

## Peer Review File

Article information: <https://dx.doi.org/10.21037/aob-23-17>

### Reviewer Comments

#### Reviewer A

Comment 1: The abstract needs to be revised, you are presenting results as the conclusion

Reply 1: I have revised them.

Comment 2: It is unclear if you are presenting a systematic review or a narrative review, if this is a systematic review you need to search more than one database

Reply 2: Line 34 has described that it is a narrative review.

Comment 3: Did you only search the term 'biomarkers' and not any specific terms for each biomarker?

Reply 3: I have tried to search specific terms such as D-dimer, VWF, ENDOTHELIN, etc. These searched issues were not beyond the results of biomarkers when combined with TTP.

Comment 4: The box for the key findings, what is known, and what is the implication needs to be revised because currently, you aren't answering the questions presented

Reply 4: According to the editor's comments, this manuscript is a Narrative Review Article, and it doesn't need the Highlight Box. So I deleted it.

Comment 5: 1) Did only one person extract data? 2) Did you use a standard form? 3) Did you include case reports? 4) What does it mean that the author determined the biomarkers that were really involved in iTTP? 5) Did you have a list a priori or what type of standard method was used?

Reply 5: 1) Yes, there is only one author who extract data and write this article. 2) I did not use a standard form. 3) I did not include case reports because this article focuses on Clinical biomarkers that predict the value of iTTP. As iTTP is a rare disease, sporadic data from case reports cannot provide enough materials. 4) If biomarkers be determined to be involved in iTTP, clinicians can use these indicators to determine the severity of the disease and guide treatment. 5) Through reading the retrieved literature, it was found that the biomarkers involved in iTTP include the following aspects, endothelial injury, acute inflammation, complement activation, cardiac biomarkers, and coagulation parameters. Then I use these categories as a list when analyzing and writing.

Comment 6: The majority of the manuscript describes the different types of biomarkers as more of a clinical review and not as a systematic review. So again I'm confused about the goal of the article. If this is a systematic review then you need to describe how many articles you found focused on Big endothelin-1 for example and what those articles agreed on what they disagreed on etc.

Reply 6: Line 34 has described that it is a narrative review. And iTTP is a rare disease, there are no more than 3 articles focused on Big endothelin-1 in TTP.

Comment 7: There are grammatical errors throughout the manuscript

Reply 7: I have revised them as possible as I can.

## **Reviewer B**

Comment 1: The authors need to modify the method section to more details. You may follow the PRIMSA statement on the method of reporting - for a systematic review. The method section is quite lacking.

Reply 1: Line 34 has described that it is a narrative review.

Comment 2: Discussion will be more helpful for the readers to discuss what is clinically relevant. Some of the tests are more in research settings. Developing a strategy to help clinicians manage iTTP would be helpful.

Reply 2: I have revised them.

Comment 3: I would recommend summarizing all the biomarkers in one or various tables in the subcategories that you used: to view its outcome (mortality +/- sensitivity if available)

Reply 3: I have compiled a table, as shown in Table 2

Comment 4: Please define ADAMTS13 in the introduction and MDTCS in the results

Reply 4: I have revised them

Comment 5: In the introduction, the authors stated that 'hematologists hope to find those ...'. There are other different specialists who manage iTTP depending on the center, including critical care and nephrology, etc. I would generalize the statement rather than limit it to hematologists.

Reply 5: I have revised hematologists to clinicians

Comment 6: Please do not interchange iTTP and TTP in the article. Please be consistent. It is difficult to know if you include cTTP when you are using the term TTP.

Reply 6: I have revised them.

Comment 7: Please expand if some of the biomarkers are available clinically: VWF-CBA, BIG ENDOTHELIN-1

Reply 7: They are not available clinically.

Comment 8: References are required in certain statements including:

Line 198: We demonstrated that the plasma level of big ET-1 ...

Line 247: In our recent TTP patient research, we found

Line 249: Similar to sTM...

Reply 8: I have revised them.

