Evaluation of coagulation stages of hemorrhaged swine: comparison of thromboelastography and rotational elastometry

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Thromboelastography (TEG) or rotational thromboelastometry (ROTEM) assesses blood viscoelastic properties and clotting kinetics that can be measured by Haemoscope TEG and Pentapharm ROTEM devices using slightly different methodologies. These devices were compared by measuring blood samples associated with various degrees of coagulopathy. Blood samples, collected from swine undergoing three types of severe injury and resuscitation protocol resulting in normal, hypercoagulopathy, and hypocoagulopathy, were assessed with TEG or ROTEM before the surgical procedures, and after injury, fluid resuscitation, and simulated hospital phase. Standard clotting parameters were compared by Student's *t*-test at a significance of a *P* value less than 0.05. Regression analysis indicated a positive correlation between TEG and ROTEM for reaction time (*R*), clotting rate (*K*), and maximum amplitude (M_a) parameters. With samples of normal coagulation, *R* (440 ± 136 vs. 391 ± 73 s), *K* (99 ± 39 vs. 81 ± 20 s), and M_a (74 ± 4 vs. 69 ± 5 mm) were higher, whereas (α) (68 ± 8 vs. 75 ± 3 mm) was lower with TEG than ROTEM, respectively; a *P* value is less than 0.05. The magnitude of changes from baseline in hypercoagulable or hypocoagulable samples due to level of injury was equivalent with TEG and ROTEM indicating comparable use of the instruments. However, when samples were extremely hypocoagulopathic due to resuscitation fluid, the TEG values could not be readily determined. Overall, TEG readings were higher than ROTEM readings; this disparity between the two instruments was attenuated with hypercoaguable samples. Both devices yielded similar information regarding the status of coagulation related to trauma. Because of operating characteristics, the same instrument should be used for monitoring the same patient or study. *Blood Coagul Fibrinolysis* 21:20–27 © 2010 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Introduction

Understanding the coagulation process (kinetics of clot formation, stability, and lysis) relies on measurement of in-vitro parameters offering diagnostic value for the detection of coagulation, hemostasis, or thrombosis abnormalities. First demonstrated in 1948, thromboelastographs visualized fibrin polymerization [1]. The technique was unpopular due to its variability until its computerization [2] and demonstration of its benefit during hepatic surgeries to monitor blood components [3]. Integration of software-controlled rotation and data collection have facilitated the attainment of reliable quantitative data for measuring in-vitro parameters representative of clot dynamics that might occur *in vivo*. In recent years, thromboelastography (TEG) and rotational thromboelastometry (ROTEM) have been increasingly refined and commonly used as measures of hemostasis for a variety of procedures in clinical settings [4]. TEG, using TEG-5000 (Haemoscope, Niles, Illinois, USA), is a popular technique for measuring in-vitro parameters. This machine operates on pin/wire transduction methodology to record a clotting curve representative of clot formation, strength, and breakdown by fibrinolysis. Recently, a new device based on ROTEM, (ROTEM; Pentapharm GmbH, Munich, Germany), uses alternative pin rotation and recording mechanisms. Each machine has been designed to measure the clotting curve and give quantitative results in the form of common in-vitro parameters. Since the 1980s, results have been predominantly reported using TEG [4,5], and it is likely that with the introduction of ROTEM, both machines will be used in parallel as laboratory and clinical diagnostic tools [6]. This practice may require comparison of parameters generated on each instrument, particularly for laboratories having

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experience with only one of the devices. As such, it is important to understand how interchangeable the data are between the two machines, and also to justify the interpretation of the results using the respective instruments. Having a foundation regarding the quantitative differences between TEG and ROTEM can help prevent variations in research data and potential errors in treatment in clinical settings.

Recently, Nielsen [6] reported findings using both devices with human blood samples that were artificially prepared to offer hypocoagulopathic or hypercoagulopathic properties. In a similar manner, we routinely assess swine blood samples originating from animals undergoing severe injuries and fluid resuscitation procedures, thus presenting various stages of actual clinical coagulopathy. We used this opportunity to compare clinical blood samples with various degrees of coagulopathy, ranging from normal, to hypercoagulopathic, or hypocoagulopathic, using TEG or ROTEM.

Materials and methods

Elastography

TEG and ROTEM operate on slightly different principles in how they execute and record the formation of a thromboelastograph. They have been described previously for monitoring clot formation, stability, and lysis [4]. TEG measures clotting parameters using shear elastic modulus that relies on a cylindrical cup oscillating through a 4°45' angle for 5 s. When the clot is initiated, the motion is transmitted to a pin and further converted into an electrical signal. ROTEM measures these parameters using a fixed cup and a mobile pin supported by a ball bearing mechanism and oscillating through a 4°75' angle for 6 s. The rotation of the pin is recorded optically using a charge-coupled device (CCD) image sensor system.

Blood samples

Fresh swine blood samples were collected from Yorkshire swine in 3.8% sodium citrated vacutainers (Becton Dickinson, Franklin Lakes, New Jersey, USA). The samples were processed within 60 min. In the case of TEG, 20 μl of $CaCl_2$ was added in the cup followed by 340 μl of whole blood and mixed once and run for approximately 1 h. In the case of ROTEM, we deviated from the recommended procedure (Table 1) by adding 17.7 μl $CaCl_2$ to the cup followed by 300 μl of whole blood and mixed once. However, this keeps the ratio of blood to $CaCl_2$ constant (ratio = 18) in both systems (rather than the 20 μl $CaCl_2$ recommended by the manufacturer). All tests were performed in parallel on the TEG and ROTEM instruments at 37°C using native blood. After loading, the cup was engaged to the pin, this denoted the initiation of the test.

Instrumentation

TEG consisted of two TEG-5000 devices (Haemoscope) (two channels/device) allowing four usable channels that were connected to a laboratory computer (Software version 4.2.97). One ROTEM device (ROTEM gamma; Pentapharma) offers four channels linked to a separate but dedicated computer running with a software version 1.0.04. Both instruments (TEG and ROTEM) used disposable cups and pins specific to the instrument and 0.2 mol/l $CaCl_2$ for blood recalcification. Both machines were periodically checked and maintained to operate within the manufacturer's specified range. The TEG was monitored by using hypercoaguable and hypocoaguable plasma controls. Channel baselines were adjusted if they fell out of range. ROTROL-N plasma standards were used as native samples (NATEM) for quality control of ROTEM. Differences between these devices and running conditions are listed in Table 1(a).

The blood samples were tested as native blood and were not spiked with activators or blockers to detect deficiency.

Clot kinetics parameters

We compared four classical parameters with both devices (Table 1b):

Table 1 Comparative characteristics between thromboelastography and rotational elastometry

(a) Characteristic	TEG	ROTEM	
Pipetting	Manual	Automated	
Cup motion	Moving	Fixed	
Pin motion	Fixed	Moving	
Angle of rotation	4°45/5 s	4°75/6 s	
Detection	Pin transduction	Impedance of rotation	
Temperature control (°C)	24–40	30–40	
Temperature regulation	Heated cup	Heated metal block	
Cup interior	Smooth	Ridged (thickness 0.6–0.9 mm)	
Cup material	Cryolite (acrylic polymer)	Polymethylmethacrylate	
Usage	**Recommended**	**Recommended**	**Modified[a]**
Pipetting	NA	Automated	Manual
Blood volume (μl)	340	300	300
$CaCl_2$ volume (μl)	20	20	17.7
Ratio blood/$CaCl_2$	18	16	18

(b) TEG	ROTEM	Functional parameter description
R	CT	Time from addition of activator to 2-mm amplitude
K	CFT	Time between 2 and 20-mm amplitude
Angle	α	At the 2-mm point, the angle is the tangent to the curve
M_a	MCF	Maximum amplitude reached by the clotting curve
Lys30	LI30	A measure of fibrinolysis up until 30 min

(a) Major mechanical differences and variation in sample testing between TEG and ROTEM devices. (b) Names and descriptions of the measured coagulation parameters. CFT, clot formation time; CT, clotting time; MCF, maximum clot firmness; NA, not applicable; ROTEM, rotational thromboelastometry; TEG, thromboelastography. [a]Note the deviation from manufacturer recommendations for ROTEM.

(1) the reaction time (R) or clotting time measures the time for initial fibrin formation;
(2) the kinetics (K) indicates the initial clot formation, indicated by 2 mm of amplitude, or clot formation time, which is the time between 2 and 20 mm of amplitude and represents the rate of clot formation;
(3) the angle (α) between the baseline and a tangent to the curve running through the 2-mm amplitude point; and
(4) the maximum amplitude (M_a) or maximum clot firmness (MCF) is the amplitude reached by the clotting curve prior to fibrinolysis (Lys).

Animal models and blood sampling

The experiments reported herein were conducted according to the principles set forth in the *Guide for the Care and Use of Laboratory Animals*, Institute of Laboratory Animals Resources, National Research Council, National Academy Press; 1996. The study was approved by the Naval Medical Research Center/Walter Reed Army Institute of Research Institutional Animal Care and Use Committee; all procedures were performed in an animal facility approved by the *Association for Assessment and Accreditation for Laboratory Animal Care International.*

Anesthetized (ketamine/isofluorine) and instrumented (carotid and jugular catheters) Yorkshire swine (Animal Biotech Industries, Danboro, Pennsylvania, USA) were used in three surgical procedures inflicting various degrees of severity that were described previously: hemorrhagic shock by liver injury (LIV) [7], traumatic brain injury (TBI) [8], and vascular injury (VAS) [9]. The blood samples collected at various time points during these three different experimental procedures represent different stages of hemostasis. At time 0 (T0), the samples represented normal baseline blood before intervention.

(1) In the TBI model ($n = 10$), after all craniotomy sites were prepared, a fluid percussion injury was inflicted in the standard fashion by means of a weighted mallet allowing it to create an impact on the animal's forehead. At 15 min (T15), care was provided by bolus infusion (4 ml) of recombinant factor seven (rFVIIa). At 60 min (T60), a last blood sample was collected (T60). As no severe hemorrhage occurred in this TBI protocol, no large volumes of resuscitation fluid were given and there was no hemodilution.
(2) A grade III LIV ($n = 8$) was performed by lobe crush to produce an uncontrolled bleeding; at T15 after blood sample collection, a hemoglobin-based oxygen carrier (HBOC-201; Biopure, Cambridge, Massachusetts, USA) resuscitation fluid was infused and another blood sample was collected at the end of the resuscitation phase (T60). The animals were recovered, and at 24 h (T1440), a last sample was collected from HBOC-201-treated animals that did not require blood transfusion at this time point; thus, the full effect of the infusion fluid and hypocoagulation was apparent.
(3) In the VAS model ($n = 11$), hemorrhage was created by puncture of the femoral artery. After 45 s of free bleed, a hemostatic dressing was placed on the wound, and at T15, the animal received 500 ml of Hextend (HEX, Hospira, Emeryville, California, USA) over 30 min as resuscitation fluid. At T60, the final blood sample was collected.

These three models supported larger studies with endpoints beyond 60 min at which time all animals were euthanized by injection (100 mg/kg) of Euthasol solution. However, only a few samples were being compared on TEG and ROTEM for the purpose of this study and referred as the test population (t).

Several stages of coagulation could be obtained from these various procedures and times of blood sample collection. Blood collected at T0 was an indication of normal coagulation. At T15, after injury and before resuscitative treatment, injury was anticipated to result in hypercoagulation; at T60, after fluid resuscitation (in LIV and VAS), hemodilution was present likely causing hypocoagulation; at T1d, the animals were left to recover but cogulopathy caused by physiologic abnormalities could be observed. Because rFVIIa was tested in TBI, this offered an opportunity to examine a state of possible hypercogulation mediated by the procoagulant. Blood samples were also assessed for complete blood count profile (Pentra 60 C+; HoribaABX, Irvine, California, USA) and standard coagulation prothrombin time (PT; Diagnostica Stago, Parsippany, New Jersey, USA).

Data analysis

Data on the four parameters was collected from the TEG and ROTEM instruments and was grouped according to the time point and the protocol from which the blood was taken. Samples for the comparative TEG–ROTEM study (test population) were derived from a larger physiology study (parent population), and the test and parent populations were compared using comparison of the mean Student's t-test. Data are presented as average and standard deviation for each time point group. A paired two-tailed Student's t-test was used to assess the differences between the TEG and ROTEM data sets. Linear regression was performed between TEG and ROTEM parameters. The level of significance was at a P value of less than 0.05.

Results

Severity of injury: information about the model

In the parent population (p), rate of blood loss was initially less in LIV than VAS injury group, but LIV animals bled longer and eventually the hemorrhage volume at T15 exceeded that of the animals in the

Table 2 Blood loss and survival in three injury models

	Blood loss at injury		Survival			
	Initial rate (first 5 min)	Shed volume (at 15 min)	Rates			Time
Injury	ml/min	% EBV	T15	T60	T1440	min
TBI t	0	0	10/10	10/10	N/A	60
TBI p	0	0	20/20	20/20	N/A	60
LIV t	80.6 ± 13.3	30.0 ± 7.6	6/6	8/8	8/8	1440
LIV p	74.7 ± 31.3	27.2 ± 9.0	36/36	36/36	36/36	1440
VAS t	507 ± 133	21.2 ± 7.6	10/11	9/11	N/A	54.2
VAS p	462 ± 128	18.8 ± 5.1	64/65	58/65	N/A	56.7

LIV, grade III liver injury; TBI, traumatic brain injury; VAS, groin vascular injury. t denotes the test population and p the parent population.

VAS group (Table 2). TBI animals were not hemorrhaged. Survival at T60 in the VAS group was 89% (58/65 in the parent population) compared with 100% for the other two groups. We confirmed that the test population (t) was a representative sampling of the parent population (p) regarding these indices in all three models. This allows ranking the VAS injury model as the most severe, followed by LIV, and finally TBI models.

Systemic coagulation in relation with the resuscitation regimen

Timely changes in the hematocrit (Hct) and platelet count (PLT) of the blood samples are shown for the three experimental groups in Table 3. Hct and PLT remained similar from T0 to T15, regardless of the injury. Differences were observed at T60 when Hct and PLT were significantly reduced ($P < 0.05$) in LIV and VAS protocols compared with T0 due to fluid resuscitation. This hemodilution contributed also to elevated PT. In contrast, use of rFVIIa in TBI caused a reduction of PT at T60 ($P < 0.05$) compared with baseline, indicating induced possible hypercoagulation. At T1440 in the LIV group, Hct and PLT were still significantly reduced and PT was elevated. This allows categorizing T60 samples for LIV and VAS as hemodiluted, but still under influence of the injury and thus likely to be coagulopathic. The T60 samples in the TBI group were likely hypercoagulopathic due to the injury, no resuscitation fluid, and the presence of FVIIa. The T1440 samples in LIV were still highly hemodiluted and did not receive a blood transfusion, and were thus likely to be hypocoagulopathic.

Effect of treatment on clotting parameters

Results for the all TEG parameters are presented in Table 4 for the different groups at different time points of the experimental procedure. All parameters from the test population were comparable to those of the parent population (data not shown).

At T0, blood samples were identical to normal swine blood and were similar for all treatment groups when measured on each instrument (TEG or ROTEM). These values represent baseline parameters and were averaged in Table 4. When compared between devices, the R, K, and M_a parameters were higher and α was lower with TEG than ROTEM ($P < 0.05$, paired t-test) in all the three injury models. The same numerical pattern was observed at T15 and at T60 in the various groups with various levels of significance. At T1440 in the LIV group, there was a difference between TEG and ROTEM. However, 50% of the samples did not react with TEG or showed abnormally long R, which caused abortion of the test. Lys was the least affected parameter at all time points. Apart from the paired differences seen between TEG and ROTEM samples, parameter values varied according to injury and treatment. At T15, R and K parameters were reduced from T0 when measured with both TEG and ROTEM instruments. These values were significant for TBI and VAS when measured with ROTEM ($P < 0.05$), but not for LIV. All other parameters were unchanged. At T60, R was unchanged from T15 in all groups. K, α, and M_a were unchanged for TBI but were increased (K) or decreased (α and M_a) for VAS and LIV, but only with a higher significance when measured with ROTEM ($P < 0.01$). At T1440, R and K parameters

Table 3 Hematologic parameters for the test population

Protocol	Hct (%)				PLT (10^6/ml)				PT (s)			
Time	T0	T15	T 60	T 1440	T0	T15	T60	T 1440	T0	T 15	T 60	T 1440
TBI	29 ± 3	29 ± 4	29 ± 3	N/A	368 ± 103	353 ± 102	345 ± 102	NA	14 ± 1	13 ± 2	11 ± 2*	NA
LIV	28 ± 3	26 ± 2	12 ± 4*	17 ± 3*	391 ± 99	344 ± 87	211 ± 86*	161 ± 45*	14 ± 1	14 ± 1	16 ± 3*	16 ± 3*
VAS	25 ± 2	23 ± 2	17 ± 4*	NA	331 ± 94	344 ± 94	197 ± 78*	NA	14 ± 1	14 ± 1	15 ± 2*	NA

Hct, hematocrit; LIV, liver injury; NA, not applicable; PLT, platelet count; PT, prothrombin time, of blood sample collected at various time during three different protocols; TBI, traumatic brain injury; VAS, vascular injury. * Indicate $P < 0.05$ between the selected time point and T0 for a given protocol.

Table 4 Experimental parameters

TBI-VAS-LIV	R (s)	K (s)	α (°)	M_a (mm)	Lys30
Parameters from test population during experimental course					
Baseline T0					
TEG	440 ± 136	99 ± 39	68 ± 8	74 ± 5	2.2 ± 1.2
ROTEM	391 ± 73*	81 ± 20*	75 ± 3*	69 ± 4*	2.2 ± 1.3
P	<0.05*	<0.05*	<0.001*	<0.001*	NS
TBI T15					
TEG	326 ± 71	81 ± 28	70 ± 10	74 ± 4	1.8 ± 0.8
ROTEM	316 ± 69#	66 ± 12	76 ± 5*	70 ± 4	1.8 ± 1.1
P	NS	NS	<0.01*	NS	NS
Significance from T0	<0.01#	NS	NS	NS	NS
TBI T60 with FVIIa					
TEG	321 ± 73	85 ± 27	73 ± 4	74 ± 3	2.0 ± 0.8
ROTEM	309 ± 79	72 ± 20	76 ± 4*	72 ± 5	1.5 ± 1.4
P	NS	NS	<0.05*	NS	NS
Significance from T15	NS	NS	NS	NS	NS
VAS T15					
TEG	311 ± 122	84 ± 35	71 ± 7	72 ± 5	3.5 ± 1.0
ROTEM	276 ± 43#	68 ± 13#	77 ± 3*	70 ± 5	3.0 ± 1.3
P	NS	NS	<0.05*	NS	NS
Significance from T0	<0.01#	<0.01#	NS	NS	NS
VAS T60					
TEG	280 ± 54	101 ± 27	67 ± 6#,1	63 ± 7#,1	3.7 ± 1.2
ROTEM	289 ± 52	109 ± 33#	69 ± 5#,2	56 ± 9*,#,2	2.5 ± 1.8
P	NS	NS	NS	<0.05*	NS
Significance from T15	NS	<0.01#	<0.05#,1, <0.01#,2	<0.05#,1, <0.01#,2	NS
LIV T15					
TEG	404 ± 125	93 ± 40	69 ± 8	73 ± 4	1.8 ± 0.7
ROTEM	358 ± 76	76 ± 25	75 ± 5	68 ± 4*	2.4 ± 2.5
P	NS	NS	NS	<0.05*	NS
Significance from T0	NS	NS	NS	NS	NS
LIV T60					
TEG	365 ± 98	105 ± 30	65 ± 6	61 ± 7	2.3 ± 1.1
ROTEM	358 ± 62	115 ± 48#	68 ± 8#	52 ± 9*	2.7 ± 2.2
P	NS	NS	NS	<0.05*	NS
Significance from T15	NS	<0.05#	<0.05#	<0.01#	NS
LIV T1440 Hemodil					
TEG	2362 ± 2231#	274 ± 156#	60 ± 15	67 ± 19	0.2 ± 0.4
ROTEM	648 ± 229*,#	188 ± 95#	55 ± 17	71 ± 11#	1.0 ± 1.4
P	<0.05*	NS	NS	NS	NS
Significance from T60	<0.01#	<0.01#	NS	<0.01#	NS

Summary of the reaction time (*R*), clot kinetics (*K*), angle (α), maximum amplitude (M_a), and lysis at 30 min (Ly30) with ± SD for two TEG machines using blood collected from three protocols at varied time points. FVIIa, factor VIIa; LIV, liver injury; NS, not significant; ROTEM, rotational thromboelastometry; TBI, traumatic brain injury; TEG, thromboelastography; VAS, vascular injury. * Indicates significant differences (paired Student's *t*-test) between values from TEG and ROTEM. # Indicates significant differences (paired Student's *t*-test) between T0 and other time points. [1] Indicates level of difference from T0 for TEG. [2] Indicates level of differences from T0 for ROTEM.

were significantly different ($P < 0.01$) from T60 with the two instruments.

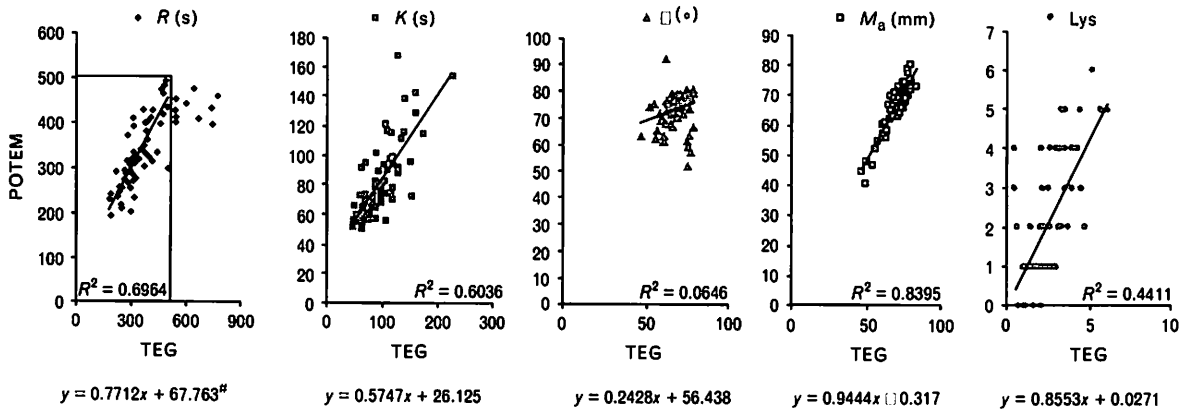
Correlation between thromboelastography and rotational thromboelastometry

A linear regression was performed between the TEG and ROTEM's *R*, *K*, α, M_a, and Lys parameters (Fig. 1). Despite the important variation around TEG data, there was a significant positive correlation for *R*, *K*, and M_a ($P < 0.01$), with the TEG parameters being higher as indicated by the slope. Alpha showed no correlation. Interestingly, when samples were highly hypocoagulopathic, *R* values were more than 500 s and *K* values were above 200 s with TEG, suggesting that TEG will not determine initial coagulation and give abnormal values.

Discussion

Definition of coagulopathy can be complex, and diagnostic decisions made solely on a single assay can be misleading. Diagnosis of clinical coagulopathy is usually based on abnormal PT or international normalized ratio (INR) (derived from PT). These indices are greatly affected by anticoagulant (e.g. warfarin that increases PT [10]), or procoagulant (e.g. rFVIIa that reduces PT [11]) and do not necessarily indicate a clinical condition of serious coagulopathy. It is clear that a patient's coagulation diagnoses should rely on more than one test. Lately, TEG has provided additional information for the detection of clinical clotting [3,4,13]. Its rapid execution has made it a valuable assay to document coagulation and hemostasis at the bedside [14,15]. Coakley *et al.* [12] showed that clinical coagulation management in liver transplanted patients may vary depending on the TEG or ROTEM diagnostics tools used. It is more and more likely that test results will be compared on the two current instruments – TEG and ROTEM – for analytical measurement of clot dynamics. Therefore, the present study compared values of clotting characteristics of blood samples with various degrees of clinical coagulopathy using both devices.

Fig. 1



Correlation between all measurement from thromboelastography and rotational elastometry parameters R, K, α, M_a, and fibrinolysis. Level of significance ($P < 0.01$) was found for R, K, M_a, and Lys. Regression coefficients and slopes are indicated. # refers to the regression of points included in the box. α, angle; K, kinetics; Lys, fibrinolysis; M_a, maximum amplitude; R, reaction time; ROTEM, rotational thromboelastometry; TEG, thromboelastography.

Overall, the findings indicated that TEG generated higher R and K values and a lower α than ROTEM, leading to an interpretation toward hypocoagulation for native whole blood samples. This confirms results from Nielsen [6]. Reasons for this difference are probably related to the equipment function (thickness of the cup, surface contact, electrostatic charge of the plastic, and pin motion) as stated by Nielsen [6]. M_a was consistently higher with TEG, not always reaching significance, but this difference was particularly noticeable on baseline samples. However, in the absence of platelets in Nielsen's [6] study, M_a was significantly lower with TEG. This may be due to stronger activation of platelets by the rotational movement and the nature of the plastic of the TEG cup and pin. In the present study, the plasmatic response (fibrin clot) could have been obtained by neutralization of the platelet component using GPIIb/IIIa membrane blocker, but this was not part of this study. In hypercoagulopathic samples (after injury), the R absolute values were smaller and the differences between TEG and ROTEM were attenuated compared with native. For most hypocoagulopathic conditions representing less fibrin polymerization, kinetic values also exhibited a trend towards higher K or lower α values with TEG as compared with ROTEM. With substantial hypocoagulation as observed at T1440, initiation of coagulation failed numerous times with TEG, pushing R towards infinity, whereas finite high R and K values were obtained with ROTEM. Despite this severe hypocoagulation, animals survived to the hospital phase [16]. At T60 in LIV and VAS groups when resuscitation fluid was given, we saw significant differences from the previous state (increased K and decreased α) with ROTEM only. The high variability in TEG measurements prevented data between different stages of the experiment from reaching statistical significance. Numerical differences between TEG and ROTEM were noticeable and showed a strong correlation for R, K, and M_a parameters. The Lys parameter was similar on both instruments regardless of the state of coagulation in this study. Offering a more robust construction, the ROTEM instrument was less subject to external shock leading to less motion changes in the cup and pin coupling.

Nielsen [6] previously compared TEG and ROTEM. Despite the major methodology differences, Nielsen used human plasma, whereas we used swine whole blood, both studies supported the fact that TEG readings tended towards hypocoagulation on native samples [higher R, K (or lower α), and M_a]. However, in the Nielsen study, TEG and ROTEM yielded equivalent results following activation of human samples with celite. Had we used celite or kaolin this might have resulted in similar findings. Other variations in Nielsen's method reside in the fact that they utilized in-vitro activated prediluted samples from human origin, whereas the present study assessed ex-vivo native blood samples directly collected on experimental animals induced to various degrees of coagulopathy. In both studies, the ratio of $CaCl_2$ to blood or plasma was the same, but Nielsen used 340 µl as compared with 300 µl used here in ROTEM cups. Also, the R values of human blood were lower than native porcine blood at T0, confirming that swine blood is more hypercoagulable.

The animal models used here were relevant to military trauma, including organ injury or hemorrhagic shock and their respective resuscitative management. Therefore, the collected blood represented relevant hypercoagulable or hypocoagulable stages associated with relevant military trauma scenarios. A limitation in this study is that the state of coagulopathy obtained may differ from

patients with other disorders. However, TEG techniques supplement PT or the INR. Regarding coagulopathy caused by these protocols, TEG and ROTEM both yielded the same interpretation of the results. They indicated that the vascular injury (the model with the most rapid bleeding rate) induced the maximum hypercoagulopathy. T15 and T60 parameters were comparable in TBI model despite the fact that rFVIIa was administrated in this model. The VAS group exhibited a reduced R value at T60, indicative of a high rate of thrombin formation, and an elevated K (or decreased α) and M_a resulting from the hemodilution (predicted by decreased Hct and PLT). This hemodilution was similar to that in the LIV model inducing hypocoagulopathy by dilution of the factors and platelets.

Kheirabadi *et al.* [10] used TEG to address measurement of various levels of induced coagulability in splenic injury in an in-vivo rabbit model. This study indicated that at 2 h after injury, R and K values increased with dilution, whereas only R increased and K decreased after warfarin injection. The authors indicated that V_{max} (related to K) was a sensitive predictor of coagulopathy. Comparably, we found that the kinetics of clotting, or K, may be a better indicator of hypocoagulation following dilution, whereas R reflected a hypercoagulable state as observed in trauma. Recently, Jackson *et al.* [18] compared the two instruments at bedside for ease of use but did not report data analysis. In a study to determine a standardized diagnosis for plasma or platelet transfusion for liver transplanted patients, Coakley *et al.* [12] reported poor agreement between PT and either TEG or ROTEM.

Of interest, swine present relatively faster clotting times than humans, with shorter R and K values for native swine blood as compared with human blood tested in the same conditions [17]. The hypercoagulability of porcine blood is a reason why we did not initiate clotting using activators of coagulation (kaolin or celite), which reduces the span of the reaction, and would likely mask the difference between TEG and ROTEM; also, activators may vary between companies in their nature and concentrations [6] and may lead to difficulties interpreting the results [11]. Because we tested various situations relevant to trauma, we cannot make definitive clinical conclusions regarding coagulopathy on human patients. Likewise, it should be stated that we cannot extrapolate our animal model data to human coagulopathies (i.e., factor deficiencies) as the animal models initially exhibited normal coagulation parameters.

Conclusion

The assessed parameters clearly display a trend towards divergent numerical data between TEG and ROTEM when using nonactivated native normal swine whole blood; ROTEM exhibited a consistent trend towards faster coagulation dynamics. However, the interpretation of data in the trauma protocols tested with both instruments was similar and would lead to similar clinical diagnoses while testing samples on the same instrument. Both devices yielded reliable data on coagulation indicating the same relative degree of hypercoaguablilty and hypocoaguablilty. However, when comparing numerical results from different studies, it is important to keep in mind the type of instruments and conditions of the test.

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