

Coronary syndromes associated with COVID-19: A literature review



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ABSTRACT

In January 2020, the World Health Organization (WHO) declared a state of Public Health Emergency of International Concern. The rapid population illness and the increase in the number of deaths from unknown causes generated a social panic. In view of this, it was understood that the broad spectrum of symptoms related to the respiratory infection of SARS-CoV-2 has a direct impact on the cardiovascular and immune systems and can cause conditions both in the acute phase of the infection and in a later phase. This study was developed from a meticulous and integrated review of the literature in recent publications, including articles in scientific journals, gathered in search engines dated between the period 2019 and 2021. Pooled data from the Pan American Health Organization, the Ministry of Health, and the World Health Organization were also used. Thus, it aims to highlight the various implications of COVID on the cardiovascular system. It should be remembered that the symptoms of the coronavirus are quite nonspecific and varied, and may include: headache, dry cough, hyperthermia, sore throat, anosmia, hypogeusia, dysgeusia, rash and skin irritation, myalgia, diarrhea, dyspnea and other respiratory discomforts. In view of the immune system and other morbidities, the evolution of the condition can lead to a worse prognosis. In the compilation of reviewed articles, it was observed that myocardial injury caused by SARS-CoV-2 is related to ACE-2, since the virus uses these ACE receptors to enter the cell, and, even understanding this mechanism of action, the use of enzyme blockers that act directly on this factor as a possible form of treatment is still a distant reality. There is no scientific evidence to support the use of these medications in suppressing ACE activity to reduce the viral effect on the body.

Keywords: COVID-19, Cardiology, Myocarditis, Health.



1 INTRODUCTION

In December 2019, the new coronavirus infection (COVID-19) had its first outbreak in the city of Wuhan in China, however, it was only in January 2020 that the World Health Organization (WHO) declared a state of Public Health Emergency of International Concern (PHEIC). This corresponds to a risky situation in which a coordinated international response is needed.

In March 2020, the disease caused by the mutation of the coronavirus was classified as a pandemic by the WHO, this fact is not related to the severity of the disease, but rather to its geographical distribution by recognizing that it is present in several places and countries. The lack of knowledge of the disease and its rapid spread resulted in a turbulent moment for the medical society and health authorities. In addition, the rapid population illness and the increase in the number of deaths from unknown causes generated a social panic.

In view of this, it was understood that the broad spectrum of symptoms related to the respiratory infection of SARS-CoV-2 has a direct impact on the cardiovascular and immune systems, causing conditions both in the acute phase of infection and in a later phase. It is also worth noting that COVID-19 causes organic damage that lasts weeks to months after the patient recovers from the acute phase, defined as post-covid syndromes. (GUIMARÃES et al., 2020)

2 OBJECTIVES AND METHODS

This chapter was developed from a meticulous and integrated review of the literature and recent publications comprising articles and scientific journals from search engines such as *Scielo*, *Pubmed* and *Google Scholar* dated between 2019 and 2021. The following descriptors were used: covid-19; myocarditis; endothelial injury; post-covid syndrome; Brazil. Articles and studies that did not include a robust analysis methodology were excluded. Pooled data from the Pan American Health Organization, the Ministry of Health, and the World Health Organization were also used. Thus, it aims to highlight the various implications of COVID on the cardiovascular system.

3 DISCUSSION AND RESULTS

Covid-19 is classified as a viral acute respiratory syndrome, which presents a broad clinical picture subdivided into mild, moderate and severe. It is known that it has an accelerated infection rate and low mortality, as shown by the following data for Brazil. In April 2020, 49,500 new cases and 3,310 deaths were recorded (FERRARI, 2020). According to the Brazilian Ministry of Health, the latest data from April 2021 record 67,636 new cases and 2,929 deaths. In November, the number of new cases registered in Brazil was 5,638 and 126 deaths, which shows a significant reduction in both new cases and deaths. This significant reduction is likely due, in large part, to health teams' better understanding and management of the coronavirus and the "mass vaccination" that began in January



2020 in the country. In addition, social isolation was one of many prevention measures used to reduce the exponential growth of the contagion curve for the control of a silent disease.

The impacts of the disease and the partial confinement, necessary to contain the virus, have increased the reports of uncontrolled chronic diseases such as diabetes and hypertension, which leads to a negative implication in personal well-being, since the confinement contributed to an unregulated diet and to the decrease in physical activity, a fact that favors the increase of practices that are harmful to health. (BRAZILIAN SOCIETY OF CARDIOLOGY, 2020).

However, although there are still uncertainties regarding the dynamics of the pandemic, effective strategies to control the disease, and even in relation to the appropriate antiviral treatment, the data show that the world is on an appropriate path of discoveries and innovations regarding SARS-CoV-2. Today, knowledge of the disease allows us to divide it into three main phases: (1) infection, (2) pulmonary phase, and (3) hyperinflammation. In the first, viral infiltration and replication occur; It then progresses to the pulmonary phase in which the patient presents clinical and radiological changes. Finally, taking into account the host's immune system, the disease progresses with a generalized and exacerbated inflammatory response that secretes patients into mild to severe clinical conditions.

The symptomatology of the coronavirus is quite non-specific and varied. It may present with headache, dry cough, hyperthermia, sore throat, anosmia, hypogeusia, dysgeusia, rash and skin irritation, myalgia, diarrhea, dyspnea, and other respiratory discomforts. Depending on the immune system and other morbidities, the evolution of the condition can lead to a worse prognosis and, consequently, to hospitalizations in intensive care units (ICU) specialized in the treatment of SARS-CoV-2. In June 2021, an article developed by ARANDA et al. was published that correlated previous sedentary lifestyle with increased mortality in patients hospitalized for Covid, regardless of other risk factors. (COLOMBO et al., 2021)

It should be noted that the coronary involvement of SARS-CoV-2 is sometimes insidious, being visible only in alterations in exams such as electrocardiogram, echocardiogram, echostress, ergospirometry, and stress test performed long after the disease has already established itself (XIONG et al., 2021). It is worth noting that at the beginning of the pandemic in Wuhan, of the first 41 patients diagnosed with Covid-19, five had myocardial injury. Recent data, released in research carried out during the pandemic, also showed that the virus has several important cardiac manifestations in the short and long term. These range from myocardial injury, arrhythmia, myocarditis to Takotsubo Syndrome (TS) to shock. Some patients still demonstrate late clinical signs and symptoms such as tachycardia, postural tachycardia orthostatic syndrome, fatigue, nausea, headache, chest pain, dyspnea at rest or during exertion, palpitation or irregular pulse, feeling faint, and sleep disturbance (JOHANSSON et al., 2021).



According to Liu et al., the manifestations are multifactorial, resulting from an imbalance between metabolic demand and cardiac reserve. Cardiac stress, generated by direct SARS-CoV-2 infection, is connected to low saturation and respiratory stress, leading to a worsening of the condition. In view of this, hypoxemia arises as a consequence of these factors and in association with acute coronary syndrome (NETO et al., 2020). In addition, systemic inflammation, thromboembolic disorders of viral infection, and pre-existing risk factors lead to an exacerbated response, in addition to the elevation of biological markers – D-dimer, procalcitonin, C-reactive protein, interleukin-6, ferritin, and troponin – (LIU; BLET; SMYTH; LI, 2020).

From this perspective, it has been noted that hospitalized patients with moderate and severe COVID and those who have a negative prognosis have a prolonged prothrombin time, D-dimer elevation, and greater activation of thromboplastin time. Likewise, clinically, there are findings of thrombotic intravascular dissemination, that is, we can say that COVID-19 may be associated with venous and arterial thrombosis. In addition, more recent studies of the coronavirus also report a disorder of the fibrinolytic and coagulation system (ATRI et al., 2020).

The sustained systemic inflammatory response is probably one of the most curious mechanisms of cardiac injury present in severe COVID patients (COSTA, 2020). For example, 16.7% of 138 patients hospitalized with Covid-19 developed a nonspecific arrhythmia. When compared to patients admitted to the intensive care unit, this number was even higher (ATRI et al, 2020). Patients with severe symptoms, including acute myocardial injury, are more prone to a greater number of complications. This hypothesis corroborates the cases of patients treated in the ICU and had significantly higher blood pressure levels and higher levels of biological markers than those who were not treated (ZHENG, 2020).

Several studies have shown myocarditis to be an important manifestation of Covid-19. A study conducted in Germany on patients who had recently recovered from the coronavirus, with the aid of magnetic resonance imaging, revealed cardiac involvement in 78% and myocardial inflammation in 60% of the participants (DEL RIO; COLLINS; MALANI, 2020). Accordingly, another study, conducted in New York, in a total of 2,736 patients, 36% of them had evidence of myocardial injury. The latter are significantly more likely to be associated with a high risk of in-hospital mortality (GIUSTINO et al., 2020).

There is particular concern around the acute phase of viral myocarditis, as there are risks of it exacerbating or prolonging the disease and serving as a trigger for serious arrhythmias. Cardiac complications, including ventricular heart failure, arrhythmias, cardiogenic shock, and even death have been described in up to a quarter of patients hospitalized for COVID-19 (PHELAN et al., 2020).



Myocarditis is defined as an inflammation of the heart muscle with necrosis of the myocytes. Predominantly insidious, usually asymptomatic, it is an important cause of sudden death that occurs mainly in adult patients and young athletes under 40 years of age. According to Figueiredo et al (2005):

"*Post-mortem* studies suggest that myocarditis is a major cause of sudden and unexpected death, approximately 20% of cases, in adults under 40 years of age and young athletes, although it is more frequent in children. Other studies have identified myocardial inflammation in 1% to 9% of autopsies."

Myocardial inflammation is divided into three phases. The acute phase lasts a few days; The subacute one, from weeks to months, while chronicity of the inflammatory process can result in a dilated cardiomyopathy. Its diagnosis is based on cardiac enzymes, a 12-lead electrocardiogram and cardiac images. Troponin and CK-MB are the cardiac enzymes that may be increased. Myocarditis, diffuse or focal, may extend to the pericardium, and this involvement often results in heart failure, arrhythmia, and sudden death. The treatment of myocarditis is non-specific, basically consisting of the management and support of symptomatic patients. As an example, analgesia is performed in patients with chest pain, which may or may not be associated with the use of corticosteroids. Treatment of the underlying disease is also necessary in order to prevent the progression of clinical worsening. (DRIGGIN et al., 2020)

Acute myocardial injury from SARS-CoV-2 is related to angiotensin-converting enzyme-2 (ACE-2). Its function is to convert angiotensin II into angiotensin-(1-7,) acting in the opposite way to ACE. Both, in harmony, are responsible for the control and balancing of the renin-angiotensin-aldosterone system (RAAS), acting on blood pressure control. The medical importance of this enzyme lies in the fact that ACE-2 is present in several tissues including lung, heart and kidney, in addition to being involved in the pathogenesis of several cardiovascular disorders. It has been discovered that the ACE-2 receptor is a gateway for SARS-CoV-2 to enter the body through the S glycoprotein, contained in the virus that competes with angiotensin-2 for its enzyme receptor to enter cells, disrupting the cascade (AKHMEROV; MARBAN; 2020).

In order to reduce hospital admissions related to the typical symptoms of Covid-19, early diagnosis is necessary. However, the assertive realization of this diagnosis is difficult due to the similarity of the symptoms with other viral and autoimmune diseases. The post-covid period generates future impairments and new comorbidities, becoming a challenge for the medical community. As an example, it is interesting to mention that the *National Health Commission of China* (NHC) published an article reporting that some patients only seek medical help after cardiovascular symptoms appear. These symptoms included palpitations and chest pain to the detriment of respiratory and systemic symptoms such as fever and cough, thus leading to a late diagnosis of COVID-19 (ZHENG; MA; ZHANG; XIE, 2020).



4 FINAL THOUGHTS

SARS-CoV-2 infection is a highly transmissible disease, due to its virulence, which, despite its low mortality, has generated a series of chronic organic diseases in infected individuals. Classified as an acute viral syndrome, it still lacks studies due to its high mutation capacity to obtain consistent data regarding its prevention and treatment. However, recent concerns are not limited only to the immediate consequences of covid-19, but also to the medium and long-term sequelae that characterize post-covid syndromes. Cardiac involvement proved to be an important object of study, especially in patients with other comorbidities in post-covid conditions. This group includes elderly patients, as previously described. Some studies propose that the progression of myocardial injury is intrinsically related to the patient's age and cardiovascular risks. Among the various cardiac lesions, myocarditis resulting from SARS-CoV-2 infection was found to be linked to the systemic increase in pro-inflammatory factors. (MARTINS et al., 2020)

Complications and mortality from the coronavirus increase in patients admitted to the ICU with pathologies associated with previous cardiovascular diseases. According to the data identified, approximately 50% of the hospitalized cases had heart disease. Based on the above, it is verified that patients with heart disease have a poor prognosis in SARS-CoV-2 infection. In addition, it is noteworthy that insidious cardiac involvement in both healthy and elderly young patients leads to complications of post-covid syndromes. These have clinical outcomes of myocarditis, arrhythmias, ventricular dysfunction, heart failure, and others. Apparently, depending on environmental, socioeconomic, genetic, immunological, and personal factors, any patient with COVID-19 may have coronary involvement.

In this compilation of reviewed articles, it was observed that myocardial injury caused by SARS-CoV-2 is related to ACE-2, since the virus uses these ACE receptors to enter the cell, even understanding this mechanism of action, the use of enzyme blockers that act directly on this factor as a possible form of treatment is still a distant reality. There is no scientific evidence to support the use of these medications in suppressing ACE activity in order to reduce the viral effect on the body.

Finally, it is understood that the deleterious effects of COVID-19 on the body can be numerous and need special attention on several fronts. Such as research aimed at understanding and treating post-covid syndromes, a fact that generates physical, financial and social losses. At the moment, prevention is the main way to control and combat this generated pandemic.



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