# Introduction to the Review Series on venous thromboembolism: emerging issues in pathophysiology and management

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Significant advances have been made in the diagnosis, prevention, and treatment of venous thromboembolism (VTE), yet several pathophysiological aspects that may influence the management of these conditions remain unresolved. In this issue of *Haematologica*, leading experts address three emerging topics that are critical to advancing our understanding of VTE.

## Enhancing the understanding of venous thromboembolism risk and prophylaxis in trauma patients

Venous thromboembolism remains a serious and potentially fatal complication following traumatic injury. In their review, Tran *et al*. emphasize the variability in trauma cases, pointing out that while severe injuries are widely recognized as major VTE risk factors, the risks associated with minor injuries are less well understood.[1] A key takeaway from this review is the need for personalized care when managing VTE risk in trauma patients. Although clinical guidelines provide a broad framework, the diversity of trauma cases means that a uniform approach is unlikely to be effective. For hospitalized patients, especially those with moderate to severe injuries, the benefits of pharmacological thromboprophylaxis are well-established. However, for those with minor injuries, particularly those managed in outpatient settings, the decision to initiate prophylaxis requires more nuanced consideration. The review references several studies, such as the PRONOMOS[2] and the CASTING[3] studies, which offer insights into this decision-making process. These studies suggest that while thromboprophylaxis can lower the risk of VTE, careful deliberation is needed regarding the choice of agent and patient selection. Overall, the article offers a comprehensive analysis of VTE risk and thromboprophylaxis in trauma patients, highlighting the significant progress made in managing VTE in those who have received serious injuries. However, further research is needed to better understand the risks and benefits of thromboprophylaxis in those with minor injuries. Future management of VTE in trauma patients will likely rely on more sophisticated risk stratification tools and a stronger focus on individualized care.

## Addressing multimorbidity in venous thromboembolism risk and management

Traditionally, VTE risk has been associated with specific factors such as surgery, hospitalization, or cancer. However, as highlighted in the review by Zöller and Connors, growing evidence indicates that multimorbidity - the presence of two or more chronic conditions like cancer, obesity, heart failure, or kidney disease - may significantly impact VTE risk.[4] This evolving understanding requires a new framework for assessing and managing VTE in patients with multiple chronic diseases. Studies such as that by Ahren *et al*., using data from Swedish registries, show a clear and graded relationship between the number of chronic conditions a person has and their VTE risk.[5] Strikingly, individuals with two or more chronic conditions are over three times more likely to develop VTE than those without multimorbidity, and the risk continues to rise as the number of conditions increases. The concept of multimorbidity overlaps with related terms such as comorbidity (the presence of additional diseases alongside a primary condition) and frailty (a state of reduced physiological function and increased

vulnerability to stressors, especially in older adults). Both comorbidity and frailty have been shown to influence VTE risk and outcomes, complicating the clinical landscape.[6,7] As the review underlines, incorporating multimorbidity into VTE risk assessment and management protocols offers an opportunity to improve patient outcomes. To achieve this, a concerted effort in research, clinical practice, and policy-making is needed to prioritize the study of multimorbidity in VTE and to ensure healthcare systems can meet the complex needs of patients with multiple chronic conditions.

## Navigating the double-edged sword of targeted therapies in cancer treatment

Targeted therapies have revolutionized cancer treatment by shifting the focus from the broad, often debilitating effects of traditional chemotherapy to more precise interventions. Drugs like monoclonal antibodies and tyrosine kinase inhibitors (TKI) have been game-changers for cancers such as lung, breast, and colorectal cancer. However, as Verso *et al*. highlight in their review, these therapies may also increase the risk of VTE.[8] The review provides a detailed analysis of various classes of targeted therapies and their associated risks. Anti-angiogenic therapies, which inhibit the vascular endothelial growth factor pathway (e.g., bevacizumab), and TKI have both been linked to an increased risk of VTE, although reports have been inconsistent.[9,10] Further research is needed to understand the underlying mechanisms, particularly at the molecular level, to guide the development of safer treatment strategies. A better understanding of the role of specific genetic mutations and their interactions with targeted therapies could lead to predictive biomarkers that help identify patients at the greatest risk for VTE. As the use of targeted therapies in oncology continues to grow, clinicians must remain vigilant and adopt a proactive approach to monitoring and risk management.

## Conclusion

Advancements in the understanding and management of VTE in trauma patients, individuals with multimorbidities, and cancer patients on targeted therapies continue to evolve. In trauma care, the challenge remains to determine the appropriate use of thromboprophylaxis, particularly for minor injuries, while personalized care remains essential. In multimorbid patients, integrating multimorbidity into VTE risk assessments offers a potential improvement in patient outcomes. Meanwhile, as the use of targeted cancer therapies grows, balancing the benefits of these treatments with their associated VTE risk is crucial. By addressing these emerging issues, healthcare providers may be better able to manage VTE risk and improve patient outcomes across these diverse populations.

**Disclosures**

*No conflicts of interest to disclose.*

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