Dear Editor,

Enclosed please find our revised manuscript entitled "Severe/Critical COVID-19 Early Warning System Based on Machine Learning Algorithms Using Novel Imaging Scores" which is intended to be submitted to ***World Journal of Clinical Cases***. We would like to express our sincere thanks to you for the constructive and positive comments. According to the comments, we have carefully revised the related text. We have carefully read the comments from you, the responses to the comments are included at the bottom of this letter.

We are looking forward to hearing good news from you soon.

Sincerely Yours,

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Responese to comments:

Reviewer 1

Q1: But there is some inconsistency in writing (algorithm names), and it has grammar issues. The manuscript needs to be proofread before publishing. The formatting of the text is not complete (the file contains a comment), and the numbering in the body is confusing. The authors should improve the figures' quality (especially figure 1).

Author response: Thank you for your corrections. We apologize for the inconsistency in writing the algorithm names and have corrected them. We have also enlisted the assistance of a professional AJE team to proofread and polish the grammar of the entire manuscript. We appreciate your concerns regarding the formatting and numbering of the text, and we have thoroughly reviewed the entire document, making improvements and re-numbering sections for better reader comprehension. In addition, the quality of all figures has been improved and we have provided new high-quality images.

Reviewer 2

Q1: The subject is intereasting. The abstract is very long. Please summarize. Please avoid the phrase “It is found that”. Is very repetitive.

Author response: Thank you for your correction. We have shortened and summarized the abstract per your guidance and reduced the use of repetitive phrases, such as "It is found that," through professional language editing services. Additionally, grammatical errors have been corrected.

Q2: Please explain if there are some confounder factors in predicting severe covid 19 disease. There are some pathologies with increase IL value coexisting with covid 19 disease.

Author response: Thank you for your inquiry about the confounder factors in predicting severe COVID-19 cases and the increase of IL levels in COVID-19 patients.

Predicting severe/critical COVID-19 cases is a complex task and involves several factors that can impact the accuracy of the predictions. In this study, the authors used various machine learning models and selected important predictors such as clinical experience, age, IL-6/IL-10, ALT, oxygen saturation, qSOFA, and consolidation score to be included in the model. However, it is important to note that the performance of these models may be influenced by several confounding factors. These factors include:

The dataset used in this study may not be representative of the general population, and the results may not be generalizable to other populations.

- The choice of predictors is subjective and may not capture all of the important variables that contribute to the severity of the disease.
- The models used in this study may not be the most suitable for the problem at hand, and different models may yield different results.

- The performance of the models may be influenced by the choice of hyperparameters, the size of the sample, and the quality of the data.

With regards to the increase of IL levels in COVID-19 patients, we agree that Interleukin (IL) levels play an important role in the progression of the disease. IL levels are a type of cytokine produced by the immune system in response to infections, including COVID-19. Elevated IL levels can indicate an overactive immune response, which can be seen in severe or critical cases of COVID-19. However, it is important to consider other factors such as autoimmune diseases, chronic inflammation, and some cancers that can lead to increased IL levels, as they can impact the interpretation of the results. More research is needed to fully understand the relationship between IL levels and COVID-19, and to determine the optimal use of IL levels as a diagnostic or prognostic tool for this disease.

In conclusion, while this study provides valuable insights into the predictors of severe/critical COVID-19 cases, it is important to consider the limitations mentioned above and to use the results with caution. Further research is needed to confirm the findings and to improve the accuracy of the predictions.

We have incorporated these two issues into our discussion and made the necessary revisions. Please refer to the revised discussion section for more information.