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ORIGINAL ARTICLE

# Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography

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**Summary.** *Background:* Reagent-supported thromboelastometry with the rotation thrombelastography (e.g. ROTEM®) is a whole blood assay that evaluates the visco-elastic properties during blood clot formation and clot lysis. A hemostatic monitor capable of rapid and accurate detection of clinical coagulopathy within the resuscitation room could improve management of bleeding after trauma. *Objectives:* The goals of this study were to establish whether ROTEM correlated with standard coagulation parameters to rapidly detect bleeding disorders and whether it can help to guide transfusion. *Methods:* Ninety trauma patients were included in the study. At admission, standard coagulation assays were performed and ROTEM parameters such as clot formation time (CFT) and clot amplitude (CA) were obtained at 15 min ($CA_{15}$) with two activated tests (INTEM, EXTEM) and at 10 min ($CA_{10}$) with a test analyzing specifically the fibrin component of coagulation (FIBTEM). *Results:* Trauma induced significant modifications of coagulation as assessed by standard assays and ROTEM. A significant correlation was found between prothrombin time (PT) and $CA_{15}$-EXTEM ($r = 0.66$, $P < 0.0001$), between activated partial thromboplastin time and CFT-INTEM ($r = 0.91$, $P < 0.0001$), between fibrinogen level and $CA_{10}$-FIBTEM ($r = 0.85$, $P < 0.0001$), and between platelet count and $CA_{15}$-INTEM ($r = 0.57$, $P < 0.0001$). A cutoff value of $CA_{15}$-EXTEM at 32 mm and $CA_{10}$-FIBTEM at 5 mm presented a good sensitivity (87% and 91%) and specificity (100% and 85%) to detect a PT $> 1.5$ of control value and a fibrinogen less than 1 g $L^{-1}$, respectively. *Conclusions:* ROTEM is a point-of-care device that rapidly detects systemic changes of *in vivo* coagulation in trauma patients, and it might be a helpful device in guiding transfusion.

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## Introduction

Trauma is a serious global health problem, accounting for approximately 10% of deaths worldwide [1]. Massive hemorrhage is one of the leading causes of death and despite improvement in trauma care it is still responsible for approximately 40% of trauma deaths [2]. Coagulopathy, which is encountered in 25–30% of trauma patients, is associated with a worse outcome [3,4], and constitutes one of the components of the classic lethal triad with hypothermia and metabolic acidosis [5,6]. Coagulopathy-related diffuse bleeding is complex and extremely difficult to manage. The multifactorial nature of post-traumatic coagulopathy involves consumption and dilution of clotting factors, dysfunction of platelets and the coagulation system, increased fibrinolytic activity, hypothermia, and metabolic acidosis [1]. Diagnosis of coagulopathy can be made clinically but coagulation monitoring is essential to directed care. Thrombelastography is a whole blood coagulation technique providing information on the initiation of coagulation, propagation kinetics, fibrin–platelet interaction, clot firmness and fibrinolysis [7,8].

Recently, the modified rotation thrombelastogram analyzer (ROTEM®; Pentapharm, Munich, Germany) has overcome some of the limitations of classic thrombelastography, such as the long observation time when coagulation is not initiated by biochemical agonists and the susceptibility to vibrations and mechanical shocks. Moreover, by using an electronic pipette reproducibility and performance have increased. Also, depending on the parameters measured, ROTEM results are available as quickly as 10 min from commencement, and therefore ROTEM may be used as a point-of-care device to monitor hemostasis, as previously shown in various clinical setting of coagulation disorders, such as liver transplantation and cardiac surgery [9–11].

It is currently unknown whether ROTEM parameters are sensitive to systemic changes of *in vivo* coagulation in trauma patients. The aim of this study was to evaluate the ability of

ROTEM to detect various coagulation disorders in trauma patients and its potential usefulness as a transfusion guiding tool.

## Materials and methods

### *Study design*

This prospective observational study was approved by the Institutional Review Board of the Hospices Civils de Lyon and informed consent was obtained from all participants. We included in the study all patients consecutively admitted to the trauma center of our teaching hospital between July and October 2004. Patient demographics and the injury severity score (ISS) were recorded [12]. The ISS, derived from the abbreviated injury score (AIS) has been demonstrated to correlate well with probability of mortality. The AIS divides the body into six separate regions (head and neck, face, thorax, abdomen and visceral pelvic content, bony pelvis and extremities, and external structures) and assigns each a severity value, from 1 (minor) to 6 (nearly always fatal). The ISS is the sum of squares of the largest AIS severity value from each of the three most severely injured body regions. Any patient with an AIS value of 6 is automatically scored 75 on the ISS scale.

### *Measurements of coagulation parameters, hemoglobin and platelets*

An MDA II instrument (Biomérieux, Marcy l'Etoile, France) was used to analyze prothrombin time (PT) and International Normalized Ratio (INR) (Neoplastin® CI plus, Diagnostica Stago, Asnières, France), and activated partial thromboplastin time (APTT) (MDA Platelin® LS; Biomérieux). Levels of fibrinogen were assayed using Fibriquick® reagent (Biomérieux) according to Clauss technique. Platelets and hemoglobin values were determined using SE-9500® (Sysmex, Kobe, Japan). Fibrinolysis was evaluated by measuring D-dimer levels (Asserachrom®; D-DI, Diagnostica Stago). We defined trauma coagulopathy at admission as an INR spontaneously > 1.6 and/or an APTT > 60 s and/or a platelet count < $100.10^9$ $L^{-1}$ and/or a fibrinogen less than 1 g $L^{-1}$.

### *The ROTEM modified rotation thrombelastogram analyzer*

The method and the parameters of thrombelastography and the ROTEM coagulation analyzer have previously been described in detail [13,14]. Briefly, thrombelastography measures shear elastic modulus during clot formation and subsequent fibrinolysis. The ROTEM uses a ball-bearing system for power transduction, which makes it less susceptible to mechanical stress, movement and vibration.

In the ROTEM analyzer, coagulation is mildly activated either with ellagic acid (INTEM test) or tissue factor from rabbit brain (EXTEM test). This is performed in order to standardize the *in vitro* coagulation process and also to speed up the analysis. The test time for ROTEM is typically 15–20 min [15]. Apart from the basic INTEM and EXTEM screening tests, an additional reagent such as cytochalasin D (which inhibits platelets) can be used in order to study the contribution of platelets to whole blood coagulation (FIBTEM) [16]. With FIBTEM the fibrinogen component (concentration and function in clot polymerization) of blood coagulation can be evaluated [15]. All pipetting steps and also the mixing are performed in a standardized way by following an automated electronic pipette program. The ROTEM analysis was performed at 37 °C in parallel on the three channels (INTEM, EXTEM, FIBTEM).

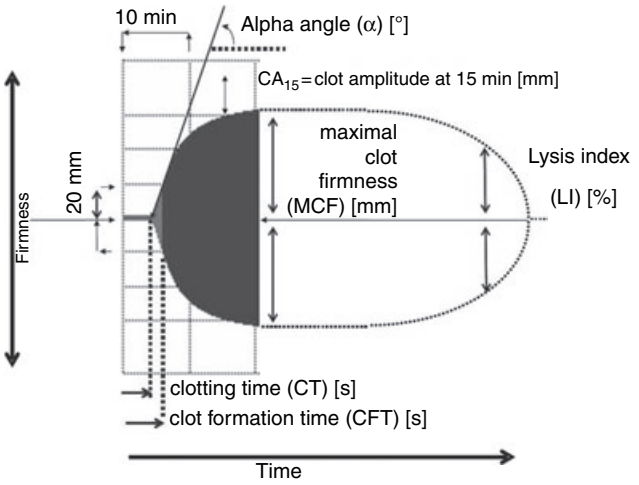


**Fig. 1.** Main parameters of ROTEM® thromboelastometry. CT, clotting time; CFT, clot formation time; ALP, alpha angle; MCF, maximum clot firmness; $CA_{15}$, clot amplitude at 15 min; $CLI_{60}$, clot lysis index at 60 min after CT.

We analyzed the following ROTEM parameters (Fig. 1): the clotting time (CT); the clot formation time (CFT); the maximum clot firmness (MCF); and the amplitude of clot at 10 min ($CA_{10}$) and 15 min ($CA_{15}$). The clot lysis index at 30–60 min ($CLI_{30}$–$CLI_{60}$) describes the ratio between the MCF and the amplitude 30–60 min after the CT and thus describes the progress of fibrinolysis at that particular time. For the FIBTEM, only MCF and $CA_{10}$ were recorded.

Normal values of ROTEM parameters were determined from blood samples of healthy subjects collected by the blood bank. Blood samples from 49 males and 21 females were analyzed [male sex 70%; age (mean ± SD) 40 ± 13 years].

### *Sampling and study protocol*

Blood samples were collected immediately after the patient's arrival to the trauma room ($H_0$) and at 6 h ($H_6$), 12 h ($H_{12}$) and 24 h ($H_{24}$) after admission, representing a total of 270 samples. Blood samples were collected by venipuncture into vacutainer tubes (Becton Dickinson, Plymouth, UK) containing citrate (0.129 M trisodium citrate) for standard tests and thrombelastogram [17,18] and ethylenediaminetetraacetic acid (EDTA) for platelet and hemoglobin counts. The ROTEM measurements and standard coagulation tests were realized within 2 h

of collection of blood samples and at least 15 min after venipuncture. As described by Lang *et al.* [15], the stability of INTEM, EXTEM and FIBTEM parameters was good within 6 h. Clinicians were not informed of ROTEM results.

To study the correlation between ROTEM parameters and standard coagulation assays, we pooled together all the samples taken for ROTEM analysis regardless of sampling time and we compared these with standard coagulation assays. Thus, ROTEM variables were compared with each corresponding coagulation test: PT compared with EXTEM parameters; APTT with INTEM parameters; and fibrinogen level with FIBTEM parameters [19–22]. The INTEM values were also compared with platelets counts, as suggested by Vorweg *et al.* [23].

To determine whether ROTEM can help to guide transfusion, we defined a cutoff value for ROTEM parameters using receiver operating characteristic (ROC) curves. ROTEM parameters that presented the best correlation with standard coagulation assays were used. Requirements for blood product administration were based on French (http://agmed.gouv.fr) and international blood products transfusion guidelines: fresh frozen plasmas were given when PT and/or APTT was greater than 1.5–1.8 of control values; platelets concentrates when platelet count was $< 50 \times 10^9$ L$^{-1}$; and fibrinogen concentrates when fibrinogen was less than 1 g L$^{-1}$ [24,25].

### *Statistical analysis*

Results are expressed as median (IQR) and observed range. The Mann–Whitney *U*-test and ANOVA with Newman–Keuls test were used for continuous variables as appropriate, after the normality of the distribution was tested using a Shapiro–Wilk test. Statistical differences between groups were evaluated by chi-squared test or by Fisher's exact test when appropriate. Correlations were tested using Spearman's rank test. The best cutoff value for ROTEM parameters was chosen using Youden's Index. ROC curves and the respective areas under the curves (AUC) were determined, and sensitivity, specificity, positive and negative predictive values were calculated. A two-tailed *P*-value $< 0.05$ was considered significant. All statistical tests were performed using commercially available statistical software (JMP version 5.1; SAS Inc., Cary, NC, USA).

## Results

Ninety patients were admitted to our trauma resuscitation unit (TRU) during the study period. Two patients using oral anticoagulant treatment were excluded. Eighty-eight patients were finally included in the study and presented the following baseline characteristics: male sex, 68 of 88 (77.2%); age (mean ± SD), 34 ± 16 years; and admission temperature (mean ± SD), 36.3 ± 1.6 °C. All of the patients were severely injured as attested by an ISS score of 22 (12–34).

### *Results of standard coagulation assays, platelets and hemoglobin*

Details of standard coagulation parameters are presented in Table 1. Coagulopathy was observed on admission in 28% of trauma patients, who also presented the most severe trauma when compared with the non-coagulopathic patients [ISS 48 (17–75) vs. 18 (9–25), $P = 0.0002$]. D-dimers were also significantly more elevated in coagulopathic patients (Table 1).

### *Comparison of ROTEM parameter values in healthy subjects and trauma patients*

Values for healthy subjects are reported in Table 2. As previously described by Lang *et al.* [15], we observed in the control group a trend for the female subclass to have a faster coagulation activation (shorter CT and CFT), greater clot firmness (higher MCF) and amplitude ($CA_{10}$, $CA_{15}$) compared with the male subclass. The difference was statistically significant in the MCF, $CA_{10}$ and $CA_{15}$ of INTEM, EXTEM and FIBTEM, and in the CT of EXTEM. However, we did not find such a difference in the trauma group, whatever the ROTEM parameters (data not shown).

When compared with control subjects, trauma significantly altered almost all of the ROTEM tests because there was a significant increase in CT and CFT and a shortening of MCF, $CA_{10}$ and $CA_{15}$ for each test. These modifications were essentially observed in the most severely injured, i.e. coagulopathic, patients (Table 2). In addition, five patients in the coagulopathic group had a $CLI_{60}$ that was below normal range

**Table 1** Standard coagulation parameters, hemoglobin, platelet count and D-dimers in trauma patients at admission

| | All traumas | Traumas without coagulopathy | Traumas with coagulopathy |
|---|---|---|---|
| *n* (%) | 88 (100) | 63 (71) | 25 (28) |
| Prothrombin time (s) | 16 (15–17) [13–80] | 15 (15–16) [13–18] | 20* (17–30) [14–80] |
| International Normalized Ratio | 1.3 (1.2–1.5) [1.0–10.0] | 1.2 (1.1–1.3) [1.0–1.5] | 1.9 (1.6–4) [1.1–10] |
| Activated partial thromboplastin time (s) | 27 (25–33) [21–300] | 27 (25–28) [21–36] | 39* (31–126) [21–300] |
| Fibrinogen (g L$^{-1}$) | 2.1 (1.4–2.6) [0.0–3.9] | 2.3 (1.9–2.8) [1.3–3.9] | 0.9* (0.5–1.5) [0.0–2.5] |
| Hemoglobin (g L$^{-1}$) | 128 (103–140) [41–164] | 134 (123–143) [90–164] | 84* (61–109) [41–143] |
| Platelets ($10^9$ L$^{-1}$) | 209 (159–262) [28–500] | 224 (192–278) [141–500] | 148* (100–195) [28–334] |
| D–dimers (μg L$^{-1}$) | 7.9 (2.9–26.7) [0.1–888.4] | 6.1 (1.6–14.0) [0.1–74.7] | 29.2* (7.4–85.1) [0.4–888.4] |

Values are median (IQR) and [range]. *$P < 0.05$: comparison between coagulopathic and non-coagulopathic trauma patients using Mann–Whitney *U*-test.

**Table 2** ROTEM® parameters in healthy control subjects and trauma patients at admission

| | CT (s) | CFT (s) | MCF (mm) | $CA_{10}$ (mm) | $CA_{15}$ (mm) | $CLI_{30}$ (%) | $CLI_{60}$ (%) |
|---|---|---|---|---|---|---|---|
| Healthy subjects ($n = 71$) | | | | | | | |
| INTEM | 157 (150–176) [107–240] | 66 (59–76) [46–102] | 59 (57–62) [52–67] | 53 (51–57) [46–61] | 57 (54–61) [50–65] | 98 (97–98) [94–98] | 91 (88–93) [84–96] |
| EXTEM | 53 (48–58) [17–139] | 94 (78–113) [58–179] | 60 (57–62) [51–67] | 52 (48–55) [40–60] | 56 (53–59) [45–65] | 98 (98–98) [97–98] | 92 (90–93) [82–96] |
| FIBTEM | 52 (48–57) [35–77] | (–) | 14 (11–16) [4–22] | 12 (10–14) [4–19] | 12 (10–14) [4–19] | (–) | (–) |
| Trauma patients ($n = 88$) | | | | | | | |
| INTEM | 146* (129–167) [91–10000] | 81* (68–123) [36–10000] | 58* (51–62) [0–68] | 50* (42–54) [0–62] | 54* (47–58) [0–65] | 98 (98–98) [5–98] | 92 (90–95) [1–98] |
| EXTEM | 61* (55–77) [37–10000] | 116* (87–179) [46–10000] | 58* (50–62) [0–69] | 48* (39–52) [0–63] | 53* (44–57) [0–67] | 98 (98–98) [0–98] | 94 (91–96) [0–98] |
| FIBTEM | 59* (55–70) [44–10000] | (–) | 10* (8–15) [0–30] | 8* (6–12) [0–20] | 9* (6–12) [0–24] | (–) | (–) |
| Trauma patients without coagulopathy ($n = 63$) | | | | | | | |
| INTEM | 136 (127–156) [91–209] | 73 (63–90) [36–169] | 60 (56–63) [49–68] | 52 (49–56) [36–62] | 57 (53–60) [42–65] | 98 (98–98) [95–98] | 92 (91–95) [86–98] |
| EXTEM | 60 (55–69) [37–146] | 101 (80–127) [46–243] | 60 (56–64) [47–69] | 51 (46–55) [36–63] | 55 (51–59) [42–67] | 98 (98–98) [96–98] | 94 (91–96) [88–97] |
| FIBTEM | 58 (55–65) [44–146] | (–) | 13‡ (10–15) [5–30] | 10 (7–14) [4–20] | 11 (8–14) [4–24] | (–) | (–) |
| Trauma patients with coagulopathy ($n = 25$) | | | | | | | |
| INTEM | 173‡ (142–257) [102–10000] | 151‡ (121–394) [58–10000] | 49‡ (37–53) [0–66] | 38‡ (24–43) [0–59] | 43‡ (29–49) [0–62] | 98‡ (98–98) [5–98] | 92‡ (35–96) [1–98] |
| EXTEM | 84‡ (56–151) [48–10000] | 220‡ (162–428) [80–10000] | 48‡ (37–52) [0–66] | 35‡ (22–40) [0–57] | 41‡ (27–47) [0–62] | 98‡ (98–98) [0–98] | 94‡ (13–97) [0–98] |
| FIBTEM | 81‡ (57–10000) [45–10000] | (–) | 6‡ (0–9) [0–14] | 4‡ (0–7) [0–11] | 4‡ (0–8) [0–11] | (–) | (–) |

Values are median (IQR) and [range]. CA, amplitude of clot firmness; CFT, clot formation time; CLI, clot lysis index; CT, clotting time. *$P < 0.05$: comparison between healthy and trauma patients (Mann–Whitney *U*-test); ‡$P < 0.05$: control and trauma patients without coagulopathy vs. trauma patients with coagulopathy (Newman–Keuls Test); (–), data not reported.

(healthy group, Table 2), which may suggest an increase in fibrinolytic activity. This phenomenon was not illustrated by differences in median values of CLI among groups but by larger IQRs and ranges (Table 2).

### *Correlation of ROTEM parameters with standard coagulation parameters and platelets*

We observed good correlation between $CA_{15}$ and MCF from EXTEM ($r = 0.98$, $P < 0.001$) and from INTEM ($r = 0.97$, $P < 0.001$), as well as between $CA_{10}$ and MCF ($r = 0.96$, $P < 0.001$) from FIBTEM. Thus, $CA_{10}$-FIBTEM and $CA_{15}$-EXTEM and -INTEM were retained as satisfying clot firmness parameters in this study.

The correlation of standard coagulation parameters with ROTEM parameters (CT, CFT, $CA_{10}$ and $CA_{15}$) was tested (Table 3) and significant correlations were observed between PT and $CA_{15}$-EXTEM, between APTT and CFT-INTEM and $CA_{15}$-INTEM, between fibrinogen and $CA_{10}$-FIBTEM, and between platelet count and $CA_{15}$-INTEM (Table 3 and Fig. 2). We also found similar correlations between standard coagulation and ROTEM parameters when only samples taken at admission (before any potential transfusion) were analyzed ($CA_{15}$-EXTEM and PT: $r = 0.70$, $P < 0.001$; $CA_{10}$-FIBTEM and fibrinogen: $r = 0.91$, $P < 0.001$; CFT-INTEM and APTT: $r = 0.70$, $P < 0.001$; and $CA_{15}$-INTEM and platelets: $r = 0.79$, $P < 0.001$).

### *Prediction by ROTEM of the need for blood products*

Cutoff values for $CA_{15}$-EXTEM, $CA_{10}$-FIBTEM, CFT-INTEM and $CA_{15}$-INTEM are summarized in Table 4. Cutoff values for $CA_{15}$-EXTEM and $CA_{10}$-FIBTEM had a good sensitivity, specificity, positive and negative predictive value in predicting a PT > 1.5 of control value and a fibrinogen less than 1 g $L^{-1}$. On the other hand, cutoff values for CFT-INTEM and $CA_{15}$-INTEM were found to have poor positive predictive values in the diagnosis of an APTT > 1.5 of control value and platelet count lower than $50 \times 10^{-9}$ $L^{-1}$.

**Table 3** Correlation (*r*) between ROTEM® and standard coagulation

| | Prothrombin time | Activated partial thromboplastin time | Fibrinogen | Platelets |
|---|---|---|---|---|
| EXTEM | | | | |
| CT | 0.53* | (–) | 0.40* | (–) |
| CFT | 0.62* | (–) | (–) | 0.33* |
| $CA_{15}$ | **0.66*** | (–) | 0.69* | 0.56* |
| INTEM | | | | |
| CT | (–) | 0.47* | (–) | (–) |
| CFT | (–) | **0.91*** | (–) | 0.32* |
| $CA_{15}$ | (–) | 0.70* | 0.66* | **0.57*** |
| FIBTEM | | | | |
| $CA_{10}$ | (–) | (–) | **0.85*** | (–) |

*$P < 0.001$. CA, amplitude of clot firmness; CFT, clot formation time; CT, clotting time; (–), data not reported.

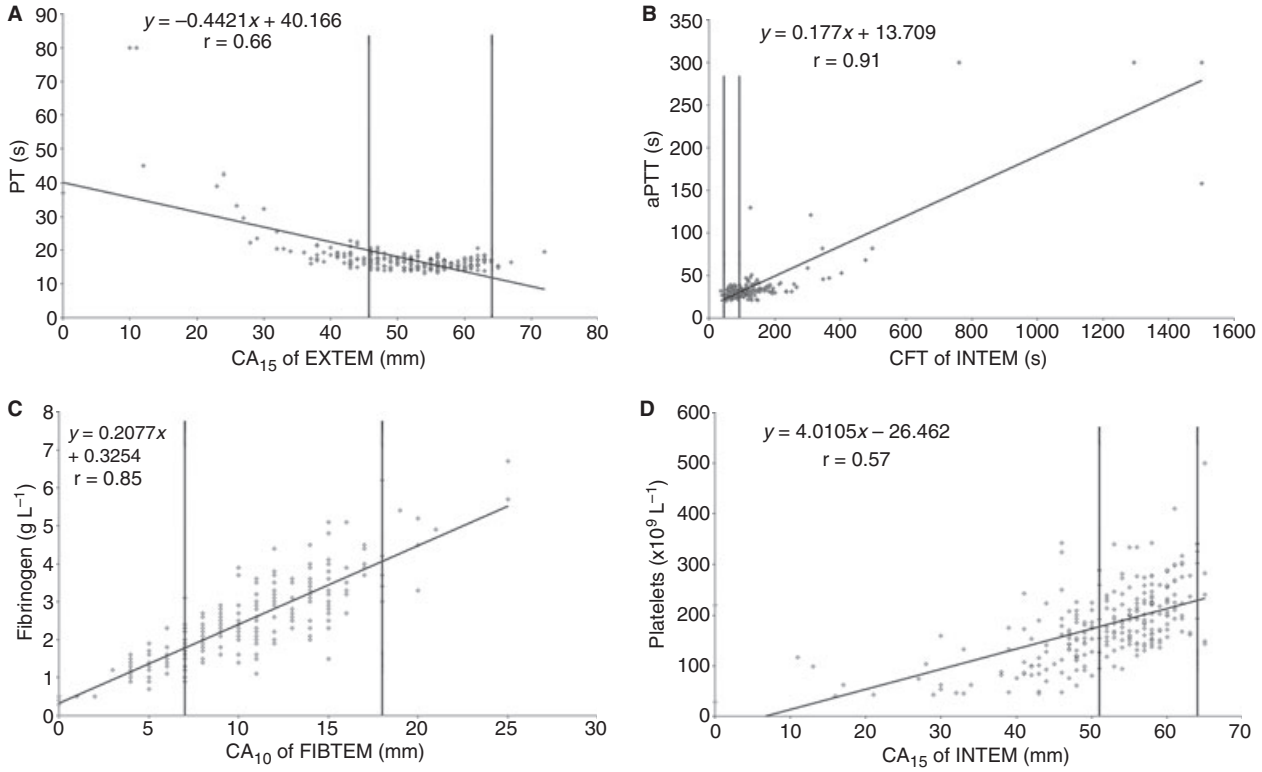


**Fig. 2.** Best linear regression depicting the relation between ROTEM® parameters and prothrombin time (A), activated partial thromboplastin time (B), fibrinogen (C) and platelets (D). The vertical lines represent the lower and upper limits of normal ranges defined according to the healthy group (2.5–97.5% percentiles). These values are very similar to those described previously by Lang *et al.* [15].

**Table 4** Cutoff values for ROTEM® parameters

| Transfusion values | ROTEM® Cutoff values | Sensitivity % (95% CI) | Specificity % (95% CI) | PPV % (95% CI) | NPV % (95% CI) | AUC |
|---|---|---|---|---|---|---|
| Prothrombin time > 1.5 of control value | $CA_{15}$-EXTEM = 32 mm | 87 (72–87) | 100 (99–100) | 100 (83–100) | 99 (98–99) | 0.98 |
| APTT > 1.5 of control value | CFT-INTEM = 112 s | 100 (84–100) | 74 (73–74) | 23 (19–23) | 100 (98–100) | 0.94 |
| Fibrinogen < 1 g $L^{-1}$ | $CA_{10}$-FIBTEM = 5 mm | 91 (72–93) | 85 (84–86) | 55 (45–60) | 99 (97–100) | 0.96 |
| Platelets < $50 \times 10^9$ $L^{-1}$ | $CA_{15}$-INTEM = 46 mm | 100 (71–100) | 83 (82–83) | 17 (12–17) | 100 (98–100) | 0.92 |

Cutoff values were determined according to transfusion threshold values based on standard coagulation parameters. APTT, activated partial thromboplastin time; AUC, area under the curve; CA, amplitude of clot firmness; CFT, clot formation time; NPV, negative predictive value; PPV, positive predictive value.

## Discussion

In this study, we showed that (i) rotation thrombelastogram (ROTEM) can detect early changes of *in vivo* coagulation in trauma patients; (ii) ROTEM parameters correlate with standard coagulation parameters and platelet counts; and (iii) it is possible to define cutoff value for ROTEM parameters according to transfusion threshold values based on standard coagulation parameters.

We observed that trauma led to significant and early coagulation abnormalities, as depicted by modifications in standard coagulation as well as ROTEM parameters (Table 1). On admission to the TRU, almost a third of the patients presented a significant coagulopathy with significant prolongation of CTs and thrombocytopenia. This is in agreement with previous reports that also underlined the relationship between severity of trauma and the occurrence of a coagulopathy [3,4].

Point-of-care devices such as rotation thrombelastography might allow physicians to detect and treat early trauma coagulopathy and have the advantage of measuring all parts of the coagulation process, including fibrinolysis. We observed significant modifications of ROTEM parameters in trauma patients. Decreases in CT as well as CFT suggested that initiation of coagulation (CT) as well as its propagation (CFT) may be sensitive to trauma. Furthermore, MCF and CA were significantly decreased in the trauma group and that effect was even more pronounced in the coagulopathic patients in whom

a significant platelet decrease was observed (Table 1). MCF has been reported to be dependent on platelet function and count [26,27] and it is probably also dependent on dilution or consumption of coagulation factors. Moreover, Gando *et al.* [28] described that severe thrombocytopenia occurred secondary to the decrease of coagulation factors. Two studies have previously shown that trauma could modify ROTEM parameters and suggested that trauma could induce a hyper or hypercoagulable state [29,30]. We did not observe a hypercoagulable profile in our trauma population, probably because we considered only the first hours after trauma and because our patients were more severely injured, hence more likely to have bleeding disorders (i.e. hypercoagulable).

Many other reports have been published [11,29,31,32] since the first report of a correlation between MCF and fibrinogen in the normal population, and between MCF and both platelet count and fibrinogen concentration in a hypercoagulable population [33]. The association between MCF and both platelet count and fibrinogen concentration was confirmed in 1985 [11]. In our study, we also demonstrated few significant correlations (Table 3). For example, $CA_{15}$-EXTEM correlated with both PT and fibrinogen, whereas $CA_{10}$-FIBTEM correlated with fibrinogen and CFT-INTEM with APTT. In trauma, Schreiber *et al.* [29] suggested correlations between TEG® parameters and APTT (*r*-time) or platelets (MA), whereas in cardiac surgery, Kettner *et al.* [32] found a correlation between fibrinogen and MA. Vorweg *et al.* [22] proposed that CFT-INTEM could guide platelet transfusion. However, we did not find any satisfying correlation between ROTEM parameters and platelet count, especially with CFT-INTEM. Furthermore, we found this parameter to have the poorest correlation with platelet count. $CA_{15}$-INTEM was the parameter for which we found the best correlation with platelets although the correlation was not very good ($r = 0.32$), with a very poor positive predictive value (17%) for platelet transfusion.

Our data suggest that ROTEM may be also useful in guiding transfusion, as previously suggested in liver transplantation and cardiac surgery [10,11]. Hence, the cutoff values for $CA_{15}$-EXTEM, $CA_{10}$-FIBTEM, CFT-INTEM and $CA_{15}$-INTEM exhibited a high sensitivity and specificity in the diagnosis of an increased PT/APTT or a decrease of fibrinogen and platelet count. However, CFT-INTEM (increase of APTT) and $CA_{15}$-INTEM (decrease in platelet count) were probably not reliable guides to fresh frozen plasma or platelet transfusion because of a very low positive predictive value and the attendant excessive risk of transfusion.

Of particular interest, we observed a decrease in CLI (increased fibrinolytic activity) that predominated in the coagulopathic patients and that was paralleled by an increase in D-dimers. This suggested an activation of fibrinolysis but this study was not designed to study fibrinolysis in detail. So far, monitoring of hyperfibrinolytic states by thrombelastography has been performed in other clinical settings, e.g. orthotopic liver transplantation [11,34], and thrombelastogram has been shown to be useful in the early detection of hyperfibrinolysis [35]. Kang *et al.* [11] also described a significant correlation between clot lysis time with euglobulin clot lysis time.

Our study suffers from several limitations. Firstly, we based the determination of cutoff values for transfusion on the CA rather than more classical parameters such as MCF or CT. Hence, we believe that CA is more reliable to clinical practice because obtained after 10 min (FIBTEM) and 15 min (EXTEM) rather than an unpredictable time of 5–30 min for realization of MCF. Moreover, we found that these parameters correlated well. Secondly, we used citrated blood rather than native blood, as previously reported [17]. This may have affected our results because citrated blood has been reported to induce a hypercoagulability profile by incomplete inhibition of the activation of the coagulation cascade [36]. However, our control population was studied under the same conditions and we proceeded with ROTEM analysis in the following 2 h. In addition, Lang *et al.* [15] had shown that the reproducibility was good between 15 min and 2 h. Thirdly, vessel disorders, adhesion of platelets to collagenous fibers, and the effect of aspirin on coagulation still cannot be estimated. Fourthly, sex difference may have impacted upon our results because it has been shown that females may have shorter CTs and greater clot firmness [15]. However, there was no difference in the sex ratio between the trauma and the control group (chi-squared test, $P = 0.30$).

In conclusion, rotation thrombelastogram is a point-of-care device that rapidly detects systemic changes in *in vivo* coagulation in trauma patients and might be a helpful device in guiding transfusion. Further studies are required to test whether ROTEM can reduce mortality and morbidity associated with bleeding and transfusion therapy.

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## Disclosure of Conflict of Interests

The authors state that they have no conflict of interest.

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