Predictive Factors for Red Blood Cell Transfusion in Children Undergoing Noncomplex Cardiac Surgery

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Background. Red blood cell (RBC) transfusion is frequently required in pediatric cardiac surgery and is associated with altered outcome and increased costs. Determining which factors predict transfusion in this context will enable clinicians to adopt strategies that will reduce the risk of RBC transfusion. This study aimed to assess predictive factors associated with RBC transfusion in children undergoing low-risk cardiac surgery with cardiopulmonary bypass (CPB).

Methods. Children undergoing surgery to repair ventricular septal defect or atrioventricular septal defect from 2006 to 2011 were included in this retrospective study. Demography, preoperative laboratory testing, intraoperative data, and RBC transfusion were reviewed. Univariate and multivariate logistic regression analysis were used to define factors that were able to predict RBC transfusion. Then, we employed receiver operating characteristic analysis to design a predictive score.

Results. Among the 334 children included, 261 (78%) were transfused. Age (< 18 months), priming volume of the CPB (> 43 mL/kg), type of oxygenator used, minimal temperature reached during CPB (< 32°C), and preoperative hematocrit (< 34%) were independently associated with RBC transfusion in the studied population. A predictive score 2 or greater was the best predictor of RBC transfusion.

Conclusions. The present study identified several factors that were significantly associated with perioperative RBC transfusion. Based on these factors, we designed a predictive score that can be used to develop a patient-based blood management program with the aim of reducing the incidence of RBC transfusion.

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Children undergoing cardiac surgery with cardiopulmonary bypass (CPB) frequently require red blood cell (RBC) transfusion [1]. Although RBC transfusion is safer than ever, it is still associated with side effects such as transfusion-associated lung injury and anaphylactic reaction [2, 3]. In pediatric cardiac surgery, RBC transfusion has been associated with several side effects, including increased postoperative nosocomial infection [4] and prolonged hospital stay [5].

Although the reported associations do not imply causality, there is universal agreement that all efforts should be undertaken to decrease exposure to RBCs [6]. However, few studies have tried to define predictors for RBC transfusion in children undergoing cardiac surgery [4, 7, 8]. These studies evaluated their pediatric cardiac population as a whole, although such a population is relatively heterogeneous regarding patients' characteristics and the procedures undergone. The transfusion policy might differ significantly between children undergoing the repair of different congenital heart defects, as some will be transfused during the CPB prime to maintain a reasonable hematocrit level, while other sicker children will be transfused in cases of hemorrhage in the context of complex surgery, or to increase oxygen delivery in cases of persistent lactic acidosis [9].

We designed this study with the primary objective of determining the predictive factors associated with RBC transfusion in a more homogeneous population; children undergoing ventricular septal defect (VSD) or atrioventricular septal defect (AVSD) repair surgery. The study's secondary objective was to examine the relationship between a predictive score and the incidence of RBC transfusion in the studied population.

Material and Methods

After obtaining approval by the local ethics committee (Queen Fabiola Children's University Hospital Ethic Committee), we performed a retrospective analysis of our departmental database, which included all consecutive children who underwent cardiac surgery with CPB between January 2006 and December 2011. We included all children scheduled for VSD or AVSD repair surgery.

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Children in a moribund state (American Society of Anesthesiology 5), and Jehovah's Witnesses were excluded from our analysis. The local ethics board waived the requirement for written informed consent given the retrospective nature of the protocol.

The same 2 surgeons performed all procedures during the study period. A senior anesthesiologist systematically performed preoperative evaluation. Preoperative laboratory testing included hemoglobin level, hematocrit, platelet count, coagulation assays (including fibrinogen level measured by the Clauss method [10]), creatinine level, blood urea nitrogen, and liver enzymes.

In the operating room, standard monitoring included pulse oxymetry, 5-lead electrocardiogram, noninvasive arterial pressure, arterial and central venous pressure, urinary output, and cutaneous and rectal temperature probes. Intravenous anesthesia based on midazolam, sufentanil, and rocuronium was preferred in all children. All patients received cefazolin 25 mg/kg, methylprednisolone 30 mg/kg after anesthesia was induced. Aprotinin was systematically used before 2008 [11]; tranexamic acid was used thereafter. Before aortic cannulation, 4 mg/kg unfractionated heparin (UFH) was administered to reach an activated clotting time greater than 480 seconds. Anticoagulation level was regularly checked during CPB using repeated activated clotting time measures, and additional UFH boluses were administered to maintain activated clotting time greater than 480 seconds throughout the entire CPB.

During the study period, the CPB circuit was primed primarily 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), sodium bicarbonate (20 mEq/L), and UFH (50 mg/L). Different models of oxygenator chosen based on body weight were used during the study period. In addition, new "miniaturized" oxygenators, which require a smaller prime volume, were introduced in our department in 2008.

When preparing the CPB prime, the hematocrit on bypass was calculated based on the volume of the prime and the estimated blood volume (EBV) of the patient. Packed RBCs were added to the prime when calculated hematocrit after cardioplegia (crystalloid cold balanced solution enriched in potassium chloride [30 mmol/L]) was estimated to fall below 20%. During CPB, body temperature was decreased according to the aortic clamp duration and surgical complexity. All patients were rewarmed to greater than 35.5°C before weaning from CPB. After weaning, modified ultrafiltration (MUF) was used to increase the hematocrit of the residual blood volume in the circuit.

Our RBC transfusion policy was standardized in agreement with the Anesthesiology Department and the Pediatric Intensive Care Unit (PICU). After separation from CPB, RBCs were transfused to maintain a hematocrit greater than 24%. In addition, RBC transfusion was considered in cases of abnormal bleeding or persistent lactic acidosis, in order to increase oxygen delivery after optimizing cardiac output with inotropes, vasoactive agents, or both.

Recorded data, including age (months), preoperative weight (kg), height (cm), preoperative oxygen saturation (%), American Society of Anesthesiology, and the risk adjustment for congenital heart surgery (RACHS) [12]. The RACHS score uses 6 categories of surgical risk, ranging from 1 (lowest) to 6 (highest). We also recorded the incidences of preoperative cardiac failure and previous cardiac surgery with or without sternotomy. Preoperative laboratory testing was included in the analysis; hemoglobin level (g/dL), hematocrit (%), platelet count ($\times$ 10^3/µL), fibrinogen level (mg/dL), prothrombin time (seconds), activated partial thromboplastin time (seconds), creatinin level (mg/dL), and blood urea nitrogen (mg/dL). Finally, the degree of hemodilution was measured in mL/kg using the ratio between the CPB prime volume (mL/kg), and the patient's EBV (mL/kg) [13]. The type of oxygenator, use of MUF, and amount of MUF (mL/kg) were also recorded. The RBC transfusion was defined as any intraoperative exposure to RBCs (during or outside CPB), as well as exposure during the entire PICU stay. We weighed sponges and measured surgical suction and chest tube drainage to calculate intraoperative and postoperative blood loss. We also calculated blood losses from the patients' EBV, preoperative and postoperative hematocrit (day 1), and the volume of RBCs transfused. No washed or unwashed cell salvage system was used during the study period.

Statistical Analysis

We used the Shapiro-Wilk normality test to assess continuous variables for normality. Because of the non-Gaussian distribution of the population, data are presented as median and interquartile range [25th percentile to 75th percentile]. Categoric variables are expressed as number and percentage (%). Groups were compared using the Wilcoxon rank sum test for continuous variables and the χ^2 test for categoric variables.

Univariate logistic regression analysis was performed for all possible determinants of RBC transfusion. We defined, a priori, that all variables with a p value less than 0.05 were considered relevant and included in the stepwise multivariate logistic regression analysis. This second analysis was used to define factors that were able to predict RBC transfusion in children undergoing VSD or AVSD repair surgery.

Next, we built separate receiver operating characteristic (ROC) curves for variables that significantly predict RBC transfusion. Results are expressed as area under the ROC curve with 95% confidence intervals (95% CI), Younden criterion, sensitivity, and specificity. Finally, those parameters were used to design a predictive score of RBC transfusion, which was validated using another ROC curve analysis. This analysis aimed to determine the sensitivity, the specificity, and the percentage of children correctly classified in the "transfused group," as well as the positive and negative predictive values and likelihood ratios.

Statistical analyses were performed using STATA version 13.1 for Mac OS (StataCorp, College Station, TX) and GraphPad Prism 6 version 6.0d for Mac OS