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Early thromboelastometry variables predict maximum clot firmness in children undergoing cardiac and non-cardiac surgery

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Abstract

Background: Early clot amplitudes measured on thromboelastometry (ROTEM®) predict maximum clot firmness (MCF) in adults. In this multicentre, retrospective study, we aimed to confirm the suspected relationship between early ROTEM® variables and MCF, in children undergoing cardiac or non-cardiac surgery.

Methods: 4762 ROTEM® tests (e.g. EXTEM, INTEM, FIBTEM, APTEM, and HEPTEM) performed in children undergoing cardiac or non-cardiac surgery at three University hospitals between January 2011 and June 2014 were reviewed. To assess the correlation between clot amplitudes measured after 5, 10 and 15 min and MCF, each variable was compared with the corresponding MCF by calculating Spearman's correlation coefficient.

Results: For the EXTEM® test, we observed that amplitude measured after 5 min (A5: r=0.91, P<0.001), 10 min (A10: r=0.95, P<0.001) and 15 min (A15: r=0.96, P<0.001) were strongly correlated to MCF. The same correlations were observed for INTEM® test (A5: r=0.93, P<0.001; A10: r=0.97, P<0.001; A15: r=0.97, P<0.001), and FIBTEM® test (A5: r=0.93, P<0.001; A10: r=0.94, P<0.001; A15: r=0.96, P<0.001). In addition, the amplitudes measured after five, 10 and 15 min were also strongly correlated with MCF in the APTEM® and the HEPTEM® tests. Receiver operating characteristics (ROC) analysis confirmed that A5, A10, A15 strongly predicted decreased MCF on all ROTEM® tests.

Conclusions: This study confirmed that early values of clot amplitudes measured as soon as five, 10 or 15 min after clotting time could be used to predict maximum clot firmness in all ROTEM® tests.

Key words: blood transfusion; blood coagulation; children; measurement techniques; thromboelastometry; transfusion algorithm

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Editor's key points

- Point-of-care (POC) coagulation testing is increasingly used and several devices are commercially available.
- Maximum clot firmness (MCF) relates to early clot amplitudes measured using the ROTEM® device in adults but there are limited data in children.
- In this retrospective study, there were close correlations between clot amplitudes as early as 5 min and subsequent maximum clot firmness.
- Early availability of this information could aid the management of coagulopathy, but further data are needed.

Standard coagulation assays have been used for a long time for the diagnosis of congenital and acquired coagulopathies, and to guide the administration of anticoagulation both in adults and children.[1 2] Although considered as the 'gold standard', these tests were not designed to monitor perioperative coagulopathy, and to guide the administration of haemostatic agents in bleeding situations.[3] As it usually takes 30–45 min to obtain the results from standard coagulation assays, limited information are provided by these tests in the context of acute bleeding.[4] In addition, standard laboratory tests are performed on platelet poor plasma (PPP) and do not allow for a global assessment of coagulation, giving no information about clot firmness and clot lysis.[5]

Over the past decade, thromboelastometry (ROTEM®, TEM International GmbH, Munich, Germany) has been increasingly used in different clinical conditions, and is now integrated in all recent guidelines for bleeding management.[6 7] Different tests performed on whole blood are available, allowing for an assessment of the intrinsic coagulation pathway (INTEM: in-tem®, ellagic acid), the extrinsic pathway (EXTEM: ex-tem®, tissue factor), the fibrinogen function (FIBTEM: fib-tem®, tissue factor and cytochalasin D), the fibrinolysis (APTEM: ap-tem®, tissue factor and aprotinin), and the presence of residual heparin activity (HEPTEM: hep-tem®, ellagic acid and heparinase). In adults undergoing cardiac and non-cardiac surgeries, clot amplitudes measured 5–10 min after initiation of coagulation have been shown to predict maximum clot firmness (MCF), allowing for a rapid detection and management of decreased clot strength.[8–11] In children undergoing cardiac surgery, Romlin and colleagues[12] reported a good correlation between clot amplitude measured 10 min after clot initiation and MCF, both in HEPTEM (r=0.95, P<0.001) and FIBTEM (r=0.96, P<0.001). Comparable results were also reported in another cardiac study, showing that the clot amplitude measured as soon as 10 min after clot initiation, offered the same predicted value for postoperative bleeding, when compared with the amplitude measured after 20 min or MCF.[13]

In this multicentre, retrospective study, we aimed to confirm the suspected relationship between early ROTEM® variables and MCF in children undergoing cardiac or non-cardiac surgery.

Methods

This retrospective study was approved by the local ethics committee at La Paz University Hospital (Madrid, Spain), and the ethics committee waived the requirement for written informed consent, as only de-identified ROTEM® variables were collected from the ROTEM® databases (30/03/2015, HULP: PI-1998). The study and the decision made by the principal ethics committee was also reviewed and approved by the other ethics committees.

Three authors (APF, MDCL, and DF) respectively reviewed the ROTEM® databases, including all tests performed in children undergoing cardiac and non-cardiac surgeries (e.g. visceral surgery, liver transplantation, trauma, orthopaedic surgery) at La Paz University Hospital (Madrid, Spain), University Hospital Virgen de la Arrixaca (Murcia, Spain), and Queen Fabiola Children's University Hospital (Brussels, Belgium) between January 2009 and June 2014. Five different tests (e.g. EXTEM, INTEM, FIBTEM, APTEM, and HEPTEM) were reviewed for adequacy. Exclusion criteria were: tests performed in patients ≥18 yr, total runtime <35 or >90 min and signs of hyperfibrinolysis defined as a lysis index, measured after 30 min (LI30) <75%.

In all centres, ROTEM® assays were performed in the operating room by experimented doctors, and respecting the recommendations published by the manufacturer.[14] The following parameters were obtained from the different ROTEM® tests: clotting time (CT, s), clot formation time (CFT, s), alpha angle (α, degree), amplitudes measured after five, 10, 15 min (A5, A10, A15, mm) and the maximum clot firmness (MCF, mm).

Statistical analysis

Data were analysed separately for each ROTEM® assays. Distribution of data was tested for normality using the Kolmogorov-Smirnov test. Continuous variables are reported as mean and standard deviation (SD). To assess the correlation between CT, CFT, α angle, A5, A10, A15 and MCF, each variable was compared with the corresponding MCF by calculating Spearman's correlation coefficient. The Bland-Altman analyses were performed to calculate the mean difference (bias) and the standard deviation (SD) between A5, A10, A15 and MCF. Optimal thresholds for all tested variables to predict a subnormal MCF on EXTEM®, INTEM®, APTEM® (MCF <50 mm), and FIBTEM® (MCF <9 mm) were calculated, using receiver operating characteristics (ROC) analysis. These cut-offs were defined a priori using the 2.5th percentile of the normal paediatric reference ranges defined by Ostwald and colleagues[15] Results are expressed as area under the ROC curve, sensitivity and specificity, and their 95% confidence intervals (CIs).

A P-value <0.05 was considered statistically significant for all comparisons. Statistical analysis was performed using IBM SPSS Statistics (version 21.0, IBM, Armonk, NY).

Results

From the 4762 ROTEM® assays obtained from children who underwent cardiac or non-cardiac surgery in this multicentre retrospective analysis, data from 1580 EXTEM®, 1227 INTEM®, 1415 FIBTEM®, 428 HEPTEM® and 112 APTEM® were analysed (Supplementary data, Table 1).

For all assays, correlations between CT, CFT, alpha angle and MCF were significant, but associated with weak correlation coefficients (Fig. 1A–C). For the EXTEM® test, we observed that amplitude measured five min (A5) after the clotting time was strongly correlated with MCF (Fig. 1D: r=0.91, P<0.001). The same strong correlations were reported for the amplitudes measured after 10 min (Fig. 1E: r=0.95, P<0.001) and 15 min (Fig. 1F: r=0.96, P<0.001). Amplitudes measured after 5, 10 and 15 min were also strongly correlated with MCF in the INTEM®, APTEM® and the HEPTEM® tests (Table 1). For the FIBTEM® test, we observed that amplitude measured after 5 min (A5) was strongly correlated with MCF (Fig. 2A: r=0.93, P<0.001). The same strong correlations were reported for the amplitudes measured after 10 min (Fig. 2B: r=0.94, P<0.001) and 15 min (Fig. 2C: r=0.96, P<0.001). In addition,