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Comparison of the Effects of Albumin 5% versus Ringer's Lactate on Blood Loss and Coagulation after Vascular Surgery Using Thromboelastography

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Keywords: Albumin 5%; Ringer's lactate; Vascular surgery; Blood loss; Coagulation, Thromboelastography

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Abstract

AIM: Comparing the effects of Albumin 5% versus Ringer's lactate on blood loss and coagulation after vascular surgery using

METHODS: In this randomised study, 60 patients, aged (18-60 years) ASA physical status (I-III) undergoing vascular surgery were included in the study and randomly allocated into two groups using a random number generator, to receive either Human albumin or Ringer lactate after obtaining written informed consent. Group A received 1-2 ml per minute of human albumin 5% combined with normal saline (0.9%). Group B received Ringer's lactate only as of the main solution. Variables were measured after administration of fluids as postoperative measures. The amount of blood needed for testing was 4 ml drawn before the operation and at the end of surgery with a citrate tube (blue tube) from the venous line or using a regular needle. The standard time of 15 minutes was considered to begin processing.

RESULTS: There was no statistically significant difference observed between both groups regarding demographic data, surgical wound drainage, haemoglobin level, hematocrit level and coagulation profile. Regarding ROTEM thermoelectrometry variables showed that there was no statistically significant difference was found between the two groups In-TEM variables (Ex-TEM Clotting time, TEM Clot Formation Time) but In-TEM Alpha Angel measured in degrees showed a Statistically significant difference between the two groups. $P < 0.001$ and Ex-TEM Maximum Clotting Firmness MCF values measured in mm, there was a statistically significant difference between the two groups $P = 0.045$.

CONCLUSION: This study concluded that the use of human albumin (5%) in vascular surgeries before reaching the trigger point for blood transfusion didn't improve blood loss or coagulation profile compared to the use of ringer lactate only. Therefore, ringer lactate can be used as a good replacement for human albumin. Ringer lactate is readily available and inexpensive while human albumin may be costly.

Introduction

Anesthesiologists always seek for the optimum fluid to be used especially in bloody operations like vascular surgeries before reaching the trigger for blood transfusion, Crystalloids, in the form of Ringer's lactate (RL), or and colloids such as 5% human serum albumin (HA) are commonly used for intra-operative fluid management during surgery [1].

Monitoring perioperative coagulation competence has relied on clinical estimates besides on plasma coagulation tests [2]. Plasma coagulation tests were, however, introduced to evaluate the lack of coagulation factors and not to predict the risk of bleeding or for guiding hemostatic therapy [3].

In contrast, viscoelastic evaluation of whole blood enables rapid diagnosis of coagulation competence and may be displayed in real time within the operating theatre. Thus, the use of perioperative coagulation monitoring by, e.g. Thromboelastography (TEG) is recommended [4].

Rotation thermoelectrometry (ROTEM®, TEM® Innovations, Munich, Germany) offers a recent alternative approach to assess perioperative coagulation disorders using the visco-elastic analysis of clotting. Trials specifically examining bleeding management in vascular surgery are lacking, and much of the literature and guideline are derived from studies on patients with trauma [5].

ROTEM® provides the most complete and rapid information on hemostasis.

The ROTEM for the evaluation of fluid management during vascular surgery using either Albumin or Ringer lactate was adopted in this study.

Methods

After obtaining an approval from the departmental ethics and research committee of Cairo University hospitals (Kasr Alainy hospital) 60 patients aged (18-60 years) ASA physical status (I-III) undergoing vascular surgery were included in the study and randomly allocated into two groups using a random number generator, to receive either Human albumin or Ringer lactate after obtaining a written informed consent (Figure 1).

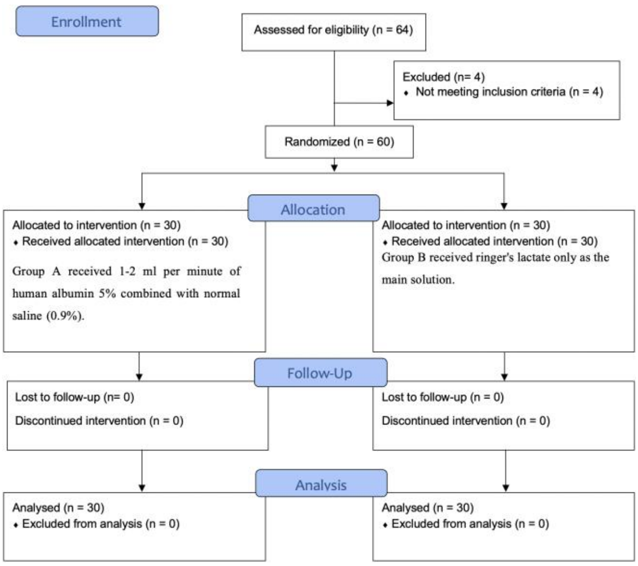

Figure 1: CONSORT Flow Diagram

After preoperative assessment and full medical history as well as laboratory investigations, patients were premedicated with 3 mg midazolam, and standard monitoring was applied.

General anaesthesia was induced with Propofol (2 mg/kg), Rocuronium (0.6 mg/kg) and Fentanyl (2 µg/kg), followed by endotracheal intubation, isoflurane 1.5%. Mechanical ventilation was initiated using 50% oxygen in air through a closed-circuit system to keep SaO_2 > 97% and end-expiratory CO_2 between 35 and 40 mm Hg.

Additional Fentanyl 50 mcg was given when heart rate or arterial blood pressure increased 20% above the baseline. Rocuronium top up was given as 1/5 of the initial dose every 20 minutes.

Fluid requirements were given based on fluid losses before the start of anaesthesia, maintenance requirements, normal fluid losses that occur during surgery, and response to unanticipated fluid (blood) loss.

At the end of the surgical procedure, muscle relaxant was reversed with neostigmine 0.08 mg/kg and atropine 0.01 mg/kg. All patients were extubated and transferred to the postoperative care unit (PACU).

ROTEM is a modern modification of the TEG technology originally described by Hartert in 1948 [6], and it was used in the present study.

These technologies provide a visual assessment of clot formation and subsequent lysis under low shear conditions (0.1/sec) similar to those present in the vena cava and well below those seen in venules, large veins, and the arterial system. Multiple test reagents are available for ROTEM; EXTEM (tissue factor activation), INTEM (ellagic acid/phospholipid activation). The commonly used ROTEM variables include clotting time (CT sec), clot formation time (CFT sec), α-angle (degree), maximum clot firmness (mm), and Lysis index (%). CT represents the onset of clotting, while CFT and α-angle both represent the initial rate of fibrin polymerisation. MCF is a measure of the maximal viscoelastic strength of clot. Lysis index issued for the diagnosis of premature lysis or hyper-fibrinolysis.

Enrolled patients were randomly allocated in two groups:

Group A received 1-2 ml per minute of human albumin 5% combined with normal saline (0.9%).

Group B received Ringer's lactate only as of the main solution.

ROTEM variables, coagulation profile, and complete blood count were recorded for all patients' pre-operative (baseline). ROTEM variables were measured after administration of fluids as postoperative measures.

The amount of blood needed for testing was 4 ml drawn before the operation and at the end of surgery with a citrate tube (blue tube) from the venous line or using a regular needle. The standard time of 15 minutes was considered to begin processing.

For ROTEM analysis, samples of blood were immediately mixed with 0.5 ml of a 3.2% citrate sodium solution (9 NC; Becton, Dickinson and Co., Franklin Lakes, NJ). After gentle mixing, the blood sample was analysed at 37°C.

The following ROTEM assays were performed, Ex-TEM which evaluates the extrinsic pathway, In-TEM evaluates the intrinsic pathway, and FIBTEM assess fibrinogen level after tissue. CT, CFT, ALP, MCF and ML parameters were measured in Ex-TEM and In-TEM assays while only the MCF was reported in the FIBTEM. All ROTEM analyses were observed for 60 minutes and then stopped.

Pain, vital signs, oxygen saturation, ventilation, and wound drainage were monitored during post-operative care.

Statistical Analysis

Data are presented as mean and standard deviation (SD). Non-normally distributed variables are expressed as median (25% and 75% percentiles). Non-parametric statistical tests were used for analysis if no normal distribution could be achieved by log transformation.

Repeated Measures Analysis of covariance (ANCOVA) is used to test the statistical differences between ROTEM thromboelastometry

All P-values are reported as results of two-sided tests and values of P < 0.05 were considered statistically significant.

Results

Demographic data

Patient characteristics including age and gender of both groups were comparable (Table 1).

Table 1: Demographic variable

Group	Range	Mean	μ ± σ (95%)[a]	Between-Groups Effects, P-Value
Age				
5% Human Serum Albumin	21 – 53	40.87	36.53 - 45.20	P-Value (F_c) =0.475
Ringers Lactate	21 - 60	43.07	38.73 - 47.40	
Gender	Male		Female	
5% Human Serum Albumin	17		13	*P* Value (χ^2) =0.2879
Ringers Lactate	21		9	

[a] μ = Mean; σ = Standard Deviation.

Regarding Surgical Wound Drainage: There was no statistically significant difference observed between both groups. Regarding haemoglobin level (Hb): No statistically significant difference was observed in Hb level between both groups. Regarding hematocrit level: No statistically significant difference was observed between both groups. Regarding coagulation profile: international normalised ratio (INR), prothrombin time (PT), and partial thromboplastin time (PTT). There was no statistically significant difference between both groups (Table 2).

Table 2: Coagulation profile

Parameter	Mean	μ ± σ (95%)[a]	Pairwise comparisons, P-Value
Coagulation Profile			
INR			
5% Human Serum Albumin	1.04	1.00 - 1.08	0.286
Ringers Lactate	1.07	1.03 - 1.11	
PT (seconds)			
5% Human Serum Albumin	12.80	12.39 - 13.21	0.302
Ringers Lactate	12.50	12.09 - 12.91	
aPPT(seconds)			
5% Human Serum Albumin	30.00	28.83 - 31.17	0.503
Ringers Lactate	30.10	28.93 - 31.27	

[a] μ = Mean; σ = Standard Deviation.

ROTEM thromboelastometry variables

In-TEM variables

In-TEM clotting time measured in seconds showed that there was no statistically significant difference was found between the two groups = 0.75. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.001. That revealed that both liquids have a significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001, (Figure 2).

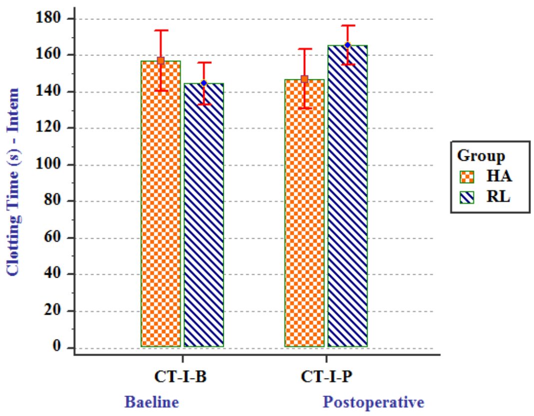

Figure 2: Clotting time, In-TEM

In-TEM Clot Formation Time measured in seconds; there was no statistically significant difference between the two groups p = 0.77. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed non-significant differences, P < 0.357. That revealed both liquids have a non-significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001, (Figure 3).

In-TEM Alpha Angel measured in degrees

showed a statistically significant difference between the two groups, P < 0.001. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.001.

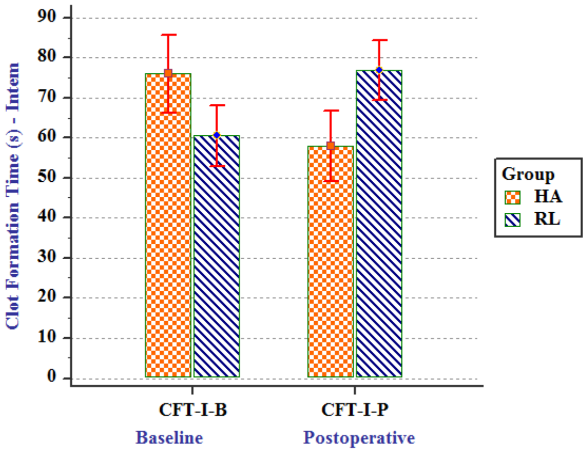

Figure 3: Clot Formation Time, In-TEM

That revealed both liquids have a non-significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001, (Figure 4).

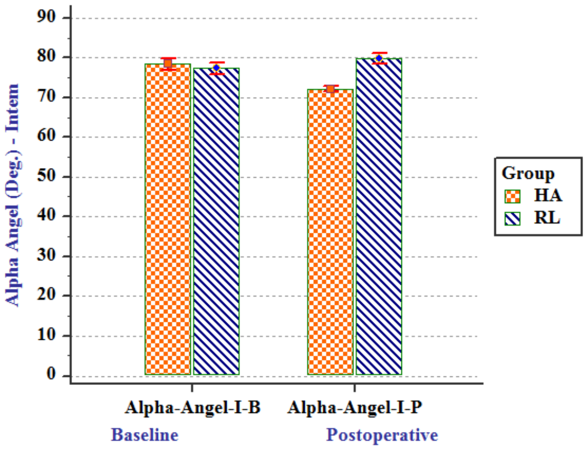

Figure 4: Alpha Angel, In-TEM

In-TEM Maximum Clot Firmness measured in mm there was no statistically significant difference between the two groups P = 0.085. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.001. That revealed that both liquids have a significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001, (Figure 5).

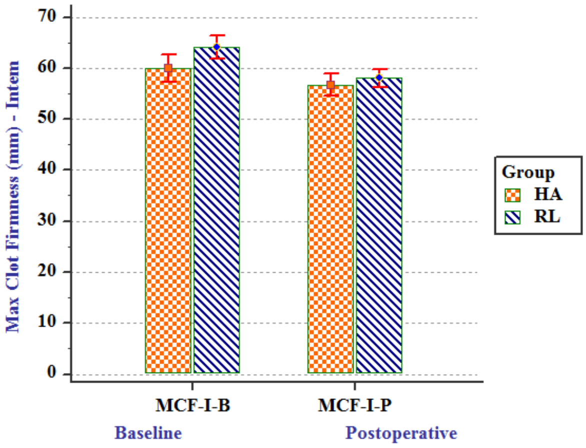

Figure 5: Max Clot Firmness, In-TEM

Ex-TEM variables

Ex-TEM Clotting time values measured in seconds. There was a statistically significant difference between the two groups P < 0.001. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.001. That revealed that both liquids have a significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001, (Figure 6).

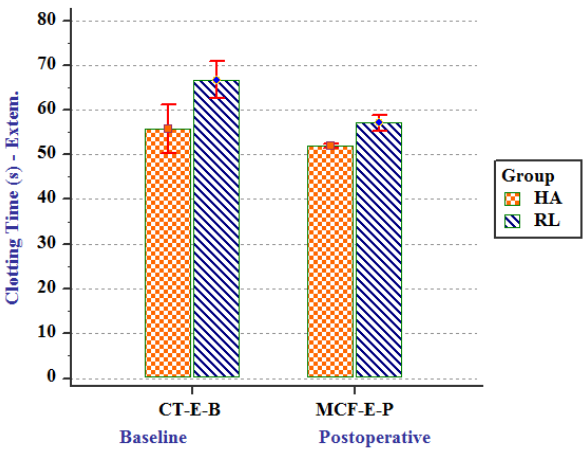

Figure 6: Clotting Time, Ex-TEM

Ex-TEM Clot Formation Time CFT values measured in seconds, Showed no statistically significant difference between the two groups P = 0.104. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.008. That revealed that both liquids have a significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001 (Figure 7).

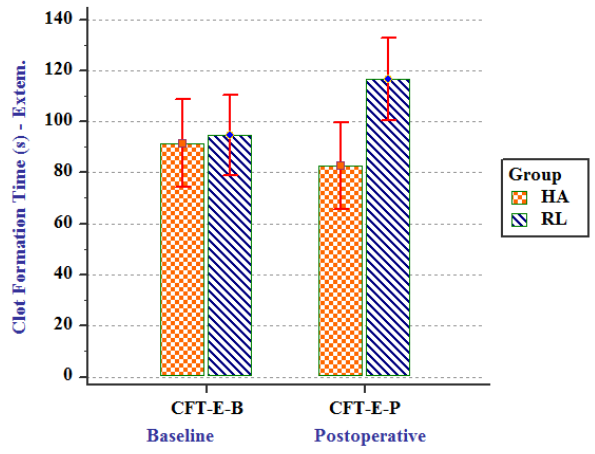

Figure 7: Clot Formation Time, Ex-TEM

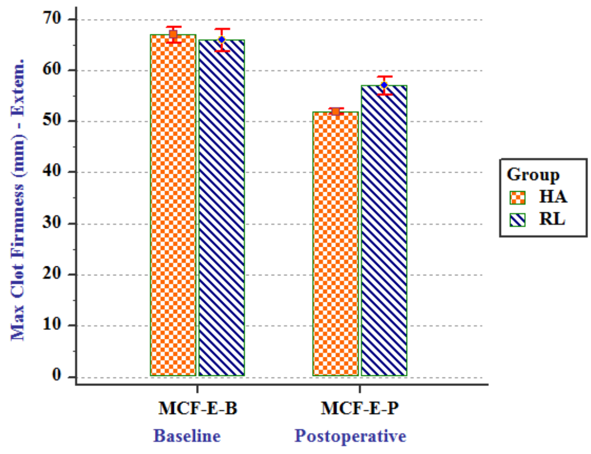

Figure 9: Max Clot Firmness, Ex-TEM

Ex-TEM Alpha Angel values measured in degree showed no statistically significant difference between the two groups P = 0.902. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.008. That revealed that both liquids have a significant impact on this parameter. The interaction between different effects and liquid effects showed non-significant differences, P = 0.208, (Figure 8).

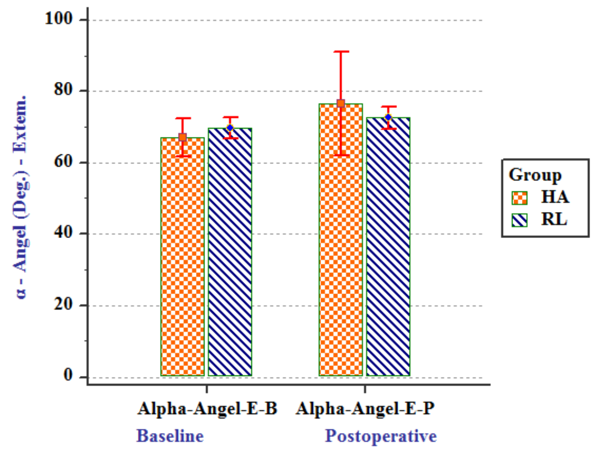

Figure 8: Alpha Angel, Ex-TEM

Ex-TEM Maximum Clotting Firmness MCF values measured in mm, There was a statistically significant difference between the two groups P = 0.045. Within-group effects (the difference between baseline and postoperative regardless of the type of liquid) showed significant differences, P < 0.001. That revealed that both liquids have a significant impact on this parameter. The interaction between different effects and liquid effects showed significant differences, P < 0.001 (Figure 9).

Discussion

Maintenance of intravascular volume is important to achieve optimal perioperative outcomes. There is continuing debate regarding the quantity and the type of fluid resuscitation during elective major surgery [7].

In terms of the effect of albumin versus ringer lactate on blood loss, the results of this study were in line with published studies and meta-analyses comparing crystalloids and colloids for cardiac surgery [8] postoperative bleeding often did not differ between crystalloids and colloids. Studies comparing albumin with non-protein colloids during cardiac surgery were in the majority in favour of albumin regarding transfusion requirements and mortality [9], [10], [11].

In contrast to this study, Johan AB Groeneveld found that Colloids are more efficient than crystalloids in attaining resuscitation endpoints since much less fluid volume is required [12].

Thromboelastography (TEG) and rotational thromboelastometry (ROTEM); are devices that provide the continuous measurement and display of the viscoelastic properties of a whole blood sample from the initial phase of fibrin formation to clot retraction and ultimately fibrinolysis [13].

Numerous studies have reported the utilisation of TEG and ROTEM as a monitoring device for hemostasis and transfusion management in various clinical settings, for example, cardiac surgery, liver transplantation, identification of patients with overt disseminated intravascular coagulation [14], hypercoagulability, and prediction thromboembolic events in surgical patients [15].

Studies claim that TEG is a point of care device for rapid diagnosis and differentiation of hypercoagulable and hyperfibrinolytic conditions [16].

TEG's ability to assess hemostasis in whole blood renders it to be ideal for rapidly identifying patients with trauma-induced coagulation and transfusion guidance [17]. Rotation thromboelastometry (ROTEM®, TEM® Innovations, Munich, Germany) offers an alternative approach to assess perioperative coagulation disorders using the visco-elastic analysis of clotting in vitro. First results are available within 10 min of test initiation, and clot formation can be observed online by a bedside monitor. ROTEM® measurements of EXTEM and INTEM are reproducible and stable over time, regardless of a delay from blood withdrawal to analysis (range 0–120 min after blood withdrawal).

Along with this present study, some studies report TEG and ROTEM to be a useful research tool in comparison to six common tests, hematocrit, platelet count, fibrinogen, PT, aPTT, and fibrin split degradation [18], suggesting a strong relationship.

Tripodi and colleagues [19] stated that standard coagulation tests failed to reflect the balance between the actions of pro- and anticoagulant factors.

By this study, Wang and colleagues [20] showed a significant decrease in transfused allogeneic blood products following a transfusion algorithm using ROTEM® compared with standard laboratory tests in liver transplant surgery.

Data from Schöchl and colleagues revealed the effective use of ROTEM®-guided coagulation management in trauma patients by reducing the amount of allogeneic blood product transfusion [21].

Koray et al. have demonstrated that a ROTEM®-based coagulation algorithm decreased total transfusion costs in cardiac surgery which is consistent with results of the current study [22].

In line with this study, a previous thrombelastographic study in patients undergoing knee replacement surgery and exhibiting even minor blood loss and intravascular volume replacement already showed that colloid administration reduces final clot strength more than Ringer lactate solution does [23].

Limitations: 1. Although ROTEM® can guide the clinician as to which type of treatment may be most helpful to treat coagulopathy during surgery or in trauma ROTEM® results cannot give exact recommendations on the number of blood products or coagulation factors to be administered; 2. Thromboelastometry/Thromboelastography is a valuable addition to the diagnostics of perioperative coagulation management, but it should not be overlooked that this method by no means provides a complete picture of clotting SO as to avoid this drawback correlation between thrombo-elastographic coagulation time and conventional PT and PTT should be considered; 3. Thromboelastography should be performed by trained personnel, and its technique requires standardisation. Standard parameters of ROTEM do not directly examine platelet function; recently specific "platelet mapping assay" for ROTEM had been introduced to practice; 4. ROTEM® analyses were performed not as bedside tests but in a central laboratory with a certain time delay for sample transport.

This study concluded that the use of human albumin (5%) in vascular surgeries before reaching the trigger point for blood transfusion didn't improve blood loss or coagulation profile compared to the use of ringer lactate only. Therefore, ringer lactate can be used as a good replacement for human albumin. Ringer lactate is readily available and inexpensive while human albumin may be costly.

References

1. Senzolo M, Coppell J, Cholongitas E, Riddell A, Triantos CK, Perry D, Burroughs AK. The effects of glycosaminoglycans on coagulation: a thromboelastographic study. Blood Coagulation & Fibrinolysis. 2007; 18(3):227-36. https://doi.org/10.1097/MBC.0b013e328010bd3d PMid:17413758

2. Enriquez LJ, Shore-Lesserson L. Point-of-care coagulation testing and transfusion algorithms. British journal of anaesthesia. 2009; 103(Suppl 1):i14-22. https://doi.org/10.1093/bja/aep318

3. Haizinger B, Gombotz H, Rehak P, Geiselseder G, Mair R. Activated thrombelastogram in neonates and infants with complex congenital heart disease in comparison with healthy children. BJA: British Journal of Anaesthesia. 2006; 97(4):545-52. https://doi.org/10.1093/bja/ael206 PMid:16873390

4. Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, Fries D, Goerlinger K, Haas T, Imberger G, Jacob M. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. European Journal of Anaesthesiology (EJA). 2013; 30(6):270-382. https://doi.org/10.1097/EJA.0b013e32835f4d5b PMid:23656742

5. Mahla E, Lang T, Vicenzi MN, Werkgartner G, Maier R, Probst C, Metzler H. Thromboelastography for monitoring prolonged hypercoagulability after major abdominal surgery. Anesthesia & Analgesia. 2001; 92(3):572-7. https://doi.org/10.1213/00000539-200103000-00004

6. Hartert H. Blutgerinnung studien mit der thromboelastographie, einen Neuen Untersuchingsverfahren. Klin Wochenschrift. 1948; 26:577-83 cited by Whitten CW and Greilich PE. Thromboelastography® Past, Present, and Future. Anesthesiology. 2000; 92:1223-5.

7. Joshi GP. Intraoperative fluid restriction improves outcome after major elective gastrointestinal surgery. Anesthesia & Analgesia. 2005; 101(2):601-5. https://doi.org/10.1213/01.ANE.0000159171.26521.31 PMid:16037184

8. Solomon C, Sørensen B, Hochleitner G, Kashuk J, Ranucci M, Schöchl H. Comparison of whole blood fibrin-based clot tests in thrombelastography and thromboelastometry. Anesthesia & Analgesia. 2012; 114(4):721-30. https://doi.org/10.1213/ANE.0b013e31824724c8 PMid:22314689

9. Wilkes MM, Navickis RJ, Sibbald WJ. Albumin versus hydroxyethyl starch in cardiopulmonary bypass surgery: a meta-analysis of postoperative bleeding. The Annals of thoracic surgery. 2001; 72(2):527-33. https://doi.org/10.1016/S0003-4975(01)02745-X

10. Sedrakyan A, Gondek K, Paltiel D, Elefteriades JA. Volume

expansion with albumin decreases mortality after coronary artery bypass graft surgery. Chest. 2003; 123(6):1853-7. https://doi.org/10.1378/chest.123.6.1853 PMid:12796160

11. Knutson JE, Deering JA, Hall FW, Nuttall GA, Schroeder DR, White RD, Mullany CJ. Does intraoperative hetastarch administration increase blood loss and transfusion requirements after cardiac surgery? Anesthesia & Analgesia. 2000; 90(4):801-7. https://doi.org/10.1213/00000539-200004000-00006

12. Groeneveld AB. Albumin and artificial colloids in fluid management:where does the clinical evidence of their utility stand? Crit Care. 2000; 4(Suppl 2):S16-S20. https://doi.org/10.1186/cc965

13. Spiel AO, Mayr FB, Firbas C, Quehenberger P, Jilma B. Validation of rotation thrombelastography in a model of systemic activation of fibrinolysis and coagulation in humans. Journal of Thrombosis and Haemostasis. 2006; 4(2):411-6. https://doi.org/10.1111/j.1538-7836.2006.01715.x PMid:16420574

14. Sharma P, Saxena R. A novel thromboelastographic score to identify overt disseminated intravascular coagulation resulting in a hypocoagulable state. American journal of clinical pathology. 2010; 134(1):97-102. https://doi.org/10.1309/AJCPPZ4J6CAFYDVM PMid:20551273

15. Kashuk JL, Moore EE, Sabel A, Barnett C, Haenel J, Le T, Pezold M, Lawrence J, Biffl WL, Cothren CC, Johnson JL. Rapid thrombelastography (r-TEG) identifies hypercoagulability and predicts thromboembolic events in surgical patients. Surgery. 2009; 146(4):764-74. https://doi.org/10.1016/j.surg.2009.06.054 PMid:19789037

16. Royston D, Von Kier S. Reduced haemostatic factor transfusion using heparinase-modified thrombelastography during cardiopulmonary bypass. British journal of anaesthesia. 2001; 86(4):575-8. https://doi.org/10.1093/bja/86.4.575 PMid:11573637

17. Trapani LM. Thromboelastography: current applications, future directions. Open journal of Anesthesiology. 2013; 3(01):23-27. https://doi.org/10.4236/ojanes.2013.31007

18. Afshari A, Wikkelsø A, Brok J, Møller AM, Wetterslev J. Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion. Cochrane database of systematic reviews. 2011; (3):CD007871. https://doi.org/10.1002/14651858.CD007871.pub2

19. Tripodi A, Primignani M, Chantarangkul V, Viscardi Y, Dell'Era A, Fabris FM, Mannucci PM. The coagulopathy of cirrhosis assessed by thromboelastometry and its correlation with conventional coagulation parameters. Thrombosis research. 2009; 124(1):132-6. https://doi.org/10.1016/j.thromres.2008.11.008 PMid:19135704

20. Wang SC, Shieh JF, Chang KY, Chu YC, Liu CS, Loong CC, Chan KH, Mandell S, Tsou MY. Thromboelastography-guided transfusion decreases intraoperative blood transfusion during orthotopic liver transplantation: randomized clinical trial. Transplantation proceedings. 2010; 42(7):2590-2593. https://doi.org/10.1016/j.transproceed.2010.05.144 PMid:20832550

21. Schöchl H, Nienaber U, Hofer G, Voelckel W, Jambor C, Scharbert G, Kozek-Langenecker S, Solomon C. Goal-directed coagulation management of major trauma patients using thromboelastometry (ROTEM®)-guided administration of fibrinogen concentrate and prothrombin complex concentrate. Critical care. 2010; 14(2):R55. https://doi.org/10.1186/cc8948

22. Ak K, Isbir CS, Tetik S, Atalan N, Tekeli A, Aljodi M, Civelek A, Arsan S. Thromboelastography-based transfusion algorithm reduces blood product use after elective CABG: a prospective randomized study. Journal of cardiac surgery. 2009; 24(4):404-10. https://doi.org/10.1111/j.1540-8191.2009.00840.x PMid:19583608

23. Martin G, Bennett-Guerrero E, Wakeling H, Mythen MG, El-Moalem H, Robertson K, Kucmeroski D, Gan TJ. A prospective, randomized comparison of thromboelastographic coagulation profile in patients receiving lactated Ringer's solution, 6% hetastarch in a balanced-saline vehicle, or 6% hetastarch in saline during major surgery. Journal of cardiothoracic and vascular anesthesia. 2002; 16(4):441-6. https://doi.org/10.1053/jcan.2002.125146 PMid:12154422