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Original Article

Transfusion Threshold of Hemoglobin 80 g/L Is Comparable to 100 g/L in Terms of Bleeding in Cardiac Surgery: A Prospective Randomized Study

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Objective: Anemia is common after cardiac surgery and, according to some suggestive evidence, may be associated with increased bleeding, other morbidity, and mortality. However, transfusion of red blood cells (RBC) may cause adverse effects and increase cost. The authors hypothesized that the restrictive hemoglobin threshold (Hb of 80 g/L) may aggravate bleeding more than the higher Hb threshold (Hb 100 g/L).
Design: Prospective randomized trial.
Type of Hospital: University Hospital of Helsinki, Finland.
Participants: Eighty patients with written informed consent, scheduled for elective open-heart surgery were randomized in 2 groups.
Interventions: Two study groups had RBC transfusion threshold of either Hb 80 g/L or 100 g/L. These triggers were followed for a 24-hour period postoperatively. A medical follow-up was carried out for 7 days after surgery.
Measurements and Main Results: Rotational thromboelastometry (ROTEM) and conventional laboratory tests were performed to evaluate coagulation. There was no significant difference in bleeding or ROTEM parameters between the groups. Complication rate and Hb concentration after 7-day follow-up were not different between the groups, but Group 100 g/L had received twice the amount of RBC transfusions.
Conclusion: Hb threshold of 80 g/L for RBC transfusion in cardiac surgery is comparable to 100 g/L in terms of bleeding and possibly short-term complications.

Key Words: cardiac surgery; transfusion, bleeding

HEMOGLOBIN (Hb) has a crucial role in carrying oxygen to tissues. Evidence supports that red blood cells (RBCs) play an active role in hemostasis.[1] Anemia is common during and after cardiac surgery, and it is associated with increases in morbidity and mortality.[2–4] Transfusion of allogeneic RBC is typically the treatment of choice. Cardiac surgery has one of the highest associated transfusion rates with over 50% of patients receiving transfusions.[5] On the other hand, transfusion of RBC, or other blood components, is associated with numerous harmful effects, such as infection, acute kidney injury, ischemic events, prolonged hospital stay, increased early and late mortality, and hospital costs.[2,6–8]

A recent guideline from the AABB recommends restrictive transfusion strategy in most clinical settings, including cardiac surgery.[9] The results of trials studying critically ill patients (ie, TRICC [Transfusion Requirements in Critical Care] or TRISS

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[Transfusion Requirements in Septic Shock]) also support the idea of lower transfusion thresholds because there was no significant difference in 30- and 90-day mortality when comparing higher (Hb 90 g/L) versus lower (Hb 70 g/L) transfusion thresholds.[10,11] However, particularly in cardiac surgery,[12–14] recent studies have conflicting results regarding restrictive transfusion strategies, and no clear consensus exists. Transfusion thresholds in cardiac surgery have generally been more liberal in clinical practice, partly due to justified concern of cardiac ischemia, bleeding, and other undesired sequelae.

It has been shown that lower hematocrit (Hct) influences coagulation in vivo.[15] Rotational thromboelastometry (ROTEM), a point-of-care whole blood coagulation test, gives more rapid and detailed information about patients' coagulation status, compared with conventional laboratory tests performed with cell free plasma.[16,17] The use of ROTEM-guided transfusion protocols also has been shown to reduce the need for transfusions in cardiac surgery.[18]

The aim of this prospective randomized study was to compare the effect of 2 different RBC transfusion thresholds (80 g/L *v* 100 g/L) perioperatively on bleeding and coagulation parameters measured by ROTEM in cardiac surgical patients.

Methods

After registering the study at the Hospital District of Helsinki and Uusimaa (§94,9.05.2014) and receiving approval from the institutional Ethics Committee for Surgery in Helsinki University Hospital 2014 (D-number 58/13/03/02/2014), the authors gathered 80 patients scheduled for non-emergency coronary artery bypass grafting (CABG), simple one valve (aortic or mitral) replacement or both, requiring cardiopulmonary bypass (CPB). Patients were operated on between June 2014 and December 2015. Exclusion criteria included any hereditary or acquired hemostatic disorders, any malignancies, and severe chronic kidney disease (glomerular filtration rate < 30 mL/min). Patients' medical history and severity of the surgery was described with European System for Cardiac Operative Risk Evaluation, (numeric) EuroSCORE I.[19] After providing written informed consent, patients were randomized in 2 groups: (1) "Group 80," RBC transfusion threshold of 80 g/L, and (2) "Group 100," RBC transfusion threshold of 100 g/L. Randomization was done in blocks of 20 patients and using closed envelopes (Fig 5). Use of other blood components and medications was left to clinicians' discretion and based on Helsinki University Hospital treatment protocols; that is, if postoperative bleeding is severe (> 200 mL/h), activated coagulation time (ACT, s), thromboplastin time value (TT, %), and platelet count (PLC) are measured. If ACT is prolonged more than 10 seconds compared with pre-bypass level, 25 mg of protamine is administered. Pooled human plasma (5 mL/kg) is given if TT is $< 50\%$ and platelets (1 U/10 kg) transfused if PLC is $< 50 \times 10^9$/L. If bleeding continues, 1 g of tranexamic acid is administered. Intervention started at the beginning of surgery, and it lasted 24 hours. The study was unblinded due to the Finnish practice of anesthetists performing transfusions themselves.

Patients' own medication was continued until surgery according to hospital protocol. Patients did not receive any low molecular weight heparin for 24 hours before surgery. The possible acetylsalicylic acid treatment was continued until surgery, but the cessation of oral anticoagulation was performed according to the hospital protocol: Warfarin 3 days and new oral anticoagulants 5 days preoperatively. Patients received a 1-g bolus of tranexamic acid during anesthesia induction. CPB was performed according to institutional standards described elsewhere.[20] Before cannulation a bolus of heparin (300-400 IU/kg body weight) was administered. Another 1 to 2 g bolus of tranexamic acid also was administered in the CPB routinely. Intraoperatively ACT was measured repeatedly to monitor the efficiency of anticoagulation. In the case of ACT < 480 s, a further bolus of heparin was administered. After finishing the CPB, heparin was antagonized with protamine sulfate administered at 1 mg to 100 IU ratio to initial dose of heparin.

Conventional laboratory tests were performed preoperatively and at predetermined time intervals. During surgery and postoperative intensive care, Hb concentrations were monitored hourly during surgery, every 30 minutes during CPB, and every 2 to 3 hours in the intensive care unit (ICU), or more frequently, if needed. If Hb level was 79 g/L or less, 99 g/L or less, respectively, the patient received 1 unit of packed RBC, and Hb was measured again. Transfusions were carried out until Hb level reached 80 g/L or more, 100 g/L or more, respectively. Cell salvage was used only in few isolated cases, as procedures were estimated to be simple and patients did not have predisposing risk factors for extensive bleeding.

ROTEM (TEM International GmbH, Munich, Germany) was performed at 3 predetermined time points: before anesthesia induction, immediately after CPB/surgery, and on the first postoperative morning. Tissue factor with (FibTEM) or without (ExTEM) cytochalasin D was used for coagulation activation. In FibTEM, platelet function is inhibited completely, therefore it is possible to measure the isolated effect of fibrinogen on blood coagulation. The following variables were recorded: clotting time (CT, s), clot formation time (CFT, s), maximum rise in clot firmness (given as the angle α), maximum clot firmness (MCF, mm), and clot lysis after 30 minutes. The clinical staff was blinded to the ROTEM data. Other data collected during the study period were the amount of bleeding during the surgery (estimate done by surgeons/anesthetists) and postoperatively from the chest tubes, RBC and blood product transfusions, diuresis, and cumulative fluid balance. Patient data during the surgery and intensive care were collected with PI Client Information System (Caresuite 8.2, PiCIS Inc, San Francisco, CA).

Statistical Analysis

Based on results of the authors' previous study,[21] the group size was calculated with power (1-β) = 80% and α = 0.05

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