Peer Review File
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Reviewer Comments
Reviewer A
This is a well-written Review article which summarises the current literature on the entity "Sticky Platelet Syndrome". The authors highlight the need for a more standardised laboratory test system to diagnose this entity. 1. In this light, I would suggest discussion of the possible utility of whole blood platelet aggregation studies which have been shown to identify patients with myeloproliferative neoplasms(MPN) who are at risk of developing thrombosis(Manoharan et al, Clinical and Applied Thrombosis/Hemostasis July 2022). 2, The authors should also discuss the possibility that SPS may be a forme fruste presentation of MPN; hence the need to include molecular studies for diagnostic driver mutations (JAK-2, CALR, MPL) in patients with suspected SPS.

Reply to the comment 1: The alternative methods of hyperaggregability evaluation are discussed in a new part of the article. The weakness of the mentioned article is low number of healthy controls, which can result in misleading conclusions.
Reply to the comment 2: The issue of platelet aggregability in patients with MPN is very complex and the investigation of platelet aggregability with low concentrations of epinephrine and ADP is inspirational. We can speculate about the usefulness of molecular studies for MPN associated mutations in people with SPS, but very limited data are yet available.

Reviewer B
Comments:
Thank you to the authors for providing a comprehensive overview of the diagnostic issues and controversies surrounding SPS. The article highlights the complexity of diagnosing this thrombophilic condition and raises important questions regarding the validity of traditionally used diagnostic criteria. Given that the manuscript provides the authors' reflections and recommendations based on clinical practice experience, we suggest considering publishing this article as a "Clinical Practice Review".

Major concerns:
1. Please change the "Summary" to "Abstract". Perhaps it would be helpful to specify in the abstract which year and by whom/which organization the "traditionally used diagnostic criteria" were established. This would provide clarity for readers on which diagnostic criteria controversy the paper is aiming to address.

2. And, it is recommended to briefly introduces the key issues addressed in this article in the abstract, not only limited to the problem of inductor concentration.

3. According to the requirements of AOB, please expand the abstract to 200-350 words.

4. It is suggested that the authors include "thrombophilia" as a keyword.

5. For a clinical practice review, the main text should be structured with Introduction, Main Body, and Conclusions. Therefore, the Introduction should not only include background information on the topic, but also clearly articulate the purpose and necessity of the review. Meanwhile, according to the latest requirements of AOB, the Introduction of a review should be structured into three parts: a) Background, b) Rationale and knowledge gap, c) Objective. The template can be downloaded from this link: https://cdn.amegroups.cn/static/public/2.2.4-Structure%20of%20Clinical%20Practice%20Reviews-template-V2022.11.4.docx?v=1677579797105

6. The authors also mentioned that the laboratory evaluation of platelet aggregation is complicated and lacks standardization, leading to significant interlaboratory variability. Although LTA is the current standard method for evaluating platelet hyperaggregability, it is time-consuming and technically challenging, and affected by many pre-analytical and analytical variables. To establish universal standards, it is necessary to have a widely available and feasible method to measure platelet aggregation. Therefore, the authors may consider discussing alternative methods currently used by various clinical units and research institutions to measure platelet aggregation and suggest a feasible approach for developing new diagnosis criteria in the future.

7. Since several widely used medical agents (e. g. nonsteroid anti-inflammatory agents, ASA, and ADP receptor antagonists) are known to have a prolonged effect on platelet function, it is of utmost importance to carefully and extensively evaluate medication and diet and exclude such interfering agents for a sufficient time period before testing. It is also important to perform tests outside conditions that may influence results (stressful events, recent TE event, and pregnancy). Neglecting or underestimating patient variables may lead to significant differences and conflicting results in the same patient.

8. Although the author raises some controversial considerations based on testing healthy samples, it seems that external conditions (such as stressful events, recent thromboembolic event, and pregnancy) and patient factors such as medication use that may have a prolonged effect on platelet function also need to be considered.

9. We suggest the authors provide a more comprehensive conclusion that summarizes the constructive viewpoints presented in this article.

Format issues:
10. We suggest combining Figures 1 and 2 under a common title, and sorting the images by EPI and ADP categories and their respective concentrations. Also, the legend should be provided for the figure, including the figure title, the full name of any abbreviation in the figure, a detailed description of any symbol in the figure (e.g., some color notation or arrows), and a separate description of each figure if it is a combination of several figures, etc.

11. Since the author has already discussed each of the controversial issues in separate paragraphs with subheadings, we suggest that Table 2 may not be necessary and could be removed.

12. For tables, each column must have an appropriate heading and, if measurements are given, the units should be provided in the column heading. Column headings should be brief, with units of measurement in parentheses; all abbreviations must be defined in footnotes.

13. We suggest keeping the R values in Table 4 to three decimal places, and adjusting the precision of the P values according to the following suggestions:
The description of the P-value should be in uppercase italic format, i.e., "P".
If P<0.001, please report "P<0.001" to avoid reporting unnecessarily excessive precision (with the exception of hypothesis tests that include correlations or studies with exponentially small P-values, such as genetic association studies, which can be reported exponentially, e.g., P=1×10-5);
If 0.001≤P<0.01, please report the specific P-value to 3 decimal places, e.g., "P=0.001", "P=0.009";
If P≥0.01, please report the specific P-value to 2 decimal places, e.g., "P=0.01", "P=0.06", "P=0.10", "P=0.90";
If P>0.99, report "P>0.99".
Do not round P-values, do not report "not significant" simply when the data is greater than an arbitrary value, and do not report only vague bounds, such as P<0.05, as described above, but report the exact P-value.

14. L38-39: "These diagnostic criteria have been used in most publications until present time." Please cite corresponding references.

Reply to the comment 1: Summary has been changed to Abstract. The authors of traditional diagnostic criteria have been specified.

Reply to the comment 2 and 3: The abstract has been expanded and the additional key issues have been included in the abstract.

Reply to the comment 4: The keyword Thrombopilia has been added,

Reply to the comment 5: The review has been structured according to the suggestion.

Reply to the comment 6: The alternative methods of hyperaggregability evaluation are discussed in a new part of the article.

Reply to the comment 7 and 8: The factors, which influence the platelet aggregability are newly discussed

Reply to the comment 9: The conclusions are enlarged.

Reply to the comment 10: The titles and footnotes have been added. The combination of Fig.1 and

Fig 2 in a common figure I consider as not optimal.

Reply to the comment 11: The table 2 has been removed.

Reply to the comment 12: The abbreviations are defined in footnotes. No measurements are given, no units are thus provided in column headings.

Reply to the comment 13: All P-values are exact. The R-values are adjusted according to the reviewer's suggestion.

Reply to the comment 14: The references are added.