

## Peer Review File

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### Reviewer A:

1. The influencing factors related to elevated troponin-I were explored by comparing the clinical characteristics of COVID-19 patients to provide a clinical reference for identifying high-risk COVID-19 patients. However, my main concern was the lack of evidence for the clinical significance of the troponin-I elevations. Furthermore, we don't know whether the cardiac injury affected outcome. The author should add the included patient's prognosis or at least add relevant references to confirm the relationship between elevated troponin-I and prognosis.

Reply 1: Thank you for your advice. Many studies have shown that cardiac injury is a common condition among hospitalized patients with COVID-19, and it is associated with higher risk of in-hospital mortality (See **References 3,4,9**). We have added a recent study (Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019. *Eur Heart J.* 2020;41(22):2070-2079.) to further confirm that the increased troponin-I is associated with poor prognosis.

Changes in the text: We have added this reference in the current revised manuscript. (See **References 10**)

2. I couldn't find any information about the extent of troponin-I elevation or the distribution of values. Can the author add it?

Reply 2: Thank you for your advice. According to TnI level, patients were divided into TnI normal group ( $<0.01\mu\text{g/L}$ ) and TnI elevated group ( $>0.01\mu\text{g/L}$ ). However, because the sample size of TnI elevated group ( $>0.01\mu\text{g/L}$ ) is relatively small and data is scattered, we can not analyze the extent of troponin-I elevation further. Hence, we analyzed the influencing factors related to elevated serum troponin I level by comparing the clinical characteristics of TnI normal group ( $<0.01\mu\text{g/L}$ ) and TnI elevated group ( $>0.01\mu\text{g/L}$ ) last.

3. As we know, Yichang is another city out of Wuhan in Hubei Province. The included COVID-19 patients in this paper may mainly second or third generation cases. I wonder there also existed difference between Yichang and Wuhan, the author should mention this in discussion.

Reply 3: Thank you for your advice. Many researches carried out in Wuhan (See **References 3,4,10**) have indicated that some patients with COVID-19 have troponin levels that increase as the disease progresses, and this trend is associated with poor prognosis. In clinical practice, we also observed that cardiac injury (troponin-I elevations) is a common condition among hospitalized patients with COVID-19 in Yichang, and it is associated with higher risk of in-hospital mortality. Therefore, it can be concluded that the TnI level can be used to evaluate the prognosis of COVID-19 patients. A thorough analysis of the influencing factors related to myocardial injury in

COVID-19 patients will help to establish an effective early warning monitoring system to initiate early treatment and minimize the number of patient deaths caused by myocardial injury. At the same time, just like the reviewer mentioned, Yichang is a city out of Wuhan in Hubei Province. The included COVID-19 patients in this paper may mainly second or third generation cases. Hence, we speculated that the virulence of the virus may be weakened compared with Wuhan and the degree of TnI elevation may be different. Currently, related researches in this area also have been carried out. Changes in the text: We have added this in discussion in the current revised manuscript. **(See Discussion)**

4. Currently, many paper have suggested myocardial injury was associated with poor prognosis and high mortality. Troponin is the most sensitive and specific marker for assessing myocardial injury. While, CK-MB is also an another sensitive and specific marker for assessing myocardial injury. Have the author analyzed the relationship between elevation CK-MB and prognosis, and influencing factors related to elevated CK-MB? If so, was there a similar results?

Reply 4: Thank you for your advice. The related research data about CK-MB is being collated. Preliminary research findings indicated that the increased CK-MB is also associated with poor prognosis.

#### **Reviewer B:**

1. The author indicated that TnI was an indicator of risk factors and it was associated with significant cardiac injury. However, the literature support for the relationship between TnI elevation and prognosis is not sufficient, and relevant literature data needs to be added.

Reply 1: Thank you for your advice. TnI was an indicator of poor prognosis and it was associated with significant cardiac injury **(See References 3,4,9)**. We have added a recent study (Characteristics and clinical significance of myocardial injury in patients with severe coronavirus disease 2019. Eur Heart J. 2020;41(22):2070-2079.) to further confirm that the increased troponin-I is associated with poor prognosis.

Changes in the text: We have added this reference in the current revised manuscript. **(See References 10)**

2. "According to TnI level, patients were divided into TnI normal group ( $<0.01\mu\text{g/L}$ ) and TnI elevated group ( $>0.01\mu\text{g/L}$ )". While, the patients may have multiple tests for TnI after admission. Which test result would be used to determine the TnI level, the highest or admission?

Reply 2: Thank you for your advice. The patients may have multiple tests for TnI after admission. The highest level was used to determine the grouping.

3. It is recommended to establish a nomogram model to predict the elevation of TnI according to the binary logistic regression analysis results, which gives the TnI

elevation probability of COVID-19 patients.

Reply 3: Thank you for your advice. We had established a nomogram model.

Changes in the text: We have established a nomogram model in the current revised manuscript. (See **Statistical analysis, Results, Discussion, Figure 1 and Figure legend**)

### **Reviewer C:**

This manuscript addresses an important and interesting problem that analysis of influencing factors related to elevated serum troponin I level for COVID-19 patients in Yichang, China. Overall the article is well organized and its presentation is good. However, some minor issues still need to be improved:

1. In order to state the relationship between elevated serum troponin I and adverse events for COVID-19 patients in Yichang, China, you can combine both table 1 and table 4 into one table, named clinical characteristics of patients in the two groups.

Reply 1: Thank you for your advice. To emphasize the effect of elevated TnI on the complications of COVID-19 patients, we listed the complications separately in Table 4.

2. With TnI level 0.01 µg/L as the cut-off point, patients were divided into a normal TnI group and an elevated TnI group, why your team set this cut-off point.

Reply 2: Thank you for your advice. Patients were divided into a normal TnI group and an elevated TnI group according to the reference range of our hospital laboratory. It is negative when TnI level is less than 0.01 µg/L. While, it is positive when TnI level exceeds 0.01 µg/L.

3. MYO was significantly increased in patients with elevated TnI level, but MYO was released mainly from cardiomyocytes and skeletal muscle, in your study, which one you think is the main source, and then do you think MYO is the independent influencing factors of elevated TnI?

Reply 3: Thank you for your advice. MYO exists in skeletal muscle and the myocardium and is a sensitive and specific biomarker for the diagnosis of myocardial infarction coronary heart disease in the acute phase. After myocardial injury, the rise of serum MYO occurs earlier than the rise of TnI, possibly a reason why MYO is independently related to elevated TnI. According to the results of this study, we speculated the main source was cardiomyocytes.

4. You'd better present the results of logistic regression analysis of another influencing factors (like LDH, albumin) in table 3.

Reply 4: Thank you for your advice. Binary Logistic regression analysis was used to analyze the influencing factors related to elevated TnI in COVID-19 patients. After analysis, CRP, PT, LDH, and albumin were excluded from the final modeling. Hence,

no results about CRP, PT, LDH, and albumin were presented in table 3.