Peer Review File

Article information: https://dx.doi.org/10.21037/jtd-23-808

Reviewer A

I would recommend that, in a future submission, the authors choose a main objective and develop a robust methodology that specifically addresses that objective (whether it is related to sepsis, biomarkers or the Omicron variant). For example, if the objective is to study sepsis, it would be important to use the Sepse 3.0 criteria for diagnosis and define the focus of the research, such as whether the cause of sepsis was always viral and, if so, what was the specific focus (pulmonary, gastrointestinal tract, etc.). Additionally, it is necessary to clarify whether all patients were indeed contaminated with the Omicron variant and how tests were conducted to confirm this. These details will help in the understanding and evaluation of the study.

Reply to Reviewer A: We thank you for your valuable insights concerning the focus and methodology of our study. In response to your recommendations, we have revised our manuscript to define and emphasize our primary objective more clearly. This objective is to investigate the incidence of Omicron-associated sepsis, as per the Sepsis 3.0 definition, in hospitalized patients, and to explore its relationship with their clinical characteristics and prognosis.

In accordance with your suggestions, we have enhanced the Methods section of our manuscript. We now provide a more detailed description of the diagnostic process for sepsis, strictly adhering to the Sepsis 3.0 criteria. This revision aims to address your concerns regarding the specificity of our research focus and the clarity of our methodology.

Furthermore, we have undertaken genomic sequencing on samples from 240 patients to definitively identify the Omicron variant in our patient cohort. The sequencing results confirmed the presence of the Omicron variant in all these cases (data not reported in this manuscript). This finding is particularly relevant to the context of the COVID-19

pandemic situation in China during the period of late 2022 to early 2023, as reported by the CDC of China (Emerg Infect Dis. 2023;29(10):2121-2124.).

We believe these enhancements substantially improve the rigor and clarity of our study.

Changes in the text: The revised manuscript now includes as follows:

1. Objective in Abstract. (line 50 to 51)
2. Objective and clinical outcomes in Methods (line 158 to 160).

Reviewer B

Comment 1: The manuscript is well-written and discussed. The main ideas are well presented in the introduction and with adequate references to the literature. The results are well presented and the main ideas are expressed in the "Discussion" section. It is a relevant topic to the field, and the author shows the association between sepsis and poor clinical prognosis in SARS-CoV-2 patients, along with the importance of early recognition of SOFA score deterioration.

Reply 1: Thank you for your positive feedback.

Changes in the text: As per your feedback, no changes are required in the text.

Comment 2: Define the acronym the first time it appears in the text. For instance, CRP, PCT or IL-6 are not defined in line 199.

Reply 2: We apologize for the oversight. We have revised the manuscript to ensure that all acronyms, including CRP, PCT, and IL-6, are defined upon their first mention.

Changes in the text: The definitions for CRP (C-reactive protein), PCT (Procalcitonin), and IL-6 (Interleukin-6) have been added at their first mention in the manuscript, starting from line 132 to 134 and consistently applied throughout the document.

Comment 3: Add point 408 1% to make it 40.81% in line 240.

Reply 3: Thank you for your reminder. We added point in 4081% to make it 40.81% in line 207.

Changes in the text: The corrected percentage now reads "40.81%" in line 207 of the

revised manuscript.

Comment 4: Add 95% confidence interval of AUC and p value for SOFA, IL-6, CRP and PCT ROC curves.

Reply 4: We appreciate your suggestion to include the 95% confidence intervals and p-values for the AUC of the SOFA, IL-6, CRP, and PCT ROC curves. We have incorporated these numbers into the revised manuscript.

Changes in the text: We have included the 95% confidence intervals and p-values in the results section, specifically in lines 235 to 238 and 245 to 248.

Comment 5: Revise number of patients in each group in Table 2, For instance, serious group shouldn't be 147 and non-serious group 152?

Reply 5: We appreciate your attention to the details in Table 2 regarding the number of patients in each group. Upon re-examining our data, we realized that there was indeed a discrepancy in the numbers reported for the serious and non-serious groups. We have corrected this error to accurately reflect the number of patients in each group.

Changes in the text: In the revised manuscript, Table 2 has been updated to correctly display the number of patients in the serious and non-serious groups.

Comment 6: On section "Impact of sepsis on patients' prognosis" says: " Of the 299 patients, 30 were directly admitted to the ICU, and the other 269 were in the general ward at admission. Sepsis was present in 118 (43.9%) patients in the general ward, and of these patients, 34 (28.8%) later needed to be transferred to the ICU during hospitalization". That makes 64 ICU patients. Revise number of patients in each group in Table 3.

Response to Comment 6: We appreciate your detailed review and comments on the patient numbers in the "Impact of sepsis on patients' prognosis" section and in Table 3. Upon re-examining our data, we affirm that the figures presented in Table 3 are indeed accurate. The count of patients transferred to the ICU, as detailed in Table 3, is specific to the 269 patients initially admitted to the general ward. This includes 34 patients

(28.8%) in the sepsis group and none in the non-sepsis group who were later transferred to the ICU. To ensure clarity and better understanding, we have added a footnote in Table 3, explicitly stating that these numbers pertain only to patients initially admitted to the general ward.

Changes in the text: After a thorough review, we confirm that the numbers in Table 3 correctly represent our data as intended and we added a footnote to clarity that clearly.