EDITORIAL

Cause or Consequence? What is the Relationship between Cardiac Injury and COVID-19 Severity?

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Editorial referring to the article: Predictive Value of Myocardial injury in Patients with COVID-19 Admitted to a Quaternary Hospital in the City of Rio de Janeiro

“I know nothing and my heart aches”

Fernando Pessoa, The Book of Disquiet

In most patients, coronavirus disease-2019 (COVID-19) causes minor respiratory symptoms or even no symptoms. SARS-CoV-2 infection can also cause extrapulmonary manifestations and complications. COVID-19 is more severe and fatal among patients with pre-existing cardiovascular risk factors or diseases.¹ Increases in cardiac troponin (cTn) are indicative of myocardial injury and frequently found in patients with COVID-19.² The Chinese Center for Disease Control and Prevention published a survey demonstrating that among patients diagnosed with COVID-19, 13% had hypertension, 5% had diabetes mellitus, and 4% had a history of cardiovascular disease. However, in this same cohort, among patients who had not survived, 40% had hypertension, 20% had diabetes, and 22% had pre-existing cardiovascular disease.³ Patients with cardiovascular disease had the highest case fatality rate (10.5%).

In this issue of the International Journal of Cardiovascular Sciences, Rocha et al.,⁴ studied 192 patients admitted with COVID-19 in a quaternary care cardiac hospital in Rio de Janeiro, Brazil. Mortality rate was 28%. Multivariate analysis demonstrated that elevated cTnI levels (OR=9.504; 95% CI=1.281–70.528; P=0.028) upon admission and the need for mechanical ventilation

during hospitalization (OR=46.691; 95% CI=2.360–923.706; P=0.012) were independent predictors of death during hospitalization.⁴ The main limitations of the study are a sample from a single Brazilian metropolitan region and a short follow-up period. However, these limitations do not invalidate the main message of the study: the measurement of cardiac troponin at hospital admission may be useful for identification of high-risk patients infected by SARS-CoV-2.

Cardiac troponins are not specific markers of ischemic injury of the heart. The Fourth Universal Definition of Myocardial Infarction defines myocardial injury (acute or chronic) as cTn concentrations >99th percentile upper reference limit (URL). While dynamic changes in cardiac troponins characterize acute injury, patients without these changes have chronic injury.⁵ Patients with COVID-19 have several conditions that may be associated with myocardial injury such as myocarditis, stress cardiomyopathy, acute heart failure, pulmonary embolism, critical illness, and sepsis.² Garcia de Guadiana-Romualdo et al.,⁶ demonstrated that elevated troponin levels were common in patients with COVID-19. These authors found abnormal levels of cTn in 26.9% of the patients and in 30% when sex-specific cut-offs were used to detect myocardial injury.⁶ Some factors increase the risk of abnormal cTn levels, including older age and the type of troponin measured (troponin T is associated with higher levels). Nascimento et al.,⁷ studied 61 patients admitted to intensive care unit with COVID-19 in a Brazilian hospital and found a high incidence of myocardial infarction in patients with severe COVID-19, with impact on in-hospital mortality.⁷

COVID-19 can damage the cardiovascular system in many ways. A myocardial oxygen supply-demand

Keywords

Cardiovascular Diseases/complications; COVID-19/complications; SARS-CoV-2; Risk Factors; Hypertension; Diabetes Mellitus; Troponin I; Hospitalization; Mortality.

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mismatch (type 2 myocardial infarction) can result from an imbalance between high metabolic demand and low cardiac reserve, systemic inflammation and thrombogenesis, in addition to direct cardiac damage from the virus.⁸ Cardiovascular complications occur mainly in patients with cardiovascular risk factors (advanced age, hypertension and diabetes) or preexisting cardiovascular diseases. There are few reports of COVID-19 patients who presented with acute ST-segment elevation myocardial infarction (STEMI) that the final diagnosis was myocarditis. This diagnosis is supported by elevated cardiac troponins, moderate decrease of left ventricular ejection fraction, and absence of flow-limiting coronary artery disease by invasive coronary angiography.⁹ Autopsy findings support the concept that the pathogenesis of severe COVID-19 involves a virus-induced injury of multiple organs, including heart and lungs, coupled with the consequences of a procoagulant state with coagulopathy, although overt myocarditis is very rare.¹⁰ Together, these data suggest that in most cases, myocardial injury detected by increased cardiac troponins are not causes of severe COVID-19, but rather consequences/effects of high risk COVID-19.

Type I myocardial infarction is not commonly associated with COVID-19 and some studies have shown even a decreased incidence of hospitalization for acute myocardial infarction during the Covid-19 pandemic. Solomon et al.,¹¹ reported a decrease by up to 48% in weekly rates of hospitalization for acute myocardial infarction during the COVID-19 period.¹¹ De Filippo et al.,¹² found similar reductions in 15 hospitals in northern Italy. This decrease may also be associated with the

anxiety and fear of catching COVID-19 in the emergency department, commonly seen among patients during the initial months of the pandemic. Consequently, parallel to this decrease in myocardial infarction hospitalizations, a transient increase in the incidence of out-of-hospital cardiac arrest (AOHCA) was observed when compared with the equivalent time period in previous years with no pandemic.¹³ The same trend was demonstrated in a Brazilian study by Guimarães et al.,¹⁴ who found a proportional increase of 33% of home deaths in March 2020, which is when the World Health Organization declared the COVID-19 pandemic.¹⁴ The increase of AOHCA can be linked to COVID-19 infections and to the potential increase of patients with acute cardiac diseases that did not seek emergency care.

We are entering a new phase of the COVID-19 pandemic. The United Kingdom's Medicines and Healthcare products Regulatory Agency has issued temporary authorization of the antiviral drug molnupiravir for the treatment of mild to moderate COVID-19 in adults with at least one risk factor for severe illness.¹⁵ The approval of effective oral drugs, combined with the use of effective vaccines against COVID-19, can potentially change the scenario and contribute to a consistent decrease in the number of cases and the adverse effects of SARS-COV-2 infections.^{16,17} However, we must remember that there is a long way to go to let our guard down. Science needs to be protected and valued; now more than ever.

Sources of Funding

Dr. Claudio Tinoco Mesquita receives funding from CNPq and FAPERJ.

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