

Dear Dr. Wang and the reviewers of the World Journal of Clinical Cases,

Thank you for your comments on our manuscript “Associations between coagulation factor XII, coagulation factor XI, and stability of venous thromboembolism: A case-control study” (Manuscript NO.: 69890, Case Control Study). These comments are important for improving the quality of our work, and we have revised our manuscript accordingly. The revisions are highlighted in red, and a detailed response letter has been attached. We hope this version of the manuscript could be accepted by the World Journal of Clinical Cases.

By the way, the author Yang-yang Deng did not receive the letter of notification on Copyright License Agreement, so she signed it by hand written.

Look forward to hearing from you soon.

Best regards,

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Reviewer 1

Overall, the manuscript was well-written and only contain a few errors which I have highlighted in the revised manuscript, although I still do have several questions:

1. What were the potential sources bias which might have occurred in the study?

Authors' response: Thank you for your comment. As mentioned in the limitation section, this was a small-scale, case-control study that only included Chinese patients from a single-centre, and only patients with no previous antithrombotic therapies were included. These factors might have led to selection bias, and the results of this study should be validated in large-scale studies in other centers. Although the baseline characteristics included age, gender, smoking status, and comorbidities that might affect the coagulative status of the patients, due to the limited sample size, only univariate analysis was performed. The potential effect of other study characteristics could not be excluded, such as prophylactic anticoagulants and concurrent medication used by each patient, which might also affect the results. These have been mentioned in the revised discussion.

2. Briefly describe in the abstract the urgency/importance of this study and how it will tackle the problem of PE in DVT.

Authors' response: Thank you for your comment. We have added a sentence to highlight the importance and urgency of this study in the abstract of the revised

manuscript as “However, clinical and biochemical factors that are related to the stability of DVT are not fully understood”.

3. What were the statistical methods used to control for confounding factors?

Authors’ response: Thank you for your comment. Due to the limited sample, we did not apply multivariate analysis to control the confounding factors. This has been mentioned as a limitation of our study as “Although the baseline characteristics included age, gender, smoking status, and the comorbidities that might affect the coagulative status of the patients, due to the limited sample size, only univariate analysis was performed. The potential effect of other study characteristics could not be excluded, such as prophylactic anticoagulants and concurrent medication used by each patient, which might affect the results”. As a pilot investigation, our study is potentially hypothesis-generating. Large-scale studies with multivariate analysis and adequate control of the possible confounding factors are required to validate our findings in the future.