

Dear reviewers,

We have corrected the different recommendations that you have communicated to us. The changes are highlighted in yellow in the new version of the manuscript.

Reviewer 1 – 02894577

The manuscript entitled "Cardiovascular disease and COVID19 a deadly combination, a review about the direct and indirect impact of a pandemic" aims to outline the recent findings on the deadly relation of COVID19 with cardiovascular events and the wider impact on several cardiovascular care areas by the pandemic situation. The manuscript is written well; however, it has a number of limitations.

Thank you very much for your constructive comments.

1. Please add the related references in the tables.

The references related with the tables if needed have been added to the manuscript

2. Figure 1 is not clear enough for the mechanism of Cardiac Arrhythmias described in patients with COVID-19 Infection

The figure 1 as has been redesigned to improve the understanding

3. Lack of therapy strategies discussion.

The focus of the review was on the direct and indirect impact of a pandemic in the cardiovascular diseases, the approach to the therapies goes beyond our review. Some lines to highlight the focus of paper has been added mentioning that therapeutic for COVID19 was not the objective of the paper

Reviewer 2- 06144315

I accepted this manuscript for publication after answering the following questions

Thank you very much for your appreciation about our paper

1-The relation between these mentioned acute cardiovascular complications were associated or causative??? I need more explanation

We thank the reviewer for raising this important point. In fact, in the absence of larger datasets it cannot be proven whether the observed associations are causative or merely bystanders. In accordance with the reviewers' kind suggestion, we therefore adjusted the phrasing as follows:

'In line with this, COVID-19 might both trigger AHF in patients with a known history of HF as well as lead to a first episode of hospitalization in patients with occult heart failure [26, 27]. **Whether these factors are causative or just coincident is currently within the scope of scientific research.** **However,** several factors induced by COVID-19 might be contributing to mechanisms of AHF...'

2-COVID-19 vaccination related myocarditis cases happened after receiving vaccines,,,were those cases are related direct to vaccine or may be chronic COVID-19 sequale?

We appreciate the reviewer's pertinent comment. In fact, whether myocardial damage and cardiovascular symptoms are attributable to COVID-19 itself or the vaccine is often difficult to discern in clinical practice.

However, in most of the cited papers in the section dedicated to Myocarditis of this article (page 10/45), data from cardiac MRI was reported, using T1/T2 mapping abnormalities (as evidence of myocardial edema) or the Lake Louise criteria to corroborate the diagnosis of myocarditis. Despite the poor understanding we still have of COVID-19 sequelae and COVID-19/COVID-19 vaccines myocarditis, the mentioned imaging abnormalities most likely suggest acute/subacute inflammation that, in the appropriate setting (mRNA

vaccine, temporal association with vaccine administration, absence of recent COVID-19 infection), may correlate with vaccine-related myocarditis

3-Were these cardiovascular complications acute only or some of them will continue as the chronic COVID-19 syndrome

In fact, there has been a rising body of evidence supporting the presence of 'Long COVID' contributing to cardiovascular disease. Therefore, the manuscript has been adjusted as follows:

'..., irrespective of heart failure state [37]. **Furthermore, there has been recent evidence that patients following COVID-19 infection are at increased risk for developing cardiovascular disease even after the acute phase of infection often referred to as 'Long COVID'[38].'**

Accordingly, the following reference has been added DOI: '10.1038/s41591-022-01689-3'.

4-The impact of COVID-19 era on cardiac imaging has direct burden on morbidity and mortality especially for acute cases??? more explanation

We appreciate the reviewer's question. As stated in the manuscript, early in the first wave of the pandemic, the EACVI issued recommendations designed to ensure that imaging studies in acute/life threatening situations would still be safely performed, while futile exams (unlikely to alter the patient's management at that unique time) would be deferred. In the acute setting, despite the panic generated during the first lockdown, the use of cardiovascular imaging (specially echo) remained part of the evaluation of patients in need of acute cardiovascular care. This is important given the unprecedented number of patients that presented with acute heart failure/cardiogenic shock or with mechanical complications from acute coronary syndromes, as discussed in the manuscript. Moreover, an increase in the use of lung ultrasound and point of care echo was witnessed, and these imaging modalities are being increasingly used by intensivists, internists and emergency practitioners.

Still, the deferral of routine exams likely impacted on CV disease diagnosis and timely management, as we mentioned (page 22/45).

EDITORIAL OFFICE'S COMMENTS

(1) Science editor:

The manuscript entitled "Cardiovascular disease and COVID19 a deadly combination, a review about the direct and indirect impact of a pandemic" aims to outline the recent findings on the deadly relation of COVID19 with cardiovascular events and the wider impact on several cardiovascular care areas by the pandemic situation. This article can be accepted if it completes the following modifications :

1. the number of references cited in Minireview manuscripts should be less than 99.

The number of references cited has been reduced as maximum to not lose information on the review planned and also to answer the reviewers as some questions has been addressed adding new references. We hope the reduction will be satisfactory for the current type of manuscript

2. The form of the table in the article should adopt the form of a three-line table.

The format of the table has been changed accordingly

3. modify the minireview according to the reviewer's comments.

The suggested changes to the manuscript have been done

(2) Company editor-in-chief:

I have reviewed the Peer-Review Report, full text of the manuscript, and the relevant ethics documents, all of which have met the basic publishing requirements of the World Journal of Clinical Case, and the manuscript is conditionally accepted. I have sent the manuscript to the author(s) for its revision according to the Peer-Review Report, Editorial Office's comments and the Criteria for Manuscript Revision by Authors.

The suggested changes to the manuscript have been done