

**ROUND 1**  
**REVIEWER: #1**

Scientific Quality: Grade D (Fair)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Major revision

Specific Comments to Authors: Dear author, The article represents the clinical case with a focus on extensive right coronary artery thrombosis in a COVID-19 patient. The article is written with the acceptable English-speaking adduction of the arguments. The article is sufficiently novel and very interesting to warrant publication. All the key elements are presented and described clearly. The most discussable options in the article are:

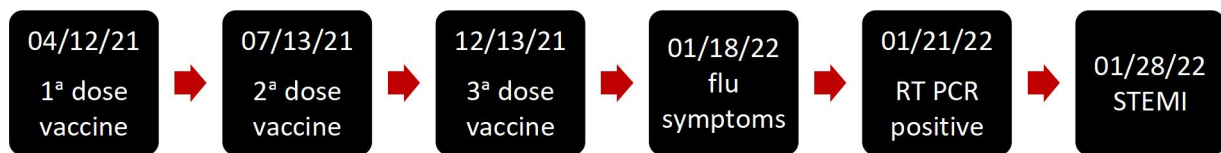
1) Please correct all your multiple grammar errors and typos.

**Thank you for pointing this out. We have provided corrections for all grammatical errors and typos.**

2) This is technically a case of the complication or adverse effect after vaccination. Or how many days later he has developed a complication? Why you would not you emphasize on that? Frankly, the case is confusing in case of timing. When all vaccine doses were applied exactly? Please, draw a timeframe.

**The patient received the first dose on 04/12/21 (Astrazeneca/Fiocruz), the second dose on 07/13/21 (Astrazeneca/Fiocruz), and the third dose on 12/13/21 (Pfizer). On 01/18/22 the patient's flu-like symptoms began, and on 01/28/22 she presented with ST-segment elevation infarction.**

**Timeframe:**



**We did not emphasize the possibility that the patient's clinical condition was due to an adverse effect of the vaccine because the event occurred more than 30 days after the third dose; additionally, she had a positive PCR test indicating active infection.**

3) Please mention what kind of the imaging analysis is that? How many experts were involved? Did you use any imaging software? Please mention what kind of the imaging analysis is that?

**Figures 2, 3, and 5 are of the coronary angiogram. Figure 4 shows the findings of intracardiac ultrasound (right column) indicating the corresponding locations on the angiogram (left column) so that the reader can locate where the IVUS probe was in the coronary artery when the photo was taken. Figure 6 shows the optical coherence tomography findings (right column) indicating the corresponding locations on the angiogram (left column) so that the reader can locate where in the coronary artery the optical coherence tomography probe was when the photo was taken.**

How many experts were involved?

**Three interventional cardiologists were involved. Figure 7 is a photo of the result of the invasive physiology assessment of the coronary artery by resting full-cycle ratio.**

Did you use any imaging software?

Horos Mac 64-bit medical image viewer for Mac OS X.

4 Regarding treatment it must be clear how is that correspondent to the international Guidelines

**In patients with known or suspected COVID-19, treatment of ST-segment elevation myocardial infarction is similar to that for patients without COVID-19, using aspirin, nitrate, beta-blockers, anticoagulation, antiplatelet aggregation with a P2Y12 agent, statins, and reperfusion therapy with fibrinolytics or primary angioplasty. We detail this further in the manuscript.**

5) The quality of figures is extremely low. I cannot evaluate it properly. Please provide the reader with the higher quality images.

**Thank you for noting this. We have downloaded the images in higher resolution.**

6) Did you find a source of the thrombosis? I mean signs of plaque erosion or rupture? Regarding your thereafter angio, do you see any culprit lesions? Figure 6: your OCT examination does not make any sense if you do not show the exact location of the lesion and possible source of the thrombosis.

**On angiography, we were unable to identify any culprit lesions. Therefore, we used OCT to look for signs of erosion or plaque rupture, which could have explained the condition and guided treatment. However, we did not find plaque erosion or rupture on OCT.**

## **REVIEWER #2**

**Scientific Quality:** Grade C (Good)

**Language Quality:** Grade B (Minor language polishing)

**Conclusion:** Major revision

**Specific Comments to Authors:** The authors reported a case of AMI in a patient with COVID-19 infection. The author weighed the significance of this case on the uses of IVUS and OCT findings before and after the treatment respectively. This reviewer has several concerns about this case report.

Major:

1. Please discuss about whether there is any specific findings that confirm the relationship COVID-19 infection and AMI and the difference between this case and previous literatures. AMI without plaque rupture (type 2) may occur besides the COVID-19 infection. There are similar case reports of AMI in patients with COVID-19. Please discuss about large thrombus burden in COVID-19 cases. I think the following cases can be referred. a. Pandit B N, et al. Impact of COVID-19 on Thrombus Burden and Outcome in Acute Myocardial Infarction. Cureus 13(8): e16817. [DOI: [10.7759/cureus.16817](https://doi.org/10.7759/cureus.16817)] (August 01, 2021) b. Trivi M et al. Medicina (Buenos Aires) 2020; Vol. 80 (Supl. VI): 97-99.

**There is no specific finding that confirms the relationship between COVID-19 infection and AMI other than the known extensive thrombotic burden, which is not a specific finding. The high thrombotic load in patients with AMI and COVID is known. In addition to the findings of the study by Pandit et al., there are also other important works addressing this issue, such as a statement from the American College of Cardiology in which the authors concluded that patients with STEMI and concurrent COVID-19 infections experienced a higher thrombotic burden, worse than patients**

**without concurrent COVID -19 infection (Choudry F, Hamshire S, Rathod K, et al. High Thrombus Burden in Patients With COVID-19 Presenting With ST-Segment Elevation Myocardial Infarction. (J Am Coll Cardiol 2020, 76:1168–1176).**

**AMI without plaque rupture (type 2) can indeed occur in addition to COVID-19 infection; but we did not identify any other causes of type 2 AMI, such as coronary dissection, vasospasm, emboli, microvascular dysfunction, or increases in demand with or without underlying coronary artery disease.**

**The difference between this case and those previously published is that we were able to document the absence of plaque rupture or erosion in a patient with coronary artery disease, and also to demonstrate that the plaque had no hemokinetic repercussions shown via invasive physiology. We believe that our case corroborates a body of evidence that has been building toward an understanding of COVID and AMI.**

2. More detailed clinical findings of COVID-19 such as disease severity, other organ involvement, and systemic thrombogenicity during the entire course of COVID-19.

**The patient in question showed signs and symptoms of mild COVID, similar to the flu, until on the tenth day of illness when she presented the heart attack. We did not detect any involvement of other organs. Laboratory blood tests (with the exception of myocardial necrosis markers), chest tomography, and oxygen saturation were normal. In short, there was no clinical evidence of the involvement of other organs. The patient has been under follow-up until the present day by our team, with 6 months of follow-up completed thus far, and remains asymptomatic without any other clinical condition since then.**

3. Regarding subacute and acute thrombus formation, please add the references that reveals the echocardiographic and clinical findings between acute and subacute thrombus. What do two stage thrombus formation mean in this case?

**This reference has been added to the list: Groenland FTW, Ligthart JMR, Witberg KT, Daemen J. Patterns of intracoronary thrombus by high-definition intravascular ultrasound. EuroIntervention. 2022 Jun 3;18(2):e158-e159. [DOI: [10.4244/EIJ-D-21-00796](https://doi.org/10.4244/EIJ-D-21-00796)]. PMID: 34984982.**

What do two stage thrombus formation mean in this case?

**We believe that the presence of thrombi on intravascular ultrasound in the acute and subacute stages was due to the fact that, at the time the patient was studied, the process had already been evolving for over 24 hours, and the thrombotic process (when it does not culminate with vessel occlusion) is a continuum of thrombus stages.**

4. I don't think OCT was necessary to confirm the disappearance of thrombi. OCT is invasive and much cost compared with angiogram alone. Was there any possibility of treatment option by using OCT?

**We agree that OCT was not required solely to demonstrate the disappearance of thrombi. The actual reason that it was used was that there would be a change in conduct if the OCT showed signs of plaque rupture or erosion, in which case we would change the therapeutic proposal, as we would tend to have implanted a stent for mechanical passivation of the plaque.**

Minor:

Please show the full spelling for COVIT-19 and SARS CoV-2 at the first presentation.

Page 1 short title I don't think authors name is necessary in the short title.

Page 3 line 11 Please add branches after RPD and RPV

Page 3 line 17 RVP branc. →RVP branch

Page 4 core tip second line duplicated "we" third line STEMI please show the full spelling at the first presentation. 5th line don't show the full spelling for RPR. 8th line ACS Page 5 line APRESENTATION→PRESENTATION Page 5 tiboline Please show the dose and company Page 5 Please show the date of 3rd vaccination. When the patient vaccinated? Before or after infection? Page Doppler echocardiography showed regional akinesis? Page 7 final diagnosis The authors doesn't show the data showing Kilipp grade 1. Page 7 treatment Please show the dose of enoxaparin What the authors mean specifically by "complete" anticoagulation? Discussion Line 1-5 please add the reference about this context Figure 3 in the legend capitals should be used.(a, b) (c, d) Please indicate diastolic/systolic in the figures C and D Figure 4 in the legend capitals should be used. Figure 6 in the legend capitals should

be used. In all figures indicate the views the pictures were taken I don't think Figure 7 is necessary.

**All of the above minor changes have been completed in the manuscript.**



## **ROUND 2**

### **RESPONSES TO REVIEWER – SECOND ROUND**

Thank you for your comments; they have greatly enriched the article.

1- Regarding the fact that our responses to reviewer 1 do not appear in the body of the article and only in the document for the reviewers, we have now provided the correction in the body of the manuscript.

2- In terms of tibolone, we have added details regarding the reason that we do not believe tibolone was related to the cause of this patient's infarction in the manuscript (Page 10):

The Long-term Intervention on Fracture with Tibolone study, which was designed to determine the effect of tibolone on vertebral fracture risk in postmenopausal women (n=4,538, mean 68 years), was stopped early due to an excessive risk of stroke in women receiving tibolone compared with those receiving a placebo (relative risk 2.2) [52]. However, there were no significant differences in terms of the risk of coronary heart disease or venous thromboembolism between the two groups.

3- Yes we have D-dimer results (2.540 mcg/L FEU), as well as results for other inflammatory markers: C-reactive protein: 75.8 mg/dL and lactic dehydrogenase: 1510 U/L. This was an oversight on our part, and we have added these results to the manuscript (Page 7).

### **RESPONSES TO THE EDITOR – SECOND ROUND**

1- The copyright agreement has been signed by all missing authors.

2- The specific comments in the second-round review (document 77676\_Revision ReviewReport) have been answered.

3- Funding documents regarding support from the Department of Hemodynamic and Interventional Cardiology of Advanced Hemodynamic Therapy Center, Brazilian Society of Health Support Hospital were not provided, because no funding was received for this research.

4- The figures cited in the original manuscript are in PPT format. All figures are provided in PPT format, except for Figure 2 because it is an electrocardiogram.

5- All subtitles have been corrected.

6- The correct version of [CAREchecklist-Eng-20160131] has been provided.

7- The page numbers have been added.

