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Review Article

# Cardiovascular Damage of Covid 19 in Adults

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## Abstract

Throughout history, disease outbreaks have complicated mankind, many times devastating civilizations, consistent with the above. In December 2019, an outbreak of pneumonia by a designated novel coronavirus was detected in the city of Wuhan. as SARS-CoV-2, the causal agent of the disease known as Covid 19. The few initial reports limited the involvement of the lower respiratory tract. With the progress of the disease and the accumulation of scientific evidence, the fundamental role played by cardiovascular involvement in the development and prognosis of the infection has been demonstrated. Cardiac injury can be direct or indirect, including acute myocardial damage, myocarditis, acute myocardial infarction, heart failure, arrhythmias, and venous thromboembolic events. This monograph reviews cardiovascular damage from COVID-19 in adults.

**Keywords:** SARS-CoV-2; Covid 19; Cardiovascular Damage

## Introduction

Currently the whole world is experiencing the desolation and devastation of a deadly virus, such a statement is reflected today through the great evolution that has presented the SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2) identified in 2019, in Wuhan, China, as a new variety of coronavirus responsible for the COVID-19 pandemic (Coronavirus Disease 2019) [1,2]. The main manifestation of this disease is respiratory involvement, which in its clinical spectrum can range from asymptomatic patients with mild respiratory symptoms, to adult respiratory distress syndrome (ARDS), with potentially fatal outcomes [3,4].

During the initial stages of the pandemic and given the little scientific evidence available, it was thought that this coronavirus caused symptoms limited to the respiratory system [5]. With the publication of reports on large series of the disease in different countries, it was observed that cardiovascular involvement has a fundamental role in the development and prognosis of infection [6,7].

Although at the beginning of the appearance of Covid-19 it was believed that the damage caused by the virus clearly concerned the elderly who were the individuals who had the most cardiovascular risk factors [8], it is important to know that the direct myocardial involvement that occurs in the course of severe infection in healthy individuals, promotes acute cardiovascular damage [9]. Its expression through de novo cardiac complications, such as acute myocardial injury, myocarditis and arrhythmias, show the need to study the pathophysiological mechanisms related to cardiovascular damage in SARS-CoV-2 (COVID-19) infection [10].

### History of coronavirus infection.

Throughout history, disease outbreaks have complicated humanity, many times, devastating civilizations [11]. Since 1930, numerous coronaviruses have been discovered as the etiology of respiratory, gastrointestinal, hepatic and neurological diseases in animals [12].

In 1965, Dorothy Hamre, a researcher at the University of Chicago, discovered a new type of virus, now known as 229E. This

turned out to be a coronavirus, the first to infect humans and be responsible for the cold or common cold [13].

Already in the twenty-first century, three of these viruses have been responsible for major outbreaks of pneumonia of varied mortality [14]. In 2002, SARS-CoV was identified in southern China as the cause of an outbreak of severe acute respiratory syndrome (SARS) and spread rapidly to 28 other countries [15]. More than 8,000 people were infected in July 2003, and 774 died. In 2012, MERS-CoV was identified as the cause of Middle East respiratory syndrome (MERS), which began in Saudi Arabia in 2012 and affected 2500 people [16]. A virus much less contagious than SARS, but that caused a higher mortality, 858 deaths.

### SAR-COV-2 infection

In December 2019, the first cases of an unknown pneumonia that did not respond to traditional treatments began to be reported in Wuhan, a city in China's Hubei province [17]. On January 30, 2020, the World Health Organization declared a global state of emergency and on March 11 of the same year, it declared a state of pandemic due to the high number of infected people worldwide [18]. The pathogen, which came to be identified as SARS-CoV-2, is a novel coronavirus that is now known to be responsible for the COVID-19 disease. This new virus belongs to the same family of SARS-coronavirus (SARS-CoV) and MERS-coronavirus (MERS-CoV) [19,20]. This contagious variable virus has a high reproduction number, so the number of cases has increased exponentially.

It is transmitted through Flügger droplets when they penetrate the airway through inhalation or when they are left on contaminated surfaces or objects that, then through the hands, can come into contact with the oral, nasal and ocular mucous membranes [21].

### Epidemiology

Infection to date (October 2021) had affected more than 215 countries, with more than 77,228,903 million cases, nearly 44,300,000 recovered patients and more than 1,718,470 deaths [22].

In the Americas region, 934,355 infections have been reported, with 49,605 deaths associated with COVID-19, with a case fatality rate of 5.31%. The most affected country in terms of the number of cases is the United States, with about 18,090,260 patients diagnosed and 320,180 deaths [23]. The first Latin American country affected was Brazil, which reported the first case on February 26, the first death was recorded in Argentina on March 7. Brazil is today the Latin American country with the highest number of cases, with about 7,318,821 and 188,259 deaths [24].

Worldwide, cardiovascular disorders have been observed in patients sick with COVID-19, a situation that is becoming increasingly remarkable [25]; which makes it necessary to have existing knowledge regarding the relationship between this disease and the effects it produces on the cardiovascular system [26]. The aim of this review is to describe the relationship between COVID-19 and cardiovascular disease.

## Material and Method

An exhaustive literature review was carried out in the period from January to October 2021. The review covered wide-ranging journals from Web of Science, national and international journals, mostly from studies conducted in China. The Pubmed, MEDLINE and Scielo databases were consulted using the terms "coronavirus", "COVID-19", "cardiovascular system", "angiotensin-converting enzyme II"; for English and Spanish, being the search strategy: COVID-19 OR coronavirus AND cardiovascular system AND angiotensin II converting enzyme. A total of 42 articles were consulted, 25 being selected, which were specifically adjusted to the topic in question, excluding those with possible biases in their methods and written in languages different from those mentioned above. A large percentage of the bibliography used is from the last 5 years and its validity has been verified.

### Sar-Cov2 and cardiovascular damage

SARS-CoV-2 is a single-stranded (single-stranded) RNA virus of the genus beta-coronavirus, family Coronaviridae with envelope. The 2/3 of the genetic material translates to 16 non-structural proteins and 1/3 corresponds to 4 structural proteins: protein S, which has an S1 subunit which intervenes in the affinity of the virus for the angiotensin-converting enzyme 2 (ACE2) [27].

In addition to the interaction of the virus with the ACE2 receptor in the pulmonary alveolar cells, the main scenario of contagion and infection, a high incidence of cardiovascular involvement has been recorded in these patients, determining that the heart and vascular endothelium show a high expression of this enzyme [28].

The semiogenesis of COVID-19 is not defined, [29] it is assumed that sars-CoV and SARS-CoV-2 viruses could cause damage to myocardiocytes by equal mechanisms due to the similarity of their

genomes [30,31]. Both penetrate human cells by binding to viral receptors mediated by endocytosis, in particular the angiotensin-converting enzyme receptor 2 (ACE2) and affect the signaling pathways that are related to this enzyme. Thus SARS-CoV-2 injures the lung, heart, kidney, nervous, and cardiac tissues (cardiomyocytes, cardiac fibroblasts, and coronary endothelium cells) where these receptors are expressed.

Several mechanisms have been proposed for the explanation of cardiovascular involvement in COVID-19 disease, including the following

- **Myocardial inflammation:** SARS-CoV2 causes an acute systemic inflammatory response by penetrating host cells by binding the spike protein to ACE2, with the release of pro-inflammatory cytokines, which causes a macrophagic activation syndrome and myocardial inflammation [32,33]. The presence of viral RNA in myocardial tissue and the expression of ACE2 receptors in this tissue have been documented, so an intrinsic cardioselective potential of the virus is suggested [34]. An autopsy of the deceased showed interstitial infiltration of mononuclear predominance with inflammation of the myocardium, increased vascular permeability and pulmonary edema [35].

- **Endothelial damage:** The systemic inflammatory response produces endothelial inflammation. The involvement of the coronary circulation causes instability or rupture of atheromatous plaques and generates thrombogenicity and vasospasm, which can cause an acute myocardial infarction (AMI) type 1. Microvascular injury along with cardiac dysfunction decreases tissue perfusion, and microangiopathic damage may result in coagulation disorders [32,36].

- Imbalance between the supply and demand of oxygen by the myocardium: the systemic inflammatory response produces Acute Respiratory Dysfunction Syndrome and secondary hypoxia increases the oxygen demand of the myocardium, increases oxidative stress, generates intracellular acidosis and mitochondrial damage, which increases the risk of myocardial ischemia and can cause a type 2 AMI, heart failure (HF) and arrhythmias [37].

- Influence of adverse effects of pharmacological therapies: Chloroquine and hydroxychloroquine (HCQ) have arrhythmogenic effect: they prolong the depolarization and refractory period of Purkinje fibers, which disrupts cardiac conduction; both increase lysosomal pH and induce atrial and ventricular arrhythmias, fascicular and atrioventricular block; HCQ can induce QT prolongation, and lead to polymorphic ventricular tachycardia and sudden cardiac death [38-40].

- Electrolyte imbalance: systemic involvement can lead to hypokalemia, which favors the genesis of arrhythmias [38].

Its effect on cardiovascular homeostasis through RAAS (Renin-Angiotensin System) generates directly by this mechanism, myocardial injury. Munster., *et al*. [41]. in their article: A new emerging coronavirus in China; argued that myocardial damage was observed in 5 of 41 patients diagnosed in Wuhan in a retrospective study, in which an affinity of entry of the virus through this enzyme was detected in these patients and in turn caused respective cardiovascular lesions.

Munster., *et al*. [41] further added that the observed high incidence of cardiovascular symptoms appears to be related to systemic inflammatory response, the effect of ACE2 dysregulation, as well as lung dysfunction itself and hypoxia. All this would result in acute damage to myocardial cells.

COVID-19 can lead to severe infection with significant implications in patients with heart disease. Patients with cardiovascular disease have an increased risk of severe symptoms and death [31]. In addition, SARS-CoV-2 infection has been associated with multiple direct and indirect complications in the cardiovascular system. In a research conducted by Barnes., *et al.* [42], it was proposed that cardiovascular complications directly related to COVID-19, reported so far in case series or anecdotally include: myocarditis, myocardial injury, acute coronary syndrome, congestive heart failure, cardiogenic shock and arrhythmias of varying complexity. It is reasonable to expect significant cardiovascular complications related to COVID-19 to occur in severe symptomatic patients due to the high inflammatory response associated with this disease [43]. Among the mechanisms involved are: direct cell injury mediated by ACE2, hypoxia (intracellular acidosis and mitochondrial damage), inflammation with procoagulant activity (thrombosis), microvascular damage (spasm, increased permeability, perfusion defects) and cytokine storm [35,37].

Damage to heart cells caused by SARS-CoV-2 infection defines myocardial injury [44]. The frequency of this complication varies, influenced largely by its definition and by the type and severity of hospitalized patients. It is usually associated with non-ischemic etiology, such as acute inflammatory cardiomyopathy or takotsubo

syndrome, and ischemic cardiomyopathy with infarction [6,9,10] types 1 and 2, already described above. These patients with myocardial injury usually have electrocardiographic alterations of the ST segment and the T wave, and disorders of the regional motility of the walls of the left ventricle and cardiac function, identified from the Echocardiogram.

The mechanism invoked in patients with myocardial damage due to COVID-19 is the result of the imbalance between oxygen supply and demand to the myocardium [45]. The increase in myocardial oxygen consumption, favored by severe sepsis, tachyarrhythmias, arterial hypertension, hypoxia, coronary spasm, right claudication and secondary biventricular, requires significant increases in coronary flow (demand) [25,26]. This increase in flow (contribution) cannot be supplemented especially in patients with coronary heart disease where there is already a compromise of the flow due to fixed coronary stenosis, aggravated by infectious, inflammatory, neurogenic, humoral mechanisms, endothelial dysfunction and dysregulation and vascular hyperreactivity [28,32].

### Natural history of the COVID-19 patient from the cardiovascular perspective

Factors of poor prognosis are age over 60 years, male sex, history of high blood pressure, diabetes mellitus, ischemic heart disease, cardiomyopathy, HF, complex congenital heart disease, cerebrovascular disease, chronic renal failure, chronic obstructive pulmonary disease of cardiotoxicity by oncological treatment. The risk is also increased in patients who present with acute cardiac, renal or hepatic dysfunction, altered consciousness, persistent fever, coagulopathy, leukocytosis/leukopenia, lymphopenia, pancytopenia and the elevation of markers of myocardial damage, among others [28,43].

It is assumed that as in other coranovirus infections, the systemic and procoagulant inflammatory response persists after resolution of SARS-CoV-2 infection and is related to an increased risk of CV disease [31,44] since myocardial inflammation may generate myocardial fibrosis and be a substrate for cardiac arrhythmias [46].

Although this is not a systematic review, it does not use rigorous methods such as meta-analysis for the selection of articles, which could be a limitation; This study constitutes a descriptive review that provides the reader with an update on the relationship between COVID-19 and cardiovascular diseases, which is constantly evolving in the midst of the current situation. It has great utility and can be of interest to all those interested in the subject.

## Conclusions

The scientific evidence that is appearing at the same time as the evolution of the COVID-19 pandemic, as a result of multicenter studies and epidemiological series worldwide, allows us to better understand the systemic effects of the disease beyond the initial lung damage and its extension to the cardiovascular system, which determines the prognosis and survival of patients.

COVID-19 is closely related to cardiovascular diseases, which corresponds to the pathophysiology of the disease and the body's response to it.

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