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Roles of Thrombelastography and Thromboelastometry for Patient Blood Management in Cardiac Surgery☆

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ABSTRACT

The value of thrombelastography (TEG) and thromboelastometry (ROTEM) to improve perioperative hemostasis is under debate. We aimed to assess the effects of TEG- or ROTEM-guided therapy in patients undergoing cardiac surgery on the use of allogeneic blood products. We analyzed 12 trials including 6835 patients, 749 of them included in 7 randomized controlled trials (RCTs). We collected data on the amount of transfused allogeneic blood products and on the proportion of patients who received allogeneic blood products or coagulation factor concentrates. Including all trials, the odds ratios (ORs) for transfusion of red blood cell (RBC) concentrates, fresh-frozen plasma (FFP), and platelets were 0.62 (95% confidence interval [CI], 0.56-0.69; $P < .001$), 0.28 (95% CI, 0.24-0.33; $P < .001$), and 0.55 (95% CI, 0.49-0.62; $P < .001$), respectively. However, more than 50% of the patients in this analysis were derived from one retrospective study. Including RCTs only, the ORs for transfusion of RBC, FFP, and platelets were 0.54 (95% CI, 0.38-0.77; $P < .001$), 0.36 (95% CI, 0.25-0.53; $P < .001$), and 0.57 (95% CI, 0.39-0.81; $P = .002$), respectively. The use of coagulation factor concentrates was reported in 6 studies, 2 of them were RCTs. The ORs for the infusion of fibrinogen and prothrombin complex concentrate were 1.56 (95% CI, 1.29-1.87; $P < .001$) and 1.74 (95% CI, 1.40-2.18; $P < .001$), respectively. However, frequencies and amounts were similar in the intervention and control group in the 2 RCTs. It is presumed that TEG- or ROTEM-guided hemostatic management reduces the proportion of patients undergoing cardiac surgery transfused with RBC, FFP, and platelets. This presumption is strongly supported by similar ORs found in the analysis including RCTs only. Patient blood management based on the transfusion triggers by TEG or ROTEM appears to be more restrictive than the one based on conventional laboratory testing. However, evidence for improved clinical outcome is limited at this time.

MASSIVE BLEEDING, MEDIASTINAL reexploration, and transfusion of allogeneic blood products have been associated with increased morbidity and mortality after cardiac surgery [1-6]. Timely diagnosis and treatment of bleeding diathesis are thus important to prevent such adverse events. Various hematologic causes of increased bleeding have been identified, including dual-antiplatelet therapy [7,8], reduced thrombin generation due to oral anticoagulants (eg, warfarin and dabigatran) [9], and hypofibrinogenemia [10]. In addition, residual heparin, hyperfibrinolysis, prolonged cardiopulmonary bypass, and intraoperative deep hypothermic cardiac arrest contribute to abnormal bleeding after cardiac surgery [11,12]. Multiple blood conservation strategies have thus been recommended for perioperative patient blood management in cardiac surgery [6,7,13]. Examples of such strategies include early cessation of antiplatelet and antithrombotic agents, acute normovolemic hemodilution, intraoperative cell scavenging, and the prophylactic use of tranexamic acid or ε-aminocaproic acid [7]. Furthermore, implementing transfusion algorithms has been repeatedly shown to reduce transfusion of allogeneic blood products [6,14,15].

Screening for coagulation abnormalities and selected application of hemostatic interventions in the transfusion algorithms have been dependent on coagulation tests including platelet count, prothrombin time (PT), activated partial thromboplastin time (aPTT), and the Clauss fibrinogen assay. Most trigger values recommended in the recent guidelines [16-18] have been empirically established. Indeed, PT and aPTT cutoff values set outside the reference range can be useful in predicting bleeding after cardiac surgery under best conditions [19]. However, a keen interest in viscoelastic point-of-care (POC) testing including thrombelastography (TEG) and rotational thromboelastometry (ROTEM) has emerged because of a long turnaround time of the conventional laboratory testing, generally limited predictive value, and inability to assess the interaction between cellular and plasma hemostatic elements (according to the cell-based model of

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coagulation) [20,21]. Although TEG and ROTEM have been reported to have low predictive values in the statistical models of postoperative bleeding after cardiac surgery [19,22], the mainstay use of these POC viscoelastic tests is to choose optimal allogeneic blood product(s) or coagulation factor concentrate(s) in the presence of clinical bleeding [13,21,23]. A timely decision for transfusion and proper selection of hemostatic components are pivotal in the patient blood management because a variety of allogeneic blood products and coagulation factor concentrates are currently available in many countries.

In this article, we aimed to assess the effects of TEG- or ROTEM-guided transfusion therapy in patients undergoing cardiac surgery regarding transfusion of allogeneic blood products. We hypothesized that the TEG- or ROTEM-guided treatment algorithm reduces the transfusion of allogeneic blood products.

Patients and Methods

We performed an electronic search of the MEDLINE database to identify published prospective and retrospective clinical trials comparing the patient cohort, in which hemostatic therapy and transfusion of allogeneic blood products were guided by TEG or ROTEM (intervention group), and the other cohort, which was guided either by standard laboratory coagulation testing or by clinical judgment (control group). The search covered the period between January 1995 and February 2013 and was restricted to publications in English. The following search terms were applied: "thrombelastography" and "thromboelastometry." Additional studies were identified by searching of reference lists and reviews as well as contacts with experts in the field.

One hundred seventy-seven publications were identified by the initial search. After excluding 135 publications, which were animal studies, laboratory investigations, or unrelated to cardiac surgery, a total of 42 relevant publications were available for further assessment. Of them, 12 trials were finally selected because they provided data on frequency and median amounts of transfusion in TEG- and ROTEM-guided groups in comparison with control groups [12,14,15,24-32].

The trials were initially categorized into 3 types; (i) retrospective cohort studies comparing 2 cohorts before and after the introduction of a TEG- or ROTEM-guided transfusion algorithm, (ii) matched case-control studies, and (iii) randomized controlled trials (RCTs). Treatment algorithms including threshold values (triggers) for component transfusion based on TEG or ROTEM parameters in the intervention group or on conventional laboratory values in the control group were summarized. The methodologies and pertinent parameters of TEG and ROTEM have been extensively reviewed before [21]. The transfused units of allogeneic blood products and the infused amounts of coagulation factor concentrates were summarized from the publications.

The primary aim of this review was to compare the proportion of patients transfused with allogeneic blood products including red blood cell (RBC) concentrates, fresh-frozen plasma (FFP), and platelet concentrates between the intervention and control groups. The secondary aim was to compare the proportion of patients who received hemostatic agents including fibrinogen concentrate, cryoprecipitate, prothrombin complex concentrate (PCC), and recombinant activated factor VII (rFVIIa). The median amounts of transfused allogeneic blood products and infused hemostatic agents were evaluated, where available.

Finally, we evaluated the incidence of massive bleeding or massive transfusion, surgical reexploration, and hematocrit/hemoglobin levels and platelet count before and after surgery, where available.

Statistics

Data were summarized as numbers (percentages) of patients with transfusion of each blood product or median amount (interquartile range or range). Overall frequencies were compared by χ^2 test and reported as odds ratios (ORs). A P value less than .05 was considered significant. Statistical analyses were performed using IBM SPSS Statistics 21 (IBM Corp, Armonk, New York).

Results

Study Characteristics

The characteristics and numbers of analyzed patients in the 12 included studies [12,14,15,24-32] are presented in Table 1. In total, these studies included 6835 patients; 3687 of them were included in the intervention groups. More than 50% of the patients (3865/6835) were included in one retrospective observational study [27]. In the subgroup of RCTs (n = 7), 739 patients were included; 366 of them were included in the intervention groups. One nonrandomized study including 100 patients was performed in pediatric cardiac surgery [28], whereas all the other studies were performed in adult patients. Sample size varied from 56 to 3865 in all studies and from 56 to 224 in the 7 RCTs.

The studies included all types of cardiac surgery with varying risks of transfusion. Five studies included patients with high risk of transfusion; 2 of them solely included patients with bleeding after cardiac surgery [15,31], 2 studies included patients undergoing hypothermic circulatory arrest [12,26], and 1 study included pediatric patients undergoing cardiac surgery (median age, 5 months; median weight, 5.7 kg) [28].

Table 1
Study characteristics

Author and year	Type of study	No. of participants	Population	Intervention algorithm	Control group algorithm	Follow-up transfusion
Ak et al, 2009 [24]	RCT	224	CABG	TEG only	No; clinical judgment	Hospital discharge
Anderson et al, 2006 [25]	RC	990	Mixed cardiac surgery	ROTEM only	No; clinical judgment	Hospital discharge
Avidan et al, 2004 [14]	RCT	102	CABG	TEG + PFA + HMS	SLT-based algorithm	24 h perioperatively
Fassl et al, 2013 [12]	MCC	62	HCA	ROTEM only	No; clinical judgment	24 h perioperatively
Girdauskas et al, 2010 [26]	RCT	56	HCA	ROTEM only	SLT-based algorithm	Hospital discharge
Görlinger et al, 2011 [27]	RC	3865	Mixed cardiac surgery	ROTEM + MEA	No; clinical judgment	Hospital discharge
Nuttall et al, 2001 [15]	RCT	92	Patients with bleeding	TEG + POC	No; clinical judgment	Hospital discharge
Romlin et al, 2011 [28]	MCC	100	Pediatric cardiac surgery	ROTEM only	No; clinical judgment	24 h perioperatively
Royston and von Kier, 2001 [32]	RCT	60	Mixed cardiac surgery	TEG only	SLT-based algorithm	48 h perioperatively
Shore-Lesserson et al, 1999 [29]	RCT	105	Mixed cardiac surgery	TEG only	SLT-based algorithm	48 h perioperatively
Spiess et al, 1995 [30]	RC	1079	Mixed cardiac surgery	TEG only	No; clinical judgment	Hospital discharge
Weber et al, 2012 [31]	RCT	100	Bleeding patients	ROTEM + MEA	SLT-based algorithm	Hospital discharge

Abbreviations: CABG, coronary artery bypass graft surgery; HCA, hypothermic circulatory arrest; HMS, heparin monitoring system (Hepcon); MCC, matched case-control study; MEA, multiple-electrode aggregometry (Multiplate); PFA, platelet function analyzer (PFA-100); RC, retrospective cohort study; SLT, standard laboratory tests.

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Transfusion Algorithms

Eight studies used TEG or ROTEM in the intervention group as a sole guide for hemostatic intervention(s), whereas the other 4 studies used TEG or ROTEM in combination with POC PT and aPTT measurements, with platelet function analyzers (PFA-100, Dade-Behring, Marburg, Germany or multiple-electrode aggregometry, Roche Diagnostics, Rotkreuz, Switzerland), and with heparin concentration–based anticoagulation (Hepcon, Medtronic, Minneapolis, MN heparin monitoring system; Table 1).

The triggers for RBC, FFP, and platelet transfusion are indicated in Table 2. The threshold values of hemoglobin and hematocrit triggering RBC transfusion varied between 7 and 11 g/dL and between 21% and 25%, respectively. The selected levels were identical between the intervention and control groups in the respective study. However, the triggers for FFP and platelet transfusion based on TEG/ROTEM and on standard laboratory testing varied widely among different studies. In 4 studies, there was no algorithm for FFP and platelet transfusion in the control group, and it was administered by clinical judgment. The triggers for platelet transfusion were based on amplitude/clot firmness in the intervention groups and/or platelet function analyzers, where available. Thereby, different threshold levels of maximal amplitude (MA) and maximal clot firmness (MCF) were used on TEG and ROTEM, respectively (Table 2). In the case of ROTEM, the amplitudes of clot firmness at 10 or 15 minutes (A10 or A15) were preferably used as a treatment trigger because they can be assessed earlier than MCF and they are highly predictive of MCF [33]. In the control groups, a platelet count below $100 \times 10^3/\mu L$ was most frequently used as a transfusion trigger.

The triggers for administration of coagulation factor concentrates or cryoprecipitate varied widely among studies (Table 2). In 5 studies conducted in Europe [12,26-28,31], fibrinogen concentrate was dosed according to the low amplitude/clot firmness on FIBTEM, whereas cryoprecipitate was a treatment option in 2 studies from the United States using the TEG device [29,30]. Prothrombin complex concentrate was used in 4 studies using the ROTEM device [12,26,27,31]. In most studies, rFVIIa was used as a rescue medication, but there was no clear protocol or treatment trigger.

Frequencies of Transfusions of Allogeneic Blood Products and Administration of Coagulation Factor Concentrates

Frequencies of transfusion of RBC, FFP, and PC were available in 10 of the 12 included studies (Table 3). The frequency of transfusion of any of these allogeneic blood products was available in 6 studies. The proportion of patients with RBC, FFP, and platelet transfusion in all studies and in RCTs only is shown in Figure A/B. Including all studies, the ORs were 0.62 (95% confidence interval [CI], 0.56-0.69; $P < .001$) for RBC transfusion, 0.28 (95% CI, 0.24-0.33; $P < .001$) for FFP transfusion, and 0.55 (95% CI, 0.49-0.62; $P < .001$) for platelet transfusion. Including RCTs only, the ORs were 0.54 (95% CI, 0.38-0.77; $P < .001$) for RBC transfusion, 0.36 (95% CI, 0.25-0.53; $P < .001$) for FFP transfusion, and 0.57 (95% CI, 0.39-0.81; $P = .002$) for platelet transfusion. Odds ratios for any transfusion in all studies and in RCTs only were 0.65 (95% CI, 0.58-0.72; $P < .001$) and 0.62 (95% CI, 0.47-1.83; $P = .002$), respectively. The median amounts of transfused allogeneic blood products were lower in the intervention groups of most studies. No study showed higher median amounts of transfused allogeneic blood products in the intervention group (data not shown).

Coagulation factor concentrates were used in 5 studies from Europe using the ROTEM device. Cryoprecipitate was a treatment option in 2 studies from the United States [29,30], but transfusion of cryoprecipitate was reported in only 1 of these studies [30]. The ORs for using factor concentrates were higher in the intervention group including 5262 patients from all studies (Table 4); ORs were 1.56 (95% CI, 1.29-1.87; $P < .001$) for fibrinogen concentrate/cryoprecipitate and 1.74 (95% CI, 1.40-2.18; $P < .001$) for PCC. These data may indicate that factor concentrates are favored over FFP under ROTEM guidance. However, there was no higher frequency or amount of coagulation factor concentrate in the ROTEM group in 2 RCTs including 156 patients by Girdauskas et al [26] and Weber et al [31] or in the matched case-control study by Fassl et al [12] including 62 patients. In 4 studies, the administration of rFVIIa was reported. In one study [31], rFVIIa was used more frequently in the control group, whereas there was no difference in the other 3 studies [12,26,27].

Massive Bleeding and Surgical Reexploration

The massive bleeding was reported in 2 studies and was defined as (i) mediastinal drainage volumes more than 1000 mL in 24 hours [12] and (ii) blood loss of more than 400 mL within the first hour or more than 100 mL per hour for 4 consecutive hours [24]. The massive transfusion was reported in 2 studies and was defined as (i) more than 10 U of RBC transfusion [27] or (ii) more than 20 U of any allogeneic blood product [26]. Massive bleeding and/or transfusion was found in 38 (1.6%) of 2319 patients in the intervention group and 69 (3.7%) of 1888 patients in the control group (OR, 0.44; 95% CI, 0.29-0.66; $P < .001$).

The incidence of surgical reexploration was indicated in 9 studies [12,15,24-27,30-32]. Surgical reexploration was performed in 67 (2.2%) of 3031 patients in the intervention group and in 128 (5.1%) of 2507 patients in the control group (OR, 0.42; 95% CI, 0.31-0.57; $P < .001$). Including RCTs only, the OR for reexploration was 0.34 (95% CI, 0.19-0.61; $P < .001$).

Hemoglobin levels before and after surgery were similar in the intervention and control groups in all studies who provided these data. Platelet count was similar in the intervention and control groups in all studies before surgery, but higher platelet counts after surgery in the intervention group were reported in 3 studies [12,28,31].

Discussion

Based on our analysis, we presume that the transfusion triggers based on TEG or ROTEM analyses reduced the proportion of patients transfused with platelets and FFP in patients undergoing cardiac surgery. Also, the proportion of patients transfused with RBC was significantly lower under transfusion guidance by TEG or ROTEM despite identical RBC transfusion triggers. We found the similar ORs whether we included all type of studies or RCTs exclusively, which strongly support our presumption. In the European studies, reduction of transfused allogeneic blood products seemed to be accompanied by increased administration of coagulation factor concentrates. However, in 2 newer RCTs [26,31] and a recent matched case-control study [12], there was no difference in the frequency and amount of administered coagulation factor concentrates.

The administration of allogeneic blood products including RBC, FFP, and platelets in cardiac surgery and in critically ill patients has been associated with increased mortality and morbidity [1-3,6,34-37]. Therefore, the reduction or even avoidance of transfusion of allogeneic blood products is the goal of patient blood management and has been advocated by the recent guidelines of the European and American Society of Cardiothoracic Surgeons and Anesthesiologists as a 1A recommendation [7,38]. In recent years, POC-guided hemostatic transfusion algorithms have been suggested to be advantageous in terms of time efficiency and clinical efficacy of hemostatic therapies as well as total treatment costs [27,31,39]. The implementation of TEG- and ROTEM-guided transfusion algorithms has, therefore, been advocated in the recent European guidelines for the management of perioperative bleeding as a 1C recommendation [38]. However, the recent systematic reviews by Wikkelsoe et al [40] and by Afshari et al [41] questioned the efficacy of viscoelastic tests in reducing postoperative bleeding, transfusion requirements, adverse events, and

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Table 2
Transfusions triggers

Author and year	RBC trigger		FFP trigger		Platelet trigger		Fibrinogen/Cryo Trigger	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Ak et al, 2009 [24]	Hct <25%	Hct <25%	R >14 min	PT >14 s or aPTT > 1.5 × normal	MA <48 mm	PC $<100 \times 10^3/\mu L$	NA	NA
Anderson et al, 2006 [25]	Hct <21%	Hct <21%	CT_{INTEM} and CT_{HEPTEM} prolonged and MCF_{FIBTEM} <6 mm	INR >1.5 or surgical request	CT_{INTEM} and CT_{HEPTEM} prolonged and MCF_{FIBTEM} >6 mm	PC $<100 \times 10^3/\mu L$ or <0.5× preoperatively PC	NA	NA
Avidan et al, 2004 [14]	Hb <8 g/dL	Hb <8 g/dL	R >10 min	INR >1.5 or aPTT >1.5× normal	Prolonged closure time in PFA	PC $<50 \times 10^3/\mu L$	NA	NA
Fassl et al, 2013 [12]	Hb >7-10 g/dL	Hb >7-10 g/dL	CT_{INTEM} and CT_{HEPTEM} >240 s and MCF_{FIBTEM} >8 mm	Clinical decision	$A15_{EXTEM}$ <48 mm and $A15_{FIBTEM}$ >10 mm	Clinical decision	$A15_{FIBTEM} \leq 8$ mm or $A15_{EXTEM}$ <48 mm and $A15_{FIBTEM} \leq 10$ mm	Clinical decision
Girdauskas et al, 2010 [26]	Hb <8.5 g/dL	Hb <8.5 g/dL	CT_{HEPTEM} >260 s	aPTT >60 s or INR >1.5	MCF_{HEPTEM} <35 mm or MCF_{HEPTEM} 35-45 mm and MCF_{FIBTEM} >8 mm	PC $<100 \times 10^3/\mu L$	MCF_{FIBTEM} <8 mm	Fibrinogen < 1.5 g/L
Görlinger et al, 2011 [27]	Hb <8-10 g/dL	Hb <8-10 g/dL	CT_{EXTEM} > 90 s or CT_{HEPTEM} >240 s, only after PCC	Profuse bleeding after heparin reversal	$A10_{EXTEM}$ <40 mm and $A10_{FIBTEM}$ >10 mm, decreased platelet aggregation in MEA	PC $<100 \times 10^3/\mu L$	$A10_{FIBTEM} \leq 10$ mm and $A10_{EXTEM} \leq 40$ mm	Clinical decision
Nuttall et al, 2001 [15]	NA	NA	PT >16.6 s or aPTT >57 s (POC)	Clinical decision	MA <48 mm and PC <102 000/μL	Clinical decision	Fibrinogen <1.44 g/L	Clinical decision
Romlin et al, 2011 [28]	Hb <11 g/dL	Hb <11 g/dL	CT_{HEPTEM} >240 s	NA	MCF_{HEPTEM} <50 mm	NA	$MCF_{FIBTEM} \leq 8$ mm	NA
Royston and von Kier, 2001 [32]	NA	NA	R >14 min	PT or aPTT >1.5× normal	MA <48 mm	PC $<50 \times 10^3/\mu L$	NA	NA
Shore-Lesserson et al, 1999 [29]	Hct <25%	Hct <25%	R >20 min	PT >1.5× normal	MA <45 mm and PC $<100 \times 10^3/\mu L$	PC $<100 \times 10^3/\mu L$	Fibrinogen <1 g/L	Fibrinogen <1 g/L
Spiess et al, 1995 [30]	NA	NA	NA	NA	NA	NA	NA	NA
Weber et al, 2012 [31]	Hb <8-10 g/dL	Hb <8-10 g/dL	CT_{EXTEM} >90 s or CT_{HEPTEM} >240 s, only after PCC	aPTT >50 s or INR >1.4	$A10_{EXTEM}$ <40 mm and $A10_{FIBTEM}$ >10 mm, decreased platelet aggregation in MEA	PC $<80 \times 10^3/\mu L$	$A10_{FIBTEM} \leq 10$ mm and $A10_{EXTEM} \leq 40$ mm	Fibrinogen <1.5 g/L

Abbreviations: A10 and A15, clot firmness after 10 and 15 minutes in EXTEM, HEPTEM, or FIBTEM tests; Hb, hemoglobin; Hct, hematocrit; INR, international normalized ratio; MEA, multiple-electrode aggregometry; NA, data not available or hemostatic mean not used; PC, platelet count; PFA, platelet function analyzer; R, R time in heparinase-coated TEG test.

Table 3
Transfusions of allogeneic blood products

Author and year	RBC		FFP		Platelets		Any transfusion	
	Intervention	Control	Intervention	Control	Intervention	Control	Intervention	Control
Ak et al, 2009 [24]	52/114 (46)	60/110 (55)	19/114 (17)	31/110 (31)	17/114 (15)	29/110 (26)	NA	NA
Anderson et al, 2006 [25]	270/502 (53)	294/488 (60)	60/502 (12)	81/488 (17)	56/502 (11)	77/488 (16)	NA	NA
Avidan et al, 2004 [14]	34/51 (68)	35/51 (69)	2/51 (4)	0/51 (0)	2/51 (4)	1/51 (2)	NA	NA
Fassl et al, 2013 [12]	15/31 (48)	22/31 (71)	10/31 (33)	20/31 (65)	9/31 (29)	7/31 (23)	18/31 (58)	25/31 (85)
Girdauskas et al, 2010 [26]	24/27 (89)	27/29 (93)	9/27 (33)	25/29 (86)	14/27 (52)	23/29 (79)	24/27 (89)	29/29 (100)
Görlinger et al, 2011 [27]	868/2147 (40)	854/1718 (50)	24/2147 (1)	333/1718 (19)	280/2147 (13)	173/1718 (10)	906/2147 (42)	902/1718 (53)
Nuttall et al, 2001 [15]	NA	NA	NA	NA	NA	NA	NA	NA
Romlin et al, 2011 [28]	29/50 (58)	39/50 (78)	7/50 (14)	39/50 (78)	38/50 (76)	6/50 (12)	32/50 (64)	46/50 (92)
Royston and von Kier, 2001 [32]	NA	NA	NA	NA	NA	NA	5/30 (17)	10/30 (33)
Shore-Lesserson et al, 1999 [29]	22/53 (42)	31/52 (60)	4/53 (8)	16/52 (31)	7/53 (13)	15/52 (29)	NA	NA
Spiess et al, 1995 [30]	361/591 (74)	406/488 (83)	156/591 (26)	176/488 (36)	285/591 (48)	289/488 (59)	464/591 (79)	421/488 (86)
Weber et al, 2012 [31]	20/50 (40)	40/50 (80)	42/50 (84)	49/50 (98)	28/50 (56)	33/50 (66)	NA	NA

Data are number of patients with transfusions/all exposed patients (percentage).
Abbreviations: NA, data not available.

mortality. We found some evidence of reduced bleeding and surgical reexploration after cardiac surgery in the present study. Mortality was reported in only 3 studies [26,27,31]. Of them, one study showed reduced mortality in the intervention group [31], whereas others did not. The lack of effects on mortality might be explained by the inclusion of either low-risk or high-risk patients and patients with bleeding only. In these patients, the positive effects of TEG and ROTEM as suggested in this study might not be high enough to result in decreased mortality. However, TEG and ROTEM were developed as a POC coagulation test to guide hemostatic interventions including platelets, FFP, cryoprecipitate, or coagulation factor concentrates. Therefore, the primary aim of such systematic reviews should be the analysis of transfused allogeneic blood products and not bleeding (or prediction of bleeding) or mortality.

Regarding the different allogeneic blood products, especially FFP, transfusion is decreased by 3 to 4 times when using TEG or ROTEM. There are several reasons for this finding. First, FFP transfusions are usually triggered by prolonged PT or aPTT [19,42]. However, the triggers for PT/aPTT are merely recommendations, may vary widely (Table 2), and have not been adequately validated in the perioperative setting. In addition, the results of PT and aPTT are often impracticable to guide FFP therapy in acute bleeding because the turnaround times of these classical laboratory tests ranged from 29 to 235 minutes [43]. Point-of-care devices for these tests might be helpful [19]. In the viscoelastic tests, R time in TEG and coagulation time (CT) in ROTEM are used as a trigger for FFP transfusion. R time and CT are not prolonged in parallel with PT or aPTT [21], and the correlations between these parameters are rather poor [21,44]. The most likely reasons for these findings are that R time and CT are influenced by fibrinogen levels [45-47], by the cellular components (especially platelets) even in warfarin-treated patients [48], and potentially by decreased antithrombin levels in hemodilution [21]. Accordingly, viscoelastic tests using currently available reagents are not recommended for the assessment or hemostatic management of neither classical (warfarin) nor new oral anticoagulants (dabigatran, rivaroxaban, etc) [48,49]. Furthermore, angle and MA of viscoelastic tests are also strongly dependent on platelet counts and fibrinogen levels [45,47,50]. Second, even high amounts of FFP will lead to only small improvement in MCF. For example, about 11 to 13 mL/kg of FFP is required to improve MA in ROTEM tests by 1 mm [47]. In summary, FFP is less likely to be the primary choice for correcting coagulopathy based on TEG or ROTEM.

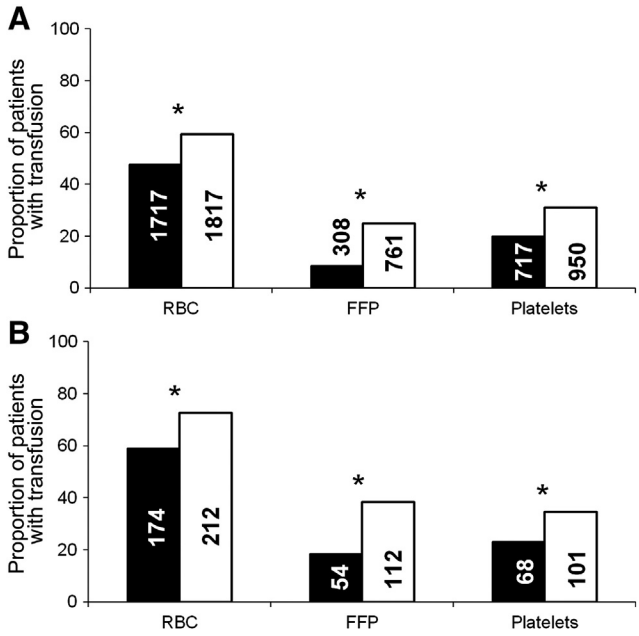

Fig. Frequency of transfusion of allogeneic blood products. Percentage of patients with transfusion of RBC concentrates, FFP, and platelets is shown. Black and white columns indicate the intervention (TEG or ROTEM guidance) and control groups, respectively. Numbers within the columns indicate patients with transfusion. A, All studies (3616 patients in the intervention group and 3067 in the control group). B, RCTs only (295 patients in the intervention group and 292 patients in the control group). *$P < .05$.

The overwhelming number of patients was included in a study comparing the use of FFP before and after the introduction of ROTEM [27]. Our findings might, therefore, be biased by this study. However, there was a consistent reduction in administration of FFP in most studies. Furthermore, the administration of FFP was reduced by nearly 40% when only RCTs were included in the analysis. This reduction in administration of FFP in TEG- or ROTEM-guided algorithms as part of patient blood management potentially reduces complications associated with FFP [31,37,51].

With regard to the use of fibrinogen concentrate, several European studies indicated the increased usage at the introduction of ROTEM and specific monitoring of fibrin polymerization (FIBTEM test) [27,28,39,52]. This is because the mainstay hemostatic interventions in the historic control groups were FFP and platelet concentrates (note: cryoprecipitate is unavailable in most European countries). Although purified factor concentrates are derived from the allogeneic human plasma pools, they are regulated as biological drugs with the national drug code. These products are infused without preceding type matching and are not considered as blood transfusion. In case of bleeding, fibrinogen levels can be estimated by ROTEM in a timely fashion (<10-15 minutes of testing) [23,50], and fibrinogen concentrate can be quickly administered to achieve the target of FIBTEM-MCF

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Table 4
Infusion of coagulation factor concentrates

Author and year	Fibrinogen/Cryoprecipitate		Administered amount of fibrinogen/cryoprecipitate	PCC		Administered amount of PCC	rFVIIa	
	Intervention	Control		Intervention	Control		Intervention	Control
Fassl et al, 2013 [12]	23/31 (73)	24/31 (77)	Similar ($P > .05$)	7/31 (23)	4/31 (13)	Similar ($P > .05$)	0/31 (0)	0/31 (0)
Girdauskas et al, 2010 [26]	21/27 (78)	26/29 (90)	Similar ($P > .05$)	4/27 (15)	26/29 (90)	Higher in control group ($P < .05$)	1/27 (4)	2/29 (7)
Görlinger et al, 2011 [27]	215/2147 (10)	64/1718 (4)	NA	191/2147 (9)	76/1718 (4)	NA	0/2147 (0)	1/1718 (0)
Romlin et al, 2011 [28]	8/50 (16)	1/50 (2)	Higher in intervention group ($P < .05$)	NA	NA		NA	NA
Spiess et al, 1995 [30]	39/591 (6)	44/488 (9)	NA	NA	NA		NA	NA
Weber et al, 2012 [31]	32/50 (64)	30/50 (60)	Similar ($P > .05$)	22/50 (44)	26/50 (52)	Similar ($P > .05$)	1/50 (2)	12/50 (24)

Data are numbers of patients with infusion/all exposed patients (percentage). *P* values are reported for differences in median amounts of coagulation factor concentrates.
Abbreviations: NA, data not available or hemostatic mean not used.

between 8 and 10 mm [12,26,27,31] corresponding to 1.5 to 2 g/L of plasma fibrinogen [53]. This is substantially higher than the threshold level of fibrinogen at 0.8 to 1 g/L recommended by most international guidelines [16,17]. However, 2 recent RCTs [27,31] and a matched case-control study with contemporary controls [12] from European countries, in which fibrinogen concentrate is licensed for the treatment of acquired hypofibrinogenemia, demonstrated that the requirements for fibrinogen concentrate were similar between the ROTEM-guided and control groups. The use of FFP is more cumbersome because each unit needs to be thawed (note: thawed plasma is unavailable in most European hospitals) and to be blood type compatible. The recent European clinical experiences with fibrinogen concentrate under ROTEM guidance [12,26,27,31] resulted in higher targeted fibrinogen levels (>1.5 g/L) and reduced FFP usage. However, acquired hypofibrinogenemia after major surgery and trauma is presumed to be an important cause of bleeding [20,54], but further trials are needed to establish the most effective fibrinogen target as assessed by ROTEM or Clauss assay in cardiac surgery or other invasive procedures.

The reduction of platelet transfusion by TEG or ROTEM was also observed, but it was not extensively different from the control group. Platelet transfusion is conventionally triggered by platelet count below $100 \times 10^3/\mu L$. The empirical trigger value was never adequately tested in the perioperative setting, and in one study, Avidan et al [14] demonstrated that platelet transfusion rates were similar in both groups using a trigger value of below $50 \times 10^3/\mu L$. In contrast, trigger value in patients with recent intake of antiplatelet medications such as aspirin and P_2Y_{12} receptor agonists might be even higher than $100 \times 10^3/\mu L$. Commonly used TEG test and all ROTEM tests are not influenced by most platelet inhibitors, and the value of platelet function monitoring in the perioperative setting is poorly standardized and its values are limited in this setting by its dependency on platelet count [55]. The indication and trigger values for its intraoperative and postoperative use of platelet concentrates remains, therefore, unclear [38], and transfusion of platelets are often triggered by educated guess based on additional information as the medical history of the patient. Earlier studies using the TEG device did not have sufficient sensitivity to differentiate between hypofibrinogenemia and thrombocytopenia [50]. Therefore, the transfusion of platelets might have been similar in the intervention and control groups in earlier TEG studies [14,30]. Finally, the triggers for platelet transfusion based on MCF or amplitude after 10 or 15 minutes (A10 and A15) in TEG and ROTEM studies are mostly empirical, and these cutoff values were never adequately validated.

Interestingly, the frequency of RBC transfusion was also consistently decreased in patients with a ROTEM- or TEG-guided transfusion algorithm in comparison with the control group, despite identical triggers for RBC transfusion. Triggers for RBC transfusion are based on hemoglobin or hematocrit measurements. Therefore, it might be concluded that hemoglobin and hematocrit levels were decreased more distinctly during and after cardiac surgery in patients with a management based on standard laboratory tests or on clinical decision. It is also speculated that the transfusion of FFP leads to a dilution of the RBCs, whereas reduced FFP transfusion or small volumes of coagulation factor concentrates might lead to higher hemoglobin levels [56] and platelet count after surgery [28,31].

The question arises whether the difference found in our study is based on too liberal transfusion triggers in the control groups [57]. In fact, we cannot exclude that a more restrictive blood management in the control groups might have led to similar transfusion rates, as in the TEG- and ROTEM-guided groups. There is a paucity of evidence to support these hemostatic trigger values because most of them were never adequately tested (eg, discriminative analysis using the receiver operating characteristic curve). Another limitation is the turnaround time of laboratory testing, and clinical judgment to transfuse with FFP and platelets might have been made when the results were unavailable within reasonable time in patients with bleeding [27,31].

Reduced transfusion rates in the TEG- or ROTEM-guided groups are reported not only in cardiac surgery but also in liver transplant [58] and trauma [59]. Particularly in liver transplantation, coagulation monitoring by TEG or ROTEM was useful in identifying coagulopathy [60], whereas standard coagulation testing is of limited value in such patients. The same seems to be true in patients with trauma. However, evidence for the use of TEG or ROTEM is limited because of the low number of RCTs in these populations, and the same limitations of inadequately triggered transfusion by conventional laboratory tests exist.

Lastly, it is important to discuss the use of antifibrinolytics in cardiac surgery. Both TEG and ROTEM can detect systemic fibrinolysis when profibrinolytic enzymes, tissue plasminogen activator and plasmin, override the endogenous antifibrinolytic system [61]. In cardiac surgery, ε-aminocaproic acid or tranexamic acid is routinely used during cardiopulmonary bypass; therefore, seeing fibrinolysis on TEG or ROTEM is rare. The lack of systemic fibrinolysis does not exclude the usefulness of antifibrinolytic therapy because lysine analogues have been repeatedly shown to reduce postoperative bleeding in cardiac and other surgical procedures [62]. In contrast, in high-risk cases for thrombosis, for example, ongoing sepsis, vegetation on native or prosthetic valves, liver dysfunction, or on extracorporeal membrane oxygenation, it may be important to selectively use an antifibrinolytic agent only when fulminant fibrinolysis is detected on TEG or ROTEM.

This review has several strengths and limitations. Compared with the previous systematic reviews [40,41], it includes newer studies [12,27,31], which partially showed an improved outcome and decreased mortality in patients with ROTEM-guided transfusion management. By assessing MEDLINE database, checking reference lists in articles of interest, and referring to experts in the field, we might have identified and included the most important studies. In addition, we included not only RCTs but also retrospective studies with historical controls and matched case-control studies. One of these studies included more than 50% of patients, thereby potentially

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overwhelming the other studies. However, ORs for transfusion were minimally altered when including RCTs only. Furthermore, exact numbers of transfused allogeneic blood products were not evaluated, and the definitions of massive bleeding and/or transfusion varied between the included studies. These limitations might have contributed to the different findings compared with earlier meta-analyses [40,41]. Finally, reliability, maintenance, and calibration of POC devices outside the central laboratory setting might be questioned. In fact, none of the included studies stated regular quality control of the device's performance.

Conclusion

It is presumed that transfusion algorithms based on TEG or ROTEM are more restricted on the use of FFP and platelets compared with the guidance based on commonly used laboratory tests without increasing bleeding diathesis after cardiac surgery. Furthermore, it is speculated that viscoelastic testing leads to lesser transfusion of RBCs because of the lack of hemodilution by FFP transfusion. These views are strongly corroborated by the findings in 7 RCTs. In addition, the use of TEG or ROTEM is acceptable in guiding the selective use of factor concentrates in a timely manner. There is still a lack of clear evidence for improved patient outcome with TEG or ROTEM, which warrants further studies.

References

[1] Johnson JL, Moore EE, Kashuk JL, Banerjee A, Cothren CC, Biffl WL, et al. Effect of blood products transfusion on the development of postinjury multiple organ failure. Arch Surg 2010;145:973–7.
[2] Karkouti K, Wijeysundera DN, Yau TM, Beattie WS, Abdelnaem E, McCluskey SA, et al. The independent association of massive blood loss with mortality in cardiac surgery. Transfusion 2004;44:1453–62.
[3] Koch CG, Li L, Duncan AI, Mihaljevic T, Loop FD, Starr NJ, et al. Transfusion in coronary artery bypass grafting is associated with reduced long-term survival. Ann Thorac Surg 2006;81:1650–7.
[4] Spiess BD, Royston D, Levy JH, Fitch J, Dietrich W, Body S, et al. Platelet transfusions during coronary artery bypass graft surgery are associated with serious adverse outcomes. Transfusion 2004;44:1143–8.
[5] Isbister JP, Shander A, Spahn DR, Erhard J, Farmer SL, Hofmann A. Adverse blood transfusion outcomes: establishing causation. Transfus Med Rev 2011;25:89–101.
[6] Vamvakas EC, Blajchman MA. Blood still kills: six strategies to further reduce allogeneic blood transfusion–related mortality. Transfus Med Rev 2010;24:77–124.
[7] Ferraris VA, Saha SP, Oestreich JH, Song HK, Rosengart T, Reece TB, et al. 2012 Update to the Society of Thoracic Surgeons guideline on use of antiplatelet drugs in patients having cardiac and noncardiac operations. Ann Thorac Surg 2012;94:1761–81.
[8] Carroll RC, Chavez JJ, Snider CC, Meyer DS, Muenchen RA. Correlation of perioperative platelet function and coagulation tests with bleeding after cardiopulmonary bypass surgery. J Lab Clin Med 2006;147:197–204.
[9] Crowther MA, Warkentin TE. Bleeding risk and the management of bleeding complications in patients undergoing anticoagulant therapy: focus on new anticoagulant agents. Blood 2008;111:4871–9.
[10] Karlsson M, Ternstrom L, Hyllner M, Baghaei F, Flinck A, Skrtic S, et al. Prophylactic fibrinogen infusion reduces bleeding after coronary artery bypass surgery. A prospective randomised pilot study. Thromb Haemost 2009;102:137–44.
[11] Sniecinski RM, Chen EP, Makadia SS, Kikura M, Bolliger D, Tanaka KA. Changing from aprotinin to tranexamic acid results in increased use of blood products and recombinant factor VIIa for aortic surgery requiring hypothermic arrest. J Cardiothorac Vasc Anesth 2010;24:959–63.
[12] Fassl J, Matt P, Eckstein F, Filipovic M, Gregor M, Zenklusen U, et al. Transfusion of allogeneic blood products in proximal aortic surgery with hyopthermic circulatory arrest: effects of thromboelastometry-guided transfusion management. J Cardiothorac Vasc Anesth 2013. http://dx.doi.org/10.1053/j.jvca.2013.02.009.
[13] Spahn DR, Goodnough LT. Alternatives to blood transfusion. Lancet 2013;381:1855–65.
[14] Avidan MS, Alcock EL, Da Fonseca J, Ponte J, Desai JB, Despotis GJ, et al. Comparison of structured use of routine laboratory tests or near-patient assessment with clinical judgement in the management of bleeding after cardiac surgery. Br J Anaesth 2004;92:178–86.
[15] Nuttall GA, Oliver WC, Santrach PJ, Bryant S, Dearani JA, Schaff HV, et al. Efficacy of a simple intraoperative transfusion algorithm for nonerythrocyte component utilization after cardiopulmonary bypass. Anesthesiology 2001;94:773–81.
[16] Practice guidelines for perioperative blood transfusion and adjuvant therapies: an updated report by the American Society of Anesthesiologists Task Force on Perioperative Blood Transfusion and Adjuvant Therapies. Anesthesiology 2006;105:198–208.
[17] O'Shaughnessy DF, Atterbury C, Bolton Maggs P, Murphy M, Thomas D, Yates S, et al. Guidelines for the use of fresh-frozen plasma, cryoprecipitate and cryosupernatant. Br J Haematol 2004;126:11–28.
[18] Rossaint R, Bouillon B, Cerny V, Coats TJ, Duranteau J, Fernandez-Mondejar E, et al. Management of bleeding following major trauma: an updated European guideline. Crit Care 2010;14:R52.
[19] Nuttall GA, Oliver WC, Ereth MH, Santrach PJ. Coagulation tests predict bleeding after cardiopulmonary bypass. J Cardiothorac Vasc Anesth 1997;11:815–23.
[20] Bolliger D, Görlinger K, Tanaka KA. Pathophysiology and treatment of coagulopathy in massive hemorrhage and hemodilution. Anesthesiology 2010;113:1205–19.
[21] Bolliger D, Seeberger MD, Tanaka KA. Principles and practice of thromboelastography in clinical coagulation management and transfusion practice. Transfus Med Rev 2012;26:1–13.
[22] Lee GC, Kicza AM, Liu KY, Nyman CB, Kaufman RM, Body SC. Does rotational thromboelastometry (ROTEM) improve prediction of bleeding after cardiac surgery? Anesth Analg 2012;115:499–506.
[23] Tanaka KA, Bolliger D, Vadlamudi R, Nimmo A. Rotational thromboelastometry (ROTEM)–based coagulation management in cardiac surgery and major trauma. J Cardiothorac Vasc Anesth 2012;26:1083–93.
[24] Ak K, Isbir CS, Tetik S, Atalan N, Tekeli A, Aljodi M, et al. Thromboelastography-based transfusion algorithm reduces blood product use after elective CABG: a prospective randomized study. J Card Surg 2009;24:404–10.
[25] Anderson L, Quasim I, Soutar R, Steven M, Macfie A, Korte W. An audit of red cell and blood product use after the institution of thromboelastometry in a cardiac intensive care unit. Transfus Med 2006;16:31–9.
[26] Girdauskas E, Kempfert J, Kuntze T, Borger MA, Enders J, Fassl J, et al. Thromboelastometrically guided transfusion protocol during aortic surgery with circulatory arrest: a prospective, randomized trial. J Thorac Cardiovasc Surg 2010;140:1117–24.
[27] Görlinger K, Dirkmann D, Hanke AA, Kamler M, Kottenberg E, Thielmann M, et al. First-line therapy with coagulation factor concentrates combined with point-of-care coagulation testing is associated with decreased allogeneic blood transfusion in cardiovascular surgery: a retrospective, single-center cohort study. Anesthesiology 2011;115:1179–91.
[28] Romlin BS, Wahlander H, Berggren H, Synnergren M, Baghaei F, Nilsson K, et al. Intraoperative thromboelastometry is associated with reduced transfusion prevalence in pediatric cardiac surgery. Anesth Analg 2011;112:30–6.
[29] Shore-Lesserson L, Manspeizer HE, DePerio M, Francis S, Vela-Cantos F, Ergin MA. Thromboelastography-guided transfusion algorithm reduces transfusions in complex cardiac surgery. Anesth Analg 1999;88:312–9.
[30] Spiess BD, Gillies BS, Chandler W, Verrier E. Changes in transfusion therapy and reexploration rate after institution of a blood management program in cardiac surgical patients. J Cardiothorac Vasc Anesth 1995;9:168–73.
[31] Weber CF, Görlinger K, Meininger D, Herrmann E, Bingold T, Moritz A, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. Anesthesiology 2012;117:531–47.
[32] Royston D, von Kier S. Reduced haemostatic factor transfusion using heparinase-modified thrombelastography during cardiopulmonary bypass. Br J Anaesth 2001;86:575–8.
[33] Görlinger K, Dirkmann D, Solomon C, Hanke AA. Fast interpretation of thromboelastometry in non-cardiac surgery: reliability in patients with hypo-, normo-, and hypercoagulability. Br J Anaesth 2013;110:222–30.
[34] Khan H, Belsher J, Yilmaz M, Afessa B, Winters JL, Moore SB, et al. Fresh-frozen plasma and platelet transfusions are associated with development of acute lung injury in critically ill medical patients. Chest 2007;131:1308–14.
[35] Murphy GJ, Reeves BC, Rogers CA, Rizvi SI, Culliford L, Angelini GD. Increased mortality, postoperative morbidity, and cost after red blood cell transfusion in patients having cardiac surgery. Circulation 2007;116:2544–52.
[36] Sarani B, Dunkman WJ, Dean L, Sonnad S, Rohrbach JI, Gracias VH. Transfusion of fresh frozen plasma in critically ill surgical patients is associated with an increased risk of infection. Crit Care Med 2008;36:1114–8.
[37] Watson GA, Sperry JL, Rosengart MR, Minei JP, Harbrecht BG, Moore EE, et al. Fresh frozen plasma is independently associated with a higher risk of multiple organ failure and acute respiratory distress syndrome. J Trauma 2009;67:221–7.
[38] Kozek-Langenecker SA, Afshari A, Albaladejo P, Santullano CA, De Robertis E, Filipescu DC, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. Eur J Anaesthesiol 2013;30:270–382.
[39] Spalding GJ, Hartrumpf M, Sierig T, Oesberg N, Kirschke CG, Albes JM. Cost reduction of perioperative coagulation management in cardiac surgery: value of "bedside" thrombelastography (ROTEM). Eur J Cardiothorac Surg 2007;31:1052–7.
[40] Wikkelsoe AJ, Afshari A, Wetterslev J, Brok J, Moeller AM. Monitoring patients at risk of massive transfusion with thrombelastography or thromboelastometry: a systematic review. Acta Anaesthesiol Scand 2011;55:1174–89.
[41] Afshari A, Wikkelso A, Brok J, Moller AM, Wetterslev J: Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion. *Cochrane Database Syst Rev* 2011:CD007871.
[42] Roback JD, Caldwell S, Carson J, Davenport R, Drew MJ, Eder A, et al. Evidence-based practice guidelines for plasma transfusion. Transfusion 2010;50:1227–39.
[43] Toulon P, Ozier Y, Ankri A, Fleron MH, Leroux G, Samama CM. Point-of-care versus central laboratory coagulation testing during haemorrhagic surgery. A multicenter study. Thromb Haemost 2009;101:394–401.
[44] 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;52:14–22.

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[45] Bolliger D, Szlam F, Molinaro RJ, Rahe-Meyer N, Levy JH, Tanaka KA. Finding the optimal concentration range for fibrinogen replacement after severe haemodilution: an in vitro model. Br J Anaesth 2009;102:793–9.
[46] Nielsen VG, Cohen BM, Cohen E. Effects of coagulation factor deficiency on plasma coagulation kinetics determined via thrombelastography: critical roles of fibrinogen and factors II, VII, X and XII. Acta Anaesthesiol Scand 2005;49:222–31.
[47] Rumph B, Bolliger D, Narang N, Molinaro RJ, Levy JH, Szlam F, et al. In vitro comparative study of hemostatic components in warfarin-treated and fibrinogen-deficient plasma. J Cardiothorac Vasc Anesth 2010;24:408–12.
[48] Nascimento B, Al Mahoos M, Callum J, Capone A, Pacher J, Tien H, et al. Vitamin K–dependent coagulation factor deficiency in trauma: a comparative analysis between international normalized ratio and thromboelastography. Transfusion 2012;52:7–13.
[49] Casutt M, Konrad C, Schuepfer G. Effect of rivaroxaban on blood coagulation using the viscoelastic coagulation test ROTEM. Anaesthesist 2012;61:948–53.
[50] Larsen OH, Fenger-Eriksen C, Christiansen K, Ingerslev J, Sorensen B. Diagnostic performance and therapeutic consequence of thromboelastometry activated by kaolin versus a panel of specific reagents. Anesthesiology 2011;115:294–302.
[51] Kozek-Langenecker S, Sorensen B, Hess JR, Spahn DR. Clinical effectiveness of fresh frozen plasma compared with fibrinogen concentrate: a systematic review. Crit Care 2011;15:R239.
[52] Lin DM, Murphy LS, Tran MH. Use of prothrombin complex concentrates and fibrinogen concentrates in the perioperative setting: a systematic review. Transfus Med Rev 2013;27:91–104.
[53] Ogawa S, Szlam F, Bolliger D, Nishimura T, Chen EP, Tanaka KA. The impact of hematocrit on fibrin clot formation assessed by rotational thromboelastometry. Anesth Analg 2012;115:16–21.
[54] Karkouti K, Callum J, Crowther MA, McCluskey SA, Pendergrast J, Tait G, et al. The relationship between fibrinogen levels after cardiopulmonary bypass and large volume red cell transfusion in cardiac surgery: an observational study. Anesth Analg 2013;117:14–22.
[55] Bolliger D, Seeberger MD, Tanaka KA, Dell-Kuster S, Gregor M, Zenklusen U, et al. Pre-analytical effects of pneumatic tube transport on impedance platelet aggregometry. Platelets 2009;20:458–65.
[56] Demeyere R, Gillardin S, Arnout J, Strengers PF. Comparison of fresh frozen plasma and prothrombin complex concentrate for the reversal of oral anticoagulants in patients undergoing cardiopulmonary bypass surgery: a randomized study. Vox Sang 2010;99:251–60.
[57] Ereth MH. Decision to transfuse comfort zones: move out or get pushed out. Transfusion 2012;52:2–3.
[58] Wang SC, Shieh JF, Chang KY, Chu YC, Liu CS, Loong CC, et al. Thromboelastography-guided transfusion decreases intraoperative blood transfusion during orthotopic liver transplantation: randomized clinical trial. Transplant Proc 2010; 42:2590–3.
[59] Schochl H, Nienaber U, Maegele M, Hochleitner G, Primavesi F, Steitz B, et al. Transfusion in trauma: thromboelastometry-guided coagulation factor concentrate-based therapy versus standard fresh frozen plasma-based therapy. Crit Care 2011;15:R83.
[60] 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;20:548–53.
[61] Bolliger D, Szlam F, Levy JH, Molinaro RJ, Tanaka KA. Haemodilution-induced profibrinolytic state is mitigated by fresh-frozen plasma: implications for early haemostatic intervention in massive haemorrhage. Br J Anaesth 2010;104: 318–25.
[62] Ker K, Edwards P, Perel P, Shakur H, Roberts I. Effect of tranexamic acid on surgical bleeding: systematic review and cumulative meta-analysis. BMJ 2012;344:e3054.

Please cite this article as: Bolliger D, Tanaka KA, Roles of Thrombelastography and Thromboelastometry for Patient Blood Management in Cardiac Surgery, Tranfus Med Rev (2013), http://dx.doi.org/10.1016/j.tmrv.2013.08.004