Measurement of Blood Loss in Cardiac Surgery: Still Too Much

Mark Nelson, MD, Jeffrey Green, MD, Bruce Spiess, MD, Vigneshwar Kasirajan, MD, Patricia Nicolato, DO, Hangcheng Liu, MStat, and Ryan S. Meshkin, BS

Department of Anesthesiology, Division of Cardiothoracic Anesthesiology, Department of Surgery, Division of Cardiothoracic Surgery, and Departments of Biostatistics and Biology, Virginia Commonwealth University, Richmond, Virginia

Background. **Cardiac surgery is associated with a significant decrease in hematocrit. It is unclear whether that occurs from hemodilution, loss of red cells, or both. Hematocrit is a major determinant of transfusion decisions although transfusion is associated with increased morbidity and mortality. Physicians must determine whether this anemia is the result of hemodilution or red blood cell loss as the former would be treated with packed red blood cell transfusions and the latter by diuresis. We hypothesize that the decrease in hematocrit observed in cardiac surgery is due to hemodilution.**

Methods. **Blood volume (BV), plasma volume (PV), and red blood cell volume (RBCV) were measured in 54 patients undergoing coronary artery bypass graft surgery, valve surgery, or coronary artery bypass graft/valve surgery. Measurements were made preoperatively, immediately postoperatively, and 2 hours after surgery utilizing a dilution tracer method and hematocrit measurements.**

Results. **Preoperative average BV was 6,094 mL (SD 1,904 mL), RBCV was 2,024 mL (SD 720 mL), and PV was 4,070 mL (SD 1,339 mL). Postoperative average BV was 4,834 mL (SD 1,432 mL), RBCV 1,226 mL (SD 527 mL), and PV 3,607 mL (SD 993 mL). Blood volume decreased 18% ($p < 0.0001$), RBCV decreased 38% ($p < 0.001$), and PV decreased 8% ($p < 0.012$). There were no significant changes between postoperative values and those 2 hours later in the cardiac surgery intensive care unit.**

Conclusions. **Decreases in hematocrit observed in cardiac surgery patients are due to significant red blood cell losses and not to hemodilution. Red blood cell losses averaged 38%. Plasma volume also decreased.**

(Ann Thorac Surg 2018;■:■–■)

Anemia in cardiac surgery patients is associated with significant adverse outcomes [1–4]. However, cardiac surgery with cardiopulmonary bypass (CPB) is associated with significant reductions in hematocrit [5–8]. To mitigate this effect, efforts are put forward to conserve the patient's native red cell mass as much as possible. Red cell scavenging and direct cardiotomy suction into the cardiopulmonary bypass pump are routinely used. Normovolemic hemodilution is often utilized and has been shown to decrease red cell transfusion [9–12]. Despite such interventions, substantial decreases in hematocrit are often observed and packed red blood cells (pRBC) transfusions are frequently administered, with between 27% and 92% of patients receiving at least one pRBC transfusion during a cardiac surgery hospitalization [13, 14]. Transfusion of pRBCs is associated with increased risk of adverse outcomes [15–19]. Despite guidelines, such as those published by The Society of Thoracic Surgery/Society of Cardiac Anesthesiologists in 2007 (and updated in 2011), there remains substantial variability in transfusion practices. In nearly all guidelines, hematocrit is a major determinant of decision to transfuse [9, 10].

Accepted for publication Nov 6, 2017.

Address correspondence to Dr Nelson, 1200 E Broad St, PO Box 980514, Richmond, VA 23298-0541; email: mark.nelson@vcuhealth.org.

Cardiothoracic surgery patients receive significant amounts of infusions not containing RBCs during the intraoperative period; these include carriers for other medication infusions, fluid boluses for hemodynamic instability, cardioplegia solutions to arrest the heart, cardiopulmonary bypass priming solutions, and platelet and clotting factor transfusions. Reduction of hematocrit is observed with excessive administration of non-RBC–containing solutions in general surgical, medical patients and patients undergoing cardiac surgery with CPB [20–23]. With this background information in mind and based on our clinical observations, we hypothesized firstly that much of the observed reduction in hematocrit associated with cardiac surgery was the result of hemodilution from RBC-free transfusions; and secondly that with modern blood conservation techniques, RBC mass was largely conserved, and hence, pRBC transfusions would be unwarranted.

Patients and Methods

This study was conducted in compliance with the protocol reviewed and approved by the Western Institutional Review Board (protocol number 20072128) as well as the regulations and policies of the Virginia Commonwealth University Medical Center.

Published by Elsevier Inc.

0003-4975/$36.00
https://doi.org/10.1016/j.athoracsur.2017.11.023

Abbreviations and Acronyms

BV = blood volume
CABG = coronary artery bypass graft surgery
CPB = cardiopulmonary bypass
CSICU = cardiac surgery intensive care unit
pRBC = packed red blood cells
PV = plasma volume
RBC = red blood cells
RBCV = red blood cell volume

After obtaining informed consent, 55 consecutive adult patients (aged 18 years or more) having either coronary artery bypass graft surgery (CABG) or valve surgery or a combination of CABG and valve surgery requiring CPB were consecutively enrolled between April 2009 and April 2010. Patients with recognized coagulopathy or having emergency surgery were excluded. The outcome variables included blood volume (BV), plasma volume (PV), and RBC volume (RBCV), in milliliters. All three outcome variables were measured at three timepoints; before surgery, after surgery, and cardiac surgery intensive care unit (CSICU). The presurgery measurement was taken after induction of general anesthesia, but before CPB. The postsurgery measurement was taken after the operation and after all intraoperative RBC transfusions were complete. The final measurements were obtained 2 hours after admission to the CSICU. For patients receiving blood transfusions in the operating room or in the CSICU before all data collection points, the transfused RBCV volume was recorded and subtracted from the RBCV measured after the transfusion. Transfused RBCV took into account hematocrit of 60% for pRBCs. Additional baseline information including age (year), sex (male, female), weight (kg), and surgery type was collected.

Cardiopulmonary bypass practice included anticoagulation with intravenous heparin to an activated clotting time of 480 seconds with regular monitoring throughout CPB; CPB circuit priming with crystalloid solutions and heparin, allowing the temperature to drift to between 32°C and 34°C; mean perfusion pressures between 50 mm Hg and 80 mm Hg; and cardiac index of 2.2 $L \cdot min^{-1} \cdot m^{-2}$. Cardioplegia solutions consisted of 4:1 blood to crystalloid solution with potassium concentration of 22 to 24 mEq/L administered intermittently during aortic cross clamping. Cell salvaging using the Sorin Compact Advanced cell saver (Sorin Group, Arvada, CO) was used as well as direct cardiotomy suction into the CPB pump. Retrograde autologous priming of the CPB pump was utilized unless hemodynamic instability was encountered. That was at the discretion of the anesthesiologist. After CPB, protamine was utilized to neutralize the heparin anticoagulation to an activated clotting time within 20 seconds of baseline. Epsilon-aminocaproic acid was used in all cases. Blood remaining in the CPB pump after the procedure was processed through cell salvage and reinfused before leaving the operating room.

Blood volume analysis was performed with the Daxor blood volume analyzer BVA-100 System and the Volumex HSA I-131 radiopharmaceutical (Daxor Corporation, New York, NY). This system uses a 1-mL unit dose of human serum albumin with attached iodine-131 as a dilution indicator for computation of circulating volume. This method has been utilized and published elsewhere [24–26]. For the tracer dilution method, the following blood samples were collected: baseline; first sample 12 minutes after injection (after complete mixing in the blood volume); and additional samples every 6 minutes for at least three successive timed sample points. These multiple timed sample points produce a logarithmic curve of radiation over time, as only a small fraction of albumin leaves the blood volume into the interstitial space. The Daxor machine uses a Coulter counter to measure the amount of radiation in each prepared sample and software to compute a regression curve to accurately back-calculate the concentration of the tracer (assuming perfect, immediate distribution at time 0) in the blood volume at time 0. The details of the operation of this device have been reported previously [27].

Statistical Analyses

The mean and standard deviation (SD) or frequency and percentage were calculated for each baseline characteristic. Spaghetti plots of the raw longitudinal profiles were created for each outcome. Linear mixed-effects models were used to fit each outcome over the three timepoints. Each model predicting the raw volumes included separate fixed effects of time, sex, surgery type, and the interaction of sex and time. A secondary outcome using the percentage change from baseline for BV, PV, and RBCV for each subject was modeled using a linear mixed-effects model with time, sex, and surgery type as fixed effects. An unstructured covariance matrix was used for each of the mixed-effects models. The mean and standard error (SE) were calculated for all predicted values. A preliminary assessment showed no evidence that the interaction term of sex and time had significant relationship with any of the outcomes; therefore, this interaction term was not included in secondary analysis. Statistical significance in these models and tests were defined as a p value less than 0.05.

Power Analysis

Average plasma volume for men and women is 2,950 mL (SD 590 mL) [26]. To detect a 10% increase in plasma volume from hemodilution with a power 0.80 and α error 0.05, a one-tailed normal distribution Student's t test determines a sample size of 50. To account for a 10% data loss (technical difficulty, patient withdrawal), a sample size of 55 was required.

Results

Fifty-four subjects were included in the analysis. One subject had missing or incomplete data and was not included. The summary of the baseline information is shown in Table 1. The summary of BV, PV, and RBCV