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Mini Review

The Application of Thromboelastography and Rotational Thromboelastometry in Deep Vein Thrombosis

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ABSTRACT

Deep Vein Thrombosis (DVT) is a common venous thromboembolism disorder and a major cause of hospital-related morbidity and mortality. Comprehensive assessment of DVT related coagulation abnormalities may help to early identify and prevent this life-threatening complication. Conventional coagulation assays lack sufficient information of the clotting of whole blood and are of limited value in the assessment of coagulation status of patients with DVT. In contrast, whole-blood viscoelastic coagulation tests including Thromboelastography (TEG) and Rotational Thromboelastometry (ROTEM) allow rapid identification of coagulation disorders. TEG/ROTEM have shown promising efficacy in identifying patients with increased risk of DVT and are predictive for the occurrence of DVT. Furthermore, TEG/ROTEM has been demonstrated effective in detecting DVT related hypercoagulability and identifying DVT. In addition, TEG/ROTEM may be used to guide anticoagulation therapy in patients with DVT. We suggest the routine use of TEG/ROTEM in combination with other coagulation laboratory tests to enhance effectiveness and improve quality assurance in prophylaxis, diagnosis and management of DVT.

Keywords: Deep vein thrombosis; Thromboelastography; Rotational thromboelastometry; hypercoagulability

INTRODUCTION

Deep vein thrombosis (DVT) is a major global burden that commonly affects the lower limb, with clot formation beginning in a deep calf vein and propagating proximally [1]. It is a common venous thromboembolism (VTE) disorder with a high incidence of nearly 1.6 per 1000 inhabitants each year [1,2]. The incidence of DVT is steadily increasing because of population ageing, a higher prevalence of comorbidities associated with DVT, such as obesity, heart failure and cancer, and the improved sensitivity and widespread use of imaging tests to detect DVT [3,4]. Possible symptoms of DVT usually include extremity pain, swelling, erythema and dilated superficial veins [3]. Compression ultrasonography combined with D-dimer is the first-line test for DVT diagnosis [5,6]. Anticoagulation to prevent clot extension and embolization is the standard treatment for DVT [7]. Coagulation status of patients is generally monitored by Conventional Coagulation Assays (CCAs) including Prothrombin Time (PT), Activated Partial Thromboplastin Time (APTT), Thrombin Time (TT), International Normalized Ratio (INR) and Platelet Count (PLT) to guide the use of anticoagulants. However, challenging complications of DVT such as life-threatening hemorrhage and recurrence after discharge are frequently observed, indicating the poorly monitoring of patients' coagulation status by CCAs [3,5,7]. PT, APTT, TT and INR end with the formation of the first fibrin strand and provide information about clotting factor deficiencies, and PLT reflects the number of platelets [8,9]. They only take snapshots of isolated parts of the coagulation process and lack sufficient information of the clotting of whole blood [10]. Since these plasma-based CCAs may not accurately assess the coagulation status of patients, interest in whole-blood viscoelastic coagulation tests including Thromboelastography (TEG) and Rotational Thromboelastometry (ROTEM) has increased in recent years [11-13]. TEG/ROTEM tests rely upon changes in the viscosity of blood as it coagulates, along with fibrin and platelet-dependent cross-linking between whole blood, to provide information on the sufficiency of hemostasis and detect coagulation defects [14]. The results are displayed in real time and constitute numerical readout for parameters related to time taken to form initial fibrin threads, rapidity of clot formation, and development, strength and stability of the clot

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together with assessment of fibrinolytic phase [11]. TEG/ROTEM have been proven superior to CCAs in many circumstances [11-13], resulting from their performance in whole blood combining all the cellular components of platelets and tissue-bearing cells. In addition, TEG/ROTEM take shorter time (15 min to 2 hours) compared with CCAs (12-24 hours), allowing fast identification of coagulation disorders [15]. Based on these advantages, TEG/ROTEM have been recognized as uniquely useful point-of-care devices in many clinical fields including hemophilia [16], sepsis [17], coronary artery bypass [18], trauma [19], pregnancy and postpartum hemorrhage [20]. Recently, more and more evidence showed the possible use of TEG/ROTEM in prophylaxis, identification or management of venous thromboembolism disorders. Here, we provide an overview of the application of TEG/ROTEM in DVT.

LITERATURE REVIEW

TEG/ROTEM in predicting and assessing the risk of DVT

The major risk factors for the development of DVT include trauma, injury and surgery. These risk factors could lead to dramatic disturbances in coagulation with increased risk of bleeding followed by a hypercoagulable state, which is tightly associated with the occurrence of DVT.2-4 Comprehensive assessment of these coagulation abnormalities, early identification and targeted DVT prophylaxis may prevent this life-threatening complication. In recent decades, the utility of TEG in assessing the risk of DVT among patients has been demonstrated in multiple studies. Brill, et al. [21], conducted a prospective cohort study on 938 trauma patients who were at a high risk of developing DVT. All the patients were evaluated with TEG in admission and ultrasound surveillance for DVT diagnosis. They found that 85% of the patients were tested hypercoagulable by TEG, and hypercoagulable TEG was associated with a significant higher rate of lower-extremity DVT. With the further observation that hypercoagulable TEG predicted DVT with a high sensitivity of 91.9%, they concluded that TEG would be a useful metric for assessing DVT risk. Similarly, a retrospective study on over 1800 patients with severe extremity fractures reveals that Maximum Amplitude (MA) values from TEG ≥ 65 and ≥ 72 are independent predictors of DVT and pulmonary embolus, indicating TEG could effectively identify patients with increased risk of in-hospital DVT and pulmonary embolus [22]. Other studies also showed the predictive role of TEG in DVT. Li, et al. [23], observed patients underwent neurosurgery were at high risk of DVT and TEG was able to predict the occurrence of postoperative DVT to some extent. Furthermore, a clinical study performed TEG on 172 gastric cancer patients after surgery and found the combination of reaction time (R), coagulation time (K), alpha angle (Angle) and MA from TEG was predictive for the occurrence of postoperative DVT [24] These combined results suggest that TEG has the capacity in assessing the risk of DVT and may be used to predict the occurrence of DVT.

TEG/ROTEM in identifying and detecting DVT related hypercoagulability

Patients in hypercoagulable state were demonstrated at particularly high risk for DVT. Early detection and effective monitoring of hypercoagulability are extremely valuable in reducing the incidence of thromboembolic events in surgical or injured patients. It is widely accepted the utility of TEG in identifying hypercoagulability [9,25-27] Park, et al. [26], performed TEG on critically ill and nonbleeding patients with trauma and found TEG was more sensitive than CCAs for the detection of hypercoagulable state in these patients. Spiezia, et al. [28], also reported that ROTEM was a useful tool to detect DVT-related hypercoagulability, particularly for maximum clot firmness and the area under curve values from ROTEM, which significantly correlated with the hypercoagulable state in the acute phase of DVT. In addition, Mao, et al. [9], observed that TEG parameters including Angle, MA, clot strength (G), Coagulation Index (CI) were significantly higher and K was markedly lower in DVT patients compared with healthy individuals, indicating a hypercoagulable tendency in DVT patients, whereas APTT, PT or PLT showed no significant difference between the patients and controls. They further found hypercoagulable TEG had the strongest capacity in identifying DVT compared to CCAs [9]. Moreover, a systematic review and meta-analysis based on 8939 patients showed TEG/ROTEM possessed a great ability to identify hypercoagulability in trauma and operative patients [27]. Interestingly, the study further found among all the TEG parameters, MA was consistently used to both define hypercoagulability and be predictive of VET after traumatic injury and surgical intervention, and it showed satisfactory specificity and sensitivity in identifying DVT [27]. Together, the above researches indicate that TEG is applicable in detecting DVT-related hypercoagulability and can be used as an indicator of DVT.

TEG/ROTEM in the management of DVT

Anticoagulation is the mainstay of treatment for DVT. It aims to reduce mortality, thrombus extension, recurrence, and risk of post-thrombotic syndrome. Options for the prophylaxis or treatment of DVT include low molecular weight heparin, dabigatran, rivaroxaban and apixaban.5 Evidence shows that TEG is significantly more sensitive to the presence of heparin than most other coagulation tests such as APTT, PT or INR [10,29]. In addition, Wu, et al. [30], performed TEG on 205 patients who were receiving low molecular weight heparin anticoagulant therapy in surgical intensive care unit. They observed that the R value of TEG was associated with the occurrence of DVT and hemorrhagic complications in these patients [30]. These results suggest TEG may provide guidance for low molecular weight heparin treatment among patients with DVT. Similarly, Solbeck, et al. [31], reported that the R value of TEG displayed linearity towards fixed concentrations of dabigatran and correlated strongly to the current gold-standard tests Hemoclot and Ecarin clotting time for assessing dabigatran, suggesting TEG is applicable as a rapid and precise whole blood monitoring test for dabigatran treated patients [31]. Though data

regarding the effectiveness of TEG on guidance of anti-coagulation treatment of DVT still lack, these evidence sheds light on the application of TEG in the management of patients with DVT.

CONCLUSION

TEG/ROTEM, unlike CCAs, captures the interactions between cellular components and plasma components of the coagulation cascade and provides simultaneous measurement of multiple aspects of whole-blood coagulation. TEG/ROTEM has shown promising efficacy in assessing the risk of DVT, detecting DVT related hypercoagulability and identifying DVT. Though prospective studies are needed to define the application of TEG /ROTEM in the management of DVT, we believe TEG/ROTEM will receive sufficient validity in clinical and research fields regarding DVT or other thromboembolism disorders. We suggest the routine use of these practical and effective tools in combination with other coagulation laboratory tests to enhance effectiveness and improve quality assurance in prophylaxis, diagnosis and management of DVT.

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