Outcomes and Biochemical Parameters Following Cardiac Surgery: Effects of Transfusion of Residual Blood Using Centrifugation and Multiple-Pass Hemoconcentration

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Objectives: **To determine whether or not there was a significant difference between the methods of centrifugation (CF) and multiple-pass hemoconcentration (MPH) of the residual cardiopulmonary-bypass volume in relation to biochemical measurements and patient outcomes.**

Design: **Prospective, randomized, and controlled.**

Setting: **Conducted at a western Canadian tertiary care hospital.**

Participants: **Consisted of 61 consecutive male and female patients from ages 40 to 80 who were scheduled for cardiac surgery with cardiopulmonary bypass.**

Interventions: **Either the centrifugation or multiple-pass hemoconcentration method was used to process the residual blood from the cardiopulmonary bypass circuit.**

Results: **The 12-hour postoperative levels of serum hemoglobin were not significantly different in the centrifugation group as compared to the multiple-pass hemoconcentration group. However, the serum levels of total protein and albumin were significantly higher in the multiple-pass hemoconcentration group as compared to the centrifugation group. Additionally, after 12-hours postoperatively, the serum fibrinogen and platelet counts were significantly higher in the multiple-pass hemoconcentration group as compared to those of the centrifugation group.**

The allogeneic product transfusion index and the chest-tube blood drainage indices were lower in the multiple-pass hemoconcentration group as compared to the centrifugation group.

Conclusion: **Although the CF method provided a product in a shorter turnaround time, with consistent clearance of heparin, the MPH method trended towards enhanced biochemical and clinical patient outcomes over the 12-hour postoperative period.**

KEY WORDS: centrifugation, multiple-pass hemoconcentration, allogeneic transfusion, chest tube drainage

MORE THAN 500,000 CARDIAC PROCEDURES are performed in North America every year,[1] with approximately 40-90% receiving allogeneic product transfusions. The transfusion rates related to cardiac surgery range from about 40-90% for red blood cells (RBCs) and up to 90% for fresh frozen plasma (FFP) and platelets,[2] with 20% of recipients consuming 80% of the transfused products.[2] The probability of critically ill patients experiencing a major adverse event from a blood transfusion ranges from 2.5%-40%.[3,4] Complications arising from a blood transfusion include but are not limited to acute transfusion reactions, transfusion-related lung injury, incorrect component transfusion, hemolysis, infections, storage errors, and anti-D administration errors.[4] The implication is that the higher the transfusion rate, the higher the complication rate and, thus, the more benefit is derived from reducing/eliminating transfusion requirements in cardiac surgical patients. Differing methods of the salvage of the residual cardiopulmonary bypass (CPB) circuit volume may influence patient blood product transfusion requirements over the 12-hour postoperative period.[5,6] Consequently, changes in transfusion requirements may impact patient outcomes during the 12-hour postoperative recovery period.

Current practice in cardiac surgery requiring CPB dictates the salvage of the residual circuit volume at the end of the procedure into an autologous recovery system. This system uses the centrifugation method (CF) to separate whole blood into red blood cells (RBCs) and plasma components.[7] The RBCs are washed with normal saline and re-infused into the patient while the plasma portion is discarded. Possible disadvantages of this technique include up-regulation of the systemic inflammatory response,[8,9] increased risk of fat emboli,[10] and the loss of plasma proteins including albumin, coagulation factors, and hormones.[7,10]

Ultrafiltration (hemoconcentration) of the residual volume from the CPB circuit utilizing a device called an "ultrafiltrator" (hemofilter) represents an alternative technique of autologous recovery.[11,12] Similar to the filter used during dialysis, a hemofilter removes excess plasma water while preserving plasma protein and coagulation factors thereby minimizing allogeneic blood product use.[12,13] As it concentrates plasma protein, it increases colloid osmotic pressure (COP), reducing the risk of edema.[14,15] Multiple-pass hemoconcentration (MPH) differs from conventional hemoconcentration by passing blood through the hemofilter several times, thereby enhancing the effect of blood concentration.[11,12]

The preservation of the serum protein concentration, specifically serum albumin, may have advantages, including reduced interstitial fluid accumulation and decreased fluid administration during the postoperative period.[15-18] Several clinical conditions often present in cardiac surgical patients increase the transvascular escape rate of albumin. These include the use of CPB,

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hypertension, fluid overloading, inflammation, ischemia/reperfusion, congestive heart failure, and diabetes.[15] The use of MPH also enhances preservation of clotting factors, the loss of which could negatively impact patient recovery during the 12-hour postoperative recovery period.[19-21]

The main objective of this study was to determine which of the two methods for the recovery of the residual CPB volume was better at enhancing overall patient outcomes during the 12-hour postoperative period. The means used to carry out this objective were the comparative determination of biochemical/hematologic parameters such as serum hemoglobin (Hb), albumin (ALB), total protein (TP), clotting factors, and markers of inflammation and the secondary outcome parameters previously described.

MATERIALS AND METHODS

The sample population consisted of 61 consecutive male and female patients from 40 to 80 years old scheduled for elective or urgent cardiac surgery with CPB. All of the subjects signed a written informed consent to participate in this study.

Exclusion criteria included (1) emergent cardiac surgery, (2) history of severe liver or kidney dysfunction, (3) anemia, (4) cardiogenic shock, (5) cardiomyopathy, (6) redo-cardiac procedures, (7) history of stroke (8) history of transient ischemic attacks, and (9) preoperatively documented coagulopathies.

With the University Research Ethics Committee approval, patients scheduled for elective or urgent cardiac surgery with CPB were recruited. Patients were assigned to a CF or MPH group according to a computer-generated random number table. Opaque envelopes containing this information were opened when the CPB circuit was set up, and the randomly selected CF or MPH circuit then was incorporated into the CPB circuit.

This study was a prospective, randomized, controlled trial that comprised two groups. It was blinded to the surgeons, operating room staff, ICU staff, and lab personnel. The perfusionist was not blinded for clinical necessity. Due to the inability of the hemofilter to remove all circulating heparin and for the sake of patient safety, the anesthesiologist was not blinded because of the potential need for additional protamine to be administered.

The two groups were as follows: Group I ($n = 31$), the control group, the residual volume underwent centrifugation (CF); and Group II ($n = 30$), the test group, the residual volume underwent multiple-pass hemoconcentration (MPH). Standard procedures were followed during cardiac surgery, and only the salvage of the residual volume of blood in the CPB circuit was affected.

The conduct of anesthesia was left to the discretion of the attending anesthesiologist and generally was based on a standard protocol for cardiac surgery patients. Target mean arterial pressure and heart rate were within 20% of the mean baseline values. Hemodynamic control was provided by modification of the concentration of the inhalation anesthetic or intravenous vasoactive drugs and/or volume repletion. A dose of unfractionated heparin was determined by the Medtronic heparin management system's (HMS) heparin dose-response test (Medtronic, Minneapolis, MN) and administered at the direction of the attending surgeon. Activated coagulation time (ACT) was measured and ensured to be greater than 480 seconds prior to the initiation of CPB. All patients also received 2 grams of intravenous tranexamic acid after heparinization. In coordination with the surgeon, the anesthesiologist administered FFP, platelets and cryoprecipitate based upon the presence of a coagulopathy or nonsurgical bleeding as determined by thromboelastography (TEG), HMS, and complete blood count (CBC).

A Sorin heart-lung machine (Sorin, Munich, Germany) roller pump was used with flows of 2.4 to 2.6 L/min/m^2 in the non-pulsatile setting. The oxygenator used was an Affinity with Trillium (polymer with heparin) coating with a Trillium-coated affinity twenty-micron arterial line filter (Medtronic, Minneapolis, MN). The extracorporeal circuit tubing was made by Sorin S5 with Physio (phosphorylcholine) (Sorin, Mirandola, Italy) coating. Circuits were flushed with carbon dioxide prior to priming. The prime consisted of Plasma-Lyte A (Baxter, Mississauga, ON, Canada), Voluven (Fresenius Kabi, Bad Homburg, Germany), sodium bicarbonate, mannitol, and heparin.

Heparin dosing was determined as described in the previous section. ACT during CPB were kept above 480 seconds while the heparin concentration was maintained at or above 300 u/kg through blood analysis with the HMS.

Cardiac activity was arrested with an induction dose of warm blood cardioplegia followed by intermittent cold doses for the duration of the aortic cross-clamp time. Blood gases, electrolytes, metabolites, and oximetry were monitored every 30 minutes via an 815 Flex ABL analyzer (Radiometer America Inc, Westlake, OH). During the CPB period all patients regardless of age/sex with a hemoglobin less than 70 g/L were transfused with RBCs.

Before separation from CPB, preload was optimized, and an infusion of epinephrine, dopamine, norepinephrine or phenylephrine alone or in combination was used to maintain a systolic blood pressure of greater than 110 mmHg after CPB. Intravenous nitroglycerin was administered as needed.

All patients had chest tubes placed in the anterior mediastinum (9 mm Mediastinum Drain, Axiom Medical Inc, Torrance, CA.), and the posterior pericardial (32 Fr Thoracic Drain, Axiom Medical Inc, Torrance, CA) cavity. These chest tubes were connected to a sterile system (Oasis Dry Suction, Atrium Inc, Hudson, NH) that drained shed blood over the 12-hour postoperative period.

Circulating heparin was reversed by an HMS-determined protamine dose after disconnection from CPB. All patients were transported to the intensive care unit, intubated, and sedated at the completion of the procedure.

Recovery of the residual CPB volume with the CF method used a Medtronic Autolog™ Autotransfusion system (ATS) (Medtronic Inc, Minneapolis, MN). After aortic cannula removal, the sterile end of the vent line was connected to the luer port of the arterial cannula, and the opposite end was connected to the cardiotomy reservoir of the ATS. The residual CPB circuit then was flushed antegrade with Plasma-Lyte® solution to the ATS reservoir. The bidirectional automated fluid pump of the ATS has a maximum flow of up to 600 mL/min and a centrifugation rate of up to 10,000 RPM (± 5%). The packed RBC's are washed with 0.9% NaCl and recovered into a transfusion bag, which was connected to an intravenous anesthesia catheter for infusion as needed. The CF method processed the residual CPB volume in approximately 5-7 minutes, with a mean volume and standard error of the mean (SEM) of 648.36 ± 25.6 mL.

Recovery of the residual CPB volume with the MPH method used a Sorin hemofilter (Milan, Italy) and Medtronic 20-micron cardiotomy reservoir (Milan, Italy). Following aortic decannulation, the vent line was connected to the luer on the arterial cannula while the other end was connected to the cardiotomy reservoir of the hemoconcentration system. The CPB circuit was flushed antegrade with Plasma-Lyte® solution into the reservoir of the hemoconcentration system. MPH via a roller head pump at 250-300 mL/min facilitated the removal of crystalloid under low continuous negative pressure. As determined by the perfusionist following standard protocol, MPH was discontinued when the desired pressure and hemoglobin were achieved. The MPH method processed the residual CPB volume in approximately 10-15 minutes, with a mean volume of 731 ± 54.72 mL. The volumes of processed blood from the two methods were not clinically or statistically different.