Peer Review File

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Reviewer A

Congratulations on your great study! TPE remains an area of interest in many parts of the world and your work definitely adds value to current knowledge.
Response: Thank you for your positive comments.

I have only one suggestion to expand on NRI and IDI for readers to better understand the flow of the paper.
Response: The mathematical basis of NRI and IDI is very complicated. I do not believe we can interpret them in an easy-to-understand way with ten sentences. The statistical analysis section will be unfocused if I add the mathematical basis. Therefore, to make the article simple and enhance its readability, I cited a reference there. Lines 171–174.

Reviewer B

The report assesses the utility of sFasL measurement in pleural fluid as a diagnostic marker for TPE. The findings reveal that pleural fluid sFasL exhibits a moderate level of diagnostic accuracy for TPE, comparable to the diagnostic performance of pleural ADA levels. While the report holds significant importance, it necessitates additional discussions to fully elucidate its implications.
Response: Thank you for your positive comments.

Major comments
- This study presents findings that indicate negative results. While acknowledging the importance of such outcomes, it's evident that the study might lack comprehensive insights or novel findings. The authors are urged to explore avenues for generating novel insights from the study's results.
Response: This study's strengths or novel findings have been addressed in the discussion section. Briefly, the novel findings of this study can be summarized as follows: (1) we found that age may affect the diagnostic accuracy of sFasL for TPE; (2) we analyzed the net benefit of sFasL in patients with pleural effusion, and previous studies have not addressed this issue. Compared with previous studies, the mean age of participants in our cohort is higher than previous studies, allowing us to investigate the diagnostic accuracy of sFasL in elderly patients. Diagnosing TPE in elderly patients is a challenge because many elderly patients have impaired renal, liver, and coagulation

functions. We have revised the discussion to make the novel findings of this study more straightforward. Line 217–223.

- This study's discovery of a correlation between sFasL and age holds a significant interest. Nevertheless, the current discussion primarily focuses on this specific correlation. A more comprehensive exploration would involve delving into other potential factors linked to sFasL and the reasons behind its correlation with age. Especially, the AUC of the combination of pleural ADA levels and sFasL did not significantly differ from that of ADA alone, therefore, this could imply a correlation between pleural ADA levels and sFasL.
Response: In the revised manuscript, we added a paragraph to address the possible mechanisms underlying the negative correlation between age and sFasL. Lines 266–278.

Section 4.3 highlights that the age of TPE cases in this study was lower compared to findings from previous studies. However, a study conducted by Wu et al. (reference number 23) has reported a similar median age and a higher AUC in comparison to the current study. The author should address and discuss further this point.
Response: I agree with you. These results indicate that age can only partialy explain the heterogeneity across published studies. We have revised the discussion section accordingly. Lines 258–260.

- The pleural ADA levels are generally considered to have high sensitivity and specificity for diagnosing tuberculous pleurisy, and recent studies have reported relatively low specificity. However, this study presents a sensitivity of 61% and specificity of 92% in pleural ADA levels for the diagnosis of tuberculous pleurisy, which appears comparatively lower sensitivity than findings in previous reports. This raises the question of whether the study might have included an atypical population or potentially misdiagnosed patients with tuberculous pleurisy. To provide a clearer understanding, the author should provide a more detailed description of the criteria used for diagnosing tuberculous pleurisy and further discuss any observed differences from previous studies.
Response: This is an interesting question. Actually, the sensitivity and specificity of ADA for TPE are affected by the threshold used to define positive ADA. In addition, we noted that the diagnostic accuracy reported in previous studies is heterogeneous [PLoS One, 2019,14(3): e0213728]. I have revised the methods section to clarify the reference standard for TPE. Lines 141–144.

Minor comments

- In the introduction, the author suggests that the diagnostic performance of ADA for TPE is strongly influenced by age. However, this influence might not be as strong as implied, as evidenced by a sensitivity of 77.8% and specificity of 85.6% for the diagnosis of tuberculous pleurisy when considering a cut-off value of pleural ADA as 21.4 U/L, as reported in the reference.

Response: I have revised the sentences as the follows: the diagnostic performance of ADA for TPE is influenced by many factors, such as age. Lines 94–96.

- I suggest incorporating the content of the "3.5 Studies investigating the diagnostic accuracy of sFasL for TPE" section from the Results into the Discussion section.

Response: Thank you for your comments. It has been revised accordingly. Lines 245–260.

- All analyzed data which is described in discussion section should be include in results section.

Response: I have revised it accordingly. All results have been moved to the results section.