A Systematic Review of COVID-19 and Pericarditis

Pramod Theetha Kariyanna 1, Ahmed Sahib 2, Bayu Sutarjono 3, Kanval Shah 4, 5, Alvaro Vargas Peláez 6, Jeremy Lewis 7, Rebecca Yu 7, Ekjot S. Grewal 3, Apoorva Jayarangaiah 7, Sushruth Das 9, Amog Jayarangaiah 10

1. Division of Interventional Cardiology, Icahn School of Medicine at Mount Sinai Morningside/Beth Israel Hospital, New York City, USA. 2. Internal Medicine, Kingsbrook Jewish Medical Center, Brooklyn, USA. 3. Emergency Medicine, Brookdale University Hospital Medical Center, New York City, USA. 4. Internal Medicine, Baystate Medical Center, Springfield, USA. 5. Internal Medicine, University of Massachusetts Medical School - Baystate Medical Center, Springfield, USA. 6. Cardiology, Mount Sinai Beth Israel, New York City, USA. 7. Internal Medicine, Saba University School of Medicine, Devens, USA. 8. Internal Medicine, New York City Health and Hospitals/Jacobi Medical Center, Bronx, USA. 9. Internal Medicine, Trinity School of Medicine, Kingstown, VCT. 10. Internal Medicine, Marshfield Clinic Health System, Marshfield, USA

Abstract

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was first identified in Wuhan, China in December 2019. Since then, the disease has spread globally, leading to the ongoing pandemic. It can cause severe respiratory illness; however, many cases of pericarditis have also been reported. This systematic review aims to recognize the clinical features of pericarditis and myopericarditis in COVID-19 patients.

Google Scholar, Medline/PubMed, CINAHL, Cochrane Central, and Web of Science databases were searched for studies reporting “Coronavirus” or “COVID” and “Peri-myocarditis,” “heart,” or “retrospective.” Case reports and retrospective studies published from May 2020 to February 2021 were reviewed.

In total, 33 studies on pericarditis, myopericarditis, and pericardial infusion were included in this review. COVID-19 pericarditis affected adult patients at any age. The incidence is more common in males, with a male-to-female ratio of 2:1. Chest pain (60%), fever (51%), and shortness of breath (51%) were the most reported symptoms, followed by cough (59%), fatigue (15%), myalgia (12%), and diarrhea (12%). Laboratory tests revealed leukocytosis with neutrophil predominance, elevated D-dimer, erythrocyte rate, and C-reactive protein. Cardiac markers including troponin-I, troponin-T, and brain natriuretic peptide were elevated in most cases. Radiographic imaging of the chest were mostly normal, and only 31% of chest X-rays showed cardiomegaly and or bilateral infiltration. Electrocardiography (ECG) demonstrated normal sinus rhythm with around 59% ST elevation and rarely PR depression or T wave inversion, while the predominant echocardiographic feature was pericardial effusion. Management with colchicine was favored in most cases, followed by non-steroidal anti-inflammatory drugs (NSAIDs), and interventional therapy was only needed when patient developed cardiac tamponade. The majority of the reviewed studies reported either recovery or no continued clinical deterioration.

The prevalence of COVID-19-related cardiac diseases is high, and pericarditis is a known extrapulmonary manifestation. However, pericardial effusion and cardiac tamponade are less prevalent and may require urgent intervention to prevent mortality. Pericarditis should be considered in patients with chest pain, ST elevation on ECG, a normal coronary angiogram, and COVID-19. We emphasize the importance of clinical examination, ECG, and echocardiogram for decision-making, and NSAIDs, colchicine, and corticosteroids are considered to be safe in the treatment of pericarditis/myopericarditis associated with COVID-19.

Introduction And Background

The novel coronavirus disease 2019 (COVID-19) is a global pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) [1]. The pandemic began in Wuhan, China in December 2019. While affecting dominantly the respiratory system, COVID-19 can also cause acute and chronic damage to the cardiovascular system. The cardiovascular manifestations of COVID-19 are diverse and include arrhythmia, acute coronary syndrome, left ventricular heart failure, myocarditis, and acute and subacute pericarditis with or without pericardial effusion [2-4].

Pericarditis refers to the inflammation of the pericardium, the thin fibrous sac surrounding the heart, that can present as an isolated disease or as a manifestation of a systemic disorder, diagnosed in approximately 0.1% of patients hospitalized for chest pain. Although acute pericarditis has many causes, it is most often...
idiopathic or is presumed to be viral in origin [5].

Acute effusive pericarditis is a rare manifestation of COVID-19, especially without concomitant pulmonary disease or myocardial injury; yet, very little research is available regarding pericarditis caused by SARS-CoV-2. It is important to maintain a high level of suspicion to ensure early diagnosis and treatment. Diagnosing these conditions can be challenging, and early appropriate treatment can improve the outcome. Therefore, we conducted a systematic review of COVID-19 patients with acute pericarditis to assess clinical characteristics, diagnostic testing, and current treatment therapy.

Acute pericarditis and myopericarditis share the same viral etiological agents, with myocardial involvement often found in the former [6]. Therefore, we have included myopericarditis in this study.

**Review**

**Methodology**

**Protocol and Registration**

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) checklist was followed for this systematic review [7]. The study protocol was not registered. The Joanna Briggs Institute critical appraisal tool for case reports was used in this systematic review [8].

**Inclusion Criteria**

Only articles reporting the association between COVID-19 and myopericarditis or pericarditis were included. Pericarditis is defined as an inflammatory process affecting the pericardial sac surrounding the heart [6]. The search terms that were used in our article screening were "COVID-19," "Pericarditis," "Pericardial effusion," "Pericardial disease," "Cardiac tamponade," and "Myocarditis."

**Exclusion Criteria**

Studies were excluded if: (1) they were not case reports, case series, or observational studies with a focus on myopericarditis or pericarditis; (2) they were reviews or editorials, (3) the patient tested negative for COVID-19; or (4) the study did not pass bias evaluation. The language of the article was not a limitation as all of the articles which were relevant in our literature search were written in the English language.

**Information Sources and Search Strategies**

We conducted a comprehensive literature search using Medline/PubMed, Google Scholar, CINAHL, Cochrane Central, and Web of Science databases up to and including February 28, 2021, using the terms "Coronavirus" or "COVID" and "pericarditis" or "myopericarditis."

**Study Selection**

Articles were triaged based on whether titles or abstracts met the inclusion criteria. Full-text articles were then read, and those that did not satisfy the inclusion criteria were excluded. A summary of study characteristics is given in Table 1.

| Reference, publication year | Study type | Patient profile (age in years, sex) | Symptoms                                                                 | Diagnosis          |
|-----------------------------|------------|-----------------------------------|-------------------------------------------------------------------------|--------------------|
| Amoozgar et al., 2020 [9]    | Case report| 56, Male                           | Non-radiating exertional chest pain with dyspnea for 1 week             | Acute pericarditis |
| Asif et al., 2020 [10]       | Case report| 70, Female                         | Chest pain, worsening dyspnea, myalgias for 3 days                      | Acute pericarditis |
| Blagojevic et al., 2020 [11]| Case report| 51, Male                           | Sudden but persistent chest pain for 1 day; the pain was sharp, worsened with deep breathing or a change in body position, and was alleviated while sitting | Acute pericarditis |
| Cairns et al., 2021 [12]     | Case report| 58, Female                         | Fever, diarrhea, vomiting, poor oral intake                            | Acute Myopericarditis |
| Authors                  | Type          | Age | Sex | Symptoms                                                                 | Diagnosis                      |
|-------------------------|---------------|-----|-----|--------------------------------------------------------------------------|--------------------------------|
| Cizgici et al., 2020    | Case report   | 78  | Male| Chest pain and shortness of breath                                       | Acute myopericarditis          |
| Faraj et al., 2021      | Case report   | 36  | Male| Chest pain, worse when lying or on deep breathing                        | Acute pericarditis             |
| Fox et al., 2020        | Case report   | 43  | Male| Progressive orthopnea, conversational dyspnea, and chest pain (radiating to the neck and left shoulder) for 4 days; reported mild non-productive cough and subjective fever 2 weeks prior | Acute pericarditis             |
| Fried et al., 2020      | Case series   | 64  | Female| Persistent chest pressure for 2 days                                     | Acute myopericarditis          |
| Garcia-Cruz et al., 2020| Case report   | 64  | Male| Chest pain, dry cough, fever, dyspnea                                    | Acute pericarditis             |
| Inciardi et al., 2020   | Case report   | 53  | Female| Severe fatigue for 2 days, fever, and cough the week before              | Acute myopericarditis          |
| Karadeniz et al., 2020  | Case report   | 33  | Male| Retrosternal chest pain for 5 days, worse with sitting forward, unresponsive to diclofenac, severe low back pain (for 1 week) | Acute pericarditis             |
| Kazi et al., 2020       | Case report   | 73  | Male| Dry cough, worsening fever, fatigue for 2 days before presenting to ED (6 days before transfer to ICU); dyspnea developed over next 4 days | Acute myopericarditis          |
| Khalid et al., 2020     | Case series   | 34  | Female| Chest heaviness, generalized weakness, subjective fever/chills, body aches for 3 days | Acute myopericarditis          |
| Khatir et al., 2020     | Case report   | 50  | Male| Fever, chills, generalized malaise, non-productive cough, dyspnea for 3-4 days, and an episode of near-syncpe on the day of presentation | Acute myopericarditis          |
| Kumar et al., 2020      | Case report   | 66  | Male| Acute-onset severe pleuritic chest pain for 1 day (4 episodes lasting 10-15 minutes); pain worse lying down, relieved by leaning forward | Acute pericarditis             |
| Legrand et al., 2020    | Case report   | 39  | Male| Chest pain and dyspnea for 2 days                                       | Acute myopericarditis          |
| Li et al., 2020         | Case report   | 60  | Male| Fever, cough, worsening dyspnea, mild abdominal pain, diarrhea for 8 days | Acute myopericarditis          |
| Marschall et al., 2020  | Case report   | 45  | Male| Dyspnea with minimal exertion, orthopnea, bendopnea                      | Acute pericarditis             |
| Naqvi et al., 2020      | Case report   | 55  | Male| Chest pain for 24 hours                                                  | Acute pericarditis             |
| Ortiz-Martinez et al., 2020 | Case report | 25  | Male| Myalgias, arthralgias, diarrhea, 2 days later: fever and nausea, began isolation, on 8th day: intense pleuritic centrothoracic chest pain, improved with sitting forward, worse with supine, dyspnea at rest | Acute pericarditis             |
| Öz turan et al., 2020   | Case report   | 25  | Male| Acute onset chest pain and shortness of breath, 4-day history of progressive fatigue and fever | Acute myopericarditis          |
| Patel et al., 2021      | Case report   | 63  | Male| Fever, dry cough, and malaise for 1 week; chest pain for 1 day           | Acute pericarditis             |
| Purohit et al., 2020    | Case report   | 82  | Female| Productive cough, fever with chills, intermittent diarrhea for 5 days    | Acute myopericarditis          |
| Raymond et al., 2020    | Case report   | 7   | Female| Cough, chest pain, orthopnea for 3 days                                 | Acute pericarditis             |
| Recalcati et al., 2020  | Case          |     |     |                                                                           | Acute                          |
TABLE 1: Summary of the characteristics of included articles (n = 33).

| Data Collection Process and Data Items |
|---------------------------------------|
| Data extracted from articles included the name of the first author, year of publication, country, and study design. Variables for which data were sought from all studies included patient age and sex and presenting complaints at the time of admission. Laboratory tests, diagnostic studies, management of pericarditis, and patient outcomes including complications were extrapolated from case studies. |
| **Analysis of Results and Summary of Measures** |
| Information was reviewed if it was reported by two or more articles. Subsequently, the data were tabulated, evaluated, and summarized. |
| **Risk of Bias Across Studies** |
| Potential bias across studies was analyzed within study characteristics. Two independent reviewers evaluated the methodological quality of the eligible studies. A third reviewer evaluated papers when there was no agreement. The Joanna Briggs Institute critical appraisal tool for case reports was used in this systematic review [8]. Bias was evaluated using a checklist of eight questions. Each question is specified in the Appendix concerning the risk of bias whereby an overall appraisal was made of each article: low risk of bias (included), high risk of bias (excluded), or uncertain risk of bias (more information is required). For this study, an answer of "yes" equal to or greater than 50% of the questions was considered to be low risk of bias. Similarly, an answer of "no" equal to or greater than 50% of questions was determined to be high risk of bias, whereas "unclear" answers were equal to or greater than a 50% response. |
| **Results** |
| **Study Selection** |
| From the five databases, 12,510 articles were selected concerning COVID-19 and myocarditis. In total, 34 articles were selected once assessed for eligibility [9-42]. The study by Rauch et al. [42] was removed from the analysis. |
this list as it did not meet the minimum criteria required when assessed for bias. A PRISMA flow diagram detailing the process of identification, inclusion, and exclusion of studies is shown in Figure 1.

![Flow diagram of the literature search and selection criteria adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).]

**FIGURE 1: Flow diagram of the literature search and selection criteria adapted from the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA).**

### Study Characteristics

In total, 29 articles selected for this study were case reports [9-15,17-20,22-35,38-41] while four were case series [16,21,36,37]. All articles were published in 2020 [9-11,13,15-29,31-37,39-41], except four, which were published in 2021 [12,14,30,38]. The majority of the studies were conducted in the United States [9,10,15,16,20-22,25,30-32,38-41], followed by countries from the European Union or United Kingdom [11,12,18,25,26,33,35,36,40] and the Middle East or Asia [12,19,27,29,37]. Only three studies originated from Latin America [17,28,34] and one from northern Africa [14].

### Risk of Bias Within Studies

In comparison to case reports, the majority of articles were rated to have a low risk of bias [9-41]. As mentioned previously, only one study was characterized as high risk of bias [42] and was removed from the systematic review.

### Results of Individual Studies

The common theme of the studies was either the identification of only pericarditis [10,11,14,16,19,23,26,28,30,35,37,38,40], myopericarditis [13,18,20,21,24,25,29,33,34], or the association of cardiac tamponade or pericardial effusion and either pericarditis or myopericarditis [9,12,15,17,27,31,32,36,39,41] in COVID-19 patients.

### Patient Profile

COVID-19 patients selected for the systematic review were 49.3 ± 18.5 years of age, with more males affected than females at a ratio of 2:1 [9-41]. The eldest was 82 years old [31], while the youngest was seven years old [32].

### Presenting Complaints

The predominant symptom at admission was chest pain [9,11,13-17,19,21,23,24-27,30,32,33,37,38], followed by fever [12,15,17,18,20-22,25,28-31,33-35,40,41], shortness of breath [10,13,15,17,20,22,24-26,28,29,32,34,35,38,39,41], and cough [15,17,18,20,22,25,30-32,35,38,40,41]. The mean temperature recorded was 37.5 ± 1.1°C [9-12,14-16,21,22,23,30,32,33,35,38,41] while the mean blood pressure was 112.0 ± 20.3/71.7 ± 16.0 [5-12,14-21,25,26-30,34,37,38,41]. The average heart rate was also elevated at 105.9 ± 21.3 beats/minute [9-12,14-21,25-30,32,34,37,38,41]. The mean oxygen saturation was 96.2 ± 0.1% [9-12,14-21,25-30,32,34,36-38,41]. The distribution of presenting complaints and associated symptoms are listed in Table 2.
| Symptom               | %  |
|----------------------|----|
| Chest pain           | 60.6 |
| Fever                | 51.5 |
| Shortness of breath  | 51.5 |
| Cough                | 39.4 |

**TABLE 2: Most common clinical manifestations on admission of patients with COVID-19 and pericarditis and myopericarditis as the proportion reported from all articles (n = 33).**

**Medical History**

Nearly half of the patients reported a medical history of hypertension [10-15,16,20,22,23,25,27,30,31,38,39], followed by diabetes mellitus [10,12,20,37,39] and hyperlipidemia [10,16,25,31].

**Laboratory Tests**

A summary of laboratory tests is presented in Table 3.

| Vitals                                                                 | Trends | (Standard range) |
|-----------------------------------------------------------------------|--------|------------------|
| Temperature, °C (n = 25)                                              | Elevated | (<37.5)         |
| Heart rate, beats/minute (n = 25)                                     | Elevated |                |
| Systolic blood pressure, mmHg (n = 22)                                | Normal  | (90–120)         |
| Diastolic blood pressure, mmHg (n = 21)                               | Normal  | (60–80)          |
| SaO₂, % (n = 25)                                                      | Normal  | (>94)            |

| Inflammatory markers                                                 |        |                  |
|-----------------------------------------------------------------------|--------|------------------|
| WBC, cells/mm³ (n = 17)                                              | Elevated | (4,500–11,000) |
| WBC predominance (n = 8)                                             | Neutrophils |          |
| CRP, mg/L (n = 21)                                                   | Elevated | (<8.0)          |
| ESR, mm/hour (n = 5)                                                 | Elevated | (0–20)          |
| D-dimer level, ng/mL (n = 15)                                        | Elevated | (<250)          |

| Cardiac markers                                                      |        |                  |
|----------------------------------------------------------------------|--------|------------------|
| Troponin-I, ng/mL (n = 17)                                           | Elevated | <0.04           |
| Troponin-T, ng/mL (n = 13)                                           | Elevated | <0.01           |
| CK-MB, ng/mL (n = 3)                                                 | Elevated | <5.0            |
| BNP, pg/mL (n = 10)                                                  | Elevated | <125            |

**TABLE 3: Trends of laboratory values of COVID-19 patients with pericarditis and myopericarditis from all articles (n = 33).**

SaO₂: oxygen saturation (arterial blood); WBC: white blood cell; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; CK-MB: creatine kinase-myoglobin binding; BNP: brain natriuretic peptide; COVID-19: coronavirus disease 2019.
All patients were confirmed COVID-19 positive [9-41]. The majority of studies reported leukocytosis [9,11,14,15,20,22,24-29,32-35,37,40] and neutrophil predominance [11,20,21,25,34,38-40], with a mean of 15,622 ± 2,654 cells/mm³. Increased C-reactive protein (CRP) was also reported by the majority of studies, with a mean of 15.0 ± 9.59 mg/dL [11,13-16,19-22,24-26,28-30,32-35,37-40]. Only six studies recorded erythrocyte sedimentation rate (ESR), with three reporting elevated values at a mean of 59.3 ± 25.7 mm/hour [11,21,32,30,32,38].

Two-thirds of studies showed elevated D-dimer levels [9,15,16,19,22,23,25,26,28,33-35,38,40,41], with two articles reporting values higher than 5,000 ng/mL [9,15]. Only 60.0% of studies reported either an increased troponin-I [9,11,15,16,19,21,22,24,27,29,31,32,34,36,38-40] or troponin-T [12-14,18,20,25,26,28,30,33,35,37]. The troponin-I values ranged from 0.544 ng/mL to 90.0 ng/mL, while mean troponin-T values ranged from 0.367 to 13.0 ng/mL. Nine out of 10 studies recorded elevated n-terminal brain natriuretic peptide (BNP), with a mean value of 4,770.1 ± 5,158.2 pg/mL [11,18,21,24,25,32,34,38,39,41]. Only three studies reported elevated creatine kinase-MB results, with a mean of 59.9 ± 15.3 ng/mL [22,25,29].

**Diagnostic Studies**

A summary of diagnostic studies is provided in Table 4.

| Diagnostic study               | %     |
|-------------------------------|-------|
| Electrocardiography (n = 32)   |       |
| ST-segment elevation           | 59    |
| PR depression                  | 28    |
| Tachycardia                    | 22    |
| T-wave inversion               | 13    |
| Electric alternans             | 3     |
| Echocardiography (n = 30)      |       |
| Pericardial effusion           | 67    |
| Hypokinesis                    | 20    |
| Reduced LVEF                   | 20    |
| Ventricular wall thickening    | 13    |
| Imaging (X-ray) (n = 16)       |       |
| Bilateral infiltrates          | 31    |
| Cardiomegaly                   | 31    |
| Imaging (CT) (n = 18)          |       |
| Ground-glass opacities         | 50    |
| Pericardial effusion           | 39    |
| Pleural effusion               | 33    |
| Imaging (MRI) (n = 4)          |       |
| Late gadolinium enhancements   | 50    |

**TABLE 4: Common findings found on diagnostic tests of COVID-19 patients with pericarditis and myopericarditis as the proportion recorded from all articles (n = 33).**

LVEF: left ventricular ejection fraction; CT: computed tomography; MRI: magnetic resonance imaging; COVID-19: coronavirus disease 2019

The predominant feature of electrocardiogram (ECG) recordings was sinus rhythm [10-11,15,16,20-22,32,33,36,40,41], with ST-segment elevation [10-11,13,15-18,20,22-27,30,33,35,37,38]. About one in four
articles reported PR depression [10,11,15,20,23,26,29,30,37] while one in five presented with tachycardia [15,16,21,22,32,33,41]. Finally, inverted T waves were found in one in 10 studies [10,31,29,33] while only one study had the classic presentation of electric alternans [32].

Echocardiography showed pericardial infusion in nearly three out of four studies [9-12,14,15,17-19,21-22,24,25,27,28,30-32,34,35,39,41] while one in four demonstrated either hypokinesis [16,18,20,25,29,31] or reduced left ventricular ejection fraction (<50%) [16-18,21,29].

Less than one-third of the articles reported bilateral infiltrates on chest X-ray [10,17,26,37,38], with the same proportion highlighting cardiomegaly [9,10,14,15,32]. Likewise, computed tomography (CT) imaging of the chest revealed similar results, with 50% of images demonstrating ground-glass opacities in the lungs [9,15,19,24,28,34,39] while one in three reporting pleural effusion [9,14,19,24,34,39]. Pericardial effusion was reported in slightly more than one-third of articles [9,13,19,24,28,34,39]. Magnetic resonance imaging (MRI) was the least used modality, with only half demonstrating subepicardial delayed gadolinium enhancement [24,56].

Management of Myocarditis

The most common medical management was the use of colchicine by 45.1% of studies [14,15,19,21,25,24,26,28,30,32,34,40,41], followed by either aspirin or non-steroidal anti-inflammatory drugs (NSAIDs) in 41.9% of articles [11,15,19,26-30,32,33,37,38,41] and corticosteroids in 35.3% of patients [18,21,22,25,28,34,35,38]. Regarding surgical interventions, pericardiocentesis [10,12,15,21,22,27,31,32,54] or the creation of pericardial windows [10,17,39,41] were required in 13 case reports.

Outcomes

The outcomes of the patients were documented in the majority of case reports. Only two deaths were reported [20,22], with the majority being discharged from the hospital [9-19,21,25-41].

Risk of Bias Across Studies

Due to the nature of descriptive studies, the results being presented are liable to the investigator, procedure, and selection bias.

Limitation of the Study

Statistical analyses were not performed as there were no control/comparison groups in the included studies.

Discussion

Pathophysiology

SARS-CoV-2 is thought to lead to myocardial damage and inflammation through the following processes: (1) direct invasion, (2) ischemic injury, and (3) cytokine storm. SARS-CoV-2 typically invades the respiratory epithelium through direct invasion via binding to angiotensin-converting enzyme-2 (ACE2) receptors on the host cells. These receptors are predominantly found on the respiratory epithelium and are also expressed on cardiac cells, facilitating a pathway and allowing for direct invasion and damage to cardiomyocytes [43]. Hypoxemia, which can result from pulmonary compromise from SARS-CoV-2 infection, can also lead to impaired myocardial oxygen supply resulting in a supply and demand mismatch, which then leads to ischemic injury to cardiomyocytes [43]. Cytokine storm is a known physiologic mechanism associated with SARS-CoV-2 infection, leading to the widespread production of high levels of pro-inflammatory cytokines. Large-scale production of these pro-inflammatory cytokines has also been linked to myocardial damage through recorded elevations in troponin levels during these states [43]. Autopsy reports on patients who died of COVID-19 infection have also shown findings within cardiac tissue consistent with inflammatory cellular infiltrate and multi-nucleated giant cells. Additionally, findings of pericardial effusions have also been seen in autopsy examinations [43].

Clinical Presentation

The clinical manifestations of COVID-19 in order of prevalence are fever, cough, and fatigue [2]. A common clinical manifestation of pericarditis is typically sharp and pleuritic chest pain that radiates posteriorly to the bilateral trapezius ridges, which improves on sitting up or leaning forward [44]. The presence of fever, subacute course, large effusion, or tamponade are indicators of poor prognosis [45]. Auscultation of the left sternal border typically indicates a triphasic pericardial friction rub. Here, we identified that patients with COVID-19 pericarditis commonly presented with chest pain, in addition to fever and shortness of breath.

Laboratory Findings
Our systematic review provides a comprehensive characterization of the clinical features among COVID-19 patients with pericarditis. We found that colchicine, aspirin, NSAIDs, and/or corticosteroids were used in the majority of cases. Among 10 studies to report COVID-19-related complications, eight of which were present in COVID-19 patients diagnosed with myopericarditis.

Conclusions

Our systematic review provides a comprehensive characterization of the clinical features among COVID-19 patients with pericarditis. We found that colchicine, aspirin, NSAIDs, and/or corticosteroids were used in the majority of cases. Among 10 studies to report COVID-19-related complications, eight of which were present in COVID-19 patients diagnosed with myopericarditis.
patients with pericarditis. Currently, as data are limited, more research is needed to improve our understanding of COVID-19 pericarditis.

## Appendices

| Reference, publication year | Were patient’s demographic characteristics clearly described? | Was the patient’s history clearly described and presented as a timeline? | Was the current clinical condition of the patient on presentation clearly described? | Were diagnostic tests or assessment methods and results clearly described? | Was the post-intervention clinical condition clearly described? | Were adverse events (hazms) or unanticipated events identified and described? | Does the case report provide takeaway lessons? | Total score |
|-----------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------------------------------------------|-------------|
| Amoozgar et al., 2020       | Some information missing                         | √                                              | √                                              | √                                              | √                                              | √                                              | √                                              | 87.5%       |
| Asif et al., 2020           | √                                               | √                                              | √                                              | √                                              | Some information missing                       | Some information missing                       | √                                              | 75.0%       |
| Blagojevic et al., 2020     | √                                               | √                                              | √                                              | √                                              | √                                              | √                                              | √                                              | 100.0%      |
| Cairns et al., 2021         | √                                               | √                                              | √                                              | √                                              | Some information missing                       | √                                              | √                                              | 87.5%       |
| Cizgici et al., 2020        | Some information missing                         | √                                              | Some information missing                       | √                                              | All information missing                         | All information missing                         | √                                              | 50.0%       |
| Fanj et al., 2021           | Some information missing                         | √                                              | √                                              | √                                              | √                                              | √                                              | √                                              | 87.5%       |
| Fox et al., 2020            | √                                               | √                                              | Some information missing                       | √                                              | √                                              | √                                              | √                                              | 87.5%       |
| Fried et al., 2020          | Some information missing                         | √                                              | √                                              | Some information missing                       | All information missing                         | All information missing                         | √                                              | 75.0%       |
| García-Cruz et al., 2020    | √                                               | All information missing                         | √                                              | Some information missing                       | All information missing                         | All information missing                         | √                                              | 50.0%       |
| Inciardi et al., 2020       | √                                               | √                                              | √                                              | √                                              | √                                              | √                                              | √                                              | 100.0%      |
| Karadeniz et al., 2020      | Some information missing                         | √                                              | √                                              | √                                              | √                                              | √                                              | √                                              | 87.5%       |
| Kazi et al., 2020           | √                                               | √                                              | √                                              | √                                              | Some information missing                       | √                                              | √                                              | 87.5%       |
| Khalid et al., 2020         | Some information missing                         | √                                              | √                                              | √                                              | Some information missing                       | √                                              | √                                              | 75.0%       |
| Khatri et al., 2020         | √                                               | √                                              | Some information missing                       | √                                              | Some information missing                       | √                                              | √                                              | 75.0%       |
| Kumar et al., 2020          | Some information missing                         | √                                              | √                                              | √                                              | Some information missing                       | √                                              | √                                              | 75.0%       |
| Legrand et al., 2020        | Some information missing                         | √                                              | Some information missing                       | √                                              | √                                              | √                                              | √                                              | 75.0%       |
| Reference | Li et al., 2020 [25] | Marschall et al., 2020 [26] | Nezvi et al., 2020 [27] | Ortiz-Martinez et al., 2020 [28] | Özturan et al., 2020 [29] | Naqvi et al., 2020 [27] | Sampaio et al., 2020 [34] | Purohit et al., 2020 [31] | Raymond et al., 2020 [32] | Recalcati et al., 2020 [33] | Sauer et al., 2020 [36] | Shah et al., 2020 [37] | Thupsi et al., 2021 [38] | Tung-Chen et al., 2020 [40] | Walker et al., 2020 [41] | Rauch et al., 2020 [42] |
|------------|---------------------|------------------------|-------------------|-----------------------|-----------------------|-----------------------|-------------------|-------------------|-----------------------|-----------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|
| Some information missing | √ | √ | Some information missing | √ | Some information missing | √ | Some information missing | √ | Some information missing | √ | Some information missing | √ | √ | √ | √ | √ | √ |
| Marschall et al., 2020 [26] | √ | √ | √ | √ | Some information missing | √ | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Nezvi et al., 2020 [27] | √ | √ | √ | Some information missing | √ | All information missing | All information missing | √ | √ | 62.5% |
| Ortiz-Martinez et al., 2020 [28] | √ | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Özturan et al., 2020 [29] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Naqvi et al., 2020 [27] | √ | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Sampaio et al., 2020 [34] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Purohit et al., 2020 [31] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Raymond et al., 2020 [32] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Recalcati et al., 2020 [33] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Sauer et al., 2020 [36] | Some information missing | √ | Some information missing | √ | √ | √ | √ | 62.5% |
| Shah et al., 2020 [37] | Some information missing | √ | √ | Some information missing | Some information missing | Some information missing | Some information missing | √ | √ | 50.0% |
| Thupsi et al., 2021 [38] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Tung-Chen et al., 2020 [40] | Some information missing | √ | Some information missing | √ | √ | √ | √ | 75.0% |
| Walker et al., 2020 [41] | Some information missing | √ | √ | Some information missing | √ | √ | √ | 75.0% |
| Rauch et al., 2020 [42] | No | All information missing | All information missing | All information missing | All information missing | √ | √ | 25.0% |

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TABLE 5: Risk of bias across studies.

Additional Information

Disclosures

Conflicts of interest: In compliance with the ICMJE uniform disclosure form, all authors declare the following: Payment/services info: All authors have declared that no financial support was received from any organization for the submitted work. Financial relationships: All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. Other relationships: All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

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