Validation of viscoelastic coagulation tests during cardiopulmonary bypass

E. ORTMANN,* A. RUBINO,* B. ALTEMIMI,* T. COLLIER,† M. W. BESSER‡ and A. A. KLEIN*

*Department of Anaesthesia and Intensive Care, Papworth Hospital, Cambridge; †London School of Hygiene and Tropical Medicine, London; and ‡Department of Haematology, Addenbrooke’s Hospital, Cambridge University Hospitals Foundation Trust, Cambridge, UK


Summary. Background: Viscoelastic point-of-care tests such as thromboelastography (TEG) and rotational thromboelastometry (ROTEM) are increasingly used to guide hemostatic therapy after cardiac surgery. The aim of this study was to assess their clinical utility during cardiopulmonary bypass to predict postbypass coagulation status and to guide therapy. Methods: In this prospective study, TEG and ROTEM tests were performed in 52 adult patients undergoing elective cardiac surgery at two time points: near the end of cardiopulmonary bypass and after heparin reversal with protamine. The 95% confidence intervals of the mean difference were compared with a prespecified clinically relevant limit of ±20% of the value after protamine. Results: Both viscoelastic fibrinogen assays were well within the prespecified clinically relevant limit (≥79% of patients). The laboratory Clauss fibrinogen was much lower during cardiopulmonary bypass than after protamine (mean difference 1.2 g L⁻¹, 95% CI 1.03–1.4, which was outside a clinically acceptable difference. For intrinsically activated tests, clotting times (CT) were different and outside the prespecified limit on TEG (mean difference −1.2 min, 95% CI −1.8 to −0.6) but not on ROTEM (mean difference 2.3 sec, 95% CI −8.6 to 13.2), while clot strength was well within the clinical limit on both devices (≥94% of patients). For extrinsically activated tests, clot strength on both TEG and ROTEM was within the pre-specified limit in 98% of patients. Conclusions: Results from TEG and ROTEM tests performed toward the end of cardiopulmonary bypass are similar to results after reversal of heparin. Amplitudes indicating clot strength were the most stable parameters across all tests, whereas CT showed more variability. In contrast, laboratory testing of fibrinogen using the Clauss assay was essentially invalid during cardiopulmonary bypass.

Keywords: blood coagulation tests; cardiac surgical procedures; cardiopulmonary bypass; point-of-care systems; thromboelastography.

Introduction

Both laboratory-based assays and point-of-care devices, using viscoelastic assays, are used for guiding hemostatic management during and after cardiac surgery. Viscoelastic test results are rapidly available at the patient’s bedside or in the operating theater and allow a global assessment of hemostasis, including fibrinolysis. Another potential advantage of viscoelastic tests is that they can be performed during cardiopulmonary bypass (CPB), allowing blood products to be prepared for administration immediately after CPB when required. Viscoelastic tests have now been recommended for use perioperatively in cardiac surgery by the National Institute for Health and Care Excellence (NICE) in the United Kingdom [1]. The results of laboratory tests, on the other hand, inevitably take longer to be available, due to transport and processing delays and the requirement for centrifugation before testing. However, they are usually accepted as the basis of supportive hemostatic therapy. Waiting for results of laboratory tests before preparing blood products can delay treating patients, which can be associated with further increased hemorrhage and clinical deterioration. The most widely used point-of-care devices are ROTEM (Tem International GmbH, Munich, Germany) and TEG (Haemonetics Corp., Braintree, MA, USA), both based on the principle of thromboelastography as described by Hartert [2]. However, it has been demonstrated in cardiac surgical patients that the results of the two systems are not completely interchangeable [3]. Treat-
ment algorithms using viscoelastic tests have been shown to reduce transfusion requirements (potentially for the price of increased use of factor concentrates), decrease the need for surgical revision, and improve outcome overall in cardiac surgical patients compared with only laboratory-based tests [4–6].

The ideal hemostatic assays should be available quickly, ideally while still on cardiopulmonary bypass, and predict the coagulation status after CPB to allow requesting and preparation of optimal blood component therapy. However, the literature is very sparse regarding whether viscoelastic point-of-care assays, performed during CPB and therefore full heparinization, are valid or clinically useful. The clinical value of testing during CPB is uncertain because of the potential impact of heparinization and its reversal with protamine, temperature, pH, hemodilution and the time interval between testing and therapeutic intervention. It has been shown in vitro that viscoelastic assays can be affected by the presence of heparin and protamine [7,8] and that additional protamine could lead to a prolongation of intrinsically activated clotting times (CTs) on ROTEM [9]. It is therefore uncertain to what degree blood tests performed during CPB (i.e. during full heparinization) correlate to the results after the end of CPB (i.e. after reversal of heparin with protamine).

The aim of this study was to assess the clinical utility of viscoelastic testing (TEG, ROTEM) during CPB with regard to prediction of post-CBP coagulopathy and guiding of hemostatic management.

Methods

This prospective observational study was approved by the institutional ethics committee (Papworth Hospital Research Tissue Bank Operational Group, project No. T01716). All patients gave written consent to blood sampling and use of data for research. Adult patients undergoing scheduled cardiac surgery requiring CPB at Papworth Hospital (UK) were prospectively included between March and April 2013. Patients undergoing emergency procedures, organ transplantation, pulmonary endarterectomy, or procedures requiring extracorporeal cardiopulmonary organ support or with known preoperative coagulopathy disorders were excluded.

Clinical management

All patients were treated according to institutional protocols [10]. Specifically, full anticoagulation for CPB was achieved with 300 IU kg⁻¹ unfractionated heparin. An activated CT (ACT; Hemochron Jr., ACT+; International Technidyne Corporation, Edison, NJ, USA) was measured at 30-min intervals and maintained at > 400 s for the duration of CPB. Additional boluses of 5000 IU heparin were given as required. All patients received a bolus dose of 2 g of tranexamic acid prior to the institution of CPB. After the end of CPB, heparinization was reversed with 10 mg protamine sulfate for each 1000 units of the initial heparin dose.

Assessment of coagulation

The patient’s coagulation system was assessed at two time points: on-CPB and post-protamine (Fig. 1). Toward the end of the CPB period, defined as 5–10 min after removal of the aortic cross-clamp, blood samples (9 mL in citrate-blood, 2.6 mL in EDTA-blood) were drawn (sample tubes: S-Monovette; Sarstedt AG, Nuembrecht, Germany) from the arterial cannula for the on-CPB tests. The second set of blood samples (as above) was taken ~5 min after infusion of the initial protamine dose and before systemic administration of any hemostatic products for the post-protamine tests.

The following tests were performed at both time points: on the TEG® 5000-analyzer (Haemonetics Corp.), a kaolin-activated TEG, a rapid TEG, and a functional fibrinogen assay in heparinase cups; on the ROTEM® delta-analyzer (Tem International GmbH), a hepTEM, exTEM, and a fibTEM assay; an ACT at the bedside; a platelet count (Beckman Coulter LH 500 analyser, High Wycombe, UK); and Clauss fibrinogen (HaemosIL Fibrinogen-C XL, IL TOP 500 analyzer; Instrumentation Laboratory, Warrington, UK) in the laboratory. In addition, the following tests were performed on the post-protamine samples: kaolin-activated TEG in a plain cup on the TEG® 5000-analyzer, inTEM on the ROTEM® delta-analyzer, coagulation screen in the laboratory including Clauss fibrinogen (HaemosIL Fibrinogen-C XL), prothrombin time (HaemosIL RecombiPlasTin 2G), activated partial thromboplastin time (APTT; HaemosIL SynthA-Sil), and thrombin time (HaemosIL Thrombin Time). All viscoelastic tests were performed in parallel for each sample point on whole blood anticoagulated with citrate (citrate 0.106 mol L⁻¹ blood = 1:9) by three experienced operators according to the manufacturers’ instructions as detailed below [11]. Quality controls were performed on the point-of-care analyzers at the recommended intervals, and laboratory analyzers were internally and externally quality controlled throughout the study period. The following parameters were recorded and analyzed on the point-of-care analyzers: coagulation time (R) in minutes and maximum amplitude (MA) in millimeters for TEG assays and CT in seconds and maximum clot firmness (MCF) in millimeters for ROTEM assays.

For the TEG assays, cups containing 2 IU heparin were used for all tests apart from the kaolin-activated TEG post-protamine, which was run in plain cups. First, 20 µL of 0.2 mol L⁻¹ CaCl₂ were pipetted into the cups. For the kaolin-activated assays, 1 mL of blood was mixed with kaolin, and 340 µL was pipetted into the test cups. For the functional fibrinogen assay, tissue factor and a
GPIIb/IIa inhibitor were added to 500 µL of citrated blood, and 340 µL was pipetted into the test cup. The rapidTEG™ reagent, containing tissue factor, kaolin, and phospholipid, was reconstituted with 20 µL of distilled water and incubated for 5 min. Then, 10 µL of the reconstituted reagent was mixed with 340 µL of citrated blood in the test cup.

For the ROTEM tests, the automated pipetting system of the ROTEM delta analyzer was used. For the exTEM assay, 300 µL of blood was mixed with 20 µL of ex-tem® reagent (tissue factor, phospholipids, and heparin inhibitor) and 20 µL of 0.2 mol L⁻¹ CaCl₂ (star-tem®). For the fibTEM assay, 300 µL of blood was mixed with 20 µL of ex-tem® reagent and 20 µL of fib-tem® reagent containing 0.2 mol L⁻¹ CaCl₂ and cytochalasin D, a platelet inhibitor. For the inTEM assay, 300 µL of blood was mixed with 20 µL of in-tem® reagent (partial thromboplastin phospholipid) and 20 µL of 0.2 mol L⁻¹ CaCl₂ (star-tem®). For the hepTEM assay 300 µL of blood were mixed with 20 µL of in-tem® reagent and 20 µL of reconstituted hep-tem® reagent containing heparinase and CaCl₂.

**Statistical analyses**

Sample size was estimated based on clinical equivalence for an individual patient at the two time points for the fibTEM MAs. Previous studies gave estimates for the mean (SD) fibTEM MA of 11 (3) mm after CPB [9,12,13]. A difference of > 20%, or ± 2.2 mm, was considered clinically important; that is, the two measurements would lead to different treatment decisions. Assuming no correlation between the time points, it was estimated that 40 patients would be required to provide 80% power at the 5% two-sided significance level to show that a 95% confidence interval around the difference would lie completely within ± 2.2 mm.

Patient and procedural characteristics and preoperative coagulation parameters are presented as mean (SD) or median (IQR) as appropriate. CT and amplitudes for each viscoelastic test, fibrinogen concentration measured by the Clauss method, and platelet counts were compared between the two time points using paired t-test, and a P value of < 0.05 was considered significant. The mean difference and the 95% confidence intervals between mea-

---

**Fig. 1.** Flow diagram of study procedures: Sample time 1 (‘on-CPB’) was 5–10 min after removal of the aortic-cross-clamp towards the end of cardiopulmonary bypass (CPB), and sample time 2 (‘post-protamine’) was after the end of CPB around 5 min after protamine administration. CPB, cardiopulmonary bypass; PT, prothrombin time; aPTT, activated thromboplastin time.
measurements at the two time points were calculated for each variable. These confidence intervals were examined to assess whether they lie completely within the prespecified clinical important limits of ± 20% of the mean value after administration of protamine. In addition, the proportions of patients with a difference of < 20% of the measurement after protamine were calculated for all parameters. Bland–Altman plots were drawn to investigate whether differences between the two measurements were related to the size of the measurements. Pearson correlation was calculated for corresponding test values on TEG and ROTEM for both time points and for viscoelastic test values and corresponding laboratory coagulation parameters for the results post-protamine. Analyses were performed on Prism 6.0 (GraphPad Software Inc., La Jolla, CA, USA) and STATA 13 (StataCorp LP, College Station, TX, USA).

Results

Fifty-two patients (75% male) undergoing cardiac surgery with CPB were included. Median (IQR) age was 75 (68–80) years, body mass index was 29 (25.4–32.4) kg m⁻², and the logistic EuroSCORE [14] was 5.75 (3.5–10) (Table 1). Isolated coronary artery bypass graft surgery accounted for 50% of the operations, isolated valve surgery for 17%, and combined and complex procedures for 19% and 13%, respectively, and the mean (SD) time on CPB was 108 (42) min. The baseline coagulation and full blood count results are shown in Table 1. The median (IQR) time between the on-CPB and post-protamine samples was 35 (25–43) min.

Coagulation

Results for the CTs and the MAs for the viscoelastic coagulation assays and the laboratory-based coagulation studies are summarized in Table 2 and Fig. 2.

Fibrinogen assays

The difference in mean maximum clot firmness (MCF) for fibTEM on ROTEM between on-CPB and post-protamine was not statistically significant (P = 0.07). The 95% CI of the mean difference was well within the prespecified 20% limit of the post-protamine mean (± 2.8 mm). Seventy-nine percent (41) of the patients were within this limit, that is had a difference of < 2.8 mm between the two measurements.

The mean MA for the functional fibrinogen assay (FF) on TEG was significantly different between the two sample times (P = 0.002). However, the 95% CI of the mean difference was well within the 20% limit (± 3.7 mm), and 85% (44) of patients had a difference within this limit.

The results of the laboratory Clauss fibrinogen assay were significantly lower on-CPB compared with post-protamine (P < 0.001). The mean difference of 1.2 g L⁻¹ (95% CI 1.03–1.4) was well outside the acceptable 20% limit of 0.4 g L⁻¹. Only 10% (5) patients had a difference between the two time points of < 20% of the post-protamine value.

The viscoelastic fibrinogen assays correlated well across all measurements between the TEG and ROTEM analyzers (Pearson r = 0.69, 95% CI 0.57–0.78) (Fig. 3A), but Bland–Altman analysis showed a bias of 5.4 mm consistently across all averages for FF on TEG vs. fibTEM (Fig. 4).

For the post-protamine samples, both TEG and ROTEM fibrinogen assays had a good correlation with the laboratory Clauss fibrinogen (Pearson r [95% CI] 0.75 [0.59–0.85] for fibTEM and r = 0.69, 95% CI 0.51–0.81 for FF; Fig. 3A).

Intrinsically activated assays

There was no difference (P = 0.67) between the mean CT for the hepTEM assay (ROTEM) on-CPB and post-protamine, and mean difference was well within the 20% limit (± 45 s).

In contrast, the mean CT (R-time) for the heparinase TEG (TEG) was significantly different between the two sample times (P < 0.001), and the mean difference was outside the 20% limit (± 1.1 min).

The mean MAs on both devices, hepTEM MCF and heparinase TEG MA, were significantly different between the two measurements (P < 0.001 and P = 0.008). However, the 95% CI of the mean differences were very well within the 20% limits (10.7 mm for hepTEM MCF and 12.1 mm for heparinase TEG MA) for both devices, and 94% (49) (hepTEM MCF) and 98% (51) (heparinase TEG MA) of patients had a difference within this limit.

Across all measurements, the correlation between inTEM (ROTEM) and heparinase TEG was good with

| Table 1 Patient and procedural characteristics, and preoperative blood results; values are mean (SD) or median (IQR)* |
|------------------------------|-----------------|---------------|
| Age (yrs) | 52 | 73.2 (9.9) |
| BMI (kg m⁻²) | 51 | 29.2 (5.2) |
| Logistic EuroSCORE | 52 | 5.8 (3.5–10)* |
| CPB time (min) | 51 | 108 (42) |
| Preoperative | | |
| INR | 51 | 1.0 (0.1) |
| APTT (s) | 51 | 32 (8) |
| Platelet count (10⁹ L⁻¹) | 52 | 205 (70) |
| Baseline ABG | | |
| Hb (g L⁻¹) | 52 | 119 (16) |
| Hct (%) | 52 | 38 (11) |
| ACT (s) | 50 | 113 (15) |

BMI, body mass index; CPB, cardiopulmonary bypass; INR, international normalized ratio; APTT, activated partial thromboplastin time; ABG, arterial blood gas; Hb, hemoglobin; Hct, hematocrit; ACT, activated clotting time.
regard to MAs (Pearson \( r = 0.7 \), 95% CI 0.6–0.8) but only moderate for CTs (\( r = 0.5 \), 95% CI 0.35–0.64) (Fig. 3B).

The CT of the intrinsically activated assays had a good correlation with the APTT measured in the laboratory for inTEM CT (Pearson \( r = 0.65 \), 95% CI 0.45–0.78) but not for the plain TEG R-time (\( r = 0.08 \), 95% CI 0.2–0.34).

Extrinsically activated assays

The mean differences of the CTs on exTEM (ROTEM) and R-time on rapid TEG between the measurement on-CPB and post-protamine were within the 20%-limits (± 11.4 s and ± 0.14 min, respectively) However, mean exTEM CT was significantly different (\( P < 0.001 \)).

The mean maximum clot firmness (MCF) for exTEM (ROTEM) was not different between the two time points (\( P = 0.57 \)), and the mean difference was well within the 20% limits (± 11.5 mm). All but one patient (98%) had a difference of less than the prespecified 20% limit. Mean MA for rapidTEG was significantly different (\( P \leq 0.001 \)), but the mean difference was within the 20% limit (± 11.9 mm) and the difference was within this limit in almost all patients (98%).

Correlation between exTEM (ROTEM) and rapidTEG was very weak with regard to CTs (\( r = 0.2 \), 95% CI 0.04–0.38) but strong for amplitudes (\( r = 0.83 \), 95% CI 0.76–0.88) (Fig. 3C).

For the extrinsically activated CTs on the viscoelastic analyzers and the international normalized ratio (INR) from the laboratory, there was moderate correlation for exTEM CT (\( r = 0.58 \), 95% CI 0.36–0.73) but no correlation for rapidTEG R-time (\( r = 0.13 \), 95% CI −0.15–0.39).

Discussion

Our data demonstrate that, in a clinical setting, point-of-care viscoelastic tests can be used during CPB to assess the coagulation system, but not all parameters are equally valid for predicting results after CPB and after the reversal of heparin with protamine. Even though we found statistically significant differences between the two measurements for the majority of parameters, any differ-

![Table 2 Results of viscoelastic and laboratory coagulation assays at both time points (on-CPB and post-protamine), mean difference between the time points, and percentage of patients with a difference of < 20% of the post-protamine value](image-url)
Fig. 2. (A–C) Box and whiskers (min. to max.) diagrams for fibrinogen (A), intrinsically (B) and extrinsically (C) activated assays. h, heparinase cups.
ences were small (<20% of post-protamine value) except for the CT with the heparinase TEG. This means that the value on bypass would differ <20% from the value after protamine, which is clinically acceptable, as it is unlikely to result in a different treatment decision. Another way of evaluating the size of the difference between the two measurements is to calculate the proportion of individual patients, which are below the threshold difference of 20%. In our study, across all viscoelastic tests clot strength had a difference below the clinically important threshold in 79%–98% of the patients, whereas for CT only 40%–79% of patients were within that limit. Viscoelastic CTs, which are assessing mainly the plasmatic coagulation system that is clotting factor deficiency, might therefore not be as useful as predictors for post-protamine coagulopathy when tested during full heparinization on CPB. In contrast, the amplitudes measured on CPB, representing mainly the platelet and fibrinogen contribution to clot formation and strength, were very close to the measurement after protamine. The MAs tested during CPB could therefore be used to guide therapy especially considering their known correlation to postoperative chest tube drainage, fibrinogen level, and platelet count [15–17].

For the assessment of fibrinogen levels during CPB, there was a clear advantage for the point-of-care viscoelastic assays over the laboratory Clauss fibrinogen. While 79% and 85% of patients had a difference of <20% in fibTEM and TEG functional fibrinogen, respectively, only 10% of
patients were within this limit for the laboratory assay. Fibrinogen concentration measured in the laboratory during CPB underestimated the post-protamine value by 1.2 g L\textsuperscript{-1} and is therefore unacceptable for clinical use. This is in keeping with the in vitro findings of Gertler et al. [7] that the laboratory Clauss assay is affected by heparin concentrations over 2 IU mL\textsuperscript{-1}. However, the Clauss assay is a clinical standard for use after CPB—that is, after reversal of heparin. At that time point, the amplitudes of both fibTEM and TEG functional fibrinogen showed a strong correlation to the Clauss fibrinogen concentration. We have only studied the MAs but not the functional fibrinogen values calculated by the TEG analyzer, which have been shown to overestimate the laboratory (Clauss) fibrinogen concentration [18]. It is important to note here that the viscoelastic analyzers use clot firmness in a clot with minimal platelet contribution as a surrogate and do not derive fibrin concentration like the Clauss assay from a CT in the presence of high concentration of bovine thrombin against a calibration curve of fibrinogen concentration. As discussed below the viscoelastic assays are influenced by the degree of platelet inhibition in the assay and possibly also by the reduction in the levels of other clotting factors, which are needed to initiate coagulation via the extrinsic pathway. Given the small mean differences for the fibrinogen assays in amplitude of ~1 mm on TEG and ROTEM in our study, we conclude that viscoelastic fibrinogen assays performed toward the end of CPB were able to predict postbypass fibrinogen and could be used to guide therapy.

Comparison of the two analyzers produced good correlation for the MAs across all assays but only moderate to poor correlation for the CTs. However, it has to be noted that the absolute values are not interchangeable and device specific reference values need to be applied. For example, Bland–Altman analysis showed a bias between fibTEM MCF and TEG functional fibrinogen MA of 5 mm, which was consistent across all averages (Fig. 4). The higher readings on the TEG functional fibrinogen are likely attributable to a different level of platelet inhibition as crossover testing of the fibrinogen assays on both devices produced similar effects [19]. To produce a fibrin-only clot, the two assays use different platelet blocking agents, cytochalasin D on ROTEM and abciximab on TEG. A recent comparison of both assays to a third one using cytochalasin D plus a GPIIb/IIIa inhibitor showed that double inhibition of platelets produces even lower amplitudes, suggesting that both standard assays fail to fully suppress platelet activity [20,21]. Contribution of residual platelet activity to clot firmness in fibrinogen assays would be a concern as theoretically large variation in platelet count could impact on the fibrinogen reading. In this study, we did not evaluate fibrinogen assays at different platelet counts. The average platelet count in our cohort decreased by only 10% (Table 2) between the sample points, which is unlikely to have a major impact on the measurement. Similarly, the previously mentioned study did not find a correlation between platelet count and difference in amplitudes between fibTEM and functional fibrinogen. In summary, transfusion algorithms based on thresholds designed for one particular viscoelastic analyzer or test assay have to be revalidated if they are to be used with another.

The main factors that could affect the validity of on-bypass viscoelastic testing are the presence and the reversal of heparin. Even though various assays on TEG and ROTEM are designed to counteract heparin with heparinase to produce valid results during full heparinization, in vitro results demonstrated for ROTEM that higher concentrations of heparin as well as the presence of protamine could affect test results [7]. In that study, intrinsically activated tests were stable up to a heparin concentration of 8 IU mL\textsuperscript{-1}, extrinsically activated CTs significantly increased with heparin over 2 IU mL\textsuperscript{-1}, and clot firmness significantly decreased over 4 IU mL\textsuperscript{-1}. Protamine also significantly affected results. CT were prolonged from a heparin:protamine ratio of 1:1, and clot firmness was decreased for ratios of 1:1.5 and 1:2. As the
assays are comparable, it can be assumed that similar effects would be seen on TEG. Although heparin concentrations at the end of bypass are unlikely to exceed 4 IU mL⁻¹ [22,23], these findings raise concerns about the practice of using viscoelastic tests toward the end of bypass to identify and subsequently treat coagulopathy early. Comparable to those in vitro findings, our results show that CTs on point-of-care viscoelastic devices seem to be significantly affected; that is, we observed larger differences between the two time points, but the amplitudes across all assays produced good agreement between on-CPB and post-protamine measurement.

We chose to investigate the validity of viscoelastic tests during CPB in a real patient setting, whereby other known and unknown confounding factors besides heparin and protamine could have affected the results. This study design allows for a more realistic assessment of the clinical utility of performing viscoelastic tests early, while the patient is still on CPB. The question to be answered is whether an early test, done at the end of CPB, produces results, which can be used to guide therapy at a later stage, after administration of protamine, when coagulopathy becomes apparent. As the development of coagulopathy after cardiac surgery can be a very dynamic process, any type of coagulation test may become invalid after a certain period of time, depending on factors such as amount of bleeding, red cell transfusion, cell salvage, surgical complications, etc. The median time between the two samples in our study was 35 min with an IQR of 18 min. From 25 to 40 min seems to be a reasonable time between testing for and treating of coagulopathy, especially considering that the turnaround time for laboratory-based tests would be rarely < 30 min and samples can only be taken after reversal of heparin. Our results therefore support the use of certain point-of-care viscoelastic parameters to guide therapy despite the time delay between testing and treatment. Specifically, the clot firmness, represented in the MAs, can be used to assess platelets and fibrinogen at the end of CPB. Those results would then be available to the clinician at the time of heparin reversal, and if microvascular bleeding occurs, it could be acted on specifically. Early assessment of the coagulation could also aid the targeted preparation of blood products if bleeding complications are anticipated and avoid blind preparation of potentially unnecessary blood and coagulation products.

NICE has reviewed the utility and cost effectiveness of viscoelastic tests in the cardiac surgery setting in 2014. The expert committee did not distinguish between the viscoelastic methods, and on the basis of a comparison of red cell transfusion, TEG or ROTEM, was considered cost effective even if used in conjunction with conventional laboratory testing provided a site handles > 300 cases a year. NICE did not endorse a particular algorithm or combinations of tests [1].

Our study included only scheduled cardiac surgical patients, and therefore, patients undergoing emergency procedures, who might be at a higher risk of acquiring coagulopathy, were not studied. Also, most of the study patients did not present with major abnormalities of their clotting system after CPB, and therefore patients with severe coagulopathy might be underrepresented. About half of the patients received red blood cell transfusions, 8% received fresh frozen plasma, 27% received platelets, and 15% received other clotting promoting products, but all of these were administered after our testing had been completed. However, with regard to the type of surgery performed and the transfusion management, the study population closely represents the average elective patient population at our institution. Finally, the study was not designed to evaluate the impact of on-bypass testing on transfusion rates or other outcome parameters.

In conclusion, results from viscoelastic point-of-care coagulation tests performed toward the end of CPB produce clinically comparable results to the same test after reversal of heparin. The most stable parameters were the amplitudes, indicating clot strength, whereas CTs showed more variability. Laboratory testing of fibrinogen was essentially invalid during CPB, but viscoelastic fibrinogen tests were valid and therefore useful. The results suggest that on-bypass testing with viscoelastic assays is a useful tool for early planning of coagulation management, specifically with regard to substitution of fibrinogen and platelets, the two major substrates for clot formation.

Addendum

E. Ortmann was responsible for study design, sample collection, viscoelastic coagulation testing, data collection, data analysis and interpretation, and manuscript writing. A. Rubino and B. Altemimi were responsible for collecting samples, viscoelastic coagulation testing, data collection, and manuscript writing. T. Collier was responsible for data analysis and interpretation and manuscript writing. M. W. Besser and A. A. Klein were responsible for study design, data interpretation, and manuscript writing.

Acknowledgements

This work was presented in part at the Annual Autumn Meeting of the Association of Cardiothoracic Anaesthetists (ACTA), November 2013, Nottingham. We would like to thank Haemonetics Ltd. and Tem International GmbH for technical support. The companies had no influence on study design and conduct, data collection and analyses, or publication of the data.

Disclosure of Conflict of Interests

This study was partially funded by an unrestricted research grant from CSL Behring. M. W. Besser reports personal fees from Glaxo Smith Kline, Ashfield in Focus,
Pharma- Intel and GIG Consulting, outside the submitted work.

References


