Peer-review Comments and Author Responses

Reviewer 1

1. *Introduction: Although the study is between COVID-19 and MINOCA, a more detailed description of MINOCA is seemingly required. The description should include healthcare implications, general incidence, and prevalence. If the word limit is a limitation, the COVID-19 description could be reduced.*

Dear Reviewer: We thank you for your help and observations. Detailed descriptions of MINOCA were included in the Introduction and Materials and Methods sections. Information on the epidemiology (proportion of MINOCA among patients with acute myocardial infarction) and healthcare implications (all-cause mortality rate at 12 months) was also included.

2. *Material and Methods: Inclusion criteria should be in resonance with the initial objective written in the introduction ("Therefore, we have decided to perform a cross-sectional study to assess the relationship between COVID-19 active infection and MINOCA in Hispanic patients.") If racial disparity is considered as secondary outcome, it must be addressed in methods.*

Racial disparity was not considered a secondary outcome since most of the patients that are admitted to our institution are from the same region composed of Colombian (Hispanic) individuals. Changes were made to specify the type of population in our study (Hispanic) in the Study sample and Outcome sections.

3. *Regarding COVID-19 infection, is it possible to know when the swabs were done? It might help to differentiate COVID-19 infection before admission or during hospital stay.*

The swabs were performed upon the admission of the patients. This change was implemented in the text where "hospitalization" was replaced with the more specific term "admission."

4. *Discussion: In our understanding, MINOCA is a general term used to describe myocardial infarction with non-obstructive coronary arteries, and its diagnosis could be narrowed into a unique potential underlying mechanism such as coronary vasospasm, dysfunction, coronary dissection, and much more according to the American Heart Association (https://doi.org/10.1161/CIRCULATIONAHA.117.027666). Furthermore, John et al support the possibility of underlying myocarditis, vasculitis, dissection, Takotsubo, and other miscellaneous causes with COVID-19 infection (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9136718/); therefore, he used unclassified MINOCA for his review. Regarding your study, are the patients pertinent to unclassified MINOCA or is there any other specific diagnosis other than Takotsubo?*

A detailed description of MINOCA was added to the Materials and Methods section. This definition includes the differential diagnoses ruled out to achieve the MINOCA diagnosis and increase the clarity in our manuscript.

Reviewer 2

5. *In the introduction, I missed more information about the MINOCA definition.*

We thank you for your help and observations. Detailed descriptions of MINOCA were included in the Introduction and Materials and Methods sections.

6. *In the topic of data extraction and missing data, was the sample size adjusted after previously considering the existence of missing data?*

A sample size calculation was not done as this was a pilot study. Accordingly, we attempted to include all patients admitted to our center, meeting the inclusion criteria. The results from our study could potentially serve as an initial step when calculating the effect size in forthcoming similar studies done in our region.

No adjustments were made for missing data on the sample size since this was a cross-sectional study (no follow-ups or dropout rates). Adjustments for missing categorical data using imputation techniques were carried out for three patients who did not have their ejection fraction calculated.

7. *In the methods you mentioned, "The primary outcome was to evaluate the relationship between COVID-19 and MINOCA". From my understanding, in this study, you are measuring the prevalence between COVID-19 and MINOCA and building hypotheses about causal relationships. I suggest adjusting the text.*

The objective of our study was not to calculate prevalence. Instead, we aimed to calculate proportions since the prevalence calculation requires the entire population at risk, and our study is a pilot study with a reduced sample size.

We aimed to assess a proportion to hypothesize a potential relationship between COVID-19 and MINOCA. Cross-sectional studies cannot demonstrate causality. For these reasons, we opted to implement the term "relationship."

We also modified the last sentence in our discussion section to clarify and emphasize that our study cannot demonstrate causality between COVID-19 and MINOCA.

Reviewer 3

8. *The manuscript follows the STROBE statement checklist for cross-sectional studies in each section. Definitions were correctly provided to make a diagnosis. However, I'd suggest to define MINOCA. This is not mentioned in the methods section, and I believe this is important to mention. In addition, if possible, add the name of the center where you recruited your*

population. As you correctly mentioned, the study was single-centered, decreasing the external validity of the study. At the same time, the results are more specific for the population you included in the study that met the eligibility criteria. I would suggest you add in the results section you didn't find any statistically significant differences in the baseline characteristics (I know you included it in the discussion, but it might also be appropriate to include a line there mentioning these results). Besides that, the results were carefully presented in the text and the table.

We thank you for your help and observations. Detailed descriptions of MINOCA were included in the Introduction and Materials and Methods sections. The Materials and Methods section also mentions the institution where we recruited the study population. Additionally, our Results section now states there were no statistically significant differences in the groups' baseline characteristics.