Coronavirus disease 2019 (COVID-19) is a global pandemic that, at the time of this writing, has led to 178,000,000 cases worldwide and more than 3,875,000 deaths. Cardiovascular complications of COVID-19 have become the focus of investigation after many hospitalized COVID-19 patients—with or without established cardiovascular disease—incurred clinical or subclinical myocardial injury, including isolated biomarker elevations, myocardial infarction, arrhythmia, heart failure, myocarditis, and cardiogenic shock. In this review, we highlight the most recent evidence of the prevalence and potential etiologies of acute and subclinical myocardial injury in COVID-19 patients.
INTRODUCTION

For the last 2 years, the world has been facing a pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the causative agent of coronavirus disease 2019 (COVID-19). As of December 1, 2021, there were over 263 million cases of COVID-19 globally and roughly 5,223,470 COVID-19 related deaths, 782,056 in the United States alone.1 While most patients recover after experiencing mild or moderate symptoms, some patients, particularly those with risk factors and underlying comorbid conditions, can have severe manifestations and acute respiratory distress syndrome (ARDS).2

In the early phases of the pandemic, it was recognized that the virus leads to systemic disease, and cardiac, vascular, renal, and various organ system manifestations were reported.3-5 Indeed, myocardial injury in hospitalized COVID-19 patients has been observed in patients with and without established cardiovascular disease (CVD). Cardiac involvement includes isolated biomarker elevations such as troponin and brain natriuretic peptide, myocardial infarction, arrhythmia, myocardial inflammation and myocarditis, and thromboembolic events as well as heart failure and cardiogenic shock.6 The prevalence and short-term implications of myocardial injury in hospitalized COVID-19 patients have been investigated, although many questions remain regarding its mechanisms, optimal treatment strategies, and long-term consequences for cardiovascular health after recovery. In nonhospitalized COVID-19 patients and particularly those without known CVD, the incidence and prognosis of subclinical myocardial injury remains an active area of investigation with critical public health consequences for the long-term management of recovered patients. In this review, we discuss the current knowledge about the prevalence and various manifestations of acute and subclinical myocardial injury in COVID-19 patients.

SARS-COV-2 AND CARDIOVASCULAR RISK FACTORS

SARS-CoV-2 is a single-stranded RNA virus that exerts its infectious action by coupling a spike protein (S-protein) with the body’s angiotensin-converting enzyme 2 (ACE2) receptor, which is expressed mainly in the lungs.7 ACE2 is also present in high concentrations in the heart, which may partly explain myocardial injury in COVID-19.8 Other viral illnesses, including H1N1 influenza, severe acute respiratory syndrome virus (SARS), and Middle East respiratory syndrome virus (MERS), have all been associated with cardiac injury including myocarditis.9-11

Cardiovascular risk factors, mainly hypertension, obesity, and diabetes, are associated with a higher risk of hospitalization due to COVID-19.12 A meta-analysis of 13 studies with 3,207 total patients showed that the risk factors associated with disease progression and morbidity are age > 65 years, male gender, history of smoking, hypertension, preexisting cardiovascular disease (CVD), and respiratory disease (Figure 1).13 In addition, obesity has long been associated with worse clinical outcomes in viral infections.14 An analysis of the American Heart Association COVID-19 CVD registry revealed that all classes of obesity were associated with a progressively higher risk of COVID-19 complications, such as mechanical ventilation and in-hospital death. Obese patients with COVID-19 were likely to be admitted to the hospital at a younger age than non-obese patients and have a higher risk of venous thromboembolism and major cardiovascular events.15

![Figure 1 Risk factors for cardiovascular involvement of COVID-19 and possible complications.](image-url)
BIOMARKERS OF MYOCARDIAL INJURY
Studies have shown a prevalence of acute myocardial injury (as defined by troponin elevation) in hospitalized COVID-19 patients ranging from approximately 12% in one series to as high as 62% in another (Table 1). A large series from New York showed a prevalence of acute cardiac injury of 22.6% by a variety of troponin assays. Acute myocardial injury in COVID-19 is associated with in-hospital mortality. In a cohort study of 416 hospitalized COVID-19 patients, 19.7% had evidence of myocardial injury manifested by elevation of high-sensitivity troponin I levels and NT-terminal pro-B-type natriuretic peptide (NT-proBNP). These patients had a markedly higher in-hospital mortality rate (51.2%) compared with those without myocardial injury (4.5%). Furthermore, among those with myocardial injury, greater degrees of troponin elevation were associated with higher mortality rates.

It is unclear if COVID-19–related acute myocardial injury differs in prevalence in other viral infections. In a study of 1,131 patients with lab-confirmed influenza infection, only 33 (2.9%) had myocardial injury.

MYOCARDIAL INFLAMMATION AND MYOCARDITIS
Reports of myocarditis associated with coronavirus infection date back to the 1980s. Myocarditis is often a clinical diagnosis made without histopathologic confirmation because of poor utilization and sensitivity of endomyocardial biopsies. Myocardial inflammation associated with SARS-COV-2 became a focus of research studies early in the pandemic, although isolation protocols prohibited myocardial biopsy in most cases. Although early case reports localized viral particles in the myocardial tissue associated with low-grade inflammation, there is little evidence supporting direct cardiomyocyte injury through virus-mediated lysis. Histopathologic studies of myocardial biopsies or postmortem examinations have largely suggested that SARS-COV-2 myocarditis is uncommon or rare. Conversely, at least one acute histopathologic finding such as macro- or microvascular thrombi, inflammation, or intraluminal megakaryocytes was reported in almost half of postmortem cases. While acute and subclinical myocardial injury is not uncommon in COVID-19 cases, it appears that COVID-19–related nonischemic injury and myocardial inflammation have different mechanisms than in lymphocytic myocarditis.

ROLE OF CARDIAC MAGNETIC RESONANCE
Cardiac magnetic resonance (CMR) is the standard noninvasive imaging modality for myocardial tissue characterization, and diagnosis of myocarditis by CMR has established criteria. However, diagnosis by CMR carries some limitations, such as abnormalities on T1/T2 mapping that are somewhat vague. Late gadolinium enhancement (LGE) can indicate acute injury or myocardial replacement fibrosis, and the pattern and context sheds light on the diagnosis in the right clinical setting.

CMR-based research studies in COVID-19 focus predominately on patients who recovered after hospitalization. Studies have varied significantly thus far in the incidence of cardiac involvement, likely due to differences in the tested populations and, more importantly, the criteria used to define abnormalities (Table 2).

| AUTHOR             | N    | (%) WITH ELEVATED TROPNON | ASSAY USED               | PATIENT SETTING     |
|--------------------|------|---------------------------|--------------------------|--------------------|
| Metkus et al.20     | 243  | 51                        | Troponin I or T          | ICU                |
| Giustino et al.21   | 305  | 62                        | Troponin T               | Inpatient          |
| Huang et al.22      | 41   | 12                        | Hypersensitive troponin I| Inpatient          |
| Han et al.23        | 273  | 5.05% (outpatients)       | Hypersensitive troponin I| Outpatient, inpatient, ICU |
|                    |      | 23.33% (inpatients)       |                          |                    |
|                    |      | 20% (ICU)                 |                          |                    |
| Richardson et al.12 | 5,700| 22.6                      | Variety of assays        | Inpatient          |
| Petrilii et al.24   | 4,103| 11.7                      | Not reported             | Outpatient and inpatient |
| Wang et al.25       | 138  | 7.2                       | Troponin I               | Inpatient          |
| Zhou et al.26       | 191  | 17                        | High-sensitivity troponin I| Inpatient          |
| Guo et al.18        | 187  | 27.8                      | Troponin T               | Inpatient          |
| Shi et al.19        | 416  | 19.7                      | High-sensitivity troponin I| Inpatient          |

Table 1 Summary of cardiac injury prevalence (defined as troponin elevation) in COVID-19 studies. ICU: intensive care unit.
| FIRST AUTHOR, YEAR | COUNTRY | TYPE OF STUDY | NO. OF PATIENTS | RESULTS | PRIMARY END POINTS | CONCLUSION |
|--------------------|---------|---------------|----------------|---------|--------------------|------------|
| Joy38 2021         | UK      | Prospective blind study | 74 recovered patients with mild cases vs. 75 controls | No difference in end points between recovered patients and controls | Cardiac involvement 6 months after recovery from mild COVID-19 | Mild COVID-19 in healthy patients does not result in cardiovascular abnormalities. |
| Raman37 2021       | UK      | Observational cohort study | 58 recovered patients from moderate-severe COVID-19 vs. 30 matched controls | • 26% elevated basal myocardial T1 • No statistical difference in T2 and ECV | Cardiac involvement 2-3 months after recovery from COVID-19 | Multiorgan inflammation persists after recovery from moderate-severe COVID-19. |
| Starekova39 2021   | USA     | Case series | 145 competitive athletes recovering from mild-moderate COVID-19 who underwent CMR 15 days after diagnosis | 1.4% had CMR findings consistent with myocarditis | Prevalence of myocardial involvement in competitive athletes recovering from COVID-19 | There is low prevalence of myocarditis in this population. |
| Daniels40 2021     | USA     | Case series | 1,597 competitive athletes recovering from COVID-19 | 2.3% had CMR-diagnosed myocarditis, clinical and subclinical | Prevalence of myocarditis in competitive athletes recovering from COVID-19 | CMR screening in athletes recovering from COVID-19 should be considered for safe return to play. |
| Martinez41 2021    | USA     | Cross-sectional study | 789 professional athletes with COVID-19 infection, irrespective of symptoms | 0.6% had CMR findings suggesting inflammatory heart disease | Prevalence of detectable inflammatory heart disease in professional athletes with prior COVID-19 infection | Few cases of inflammatory heart disease have been detected; safe return to play has been achieved. |
| Kotecha42 2021     | UK      | Retrospective study | 148 patients with severe COVID-19 requiring hospitalization | 54% had LGE: • 26% myocarditis • 22% ischemia • 6% dual pathology | Assess myocardial injury in hospitalized COVID-19 patients after recovery | During recovery from severe COVID-19, myocarditis-like injury can be detected. Its functional consequence is not clear. |
| Puntmann36 2020    | Germany | Prospective observational cohort study | 100 recovered patients vs. 107 controls | • Abnormal CMR findings in 78% of recovered COVID-19 patients • 73% raised myocardial native T1 • 60% raised myocardial native T2 • 32% LGE • 22% pericardial involvement | Cardiac involvement after recovery from COVID-19 | CMR revealed cardiac involvement and ongoing myocardial inflammation in recovered COVID-19 patients. |
| Huang35 2020       | China   | Retrospective study | 26 recovered patients | • 58% abnormal CMR • 54% myocardial edema • 31% LGE | Cardiac involvement after recovery from COVID-19 | A proportion of recovered COVID-19 patients had cardiac involvement on CMR. |
| Rajpal43 2020      | USA     | Case series | 26 competitive athletes with mild COVID-19 | • 15% CMR findings consistent with myocarditis • 46% LGE | Detect cardiac involvement through CMR in competitive athletes recovering from COVID-19 | CMR may help stratify athletes recovering from COVID-19 as to risk of myocarditis. |
| Knight44 2020      | UK      | Cross-sectional study | 828 hospitalized patients positive for COVID-19 or with a clinical diagnosis | • 586 patients had elevated hsTNT • 51 underwent CMR: 69% of them had myocardial injury | Underlying cause of troponin elevation in COVID-19 infection | Myocardial injury detected by CMR is common in hospitalized COVID-19 patients. |

Table 2: Main findings of studies utilizing CMR in COVID-19 patients.35-44 ECV: extracellular volume fraction; CMR: cardiac magnetic resonance; LGE: late-gadolinium enhancement; hsTNT: high-sensitivity troponin T.
An early retrospective CMR study of 26 recovered COVID-19 patients with cardiac symptoms showed that 58% had abnormal CMR findings, including abnormal global native T1 and T2, LGE, and impaired right ventricular function (Figure 2). Later, a prospective cohort study by Puntmann et al. of 100 patients who recovered from COVID-19 found a 78% prevalence of cardiac involvement and 60% prevalence of ongoing myocardial inflammation based on CMR abnormalities detected by native T1/T2 mapping, LGE, and pericardial enhancement. High-sensitivity troponin T was detectable in 71% of patients and significantly elevated in 5%, showing evidence of subclinical myocardial involvement. Raman et al., who compared 58 recovered COVID-19 patients after hospital discharge with matched controls using multiorgan magnetic resonance imaging and functional assessment, found a 26% rate of elevated T1 time in the COVID-19 cohort but no significant difference in T2 time or extracellular volume fraction against controls.

In a multicenter CMR study evaluating 148 patients 2 months after being hospitalized with severe COVID-19 and elevated troponin levels, 54% of patients (80/148) had LGE and/or ischemia on CMR. The LGE pattern was inflammatory in 26% of patients, ischemic in 22%, and both in 6%. In contrast to Puntmann et al., no abnormalities on T1 or T2 mapping were seen compared with matched controls. More recently, another case-control study focused on healthcare workers free of known CVD, including 74 seropositive and 75 seronegative subjects. Of the total patients, only one was hospitalized briefly, while 11 (15%) were asymptomatic. The cohort underwent CMR and biomarker evaluation 6 months after enrollment. None of the end points—including left ventricular ejection fraction, indexed end-diastolic volume, LGE, global T1 and T2, and biomarkers such as NT-proBNP and troponin—were significantly different between the two groups.

These studies highlight the importance of future research on cardiac involvement and its implications for recovered COVID-19 patients. However, larger multicenter studies with unified selection criteria and CMR imaging analysis are needed, and isolated T1/T2 abnormalities should be considered despite their uncertain relevance based on reduced biopsy specificity. While the incidence of cardiac involvement after COVID-19 may be lower than initially reported, it still carries critical long-term consequences given the extent of the pandemic. Healthy asymptomatic individuals who have a mild COVID-19 course appear unlikely to have significant cardiac involvement, but confirmatory studies are needed.

**COMPETITIVE ATHLETES AND RETURN TO PLAY**

Early in the pandemic, there were significant concerns for the risk of myocarditis in otherwise healthy athletes with mild or no symptoms, leading to cessation of tournaments and discussions about cardiovascular screening prior to return to play after COVID-19 infection. This led to research studies evaluating the risk of SARS-COV-2 myocarditis or myocardial inflammation in athletes. In a retrospective study of 145 competitive student athletes recovering from mild-to-moderate COVID-19, only two patients (1.4%) had myocarditis. In a cohort study of 1,597 college athletes with CMR screening after COVID-19 infection, 37 athletes (2.3%) were diagnosed with clinical and subclinical myocarditis. However, there was significant variability in testing protocols and prevalence of myocarditis (eg, the prevalence was 0.31% based on symptom-based screening).

In another study of 789 professional athletes with previous COVID-19 and mild or no symptoms, a screening strategy with troponin, electrocardiogram, and...
echocardiography identified 30 athletes (3.8%) with abnormalities. Only 5 athletes (0.6%) had CMR findings suggestive of myocardial inflammation (and they were restricted from play), while no adverse events occurred in those who resumed sports participation with negative screening.41

Currently, expert opinion considers cardiovascular testing to be unnecessary in those with no or mild COVID-19 symptoms after 10 days of exercise cessation and full resolution of symptoms. New cardiovascular symptoms or moderate or severe COVID-19 symptoms after recovery warrant a medical evaluation prior to return to sports.45

OTHER CAUSES OF CARDIAC INJURY IN COVID-19

The following is a brief review of other potential etiologies that are covered elsewhere in this issue.

ACUTE CORONARY SYNDROME

Acute respiratory infections, including viral and bacterial pneumonias, are well-recognized triggers for CVD and acute coronary syndrome (ACS).46-48 A recent study showed a 3- to 6-fold increase in the risk of myocardial infarction during the week after laboratory-confirmed infection with respiratory viruses (influenza virus, respiratory syncytial, etc.) compared with the risk during the year before or after infection.49,50

Admissions and care for patients with ACS were significantly impacted by COVID-19. A prospective international registry initiated early in the pandemic reported significant delays in patients seeking medical care and longer door-to-balloon times in COVID patients with ST elevation myocardial infarction (STEMI). There also were significantly higher rates of cardiogenic shock and quadrupling of in-hospital mortality compared with pre-COVID cohort databases.51 Another observational study of STEMI patients with concurrent SARS-COV-2 infection was suggestive of a higher thrombus burden and higher biomarkers levels (troponin T, D-Dimer, and C-reactive protein) compared with non–COVID-19 STEMI patients.52

HEART FAILURE

Patients with heart failure (HF) who experience severe COVID-19 infection are particularly at risk for COVID-19-related morbidity and mortality.19,53 A cohort study of 132,000 HF patients admitted to the hospital for COVID-19 between April and September 2020 showed a 10-to-14-fold greater odds of dying versus patients with HF alone. Patients with HF and COVID-19 had more comorbidities and required more ICU stays, renal replacement therapy, and advanced cardiovascular monitoring. In addition, this cohort’s in-hospital mortality rate was almost 25% compared with 2.6% for HF patients without COVID-19 infection.54

Similar findings were shown in a retrospective study of 4,043 patients admitted for COVID-19 between March and May 2020. The 8.3% of patients with both COVID-19 and HF had a higher rate of cumulative in-hospital mortality compared with patients without HF (49% vs. 27%, P < .001) despite adjusting for age, body mass index, and comorbidities.55

Takotsubo cardiomyopathy has been described in the context of COVID-19 in several case reports and case series.56-59

CONCLUSIONS

For almost 2 years, the world has faced a global pandemic due to COVID-19. Although vaccinations are reducing infection rates, the impact of the disease on global health has been massive. Cardiovascular comorbidities increase morbidity and mortality in COVID-19 patients, and the infection itself has been associated with myocardial injury and dysfunction. This can cause several complications, including myocarditis, arrhythmia, acute myocardial infarction, venous thromboembolic events, and heart failure. Therefore, to optimally manage COVID-19 patients, it is critical to not only assess their risk factors but also to be on alert for possible fatal cardiovascular complications. Additional studies with longer observation periods are needed to gain a deeper understanding of the potential long-term cardiovascular complications of COVID-19.

KEY POINTS

- Myocardial injury is common in hospitalized COVID-19 patients, particularly those with established cardiovascular disease.
- Myocardial injury can range from subclinical biomarker elevations to myocardial infarction, inflammatory cardiomyopathy, potential myocarditis, heart failure, and cardiogenic shock.
- The prevalence, implications, and optimal management of myocardial injury in nonhospitalized COVID-19 patients is a critical area for future research.
COMPETING INTERESTS

Dr. Malahfji receives support from the Houston Methodist Research Institute; Dr. Al-Mallah receives research support from Siemens, unrelated to this work, and is a consultant for Pfizer and Philips; and Dr. Shah receives support from the National Science Foundation (CNS-1931884) and the Beverly B. and Daniel C. Arnold Distinguished Centennial Chair Endowment. All other authors have completed and submitted the Methodist DeBakey Cardiovascular Journal Conflict of Interest Statement and none were reported.

AUTHOR AFFILIATIONS

Valentina L. Crudo, MD orcid.org/0000-0002-2465-8830
Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas, US

Ahmed I. Ahmed, MD, MPH orcid.org/0000-0002-5886-7999
Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas, US

Eilidh L. Cowan, BS orcid.org/0000-0003-0738-4775
Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas, US

Dipan J. Shah, MD orcid.org/0000-0002-6179-2393
Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas, US

Mouaz H. Al-Mallah, MD, MSc orcid.org/0000-0003-2348-0484
Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas, US

Maan Malahfji, MD orcid.org/0000-0002-2701-8783
Houston Methodist DeBakey Heart & Vascular Center, Houston Methodist Hospital, Houston, Texas, US

REFERENCES

1. Jhu.org [Internet]. Baltimore, MD: Johns Hopkins University & Medicine; 2021. Coronavirus resource center: COVID-19 United States Cases by County; 2021 Dec 1 [cited 2021 Dec 1]. Available from: https://coronavirus.jhu.edu/us-map

2. Wu Z, McGoogan JM. Characteristics of and Important Lessons From the Coronavirus Disease 2019 (COVID-19) Outbreak in China: Summary of a Report of 72 314 Cases From the Chinese Center for Disease Control and Prevention. JAMA. 2020 Apr 7;323(13):1239-1242. doi: 10.1001/jama.2020.2648

3. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID-19 and Cardiovascular Disease. Circulation. 2020 May 19;141(20):1648-1655. doi: 10.1161/CIRCULATIONAHA.120.046941

4. Azevedo RB, Botelho BG, Hollanda JVGd, et al. Covid-19 and the cardiovascular system: a comprehensive review. J Hum Hypertens. 2021 Jan;35(1):4-11. doi: 10.1038/s41371-020-0387-4

5. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the `Cytokine Storm’ in COVID-19. J Infect. 2020 Jun;80(6):607-613. doi: 10.1016/j.jinf.2020.03.037

6. Long B, Brady WJ, Kayfman A, Gottlieb M. Cardiovascular complications in COVID-19. Am J Emerg Med. 2020 Jul;38(7):1504-1507. doi: 10.1016/j.ajem.2020.04.048

7. Hoffmann M, Kleine-Weber H, Schroeder S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell. 2020 Apr 16;181(2):271-280.e8. doi: 10.1016/j.cell.2020.02.052

8. Zheng Y-Y, Ma Y-T, Zhang J-Y, Xie X. COVID-19 and the cardiovascular system. Nat Rev Cardiol. 2020 May;17(5):259-260. doi: 10.1038/s41569-020-0360-5

9. Al-Amoodi M, Rao K, Rao S, Brewer JH, Magalski A, Chhatriwalla AK. Fulminant Myocarditis Due to H1N1 Influenza. Circ Heart Fail. 2010 May;3(3):e7-e9. doi: 10.1161/CIRCHEARTFAILURE.110.938506

10. Alhogybani T. Acute myocarditis associated with novel Middle east respiratory syndrome coronavirus. Ann Saudi Med. Jan-Feb 2016;36(1):78-80. doi: 10.5144/0256-4947.2016.78

11. Oudit GY, Kassiri Z, Jiang C, et al. SARS-coronavirus modulation of myocardial ACE2 expression and inflammation in patients with SARS. Eur J Clin Invest. 2009 Jul;39(7):618-25. doi: 10.1111/j.1365-2362.2009.02153.x

12. Richardson S, Hirsch JS, Narasimhan M, et al. Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized With COVID-19 in the New York City Area. JAMA. 2020 May 26;323(20):2052-2059. doi: 10.1001/jama.2020.6777

13. Zheng Z, Peng F, Xu B, et al. Risk factors of critical & mortal COVID-19 cases: A systematic literature review and meta-analysis. J Infect. 2020 Aug;81(2):e16-e25. doi: 10.1016/j.jinf.2020.04.021

14. Jain S, Chaves SS. Obesity and influenza. Clin Infect Dis. 2011 Sep;53(5):e42-e4. doi: 10.1093/cid/cir448

15. Hendren NS, de Lemos JA, Ayers C, et al. Association of Body Mass Index and Age With Morbidity and Mortality in Patients Hospitalized With COVID-19: Results From the American Heart Association COVID-19 Cardiovascular Disease Registry. Circulation. 2021 Jan 12;143(2):135-144. doi: 10.1161/CIRCULATIONAHA.120.051936

16. Chan JWM, Ng CK, Chan YH, et al. Short term outcome and risk factors for adverse clinical outcomes in adults with severe acute respiratory syndrome (SARS). Thorax. 2003 Aug;58(8):686-9. doi: 10.1136/thorax.58.8.686

17. Mehra MR, Desai SS, Kuy S, Henry TD, Patel AN. Cardiovascular Disease, Drug Therapy, and Mortality in Covid-19. N Engl J Med. 2020 Jun 18;382(25):e102. doi: 10.1056/NEJMoa2007621

18. Guo T, Fan Y, Chen M, et al. Cardiovascular Implications of Fatal Outcomes of Patients With Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020 Jul 1;5(7):811-818. doi: 10.1001/jamacardio.2020.1017
19. Shi S, Qin M, Shen B, et al. Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China. JAMA Cardiol. 2020 Jul 1;5(7):820-810. doi: 10.1001/jamacardio.2020.0950

20. Metkus TS, Sokoll LJ, Barth AS, et al. Myocardial Injury in Severe COVID-19 Compared With Non-COVID-19 Acute Respiratory Distress Syndrome. Circulation. 2021 Feb 9;143(6):553-565. doi: 10.1161/CIRCULATIONAHA.120.050543

21. Giustino G, Croft LB, Stefanini GG, et al. Characterization of Myocardial Injury in Patients With COVID-19. J Am Coll Cardiol. 2020 Nov 3;76(18):2043-2055. doi: 10.1016/j.jacc.2020.08.069

22. Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet. 2020 Feb 15;395(10223):497-506. doi: 10.1016/S0140-6736(20)30183-5

23. Han H, Xie L, Liu R, et al. Analysis of heart injury laboratory parameters in 273 COVID-19 patients in one hospital in Wuhan, China. J Med Virol. 2020 Jul;92(7):819-823. doi: 10.1002/jmv.25809

24. Petrilli CM, Jones SA, Yang J, et al. Factors associated with hospital admission and critical illness among 5279 people with coronavirus disease 2019 in New York City: prospective cohort study. BMJ. 2020 May 22;369:m1966. doi: 10.1136/bmj.m1966

25. Wang D, Hu B, Hu C, et al. Clinical Characteristics of 138 Hospitalized Patients With 2019 Novel Coronavirus-Infected Pneumonia in Wuhan, China. JAMA. 2020 Mar 17;323(11):1061-1069. doi: 10.1001/jama.2020.1585

26. Zhou F, Yu T, Du R, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. 2020 Mar 28;395(10229):1054-1062. doi: 10.1016/S0140-6736(20)30566-3

27. Harris JE, Shah PJ, Korimilli V, Win H. Frequency of troponin elevations in patients with influenza infection during the 2017-2018 influenza season. Int J Cardiol Heart Vasc. 2019 Jan 30:22:145-147. doi: 10.1016/j.ijchv.2018.12.013

28. Riski H, Hovi T, Frick M H. Carditis associated with coronavirus infection. Lancet. 1980 Jul 12;2(8185):100-1. doi: 10.1016/S0140-6736(80)92989-X

29. Trachtenberg BH, Hare JM. Inflammatory Cardiomyopathic Syndromes. Circ Res. 2017 Sep 15;121(7):803-818. doi: 10.1161/CIRCRESAHA.117.310221

30. Tavazzi G, Pellegrini C, Maurelli M, et al. Myocardial localization of coronavirus in COVID-19 cardiogenic shock. Eur Heart Fail. 2020 May;22(5):911-915. doi: 10.1002/ehjf.1828

31. Halushka MK, Vander Heide RS. Myocarditis is rare in COVID-19 autopsies: cardiovascular findings across 277 postmortem examinations. Circ Cardiovasc Pathol. Jan-Feb 2021;50:107300. doi: 10.1016/j.circpath.2020.107300

32. Kawakami R, Sakamoto A, Kawai K, et al. Pathological Evidence for SARS-CoV-2 as a Cause of Myocarditis: JACC Review Topic of the Week. J Am Coll Cardiol. 2021 Jan 26;77(3):314-325. doi: 10.1016/j.jacc.2020.11.031

33. Lindner D, Fitzek A, Bräuninger H, et al. Association of Cardiac Infection With SARS-CoV-2 in Confirmed COVID-19 Autopsy Cases. JAMA Cardiol. 2020 Nov 1;5(11):1281-1285. doi: 10.1001/jamacardio.2020.3551

34. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations. J Am Coll Cardiol. 2018 Dec 18;72(24):3158-3176. doi: 10.1016/j.jacc.2018.09.072

35. Huang L, Zhao P, Tong D, et al. Cardiac Involvement in Patients Recovered From COVID-19 Identified Using Magnetic Resonance Imaging. JACC Cardiovasc Imaging. 2020 Nov;13(11):2330-2339. doi: 10.1016/j.jcmg.2020.05.004

36. Puntmann VO, Carerj ML, Wieters I, et al. Outcomes of Cardiovascular Magnetic Resonance Imaging in Patients Recently Recovered From Coronavirus Disease 2019 (COVID-19). JAMA Cardiol. 2020 Nov 1;5(11):1265-1273. doi: 10.1001/jamacardio.2020.3557

37. Raman B, Cassar MP, Tunnicliffe EM, et al. Medium-term effects of SARS-CoV-2 infection on multiple vital organs, exercise capacity, cognition, quality of life and mental health, post-hospital discharge. EClinicalMedicine. 2021 Jan 7;31:100683. doi: 10.1016/j.eclinm.2020.100683

38. Joy G, Artico J, Kurdi H, et al. Prospective Case-Control Study of Cardiovascular Abnormalities 6 Months Following Mild COVID-19 in Healthcare Workers. JACC Cardiovasc Imaging. 2021 May 5;S1936-878X(21)00356-9. doi: 10.1016/j.jcmg.2021.04.011

39. Starekova J, Bluemke DA, Bradham WS, et al. Evaluation for Myocarditis in Competitive Student Athletes Recovering From Coronavirus Disease 2019 With Cardiac Magnetic Resonance Imaging. JAMA Cardiol. 2021 Aug 1;6(8):945-950. doi: 10.1001/jamacardio.2020.7444

40. Daniels CJ, Rajpal S, Greenshields JT, et al. Prevalence of Clinical and Subclinical Myocarditis in Competitive Athletes With Recent SARS-CoV-2 Infection: Results From the Big Ten COVID-19 Cardiac Registry. JAMA Cardiol. 2021 Sep 1;6(9):1078-1087. doi: 10.1001/jamacardio.2021.2065

41. Martinez MW, Tucker AM, Bloom OJ, et al. Prevalence of Inflammatory Heart Disease Among Professional Athletes With Prior COVID-19 Infection Who Received Systematic Return-to-Play Cardiac Screening. JAMA Cardiol. 2021 Jul 1;6(7):745-752. doi: 10.1001/jamacardio.2021.0565

42. Kotecha T, Knight DS, Razvi Y, et al. Patterns of myocardial injury in recovered troponin-positive COVID-19 patients assessed by cardiovascular magnetic resonance. Eur Heart J. 2021 May 14;42(19):1866-1878. doi: 10.1093/eurheartj/ehab075

43. Rajpal S, Tong MS, Borchers J, et al. Cardiovascular Magnetic Resonance Findings in Competitive Athletes Recovering From COVID-19 Infection. JAMA Cardiol. 2021 Jan 1;6(1):116-118. doi: 10.1001/jamacardio.2020.4916

44. Knight DS, Kotecha T, Razvi Y, et al. COVID-19: Myocardial Injury in Survivors. Circulation. 2020 Sep 15;142(11):1120-1122. doi: 10.1161/CIRCULATIONAHA.120.049252
45. Kim JH, Levine BD, Phelan D, et al. Coronavirus Disease 2019 and the Athletic Heart: Emerging Perspectives on Pathology, Risks, and Return to Play. JAMA Cardiol. 2021 Feb 1;6(2):219-227. doi: 10.1001/jamacardio.2020.5890

46. Maddj M, Miller CC, Zarubaov V, et al. Influenza epidemics and acute respiratory disease activity are associated with a surge in autopsy-confirmed coronary heart disease death: results from 8 years of autopsies in 34,892 subjects. Eur Heart J. 2007 May;28(10):1205-10. doi: 10.1093/eurheartj/ehm035

47. Maddj M, Safavi-Naeini P, Solomon SD, Vardeny O. Potential Effects of Coronavirus on the Cardiovascular System: A Review. JAMA Cardiol. 2020 Jul 1;5(7):831-840. doi: 10.1001/jamacardio.2020.1286

48. Cowan LT, Lutsey PL, Pankow JS, Matsushita K, Ishigami J, Lakshminarayan K. Inpatient and Outpatient Infection as a Trigger of Cardiovascular Disease: The ARIC Study. J Am Heart Assoc. 2018 Nov 20;7(22):e009683. doi: 10.1161/JAHA.118.009683

49. Kwong JC, Schwartz KL, Campitelli MA, et al. Acute Myocardial Infarction after Laboratory-Confirmed Influenza Infection. N Engl J Med. 2018 Jan 25;378(4):345-353. doi: 10.1056/NEJMoa1702090

50. Mushar DM, Abers MS, Corrales-Medina VF. Acute Infection and Myocardial Infarction. N Engl J Med. 2019 Jan 10;380(2):171-176. doi: 10.1056/NEJMoa1808137

51. Kite TA, Ludman PF, Gale CP, et al. International Prospective Registry of Acute Coronary Syndromes in Patients With COVID-19. J Am Coll Cardiol. 2021 May 25;77(20):2466-2476. doi: 10.1016/j.jacc.2021.03.309

52. Choudry FA, Homshere SM, Rathod KS, et al. High Thrombus Burden in Patients With COVID-19 Presenting With ST-Segment Elevation Myocardial Infarction. J Am Coll Cardiol. 2020 Sep 8;76(10):1168-1176. doi: 10.1016/j.jacc.2020.07.022

53. Sama IE, Ravera A, Santema BT, et al. Circulating plasma concentrations of angiotensin-converting enzyme 2 in men and women with heart failure and effects of renin-angiotensin-aldosterone inhibitors. Eur Heart J. 2020 May 14;41(19):1810-1817. doi: 10.1093/eurheartj/ehaa373

54. Bhatt AS, Jering KS, Vaduganathan M, et al. Clinical Outcomes in Patients With Heart Failure Hospitalized With COVID-19. JACC Heart Fail. 2021 Jan;9(1):65-73. doi: 10.1016/j.jchf.2020.11.003

55. Castagna F, Kataria R, Madan S, et al. A History of Heart Failure Is an Independent Risk Factor for Death in Patients Admitted with Coronavirus 19 Disease. J Cardiovasc Dev Dis. 2021 Jun 30;8(7):77. doi: 10.3390/jcdd8070077

56. Templin C, Ghadri JR, Diekmann J, et al. Clinical Features and Outcomes of Takotsubo (Stress) Cardiomyopathy. N Engl J Med. 2015 Sep 3;373(10):929-38. doi: 10.1056/NEJMoa1406761

57. Chao C, DeValeria PA, Sen A, et al. Reversible cardiac dysfunction in severe COVID-19 infection, mechanisms and case report. Echocardiography. 2020 Sep;37(9):1465-1469. doi: 10.1111/echo.14807

58. Dave S, Thibodeau JT, Styrvoky K, Bhatt SH. Takotsubo Cardiomyopathy in a Coronavirus Disease-2019-Positive Patient: A Case Report. A A Pract. 2020 Sep;14(11):e01304. doi: 10.1213/XAA.0000000000001304

59. Moody G, Atar S. Takotsubo syndrome during the COVID-19 pandemic, state-of-the-art review. CJC Open. 2021 May 26. doi: 10.1016/j.cjco.2021.05.011