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Multivariate model for predicting postoperative blood loss in children undergoing cardiac surgery: a preliminary study

V. Savan[1†], A. Willems[2†], D. Faraoni[3*] and P. Van der Linden[3]

[1] Department of Anaesthesia and Intensive Care 'Valeriu Ghereg', State Medical and Pharmaceutical University 'Nicolae Testemitanu', Chisinau, Republic of Moldova
[2] Department of Paediatric Intensive Care, Queen Fabiola Children's University Hospital, 15 Avenue JJ Crocq, B-1020 Brussels, Belgium
[3] Department of Anaesthesiology, Centre Hospitalier Universitaire (CHU) Brugmann-Queen Fabiola Children's University Hospital, Brussels, Belgium

* Corresponding author. E-mail: davidfaraoni@icloud.com

Editor's key points

- Bleeding after cardiac surgery is associated with worse outcomes and increased costs.
- Identification of risk factors can prompt management strategies to prevent bleeding.
- Retrospective analysis of a clinical database was performed to identify risk factors for postoperative bleeding in children.
- Risk factors were found to be low weight, cyanotic heart disease, and prolonged wound closure duration.

Background. Postoperative bleeding and blood product transfusion increase morbidity, mortality, and costs after cardiac surgery. However, factors that could accurately predict bleeding have not been well studied in children undergoing cardiac surgery. This study aims at determining factors that could be used to predict postoperative bleeding in this paediatric population.

Methods. We included 182 children undergoing congenital heart surgery. Significant bleeding was defined as a blood loss that exceeds 10% of total blood volume within the first 6 postoperative hours. Univariate and multivariate logistic regression analyses were performed to determine variables independently associated with bleeding. These variables were used to calculate a probability for each individual child to develop postoperative bleeding.

Results. According to the definition of bleeding, 44 patients were included into the 'bleeder' group and 138 into the 'non-bleeder' group. Factors independently associated with postoperative bleeding were preoperative body weight, the presence of a cyanotic disease, and the time required for wound closure. Based on these three parameters, we calculated the probability of bleeding and found a significant relationship with postoperative bleeding. Finally, a calculated probability of 0.59 can predict significant postoperative blood loss with a sensitivity of 84% and a specificity of 64%.

Conclusions. This study shows that preoperative body weight, cyanotic disease, and wound closure duration are best predictors of bleeding in the paediatric population after cardiac surgery. The combination of these three factors could be used at the end of the surgery to estimate the probability of postoperative bleeding.

Keywords: children; congenital heart diseases; postoperative blood loss; risk factors

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Cardiac surgery with cardiopulmonary bypass (CPB) is often associated with excessive blood loss and blood product transfusions, which have been associated with increased postoperative morbidity, early and late mortality, prolonged hospitalization stay, and costs.[1] Outcome may further be worsened by the presence of pre-existing cofactors (e.g. anaemia in adult), massive transfusion, and re-exploration for bleeding.[2] Excessive blood loss often results from the development of a perioperative coagulopathy which can be triggered by several factors such as contact between blood and non-endothelial surfaces, anticoagulation using unfractioned heparin (UFH), protamine overdosage, and hypothermia.[3] In the paediatric population, other specific factors have to be considered such as the immaturity of the haemostatic system, the higher degree of bypass haemodilution, and the presence of cyanotic disease.[4] Therefore, the coagulopathy observed in children undergoing cardiac surgery with CPB is more complex and has been associated with bad outcomes.[5] Rapid detection of this coagulopathy should allow early goal-directed haemostatic therapy, aiming at preventing postoperative bleeding, reducing morbidity, mortality, and costs.[6] This goal-directed therapy is best obtained through the development of specific algorithms,[7] which are applied after identification of abnormal bleeding.[8 9] Insufficient data exist to accurately predict

† These authors contributed equally to this study.

bleeding complications both in adult and paediatric cardiac surgery populations. There is urgent need for further studies that will identify patients with increased bleeding risk in order to improve their perioperative management.[10]

We therefore designed a retrospective analysis of prospectively collected data to evaluate parameters that could be used to define and/or predict postoperative bleeding in children undergoing cardiac surgery with CPB. Our goal was to develop a simple model that would allow pre- and intraoperative identification of children at higher risk for bleeding using variables available in routine clinical practice.

Methods

Study design

After approval by the local Ethics Board, we performed a retrospective analysis of data collected in our departmental database, which included children aged between 0 and 16 yr old undergoing a cardiac surgery with CPB between September 2010 and January 2012. Exclusion criteria were: pre-existing acquired and/or congenital coagulopathy [defined as platelet count $<100\,000$ mm^{-3}, activated partial thromboplastin time (aPTT) >45 s, prothrombin time (PT) $<70\%$, fibrinogen <100 mg dl^{-1}], liver (aspartate aminotransferase and alanine aminotransferase $>$ two-fold our normal range) and/or kidney diseases (creatinine level >1.5 mg dl^{-1} and/or haemodialysis), emergency procedures for life-threatening condition, and Jehovah's Witnesses. The local Ethic Board waived the requirement for written informed consent due to the retrospective nature of the protocol.

Anaesthesia protocol and intraoperative management

Standard monitoring included five-lead ECG, pulse oximeter, non-invasive arterial pressure, arterial and central venous pressures, urinary output, and rectal temperature. I.V. anaesthesia based on midazolam, sufentanil, and rocuronium was used in all children, except those with univentricular physiology undergoing a cavopulmonary connection. In this particular situation, early extubation was warranted and anaesthesia was based on propofol, remifentanil, and atracurium. All children received 30 mg kg^{-1} methylprednisolone and cefazoline 25 mg kg^{-1} after the induction of anaesthesia. Tranexamic acid was systematically administered according to the following dose scheme: a bolus of 10 mg kg^{-1} was given after anaesthesia induction, followed by a continuous infusion of 10 mg kg^{-1} h^{-1} until the end of wound closure. A second bolus of 10 mg kg^{-1} was added to the CPB prime solution.

Before aortic cannulation, 4 mg kg^{-1} UFH was administered to reach an activated clotting time (ACT, ACTII monitor, Medtronic BV, Kerkrade, The Netherlands) >480 s. The level of anti-coagulation was repeatedly checked during bypass using ACT testing and additional heparin boluses (1 mg kg^{-1}) were administered to maintain ACT >480 s. At the end of CPB, protamine was administered to antagonize UFH. We used a standardized scheme in which the protamine dose corresponds to half the total amount of UFH administered during the whole CPB duration. Heparin reversal was controlled with ACTII monitor comparing ACT measured in cartridge with and without heparinase (Medtronic BV). An additional 1 mg kg^{-1} of protamine was administered if required to ensure adequate antagonization of heparin, defined as a difference $<10\%$ between ACTs with and without heparinase.

The CPB circuit was primed with 6% hydroxyethyl starch (130/0.4) in 0.9% sodium chloride (Voluven®, Fresenius-Kabi Gmbh, Bad Homburg, Germany), 20% mannitol (1.5 ml kg^{-1}), 20 mEq litre^{-1} sodium bicarbonate, and 50 mg litre^{-1} UFH. In neonates up to 1 month of age, the colloid was replaced by fresh-frozen plasma (FFP). When preparing the CPB prime, the haematocrit on bypass was calculated based on the volume of the prime and the estimated blood volume (EBV) of the child. Packed red blood cells (RBCs) were added to the prime when predicted haematocrit was $<24\%$ after cardioplegia (crystalloid cold balanced electrolyte solution enriched with potassium chloride 30 mmol litre^{-1}). All patients were rewarmed to a rectal temperature $>35.5^{\circ}$C before weaning from CPB. After weaning from CPB, modified ultrafiltration was used to increase haematocrit of the residual blood volume in the CPB circuit.

After separation from CPB, packed RBCs were transfused to maintain a haematocrit $>24\%$ in the case of haemorrhage or to increase oxygen delivery in the case of persistent significant R- to L-shunt resulting in a low arterial oxygen saturation ($Sp_{O_2}<90\%$), or in the case of persistent lactic acidosis after optimization of cardiac output with inotropes, vasoactive agents, or both. In these conditions, the volume of blood transfused was adapted to each child according to the clinical situation. Platelet concentrates and FFP were transfused after CPB in the presence of abnormal clinical bleeding (based on surgeon and anaesthesiologist's judgement), using the algorithm developed by Despotis and colleagues, based on platelet count, PT, and aPTT.[11]

Data recorded

Several parameters, which we considered as factors that may influence postoperative blood loss in children undergoing cardiac surgery, were recorded. These parameters included: age, weight, height, anaesthetic risk (ASA score) and surgical complexity (RACHS-1),[12] cyanotic heart disease (CHD), previous sternotomy, preoperative laboratory data (haemoglobin level, platelets count, aPTT, PT, fibrinogen level, creatinine level), routine coagulation assays performed at the end of CPB (fibrinogen level, haemoglobin level, platelets count, aPTT, and PT), length of surgery, aortic clamping, and CPB, minimal temperature during CPB, intraoperative blood loss, wound closure duration, intraoperative exposition to allogeneic blood products (FFP, RBCs, platelets), and volume of priming solution.

Intraoperative blood loss was determined by weighing sponges and measuring suction volumes after separation from CPB. Postoperative blood loss was assessed by measuring chest tube drainage from admission to the paediatric intensive care unit. Clinically significant postoperative bleeding was defined as $>10\%$ of EBV blood loss in the first 6 postoperative hours, which corresponds to the 75th percentile of our population.