Indian J Med Res 152, September 2020, pp 169-171
DOI: 10.4103/ijmr.IJMR_3760_20

Quick Response Code:

Editorial

COVID cardiomyopathy: Is it time to involve the cardiologists?

SARS-CoV-2 (COVID-19) was declared a pandemic by the World Health Organization on March 11, 2020[1]. The number of individuals with confirmed infection has now exceeded 23 million worldwide with over 800,000 deaths attributed to COVID-19 as of August 23, 2020[2]. While many patients may remain entirely asymptomatic, symptomatic individuals typically present with pulmonary complaints that range from minor flu-like disease to severe pneumonia and acute respiratory distress syndrome. Some will ultimately develop multiorgan failure, and cardiac involvement is common as is being highlighted below. While the exact incidence remains unknown, approximately seven per cent of all COVID-19-related deaths are thought be due to myocarditis[3]. There is also evidence that cardiac involvement is associated with worse overall outcomes. In a cohort study from Renmin Hospital of Wuhan University, China, 82 of 416 (19%) consecutive patients hospitalized for COVID-19 infection had cardiac injury as evidenced by elevated serum biomarkers. When compared to the control group, these patients required mechanical ventilation more frequently, had higher risk of complications during their index hospitalization and had an overall increased rate of mortality[4]. In a prospective observational cohort study from Frankfurt, Germany, Puntmann *et al*[5] performed cardiac magnetic resonance imaging (MRI) on 100 patients who recently recovered from COVID-19 infection. They found that 78 patients had cardiac involvement, with 60 having ongoing myocardial inflammation. This was independent of the pre-existing medical conditions, disease severity and overall course of the acute illness[5].

Viral myocarditis is believed to be caused by a combination of direct T cell injury and T lymphocyte-mediated cardiotoxicity[6]. In another cohort study from Germany, the presence of SARS-CoV-2 was examined in myocardial tissue during autopsy from 39 individuals with documented infection. The virus was detected in 24 patients (61.5%), and a viral load above 1000 copies/µg RNA was documented in 16 cases (41%). Interestingly, there was no increase in inflammatory cell infiltrate, but the expression of six pro-inflammatory genes was upregulated in this population[7]. Though the long-term consequences remain unknown at this time due to the novelty of COVID-19, the high incidence of cardiac involvement, including myocarditis, will put patients who recovered from COVID-19 infection at elevated risk for the development of heart failure in the future, as seen with other viral causes of myocarditis.

The SARS-CoV-2 virus uses the angiotensin-converting enzyme 2 (ACE2) receptors to gain access to the cell cytoplasm. ACE2 receptors are expressed on the cell surface in most organs, including the lungs, heart, kidneys, pericytes and the vascular endothelium. Viral invasion of pericytes and vascular endothelium has been shown to initiate localized inflammation, ultimately provoking microvascular dysfunction[8-10]. In addition, the cytokine storm associated with COVID-19 infection (caused by interleukins-6 & 8) may cause platelet activation, neutrophil recruitment and blood hyperviscosity[11]. This cytokine storm, in addition to the direct viral invasion of the myocardium, is responsible for the variable cardiac presentation of COVID-19 infection that may range from minor biomarker elevation to acute cardiogenic shock.

With cases of COVID-19 rising on a daily basis and with recent literature demonstrating worse overall outcomes in patients with cardiac involvement, cardiologists need to play an important role in both the short- and long-term management of these patients. As mentioned previously, approximately about 60-70 per cent of patients infected with the

This editorial is published on the occasion of the World Heart Day - September 29, 2020.

SARS-CoV-2 virus have cardiac involvement or injury[5,7]. Therefore, it is reasonable to perform a baseline, focused clinical screening with routine laboratories and troponin testing in all individuals with documented COVID-19 infection. In the case of positive findings, further evaluation could follow using electrocardiography, natriuretic peptide levels and echocardiogram. These studies may also reveal a clinical picture of stress cardiomyopathy, a clinical presentation that is witnessing an increase in incidence from 1.8 to 7.8 per cent during the pandemic, possibly due to the cytokine storm[12]. Depending on the clinical course, the above studies may be repeated or expanded with coronary angiogram, cardiac MRI or other relevant studies at the discretion of the treating cardiologist. Unfortunately, there is a substantial overlap between the presentation of fulminant giant cell myocarditis and COVID myocarditis. Therefore, endomyocardial biopsy should be considered, especially in patients presenting with cardiogenic shock and high arrhythmia burden. Shock may develop in this group of patients rapidly, and it may be difficult to determine the exact aetiology based on non-invasive evaluation. Swan-Ganz catheter use should be considered in these scenarios as a means to guide clinical decision-making and to titrate vasoactive medications. It will also help monitor pulmonary artery pressures as hypoxia is a profound vasoconstrictor in the lung, and acute right ventricular failure may develop. At our institution, we have successfully cared for several patients requiring veno-arterial extracorporeal membrane oxygenation (ECMO) or veno-venous-ECMO support as a life-saving measure (unpublished observation). Its use in this condition is increasing.

Patients who recovered from COVID-19 disease without any evidence of cardiac involvement may be considered to have Stage A heart failure, defined as population at risk for the development of clinical heart failure. As detailed above, a large proportion of patients will have evidence of cardiac involvement for at least several months after recovery from active COVID-19 infection. At this time, we lack long-term follow up data as to what percentage of this group will develop Stage B-D heart failure. Future studies should shed light on this issue. As such, patients should be educated to report any symptoms that may suggest new onset or worsening heart failure, and clinical symptom screening should be performed during routine healthcare visits. Many institutions have initiated remote monitoring programmes for all patients who tested positive for COVID-19 infection or selectively for those who required hospital admission and management. These are instrumental at early identification of heart failure symptoms and may enable timely treatment initiation. For patients with known Stage C heart failure, remote pulmonary artery pressure monitoring may be considered to promote social distancing and to reduce the frequency of in-person clinic visits.

The SARS-CoV-2 pandemic, 2020, has created a challenging year for patients, clinicians, healthcare systems and the society. Several questions remain, such as how COVID-19 will affect the current heart failure epidemic? Are we ready to face the challenges that may be ahead us? At present, we lack answers to these questions, however we, as cardiologists, have to remain prepared for the years to come.

***Conflicts of Interest*:** None.

Mohammed Chowdhury[1], Valmiki R. Maharaj[2], Gary S. Francis[2,*], Tamas Alexy[2] & Meg Fraser[2]
[1]Advanced Heart Failure Cardiologist, North Central Heart, Sioux Falls, SD & [2]Department of Medicine, Division of Cardiology, University of Minnesota, Minneapolis, MN, USA
[*]*For correspondence*: franc354@umn.edu

Received September 4, 2020

References

1. World Health Organization. *WHO Director-General's opening remarks at the media briefing on COVID-19 - 11 March 2020*. Available from: *https://www.who.int/dg/speeches/detail/who-director-general-s-opening-remarks-at-the-media-briefing-on-covid-19---11-march-2020*, accessed on August 24, 2020.
2. World Health Organization. *Coronavirus disease (COVID-19): Weekly epidemiological update*. Available from: *https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200907-weekly-epi-update-4.pdf?sfvrsn=f5f607ee_2*, accessed on August 24, 2020.
3. Driggin E, Madhavan MV, Bikdeli B, Chuich T, Laracy J, Biondi-Zoccai G, *et al*. Cardiovascular considerations for patients, health care workers, and health systems during the COVID-19 pandemic. *J Am Coll Cardiol* 2020; *75* : 2352-71.
4. Shi S, Qin M, Shen B, Cai Y, Liu T, Yang F, *et al*. Association of cardiac injury with mortality in hospitalized patients with COVID-19 in Wuhan, China. *JAMA Cardiol* 2020; *5* : 802-10.

5. Puntmann VO, Carerj ML, Wieters I, Fahim M, Arendt C, Hoffmann J, *et al*. Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from coronavirus disease 2019 (COVID-19). *JAMA Cardiol* 2020; e203557.
6. Esfandiarei M, McManus BM. Molecular biology and pathogenesis of viral myocarditis. *Annu Rev Pathol* 2008; *3* : 127-55.
7. Lindner D, Fitzek A, Bräuninger H, Aleshcheva G, Edler C, Meissner K, *et al*. Association of cardiac infection with SARS-CoV-2 in confirmed COVID-19 autopsy cases. *JAMA Cardiol* 2020; e203551.
8. Chen L, Li X, Chen M, Feng Y, Xiong C. The ACE2 expression in human heart indicates new potential mechanism of heart injury among patients infected with SARS-CoV-2. *Cardiovasc Res* 2020; *116* : 1097-100.
9. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, *et al*. Endothelial cell infection and endotheliitis in COVID-19. *Lancet* 2020; *395* : 1417-8.
10. Epelman S, Tang WH, Chen SY, Van Lente F, Francis GS, Sen S. Detection of soluble angiotensin-converting enzyme 2 in heart failure: insights into the endogenous counter-regulatory pathway of the renin-angiotensin-aldosterone system. *J Am Coll Cardiol* 2008; *52* : 750-4.
11. Bester J, Pretorius E. Effects of IL-1β, IL-6 and IL-8 on erythrocytes, platelets and clot viscoelasticity. *Sci Rep* 2016; *6* : 32188.
12. Jabri A, Kalra A, Kumar A, Alameh A, Adroja S, Bashir H, *et al*. Incidence of stress cardiomyopathy during the coronavirus disease 2019 pandemic. *JAMA Netw Open* 2020; *3* : e2014780.