COVID-19 Infection and Myocarditis: A State-of-the-Art Systematic Review

Vikash Jaiswal1*, Zouina Sarfraz2*, Azza Sarfraz3*, Dattatreya Mukherjee4*, Nitya Batra5, Gazala Hitawala6*, Sadia Yaqoob7, Abhinav Patel8, Preeta Agarwala9, Ruchika10*, Muzna Sarfraz11, Shehar Bano2*, Nishwa Azeem12, Sidra Naz13*, Akash Jaiswal14, Prachi Sharma15, and Gaurav Chaudhary15

Abstract
Background: COVID-19 was initially considered to be a respiratory illness, but current findings suggest that SARS-CoV-2 is increasingly expressed in cardiac myocytes as well. COVID-19 may lead to cardiovascular injuries, resulting in myocarditis, with inflammation of the heart muscle. Objective: This systematic review collates current evidence about demographics, symptomatology, diagnostic, and clinical outcomes of COVID-19 infected patients with myocarditis. Methods: In accordance with PRISMA 2020 guidelines, a systematic search was conducted using PubMed, Cochrane Central, Web of Science and Google Scholar until August, 2021. A combination of the following keywords was used: SARS-CoV-2, COVID-19, myocarditis. Cohorts and case reports that comprised of patients with confirmed myocarditis due to COVID-19 infection, aged >18 years were included. The findings were tabulated and subsequently synthesized. Results: In total, 54 case reports and 5 cohorts were identified comprising 215 patients. Hypertension (51.7%), diabetes mellitus type 2 (46.4%), cardiac comorbidities (14.6%) were the 3 most reported comorbidities. Majority of the patients presented with cough (61.9%), fever (60.4%), shortness of breath (53.2%), and chest pain (43.9%). Inflammatory markers were raised in 97.8% patients, whereas cardiac markers were elevated in 94.8% of the included patients. On noting radiographic findings, cardiomegaly (32.5%) was the most common finding. Electrocardiography testing obtained ST segment elevation among 44.8% patients and T wave inversion in 7.3% of the sample. Cardiovascular magnetic resonance imaging yielded 83.3% patients with myocardial edema, with late gadolinium enhancement in 63.9% patients. In hospital management consisted of azithromycin (25.5%), methylprednisolone/steroids (8.5%), and other standard care treatments for COVID-19. The most common in-hospital complication included acute respiratory distress syndrome (66.4%) and cardiogenic shock (14%). On last follow up, 64.7% of the patients survived, whereas 31.8% patients did not survive, and 3.5% were in the critical care unit. Conclusion: It is essential to demarcate COVID-19 infection and myocarditis presentations due to the heightened risk of death among patients contracting both myocardial inflammation and ARDS. With a multitude of diagnostic and treatment options available for COVID-19 and myocarditis, patients that are under high risk of suspicion for COVID-19 induced myocarditis must be appropriately diagnosed and treated to curb co-infections.

Keywords
myocarditis, COVID–19, SARS-CoV-2, symptomatology, biomarkers, adverse events, cytokine storm, systematic review

Introduction
Coronavirus disease 2019 (COVID-19) has led to fright among populations worldwide since it was first reported. The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially only considered to be a respiratory illness, but it is now recognized as a complex multi systems disease. Current literature suggests that the increased expression of angiotensin-converting enzyme 2 (ACE2) receptors of SARS-CoV-2 in cardiac myocytes accounts for the relatively high cardiovascular involvement in COVID-19. Comorbidities such as pre-existing cardiovascular diseases, hypertension and diabetes mellitus have led to worse prognosis among patients infected with...
COVID-19. However, infected patients may experience added-on cardiovascular injuries, even in the absence of pre-existing cardiac disease. Myocarditis is an inflammation of the heart muscle with symptoms such as chest pain, shortness of breath, and palpitations. A study identified 42 COVID-19 patients with myocarditis, where fever was the most common presenting sign in 57% patients, and hypertension was the most pervasive comorbidity.

SARS-CoV-2 is posited to gain entry into human cells by binding the spike protein to the membrane protein angiotensin-converting enzyme 2 (ACE2). As depicted in Figure 1, SARS-CoV-2 gains entry into the bloodstream, making its way to the heart and cardiac muscle. In the cardiomyocytes, the binding to ACE2 upregulates the receptor eventually leading to apoptosis, releasing viral and cardiac antigens. These antigens, when fixed to the antigen presenting cells (APCs), lead to the release of interleukins (IL1, IL6, IL12, TNF alpha), which when presented to CD4 + T helper cells, CD8 + T cells, and B cells, lead to autoreactive virus specific antibodies. The entire mechanism is posited to lead to myocarditis, with elevated inflammatory biomarkers, cardiac biomarkers, EKG changes, and symptoms such as shortness of breath and chest pain (Figure 1).

While our systematic review does not delve into the myocardial effects of COVID-19 vaccines, a report in the New England Journal of Medicine identified 2 cases of histologically confirmed, fulminant myocarditis within 2 weeks of COVID-19 vaccination. As of September 1, 2021, the Centers for Disease Control and Prevention writes that the risk of myocarditis is far higher after COVID-19 infection as opposed to the mRNA virus. Based on a study that identified 1.5 million inpatient records with COVID-19, myocarditis was uncommon among patients with or without COVID-19, however, there was a relatively higher risk in the 50 to 75 and over age groups. The under 16 age group could be more prone due to the related multisystem inflammatory syndromes. The paper also noted an 18-fold higher chance of developing myocarditis due to COVID-19.

The objective of this systematic review is to collate evidence about demographics, symptomatology, diagnostic techniques, and clinical outcomes of COVID-19 infected patients with myocarditis.

Methods
This systematic review was conducted and reported in conformity with the Cochrane and PRISMA (Preferred Reporting Items for Systematic review and Meta-Analyses) 2020 guidelines (Figure 2). A comprehensive literature search was done using the search engines PubMed, Google Scholar, Cochrane CENTRAL, and Web of Science database from their inception up until August 31, 2021. The search terms included “SARS-CoV-2” and/or “COVID 19” and/or “myocarditis.” Reference lists of included studies were also manually screened to identify any relevant studies that may have been missed during the search (umbrella review).

Articles retrieved from the systematic search were exported to EndNote Reference Library software (Clarivate), where duplicates were removed. 2 authors (V.J. and S.Y.) carried out an independent search and screened the titles and abstracts of the identified articles for inclusion. Afterward, full-text articles were reviewed to validate if they satisfied the inclusion criteria. Any discrepancies were resolved by discussion till consensus was achieved. Articles were included if they met all the pre-specified eligibility criteria: (1) Patients with confirmed myocarditis in association with COVID-19; (2) Age groups > 18 years; (3) Cohorts, case series and case reports.
Studies with post-mortem findings consistent with acute myocarditis were also included. All other studies were excluded.

Data extracted from articles included publication related characteristics (i.e. author/s, study design, number of patients, year of publication, and country) and patient related characteristics. In specific, demographics (age in years, gender, comorbidities), and clinical characteristics along with laboratory findings (particularly, inflammatory markers and cardiac enzymes) were documented (Tables 1-3). Additionally, features of imaging modalities including Chest X-ray/CT scan, ECG, ECHO, CMR, and endomyocardial biopsy were noted. Management pertaining to both COVID-19 and myocarditis, complications, and final clinical outcomes were also recorded. All data was extracted onto a predesigned Excel spreadsheet.

**Results**

In total, 54 case reports and 5 cohorts were identified comprising 215 adult patients. Among the 59 studies, the following comorbidities were noted among 178 patients. Hypertension ($n=92$, 51.7%), diabetes mellitus type 2 ($n=47$, 46.4%), cardiac comorbidities ($n=26$, 14.6%), hyperlipidemia ($n=6$, 3.4%), obesity ($n=5$, 2.8%), ischemic stroke ($n=2$, 1.1%), asthma ($n=2$, 1.1%), hypothyroidism ($n=2$, 1.1%), smoking ($n=2$, 1.1%), cancer ($n=2$, 1.1%), sarcoidosis ($n=1$, 0.6%), epilepsy ($n=1$, 0.6%), multiple sclerosis ($n=1$, 0.6%), tuberculosis ($n=1$, 0.6%), migraine ($n=1$, 0.6%), spondylitis ($n=1$, 0.6%), renal transplant ($n=1$, 0.6%), and sleep apnea ($n=1$, 0.6%) (Table 1).

Presenting symptoms on admission were acquired from 139 of 215 patients. They include cough ($n=86$, 61.9%), fever ($n=84$, 60.4%), shortness of breath ($n=74$, 53.2%), chest pain ($n=61$, 43.9%), diarrhea ($n=43$, 30.9%), fatigue ($n=37$, 26.6%), myalgia ($n=34$, 24.5%), dyspnea ($n=17$, 12.2%), hypoxia ($n=7$, 5%), syncope ($n=6$, 4.3%), tachycardia ($n=4$, 2.9%), hypotension ($n=4$, 2.9%), tachypnea ($n=4$, 2.9%), malaise ($n=4$, 2.9%), vomiting ($n=4$, 2.9%), ARDS ($n=1$, 0.7%) (Table 1).

Of 215, inflammatory markers were reported among 185 patients. The inflammatory markers were elevated among 181 (97.8%) patients, and were normal in the remaining 4 (2.2%) patients. The cardiac markers were documented in 212 patients, of which 201 (94.8%) had elevated levels, whereas, 11 (5.2%) patients had normal cardiac markers. The mean value of CRP was 91.6 mg/L (Normal: Less than
The mean D-dimer value was 2419.2 ng/ml (reference concentration of D-dimer is <500 ng/mL). Mean ferritin laboratory values of 908.9 ng/ml (the normal range for ferritin in blood serum is: 20 to 250 ng/mL for adult males, 10 to 120 ng/mL for adult females); and Interleukin 6 of 271.2 pg/mL (normal values: 5-15 pg/ml) were reported. Troponin values were reported as 44.85 ng/ml (normal range for troponin I is between 0 and 0.04 ng/mL but for high-sensitivity cardiac troponin (hs-cTn) normal values are below 14 ng/L).

Radiographic imaging studies particularly, CT and Chest X-ray were indicated in COVID-19 patients (Table 2). Radiographic findings were obtained from 120 individuals with COVID-19 myocarditis. Variable features were noticed, of which cardiomegaly (32.5%) was the most prominent. Precisely, 120 patient radiographic findings were noted, of which cardiomegaly (n=39, 32.5%) was the most common occurrence. This was followed by pulmonary venous congestion (n=27, 22.5%), ground glass opacity (n=23, 19.2%), consolidation (n=9, 7.5%), pericardial effusion (n=4, 3.3%), and pleural effusion (n=2, 1.7%).
Table 1. Demographics, Comorbidities, and Presenting Symptoms Among all Patients.

| Authors          | Study design | Country | Sample size | Age (y) | Gender | Comorbidities | Presenting symptoms |
|------------------|--------------|---------|-------------|---------|--------|---------------|---------------------|
| Cizgic et al13   | Case report  | Turkey  | 1           | 78      | M      | HTN, Ischemic Stroke | Chest pain, shortness of breath |
| Yokoo et al14    | Case report  | Brazil  | 1           | 81      | M      | HTN, Ischemic Stroke | Fever, shortness of breath |
| Pietsch et al15  | Case report  | Germany | 1           | 59      | F      | None           | ARDS and dyspnea           |
| Pavon et al16    | Case report  | Switzerland | 1       | 64      | M      | Isolated pulmonary sarcoidosis and epilepsy | Fever, chest pain, shortness of breath, cough |
| Khanri et al17   | Case report  | USA     | 1           | 50      | M      | HTN, Ischemic stroke | Fever with chills, malaise, shortness of breath, cough, syncope |
| Hussain et al18  | Case report  | USA     | 1           | 51      | M      | HTN           | Cough, shortness of breath, fatigue, fever |
| Falen et al19    | Case report  | Norway  | 1           | 55      | F      | None           | Fatigue, myalgia, syncope, chest pain |
| Zeng et al20     | Case report  | China   | 1           | 63      | M      | None           | Fever, cough, shortness of breath, chest pain |
| Doen et al21     | Case report  | France  | 1           | 69      | M      | HTN           | Fever, cough, shortness of breath, vomiting, diarrhea |
| Fairdoth et al22 | Case report  | USA     | 1           | 60      | M      | Multiple sclerosis | Fever, tachycardia, hypotension, shortness of breath, tachypnea, hypoxia |
| Goyle et al23    | Case report  | USA     | 1           | 57      | M      | HTN           | Fever, myalgia, cough, shortness of breath, decrease appetite, nausea, diarrhea |
| Luukiers et al24 | Case report  | Germany | 1           | 79      | M      | Asthma        | Fatigue, syncope, shortness of breath, wheeze |
| Jain et al25     | Case report  | India   | 1           | 60      | M      | HTN, DM II    | Cough, shortness of breath, hypoxia (75% SpO2) |
| Mustafa et al26  | Case report  | USA     | 1           | 56      | M      | None           | Fatigue, myalgia, chest pain, cough, shortness of breath |
| Manosor et al27  | Case report  | USA     | 1           | 72      | F      | HTN           | Myalgia, fever, tachycardia, cough, cold, tachypnea, hypoxia (60% SpO2) |
| Al-azzaf et al28 | Case report  | UAE     | 1           | 58      | M      | HTN           | Asymptomatic |
| Khalid et al29   | Case report  | USA     | 1           | 76      | M      | HTN, hyperlipidemia, hypothyroidism | Fever, dyspnea, cough, tachycardia, tachypnea, hypoxia (79%SpO2) |
| Incaridi et al30 | Case report  | Italy   | 1           | 53      | F      | None           | Fatigue, fever, hypotension, cough |
| Fried et al31    | Case report  | USA     | 1           | 64      | M      | HTN, hyperlipidemia | Asymptomatic |
| Halh et al32     | Case report  | Argentina | 1       | 68      | M      | HTN, obesity, DM II | Tachyarrhythmia, shortness of breath, hypoxia, confusion |
| Butler et al33   | Case report  | USA     | 1           | 50      | M      | HTN, DM II    | Fever, cough, shortness of breath |
| Laguna et al34   | Cohort Italy | Italy   | 12 (Mean)   | 76( Mean) | F | HTN, hyperlipidemia | Fever, cough, shortness of breath |
| Kall et al35     | Case report  | USA     | 1           | 56      | M      | Diabetes, obesity | Fever, myalgia, chest pain, cough, hypoxia |
| Ghugre et al36   | Case report  | Canada  | 1           | 62      | M      | HTN, dyslipidemia | Fever, fatigue, cough, shortness of breath, tachypnea, lathyria |
| Fish et al37     | Case report  | USA     | 1           | 61      | M      | HTN, obesity, hyperlipidemia | Fatigue, myalgia, hypotension, tachypnea, hypoxia (SpO2 85%), shortness of breath |
| Dabbagh et al38  | Case report  | USA     | 1           | 67      | M      | Non-ischemic cardiomyopathy with LVEF of 40% | Cough, shortness of breath, left shoulder pain |
| Inbringer-Otto et al39 | Case report | Spain   | 1           | 59      | F      | HTN, lymph node tuberculosis diagnosed by presence of erythema nodosum, and migraines | Fever, squeezing chest pain |
| Albert et al40   | Case report  | USA     | 1           | 49      | M      | None           | Fever, dyspnea |
| Escher et al41   | Case report  | Germany | 1           | 39      | M      | None           | Fever, dyspnea |
| Ford et al42     | Case report  | USA     | 1           | 53      | M      | Dyslipidemia   | Malaise, fever, chest pain |
| Guenot et al43   | Case report  | France  | 1           | 69      | M      | DM II, HTN, IHD | Fever, fatigue, abdominal pain |
| Hua et al44      | Case report  | UK      | 1           | 47      | F      | None           | Fever, dry cough, chest pain, shortness of breath |
| Jacobs et al45   | Case report  | Belgium | 1           | 48      | M      | HTN           | Diarrhea, cough, dyspnea |
| Labani et al46   | Case report  | French  | 1           | 71      | F      | Breast Cancer  | Flu-like symptoms, chest pain |
| Spano et al47    | Case report  | Switzerland | 1       | 49      | M      | None           | Dyspnea, fatigue, intermittent epigastric pain, nocturia |
| Tanzi et al48    | Case report  | Italy   | 1           | 69      | M      | None           | Cough, dyspnea, weakness |
| Traeger et al49  | Case report  | USA     | 1           | 69      | M      | Obesisty, asthma, spondyloarthritis | Fever, neck pain, diarrhea, vomiting |
| Warg et al50     | Case report  | N/A     | 1           | 71      | M      | Renal transplant, CAD, HTN | Dyspnea, fever, tachycardia, confusion |
| Warchol et al51  | Case report  | Poland  | 1           | 74      | M      | Atrial fibrillation, arterial HTN | New-onset ventricular tachycardia |

(continued)
| Authors         | Study design | Country | Sample size | Age (y) | Gender | Comorbidities       | Presenting symptoms                                                                 |
|-----------------|--------------|---------|-------------|---------|--------|---------------------|--------------------------------------------------------------------------------------|
| Sardari et al. | Case report  | Iran    | 1           | 31      | M      | None                | Dyspnea, fever,                                                                     |
| Dahl et al.    | Case report  | Norway  | 1           | 37      | M      | None                | Fever, headache, unilateral left painful neck swelling                               |
| Hu et al.      | Case Report  | China   | 1           | 37      | M      | None                | Chest pain, dyspnea, diarrhea                                                        |
| Volk et al.    | Case report  | Israel  | 1           | 21      | M      | None                | Chest pain, cough, dyspnea, fever                                                    |
| Besler et al.  | Case report  | Turkey  | 1           | 20      | M      | None                | Chest pain, fever                                                                   |
| Gane et al.    | Case report  | Ireland | 1           | 58      | M      | Smoking             | Polyarthrom, dyspnea                                                                 |
| Sheikh et al.  | Case report  | USA     | 1           | 28      | M      | None                | Chest pain, cough, dyspnea                                                           |
| Salamanca et al.| Case report  | Spain   | 1           | 44      | M      | None                | Dyspnea, syncope                                                                     |
| Naneishvili et al. | Case report  | UK      | 1           | 44      | M      | None                | Syncope, fever, lethergy                                                              |
| Kim et al.     | Case report  | Korea   | 1           | 21      | F      | None                | Fever, dyspnea, cough                                                                |
| Nidir et al.   | Case report  | Iran    | 1           | 38      | F      | None                | Chest pain, nausea, vomiting, malaise                                                |
| Saka et al.    | Case report  | Italy   | 1           | 43      | F      | Unremarkable        | Dyspnea, fever, chest pain                                                           |
| Yuan et al.    | Case report  | China   | 1           | 33      | M      | N/R                 | Fever, chest pain                                                                   |
| Warchal et al. | Case report  | Poland  | 1           | 74      | M      | Atrial fibrillation, atrial HTN, type II DM, hyosypothyroidism | No symptoms                                                                          |
| Asif and AP    | Case series  | USA     | 2           | 64.71   | P1: M, P2: F | P1: HTN, Hyperlipidemia, P2: Multiple Myeloma | P1: dyspnea, hypertension, P2: fever, cough, dyspnea                                    |
| Khald et al.   | Case series  | USA     | 2           | 48.34   | P1: M, P2: F | P1: Obesity, Diabetes, Obstructive sleep apnea, P2: None | P1: fever, chills, myalgias, diarrheas, nonproductive cough and shortness of breath. P2: Fever, chills, body ache |
| Ng et al.      | Cohort       | China   | 16          | 68      | 9M,7F | None                | All have chest pain, cough, shortness of breath                                      |
| Jlrak et al.   | Cohort       | Europe  | 76          | 66.8    | 53M,23F | Arterial hypertension—56.6% | N/A                                                                                  |
| Xu yan et al.  | Cohort       | China   | 27          | 69      | 10M, 17F | CHD—11% | Fever (82.4%), chest pain (7.6%), cough (61.1%), shortness of breath (40.3%), diarrheas (11.1%) |
| Koral et al.   | Cohort       | India   | 28          | 60±15.1 | 14M,14F | Diabetes=71.4%, HTN =64.3% | Myalgia, fever, fatigue, chest pain, cold, cough, shortness of breath, confusion, headache, diarrheas |
effusion (n=3, 2.5%), pleural effusion (n=1, 0.83%), and no abnormal finding (n=5, 4.2%) were noted in the cohort of included patient (Table 2).

Electrocardiography (ECG) findings were obtained for 96 patients, which were normal in 2 (2%) patients while other patients had varied ECG findings comprising of ST segment elevation among 43 (44.8%) patients, T wave inversion in 7 (7.3%) patients, ST depression in 5 (5.2%) patients, sinus tachycardia in 11 (11.5%) patients, atrial fibrillation in 3 (3.1%) patients, sinus bradycardia in 1 (1%) patient, ventricular tachycardia in 2 (2%) patients, and finally LBBB was reported in 1 (1%) patient as well (Table 2). Echocardiography was conducted in 175 patients, where 9 (51.4%) patients showed normal ejection fractions while 55 (31.4%) patients demonstrated reduced ejection fraction with a mean EF% of 35. Pericardial effusion was demonstrated in 12 (6.9%) patients, left ventricular hypertrophy in 7 (4%) patients, cardiomegaly in 7 (4%) patients, myocardial dyskinesia in 19 (10.9%) patients, and LV thrombus in 1 (0.6%) patient (Table 2).

Cardiovascular magnetic resonance (CMR) imaging is a non-invasive, gold standard test for diagnosing myocarditis. Our synthesis identifies that 42 of 215 patients underwent CMR and 36 of them were diagnosed with Myocarditis by the Lake Louis Criteria. The most common findings were increased signal intensity in T2 weighted imaging that is, myocardial edema (30/36; 83.3%) suggestive of myocardial inflammation and/or ischemia. Late Gadolinium enhancement was observed in 23/36 (63.9%) patients in both ischemic and non ischemic patterns. Hypokinesis and decreased systolic function were present in 8/36 (22.2%) and 6/36 (16.7%) patients respectively. Myocardial fibrosis was found in 1/36 (2.8%) patients. In total, 6 (14.3%) of 42 patients were found to have normal CMR findings (Table 2).

On noting the biopsy and histopathological examination findings, and considering the invasive in nature, these findings were reported in 9 (4.2%) patients out of 215 (Table 2). The most common findings were multifocal or diffuse lymphocytic infiltrates in the myocardium and endothelium along with myocardial edema and necrosis. Other findings included positive myocardial anti-SARS COV nucleocapsid protein antibodies, cardiac hypertrophy, and multiple sites of ischemia and thrombosis with a left atrial and left pulmonary artery thrombus in one patient. Only 1 (11.1%) patient had normal findings on biopsy.

The in-hospital management acquired from 165 patients comprised of azithromycin (n=42, 25.5%), hydroxychloroquine (n=41, 24.9%), methylprednisolone/steroid (n=14, 8.5%), norepinephrine (n=10, 6%), dobutamine (n=7, 4.3%), tocilizumab (n=6, 3.6%), and remdesivir (n=1, 0.6%) (Table 3). Standard care of treatment for COVID-19 was used for majority of the patients.

Complications during in-hospital stay reported in 128 patients included ARDS (n=85, 66.4%), cardiogenic shock (n=18, 14%), pleuritic chest pain (n=6, 4.7%), multiorgan failure (n=4, 3.1%), septic shock (n=3, 2.3%), distributive shock (n=2, 1.6%), sepsis (n=2, 1.6%), and pulmonary thrombosis (n=1, 0.8%) (Table 3). Of 85 patients, 55 (64.7%) survived, whereas 27 (31.8%) died. Three patients (3.5%) were in critical care unit on the last follow-up (Table 3).

**Discussion**

This systematic review aimed to describe the symptomatology, prognosis, and clinical findings of patients with probable and confirmed COVID-19-related myocarditis. Frequent clinical findings of COVID-19 infection constitute fever, cough, shortness of breath, and fatigue. The World Health Organization has cited fever and cough as striking features of COVID-19. Fever, dyspnea, and/or chest pain are typical manifestations of myocarditis that tend to overlap with COVID-19 symptomatology, thus making the diagnosis challenging. Laboratory investigations such as rising levels of cardiac biomarkers and electrocardiogram findings may assist in diagnosing COVID-19 induced myocarditis.

Our systematic review finds hypertension was the most common comorbidity with prevalence among 51.7% patients. This was followed by diabetes mellitus type 2 (46.4%) and cardiac comorbidities (14.6%). Our synthesis also finds that the most common presenting symptoms on admission comprised of 61.9% patients with cough, 60.4% with fever, and 53.2% with shortness of breath. The inflammatory markers were elevated among 97.8% patients, and the cardiac markers were increased in 94.8% of patients. The mean CRP levels were 91.6 mg/L, mean D-dimer values were 2419.2 ng/ml, and mean ferritin was 908.9 ng/ml. The most distinct inflammation and/or ischemia. Late Gadolinium enhancement was observed in 63.9% patients. The biopsy and histopathological examination findings found multifocal or diffuse lymphocytic infiltrates in the myocardium and endothelium suggesting myocardial ischemia/inflammation. Late gadolinium enhancement was observed in 63.9% patients. The biopsy and histopathological examination findings found multifocal or diffuse lymphocytic infiltrates in the myocardium and endothelium along with myocardial edema and necrosis. In-hospital management comprised of 22.5% patients treated with azithromycin, 24.9% with hydroxychloroquine, 8.5% with methylprednisolone/steroid and 6% with norepinephrine. Standard of care and treatment was used for the
### Table 2. Biomarkers, Radiographic, Electrocardiography, Echocardiography, and Biopsy Findings.

| Authors          | Inflammatory markers | Cardiac markers | Radiographic findings | Electrocardiography | Echocardiography | CTPM | Myocardial biopsy |
|------------------|----------------------|----------------|----------------------|---------------------|------------------|------|------------------|
| Gzic et al. 13   | C-reactive protein 94.6 mg/L | Troponin 1 1 g/L | CT: chest small pericardial effusion and ground glass opacities with consolidation | Abnormal T wave in leads II, III, aVF, and ST depression in L, AVL | N/A | N/A |
| Yakoo et al. 14  | N/A                  | Troponin T 33.9 pg/mL | Chest CT: small round ground glass opacities, with multifocal distribution in both lungs | N/A | Reduction in the ejection fraction to 35% | Late enhancement areas with an ischemic pattern on the left ventricle base septum wall, with diffuse hypokinesis, and global systolic function | N/A |
| Preach et al. 15 | N/A                  | Troponin 3.56 g/L, CK-MB 7.14 mg/mL | NA | N/A | Severe diastolic dysfunction III with an increased wall thickness (interventricular septum, 14 mm), and pericardial effusion | N/A |
| Pavan et al. 16  | C-reactive protein 46.6 mg/mL, D-dimer 1210 ng/mL | Troponin (peak) 1840 mg/L | Chest x-ray: bilateral reticulation and ill-defined opacities, indicative of interstitial edema | NA | Moderately reduced left ventricular ejection fraction of 45%/72% after CPR | Reduced left-ventricular (LV) systolic function (42%/30%), mild hypokinesia of the basal wall. T2-mapping sequences showed myocardial edemas (segmental T2 >55-67 ms) | N/A |
| Khair et al. 17  | D-dimer 10.68 mg/mL, procalcitonin 16.6 ng/mL, C-reactive protein 10.65 mg/mL, Ferritin 46 mg/mL | Troponin 1 54.8 mg/mL, CK-MB 54.3 mg/mL | NA | Sinus tachycardia along with ST elevation in leads II, III, aVF, and ST depression in L, AVL | Severe left ventricular systolic dysfunction, right ventricular (RV) enlargement causing its systolic dysfunction and moderate-to-large pericardial effusion anterior to the right ventricle | N/A |
| Huasi et al. 18  | Troponin 1 8 mg/mL, and CK-MB 14.7 mg/mL | N/A | Diffuse ST elevation | N/A | N/A |
| Dalen et al. 19  | Troponin T 108 mg/mL, NTproBNP 102.5 pg/mL | N/A | Sinus tachycardia, integrant ST elevation in inferior leads with a T-wave inversion in precardial leads | N/A | Left ventricular ejection hypertrophy | T1-mapping exhibited relaxation times of 120-127 ms in the anterolateral wall correlated with 109 ms in the septum. Late gadolinium enhancement in the anterolateral wall | N/A |
| Zeng et al. 20   | Interleukin 4 (peak) 272.4 pg/mL | Troponin 1 (peak) 11.37 pg/mL, myoglobin (peak) >390 97 pg/mL, NTproBNP 22.39 pg/mL | Chest X-ray: Typical ground glass changes indicative of viral pneumonia | N/A | Left ventricular ejection fraction of 32%, pulmonary hypertension, and normal RV function | N/A |
| Dagen et al. 21  | N/A                  | Troponin 1 402 mg/mL | Chest CT: bilateral early stage pattern, ground glass opacities and consolidation | Diffuse T-wave inversion with the sign of left ventricular hypertrophy | N/A | N/A |
| Fard et al. 22   | C-reactive protein 20.2 mg/mL, Ferritin 73.7 ng/mL | Troponin 2 5000 ng/mL | N/A | Sinus tachycardia, with normal ST/T wave | N/A | N/A |
| Goyle et al. 23  | Troponin (peak) 7.33 on day 3 | N/A | Sinus tachycardia, with normal ST/T wave | Diffuse hypokinesis with relative apical sparing, with a left ventricular ejection fraction of 35-40%, no pericardial effusion | Diffuse demins of both aorta and both vena cava along with small foot of left atrial enlargement | N/A |
| Luikman et al. 24 | C-reactive protein (free) 6.4-23 mg/L | Troponin T 63.5 mg/mL, NTproBNP 117.8 pg/mL | Chest CT: pulmonary ground glass parenchymal infiltrates in the left upper lobe and lower lobe and posterior and para nasal effusion | Normal | Diffuse interstitial myocardial edema with an increased T2 signal in the myocardium. T2-mapping showed diffuse myocardial inflammation (on day 10) | N/A |
| Jain et al. 25    | Elevated inflammatory markers | Elevated troponin | Elevated inflammatory markers | Normal | N/A | N/A |
| Mustak et al. 26  | C-reactive protein 160 mg/mL | Troponin 1 8.6 mg/mL | Chest X-ray suggestive of increased intraventricular prominence | N/A | N/A | N/A |
| Masoor et al. 27  | C-reactive protein 27.5 mg/mL, Ferritin 928.8 mg/L, CRP 85.7 mg/L, WBC 20400, D-dimer 6450 mg/mL | NT-proBNP 46.9 pg/mL, Troponin T (inIU) 118 ng/mL | N/A | N/A | N/A | N/A |
| Al-awadi et al. 28 | Normal ranges of inflammatory markers and contact biomarkers | N/A | Sinus bradycardia, no ST-T changes | Unremarkable study showing only a mildly dilated ascending aorta | T1-mapping showing a high value of 116.2 | T2 mapping showing an abnormal value of ST | N/A |

(continued)
| Authors          | Inflammatory markers                                                                 | Cardiac markers                                                                 | Radiographic findings                                                                 | Electrocardiography                                  | Echocardiography                                  | CMR | Myocardial biopsy   |
|------------------|---------------------------------------------------------------------------------------|--------------------------------------------------------------------------------|---------------------------------------------------------------------------------------|-----------------------------------------------------|------------------------------------------------|------|---------------------|
| Khalid et al     | C-reactive protein 2.310 mg/L, Interleukin-1 (IL-1) 78 mg/L, elevated lactate dehydrogenase 2.34 U/L, and ferritin 457 ng/mL | Troponin 30.3 mg/L, NT-proBNP 35,000 pg/mL | Normal sinus rhythm with a short PR interval                                           | Severe left ventricular systolic dysfunction with segmental wall motion anomalies | N/A                                           | N/A  |                     |
| Inceri et al     | C-reactive protein 1.3 mg/dL, D-dimer 500 U/L                                         | Troponin T peak 0.8 mg/L, CK (peak) 399 mg/mL, NT-proBNP 469 mg/mL              | Minimal diffuse ST depression, low voltage in limb leads, ST depression, and T wave inversion in V1 and V | Increased left ventricular wall thickness with diffuse hypokinesis, and LVEF of 45%. Large circumferential pericardial effusion of size 11 mm with the drama of tamponade | N/A                                           | N/A  | Diffuse biventricular apical hypokinesia, severe LV dysfunction (LVEF of 35%). Short PR interval recovery and T2 mapping sequences showed marked biventricular myocardial interstitial edema. | N/A  |
| Fried et al      | C-reactive protein 0.034 mg/dL, ferritin 5764 ng/mL ESR 144 mg/mL                     | Troponin 9.9 mg/mL                                                             | Sino-tachycardia, ST segment elevation in leads V1, V2, V3, V4, and PR depression and ST depression in V1. Low voltage QRS complexes in the limb leads. | EF 30% (reduced)                                      | BP 80/50 (reduced)                                 | N/A  |                     |
| Wehit et al      | LDH 22.3 U/L, ferritin 72.3 mg/mL, Dimer 0.306 mg/mL                                  | Troponin T 16.6 mg/mL, NT-proBNP 45.29 ng/mL                                    | Chest radiography revealed right basal opacities                                         | N/A                                                 | N/A                                           | N/A  | Deterioration in both global and segmental longitudinal strain | N/A  |
| Lagan et al      | C-reactive protein 59.9 mg/mL, NT-proBNP 1557.6 mg/mL                                 | Troponin 39.95 mg/mL                                                           | N/A                                                                                           | N/A                                                 | N/A                                           | N/A  |                     |
| Kallel et al     | C-reactive protein 315 mg/l, WBC count 9.67 × 10⁹/L, Creatinine 45 mg/l, D-dimer 1.64 mg/L | Troponin I 477 mg/L, CK (peak) 19 U/L                                           | CT chest showed typical findings of COVID-19 with ground-glass opacification               | Diffuse ST elevation and simple monomorphic supraventricular extrasystoles               | N/A                                           | N/A  |                     |
| Ghoge et al      | NA                                                                                   | NA                                                                              | NA                                                                                           | Normal ejection fraction                           | N/A                                           | N/A  | Normal left ventricular (LV) and right ventricular (RV) size and function, LV ejection fraction was 62%, area of red myocardial/subendocardial left ventricular infarction in the basal inferolateral wall in a nonischemic pattern more consistent with a myocarditis type pattern, abnormal ST elevation, T wave inversion associated with the presence of edema. Abnormal T2 hypointense relaxation associated with the presence of edema. | N/A  |
| Fish et al       | Creatinine 1.14 mg/L, INR 1.5, CRP 34.6 mg/L, LDH 170 U/L, SAA 10 mg/L, D-dimer 52 mg/mL | Elevated Troponin I 7.46 mg/mL                                                  | NA                                                                                           | Diffuse, mainly anterior, ST elevation               | Reduced ejection fraction                          | N/A  | Multiple microscopic areas of myocardial necrosis together with thrombus in the left atrium and pulmonary vasculature and scattered microscopic capillary congestion. Myocardial edema also revealed an adherent organizing left atrial thrombus (4.5 cm) and marked chronic inflammation of the left pulmonary artery. | N/A  |
| Dabbagh et al    | C-reactive protein 15.9 mg/l, ferritin 39 mg/ml, D-dimer 6.42 mg/L, CK 2801.22 mg/l | Troponin I < 11 mg/ml, pro-BNP 5.4 mg/ml                                         | Chest X-ray showed cardiac silhouette                                                      | Shallow voltage in limb leads, non-specific ST abnormal                                           | N/A                                           | N/A  |                     |
| Indriat-Oraz et al | C-reactive protein 10 mg/l                                                        | Troponin T peak 1.8 mg/ml, NT-proBNP 441 mg/mL                                 | Chest X-ray showed signs of vascular redistribution, with no evidence of infection          | Diffuse ST elevation and PR-segment depression                                                | N/A                                           | N/A  |                     |
| Albert et al     | NA                                                                                   | Elevated troponin, NT-proBNP                                                   | No pathological features                                                                   | Sinus tachycardia, no ST-T changes                                                             | N/A                                           | N/A  | Globally depressed LVEF of 25% with LVEDD of 58 mm increased wall thickness. | N/A  |
| Escher et al     | NA                                                                                   | Troponin 3.264 pg/mL, BNP 12230 pg/mL                                           | N/A                                                                                           | N/A                                                 | N/A                                           | N/A  | Inflammatory infiltrates with visualization of viral particles Active myocarditis with CD3+ 106 cell/ mm² | N/A  |
| Ford et al       | NA                                                                                   | Troponin 588 pg/mL, TNF normal                                                  | Mild LV dilation with hypokinesis (EF 15%), New transcranial echo revealed LV thrombus and worsening LV dilation | LV dilation with global hypokinesis, increased T2 signal, hypodense, and edema               | N/A                                           | N/A  |                     |
Table 2. (continued)

| Authors          | Inflammatory markers | Cardiac markers | Radiographic findings | Electrocardiography | Echocardiography | CPR | Myocardial biopsy                                                                 |
|------------------|----------------------|-----------------|-----------------------|---------------------|------------------|-----|-----------------------------------------------------------------------------------|
| Gauchotte et al. | N/A                  | Troponin I 8966 pg/mL and CK-MB 2103 U/L | Normal               | Normal              | Severe and diffuse LV hypokinesis, LVEF<30% | N/A | Post mortem: Multifocal inflammatory infiltration, in both ventricles and septum, composed in a majority of macrophages and lymphocytes. The myocardium was edematous, containing dystrophic cardiomyocytes, without necrosis. Strong presence of anti-SARS-CoV2 nucleocapsid protein antibody in the myocardium |
| Hua et al.       | N/A                  | Troponin I 8966 pg/mL and CK-MB 2103 U/L | Normal               | Normal              | N/A              | N/A | Post Mortem: Myocarditis; focal inflammatory infiltrates, predominantly in the myocardium adjacent to the foci of myocarditis |
| Jacobs et al.    | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | Left ventricular ejection fraction was normal with pericardial effusion of size 11 mm and absence of cardiac tamponade   | N/A | Hypodynamic ventricular function (pericarditis): IVS 12mm, PW 11mm, LVEDD 48mm |
| Labani et al.    | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | Diffuse inverted T waves and prolonged QT     | N/A | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Spaso et al.     | Elevated C-reactive protein | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Tawazzu et al.   | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | Right atrial enlargement, LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Trangen et al.   | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Varga et al.     | C-reactive protein: 52.7 mg/L | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Warchoł et al.   | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Sardari et al.   | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Dahl et al.      | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Hu et al.        | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |
| Vefs et al.      | Ferritin: 32 492 pg/mL, interleukin 6 level: 381 pg/mL | Troponin I 8966 pg/mL and CK-MB 2103 U/L | N/A                  | Normal               | LV wall motion, normal LVEF 41% and persistence of a mild pericardial effusion: STT and T2 map showed suggestive of myocardial edema in the basal inferior LV wall: LCE multiple areas of inferior subepicardial and mid-wall |

(continued)
| Authors | CRP (mg/L) | Troponin-I (ng/mL) | CK-MB (U/L) | NT-proBNP (pg/mL) | Cardiac markers | Radiographic findings | Electrocardiography | Echocardiography | CMR | Myocardial biopsy |
|---------|------------|--------------------|-------------|-------------------|----------------|----------------------|---------------------|-------------------|-----|------------------|
| Besler et al. | 56 CRP-0.0812 g/L | Troponin-I 17.621 ng/mL, CK-MB 21.9 μg/L, NT-proBNP 323.1 μg/L | N/R | N/R | Cardiac markers | CXR: focal consolidation on the upper zone of left lung, CHEST CT: subepicardial consolidation with ground-glass opacification in the left upper lobe | N/R | N/R | Myocardial wall edema, subepicardial late gadolinium enhancement of the posterior wall in the mid ventricle, suggestive of myocarditis of 64% | N/R |
| Shehory et al. | 32.5 mg/L | Troponin-I 0.415 g/mL, BNP 1940 pg/mL | N/R | N/R | Cardiac markers | CXR: pericardial effusion, increased interstitial markings | N/R | N/R | Ventricular septal defect | N/R |
| Sabir et al. | 47 mg/L | Troponin-I 1.546 ng/mL, CK-MB 0.414 g/mL, CKI 40.1 mg/L | N/R | N/R | Cardiac markers | CXR: pericardial effusion, increased interstitial markings | N/R | N/R | Ventricular septal defect | N/R |
| Kim et al. | 124 mg/mL | Troponin-I 1.274 mg/mL, NT-proBNP 212 pg/mL | N/R | N/R | Cardiac markers | CXR: multifocal consolidation on both lung fields and cardiomegaly, CHEST CT: multifocal consolidation and ground-glass opacification in both lungs in the lower lobe | N/R | N/R | Severe left ventricular systolic dysfunction | N/R |
| Nikoo et al. | 23 mg/L | Troponin-I 11.032 ng/mL, CK-MB 0.81 IU/L | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Sustained ventricular tachycardia | N/R |
| Sae et al. | 18 mg/L | Troponin-I 1.385 ng/mL, NT-proBNP 51.2 pg/mL | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Ventricular tachycardia | N/R |
| Yuan et al. | 94 mg/L | Troponin-I 1.031 mg/mL, NT-proBNP 245.3 pg/mL | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Ventricular tachycardia | N/R |
| Asif and Ali | P1: CRP 32.5 mg/dL, ESR 12.2 mg/L | Troponin-I 0.174 ng/mL, CK-MB 22.1 μg/L, NT-proBNP 319 pg/mL | P1: 0.17 ng/mL | P2: 1.6 ng/mL | Cardiac markers | CXR: right atrial and ventricular enlargement, diffuse peribronchial infiltrates, diffuse ground glass opacities, peripheral consolidation, and pleural effusion, chest CT: diffuse ground-glass opacities, patchy consolidation, and pleural effusion | P1: ST-elevation in leads V1-V2, aVL, V6, and V1-4.4 T wave changes, P2: ST-depression in leads V2-V6, and Q wave in lead V4-V6 | P1: EF = 0.17%, P2: EF = 0.17% | P1: EF = 0.17%, P2: EF = 0.17% | N/R |
| Khalil et al. | 8.5 mg/L | Troponin-I 1.6 ng/mL, CK-MB 27 ng/mL, NT-proBNP 971 pg/mL | P1: 0.1 ng/mL | P2: 0.1 ng/mL | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | P1: EF = 0.17%, P2: EF = 0.17% | N/R |
| Ng et al. | Elevated CRP: 4 WBC: 4 | Elevated Troponin: 7 patients | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Elevated CRP: 4 WBC: 4 | N/R |
| Jink et al. | 80 U/L | Troponin-I 3.3 ng/mL, CK-MB 2.6 ng/mL, NT-proBNP 31 pg/mL | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Elevated CRP: 4 WBC: 4 | N/R |
| Yan et al. | 80 U/L | Troponin-I 8.5 ng/mL, CK-MB 2.6 ng/mL, NT-proBNP 221 pg/mL | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Elevated CRP: 4 WBC: 4 | N/R |
| Khand et al. | D-dimer 442% (elevated) | Troponin-I 0.446 ± 12.8 μg/L, CK-MB 59 ± 30.1 | N/R | N/R | Cardiac markers | CXR: apical opacity in lungs | N/R | N/R | Elevated CRP: 4 WBC: 4 | N/R |
| Authors          | In-hospital management                                                                 | Complications                                      | Outcomes                |
|------------------|----------------------------------------------------------------------------------------|-----------------------------------------------------|-------------------------|
| Cizgic et al.    | Furosemide, angiotensin-converting enzyme (ACE) inhibitor and, beta-blocker along with Covid-19 specific therapy | ARDS on 2nd day                                     | Discharged              |
| Yokoo et al.     | Antibiotics, steroids                                                                  | —                                                  | Discharged              |
| Pletsch et al.   | N/A                                                                                    | —                                                  | N/R                     |
| Pawan et al.     | Piperacillin-tazobactam, catecholamine, Intubated                                      | —                                                  | Discharged              |
| Khatri et al.    | Hydroxychloroquine (400 mg twice on the first day, succeeded by 200 mg twice a day for 4 days), IV azithromycin, IV vancomycin, IV cephalosporin, and methylprednisolone (200 mg/d) on 3 day, dobutamine, vasopressin, and norepinephrine | Cardiogenic and distributive shock, with multi-organ failure | Died on day 4            |
| Hussain et al.   | Remdesivir, hydroxychloroquine and azithromycin, and Indomethacin 7th day, methylprednisolone and colchicine, mechanical ventilation | ARDS on 2nd day                                     | N/R                     |
| Dalen et al.     | IV fluids, norepinephrine, and dobutamine                                              | Cardiogenic shock                                   | Recovered               |
| Zeng et al.      | High-flow oxygen, lipoprotein-racumin, interferon α-1b, immunoglobulin, piperacillin-tazobactam, and continuous renal replacement therapy, IV methylprednisolone, vasopressors used from day 2A, ECMO on day 1 | Cardiogenic shock on day 11, Septic shock on day 26, ARDS day 1 | Passed away on day 33    |
| Doyen et al.     | Aspirin, fondaparinux, IV hydrocortisone for 9 days, Mechanical ventilation            | ARDS                                               | Discharged from ICU after 3 weeks |
| Fairdoth et al.  | Norepinephrine, vasopressin, dobutamine, and methylprednisolone                         | —                                                  | Discharged              |
| Pavon et al.     | Piperaclill-tazobactam, catecholamine, Intubated                                      | —                                                  | Discharged              |
| Khatri et al.    | Hydroxychloroquine (200 mg 2 times a day), lipoprotein-racumin (250 every 12h), kanamirone (50 mg), fosfomycin (25-50mg), and biopress (25 mg), IV methylprednisolone 1 mg/kg for 3 days, dobutamine | Mechanical ventilation                             | Cardiogenic shock on day 4 |
| Luetkens et al.  | N/R                                                                                    | —                                                  | Cardiogenic shock on day 4 |
| Jain et al.      | Vasoactive drugs, vancomycin and cephalosporin, PMG, pulse dose steroids, and mechanical ventilation | —                                                  | Discharged on day 19    |
| Mustafa et al.   | Aspirin, unfractionated heparin and nitroglycerin infusion for acute coronary syndrome. | Multisorb system failure and pulseless electrical activity. | Mortality on day 6 in ICU |
| Mansoor et al.   | Vancomycin, meropenem, chloroquine, and azithromycin, norepinephrine, vasopressin, diuretics, and subcutaneous heparin | —                                                  | —                       |
| Allassa et al.   | Enoxaparin, anidolide, and scheduled a permanent pacemaker implant.                   | —                                                  | —                       |
| Khaid et al.     | Todixubam (2 dose of 480 mg and 240mg), intravenous immunoglobulin (25 g for 5 days), ceftriaxone, cefdinir, and cefapime, norepinephrine, Intubated | —                                                  | —                       |
| Incand et al.    | Hydroxychloroquine (250 mg 2 times a day), lipoprotein-racumin (250 every 12h), kanamirone (50 mg), fosfomycin (25-50mg), and biopress (25 mg), IV methylprednisolone 1 mg/kg for 3 days, dobutamine | —                                                  | —                       |
| Fried et al.     | Intraaortic balloon pump was inserted and dobutamine infusion                         | Cardiogenic shock                                   | Discharge               |
| Weihl et al.     | Amoxicillin/sulbactam, lipoprotein-racumin and hydroxychloroquine, orotracheal intubation and mechanical ventilation | On day 15, bacteraemic sepsis and multi-organ failure | Patient was still in the intensive care unit |
| Butler et al.    | Rehabilitation                                                                         | —                                                  | —                       |
| Lagana et al.    | Methyl prednisolone (100%), Ace Inhibitor (75%)                                        | Cardiogenic shock                                   | N/R                     |
| Kael et al.      | Oxygen therapy with a high concentration mask (10 liters/minute) for acute respiratory failure on admission. | Cardiogenic shock on day 1                          | N/R                     |
| Fishe et al.     | Dobutamine (5 μg/min) and noradrenaline (3 μg/ml)                                       | Cardiogenic shock (53.33%)                          | 3(25%)                  |
| Fishe et al.     | One dose of 800mg of Todixubam, cortisosteroi, and azithromycin; (300 mg the first day than 25 mg/day for 4 days) | Discharged 7 days later in-patient management       | —                       |
| Fish et al.      | Aspirin and scangrelor, along with the heparin infusion and inotopic support with norepinephrine, vasopressin, and dobutamine for acute coronary syndrome. | Cardiac arrest                                       | Died                    |
| Dabbagh et al.   | Hydroxychloroquine, glucocorticoids, and colchicines; Intubated                         | —                                                  | —                       |
| Irabien-Oroz et  | Immunglobulins (80mg/d), interferon-β (0.25 mg every 48h) and ritonavir/lipocurvin, IV methylprednisolone 500 mg daily at decreasing doses for 14 days, and noradrenaline, ECMO | —                                                  | —                       |
| Albert et al.    | Todixubam, Methyl prednisolone, IV immunoglobulin, Inotropes, ECMO                        | Cardiogenic shock on day 1                          | N/R                     |
| Escher et al.    | Cyclophosphamide and steroids.                                                         | —                                                  | —                       |
| Ford et al.      | Amiodarone load, ceftriaxone/azithromycin, tissue plasminogen activator, warfarin.     | N/R                                                  | —                       |
| Gauchotte et al. | Vasopressors, Inotropic support, ECMO, infusion.                                        | —                                                  | —                       |
| Hua et al.       | Hydroxychloroquine, azithromycin, noradrenaline, adrenaline, and dobutamine             | N/R                                                  | —                       |
| Labani et al.    | N/R                                                                                   | —                                                  | —                       |
| Spano et al.     | N/R                                                                                   | —                                                  | —                       |
| Tawzzi et al.    | Adrenaline (0.07 μg/kg/min), and noradrenaline (0.1 μg/kg/min), ECMO and IABP          | —                                                  | —                       |
| Authors          | In-hospital management                                                                 | Complications                                      | Outcomes                  |
|------------------|-----------------------------------------------------------------------------------------|---------------------------------------------------|---------------------------|
| Trogen et al.    | Hydroxychloroquine, piperacillin/tazobactam, enoxaparin                               | Septic shock                                      | Discharged                |
| Varga et al.     | N/R                                                                                     | N/R                                               | Died                      |
| Warchol et al.   | Azithromycin, oseltamivir, magnesium, and amiodarone                                      | N/R                                               | N/R                       |
| Sardari et al.   | Bisoprolol and lisinopril                                                               | Pluertic chest pain                               | N/R                       |
| Dahl et al.      | Cefotaxime, dindamycin, 3 L/min oxygen, Furosemide, norepinephrine, Continuous positive airway pressure | Respiratory distress, right side ball's pulsy     | Discharged on day 11      |
| Hu et al.        | methylprednisolone, immunoglobulin, norepinephrine, torasemide, furosemide/magnesium    | Cardiogenic shock and pulmonary infection          | Discharged                |
| Vais et al.      | N/R                                                                                     | Pleuertic chest pain, dyspnea                      | Discharged                |
| Besler et al.    | Hydroxychloroquine, azithromycin, ceftriaxone, tigecycline, favipiravir, colchicine     | Pleuertic chest pain, dyspnea                      | Discharged                |
| Gaine et al.     | Diuretics, rate-control agents, anticoagulants, ACE inhibitor, mineralocorticoid antagonist | Heart failure                                     | discharge                 |
| Sheikhi et al.   | Metoprolol, lisinopril, low-dose aspirin, hydrochloroquine, deoximorisin                | Diabetes insipidus                                 | Discharged                |
| Salmans et al.   | Dobutamine, norepinephrine, methylprednisolone, tocilizumab, hydroxychloroquine, azithromycin, lopinavir-ritonavir, temporary pacemaker, extracorporeal membrane oxygenation, inra-aortic balloon pump | Cardiogenic shock                                  | Discharged                |
| Naneishvili et al. | Methylprednisolone, dobutamine, amiodarone, minithinone, norepinephrine, antibiotics | Cardiogenic shock                                  | Discharged                |
| Kim et al.       | N/R                                                                                     | N/R                                               | N/R                       |
| Nile et al.      | Amiodarone, dexamethasone, standard heart failure therapies (details n/r), therapeutic anticoagulation, temporary pacemaker | Cardiogenic shock                                  | Discharged                |
| Long ma et al.   | NA                                                                                      | N/R                                               | N/R                       |
| Sah et al.       | Lopinavir, Hydroxychloroquine                                                            | NA                                                | NA                        |
| Yuan et al.      | N/R                                                                                     | Chest Pain, dyspnea                               | Discharge                 |
| Warchoł et al.   | Azithromycin, oseltamivir                                                               | Chest Pain, dyspnea                               | Discharge                 |
| Asif and Ali     | P1: Aspirin, dopedogrol and heparin, azithromycin, hydroxychloroquine, tocilizumab, meroenoem, norepinephrine. P2: Azithromycin, tocilizumab, nor epinephrine, midaanol | Hemodynamically unstable                          | N/R                       |
| Khalid et al.    | P1: Aspirin, dopedogrol and duretics 2: Methylprednisone, colcholine                   | P1: ARDS, P2: ARDS                                | P1: Died, P2: ICI         |
| Ng et al.        | N/R                                                                                     | P1: N/R, P2: Refractory shock                      | P1: Discharge, P2: Discharge |
| Jin et al.       | Catecholamine, extracorporeal membrane oxygen therapy, Antibiotics                     | N/R                                               | ARDS,                     |
| Yan et al.       | N/R                                                                                     | N/R                                               | N/R                       |
| Kunal S et al.   | Hydroxychloroquine, Azithromycin                                                        | N/R                                               | 57 % Died                 |
The majority of patients, complications during in-hospital stay included 66.4% patients acquiring ARDS and 14% with cardiogenic shock, in addition to others. Overall, 64.7% of patients survived. A summary of the findings obtained is depicted in Figure 3.

Pirzada et al79 elucidated the features of myocarditis found during the initial waves of the COVID-19 pandemic. The authors write that while the exact pathophysiology of severe COVID-19 was still elusive, a consistent observation of the pro-inflammatory surge, namely the cytokine storm was made.79 Observations of elevated interleukins (IL-2R, IL-6, IL-10, TNF- α) were presented in a single-center cohort.80 Viral myocarditis may be considered a direct response of autoimmune, inflammation, or both.81 Based on a cohort of 416 patients at the Renmin Hospital of Wuhan University conducted from January 20, 2020 until February 10, 2020, 82 (19.7%) patients had cardiac injury.82 The cardiac involvement in the cohort of patients had a hazard ratio of 4.26, which is notably high.82 Mortality in the myocardial injury group versus the general group was significantly higher (51.2% vs 4.5%, P<.001).82 The symptoms of myocarditis among COVID-19 patients range from mild symptoms such as chest pain, fatigue, and palpitations to life-threatening symptoms such as sudden cardiac death associated with ventricular arrhythmia or cardiogenic shock. Classically, myocarditis has a viral prodrome including myalgias, fever, and gastrointestinal/respiratory symptoms, with ranges of 10% to 80%.79

Sawalha et al83 identified COVID-19 related myocarditis focusing on management and outcomes until June 30, 2020, including a total of 14 cases. The authors found a male predominance (58%), with a median age of 50.4 years.83 One thirds of all cases were younger than 40 years, and a majority of patients did not have comorbidities (50%), but among those that did have pre-existing conditions, hypertension was the most prevalent (33%).83 Among the 14 patients, dyspnea/shortness of breath were the most common presenting features (75%), in addition to fever (75%).83 On noting the hemodynamic status, 64% patients were in shock, of which 71% of the patients had cardiogenic shock, whereas 29% had a mixed septic and cardiogenic shock.83 Around 42% of the patients had acute respiratory distress syndrome or developed it during the in-hospital period.83 ECG findings were variable with ST-segment depression, ST-segment elevation, and T wave inversion occurring at 25% each.83 Troponin was elevated in 91% of the cases, whereas pro-BNP and CK-MB were less frequently checked.83 Among the 14 patients, echocardiography was performed in 83% of the case and 60% had a reduced ejection fraction.83 Cardiac tamponade was reported in 20% of all echocardiograms, where diffuse hypokinesis was prevalent among 30% patients.83 None of the patients had obstructive coronary disease. Around 50% patients required vasopressor support, with 25% of them warranting inotropic support.83 Mechanical ventilation was utilized for 17% of the patients, of which ECMO was the most commonly used modality.83 Many treatment modalities were used to manage myocarditis of which glucocorticoids (58%) were mostly used, followed by immunoglobulin therapy (25%) and colchicine (17%). Therapies to mitigate cytokine storm were interferon and tocilizumab (17% each).83 Sawalha et al83 found that 81% survived to discharge whereas 19% did not survive; the patients who did not survive were noted to have both myocarditis and ARDS.

Castiello et al84 identified 38 case reports of COVID-19 patients with myocarditis based on the WHO/IFSC or ESC criteria. Around 45% of the cases had fever or a mild temperature increase; 21.1% had gastrointestinal symptoms, and 10.5% had a presenting or previous syncope.84 Troponin levels varied substantially whereas BNP was raised in 57.9% patients. ECG findings were normal in 10.5% patients with variations among the rest.84 Of 34 patients, only 18.4% patients had no functional or structural abnormality.84 On noting CMR findings, myocardial inflammation and diffuse edema were captured in 50% patients.84 EMB was performed only in 21.2% patients, where only 1 case reported the presence of SARS-CoV-2 in the cardiomyocytes.84 Histological data obtained from autopsies were available for 10.5% patients, of which inflammatory infiltrates, accumulated inflammatory cells in the endothelium and signs of ferroptosis were noted.84 The medical treatment was variable ranging from hydroxychloroquine (26.3%), tocilizumab (10.5%), lopinavir/ritonavir (7.9%), antibiotics (36.8%), steroids (34.2%), heart failure medications (36.8%), and anticoagulants (21.1%). Of 33 cases with reported outcomes, 84.8% patients survived, whereas 15.2% did not survive.84

Rathore et al8 present recent data, until January 5, 2021, of 42 patients with myocarditis and COVID-19, with 71.4% being males, and with a median age of 43.4 years. Hypertension was the most common finding in these patients, where cardiac biomarkers BNP and troponin were raised in 87% and 90% of the patients respectively.8 ECG findings were non-specific with T-wave and ST-segment changes noted. Echocardiogram commonly showed ventricular systolic dysfunction with cardiomegaly.8 The commonest histopathological feature was diffuse lymphocytic inflammatory infiltrates.8 Moreover, corticosteroids and antivirals were most frequently used. Around 40% of the patients required vasopressor support.8 Of 41 patients, 67% survived, whereas 33% died.8 Due to the sudden risk of worsening patient conditions and associations with myocarditis, knowledge of this cardiac complication due to COVID-19 is critical for healthcare workers across all settings. Kamarullah et al85 also conducted a search until January 2021 where 18 patients were included. The findings were suggestive of the beneficial effects of corticosteroids in treating myocarditis associated with COVID-19; the most commonly applied
Steroids were hydrocortisone (5.5%), methylprednisolone (89%), and prednisolone (5.5%), with the intravenous route being the most common and duration of treatment ranging from 1 to 14 days.85,86

**Strengths and Limitations**

This systematic review synthesizes the most recent evidence of COVID-19 infection and myocarditis, until August 31, 2021. Published literature obtained during the systematic search presents data collected until January 2021, enabling our collated findings, obtained until August 2021, to be a critical piece of information for healthcare workers worldwide. We present key findings about demographics, COVID-19 and myocarditis symptomatology, essential diagnostic techniques of use to clinicians, and clinical outcomes of interest of COVID-19 infection and myocarditis. The findings further strengthen the benefits of evidence-based healthcare where we gather evidence from reliable published literature to inform healthcare decisions, and reduce variations in healthcare delivery during the COVID-19 pandemic.

This systematic review has certain limitations. First, COVID-19 and myocarditis symptomatology may be overlapping, suggesting difficult clinical demarcations. Second, COVID-19 infections compounded with myocarditis were expected to be underreported as patients who did not previously have comorbidities presented with newly diminished ejection fractions and elevated myocardial markers. Thirdly, our systematic review presents that a low proportion of patients had confirmed myocarditis via MRI/endomyocardial biopsy. A plausible reason was the fear of contracting COVID-19 infection on undergoing MRI/endomyocardial biopsy. Fourthly, ECG and echocardiography were considered to be reliable screening tests, but not diagnostic tests, except for pericardial effusion. Lastly, while biomarkers such as troponin, BNP, and CK-MB were useful in diagnosing myocarditis, they are non-specific because the levels may also rise in other conditions such as demand ischemia and acute heart failure.

**Conclusion**

This systematic review presents findings about demographics, symptomatology, diagnostic techniques, and clinical outcomes of adult COVID-19 patients with myocarditis. A total of 229 patients were included in this analysis, who were diagnosed with myocarditis. The patients commonly presented with fever, cough, and shortness of breath making the clinical presentations difficult to differentiate. Elevated inflammatory and cardiac marker in addition to ECG and echocardiographic findings were useful indicators of myocardial disease. Gold standard testing such as MRI and endomyocardial biopsy were under-utilized suggesting that a definitive diagnostic approach may be required for those patients who fall under a high risk of suspicion for COVID-19 induced myocarditis. Due to the peaked risk of death among patients contracting both...
ARDS and myocardial inflammation, it is essential that healthcare workers are aware that myocarditis may be associated with COVID-19 infections. While the treatment approaches were variable across the cohort of patients included in this systematic review, further large-scale randomized controlled trials may help in establishing the best care of treatment for those with a definitive diagnosis of myocarditis with COVID-19.

**Acknowledgments**

We would like to thank Janelle Tayo, Yoandra Diaz, Furqan Ahmad Jarullah for their early contributions to the manuscript.

**Declaration of Conflicting Interests**

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

**Funding**

The author(s) received no financial support for the research, authorship, and/or publication of this article.

**ORCID iDs**

Vikash Jaiswal [i] https://orcid.org/0000-0002-2021-1660

Zouina Sarfraz [i] https://orcid.org/0000-0002-5132-7455

Azza Sarfraz [i] https://orcid.org/0000-0001-8206-5745

Dattatrey Mukherjee [i] https://orcid.org/0000-0001-7566-3843

Gazala Hitawala [i] https://orcid.org/0000-0002-5819-4157

Ruchika [i] https://orcid.org/0000-0003-0227-3175

Shehar Bano [i] https://orcid.org/0000-0002-6429-797X

Sidra Naz [i] https://orcid.org/0000-0001-6390-9658

**References**

1. Mantica G, Riccardi N, Terrone C, Gratarola A. Re: letter to the editor of Public Health in response to ‘Non-COVID-19 visits to emergency departments during the pandemic: the impact of fear’. Public Health. 2020;186:17. doi:10.1016/j.puhe.2020.07.003

2. Jaiswal V, Alquraish D, Sarfraz Z, et al. The influence of Coronavirus disease-2019 (COVID-19) On Parkinson’s disease: an updated systematic review. J Prim Care Community Health. 2021;12:21501327211039709. doi:10.1177/21501327211039709

3. Sarfraz Z, Sarfraz A, Barrios A, et al. Cardio-Pulmonary sequelae in recovered COVID-19 patients: considerations for primary care. J Prim Care Community Health. 2021;12:21501327211023726. doi:10.1177/21501327211023726

4. Guo J, Huang Z, Lin L, Lv J. Coronavirus disease 2019 (COVID-19) and Cardiovascular disease: a viewpoint on the potential influence of angiotensin-converting enzyme inhibitors/angiotensin receptor blockers on onset and severity of severe acute respiratory syndrome Coronavirus 2 infection. J Am Heart Assoc. 2020;9(7):e016219. doi:10.1161/JAHA.120.016219

5. Zaim S, Chong JH, Sankaranarayanan V, Harky A. COVID-19 and multiorgan response. Curr Probl Cardiol. 2020;45(8):100618. doi:10.1016/j.cpcardiol.2020.100618

6. Khan IH, Zahra SA, Zaim S, Harky A. At the heart of COVID-19. J Card Surg. 2020;35(6):1287-1294. doi:10.1111/jocs.14596

7. Myocarditis and pericarditis following mRNA COVID-19 vaccination | CDC. Accessed September 2, 2021. https://www.cdc.gov/coronavirus/2019-ncov/vaccines/safety/myocarditis.html

8. Rathore SS, Rojas GA, Sondhi M, et al. Myocarditis associated with Covid-19 disease: a systematic review of published case reports and case series. Int J Clin Pract. 2021;75(11):e14470. doi:10.1111/i tcp.14470

9. 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(9):1463-1471. doi:10.1016/j.hrthm.2020.05.001

10. Tissières P, Teboul J-L. SARS-CoV-2 post-infective myocarditis: the tip of COVID-19 immune complications? Ann Intensive Care. 2020;10(1):98-104. doi:10.1186/s13613-020-00717-0

11. Verma AK, Lavine KJ, Lin C-Y. Myocarditis after covid-19 mRNA vaccination. New Engl J Med. 2021;385:1332-1334. doi:10.1056/NEJMc2109975.

12. Boehmer TK, Kompaniyets L, Lavery AM, et al. Association between COVID-19 and myocarditis using hospital-based administrative data - United States, march 2020-january 2021. MMWR Morb Mortal Wkly Rep. 2021;70(35):1228-1232. doi:10.15585/mmwr.mm7035e5

13. Cizgici AY, Zencirkiran Agus H, Yildiz M. COVID-19 myopericarditis: it should be kept in mind in today's conditions. Am J Emerg Med. 2020;38(7):1547.e5-1547.e6.

14. Yokoo P, Fonseca EKUN, Neto RS, et al. COVID-19 myocarditis: a case report. Einstein (São Paulo). 2020;18:eRC5876.

15. Pietsch H, Escher F, Aleshcheva G, et al. Proof of SARS-CoV-2 genomes in endomyocardial biopsy with latency after acute infection. Internet J Infect Dis. 2021;102:70-72.

16. Pavon AG, Meier D, Samim D, et al. First documentation of persistent SARS-Cov-2 infection presenting with late acute severe myocarditis. Can J Cardiol. 2020;36(8):1326.e5-1326.e7.

17. Khatri A, Wallach F. Coronavirus disease 2019 (Covid-19) presenting as purulent fulminant myopericarditis and cardiac tamponade: a case report and literature review. Heart Lung. 2020;49(6):858-863.

18. Hussain H, Fadel A, Alwaeli H, Guardiola V. Coronavirus (COVID-19) fulminant myopericarditis and acute respiratory distress syndrome (ARDS) in a middle-aged male patient. Cureus. 2020;12(6):e8808.

19. Dalen H, Holte E, Guldal AU, et al. Acute perimyocarditis with cardiac tamponade in COVID-19 infection without respiratory disease. BMJ Case Rep. 2020;13(8):e236218. doi:10.1136/bcr-2020-236218.
20. Zeng J-H, Liu Y-X, Yuan J, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. *Infection*. 2020;48(5):773-777.
21. Doyen D, Moceri P, Ducrues D, Dellamonica J. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. *Lancet*. 2020;395(10235):1516.
22. Faircloth E, Conner C, Dougherty K, Arora S, Thorevska N. Viral heartbeat: a case of covid-19 myocarditis vs stress-induced cardiomyopathy. *Chest*. 2020;158(4):A173.
23. Coyle J, Igbinomwanhi E, Sanchez-Nadales A, Danciu S, Chu C, Shah N. A recovered case of COVID-19 myocarditis and ARDS treated with corticosteroids, tocilizumab, and experimental AT-001. *Case Rep. 2020*.2(9):1331-1336.
24. Luetkens JA, Isaak A, Zimmer S, et al. Diffuse myocardial inflammation in COVID-19 associated myocarditis detected by multiparametric cardiac magnetic resonance imaging. *Circ Cardiovasc Imaging*. 2020;13(5):e010897.
25. Jain A, Deval N, Paul L. A recovered case of covid-19 myocarditis treated with IV immunoglobulin. *Chest*. 2020;158(4):A281.
26. Mustafa S, Zafar M, Agrawal N, Shahbaz A, Al-khafaji N. COVID-19-associated myocarditis mimicking ST elevation myocardial infarction. *Chest*. 2020;158(4):A572.
27. Mansoor A, Chang D, Mitra R. Rhythm, conduction, and ST elevation with COVID-19: myocarditis or myocardial infarction? *HeartRhythm Case Rep*. 2020;6(10):671-675.
28. Al-Assaf O, Mirza M, Musa A. Atypical presentation of COVID-19 as subclinical myocarditis with persistent high degree atrio-ventricular block treated with pacemaker implant. *HeartRhythm Case Rep*. 2020;6(11):884-887.
29. Khalid Y, Dasu N, Dasu K. A case of novel coronavirus (COVID-19)-induced viral myocarditis mimicking a Takotsubo cardiomyopathy. *HeartRhythm Case Rep*. 2020;6(8):473-476.
30. Inciardi RM, Lupi L, Zacccone G, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). *JAMA Cardiol*. 2020;5(7):1-6.
31. Fried JA, Ramasubbu K, Bhatt R, et al. The variety of cardiovascular presentations of COVID-19. *Circulation*. 2020;141(23):1930-1936.
32. Wehit JM, Sosa FA, Merlo P, Roberti J, Osatnik J. Identification of COVID-19-associated myocarditis by speckle-tracking transthalogal echocardiography in critical care. *Acta Colomb Cuidado Intensivo*. Published online November 24, 2020. doi:10.1016/j.acci.2020.11.008
33. Butler K, Clancy MJ, Adler J, Tevald MA. Acute rehabilitation of a patient with COVID-19 myocarditis: a case report. *Phys Ther*. 2021;101(1):aa190.
34. Laganà N, Cei M, Evangelista I, et al. Suspected myocarditis in patients with COVID-19: a multicenter case series. *Medicine*. 2021;100(8):e24552.
35. Kallel O, Bourouis I, Bougrine R, Housni B, El Ouafi N, Ismaili N. Acute myocarditis related to covid-19 infection: 2 cases report. *Ann Med Surg*. 2021;66:102431.
36. Ghugre NR, Orbach A, Biswas L, et al. Suspected subclinical myocarditis detected by cardiac magnetic resonance imaging late post COVID-19 recovery. *J Cardiol Cases*. Published online May 14, 2021. doi:10.1016/j.jccase.2021.04.014.
37. Fath AR, Aglan A, Varkoly KS, et al. Distinct coagulopathy with myocardial injury and pulmonary embolism in COVID-19. *J Investig Med High Impact Case Rep*. 2021;9:23247096211019560.
38. Dabbagh MF, Aurora L, D’Souza P, Weinmann AJ, Bhargava P, Basir MB. Cardiac tamponade secondary to COVID-19. *Case Rep*. 2020;2(9):1326-1330.
39. Iribien-Ortiz Carreras-Mora J, Sionis A, Pamiès J, Montiel J, Tauron M. Fulminant myocarditis due to COVID-19. *Rev Esp Cardiol*. 2020;73(6):503-504.
40. Albert CL, Carmona-Rubio AE, Weiss AJ, Procop GG, Starling RC, Rodriguez ER. The enemy within: sudden-onset reversible cardiogenic shock with biopsy-proven cardiac myocyte infection by severe acute respiratory syndrome coronavirus 2. *Circulation*. 2020;142(19):1865-1870.
41. Escher F, Pietsch H, Aleshecheva G, et al. Detection of viral SARS-CoV-2 genomes and histopathological changes in endomyocardial biopsies. *ESC Heart Fail*. 2020;7(5):2440-2447.
42. Ford JS, Holmes JF, Jones RF. Cardioembolic stroke in a patient with coronavirus disease of 2019 (COVID-19) myocarditis: a case report. *Clin Pract Cases Emerg Med*. 2020;4(3):332-335.
43. Gauchotte G, Venard V, Segondy M, et al. SARS-CoV-2 fulminant myocarditis: an autopsy and histopathological case study. *Int J Legal Med*. 2021;135(2):577-581.
44. Hua A, O’Gallagher K, Sado D, Byrne J. Life-threatening cardiac tamponade complicating myo-pericarditis in COVID-19. *Eur Heart J*. 2020;41:2130-2130.
45. Jacobs W, Lammens M, Kerckhofs A, et al. Fatal lymphocytic cardiac damage in coronavirus disease 2019 (COVID-19): autopsy reveals a ferroptosis signature. *ESC Heart Fail*. 2020;7(6):3772-3781.
46. Labani A, Germain P, Douchet M-P, et al. Acute myopericarditis in a patient with mild SARS-CoV-2 respiratory infection. *CJC open*. 2020;2(5):435-437.
47. Siano G, Fischer K, Maillat C, Vicario G, Huber AT, Gräni C. Delayed isolated peri-myocarditis in a covid-19 patient with respiratory symptoms but without lung involvement. *Int J Cardiovasc Imaging*. 2020;36(11):2279-2280.
48. Tavazzi G, Pellegrini C, Maurelli M, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. *Eur J Heart Fail*. 2020;22(5):911-915. doi:10.1002/ejhf.1828
49. Trogen B, Gonzalez FJ, Shust GF. COVID-19-associated myocarditis in an adolescent. *Pediatr Infect Dis J*. 2020;39(8):e204-e205.
50. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endothelitis in COVID-19. *Lancet*. 2020;395(10234):1417-1418. doi:10.1016/S0140-6736(20)30937-5
51. Warchol I, Debska-Kozlowska A, Karcz-Socha A, Książczyk J - Cardiovasc Imaging. Published online May 14, 2021. doi:10.1016/j.jccase.2021.04.014.
52. Sardari A, Tabarsi P, Borhany H, Mohiaddin R, Houshmand G. Myocarditis detected after COVID-19 recovery. *Eur Heart J - Cardiovasc Imaging*. 2021;22(1):131-132.
53. Dahl EH, Mosevoll KA, Cramariuc D, Vedeler CA, Blomberg B. COVID-19 myocarditis and postinfection bell’s palsy. BMJ Case Rep. 2021;14(1):e240095. doi:10.1136/BCR-2020-240095

54. Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminating myocarditis treated with glucocorticoid and human immunoglobulin. Eur Heart J. 2021;42(2):206. doi:10.1093/eurheartj/ehaa190

55. Volis I, Livneh I, Hussein K, Raze-Pastueur A. COVID-19-Associated suspected myocarditis as the etiology for recurrent and protracted fever in an otherwise healthy adult. Am J Med Sci. 2021;361(4):522-525. doi:10.1016/j.amjms.2020.11.001

56. Beşler MS, Arslan H. Acute myocarditis associated with COVID-19 infection. Am J Emerg Med. 2020;38(11):2489.e1-2489.e2. doi:10.1016/j.ajem.2020.05.100

57. Gaine S, Devitt P, Coughlan JJ, Pearson I. COVID-19-associated myocarditis presenting as new-onset heart failure and atrial fibrillation. BMJ Case Rep. 2021;14(7):e244027. doi:10.1136/BCR-2021-244027

58. Sheikh AB, Javed N, Sheikh AAE, Upadhyay S, Shekhar R. COVID-19 and myocarditis: a systematic review and overview of COVID-19 related myocarditis. Current challenges. J Investig Med High Impact Case Rep. 2020;8:1-11. doi:10.1007/s12378-021-10087-9

59. Eichhorn C, Bière L, Schnell F, et al. Myocarditis in athletes - an ominous association. Cardiovasc Revasc Med. 2021;24:177-185. doi:10.1016/j.carrev.2020.08.028
85. Kamarullah W, Nurcahyani N, Mary Josephine C, Bill Multazam R, Ghaezany Nawing A, Dharma S. Corticosteroid therapy in management of myocarditis associated with COVID-19: a systematic review of current evidence. *Arch Acad Emerg Med*. 2021;9(1):e32. doi:10.22037/aaem.v9i1.1153.

86. Sarfraz A, Sarfraz Z, Sarfraz M, Aftab H, Pervaiz Z. Tocilizumab and COVID-19: a meta-analysis of 2120 patients with severe disease and implications for clinical trial methodologies. *Turk J Med Sci*. 2021;51(3):890-897. doi:10.3906/SAG-2010-131