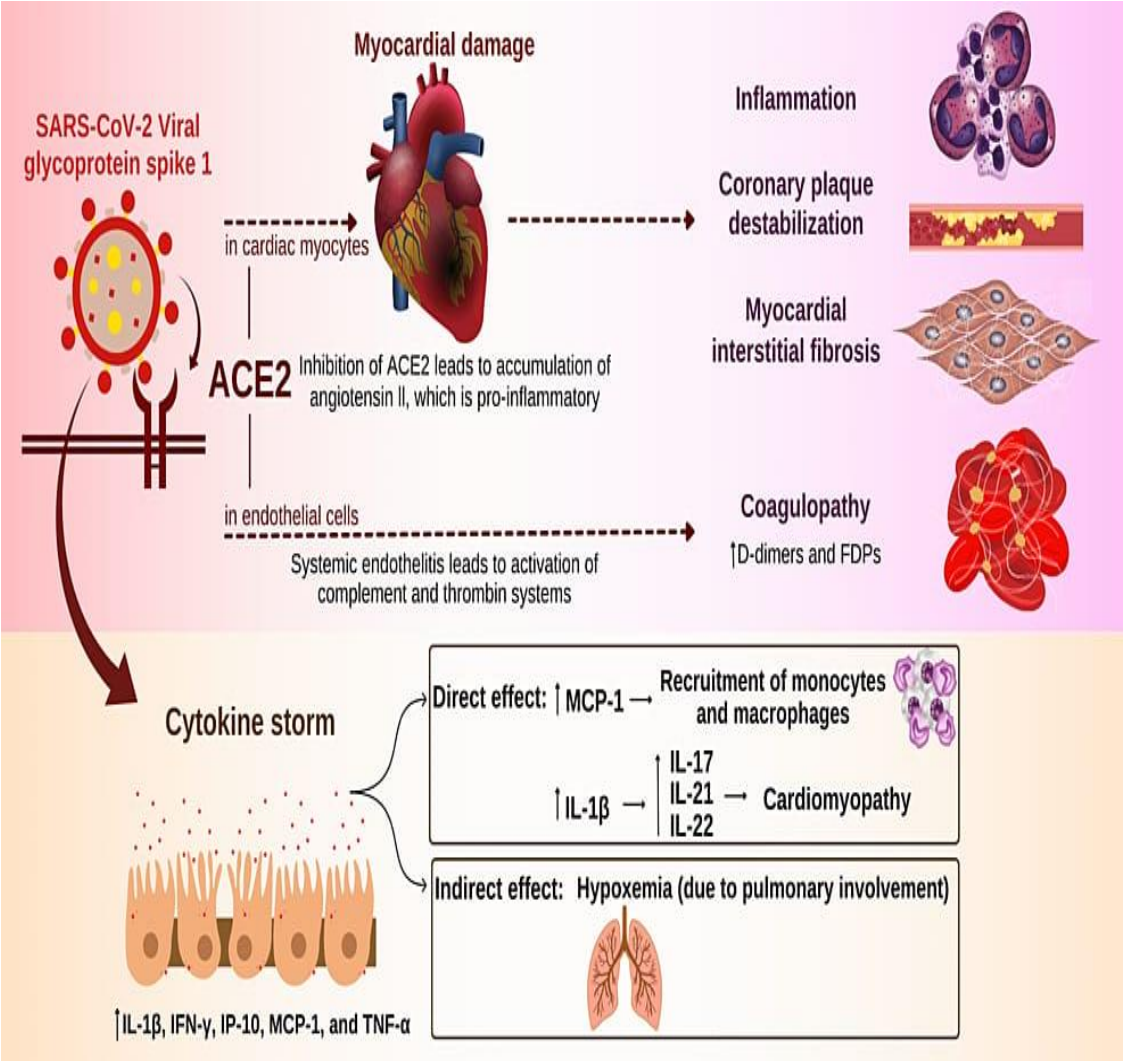
Cytokine storm's indirect effect on the heart is attributed to its effects on the lungs, which result in hypoxemia and a reduction in blood flow to the heart's vasculature[15].

Role of Coagulopathy

Higher levels of fibrin degradation products (FDPs) and D-dimers indicate a significant risk of thromboembolism in COVID-19 patients, especially in critically ill patients[16–17]. The virus targets endothelial cells that express ACE2, which damages

endothelium throughout the body. The activation of the complement and thrombin systems, as well as the aggregation of platelets and white blood cells, can result from this systemic endothelium and cause coagulopathy[18]. Furthermore, immobility is another independent risk factor that contributes to coagulopathy in critically ill individuals. A coronary artery occlusion may occur after the prothrombotic state[19].

COVID-19, particularly in its more severe and complicated stages, has been characterized by Libby and Lüscher[20] as an endothelial disease. It clarifies how important the endothelium is to fibrinolysis and thrombosis. In addition to serving as the barrier, the endothelium also possesses the balances of vasodilator/vasoconstrictor, endothelial inflammatory, and antioxidant/pro-oxidant. These processes' disruption in disease has been proposed as the primary pathophysiological alteration causing endothelium damage, coupled with the cytokine storm. Figure 1 summarizes the pathophysiology of cardiac damage in individuals inflicted by COVID-19. (Summarized in figure 1.)



NOTE**: ACE-2:** Angiotensin-converting enzyme 2

FDPs: Fibrin degradation products

Figure 1: Illustrating pathogenesis involved in myocardial insult by COVID-19

Cardiac Clinical Manifestations of COVID-19

Myocardial Infarction

There are several pathogenic pathways linked to myocardial infarction (MI) in COVID-19. Glycoproteins in the viral envelope may bind to hemoglobin's β-chain as well as porphyrin, resulting in hypoxia and type 2 acute myocardial infarction (AMI), which is defined as an imbalance between the oxygen supply and demand of the heart due to infection[9,20–21]. Type 1 AMI can also be made worse by the pro-thrombotic state brought on by the pro-inflammatory state[19,22].

Heart rhythms

Another potentially fatal consequence linked to COVID-19 individuals is arrhythmias, which can lead to both bradyarrhythmia and tachyarrhythmia [23]. Electrolyte imbalances could be a possible mechanism in addition to direct cardiac damage caused by SARS-CoV-2. For example, tachyarrhythmia risk is increased in hypokalemia caused by renin-angiotensin-aldosterone system (RAAS) disruption[15,24]. Research examining the origins of arrhythmias in COVID-19 patients with myocarditis have identified a number of factors, including scarring, pericarditis, ischemia, direct cell injury, and ruptured cell membranes. Plakoglobin is a desmosomal protein that is dislodged by inflammatory cytokines, which is a powerful cause of arrhythmogenic cardiomyopathies[25].

Heart Failure

Another clinical symptom that has been observed in COVID-19 individuals is heart failure[19]. NEC arises from both direct myocardial injury and a hyper-inflammatory condition. In addition, endothelial injury and microthrombosis contribute to endocardial damage. These may ultimately result in the heart's systolic and diastolic collapse, which can induce cardiogenic shock[13]. Right heart failure and pulmonary hypertension may result from the pulmonary vascular bed's impairment[26].

Heart Myopathy

Myocarditis can result from both direct heart injury and hyperinflammation brought on by cytokine storms. Inflammatory cells linked to edema, such as neutrophils, lymphocytes, macrophages, and monocytes, are drawn in by viral Inclusions. This virus-induced myocarditis manifests as cardiac edema, myocardial cell necrosis, and connective tissue interstitium. Myocarditis can also result from the virus's cell-mediated auto-immune response [27]. Because epicardial fat releases adipokines and serves as a reservoir for the COVID-19 virus, it is associated with myocarditis. In COVID-19 patients, the degree of cardiac inflammation is closely correlated with the thickness of epicardial fat[28].

Takotsubo Heart Disease

This condition is characterized by transient left ventricular failure, both systolic and diastolic [29–30]. There is evidence that a psychological and emotional trigger occurs prior to the disease[31]. There has been much research and discussion on the function catecholamines play in its pathogenesis [32]. Research has indicated that patients with COVID-19 have a higher incidence of this stress cardiomyopathy[33]. In addition to the cytokine storm caused by COVID-19, ongoing stress, worry, terror, and panic attacks can result in excessive catecholamine release, which can cause Takotsubo cardiomyopathy.

Myocardial Effects due to Post-COVID-19 Syndrome (PCS)

One pathogenesis associated with post-COVID-19 syndrome (PCS) is disruption of the autonomic nerve system (ANS). It presents as blood pressure fluctuations, orthostatic disorders, inappropriate sinus tachycardia (IST), palpitations, chest pain, and rhythm abnormalities in the cardiovascular system. Patients with PCS frequently have IST, which is important in treating cardiac symptoms like palpitations, reduced exercise tolerance, and exhaustion[34].

Psychological Effects of COVID-19 on Heart

Research on the cardiovascular effects of social separation has been published in both clinical and experimental settings. The effects of mandatory isolation periods and loneliness on cardiac illnesses are significant. One major risk factor for cardiovascular death is the absence of healthy relationships[35–36]. We have already covered Takotsubo cardiomyopathy caused by psychological stress. The isolation time that COVID-19 patients must adhere to intensifies the emotional pressures that precipitate Takotsubo cardiomyopathy[33]. (Figure 2 Summarizes the clinical symptoms of COVID-19 in the heart).

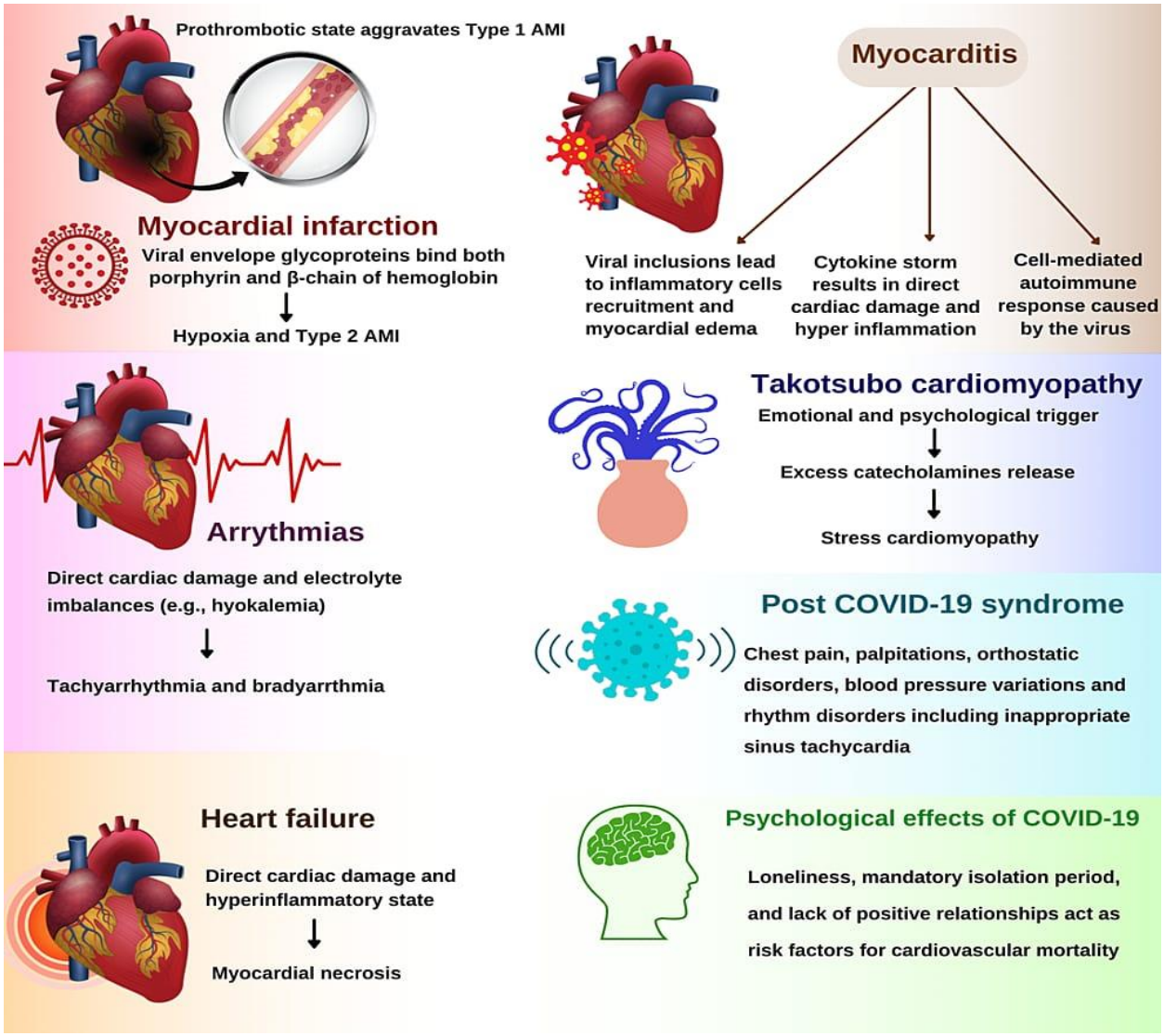


Figure 2 Summarizes the clinical symptoms of COVID-19 in the heart

Diagnosing Cardiac Injury among COVID-19 Patients

In addition to standard laboratory testing, research is being done to determine the function of several biomarkers in the reliable and low-misdiagnosis diagnosis of COVID-19. When starting treatment and keeping an eye on COVID-19 patients, biomarkers can help clinicians. Patients with COVID-19 have been shown to have elevated levels of various cardiac biomarkers[37]. According to

numerous research, the majority of COVID-19 patients have elevated serum lactic dehydrogenase (LDH) values. Higher death rates in COVID-19 patients have been associated with elevated LDH levels[38].

In COVID-19 individuals with acute myocardial damage, CK-MB levels are elevated. The patients with elevated CK-MB levels were identified as those who did not recover from the COVID-19 infection. In COVID-19 patients, however, elevated myoglobin levels are more specific for cardiac insult[39].

Interleukin-6 plasma concentrations are higher in COVID-19 patients who have experienced cardiac injury[5]. One meta-analysis found that individuals with complex illnesses had mean interleukin-6 levels that were 2.9 times greater than those with simple illnesses[40].

Acute myocardial infarction, pulmonary embolism, and venous thromboembolism are all more likely when COVID-19 causes prothrombotic endothelial damage. Raised D-dimers and fibrin degradation products in COVID-19 patients are indicative of the onset of pulmonary embolism and disseminated intravascular coagulation, both of which have an effect on hemodynamic stability. Additionally, compared to individuals without an increase in D-dimers, COVID-19 patients with elevated D-dimer levels have been linked to higher mortality rates [38].

Myocardial damage and myocarditis, which can be brought on by an inadequate oxygen supply, a direct lesion to the heart, or both, cause high troponin levels. Patients with COVID-19 who have elevated troponin levels are directly at risk for serious consequences, including death. Troponin levels have also been shown to have predictive value in sepsis. A negative troponin profile does not, however, rule out cardiac damage. For the diagnosis of myocardial damage, high-sensitivity Troponin I (hs-TnI) is more dependable[38–39].

Patients with COVID-19 who have cardiac disease have elevated NT-proBNP levels. Regardless of cardiac damage, patients with increased NT-proBNP or BNP levels may also exhibit no symptoms or indicators of fluid overload[41].

Patients with COVID-19 who have cardiac damage have been reported to have elevated levels of neutrophils, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), hyperglycemia, and neutrophil/lymphocyte ratio—all indicators of systemic inflammation. These biomarkers might, however, be less sensitive and non-specific[28].

ECG Examination

Electrocardiography (ECG) may reveal ST elevation and PR depression in COVID-19 patients with myocarditis, which are indicative of pericardial damage. However, an ECG may also show premature ventricular complexes, arrhythmia, QT interval prolongation, and bundle branch block[26]. T wave inversion and non-specific ST segment disruption may also be seen in cardiac consequences from COVID-19 that are captured on ECG[42].

Some patients' de-novo production of fragmented QRS complexes may be seen on an ECG[43]. An ECG can be utilized as a screening tool for COVID-19-related cardiac problems.

Cardiac Magnetic Resonance Imaging and Echocardiogram

The American Heart Association (AHA) advises echocardiography (ECHO) and cardiac magnetic resonance imaging (CMR) to confirm myocarditis in COVID-19 patients[44]. Though endomyocardial biopsy (EMB) remains the gold standard for diagnosing myocarditis, there are other options. However, EMB is less sensitive when viral myocarditis causes focal and patchy myocardial involvement. Non-invasive imaging tests are therefore a crucial component of the workup. Therefore, the most useful test for viral myocarditis

is CMR [45]. In a research, people with COVID-19-related myocarditis had cardiac inflammation, edema, and scarring visible on CMR. Despite being a superior approach to ECHO, CMR is not as widely recommended due to its slower output and requirement for post-usage decontamination.

Echocardiography is advised because it can reveal a wall defect that is indicative of myocardial injury from acute coronary syndrome (ACS)[46]. The drawbacks of CMR includeincludee its limited availability, high expense, prolonged examination duration, and patient-specific problems such arrhythmia, dyspnea, claustrophobia, metallic implants, and contrast hypersensitivity[47].

When a patient is stable, computed tomography (CT) is the most important diagnostic test for the diagnosis of acute myocarditis. Transporting COVID-19 patients who are unstable presents certain problems, however echocardiography, as opposed to CMR, allows us to undertake a bedside diagnostic and prognostic assessment[48].

EMB (Endomyocardial Biopsy)

Endomyocardial biopsy (EMB) was introduced as the gold standard for myocarditis diagnosis by the American Heart Association and the European Society of Cardiology [49]. When confirming the presence of myocarditis, EMB is regarded as the gold standard Investigation [45]. EMB showed a high level of macrophages and lymphocytic infiltration in COVID-myocarditis patients[47]. EMB can also provide tissues for the purpose of searching for biomarkers in order to diagnose COVID-related myocarditis more precisely. Nevertheless, EMB has drawbacks, such as low sensitivity, the need for specialized knowledge, and the possibility of COVID-19 spreading. To lower the chance of infectious dissemination, EMB should be performed concurrently with invasive right cardiac catheterization if necessary[25].

Only life-threatening clinical situations when histology information could influence therapy decisions should consider using the invasive EMB method[48].

CT-Scan, or Computerized Tomography

The thickness of epicardial fat was assessed using computerized tomography (CT-Scan) in a study by Özer et al.[27]. In patients with COVID-19, epicardial fat serves as a reservoir for the virus and fuels cytokine-mediated cardiac inflammation.

Bihan et al. discovered that in the chosen cohort with a large percentage of obese people affected by COVID-19, the mean epicardial adipose tissue volume was associated with death or transfer from a non-ICU hospital medical department to an ICU. Measuring the volume of fat in the epicardium at the time of admission may be useful in properly predicting the outcome of COVID-19 [50].(Figure 3 summarizes the diagnostic techniques employed for COVID-19-related myocardial damage).

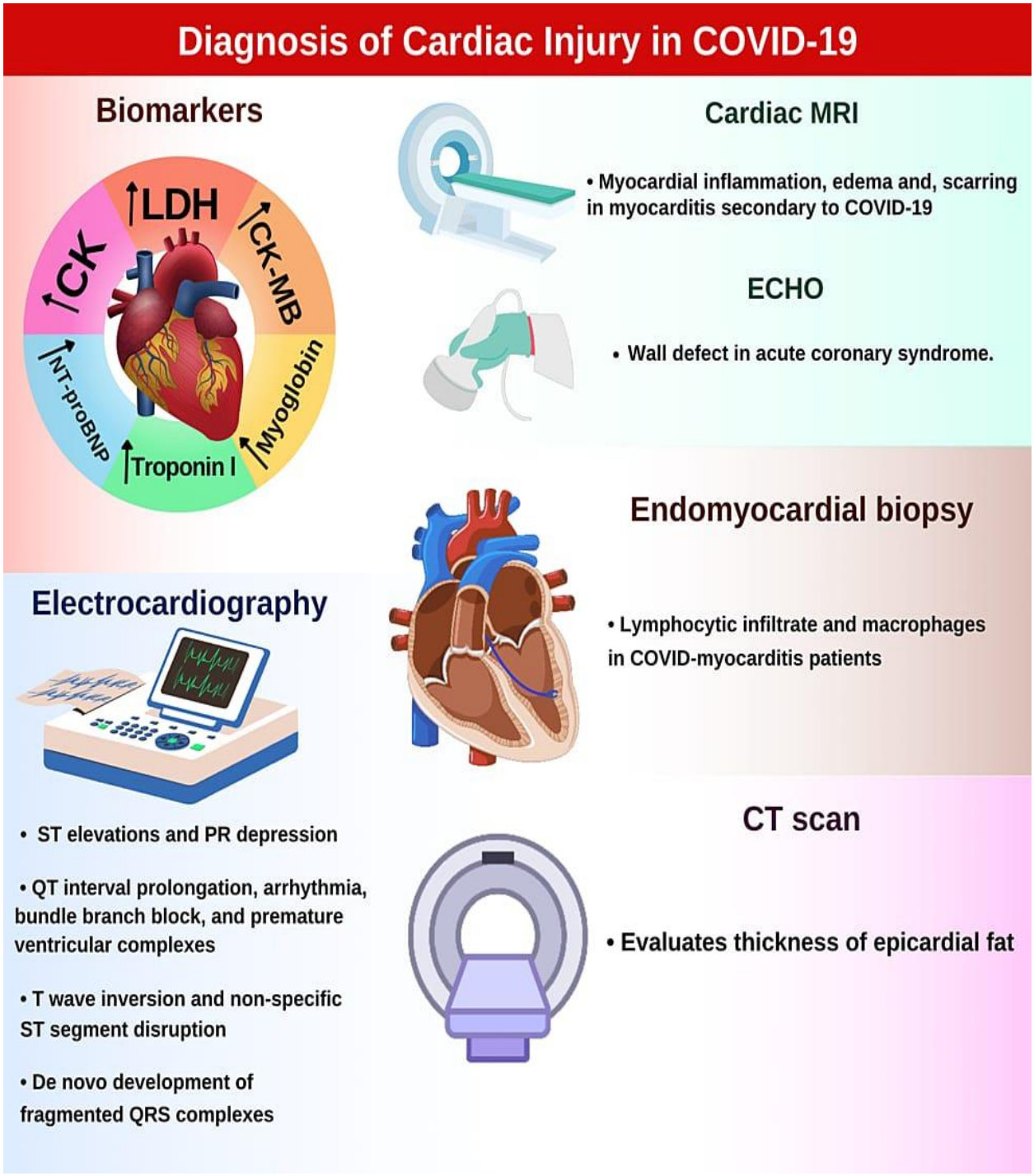


Figure 3: Illustrating modalities for diagnosing myocardial injuries due to COVID-19.

Conclusions

COVID-19 and the injuries it causes have been linked to numerous serious outcomes, including death, making this a public health concern. One of the most important side effects of COVID-19-induced insults is still myocardial damage. In order to finally decipher the intricate mechanisms at play, scientific studies into the underlying pathophysiology and clinical symptoms are still in progress. Some of the main causes of COVID-19's cardiac symptoms include ACE2, cytokine storm, endothelial injury, and coagulopathy. A number of

diagnostic techniques, including CT scan, ECG, Echo, CMR, EMB, and EMB, are utilized to identify the pathological alterations brought on by COVID-19. Since the start of the pandemic, a number of studies on this subject have been published; nevertheless, further research is needed to bolster the data.

References

1. Wu Z, McGoogan JM: Characteristics of and important lessons from the coronavirus disease 2019 (COVID-19) outbreak in China: summary of a report of 72 314 cases from the Chinese Center for Disease Control and Prevention. JAMA. 2020, 323:1239-1242. 10.1001/jama.2020.2648
2. Coronavirus Cases: Statistics and Charts – Worldometer. (2023). Accessed: January 09, 2023: https://www.worldometers.info/coronavirus/coronavirus-cases/.
3. Parohan M, Yaghoubi S, Seraji A: Cardiac injury is associated with severe outcome and death in patients with Coronavirus disease 2019 (COVID-19) infection: a systematic review and meta-analysis of observational studies. Eur Heart J Acute Cardiovasc Care. 2020, 9:665-677. 10.1177/2048872620937165
4. Lala A, Johnson KW, Januzzi JL, et al.: Prevalence and impact of myocardial injury in patients hospitalized with COVID-19 infection. J Am Coll Cardiol. 2020, 76:533-546. 10.1016/j.jacc.2020.06.007
5. Guzik TJ, Mohiddin SA, Dimarco A, et al.: COVID-19 and the cardiovascular system: implications for risk assessment, diagnosis, and treatment options. Cardiovasc Res. 2020, 116:1666-1687. 10.1093/cvr/cvaa106
6. Klein NP, Lewis N, Goddard K, et al.: Surveillance for adverse events after COVID-19 mRNA vaccination. JAMA. 2021, 326:1390-1399. 10.1001/jama.2021.15072
7. Chen L, Li X, Chen M, Feng Y, Xiong C: The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. Cardiovasc Res. 2020, 116:1097-1100. 10.1093/cvr/cvaa078
8. Li W, Moore MJ, Vasilieva N, et al.: Angiotensin-converting enzyme 2 is a functional receptor for the SARS coronavirus. Nature. 2003, 426:450-454. 10.1038/nature02145
9. Azevedo RB, Botelho BG, Hollanda JV, et al.: COVID-19 and the cardiovascular system: a comprehensive review. J Hum Hypertens. 2021, 35:4-11. 10.1038/s41371-020-0387-4
10. Kuba K, Imai Y, Rao S, et al.: A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat Med. 2005, 11:875-879. 10.1038/nm1267
11. Huang C, Wang Y, Li X, et al.: Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020, 395:497-506. 10.1016/S0140-6736(20)30183-5
12. Deshmane SL, Kremlev S, Amini S, Sawaya BE: Monocyte chemoattractant protein-1 (MCP-1): an overview. J Interferon Cytokine Res. 2009, 29:313-326. 10.1089/jir.2008.0027
13. Adeghate EA, Eid N, Singh J: Mechanisms of COVID-19-induced heart failure: a short review. Heart Fail Rev. 2021, 26:363-369. 10.1007/s10741-020-10037-x
14. Chen H, Wang C, Li J, et al.: Chinese herbal formula, huayu tongbi fang, attenuates inflammatory proliferation of rat

synoviocytes induced by IL-1β by regulating proliferation and differentiation of T lymphocytes. Evid Based Complement Alternat Med. 2020, 2020:1706837. 10.1155/2020/1706837

15. Xie Y, Wang X, Yang P, Zhang S: COVID-19 complicated by acute pulmonary embolism. Radiol Cardiothorac Imaging. 2020, 2:e200067. 10.1148/ryct.2020200067
16. Danzi GB, Loffi M, Galeazzi G, Gherbesi E: Acute pulmonary embolism and COVID-19 pneumonia: a random association?. Eur Heart J. 2020, 41:1858. 10.1093/eurheartj/ehaa254
17. McFadyen JD, Stevens H, Peter K: The emerging threat of (micro)thrombosis in COVID-19 and its therapeutic implications. Circ Res. 2020, 127:571-587. 10.1161/CIRCRESAHA.120.317447
18. Zhou F, Yu T, Du R, et al.: Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020, 395:1054-1062. 10.1016/S0140-6736(20)30566-3
19. Wenzhong L, Hualan L: COVID- 19: attacks the 1-beta chain of hemoglobin and captures the porphyrin to inhibit human heme metabolism [PREPRINT]. ChemRxiv. 2020, 10.26434/chemrxiv.11938173.v9
20. Libby P, Lüscher T: COVID-19 is, in the end, an endothelial disease. Eur Heart J. 2020, 41:3038-3044. 10.1093/eurheartj/ehaa623
21. Wiessman M, Shlomai A: Acute myocardial infarction after laboratory-confirmed influenza infection. N Engl J Med. 2018, 378:2539. 10.1056/NEJMc1805679
22. Wang D, Hu B, Hu C, et al.: Clinical characteristics of 138 hospitalized patients with 2019 novel coronavirus-infected pneumonia in Wuhan, China. JAMA. 2020, 323:1061-1069. 10.1001/jama.2020.1585
23. Chen D, Li X, Song Q, et al.: Hypokalemia and clinical implications in patients with coronavirus disease 2019 (COVID-19) [PREPRINT]. MedRxiv. 2020, 10.1101/2020.02.27.20028530
24. Siripanthong B, Nazarian S, Muser D, et al.: Recognizing COVID-19-related myocarditis: the possible pathophysiology and proposed guideline for diagnosis and management. Heart Rhythm. 2020, 17:1463-1471. 10.1016/j.hrthm.2020.05.001
25. Tajbakhsh A, Gheibi Hayat SM, Taghizadeh H, et al.: COVID-19 and cardiac injury: clinical manifestations, biomarkers, mechanisms, diagnosis, treatment, and follow up. Expert Rev Anti Infect Ther. 2021, 19:345-357. 10.1080/14787210.2020.1822737
26. Esfandiarei M, McManus BM: Molecular biology and pathogenesis of viral myocarditis. Annu Rev Pathol. 2008, 3:127-155. 10.1146/annurev.pathmechdis.3.121806.151534
27. Özer S, Bulut E, Özyıldız AG, Peker M, Turan OE: Myocardial injury in COVID-19 patients is associated with the thickness of epicardial adipose tissue. Kardiologiia. 2021, 61:48-53. 10.18087/cardio.2021.8.n1638
28. Hurst RT, Prasad A, Askew JW 3rd, Sengupta PP, Tajik AJ: Takotsubo cardiomyopathy: a unique cardiomyopathy with variable ventricular morphology. JACC Cardiovasc Imaging. 2010, 3:641-649. 10.1016/j.jcmg.2010.01.009
29. Medeiros K, O'Connor MJ, Baicu CF, et al.: Systolic and diastolic mechanics in stress cardiomyopathy. Circulation. 2014,

129:1659-1667. 10.1161/CIRCULATIONAHA.113.002781

30. Tsuchihashi K, Ueshima K, Uchida T, et al.: Transient left ventricular apical ballooning without coronary artery stenosis: a novel heart syndrome mimicking acute myocardial infarction. J Am Coll Cardiol. 2001, 38:11-18. 10.1016/S0735-1097(01)01316-X
31. Wittstein IS, Thiemann DR, Lima JA, et al.: Neurohumoral features of myocardial stunning due to sudden emotional stress. N Engl J Med. 2005, 352:539-548. 10.1056/NEJMoa043046
32. Jabri A, Kalra A, Kumar A, et al.: Incidence of stress cardiomyopathy during the coronavirus disease 2019 pandemic. JAMA Netw Open. 2020, 3:e2014780. 10.1001/jamanetworkopen.2020.14780
33. Aranyó J, Bazan V, Lladós G, et al.: Inappropriate sinus tachycardia in post-COVID-19 syndrome. Sci Rep. 2022, 12:298. 10.1038/s41598-021-03831-6
34. Heidari Gorji MA, Fatahian A, Farsavian A: The impact of perceived and objective social isolation on hospital readmission in patients with heart failure: a systematic review and meta-analysis of observational studies. Gen Hosp Psychiatry. 2019, 60:27-36. 10.1016/j.genhosppsych.2019.07.002
35. Pantell M, Rehkopf D, Jutte D, Syme SL, Balmes J, Adler N: Social isolation: a predictor of mortality comparable to traditional clinical risk factors. Am J Public Health. 2013, 103:2056-2062. 10.2105/AJPH.2013.301261
36. Kermali M, Khalsa RK, Pillai K, Ismail Z, Harky A: The role of biomarkers in diagnosis of COVID-19 – A systematic review. Life Sci. 2020, 254:117788. 10.1016/j.lfs.2020.117788
37. Dawson D, Dominic P, Sheth A, Modi M: Prognostic value of cardiac biomarkers in COVID-19 infection: a meta-analysis [PREPRINT]. Res Sq. 2020, 10.21203/rs.3.rs-34729/v1
38. Zhu Z, Wang M, Lin W, et al.: Cardiac biomarkers, cardiac injury, and comorbidities associated with severe illness and mortality in coronavirus disease 2019 (COVID-19): a systematic review and meta-analysis. Immun Inflamm Dis. 2021, 9:1071-1100. 10.1002/iid3.471
39. Coomes EA, Haghbayan H: Interleukin-6 in COVID-19: a systematic review and meta-analysis. Rev Med Virol. 2020, 30:1-9. 10.1002/rmv.2141
40. Long B, Brady WJ, Koyfman A, Gottlieb M: Cardiovascular complications in COVID-19. Am J Emerg Med. 2020, 38:1504-1507. 10.1016/j.ajem.2020.04.048
41. Iorio A, Lombardi CM, Specchia C, et al.: Combined role of troponin and natriuretic peptides measurements in patients with COVID-19 (from the Cardio-COVID-Italy Multicenter Study). Am J Cardiol. 2022, 167:125-132. 10.1016/j.amjcard.2021.11.054
42. Stavileci B, Özdemir E, Özdemir B, Ereren E, Cengiz M: De-novo development of fragmented QRS during a six-month follow-up period in patients with COVID-19 disease and its cardiac effects. J Electrocardiol. 2022, 72:44-48. 10.1016/j.jelectrocard.2022.02.012
43. Kochi AN, Tagliari AP, Forleo GB, Fassini GM, Tondo C: Cardiac and arrhythmic complications in patients with COVID-19. J Cardiovasc Electrophysiol. 2020, 31:1003-1008. 10.1111/jce.14479
44. Kociol RD, Cooper LT, Fang JC, et al.: Recognition and initial management of

fulminant myocarditis: a scientific statement from the American Heart Association. Circulation. 2020, 141:69-92. 10.1161/CIR.0000000000000745

45. Adeboye A, Alkhatib D, Butt A, Yedlapati N, Garg N: A review of the role of imaging modalities in the evaluation of viral myocarditis with a special focus on COVID-19-related myocarditis. Diagnostics (Basel). 2022, 12:549. 10.3390/diagnostics12020549
46. Cau R, Bassareo P, Saba L: Cardiac involvement in COVID-19-assessment with echocardiography and cardiac magnetic resonance imaging. SN Compr Clin Med. 2020, 2:845-851. 10.1007/s42399-020-00344-7
47. Weckbach LT, Curta A, Bieber S, et al.: Myocardial inflammation and dysfunction in COVID-19-associated myocardial injury. Circ Cardiovasc Imaging. 2021, 14:e012220. 10.1161/CIRCIMAGING.120.011713
48. D'Andrea A, Cante L, Palermi S, et al.: COVID-19 myocarditis: prognostic role of bedside speckle-tracking echocardiography and association with total scar burden. Int J Environ Res Public Health. 2022, 19:5898. 10.3390/ijerph19105898
49. Caforio AL, Pankuweit S, Arbustini E, et al.: Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. Eur Heart J. 2013, 34:2636-2648. 10.1093/eurheartj/eht210
50. Bihan H, Heidar R, Beloeuvre A, et al.: Epicardial adipose tissue and severe Coronavirus Disease 19. Cardiovasc Diabetol. 2021, 20:147. 10.1186/s12933-021-01329-z