

Myocardial injury in COVID-19: A case series



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ABSTRACT

The COVID-19 pandemic has affected nearly millions of populations worldwide. The range of symptomatology is vast, though predominantly respiratory, and ranges from mild flu-like symptoms to severe respiratory illness with acute respiratory distress syndrome. COVID-19 is associated with many non-respiratory complications affecting the heart, kidneys, gastrointestinal system, central nervous system, and blood vessels. Myocardial injury in COVID-19 patients has varied presentations ranging from arrhythmias, myocardial infarction, myocarditis, and cardiomyopathy to cardiogenic shock. It is usually associated with elevated levels of cardiac biomarkers, with or without any changes in electrocardiography or cardiac imaging. Diagnosis may be difficult based on clinical symptoms or electrocardiogram changes alone, and it can be made using 2D echocardiography, coronary angiogram, CT coronary angiogram, or cardiac magnetic resonance imaging, depending on clinical suspicion. COVID-19-associated cardiac injury increases overall morbidity and mortality. In this case series, five COVID-19 cases with different cardiac manifestations were reported with the intention of presenting the various manifestations of cardiac complications, the course of the disease, and the challenges associated with the complications. This case series showed that cardiac complications are common in the 2nd week during the cytokine storm phase, and timely case-specific specialized diagnostic and therapeutic cardiac interventions might improve the chances of patient survival.

Key words: COVID-19; Myocardial injury; Myocarditis; Electrocardiogram; Troponin

INTRODUCTION

The COVID-19 pandemic has affected nearly millions of populations worldwide.¹ The range of symptomatology is wide, though predominantly respiratory, and ranges from mild flu-like symptoms to severe respiratory illness with acute respiratory distress syndrome (ARDS). COVID-19 is associated with many non-respiratory complications affecting the heart, kidneys, gastrointestinal system, central nervous system, and blood vessels. Myocardial injury in COVID-19 patients has varied presentations ranging from arrhythmias, myocardial infarction, myocarditis, and cardiomyopathy to cardiogenic shock and is usually associated with elevated levels of cardiac biomarkers with or without any changes in electrocardiography or cardiac imaging.^{2,3} In this case series, five COVID-19 cases with different cardiac manifestations were reported with the intention of presenting the different manifestations of cardiac complications, the course of the disease, and the challenges associated with the complications.

CASE 1

A 55-year-old male was admitted with a history of fever, cough, and expectoration for 3 weeks, shortness of breath, and generalized body swelling. There was no history of diabetes mellitus, hypertension, coronary artery disease, chronic kidney disease, or cerebrovascular accidents in the past. The patient's reverse transcription polymerase chain reaction (RT-PCR) for the COVID-19 report came back positive. Vitals were PR: 110 beats/min, BP: 110/80 mmHg, and SpO₂:88%. Baseline arterial blood gas analysis showed pO₂ of 66 mmHg on fI_O₂-0.5. The electrocardiogram (ECG) depicted a normal sinus rhythm at 110 beats/min. He was admitted to the intensive care unit (ICU) and put on high-flow oxygen therapy with a non-rebreathing mask (NRBM) at 15L/min. Investigation revealed hemoglobin 4 g/dL (13–17 g/dL), total leucocyte count 59300/mm³ (4500–11000/mm³), platelet count 1.3 lakhs/mm³ (1.5–4.5 lakhs/mm³),

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D-dimer 1125 ng/mL (normal <250 ng/mL), serum ferritin 396.38 ng/mL (normal 20–250 ng/mL), and IL6 181.36 pg/mL (5–15 pg/mL). His cardiac biomarkers were troponin-I 0.09 ng/mL (N: <0.1 ng/mL) and NT-proBNP 566 pg/mL (N: <300 pg/mL). The patient was started on injection of Remdesivir, intravenous antibiotic piperacillin-tazobactam, and subcutaneous low-molecular-weight heparin (Clexane 60 mg twice daily). Four units of packed red cells were transfused, and hemoglobin was 7 g/dL post-transfusion. Given the increased leucocyte count, a hematological evaluation was done, which suggested suspicion of chronic myeloid leukemia.

On day 4, the patient developed an acute episode of palpitation that was not associated with any giddiness, syncope, or increased severity of breathlessness or oxygen requirement. PR was 200 beats/min, irregularly irregular, BP 100/70 mmHg, and SpO₂ 95% (face mask as 6 L/min). The ECG showed new-onset atrial fibrillation (AF). The echocardiogram showed hypokinesia of the anterior, anteroseptal, and anterolateral walls with a left ventricular ejection fraction of 45%. There was no evidence of any clot in the left atrial appendage. There was also no evidence of acute pulmonary embolism in the form of a dilated right atrium, a dilated right ventricle, or tricuspid regurgitation. The patient's repeat cardiac markers at the time of AF were elevated with cardiac troponin I of 0.77 ng/mL (normal <0.1 ng/mL) and NT-ProBNP of 35000 pg/mL (normal <300 pg/mL). The possibility of acute myocarditis was kept.

The patient was started on an injection of methylprednisolone at a dose of 1 mg/kg for 3 days. For AF, pharmacological cardioversion was tried with a loading dose of intravenous amiodarone 150 mg. However, there was no response to the

amiodarone dose. Following this, a rate-control strategy was tried by injecting diltiazem at a dose of 15 mg intravenously. The patient's heart rate came down to 90 beats/min (Figure 1), and he remained hemodynamically stable after that. On day 6, the ECG showed normal sinus rhythm with a heart rate of 88 beats/min (ECG 1). The patient was shifted to the general ward on day 10 on room air and discharged 1 week after his RT-PCR became negative for COVID-19. Later, cardiac magnetic resonance imaging (MRI) was done, which showed no evidence of any myocarditis with a normal left ventricular ejection fraction.

CASE 2

An 80-year-old male presented with a history of dry cough for 5 days. He had hypertrophic obstructive cardiomyopathy (HOCM) and was on beta-blocker therapy for the last 10 years. He had chronic obstructive pulmonary disease and was on regular treatment with Salmeterol and Budesonide inhaler therapy for 10 years. Vitals were HR 66 beats/min, BP 110/60 mmHg, and SpO₂ at room air 98%. RT-PCR for COVID-19 was positive. On day 11 in the isolation ward, he developed an acute onset of palpitations with chest pain. There was no history of giddiness, syncope, or perspiration. At the time of palpitation, his PR was 170 beats/min, and his ECG revealed broad complex regular tachycardia with no evidence of atrioventricular dissociation, fusion beat, or capture beat. Tachycardia spontaneously reverted to a normal sinus rhythm. Following this, the patient was shifted to the ICU for continuous cardiac monitoring. In the ICU, his PR was 142 beats/min with a BP of 94/60 mmHg. His investigations were serum creatinine of 1.7 mg/dL (0.8–1.2 mg/dL), Troponin-I 0.77 ng/mL (normal 0.1 ng/dL),

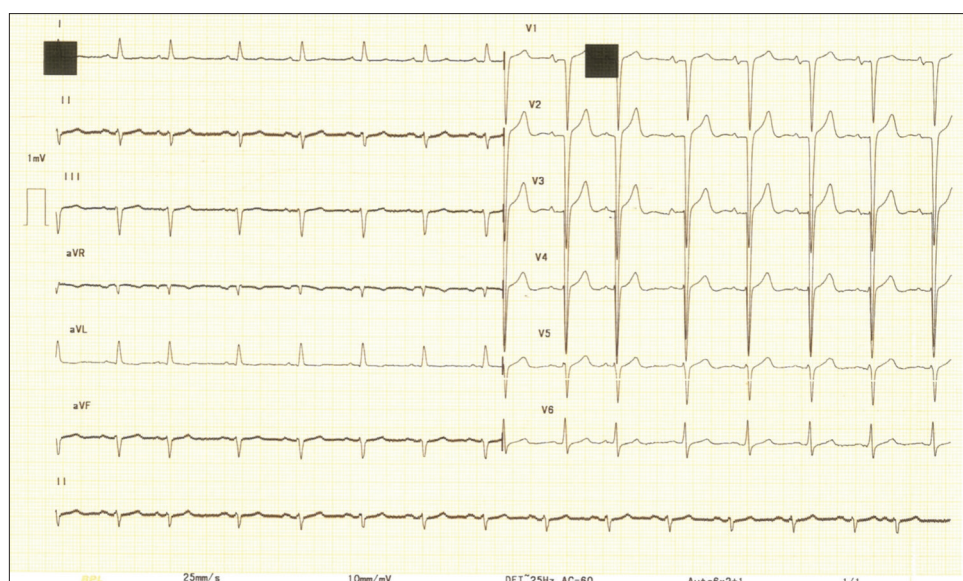


Figure 1: Electrocardiogram after giving injection diltiazem is showing normal sinus rhythm, left axis deviation with heart rate of 88 bpm

NT-pro BNP 12315 pg/mL (normal <300 pg/mL), D-Dimer 1977 ng/mL (normal <250 ng/mL), and fibrinogen 394 mg/dL (normal 200–400 mg/dL).

In the ICU, he developed another episode of broad complex tachycardia that terminated spontaneously. The patient was given an amiodarone loading dose of 150 mg i.v. He received IV antibiotics: inj methylprednisolone 50 mg twice a day, inj clexane 50 mg s.c. once daily, and tab metoprolol 50 mg daily. Repeat cardiac markers on day 2 revealed an increasing trend of serum troponin-I (16.06 ng/mL) and NT-Pro BNP (17712 pg/mL). On day 3, his serum troponin-I levels decreased (6.04 ng/mL). Hemodynamically, he became stable. His 2D echocardiogram revealed severe mitral regurgitation, a dilated left atrium, and asymmetrical septal hypertrophy. There was no evidence of any regional wall motion abnormalities or a left ventricular ejection fraction >60%. There was no evidence of pulmonary embolism, vegetation, clots, or pericardial effusion. The patient was shifted to the ward on day 5 and discharged after 12 days. The patient was advised to get a cardiac MRI done for further evaluation.

CASE 3

An 80-year-old female was admitted with fever, generalized weakness, and shortness of breath for 4 days. She had no comorbid illnesses like hypertension, diabetes, seizure disease, or cardiorespiratory diseases. She had a history of typhoid fever 1 month back. On examination, she had altered sensorium with a Glasgow coma scale (GCS) of 9/15, dyspnea with room-air SpO₂ of 75%, and diffuse bilateral crackles on auscultation. Her hemodynamic parameters and temperature were within normal limits. On

oxygen therapy using a NRBM with a flow of 15 l/min, SpO₂ went up to 90%. The initial ECG showed a normal sinus rhythm. A chest radiograph revealed bilateral reticulonodular opacities. A nasopharyngeal swab sample was sent for RT-PCR for COVID-19, which was positive. She was transferred to the COVID-19-positive ICU.

Her baseline investigations were within normal limits. Standard COVID-19 management was initiated as per protocol, including remdesivir, methylprednisolone, and anticoagulants. She was intubated in view of gradually decreasing oxygen saturation in the background of low GCS on day 2 (SpO₂ below 85% with fiO₂ of 1.0, GCS-9/15). She was put on 'volume assist control' mode with low tidal volume and high PEEP (Vt-350 mL, RR-24/min, PEEP-10 cm H₂O). Ventilatory settings were titrated according to the ARDS net trial. Her oxygenation status improved gradually with oxygen saturation in the range of 90–92% with a fiO₂ of 0.8. On day 5, she became hypotensive, which necessitated initiating a vasopressor infusion of noradrenaline and vasopressin. The ECG showed atrial tachycardia with a rate of around 150/min (Figure 2). Troponin-I and pro-BNP were 1.45 ng/mL and 6847 pg/mL, respectively. Her 2D echocardiography showed an ejection fraction of 30–35% with a regional wall motion abnormality in the anterolateral wall. Management was started in line with cardiogenic shock, including initiating an inotropic drug infusion of dobutamine at 5 mic/kg/min. On day 6, her hemodynamic parameters were worsening, further necessitating an escalation of vasopressor dosage. Her repeat Troponin-I and pro-BNP were 1.03 ng/mL and 6742 pg/mL, respectively, on day 6. There was a progressive deterioration of the kidney profile, with a subsequent decline in urine output. Due to the lack

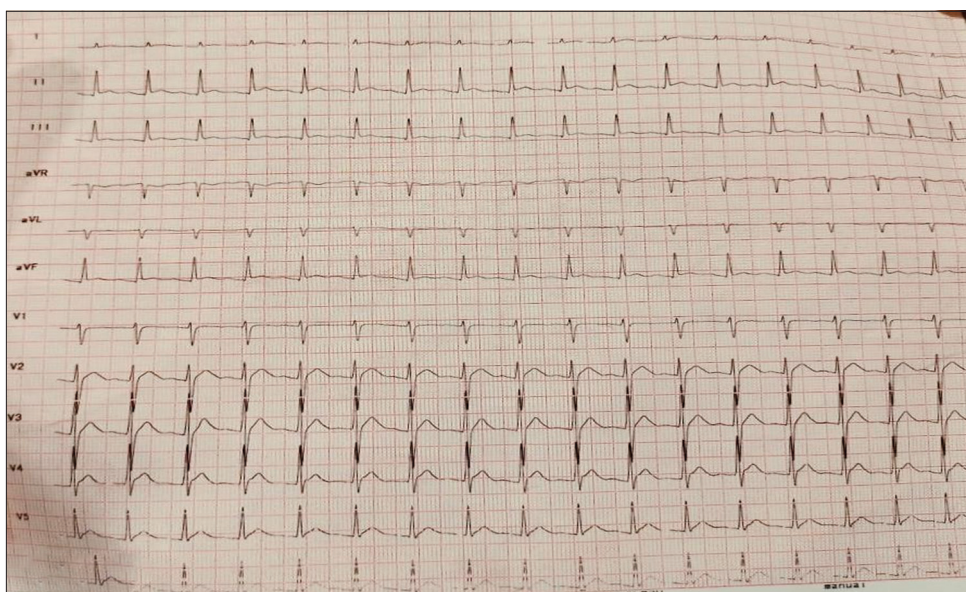


Figure 2: 12 lead electrocardiogram showing atrial tachycardia with a heart rate around 150 bpm

of COVID-19--specific superspeciality infrastructure and equipment, some needed procedures could not be attempted. On day 7, she had two episodes of cardiac arrest and could not be revived.

CASE 4

A 76-year-old female, a known diabetic patient on irregular treatment, was admitted with complaints of fever, cough, and shortness of breath for the last 7 days. On admission, she had dyspnea with a respiratory rate of 25 breaths/min and oxygen saturation of 93% on the NRBM with an oxygen flow of 15 L/min. Her hemodynamic profile was within normal limits with a temperature of 99°F, and random blood sugar was 99 mg/dL. Her HRCT chest revealed multiple patchy ground glass opacities with a CT score of 10/25. Her ECG showed no abnormality. She was shifted to the COVID ICU as her nasopharyngeal sample for RT-PCR came positive for COVID. As per ICU protocol, she was started on remdesivir, methylprednisolone, anticoagulants, and antibiotics. Her baseline investigations were within the normal limits.

On day 3, her hemodynamic profile rapidly deteriorated with desaturation to 84–86%, which necessitated intubation and vasopressor support. Lung protective ventilation was initiated with low tidal volume and high respiratory rate, and PEEP was increased gradually to maintain saturation of 92–94% (VAC mode: Vt-320ml, RR-28/min, PEEP-10 cm of H₂O, FiO₂-0.8). Cardiac biomarkers were elevated: Trop-I 10.31 ng/mL and Pro BNP 35000 pg/mL. Her C-reactive protein (CRP) was 136 mg/L (n = <10 mg/L) and LDH was 1070u/L (n=140–280 u/L).

Her 2D echocardiography revealed abnormal movement of the septum due to the left bundle branch block, no RWMA, and a normal ejection fraction. Her urine output started declining with an abnormal kidney function test on day 5. She had three episodes of rectal bleeding, for which anticoagulant therapy was withheld, and she was transfused with four units of fresh frozen plasma and two units of packed red cells. Her post-transfusion Hb was? Her abdominal ultrasound showed no abnormality with minimally raised bilateral renal cortical echogenicity. On day 6 of the ICU stay, she became hemodynamically unstable and non-responsive to vasopressor therapy. Gradually, she went into cardiac arrest and could not be revived.

CASE 5

A 72-year-old female with a history of diabetes and hypertension for the past 20 years on regular treatment was admitted with a recent seizure episode and loss of

consciousness. She tested COVID positive 9 days back. She was intubated and put on a mechanical ventilator in view of her low GCS. On day 3, she became conscious of the GCS of E₄V₁M₄. She was in the pressure control mode of ventilation with an inspiratory pressure of 16 cm H₂O, a PEEP of 6 cm H₂O, a FiO₂ of 0.4, and a respiratory rate of 16/min. Her BP was 150/94 mm of Hg, her heart rate was 79 per minute, her SpO₂ was 100%, and her random blood sugar was 196 mg/dL.

Her MRI brain showed an acute vascular event and a small infarct in the left parietal lobe. Her EEG revealed generalized slowing of waves, periodic slow waves, and triphasic waves, suggesting encephalopathy (metabolic or hypoxic). HRCT thorax showed severe lung involvement with a CT severity score of 16/25 and bilateral pleural effusion with collapse and consolidation. ECG showed PR prolongation, ST depression, and left axis deviation. She was on insulin therapy: tablet glimepiride 2 mg and metformin 1000 mg for diabetes, tablet losartan 50 mg, and tablet metoprolol 12.5 mg for hypertension. After admission, she received meropenem, teicoplanin, levetiracetam, low-molecular-weight heparin, dexamethasone, aspirin, insulin, and antihypertensives.

Her ultrasound chest showed a right-sided pleural effusion with a maximum depth of 6 cm. Under ultrasound guidance, tapping was done, and only 10 mL of straw-colored transudative fluid could be aspirated from the right-sided pleural space. A neurological review was done in view of fluctuating GCS (E₃V₁M₂) and abnormal findings on neurological investigation. She was prescribed injection eptoin, injection lorazepam, and injection acyclovir as per the neurologist's advice.

Her cardiac biomarkers were elevated with a Trop-I level of 8 ng/mL on day 2 of the ICU stay. Her 2D echo showed global hypokinesia with an LV ejection fraction of 30% and signs of myocarditis. Serial cardiac biomarkers over the next week had a decreasing trend, and it normalized on the 9th day. Her neurological status did not improve much, though she remained hemodynamically stable in the initial days. On the 28th day of her ICU stay, she had a sudden episode of hypotension and ST-T changes on the ECG, following which cardiac markers were repeated. The report revealed Trop-I 4.57 ng/mL, pro-BNP 9003 pg/mL, CRP 18 mg/L, and procalcitonin<0.5. A repeat 2D echo showed global hypokinesia with an LV ejection fraction of 25%. Inotropic support was initiated, but she went into cardiac arrest and expired on day 31 of her ICU stay.

DISCUSSION

Acute cardiac injury is a known complication in COVID-19 patients of all age groups.^{4,5} Various mechanisms

have been proposed and elaborated upon regarding cardiac symptomatology. Evidence from autopsies of COVID patients revealed the presence of SARS-CoV-2 in the myocardial tissue.⁶ Research on SARS-CoV, which is genetically related to SARS-CoV-2, revealed that it was a cardiotropic virus that attacked the cardiomyocytes by binding to ACE-2 receptors on the cardiomyocytes and endothelium.⁷

In case 1, cardiac manifestations (supraventricular tachycardia, elevated Troponin-I) could be due to the imbalance between the oxygen supply and demand due to anemia, a manifestation of COVID-19, or both. Conservative management was followed, including anticoagulants and beta blockers. Myocarditis was ruled out in view of a normal echo and cardiac MRI.

In case 2, the patient had HOCM and a low cardiac reserve. The myocardial oxygen supply was further decreased because of hypoxia secondary to COVID-19 pneumonia, resulting in ischemic changes, chest pain, and ventricular tachycardia, which further caused an oxygen supply-demand imbalance. However, with oxygen supplementation and amiodarone-assisted ventricular rate control, the oxygen demand was reduced, and the patient showed clinical improvement. Myocarditis could not be ruled out as the cardiac MRI could not be performed.

Case 3 presented with hypoxia and altered mentation. Cardiac symptoms began on the 9th day, most likely in the cytokine storm phase, as a symptom of multiorgan dysfunction syndrome (ARDS, myocarditis, and cardiogenic shock with acute renal injury).

Similarly, in case 4, the hemodynamics deteriorated on day 10 of the symptom onset. With the existing COVID infrastructure, mechanical cardiac support like IABP/extracorporeal membrane oxygenation (ECMO) and other diagnostic investigations could not be performed to identify exact cardiac pathology.

In case 5, investigations revealed increased cardiac biomarkers 10 days after the onset of symptoms. She had a history of seizures, was diabetic, and had high blood pressure. Poor left ventricular function was found on echo, along with generalized hypokinesia and myocarditis-related symptoms. Neither cardiac MRI nor endomyocardial biopsy could provide a conclusive diagnosis of myocarditis. Over 1 week, the increased biomarkers progressively returned to normal, but by the 4th week, there was a new rise of cardiac biomarkers with hemodynamic instability.

SARS-CoV-2 utilizes its spike protein to bind to the membrane-bound ACE-2 receptors on host cells to

facilitate the entry.⁸ Once inside the cell, it inhibits stress granule formation, facilitating intracellular viral replication and cellular damage. It has been found that downregulation of ACE-2 receptors is associated with increased angiotensin-2 levels, a potent vasoconstrictor. It is associated with an increase in bradykinin levels, which has a negative effect through the release of the proinflammatory cytokine IL-6.⁹ This is associated with the release of large amounts of inflammatory mediators such as TNF-alpha, IL-1, IL-6, and IFN- γ . Elevated levels of high-sensitivity troponin (hs-cTnI), creatine kinase-MB (CK-MB), IL-6, and procalcitonin are associated with a decrease in T-lymphocytes and the CD4/CD8 ratio, suggesting a damaging effect.¹⁰ The inflammatory mediators can activate the coagulation pathways and cause thromboembolic complications.¹¹ Autopsy studies in COVID patients have shown the presence of mononuclear infiltrates in the cardiac myocytes, implicating inflammatory damage.¹²

By creating an imbalance in the oxygen demand-supply ratio, hypoxemia related to a deteriorating pulmonary condition can negatively impact heart performance. This can result in mitochondrial injury, lactic acidosis, the generation of oxygen-free radicals, or hypoxic inflammatory responses.¹³ Patients with an underlying cardiovascular disease have low cardiac reserve and are at higher risk for cardiovascular complications.¹⁴ COVID-19 patients with myocardial injuries may present with varying symptoms, depending on the severity of the affection. Symptoms may be mild in the form of fatigue or breathlessness, chest pain, or chest tightness.¹⁵ In severe cases, they may present with arrhythmias, cardiogenic shock, or heart failure.¹⁶ A global survey conducted by the Heart Rhythm Society observed that the prevalence of arrhythmias was higher in patients with myocardial injury, and 6–17% of patients with COVID-19 infection were found to have some arrhythmia.¹⁷ AF was found to be the most common form of cardiac arrhythmia seen among COVID-19 patients. High levels of hs-cTnI and NT-pro BNP are essential markers for myocardial injury.^{18,19} Differential diagnoses for patients with suspected myocardial injury with raised hs-cTnI levels include acute or chronic myocarditis, type-1 or type-2 myocardial infarction, stress-induced cardiomyopathy, and sepsis-induced cardiomyopathy.

Patients developing myocarditis may present in the acute stage after an inflammatory response to cytokines. Fulminant myocarditis may mimic features of sepsis like fever, sinus tachycardia, and cold peripheries.²⁰ Myocarditis is frequently associated with ventricular arrhythmias and monomorphic ventricular tachycardias.²¹ ECG abnormalities (ST elevation, PR depression, AF, sinus bradycardia, bundle branch block, QT prolongation) and elevation of cardiac biomarkers like hs-cTnI and NT-pro

BNP may be observed. Still, non-elevation of troponin cannot completely rule out myocarditis.^{6,7} Inflammatory markers such as CRPs, erythrocyte sedimentation rate, and procalcitonin may often be elevated in myocarditis. American Heart Association recommendations for patients with suspected myocarditis include cardiac imaging in the form of echocardiography or cardiovascular magnetic resonance (CMR).²⁰ Echocardiographic features of myocarditis include increased wall thickness, chamber dilatation, ventricular systolic dysfunction, and pericardial effusion.

Cardiovascular MRI is interpreted as per revised Lake Louise consensus criteria, which include edema, irreversible cell injury, hyperemia, and capillary leak.²¹ In patients where CMR is not possible, contrast-enhanced computed tomography with ECG gating is indicated.²² For a definitive diagnosis of myocarditis, an endomyocardial biopsy is recommended. Management of fulminant myocarditis includes management of cardiogenic shock using inotropes and vasopressors, antiarrhythmic drugs to treat arrhythmias, the use of an intra-aortic balloon pump, ventricular assist devices, and ECMO. The beneficial effects of intravenous immunoglobulin and corticosteroids in treating myocarditis are controversial.²³ A systematic review by Castiello et al. highlighted that the occurrence of myocarditis with and without direct myocyte damage suggested different pathophysiologic mechanisms and diverse therapeutic approaches.²⁴ According to the review, the presence or absence of virus in the myocytes was required to confirm the diagnosis and decide the management; virus-negative patients most likely benefitted from immunosuppressant therapy, while viral-positive patients responded to antiviral drugs.

Acute coronary syndrome is diagnosed based on clinical symptoms, elevated cardiac biomarkers, and ECG changes and confirmed with a CT coronary angiogram. Patients with ST-elevation myocardial infarction (STEMI) are candidates for percutaneous coronary intervention (PCI).²⁵ If PCI facilities are unavailable, then fibrinolysis is indicated. Mechanical circulatory support (intra-aortic balloon pump, or ECMO) is indicated for hemodynamic instability. Patients with non-STEMI can be managed conservatively with medical stabilization unless they present with hemodynamic instability.

Takotsubo cardiomyopathy (TCM), also known as stress-induced cardiomyopathy, is a reversible non-ischemic systolic dysfunction of the left ventricle classically seen after stress exposure, characterized by the transient weakening of the myocytes and ballooning of the apical region.^{26,27} ECG abnormalities and cardiac biomarkers mimic an ACS. The primary mechanism appears to be excessive catecholamine levels in circulation and their effects on cardiomyocytes.²⁸ Levels of cortisol and catecholamine are increased

secondary to inflammation, and cytokine storms might be the cause of the direct toxic effect on cardiomyocytes in COVID patients, resulting in TCM. In the acute phase, patients with TCM may present with cardiogenic shock, left ventricular outflow obstruction, free wall or septal rupture, arrhythmias, or thromboembolic complications. Special care must be taken to rule out LV outflow obstruction, as diuretics and underfilling the left ventricle may worsen the clinical condition. Inotropic agents result in deleterious consequences, as catecholamines have been presumed to be the primary cause of TCM. For rate regulation, beta-blockers or ivabradine can be taken into consideration. Early placement of mechanical support, such as an intra-aortic balloon pump, ventricular assist device, or veno-arterial ECMO, may improve the outcome for these patients.

Sepsis-related cardiomyopathy is a reversible condition characterized by left ventricular dilatation, impaired ejection fraction, and recovery in 7–10 days. It has been reported in many critically ill COVID patients on vasopressor therapy for coexisting septic shock.²⁹

A systematic review by Brogi et al., in 2022 evaluated the types of cardiac complications and their risk factors in COVID-19 patients and identified acute cardiac injury as the most prevalent cardiac complication observed (20–45%).³⁰ It was more prevalent in older patients with comorbidities, resulting in higher mortality rates. Because of the scarcity of evidence regarding Takotsubo, myocarditis, pleural effusion, and right ventricular dysfunction in COVID-19 patients, they could not come to any valid conclusion. The incidence of arrhythmia was found to range from 3% to 60% in COVID patients and was responsible for the consequent hemodynamic instability and morbidity. The most common comorbidity in COVID-19 patients was hypertension (30–59.8%), with a high prevalence of cardiovascular disease in this group (up to 57%), with coronary artery disease accounting for 10%.

CONCLUSION

The clinical manifestation of myocardial damage caused by COVID-19 varies. Only based on clinical symptoms or ECG alterations, the diagnosis may be challenging. Depending on the clinical suspicion, a diagnosis may be made using 2D echocardiography, coronary angiography, CT coronary angiogram, or cardiac MRI. Heart damage caused by COVID increases the overall morbidity and mortality rate. This case series demonstrated that cardiac problems are frequent during the cytokine storm phase in the 2nd week and that prompt, case-specific, specialized diagnostic and therapeutic cardiac interventions may increase patient survival rates.

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REFERENCES

- Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, 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(10229):1054-1062. [https://doi.org/10.1016/S0140-6736\(20\)30566-3](https://doi.org/10.1016/S0140-6736(20)30566-3)
- Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, et al. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol*. 2020;5(7):802-810. <https://doi.org/10.1001/jamacardio.2020.0950>
- Guo T, Fan Y, Chen M, Wu X, Zhang L, He T, et al. Cardiovascular implications of fatal outcomes of patients with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):811-818. <https://doi.org/10.1001/jamacardio.2020.1017>
- Rodriguez-Morales AJ, Cardona-Ospina JA, Gutiérrez-Ocampo E, Villamizar-Peña R, Holguin-Rivera Y, Escalera-Antezana JB, et al. Clinical, laboratory and imaging features of COVID-19: A systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;34:101623. <https://doi.org/10.1016/j.tmaid.2020.101623>
- Li B, Yang J, Zhao F, Zhi L, Wang X, Liu L, et al. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clin Res Cardiol*. 2020;109(5):531-538. <https://doi.org/10.1007/s00392-020-01626-9>
- Lindner D, Fitzek A, Bräuninger H, Aleshcheva G, Edler C, Meissner K, et al. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases. *JAMA Cardiol*. 2020;5(11):1281-1285. <https://doi.org/10.1001/jamacardio.2020.3551>
- Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 Cell entry Depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. *Cell*. 2020;181(2):271-280.e8. <https://doi.org/10.1016/j.cell.2020.02.052>
- Komarowska I, Coe D, Wang G, Haas R, Mauro C, Kishore M, et al. Hepatocyte growth factor receptor c-met instructs T cell cardiotropism and promotes T cell migration to the heart via autocrine chemokine release. *Immunity*. 2015;42(6):1087-1099. <https://doi.org/10.1016/j.immuni.2015.05.014>
- Santoso A, Pranata R, Wibowo A, Al-Farabi MJ, Huang I and Antariksa B. Cardiac injury is associated with mortality and critically ill pneumonia in COVID-19: A meta-analysis. *Am J Emerg Med*. 2021;44:352-357. <https://doi.org/10.1016/j.ajem.2020.04.052>
- Van der Poll T and Levi M. Crosstalk between inflammation and coagulation: The lessons of sepsis. *Curr Vasc Pharmacol*. 2012;10(5):632-638. <https://doi.org/10.2174/157016112801784549>
- Xu Z, Shi L, Wang Y, Zhang J, Huang L, Zhang C, et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. *Lancet Respir Med*. 2020;8(4):420-422. [https://doi.org/10.1016/S2213-2600\(20\)30076-X](https://doi.org/10.1016/S2213-2600(20)30076-X)
- Peng W, Wu H, Tan Y, Li M, Yang D and Li S. Mechanisms and treatments of myocardial injury in patients with corona virus disease 2019. *Life Sci*. 2020;262:118496. <https://doi.org/10.1016/j.lfs.2020.118496>
- Guan W, Ni Z, Hu Y, Liang WH, Ou C, He J, et al. Clinical characteristics of corona virus disease 2019 in China. *N Engl J Med*. 2020;382:1708-1720. <https://doi.org/10.1056/NEJMoa2002032>
- Inciardi RM, Lupi L, Zacccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):819-824. <https://doi.org/10.1001/jamacardio.2020.1096>
- Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, et al. First case of COVID-19 complicated with fulminant myocarditis: A case report and insights. *Infection*. 2020;48(5):773-777. <https://doi.org/10.1007/s15010-020-01424-5>
- Bhatla A, Mayer MM, Adusumalli S, Hyman MC, Oh E, Tierney A, et al. COVID-19 and cardiac arrhythmias. *Heart Rhythm*. 2020;17(9):1439-1444. <https://doi.org/10.1016/j.hrthm.2020.06.016>
- Gopinathannair R, Merchant FM, Lakkireddy DR, Etheridge SP, Feigofsky S, Han JK, et al. COVID-19 and cardiac arrhythmias: A global perspective on arrhythmia characteristics and management strategies. *J Interv Card Electrophysiol*. 2020;59(2):329-336. <https://doi.org/10.1007/s10840-020-00789-9>
- Gordon JS and Drazner MH. Biomarkers of cardiac stress and cytokine release syndrome in COVID-19: A review. *Curr Heart Fail Rep*. 2021;18(3):163-168. <https://doi.org/10.1007/s11897-021-00505-2>
- Kociol RD, Cooper LT, Fang JC, Moslehi JJ, Pang PS, Sabe MA, et al. Recognition and initial management of fulminant myocarditis: A scientific statement from the American heart association. *Circulation*. 2020;141(6):e69-e92. <https://doi.org/10.1161/cir.0000000000000745>
- Peretto G, Sala S, Rizzo S, Palmisano A, Esposito A, De Cobelli F, et al. Ventricular arrhythmias in myocarditis: Characterization and relationships with myocardial inflammation. *J Am Coll Cardiol*. 2020;75(9):1046-1057. <https://doi.org/10.1016/j.jacc.2020.01.036>
- Friedrich MG, Sechtem U, Schulz-Menger J, Holmvang G, Alakija P, Cooper LT, et al. Cardiovascular magnetic resonance in myocarditis: A JACC white paper. *J Am Coll Cardiol*. 2009;53(17):1475-1487. <https://doi.org/10.1016/j.jacc.2009.02.007>
- Caforio AL, Pankuweit S, Arbustini E, Basso C, Gimeno-Blanes J, Felix SB, et al. European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. 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(33):2636-48, 2648a-2648d. <https://doi.org/10.1093/eurheartj/ehd210>
- Li Y, Yu Y, Chen S, Liao Y and Du J. Corticosteroids and intravenous immunoglobulin in pediatric myocarditis: A meta-analysis. *Front Pediatr*. 2019;7:342. <https://doi.org/10.3389/fped.2019.00342>
- Castiello T, Georgiopoulos G, Finocchiaro G, Claudia M, Gianatti A, Delialis D, et al. COVID-19 and myocarditis: A systematic review and overview of current challenges. *Heart Fail Rev*. 2022;27(1):251-261. <https://doi.org/10.1007/s10741-021-10087-9>
- Mahmud E, Dauerman HL, Welt FG, Messenger JC, Rao SV,

- Grines C, et al. Management of acute myocardial infarction during the COVID-19 pandemic: A position statement from the society for cardiovascular angiography and interventions (SCAI), the American college of cardiology (ACC), and the American college of emergency physicians (ACEP). *J Am Coll Cardiol.* 2020;76(11):1375-1384.
<https://doi.org/10.1016/j.jacc.2020.04.039>
26. Ghadri JR, Wittstein IS, Prasad A, Sharkey S, Dote K, Akashi YJ, et al. International Expert consensus document on takotsubo syndrome (Part I): Clinical characteristics, diagnostic criteria, and pathophysiology. *Eur Heart J.* 2018;39(22):2032-2046.
<https://doi.org/10.1093/eurheartj/ehy076>
27. Wittstein IS, Thiemann DR, Lima JA, Baughman KL, Schulman SP, Gerstenblith G, et al. Neurohumoral features of myocardial stunning due to sudden emotional stress. *N Engl J Med.* 2005;352(6):539-548.
<https://doi.org/10.1056/nejmoa043046>
28. Tan T, Khoo B, Mills EG, Phylactou M, Patel B, Eng PC, et al. Association between high serum total cortisol concentrations and mortality from COVID-19. *Lancet Diabetes Endocrinol.* 2020;8(8):659-660.
[https://doi.org/10.1016/s2213-8587\(20\)30216-3](https://doi.org/10.1016/s2213-8587(20)30216-3)
29. Neu C, Baumbach P, Scherag A, Kortgen A, Götze J and Coldewey SM. Identification of cardiovascular and molecular prognostic factors for the morbidity and mortality in COVID-19-sepsis (ICROVID): Protocol for a prospective multi-centre cohort study. *PLoS One.* 2022;17(6):e0269247.
<https://doi.org/10.1371/journal.pone.0269247>
30. Brogi E, Marino F, Bertini P, Tavazzi G, Corradi F and Forfori F. Cardiac complications in patients with COVID-19: A systematic review. *J Anesth Analg Crit Care.* 2022;2(1):18.
<https://doi.org/10.1186/s44158-022-00046-7>

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