Change in Hemostatic Intervention After Implementation of Thromboelastometry

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Objective: **To monitor the use of blood products and hemostatic intervention after implementation of thromboelastometry.**

Design: **Observational prospective study using a historic control.**

Setting: **Single-center university hospital.**

Participants: **Patients undergoing cardiac surgery during 2008 (n = 811) were compared with similar patients in 2009 (n = 865).**

Interventions: **Thromboelastometry was implemented in December 2008. Changes in transfusion of blood products and changes in use of recombinant factor VIIa and fibrinogen were studied.**

Measurements and Main Results: **Use of blood products was not decreased significantly after implementation of thromboelastometry. However, in patients receiving blood products, the units of red blood cells were decreased significantly ($p = 0.04$). Regarding hemostatic reagents, the use of recombinant factor VIIa was decreased significantly ($p = 0.04$), and the use of fibrinogen increased significantly ($p < 0.001$). Most blood products (>70%) were given to a minority of patients (~10%) in 2008 and 2009. In 2009, thromboelastometry was performed in 146 patients (17%), and the use of blood products ($p < 0.0001$), recombinant factor VIIa ($p < 0.001$), and fibrinogen ($p < 0.001$) was significantly higher compared with patients in whom thromboelastometry was not performed.**

Conclusions: **After implementation of thromboelastometry, the use of recombinant factor VIIa was decreased significantly, whereas the use of blood products was not decreased significantly in patients undergoing cardiac surgery.**

KEY WORDS: cardiac surgery, cardiopulmonary bypass, diagnostic strategy, hemostasis, intervention, transfusion, thromboelastogram, ROTEM

CARDIAC SURGERY carries an inherent risk of bleeding complications. In industrialized countries, 10% to 20% of the blood supply is used by this group of patients.[1,2] Transfusion requirements vary considerably, depending on patient characteristics and perioperative risk factors.[1] Knowing this, the authors previously studied a group of patients classified according to type of cardiac surgery.[3] They found that complexity of surgery, previous cardiac surgery, and emergency surgeries were associated with an increased need for blood transfusions.[3] Because the consumption of blood products varies considerably among cardiac surgical patients, an evaluation of a new diagnostic test to decrease blood product consumption cannot be performed in the entire group of cardiac surgical patients without considering the distribution of risk factors before and after introduction of an intervention.

Management of the coagulopathy associated with cardiopulmonary bypass (CPB) should be tailored according to the risk profile of the individual patient. Thus, several point-of-care tests have become available, including rotation thrombelastography (TEG; Haemoscope, Niles, IL) and thromboelastometry (ROTEM; Tem International, GmbH, Munich, Germany). In contrast to conventional coagulation analyses, ROTEM and TEG are performed bedside using whole blood and provide information on the contribution of fibrinogen and platelets to clot formation.[4] Although conflicting data exist on the predictive value of TEG for perioperative blood loss in patients undergoing cardiac surgery,[5-8] the authors decided to implement a similar device, the ROTEM. The aim of the present study was to monitor the use of blood products and hemostatic intervention after implementation of ROTEM. The authors hypothesized that the amount of blood products given would decrease significantly (primary endpoint) and that the use of recombinant factor VIIa (rVIIa) would decrease significantly (secondary endpoint) in well-defined groups of patients undergoing cardiac surgery.

METHODS

Data on consecutive patients (n = 865) admitted to the cardiothoracic intensive care unit from January 1, 2009 through December 31, 2009 were collected prospectively from standardized electronic patient case-report forms and compared with prospectively collected data obtained in 2008 (n = 811).[3] An identical data collection method was used in 2008 and 2009. Patient data contained detailed perioperative information, including demographics, medication, type of surgery, preoperative co-morbidity, and duration of CPB. Data were entered into a database in combination with other clinical data on transfusion of various blood products and hemostatic medication.

Patients were classified in accordance with the indication for cardiac surgeries, ie, coronary artery bypass grafting (CABG) on and off pump, valve replacement, and combined CABG and valve replacement. Patients undergoing valve replacement because of endocarditis were grouped separately, and patients requiring surgery involving the thoracic aorta were categorized as a separate entity. Other types of surgical patients (eg, pulmonary thromboendarterectomy, adult congenital heart surgery) were not included (n = 75).

Anesthesia, surgical procedures, and CPB were standardized as described previously[3] and remained unchanged during the entire observation period (2008 through 2009). In short, general anesthesia was induced and maintained with propofol, sufentanil, and rocuronium. Bovine unfractionated heparin was administered for anticoagulation before the initiation of CPB (300 IU/kg), and the dose was adjusted to achieve a target activated coagulation time (ACT) longer than 400 seconds (Celite activated). As routine clinical practice, standard-dose tranexamic acid was administered.

The CPB circuit was primed with crystalloids (total volume 1,700 mL). Most patients were kept normothermic (35°C to 37°C) unless the surgical procedure required a lower temperature (ie, circulatory arrest), with a decrease of the core temperature to 18°C. The myocardium was

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protected by intermittent antegrade crystalloid cardioplegia. Standard surgical techniques were used in patients undergoing coronary revascularization on the beating heart without CPB. Cell saver was not used in any patient. At the end of CPB, when stable hemodynamics were obtained, the CPB circuit and oxygenator were emptied and the blood solution transfused back to the patient, unless there was evidence of ongoing hemolysis.

Similar to 2008, a standardized transfusion protocol was used for prescribing red blood cells (RBCs) in patients in the postoperative period. Hematocrit levels of 26% were tolerated in the postoperative period unless the patient showed signs of metabolic acidosis or lactate accumulation, which could not be related entirely to impaired hemodynamics. In this situation, RBCs could be administered at the discretion of the anesthesiologist. Autologous blood was returned to the patient before allogeneic transfusion was initiated, except in patients with obvious signs of hemolysis. In general, mediastinal blood loss >400 mL within the first 5 hours was autotransfused back to the patient.

Medical staff underwent an introductory course in interpretation of the ROTEM (Pentapharm, GmbH, Munich, Germany); after 3 months, an evaluation and refresher course were given. According to the authors' treatment algorithm, indications for ROTEM analysis perioperatively were excessive bleeding, long CPB duration (>180 minutes), and thoracic aorta dissection; and in the postoperative period, indications were chest tube drainage (>300 mL during 1st hour, >200 mL during 2nd hour, and >100 mL during 3rd hour). ROTEM analysis could be repeated at the discretion of the treating clinician, but with a minimum of 30 minutes between 2 consecutive ROTEM analyses.

Blood samples were obtained from an indwelling arterial catheter and anticoagulated with 3.2% sodium citrate. ROTEM analysis was performed by trained laboratory technicians. Standard assays were performed using the 4 assays: in-tem, ex-tem, fib-tem, and hep-tem. Using the software DyCoDerivAn GOLD (Avordusol, Risskov, Denmark), the authors obtained dynamic parameters of clot initiation (clotting time in seconds) and clot propagation, such as the maximum velocity of clot formation (millimeters × 100/second) and the time until maximum velocity of clot propagation (in seconds). Whole-blood clot strength was assessed by the evaluation of maximum clot firmness (millimeters × 100). The ROTEM graphs were displayed on a computer in the operating room or intensive care unit in close proximity to the bleeding patient. Online results often were available within the first 5 minutes after blood sampling; 15 minutes was the longest time span from blood sampling until online view of the analysis. The coagulation process analyzed by ROTEM could be followed online for up to 60 minutes. A printout of the ROTEM analysis was available for the patient record. A full coagulation profile using conventional coagulation tests always was requested at the same time as the ROTEM analysis, including measurement of prothrombin time, thrombin time (with and without protamine), activated partial thromboplastin time (PTT), fibrinogen and antithrombin concentrations, and platelet count. Turnaround time for the standard coagulation test was approximately 40 to 60 minutes.

To optimize the coagulation capacity, hypocalcemia, acidosis, and hypothermia were corrected. All clinicians carried a simplified interpretation and treatment algorithm based on recommendations by an international expert group.[9] Additional protamine sulfate was recommended if the in-tem assay showed a clotting time >25% longer than the hep-tem assay. Fibrinogen (Haemocomplettan, Csl Behring, GmbH, Hannover, Germany) was recommended if fib-tem maximal clot formation was <9 mm. Platelet administration was recommended if hep-tem maximal clot formation was <45 mm and fib-tem maximal clot formation was >9 mm; similarly, if therapy with platelet inhibitors had not been withheld before surgery. Fresh frozen plasma (FFP) was recommended if hep-tem clotting time was >300 seconds or ex-tem clotting time was >100 seconds. In case of normal ROTEM analysis despite continuous bleeding, a resternotomy was indicated to exclude surgical bleeding complications.

If ROTEM analysis was not required, allogeneic blood products were given at the discretion of the individual clinician. Reversal of heparin was performed by protamine, with an initial dose of protamine 1 mg/heparin 100 IU. Dose adjustments were performed using protamine until the patient's preoperative ACT and activated PTT level were achieved.

Transfusion requirements were recorded during surgery and in the subsequent 24 hours. Data on blood products were collected from an electronic record system at the hospital blood bank. Blood products were recorded on delivery and tagged by the unique civil registration number of each patient. Blood products delivered on the day of surgery and for the next 24 hours were extracted from this database. If blood products were unused and returned to the blood bank, data were erased from the electronic database.

The study and data extractions were approved by the Danish Data Protection Agency. According to the Danish law of ethics, the study did not need approval by the Central Denmark Region Committee on Biomedical Research Ethics.

Multivariate analyses were performed by logistic regression analysis calculating odds ratio of using blood products in 2009 versus 2008, adjusted for type of surgery, acute surgery, and use of antithrombotic medications. Linear regression was performed; after linear regression with log(units) as the dependent variable, the regression coefficient was transformed to express the average number of units of blood products used in 2009 compared with 2008. This analysis also was adjusted for type of surgery, acute surgery, and use of antithrombotic medications. Unpaired comparison between groups was performed using the Mann-Whitney U test. All p values <0.05 were considered statistically significant. Statistical analyses were performed using Stata 11.0 (StataCorp, College Station, TX).

RESULTS

In 2008, 811 patients undergoing cardiac surgery were included[3]; in 2009, 865 patients were included. In 2009, a

Table 1. Demographics and Clinical Characteristics in Patients Undergoing Cardiac Surgery During 2008 and 2009

Characteristics	2008 (n = 811)	2009 (n = 865)	*p* Value
Age (y), mean ± SD	66 ± 12	68 ± 12	0.99
Sex, n (%)			0.91
Male	573 (71)	614 (71)	
Female	238 (29)	251 (29)	
Procedure, n (%)			
Endocarditis	35 (4)	29 (3)	0.30
Valve replacement	230 (28)	290 (34)	0.02
CABG	393 (49)	405 (47)	0.50
CABG + valve replacement	98 (12)	87 (10)	0.19
Thoracic aorta	19 (2)	29 (3)	0.22
Thoracic aorta ± valve ± CABG	36 (4)	25 (3)	0.09
Urgency, n (%)			0.01
Elective	740 (91)	819 (95)	
Emergency	71 (9)	46 (5)	
Renal insufficiency, n (%)	35 (4)	40 (5)	0.76
Previous cardiac surgery, n (%)	66 (8)	60 (7)	0.35
CPB time (min), mean ± SD	89 ± 61	86 ± 53	0.38
CA time (min), mean ± SD	14 ± 11	13 ± 9	0.71

Abbreviations: CA, circulatory arrest; CABG, coronary artery bypass grafting; CPB, cardiopulmonary bypass; SD, standard deviation.