

## **Global haemostasis assays: what will be the future?**

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Haemostasis is the result of a complex interplay between the vascular endothelium, and in the blood circulating blood platelets, coagulation factors and anticoagulant proteins. Congenital as well as acquired defects in the haemostatic system may result in a pathological conditions like thrombosis or bleeding disorders.

Growing knowledge of the haemostatic mechanisms went hand in hand with the development of laboratory tests that were aimed at probing the function of the clotting system in order to diagnose haemostatic defects, monitor treatment and predict the risk of thrombotic or bleeding disorders of individuals with defects in the haemostatic system.

Individual risk assessment is a major challenge particularly in individuals with known haemostatic defects. Since both venous thrombosis and bleeding disorders are multifactorial diseases resulting from the complex interplay of genetic and acquired risk factors, screening tests are required that reflect the overall effect of all risk factors.

Classical clotting tests often probe only a limited part of the haemostatic process and therefore do not meet the criteria of a functional test that reflect the overall effect of all risk factors and factors protecting against the disease.

More recently global haemostasis assays were developed that more closely reflect the physiological condition than classical clotting tests and that may find their way to the routine clinical laboratory. Two of these assays (thromboelastography and thrombin generation), which both provide more information of the haemostatic process than routine clotting tests, will be discussed in my presentation.

Thromboelastography measures the physical properties of clot that is formed in whole blood or in platelet-rich plasma (PRP). Although thromboelastographic analysis enables identification of fibrinolytic, thrombotic and bleeding abnormalities, it is most intensively used as a point-of-care test to diagnose bleeding and monitor the transfusion of blood products during cardiac surgery. There are several reports that indicate that thromboelastography may also provide valuable information on the effectivity of treatment of haemophilia patients particularly of patients with acquired FVIII inhibitors.

The thrombin generation assay monitors the formation and inhibition of thrombin in plasma, platelet-rich plasma or whole blood. A high-throughput method, called calibrated automated thrombinoscopy (CAT), enables simultaneous measurement of thrombin generation in 96 plasma samples. Thrombin generation is not only an excellent tool in research laboratories to study coagulation mechanisms in plasma, but is also very useful in pre-clinical studies to test the effects of new drugs *e.g.* anticoagulants or hormonal contraceptives on the coagulation system. Depending on the assay conditions (coagulation trigger and/or presence of thrombomodulin or APC) CAT can be used in thrombophilia screening, in assessing the bleeding risk in haemophilia patients and to monitor treatment.

However, and this is also true for thromboelastography, the use CAT is limited to specialised haemostasis laboratories and the thrombin generation assay is rarely used routine clinical laboratories. The reason for this is that global haemostasis assay are very sensitive for pre-analytical variables (*e.g.* blood collection and plasma preparation) and analytical variables (assay conditions). Rigorous standardization of both plasma collection and test conditions and detailed knowledge on the determinants of the tests will be required for future application of global haemostasis test in clinical practice and to enable fruitful use of thrombin generation assays in the routine laboratory.