Fibrinolysis, what and how to measure?

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The fibrinolytic system is involved in degradation of the fibrin clot. Furthermore, the fibrinolytic system is important in other processes, such as wound healing, angiogenesis and tumor growth. Activation of the fibrinolytic system immediately starts upon the formation of the fibrin network. Plasmin is formed after binding of plasminogen and its activator, tissue-type plasminogen activator, to partially degraded fibrin. C-terminal lysine residues on fibrin play an essential role for the optimal activation of the fibrinolytic system. Regulation of fibrinolysis occurs via the inhibition of the enzymes of the fibrinolytic system by plasminogen activator inhibitor-1 (PAI-1) or alpha2-antiplasmin (AP). In addition, the C-terminal lysine residues of fibrin can be cleaved off by activated TAFI (thrombin-activatable fibrinolysis inhibitor). Currently, assays are available for all the components of the fibrinolytic system. As with all assays that are performed in a clinical laboratory, it is highly recommended to use well-validated assays that whenever possible are calibrated against international standards. Unfortunately, the relevance of measuring fibrinolytic parameters is limited. Only in rare cases will a disturbance in fibrinolysis lead to a bleeding tendency. Examples are the rare deficiencies in AP, PAI-1 and factor XIII. Also, hyperfibrinolysis such as seen in acute promyelocytic leukemia may cause a bleeding tendency.

The situation in thrombosis is even less clear. There are not many fibrinolytic tests that benefit the thrombotic patient. The relevance of d-dimer in the exclusion of venous thrombosis is without doubt. For other fibrinolytic parameters, there is no consistent pattern in patients with thrombosis. A striking example is the determination of TAFI levels which constitute a risk factor for venous thrombosis. In contrast, in arterial thrombosis both high and low levels of TAFI have been shown to be associated with the disease. Differences in methods and study populations could be reasons for this discrepancy. Therefore, the jury is still out for the relevance of determining individual fibrinolytic parameters for the patient with thrombosis.

Is there no hope for fibrinolytic parameters? Over the last few years a number of studies have investigated the use of overall assays of fibrinolysis. These assays show promise since they show hyperfibrinolysis (in case of thromboelastography) or hypofibrinolysis (in case of so-called ‘clot-lysis’ assays). Hypofibrinolysis has been shown to be an important risk factor for both venous and arterial thrombosis. The relevance of these assays for the individual patient needs further investigation.