

Preoperative thromboelastometry for the prediction of increased chest tube output in cardiac surgery

A retrospective study

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Abstract

Bleeding following cardiac surgery is a serious event with potentially life-threatening consequences. Preoperative recognition of coagulation abnormalities and detection of cardiopulmonary bypass (CPB) related coagulopathy could aid in the start of preventive treatment strategies that minimize perioperative blood loss. Most algorithms that analyze thromboelastometry coagulation tests in elective cardiac surgery do not include test results performed before surgery. We evaluated preoperative rotational thromboelastometry test results for their ability to predict blood loss during and after cardiac surgery.

A total of 114 adult patients undergoing cardiac surgery with CPB were included in this retrospective analysis. Each patient had thromboelastometry tests done twice: preoperatively, before the induction of anesthesia and postoperatively, 10 minutes after heparin reversal with protamine after decannulation.

Patients were placed into 1 of 2 groups depending on whether preoperative thromboelastometry parameters deviated from reference ranges: Group 1 [N=29; extrinsically activated test (EXTEM) or INTEM results out of normal range] or Group 2 (N=85; EXTEM and INTEM results within the normal range). We observed that the total amount of chest tube output was significantly greater in Group 1 than in Group 2 (700 mL vs 570 mL, $P=.03$). At the same time, the preoperative values of standard coagulation tests such as platelet count, aPTT, and INR did not indicate any abnormalities of coagulation.

Preoperative coagulation abnormalities diagnosed with thromboelastometry can predict increased chest tube output in the early postoperative period in elective adult cardiac surgery. Monitoring of the coagulation system with thromboelastometry allows rapid diagnosis of coagulation abnormalities even before the start of the surgery. These abnormalities could not always be detected with routine coagulation tests.

Abbreviations: A10 min = clot firmness after 10 minutes, ACC = aortic cross-clamping, AVR = aortic valve replacement, CABG = coronary artery bypass grafting, CFT = clot formation time, CPB = cardiopulmonary bypass, CT = clotting time, FAP/ FAC = paroxysmal atrial fibrillation/continuous atrial fibrillation, MCF = maximum clot firmness, ML = maximum lysis, MVR = mitral valve replacement, POC = point-of-care.

Keywords: critical care, point-of-care testing, thromboelastometry

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1. Introduction

Bleeding following cardiac surgery is a serious event with potentially life-threatening consequences. Preoperative recognition of coagulation abnormalities, as well as detection of cardiopulmonary bypass (CPB) related coagulopathy could aid in the start of preventive treatment strategies that minimize perioperative blood loss and transfusion requirements. Conventional laboratory tests, although often used, are not very helpful in directing transfusion management in these situations, due to the long turn-around time. A point-of-care (POC) diagnostic tool such as thromboelastometry, which is based on analyzing samples of whole blood, is becoming more commonly used to detect coagulopathy. The results are also used to monitor therapy with blood products.^[1] This type of method measures various parameters of the actual coagulation process, including clot development and the maximal strength of a clot.^[2] Thromboelastometry not only gives a comprehensive picture of the hemostatic status, but also indicates major underlying pathomechanisms of coagulopathy. Thromboelastometry test results can be obtained directly after taking samples, and therefore, goal-directed therapy can be started in a timely manner^[3]; algorithms that incorporate detailed thromboelastometry analysis can be used to diagnose the cause of bleeding and indicate treatment.

The information obtained from these algorithms can lessen the need for transfusing blood products, in contrast to empiric therapy or transfusion algorithms based on standard laboratory coagulation tests.^[4–6]

Most algorithms that analyze POC thromboelastometry tests in elective cardiac surgery do not include preoperative test results performed before surgery, because of the assumption that there were no abnormalities in the coagulation system.^[7] The assumption is based on routine coagulation tests, the patient's general condition, and/or pharmacological treatment.

In this study, we examined the predictive value of preoperative thromboelastometry test indices in adult patients scheduled for first time cardiac surgery with CPB. Specifically, we examined whether excessive postoperative chest tube output was associated with abnormal preoperative values of thromboelastometry extrinsically activated test (EXTEM) and INTEM tests and other standard preoperative coagulation tests.

1. Subjects and methods

1.1. Patients

The study was designed as an observational, retrospective analysis of adult patients scheduled for first time cardiac surgery with cardiopulmonary bypass (CPB). The Bioethics Committee of Wroclaw Medical University approved the study and informed consent was not required due to the retrospective, observational character of the study (No. KB-528/2013). The study was conducted in accordance with the principles expressed in the Declaration of Helsinki. The surgery was performed at the Department of Cardiothoracic Surgery and postoperative care was at the Department of Anesthesiology and Intensive Therapy University Hospital between December 2013 and May 2014. Patients' medical records were searched for data. Patient data for analysis were analyzed anonymously.

Inclusion criteria: included in the study were consecutive patients scheduled for first time cardiac surgery with CPB who had thromboelastometry tests done twice, before and after surgery. The first thromboelastometry measurement was performed preoperatively, before the induction of anesthesia and the second measurement was performed postoperatively, 10 minutes

after heparin reversal with protamine after decannulation and activated clotting time confirmation.

Exclusion criteria: excluded from the study were patients scheduled for off-pump cardiac surgery, patients scheduled for repeated cardiac surgery, patients scheduled for non-elective surgery, patients who had not had thromboelastometry measurements done before and after surgery. Flow chart illustrating selection of the study group is presented in Fig. 1.

All patients included in the final analysis were stratified according to thromboelastometry results done before surgery (baseline). Patients were placed into 1 of 2 groups depending on whether there had been any deviation in the reference ranges of the EXTEM or INTEM parameters.

Group 1 with coagulation abnormalities at baseline; at least one of the following baseline EXTEM or INTEM parameters was out of the reference range: clotting time (CT) above the upper limit, clot formation time (CFT) above the upper limit, an alpha angle below the lower limit, clot firmness after 10 minutes (A10 min) or maximum clot firmness (MCF) value below the lower limit.

Group 2 with a normal coagulation pattern; EXTEM or INTEM parameters (CT, CFT, alpha angle, A (10 min), and MCF were within reference ranges at baseline (see supplemental material for reference ranges for ROTEM tests).

Patients who had been treated with acetylsalicylic acid to prevent cardiovascular disease had therapy maintained until the operation, and for patients treated with clopidogrel, the therapy was stopped 5 days before the planned surgery. None of the patients was treated with heparin before surgery.

1.2. Anesthetic and surgical procedures

The anesthetic and surgical procedures were previously described in detail.^[8] General anesthesia was induced with sufentanil and propofol. Rocuronium at a dose of 0.6 mg/kg was administered to facilitate intubation. For maintenance of general anesthesia, 1 to 3 vol% sevoflurane and continuous sufentanil infusion at 0.2–0.5 µg/kg/h were used. Uniform surgical and myocardial protective techniques were the same for all patients according to institutional protocols. In all patients, a standard open bypass circuit was used, composed of uncoated polyvinylchloride tubing,

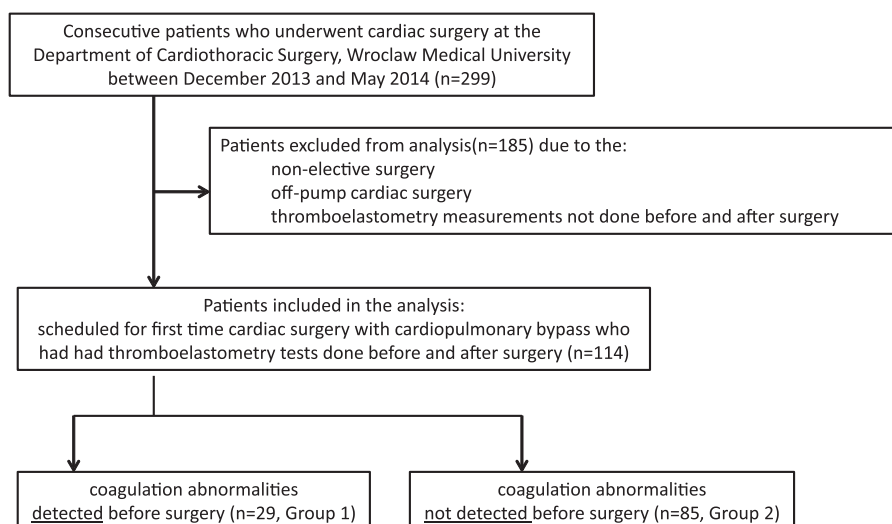


Figure 1. Flow chart illustrating selection of the study groups.

a hard-shell venous reservoir (Affinity CVR Reservoir), a hollow fiber membrane oxygenator (Affinity NT Oxygenator CB 511 from Medtronic Cardiac Surgery, Minneapolis, MN), and a roller pump with no pulsatile flow 2.2 to 2.4 L/min/m² (Stockert S3, Sorin Group, Germany). Heparin was administered after an initial bolus of 300 IU/kg to maintain activated clotting time (ACT) > 480 seconds. Heparin activity was reversed with protamine administration after decannulation. A dose of 1 g tranexamic acid was given at the induction of anesthesia and after protamine administration. Weaning from the bypass was initiated once the cardiac rhythm had stabilized and normothermia had been achieved. Packed red blood cells were transfused if the hematocrit was < 22% during the bypass and < 25% after terminating the bypass. Blood products supplementation was based on the hemostatic therapy algorithms provided by Weber et al.^[9]

After surgery, patients were transferred to the intensive care unit. Propofol sedation 0.5 to 1.0 mg/kg/h was continued until the patient was weaned from the ventilator and extubated, according to the institutional protocol. Symptoms of myocardial ischemia, the need for inotropic support, and heart rhythm disturbances were recorded postoperatively.

1.3. Thromboelastometry method

For each patient indicated by the attending anesthesiologist, the standard procedure was done twice by the same *laboratory technician immediately after sample collection and always using the same instrument* (ROTEM thromboelastometry analyzer, Pentapharm GmbH, Germany). All EXTEM, INTEM, FIBTEM, and APTEM experiments were conducted rigorously, with appropriate controls; tests were performed according to the manufacturer's procedures. All measurements were done promptly after collecting blood as *point-of-care tests*. Thromboelastometric parameters analyzed were: (1) clotting time (CT), (2) clot formation time (CFT), (3) clot firmness after 10 minutes (A10 min), and maximum clot firmness (MCF) and maximum lysis at 60 minutes (ML). CT describes the beginning of clotting, indicates the dynamics of clot formation, and is dependent on clotting factors and anticoagulants. CFT describes the next phase of clotting—the kinetics of clot formation between a 2 mm and 20 mm amplitude of the clotting signal; it is impacted by platelets and fibrinogen that contribute to clot firmness. Parameters A10 and MCF give information about clot formation, clot strength, and stability after 10 and 30 minutes and are impacted by platelets, the concentration of fibrinogen and its ability to polymerize, other clotting factors, and the status of fibrinolysis. The parameter of maximum lysis measured in EXTEM and INTEM tests describes the degree of fibrinolysis.

In the EXTEM test, extrinsic activation is observed by adding a tissue factor to stimulate coagulation. EXTEM is sensitive to disturbances of the extrinsic coagulation factors, platelets, fibrinogen, and fibrin polymerization. In the INTEM test, ellagic acid is used to activate coagulation to observe intrinsic activation. The INTEM test is designed for global analysis of coagulation, to assess the interaction between intrinsic coagulation factors and platelets. In the ATPEM test aprotinin, a plasmin antagonist is added to inhibit fibrinolysis. The APTEM test allows for early recognition of hyperfibrinolysis in the blood sample. In the FIBTEM test, the platelet function is blocked with cytochalasin D; therefore, the obtained clot is mainly a fibrin clot. With the FIBTEM test, a differentiation can be made between disturbances in platelet function and the fibrin polymerization process.

1.4. Outcomes and statistical analysis

Patient medical records were reviewed for demographic data, surgical procedures and clinical data, routine laboratory test results, and chest tube output. The information about the presence of arterial hypertension, left main stenosis, triple vessel disease, and previous myocardial infarction were collected. The chest tube output was recorded at day 0 (day of surgery), day 1 (24 hours after surgery), and day 2 (48 hours after surgery). The hospital survival rate was recorded. For each patient, thromboelastometry was done twice: before surgery and after surgery.

Data were analyzed with Statistica version 12.0 (StatSoft, Inc. Tulsa). Continuous variables are presented as medians and interquartile range (25th and 75th percentiles). The distribution of the data was not normal, as revealed by a Shapiro-Wilk test and statistical analysis was performed using nonparametric methods—the Mann-Whitney *U* test or Wilcoxon matched pairs test. Categorical variables were analyzed using a Pearson Chi-square test or Fisher exact test when necessary. The study sample size was calculated based on the preliminary data with Statistica 12 for a power of 60% and alpha level at 0.05. For the chest tube output data, the Box-Cox transformation was applied to stabilize variances and the *t*-test was used to compare differences between Group 1 and Group 2. Statistical significance was determined as $P \leq .05$.

2. Results

Out of 299 patients who underwent cardiac surgery with CPB, 114 met the criteria and were included in the final analysis. Depending on the baseline results of EXTEM and INTEM thromboelastometry tests, patients were placed into Group 1 (N=29; EXTEM or INTEM results out of normal range) or Group 2 (N=85; EXTEM and INTEM results within normal range). Patients with coagulation parameters out of normal range before the start of surgery accounted for 25% of the study population. The most common co-morbidities diagnosed in studied patients were previous myocardial infarction and arterial hypertension. The baseline characteristics were comparable between the 2 groups of patients (Table 1).

Table 1
Baseline characteristics of patients.

	Group 1 (N=29)	Group 2 (N=85)	P
Age, years	70 (60–75)	66 (58–72)	.29
Gender: female/male, % male	8/21 (72)	30/55 (65)	.44
Co-morbidities, n, %			
Previous myocardial infarction	10 (34)	43 (51)	.12
Arterial hypertension	25 (86)	67 (79)	.44
FAP/FAC	7 (24)	20 (24)	.97
Kidney failure stage III	4 (14)	11 (13)	.94
Anticoagulation drugs before surgery, n, %			
Clopidogrel	4 (14)	17 (20)	.87
Acetylsalicylic acid	7 (24)	29 (34)	.86
Previous stroke, n, %	6 (20)	9 (10)	.18
Diabetes	5 (17)	18 (21)	.70
Ejection fraction, %	58 (43–60)	60 (45–60)	.83
	(min 30, max 65)	(min 20, max 70)	

Data presented as medians with 25th and 75th percentiles, unless other stated.
FAP/ FAC: paroxysmal atrial fibrillation/continuous atrial fibrillation.

Table 2

Thromboelastometry EXTEM, INTEM, and FIBTEM results measured before and after surgery.

	Ref. range	Before surgery		P*	After surgery		P*
		Group 1	Group 2		Group 1	Group 2	
EXTEM							
CT, s	38–79	89 (80–112)	56 (50–62)	<.001	131 (89–180)	67 (59–77)	<.001
CFT, s	34–159	76 (63–93)	65 (57–77)	.01	112 (92–125)	90 (78–104)	<.001
A (10), mm	43–65	61 (52–67)	61 (58–64)	.86	58 (48–62)	54 (50–57)	.12
MCF, mm	50–72	68 (61–72)	67 (64–69)	.82	65 (58–69)	62 (59–64)	.13
ML, %	<15	12 (7–14)	12 (9–15)	.21	5 (3–8)	6 (3–9)	.83
INTEM							
CT, s	100–240	165 (146–204)	165 (151–180)	.63	196 (170–229)	200 (175–216)	.99
CFT, s	30–110	65 (52–115)	60 (51–68)	.06	75 (63–124)	85 (72–99)	.71
A (10), mm	44–65	59 (52–64)	60 (55–64)	.32	55 (45–59)	53 (49–56)	.99
MCF, mm	50–72	65 (58–69)	65 (61–69)	.47	63 (57–667)	61 (57–65)	.84
ML, %	<15	11 (10–14)	12 (9–15)	.74	5 (3–7)	5 (2–8)	.80
FIBTEM							
MCF, mm	9–25	21 (17–25)	20 (17–25)	.85	17 (11–20)	15 (13–19)	.71

Data presented as medians with 25th and 75th percentiles.

CFT=clot formation time, CT=clotting time, MCF=maximum clot firmness, ML=maximum lysis.

* P in comparison between groups.

2.1. Indices of coagulation parameters

2.1.1. Before surgery. Preoperatively, 72% of patients (n=21) had elongated CT in the EXTEM test and 18% (n=8) had elongated CFT in the INTEM test in Group 1 (Table 2). The values of other parameters (alpha angle, A (10), MCF and ML) measured in EXTEM and INTEM were within normal range in Group 1 and all thromboelastometry parameters were within the reference range in Group 2. The difference in EXTEM CT was significant between groups before surgery (P<.001) (Fig. 2). At the same time, the preoperative values of standard coagulation tests such as platelet count, aPTT, and INR values were within the normal range and did not indicate any abnormalities of coagulation; no marked differences in platelet count, aPTT, and INR values were recorded between groups (Table 3).

In the FIBTEM test, the values of clot firmness (MCF) were similar in both groups and did not indicate any fibrin deficiency and/or disturbances in the process of fibrin polymerization before

surgery (Table 2). Abnormal values of parameters measured in EXTEM were not corrected in the APTEM test; therefore, hyperfibrinolysis was not detected in any sample.

2.1.2. After surgery. After CPB, the differences between groups in EXTEM CT remained significant (P<.001) (Fig. 1). Moreover, the median CT was almost twice longer in Group 1 than in Group 2 (131s vs 67s). There were no significant differences between groups in INTEM CT, CFT, alpha angle, A (10), MCF, and ML measured after CPB.

In the FIBTEM test, the values of clot firmness (MCF) were similar in both groups and did not indicate any fibrin deficiency and/or disturbances in the process of fibrin polymerization after CPB (Table 2). Similarly like before surgery, abnormal values of parameters measured in EXTEM were not corrected in the APTEM test; therefore, hyperfibrinolysis was not detected in any sample. The median platelet count was within the reference range on the 1st and 2nd day after surgery (Table 3).

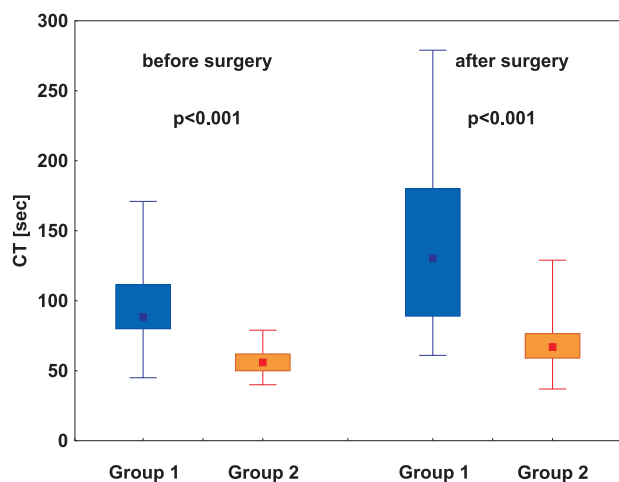


Figure 2. EXTEM clotting time (CT) measured in Group 1 (blue bars) and Group 2 (orange bars) before and after surgery. Data are expressed as median (middle point), interquartile ranges (box), and minimum and maximum (whiskers); P value represents the difference between groups. EXTEM=extrinsically activated test.

2.2. Surgery procedures and chest tube output

The main surgical procedures were CABG (coronary artery bypass grafting) and AVR/MVR (aortic valve replacement / mitral valve replacement). The mean CPB duration and ACC time

Table 3

Indices of the coagulation process collected before surgery (0), on the 1st (1) and 2nd day (2) after surgery.

		Group 1 (N=29)	Group 2 (N=85)	P*
Platelets	0	200 (150–228)	223 (176–263)	.01
Ref. range:	1	140 (111–179)	166 (124–205)	.05
140–440 10 ³ /μL	2	142 (111–166)	169 (131–205)	.03
APTT	0	31 (28–36)	30 (28–33)	.48
Ref. range:	1	35 (32–37)	36 (31–43)	.47
25–37 s	2	39 (33–44)	38 (33–47)	.73
INR	0	1.1 (1.0–1.2)	1.0 (0.9–1.1)	.09
Ref. range:	1	1.3 (1.2–1.4)	1.2 (1.2–1.3)	.10
0.9–1.3	2	1.2 (1.1–1.3)	1.1 (1.0–1.2)	.01

* P in comparison between groups.

Table 4**Surgery and follow up in Group 1 and Group 2.**

	Group 1 (N=29)	Group 2 (N=85)	P
Type of surgery, n, %			.23
CABG	13 (44)	48 (56)	
AVR/MVR	6 (21)	17 (20)	
CABG + AVR/MVR	6 (21)	17 (20)	
Aortic aneurysm	4 (14)	3 (4)	
CPB, min.	107 (87–149)	100 (75–140)	.29
ACC, min.	57 (48–89)	53 (37–81)	.28
Surgical reexploration, n	5	6	.11
Time to extubation, h	6 (4–7)	5 (4–8)	.77
Inotropes, n, %*	36 (45)	46 (54)	.43
Hospital mortality, n, %	1 (3.4)	4 (4.7)	.66

Data are presented as medians with 25th and 75th percentiles.

ACC=aortic cross-clamping, AVR=aortic valve replacement, CABG=coronary artery bypass grafting, CPB=cardiopulmonary bypass, MVR=mitral valve replacement.

*Inotropes administered during and after surgery.

were similar in both groups. Surgical re-exploration had to be performed in 10 patients (4 patients from Group 1 and 6 patients from Group 2) (Table 4). Surgical reasons of postoperative bleeding were found only in 3 cases. In the first case, after the Bentall procedure, there was a problem with tightness of the prosthesis; it was not possible to seal it efficiently. After re-exploration, the procedure was completed with packing and cell-saver use. In the second case after combined mitral and tricuspid valve surgery, the surgical cause of bleeding was noted. In the third case, surgical bleeding from vascular anastomosis was noted. In 7 other patients who needed surgical re-exploration, surgical reasons of postoperative bleeding were not found. In these patients, the reasons for re-exploration were as follows: in the Group 1, in 1 patient combined mitral and tricuspid valve surgery and in 1 patient surgical correction of dysfunctional vascular graft were performed; in the Group 2, in 2 patients surgical correction of dysfunctional vascular graft, in 1 patient combined aortic, mitral and tricuspid valves surgery, and in 2 other patients aortic valves surgery were performed during surgical re-exploration.

The total chest tube output was significantly higher in Group 1 than in Group 2 (700 mL (330–1060) vs 530 mL (390–770), $P=.03$). It was higher in Group 1 (430 mL (310–630) compared to Group 2 (380 (255–500), on day 0 ($P=.04$), and similar for both groups after surgery (180 mL (0–310) vs 150 mL (0–260), $P=.075$ on the 1st day and 0 mL (0–150) vs 0 mL (0–0), $P=.016$) on the 2nd day) (Fig. 3).

In the post-operative period, there were 34 patients who had blood products supplemented: 8 patients from Group 1 (28%) and 26 (30%) from Group 2. The average amount of red blood concentrate was similar for both groups (520 mL in Group 1, 520 mL in Group 2). The average amount of fresh frozen plasma was 2 times higher in Group 1 (960 mL) than in Group 2 (460 mL) ($P=.05$). Also, platelet concentrate supplementation was 2 times higher in Group 1 (10 units) than in Group 2 (5 units), but the differences did not reach statistical significance due to the low number of patients requiring platelet supplementation.

3. Discussion

In our study, 25% of patients referred for elective cardiac surgery had abnormal values in thromboelastometry EXTEM or INTEM

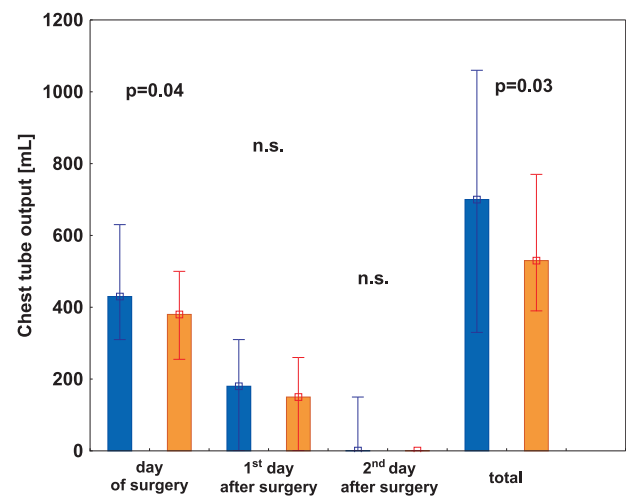


Figure 3. Chest tube output in Group 1 (blue bars) and Group 2 (orange bars) calculated on the day of surgery, 1st and 2nd day after surgery. Data are presented as medians with 25th and 75th percentiles; P value represents the difference between groups.

tests recorded before surgery. At the same time, the preoperative values of standard coagulation tests such as platelet count, aPTT, and INR did not indicate any abnormalities of coagulation. Abnormal preoperative values of thromboelastometry indices were associated with postoperative increased chest tube output in adult patients undergoing elective cardiac surgery.

Our observations showed the usefulness of thromboelastometry as a point of care screening tool for coagulation abnormalities before surgery and during the postoperative period. The first thromboelastometry POC tests were carried out immediately after insertion of the arterial cannula and before the induction of anesthesia. Thus, resulting effects of the anesthetic drugs, hemodilution, or temperature changes can be ruled out. Of note is that these observations were made in patients referred for elective surgery, without any abnormalities in standard coagulation tests done before surgery. Most algorithms in cardiac surgery do not recommend thromboelastometry tests before the surgery; the first thromboelastometry test is performed after aorta declamping during surgery.^[9,10]

In our study, thromboelastometry revealed differences between groups in EXTEM CT, CFT, and alpha angle values. According to generally accepted principles, it can be assumed that there is a deficiency of vitamin K-dependent plasma factors II, VII, IX, and/or X, if the CT in EXTEM is elongated.^[11] A prolonged CT may indicate plasma coagulation disorders and this may call for the administration of FFP or prothrombin complex concentrate (PCC). Fibrin formation and polymerization directly impact the viscoelastic properties of blood clotting as measured by thromboelastometry tests.^[12] According to the Essener Runde algorithm, if the EXTEM CFT is prolonged, the reason for bleeding is likely to be a fibrinogen deficiency, a reduced platelet count or platelet dysfunction. Possible reasons can be identified with FIBTEM clot firmness parameters A (10) and MCF.^[11] Because all the above mentioned possible reasons were excluded in our study, it can be assumed that the abnormalities observed in the EXTEM tests were caused by a deficiency of plasma coagulation factors. However, it should be noted that in Group 1, the platelet count was significantly lower before surgery in comparison to Group 2 and this difference was seen until the end

of the observation period. Furthermore, platelet count significantly correlated with CFT, alpha angle, A (10), and MCF recorded preoperatively. Prolonged EXTEM clotting time over 80–100 seconds (normal range 35–80s) was used as a cut-off value for hemostatic intervention with PCC in patients suffering trauma or experiencing major blood loss during the surgery.^[13,14] In a randomized clinical trial by Weber and colleagues,^[9] 2 algorithms were compared, the first based on routine coagulation tests and the second on thromboelastometry and aggregometry. The need for plasma transfusion occurred much less often (40% vs 80% $P=.001$) when thromboelastometry was used as a guide. Plasma or PCC administration guided by thromboelastometry is an appealing approach in the management of coagulation disorders; however, in our study, there was no correlation between preoperative EXTEM and INTEM parameters and APTT and INR values. In a study by Ogawa and colleagues,^[15] in contrast to our study, a strong correlation between PT and EXTEM CT and CFT and between aPTT and INTEM CT and CFT was found. PT/INR is also more standardized than thromboelastometry parameters for warfarin reversal using PCC.^[16] Additionally, optimal cut-off values for CT have not been evaluated or standardized.^[17–19]

The importance of thromboelastometry for predicting bleeding following cardiac surgery is controversial. Clinical studies often use small, single center, randomized protocols with different controls, with and without analyzing platelet function with aggregometry and with different study endpoints.^[1] In a recent cohort, 2-phase study, it was found that if rotational thromboelastometry was used in addition to the clinical model of bleeding management, there was no improved prediction of bleeding; however, this analysis started 5 minutes after post-CPB protamine administration and did not include observations before surgery.^[20] Based on a Cochrane review, algorithms that incorporate thromboelastometry can be used to reduce microvascular bleeding and lower the need for transfusions in cardiovascular surgery.^[21] In a meta-analysis by Wikkelse and colleagues,^[22] thromboelastometry-guided transfusion protocols led to a lower amount of blood lost in patients who had been given mass transfusions, although there was no related reduction in blood transfused, lower morbidity or mortality.

The results of this study confirmed that preoperative thromboelastometry measurements are useful in predicting an increased likelihood of perioperative bleeding in patients undergoing CABG. It is commonly agreed that patients experiencing perioperative bleeding have much worse outcomes than those without bleeding, along with longer length of hospital and/or ICU stays, higher mortality rates, and higher healthcare costs.^[23]

We are aware of the study limitations, one of them being that it is retrospective in nature and also that it did not include routine determinations of fibrinogen concentration, since it is not a standard measure in our unit. Rotational thromboelastometry can analyze all phases of coagulation, from the initial phase of fibrin formation to clot retraction and ultimately fibrinolysis. However, the measurement does not reflect the contribution of the endothelium to coagulation. It lacks platelet function testing and detection of conditions that affect platelet adhesion, for example, von Willebrand's disease cannot be detected. The standard practice in our center is to suspend clopidogrel at least 5 days before surgery; however, this does not exclude the possibility that the platelet function is still impaired. There may also be concerns about blood sample collection and processing. In order to overcome these limitations *all measurements were*

performed immediately after sample collection by the same laboratory technician and always using the same instrument. We also realize that the results of a single center study cannot be extrapolated to the entire population of patients undergoing cardiac surgery, because of the different surgical and heart protection methods together with different CPB methods in other heart surgery centers. The low number of patients is a limitation of this study and further studies are needed to investigate our observation in a larger group of patients.

The results of our study show that thromboelastometry performed before surgery provides additional data beyond routine coagulation testing. Therefore, it would be useful if the ability to perform thromboelastometry tests could be ensured before and during cardiac surgery. However, there will be additional costs to cover expenses for reagents and maintenance and this economic factor might be difficult to accept in some centers.

Potential clinical application of results of our study

4. Conclusions

1. Based on the analysis of the presented results, we can conclude that careful supervision and point of care monitoring of the coagulation system with thromboelastometry allows rapid diagnosis of coagulation abnormalities even before the start of surgery. These coagulation abnormalities were not possible to detect with routine coagulation screening tests.
2. Results of study indicate that preoperative thromboelastometry indices can predict postoperative increased chest tube output in adult patients undergoing elective cardiac surgery.

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References

- [1] Whiting D, DiNardo JA. TEG and ROTEM: Technology and clinical applications. *Am J Hematol* 2014;89:228–32.
- [2] Solomon C, Schöchl H, Ranucci M, et al. Can the viscoelastic parameter α -angle distinguish fibrinogen from platelet deficiency and guide fibrinogen supplementation? *Anesth Analg* 2015;121:289–301.
- [3] Görlinger K, Jambor C, Hanke AA, et al. Perioperative coagulation management and control of platelet transfusion by point-of-care platelet function analysis. *Transfus Med Hemotherapy* 2007;34:396–411.
- [4] Görlinger K, Dirkmann D, Hanke AA. Potential value of transfusion protocols in cardiac surgery. *Curr Opin Anaesthesiol* 2013;26:230–43.
- [5] Kozek-Langenecker SA, Afshari A, Albaladejo P, et al. Management of severe perioperative bleeding: guidelines from the European Society of Anaesthesiology. *Eur J Anaesthesiol* 2013;30:270–382.
- [6] Ak K, Isbir CS, Tetik S, et al. Thromboelastography-based transfusion algorithm reduces blood product use after elective CABG: a prospective randomized study. *J Card Surg* 2009;24:404–10.
- [7] Karkouti K, Callum J, Wijeyesundera DN, et al. Point-of-care hemostatic testing in cardiac surgery clinical perspective: a stepped-wedge clustered randomized controlled trial. *Circulation* 2016;134:1152–62.
- [8] Gozdzik W, Adamik B, Gozdzik A, et al. Unchanged plasma levels of the soluble urokinase plasminogen activator receptor in elective coronary artery bypass graft surgery patients and cardiopulmonary bypass use. *PLoS One* 2014;9:e98923.
- [9] Weber CF, Görlinger K, Meininger D, et al. Point-of-care testing: a prospective, randomized clinical trial of efficacy in coagulopathic cardiac surgery patients. *Anesthesiology* 2012;117:531–47.
- [10] Ng W, Jerath A, Wasowicz M. Tranexamic acid: a clinical review. *Anaesthesiol Intensive Ther* 2015;47:339–50.

- [11] Lier H, Vorweg M, Hanke A, et al. Thromboelastometry guided therapy of severe bleeding: Essener Runde algorithm. *Hämostaseologie* 2013;33:51–61.
- [12] Tanaka KA, Mazzeffi M, Durila M. Role of prothrombin complex concentrate in perioperative coagulation therapy. *J Intensive Care* 2014;2:60.
- [13] Tanaka KA, Esper S, Bolliger D. Perioperative factor concentrate therapy. *Br J Anaesth* 2013;111(suppl 1):i35–49.
- [14] Rugeri L, Levrat A, David JS, et al. Diagnosis of early coagulation abnormalities in trauma patients by rotation thrombelastography. *J Thromb Haemost* 2007;5:289–95.
- [15] Ogawa S, Szlam F, Chen EP, 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.
- [16] Pabinger I, Brenner B, Kalina U, et al. Prothrombin complex concentrate (Beriplex[®] P/N) for emergency anticoagulation reversal: a prospective multinational clinical trial. *J Thromb Haemost* 2008;6:622–31.
- [17] Görlinger K, Dirkmann D, Hanke AA, 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;115:1171–91.
- [18] Fassl J, Matt P, Eckstein F, et al. Transfusion of allogeneic blood products in proximal aortic surgery with hypothermic circulatory arrest: effect of thromboelastometry-guided transfusion management. *J Cardiothorac Vasc Anesth* 2013;27:1181–8.
- [19] Davidson S. State of the Art—how I manage coagulopathy in cardiac surgery patients. *Br J Haematol* 2014;164:779–89.
- [20] Lee GC, Kicza AM, Liu K-Y, et al. Does rotational thromboelastometry (ROTEM) improve prediction of bleeding after cardiac surgery? *Anesth Analg* 2012;115:499–506.
- [21] Afshari A, Wikkelso A, Brok J, et al. Thrombelastography (TEG) or thromboelastometry (ROTEM) to monitor haemotherapy versus usual care in patients with massive transfusion. *Cochrane Database of Systematic Reviews* 2011;3:CD007871.
- [22] Wikkelsoe AJ, Afshari A, Wetterslev J, et al. Monitoring patients at risk of massive transfusion with thrombelastography or thromboelastometry: a systematic review: TEG/ROTEM to guide massive transfusion. *Acta Anaesthesiol Scand* 2011;55:1174–89.
- [23] Zbrozek A, Magee G. Cost of bleeding in trauma and complex cardiac surgery. *Clin Ther* 2015;37:1966–74.