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RESPONSE TO LETTER

Unaddressed Biases in a Retrospective Study of Anticoagulant Prophylaxis in Trauma Patients [Response to Letter]

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Dear editor

We extend our gratitude for the opportunity to address the methodological comments provided by Lu et al on our manuscript, "A Retrospective Study of Preventive Anticoagulant Therapy Among Trauma Patients in the Yichang Area Through Clinical Data Review and Clinician Survey" (IJGM-595896). We appreciate their thorough review of our work and recognize the significance of the points they have raised. Herein, we respond to each of their four principal observations.

Differential Imaging Intensity and Surveillance

The authors accurately observe that patients administered anticoagulation underwent lower extremity ultrasound and pulmonary computed tomography (CT) re-examinations more frequently (84.47% vs. 47.15%), and that this discrepancy may amplify thrombotic event detection in the anticoagulation group. We entirely concur that surveillance bias constitutes a well-established phenomenon in venous thromboembolism (VTE) research. In our logistic regression analysis (Table 7), we incorporated re-examination status as a covariate, thereby partially adjusting for this imbalance. Nonetheless, as highlighted in the letter, this adjustment does not comprehensively address the mechanistic pathway by which imaging frequency enhances event detection. We agree that limiting analyses to patients with complete imaging workups or employing blinded outcome adjudication would represent more robust methodologies. In future prospective or multicenter studies, we intend to standardize screening protocols across groups to minimize detection bias.

Confounding by Indication and Analytical

The letter appropriately emphasizes that anticoagulated patients in our cohort were older, experienced longer hospital stays, and had a higher prevalence of prior thrombotic events-reflecting clinician-driven selection rather than random allocation. Although binary logistic regression adjusted for measured covariates, we acknowledge that residual confounding due to unmeasured factors or systematic selection biases cannot be excluded. Propensity score matching or inverse probability of treatment weighting would indeed better equilibrate baseline risk. We note that the Nagelkerke R^2 values of 0.325 and 0.160 in Tables 3 and 7 indicate limited explanatory power, underscoring the necessity for more advanced causal inference techniques. We plan to implement these methods in future analyses, contingent upon sufficient sample size and data granularity.

Absence of Bleeding Complication

We fully concur that reporting thrombotic events in the absence of corresponding bleeding outcomes constrains the clinical interpretability of the benefit–risk balance associated with anticoagulation in trauma patients. Trauma consensus guidelines appropriately conceptualize thromboprophylaxis as a risk–benefit calculus. In our retrospective dataset,

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bleeding events were not systematically captured in a standardized fashion, precluding their inclusion as a secondary endpoint. We strongly endorse the recommendation to adopt the International Society on Thrombosis and Haemostasis (ISTH) definition of major bleeding as a prespecified endpoint in future investigations. This limitation has been incorporated into the revised discussion section of our manuscript.

Drug Dose Reporting and Immortal Time

The letter identifies two practical concerns. First, the documentation of anticoagulant doses in milliliters, rather than milligrams or weight-adjusted units, precluded the determination of whether patients received standard prophylactic, weight-adapted, or therapeutic regimens. This reflects the real-world documentation practices within our electronic medical records; however, we agree that future studies should report doses in standardized units, concomitant with body weight and renal function parameters. Second, treating anticoagulation initiation as a static binary exposure indeed introduces the risk of immortal time bias, as patients must survive sufficiently long to receive the initial dose. Modeling anticoagulation as a time-varying covariate within a survival analysis framework, supplemented by multiple imputation for missing data, would yield more reliable estimates. We intend to employ this approach in subsequent research.

Conclusion

We thank Lu et al for their constructive critique, which will help improve the design and analysis of future studies in this important area. Our study remains, to our knowledge, one of the larger single-centre series from China characterising real-world thromboprophylaxis practice in trauma care, and we hope the limitations identified here will inform the multicentre prospective research we ourselves advocate.

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