

Sonoclot Analyzer Guided Transfusion Therapy in Patients Undergoing On-Pump Cardiac Surgeries

Khan Afroz Shahana M¹, Vaishali A Mohod², Quazi Mohammed Azhar³

¹ Assistant Professor, ² Associate Professor, Department of Anaesthesia and Critical Care, ³ Associate Professor, Department of Plastic Surgery, Grant Government Medical College, Mumbai, Maharashtra 400008, India

Abstract:

Context: The study was conducted to establish a co-relation between Sonoclot parameters and blood and blood product during on-pump cardiac surgeries. **Aims:** To estimate the amount of blood and blood product transfusion and post-operative drain are affected by Sonoclot-guided transfusion therapy. **Settings and Design:** Randomised controlled Study **Methods and Material:** Total of 120 patients were randomly assigned by computer generation to either Sonoclot guided therapy or routine hospital therapy. Patients of either sex undergoing on-pump complex cardiac surgical procedures. Patients having pre-existing hepatic disorders, a renal disease requiring dialysis, and those who received anticoagulant or antiplatelet drugs within one week of surgery were excluded. **Statistical analysis used:** Data were analyzed using descriptive statistics to get the frequency distribution & the Independent Sample T-test was used for inter-group Comparison. *p*-value of <0.05 is considered as statistically significant. SPSS (Statistical Software for Social Sciences) version 20 was used. **Results:** The whole blood transfusion in the two groups was non-significant both intra-operative and post-operative period. While a comparison of FFP transfusion during an intra-operative period in Sonoclot group was significant. Platelets were administered in the post-operative period and comparison in the two groups was not significant. A comparison of 24 hr drain output in two groups of patients was non-significant. **Conclusions:** It allows the diagnosis of an exact cause of hemostatic abnormality i.e. deficiency of coagulation factors or fibrinogen or platelet function.

Keywords: Point of care test, Sonoclot, Transfusion, On-pump cardiac surgeries.

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Introduction:

The incidence of blood loss is higher in cardiac surgical procedures, leading to transfusion of allogeneic blood products in as much as 10%-20% of cases^{1,2}. The main cause of this is, coagulopathy caused by multiple factors like changes in the hemostatic system associated with increased age, preoperative medication with platelet and/or coagulation inhibitors and transient platelet

dysfunction associated with cardiopulmonary bypass (CPB)³⁻⁹. The Systemic inflammatory response caused by exposure to CPB with activation of coagulation and fibrinolytic systems leads to coagulopathy caused by factor consumption and transiently reduced platelet count and function^{10,11}. Strategies to decrease an amount of blood loss have been incorporated such as the collection and reinfusion of autologous blood products¹²,

Corresponding Author: Vaishali A Mohod, Associate Professor, Department of Anaesthesia and Critical Care, Grant Government Medical College, Mumbai, Maharashtra 400008, India

E-mail: vamohod2001@yahoo.co.in

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alterations in heparin and protamine dosing¹³, and the prophylactic use of anti-fibrinolytic therapy¹⁴ however, microvascular bleeding and transfusions still occur¹⁵.

Laboratory-based coagulation tests take a long time and reflect only initial thrombin formation and do not give information about clot stability and fibrinolysis which leads to the practice of inappropriate and empirical blood transfusions resulting in increased morbidity and mortality and hospital costs¹⁶⁻¹⁸.

Perioperative coagulation monitoring with point-of-care (POC) devices is routinely done and has been recommended in cardiac patients as it helps in the identification of an exact cause of bleeding and to guide the clinician in appropriate specific therapy^{19,20}. Viscoelastic point of care coagulation instruments like Thromboelastographic (TEG), the thromboelastometer (ROTEM) and the Sonoclot have been used in clinical practice for perioperative monitoring of excessive bleeding in cardiac surgery²¹⁻²³. They measure clot formation and clot dissolution that assess coagulation, platelet function²⁴, platelet-fibrinogen interactions and fibrinolysis. They indicate any alterations in hemostasis in a timely fashion and correlate well with conventional coagulation tests and may be used to predict transfusion of red cells, plasma and, platelets. Patients undergoing cardiac surgical procedures are at risk for major perioperative blood loss and life-threatening postoperative bleeding require multiple transfusions²⁵. Blood and blood product transfusions are associated with increased risk of patient morbidity and mortality²⁶⁻²⁸. Thus, effective blood loss management must focus on the real rather than an assumed cause of bleeding with targeted hemostatic therapy administered with minimal delay. Sonoclot analyzer provides information on the hemostasis process including coagulation, fibrin gel formation, fibrinolysis, and able to assess platelet function²⁹. It takes 20-30 minutes for the complete assessment of whole blood including platelet function³⁰⁻³¹. So useful for evaluating intraoperative hemostatic changes³².

This study was conducted to establish a correlation between Sonoclot signature parameters and blood and blood product transfusion decisions taken by the anesthesiologist during on-pump cardiac surgeries. Sonoclot signature parameters studied included sonoclot activated clotting time (Son ACT), clot rate (CR), platelet function (PF). We compared transfusion requirements after

cardiopulmonary bypass (CPB) using Sonoclot analyzer and routine transfusion therapy which is based on clinical judgment and without strict adherence to any algorithm. The main objective of the study was to determine, whether an amount of blood and blood product transfusion and post-operative drain were affected by Sonoclot-guided transfusion therapy.

Materials and Methods

After Institutional Ethics Committee approval, a total of 120 patients were randomly assigned by computer generation to either Sonoclot guided transfusion therapy (case) or routine hospital transfusion therapy (control) group of 60 each. Patients of either sex undergoing on-pump cardiac surgical procedures like single or multiple valve repair or replacement, coronary artery bypass grafting (CABG), combined CABG with valve repair or replacement, isolated aortic root or arch repair, or combination of aortic root or arch with valve repair or replacement or CABG were included. Patients having pre-existing hepatic disorders, a renal disease requiring dialysis, and those who received anticoagulant or antiplatelet drugs within one week of surgery were excluded. Sonoclot® Coagulation & Platelet Function Analyzer, Sienco, Inc. CO, USA was used to perform point of care coagulation monitoring in all patients undergoing on-pump cardiac surgeries.

At the onset of surgery, prophylactic antifibrinolytic (tranexamic acid) was administered. Cardiopulmonary bypass was conducted in the standard manner using moderate hypothermia, membrane oxygenator, arterial line filtration and, heparin-coated circuits. Baseline K-ACT (kaolin activated clotting time) was used in all patients. Anticoagulation for CPB was achieved with bovine heparin 300IU/kg administered via an internal jugular catheter with confirmation by the backflow of blood. ACT >480 seconds was accepted as adequate anticoagulation for CPB. Additional heparin in doses of 100 IU/kg was administered to maintain the ACT at least >400 seconds. ACT was monitored every 30 minutes. Protamine was administered slowly over a 20 minutes period in a ratio of 1mg/100 U of the first dose of heparin. In both, the groups' baseline coagulation tests included hemoglobin, hematocrit, platelet count, prothrombin time (PT), INR. In the control group, K-ACT was monitored. In Sonoclot group baseline glass beads-activated ACT was done and after protamine administration again glass beads

activated ACT was done. All intraoperative results of the Sonoclot parameter such as an ACT, clot rate and Platelet function were interpreted by the anesthesiologist directly involved in the study. During CPB hematocrit of 21% was accepted. In control group routine transfusion therapy, which was based on the clinical judgment was followed i.e. in case of absence of clot in the surgical field and presence of obvious clinical bleeding, patients were transfused with FFP (15ml/kg) and platelet concentrate (10 mL/kg). In Sonoclot group transfusion of non-red blood cell (RBCs) component therapy was according to abnormal Sonoclot parameters. In both, the groups packed RBCs were transfused when hematocrit was less than 27% in the post-bypass period.

All the patients were shifted to the ICU for elective mechanical ventilation.

Post-operative blood loss as measured by chest tube drain at 24 hr was recorded. The data were analyzed for differences between Sonoclot and control groups with regard to transfusions and post-op bleeding. Data were analyzed using descriptive statistics to get the frequency distribution & the Independent Sample t-test was used for inter-group Comparison. *p*-value of < 0.05 is considered as statistically significant. SPSS (Statistical Software for Social Sciences) version 20 was used.

Results

One hundred twenty patients were taken for the study (60 in each patient). Baseline patient characteristics age, sex, BMI, preoperative hematocrit was comparable. Intra-operative variables like CPB duration, minimal temperature, total heparin and, protamine dose did not vary by study group (Table 1).

Various hematological and coagulation parameters (Table 2) derived from Sonoclot analyzer parameters were comparable in two groups except for the clot rate (Table 3) which was significantly deteriorated after heparin neutralization (*p* < 0.05).

A Comparison of an average number of units of whole blood and FFP transfused in the Sonoclot and control group (Tables 5,6) showed that there was no significant difference in whole blood transfusion in the two groups both intra-operative and post-operative period. While a comparison of FFP transfusion in two groups during an intra-operative period was significant and during the post-operative period transfusion of FFP was comparable. Platelets were administered in the post-operative period and comparison in the two

groups was not significant (Table 6) (Fig. 1 and 2). A comparison of 24 hr drain output in two groups of patients is shown in table 7 which was non-significant.

Table 1: Baseline Information

Parameters	Groups	N	Mean	Std. Deviation	Std. Error Mean	<i>p</i> Value
Age	cases	60	47.50	15.83	2.04	> 0.05
	controls	59	44.80	17.02	2.21	
BMI	cases	60	27.15	6.706	0.86	> 0.05
	controls	60	27.00	6.494	0.83	
PB HCT	cases	60	38.02167	5.37	0.69	> 0.05
	controls	60	38.71000	6.20	0.80	
CPB time	cases	60	171.83	66.21	8.54	> 0.05
	controls	60	182.00	84.44	10.90	
Min temp	cases	60	28.65	1.999	0.26	> 0.05
	controls	60	28.60	.924	0.11	
Total heparin	cases	60	27100	8605.532	1110.96	> 0.05
	controls	60	28500	10023.103	1293.9	
Protamine	cases	60	185.00	52.513	6.779	< 0.05
	controls	60	170.67	38.746	5.002	

BMI- Body mass index, PB HCT- Pre-bypass haematocrit, CPB- Cardiopulmonary bypass

Table 2: Haematological and Sonoclot Profile

Parameters	Groups	N	Mean	Std. Deviation	Std. Error Mean	<i>p</i> Value
HB	cases	60	12.65	1.790	0.23	> 0.05
	controls	60	12.85	2.07	0.26	
PB HCT	cases	60	38.02	5.37	0.69	> 0.05
	controls	60	38.71	6.20	0.8	
PB ACT	cases	60	130.98	38.49	4.969	> 0.05
	controls	60	125.72	27.37	3.534	
OB HCT	cases	60	24.66	3.72	0.48	> 0.05
	controls	60	24.44	4.41	0.56	
OB ACT	cases	60	614.25	185.932	24.0	> 0.05
	controls	60	608.77	183.056	23.63	
OBCR	cases	60	2.62	1.68	0.21	NA
	controls	0a	.	.	.	
Off Hct	Cases	60	27.0	3.5	0.45	> 0.05
	Control	60	26.88	4.52	0.58	
Off ACT	Cases	60	140.93	31.70	4.09	> 0.05
	Control	60	134.45	30.84	3.98	

HB- haemoglobin, PB HCT- Pre-bypass haematocrit, PB ACT- Pre-bypass Activated clotting time, OB- On bypass, CR- Clot rate

Table 3: Prebypass and off bypass CR (clot rate)

Sonoclot N=60	Mean CR	N	Std Dev	T- value	p Value
Prebypass	36.05	60	6.133	3.08	<0.05
Offbypass	37.03	60	7.73		(0.003)

Table 4: Prebypass and off bypass PF (platelet function)

Sonoclot N=60	Mean PF	N	Std Dev	T- value	p Value
Prebypass	3.53	60	0.75	-0.19	>0.05
Offbypass	3.35	60	1.17		

Table 5: Intraoperative Blood and Blood Products transfusion

	Groups	N	Mean	Std. Devi- ation	Std. Error Mean	p Value
IO Blood	cases	60	1.18	0.948	0.12	> 0.05
	controls	60	1.23	1.015	0.13	
IO FFP	cases	60	2.33	1.989	0.26	< 0.05
	controls	60	3.20	1.614	0.20	(0.001) **
IO Platelets	cases	0a	.	.	.	NA
	controls	0a				

IO- Intraoperative, FFP- Fresh frozen plasma

Table 6: Postoperative Blood and Blood Products transfusion

	Group	N	Mean	Std. Devi- ation	Std. Error Mean	p Value
PO blood	Cases	60	.38	0.66	0.08	> 0.05
	Control	60	.28	0.61	0.07	
PO FFP	Cases	60	.43	1.17	0.15	> 0.05
	Control	60	.47	1.29	0.16	
PO Platelets	Cases	60	.23	0.74	0.09	> 0.05
	Control	60	.15	0.63	0.08	

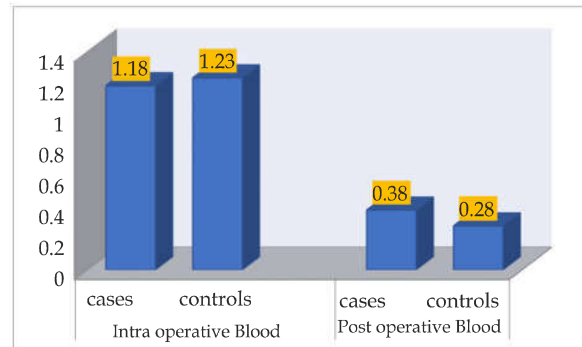
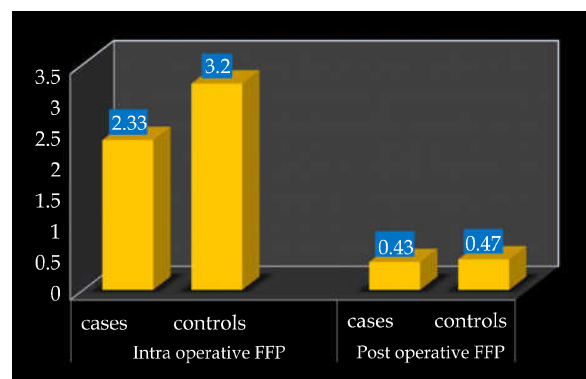
PO- Postoperative

Table 7: 24 Hrs Drain Output

	Group	N	Mean	Std. Devi- ation	Std. Error Mean	p Value
24 h drain	Cases	59	228.81	92.942	12.100	> 0.05
	Control	60	234.17	80.513	10.394	

Discussion

In our study we have determined the utility of Sonoclot analyzer in directing appropriate blood component therapy thereby any reduction in blood and blood product transfusion during on-pump cardiac surgical procedures. We found that transfusion of intra-operative FFP was significantly less in the Sonoclot analyzer group compared to the routine transfusion group. But both intra-operative and post-operative transfusion of packed red blood

**Fig. 1:** Intraoperative and Postoperative Blood transfusion**Fig. 2:** Intraoperative and postoperative FFP

cells and post-operative FFP transfusion in both the groups were similar in our study. Similarly, platelets were administered postoperatively in all patients and overall exposure was the same in both the groups. Furthermore, a comparison of post-operative 24 hr chest drain in two groups was non-significant.

Our results suggest that using Sonoclot to determine the need for blood products reduced the proportion of patients exposed to intra-operative FFP. Although the overall transfusion of packed red blood cells in two groups was similar which could be explained by the fact that the decision of red blood cell transfusion was based on hematocrit in our study. We also found out that there is no transfusion disparity in both FFP and platelets administered in the two groups in the postoperative period which could be suggested by the fact that Sonoclot guided algorithm was no longer enforced in the post-operative period.

The study conducted by Linda Shore-Lesserson et al on TEG-guided (point of care coagulation test) transfusion in cardiac patients found intraoperative transfusion rates did not differ but there was significantly fewer postoperative and total

transfusion rate in the TEG group hence, concluded that reduction in transfusions may have been due to improved hemostasis in these patients who had earlier and specific identification of the hemostasis abnormality and thus received more appropriate intraoperative transfusion.³³ Dominique B. Bischof et al. determined if Sonoclot with its sensitive glass bead-activated, the viscoelastic test could predict postoperative bleeding in cardiac surgical patients at predefined time points and concluded that only glass bead measurements by Sonoclot after heparin reversal before chest closure but not preoperatively were predictive for increased postoperative bleeding.³⁴

The viscoelastic tests and the response to a platelet agonist are some of the dynamic tests which are more reflective of platelet function over time. The specific agonist like thrombin or collagen can be used for assessment of platelet response to endothelial injury and its ability for normal hemostasis in vivo and are utilized in transfusion algorithms for bleeding patients. Platelet transfusion is often empirical in the management of bleeding patients. Although there are many platelet functions tests available³⁵, many of them are not suitable or bedside monitoring as they are time-consuming. The time to peak in Sonoclot correlates with the general platelet function.³⁶ Rajkumar V et al. have studied the utility of Sonoclot in pediatric patients undergoing cardiac surgery with CPB for congenital heart disease for the prediction of postoperative bleeding. Both laboratory parameters (prothrombin time, INR, activated partial thromboplastin time fibrinogen, D-dimer) as well as POC Sonoclot glass bead activation time, clot rate and platelet function (gbPF) were done before induction of anesthesia and following heparin reversal after the termination of CPB in all patients. Their conclusion was clot rate and platelet function (gbPF) have maximum predictive value.³⁷

Espinosa et al compared laboratory tests of coagulation, TEG, and Sonoclot for prediction of post-CPB bleeders in adult patients undergoing elective cardiac surgery, and concluded that although laboratory tests had maximal sensitivity and specificity for prediction of postoperative bleeding, Sonoclot variables that reflect platelet function (R1 & R2)

had a statistically significant correlation with blood loss.³⁸ Like previous studies correlation between various POC variables and fibrinogen concentrations was consistent.^{39,40} The role of fibrinogen has been underscored in coagulation and hemostasis and as a contributor to the clot

strength. Reduced levels of fibrinogen during CPB could predict the risk of postoperative bleeding and transfusion requirements. They found that Son ACT and Clot rate correlated significantly with aPTT. An aPTT is prolonged in hypocoagulable states so as low clot Rate. The POC devices assess platelet function rather than platelet counts so, clinically more useful than standard platelet counts. The routine coagulation tests will have to remain the gold standard for assessment of many aspects of hemostasis.

There are many limitations to our study. Postoperative outcome i.e. any improvement in morbidity and mortality or decrease in ICU stay and any cost reduction because of appropriate administration of blood and blood products in the postoperative period were not investigated.

Conclusion

Sonoclot is a point of care method of monitoring of coagulation status during on-pump cardiac surgeries which is easily performed and reproducible. It allows the diagnosis of an exact cause of hemostatic abnormality i.e. deficiency of coagulation factors or fibrinogen or platelet function. With Sonoclot guided transfusion algorithm we were able to demonstrate intraoperative reduction of blood products i.e. fresh frozen plasma administration. But, the use of point of care test should be extended in the postoperative period till 24 hrs as well to demonstrate an overall advantage of this device for the reduction of blood and blood product transfusion and improvement of patient's outcome.

Key Messages: Sonoclot analyzer directs appropriate blood component therapy. With Sonoclot guided algorithm we were able to demonstrate intraoperative reduction of blood product administration. But its use should be extended in the postoperative period till 24 hrs to demonstrate an overall advantage of this device and improvement of patient's outcome.

Conflict of Interest: Nil

Acknowledgement: Nil

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