

## CASE REPORT

## The Association between Covid-19 and ST Elevation Myocardial Infarction: Variable Clinical Presentations on a Case Report Series

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### Introduction

The current global pandemic caused by the new coronavirus (COVID-19) already reaches 185 countries with approximately 3 million infected people and more than 200 thousand deaths.<sup>1,2</sup> With continental dimensions and an elevated socioeconomic disparity, Brazil, by the beginning of May, presents with increasing infection rates and mortality close to 8%. The numbers may be higher considering the lack of adequate testing of the population and healthcare professionals.<sup>3</sup>

According to the World Health Organization (WHO), cardiovascular diseases represent the leading cause of deaths around the world.<sup>1</sup> Recent reports confirmed that patients with cardiovascular comorbidities are at a higher risk to develop the most severe form of the COVID-19.<sup>4-6</sup> The association between these two pathologies can lead to high morbidity and mortality rates and has been the object of continuous efforts by the medical community. In this sense the management of Acute Coronary Syndrome (ACS) has undergone changes in both diagnosis and treatment since the beginning of the pandemic.<sup>7-10</sup> Another aggravating factor regarding the approach of ACS during this period is the multiple clinical

presentations and differential diagnosis associated with COVID-19, such as myopericarditis, pulmonary embolism and arrhythmia.<sup>4-6</sup>

We report a series of three cases of ST-elevation myocardial infarction (STEMI) that represent the impact of COVID-19 in the management of ACS and the main protocol adaptations in the largest private hospital group in Brazil (Rede D'OR São Luiz). This report was approved by the responsible Ethics Committee and the Informed Consent Form was not required.

### Case 1

We report the case of a 71-year-old male with systemic arterial hypertension (in use of angiotensin II receptor blocker), insulin dependent diabetes mellitus and dyslipidemia referred to the cardiovascular emergency unit due to oppressive chest pain initiated in the previous 24 hours, which worsened within the next 2 hours. He denied flu-like symptoms and reported fear of going to a hospital due to the risk of contamination by SARS-CoV-2.

At admission, vital signs were stable and physical examination revealed no significant changes. The electrocardiogram (ECG) showed ST-Elevation at inferior leads and ST depression in V2-V4 (Figure 1).

According to the institutional protocol, the patient was treated with Aspirin 300 mg, Ticagrelor 180 mg, Atorvastatin 80 mg and was immediately sent to the Cardiac Catheterization Laboratory (CCL). A total obstruction in the proximal segment of the right coronary artery (RCA) associated with a large amount

### Keywords

Coronavirus; COVID-19; Pandemics; ST Elevation Myocardial Infarction; Morbidity and Mortality; Acute Coronary Syndrome; Diabetes Mellitus; Hypertension; Chest Pain; Severe Acute Respiratory Syndrome.

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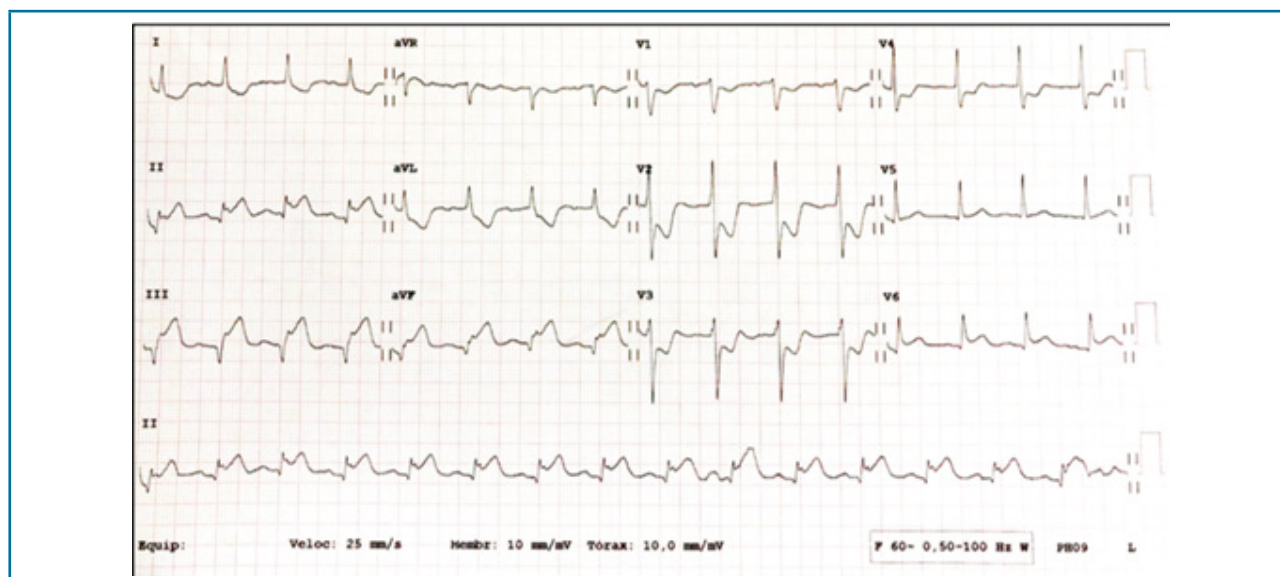


Figure 1 – EKG with ST elevation in II, III, aVF and ST depression in V2,V3, V4.

of thrombus was found and a primary percutaneous intervention (PCI) with 2 drug-eluting stents (DES) was performed. There was also a severe lesion at the proximal segment of the left anterior descending artery (LAD), which was not treated in the index procedure. The treatment of the LAD, as routinely carried out in multivessel disease patients with STEMI, was successfully performed within 48 hours with one DES. Later on that day, the patient had 2 episodes of fever without any respiratory symptoms, which were initially attributed to post-infarction stress. In the next morning, due to persistence of the fever and considering the pandemic scenario, a nasopharyngeal swab was collected, which was positive for SARS-CoV-2. Computed tomography (CT) of the chest revealed infectious focus and ground-glass opacities at the right lung. The patient was transferred from the Coronary Unit to an isolated intensive care unit dedicated to COVID-19 care. At that moment, antibiotics (Azithromycin included) were started in combination with Hydroxychloroquine (HCQ), but the fever persisted until the twelfth day of hospitalization, when there was a significant worsening of the respiratory condition, with hypoxemia and need of mechanical ventilation.

Laboratory tests revealed a leukocytosis of 19.390/mm<sup>3</sup>, a D-dimer of 7.348 ng/dl new troponin-I elevation (1.85 ng/ml). Transthoracic echocardiography (TTE) did not reveal any worsening of left ventricular function.

A new chest CT showed increased consolidation area, at this point bilaterally, with approximately 50% of the parenchyma involved (Figure 2). The patient had an unfavorable evolution, which led to renal failure and refractory hypoxemia, despite the mechanical ventilation, evolving to death 14 days after hospital admission.

## Case 2

A 69-year-old man with a previous history of hypertension and no coronary artery events in the past presented to the emergency room (ER) with fever, cough and fatigue in the previous week. His symptoms worsened within the next 24 hours, with onset of dyspnea and fatigue. He was lucid, with tachydyspnea and denied chest pain. Physical examination revealed blood pressure of 200 x 110 mmHg, a heart rate of 80 bpm and oxygen saturation of 78%, with no fever. Cardiac and pulmonary auscultation showed an S3 gallop and rales. Arterial gas analysis revealed a PH 7.47, oxygen partial pressure of 66%, a carbon dioxide partial pressure of 30mmHg and lactate level of 18.8 mg/dL. Since the patient had respiratory failure and a flu-like syndrome in times of COVID-19 pandemic, orotracheal intubation and invasive ventilation were needed. Low-dose vasopressor was given after a blood-pressure drop following sedation. Only after clinical stabilization had been achieved, a 12-lead ECG was performed, which showed anterior ST elevation,

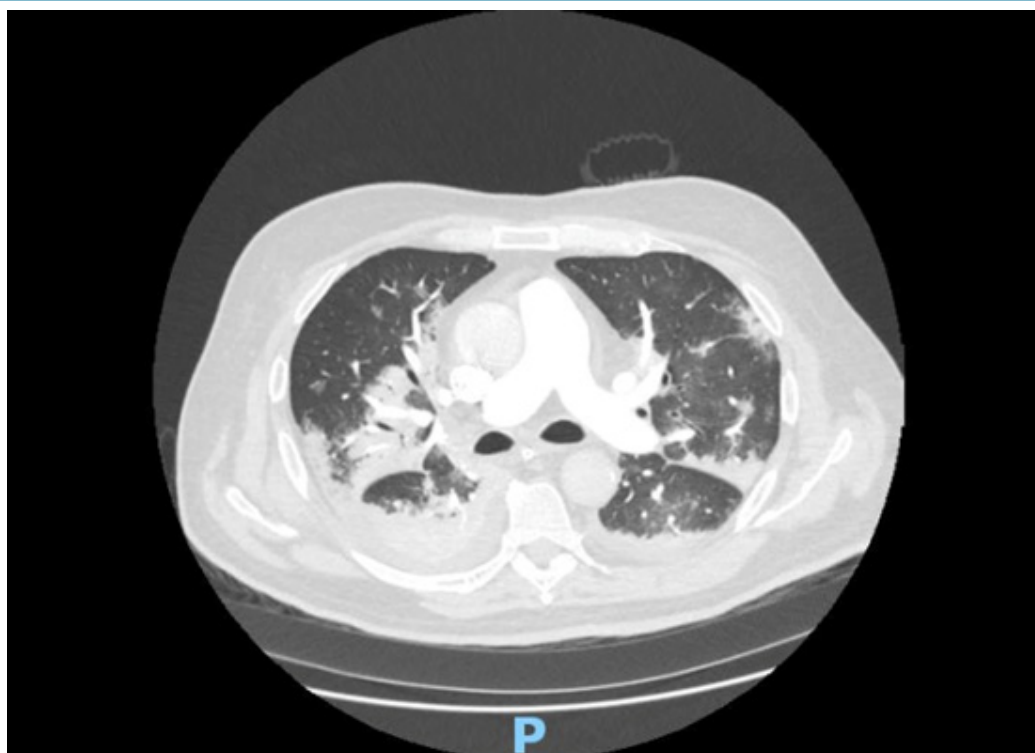


Figure 2 – Chest Computed Tomography with bilateral involvement.

Q-wave in anteroseptal leads, suggestive of a subacute transmural myocardial infarction. The chest x-ray revealed no cardiac enlargement with interstitial and alveolar edema. TTE showed normal left ventricular dimensions despite apical akinesis, with an estimated LV ejection fraction of 44%. There was no evidence of heart valve disease. In face of all these findings suggestive of an AMI combined with a flu-like syndrome, the patient was referred to CCL. The angiography revealed a thrombotic occlusion of the mid portion of the LAD artery. The patient underwent a 2 drug-eluting stent PCI in the LAD artery, with no-reflow phenomena, and was successfully treated with intracoronary adenosine. Door-to-reperfusion time was prolonged (162 min). After coronary treatment, the patient was sent to ICU hemodynamically stable, with an oxygen saturation of 99% and a FiO<sub>2</sub> of 80%. His laboratory tests showed elevated troponin, lymphopenia and a normal renal function. A nasopharyngeal swab (PCR) test confirmed SARS-Cov-2 infection and a chest CT showed findings of pulmonary edema, pleural effusion and interstitial ground-glass infiltrate pattern (Figure 3). He had good clinical improvement, with discharge 16 days after admission.

### Case 3

We present the case of a 42-year-old female without any comorbidities and onset of flu-like symptoms in the previous 7 days. She was admitted to the ER with weakness, cough and shortness of breath. She rapidly evolved with respiratory insufficiency and was submitted to orotracheal intubation and mechanical ventilation. Her initial D-dimer was 1706ng/ml and she had patterns of viral pneumonia on chest CT. Treatment with Hydroxychloroquine and Azithromycin was initiated; a nasopharyngeal swab was collected, which was positive for SARS-CoV-2. On the fourth day, the patient presented with hemodynamic instability, D-dimer elevated to 83.390 ng/ml and a troponin I level of 34.42 ng/dl. TTE revealed anterior wall hypokinesia and ECG showed anterior ST elevation. She was referred to CCL. Angiography did not reveal obstructive coronary artery disease and injection into the left ventricle showed a pattern of Takotsubo cardiomyopathy (Figure 4). Despite drug optimization and use of mechanical support, the patient had refractory shock and died within the next hours.

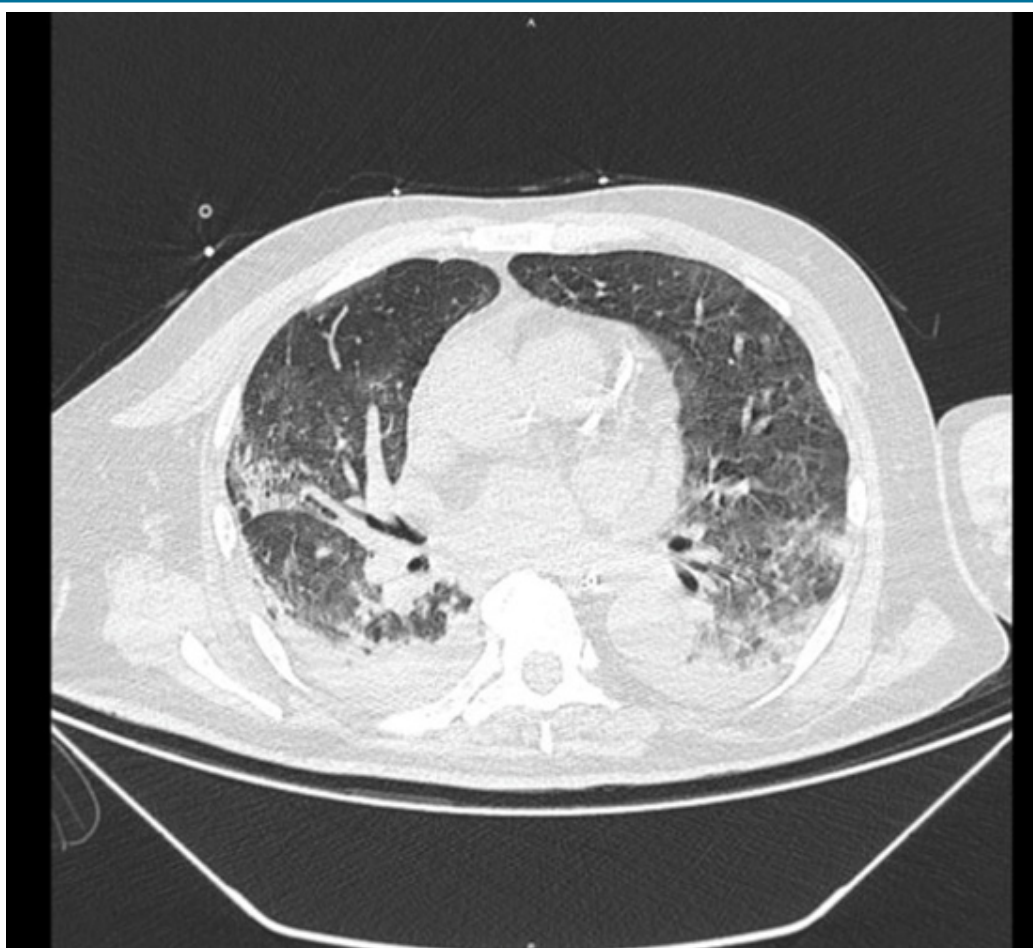


Figure 3 – Chest Computed Tomography with bilateral interstitial ground/glass infiltrate.

## Discussion

Case 1 refers to an elderly patient with STEMI treated with the usual and recommended management of this clinical presentation. Despite no flu-like symptoms at admission and **denial** of contact with people who tested positive or are suspected to have Covid-19, the patient developed pneumonia caused by SARS-CoV-2 with a fatal endpoint. The wide incubation period (4-14 days) does not allow us to determine whether contamination occurred prior to admission or during hospital stay, but the presence of fever from the first days (<72 hours) suggests community infection.

Zhou et al.<sup>4</sup> reported the clinical worsening that occurs in the second week after the onset of symptoms in advanced age and among severe comorbidity subgroups. Such clinical deterioration is caused not only by pulmonary parenchyma injury but also by

thromboembolic phenomena. There is a positive correlation between elevated fibrinogen and D-dimer levels and in-hospital death in COVID-19 patients, which emphasizes the characteristic of a prothrombotic state<sup>11</sup> and may have contributed to the unfavorable evolution of the reported patient.

Another important issue to be discussed is the complete revascularization strategy in multivessel patients with STEMI, especially at the moment of a pandemic. The institution current practice is based on recent data published in the literature,<sup>12</sup> with complete revascularization performed during the same hospital stay, usually 48-72 hours after the index procedure. There were two other possibilities in this scenario: 1) complete revascularization in the index procedure, aimed at shortening hospital length of stay and exposure to SARS-CoV-2, but with a higher contrast load; 2) to treat the culprit lesion and postpone the second procedure



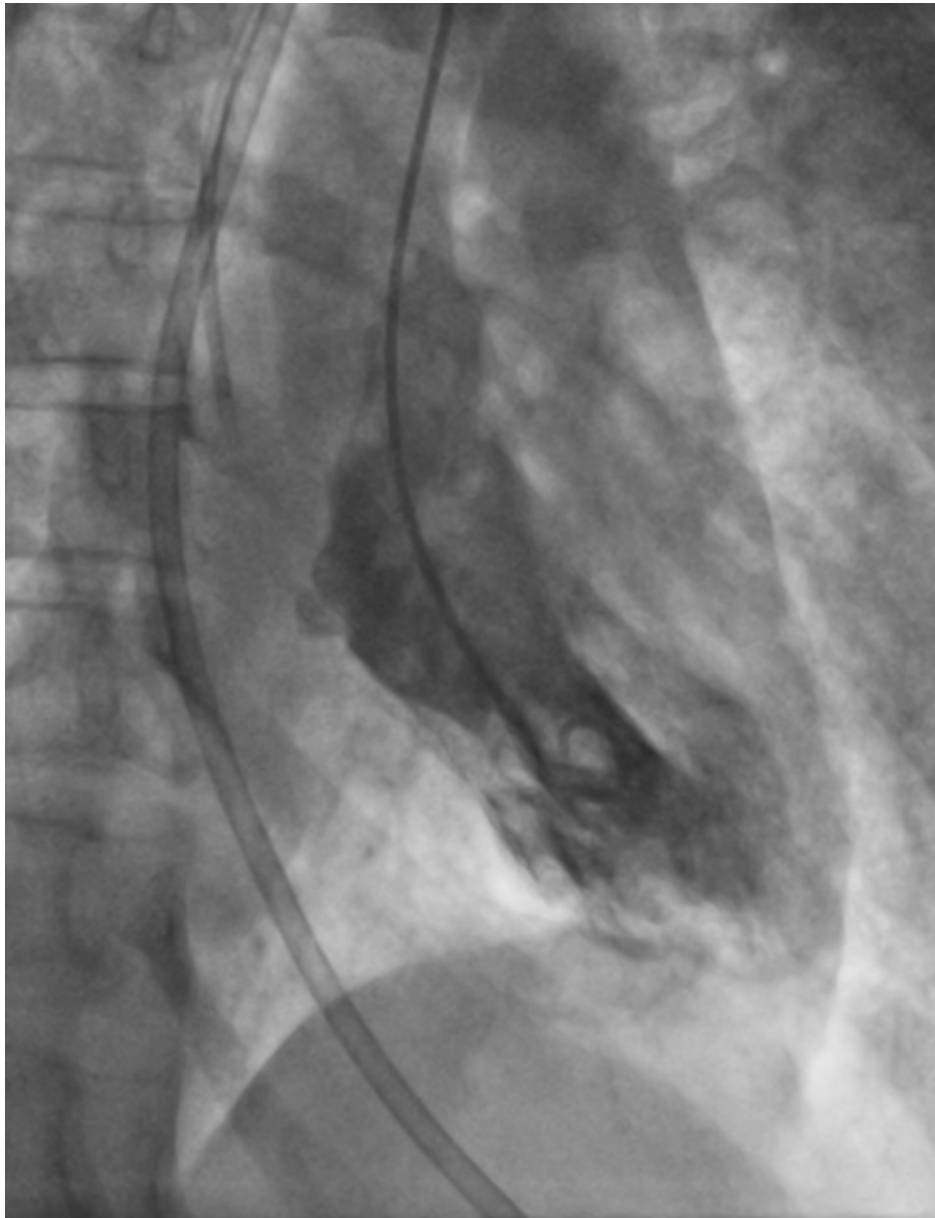


Figure 4 – Left ventriculography with akynesia of the apical portions of the left ventricle – Takotsubo Syndrome pattern.

to a second elective procedure; on the other hand, this specific patient with a severe lesion in the proximal LAD would be exposed to a higher risk for ischemic events. Considering this completely new situation, with a highly spread infectious disease and with individual experience-based evidence, it is difficult to determine which would be the best approach in this case.

Finally, it is important to emphasize the adequate use of personal protective equipment (PPE) by healthcare professionals. During both procedures performed at the CCL, the patient was not suspected of COVID-19.

Still, all the staff was fully equipped with PPE. Based on the experience of European centers,<sup>8,9,13</sup> the institution took several precautions and a new service flow chart was validated and has been applied since the reports of the first cases in Brazil. This new protocol suggests close communication between the multidisciplinary cardiology team. In addition, all cases referred to the CCL are considered suspected of infection by SARS-CoV-2, even in the absence of flu-like symptoms. Thus, all professionals in the unit are fully equipped. So far, no healthcare professional was quarantined.

The second case refers to a patient with AMI, probably triggered by a flu-like syndrome, in the context of COVID-19 pandemic. Not only can viral infections trigger cardiac events, they can also decompensate cardiac status. The known mechanisms involved are vasoconstriction, endothelial inflammation, platelet dysfunction and thrombogenicity. An increased systemic inflammatory status can raise the incidence of arrhythmias and myocarditis, destabilizing coronary plaques and leading to coronary events. In this context, there is a higher incidence of coronary events during infections.<sup>14,15</sup> This case showed an AMI with atypical clinical manifestations during a COVID-19 infection. The non-specific case of fever and myalgia, evolving after a few days into dyspnea, is typically described in severe presentations of COVID-19. Even though the patient's admission interview was brief, since he presented with respiratory failure, the absence of chest pain delayed essential specific cardiac procedures. Although the ECG was not performed immediately, as recommended, it was used to guide the treatment. The need for a differential diagnosis with an adrenergic cardiomyopathy (Takotsubo Syndrome)<sup>16</sup> made coronary angiography essential for defining the diagnosis, since Takotsubo cardiomyopathy can mimic AMI and is associated with COVID-19. As indicated by institutional protocols during pandemic, confirmed or suspected cases should be treated after all precautions and safe procedures have been taken, during transportation and inside the CCL, sometimes leading to prolonged reperfusion. Efforts have to be made to reduce reperfusion times in ST-elevation AMI during the COVID-19 pandemic.<sup>9</sup>

Case 3 reports the unfavorable outcome of a patient with a typical flu-like presentation and COVID-19 confirmation that may have triggered a cardiovascular manifestation. The association with a cardiovascular disease contributed to clinical worsening. Despite early invasive measures, such as orotracheal intubation and administration of antiretrovirals, antibiotics and anticoagulants, the clinical presentation of STEMI posed a major challenge to the medical team. The differential diagnoses were myopericarditis, acute myocardial infarction, stress myocarditis and vasospasm. Even though this was a young patient, with no cardiovascular risk, it was not possible to rule out an AMI and, in this context, the indication of a TTE before the angiography was fundamental for the diagnosis of a stress cardiomyopathy. This decision, considering

the significant alterations in the ECG, would not be the same outside the COVID-19 pandemic. This case also reinforces the exacerbated inflammatory and thrombotic reactions caused by the association between SARS-CoV-2 and cardiovascular complications. D-dimer elevation over 80.000 and interleukin 100 times over the normal values are clear parameters of this alteration that can lead to thrombotic events with AMI and/or inflammatory presentations, such as myocarditis, which hinders the diagnostic elucidation of cases and promotes changes in diagnosis and treatment protocols.

## Conclusion

COVID-19 is a global pandemic that in association with cardiovascular disease can lead to high morbidity and mortality rates. SARS-CoV-2 infection can trigger decompensation of coronary-artery plaques, leading to STEMI. Clinical presentation, ECG changes and elevated cardiac biomarkers can mimic AMI, but without obstructive coronary artery disease. Patients with COVID-19 and STEMI may require a long period of hospital stay, demanding multidisciplinary efforts to overcome critical clinical conditions.

## Learning objectives:

- 1 - Association between SARS-CoV-2 and STEMI can lead to high morbidity and mortality rates.
- 2 - COVID-19 can mimic AMI in clinical presentation and complementary exams in the absence of CAD.
- 3 - The use of personal protective equipment (PPE) by healthcare professionals is crucial to avoid system collapse.
- 4 - Cardiovascular disease clinical presentation in patients with COVID-19 is variable.

## Author Contributions

Conception and design of the research: Esteves V, deLuca F, Zukowski CN, Feldman A. Acquisition of data: Arruda G, Camiletti A, Bandeira B. Critical revision of the manuscript for intellectual content: Souza OF.

## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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There were no external funding sources for this study.

## Study Association

This study is not associated with any thesis or dissertation work.

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of the *Instituto D'Or de Pesquisa e Ensino* under the protocol number CAAE: 31478820.0.0000.5249. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

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