



# Covid-19 Related Myocarditis

Nurcan Arıkan

*Bilecik Training and Research Hospital*

Abstract:

Coronavirus Disease-2019 (COVID-19) affected the whole world and caused the death of millions of people. Pneumonia and acute respiratory distress syndrome are the most common causes of death. Many cardiovascular conditions such as myocarditis, acute myocardial infarction, heart failure, arrhythmias, cardiac arrest and cardiogenic shock are other common causes of mortality. The exact incidence of COVID-19-associated myocarditis is unknown. Sudden dyspnea, chest pain, arrhythmias, heart failure may be due to myocarditis. Patients with suspected cardiac involvement should be monitored and followed closely. Although the definitive diagnosis of myocarditis is made by endomyocardial biopsy, it is not possible to perform it in every patient and in every center, since it is an invasive method. Patients with suspected myocarditis should be followed up with troponin, electrocardiogram and, if necessary, echocardiography, and cardiac magnetic resonance imaging should be performed if possible. Although there is no definitive treatment for myocarditis, supportive treatment is the most important treatment approach.

Keywords: Coronavirus Disease-2019, myocarditis, cardiac involvement.

Copyright : © 2022 The Authors. Published by Publisher. This is an open access article under the CC BY-NC-ND license

(<https://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Supplementary information** The online version of this article (<https://doi.org/xx.xxx/xxx.xx>) contains supplementary material, which is available to authorized users.

**Corresponding Author:** *Nurcan Arıkan*, *Bilecik Training and Research Hospital*

## Introduction

Although Coronavirus Disease-2019 (COVID-19) is initially defined as a respiratory system disease, it is a disease with a wide clinical spectrum that can affect all systems. It may present with a clinical course that can progress from asymptomatic infection to multi-organ failure and death. The respiratory system was found to be the most frequently involved system, and ARDS was the most common cause of mortality (1). In recent studies, it has been reported that COVID-19 infection is frequently observed in cardiovascular involvement, except lung involvement (2-5). In a recent study, myocardial disease was detected in approximately 12% of hospitalized patients infected with COVID-19 (6). The pathogenesis of acute myocardial injury is not fully understood. Cytokine storm has been considered as the most important injury mechanism in the pathogenesis of acute lung injury, ARDS and myocardial injury. Another hypothesis is direct viral invasion via Angiotensin-Converting Enzyme II (ACE-II) receptors (7).

Viral infections are the most common causes of myocarditis (8). Covid-19-associated myocarditis develops as a result of acute ventricular dysfunction associated with diffuse myocardial edema (9). According to the criteria of the European Society of Cardiology, the clinical diagnosis of myocarditis is made by the presence of chest pain and the presence of increased troponin T or Troponin I (10). The most common symptoms in acute myocarditis are; chest pain, dyspnea, cough, weakness, palpitations, hypotension, life-threatening arrhythmias and cardiogenic shock (11). The cause of approximately 10% of sudden cardiac death in young people is acute myocarditis (12). C-reactive protein (CRP), lactate dehydrogenase and white blood cell increase can be seen in patients with COVID-19 who develop myocarditis. However, these are not specific to myocarditis (13, 14). An increase in serum troponin may indicate cardiac involvement, but it is not specific for myocarditis (15). An increase in N-terminal pro-B type natriuretic peptide (NT-pro-BNP) can be seen in COVID-19-associated myocarditis, but it is not specific (14). The normal troponin values in some patients with COVID-19-associated myocarditis also do not exclude the diagnosis of myocarditis (16, 17).

Electrocardiographic (ECG) changes that can be seen in patients who develop COVID-19 related myocarditis are sinus tachycardia, ST segment elevation/depression, T wave inversion, bradycardia, tachycardia, arrhythmias, QT interval prolongation, non-specific interventricular conduction delays, low QRS voltage due to myocardial edema (18, 19). Echocardiography is an extremely important non-invasive test in terms of excluding other causes of heart failure

such as heart valve disease and myocardial infarction (21). Transthoracic echocardiographic findings are global left ventricular or biventricular dysfunction, pericardial effusion, myocardial edema, dilated and/or hypertrophic ventricles, regional wall motion abnormalities. Cardiac magnetic resonance is the non-invasive test with the highest sensitivity in the diagnosis of myocarditis (19). Cardiac images should be interpreted according to the Lake Louise consensus criteria. These criteria show myocardial edema, necrosis, and fibrosis with early and late gadolinium uptake on T2-weighted images. It cannot distinguish whether the edema in the myocardium is of autoimmune origin or due to viral invasion (22). Its use is limited in patients who are hemodynamically unstable, intubated, and have tachyarrhythmias. In these patients; Endomyocardial biopsy, which is the gold standard diagnostic method that definitively detects the etiology of myocardial edema, should be preferred (19). Biopsy samples should be interpreted according to Dallas criteria (23). The diagnosis becomes more reliable when immunohistochemical criteria are added to the Dallas criteria (24).

If left ventricular dysfunction has developed in the management of COVID-19-associated myocarditis, ACE inhibitors, angiotensin receptor blockers or angiotensin receptor neprilysin inhibitors, beta-blockers and diuretics should be used in line with the heart failure treatment guidelines (25). Inotropic therapy support or vasopressor therapy is recommended in the acute period in patients who develop cardiogenic shock and fulminant myocarditis. In the prolonged period, mechanical circulatory support, transplantation, atropine or temporary cardiac pacemaker in patients who develop bradycardia, and antiarrhythmic drugs in patients who develop tachyarrhythmia are recommended (26). There is no definitive recommendation for the routine use of corticosteroids and intravenous immunoglobulin in the diagnosis and treatment of COVID-19-associated myocarditis. The decision should be made on a patient basis. More clinical studies and guidelines are needed on this subject.

## Discussion and Conclusion

Although the mechanism of myocarditis associated with COVID-19 has not been fully elucidated, it is a serious complication that can be seen in the course of the infection. While it may be asymptomatic in some patients, it may progress to fulminant myocarditis and cause death in some patients. In the follow-up of hospitalized patients with the diagnosis of COVID-19, troponin and ECG monitoring may help in the early detection of asymptomatic patients. Every newly developed symptom should be evaluated in detail in patients, and myocarditis should be considered in symptoms such as fever, dyspnea and chest pain. In addition to an increase in inflammatory markers and cardiac markers, ECG and echocardiographic findings should be performed to support the diagnosis of myocarditis. Cardiac MRI or endomyocardial biopsy should be considered for definitive diagnosis. Treatment of COVID-19-associated myocarditis should be tailored to the clinical arrhythmias and heart failure guidelines developed in the patient. More clinical studies are needed to guide the diagnosis and treatment of COVID-19-associated myocarditis.

## References

1. Wu C, Chen X, Cai Y, et al. Risk Factors Associated With Acute Respiratory Distress Syndrome and Death in Patients With Coronavirus Disease 2019 Pneumonia in Wuhan, China [published correction appears in *JAMA Intern Med.* 2020 Jul 1;180(7):1031]. *JAMA Intern Med.* 2020;180(7):934-943. doi:10.1001/jamainternmed.2020.0994
2. Desai AD, Lavelle M, Boursiquot BC, Wan EY. Long-term complications of COVID-19. *Am J Physiol Cell Physiol.* 2022;322(1):C1-C11. doi:10.1152/ajpcell.00375.2021
3. Ardahanli I, Akhan O, Sahin E, Akgun O, Gurbanov R. Myocardial performance index increases at long-term follow-up in patients with mild to moderate COVID-19. *Echocardiography.* 2022;39(4):620-625. doi:10.1111/echo.15340
4. Raman B, Bluemke DA, Lüscher TF, Neubauer S. Long COVID: post-acute sequelae of COVID-19 with a cardiovascular focus. *Eur Heart J.* 2022;43(11):1157-1172. doi:10.1093/eurheartj/ehac031
5. Avcı E, Ardahanlı İ, Öztaş E, Dişibeyaz S. COVID-19'da gastrointestinal semptomlar ile hastalığın seyri ve prognozu arasında bir ilişki var mı? Tek merkezli pilot çalışma. *Akademik Gastroenteroloji Dergisi.* 2020;19(3):103-108. doi: 10.17941/agd.847338

6. Clerkin KJ, Fried JA, Raikhelkar J, et al. COVID-19 and Cardiovascular Disease. *Circulation*. 2020;141(20):1648-1655. doi:10.1161/CIRCULATIONAHA.120.046941
7. Mehta P, McAuley DF, Brown M, et al. COVID-19: consider cytokine storm syndromes and immunosuppression. *Lancet*. 2020;395(10229):1033-1034. doi:10.1016/S0140-6736(20)30628-0
8. Rezkalla SH, Kloner RA. Viral myocarditis: 1917-2020: From the Influenza A to the COVID-19 pandemics. *Trends Cardiovasc Med*. 2021;31(3):163-169. doi:10.1016/j.tcm.2020.12.007
9. 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. doi:10.1093/eurheartj/ehaa253
10. Caforio AL, Pankuweit S, Arbustini E, et al. Current state of knowledge on aetiology, diagnosis, management, and therapy of myocarditis: a position statement of the European Society of Cardiology Working Group on Myocardial and Pericardial Diseases. *Eur Heart J*. 2013;34(33):2636-2648d. doi:10.1093/eurheartj/eh210
11. Kociol RD, Cooper LT, Fang JC, et al. Recognition and Initial Management of Fulminant Myocarditis: A Scientific Statement From the American Heart Association. *Circulation*. 2020;141(6):e69-e92. doi:10.1161/CIR.0000000000000745
12. Corrado D, Basso C, Thiene G. Sudden cardiac death in young people with apparently normal heart. *Cardiovasc Res*. 2001;50(2):399-408. doi:10.1016/s0008-6363(01)00254-1
13. Fried JA, Ramasubbu K, Bhatt R, et al. The Variety of Cardiovascular Presentations of COVID-19. *Circulation*. 2020;141(23):1930-1936. doi:10.1161/CIRCULATIONAHA.120.047164
14. Ho JS, Sia CH, Chan MY, Lin W, Wong RC. Coronavirus-induced myocarditis: A meta-summary of cases. *Heart Lung*. 2020;49(6):681-685. doi:10.1016/j.hrtlng.2020.08.013
15. Akhmerov A, Marbán E. COVID-19 and the Heart. *Circ Res*. 2020;126(10):1443-1455. doi:10.1161/CIRCRESAHA.120.317055.
16. Oleszak F, Maryniak A, Botti E, et al. Myocarditis Associated With COVID-19. *Am J Med Case Rep*. 2020;8(12):498-502. doi:10.12691/ajmcr-8-12-19
17. Schultz JC, Hilliard AA, Cooper LT Jr, Rihal CS. Diagnosis and treatment of viral myocarditis. *Mayo Clin Proc*. 2009;84(11):1001-1009. doi:10.1016/S0025-6196(11)60670-8
18. Omidi F, Hajikhani B, Kazemi SN, et al. COVID-19 and Cardiomyopathy: A Systematic Review. *Front Cardiovasc Med*. 2021;8:695206. Published 2021 Jun 17. doi:10.3389/fcvm.2021.695206
19. Ardahanlı İ, Akhan O, Aslan R, Çelik M, Akyüz O. A new index in the follow-up of arrhythmia of Coronavirus Disease-2019 (COVID-19) patients receiving Hydroxychloroquine and Azithromycin therapy; index of cardiac electrophysiological balance. *Cumhuriyet Medical Journal*. 2021;43(1):1-7. doi:10.7197/cmj.870158
20. Fan Q, Zhu H, Zhao J, et al. Risk factors for myocardial injury in patients with coronavirus disease 2019 in China [published online ahead of print, 2020 Oct 2]. *ESC Heart Fail*. 2020;7(6):4108-4117. doi:10.1002/ehf2.13022
21. Bière L, Piriou N, Ernande L, Rouzet F, Lairez O. Imaging of myocarditis and inflammatory cardiomyopathies. *Arch Cardiovasc Dis*. 2019;112(10):630-641. doi:10.1016/j.acvd.2019.05.007
22. Ferreira VM, Schulz-Menger J, Holmvang G, et al. Cardiovascular Magnetic Resonance in Nonischemic Myocardial Inflammation: Expert Recommendations. *J Am Coll Cardiol*. 2018;72(24):3158-3176. doi:10.1016/j.jacc.2018.09.072
23. Aretz HT. Myocarditis: the Dallas criteria. *Hum Pathol*. 1987;18(6):619-624. doi:10.1016/s0046-8177(87)80363-5
24. 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;77(3):314-325. doi:10.1016/j.jacc.2020.11.031
25. McDonagh TA, Metra M, Adamo M, et al. 2021 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure [published correction appears in *Eur Heart J*. 2021 Oct 14;:]. *Eur Heart J*. 2021;42(36):3599-3726. doi:10.1093/eurheartj/ehab368
26. Lavalley C, Magnocavallo M, Straito M, et al. Flecainide How and When: A Practical Guide in Supraventricular Arrhythmias. *J Clin Med*. 2021;10(7):1456. Published 2021 Apr 2. doi:10.3390/jcm10071456