

Article information: <https://dx.doi.org/10.21037/jtd-23-124>

Review Comments

1) First of all, my major concern of this study is the unclear focus of this study. If the focus is the diagnostic accuracy of sSema4D alone for AMI, the results suggest this is not a good diagnostic biomarker, or even this is a failed study and the results did not deserve to be reported, while if the focus is the combination of sSema4D and CRP, the research focus deserved to be studied and the findings deserved to be reported. The authors need to reconsider the focus of this study and substantially revise the whole paper.

Reply: Thank you for your comments. The focus of this study is to find specific indicators for the inflammatory status of acute myocardial infarction; Compared with the traditional inflammatory index (CRP), it is confirmed that sSema4D is more specific in evaluating the inflammatory status of acute myocardial infarction.

2) Second, I do not agree with the use of the term “predictive” since the data are not longitudinal. The authors used cross-sectional data, so they focused on diagnostic accuracy of a potential diagnostic biomarker. Please consider to revise all necessary parts of this paper and indicate the clinical research design in the title, a diagnostic test.

Reply: Thank you for your comments. We have made corresponding modifications in the article. This study focuses on evaluating the value of sSema4D index in reflecting the inflammatory status of acute myocardial infarction.

3) Third, the abstract is not adequate. The background did not indicate the clinical needs for new diagnostic biomarkers for AMI, the limitations of traditional biomarkers, and why the sSema4D is potentially sensitive and specific for the diagnosis of AMI. The methods did not describe the inclusion of subjects, assessment methods for sSema4D, indicators for the diagnostic accuracy of sSema4D, and the measurement of CRP. The results did not provide the sSema4D levels in the three groups and accurate P values for their comparisons. Sensitivity and specificity for the sSema4D alone and sSema4D+CRP should be reported. The conclusion is not clear and please have more detailed comments for the clinical implications of the findings.

Reply: Thank you for your comments. We have modified the abstract to a certain extent, and the focus of the study is on the value and clinical significance of sSema4D as an

assessment of inflammatory status in acute myocardial infarction

- 4) Fourth, in the introduction of the main text, the authors criticized the limited specificity of cTnI but they did not explain why sSema4D is more specific for the diagnosis of AMI. It is necessary to compare the potential strengths of sSema4D vs. cTnI including its diagnostic accuracy, to indicate the clinical needs for this research.

Reply: Thank you for your comments. We have revised the introduction to focus on the value of sSema4D in assessing the inflammatory status of acute myocardial infarction, rather than the diagnostic value of acute myocardial infarction.

- 5) Fifth, in the methodology of the main text, please describe the clinical research design, sample size estimation, and test method for CRP. In statistics, please describe the threshold values of diagnostic accuracy parameters such as sensitivity and AUC for a good diagnostic test. Please clearly describe how the two biomarkers, sSema4D+CRP, were combined to diagnose AMI. Please ensure $P < 0.05$ is two-sided. Finally, please consider to cite the below related paper: Hui L, Wang D, Liu T, Liu B, Wang Y, Liu B. Diagnostic performance of transthoracic echocardiography in screening acute type A aortic dissection from ST-segment elevated myocardial infarction. *Cardiovasc Diagn Ther* 2022;12(5):603-613. doi: 10.21037/cdt-22-59.

Reply: Thank you for your comments. We significantly modified our results to focus on the specificity of sSema4D compared to CRP in reflecting inflammatory status in STEMI patients. We refer to the above article in the discussion section (Ref. No. 13)