Original Article

Do Sonoclot Coagulation Parameters Correlate with Thrombelastograph Parameters?

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ABSTRACT

Postoperative hemorrhage is a major cause of morbidity after cardiopulmonary bypass. Timely coagulation test results may aid the clinician in diagnosing and treating coagulopathy. The purpose of this study is to determine if there is any correlation between parameters obtained from two viscoelastic coagulation monitors (Thrombelastograph and Sonoclot). Fifty non-heparinized blood samples were obtained from cardiac surgery patients pre-skin incision or post-Protamine. Each blood sample was placed in the Celite-activated Sonoclot cuvette and native, as well as Celite-activated TEG wells. The parameters compared were: native and Celite TEG split point, r, k, alpha angle, MA, MA60 vs. Sonoclot immersion point, SonACT, R1, shoulder point, time to shoulder, R2, peak, time to peak, R3, retraction point and time to retraction. All viscoelastic parameters were correlated with routine coagulation tests including: ACT, PT, PTT, platelet count, fibrinogen concentration, bleeding time and hematocrit.

Simple and multiple regressions were performed on these Thrombelastograph and Sonoclot parameters to determine correlation, if any.

Correlations were considered significant if $p<0.01$ and $R2 > 0.6$. The Sonoclot R1 correlated significantly with the Thrombelastograph Celite-activated k-time and alpha angle. The Sonoclot shoulder point correlated with the Thrombelastograph Celite-activated MA and Coagulation Index. The Sonoclot R1 and shoulder point correlated with fibrinogen and platelet counts. The Sonoclot time to peak and time to retraction correlated with the PTT. The Sonoclot coagulation parameters generally do not correlate with the Thrombelastograph parameters. The lack of better correlation among all parameters suggests that there are aspects of coagulation that are detected differently by each monitor. Therefore, the two viscoelastic monitors cannot be substituted for each other.

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INTRODUCTION

Postoperative hemorrhage is a major cause of morbidity after cardiopulmonary bypass (CPB). It has been reported to occur in 5-18% of patients who have undergone open-heart procedures. (1) Approximately 3% of patients require surgical re-exploration of the chest due to postoperative hemorrhage. (2) Many non-surgical abnormalities such as thrombocytopenia, fibrinolysis, coagulation factor deficits and inadequate heparin neutralization with protamine sulfate can account for hemorrhage after CPB. The open-heart team is often faced with determining the cause of hemorrhage and timely coagulation test results may aid in diagnosing and treating the coagulopathy. (2)

Coagulation screening tests include the activated clotting time (ACT), platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT) and fibrinogen concentration. The laboratory turnaround time for these tests often decreases their utility to the clinician in treating the cause of postoperative hemorrhage. (1) Readily available intraoperative monitors of all phases of clot formation, strength and breakdown may decrease the empiric administration of fresh frozen plasma and platelets to the bleeding cardiac patient postoperatively. (2) Technology now exists to assess the clotting mechanism in the operating room.

Thrombelastography (TEG) and Sonoclot analysis (SCT) both measure the viscoelastic properties of the blood clot and graphically represent it's formation and dissolution. (2) These monitors of clot viscoelastic properties have been shown to be useful in hemostasis management during hepatic transplant and cardiac surgery. (2-4)

Tuman, et al., compared the TEG and SCT viscoelastic monitors to the routine coagulation tests listed above to determine which test best predicted hemostasis after CPB. (2) Both the TEG and SCT were 100% accurate in predicting hemorrhage in patients that bled and both tests were significantly better predictors of bleeding than routine coagulation tests (RCT), such as the ACT. Accuracy was defined as: [# correctly predicted bleeders + # correctly predicted non-bleeders] / total # patients. They found the overall accuracy of coagulation tests to be: TEG-88%, SCT-74% and RCT-33%. The preoperative parameters reflecting platelet-fibrin interaction (SCT: R2, peak, R3 and TEG: alpha angle, MA, A60) were reported to be significantly different post-CPB.

Wang, et al., also studied the usefulness of the TEG and RCT for predicting post-CPB bleeding. (1) They reported that neither the RCTs nor TEG can reliably predict excessive hemorrhage after CPB. Chapin, et al., compared the TEG and SCT coagulation analyzers with RCT in detecting platelet dysfunction, factor deficiency and fibrinolysis during orthotopic liver transplantation. (3) A significant correlation between TEG and SCT evaluations of platelet function was found. They reported that viscoelastic monitors and RCT responded similarly to platelet dysfunction and factor deficiencies.

Table 1
Coagulation Parameters vs. Coagulation Events
R = R time, K = K time, MA = maximum amplitude, MA60 = maximum amplitude 60 minutes after MA, R1 = clot rate, SONACT = activated clotting time on the Sonoclot signature, R2= second slope of clot formation on the Sonoclot, R3 = slope of clot retraction measurement on the Sonoclot

COAGULATION EVENT	TEG	SCT	REFERENCES
CLOT ONSET	R	R1, SONACT	6, 6
PLATELET FUNCTION	K,MA,ALPHA ANGLE	PEAK, R3	7, 6
PLATELET/FIBRIN	K,MA, MA60	R2, PEAK, R3	7, 6
MESH CONTRACTION	MA, ALPHA ANGLE	R3	7, 2
CLOT BREAKDOWN	MA60	R3	4, 6

Table 2
Native Thrombelastograph Parameters
r = r time, k = k time, MA = maximum amplitude, MA60 = amplitude of tracing 60 minutes after the MA

PARAMETER	MEAN VALUE	STANDARD DEVIATION	FUNCTION
Split Point	13.6 min	9.6 min	initial signal on TEG
r	16.4 min	11.2 min	reaction time, initial fibrin formation
k	8 min	6.4 min	coagulation time, speed of fibrin buildup
Alpha Angle	35.3 °	7.9 °	speed of clot strengthening
MA	51.4 mm	13.1 mm	maximum clot strength
MA60	47.0 mm	12.7 mm	measure of clot destruction

*** All parameters obtained from open-heart surgical patient's non-heparinized blood pre or post cardiopulmonary bypass.

THE THROMBELASTOGRAPH

The TEG technique was developed by Hartert in 1948. (5) Whole blood (0.36 ml) is placed in a pre-warmed (37°C) metal cuvette which rotates. Once blood is placed in the cup, mineral oil is placed over the sample to prevent evaporation. A piston is suspended in the blood, and as clot forms, fibrin strands form from the walls of the cuvette to the piston. Shear elasticity is

Table 3
Celite-Activated Thrombelastograph Parameters
(n = 50), r = r time, k = k time, MA = maximum amplitude, MA60 = amplitude of tracing 60 minutes after the MA

PARAMETER	MEAN VALUE	STANDARD DEVIATION	FUNCTION
Split Point	2.9 min	1.1 min	initial signal on TEG
r	3.7 min	1.2 min	reaction time, initial fibrin formation
k	2.24 min	1.7 min	coagulation time, speed of fibrin buildup
Alpha Angle	62.9 °	13.0 °	speed of clot strengthening
MA	55.8 mm	14.6 mm	maximum clot strength
MA60	50.2 mm	13.8 mm	measure of clot destruction

*** All parameters obtained from open-heart surgical patient's non-heparinized blood pre or post cardiopulmonary bypass.

Table 4
Celite-Activated Sonoclot Parameters
(n = 50), R1 = clot rate, R2 = second slope of clot formation on the Sonoclot signature, R3 = third slope of clot formation on the Sonoclot signature

PARAMETER	MEAN VALUE	STANDARD DEVIATION	FUNCTION
Immersion Point	27.3 units	14.6 units	viscosity of sample
SonACT	135.8 secs	30.5 secs	activated clotting time
R1	28.7 u/min	12.2 u/min	clot rate, fibrin formation
Shoulder Point	66.1 units	19.4 units	point of platelet/fibrin interaction
Time to Shoulder	5.2 min	1.7 min	fibrin formation complete
R2	4.4 u/min	2.5 u/min	platelet/clot interaction
Peak	101.5 units	25.8 units	maximum clot retraction
Time to Peak	19.4 min	9.1 min	time to maximum clot retraction
R3	-2.0 u/min	2.1 u/min	platelet contraction of fibrin
Retraction Point	87.2 units	23.4 units	clot maturity
Time to Retraction	40.6 min	13.5 min	time to clot maturity

*** All parameters obtained from open-heart surgical patient's non-heparinized blood pre or post cardiopulmonary bypass.

measured as fibrin transfers motion from the cuvette to the piston. This viscous "drag" is graphically illustrated by a moving pen and paper. (6) The blood coagulation may be activated with Celite to speed up the process, but the majority of data is available for native TEGs and not for activated TEG parameters. Celite shortens coagulation time because it acts as a contact surface (analogous to glass activation) which activates Factor XII and platelets and stimulates the reserve clotting ability of a blood sample. (Haemoscope: Thrombelastograph Coagulation Analyzer Operator's Manual, 1991)

Several parameters obtained from the TEG are used to quantitate the whole blood coagulation mechanism. The split point is the time to the first deflection being recorded on the TEG tracing. The reaction time (R value) measures the time from blood being placed in the plastic cup until a 1 mm amplitude is seen on the recorder. The R value (normal 23.6 mm ± 4.8 mm) represents the time necessary for initial fibrin formation. The K value is the time from the end of the R time till the amplitude is 20 mm on the TEG tracing. The K value (normal 10.6 mm ± 2.8 mm) is a measure of the speed of fibrin buildup and crosslinking. The alpha angle is measured as the slope of a line tangent to the divergence of the tracing from the point of the split time. It is expressed in degrees (normal 36 degrees ± 7.4 degrees) and it represents the speed of clot formation and fibrin cross-linking. The maximum amplitude (MA: normal 54mm ± 5.6 mm) is a reflection of the maximal strength of the fibrin clot and is dependent on platelet number and function, as well as the fibrinogen concentration. The maximum amplitude 60 (MA60) is the amplitude of the clot sixty minutes after the MA is recorded. The change in MA is an indicator of clot dissolution and is normally less than 5 mm. A 10% decrease in MA in 60 minutes is indicative of fibrinolysis. (6,7)

THE SONOCLOT TEST

The SCT is performed by placing a similar amount of whole blood (0.4 ml) into a pre-warmed cuvette into which a vertically vibrating probe is suspended. The changes in mechanical impedance (viscosity) exerted on the probe by the forming blood clot in the cuvette are measured on a recorder and a graphic tracing, known as the Sonoclot signature, is produced. The time that the sample remains a liquid in the cuvette is the Sonoclot activated clotting time (SonACT). This time begins when the blood sample is mixed and ends when the Sonoclot signature begins to increase. The normal SonACT is 90-150 seconds. (An Approach To Interpreting A Sonoclot Signature. Sienco, Inc. Morrison, CO 80465) As fibrin strands form, the impedance on the probe sequentially increases until a peak is reached. The onset time (T1- normally 2-6 minutes) reflects the beginning of fibrin formation and includes the SonACT. The primary slope (R1) reflects the speed of clot formation and further fibrin formation. Normal R1 is 15-30 mm/min. An inflection point, or "shoulder", is often seen on the SCT signature. This represents the point at which platelets first start contracting the fibrin strands. The secondary slope (R2) reflects further fibrinogenesis and platelet-fibrin interaction. R2 is normally 15-30 mm/min. The peak

Table 5
Viscoelastic Monitors vs. Routine Coagulation Tests
PT = prothrombin time, PTT = partial thromboplastin time, K = K time, AA = alpha angle, CI = coagulation index, MA = maximum amplitude, SH. Point = shoulder point of the Sonoclot clot formation slope, R1 = Sonoclot clot rate, Retr. Time = time to clot retraction on Sonoclot signature

	NATIVE TEG	CELITE TEG	SONOCLOT
PT	NOT SIGNIFICANT	K (R^2=.685) AA (R^2=-.613) CI (R^2=-.681) MA (R^2=-.712)	NOT SIGNIFICANT
PLATELET COUNT	NOT SIGNIFICANT	K (R^2=-.570) AA (R^2=.618) CI (R^2=.690) MA (R^2=.673)	SH. POINT (R^2=.637) R1 (R^2=.681)
PTT	NOT SIGNIFICANT	NOT SIGNIFICANT	TIME TO PEAK (R^2=.615) RETR. TIME (R^2=.685)
FIBRINOGEN	MA (R^2=.643)	K (R^2=-.665) AA (R^2=.691) CI (R^2=.802) MA (R^2=.814)	SH. POINT (R^2=.694) R1 (R^2=.784)

impedance (Peak) reflects completion of fibrin formation and is normally 70-90 mm. A downward slope (R3) is produced as platelets induce contraction of the completed clot. R3 is normally negative 2-8 mm/min. (4) The Sonoclot signature either remains flat or shows a gradual upward trend at the completion of R3. This slight upward trend can be referred to as secondary retraction, but no clinical significance has been attributed to this part of the Sonoclot signature. (An Approach To Interpreting A Sonoclot Signature. Sienco, Inc. Morrison, CO 80465) The SCT Signature is indicative of fibrinolysis if the retraction point is equal to the immersion point. The Sonoclot chart recorder we used in our study measures slopes in units/minute, as opposed to the mm/minute reported in the above study. (Personal communication: Jon Morrison, Sienco, Inc.)

THE TEG VS. SCT

A diligent literature review revealed no published clinical study that directly correlates the values of parameters obtained from the two viscoelastic monitors (TEG and SCT) in the open-heart surgery patient population. The purpose of this study is to test the hypothesis that there is no correlation between the coagulation parameters obtained from the TEG and SCT in open-heart surgery patients. Table One illustrates which TEG/SCT parameters are associated with the coagulation events that make up clot formation and contraction.

Table 6
Sonoclot vs. Thrombelastograph
SCT R1 = Sonoclot clot rate, MA = maximum amplitude, CI = coagulation index, K = K time, AA = alpha angle

	NATIVE TEG PARAMETERS	CELITE TEG PARAMETERS
SHOULDER POINT	NOT SIGNIFICANT	MA (R^2=.609) CI (R^2=.614)
SCT R1	NOT SIGNIFICANT	K (R^2=-.653) AA (R^2=.694)

If the TEG and SCT measure similar aspects of clot formation, the analyzer parameters above should correlate strongly for each coagulation event.

METHODS AND MATERIALS

The comparison of coagulation parameters was made on adult patients undergoing open-heart surgery requiring CPB. Random selection was employed with respect to patient gender and type of operation. All patients with known preoperative bleeding abnormalities were excluded from the study. Blood from patients on heparin therapy preoperatively was excluded due to it's effect on the viscoelastic monitors. The machines used to obtain these parameters were the TEG[a] and the SCT[b]. Non-heparinized blood samples were drawn from the radial arterial line by the anesthesiologist either prior to skin incision or after heparin reversal with Protamine Sulfate.

The sample was taken to the SCT analyzer and 0.4 ml was placed in the machine per manufacturer's instructions. The same blood sample was then taken to the TEG machine and 0.36 ml was placed in a pre-heated plastic well per manufacturer's instructions for a native TEG. In the next plastic well, 0.33 ml blood and 0.03 ml 1% Celite was used to obtain the activated TEG parameters. The SCT parameters were compared to both the native and Celite-activated TEG parameters for possible correlations. The operator noted the time the sample was drawn and if more than 3 minutes elapsed prior to the sample being placed in the TEG, this time was added to the R time.

Quality control procedures were performed on the TEG

a Hellige Thrombelastograph, Haemoscope Corp., Morton Grove, IL 60053
b Sonoclot II Analyzer, Model DP-2951, Sienco Inc., Morrison, CO 80465

Figure 1
TEG MAc vs. SCT R1
MAc = maximum amplitude (Celite-activated), R1 = Sonoclot clot rate

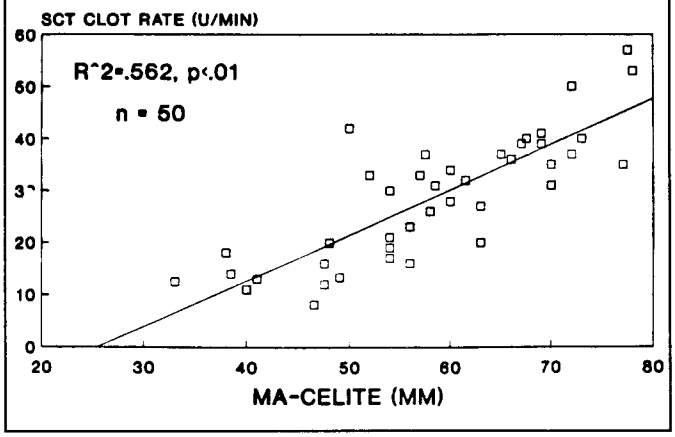
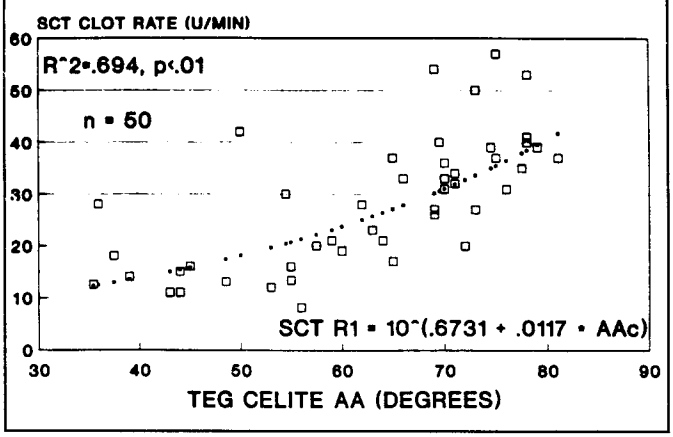


Figure 2
TEG AAc vs. Sonoclot R1
AAc = alpha angle (Celite-activated), R1 = Sonoclot cot rate



and SCT frequently during the period of data collection. The calibration spring was used on the TEG and the amplitude of the tracing was consistently 20 mm. The SonoCAL quality control system consistently showed an immersion point of 12 units and an amplitude of 62 units after ten minutes.

Fifty TEG/SCT samples were collected and analyzed. A database[c] was created that included the following parameters: Native and Celite TEG- split point, r, k, alpha angle, MA, MA60 and Coagulation Index; SCT- immersion point, SonACT, R1, shoulder point, time to shoulder, R2, peak, time to peak, R3, retraction point and time to retraction. The database was passed to a statistical program[d] for correlation and analysis. Simple and multiple regression between all TEG and SCT parameters and combinations will reveal significant correlation between the TEG and SCT parameters. Graphics software[e] was used for plotting correlation between the coagulation parameters. Correlations were considered statistically significant if $p<.01$ and $R^2 > 0.6$. It may be that parameters with a significant correlation are measuring similar coagulation cascade events.

RESULTS

Table 2 shows the native TEG parameters measured and the mean and standard deviations found for each. Table 3 shows the Celite-activated TEG parameters measured and the mean and standard deviation found for each. Table 4 shows the Celite-activated Sonoclot parameters measured and the mean and standard deviation found for each. Table 5 shows significant correlations found between the viscoelastic analyzers and routine coagulation tests. Table 6 shows significant correlations found between the TEG and SCT coagulation parameters.

DISCUSSION

The Sonoclot and Thrombelastograph parameters that correlate appear to measure similar aspects of coagulation. The SCT R1 correlates with the Celite-activated TEG parameters (K and alpha angle) that measure the speed of clot formation and fibrin cross-linking. The correlation between the SCT R1 and the TEG MA (Celite) may be best explained by the fact that both of these parameters are dependent on, and correlate with platelet count and fibrinogen concentration. Figure 1 shows the correlation found between the SCT R1 and TEG MA (Celite).

The SCT shoulder point correlated with the Celite-activated TEG MA. This may be explained by the shoulder point being related to the beginning of platelet-fibrin interaction and, the TEG MA strongly correlating with both of these procoagulants. The fact that more TEG and SCT parameters do not correlate may indicate that some parameters measure different aspects of clot formation and dissolution.

LaForce, et al., conducted a study to evaluate the coefficients of variation of the different parameters ohtainned from the SCT Signature. They stated that the slopes calculated from the SCT Signature cannot be reasonably reproduced by either the same individual or different individuals using the same instrument. They reported that the coefficients of variation ranged from 9.2 to 41.7 percent and therefore, concluded that the SCT analyzer couldn't be recommended for quantitatively examining the clotting function of whole blood. (8)

There have been no published studies citing the coefficients of variation on the parameters obtained from the Thrombelastograph tracing. A study currently in press by Norton, et al., reports coefficients of variation of 8 to 40 percent in the computerized Thrombelastograph (CTEG) coagulation param-

c Lotus 1-2-3, Software Publishing Inc., Mountain View, GA 94093
d Minitab, Minitab Inc., State College, PA 16801
e Harvard Graphics, Software Publishing Inc., Mountain View, CA 94039

eters. It may be that the lack of more TEG/SCT correlation is due to each machine having large and inconsistent coefficients of variation.

The lack of better correlation of TEG/SCT parameters may also be explained by the TEG being more sensitive to coagulation changes in hypocoagulable patients. Patients are often hypocoagulablle after open-heart surgery involving CPB, and some of the TEG/SCT data in this study was obtained from post-CPB patients' blood. Figure 2 shows how the TEG AA (Celite) detects an increase in coagulability while the SCT R1 is essentially unchanged in the lower coagulability range. This seems to suggest a greater sensitivity to coagulability changes by the TEG AA (Celite).

Due to lack of better correlation in the coagulation parameters measured by the TEG and SCT, it appears that the TEG and SCT are measuring different aspects of clot formation. Therefore, the TEG and SCT parameters cannot be substituted for each other.

CONCLUSIONS

1) The Sonoclot coagulation parameters correlate best with the Celite-activated Thrombelastograph parameters.
2) The TEG may be more sensitive than the SCT to changes in the coagulation status in hypocoagulable patients, i.e., post-CPB patients.
3) The lack of more significant correlation between the TEG and SCT coagulation parameters may be due to large and inconsistent coefficients of variation reported for the Sonoclot and proposed for the Thrombelastograph.
4) Due to lack of significant correlation between a greater number of TEG and SCT parameters, the TEG remains this institution's primary point-of-care viscoelastic monitor.

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