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CLINICAL PRACTICE

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

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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,

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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, 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 Lillliefors' 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 mm) and FIBTEM® (MCF<9 mm) were calculated using receiver operating characteristics (ROC).[35][36] Results for ROC analyses are given as area under the curve (AUC), P-value, sensitivity [95% confidence interval (CI)], and specificity (95% CI). Optimal cut-off values (threshold) were calculated as the Youden index.[37] Where applicable, a P-value of <0.05 was considered statistically significant.

Results

Descriptive data

Data were collected from our database of patients undergoing different kinds of non-cardiac surgery (visceral surgery and liver transplantation, severe trauma, orthopaedic surgery, neurosurgery, urological surgery, gynaecological surgery, and postpartum haemorrhage). A total of 14 162 ROTEM® analyses were included (3939 EXTEM®, 3654 INTEM®, 3287 FIBTEM®, and 3282 APTEM® assays, respectively). Descriptive data of all analysed ROTEM® variables (i.e. CT, CFT, α-angle, A5, A10, A15, and MCF) are shown as median (25th; 75th percentile) (range) in Table 1 indicating a wide range for all variables analysed. According to EXTEM® MCF, 1935 analyses (49.1%) present subnormal MCF values (EXTEM® MCF<50 mm), 1864 analyses (47.3%) were within the reference range of 50–70 mm, and 140 analyses (3.6%) presented supranormal MCF values (EXTEM® MCF>70 mm). With regard to FIBTEM® MCF, 469 analyses (14.3%) presented values below the reference range (FIBTEM® MCF<9 mm), 2552 analyses (77.6%) were within the reference range of 9–25 mm, and 266 analyses (8.1%) presented values above the reference range (FIBTEM® MCF>25 mm) (Table 2).

Spearman's correlation

Correlation coefficients for all variables and assays analysed are listed in Table 3. Specifically, CT showed neither good linear nor non-linear correlation (r=0.18–0.49). Accordingly, no line of agreement is given in the figures (Figs 1A and 2A). CFT (Fig. 1B) and α-angle (Fig. 1C) fared better, but linear regression did not fit appropriately. Accordingly, non-linear regression (r=0.89–0.92 and 0.85–0.88, respectively) was used and a runs test (Wald–Walfowitz test) demonstrated a good fit for these variables. Early values of clot firmness (A5, A10, and A15) showed an excellent linear correlation with MCF for all assays analysed (r=0.93–0.95, 0.96, and 0.97–0.98, respectively). Data given above in parentheses represent the worst and the best correlation coefficient obtained from the four different assays (EXTEM®, INTEM®, FIBTEM®, and APTEM®). Exemplary graphs demonstrating the respective correlations for all variables of EXTEM® and FIBTEM® assays are shown in Figures 1 and 2.

Table 1 Descriptive data for all ROTEM® variables analysed. Data are shown for each assay and are presented as median (25th; 75th percentile) (range). CT, clotting time; CFT, clot formation time; A5, A10, A15, amplitude of clot firmness 5, 10, and 15 min after CT; MCF, maximum clot firmness

Assay (n)	CT (s)	CFT (s)	α-Angle (°)	A5 (mm)	A10 (mm)	A15 (mm)	MCF (mm)
EXTEM® (n=3939)	63 (51; 86) (20–1057)	153 (100; 248) (11–5160)	64 (53; 72) (14–87)	29 (22; 38) (3–79)	39 (31; 39) (2–83)	44 (35; 53) (2–84)	50 (42; 57) (5–90)
APTEM® (n=3282)	74 (59; 100) (21–905)	162 (106; 262) (18–3943)	63 (51; 71) (12–86)	28 (21; 37) (3–78)	38 (29; 47.5) (4–84)	43 (34; 52) (3–86)	49 (42; 57) (5–88)
FIBTEM® (n=3287)	63 (51; 81) (21–1100)	n.a.	n.a.	9 (7; 13) (2–55)	10 (7; 14) (2–65)	11 (8; 15) (2–68)	14 (10; 18) (4–79)
INTEM® (n=3654)	211 (173; 270) (101–1166)	142 (92; 238) (25–3466)	67 (56; 74) (14–85)	30 (22; 38) (4–76)	39 (30; 48) (2–82)	44 (35; 52) (3–84)	49 (42; 49) (5–88)

Table 2 Bias for A10 values of EXTEM® and FIBTEM® in patients with subnormal, normal, and supranormal MCF and pooled data as obtained from the Bland–Altman analyses. The reference range for EXTEM® MCF is 50–70 mm and for FIBTEM® MCF 9–25 mm.[32] Bias data are presented as means (SD). r, Spearman's coefficient ρ for each assay and range for linear regression; MCF, maximum clot firmness; A10, amplitude of clot firmness 10 min after CT

Assay (n)	MCF range (mm)	A10 bias (mm)	r
EXTEM® (n=3939)	Overall	10.03 (3.86)	0.96
EXTEM® (n=1935)	<50	11.08 (3.60)	0.90
EXTEM® (n=1864)	50–70	9.27 (3.63)	0.89
EXTEM® (n=140)	>70	5.64 (4.87)	0.56
FIBTEM® (n=3287)	Overall	3.44 (2.06)	0.96
FIBTEM® (n=469)	<9	1.95 (0.86)	0.70
FIBTEM® (n=2552)	9–25	3.43 (1.49)	0.93
FIBTEM® (n=266)	>25	6.24 (4.29)	0.83

Table 3 Spearman's correlation coefficient ρ for each ROTEM® assay. Correlation coefficients are listed for non-linear regression of CT, CFT, and α-angle to MCF and for linear regression of A5, A10, and A15 to MCF. CT, clotting time; CFT, clot formation time; MCF, maximum clot firmness; A5, A10, A15, amplitude of clot firmness 5, 10, and 15 min after CT, respectively

Assay (n)	CT (s)	CFT (s)	α-Angle (°)	A5 (mm)	A10 (mm)	A15 (mm)
EXTEM® (n=3939)	0.32	0.89	0.85	0.93	0.96	0.97
APTEM® (n=3282)	0.31	0.92	0.88	0.94	0.96	0.97
FIBTEM® (n=3287)	0.18	n.a.	n.a.	0.95	0.96	0.97
INTEM® (n=3654)	0.49	0.91	0.87	0.94	0.96	0.98

Bland–Altman analyses

Specific bias as obtained from the Bland–Altman analyses for A5, A10, and A15 values for EXTEM®, APTEM®, FIBTEM® and INTEM® assays are listed in Table 4.

Difference in patients presenting subnormal, normal, or supranormal MCF values

The bias for A10 values of EXTEM® and FIBTEM® in patients with subnormal (MCF<50 or <9 mm, respectively), normal (MCF 50–70 or 9–25 mm, respectively), and supranormal MCF values (MCF>70 or >25 mm, respectively) and pooled data as obtained from the Bland–Altman analyses are presented in Table 2, and also the respective Spearman's coefficients ρ for linear regression.

Receiver operating characteristics

ROC curve analyses demonstrated that CT provided only poor AUC values (0.614–0.74), indicating a low overall test performance, for all assays analysed. In contrast, CFT and α-angle (AUC=0.943–0.967 and 0.915–0.935, respectively) (both analysed for EXTEM®, APTEM®, and INTEM® assays only) and also A5, A10, and A15 performed excellently (AUC=0.962–0.976, 0.974–0.982, and 0.981–0.985, respectively). ROC curves of variables are shown in Figure 3A–D for all assays analysed. Results of all ROC curve analyses are given in Table 5 as AUC with respective P-values and calculated optimal cut-off values (thresholds) with respective sensitivity (95% CI) and specificity (95% CI).

Discussion

Our retrospective study analysing data of 14 162 ROTEM® assays from non-cardiac patients demonstrates that early values of clot firmness (A5, A10, or A15, respectively) serve best in approximating the MCF achieved in ROTEM® measurements. In contrast, CFT and α-angle performed worse and furthermore showed non-linear correlation, making it difficult to apply clinically. CT showed the worst correlation with MCF and seems not useful for the prediction of MCF.

In EXTEM®, the bias between A10 and MCF decreases slightly with increasing MCF. This might be due to progressive platelet retraction in the case of a high platelet count or platelet hyperreactivity.[38] However, the difference between the bias in the group presenting subnormal MCF values and the bias calculated for all EXTEM® analyses is only 1.05 mm (about 2% of the corresponding MCF). Therefore, this can be neglected for therapeutic decisions. In patients presenting supranormal MCF values, the bias is remarkably lower [5.64 (4.87) vs 10.03 (3.86) mm], but in this patient population, a procoagulant haemostatic intervention is not indicated.

Notably, in FIBTEM®, the bias between A10 and MCF increases with increasing MCF. This might be due to progressive fibrin polymerization due to high plasma fibrinogen concentrations. Since the bias in patients presenting subnormal MCF values is 1.49 mm lower compared with that in the whole patient population, the calculated dose of fibrinogen substitution tends to turn out a bit lower (about 10 mg fibrinogen per kilogram bodyweight).[29] On the other hand, the risk of fibrinogen overdose is reduced by this difference in the bias.

MCF in FIBTEM® assays has been demonstrated to correlate well with plasma fibrinogen concentration in patients undergoing major surgery or liver transplantation or suffering from trauma or postpartum haemorrhage.[3 13 15–18 39] Accordingly, fast and reliable assessment of plasma fibrinogen concentration is of interest since plasma fibrinogen concentration and MCF in FIBTEM® assays have been shown to have an excellent predictive value for perioperative bleeding complications and need for massive transfusion in trauma, scoliosis surgery, postpartum haemorrhage, and cardiac surgery.[2 17 40–43] Furthermore, FIBTEM®-guided administration of fibrinogen concentrate has been shown to be associated with reduced transfusion requirements in patients after severe trauma or undergoing
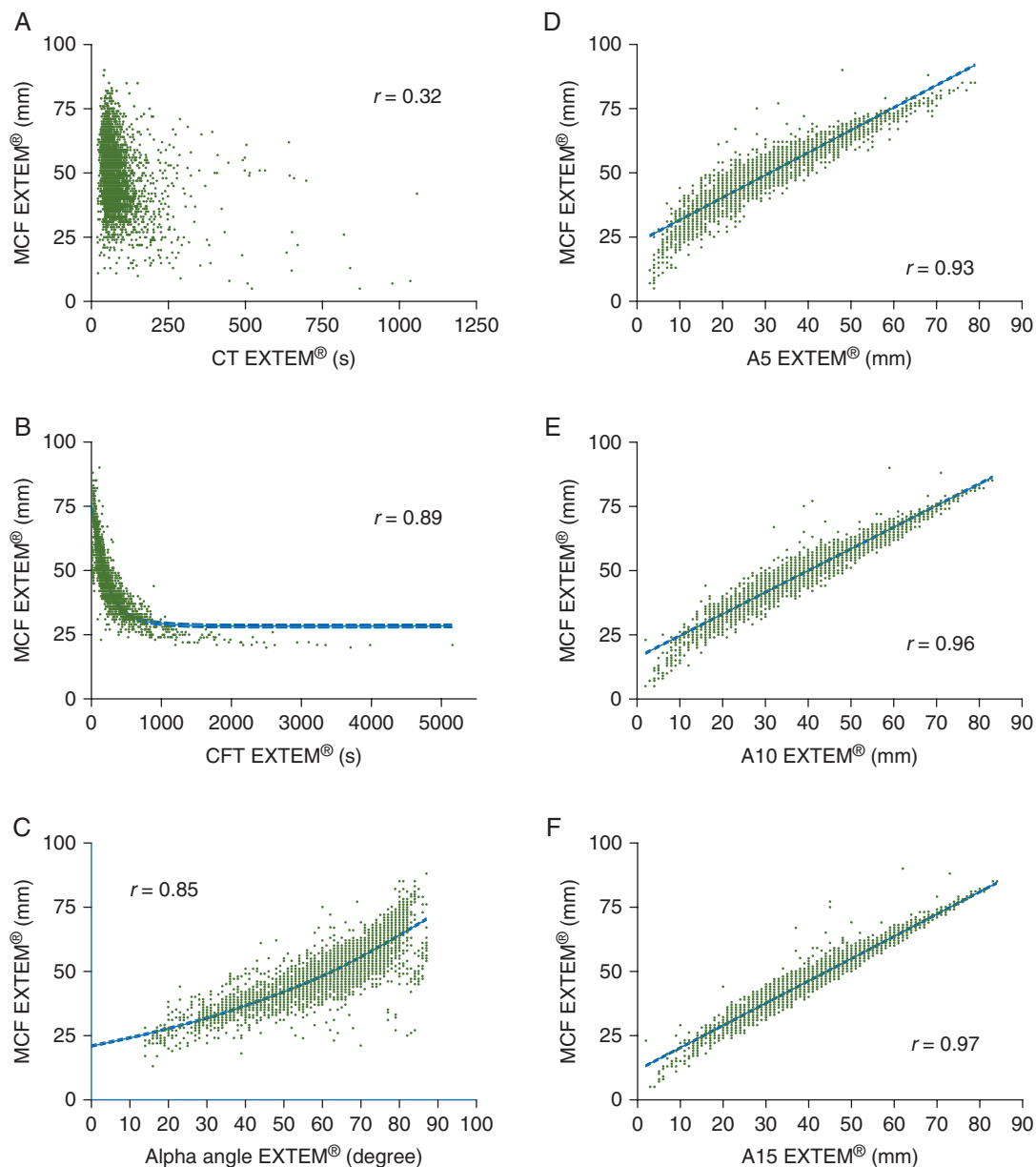
Fig 1 Graphs for EXTEM® variables demonstrating poor correlation between CT and MCF (A) and good non-linear correlation between CFT (B) and α-angle (C) and MCF, and excellent linear correlation between A5 (D), A10 (E), and A15 (F) and MCF, respectively. CT, clotting time; MCF, maximum clot firmness; CFT, clot formation time; A5, A10, A15, amplitude of clot firmness 5, 10, and 15 min after CT, respectively.

major surgery without an increased incidence of thromboembolic events.[20] [23–30] [44] Accordingly, an early and reliable assessment of plasma fibrinogen concentration and the detection of fibrin polymerization disorders by MCF in FIBTEM® assays should accelerate clinical decision-making with regard to therapy with fibrinogen containing blood products such as fresh-frozen plasma, cryoprecipitate, or fibrinogen concentrate. Furthermore, FIBTEM® provides not only an alternative assessment for plasma fibrinogen concentration but also adds additional information on fibrinogen polymerization defects due to dysfibrinogenaemia, often present in liver

cirrhosis, colloid infusion, or factor XIII deficiency.[45] In addition, hydroxyethylstarch solutions can evoke erroneously high fibrinogen concentration measurements yielded by coagulation analysers based on optical measurements.[46] Thus, assessing FIBTEM® MCF seems to be preferable to assess fibrin polymerization in patients after infusion of colloids, such as hydroxyethylstarch solutions. It is important to consider that ROTEM® results are influenced by haematocrit. Reduced haematocrit results in increased plasma fraction in the whole blood sample which can result in increased MCF.[47–49]
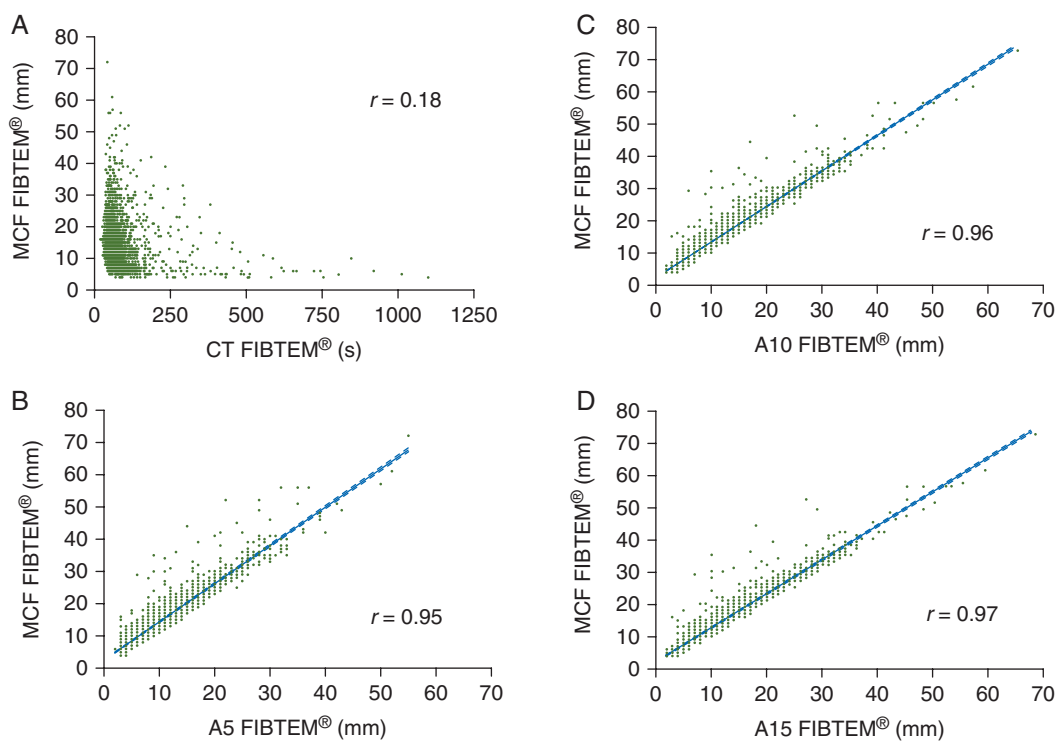
Fig 2 Graphs for FIBTEM® variables demonstrating poor correlation between CT and MCF (A) and excellent linear correlation between A5 (B), A10 (C), and A15 (D) and MCF, respectively. CT, clotting time; MCF, maximum clot firmness; A5, A10, A15, amplitude of clot firmness 5, 10, and 15 min after CT, respectively.

Table 4 Bias for A5, A10, and A15 values of all assays as obtained from the Bland–Altman analyses. Data are presented as means (SD). A5, A10, A15, amplitude of clot firmness 5, 10, and 15 min after CT, respectively

Assay (n)	A5 (mm)	A10 (mm)	A15 (mm)
EXTEM® (n=3939)	19.07 (4.52)	10.03 (3.86)	5.76 (3.22)
APTEM® (n=3282)	19.07 (4.34)	10.15 (3.79)	5.92 (3.22)
FIBTEM® (n=3287)	4.47 (2.51)	3.44 (2.06)	2.84 (1.91)
INTEM® (n=3654)	18.63 (4.14)	9.89 (3.53)	5.67 (2.93)

According to our data, early values of clot firmness can be used as an alternative assessment of MCF. A5 or A10 values in FIBTEM® assays can predict MCF. Based on our data, it seems appropriate to use A5 values by adding 4 mm ($\pm$3 mm) or A10 values by adding 3 mm ($\pm$2 mm) to predict MCF when using FIBTEM® assays. The difference in bias in FIBTEM® assays between patients with subnormal and normal MCF values was very small (<1.5 mm) and therefore, can be neglegted for clinical decision making.

MCF in EXTEM®, INTEM®, and APTEM® assays, respectively, is influenced by both, fibrinogen concentration/fibrin polymerization and platelet count with platelets responsible for the main part of clot firmness. MCF in EXTEM® assays correlates well with platelet count and allows detection of thrombocytopenia during orthotopic liver transplantation.[16][18][39] For EXTEM® assay, 19 mm ($\pm$5 mm) have to be added to A5 values or 10 mm ($\pm$4 mm) to A10 values in order to approximate MCF. However, early parameters of ROTEM® are not clinically interchangeable with TEG® results because clot formation kinetics are strongly influenced by different reagents.[50]

In conclusion, our data demonstrate that 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. We recommend the use of A5 or A10 values since they exhibit an excellent linear correlation to MCF with a fixed bias for each ROTEM® test. This enables easy and fast calculation of MCF and a calculated targeted haemostatic therapy in daily clinical practice. We recommend using A10 values in routine and A5 values in the case of severe life-threatening bleeding. In contrast, CT, CFT, and α-angle correlate poorly and non-linearly to MCF which makes them inappropriate to guide haemostatic therapy with regard to clot firmness in severe bleeding. However, this does not impair their value to estimate thrombin generation in this setting.
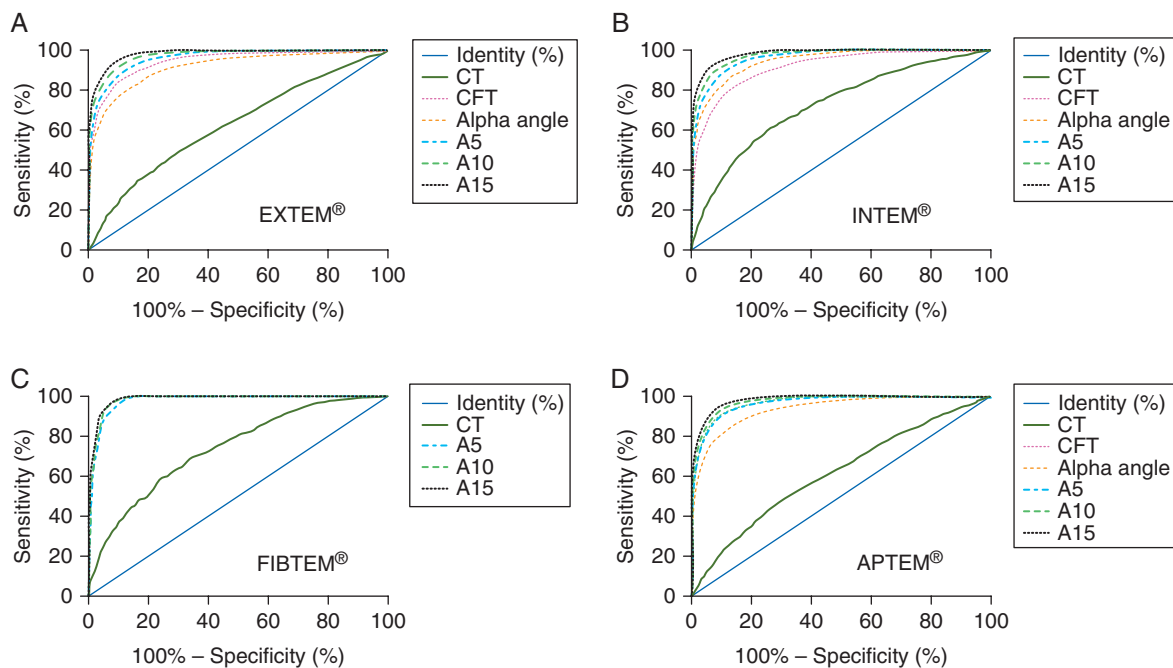
227

Fig 3 ROC curves of CT, CFT, α-angle, A5, A10, and A15 assays to predict subnormal MCF in (A) EXTEM®, (D) APTEM®, and (B) INTEM® (<50 mm) and in (C) FIBTEM® (<9 mm) assays. ROC, receiver operating characteristics CT, clotting time; CFT, clot formation time; A5, A10, A15, amplitude of clot firmness 5, 10, 15 min after CT; MCF, maximum clot firmness.

Table 5 Results obtained from ROC. AUC as obtained from ROC shown with respective *P*-values, optimal cut-off values to predict subnormal MCF values (MCF<50 mm for EXTEM®, APTEM®, and INTEM® and MCF<9 mm for FIBTEM®), corresponding sensitivity (CI), and specificity (CI). CT, clotting time; CFT, clot formation time; A5, A10, A15, amplitude of clot firmness 5, 10, and 15 min after CT, respectively; MCF, maximum clot firmness

Assay (n)	Variable	AUC; *P*-value	Optimal cut-off	Sensitivity in % (CI)	Specificity in % (CI)
EXTEM® (n=3939)	CT (s)	0.625; <0.0001	>71.5	48.04 (45.79–50.29)	71.1 (69.06–73.08)
	CFT (s)	0.943; <0.0001	>163.5	84.46 (82.74–86.06)	89.77 (88.26–91.06)
	α-Angle (°)	0.915; <0.0001	<62.5	80.81 (78.95–82.57)	86.58 (85.01–88.04)
	A5 (mm)	0.962; <0.0001	<29.5	89.82 (88.38–91.13)	87.87 (86.36–89.27)
	A10 (mm)	0.974; <0.0001	<39.5	92.56 (91.3–93.69)	89.22 (87.78–90.55)
	A15 (mm)	0.982; <0.0001	<43.5	91.94 (90.63–93.11)	92.86 (91.65–93.95)
APTEM® (n=3282)	CT (s)	0.614; <0.0001	>83.5	46.42 (44.05–48.8)	71.33 (69.01–73.57)
	CFT (s)	0.967; <0.0001	>161.5	91.36 (89.85–92.72)	89.82 (88.21–91.28)
	α-Angle (°)	0.935; <0.0001	<62.5	84.44 (82.61–86.15)	87.11 (85.34–88.74)
	A5 (mm)	0.966; <0.0001	<28.5	88.5 (86.9–89.96)	91.95 (90.48–93.25)
	A10 (mm)	0.975; <0.0001	<39.5	94.16 (92.95–95.22)	89.69 (88.07–91.16)
	A15 (mm)	0.981; <0.0001	<43.5	93.18 (91.89–94.32)	92.65 (91.24–93.9)
FIBTEM® (n=3287)	CT (s)	0.740; <0.0001	>69.5	69.08 (64.68–73.24)	65.97 (64.19–67.72)
	A5 (s)	0.976; <0.0001	<6.5	98.51 (96.95–99.4)	88.18 (86.93–89.35)
	A10 (mm)	0.982; <0.0001	<6.5	95.95 (93.75–97.54)	93.83 (92.87–94.69)
	A15 (mm)	0.985; <0.0001	<7.5	99.57 (98.47–99.95)	89.63 (88.45–90.73)
INTEM® (n=3654)	CT (s)	0.726; <0.0001	>222.5	60 (57.73–62.24)	74.56 (72.48–76.55)
	CFT (s)	0.946; <0.0001	>139.5	87.73 (86.12–89.21)	85.92 (84.23–87.49)
	α-Angle (°)	0.918; <0.0001	<66.5	80.55 (78.64–82.36)	86.59 (84.93–88.13)
	A5 (mm)	0.963; <0.0001	<29.5	88.27 (86.72–89.7)	89.86 (88.37–91.21)
	A10 (mm)	0.975; <0.0001	<38.5	88.97 (87.46–90.36)	93.02 (91.74–94.15)
	A15 (mm)	0.983; <0.0001	<43.5	92.16 (90.84–93.35)	93.57 (92.34–94.66)

Declaration of interest

Funding

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