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Thromboelastography and Thromboelastometry in Patients with Sepsis - A Mini-Review

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Introduction

Coagulopathy is a common finding in patients with sepsis and is considered to be a risk factor for mortality [1]. Mechanisms like imbalance between coagulation and fibrinolysis have been attributed to coagulopathy in sepsis. The spectrum of coagulopathy can range from a hypercoagulable state to a hypocoagulable state [2]. Conventional coagulation assays (CCAs) like prothrombin time (PT) and activated partial thromboplastin time (aPTT) are routinely done to assess coagulation status in patients with sepsis. However, these coagulation tests have certain inherent limitations associated with them [3]. These limitations include their inability to detect hypercoagulable state and also cannot assess the fibrinolytic system. Rotational thromboelastography (TEG) and thromboelastometry (ROTEM) evaluate whole clot formation and can be useful point-of-care tests [3]. There is ongoing research to establish the efficacy of TEG/ROTEM over conventional coagulation tests in detection of hypo- or hypercoagulable states in sepsis and in guiding transfusion practices [4].

Basic principles of conventional thromboelastography (TEG®) and thromboelastometry (ROTEM®): [3,4]. The basic principle of functioning is similar in both thromboelastography (TEG®) and thromboelastometry (ROTEM®) with only subtle differences. Rotational thromboelastograph (TEG®) analyzer has a pin and an oscillating cup. However, in thromboelastometry (ROTEM®), the pin rotates and the cup remains fixed. Once blood begins to clot, fibrin strands are formed which influence the movement between the cup and the pin. This process is detected electromechanically and finally presented as a computerized tracing known as the thromboelastograph. Thromboelastograph is a waveform which depicts certain parameters that reflect different phases of the clotting process. These parameters are mentioned below:

An overview of TEG/ ROTEM with terminologies is presented below

A. Clot formation

Reaction time (R): R time represents the time of latency from start of test to the first evidence of clot or initial fibrin (or time taken for clot to achieve an amplitude of 2 mm) and it correlates with the level of clotting factors. In ROTEM®, R time is represented by clotting time (CT).

B. Clot kinetics

K time: K time is a measure of clot strength and it reflects the time taken for clot to reach an amplitude of 20 mm from the start of clot formation. It is recorded from the end of R time. In ROTEM®, K time is represented by clot formation time (CFT).

α angle: α angle is the angle along horizontal axis of thromboelastograph and it measures the speed at which fibrin build up and cross linking takes place. Hence, it assesses the rate of clot formation. α angle is the common terminology for this angle in both conventional thromboelastography (TEG®) and thromboelastometry (ROTEM®).

Either K time (or CFT) and α angle correlate with fibrinogen levels.

i.Clot strength

Maximum amplitude (MA): MA measures the ultimate strength of fibrin clot and correlates with the level of platelets. In ROTEM®, MA is represented by maximum clot firmness (MCF).

ii. Coagulation index (CI)

CI is calculated by a complex mathematical formula calculated from R, K, α and MA and has a normal reference range between -3 to 3. It is an overall indicator of coagulation and

represents hypocoagulable (CI<-3), normocoagulable (CI -3 to 3) or hypercoagulable states (CI >3).

iii. Clot lysis (Fibrinolysis)

A30: A30 is the amplitude at 30 minutes post-MA (in both conventional thromboelastography and thromboelastometry).

Lysis index (CL 30%): CL 30 indicates the percentage decrease in amplitude 30 minutes post-MA. LY 30% represents the lysis index in thromboelastometry.

Estimated platelet lysis (EPL %): EPL is the computer prediction of diminution of amplitude 30 seconds post-MA and it is the earliest indicator of abnormal clot lysis (in both conventional thromboelastography and thromboelastometry).

Hypocoagulability is defined as increased CT/R and CFT/K times and/or decreased MCF/MA and alpha angle.

Hypercoagulability is defined as decreased reaction times (CT/R and CFT/K times) and increased clot formation (increased alpha angle or high maximal amplitude (MCF/MA).

The thromboelastograph parameters are also useful in the diagnosis and management of hypocoagulability and hypercoagulability, identification of primary and secondary hyperfibrinolysis and differentiating between medical and surgical causes of bleeding (Table 1).

Table 1: Diagnosis of haemostatic abnormality based on TEG®/ROTEM® parameters.

Haemostatic Abnormality	TEG®/ROTEM® Parameter		
	R time (or CT)	α angle	MA (or MCF)
No abnormality	Normal	Normal	Normal
Clotting factor deficiency	High	Low/normal	Low/normal
Fibrinogen deficiency	Normal	Low	Low/normal
Low platelet counts	Normal	Normal	Low
Primary hyperfibrinolysis	Normal	Normal	Low
DIC: (Initial) Hpercoagulability with secondary fibrinolysis	Low	High	High
DIC: (Late) Hpocoagulability	High	Low	Low

Studies on the ability of ROTEM® and TEG® to detect sepsis–induced coagulopathy or disseminated intravascular coagulation (DIC)

Results of TEG®/ROTEM® in sepsis have varied widely across the studies. Some patients have shown distinct hypocoagulabilty while others have shown a predominant hypercoagulable pattern. There are several reasons to explain this lack of uniformity in test results. The timing of measurement has varied widely in the studies. The initial phase of sepsis is characterized by formation of microvascular thrombi and the later phase manifests as a hypocoagulant phase secondary to consumptive caogulopathy. So, the timing of measurement has a bearing on test results. This heterogeneity can also be explained by the difference in disease severity of study population. Interestingly, there is no universally validated reference value and definition of hypocoagulability and hypercoagulability of ROTEM®/TEG® in the available studies. Overall, if sepsis-induced coagulopathy was present, ROTEM®/TEG® could detect it in 43-100% patients.

Some of these studies are mentioned below

i. Sivula and co-workers in 2009 assessed the role of thromboelastometry (ROTEM®) in severe sepsis and investigated its applicability in diagnosing sepsis-induced coagulopathy. They studied 28 patients with severe sepsis, out of which 12 patients fulfilled the criteria of overt DIC on admission. A total of 10 healthy persons were taken as controls. MCF, CFT and alpha angle values differed significantly between patients with overt DIC, severe sepsis without DIC and healthy controls respectively (MCF 52, 68 and 63 mm, CFT 184, 73 and 88 sec and alpha angle 58, 76 and 72 degrees respectively). There was a trend towards hypercoagulability in patients with severe sepsis without DIC and a trend towards hypocoagulability in those with overt DIC. They concluded that thromboelastometry can easily demonstrate the coagulation capacity of patients with sepsis [5].

ii. In 2011, Cortegiani and co-workers studied 31 patients with severe sepsis (within 12 hours of diagnosis of severe sepsis) and compared them with 31 postoperative patients by using TEG®. R time, K time, MA, lysis index, and coagulation index were similar between these groups but α angle was significantly lower in the severe sepsis group indicating hypocoagulability in those patients [6].

iii. Kilic and co-workers in 2014 studied 21 patients with SIRS-sepsis and compared them with 34 patients (without SIRS-sepsis). Blood samples were withdrawn on admission and on day 3 of ICU stay for TEG® analysis. In patients with SIRS-sepsis, hypercoagulability was observed in the form of a significantly higher α angle and lower K value as compared to the control group. They concluded that TEG® can be a useful tool for diagnosing coagulation abnormalities in sepsis [7].

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iv. Additional value of ROTEM® and TEG® in diagnosing coagulation abnormalities as compared to CCAs:

Collins and co-workers investigated 38 patients with severe sepsis by performing global tests of haemostasis and compared them with 32 controls. They found that although patients with severe sepsis had a delayed activation of haemostasis but once initiated, thrombin generation and clot formation were normal or even enhanced in this group. Routine coagulation assays, which measure only the initiation of clotting process and not its propagation, poorly evaluate the coagulation capacity of such patients [8].

v. Luckner and co-workers in 2008 studied a case series of patients with severe sepsis and septic shock who were planned for emergency laparotomy. All patients had significantly prolonged coagulation times with a putatively increased risk of bleeding as per the routine coagulation assays. On the contrary, ROTEM® revealed normal clotting times and even signs of hypercoagulability in these patients (unlike CCAs) and surgery could be performed with minimal blood loss and no transfusions [9].

vi. Involvement of fibrinolytic system can also be detected by TEG® and ROTEM® (unlike CCAs). Adamzik and co-workers in 2010 studied 56 patients with severe sepsis and compared them with 52 postoperative patients (controls). Blood sampling for thromboelastometry (ROTEM®) was done within 24 hrs of diagnosis of severe sepsis and immediately after surgery in postoperative patients. CRP, procalcitonin (PCT), IL-1 levels, SAPS II and SOFA scores were simultaneously analyzed. ROTEM® parameters like CT, CFT, α angle and MCF were similar between these groups but lysis index was significantly increased indicating an early involvement of fibrinolysis in patients with severe sepsis [10].

Role of ROTEM® and TEG® for anticoagulant treatment in sepsis

There are only few studies attending to this area with very small series of patients [11].

Role of ROTEM® and TEG® in prediction of outcome in sepsis

Hypocoagulability has been found to be an independent predictor of poor outcome in some studies as mentioned below:

I. Daudel and co-workers in 2009 studied 30 patients with sepsis. Routine clotting tests and thromboelastometry (ROTEM®) were done every 12 hrs during first 48 hrs of admission, and finally at discharge from ICU. It was observed that patients with more severe organ failure (SOFA>10) had higher CFT (125±76 sec vs 69±27 sec) and lower MCF (57±11 mm vs 69±27 mm) as compared to those with less severe organ failure (SOFA<10). The values changed significantly with the intensity of sepsis. Improved organ dysfunction upon discharge from ICU was associated with shortened coagulation time, accelerated clot formation and increased firmness of blood clot [12].

II. Adamzik and co-workers in 2011 performed a study in 98 patients with severe sepsis to investigate the role of thromboelastometry (ROTEM®) as a potential predictor of 30-day survival in severe sepsis and compared ROTEM® with simplified acute physiology II (SAPS II) and SOFA scores. CT, CFT, α angle, MCF and SAPS II and SOFA scores were recorded on the day of diagnosis of sepsis. Mean CFT was significantly prolonged (276 ± 194 sec vs. 194 ± 109 sec) and both MCF (52.7 ± 12.1 mm vs. 57.3 ± 11.5 mm) and α angle (53.4 ± 12.8 degrees vs. 58.9 ± 11.8 degrees, P = 0.028) were significantly reduced in non-survivors. SAPS II and SOFA scores were not different between survivors and non-survivors [13].

III. Ostrowsky and co-workers in 2013 studied 50 patients with severe sepsis. Patients were divided into 3 groups on the basis of MA value of TEG® on admission: hypocoagulable MA, normocoagulable MA or hypercoagulable MA. Patients progressing to hypocoagulability had higher SOFA and DIC scores and they also showed a higher early mortality [14].

Conclusion

In summary, both thomboelastography (TEG®) and thromboelastometry (ROTEM®) seem to have a promising role in the evaluation of coagulation abnormalities in sepsis. But the available studies in sepsis show heterogeneous results and are of limited quality [4].

TEG/ROTEM measurements in sepsis can show both hypo- and hypercoagulability. Hypercoagulability is seen more in acute phase of sepsis. Timing can influence the results because sepsis is a dynamic process. Sequential measurements of TEG/ROTEM can enlighten us more about coagulation derangements associated with sepsis. The current evidence is limited due to heterogeneity, small sample size, lack of standardized definitions for hypo- and hypercoagulable states. Larger trials can establish the utility of TEG/ROTEM to detect coagulation abnormalities to diagnose DIC and to guide transfusion therapy.

References

1. Levi M, Cate HT (1999) Current concepts: Disseminated intravascular coagulation. N Engl J Med 341: 586-592.
2. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, et al. (2013) Surviving sepsis campaign: International guidelines for management of severe sepsis and septic shock. Intensive Care Med 39(2): 165-228.
3. Bollinger D, Seeberger MD, Tanaka KA (2012) Principles and practice of thromboelastography in clinical coagulation management and transfusion practice. Transfus Med Rev 26(1): 1-13.
4. Müller MC, Meijers JC, Vroom MB, Juffermans NP (2014) Utility of thromboelastography and/or thromboelastometry in adults with sepsis: a systematic review. Crit Care 18(1): R30.

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5. Sivula M, Pettila V, Niemi TT, Varpula M, Kuitunen AH (2009) Thromboelastometry in patients with severe sepsis and disseminated intravascular coagulation. Blood Coagul Fibrinolysis 20(6): 419-426.

6. Cortegiani A, Marino L, Montalto F, M Milana, A Di Benedetto, et al (2011) Use of thromboelastography in severe sepsis: a case-control study [abstract]. Crit Care 15(Suppl 1): 444.

7. Kilic Y, Topcu I, Bambal H, Civi M (2014) Thromboelastography in the evaluation of coagulation disorders in patients with sepsis. Turk J Med Sci 44(2): 267-272.

8. Collins PW, Macchivello LI, Lewis SJ, Macartney NJ, Saayman AG, et al. (2006) Global tests of haemostasis in critically ill patients with severe sepsis syndrome compared to controls. Br J Haematol 135(2): 220-227.

9. Luckner G, Mayr VD, Fries DR, Innerhofer P, Jochberger S, et al. (2008) Uncovering hypercoagulability in sepsis using ROTEM® thromboelastometry: a case series. The Open Critical Care Journal 1: 1-6.

10. Adamzik M, Eggmann M, Frey UH, Görlinger K, Bröcker-Preuss M, et al. (2010) Comparison of thromboelastometry with procalcitonin, interleukin 6, and C-reactive protein as diagnostic tests for severe sepsis in critically ill adults. Crit Care 14(5): R178.

11 Altmann DR, Korte W, Maeder MT, Fehr T, Haager P, Rickli et al. (2010) Elevated Cardiac Troponin I in Sepsis and Septic Shock: No Evidence for Thrombus Associated Myocardial Necrosis. Plos One 5(2): e9017.

12. Daudel F, Kessler U, Folly H, Lienert JS, Takala J, et al. (2009) Thromboelastometry for the assessment of coagulation abnormalities in early and established adult sepsis: a prospective cohort study. Crit Care 13(2): R42.

13. Adamzik M, Langemeier T, Frey UH, Görlinger K, Saner F, et al. (2011) Comparison of thrombelastometry with simplified acute physiology score II and sequential organ failure assessment scores for the prediction of 30-day survival: a cohort study. Shock 35(4): 339-342.

14. Ostrowski SR, Windelov NA, Ibsen M, Haase N, Perner A, et al. (2013) Consecutive thrombelastography clot strength profiles in patients with severe sepsis and their association with 28-day mortality: a prospective study. J Crit Care 28(3): 317.

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