REVIEW ARTICLE
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The Impact of COVID-19 on the Cardiovascular System

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SUMMARY

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) induces coronavirus-19 disease (COVID-19), has affected many people in Brazil and worldwide. This disease predominantly affects the organs of the respiratory system, but it also damages the brain, liver, kidneys and especially the heart. In the heart, scientific evidence shows that this virus can damage the coronary arteries, generating microvascular dysfunction, favoring acute myocardial infarction. Furthermore, with the increased expression of pro-inflammatory cytokines, it can lead to myocarditis and cardiac fibrosis, inducing changes in the electrical conduction system of the heart, generating cardiac arrhythmias. All these factors mentioned are protagonists in promoting the increase in the mortality outcome. This outcome may be even higher if the individuals are elderly, or if they have other diseases such as type 2 diabetes mellitus or hypertension, because they may already have cardiomyopathy. In this context, this review focused on the impact that COVID-19 can have on the heart and cardiovascular system and the association of this impact with aging, type 2 diabetes mellitus, cardiac arrhythmias and arterial hypertension

KEYWORDS: Coronavirus. Infection. Betacoronavirus. Cardiovascular System.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an infectious disease that was first identified at the end of 2019 in the city of Wuhan, China. The causative agent is severe acute respiratory syndrome (SARS-CoV-2), a single-stranded RNA virus[1,2] with different replication kinetics, depending on the type of host cell[3]. According to the data from the World Health Organization (WHO)[4], until May 14, 2021, the number of confirmed positive cases for COVID-19 were 160,813,869 and confirmed deaths were 3,339,002 due to COVID-19.

Clinically, the main symptoms are fever, cough, myalgia or fatigue, sputum, and dyspnea. In a meta-analysis of 10 studies involving 1,994 patients, a higher prevalence among men (60%) and a mortality rate of 7% were observed, with 43% of deaths affecting the patients aged over 60 years, or those with cancer, comorbidities, or other infections[5].

Different organ systems, such as heart, lung, liver, brain, and kidneys, are severely affected by the COVID-19 virus. This virus binds to the angiotensin-converting enzyme 2 (ACE2) receptor, causing damage to these organs, and specifically in the coronary arteries, pericytes have high ACE2 expression. These cells are damaged inducing endothelial and microvascular dysfunction[6]. Among cardiovascular complications, infection can lead to myocardial damage with elevated troponin and electrocardiographic abnormalities, as well as outcomes such as cardiogenic shock, arrhythmias, myocarditis, pericarditis, and death[7] (Figure 1).

In view of the possible cardiovascular complications evidenced in COVID-19 patients, this study performed a literature review with

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the aim to investigate the COVID-19 complications related to the myocardium. We also tried to associate the ratio of age and mortality, the data over acute myocardial infarction (AMI), diabetes mellitus, cardiac arrhythmias, and hypertension related to COVID-19.

STUDY VARIABLES

For this review, acute myocardial infarction (AMI) was defined as myocardial injury, with necrosis, through an increase in cardiac troponin values, in a clinical context consistent with cardiac ischemia[7]. As defined by the American Diabetes Association, diabetes is a metabolic disorder characterized by persistent hyperglycemia, resulting from deficiency in the production of insulin or in its action[8], or in both mechanisms[9]. Chronic and acute heart failure was defined as a complex clinical syndrome, which occurs when the heart is unable to meet the tissue demand for blood supply due to the incompetence of its pump activity, or when it does so only under high filling pressures[10]. From definition of JNC 8 guidelines for hypertension, systolic blood pressure levels >130 mmHg or diastolic blood pressure levels >80 mmHg was considered[11].

RELATIONSHIP BETWEEN AGE AND MORTALITY

Lian et al.[12] divided their study population into over and above 60 years old and less than 60 years old. It was demonstrated that there was a higher discharge rate for patients in the younger group compared with those in the older group (44.6 vs. 22.8%, p<0.001), with no deaths recorded. Age above 60 years was associated with the symptoms of severity and intensive care unit (ICU) admission (9.56 vs. 1.38%, p<0.001). Deng et al.[13] pointed out that the mean age of the group of deaths was higher than that of the group of survivors (69 [range, 62–74] years vs. 40 [33–57] years, Z=9,738, p<0.001), which corroborates with the findings of He et al.[14] Also, Wang et al.[15] compared patients in relation to the need for admission to the ICU and showed that this variable was associated with a higher mean age (66 years [IQR, 57–78] vs. 51 years [IQR, 37–62]; p<0.001), as well as other associated comorbidities such as hypertension, diabetes, and cardiovascular disease.

AMI, TROPONIN, AND BNP

Huang et al.[16] found a significant relationship between COVID-19 and the elevation of ultrasensitive troponin >28 pg/mL (99th percentile) in 12% of patients, and this was even higher for those admitted to ICU (31%). Wang et al.[15] pointed out that 7.2% of the patients evolved with AMI, of which 80% required admission to the ICU, totaling 22% of the population. A higher mean troponin value was found for patients admitted to ICU compared with those without ICU admissions (11.0 [5.6–26.4] vs. 5.1 [2.1–9.8]). Shi et al.[17] described

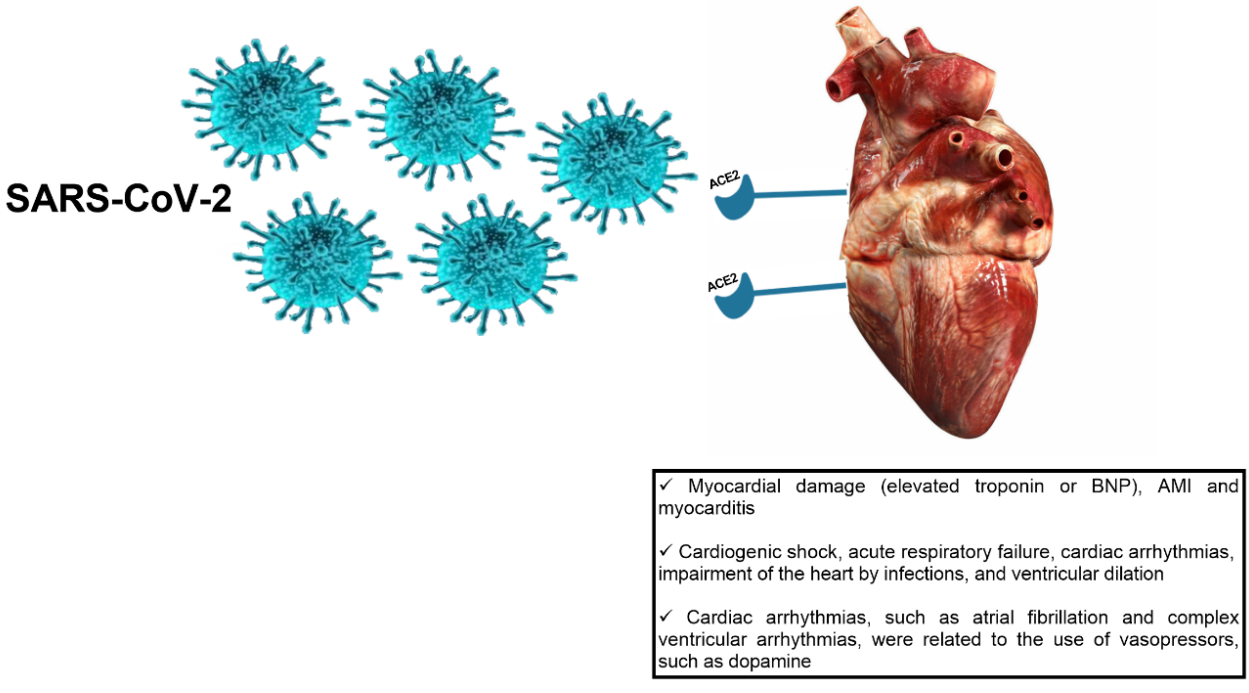

Figure 1. Impact of SARS-COV-2 and COVID-19 on cardiac structure and function.

the clinical characteristics of 82 patients (19.7%) who developed AMI. These patients were older with an average age of 74 years [34–95] vs. 60 years [21–90] (p<0.001), and more hypertensive 49 [59.8] vs. 78 [23.4%] (p<0.001). The mean value for ultrasensitive troponin in these patients was 0.19 (0.08–1.12). Deng et al.[13] showed that AMI was a more frequent complication among nonsurvivors than survivors (59.6 vs. 0.8%, c2=93,222, p<0.001). Chen et al.[18] compared the patients who underwent ultrasensitive troponin testing (only 203) and reported the relationship between increased troponin and a higher number of deaths (68/94 [72%] vs. 15/109 [14%]), in addition to the higher values of this marker (concentration) among patients who died (40.8 pg/mL) in relation to those who recovered (3.3 pg/mL). In this line, he also described the serum brain natriuretic peptide (BNP) levels and their relationship with mortality and cardiovascular diseases, finding more patients with high BNP among the group who died (68/80 [85] vs. 17/93 [18%]), and also higher BNP values (800.0 pg/mL vs. 72.0 pg/mL).

He et al.[14] found that 44.4% of the patients had myocardial injury and separated their population from this condition. Patients with myocardial injury had significantly higher BNP (p<0.01) and higher mortality rate (75 vs. 26.7%, p=0.001). Guo et al.[19] reported that there was a statistical significance in the elevation of troponin T level in patients with diabetes mellitus when compared with patients with normal troponin T level (30.8 vs. 8.9%, p<0.001) hospitalized with COVID-19 disease. Zhou et al.[20] found elevated serum troponin in 17% of the study cohort, and that the proportion of patients with high troponin was higher in nonsurvivors vs. survivors (46 vs. 1%). AMI was observed in 59% of patients who died, but in only 1% of survivors. Zhou et al.[21] reported an association between elevated serum troponin levels and disease severity. In the very severe group (respiratory failure and the need for mechanical ventilation, shock, or other organ dysfunction), 100% had elevated troponin, while in the severe group (respiratory rate >30; O_2 saturation <93%; PaO_2/FiO_2 <300 mmHg), this was 3.84%. Chen et al.[22] summarized the patients as critical and noncritical and observed that 62.5% of the critical patients had high serum troponin and 79.2% had elevated BNP.

Patients with respiratory symptoms resulting from viral infections often have pulmonary tomographic changes such as ground-glass interstitial infiltrates, a finding that is similar to pulmonary congestion in congestive heart failure. This may present diagnostic difficulties in these affected patients[15,23,24]. We observed that the elevation of cardiac enzymes, such as troponin, is associated with the clinical status and electrocardiographic abnormalities[25-28].

DIABETES MELLITUS

The prevalence of diabetes ranged from 7.2[12] to 24.1%[14] with an overall rate of 12.5%. Lian et al.[12] demonstrated that a significant difference in prevalence between older and younger groups (5 vs. 17.65%). Deng et al.[13] found that the mortality rate was similar between older and younger groups (15.6 vs. 7.8%, p=0.066). A proinflammatory state is usually noted in all diabetic patients who did not present COVID-19 infection symptoms.

The SARS-COV-19 pandemic in 2020–2021 has placed severe burdens on different health systems worldwide. In addition to high viral infectivity, this virus generates a systemic inflammatory process[16], due to the high replication kinetics and damage to host cells, increasing the expression of proinflammatory cytokines, such as interleukin-6 (IL-6), interleukin-1-beta (IL-1β), interferon-gamma (IFNγ), and monocyte chemoattractant protein 1 (MCP-1), inducing the state of hyperinflammation or cytokine storm[29-34], which can promote complications from cardiogenic shock leading to mortality, and acute respiratory failure with extensive pneumonic conditions and impairment of the heart by infections, ventricular dilation, and cardiac arrhythmias[19,22,26,35,36].

CARDIAC ARRHYTHMIAS

Cardiac arrhythmias were not reported frequently in the studies observed, having been reported only in two studies. Wang et al.[15] reported that 23% of the observed patients had arrhythmias, of which 69.5% required intensive care, corresponding to 44.4% of the total ICU stay (p<0.001). Guo et al.[19] observed that malignant arrhythmias (ventricular tachycardia and ventricular fibrillation) were more frequent in patients with previous cardiovascular disease and elevated troponin T (9 [17.3] vs. 2 [1.5%], p<0.001).

HYPERTENSION

Liu et al.[37] described the prevalence of comorbidities of 20%, but only 9.5% of patients were hypertensive with an average age of 57 years [20–83]; however, the overall mortality rate was elevated at 11.7%. Lian et al.[12] demonstrated that older adults had more comorbidities compared with young people (55.15 vs. 21.93%, p<0.001), e.g., hypertension (38.97 vs. 11.20%, p< 0.001). Deng et al.[13] found that a higher number of deaths were associated with previous comorbidities (72.5 vs. 41.5%, c2=22,105, p<0.001), e.g., hypertension (36.7 vs. 15.5%, c2=14,184, p<0.001). On the other hand, despite finding a high prevalence of hypertension in the population studied (44.4%), He et al.[14] did not observe a statistical significance

between survivors with hypertension and nonsurvivors (46.2 vs. 42.9%). As an unfavorable clinical outcome, the variable "ICU stay," Huang et al.[16] found no association between hypertension vs. ICU stay (15 vs. 14%). However, hypertension was documented in 15% of the sample with an average age of 49 years. Thus, arterial hypertension is an important and very common risk factor, affecting 30% of the adult population[10]. Hypertension was a common comorbidity with a prevalence between 17 and 40%, and was a significant risk factor of mortality. Together with age, other cardiovascular risk factors such as diabetes mellitus (16%) and arterial hypertension contribute to greater disease severity, ICU admission, and mortality[15,23,38-40].

CONCLUSIONS

There is a high prevalence of cardiovascular involvement in patients with COVID-19 with conditions such as myocardial damage (elevated troponin or BNP), AMI, and myocarditis. This subset of patients was at a significantly higher risk of mortality. Cardiac arrhythmias, such as atrial fibrillation and complex ventricular arrhythmias, were related to the use of vasopressors, such as dopamine. COVID-19 often affects various organ systems including the liver, lungs, kidneys, brain, and heart. The mortality due to COVID-19 infection is higher for the elderly people (>60 years) and in patients with cardiovascular comorbidities, elevated troponin, and cardiac arrhythmias.

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