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Araştırma/*Research Article*

The Impact of Perioperative Viscoelastic Test Application on Blood Product Usage and Outcome in Cardiac Surgery; Regional Cardiac Surgery Center Experience

Murat Aksun
Saliha Aksun
Mehmet Ali Coşar
Elif Neziroğlu
Senem Girgin
Ezgi Balıkoğlu
Nagihan Karahan
Ali Gürbüz

Kalp Cerrahisinde Perioperatif Viskoelastik Test Uygulamasının Kan Ürünü Kullanımına ve Sonuca Etkisi; Bölgesel Kalp Cerrahisi Merkezi Deneyimi

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ABSTRACT

Objective: *Thromboelastography (TEG) is a diagnostic modality that gives information about coagulation. Despite all blood-preserving precautions in open heart surgery there are blood losses and the use of blood and blood products becomes inevitable. TEG is mostly not available in every center and habits, trends and clinical experience in blood use create the possibility of causing unnecessary use of blood and blood products. In this study, it was aimed to determine the effect of the use of thromboelastography on the use of blood and blood products in cardiac surgery.*
Methods: *Two hundred patients between 18-70 years old who underwent open heart surgery were included in the study. After the cardiopulmonary bypass (CPB), the cases were confirmed to have an Activated Clotting Time (ACT) value in the range of 120-150 sec after protamine administration. In 100 patients in the TEG group, the coagulation status was evaluated with TEG and it was decided how to apply blood and blood product use. Blood and blood product use was applied to 100 patients in the control group based on clinical experience and foresight. The total amount of blood and blood product used, fluid balance, need for inotropics, mechanical ventilator time, complications, duration of intensive care and discharge times were recorded.*
Results: *Use of Fresh Frozen Plasma (FFP) at the after CPB in the TEG group was statistically significantly lower than that of the control group FFP (p<0.05). Postoperative FFP and postoperative platelet use in the study group were statistically significantly lower than in the postoperative FFP and postoperative platelet values of the control group (p <0.05).*
Conclusion: *The use of thromboelastography is a very useful monitoring in terms of reducing FFP use after CPB and reducing FFP and platelet usage in the postoperative period. In this way, the unnecessary use of blood and blood products can be prevented.*

Keywords: *thromboelastography, blood product, open heart surgery*

ÖZ

Amaç: *Tromboelastografi (TEG), pıhtılaşma hakkında bilgi veren bir tanı yöntemidir. Açık kalp cerrahisinde tüm kan koruyucu önlemlere rağmen kan kayıpları olur, kan ve kan ürünlerinin kullanımı kaçınılmaz hale gelir. TEG çoğunlukla her merkezde bulunmamakta ve kan kullanımındaki alışkanlıklar, eğilimler ve klinik deneyimler gereksiz kan ve kan ürünleri kullanımına neden olma ihtimalini yaratmaktadır. Bu çalışmada kalp cerrahisinde tromboelastografi kullanımının kan ve kan ürünleri kullanımına etkisinin belirlenmesi amaçlanmıştır.*
Yöntem: *Çalışmaya 18-70 yaş arası açık kalp ameliyatı geçirmiş 200 hasta dahil edildi. Kardiyopulmoner baypas (KPB) sonrası protamin uygulaması sonrasında vakaların 120-150 sn aralığında Aktive Pıhtılaşma Süresi (ACT) değerine sahip olduğu doğrulandı. TEG grubundaki 100 hastada pıhtılaşma durumu TEG ile değerlendirildi ve kan ve kan ürünü kullanımının nasıl yapılacağına karar verildi. Kontrol grubundaki 100 hastaya klinik deneyim ve öngörüye dayalı olarak kan ve kan ürünü kullanımı uygulandı. Toplam kullanılan kan ve kan ürünü miktarı, sıvı dengesi, inotrop ihtiyacı, mekanik ventilatör süresi, komplikasyonlar, yoğun bakım süreleri ve taburcu süreleri kaydedildi.*
Bulgular: *TEG grubunda KPB sonrası Taze Dondurulmuş Plazma (TDP) kullanımı, kontrol grubu TDP kullanımından istatistiksel olarak anlamlı derecede düşüktü (p <0.05). Çalışma grubunda ameliyat sonrası TDP ve ameliyat sonrası trombosit kullanımı, kontrol grubunun ameliyat sonrası TDP ve ameliyat sonrası trombosit değerlerinden istatistiksel olarak anlamlı derecede düşüktü (p<0.05).*
Sonuç: *Tromboelastografi kullanımı, KPB sonrası TDP kullanımının azaltılması ve postoperatif dönemde TDP ve trombosit kullanımının azaltılması açısından oldukça faydalı bir izlemdir. Bu sayede gereksiz kan ve kan ürünleri kullanımının önüne geçilebilir.*

Anahtar kelimeler: *tromboelastografi, kan ürünü, açık kalp cerrahisi*

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Murat Aksun
Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı
İzmir - Türkiye
muratakSun@yahoo.com
ORCİD: 0000-0002-8308-3045

M.A. Coşar 0000-0002-2327-5192
E. Neziroğlu 0000-0003-2639-3159
S. Girgin 0000-0003-0715-7695
E. Balıkoğlu 0000-0003-4373-0022
N. Karahan 0000-0002-8042-0501
Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Anesteziyoloji ve Reanimasyon Anabilim Dalı, İzmir, Türkiye

S. Aksun 0000-0002-7991-1645
Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Klinik Biyokimya Anabilim Dalı, İzmir, Türkiye

A. Gürbüz 0000-0002-4344-992X
Katip Çelebi Üniversitesi Atatürk Eğitim ve Araştırma Hastanesi, Kalp ve Damar Cerrahisi Anabilim Dalı, İzmir, Türkiye

INTRODUCTION

Platelet dysfunction and increased fibrinolysis caused by cardiopulmonary bypass (CPB) are the most common causes of postoperative microvascular bleeding, which increases postoperative transfusions, transfusion-related complications, and mortality rate [1].

Thromboelastography (TEG) is a diagnostic modality that gives us information about coagulation [2]. Despite all blood-preserving precautions in open heart surgery there are blood losses and the use of blood and blood products becomes inevitable [1]. Although the use of TEG has become widespread in recent years and has started to be included in the guidelines [2], it is still not used sufficiently. Despite the device is not available in every center and habits and trends in blood use create the possibility of causing unnecessary use of blood and blood products. This causes surgeons and anesthetists to base their decisions on the use of blood and blood products on empirical experiences than on calculated, actual need. This results in the unnecessary use of blood and blood products.

The thromboelastogram (TEG) is used to monitor coagulation [3]. Although TEG is used more frequently in liver transplantation it has not reached the desired level in terms of its use in cardiac surgery [4]. With a rotational force applied continuously in the TEG device, it measures changes in clot formation and evaluates clot formation, melting kinetics, and hardness [3].

Due to its processing whole blood, the TEG device also shows the relationship between platelets and red cells [5]. To accelerate the reaction, 1 mL of blood is placed into the tube containing kaolin and then 360 µL is pipetted and placed into the device's pin system. With the graphic generated by the device and the values it displays, clinicians can obtain information about the patient's coagulation status. In this graph, r-time shows coagulation activation, k-value, α-angle fibrin formation and velocity, MA (maximum amplitude) value, strain of the clot, and Ly30 value is fibrinolysis.

With the use of the TEG, we can obtain information about clot formation, clotting factors, and clot resolution [5] and clinicians can determine whether the patient should be given any blood product and, if necessary, which blood product is needed [1,3]. Clinicians can then apply treatment in accordance with the protocol in Table 1.

Table 1. Treatment protocol.

TEG value	Etiology	Recommended Treatment
R 7-10 min	↓Coagulation factors	1 unit of FFP or 4 ml/kg
R 11-14 min	↓↓Coagulation factors	2 units of FFP or 8 ml/kg
R >14 min	↓↓↓Coagulation factors	4 units of FFP or 16 ml/kg
MA between 49-54 mm	↓Platelet function	0.3 mcq/kg DDAVP
MA between 41-48 mm	↓↓Platelet function	5 units of platelets
MA 40 mm or less	↓↓↓Platelet function	10 units of platelets
45 °> angle α-	Low Fibrinogen level	0.06 Units/kg cryo
LY30 7.5% or greater, CI <3	Primary fibrinolysis	Antifibrinolytic selection
LY30 7.5% or greater, CI> 3	Secondary fibrinolysis	Anticoagulant selection
LY30 <7.5%, CI> 3	Prothrombotic state	Anticoagulant selection

R: Reaction time, MA: maximum amplitude, LY 30: Lysis 30 minutes, CI: Coagulation index, FFP: Fresh frozen plasma, DDAVP: Desmopressin

In this study, we aimed to evaluate coagulation, reduce unnecessary blood and blood product consumption, and improve postoperative parameters by using the TEG device in open heart surgery and investigate whether clinical outcomes, including mediastinal reexploration, postoperative length of stay (LOS), and short-term mortality, were affected by TEG-guided transfusion therapy.

MATERIALS and METHODS

Study design

This prospective, single center (large regional cardiac care & surgery center), randomized trial was

Tablo 2. Demographic data and distribution of categorical variables.

		Group				p
		TEG group		Control group		
		n	%	n	%	
Gender	Male	83	83.0	86	86.0	0,558
	Female	17	17.0	14	14.0	
		100	50	100	50	
Age (n) (Mean. ± SD)		61.51±9.54		59.42±10.65		0,145
Number of Anastomosis	1	-	-	1	1.0	0,083
	2	13	13.0	19	19.0	
	3	62	62.0	62	62.0	
	4	21	21.0	16	16.0	
	5	4	4.0	2	2.0	
	Mean ± SS (Min-Max)	3.16 ± 0.69 (2-5)		2.99 ± 0.69 (1-5)		

Independent sample t test, Mann Whitney u analysis

approved by the ethics committee of the Katip Çelebi University Atatürk Research and Education Hospital in İzmir, Turkey (date 12.11.2014 / number 173). Each participant gave written informed consent. Two-hundred consecutive patients undergoing elective first-time CABG were enrolled into the study. Exclusion criteria for the study were preoperative hemodynamic instability, malignancies, history of bleeding diathesis, use of low-molecular-weight heparin molecules until the day of operation, and recent treatment (<5 days) with a glycoprotein IIb/IIIa antagonist or clopidogrel. Also, patients with impaired renal function (creatinine >2 mg/dL) and any liver disease resulting in elevated liver function tests were excluded. According to transfusion strategy, Patients were randomly assigned in a 1:1 ratio on the day of surgery with a dedicated software using the minimization technique to balance groups to either TEG group (group 2, TEG, n=100), clinician-directed transfusion group (Control, n=100). The anesthesiologists in the operating rooms were necessarily aware of group assignment, while patients and research personnel were blinded to the study-group assignment.

Procedure

After CPB, 100 patients who underwent a coronary artery bypass graft (CABG) operation were confirmed to have an ACT value in the range of 120–150 sec after protamine administration. Later, each patient's coagulation status was evaluated with TEG; taking these values into consideration, clinicians decided how to apply blood and blood product use.

In the control group, 100 patients underwent the CABG operation with CPB; after confirming the ACT value

was in the range of 120-150 sec following the end of the CPB, clinicians decided upon the use of blood and blood products based on their clinical experience. TEG evaluations were performed once for each patient at the end of the CPB and at least once in the intensive care unit within the first 3 hours. In case of drainage or in suspected clinical situations, measurements were repeated. Total amount of blood and blood product used, fluid balance, need for inotropics, duration of stay in the mechanical ventilator, complications, duration of intensive care, and discharge times were recorded.

Table 3. Intraoperative and postoperative blood and blood product usage.

		Group				Total		p
		TEG group		Control group				
		n	%	n	%	n	%	
After CPB ERT	Yes	35	35.0	26	26.0	61	30.5	0,167
	No	65	65.0	74	74.0	139	69.5	
	Mean ± SS (Min-Max)	1.43 ± 0.81 (1-5)		1.31 ± 0.47 (1-2)		1.38 ± 0.69 (1-5)		0,843
After CPB Platelet	Yes	-	-	3	3.0	3	1.5	0,246
	No	100	100.0	97	97.0	197	98.5	
	Mean ± SS (Min-Max)	1.32 ± (-)		1 ± 0 (1-1)		1 ± 0 (1-1)		-
After CPB FFP	Yes	10	10.0	26	26.0	36	18.0	***0,003***
	No	90	90.0	74	74.0	164	82.0	
	Mean ± SS (Min-Max)	1.3 ± 0.48 (1-2)		1.38 ± 0.5 (1-2)		1.36 ± 0.49 (1-2)		0,641
After CPB Criopecipitate	Yes	-	-	-	-	-	-	
	No	100	100.0	100	100.0	200	100.0	
	Mean ± SS (Min-Max)	0 ± 0 (0-0)		0 ± 0 (0-0)		0 ± 0 (0-0)		1,000
Postoperative ERT	Yes	37	37.0	45	45.0	82	41.0	0,250
	No	63	63.0	55	55.0	118	59.0	
	Mean ± SS (Min-Max)	1.7 ± 1.08 (1-6)		1.69 ± 0.79 (1-4)		1.7 ± 0.93 (1-6)		0,595
Postoperative Platelet	Yes	4	4.0	15	15.0	19	9.5	***0,008***
	No	96	96.0	85	85.0	181	90.5	
	Mean ± SS (Min-Max)	1.5 ± 1 (1-3)		3.2 ± 2.88 (1-8)		2.84 ± 2.67 (1-8)		0,385

Table 3. ***(continue)***

Postoperative FFP	Yes	23	23.0	38	38.0	61	30.5	***0,021***
	No	77	77.0	62	62.0	139	69.5	
	Mean ± SS (Min-Max)	1.83 ± 0.83 (1-4)		2.34 ± 0.94 (1-5)		2.15 ± 0.93 (1-5)		***0,029***
Postoperative Criopecipitate	Yes	3	3	2	2	5	2,5	0,683
	No	97	97	98	98	195	97,5	
	Mean ± SS (Min-Max)	0,12±0,79(0-6)		0,02±0,14 (0-1)		0,07±0,56 (0-6)		0,630

Pearson Chi-Square, Chi-square trend analysis, Fisher's Exact test, Mann Whitney U analysis
ERT: Erythrocytes , FFP: Fresh frozen plasma, CPB: Cardiopulmonary bypass,

Statistical analysis of the data was done using the IBM SPSS Statics Version 24.0 program. Pearson Chi-Square, Chi-Square Trend Analysis, and Fisher's Exact Test were used to compare categorical data between the control and study groups. The Mann Whitney U test was used for comparisons between groups since continuous data were not parametric. p 0.05 was considered statistically significant.

RESULTS

When we examined the demographic data of the cases, we found there was no statistically significant difference between the control and TEG groups (p>0.05) (Table 2).

There was no statistically significant difference between the groups in terms of the number of the anastomosis (p> 0.05) (Table 2).

The use of FFP at the end of CPB in the study group was statistically significantly lower than that of the control group FFP (p <0.05). Postoperative FFP and postoperative platelet use in the TEG group were statistically significantly lower than in the postoperative FFP and postoperative platelet values of the control group (p <0.05) (Table 3).

There was no statistically significant difference between the groups in terms of the fluid using, balance values and inotropic agent using (p>0.05) (Table 4).

There was no statistically significant difference between the groups in terms of mechanical ventilator time, intensive care unit stay, hospital stay and mortality (p>0.05). While 6 patients in the TEG group and 10 patients in the control group were re-operated for drainage, 2 patients in each group were re-operated for anastomosis problems (Table 5).

DISCUSSION

Our results demonstrated that a TEG-based algorithm causes a significant reduction in the risk for allogeneic blood product (FFP and platelet suspension) exposure and diminished the amount of allogeneic blood products transfused after elective CABG.

Bleeding after CPB is an important problem. The disruption of the integrity of the inflammatory, coagulation and fibrinolytic systems by contact of the blood with the extracorporeal circuit causes microvascular bleeding after open heart surgery [6]. Thus, platelet activation, leukocyte activation, tissue factor expression, and stimulation of complement and inflammation develop. Technological and pharmacological procedures have shown variable success

Table 4. Fluid management and inotropic agent usage.

	TEG Group Mean±SS (Min.-Max.)	Control Group Mean±SS (Min.-Max.)	p
After CPB Dopamine (µg/kg/min)	6.22±5.94 (0-50)	5.63±6.06 (0-50)	0.304
After CPB Dobutamine (µg/kg/min)	3.45±6.1 (0-20)	3.15±5.53 (0-20)	0.908
After CPB Adrenaline (µg/kg/min)	0.14±0.62 (0-5)	0.08±0.28 (0-2)	0.216
After CPB Levosimendan (µg/kg/min)	0.13±0.34 (0-1)	0.14±0.35 (0-1)	0.836
Intraoperative fluid (ml)	2745±945.12 (1000-7000)	2699.5±1128.9 (200-6700)	0.417
Intraoperative urine (ml)	1020.9±610.69 (200-5000)	1070.9±676.47 (0-3800)	0.861
Balance at the CPB (ml)	1595.5±744.27 (200-4450)	1451.7±627.48 (150-2850)	0.262
Postoperative Dopamine (µg/kg/min)	4.86±3.94 (0-10)	5.34±4.39 (0-20)	0.498
Postoperative Dobutamine (µg/kg/min)	3.16±5.55 (0-20)	3.65±5.85 (0-20)	0.516
Postoperative Adrenaline (µg/kg/min)	0.08±0.31 (0-2.5)	0.1±0.32 (0-2)	0.435
Postop Levosimendan (µg/kg/min)	0.12±0.33 (0-1)	0.12±0.32 (0-1)	1.00
Postoperative fluid (ml)	5100.6±1066.17 (2210-8330)	5039.25±1311.95 (960-9080)	0.502
Postoperative urine (ml)	3478.9±1051.48 (280-6460)	3499.38±1282.53 (0-8250)	0.924
Postoperative drainage (ml)	630.1±417.82 (0-3540)	688.7±580.81 (0-4330)	0.650
Postoperative balance (ml)	1076.5±1115.68 (-1230-5430)	968.39±1423.7 (-4530-5690)	0.710

Mann Whitney U analysis
Hb: Hemoglobin, Htc: Hematocrit, Plt: Platelet, PT: Prothrombin time, APTT: Activated partial thromboplastin time, ACT: Activated clotting time, INR:international normalized ratio, CPB: Cardiopulmonary bypass

Table 5. Intraoperative and postoperative data.

	TEG Group Mean±SS (Min.-Max.)	Control Group Mean±SS (Min.-Max.)	p
Cross- clamp time (min)	45.67±13.99 (17-98)	44.74±15.34 (14-82)	0.563
CPB time (min)	89.94±29.96 (42-270)	87,62±24,63 (25-150)	0.929
Operation time (min)	254.67±50.04 (0-360)	248.1±43.55 (0-330)	0.264
Re-operation (n)	8	12	0.346
Mechanical ventilator time (hr)	16.25±24.07 (2-168)	21±52.97 (2-480)	0.410
Intensive care stay (days)	3.15±2 (1-16)	3.74±3.17 (1-20)	0.770
Hospital stay (days)	8.69±4.82 (1-35)	9.59±9.67 (2-91)	0.830
Exitus (n)	4	9	0.152

Mann Whitney U analysis

in reducing cardiac transfusion requirements in cardiac surgery [7]. Rapid and accurate diagnosis of hemostatic abnormalities after CPB supplies important information clinicians need when deciding upon the appropriate treatment for postoperative bleeding [8]. The use of TEG to monitor coagulation will guide clinicians in the use of blood and blood products in cardiac surgery.

Current methods available for the management of current blood and blood product use are limited and offer unreliable administrations blood and blood products. After the end of the CPB, ACT measurement and normal values, blood count and blood gas evaluations, and observation of the surgical field are very valuable evaluation parameters, but unfortunately, they cannot provide sufficient data to clinicians. Although ACT measurement is normal, sometimes the reason for post-operative bleedings seen in the surgical field may not be fully understood. Assessing coagulation with TEG in such cases involves a monetary cost, but provides more objective indications of the state of coagulation and what blood and blood products should be given, if needed.

The most important hemostatic disorders observed early in the postoperative period after CPB are thrombocytopenia and platelet dysfunction. Thrombocytopenia is caused by hemodilution, mechanical breakdown of platelets, and platelets

adhesion to CBP surfaces. The most important reason for platelet dysfunction is that platelets are activated by attaching to synthetic surfaces in the pump system. In addition, heparin, protamine, and hypothermia are known to have direct platelet dysfunctional effects [1,9]. In blood management after CPB, even if blood counts are performed, platelet dysfunction cannot be revealed.

Sometimes it will not be possible to determine by routine coagulation tests whether bleeding is related to surgery or the need for blood and blood products. In these instances, TEG provides clinicians with useful information and reveals the cause of bleeding. This helps clinicians prevents the unnecessary use of blood and blood products [10,11]. In our study, while the reason of reoperation for drainage in the TEG group was not caused by coagulation abnormalities, but due to surgery, in the control group this distinction could not be clearly demonstrated and reoperation was considered. TEG measurements were made both before and after the reoperation.

In the TEG evaluation performed during hypothermia (33°C) during cardiopulmonary bypass, the MA value does not change and the decrease in R, K values, and a decrease in angle α are detected. Therefore, while hypothermia decreases clot formation rate, it does not make a meaningful change in clot quality (normal MA). Changes in R, K time, and α angle obtained during hypothermia can cause misinterpretation of the hemostatic system. Therefore, normothermic (37°C) TEG measurements are important for the correct interpretation of the hemostatic system [12]. We made the measurements after patients exited CPB. In this way, we eliminated the interpretation errors because normothermia was provided by reheating at the end of the CPB.

Yıldırım et al. [8] compared the patients who were given blood transfusions according to conventional laboratory data and those given blood transfusion according to the results of rotational TEG in their study, which included 164 patients undergoing coronary artery bypass graft surgery. They found a significant decrease in intraoperative and postoperative erythrocyte and postoperative whole blood use in the TEG group. They showed that postoperative bleeding significantly decreased in the TEG group. They did not find any difference in terms of FFP use.

In our study, we found the use of FFP after CPB and the use of FFP and platelets significantly lower in the TEG group in the postoperative period. In conventional coagulation management, we found clinicians used more blood products because of the routine application of some clinical behaviors and the surgeons' attempts to prevent this by using blood products to address the patient's drainage in the postoperative period. We think that sometimes the use of FFP is due only to the volume effect. All these situations lead to ineffective blood and blood product use.

CONCLUSION

According to the results we obtained from our study, the use of TEG reduces FFP after CPB and both FFP and platelet use in the postoperative period. With the use of TEG, unnecessary use of blood and blood products can be prevented.

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