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A Novel Assay for Determining Bleeding Risk in Factor XI Deficiency

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Factor XI (FXI) plays a modulating role in coagulation, with three different activation pathways. FXI deficiency is associated with bleeding under certain conditions. Low levels detected by activated partial thromboplastin time (APTT) methods (non-physiological and dependent on contact activation via factor XII) do not necessarily predict bleeding.[1] The APTT does indeed not reflect clinically relevant FXI function as it measures the initiation of coagulation and not the amount or solidity of clot formation. Following tissue injury, tissue factor (TF) VII is activated, which in turn leads to FXI activation by thrombin. This results in feedback enhancement of the TF-independent pathway via FIX. Polyphosphates released from platelets enhance FXI activation considerably.[2] Global coagulation tests can now help to understand this mechanism further. Thrombin generation testing (TGT) can predict the bleeding tendency when measured in platelet-rich plasma (when contact activation is inhibited).[3] The TGT is however not easily automated and not generally available for patient assessment. In this issue of *Thrombosis and Haemostasis*, Calderara and colleagues described a novel method of coagulation assessment, called thrombodynamics.[4] They provided a three-dimensional measure of coagulation, based on clot development after the initial thrombin burst (which is the time point measured by the APTT). In this assay, TF was fixed on the surface to trigger coagulation, but the subsequent three-dimensional trace was TF-independent and reflected action of the FXI feedback loop on the rate of clot growth and size. This method could also discriminate between patients with or without a bleeding history, although only a small number of patients were studied. Further evidence is required, but development of global assays is beginning to assist prediction of bleeding risk in FXI-deficient patients. It is important to decide carefully who requires replacement therapy since treatment with FXI concentrate is associated with an increased risk of thrombosis.

Conflict of Interest
None declared.

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