Rotational thromboelastometry produces potentially clinical useful results within 10 min in bleeding Emergency Department patients: the DEUCE study

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Objectives and background For the first time in the Emergency Department (ED), to assess the use of rotational thromboelastometry (ROTEM) in patients presenting with all-cause haemodynamic shock, specifically (a) to establish whether a 5-min (A5) or a 10-min result (A10) is accurate compared with a final maximum clot firmness (MCF) result; (b) to compare time to A10 and formal laboratory coagulation result; (c) to assess whether bleeding ED trauma, gastrointestinal and aortic aneurysm patients are coagulopathic according to ROTEM; and (d) to compare ROTEM results with formal laboratory coagulation parameters.

Methods Patients presenting to the ED in haemodynamic shock were recruited. A citrated coagulation sample was taken and once a ROTEM researcher arrived in the ED, was subjected to ROTEM analysis.

Results Between 28 September 2010 and 31 August 2011, 40 patients were recruited (15 gastrointestinal bleeds, 20 major trauma cases and five ruptured abdominal aortic aneurysms). A10 and MCF correlated well ($\chi = 0.98$); A5 and MCF correlated less well ($\chi = 0.91$). The mean time to result (SD) was 57 (28) min for the formal laboratory coagulation result and 50 (45) min for the ROTEM A10 result (including delay to start of analysis). Seven patients were coagulopathic on ROTEM.

Conclusion Eighteen percent of bleeding ED patients are coagulopathic using ROTEM including 25% of trauma patients. A 10-min ROTEM clot firmness (A10) is an excellent surrogate for MCF and allows a result to be obtained earlier than formal laboratory results and potentially within 10 min of the patient arriving in the ED. European Journal of Emergency Medicine

Introduction

Background Recent developments in the field of emergency transfusion are leading to changes in the way that trauma patients presenting to the Emergency Department (ED) are being transfused. Traditional transfusion protocols still followed in the majority of institutions advocate packed red blood cell transfusions according to shock status and advanced trauma life support teaching [1]. Formal coagulation testing in the hospital laboratory using assays such as the prothrombin time ratio (PTR), the activated partial thromboplastin time ratio (APTTR) and the platelet concentration is then used to guide transfusion of fresh-frozen plasma, platelets and sometimes cryoprecipitate according to current trauma guidelines [2]. These laboratory results, however, are commonly delayed, leading to a reactive rather than a proactive approach to transfusion, the blind transfusion of products and an underestimation of product requirement [3,4].

Rotational thromboelastometry (ROTEM; Pentapharm, Munich, Germany) and thromboelastography are bedside viscoelastic tests that test the efficiency of blood coagulation. When blood is taken from the patient, it is mixed with an inhibitor to prevent clot formation in the citrated tube while it is stored before analysis. A standard ROTEM test involves four channels, each of which assesses a different part of the clotting pathway simultaneously. With the addition of coagulation activators or inhibitors, the clotting process can be restarted and analysed (Fig. 1).

Importance In the trauma setting, many studies have reported that coagulopathy (defined as PTR or APTTR $\geq 1.5$) is present in a quarter of all ED trauma patients [5–9]. Coagulopathy on arrival in the ED has been shown to be an independent prognostic indicator and patients whose coagulopathy is treated aggressively have increased survival [10]. Work in elective vascular, cardiothoracic
and organ transplantation surgery has also shown that both the early detection and management of coagulopathy [11], and the use of ROTEM [12], result in a better outcome. Most of the work already published on the use of ROTEM in the ED has focused on trauma patients. Major trauma presentations are decreasing in the developed world and massive transfusion is now more commonly associated with ruptured abdominal aortic aneurysm (AAA) or gastrointestinal (GI) bleeding (the most common cause of haemodynamic shock in the ED), but very little is known about the coagulative state of these patients on arrival to the ED.

Fig. 1

(a) Standard rotational thromboelastometry (ROTEM) trace and (b) abnormal tracing from DEUCE study patient 7.
Goals of this investigation
To assess the use of ROTEM in patients presenting to the ED with haemodynamic shock, specifically (a) to establish whether a 5-min (A5) or a 10-min result (A10) is accurate compared with a final maximum clot firmness (MCF) result; (b) to compare time to A10 and a formal laboratory coagulation result; (c) to assess whether bleeding trauma, GI and aortic aneurysm patients are coagulopathic in the ED according to ROTEM; and (d) to compare ROTEM results with formal laboratory coagulation parameters by comparing EXTEM A10 and the formal platelet count and FIBTEM A10 and formal fibrinogen.

Methods
Study design and setting
This is a single-centre, prospective, observational cohort study carried out in the ED of the Royal Infirmary of Edinburgh (RIE). This large UK tertiary referral centre treats 110 000 adult patients annually.

Inclusion criteria
Patients presenting to the RIE ED with any evidence of blood loss were enrolled, provided they were 13 years of age and older and fulfilled one of the DEUCE (Detection of Early Untreated Coagulopathy in the ED) study eligibility criteria: pulse rate more than 100 beats/min, systolic blood pressure less than 100 mmHg, lactate more than 2 mmol/l, base excess more than –2 mEq/l, indication of more than 500 ml blood loss, recent fresh red blood cells, recent fresh frozen plasma, coagulopathy, the relationship between ROTEM results and formal laboratory coagulation result; (c) to assess whether coagulopathic and noncoagulopathic patients.

Exclusion criteria
Patients younger than 13 years of age were excluded.

Methodology
Once the treating doctor identified a patient for inclusion and intravenous access had been achieved, two paediatric citrated blood coagulation tubes (1.3 ml) were filled (instead of the standard adult 3 ml citrated tube) and a member of the DEUCE study team was called. One of the paediatric citrated tubes was sent for formal laboratory testing after labelling (a full 1.3 ml tube is sufficient for formal laboratory coagulation studies in our hospital). The second 1.3 ml citrated tube was used for ROTEM analysis (Tem International GmbH; Munich, Germany). No additional blood sample was therefore taken from the patient compared with routine care, and the ROTEM analysis was performed on the leftover blood. Following advice from the South East Scotland Research Ethics Service, ethical approval and patient consent were deemed not to be necessary. No patients received tranexamic acid or any other blood products before the sample was drawn.

Data collection
Studies have shown the consistency of ROTEM results within 6h and thus it was ensured that all samples were analysed within 4h of them being taken [13]. The samples were stored on the ROTEM machine until they could be tested. All samples were pipetted in a standardized manner using the automated ROTEM pipette program. The four channels tested were EXTEM, INTEM, FIBTEM and APTEM. All four channels were analysed simultaneously and the results obtained (clotting time, clot formation time, clot firmness after 5 min; A5, clot firmness after 10 min; A10, MCF and maximum clot lysis; Fig. 2) were recorded along with the patient’s age, sex, underlying diagnosis, pulse, systolic and diastolic blood pressure on arrival to the ED, respiratory rate, the Glasgow Coma Score, the Rockall and Blatchford score for patients with GI bleeding, injury severity score (ISS) for patients with trauma, lactate and base excess on arrival to the ED, and the results of standard laboratory assays of PTR, APTTR, fibrinogen, platelet count and full blood count. Information was also collected on the time the ROTEM sample was taken, the time to obtain a 10-min A10 ROTEM result, the time the formal coagulation sample was received by the hospital laboratory and the time the formal coagulation result was received by the ED clinician. Results were analysed to establish the number of patients presenting to the ED with coagulopathy, the relationship between ROTEM results and formal laboratory coagulation profiles and the time both ROTEM and formal laboratory coagulation results were available to the ED clinician. A search of all ED Electronic Patient Records was carried out to identify patients who were eligible but not recruited.

Data analysis
Results were printed and saved to the machine’s database electronically and then entered into a specially designed Microsoft Excel (Microsoft Corporation, Redmond, Washington, USA) database and then analysed using SPSS (SPSS Incorporated, Chicago, Illinois, USA) and GraphPad (GraphPad Software Incorporated, La Jolla, California, USA). The mean values and SD were calculated for normally distributed variables, and the median values with interquartile ranges (IQR) were calculated for variables that were not normally distributed. x2 values were calculated for correlations and χ2 was used to compare the ‘missed’ and the ‘recruited’ groups. An unpaired Student’s t-test, two tailed, was used to compare coagulopathic and noncoagulopathic patients. The ROTEM parameter FIBTEM A10 (which provides an assessment of fibrinogen function) was compared with formal laboratory fibrinogen and the ROTEM parameter EXTEM A10 (which provides a combined assessment of platelet and fibrinogen function) was compared with formal laboratory platelets. Some authors have suggested that the calculated variable (EXTEM A10-FIBTEM A10) yields a better assessment of platelet function alone, and
therefore, this was also compared with formal laboratory platelets.

**Results**

Between 28 September 2010 and 31 August 2011, 40 patients were recruited. A flow chart of patient recruitment is detailed in Fig. 3. There were 30 men (75%) and 10 women (25%). The mean age (SD) of the patients was 58.9 (19.8) years (range 15–96). There were five ruptured AAAs, 15 GI bleeds and 20 major trauma cases. Out of the trauma patients, eight had an ISS of less than 15 and seven patients had an ISS of 16 or greater. The median ISS score was 10 (IQR 1–19.75). In patients presenting with upper GI bleeding, the median Rockall score was 4 (IQR 3–5) and the median Blatchford score was 11 (IQR 8–14). Table 1 details the selected baseline characteristics of the study population included.

A10 and MCF correlated well ($\kappa = 0.98$; Fig. 4); A5 and MCF correlated less well ($\kappa = 0.91$; Fig. 5). The mean time to the result (SD) was 57 (28) min for the formal laboratory coagulation result and 50 (45) min for the ROTEM A10 result. The majority of this 50 min was the delay to the start of the analysis while awaiting the ROTEM technician to arrive. Once the ROTEM technician arrived, the sample, which had already been obtained and was being kept warm on the ROTEM machine, took only between 1 and 6 (mean 2.2) min to process on all four ROTEM channels.

Out of the 40 recruited patients, seven (18%) had an abnormal ROTEM tracing including five trauma patients (5/20 = 25%), two GI bleeds (2/15 = 13%) and no AAAs (0/5 = 0%; Table 2). Six patients were coagulopathic according to formal laboratory tests (five patients had a PTR $>1.5$; patients 2, 19, 29, 34 and 37; one patient had an APTTR $>1.5$; patient 19) and two patients had platelets less than $50 \times 10^9/l$ (patients 2 and 4). Patients with coagulopathy on ROTEM had a significantly lower systolic blood pressure (91.8 vs. 117.6 mmHg; $P = 0.017$) and a lower Glasgow Coma Score (10.8 vs. 14.3; $P = 0.015$) than patients without coagulopathy and a nonsignificant trend towards a lower diastolic blood pressure (53.4 vs. 64.6 mmHg; $P = 0.128$), a higher respiratory rate (20 vs. 18; $P = 0.441$) and a higher lactate (5.2 vs. 4.5 mmol/l; $P = 0.766$). There was no significant difference in the ISS score between trauma patients with coagulopathy (15; SD 8.5) and trauma patients without coagulopathy (12; SD 8.5; $P = 0.50$, NS). Two patients had a normal ROTEM tracing while having abnormalities in their traditional laboratory coagulation tests (patients 19 and 37).

**FIBTEM A10 versus fibrinogen** correlated with a $\kappa$ coefficient of 0.33, **EXTEM A10 versus platelet count** correlated with a $\kappa$ coefficient of 0.24 and **EXTEM A10-FIBTEM A10 versus platelets** correlated with a $\kappa$ coefficient of 0.06.

**Missed patients**

During the study period, 364 patients who fulfilled the inclusion criteria of the study presented to the ED but were not recruited. A total of 189 were trauma patients, 38 were AAA patients, 104 were GI bleeds and 33 patients had other diagnoses. There was no statistical difference between the number who died in the ‘missed’ group (57/364 = 16%) and the number who died in the ‘recruited’ group (6/40 = 15%; $P = 0.91$, NS), the sex ratio (M:F) between the ‘missed’ (257:101) and the ‘recruited’ groups (30:10; $P = 0.69$, NS) or the number going to critical care between the ‘missed’ (147/364 = 40%) and the ‘recruited’ groups (23/40 = 58%; $P = 0.06$, NS).

**Discussion**

This study has confirmed findings from previous studies showing that 25% of ED trauma patients are coagulopathic;
however, our study has utilized the ROTEM bedside testing technology. Only 13% of GI patients and no AAA patients were coagulopathic, indicating that while making up a large proportion of bleeding ED patients, this group may benefit less from ROTEM technology in the ED than the trauma group.

Our study shows that a 10-min ROTEM clot firmness (A10) is an excellent surrogate for MCF and allows a result to be obtained at least 7 min earlier than formal laboratory results and potentially within 10 min of the patient arriving in the ED if ROTEM trained personnel are available on the arrival of the patient in the ED. A 5-min result (A5) is probably not sufficiently accurate to recommend routine use.

Flow diagram of patient recruitment. AAA, abdominal aortic aneurysm; ED, Emergency Department; GI, gastrointestinal.

Table 1  Selected baseline characteristics of the study population included

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Value</th>
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<tbody>
<tr>
<td>Demographics</td>
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<tr>
<td>Age (years)</td>
<td>58.9 (19.8)</td>
<td>40</td>
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<tr>
<td>Male sex</td>
<td>30 (75)</td>
<td>40</td>
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<td>Warfarin</td>
<td>1 (2.5)</td>
<td>40</td>
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<td>Past medical history of liver disease</td>
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<td>40</td>
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<td>Presenting condition</td>
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<td>Ruptured abdominal aortic aneurysm</td>
<td>5 (12.5)</td>
<td>40</td>
</tr>
<tr>
<td>Gastrointestinal bleeds</td>
<td>15 (37.5)</td>
<td>40</td>
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<td>Rockall score, median (IQR)</td>
<td>4 (IQR 3–5)</td>
<td>15</td>
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<tr>
<td>Blatchford score, median (IQR)</td>
<td>11 (IQR 8–14)</td>
<td>15</td>
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<td>Major trauma</td>
<td>20 (50)</td>
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<td>ISS, median (IQR)</td>
<td>10 (1–19.75)</td>
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<tr>
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<td>7 (47)</td>
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<td>Initial examination findings</td>
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<td>Pulse (beats/min)</td>
<td>89.6 (24.4)</td>
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<td>Systolic BP (mmHg)</td>
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<tr>
<td>Diastolic BP (mmHg)</td>
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<td>Glasgow coma score</td>
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<tr>
<td>Respiratory rate (breaths/min)</td>
<td>18.4 (5.8)</td>
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<tr>
<td>Lactate (mmol/l)</td>
<td>4.7 (3.7)</td>
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<tr>
<td>Base excess (mEq/l)</td>
<td>–6.5 (6.9)</td>
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</tr>
</tbody>
</table>

Values are presented as mean (±SD) or n (%) unless stated otherwise. BP, blood pressure; IQR, interquartile range; ISS, injury severity score.

Correlation of A10 with MCF ($R^2 = 0.98$). MCF, maximum clot firmness.
ROTEM and thromboelastography assess the clotting process in a way that is different from formal laboratory coagulation, and thus cannot reasonably be directly compared with formal laboratory testing. This is the reason for the poor correlation between FIBTEM A10 and formal laboratory fibrinogen, EXTEM A10 and a formal laboratory platelet count and EXTEM A10-FIBTEM A10 and a formal laboratory platelet count. This poor correlation does not make the ROTEM results any less reliable or question the validity of the technique; ROTEM detects clotting by mechanical properties through an electric current and laboratory testing involves turbidimetry.

Limitations

The two main limitations of this study are the small number of patients recruited and the small percentage of eligible patients recruited. This was because a ROTEM trained researcher had to be called into the ED to perform the ROTEM test. Recruitment therefore relied on a ROTEM trained researcher being available and being called by the treating physician. In 90% of cases, either the clinician did not call the researcher or the researcher was not available to attend. There was no statistical difference in any parameter, however, between those recruited compared with those missed, suggesting that the patients recruited in the study are typical of the entire population of unwell ED bleeding patients.

A limitation of the clinical applicability of this study is that to use the ROTEM technology routinely, members of the ED need to be trained. EDs are typically unpredictable places with a huge staff and a high staff turnover. Training staff to use a technology that may not be used on a daily basis may lead to deskilling. Our study has shown that in an ED with 110 000 attendances a year, about one patient a day may fulfil the criteria that may benefit from ROTEM. In the theatre setting, tests are run more regularly and a dedicated ever-present member of theatre staff can take on the testing role. This is not possible in the ED setting.

We originally hoped to measure serial samples on our patients, but because our patients were unwell and bleeding, the majority of them were soon transferred to either the operating theatre, angiography or to the GI endoscopy suite; thus, serial ED samples could not be obtained. Although this may reduce the clinical use of the ROTEM within the ED, a baseline ROTEM reading may be extremely useful for the intensivists/anaesthetists looking after this patient group an hour or so down the line.

Finally, before being accepted into standard ED practice, more evidence is still required to show that the use of ROTEM in the ED can impact on patient outcome. A study investigating how ROTEM might impact on important patient outcomes such as mortality and hospital length of stay is required. Such a study may have to be multicentre.

Conclusion

This is the first ED study to use ROTEM to detect coagulopathy in all bleeding patients, not just trauma

![Fig. 5](image-url)
patients. Although 18% of bleeding ED patients are coagulopathic, the majority of these are trauma patients (25% of trauma patients were coagulopathic). A 10-min ROTEM clot firmness (A10) is an excellent surrogate for MCF and allows a result to be obtained earlier than formal laboratory results and potentially within 10 min of the patient arriving in the ED. A 10-min ROTEM clot firmness (A10) should be routinely used when using ROTEM to detect coagulopathy in bleeding ED patients.

Acknowledgements

Thanks are due to all the staff in the Emergency Department of the Royal Infirmary of Edinburgh for their help with patient recruitment for this study.

The ROTEM machine was provided by Pentapharm (Munich, Germany). Reagents were supplied by the Scottish National Blood Transfusion Service.


Conflicts of interest

There are no conflicts of interest.

References