Res Cardiovasc Med. 2016 November; 5(4):e33227. doi: 10.5812/cardiovascmed.33227.

Published online 2016 June 19. **Research Article**

Role of ROTEM in Hemostatic Management During Adult Cardiac Surgery

Hooman Bakhshandeh,[1] Mostafa Alavi,[1] Behshid Ghadrdoost,[1] Fariborz Farsad,[1] Abbas Zavarei,[1] Mohsen Ziaeifard,[1] Rasoul Farasatkish,[1] Tooraj Babaei,[1] Bahador Baharestani,[2] and Reza Golpira[1,*]

[1]Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran
[2]Heart Valve Disease Research Center, Rajaie Cardiovascular Medical and Research Center, Iran University of Medical Sciences, Tehran, IR Iran

[*]*Corresponding author*: Reza Golpira, Rajaie Cardiovascular Medical and Research Center, Vali-Asr St., Niayesh Blvd, P. O. Box: 15745-1341, Tehran, IR Iran. Tel: +98-2123922194, E-mail: rg@rhc.ac.ir

Received 2015 September 17; **Revised** 2015 November 07; **Accepted** 2015 November 08.

Abstract

Background: Coagulopathy after cardiopulmonary bypass (CPB) may lead to increased morbidity and mortality. Routine conventional coagulation tests are not always suitable to detect rapid changes in patient's coagulation status. A point-of-care instrument such as ROTEM (rotational thromboelastometry) is a timely and comprehensive method to evaluate hemostasis during cardiac surgery may reduce the need for blood transfusion.
Objectives: In this study, ROTEM was compared to coagulation tests routinely performed during cardiac surgery for postoperative bleeding volume and consumption of blood products.
Patients and Methods: Fifty patients undergoing cardiac surgical procedures were enrolled. Blood was obtained before the operation and after CPB weaning. Twenty-five of patients were checked only by traditional blood coagulation test and 25 other patients were checked by ROTEM in addition to routine coagulation tests. The results of these two groups of patients were compared.
Results: There was a significant correlation between platelet count (PLT) and fibrinogen level with EXTEM-MCF (r = 0.79, P value: 0.008, r = 0.55, P value: 0.04 respectively). EXTEM-CT was correlated with prothrombin time (PT) (r = 0.56, P value: 0.01) and International normalized Ratio (INR) (r = 0.57, P value: 0.01). There was a significant correlation between PLT count and fibrinogen level with INTEM-MCF (r = 0.69, P value: 0.02, r = 0.71, P value: 0.01, respectively). INTEM-CT was correlated with partial thromboplastin time (PTT) (r = 0.57, P value: 0.02). There was a significant correlation between FIBTEM-MCF and fibrinogen level (r = 0.80, P value: 0.001). HEPTEM was not correlated with any of the coagulation variables. Postoperative consumption of packed blood cell (BPC) was increased in non-ROTEM group in comparison with ROTEM group (645.17 ± 279.16 in Non-ROTEM vs. 387.50 ± 262.88 in ROTEM, P: 0.03)
Conclusions: ROTEM can be used to detect postoperative hemostatic changes following cardiac surgery appropriately and can be useful to choose suitable blood products that may reduce the need for blood transfusion, contributing to better patient blood management.

Keywords: Rotational Thromboelastometry, Routine Conventional Coagulation Tests, Hemostatic Management, Cardiac Surgery

1. Background

Excessive bleeding following major cardiac surgery is associated with increased mortality and morbidity. Timely diagnosis and treatment of bleeding are very important to prevent such adverse events (1, 2).

Hemodilution and imbalance between procoagulant and anticoagulant factors during on-pump cardiovascular surgery disturb the hemostatic function (3). Although routine preoperative coagulation tests including platelet count, prothrombin time (PT) and activated partial thromboplastin time (aPTT) are important in management of bleeding, the value of these tests has not been clearly understood because they are plasma-based assay so do not give information about platelet function and cellular components. Because routine tests in coagulation assessment are not points of care, golden time in management of bleeding would be lost (2). For these reasons, using viscoelastic point-of-care (POC) coagulation instruments such as rotational thromboelastometry (ROTEM) that simply provide information about the quality and dynamics of clot for perioperative monitoring of bleeding in cardiac surgery is growing (4, 5).

Although, ROTEM has been increasingly used in clinical practice for perioperative monitoring of excessive bleeding and a quick decision for transfusion and proper selection of hemostatic components in cardiac surgery.

Despite increasingly use of ROTEM in clinical practice in many countries, there is no statistical picture of this method results in perioperative monitoring of bleeding after cardiac surgery in our country.

2. Objectives

In this study, we aimed to compare different parameters related to hemostasis management between patients in whom ROTEM was applied and those managed by routine coagulation tests after cardiac surgery.

3. Patients and Methods

3.1. Study Population

In this historical cohort, fifty patients undergoing cardiac surgical procedures in a referral university hospital, Rajaie cardiovascular medical and research center, were divided into two groups; 25 patients in ROTEM group and 25 patients in non-ROTEM group. Coagulation status of patients in ROTEM group evaluated via ROTEM test simultaneously with conventional coagulation tests but in non-ROTEM group, only routine coagulation tests were performed. The study protocol was approved by the review board. Inclusion criteria were all adult patients who underwent cardiac surgery including coronary artery bypass grafting (CABG) and CABG + valve surgery. Patients with renal failure, liver failure and those undergoing emergency surgery were excluded from the study. Patients with major bleeding four hours after the operation or those treated with Clopidogrel within five days prior to operation or patients who had symptoms of tamponade were excluded.

3.2. Study Design

For all patients, anesthesia was induced by benzodiazepine (midazolam 0.05 to 0.1 mg/ Kg), opioids (fentanyl 25 to 40 μg/ Kg or sufentanil 2.5 to 4 μg/ Kg) and muscle relaxants (atracurium 0.5 mg/ Kg or pancuronium 0.1 mg/ Kg) before tracheal intubation. Then anesthesia was maintained with midazolam, sufentanil, atracurium and isoflurane up to 1%. All operations were performed with CPB at mild to moderate core hypothermia (28 to 32°C). The circuit of CPB was primed with crystalloid solution (1000 to 1400 mL), 10000 U of heparin and 37.5 g mannitol. Heparin 300U/kg was given before cannulation until ACT increased to 480. After weaning of CPB, Heparin was reversed by 200 to 250 mg of protamine sulfate till ACT decreased to 130. Preoperative transfusion of packed red blood cell was used when hematocrit (HCT) reduced to less than 24.

3.3. Laboratory Measurements

Laboratory variables were assessed twice, before the operation and after CPB when heparin was completely reversed. Hemoglobin and PLT count were measured in a hematology analyzer (Sismex k800-K1000 and celltac ES). PT, PTT, INR and fibrinogen level were measured by a coagulation analyzer (diagnostic stago) using manufacturer's kits.

3.4. ROTEM Variables Measurements

ROTEM (ROTEM@ delta, Switzerland) was used for evaluating viscoelastic properties of clot. Blood samples were collected at two different time points: preoperatively (immediately before anesthesia induction) and postoperatively after weaning of CPB. Blood samples for ROTEM analyses were drawn into a tube containing citrate and analyzed within one hour. All tests for ROTEM were performed by the same investigator.

3.5. Statistical Analysis:

All study data were analyzed using SPSS 15.0 for Windows (SPSS Inc. Chicago, IL, USA). One sample Kolmogorov-Smirnov test was applied to investigate the fitness of interval data to normal distribution. Data was described as mean $\pm$ standard deviation or median (inter-quartile range) for interval and count (percent) for categorical variables. For comparing continuous variables between the two study groups, independent samples t test or Mann-Whitney U test was used. Repeated measures analysis of variance (ANOVA) was used for analysis of changes in continuous variables by time. Correlation between the variables was assessed via Pearson correlation coefficient (r). Significant level was considered as $P \leq 0.05$.

4. Results

All patient characteristics and intraoperative data are shown in Table 1. There were no significant differences between groups regarding demographic data such as age, sex and BMI (P: 0.08, P: 0.10 and P: 0.11, respectively). According to the same protocol anesthesia, intraoperative data including pump time, operation time and extubation time had no significant differences between the two groups (Table 1).

Five patients needed a surgical re-exploration due to major and persistent postoperative bleeding; two of them were in ROTEM group. These patients received packed blood cell (6 - 10 units), platelet concentrates (maximum 4 units) and FFP (maximum 5 units). None of the bleeding patients in non-ROTEM group had abnormal baseline values for routine coagulation tests. Only one patient in

Table 1. Comparison of Characteristics and Intraoperative Data Between the Groups

	ROTEM, n = 25	Non-ROTEM, n = 25	P Value
Age	56.04 ± 12.49	66.19 ± 12.21	0.08
BMI	28.69 ± 5.19	26.66 ± 2.76	0.11
Sex, M/F	12/13	14/11	0.10
EF, %	41.60 ± 13.12	40.48 ± 7.73	0.41
Pump time, min	100.60 ± 37.17	116.33 ± 22.73	0.06
Operation time, min	283.20 ± 71.80	361.90 ± 141.91	0.06
Extubation time, min	350.66 ± 124.12	462.80 ± 168.09	0.12
Bleeding Volume, cc	270 ± 256.46	458 ± 354.00	0.01
Graft number	3 (2 - 4)	3 (2.5 - 4)	0.25

Abbreviation: BMI, body mass index; EF, ejection fraction.

ROTEM group showed reduction in ROTEM FIBTEM and plasma fibrinogen values in early postoperative period.

Postoperative bleeding volume was significantly higher in non-ROTEM group compared to ROTEM group (458 ± 354.00 in non-ROTEM vs. 270 ± 256.46 in ROTEM, P: 0.01).

Most of conventional coagulation variables had statistically significant changes during time in the both groups (Table 2). Fibrinogen level in the both groups had significant changes during time (P < 0.05).

ROTEM variables EXTEM and FIBTEM MCF (clot strength) changed over time. There were no significant changes in CT of INTEM and HEPTEM during the time and correlated with reverse of heparin (ACT < 130) (Table 3).

Correlations between ROTEM variables and coagulation tests are shown in Table 4. There was a significant correlation between PLT count and fibrinogen level with EXTEM-MCF (r = 0.79, P value: 0.008, r = 0.55, P value: 0.04 respectively). EXTEM-CT was correlated with PT(r = 0.56, P value: 0.01) and INR (r = 0.57, P value: 0.01). There was a significant correlation between PLT count and fibrinogen level with INTEM-MCF (r = 0.69, P value: 0.02, r = 0.71, P value: 0.01 respectively). INTEM-CT was correlated with PTT(r = 0.57, P value: 0.02). There was a significant correlation between FIBTEM-MCF and fibrinogen level (r = 0.80, P value: 0.001). HEPTEM was not correlated with any of the coagulation variables.

Consumption of blood products in the two groups are depicted in Table 5. As shown in table, use of packed blood cell (BPC) during the operation was not significantly different between the two groups (271 ± 29.15 in Non-ROTEM vs. 195 ± 72.45 in ROTEM, P: 0.85), but postoperative use of BPC was increased in non-ROTEM group compared with ROTEM group (645.17 ± 279.16 in Non-ROTEM vs. 387.50 ± 262.88 in ROTEM, P: 0.03). FFP was not used intra-operatively in any of the groups. After the operation, consumption of FFP in non-ROTEM group was 450 ± 173.20 mL, while in ROTEM group FFP was not used at all. In ROTEM group, patients used significantly higher concentration of fibrinogen than those who did not received ROTEM (P value > 0.001). We did use platelets neither during the operation nor after it.

5. Discussion

In nearly a half of patients undergoing re-exploration, certain cause of bleeding has a microvascular origin (2, 6, 7). Various causes of microvascular bleeding related to changes in hemostatic system have been identified, including increased age, prolonged cardiopulmonary bypass, residual heparin and preoperative medication with platelet or coagulation inhibitors (8, 9).

Bleeding management after CPB is commonly guided by hematology and coagulation tests including PLT, PT, PTT, INR and fibrinogen level routinely. Viscoelastic point-of-care (POC) coagulation instruments such as rotational thromboelastometry (ROTEM) have been increasingly used for more timely assessments of whole blood clotting in major cardiac surgery and prompt decision making for re-exploration (10).

Despite long turnaround time of PT and PTT (30 - 60 minutes) in central laboratory, ROTEM is applied for a more timely assessment of fibrinogen levels (5 - 20 min), which is important for preventing blood loss. FIBTEM as an indicator of fibrin-specific clot formation can assess clot firmness in the fibrin clot. EXTEM and INTEM can be separately used to evaluate the interaction of activated PLTs and fibrin polymerization (3).

In our study, results of HEPTEM were not changed during the study, which shows that extent of heparin rever-

Table 2. Hematologic and Coagulation Test Results

	Pre-operation	Post-CPB	P Value
ROTEM			
PT	14.16 ± 2.22	16.17 ± 1.55	< 0.0001
PTT	34.91 ± 16.80	44.73 ± 14.04	0.003
INR	1.17 ± 0.23	1.37 ± 0.16	< 0.0001
Fibrinogen Level, g/L	3.6 ± 0.93	2.9 ± 0.51	0.05
Hb	13.49 ± 1.53	8.55 ± 1.24	< 0.0001
PLT, ×1000	209.50 ± 56.20	163.09 ± 32.77	< 0.0001
Non-ROTEM			
PT	15.59 ± 4.01	16.23 ± 1.50	0.04
PTT	31.45 ± 7.55	49.23 ± 16.04	< 0.0001
INR	1.34 ± 0.43	1.59 ± 0.17	0.04
Fibrinogen level, g/L	3.4 ± 0.81	1.9 ± 44	0.001
Hb	13.40 ± 1.50	8.34 ± 0.85	< 0.0001
PLT, ×1000	233.52 ± 50.78	179.33 ± 48.11	< 0.0001

Abbreviation: Hb, hemoglobin; INR, international normalized ratio; PLT, platelet; PT, prothrombin time; PTT, partial thromboplastin time.

Table 3. Comparison of ROTEM-MCF Variables at the Two Time Points

ROTEM Parameters	Baseline	Post-Operation	P Value
Mcf-INTEM	59.14 ± 9.75	57.30 ± 7.31	0.9
Mcf-EXTEM	64.23 ± 6.64	57.09 ± 8.12	0.05
Mcf-HEPTEM	50.79 ± 15.19	49.81 ± 13.59	0.7
Mcf-FIBTEM	23.00 ± 17.83	15.62 ± 7.88	0.03
CT-HEPTEM	66.00±12.15	60.17 ± 14.73	0.8
CT-INTEM	170.25 ± 23.12	166.13 ± 33.40	0.8

Abbreviation: EXTEM, extrinsically activated; FIBTEM, fibrin-specific clot formation; INTEM, intrinsically activated.

sal was not remarkable and it may help to prevent protamine overdosing. Non-heparin related coagulation disorders and accidental exposure to heparin (e.g. leakage from catheters) may lead to bleeding. During the HEPTEM assay, heparinase rapidly degrades heparin via the intrinsic pathway and allows for the assessment of hemostasis in patients who underwent CPB (11). We have seen the greatest change in FIBTEM with time. Because FIBTEM contains a powerful platelet inhibitor, only the remaining fibrin mass can be measured (12).

Our findings showed significant changes in EXTEM during the time. EXTEM assay that mildly activates hemostasis via the extrinsic pathway is influenced by platelets and fibrinogen, but not by heparin. It is used for therapeutic decisions regarding administration of FFP and platelets (13).

This comparative study of coagulation assays in cardiac surgery tried to show that some ROTEM variables can be used instead of routine coagulation test. In this study, MCF of EXTEM was found to have significant correlations with PLT and fibrinogen. EXTEM is a screening test for extrinsic coagulation factors, platelets and fibrinogen. On the other hand, PT and INR represent the function of extrinsic coagulation cascade. In our study, EXTEM-CT had a significant correlation with PT and INR.

We demonstrated that MCF of INTEM had a significant correlation with PLT and fibrinogen and INTEM-CT had a significant correlation with PTT. INTEM is an intrinsically activated test that can be used to evaluate the interaction of activated PLTs and fibrin polymerization (3). PTT is a performance indicator of the efficacy of both “intrinsic” and common coagulation pathways (14).

Table 4. Correlation Between Postoperative ROTEM Parameters and Coagulation Variables

	ROTEM Variable	P Value	r
Fibrinogen level			
	EXTEM- MCF	0.04	0.55
	INTEM-MCF	0.01	0.71
	FIBTEM-MCF	0.001	0.80
PLT			
	EXTEM-MCF	0.008	0.79
	INTEM-MCF	0.02	0.69
PT			
	EXTEM- CT	0.01	0.56
INR			
	EXTEM- CT	0.01	0.57
PTT			
	INTEM-CT	0.02	0.57

Table 5. Comparison of Using Blood Products in the Two Groups

	ROTEM	Non-ROTEM	P Value
PBC (intra-OP), mL	195 ± 72.45	271 ± 29.15	0.85
PBC (post-OP), mL	387.50 ± 262.88	645.17 ± 279.16	0.03
FFP (post-OP), mL	0	450 ± 173.20	< 0.001
Fibrinogen Concentrate, g	2.0 ± 0.28	0.5 ± 0.13	< 0.001

FIBTEM allows detection of fibrinogen deficiency and may identify rapidly the need to substitute fibrinogen (13). In our study, MCF FIBTEM was shown to have an excellent correlation.

Another important finding of our study was that POC reduces postoperative consumption of packed blood cell. In our center, for all patients, postoperative hemoglobin target was hematocrit higher than 24 and if central venous saturation was lower than 65% with atrial saturation higher than 95%, there was a need to raise hemoglobin by transfusion of packed blood cell.

According to current guidelines for blood conservation in cardiac surgery (15), hemoglobin level and platelets count are used for red cells and platelets transfusion, respectively. There is more accurate means to estimate the need for red blood cell transfusions including oxygen consumption, oxygen extraction ratios and oxygen delivery. Guidelines recommend that hemoglobin level below 7 gm/dL is a trigger for red cells transfusion except in evident cardiac or non-cardiac end organ ischemia where adequate haemoglobin level is 10 gm/dL. Patients with hemoglobin level more than 10 gm/dL do not need blood product transfusion, because there is no favourable improvement in oxygen transportation by transfusion therapy. Surgical patients with microvascular bleeding usually require platelet transfusion if the platelet count is less than 50×10^9/L and rarely require therapy if it is greater than 100×10^9/L. FFP is used for intravascular volume replacement in cases of acute blood loss (16).

We found that fibrinogen consumption in patients managed with ROTEM were significantly more than other ones. It can be explained by considering the fact that goal-directed management of coagulopathy with ROTEM leads to appropriate prescription of fibrinogen concentrate in these patients, unlike the other group.

The use of point-of-care (POC) transfusion and coagulation management algorithms based on viscoelastic tests such as thromboelastometry (ROTEM) have been shown to be associated with reduced use of allogeneic blood transfusion, reduced transfusion-related adverse events and improved outcomes in cardiac surgery (17). ROTEM may be more suitable for perioperative bleeding management; somehow it provides information ready for interpretation within 15 - 30 minutes. These instruments may be helpful as a guide for blood products transfusion and to decide whether to re-explore a patient (2).

In non-ROTEM group, PBC administration in patients with bleeding after CPB was not based on direct assessment of hemostasis, because times of laboratory-based tests are too long (18).

Guidelines are now available for POC assessment of coagulation to allow appropriate, targeted therapy for perioperative hemostatic defects in cardiac surgery.

The most common cause of coagulopathies after excluding heparin-induced coagulopathy is related to lower levels of fibrinogen (19). According to studies, the extent of surgical incision, duration of operation and pump time and perioperative blood loss are the most important factors able to reduce the level of fibrinogen followed by increase in bleeding and blood transfusion during the operation. ROTEM can be used to detect timely postoperative hemostatic changes following cardiac surgery appropriately and can be a good alternative for routine coagulation test after CPB.

Acknowledgments

We would like to thank all cardiac anesthesiology staff in Rajaie cardiovascular research center for their help in preparing this manuscript.

Footnotes

Authors' Contributions: Study concept and design: Hooman Bakhshandeh; Technical and material support, conducting the project: Reza Golpira; Revising the manuscript: Mostafa Alavi, Abbas Zavarei and Fariborz Farsad; Collecting data and review of literature: Mohsen Ziaeifard, Mostafa Alavi, Tooraj Babaei, Rasoul Farasatkish and Bahador Baharestani; Data analysis and preparing the manuscript: Behshid Ghadrdoost, Hooman Bakhshandeh.

Funding/Support: The design, management and conduction of the study were all supported by the staff of Rajaie cardiovascular medical and research center.

References

1. Bolliger D, Tanaka KA. Roles of thrombelastography and thromboelastometry for patient blood management in cardiac surgery. *Transfus Med Rev.* 2013;**27**(4):213–20. doi: 10.1016/j.tmrv.2013.08.004. [PubMed: 24075802].
2. Espinosa A, Stenseth R, Videm V, Pleym H. Comparison of three point-of-care testing devices to detect hemostatic changes in adult elective cardiac surgery: a prospective observational study. *BMC Anesthesiol.* 2014;**14**:80. doi: 10.1186/1471-2253-14-80. [PubMed: 25276093].
3. Ogawa S, Szlam F, Chen EP, Nishimura T, Kim H, Roback JD, et al. A comparative evaluation of rotation thromboelastometry and standard coagulation tests in hemodilution-induced coagulation changes after cardiac surgery. *Transfusion.* 2012;**52**(1):14–22. doi: 10.1111/j.1537-2995.2011.03241.x. [PubMed: 21756263].
4. Ronald A, Dunning J. Can the use of thromboelastography predict and decrease bleeding and blood and blood product requirements in adult patients undergoing cardiac surgery?. *Interact Cardiovasc Thorac Surg.* 2005;**4**(5):456–63. doi: 10.1510/icvts.2005.115154. [PubMed: 17670456].
5. Reinhofer M, Brauer M, Franke U, Barz D, Marx G, Losche W. The value of rotation thromboelastometry to monitor disturbed perioperative haemostasis and bleeding risk in patients with cardiopulmonary bypass. *Blood Coagul Fibrinolysis.* 2008;**19**(3):212–9. doi: 10.1097/MBC.0b013e3282f3f9d4. [PubMed: 18388501].
6. Woodman RC, Harker LA. Bleeding complications associated with cardiopulmonary bypass. *Blood.* 1990;**76**(9):1680–97. [PubMed: 2224118].
7. Paparella D, Brister SJ, Buchanan MR. Coagulation disorders of cardiopulmonary bypass: a review. *Intensive Care Med.* 2004;**30**(10):1873–81. doi: 10.1007/s00134-004-2388-0. [PubMed: 15278267].
8. Pleym H, Wahba A, Videm V, Asberg A, Lydersen S, Bjella L, et al. Increased fibrinolysis and platelet activation in elderly patients undergoing coronary bypass surgery. *Anesth Analg.* 2006;**102**(3):660–7. doi: 10.1213/01.ane.0000196526.28277.45. [PubMed: 16492812].
9. Leong JY, Baker RA, Shah PJ, Cherian VK, Knight JL. Clopidogrel and bleeding after coronary artery bypass graft surgery. *Ann Thorac Surg.* 2005;**80**(3):928–33. doi: 10.1016/j.athoracsur.2005.03.074. [PubMed: 16122457].
10. Mittermayr M, Velik-Salchner C, Stalzer B, Margreiter J, Klingler A, Streif W, et al. Detection of protamine and heparin after termination of cardiopulmonary bypass by thrombelastometry (ROTEM): results of a pilot study. *Anesth Analg.* 2009;**108**(3):743–50. doi: 10.1213/ane.0b013e31818657a3. [PubMed: 19224778].
11. Coakley M, Reddy K, Mackie I, Mallett S. Transfusion triggers in orthotopic liver transplantation: a comparison of the thromboelastometry analyzer, the thromboelastogram, and conventional coagulation tests. *J Cardiothorac Vasc Anesth.* 2006;**20**(4):548–53. doi: 10.1053/j.jvca.2006.01.016. [PubMed: 16884987].
12. Konstantinidis K, Gerasimidis T, Verdy E, Elalamy I, Samama MM, Gerotziafas GT. Inhibition of clot formation process by treatment with the low-molecular-weight heparin nadroparin in patients with carotid artery disease undergoing angioplasty and stenting. A thromboelastography study on whole blood. *Thromb Haemost.* 2007;**97**(1):109–18. [PubMed: 17200777].
13. Lang T, Toller W, Gutl M, Mahla E, Metzler H, Rehak P, et al. Different effects of abciximab and cytochalasin D on clot strength in thrombelastography. *J Thromb Haemost.* 2004;**2**(1):147–53. [PubMed: 14717978].
14. Korte W, Clarke S, Lefkowitz JB. Short activated partial thromboplastin times are related to increased thrombin generation and an increased risk for thromboembolism. *Am J Clin Pathol.* 2000;**113**(1):123–7. doi: 10.1309/C7N9-J2AU-5TB9-5FRL. [PubMed: 10631865].
15. Mehta Y, Sharma J. Current guidelines for blood conservation in cardiac surgery. *Indian J Anaesth.* 2009;**53**(3):265–7. [PubMed: 20640132].
16. Miller R. Miller's anesthesia. ; 2015. pp. 1860–1.
17. Gorlinger K, Dirkmann D, Hanke AA. Potential value of transfusion protocols in cardiac surgery. *Curr Opin Anaesthesiol.* 2013;**26**(2):230–43. doi: 10.1097/ACO.0b013e32835ddca6. [PubMed: 23407150].
18. Despotis GJ, Joist JH, Goodnough LT. Monitoring of hemostasis in cardiac surgical patients: impact of point-of-care testing on blood loss and transfusion outcomes. *Clin Chem.* 1997;**43**(9):1684–96. [PubMed: 9299961].
19. Olde Engberink RH, Kuiper GJ, Wetzels RJ, Nelemans PJ, Lance MD, Beckers EA, et al. Rapid and correct prediction of thrombocytopenia and hypofibrinogenemia with rotational thromboelastometry in cardiac surgery. *J Cardiothorac Vasc Anesth.* 2014;**28**(2):210–6. doi: 10.1053/j.jvca.2013.12.004. [PubMed: 24630470].