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To:

Dr Jia-Ping Yan,

Director, Science Editor Development Department

World Journal of Virology

Athens, 02nd June, 2022

Dear Editor,

We would like to thank you for the thoughtful evaluation of our letter to the editor about the paper "***Heart failure in coronavirus disease 2019 patients: Critical care experience***", and for the most welcome comments that helped us improve the presentation of our work.

COVID-19 disease has led to clinical exacerbation of patients with pre-existing heart failure and accounts for a great morbidity and mortality of patients with cardiovascular diseases, in general. There is evidence that COVID-19 induces deleterious effects on the myocardium through a variety of mechanisms such as excessive inflammation, thrombogenicity and endothelial dysfunction. According to literature, patients have developed myocarditis, Takotsubo cardiomyopathy and ischemia (type 1 or type 2) due to myocardial injury, which possibly is responsible for the development of new onset heart failure. Nevertheless, further studies are needed in order to elucidate the exact pathophysiology of the disease.

In the revised manuscript, all the changes have been highlighted in yellow color. We also provide a point-by-point response to all comments in a separate rebuttal letter. Please find listed below our point-by-point response (in normal font) to the referee comments (in bold). Moreover, our revised manuscript has been adjusted to all the requirements, as per journal style.

We hope that the revised version of this manuscript is appropriate for publication in your prestigious journal, after responding to the reviewers' comments.

All authors have seen and approved the paper. The article is the original work of all the authors listed. This manuscript has not been published and is not under consideration for publication elsewhere. We have no conflicts of interest to disclose. Potential publication of our article in your journal would be a great honor for our study group.

We thank you for your time and consideration.

Sincerely,

Dr Vasiliki Tsigkou, MD, MSc, PhD Candidate

Response to the reviewers comments

1. ID 05630740:

“My comments to the authors: The title of this manuscript reflects the main subject appropriately. The abstract summarizes and reflect the work described in the manuscript as well as key words reflective of its main focus. The background is adequately described as a "letter to the editor" based their reflections of a systematic review (John et al.) along with their observed clinical experiences on the subject matter. However, I did not find that the authors were reporting any new concepts on clinical practice or therapeutics aspects. Please consider the questions suggested in the highlighted areas of the main manuscript text. Please see attached file with comments highlighted in yellow and red. Overall, the underlying quality of manuscript is coherently organized and nicely presented. In addition, the language and grammar are accurate and appropriate as well. Thank you for using the language services with certificate appropriately submitted”.

We would like to thank the reviewer for the valuable comment that aims at the improvement of the quality of the content of our manuscript. In the revised version of the manuscript we have responded to your comments (please see page 4, lines 94-103; pages 4-5, lines 112-115; page 5, lines 123-126; pages 6-7, lines 170-179).

2. ID 02353723

“The manuscript of Tsigkou et al. seems to have more of the characteristics of a mini review than that of a letter to the editor finalized to comment the article of John et al (ref. 1). This is also suggested by the high number of references reported (a total of 24 references). Finally, the comments to the article of John et al. are limited to the 4 initial lines of page 5. On the

other hand, most of the "letter" deeply analyzes cardiological aspects which are related or not related to COVID-19”.

We would like to thank the reviewer for the valuable comment that aims at the improvement of the quality of our manuscript. Indeed, we have presented the pathophysiological aspects of COVID-19 and the development of new onset heart failure as well as relative aspects of medical care for patients with heart failure. The reason is that the development of new onset heart failure is a crucial aspect of COVID-19, which is under investigation due to the detrimental effects on patients quality of life, impact on medical care and mortality. In the revised manuscript we have extended our comments on the work of John *et al.* (please see pages 3-4, lines 80-87; page 4, lines 90-93, 105-109; page 5, lines 119-120, 123-126, 128-130; page 6, lines 168-170).

3. ID 05229914

“I had similar ideas when I read the original article. I missed pathophysiological explanations in the initial review. This letter is a welcomed addition. References 10 and 16 are the same”.

We would like to thank the reviewer for the valuable comments. Indeed, our aims were to provide some pathophysiologic aspects about COVID-19 and the development of new onset heart failure. In the revised manuscript we have corrected the references according to the journal’s style (pages 7-11).

4. ID 05382654

“This letter to the editor mainly discussed the pathophysiologic mechanisms and their association between COVID-19 and heart failure, which can help us in getting a better understanding of their interaction, therefore, may result in optimal management in those patients. However, below revisions are still needed before being published in World Journal of Virology. 1. It is suggested that the authors should give more specific advice on how to manage these COVID-19 patients with pre-existing or induced new-onset heart failure in the last paragraph of this manuscript. 2. Please refer to recent papers published in World Journal of Virology and correct the format. In page 1, the first author’s affiliated institutions should be described firstly, not the second author’s. In Author contributions section, “Siasos G, Oikonomou E, Vavuranakis M, and Tousoulis D gave final approval...”, not all authors? It is suggested that these four authors’ contributions should be stated clearly. In page 3, “LETTER TO THE EDITOR” should be changed to “TO THE EDITOR” according to the

journal's requirements. 3. In references, all journal names should be italic, volume number should be bold, issues should be deleted, and "doi" should be changed to "DOI". In reference 2, "JAMA. 2020 Apr 28;323(16)" should be changed to "JAMA 2020; 323". Please check other references including content and format carefully according to the journal's requirements. Other suggestions have been listed in the uploaded revised version".

Again, we would like to thank the reviewer for the above comments. We have provided advice on the management of patients with pre-existing or de novo heart failure and COVID-19 disease in the last paragraph of the manuscript (please see pages 6-7, lines 170-179). Furthermore, we have corrected the format of affiliations and author contributions as well as the title of the manuscript ("to the editor") (please see pages 1 and 3). Lastly, we have corrected the references style according to the journal's requirements (pages 7-11).