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Fast interpretation of thromboelastometry in non-cardiac surgery: reliability in patients with hypo-, normo-, and hypercoagulability

K. Görlinger[1*†], D. Dirkmann[1†], C. Solomon[2] and A. A. Hanke[3]

[1] Klinik für Anästhesiologie und Intensivmedizin, Universitätsklinikum Essen, Universität Duisburg-Essen, Hufelandstraße 55, D-45122 Essen, Germany
[2] Klinik für Anästhesiologie, Perioperative Medizin und Allgemeine Intensivmedizin, Salzburger Landesklinikum SALK, Universitätsklinikum der Paracelsus Medizinischen Privatuniversität, Müllner Hauptstraße 48, A-5020 Salzburg, Austria
[3] Klinik für Anästhesiologie und Intensivmedizin, Medizinische Hochschule Hannover, Carl-Neuberg-Straße 1, D-30625 Hannover, Germany

* Corresponding author. E-mail: klaus@goerlinger.net

Editor's key points

- Rapid analysis of coagulation function is critical to intraoperative haemostatic therapy.
- Early variables assessed by rotational thromboelastometry might rapidly predict clot formation (maximum clot firmness, MCF).
- In a large retrospective analysis of patients undergoing non-cardiac surgery, the clot amplitude at 5, 10, or 15 min provided early linear correlation with MCF, which should be useful in managing severe bleeding.

Background. Conventional coagulation test are not useful to guide haemostatic therapy in severe bleeding due to their long turn-around time. In contrast, early variables assessed by point-of-care thromboelastometry (ROTEM®) are available within 10–20 min and increasingly used to guide haemostatic therapy in liver transplantation and severe trauma. However, the reliability of early ROTEM® variables to predict maximum clot firmness (MCF) in non-cardiac surgery patients with subnormal, normal, and supranormal MCF has not yet been evaluated.

Methods. Retrospective data of 14 162 ROTEM® assays (3939 EXTEM®, 3654 INTEM®, 3287 FIBTEM®, and 3282 APTEM® assays) of patients undergoing non-cardiac surgery were analysed. ROTEM® variables [clotting time (CT), clot formation time (CFT), α-angle, A5, A10, and A15] were related to MCF by linear or non-linear regression, as appropriate. The Bland–Altman analyses to assess the bias between early ROTEM® variables and MCF and receiver operating characteristics (ROC) were also performed.

Results. Taking the best and worst correlation coefficients for each assay type, CT (r=0.18–0.49) showed the worst correlation to MCF. In contrast, α-angle (r=0.85–0.88) and CFT (r=0.89–0.92) demonstrated good but non-linear correlation with MCF. The best and linear correlations were found for A5 (r=0.93–0.95), A10 (r=0.96), and A15 (r=0.97–0.98). ROC analyses provided excellent area under the curve (AUC) values for A5, A10, and A15 (AUC=0.962–0.985).

Conclusions. Early values of clot firmness allow for fast and reliable prediction of ROTEM® MCF in non-cardiac patients with subnormal, normal, and supranormal MCF values and therefore can be used to guide haemostatic therapy in severe bleeding.

Keywords: blood coagulation; liver transplantation; measurement techniques; postpartum haemorrhage; thromboelastometry; trauma

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Severe bleeding due to acquired coagulopathy is a major issue in several kinds of non-cardiac surgery such as liver transplantation, severe trauma, and postpartum haemorrhage. However, due to their long turn-around time, conventional coagulation tests performed in the central laboratory are not useful to guide haemostatic therapy in these clinical settings.[1–4] Therefore, many clinicians decide to base their haemostatic therapy on their own experience or on red blood cell to fresh-frozen plasma ratios.[5–7] This practice can result in inappropriate transfusion of allogeneic blood products, which is associated with increased morbidity, mortality, and hospital costs.[8–12] In contrast, early variables assessed by point-of-care thromboelastometry (ROTEM®) are available within 10–20 min and are increasingly used to guide haemostatic therapy in patients with acquired coagulopathy.[2 3 13–19] Accordingly, coagulation management algorithms based on point-of-care testing and goal-directed first-line therapy with specific coagulation factor concentrates such as fibrinogen concentrate and prothrombin complex concentrate have recently been shown to be associated with a reduction in transfusion requirements and transfusion-associated adverse events,

† These authors contributed equally to this manuscript.

and also improved outcomes and reduced hospital costs.[20–30]

Maximum clot firmness (MCF) is one of the most important ROTEM® variables.[2 4 13–18 26–30] However, the reliability of early ROTEM® variables to predict MCF in non-cardiac patients with subnormal, normal, and supranormal MCF has not yet been evaluated for either ROTEM® or TEG®. Therefore, we tested the hypotheses that variables obtained early during point-of-care ROTEM® tests reliably predict the MCF that will be achieved. Specifically, we tested whether clotting time (CT), clot formation time (CFT), α-angle, or early values of clot firmness (i.e. A5, A10, and A15) allow prediction of MCF in non-cardiac surgery patients with subnormal, normal, and supranormal MCF values using four different commercially available ROTEM® assays (EXTEM®, INTEM®, FIBTEM®, and APTEM®).

Methods

Ethics approval

This retrospective study was approved by the institutional Ethics Committee of the University Hospital Essen, Germany, and abides by the ethical principles for medical research outlined in the Declaration of Helsinki.

Data collection

We retrospectively analysed data from our database including 14 162 ROTEM® assays performed in patients undergoing non-cardiac surgery (i.e. visceral surgery and liver transplantation, severe trauma, orthopaedic surgery, neurosurgery, urological surgery, gynaecological surgery, and postpartum haemorrhage). Four different commercially available ROTEM® assays (i.e. EXTEM®, APTEM®, FIBTEM®, and INTEM®) were included and reviewed for adequacy. Exclusion criteria were total runtime $<$35 or $>$120 min and signs of hyperfibrinolysis (i.e. clot lysis index after 30, 45, or 60 min $<$85% or any detected lysis onset time=time until clot firmness decreased by 15% compared with MCF). Overall, 3939 EXTEM®, 3282 APTEM®, 3287 FIBTEM®, and 3654 INTEM® assays were included in the study. The following ROTEM® variables were determined: CT, CFT, α-angle, amplitude of clot firmness 5, 10, and 15 min after CT (A5, A10, and A15, respectively), and MCF.

ROTEM® measurements

Thromboelastometry (ROTEM®, TEM International GmbH, Munich, Germany) is a whole blood viscoelastic test measuring CTs (CT and CFT), clotting dynamics (CFT and α-angle), clot firmness (A5, A10, A15, and MCF), and clot stability over the time [CLI30, CLI45, CLI60, maximum lysis (ML), and lysis onset time]. Owing to its high resistance to movement and agitation artifacts, it can be used as a mobile point-of-care device in the operating theatre or at the intensive care unit. The ROTEM® device provides four independent measuring channels and uses several test assays with two different activators. All assays analysed in the present study were performed according to the manufacturer's instructions using commercially available assays by a limited number of trained anaesthetists and nurses. In our institution, ROTEM® analysis is routinely performed at certain time points during liver transplantation and in cases of diffuse bleeding during other kinds of surgery. For screening purposes, we routinely perform different extrinsically activated assays (EXTEM®, FIBTEM®, and APTEM®) and a single intrinsically activated test (INTEM®). EXTEM® assays are activated using tissue factor and are thought to serve as a screening test sensitive to deficiencies of vitamin K-dependent coagulation factors, fibrinogen, factor XIII, and platelets. In the FIBTEM® assay, platelet function is abolished using cytochalasin D, a potent inhibitor of actin polymerization, an essential part of the platelets' cytoskeleton-mediated contractility apparatus. Accordingly, FIBTEM® allows for the detection of fibrinogen deficiency or fibrin polymerization disorders, for example, induced by dysfibrinogenaemia, infused colloids, or by factor XIII deficiency. The APTEM® assay is similar to the EXTEM® test but contains additional aprotinin to block a potential fibrinolysis. Comparison of EXTEM® and APTEM® assays gives further insight in the diagnosis of hyperfibrinolysis and allows estimation of the efficacy of antifibrinolytic therapy. The INTEM® assay is based on intrinsic activation by ellagic acid providing information on the coagulation factors involved in the intrinsic pathway. Further details about thromboelastometry are described elsewhere.[31]

Data analyses and statistics

Data were analysed separately for each ROTEM® assay. Furthermore, EXTEM® and FIBTEM® analyses were separated into three subgroups with subnormal (MCF$<$50 or $<$9 mm, respectively), normal (MCF=50–70 or 9–25 mm, respectively), and supranormal MCF (MCF$>$70 or $>$25 mm, respectively) according to the reference range for EXTEM® (MCF 50–70 mm) and FIBTEM® (MCF 9–25 mm).[32] Since data were not normally distributed, according to a Kolmogorov–Smirnov test using the Dallal and Wilkinson approximation to Lilliefors' method, data are shown as median (25th; 75th percentile) (range). To test our hypothesis that CT, CFT, α-angle, A5, A10, and A15 values correlate with MCF, each variable was compared with the corresponding MCF by fitting a linear regression and calculating Spearman's correlation coefficient ρ. A runs test (Wald–Wolfowitz test) was performed for each analysis to test if the curve fits by non-linear regression deviates significantly from the data.

The Bland–Altman analyses[33 34] were performed to calculate the mean difference (bias) [standard deviation (SD)] between the early values of clot firmness (A5, A10, and A15, respectively) and MCF. For EXTEM® and FIBTEM® A10 values, this was done separately for analyses presenting subnormal, normal, supranormal MCF, and pooled data, as well, to see whether this resulted in different bias values.

Optimal threshold values for all tested variables to predict a subnormal MCF in EXTEM®, APTEM®, and INTEM® (MCF$<$50