Thrombelastography Today: Practicability and Analytical Power

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Key Words

Rotational thrombelastography · RoTEM® · Robustness · Accuracy · Sample · Cytochalasin D

Summary

Today, rotational thrombelastography as a further development of the classical thrombelastography is increasingly applied to assess haemostasis and to predict complications of coagulation. Due to the improved robustness of the method, RoTEM® analyses are now also performed outside specialised coagulation laboratories and applied in emergency settings. Since coagulation testing, particularly when performed with different activators, is very sensitive to artifacts due to variations in the proportion to anticoagulants, temperature and concentration of activators, meticulous quality control is indispensable. For this reason, the German Federal Chamber of Physicians has issued rigorous validity ranges for the classic coagulation tests, such as the prothrombin time (PT/INR) or the activated partial thromboplastin time (aPTT) for variation coefficient acceptance, which are audited 4 times a year by external quality control circles. At present, no comparable quality assurance setup exists for whole blood coagulation testing. Thus, knowledge of the analytical limits, restrictions and caveats of this method is central for critical interpretation of the results and reliable clinical application. This review gives an outline of the practicability and accuracy of the RoTEM methodology and illustrates some pitfalls for the use in detecting and predicting disturbances of haemostasis in a case report.

This work contains parts of the doctoral thesis in medicine of P.H.

Schlüsselwörter

Rotationsthrombelastographie · RoTEM® · Robustheit · Präzision · Probenmaterial · Cytochalasin D

Zusammenfassung

Gegenwärtig wird die Rotationsthrombelastographie als eine Weiterentwicklung der klassischen Thrombelastographie zunehmend zur Überprüfung des Hämostasepotentials eingesetzt. Eine robustere Messanordnung hat dazu geführt, dass der RoTEM®-Analyser zunehmend auch außerhalb spezialisierter hämostaseologischer Laboratorien in Notfalleinheiten eingesetzt wird. Die Gerinnungstests werden mit verschiedenen Aktivatoren durchgeführt und sind störepfindlich gegenüber unterschiedlichen Einflüssen wie Temperaturschwankungen und Volumenfehlern, sowohl was den Antikoagulantengehalt als auch was die Konzentration der Aktivatoren betrifft, so dass eine sorgfältige Qualitätskontrolle unverzichtbar wäre. Aus diesem Grund hat die Deutsche Ärztekammer restriktive Vorgaben für die minimalen Anforderungen der Variationskoeffizienten für die klassischen Gerinnungstests wie die Prothrombinzeit (Quick/INR) oder die aktivierte partielle Thromboplastinzeit (PTT) herausgegeben, die viermal jährlich durch eine externe Qualitätskontrolle überprüft werden. Für Vollblut-Gerinnungstests existiert zurzeit keine vergleichbare Qualitätssicherung. Somit ist die Kenntnis der analytischen Grenzen und Schwächen der Methode von zentraler Bedeutung für die kritische Interpretation der Ergebnisse und zuverlässige klinische Anwendung. Diese Übersichtsarbeit gibt einen Überblick über die Praktikabilität und die analytische Leistungsfähigkeit des RoTEM-Verfahrens und beschreibt Schwierigkeiten bei der Identifikation und der Prädiktion des Risikos von Gerinnungsstörungen anhand eines Fallbeispiels.

Introduction

Rotational thrombelastography (ROTEG) as introduced by Calatzis and Fritzsche in 1996 is a variant of the classic thrombelastography (TEG) [1] developed by Hartert in 1948. Thrombelastography provides a continuous overall measurement of whole blood clot formation and subsequent dissolution related to the resulting fibrinolytic process. The sensor system forms the basic difference between the 2 measuring systems (fig. 1). In the case of ROTEG, there is only one rotational degree of freedom, whilst in the case of Hartert, the pin is freely moveable in all directions. Furthermore, ROTEG uses a permanently fixed cup as opposed to classical TEG where the cup rotates [2–4].

Practicability of Rotational Thrombelastography

The changes described above result in a more robust measurement configuration as compared to Hartert's TEG. The lower susceptibility to errors is an important prerequisite for the

routine application of ROTEG at sites, for example, where there is no scale table. The corresponding measuring device is sold under the name RoTEM® Vollblutgerinnungsanalyser (at present by Matel Medizintechnik GmbH, Munich, Germany), and is equipped with disposable items (pin, cup). Consequently, complicated cleaning procedures are no longer necessary, and there is less danger of erroneous interpretations caused by remnant artefacts [5]. Items of equipment positioned at the exterior of the measuring device (e.g. pre-heating block, measuring blocks) can cause temperature fluctuations, and air currents may further result in disturbances (table 1). The automatic pipette connected to the RoTEM analyser is intended to enhance the degree of standardisation. Similarly, the automatic recording of the measurements provides standardised detection as compared to the manual depiction using stencils in the case of classical TEG.

For better orientation, the 4-channel operation of the RoTEM analyser provides a parallel representation of different essential thrombelastographic variants for distinct diagnostic investigations. Moreover, these 4 channel measurements can be documented by means of a separate printer. The measurement vari-

Fig. 1. Principle of rotational thrombelastography: **a** configuration of measurement, **b** normal thrombelastogram.

Table 1. Effect of environmental factors on NaTEG measured by RoTEM

	Stable ambient temperature (21 ± 0.5 °C)			Air current, varying ambient temperature (16–21 °C)		
	CT, s	CFT, s	MCF, mm	CT, s	CFT, s	MCF, mm
Mean	769.6	280.7	53.7	752.5	348.5	59.5
Minimum	637	233	51	575	196	56
Maximum	881	395	56	1,030	446	62
CV, %	9.0	13.5	2.0	26.4	30.7	4.4
Measurements, n	20	20	20	20	20	20

CT = Coagulation time; CFT = clot formation time; MCF = maximum clot firmness;
CV = coefficient of variation.

ables – intrinsic thrombelastography (InTEG), extrinsic thrombelastography (ExTEG), fibrinogenic thrombelastography (FibTEG), aprotinin thrombelastography (ApTEG), heparin thrombelastography (HepTEG), and ecarin thrombelastography (EcaTEG) – differ mainly by the use of different activators or inhibitors of coagulation. In contrast to conducting the test with recalcification (native thrombelastography, NaTEG) only, which would most closely correspond to Hartert's TEG, the additives used in the case of ROTEG allow much quicker results. For example, in the absence of activators, the reaction time 'r', which represents the period of time in the beginning of the thrombelastogram in the absence of measurable coagulation, is usually about 10 min in the case of classical TEG, whilst the comparable coagulation time 'CT' using activation of coagulation (e.g. by thromboplastin) is approximately only 1 min in the case of ROTEG. This activation-dependent shorter response time of patient-near ROTEG compared to conventional laboratory analyses performed in the clinical laboratory are considered as one advantage favouring the application of ROTEG in a point-of-care setting [6–9]. However, the response times of ROTEG depend largely on the analysis times which may also be extremely prolonged in patients with coagulation disorders, abrogating the potential saving of time.

Principle of Rotational Thrombelastography

ROTEG is a viscoelastic method which particularly focuses on examining the mechanical properties of the developing

fibrin clot. In general, citrated whole blood is used as the sample material and is placed in a cup into the centre of which a pin is immersed. Besides clinical diseases and conditions, numerous endogenous and exogenous factors influence thrombelastography measurements (table 2). Notably, the blood of heparinised patients may have an adverse effect on the measurements, irrespective of the presence or absence of activators. The anticoagulatory effects of heparin cause a prolongation of the coagulation time and of the clot formation time, which describe the kinetics of the coagulation process, and make the maximum amplitude as the place of the maximal firmness thinner up to the point of non-measurability of the sample. Besides heparin, many further substances may interfere with ROTEG results, including local anaesthetics or protamine [10–12]. Currently, the haemostatic potential of transfused blood products or reinfused autologous blood and their influence on the fibrinolytic system, respectively, have not been systematically evaluated. In cardiac bypass surgery, significant improvement of coagulation and fibrinolytic parameters in thrombelastography have been observed after transfusion of blood [13]. Since many patients in surgery, emergency medicine, or intensive care units receive one of these substances or blood products during treatment, particular caution has to be taken when interpreting data of whole blood thrombelastography.

During RoTEM measurements, the axis holding the pin, which serves as the sensor, is rotated alternately to the right and left at 4.75° by means of a spring mechanism. The rotations are optically monitored by means of a mirror, a light

Table 2. Typical readouts for pathological thrombelastograms in specific clinical diseases and conditions. Thrombelastography parameters are given in detail in relation to clinical disease [16–19]

Classical TEG	ROTEG	Unit	Clinical conditions	
			r/CT, k/CFT longer, MCF thinner	r/CT, k/CFT shorter, MCF wider
Reaction time	CT	min ^a /s	factor deficiency hypo-/dysfibrinogenaemia fibrinogen FDPs heparin pathologic inhibitors	hyperfibrinogenaemia thrombocytosis hyperlipidaemia
Clot formation time	CFT	min ^a /s	factor deficiency hypo-/dysfibrinogenaemia FDPs heparin pathologic inhibitors thrombocytopenia thrombocytopathy	hyperfibrinogenaemia thrombocytosis hyperlipidaemia
Maximum amplitude	MCF	mm	hyperfibrinogenaemia thrombocytosis hyperlipidaemia	factor XIII deficiency hypo-/dysfibrinogenaemia FDPs heparin thrombocytopenia thrombocytopathy paraproteinaemia

^aClassical TEG.

FDPs = fibrinogen degradation products CT = coagulation time; CFT = clot formation time; MCF = maximum clot firm

source, and a light beam detector, and are eventually converted into a real time measurement by an integrated computer system (Motorola 68000s assembler programme) (fig. 1a) [14]. Initially, the rotation of the pin is unhindered, which is represented at this stage by a straight line in function of time (fig. 1b). Classical TEG defines this time period as reaction time r , whilst in ROTEG it is defined as coagulation time CT. With the initiation of the coagulation process, the rotational movements are influenced by adhesion of fibrin threads developing between the cup and pin. Graphically, this is shown as a continuous symmetrical widening of the thrombelastograms up to a variable maximum. According to the definition of classical TEG, the period of time to reach a width of 20 mm is the clot formation time k , and in the case of ROTEG, it corresponds to the clot formation time CFT (fig. 1b). CT and CFT are usually expressed in seconds. In classical TEG, the maximum width of the thrombelastogram corresponds to the maximum amplitude 'ma', which in the case of ROTEG corresponds to the parameter maximum clot firmness MCF. The maximum width of the thrombelastogram is measured in millimetres (fig. 1b, table 2). On reaching the maximum amplitude, the productive coagulation phase is completed. Subsequently, the amplitude is reduced by fibrinolytic processes.

Apart from the parameters CT, CFT and MCF, there are several further parameters such as the maximum lysis (ML) and the fibrinolysis index (LI), which may be measured after 30, 45 and 60 min, respectively, describing the fibrinolytic process. In addition, the alpha angle (alp) may be used, which demonstrates the kinetics of clot formation. As these parameters in many cases are currently of limited practical significance, they will not be discussed in further detail. During the hypercoagulable phase of liver transplantation, the clot lysis index was not helpful to differentiate between platelet- versus fibrin-related causes [15]. In this setting, the application of the alp has been effectively applied to estimate coagulation capacity during liver transplantation [15].

Analytical Power of Rotational Thrombelastography

The measurement inaccuracy is an important characteristic of the quality of analytical procedures and test parameters. Consequently for accreditation of analytical laboratories, practices to evaluate the measurement accuracy according to DIN EN ISO/ IEC 17025:2005, as outlined in the ISO Guide to the Expression of Uncertainty in Measurement or DEV-A0-4 have to be routinely applied. The analytic efficiency of ROTEG for the detection of disturbances of haemostasis was investigated. To investigate the efficiency of an analytic method, it is necessary to determine various parameters for example the precision, the accuracy, the linearity, the stability, the sensitivity, the specificity, the recovery, and the practicability. These parameters relate uniquely to the reliability of the analytical method and laboratory parameter measured,

however, even if valid, they do not allow any conclusions to be drawn about the value in clinical utility with regard to diagnostic requirements. Any unassertive analytic result is, however, definitely of no value whatsoever in the diagnostic process [20]. The imprecision, defined as the random deviation of measurements or the coincidental variation range of measured values from the mean will be discussed for the ExTEG, FibTEG, InTEG, and NaTEG. The calculations were performed using the following formulas in which x_i represents measure values, $\bar{x}$ is the mean, n is the number of values, SD is the standard deviation, and CV is the coefficient of variation:

$$\bar{x} = \sum \frac{x_i}{n} \quad (1).$$

$$SD = \pm \sqrt{\sum \frac{(x_i - \bar{x})^2}{(n-1)}} \quad (2).$$

$$CV = \left(\frac{s}{\bar{x}} \right) \times 100 \quad (3).$$

The second most important means to describe the validity of laboratory tests is the incorrectness, which is defined as the systematic deviation of measurements or the difference of the mean from the correct (real) value caused by a systematic error. The incorrectness is analysed by means of standard control materials, and the target values are determined by reference methods. Thus, for the whole blood coagulation assays, it is not possible to provide a description of the incorrectness, since neither standardised control material nor a defined reference method nor a definition of the target values to be expected, are available. The current commercially available control material (RoTROL N®, Pentapharm, Munich, Germany) is a specifically prepared test plasma, while the RoTEG assay is performed in whole blood [21]. The guidelines of the German Federal Chamber of Physicians pertaining to the quality assurance of quantitative tests carried out in medical laboratories require, however, that the composition of the control samples, in particular the matrix, is as close as possible to that of the test samples [22]. Moreover, the validity and measurement accuracy of an analytical procedure or test are always method- and matrix-specific and have to include all relevant factors to ascertain quality. Thus, the major prerequisite for quantitative measurements in a quality-assured process is not given.

Quality Assessment

We performed a quality assessment to determine the test performance of whole blood coagulation measurements using the RoTEG Vollblutgerinnungsanalyser. The measurements were performed with citrated whole blood (table 3) as well as with citrated plasma (table 4) obtained from 120 healthy blood donors. For all types of analyses, the following reagent addi-

Table 3. Imprecision in series of citrated whole blood in ExTEG, FibTEG, InTEG, and NaTEG measured by RoTEM^a

	Mean CT, s (CV, %)	Mean CFT, s (CV, %)	Mean MCF, mm (CV %)
ExTEG	38.0 (6.0)	84.6 (6.0)	54.6 (1.4)
FibTEG	not valid	not valid	19.9 (4.6)
InTEG	127.4 (3.0)	67.5 (4.6)	57.1 (1.9)
NaTEG	769.6 (9.0)	280.7 (13.5)	53.7 (2.0)
Measurements, n	20	20	20

ExTEG = Extrinsic thrombelastography; FibTEG = fibrinogenic thrombelastography; InTEG = intrinsic thrombelastography; NaTEG = native thrombelastography; CT = coagulation time; CFT = clot formation time; MCF = maximum clot firmness; CV = coefficient of variation.

^aFor determination of the imprecision, 5 measurement runs for each TEG variant were performed per channel, and the difference of the 20 determinations was analysed per variant.

Table 4. Imprecision in series of citrated plasma in ExTEG, FibTEG, InTEG, and NaTEG measured by RoTEM^a

	Mean CT, s (CV, %)	CFT, s (CV, %)	MCF, mm (CV, %)
ExTEG	30 (8.1)	145 (77.1)	38 (19.9)
FibTEG	not valid	not valid	25 (25.5)
InTEG	142 (2.1)	93 (47.2)	37 (13.2)
NaTEG	754 (17.1)	341 (22.9)	39 (17.6)
Measurements, n	20	20	20

ExTEG = Extrinsic thrombelastography; FibTEG = fibrinogenic thrombelastography; InTEG = intrinsic thrombelastography; NaTEG = native thrombelastography; CT = coagulation time; CFT = clot formation time; MCF = maximum clot firmness; CV = coefficient of variation.

^aFor determination of the imprecision, 5 measurement runs for each TEG variant were performed per channel, and the difference of the 20 determinations was analysed per variant.

Table 5. Imprecision in series for the automatic pipette^a

	Volume		
	10 µl	20 µl	300 µl
Mean volume, µl	9.4	19.3	296.8
CV, %	3.0	2.2	0.3
Measurements, n	30	30	30

CV = Coefficient of variation.

^aVolumes of 10, 20, und 300 µl were pipetted by the automatic pipette of the RoTEM and the amount of water was weighed in a series of 30 measurements for each volume.

tives were used: for all variants: StarTEG[®] (Pentapharm) as a start reagent for the recalcification with calcium chloride 0.2 mol/l; for the ExTEG: recombinant human tissue factor

with synthetic phospholipids and calcium ions (Innovin[®], DadeBehring, Marburg, Germany); for the FibTEG: abciximab (ReoPro[®], Centocor, Leiden, The Netherlands); for the InTEG: partial thromboplastin-phospholipid from rabbit brain, as well as ellagic acid for the NaTEG[®] only start reagent.

Initially, the precision in the series for the whole blood assay was tested for the variants ExTEG, FibTEG, InTEG, and NaTEG for each measurement channel separately. The measurements were obtained during 5 independent measurement runs. In the case of the above mentioned TEG variants, there was no significant difference between the measurements in the 4 channels (n = 20; Friedmann-Anova test). The precision per series could then be determined independently of the channel for the variants ExTEG, FibTEG, InTEG, and NaTEG in citrated whole blood. Measurements were made in 5 runs on all channels for each respective TEG variant, i.e. 20 measurement results were evaluated for each variant (table 3). The variation coefficients were less than 10%, with the exception of the CFT in the case of the NaTEG which was 13.5%.

For the evaluation of the suitability of plasma for ROTEG analysis (as the RoTROL N), citrated plasma was used which had been obtained within 30 min after taking the blood sample by means of centrifugation for 15 min at 2,500 × g and 15 °C [23]. Otherwise, the procedure corresponded to that described for citrated whole blood (table 4). In comparison to the largely acceptable variation in whole blood measurements, the unacceptably high variation coefficients from 2.1 up to 77% clearly demonstrate that citrated plasma is an inappropriate sample material for comprehensive coagulation status analysis by the RoTEG system. Generally, a day-to-day fluctuation of ±10%, assuming a 3.3% day-to-day precision and a permissible spread of ±3 s is acceptable for measurements of clinical-chemical laboratory values [24]. Thus, the determined variation and precision precludes reliable RoTEG analysis in plasma.

Besides the adequate sample material, the precision of the automatic pipette used to operate the preset volumes of 10, 20, and 300 µl is of central importance for the analytical performance and reliability of the test results. This was checked by standard quality assurance procedures using repetitive pipetting and weighing of the amount of distilled water in a series of 30 measurements. The variation coefficients obtained were 0.3, 2.2, and 3.0% based on the pipetted volumes of 300, 20, and 10 µl, respectively (table 5).

For practical purposes, ROTEG analyses and classic coagulation parameters may best be used in combination. To illustrate the requirement of the parallel availability of information on whole blood coagulation measurements and on conventional coagulation parameters to correctly adapt the analytical procedure and to interpret ROTEG data, an instructive clinical case is presented.

Instructive Case

Background

Elevated platelet counts are a hallmark of essential thrombocytosis/thrombocythaemia. Thromboembolic complications are related to the platelet levels, and control of the platelet pathology by anti-platelet therapy leads to a significant reduction of thrombosis and other coagulation complications.

Case

A 70-year-old male patient presented with essential thrombocytosis. Laboratory measurements showed a continually increasing platelet count of at last 1,290,000/ μ l, fibrinogen 3.1 g/l, prothrombin time (PT) 103%, activated partial thromboplastin time (aPTT) 34 s. There had been no thromboembolic complications in the past.

The question was, is the extremely elevated platelet number associated with insufficient platelet function, precluding the intake of aspirin as a prophylactic medication? Could aspirin have caused bleeding in this patient with pronounced thrombocytosis [25]?

Results of Platelet Function Measurements

ExTEG: CT 52 s (38–79 s), CFT 44 s (34–159 s) and a borderline MCF 72 mm (50–72 mm). The respective reference ranges of the manufacturer are given in brackets [26]. Refined measurements of the maximum amplitude of the FibTEG in the presence of cytochalasin D as an in vitro additive revealed a surprisingly wide readout as compared to the ExTEG without

cytochalasin D and with a fibrinogen concentration of 3.1 g/l (fig. 2). The reference range for FibTEG is given with MCF 9–25 mm [4]. Originally, abciximab (ReoPro 10 mg / 5 ml) was used to target the inhibition of the GP IIb/IIIa receptors in the case of FibTEG, which was then changed by the manufacturer so that the reagent now contains cytochalasin D to eliminate platelet influence through inhibition of the actin/myosin system [27, 28]. The excessive platelet count in this patient could possibly indicate that the quantity of cytochalasin was not sufficient to inhibit all platelets leading to an artefact in the measurement of the maximum FibTEG/ maximum amplitude. In fact, after doubling the concentration of cytochalasin D added to the in vitro system, a corresponding significant reduction of FibTEG ensued, supporting the above hypothesis (fig. 3).

Conclusion and Interpretation

This case clearly illustrates the significance of a comprehensive analysis by integrating information from conventional laboratory analytes (e.g. platelet count, fibrinogen) into the interpretation of thrombelastograms. In the absence of these traditional conventional haematological laboratory data, the exclusive ROTEG analysis would have lead to conceivable misinterpretations. Further confounding factors which in this case could lead to similar misinterpretations include hyperfibrinogenaemia, which could also lead to the pathologic ExTEG and FibTEG measurements. For the correct interpretation of this case, knowledge of conventional laboratory analytes was indispensable. The addition of cytochalasin D could thus be

Fig. 2. RoTEM analysis of a patient with thrombocytosis. The laboratory tests results are given: platelet count: 1,290,000/ μ l; MCF_{Ex} = 72 mm, MCF_{Fib} = 33 mm with cytochalasin D as provided by the manufacturer. Conventional laboratory tests: fibrinogen 3.1 g/l, PT 103%, aPTT 34 s.

Fig. 3. Modified RoTEM analysis of the same patient: FibTEG with cytochalasin D in double concentration: $MCF_{Fib} = 17$ mm.

5: 04.01.06 13:29:19 : FIBTEM: ROTEG Analysis (4)
 CT: 51s alp: 70° A10: 15mm A25: 16mm
 CFT>1800s ML: 2% A15: 16mm A30: 16mm
 MCF: 17mm A5: 13mm A20: 16mm LI30: 98%

based on the elevated platelet number. However, this procedure leads to a different test conception, which is not specified by the manufacturer. Even with the test adaptation, the results of the modified RoTEM analysis did not permit to assess the functionality of the platelets and could also not add to the clinical question of the potential risk or benefit of aspirin intake in this patient with essential thrombocytosis. The limited suitability of the RoTEM analysis to provide information on the functional status of platelets in the presence of excessive numbers is unfortunate, since effective anti-platelet therapy is associated with reduced frequency of thromboembolic events and complications both in essential thrombocythaemia and other conditions associated with elevated platelet number, such as pregnancy [29–31].

Discussion

Although ROTEG has an improved and simplified handling and execution of measurements compared to Hartert's TEG, the method is still technically demanding and contains several analytical pitfalls. Despite the advent of an integrated automated pipette, considerable imprecision is a continuing problem particularly for low volumes. As exemplified for the automatic pipette provided with the system, the volume pipetted varied widely. While acceptable variation coefficients were obtained for the large sample volumes of 300 μ l, automatic pipetting of the low volumes of 20 or 10 μ l used for the activators, showed unacceptably high variations of 2.2 and 3%. These variation coefficients of 2.2 and 3.0% of the automatic pipette are inadequate according to ISO 8655–6:2002, and by far exceed the accepted error limits of 0.5 and 0.8% for the volumes of 20 and 10 μ l, respectively [32]. This may be due to different amounts of sample at the external side of the pipette tip, a well known problem with small sample volumes, which may be solved by reverse pipetting. The reverse pipetting method, however, is not possible with the automatic system. Since the measuring device is described as point-of-care testing (POCT)

suitable, increased special training, especially if non-laboratory trained personnel operates the equipment, is necessary [6, 8, 9].

An investigation of the analytic efficiency showed that RoTEM analysis seems to provide adequately reliable results in citrated whole blood for the measurement parameters CT, CFT, and MCF with variation coefficients between 1.4 and 13.5%. In contrast, ROTEG is unsuitable for citrated plasma measurements, as clearly supported by variation coefficients from 2.1 up to 77.1%. Measurements in the 4 channels were comparable and did not yield any significant differences as determined by the Friedmann-Anova test. The precision determination of the TEG variants ExTEG, FibTEG, InTEG, and NaTEG could therefore be evaluated independently of the measurement channel.

Standard concentrations of activation reagents are not generally applicable. As exemplified for the use of the FibTEG reagents in the demonstrated instructive case of essential thrombocytosis, the standard concentration of cytochalasin D was insufficient to completely inhibit all platelets. Thus, before performing a RoTEM analysis, additional information on relevant laboratory parameters such as platelet count and fibrinogen concentration have to be considered. Since reactive thrombocytosis frequently accompanies systemic inflammatory reactions in intensive care patients or patients following surgery, these conditions have to be taken into account besides essential thrombocytosis or myelodysplastic syndrome. Further studies are needed to define the exact amount of reactants to activate or inhibit platelets at different given concentrations.

One important advantage of the RoTEM system is the possibility to estimate the efficiency of the coagulation process in whole blood, which most closely resembles in vivo conditions as an attractive means for acute and intensive care medicine. However, depending on the clinical condition, the suitability of the system for providing rapid readouts is restricted by the substantial prolongation of the total analysis time in pathologic clinical coagulation status. In particular, in the case of

haemorrhagic emergencies requiring immediate treatment, it is to be expected that the CT and the CFT are considerably prolonged so that the assessment of the resulting progression of the amplitude is also correspondingly delayed. If only 1 RoTEM analyser is available, and a second run with additional TEG variants is required, additional time delays of up to several hours ensue. Therefore, since thrombelastography only provides non-specific results, with regard to the individual case it is advisable to request in parallel corresponding specific laboratory parameters (e.g. platelet count, fibrinogen, thrombin time, fibrin degradation products, closure or bleeding time, factor XIII, PT, aPTT) to support the interpretation of the thrombelastographic measurements. It is regrettable that since the introduction of RoTEM, the distributor has changed hands several times (Nobis Diagnostika GmbH, Instrumentation Laboratory GmbH, Pentapharm GmbH, Matel Medizintechnik GmbH), and reagents have been changed.

The resulting lack of continuity has meant the loss of valuable experience and lack of comparability of previous studies, which is indispensable for an accurate and comprehensive introduction of such methods into routine clinical applications.

Conclusion

ROTEG is an additional analytical procedure employed for recognising overall disturbances of haemostasis. The investigation conducted here shows adequate practicability, but still unsatisfactory analytic efficiency and measurement accuracy of the method. The integration of traditional coagulation tests and of inflammatory parameters for adaptation of the conditions and the interpretation of thrombelastography is recommended.

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