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LETTER TO THE EDITOR

Comparison of novel thrombin generation methods with established techniques is mandatory

We appreciate the attention that our publication was given by Prof. Douxfils's group. We read their comments with interest and respond accordingly.

We acknowledge that the main shortcoming of our work was the limited number of comparisons between the methods (STG-Drugscreen and calibrated automated thrombogram [CAT]). Despite this limitation, we wanted to report the findings obtained with clinical, surplus plasma samples of anticoagulated patients. Seemingly, the PPP-reagent high of CAT is the closest to the STG-DrugScreen. The tissue factor (TF) or phospholipid concentrations of the ST Genesia reagents are not provided by the manufacturer, and therefore identical test conditions cannot be reached. Indeed, we intended to compare STG-Thromboscreen, but failed to get readouts in warfarin samples (see our article). In our previous publications, we successfully used the low TF concentration in CAT with direct oral anticoagulants (DOACs).[1] Based on these findings, we decided to use the STG-DrugScreen and the low TF reagent in CAT in our study.

While the thrombin generation methods provide several variables, clinicians regard the endogenous thrombin potential (ETP; ie, the area under the curve) as an important summative marker. We agree with Douxfils et al that lag time and peak were comparable in STG-DrugScreen and CAT, whereas ETP was discrepant in our article. In accordance, Artang et al[2] studied DOAC samples in CAT with high TF, and there, ETP failed to correlate well with DOAC levels. Yet ETP significantly attenuated with high rivaroxaban and apixaban concentrations,[2] in line with our findings in CAT. In contrast, with the STG-DrugScreen, we did not observe any changes in ETP. This lack of ETP response in STG-DrugScreen is not a novel finding and has been reported previously.[3] We cannot ignore the inert response in ETP, representing the summative parameter of thrombin generation.

Overall, the automated measurement of thrombin generation in clinical setting would be advantageous. Our conclusion is that the major limitation of the STG-DrugScreen method is the lack of the detection of overanticoagulation by the major anticoagulant warfarin or heparin. We believe that further detailed investigations of the STG-DrugScreen method, including appropriate comparisons with the traditional CAT method, are needed before any firm conclusions can be reached. Our study is the first to compare STG-DrugScreen to CAT simultaneously in anticoagulated patients, including warfarin, heparin, and DOACs. We invite further research to confirm or disprove our findings.

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AUTHOR CONTRIBUTIONS

All authors were involved in formulating and finalizing the manuscript and approval of the final version of the manuscript.

RELATIONSHIP DISCLOSURE

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