Rapid and Correct Prediction of Thrombocytopenia and Hypofibrinogenemia With Rotational Thromboelastometry in Cardiac Surgery

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Objectives: **In the present study, the authors have investigated whether rotational thromboelastometry (ROTEM) could predict thrombocytopenia and hypofibrinogenemia in cardiac surgery using the clot amplitude after 5 minutes (A5). Another parameter, PLTEM, in which the contribution of fibrinogen is eliminated by subtracting a fibrin-specific ROTEM test (FIBTEM) from an extrinsically-activated ROTEM test (EXTEM), was investigated. Furthermore, the turnaround time of ROTEM was compared to conventional laboratory tests.**

Design: **Prospective cohort study.**

Setting: **Single academic medical center.**

Participants: **Ninety-seven patients undergoing cardiac surgery between July 2011 until August 2012.**

Interventions: **The correlations between EXTEM/FIBTEM A5, A10, and maximal clot formation (MCF), EXTEM/PLTEM (A5/A10, and MCF) and platelet count, and FIBTEM (A5/A10, and MCF) and fibrinogen were evaluated using the Pearson's correlation coefficient and receiver-operating characteristic curves. Turnaround times of ROTEM tests and conventional laboratory tests were assessed in the central laboratory.**

Measurements and Main Results: **EXTEM A5 and FIBTEM A5 showed an excellent correlation with A10 (R:0.99/1.00) and MCF (R:0.97/0.99). The correlation between EXTEM A5 and platelet count (R:0.74) was comparable with the correlation of A10 (R:0.73) and MCF (R:0.70) with platelet count. FIBTEM A5 predicted fibrinogen levels (R:0.87) as well as A10 (R:0.86) and MCF (R:0.87). PLTEM A5 (R:0.85) correlated better with platelet count than EXTEM A5 (R:0.74; $p = 0.04$) and showed significantly better area under the curve values than EXTEM for predicting thrombocytopenia (A5 $p = 0.012$, A10 $p = 0.019$). Turnaround time for ROTEM tests, 12 minutes, was comparable with emergency requests for platelet count, 13 minutes, and shorter than emergency requests for fibrinogen levels, 37 minutes.**

Conclusions: **Implementation of PLTEM and FIBTEM A5 in ROTEM-guided transfusion protocols may improve transfusion management.**

KEY WORDS: ROTEM, thromboelastometry, thrombocytopenia, hypofibrinogenemia, cardiac surgery, laboratory time

DURING CARDIAC SURGERY, blood coagulation is subjected to many unfavorable changes due to hemodilution, loss of platelets, and deficiencies of both coagulation factors and inhibitors.[1,2] Under such circumstances, rapid assessment of hemostatic function is necessary to guide decisions on optimal transfusion management. Conventional laboratory tests, although often used, are not very helpful to direct transfusion management in these urgent situations due to their long turnaround time. In emergency cases, blood transfusions or therapy with isolated coagulation factor concentrates (eg, fibrinogen) are, therefore, often performed empirically before laboratory results are available. This could result in suboptimal treatment.

Because of its short turnaround time, rotational thromboelastometry (ROTEM) has proven to be an important diagnostic tool in situations of massive blood loss, such as cardiac and hepatic surgery and major trauma.[3–8] In both cardiac and noncardiac surgery, an extrinsically-activated ROTEM test (EXTEM) and a fibrin-specific ROTEM test (FIBTEM) have been shown to provide information about platelet count and fibrinogen levels within 10 to 20 minutes.[5] The use of these ROTEM parameters in transfusion protocols has been reported to reduce the amount of blood loss and the incidence of blood transfusion.[9–11] Although multiple guidelines recommend the use of conventional laboratory tests in situations of major blood loss, it generally is agreed that thromboelastometry could be an important diagnostic tool to assist in guiding hemostatic therapy and characterizing the coagulopathy.[12,13]

In this study, the authors have prospectively collected data to determine whether ROTEM could predict thrombocytopenia and hypofibrinogenemia in cardiac surgery using the amplitude after 5 minutes (A5). They hypothesized that A5 could estimate platelet count and fibrinogen levels as well as A10 and the maximal clot formation (MCF), which currently are used in ROTEM-guided transfusion protocols. Since limited information about turnaround times for conventional tests for platelet count and fibrinogen levels have been reported in the literature,[14] the turnaround times of conventional tests were compared with ROTEM tests to quantify the time advantage of A5 in the clinical setting of cardiac surgery. In addition,

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Table 1. Patient Characteristics, Laboratory Results, and ROTEM Results

Patient characteristics	Sex (male/female)	70/27
	Age (years)	62 (14)
Laboratory results	Hemoglobin (mmol/L)	5.4 (0.9)
	Hematocrit	0.26 (0.04)
	Platelet count (per μL)	123,000 (50,000)
	Fibrinogen (mg/dL)	200 (90)
ROTEM results	EXTEM A5 (mm)	34 (9)
	EXTEM A10 (mm)	45 (9)
	EXTEM MCF (mm)	55 (8)
	FIBTEM A5 (mm)	9 (5)
	FIBTEM A10 (mm)	10 (6)
	FIBTEM MCF (mm)	11 (6)
	PLTEM A5 (mm)	25 (5)
	PLTEM A10 (mm)	35 (6)
	PLTEM MCF (mm)	43 (5)
Total number of transfusions during the 24 hours before/after the ROTEM test (EC/FFP/PC)	Before	601 (399/134/68)
	After	349 (144/140/65)
Patients who received at least one transfusion before performing a ROTEM test	EC	78/97
	FFP	26/97
	PC	39/97

NOTE. Data are expressed as mean (SD) or number as appropriate.

Abbreviations: A(x), maximal clot formation after (x) minutes; CPB, cardiopulmonary bypass; EC, erythrocyte concentrate; EXTEM, extrinsically-activated ROTEM test; FIBTEM, fibrin-specific ROTEM test; FFP, fresh frozen plasma; MCF, maximal clot formation; PC, platelet concentrate; PLTEM(x), EXTEM(x) − FIBTEM(x); ROTEM, rotational thromboelastometry; SD, standard deviation.

the authors calculated another ROTEM variable (PLTEM) by subtracting FIBTEM from EXTEM. They hypothesized that PLTEM could estimate platelet count more accurately than EXTEM.

MATERIALS AND METHODS

This study was part of a planned evaluation after the introduction of ROTEM as a diagnostic tool during cardiac surgery in a single university hospital. From July 2011 until August 2012, all patients with ROTEM results, both during and after cardiopulmonary bypass (CPB), were included. ROTEM tests were not performed on fixed time points. Indications for ROTEM tests were an increased preoperative bleeding risk, redo-thoracotomy, combined surgery, aorta surgery, active endocarditis, deep hypothermic circulatory arrest, emergency surgery, CPB time more than 180 minutes, excessive blood loss after protamine administration, more than 200 mL of blood loss in the first hour in the intensive care unit, and more than 100 mL/hour during further ICU stay. The final decision whether or not a ROTEM test should be performed was made by the anesthesiologist or intensivist in charge. ROTEM-based transfusion algorithms were adopted from literature.[10] Data acquisition and analyses were performed anonymously in accordance with the Dutch law for approving medical research.

Blood was collected in 4.0-mL tubes with 7.2-mg spray dried K_2EDTA for analysis of platelet count, and in 4.5-mL, 3.2% citrate tubes for ROTEM tests and analysis of fibrinogen (BD Vacutainer, Becton Dickinson, Franklin Lakes, NJ). Platelet measurements were performed on a Sysmex XE-5000 analyzer (Sysmex Corporation, Kobe, Japan), and fibrinogen measurements were performed on a Sysmex CA-7000 analyzer after centrifugation for 10 minutes at 2000 g. Fibrinogen levels were determined using the Clauss coagulation method[15] (Dade Thrombin Reagent, Siemens Healthcare Diagnostics Products, Marburg, Germany).

Thromboelastometric measurements were performed with the ROTEM device (ROTEM®, TEM International GmbH, Munich, Germany). Measurements were performed at 37ºC according to the instructions of the manufacturer. Analyzed ROTEM parameters were EXTEM A5/A10/MCF, FIBTEM A5/A10/MCF, and PLTEM A5/A10/MCF, the last of which were calculated by the investigator by subtracting FIBTEM from EXTEM. In EXTEM and FIBTEM tests, coagulation is extrinsically activated by tissue factor. In the FIBTEM tests a platelet inhibitor was added (cytochalasin D) to correct for the contribution of platelets to the clot strength. ROTEM tests and conventional laboratory tests were performed simultaneously in the central laboratory by trained laboratory staff. Both conventional laboratory tests and ROTEM tests were part of the standard diagnostic procedure during cardiac surgery and were therefore, performed, instantly.

From October 2010 until October 2012, the turnaround time of conventional laboratory tests was retrospectively analyzed in the central laboratory for emergency requests (<30 minutes). Turnaround time was defined as the time that passed between arrival of the sample at the laboratory, after pneumatic tube transport, and the moment results were reported in the laboratory information system. Handling time of 1 single ROTEM request was analyzed perspectively. Time to perform 1 ROTEM test was calculated by collecting data of 264 ROTEM tests. Pneumatic tube transport time from the operating room to the laboratory was not included in this study but has been reported to be equal for all sample transports (between 83 and 100 seconds).[16]