Preface

Point-of-Care Testing in Acute Hemorrhagic and Thrombotic States

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Monitoring of the coagulant state in patients who present with acute hemorrhagic or thrombotic conditions can be done by conventional coagulation assays; however, there is increasing attractiveness to the use of point-of-care tests that may yield not only a more rapid result than clinical laboratory testing but may also provide a more complete picture of the condition of the hemostatic system. Most widely used areas of study and application of point-of-care test concern patients who present with massive blood loss (such as in trauma or during major surgery), patients with a hypercoagulable state (such as in sepsis or other systemic inflammatory states), and patients who may need monitoring of antithrombotic treatment for acute coronary syndromes and revascularization procedures.

Point-of-Care Monitoring in Hemostasis and Thrombosis

Monitoring of coagulation in acute patients presenting with thrombotic or hemorrhagic disorders is complex for several reasons. First, in some situations, the routinely available laboratory tests poorly reflect in vivo coagulation. Elongation of global tests such as prothrombin time and activated partial thromboplastin time provides a reflection of overall reduced clotting factor concentrations but do not provide specific and exact information about the origin of the hemostatic defect. Thus, the routinely available tests may overlook large and relevant parts of hemostasis, such as platelet function or endogenous fibrinolysis. Second, routine coagulation assays may be spuriously abnormal in patients with brain injury, antiphospholipid antibodies, or other clinical settings that are not uncommon.

Also, in some situations involving acutely ill patients, conventional coagulation monitoring may simply take too much time. In patients with massive bleeding, for example, after trauma, prohemostatic interventions, such as administration of plasma, factor concentrates, or antifibrinolytic agents, should preferably be guided by insight in the current hemostatic status of the patient. However, results of routine coagulation testing become available only after 30 to 60 minutes, which may be too slow to yield up-to-date clinically useful information as in that time frame, the situation may have changed drastically.

To overcome these limitations of conventional coagulation monitoring, point-of-care coagulation testing has become popular. First, these tests can be done at the bedside, providing quicker and hence more relevant information on the hemostatic status of the patient. Furthermore, some of these assays claim to deliver a better overall picture of the coagulation system, including platelet function, fibrin clot formation, and fibrinolysis. An example of these tests is thrombelastography, which has been available since 1948 but has recently re-emerged in various automated and computerized forms as a point-of-care test. Thrombelastography is a whole blood clotting test in which a small aliquot of blood is rotated in a cuvette and the strength, elasticity, and dissolution of the forming clot are assessed by a torsion wire or by optical detection.[1] By means of several parameters, the various steps in clot formation and degradation can be assessed. By addition of various reagents, specific function of parts of the hemostatic system (e.g., kaolin for measurement of the intrinsic pathway) or the relative contribution of anticoagulants, (e.g., heparinase for the assessment of heparin effects) can be assessed. A widely used variant of thromboelastography is thromboelastometry or rotational thromboelastometry, in which a rotating pin is placed in a cuvette with whole blood and clotting is detected by increasing restriction of rotation of the pin. As the principle and read out of the various thromboelastographic and thromboelastometric techniques are essentially similar, we will only refer to the term thromboelastography (encompassing all different variants) in this article.

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Point-of-care tests may also be used for assessment of the intensity of anticoagulant treatment. Examples are the activated clotting time that is used to monitor heparinization during extracorporeal bypass and handheld devices that can measure the international normalized ratio in patients using vitamin K antagonists, such as the CoaguChek monitor. These devices facilitate management of vitamin K antagonist treatment and may allow for self-management of this therapy avoiding the need for anticoagulation clinics.[2]

Another series of point-of-care tests that gain increasing attention are platelet function analyzers (PFAs).[3] PFA-100 is a test in which citrated blood is channeled through capillaries and a microscopic hole in a membrane, coated with platelet aggregation agonists, such as collagen/adenosine diphosphate or collagen/epinephrine. The high shear stress in the system in combination with the platelet agonists causes platelet adhesion and aggregation and the time to occlude the aperture in the membrane is monitored. This test is useful for the assessment of potential congenital of acquired defects in primary hemostasis. A point-of-care variant derived from conventional light transmission platelet aggregation assays is the PlateletWorks test that is most often used to assess platelet reactivity in patients with acute arterial thrombotic events. In the critical care setting, PFAs are mainly used to evaluate platelet function after administration of various pharmacological platelet inhibitors, for example, in patients with acute coronary syndromes. For this purpose, the VerifyNow system is most widely studied and used in clinical practice. In this system, platelet aggregation is measured in cartridges containing fibrinogen-coated polystyrene beads that agglutinate in proportion to the degree of platelet activation and expression of glycoprotein IIb/IIIa receptors. Platelet aggregation is assessed by its effect on light transmission. There are specific cartridges available for assessment of the action of specific antiplatelet agents, such as aspirin, thienopyridine derivatives, or glycoprotein IIb/IIIa antagonists.

Point-of-Care Tests in Patients Presenting with Bleeding

In patients who present with excessive blood loss, point-of-care monitoring could theoretically be helpful to rapidly assess hemostatic function and to guide transfusion and prohemostatic therapy. There is ample anecdotal evidence and series of observations on point-of-care findings in patients who present with major blood loss but controlled trials demonstrating that point-of-care assessment has a significant impact on clinically relevant outcomes are largely missing. Areas that are studied relatively intensely are trauma, perioperative management of cardiosurgical patients, and postpartum hemorrhage.

Hemorrhage is the second most frequent cause of death in patients with major trauma. Due to massive blood loss, administration of volume expanders, hypothermia, acidosis, and a systemic inflammatory response, a dilutional and consumptive coagulopathy may occur. In this issue of *Seminars in Thrombosis & Hemostasis*, Stein et al explain the concept of goal-directed point-of-care coagulation management in trauma patients and present algorithms which allow a reduction of allogeneic blood product transfusion and an improvement of trauma patient outcome.[4] Wirtz et al then provide an overview on viscoelastic testing in trauma patients.[5]

Perioperative blood loss in cardiac surgery is associated with transfusion requirements, the need for rethoracotomy and mortality. There are many factors affecting the coagulation status in patients undergoing cardiac surgery, including heparin use and platelet dysfunction in extracorporeal circulation, consumption of coagulation factors, and hyperfibrinolysis. The use of point-of-care testing in cardiac surgery is highlighted in the article by Bolliger and Tanaka.[6]

Observations on the application of point-of-care testing, mainly thromboelastography, in postpartum hemorrhage is mostly anecdotal or descriptive. It is important to realize that during pregnancy, thromboelastographic features may differ from the normal situation.[7] Karlsson describes point-of-care findings in patients with normal delivery, postpartum hemorrhage, postpartum hemorrhage with low fibrinogen, placental abruption, and preeclampsia with HELLP (hemolysis, elevated liver [enzymes], low platelet [count]).[8]

Abeysundara et al describe the use of point-of-care testing in liver disease and liver surgery.[9] They conclude that point-of-care–guided transfusion algorithms permit a reduction in blood product administration and are a key component of patient blood management programs. Also, point-of-care testing was better in identifying patients with hypercoagulability compared with conventional coagulation tests.

Hemostatic disorders can have a significant impact on the outcome of neurosurgical patients. Beynon et al report that in patients with acute brain injury, point-of-care test results were associated with relevant outcomes, such as mortality and need for neurosurgical intervention.[10] Also, in elective neurosurgical procedures, point-of-care monitoring was able to provide important information, for example, when unexpected bleeding occurred.

Immediate reversal of anticoagulant treatment may be required in case of major hemorrhage or when an urgent invasive procedure needs to be performed. Especially when using direct oral anticoagulants, reversing anticoagulation may be challenging. Iapichino et al investigated the use of point-of-care testing in patients requiring immediate reversal of anticoagulant treatment and found that these tests provided a quick, before-and-after picture in this clinical setting.[11]

Point-of-Care Testing in Thrombosis and Hypercoagulable States

In critically ill patients, systemic inflammatory responses may lead to activation of coagulation, potentially resulting in thrombosis or thrombotic obstruction of the microcirculation contributing to organ dysfunction. Point-of-care test results were demonstrated to have a good correlation with clinically important organ dysfunction and survival,[12,13] although its advantage over usual coagulation assays has not yet been confirmed.[14]

A similar situation may be present in burn patients. Wiegele et al describe point-of-care test result patterns in patients with severe burns and show the utility of this type of monitoring in this complex clinical setting.[15]

Platelets play a pivotal role in the pathogenesis of arterial thrombosis, such as in acute coronary syndromes or cerebrovascular disease, hence antiplatelet therapy is crucial for treatment and (secondary) prevention of these conditions. The cornerstone of antiplatelet treatment is aspirin, but in many situations, combined antiplatelet treatment (e.g., aspirin plus thienopyridine derivatives) is prescribed.[16] However, the antiplatelet effect of thienopyridines, in particular clopidogrel, is associated with a relatively large interindividual variability. To monitor the antiplatelet effect of these agents, several point-of-care tests that are capable of assessing (residual) platelet reactivity are used.[17] Bergmeijer et al, therefore, report on the adequate level of platelet inhibition as assessed by point-of-care testing following a clopidogrel or ticagrelor loading dose in patients presenting with acute myocardial infarction.[18]

Conclusion

Point-of-care testing is increasingly used in various clinical conditions with major blood loss or thrombosis. The test results look promising and may have a positive impact on clinically relevant outcomes, such as blood product utilization or specific tailoring of treatment. Sound clinical studies employing point-of-care testing in the various clinical settings are required to precisely establish the added value of point-of-care testing over conventional coagulation tests.

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