

Title: SARS-CoV-2 infection & Cardiology: beware of myocarditis.

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Source of Support

No funding supports.

Conflicts of Interest

All authors declare that there is no conflicts of interests.

Authors contributions

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Keywords

“SARS-COV-2”, “Covid-19”, “Myocarditis”.

Abstract

The emergence of SARS-CoV-2 is a challenge in the actual medical scenario. Besides the classical lung and respiratory disease, patients infected with the virus can present with cardiac injury, and pathogenic mechanisms point to a direct infection of the heart.

Background

SARS-CoV-2 is the virus responsible for coronavirus disease 2019 (COVID-19). The SARS-CoV-2 outbreak initiated in Wuhan, China [1] is a novel kind of coronavirus with similarities when compared to its proteomics with SARS-CoV [2]. Its main way to get access to the cells is via the angiotensin-

converting enzyme 2 (ACE2) [3]. This virus infection's main clinical features are fever (89.1%), cough (72.2%) and fatigue (42.5%). The acute severe respiratory syndrome (ARSD) affects 14.8% of the patients with 96.6% presenting with computer tomography (CT) abnormalities [4].

The cardiovascular system has been in evidence, such as the pandemic progress. Firstly because of the receptor that the virus uses to get access to the cell ACE2 [3] and the two major drugs used in cardiology the inhibitors of the angiotensin-converting-enzyme inhibitors and angiotensin II type 1 receptor blocker and a possible poor prognosis among those with SARS-CoV-2 infection [5, 6], although no evidence of harm or benefit are present in the available data [7].

Secondly, systemic arterial hypertension, which is a prevalent cardiovascular condition [8], was shown to carry a 2.36 odds ratio, in a meta-analysis involving 46248 patients, when comparing the severe patients with the no severe group [9] and cardiovascular disease a 3.42 odds ratio in the same study [9], making cardiovascular conditions the major risk factor for severe disease study until now.

In addition, as a risk factors, cardiovascular complications can appear in the progression of COVID-19 disease. These manifestations are in the form of cardiac injury (13% of patients) [10], and elevated troponin levels - 8-12% of patients with COVID-19 have values above the 99th percentile, indicating that cardiac injury may play a role a role in disease progression [11]. In this paper, we will discuss myocarditis as a possible causation of this cardiac injury and the mechanisms involved in cardiac damage caused by SARS-COV-2 infection.

Myocarditis Definition

Myocarditis is classified on histological and clinical basis. If the patient shows signs of heart injury with no better explanation, signs of on the electrocardiograph suggestive of myocardial injury or abnormal heart function measured by echocardiogram or MRI and is asymptomatic, this can be subclinical myocarditis. In addition to these findings, the patient may also have a clinical syndrome characteristic of myocarditis (acute heart failure, syncope, chest pain or myocardial pericarditis).

Therefore, an acute myocarditis case is likely. For a definitive diagnosis, an endomyocardial biopsy is required [12].

Pathophysiology

Viral etiology is a well-defined cause of acute myocarditis [12, 13]. Commonly coxsackie B viruses, influenza and parvovirus B-19 with the heart been secondary affected after the virus gain access via respiratory or gastrointestinal tract [13], the damage occurs via inflammatory response and direct induce by the virus [13], a discussed mechanism for the SARS-CoV-2 infection [14].

The SARS-CoV epidemic in 2003 brought evidence that this virus gains access to human hearts and causes cardiac damage [15]. *Oudit et al.* showed that 35% of hearts in autopsy study on SARS-COV outbreak, in Canada, were positive for the virus RNA [16]. In this same study the authors showed that the heart infection happens in ACE 2 dependent manner in a murine model [16]. In patients who needed mechanical ventilation, subclinical impairments have also been found on the echocardiography of patients with SARS-CoV [17].

Looking at the pandemic scenario today, recent studies support the hypothesis that the heart is as a potential target to the SARS-CoV-2. *Zou and colleagues* showed that 7.5% of myocardial cells have ACE 2 expression and thus being susceptible to SARS-COV-2 infection [18]. Another study also shows that the heart expresses more ACE 2 than the lungs at the site of the primary infection, even though it has a low expression in cardiomyocytes. This points to an important expression in pericytes that could play a role in myocardial injury and be a target to SARS-COV-2 in the heart by disturbing the microcirculation [19].

Cardiac involvement SARS-CoV-2

Cardiac involvement has the potential to play an important role in SARS-CoV-2 infection. In addition to previous SARS-VOC data showing the heart as a possible target, clinical findings of cardiac injury in infected patients [10,11] also show the relationship of SARS-VOC-2 to having one of its targets in

the heart [15- 19]. New evidence shows that elevated troponin levels after day 4 of hospitalization are associated with non-surviving patients [20] and cardiogenic shock can play a role in up to 33% of deaths [21]. *Chen et al.* also presented indirect evidence cardiac involvement with 27.5% and 10% of SARS-CoV-2 patients presenting with elevated N-terminal pro-B-type natriuretic peptide and troponin respectively [22].

Recently, a case of cardiac involvement without the pulmonary component was described on a 53 -year-old woman with no previous history of cardiac disease, presenting with two-day severe fatigue denying chest pain, dyspnea and other symptoms, telling just a cough and fever a week early. She had elevated cardiac enzymes, electrocardiograph suggesting ischemia, and regional wall abnormalities on the echocardiogram, with no evidence of acute coronary disease in her angiography. She received the diagnosis of acute SARS-COV-2 myocarditis [14].

In addition, other cases had fulminant myocarditis in patients with SARS-COV-2 infection. The first case presented a 63 years old male with no history of cardiovascular disease, who showed up elevated troponin (11.37g/L), sinus tachycardia and low left ventricular ejection fraction (LVEF) on the third day of evolution. After treatment the ejection fraction recovered to 68% [23].

The second one presented with fulminant myopericarditis associated with cardiac tamponade in a 47-year-old female. Other symptoms were shortness of breath, chest pain, dry cough, hypotension and tachycardia, serum troponin values also increased, but the echocardiogram showed normal ventricular function with pericardial effusion [24].

[14]

Cardiac nuclear magnetic resonance (MRI) plays an important role in the management of COVID & cardiology's cases. Therefore, it is possible to search correctly for the diagnostic criteria of myocarditis, as in the case described by Inciardi et al. with myocardial edema and late gadolinium improvement [14]. It is preferable to value the clinical diagnosis of these patients since their critical condition is usually a limiting factor for endocardial biopsy [14,22].

Treatment is usually supportive. That is, it includes ventilation, hemodynamic support and the standard approach of the intensive care unit, given that there is insufficient evidence for any other treatment, including antiretroviral drugs or corticosteroids [14,22].

Conclusion

In conclusion, cardiac injury is common [10, 11] in SARS-COV-2 infection. These can present as fulminant myocarditis [21, 22], or a focal myocarditis [14] and this diagnosis should be remembered during this pandemic even without lung disease. Although more research is needed, cardiac injuries are a marker in patients who don't survive the disease [19] and can be caused by direct infection to the heart. Finally, patients infected or suspected for SARS-COV-2 infection with troponin elevation and/or symptoms appoint to myocarditis or cardiac dysfunction should gain more attention and be submitted for a cardiology consultation.

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Acknowledgements**Financial Support**

No financial support.

Material Support

No material support.

Conflict of interest

All authors declare that there are no conflicts of interest.