

Title: Correlation between thrombopoietin and inflammatory factors, platelet indices, and thrombosis in patients with sepsis: A retrospective study

Journal: World Journal of Clinical Cases

Response to Reviewers' comments

Dear Editor,

We thank you for your careful consideration of our manuscript. We appreciate your response and overall positive initial feedback and made modifications to improve the manuscript. After carefully reviewing the comments made by the Reviewers, we have modified the manuscript to improve the presentation of our results and their discussion, therefore providing a complete context for the research that may be of interest to your readers.

We hope that you will find the revised paper suitable for publication, and we look forward to contributing to your journal. Please do not hesitate to contact us with other questions or concerns regarding the manuscript.

Best regards,

Mo Yang

Reviewer #1

Comment 1: However, what was the correlation in severe and non-sever group as per the SOFA categories.

Response: We thank the Reviewer for the comment. The Sequential Organ Failure Assessment (SOFA) is mainly used to diagnose sepsis in patients with infections. Sepsis can be diagnosed when the SOFA score is ≥ 2 points at baseline. Still, there are no clear guidelines or expert consensus suggesting that the SOFA score can be used as an indicator to judge the severity of sepsis because a given SOFA can be due to the injury of one organ or the joint effect of multiple organ injuries. Hence, the clinical judgment of sepsis severity is mainly based on the development of septic shock. Septic shock was based on sepsis with persistently low blood pressure and blood lactic acid concentration > 2 mmol/L; under complete volume resuscitation, vasoactive drugs are still needed to maintain mean arterial pressure (MAP) ≥ 65 mmHg^[1]. Theoretically, the sepsis group can be stratified according to MAP was ≥ 65 mmHg. Still, because this study was a retrospective study, and the retention time of the patients after treatment in the emergency room was inconsistent (some patients asked to give up treatment, left the hospital, or were transferred to another hospital without completing treatments), there was not enough time to evaluate the effect of fluid resuscitation fully (i.e., the changes in MAP and blood lactate index) in all patients. Only the mean arterial pressure of the patient after initial diagnosis could be found, which is presented in Table 1. Unfortunately, a single MAP measurement in time is not sufficient to determine the presence of septic shock. In addition, the number of patients with MAP < 65 mmHg in this study was very small, which could lead to a serious bias in the statistical analyses. Therefore, there were no further subgroup analyses of mild sepsis and septic shock in this study. If the follow-up sample size were fully expanded, prospective research was carried out, and the observation time were long enough, the subgroup analysis of patients with mild sepsis and septic shock could be carried out to evaluate the

difference and correlation of TPO and related indexes among different groups. We added a limitation about this point.

Comment 2: Moreover, was there any prognostic implication in survivors and non-survivors group.

Response: We thank the Reviewer. This study was a clinical retrospective study of infected patients who had just been admitted to the emergency department for examination and treatment for the first time. Only some of these patients were hospitalized, and some did not. Some of the patients receiving inpatient treatment are discharged from the hospital due to social or economic reasons. Therefore, the outcome of these patients who were not hospitalized or whose hospitalization was interrupted was not recorded. In addition, the purpose of this study was to analyze the correlation between TPO levels, platelet-related parameters, inflammatory indicators, and thrombosis-related indicators in sepsis patients and to examine the ability of TPO in the early diagnosis of sepsis. The ability of TPO to judge the prognosis of sepsis will be evaluated in future prospective studies.

Editor

Comment 1: his manuscript introduces the correlation between thrombopoietin (TPO) and inflammatory factors in patients with sepsis and the potential role of TPO in sepsis. Please add the correlation in severe and non-severe group as per the SOFA categories and prognostic implication in survivors and non-survivors group.

Response: We thank the Reviewer for the comment. The Sequential Organ Failure Assessment (SOFA) is mainly used to diagnose sepsis in patients with infections. Sepsis can be diagnosed when the SOFA score is ≥ 2 points at baseline. Still, there are no clear guidelines or expert consensus suggesting that the SOFA score can be used as an indicator to judge the severity of sepsis because a given SOFA can be due to the injury of one organ or the joint effect of multiple organ injuries. Hence, the clinical judgment of sepsis severity is mainly based on the development of septic shock. Septic

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of TPO to judge the prognosis of sepsis will be evaluated in future prospective studies.

***Comment 2:** Please prepare and arrange the figures using PowerPoint to ensure that all graphs or arrows or text portions can be reprocessed by the editor.*

Response: We now provide the figures in a ppt file.

***Comment 3:** Authors are required to provide standard three-line tables, that is, only the top line, bottom line, and column line are displayed, while other table lines are hidden. The contents of each cell in the table should conform to the editing specifications, and the lines of each row or column of the table should be aligned. Do not use carriage returns or spaces to replace lines or vertical lines and do not segment cell content.*

Response: All tables are now three-line tables and meet the requirements.

***Comment 4:** Please upload the approved grant application form(s) or funding agency copy of any approval document(s).*

Response: The document is now provided.

References

1. Singer M, Deutschman CS, Seymour CW et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA 2016; 315: 801-810. doi: 10.1001/jama.2016.0287. PMID: 26903338.