



Exploring the implications of direct oral anticoagulants in trauma

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To cite: Mahajan A, Egodage T, Ho VP. Exploring the implications of direct oral anticoagulants in trauma. *Trauma Surg Acute Care Open* 2024;**9**:e001360. doi:10.1136/tsaco-2024-001360

Since their approval in 2010, direct oral anticoagulants (DOACs) have become integral in treating and preventing thromboembolic diseases. Their predictable pharmacokinetics, negating the need for frequent dose adjustments, offer considerable advantages.¹ However, the management in patients with trauma on DOACs presents challenges, including the lack of standardized reversal protocols and the unclear clinical utility of concentration assessments in high-risk injuries.² A study by Perkins *et al* of 245 patients with trauma investigates the implications of therapeutic, subtherapeutic or supratherapeutic DOAC levels as well as the associated clinical outcomes.³

The primary finding of this study is that there is wide variability in DOAC-specific anti-Xa levels among patients with trauma. Though this study was underpowered to detect an association between anti-Xa concentrations and transfusion, reversal or outcomes, one potentially notable finding is in the small subgroup of patients with intracranial hemorrhage (ICH). Progression of ICH was observed in 30% (3/10) of patients with supratherapeutic anti-Xa levels versus 9.8% (4/41) of patients with therapeutic or subtherapeutic levels. These data suggest that there may be a clinically significant risk to patients with supratherapeutic levels. Identification of patients with supratherapeutic levels and effective strategies for reversal, therefore, becomes a critical consideration and underscores the need for further research for DOAC management in trauma care.

Another notable finding is that female patients were more likely to demonstrate supratherapeutic levels (67% vs 33%) than male group. Anti-Xa concentrations among females also had a wide variation, demonstrated by a large IQR. Despite the theoretical understanding that DOACs have a more predictable therapeutic effect that negates the need for frequent monitoring, this difference in the predictability of levels between men and women raises questions about whether there is a biological difference in how individuals respond to DOACs.⁴ The seminal DOAC trials enrolled around 40% female patients; however, these studies were not examined for sex-specific outcomes.⁵ The absence of these data makes it difficult to generate conclusions about whether testing and reversal protocols should differ for men and women.^{6,7} Furthermore, the lack of standardized anti-Xa testing, with specifically calibrated levels required for each Xa inhibitor, complicates whether and how widely testing should be adopted. Nevertheless, Perkins *et al* highlight an interesting question of who would most benefit from anti-Xa testing and reversal.

As the use of DOACs will likely continue to be omnipresent, it will be imperative that trauma providers understand their clinical implications, the utility of anti-Xa testing and when reversal is indicated. Future research should focus on understanding the clinical impacts of reversal agents and conducting pragmatic analyses for their implementation in clinical practice, paving the way for more effective and personalized care for patients with trauma on DOAC therapy.

Contributors All authors contributed to the content, literature review, drafting and editing of the manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests VPH spouse is a consultant to Zimmer Biomet, Sig Medical, Atricure, Astra Zeneca and has received research support from Medtronic.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; internally peer-reviewed.

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► <http://dx.doi.org/10.1136/tsaco-2023-001208>

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