Rapid measurement of fibrinogen concentration in whole blood using a steel ball coagulometer

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BACKGROUND: Fibrinogen plays a key role in hemostasis and is the first coagulation factor to reach critical levels in bleeding patients. Current European guidelines on the management of traumatic or perioperative bleeding recommend fibrinogen supplementation at specific threshold levels. Whole blood viscoelastic tests provide fast evaluation of fibrin deficits. Fast measurement of plasma fibrinogen concentration is not yet available. We investigated a method to rapidly determine whole blood fibrinogen concentration using standard Clauss assays and a steel ball coagulometer and provide an estimate of the “plasma-equivalent” fibrinogen concentration within minutes by adjustment of the measured whole blood fibrinogen concentration with a quickly measurable hemoglobin-derived hematocrit.

METHODS: The feasibility of this approach was tested with a Clauss assay using multiple porcine fresh blood samples obtained during in vivo bleeding, hemodilution, and after treatment with hemostatic therapy. Two different Clauss assays were then tested using multiple human volunteers’ blood samples diluted in vitro and supplemented with fibrinogen concentrate. Comparative measurements with fibrin-based thromboelastometry tests were performed.

RESULTS: Regression and Bland-Altman analyses of derived “plasma-equivalent” fibrinogen and measured plasma fibrinogen concentration was excellent in porcine and human blood samples, especially in the ranges relevant to traumatic or perioperative bleeding.

CONCLUSION: Fast whole blood fibrinogen measurements could be considered as an alternative to plasma fibrinogen measurement for acute bleeding management in trauma and perioperative care settings. Further studies are needed to prove this concept and determine the turnaround times for its clinical application in emergency departments and operating theaters. (J Trauma Acute Care Surg, 2015;78: 830–836. Copyright © 2015 Wolters Kluwer Health, Inc. All rights reserved.)

KEY WORDS: Blood coagulation tests; clinical laboratory techniques; fibrinogen; pigs.

Fibrinogen plays a key role in hemostasis and is the first coagulation factor to reach critical levels in bleeding patients.1,2 In trauma, admission fibrinogen levels are influenced by blood loss, dilution, shock, and severity of injury.3 Current European guidelines on the management of severe bleeding in trauma or the perioperative setting propose fibrinogen supplementation if plasma fibrinogen concentrations (plasma FIB) are less than 1.5 to 2.0 g/L in bleeding patients.4,5 However, long turnaround times significantly limit the current clinical value of plasma FIB measurements for the guidance of hemostatic management in trauma and perioperative bleeding.6–9 Timing is one of the reasons why the use of viscoelastic tests (VETs) in whole blood, such as thromboelastometry (ROTEM) or thrombelastography (TEG), is recommended.4,5 VETs have successfully been used to rapidly identify and treat the fibrin deficit in acutely bleeding patients.10–13 Despite recommendations, real-time and fast measurement (e.g., results in <10 minutes time) of plasma FIB is still not available. Investigations in cardiovascular surgery suggest that measurements obtained on-pump using the Clauss assay could provide an early estimation of fibrinogen deficit.14,15 Potentially, this could impact the time at which hemostatic therapy is administered, minimizing treatment delays when VETs are not available. In addition, removing the need to centrifuge the patient’s blood sample before analysis could save time. Most hospital laboratory coagulation analyzers are based on optical read out systems. However, since whole blood is not translucent, they are only able to analyze plasma. In principle, devices based on mechanical read out, for example, hook or steel ball coagulometer,16 should be able to analyze coagulation properties of both plasma and whole blood. Measuring fibrinogen in whole blood with an electromechanical coagulation analyzer has been shown.17 More recently, measurement of fibrinogen levels using the dry-hematology method in a small volume of plasma or whole blood has been demonstrated.18 For measurement of whole blood fibrinogen, an adjustment for hematocrit is required to compensate for the dynamic changes in hematocrit seen in perioperative bleeding settings.
Clot detection using a steel ball coagulometer involves monitoring the movement of a steel ball within the test solution using a magnetic sensor (Supplementary Figure, Supplemental Digital Content 1, http://links.lww.com/TA/A548). The clotting reaction is initiated with the addition of a thrombin reagent to the patient sample. As clot formation begins, the steel ball becomes incorporated into the fibrin network. This incorporation changes the position of the steel ball, which breaks the contact with the magnetic sensor and stops the previously set timer. All clotting time tests that have fibrin formation as an end point can be performed using a steel ball coagulometer. In addition, with the use of suitable reagents, both plasma and whole blood samples can be measured. We propose that whole blood fibrinogen concentrations (WB FIB) may reflect the patient’s clotting substrate availability better than the fibrinogen measurement in plasma. Whole blood, including all its cellular components (erythrocytes [RBCs], leucocytes [WBCs], platelets [PLTs]) circulating through the patient’s blood vessels, forms the hemostatic plug and not just plasma. For example, a measured plasma FIB of 2.0 g/L is mathematically equivalent to 1.5 g/L fibrinogen content in whole blood if the hematocrit is 25% or to 1.1 g/L fibrinogen content in whole blood if the hematocrit is 45%. The Clauss assay using a steel ball coagulometer reliably measures fibrinogen concentration in whole blood in the ranges relevant to the bleeding patient in the traumatic or perioperative settings. Considering current threshold/treatment recommendations on plasma FIB level in these settings, it is proposed that a “plasma-equivalent” fibrinogen concentration (deriFIB) may be accurately estimated within minutes, by adjusting the measured WB FIB with a quickly measureable hematocrit using the following equation: deriFIB (g/L) = WB FIB x (100 / [100 − hematocrit]), where hematocrit (%) = 3 × hemoglobin (g/L). The equation is simply based on the fact that the equal amount of fibrinogen after centrifugation, thus concentrated in plasma for measurement purposes only, will also be found in the original whole blood, however, “diluted” by the cell fraction. In daily clinical practice, hematocrit or hemoglobin can be obtained within minutes, using a cell counter, dedicated blood gas analyzer, or other point-of-care (POC) device.

We present a study investigating the feasibility of obtaining a fast and reliable measurement of WB FIB and a derived “plasma-equivalent” fibrinogen concentration using a Clauss assay in whole blood and a steel ball coagulometer. Comparative measurements with a viscoelastic functional fibrinogen assay were also assessed.

**MATERIALS AND METHODS**

**Porcine Study**

All experiments were performed under the conditions described in the Guide for the Care and Use of Laboratory Animals, as defined by the National Institutes of Health.

An in vivo porcine model of hemorrhagic shock, with hemodilution and treatment with hemostatic therapy, was approved by the Animal Protocol Review Board of the city government of Vienna, Austria. The model, from another experimental protocol (MA58-005750/2012/9), has been described in detail elsewhere. Briefly, after induction of anesthesia and instrumentation, hemorrhage was simulated by the withdrawal of blood through an arterial catheter, at a rate of 30 mL/min to 50 mL/min. Dilutional coagulopathy was then induced by bolus administration of 1,000 mL of a balanced acetated crystalloid solution (ELO-MEL isoton, Fresenius Kabi, Graz, Austria). After hemorrhage and fluid replacement, 80-mg/kg fibrinogen concentrate (Haemocomplettan P, CSL Behring, Marburg, Germany) was infused. Blood sampling for whole blood and plasma fibrinogen measurements were taken at several time points during this study, at baseline, after hemorrhage, after dilution, and after therapy with fibrinogen concentrate.

**Fibrinogen Measurement in Whole Blood or Plasma Samples**

Twenty-eight whole blood samples were collected from eight pigs into 3-mL tubes containing 0.3-mL buffered 3.2% trisodium citrate, giving a volume ratio of 1:9 (Vacuette; Greiner Bio-One, Linz, Austria). WB FIB was measured in triplicate by a trained laboratory technician using a Clauss fibrinogen assay (Multifibren U, Siemens, Marburg, Germany) and a steel ball coagulometer (KC-10, Amelung GmbH, Lemco, Germany). Using the same citrated whole blood samples, hemoglobin concentration was measured using a CELLDYN 3700 instrument (Abbott, Vienna, Austria) according to manufacturer’s instructions. Following this, the citrated whole blood samples were centrifuged at 2,800 G for 15 minutes to obtain the corresponding standard platelet-poor plasma for laboratory coagulation studies. The same measurement procedure was performed to obtain plasma FIB of the investigated samples.

**Human Study**

The study was approved by the official local ethics committee (Ethikkommission für die Krankenanstalten der AUVA; protocol number 14/2013). All human volunteers gave informed consent.

**Fibrinogen Measurement in Whole Blood or Plasma Samples With In Vitro Hemodilution and Fibrinogen Administration**

Plasma FIB was measured in 33 citrated human blood samples using commercially available Clauss assays (Multifibren U or TC-Thrombin [Technoclone, Vienna, Austria]) and a steel ball coagulometer (KC-10). After blood was drawn from six human volunteers, the samples were either kept undiluted or diluted in vitro with 0.9% saline in the range 33% to 75% (grade of dilution). To prove the concepts that (i) lower WB FIB are also the consequence of higher hematocrit in a whole blood sample and (ii) that plasma FIB can be accurately measured, we further adjusted nine blood samples with high hematocrit despite low fibrinogen concentrations, by centrifuging them at 400 G for 10 minutes, replacing 1-mL plasma (supernatant) with 1-mL saline and resuspending the sample. Furthermore, in six blood samples, fibrinogen concentrate (Haemocomplettan P, CSL Behring) was added in vitro to simulate fibrinogen supplementation. Measurement procedures were performed as described earlier in the porcine study.
Comparison of Clauss Assays in Plasma Only

In addition to the steel ball measurements (Multifibren, TC-Thrombin), we performed another Clauss assay with a photo-optical coagulometer (Thrombin Reagent on a Sysmex CA 1500; both Siemens) in all human plasma samples, according to manufacturer’s instructions. Correlations among the three different Clauss assays (Multifibren, TC-Thrombin, and Thrombin Reagent) were determined.

Comparison Between Modified FIBTEM and Clauss Fibrinogen Measurements in Whole Blood and Plasma

ROTEM (TEM Innovations GmbH, Munich, Germany) analysis of each whole blood and plasma sample from the human volunteer study was performed using an automated pipette and an improved FIBTEM assay, which includes the additional steps of 5-µL abciximab (2 mg/mL), a glycoprotein-IIb/IIIa inhibitor (ReoPro, Centocor B.V., Leiden, the Netherlands), being pipetted directly into the empty cup approximately 1 minute before the start of the procedure.25 For the purpose of this study only, the assay is called FIBTEM-ABC. The ROTEM channel was programed for FIBTEM, and according to the automated ROTEM pipette steps, 20 µL of ex-tem reagent (containing recombinant tissue factor and an inhibitor of heparin [hexadimethrin]) followed by 20 µL of fib-tem reagent (containing cytochalasin D and 0.2-mol/L calcium chloride) were added to the cup. Finally, 300 µL of the whole blood or plasma sample was added, and the test was initiated automatically via the pipette signal. The reaction mixture (total volume, 345 µL) was aspirated and dispensed back into the cup, and the cup was set onto the pin. ROTEM data were collected for approximately 45 minutes, and the main study parameter recorded was maximum clot firmness (MCF).

Data Collection and Statistical Analysis

For each whole blood or plasma sample, the mean and SD of a triplicate (Multifibren assay) or duplicate (TC-Thrombin assay) measurement of fibrinogen concentration was determined, and a coefficient of variation (CV), expressed as a percentage, was calculated.

In the human volunteer study, plasma FIB values obtained with all three of the earlier mentioned Clauss assays were correlated (linear regression) for reference and definition of observed variability between the assays. With regard to the main study objective, whether measured and adjusted WB FIB correlate with plasma FIB, a linear regression analysis, with regression line forced to go through 0 on both axes, was performed. The Bland-Altman limits of agreement method was used to compare the agreement between pairs of fibrinogen concentrations. Standard linear regression analysis was performed to compare FIBTEM-ABC and Clauss fibrinogen measurements for all investigated samples of the human volunteer study.

For all correlation/regression analyses, the $R^2$ values, the slope, and the 95% confidence intervals (CIs) of the slope are reported. Unless otherwise stated, values are presented as mean (SD).

RESULTS

Porcine Study

The Multifibren assay was able to detect clottable fibrinogen in all measured plasma and whole blood samples. The CV from all 28 triplicate fibrinogen measurements in plasma and whole blood samples was excellent, showing an average CV of 2.8% (range, 0.0–11.6) for plasma and 1.7% (range, 0.2–6.6) for whole blood measurements.

Porcine plasma samples revealed fibrinogen concentrations of 2.33 (0.68) g/L (range, 1.24–3.83). In the corresponding whole blood samples, fibrinogen concentration was 1.78 (0.47) g/L (range, 1.13–2.81), with hematocrit values of 18.9% (4.8%) (range, 11.9–25.7%). The accuracy of the assay was not affected at the extremes of hematocrit values studied (data not shown).

Correlation between WB FIB ($y$) and plasma FIB ($x$) resulted in a slope $y = 0.83x$ (95% CI, 0.81–0.85) and an $R^2$ of 0.91 (Fig. 1A). The WB FIB value was then adjusted (deriFIB) with the proposed hematocrit formula to approximate absolute values of plasma FIB. Correlation between deriFIB and plasma FIB resulted in a slope of $y = 1.05x$ (95% CI, 1.03–1.07) with an $R^2$ of 0.96 (Fig. 1B, Table 1). Bland-Altman analysis of deriFIB versus plasma FIB measurement is shown in Table 1.

Human Volunteer Study

The undiluted and in vitro adjusted (hematocrit, fibrinogen supplementation) whole blood samples (n = 33) showed hematocrit values of 31.4% (10.8%) (range, 10.9–43.9%). The accuracy of the Clauss assays was not affected at the extremes of hematocrit values studied (data not shown).

Comparison of Clauss Assays in Plasma Only

Measurement of plasma FIB using three different Clauss assays gave values of 1.89 (0.87) g/L (range, 0.59–3.64) for the Thrombin Reagent/Sysmex assay, 1.92 (1.02) g/L (range, 0.62–4.01) for the Multifibren/KC-10 assay, and 2.36 (1.08) g/L (range, 0.71–4.55) for the TC-Thrombin/KC-10 assay. Linear regression analysis of plasma FIB between the Clauss assays resulted in an $R^2$ of 0.98 between TC-Thrombin ($y$) and Sysmex ($x$), with a deviating slope of $y = 1.25x$ and a narrow 95% CI of 1.22 to 1.27. Linear regression analysis between Multifibren ($y$) and Sysmex ($x$) resulted in an $R^2$ of 0.92, with a slope of 1.02 but wider 95% CI of 0.97 to 1.07. Regression analysis between the TC-Thrombin and Multifibren resulted in an $R^2$ of 0.96, with a
slope of 1.20 (95% CI, 1.15–1.25). Bland-Altman mean differences (95% limits of agreement) were 0.47 g/L (−0.01 to 0.95 g/L) between TC-Thrombin and Sysmex measurement, 0.01 g/L (−0.59 to 0.57 g/L) between Multifibren and Sysmex measurement, and 0.48 g/L (0.09–0.89 g/L) between TC-Thrombin and Multifibren.

**Multifibren Assay in Whole Blood and Plasma**

When using the Multifibren assay for very low (mainly <1.0 g/L) fibrinogen concentrations in whole blood (either because of high degree of dilution or high adjusted hematocrit), the assay did not detect clotting in 10 of 33 whole blood samples. Clottable fibrinogen concentrations were also not detected in 1 of 33 plasma samples. Because of the nature of this assay, it was not possible to use a higher thrombin to sample ratio to exactly estimate such low fibrinogen values. The remaining triplicate measurements in plasma and whole blood showed an average CV of 2.6% (range, 0.2–20.9) for plasma and 7.3% (range, 0.2–29.1) for whole blood. Regression analysis between WB FIB (y) and plasma FIB (x) resulted in an $R^2$ of 0.75, $y = 0.67x$ (95% CI, 0.61–0.73; Fig. 2A). With the use of the proposed mathematical hematocrit adjustment, regression analysis between deriFIB and plasma FIB resulted in an $R^2$ of 0.92, $y = 1.04x$ (95% CI, 0.99–1.08; Fig. 2B). Bland-Altman analysis of deriFIB versus plasma FIB measurement is shown in Table 1.

**TC-Thrombin Assay in Whole Blood Versus Plasma**

The TC-Thrombin assay, which uses higher thrombin concentrations relative to fibrinogen concentration (as compared with the Multifibren assay), detected fibrinogen concentrations in all whole blood and plasma samples. The variability between duplicate measurements in plasma and whole blood samples was minimal (CV of 1.6 [range, 0.0–5.9] for plasma; 1.7 [range, 0.0–4.9] for whole blood). Regression analysis between plasma FIB and WB FIB resulted in an $R^2$ of 0.87, $y = 0.67x$ (95% CI, 0.64–0.70; Fig. 3A). With the use of mathematical hematocrit adjustment, regression analysis between plasma FIB and deriFIB resulted in an $R^2$ of 0.99, $y = 1.04x$ (95% CI, 1.02–1.05; Fig. 3B). Bland-Altman analysis of deriFIB versus plasma FIB measurements is shown in Table 1.

**Comparison Between Modified FIBTEM and Clauss Fibrinogen Measurements in Whole Blood and Plasma**

Calculating linear regression curves between the MCF values of the FIBTEM-ABC in whole blood and the corresponding Clauss plasma FIB shows that plasma FIB explains only 48% to 58% of the MCF (Table 2). However, using measurements of WB FIB raises the goodness of fit to 81% (TC-Thrombin) and 84% (Multifibren). Performing FIBTEM-ABC in plasma (instead of whole blood) raises the goodness of fit (MCF vs. plasma FIB) up to 90% to 93%. Figure 4 shows the correlation with the TC-Thrombin assay representative for the other Clauss fibrinogen assays, where applicable.

**DISCUSSION**

Our results show that a rapid and reliable fibrinogen concentration measurement can be performed in whole blood using commercially available Clauss assays and a steel ball
TABLE 2. Linear Regression Analysis Between the MCF Values of the FIBTEM-ABC in Whole Blood or Plasma and the Corresponding Clauss Whole Blood or Plasma Fibrinogen Concentrations (Where Applicable)

| ROTEM Shear Modulus | Clauss Fibrinogen Measurement | \( R^2 \) |
|---------------------|------------------------------|-----------|
| FIBTEM-ABC          | Sysmex (photo-optical)       | 0.48      |
| Whole blood         | Plasma FIB                   | 0.90      |
| Platelet-poor plasma| Plasma FIB                   | 0.90      |
| FIBTEM-ABC          | TC-Thrombin (mechanical)     | 0.55      |
| Whole blood         | Plasma FIB                   | 0.81      |
| Whole blood         | WB FIB                       | 0.93      |
| Platelet-poor plasma| Plasma FIB                   | 0.93      |
| FIBTEM-ABC          | Multifibrin (mechanical)     | 0.58      |
| Whole blood         | Plasma FIB                   | 0.84      |
| Whole blood         | WB FIB                       | 0.92      |
| Platelet-poor plasma| Plasma FIB                   | 0.92      |

Low plasma FIB has been shown to be associated with increased blood loss and/or transfusion requirements in a number of settings, including cardiac surgery, postpartum hemorrhage, and trauma\(^{27-31}\) and has recently been reported to be associated with worse outcomes in trauma patients receiving massive transfusion.\(^{32}\) It is acknowledged that fibrinogen deficit and monitoring are central to trauma-induced coagulopathy\(^{3,33}\) and early replacement of fibrinogen has been described in the recent literature.\(^{10,13,34,35}\) In major trauma patients, it has been proposed that plasma FIB could be estimated based on hemoglobin and base excess on admission to the emergency department.\(^3\) However, threshold values in guidelines\(^{4,5}\) require accurate, real-time measurement of fibrinogen concentration. In the present study, we used viscoelastic assessment of fibrin-based clot quality in whole blood and correlated the MCF with whole blood fibrinogen, achieving a curve fit of 0.81 to 0.84. From an experimental point of view (not useful in clinical application), the results show that using plasma in the ROTEM could accurately derive FIB through excellent regression fits (\( R^2 \geq 0.9 \)).

VETs in whole blood currently provide the fastest, most informative means of assessing clotting in emergency settings, and their results should be interpreted and used to guide hemostatic therapy according to the pathophysiologic clinical context. Guidelines recommend treatment based on fibrinogen levels.\(^{4,5,36,37}\) The methods tested in this study (WB FIB, deriFIB) provide a rapid and reliable measurement of coagulometer. By adjusting the WB FIB measurement with the corresponding hematocrit (derived from a fast hemoglobin measurement), a “plasma-equivalent” fibrinogen concentration can be derived accurately with a very good \( R^2 \) (0.92–0.99).

In the range of investigated fibrinogen values (1–4 g/L), mean difference between plasma-equivalent fibrinogen concentration (derived from whole blood measurement) and plasma FIB measurement methods was as low as 0.08 g/L to 0.13 g/L.

The Clauss assay was performed within minutes by a trained laboratory technician, and the CV for each duplicate or triplicate whole blood Clauss assay measurement was deemed acceptable or in the range of (or better than) the corresponding plasma Clauss assay measurement. The in vivo pig model with bleeding, hemodilution, and treatment with hemostatic therapy to prove our concept is applicable to the clinical settings of traumatic or perioperative bleeding. Furthermore, we successfully challenged the principles of the proposed fibrinogen measurement method in human whole blood with in vitro hemodilution, hematocrit adjustments simulating red blood cell transfusion, as well as simulating fibrinogen supplementation by the addition of fibrinogen concentrate.

The processing of citrated blood samples for the measurement procedure was similar to that used by VETs, such as thromboelastometry (ROTEM) or thrombelastography (TEG). By manually treating every whole blood sample the same (immediate gentle mixing of the probe) before measurement, we avoided artefacts by testing incidentally sedimented blood cells from whole blood, which could occur in automatically processed samples in large laboratory coagulation devices. The size of the device and the protocol in our study would allow POC measurement in an emergency department or operating room. When used as a POC device, where calibration curves for the thrombin reagent are preset, the device is already running at 37°C, and the citrated whole blood sample has been obtained, the procedure can be performed in less than 3 minutes. In addition, hemoglobin can usually be measured within 3 minutes, via either an operating room–based blood gas analyzer or a POC chip device. In contrast, turnaround times for plasma FIB results, which are rarely performed POC, are typically around 30 minutes to 60 minutes,\(^{31}\) although times of 78 minutes (interquartile range, 62–103 minutes)\(^8\) and 88 minutes (range, 29–295 minutes)\(^9\) have been reported. Shortened times of approximately 14 minutes (range, 6–28 minutes) have been achieved by implementing critical improvements, including fast transport of samples, extended calibration range (0.5–11.0 g/L), and rapid centrifugation.\(^{26}\)

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VETs in whole blood currently provide the fastest, most informative means of assessing clotting in emergency settings, and their results should be interpreted and used to guide hemostatic therapy according to the pathophysiologic clinical context. Guidelines recommend treatment based on fibrinogen levels.\(^{4,5,36,37}\) The methods tested in this study (WB FIB, deriFIB) provide a rapid and reliable measurement of

Figure 4. Representative correlation between MCF of the ROTEM FIBTEM + abciximab and the Clauss fibrinogen concentration (showing the TC-Thrombin Clauss assay with mechanical detection) in whole blood and plasma samples of human volunteers at baseline, after in vitro hemodilution, and in vitro fibrinogen supplementation. \( R^2 \) values (including all assays) are shown in Table 2.
fibrinogen concentration and could offer an alternative option for institutions that do not have the devices and resources needed to perform viscoelastic tests. Whether to use the WB FIB or the corresponding derived hematocrit-adjusted plasma fibrinogen value to guide hemostatic therapy would require clinical judgment. Either way, further studies are needed to correlate the use of WB FIB measurements with clinical outcome.

This study has several limitations. Although not necessary in platelet-poor plasma, the combination of FIBTEM and abciximab was added also to the plasma samples to achieve the same degree of fibrin-polymerization dependent on the assay used, as previously reported by our group. In addition, the range of fibrinogen concentration investigated was relatively narrow (1–4 g/L). In a perioperative setting, which may include admission to the intensive care unit, fibrinogen concentrations can easily reach up to 10 g/L. If the method is to be used for monitoring the coagulation pattern postpartum, a wider range would need to be validated. Finally, because of lack of availability of a standard for porcine plasma, the devices were not recalibrated for the measurement of porcine fibrinogen concentration. The effect of colloids was not investigated in this study. Synthetic colloidal solutions, such as hydroxyethyl starch, are commonly used for fluid resuscitation in patients with major bleeding and their presence has been shown to overestimate fibrinogen levels when using the Clauss assay with photo-optical detection end points. Their impact on this WB FIB measurement method as well as a potential interference of other colloids different crystalloids or blood products would need to be evaluated before firm conclusions can be made.

We conclude that measurement of fibrinogen concentration can be performed rapidly and reliably in whole blood. Adjustment of results with hematocrit provides a reliable estimation of plasma FIB. A method to rapidly estimate fibrinogen concentrations would be beneficial in clinical situations of acute traumatic and perioperative bleeding to guide hemostatic therapy. The next steps for this methodology could be to prepare such a steel ball coagulometer in a simplified form for POC and combine it with a POC method to measure hemoglobin. However, further clinical studies are needed to prove this concept and define turnaround times in a clinical setting of perioperative or traumatic bleeding.

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AUTHORSHIP

C.J.S., A.Kh., and A.Kl. contributed to data collection. C.J.S., A.Kh., A.Kl., and H.S. performed data analysis. C.J.S., C.S., G.H., M.P., H.R., and H.S. contributed to data interpretation and writing the article.

DISCLOSURE

C.J.S. has received research support and speaker fees from CSL Behring and research support from Tem International. C.S. is an employee of CSL Behring and previously received speaker honoraria and research support from Tem International and CSL Behring and travel support from Haemoscope Ltd. (former manufacturer of TEG). G.H. is an employee of CSL Behring. M.P. has received a research grant from CSL Behring. H.S. has received study grants and speaker fees from CSL Behring and Tem International. A.Kh., A.Kl., and H.R. have no conflicts of interest to declare. The study was supported by departmental funding of the AUVA Research Centre.

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