Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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COVID-19 associated myocarditis: A systematic review

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ABSTRACT

Background: Most COVID-19 infections result in a viral syndrome characterized by fever, cough, shortness of breath, and myalgias. A small but significant proportion of patients develop severe COVID-19 resulting in respiratory failure. Many of these patients also develop multi-organ dysfunction as a byproduct of their critical illness. Although heart failure can be a part of this, there also appears to be a subset of patients who have primary cardiac collapse from COVID-19.
Objective: Conduct a systematic review of COVID-19-associated myocarditis, including clinical presentation, risk factors, and prognosis.
Discussion: Our review demonstrates two distinct etiologies of primary acute heart failure in surprisingly equal incidence in patients with COVID-19: viral myocarditis and Takotsubo cardiomyopathy. COVID myocarditis, Takotsubo cardiomyopathy, and severe COVID-19 can be clinically indistinguishable. All can present with dyspnea and evidence of cardiac injury, although in myocarditis and Takotsubo this is due to primary cardiac dysfunction as compared to respiratory failure in severe COVID-19.
Conclusion: COVID-19-associated myocarditis differs from COVID-19 respiratory failure by an early shock state. However, not all heart failure from COVID-19 is from direct viral infection; some patient's develop takotsubo cardiomyopathy. Regardless of etiology, steroids may be a beneficial treatment, similar to other critically ill COVID-19 patients. Evidence of cardiac injury in the form of ECG changes or elevated troponin in patients with COVID-19 should prompt providers to consider concurrent myocarditis.

1. Introduction

The spread of COVID-19 began in late 2019, and by March of 2020 it was officially declared a pandemic by the World Health Organization (WHO). COVID-19 is the viral syndrome caused by SARS-CoV-2, a novel zoonotic RNA coronavirus [1]. The most common symptoms of COVID-19 are those of most viral syndromes and include fever, cough, shortness of breath, fatigue, and myalgia. Severe cases of COVID-19 manifest as multifocal pneumonia and acute respiratory distress syndrome (ARDS), with cardiovascular complications developing in many [1,2].

The cardiovascular complications of COVID-19 include myocardial injury, thrombotic events, and heart failure [2]. These are believed to be secondary to severe pulmonary disease, the result of inflammatory cytokines, or due to thrombotic occlusion of the cardiopulmonary vasculature, including pulmonary embolism and myocardial infarction [2]. Emerging in the literature, however, is a subset of patients with COVID-19 who appear to have primary cardiac dysfunction consistent with myocarditis.

In order to better understand COVID-19-associated myocarditis, including clinical presentation, risk factors, and prognosis, we performed a systematic review of the medical literature. Here we discuss the details of the reported cases of COVID-19-associated myocarditis.

2. Methods

2.1. Search strategy

This systematic review was conducted according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines [3]. Search terms were designed by a medical

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librarian after discussion of study aims with the authors. The search was run on the following databases: MEDLINE (via PubMed), Embase, The Cochrane Library, and Web of Science. The initial search was run on June 3, 2020 and repeated on November 13, 2020 to ensure that no relevant studies were missed in the intervening time frame. Controlled vocabularies and text words were used in the development of the search strategies in PubMed, Embase, and Cochrane. Web of Science does not employ a controlled vocabulary, so it was searched using only keywords. Search results were combined in a bibliographic management tool (EndNote), and duplicates were eliminated both electronically and through manual review. Search results were then imported into the systematic review support tool, Covidence, for further reference management and screening.

2.2. Search terms

The search terminology included two major components; both concepts were linked together with the AND operator: 1) COVID-19 including SARS-CoV-2 novel coronavirus and variations of the disease name; 2) myocarditis including cardiomyopathy inflammation of the heart and variations of cardiac inflammation terms. For a complete list of MeSH and keyword terms used please refer to the MEDLINE search strategy accompanying this paper. To investigate the grey literature perspective of this systematic review topic publication types from Embase and Web of Science such as conference proceedings research and other reports and theses/dissertations were screened.

2.3. Inclusion and exclusion criteria

We included case reports, retrospective studies, and prospective studies involving living patients diagnosed with COVID-19-associated myocarditis. Non-English articles that could not be found in translation, post-mortem diagnoses of myocarditis, and animal studies were excluded.

2.4. Selection protocol

Covidence Systematic Review software (Veritas Health Innovation, Melbourne, Australia) was used to organize the search strategy and reporting of data. 2 reviewers (WH, JK) screened 330 non-duplicate article abstracts with 146 articles assessed via full-text review for eligibility. A 3rd reviewer (KS) served as a tie-breaker in the event of discrepancy. A PRISMA flow diagram detailing the selection of relevant studies is shown in Fig. 1.

2.5. Assessment of case series

The Joanna Briggs Institute Quality Assessment Tool for Case Studies was used to evaluate the quality of evidence.

3. Results

There was 90% agreement among the reviewers for the selected studies in the systematic review. The remaining 10% required a third reviewer to resolve the discrepancy. A total of 43 articles were included in the final analysis, and 51 patients were identified with COVID-19-associated myocarditis based on clinical diagnosis, some with confirmatory testing. Cases were reported from 19 countries with the vast majority from the United States.

Details of the included articles are described in Table A-1. An assessment of the quality of the individual articles is detailed in Table A-2.

Among the 51 cases of COVID-19-associated myocarditis in the literature as of November 13, 2020, the average age was 56.3 years (median 58.5). The most common reported clinical signs and symptoms were tachycardia (76.4%), dyspnea (74.5%), shock (52.9%), and fever (37.3%). The patients' comorbidities included hypertension (41.1%), diabetes (17.6%), obesity (9.8%), and asthma/COPD (4%), with no comorbidities reported in 42%. All patients had signs of cardiac damage determined by ECG changes or elevation of troponin. Confirmatory diagnoses were performed by echocardiography alone (47.1%), MRI

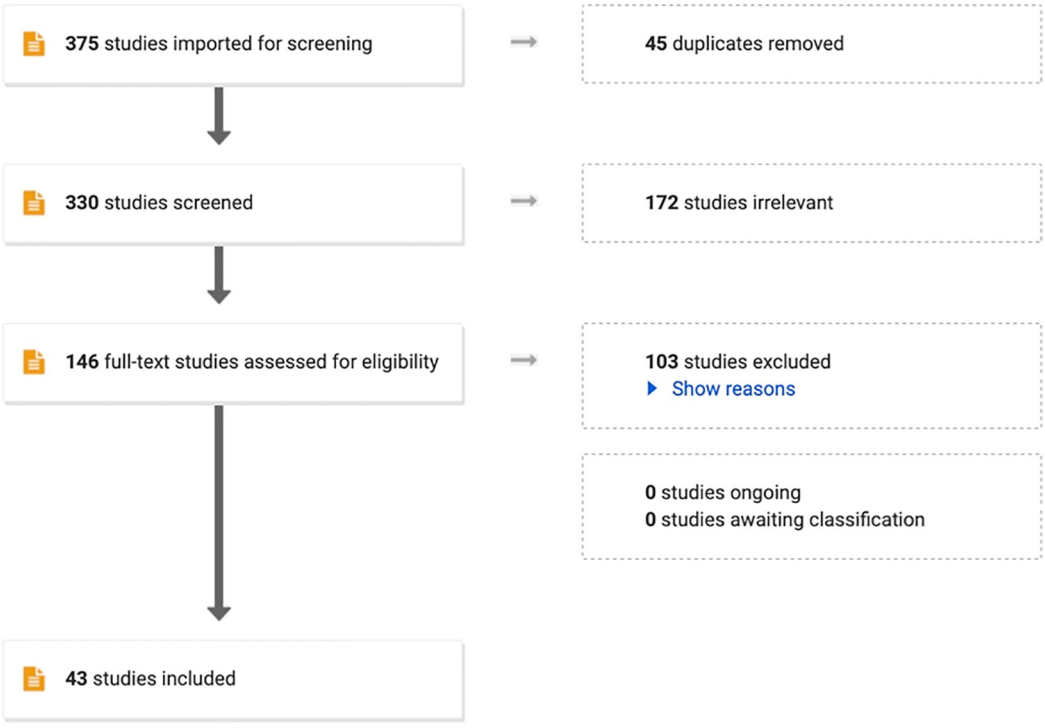

Fig. 1. Preferred Reporting Items for Systematic Reviews and Meta- Analyses (PRISMA) diagram demonstrating excluded and relevant studies.

(23.5%), cardiac catheterization (15.7%), and myocardial biopsy (9.8%). The average length of stay was 14.9 days (median 14). Nearly half of the patients (43.1%) were ultimately diagnosed with Takotsubo cardiomyopathy.

Among the 22 patients with Takotsubo cardiomyopathy, the average age was 58.9 years. The average age was 53.8 years in the remaining 29 patients. No comorbidities were reported in only 29.2% of the patients with Takotsubo cardiomyopathy. Whereas 66.7% of patients without Takotsubo cardiomyopathy had no medical problems. One patient with Takotsubo cardiomyopathy, though clinically was diagnosed with COVID-19, was COVID negative on PCR swab and myocardial biopsy.

Selected treatments for COVID-19-associated myocarditis were variable, but the most common approach was supportive treatment alone (43.1%). Supportive therapy included intravenous/oral hydration, beta-blockers, or diuretics. Additional interventions were vasopressor or inotropic support (31.3%), steroids (19.6%), and antivirals (7.8%). The overall mortality rate was 13.7, with a mortality rate of 27.3 in the Takotsubo group and 3.4 in the remaining patients without Takotsubo cardiomyopathy. Of the seven patients who died, three (42.9%) were treated with vasopressors only, two (28.6%) were treated with antivirals, one (14.3%) received steroids and vasopressors, and one (14.3%) received supportive care only. In the patients with Takotsubo cardiomyopathy, 64% presented with shock, compared to 41% of the remaining patients presenting with shock.

4. Discussion

The symptomatology of viral myocarditis and severe COVID-19 are almost indistinguishable. Both present with dyspnea and fever though the underlying pathophysiology is quite different. Myocarditis produces acute cardiac dysfunction, sometimes with reduced ejection fraction and infrequently, cardiogenic shock. The dyspnea associated with severe COVID-19, however, is usually secondary to a multifocal pneumonia and ARDS. Here we discuss from the current literature, a subset of patients diagnosed with COVID-19-associated myocarditis.

The incidence of critical illness in patients with COVID-19 has been estimated at 5% overall and 22% in those requiring hospitalization [4]. All reported patients with COVID-19-associated myocarditis required hospitalization, and 54% were critically ill, making it a morbid disease entity. The mortality of all patients with COVID-19 has been estimated to be between 0.8% to 3.0%, with a significant rise in mortality in those with severe COVID-19 to an estimated 17.4% [5,6]. COVID-19-associated myocarditis appears to carry a similarly high mortality rate: among the reported cases in this review, the mortality rate was 14.0%.

Patients with COVID-19-associated myocarditis had similar risk factors to those with severe COVID-19. Critical illness and mortality in patients with COVID-19 have been associated with older age and comorbidities, including diabetes, cardiovascular disease and respiratory disease [6]. About 50% of patients with severe COVID-19 had at least one of these risk factors [4]. Similarly, 58% of patients with COVID-19-associated myocarditis had at least one of the following comorbidities: hypertension, diabetes, obesity, and asthma/COPD.

Patient-reported or measured fever is present in approximately 85% of all COVID-19 cases [7]. While only 36% of patients in this cohort had fever at presentation, a large predominance reported fever prior to hospital admission. Therefore, fever is not a distinguishing factor. Dyspnea was present in 76.9% of patients in this case series, compared to only 16.4% in all patients with COVID-19 and 53.7% of patients with severe COVID-19 (those necessitating intensive care) [6]. COVID-19-associated myocarditis is more likely to cause respiratory distress compared to other forms of COVID-19. This falls in line with prior data on myocarditis, where mild dyspnea is frequently seen due to acute heart failure [8,9].

COVID-19-associated myocarditis may be differentiated from other forms of severe COVID-19 by an early shock state. The true incidence of shock in severe COVID-19 is unclear, with studies reporting vastly different rates, ranging from 35 to 94% [10]. In patients with severe COVID-19, shock tends to develop secondary to respiratory failure and occurs days to weeks after the initial presentation to the hospital [10]. This is in contrast to the 52% of patients with COVID-19 myocarditis who were in shock on presentation, hence, an early shock state.

The diagnosis of myocarditis was made most commonly by echocardiogram (48%). Findings suggestive of myocarditis were decreased ejection fraction or dilated cardiomyopathy [11]. In some cases, MRI was used adjunctively (24%) to determine a presence of enhancement within the myocardium. This finding indicates cardiac hyperemia and increased capillary permeability, which suggest an acute inflammatory pathology [12]. In 8 cases (16%), clinicians felt inclined to utilize cardiac catheterization to exclude occlusive myocardial infarct as a cause of symptoms. Only rarely was a myocardial biopsy performed (10%) to determine that SARS-CoV-2 had directly infected the myocardium [11,12].

Curiously, this review has uncovered two distinct etiologies of acute heart failure in patients with COVID-19: viral myocarditis and Takotsubo cardiomyopathy. Takotsubo cardiomyopathy was diagnosed in 48.0% of patients in this series. Takotsubo cardiomyopathy (also called stress cardiomyopathy) is characterized by a reversible cardiomyopathy with pathognomonic ballooning of the apical left ventricle [13]. Sympathetic response is cited as the primary driver of its pathophysiology [13]. In our patients, Takotsubo cardiomyopathy was diagnosed by echocardiography showing apical left ventricular ballooning and MRI demonstrating lack of enhancement of the myocardium (thus excluding viral myocarditis). It is notable that the mortality of patients with Taktosubo was higher than those with viral myocarditis (27.3 vs 3.4%); however the signifance of this is unclear in this small sample.

Notable within this data set is a low utilization of specific treatment for COVID-19 (44% received supportive treatment only). Only seven patients (14%) received steroids, an established therapy for patients with COVID-19 requiring supplemental oxygen [14]. Of the seven patients who received steroids, six survived (85.7%), demonstrating a potential utility of corticosteroids in the treatment of COVID-19-associated myocarditis. The success of supportive treatment (survival) may be attributed to a reduction in sympathetic drive, especially in patients with Takotsubo cardiomyopathy. However, more research is needed in this realm to make conclusive statements.

4.1. Limitations

COVID-19-associated myocarditis is a relatively new diagnostic entity for clinicians. Our knowledge is limited by the number of cases reported in the literature to date, and thus the conclusions we can extrapolate from this review are also limited. Hopefully there will be observational studies and randomized trials reported in the future.

5. Conclusion

COVID-19-associated myocarditis is a distinct clinical entity that differs from COVID-19 respiratory failure by an early shock state. The risk factors and presenting signs and symptoms are similar to those of patients with severe COVID-19, with dyspnea being more prevalent in those with COVID-19-associated myocarditis. Steroids seem to be beneficial in this subset as well, similar to critically ill COVID-19 patients. Evidence of cardiac injury in the form of ECG changes or elevated troponin in patients with COVID-19 should urge providers to consider concurrent myocarditis. Echocardiography is usually sufficient for diagnosis, but more advanced methods can be used if available. Finally, Takotsubo cardiomyopathy produces a clinical picture similar to viral myocarditis and should be simultaneously considered in COVID-19 patients with acute cardiac dysfunction.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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Appendix A. Appendix

Table A-1
Summary of patient characteristics from included articles [15,18–20,22,24–29,31–60].

Paper	Age	Comorbidities	Fever	Tachycardia	Dyspnea	Shock	Treatment	Diagnostic Modality	Mortality	Length of Stay (d)	Location	Takotsubo
Anupama 2020	66	DM, HTN, HLD	Yes	Yes	Yes	Yes	Vasopressors	US/MRI	No	19	USA	No
Bhattacharyya 2020	32	Pregnant	No	No	Yes	No	Supportive	US	No	7	India	Yes
Bobeck 2020	80	HTN, HLD, breast CA	Yes	Yes	Yes	Yes	Vasopressors	US	No	15	USA	Yes
Bonnet 2020	27	None	No	Yes	Yes	No	Supportive	US	No	9	USA	No
Cizgici 2020	78	HTN	No	Yes	Yes	No	Supportive	Catherization/Troponin	No	–	Turkey	No
Dalen 2020	55	None	No	Yes	Yes	No	Supportive	US/MRI	No	17	Norway	No
De Vita 2020	25	Pregnant	No	yes	Yes	No	Vasopressors, Steroids	US/MRI	No	4	Italy	Yes
Doyen 2020	69	HTN	No	Yes	Yes	No	Supportive	US/MRI	No	21	France	No
Faqihi 2020	40	none	No	Yes	No	Yes	Steroids	US	No	17	Saudi Arabia	Yes
Hegde 2020	71	DM, HTN, HLD	No	Yes	No	Yes	Vasopressors	US	Yes	2	USA	Yes
	78	DM, HTN, HLD, AF, CVA	Yes	Yes	No	Yes	Vasopressors	US	No	16	USA	Yes
	70	DM, HTN, HLD	No	No	Yes	Yes	Vasopressors	US	No	25	USA	Yes
	78	DM, HTN, HLD, CVA, AF	Yes	Yes	Yes	No	Supportive	US	Yes	12	USA	Yes
	88	DM, HTN, HLD, CVA, AF, CAD, CHF	No	Yes	Yes	Yes	Vasopressors	US	Yes	8	USA	Yes
	58	HLD	No	Yes	Yes	Yes	Vasopressors	US	No	44	USA	Yes
	56	HTN, HLD, AF, Schizophrenia	Yes	Yes	Yes	Yes	Vasopressors	US	Yes	17	USA	Yes
Hu 2020	37	None	No	Yes	Yes	Yes	Steroids	US	No	21	China	No
Hua 2020	47	Myocarditis	No	Yes	Yes	Yes	Vasopressors	US	No		UK	No -tamponade
Huyut 2020	59	HTN, HLD, obesity, DM	Yes	Yes	No	Yes	Steroids, Antiviral	US	No	15	Turkey	No
Inciardi 2020	53	None	Yes	Yes	No	Yes	Pressors, Antiviral	US/MRI	No	21	Italy	No
Irabien-Ortiz 2020	59	HTN/TB	Yes	Yes	No	Yes	Steroids, IVIG, Vasopressors	US	No	12	Spain	No
Fried 2020	64	HTN, HLD	No	Yes	Yes	Yes	Vasopressors	US/Cath	No	10	USA	Yes
	38	DMII	No	Yes	Yes	Yes	Vasopressors	US	No	19	USA	No
Juusela 2020	45	Pregnant	No	Yes	No	No	Steroids	US	No	12	USA	No
	26	Pregnant, Obesity, PCOS	No	Yes	Yes	No	Supportive	US	No	7	USA	No
Kim 2020	21	None	Yes	No	Yes	No	Supportive	US/MRI	No	–	Korea	No
Legrand 2020	39	None	No	Yes	Yes	No	Supportive	US/MRI	No	10	France	No
Luetkens 2020	79	Asthma	Yes	Yes	Yes	Yes	Supportive	US/MRI	No		Germany	No
Meyer 2020	83	HTN	No	No	Yes	No	Supportive	US	No	10	Switzerland	Yes
Naneishvili 2020	44	None	Yes	Yes	No	Yes	Steroids, Vasopressors	US	No	41	UK	Yes
Newton-Cheh 2020	44	None	No	Yes	Yes	Yes	Vasopressors, IVIG	US	No	14	USA	No
Nguyen 2020	71	HTN, HLD, NPH	No	No	Yes	No	Catheterization	US/Cath	No	4	Belgium	Yes
Oyarzabal 2020	82	HTN, HLD, DM, CKD, PAD	Yes	Yes	No	No	Supportive	US/Cath	No	10	Spain	Yes
Paul 2020	35	Obesity	No	Yes	No	No	Supportive	US/MRI	No	21	France	No
Pavon 2020	64	Sarcoidosis, epilepsy	Yes	Yes	Yes	Yes	Vasopressors	US/MRI	No	12	Canada	No
Purohit 2020	82	HTN, HLD, AF, iron def anemia, tachy-brady syndrome s/p PPM	No	Yes	Yes	No	Supportive	US	No	7	USA	No -tamponade
Rivers 2020	71	None	No	No	No	No	Supportive	US/Cath	No	–	Australia	Yes (COVID negative)
Sala 2020	42	None	Yes	No	Yes	No	Supportive	US/MRI/Biopsy	No	13	Italy	No
Siddarth Dave 2020	59	HTN, smoking	No	No	Yes	Yes	Vasopressors, Steroids	US	Yes	9	USA	Yes
Solano-Lopez 2020	50	None	No	No	Yes	No	Supportive	US/Cath	No	10	Spain	Yes
Spano 2020	49	None	No	No	Yes	No	Supportive	US/Cath/MRI	No	–	Switzerland	No
Tavazzi 2020	69	None	No	Yes	Yes	Yes	Vasopressors	US/Cath/Biopsy	No	5	Italy	No
Taza 2020	52	Schizophrenia, HTN,	No	Yes	Yes	Yes	Steroids	Catherization/Troponin	No	6	USA	Yes

(continued on next page)

Table A-1 (*continued*)

Paper	Age	Comorbidities	Fever	Tachycardia	Dyspnea	Shock	Treatment	Diagnostic Modality	Mortality	Length of Stay (d)	Location	Takotsubo
Tsao 2020	59	DM Obesity	Yes	Yes	Yes	Yes	Vasopressors, AntiViral	US/Cath	No	25	USA	Yes
Warchol 2020	74	AF, HTN, DM, hypothyroid	No	Yes	No	Yes	Supportive	MRI	No	17	Poland	No
Wenzel 2020	39	Obesity, HLD	Yes	Yes	Yes	No	Supportive	US/MRI/Biopsy	No	15	Germany	No
	36	HTN, HLD, CAD, smoking	Yes	Yes	Yes	No	Supportive	US/MRI/Biopsy	No	15	Germany	No
Yan 2020	44	Obesity	Yes	Yes	Yes	No	Antiviral	US/Autopsy	Yes	6	USA	Yes
Yokoo 2020	81	None	No	No	Yes	No	Steroids	US/MRI	No	21	Brazil	No
Yuan 2020	33	None	Yes	Yes	No	Yes	Supportive	US/MRI	No	17	China	No
Zeng 2020	63	COPD	Yes	Yes	Yes	Yes	Antiviral	US	Yes	33	China	No

Table A-2

Paper/Authors	1. Were patient's demographic characteristics clearly described?	2. Was the patient's history clearly described and presented as a timeline?	3. Was the current clinical condition of the patient on presentation clearly described?	4. Were diagnostic tests or assessment methods and the results clearly described?	5. Was the intervention (s) or treatment procedure (s) clearly described?	6. Was the post-intervention clinical condition clearly described?	7. Were adverse events (harms) or unanticipated events identified and described?	8. Does the case report provide takeaway lessons?	Overall appraisal: Include/Exclude/Seek Further Info	Comments
Anupama 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Bhattacharyya 2020	No	Yes	Yes	Yes	No	No	No	Yes	Include	
Bobeck 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Bonnet 2020	No	No	No	Yes	No	Yes	No	No	Include	
Cizgici 2020	No	Yes	Yes	Yes	No	No	Yes	Yes	Include	
Dalen 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Dave 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
De Vita 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Doyen 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Faqihi 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Fried 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Hegde 2020	Yes	No	Yes	Yes	Yes	No	Yes	Yes	Include	
Hua 2020	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Include	
Huyut 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Inciardi 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Irabien-Ortiz 2020	Yes	Yes	Yes	Yes	Yes	No	Yes	Yes	Include	
Juusela 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Kim 2020	No	Yes	Yes	Yes	No	No	No	No	Include	
Legrand 2020	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Luetkens 2020	Yes	Yes	Yes	Yes	No	No	No	Yes	Include	
Meyer 2020	Yes	Yes	Yes	Yes	No	No	Yes	Yes	Include	
Naneishvili 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Newton-Cheh 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Nguyen 2020	Yes	No	Yes	Yes	No	No	No	Yes	Include	
Oyarzabal 2020	Yes	No	No	Yes	No	No	No	No	Include	
Paul 2020	Yes	No	No	Yes	Yes	Yes	No	Yes	Include	
Pavon 2020	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Include	
Purohit 2020	No	No	Yes	No	Yes	No	No	No	Include	
Rivers 2020	No	Yes	Yes	Yes	No	No	No	Yes	Include	
Sala 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	No	Include	
Solano-Lopez 2020	Yes	Yes	Yes	Yes	No	Yes	No	No	Include	
Spano 2020	Yes	No	Yes	Yes	No	No	No	No	Include	
Tavazzi 2020	No	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Taza 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Tsao 2020	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Include	
Warchol 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Wenzel 2020	Yes	Yes	Yes	Yes	No	Yes	Yes	Yes	Include	
Yan 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Yokoo 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	
Yuan 2020	No	Yes	Yes	Yes	No	Yes	Yes	Yes	Include	
Zeng 2020	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Yes	Include	

References

[1] Cevik M, Bamford CGG, Ho A. COVID-19 pandemic-a focused review for clinicians. Clin Microbiol Infect. 2020 Jul;26(7):842–7. https://doi.org/10.1016/j.cmi.2020.04.023 Epub 2020 Apr 25. PMID: 32344166; PMCID: PMC7182753.

[2] Long B, Brady WJ, Koyfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med. 2020 Jul;38(7):1504–7. https://doi.org/10.1016/j.ajem.2020.04.048 Epub 2020 Apr 18. PMID: 32317203; PMCID: PMC7165109.

[3] Moher D, Liberati A, Tetzlaff J, Altman DG, PRISMA Group, et al. PLoS Med. 2009 Jul 21;6(7):e1000097. https://doi.org/10.1371/journal.pmed.1000097 Epub 2009 Jul 21. PMID: 19621072; PMCID: PMC2707599.

[4] Gao Y. COVID-19: risk factors for critical illness. EClinicalMedicine. 2020 Aug;25:100507. https://doi.org/10.1016/j.eclinm.2020.100507 Epub 2020 Aug 19. PMID: 32835189; PMCID: PMC7434618.

[5] Acuti Martellucci C, Flacco ME, Cappadona R, Bravi F, Mantovani L, Manzoli L. SARS-CoV-2 pandemic: an overview. Adv Biol Regul. 2020 Aug;77:100736. https://doi.org/10.1016/j.jbior.2020.100736 Epub 2020 Jun 17. PMID: 32773099; PMCID: PMC7832554.

[6] Zheng Z, Peng F, Xu B, Zhao J, Liu H, Peng J, et al. Risk factors of critical & mortal COVID-19 cases: a systematic literature review and meta-analysis. J Infect. 2020 Aug;81(2). https://doi.org/10.1016/j.jinf.2020.04.021 e16-e25. Epub 2020 Apr 23. PMID: 32335169; PMCID: PMC7177098.

[7] Carpenter CR, Mudd PA, West CP, Wilber E, Wilber ST. Diagnosing COVID-19 in the emergency department: a scoping review of clinical examinations, laboratory tests, imaging accuracy, and biases. Acad Emerg Med. 2020 Aug;27(8):653–70. https://doi.org/10.1111/acem.14048 Epub 2020 Jul 26. PMID: 32542934; PMCID: PMC7323136.

[8] Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. Infection. 2020 Oct;48(5):773–7. https://doi.org/10.1007/s15010-020-01424-5 Epub 2020 Apr 10. PMID: 32277408; PMCID: PMC7146072.

[9] Cooper Jr LT. Myocarditis. N Engl J Med. 2009 Apr 9;360(15):1526–38. https://doi.org/10.1056/NEJMra0800028 PMID: 19357408; PMCID: PMC5814110.

[10] Michard F, Vieillard-Baron A. Critically ill patients with COVID-19: are they hemodynamically unstable and do we know why? Intensive Care Med. 2021 Feb;47(2):254–5. https://doi.org/10.1007/s00134-020-06238-5 Epub 2020 Sep 10. PMID: 32910203; PMCID: PMC7482382.

[11] Sagar S, Liu PP, Cooper Jr LT. Myocarditis. Lancet. 2012 Feb 25;379(9817):738–47. https://doi.org/10.1016/S0140-6736(11)60648-X Epub 2011 Dec 18. PMID: 22185868; PMCID: PMC5814111.

[12] Olimulder MA, van Es J, Galjee MA. The importance of cardiac MRI as a diagnostic tool in viral myocarditis-induced cardiomyopathy. Neth Heart J. 2009 Dec;17(12):481–6. https://doi.org/10.1007/BF03086308 PMID: 20087452; PMCID: PMC2804081.

[13] Amin HZ, Amin LZ, Pradipta A. Takotsubo cardiomyopathy: a brief review. J Med Life. 2020 Jan-Mar;13(1):3–7. https://doi.org/10.25122/jml-2018-0067 PMID: 32341693; PMCID: PMC7175432.

[14] Linsell L, Staplin N, Brightling C, Ustianowski A, Elmahi E, Prudon B, et al. Dexamethasone in hospitalized patients with Covid-19. N Engl J Med. 2021 Feb 25;384(8):693–704. https://doi.org/10.1056/NEJMoa2021436 Epub 2020 Jul 17. PMID: 32678530; PMCID: PMC7383595.

[15] Hu H, Ma F, Wei X, Fang Y. Coronavirus fulminant myocarditis saved with glucocorticoid and human immunoglobulin. Eur Heart J. 2020 Mar. https://doi.org/10.1093/eurheartj/ehaa190 [Epub ahead of print].

[18] Anupama BK, Thapa SS, Amzuta I. Transient cardiomyopathy in a patient with coronavirus disease-2019. J Investig Med High Impact Case Rep. 2020;8 2324709620947577.

[19] Bhattacharyya PJ, Attri PK, Farooqui W. Takotsubo cardiomyopathy in early term pregnancy: a rare cardiac complication of SARS-CoV-2 infection. BMJ Case Rep. 2020:13(9).

[20] Bobeck KA, Holtzclaw AW, Brown TE, Clark PA. Effective use of angiotensin II in coronavirus disease 19-associated mixed shock state: a case report. A and A practice; 2020 (e01221).

[22] Dalen H, Holte E, Guldal AU, Hegvik JA, Stensaeth KH, Braaten AT, et al. Acute perimyocarditis with cardiac tamponade in COVID-19 infection without respiratory disease. BMJ Case Rep. 2020;13(8).

[24] De Vita S, Ippolito S, Caracciolo MM, Barosi A. Peripartum cardiomyopathy in a COVID-19-infected woman: differential diagnosis with acute myocarditis-a case report from a hub institution during the COVID-19 outbreak. Echocardiography. 2020;37(10):1673–7.

[25] Doyen D, Moceri P, Ducreux D, Dellamonica J. Myocarditis in a patient with COVID-19: a cause of raised troponin and ECG changes. Lancet. 2020;395(10235):1516.

[26] Faqihi F, Alharthy A, Alshaya R, Papanikolaou J, Kutsogiannis DJ, Brindley PG, et al. Reverse takotsubo cardiomyopathy in fulminant COVID-19 associated with cytokine release syndrome and resolution following therapeutic plasma exchange: a case-report. BMC Cardiovasc Disord. 2020;20(1):389.

[27] Hegde S, Khan R, Zordok M, Maysky M. Characteristics and outcome of patients with COVID-19 complicated by Takotsubo cardiomyopathy: case series with literature review. Open Heart. 2020;7(2) Select study 372.

[28] Hua A, O'Gallagher K, Sado D, Byrne J. Life-threatening cardiac tamponade complicating myo-pericarditis in COVID-19. Eur Heart J. 2020;41(22):2130.

[29] Huyut MA. Novel coronavirus pneumonia and cardiomyopathy: a case report. Arq Bras Cardiol. 2020;114(5):843–5.

[31] Inciardi RM, Lupi L, Zaccone G, Italia L, Raffo M, Tomasoni D, et al. Cardiac involvement in a patient with coronavirus disease 2019 (COVID-19). JAMA Cardiology. 2020;5(7):819–24.

[32] Irabien-Ortiz A, Carreras-Mora J, Sionis A, Pamies J, Montiel J, Tauron M. Fulminant myocarditis due to COVID-19. Revista espanola de cardiologia (English Ed). 2020;73(6) 503-503.

[33] Juusela A, Nazir M, Gimovsky M. Two cases of coronavirus 2019-related cardiomyopathy in pregnancy. Am J Obstetr Gynecol MFM. 2020;2(2) 100113-100113.

[34] Kim IC, Kim JY, Kim HA, Han S. COVID-19-related myocarditis in a 21-year-old female patient. Eur Heart J. 2020;41(19):1859.

[35] Legrand F, Chong-Nguyen C, Ghanem N. Myopericarditis, rhabdomyolysis, and acute hepatic injury: sole expression of a SARS-CoV-2 infection. Circ Cardiovasc Imaging. 2020;13(7) e010907.

[36] Luetkens JA, Isaak A, Zimmer S, Nattermann J, Sprinkart AM, Boesecke C, et al. Diffuse myocardial inflammation in COVID-19 associated myocarditis detected by multiparametric cardiac magnetic resonance imaging. Circulation Cardiovasc Imaging. 2020;13(5) e010897.

[37] Meyer P, Degrauwe S, Van Delden C, Ghadri JR, Templin C. Typical takotsubo syndrome triggered by SARS-CoV-2 infection. Eur Heart J. 2020;41(19):1860.

[38] Naneishvili T, Khalil A, O'Leary R, Prasad N. Fulminant myocarditis as an early presentation of SARS-CoV-2. BMJ Case Rep. 2020;13(9).

[39] Newton-Cheh C, Zlotoff DA, Hung J, Rupasov A, Crowley JC, Funamoto M. Case 24-2020: a 44-year-old woman with chest pain, dyspnea, and shock. N Engl J Med. 2020;383(5):475–84.

[40] Nguyen D, Nguyen T, De Bels D, Castro Rodriguez J. A case of Takotsubo cardiomyopathy with COVID 19. Eur Heart J Cardiovasc Imaging. 2020;12.

[41] Oyarzabal L, Gómez-Hospital JA, Comin-Colet J. Tako-tsubo syndrome associated with COVID-19. Revista Espanola de Cardiologia (English ed). 2020;73(10):846.

[42] Paul JF, Charles P, Richaud C, Caussin C, Diakov C. Myocarditis revealing COVID-19 infection in a young patient. Eur Heart J Cardiovasc Imaging. 2020;27.

[43] Pavon AG, Meier D, Samim D, Rotzinger DC, Fournier S, Marquis P, 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.

[44] Purohit R, Kanwal A, Pandit A, Patel BM, Meininger GR, Brown JJ, et al. Acute myopericarditis with pericardial effusion and cardiac Tamponade in a patient with COVID-19. Am J Case Rep. 2020;21 e925554.

[45] Rivers J, Ihle JF. COVID-19 social isolation-induced takotsubo cardiomyopathy. Med J Aust. 2020;213(7) 336–336.e1.

[46] Sala S, Peretto G, Gramegna M, Palmisano A, Villatore A, Vignale D, et al. Acute myocarditis presenting as a reverse Tako-Tsubo syndrome in a patient with SARS-CoV-2 respiratory infection. Eur Heart J. 2020;41(19):1861–2.

[47] Solano-Lopez J, Sanchez-Recalde A, Zamorano JL. SARS-CoV-2, a novel virus with an unusual cardiac feature: inverted takotsubo syndrome. Eur Heart J. 2020;11.

[48] Spano G, Fischer K, Maillat C, Vicario G, Huber AT, Gräni C. Delayed isolated perimyocarditis in a Covid-19 patient with respiratory symptoms but without lung involvement. Int J Cardiovasc Imaging. 2020;36(11):2279.

[49] Tavazzi G, Pellegrini C, Maurelli M, Belliato M, Sciutti F, Bottazzi A, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. European journal of heart failure. 2020;22(5):911–5.

[50] Taza F, Zulty M, Kanwal A, Grove D. Takotsubo cardiomyopathy triggered by SARS-CoV-2 infection in a critically ill patient. BMJ Case Rep. 2020;13(6).

[51] Tsao CW, Strom JB, Chang JD, Manning WJ. COVID-19-associated stress (Takotsubo) cardiomyopathy. Circ Cardiovasc Imaging. 2020;13(7) e011222.

[52] Warchol I, Debska-Kozlowska A, Karcz-Socha I, Ksiazczyk M, Szymanska K, Lubinski A. Terra incognita: clinically suspected myocarditis in a SARS-CoV-2 positive patient. Pol Arch Internal Med. 2020;24.

[53] Wenzel P, Kopp S, Göbel S, Jansen T, Geyer M, Hahn F, et al. Evidence of SARS-CoV-2 mRNA in endomyocardial biopsies of patients with clinically suspected myocarditis tested negative for COVID-19 in nasopharyngeal swab. Cardiovasc Res. 2020;116(10):1661–3.

[54] Yan L, Mir M, Sanchez P, Beg M, Peters J, Enriquez O, et al. COVID-19 in a Hispanic woman. Arch Pathol Lab Med. 2020;144(9):1041–7.

[55] Yokoo P, Fonseca Ekun, Sasdelli Neto R, Ishikawa WY, Silva MMA, Yanata E, et al. COVID-19 myocarditis: a case report. Einstein (Sao Paulo, Brazil). 2020;18 eRC5876.

[56] Yuan WF, Tang X, Zhao XX. An 'asymptomatic' driver with COVID-19: atypical suspected myocarditis by SARS-CoV-2. Cardiovasc Diag Ther. 2020;10(2):242–3.

[57] Zeng JH, Liu YX, Yuan J, Wang FX, Wu WB, Li JX, et al. First case of COVID-19 complicated with fulminant myocarditis: a case report and insights. Infection. 2020;48(5):773–7.

[58] Bonnet M, Craighero Fa, Harbaoui B. Acute myocarditis with ventricular noncompaction in a COVID-19 patient. Heart Failure. 2020;8(7):599–600.

[59] Cizgici Ahmet Yasar, Agus HZ, Yildiz M. COVID-19 myopericarditis: it should be kept in mind in today's conditions. The American Journal of Emergency Medicine. 2020;38(7):1547–e5.

[60] Fried Justin A, Ramasubbi Kumudha, Bhatt Reema, Topkara VK, Clerkin Kevin J, Horn Evelyn, et al. The variety of cardiovascular presentations of COVID-19. Circulation. 2020;141(23):1930–6.