

Modified Thromboelastography in Predicting Blood Loss Post Cardiopulmonary Bypass following Cardiac Surgery

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ABSTRACT

The study protocol was approved by the Institutional Review Board and informed consent was obtained from parents / guardians of patients. The aim of the study was to evaluate the modified TEG-rTT as a Point of care (POC) test in paediatric cardiac surgery with CPB and to study the correlation of TEG-rTT parameters G and R with a 24-hour chest tube drainage. Eleven patients undergoing elective paediatric cardiac surgery for congenital defects were enrolled in the study. Patients with coagulation defects, liver dysfunction, re-do surgery and those on anticoagulants within 7 days of surgery were excluded. The baseline standard coagulation tests (SCT) included prothrombin time (PT) activated partial thromboplastin time (aPTT), platelet count, hematocrit (HCT), hemoglobin (Hb) fibrinogen and TEG-rTT values. Postoperative investigations (24 hours in ICU) included all the above-mentioned tests and measurement of cumulative 24 hour chest tube drainage. Chest tube drainage greater than 50 ml/hour was classified as excess and, in such cases, fresh whole blood was transfused. Regular preoperative laboratory measurements and radiological investigations were also performed. Baseline and 24 hour postoperative values of bedside TEG-rTT (Haemoscope Corp. IL) were carried out. Statistical analysis was carried out using Instat 3.0 software. All results were expressed as mean (range) and the correlation between standard coagulation tests and TEG-rTT to 24 hour chest tube drainage post-surgery was analyzed. The baseline values of SCT and TEG-rTT were compared with the corresponding 24 hour postoperative values. The results showed that there was a statistically significant prolongation of PT and aPTT values compared to the corresponding baseline and post-operative values. There was a significant decrease in the postoperative platelet count but other SCT did not show any significant change. The SCT, PT and aPTT values had a poor positive correlation with 24 hour chest tube drainage whereas HCT showed a negative correlation. Fibrinogen and platelet count showed a negative correlation with chest tube drainage. The TEG-rTT R value showed no correlation with 24 hour chest tube drainage whereas G value showed a good correlation. It can be concluded that TEG-rTT has a high predictive value for 24 hour postoperative chest tube drainage. TEG-rTT G values becomes clinically significant if simultaneously platelet count and HCT values are also recorded. This will enable for specific component transfusion postoperatively in cardiac surgery with CPB. Therefore TEG-rTT qualifies as a simple, cost effective POC test with a high predictive value for 24 hour chest tube drainage postoperatively.

Keywords: Tissue factor, Modified Thromboelastography, Cardiac surgery, Cardio pulmonary bypass, point of care test.

Introduction

Cardiac surgery using cardiopulmonary bypass (CPB) is commonly accompanied by excessive microvascular bleeding (EMB). This necessitates reoperations and unwarranted transfusion of blood components [1,2]. In about 20% of patients undergoing cardiac surgery there is profuse bleeding. Among the bleeders, 50% of cases are attributed to surgical and another 50% are due to disturbances in hemostasis arising during CPB [3]. The hemostatic disorder occurring during CPB post cardiac surgery is multifactorial [4-6]. Hence it is essential to have a rapid and reliable test to detect and differentiate coagulopathy from surgical cause of excessive blood loss [7].

There are various factors contributing to coagulopathy during cardiac procedure with CPB. One of them is contact activation of coagulation by the prolonged exposure to the surface of extracorporeal device. This results in platelet activation leading to reduction in the number and function

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of circulating platelets. Hypothermia during CPB causes further impairment of platelet function [8]. Heparin which is used as an anticoagulant in the CPB circuit is another important cause for platelet dysfunction and bleeding. Inadequate reversal of heparin by protamine sulphate contributes to postoperative bleeding [9]. The above discussed acquired platelet dysfunction during CPB results in impairment of hemostasis. Therefore, a rapid and reliable point-of-care (POC) test for the determination of platelet function / coagulopathy based on which judicious transfusion of blood products can be practiced is indispensable. Plasma based standard coagulation tests that are done to assess coagulation and fibrinolysis during CPB are platelet count, fibrinogen concentration, prothrombin time (PT), and activated partial thromboplastin time (aPTT). These standard coagulation tests (SCTs) measure each component of hemostasis separately in isolation [8]. The reference values for normal individuals are different for patients after surgery with massive blood loss [10]. Activated clotting time (ACT) does not yield information on platelet–fibrin interactions and clot lysis which are impacted by CPB [11]. Overall, the long processing time taken for reporting these laboratory SCTs and their poor predictive value make them less suitable for detecting CPB associated coagulopathy [12-15].

Thromboelastography (TEG) is a POC test which can be used to monitor abnormalities in hemostasis and has many advantages over SCTs. In cardiac surgery there has been a recent interest in TEG because it evaluates blood coagulation as a whole dynamic process [16,17]. The TEG method provides a global assessment of hemostasis rather than estimating individual components of blood coagulation as with SCTs.

We had earlier reported a modified TEG activated by human recombinant tissue thromboplastin (rTT) with a shorter TCT than standard TEG (TEG-0) and TEG–Celite [18]. The effect of various concentrations of platelets, fibrinogen, red blood cells, antiplatelet agents and platelet activators on TEG-rTT has been assessed and reported elsewhere [19,20]. The goal of this work was to evaluate the efficiency of TEG–rTT as a POC test in paediatric cardiac surgeries with CPB in predicting postoperative bleeding.

The correlation of TEG–rTT parameters G and R with postoperative 24 hours chest tube drainage was analysed and compared with SCT in this study.

Methods and Materials

The study protocol was approved by the Institutional Review Board and informed consent was obtained from the parents / guardians of the patients. The aim of the study was to evaluate the modified TEG–rTT as a POC test in paediatric cardiac surgery with CPB. Eleven patients undergoing elective paediatric cardiac surgery for congenital defects under 14 years of age and weighing less than 46.5 kg were

enrolled in the study. Patients with coagulation defects, liver dysfunction and re-do surgery were excluded from the study. None of the enrolled patients received anticoagulants or antiplatelet drugs 7 days prior to surgery.

Anaesthesia was induced with midazolam, fentanyl, and rocuronium bromide. Bypass circuits was established with custom tubing pack (Medtronic MN), Maquet paediatric membrane oxygenator (Germany) and Cardioplegia delivery system (Medihub Sci. Pvt. Ltd.). The priming solution consisted of heparin, bicarbonate, mannitol, ringer lactate and whole blood. The total priming volume of bypass circuit was 300 to 600 ml. The total duration of CPB ranged from 25 to 75 mins and hypothermia was maintained between 28.9 to 33°C. Anticoagulation was obtained with porcine heparin and circulating heparin was neutralized with protamine sulphate. A single mediastinal chest tube drainage was placed prior to wound closure.

The following preoperative measurements were collected as baseline data. They were prothrombin time (PT), activated partial thromboplastin time (aPTT), platelet count, haematocrit (HCT), haemoglobin (Hb), fibrinogen and TEG–rTT values. Postoperative investigations performed after 24 hours in ICU were PT, aPTT, platelet count, Hb, HCT, fibrinogen and TEG–rTT along with total 24 hour volume of chest tube drainage. Chest tube drainage of more than 50 ml/hour was classified as excess and, in such cases, fresh whole blood was transfused. Regular preoperative laboratory measurements and radiological investigations were also performed.

Blood for coagulation assays and TEG–rTT (Haemoscope Corp. IL) was collected in 3.2% citrated vacutainer tubes. Bedside TEG–rTT was carried out using 320ml of citrated whole blood (CWB), 20µl of 0.025 % rTT, and 30µl of 0.2M CaCl₂. Blood was collected in an EDTA tube and a complete blood count (CBC) was measured using Sysmex Automated Haematology analyser.

Statistical analysis was carried out using Instat 3.0 software. All results were expressed as mean (range), the correlation between standard coagulation tests and TEG–rTT to 24 hour chest tube drainage post-surgery was analysed.

Results

Table - 1 gives the demographic parameters which includes height, weight, body surface area (BSA), blood group etc.

Table -2 lists the baseline values of various parameters measured before surgery versus 24 hour postoperative values of the same.

Fig. 1a, b shows the baseline values measured by SCTs and TEG–rTT versus the corresponding 24 hour postoperative values of the patients. There was a statistically significant prolongation of PT and aPTT postoperatively compared to

Table 1 : Patient Demographics

Parameters	Mean (Range)
Age (months)	96 (48-168)
Sex M/F	3/8
Weight (kg)	27.2 (11.3-46.5)
Height (cms)	118.7 (84-156)
BSA (m ²)	0.85 (0.69-1.05)
Blood Grp A/B/O	02/05/04
Surgical Procedure:	
ASD	6
VSD	3
MVR	2
CPB time (min)	44 (25-75)
Minimum Temp (°C)	30.5 (28.9-33)
24 hrs Chest tube drain (ml)	256(150-450)

Table 2 : Baseline values versus 24 hour postoperative values

Baseline Vs 24 hr Post Op	Baseline Mean (Range)	24 hrs Post op Mean (Range)	SD	p value
Platelet (10 ³ /μl)	250 (205-298)	162 (123-228)	58	0.002
HCT (%)	35.8 (32-38)	31 (20-41)	6	0.041
PT (sec)	14.5 (14-15.5)	19 (15-24)	4	0.002
aPTT (sec)	36 (32-38)	50.5 (39-60)	8	0.0003
Fibrinogen (mg/dl)	222 (210-250)	191 (150-220)	23	0.012
TEG-rTT G x 1000 (Dynes/cm ²)	14.75 (11.8-15.2)	10.7 (7-14)	2.7	0.013

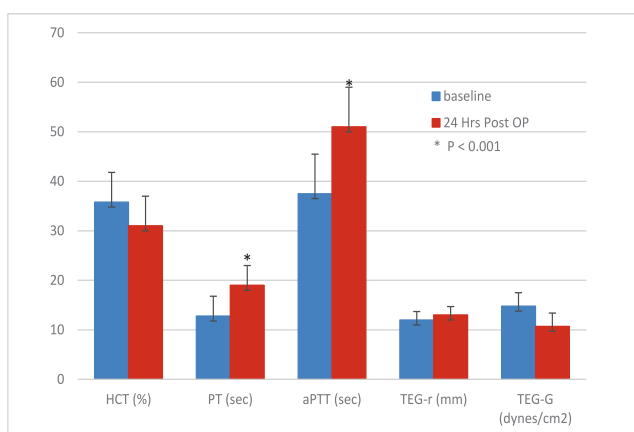


Fig: 1a

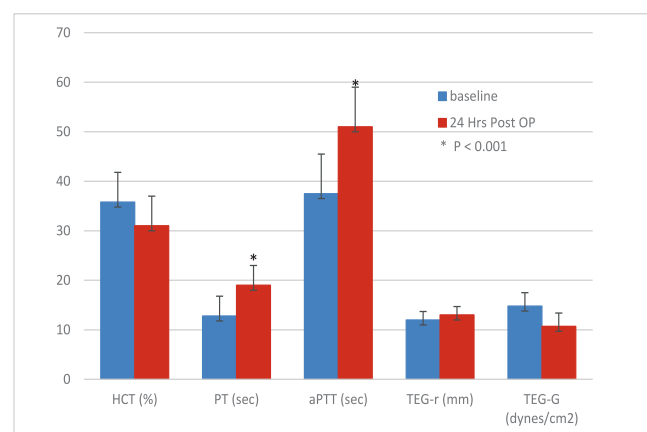


Fig: 1b

Fig. 1a,b : Baseline values of SCT and TEG-rTT versus 24 hour postoperative values.

the corresponding baseline values. There was also a significant decrease in the platelet count postoperatively. The other values analyzed did not show any significant change.

Fig.2a shows that PT and aPTT values have a poor correlation with 24 hour chest tube drainage. Fig.2b shows that there was a negative correlation between HCT and 24 hour chest

tube drainage values. Fig.2c shows that as fibrinogen and platelet count decreased there was an increase in chest tube drainage. This indicated that there was a negative correlation between these two SCTs and 24 hours chest tube drainage values.

In Fig.2d, it can be seen that there was no correlation between R and chest tube drainage whereas, as G value decreased

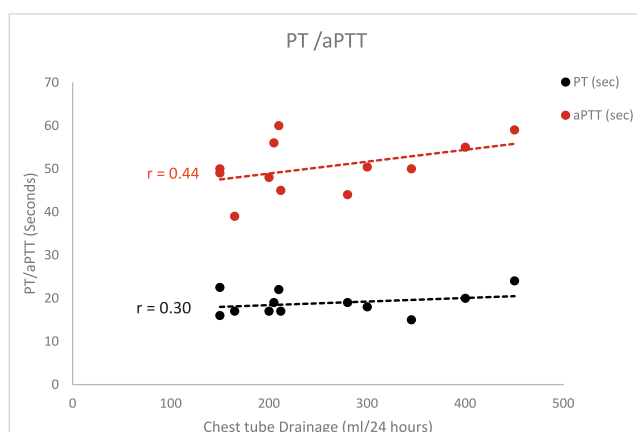


Fig: 2a

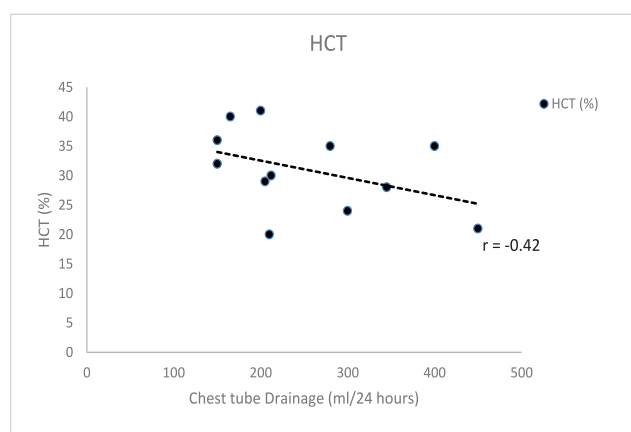


Fig: 2b

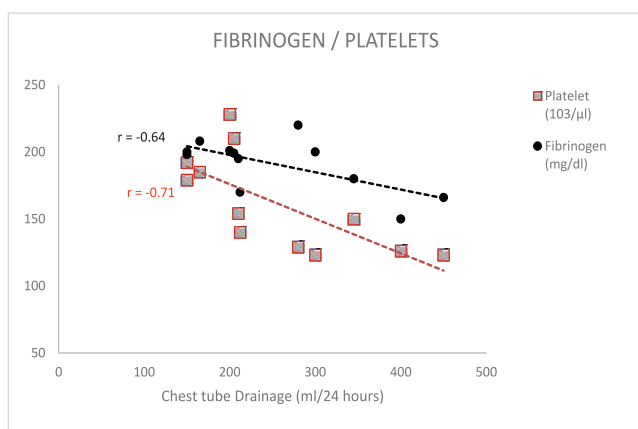


Fig: 2c

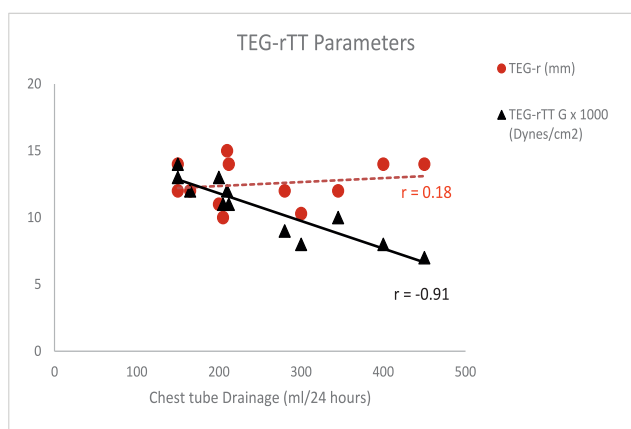


Fig: 2d

Fig. 2 a,b,c,d : Shows the correlation between 24 hour chest tube drainage versus 24-hour SCT and TEG-rTT values.

there was an increase in chest tube drainage. The TEG-rTT G value has the highest correlation when compared to any of the SCT with 24 postoperative chest tube drainage. Hence G value has the highest predictive value for postoperative chest tube drainage.

Discussion

Preoperatively patients undergoing cardiac surgery have a normal coagulation profile but during and post CPB they develop coagulopathy associated with profuse bleeding [21-23]. In the scenario of paediatric patients undergoing cardiac procedure with CPB for congenital heart defects there are several factors that might contribute to hemostatic disorder and hemorrhage [24]. One of the factors is that the priming volume becomes proportionately more than the circulating volume of blood. This results in dilution of clotting factors and subsequent excessive micro vascular bleeding (EMB) [25].

The usefulness of TEG in monitoring hemostasis in children has not been widely investigated [26,27]. The role of TEG particularly in paediatric population undergoing cardiac surgery with CPB for congenital defects is yet to be

thoroughly explored. There are some reports comparing the efficacy of TEG with SCTs in making judicious decisions regarding the type and amount of blood products to be administered to patients with EMB during CPB [28-31]. But most of their findings do not predict a decrease in the number of redo surgeries or a reduction in excessive blood loss. Most groups have not validated the usefulness of TEG with substantial results.

There are two main reasons to consider SCTs as less practical and desirable than TEG during CPB for predicting postoperative blood loss. One is the long processing time (30 to 60 mins) to obtain the test results from the laboratory. Another reason is the fact that SCTs measure each component of the coagulation independently using separate tests. When blood transfusion is done empirically by clinicians based on SCTs, it leads to irrational and excessive usage of blood products. The TEG test is different from SCTs such as PT, aPTT and platelet count by its ability to measure the dynamics involved in clot formation and lysis. Since TEG measures specific aspects of clotting the exact blood component that is deficient can be precisely identified.

In our study, among the various SCTs done 24 hours postoperatively platelet count, fibrinogen and HCT had a negative correlation with chest tube drainage. This can be attributed to the dilution factor produced by the priming volume in CPB circuit. The G value of TEG-rTT had a significant negative correlation with 24 hours postoperative chest tube drainage whereas R parameter had no correlation. Therefore, TEG-rTT parameter (G) is important in predicting postoperative bleeding because of its high correlation with chest tube drainage. The TEG-rTT (G) becomes clinically significant if platelet count and HCT are recorded concurrently. As per our study the TEG-rTT which can detect coagulopathies in 7 mins and has a high predictive value for 24 hours postoperative chest tube drainage. Hence based on TEG-rTT measurements specific blood component transfusion can be undertaken postoperatively in cardiac surgery with CPB.

As reported by some authors the data generated from TEG seems to correlate with the amount of postoperative blood loss [28,31]. But one obstacle for TEG to be useful in paediatric cardiac setting is that the reference levels of factors and inhibitors of coagulation pathway is less in infants than adults [32]. Although baseline values of TEG in infants are different from adults, the reference values have been established in young children [33]. The second obstacle is the prolonged TCT to obtain TEG results in the operating room to be able to take timely action on transfusion of blood products. To overcome the long TCT of conventional TEG, celite and tissue factor were utilized to rapidly attain α angle and MA variables which were reported to correlate with bleeding after CPB in children [34,35].

In this investigation the addition of rTT with whole blood samples of children had enabled the use of the modified TEG (TEG-rTT) as a POC test to monitor haemostasis post CPB in a paediatric cardiac intensive care room. A study has reported TF activated TEG to define baseline TEG values in children stating that clot formation is more rapid upon TF addition versus celite [36]. In terms of TCT our studies also showed that rTT was better than celite [18] and hence TEG-rTT was utilized as a POC test to predict CPB associated postoperative blood loss. In this study it was hypothesized that the TEG parameters would correlate with chest tube drainage and thereby help to predict post cardiac surgery bleeding more effectively than SCTs in children. Likewise G value of modified TEG-rTT correlated with 24 hour postoperative chest tube drainage and therefore will help identify potential bleeders post CPB.

Although TEG-platelet mapping is a relatively newer POC test, it is expensive and requires multiple channels to be run simultaneously to produce results. Whereas, TEG-rTT can be operated as a single channel instrument and is more cost effective than TEG-Platelet mapping technique. It has a high

predictive value of 24 hour postoperative chest tube drainage. TEG-rTT G value become clinically useful if simultaneous platelet count and haematocrit are recorded. This will enable for specific component transfusion post operatively. Therefore Modified TEG-rTT qualifies as a simple, cost effective POC test with a high predictive value of 24 hour chest tube drainage post operatively.

Conclusion

It can be concluded that this study conducted to evaluate the efficiency of modified TEG-rTT in predicting postoperative bleeding in paediatric cardiac surgery following CPB has established a strong correlation of G value with 24 hour chest tube drainage. The G value of TEG-rTT is a better predictor of blood loss than SCTs in view of the long turnaround time of the latter. The use of modified TEG-rTT G value will allow rapid and accurate prediction of altered coagulation due to non-surgical cause of bleeding in paediatric cardiac surgery following CPB. This in turn will pave the way for rationale use of blood products in children with acute coagulopathy associated with CPB.

Conflict of Interest:	All authors declare no COI
Ethics:	There is no ethical violation as it is based on voluntary anonymous interviews
Funding:	No external funding
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