Comparing Ultrafiltration and Centrifugation During and After Pediatric Cardiopulmonary Bypass

Traynor L, BS; Sutton R, CCP, Riley J, CCT, Crawford FA Jr, MD, Sade RM, MD
The Department of Extracorporeal Circulation Technology, College of Health Related Professions, and the Division of Cardiothoracic Surgery, Medical University of South Carolina

Keywords: ultrafiltration, centrifugation, blood processing, pediatrics

Abstract

Blood processing techniques related to pediatric cases have previously been generalized from adult experiences.

Twenty-two pediatric patients (<25 kilograms) undergoing cardiopulmonary bypass (CPB) for various congenital defects were prospectively randomized into an ultrafiltration or centrifugation group. Sixty-one variables were compared.

The blood infused from the ultrafiltration technique contained significantly more heparin ($p=0.0001$) and more plasma-free hemoglobin (PFH) ($p=0.0001$) levels than the centrifugation blood. Centrifugation patients had a significantly higher hematocrit ($p=0.0066$) than the ultrafiltration group twenty minutes postoperatively. The ultrafiltration patients (mean=431.82cc±116.8) received less total packed red blood cell volume before and during bypass than the centrifugation group (mean=534.091cc±113.07). In the centrifugation group, wash volumes showed positive correlation to postoperative blood sodium levels ($r= +0.4006$, $p< 0.05$). No significant difference was found between postoperative and preoperative sodium levels ($p> 0.05$). PFH levels for both groups showed a significant positive correlation to postoperative creatinine levels ($r= +.4029$, $p< 0.05$) suggesting decreased postoperative renal function, but a significant negative correlation to post-bypass hematocrit ($r= -.4548$, $p< 0.05$). Post-bypass heparin levels in the circuit showed a significant positive correlation to heparin levels in the reinfusion blood for the ultrafiltration group ($r= +.8025$, $p<0.05$). Post-bypass PFH level in the circuit showed a significant positive correlation to PFH levels in the reinfusion blood for both groups ($r= +.5339$, $p<0.05$). No significant difference existed between the ultrafiltration and centrifugation groups for postoperative prothrombin and partial thromboplastin times.

For pediatric cases, the centrifugation technique was found to be superior for post-bypass blood processing based on a higher postoperative patient hematocrit and the presence of less heparin and less PFH in the reinfused blood. The ultrafiltration technique was found to be superior for intraoperative blood processing due to a lower total packed red cell volume addition before and during bypass.

Address correspondence to: Laura J. Traynor
Medical University of South Carolina
CHRP, ECT
171 Ashley Avenue
Charleston, South Carolina 29425-2701

Introduction

Initiation of cardiopulmonary bypass (CPB) in the pediatric open-heart surgery patient results in considerable hemodilution. Minimization of extracorporeal circulation circuit (ECC) surface area plus the substitution of packed red blood cells (pRBCs), fresh frozen plasma (FFP), and 25% salt poor albumin (SPA) for the crystalloid prime reduces the degree of hemodilution. However, the pediatric patient's blood volume, in contrast to an adult's blood volume, is either less than or equal to the ECC priming volume. Therefore, intraoperative and post-CPB ECC blood volume salvage are important clinical practices that can minimize the use of donor blood products. Autologous blood processing has the advantage of decreasing possible patient-transfusion allergic reactions and limiting exposure to the non-A or non-B hepatitis and AIDS virus' all life-threatening hazards of donor transfusions. The current risk of such transfusion related incidents is one in every 100 transfusions[1]. Other major transfusion risks to the pediatric patient are exposure to the cytomegalovirus[2] and post-transfusion graft-versus-host disease[3]. The process of ultrafiltration and centrifugation are both resourceful and safe methods of returning autologous concentrated packed red blood cell (pRBC) volume to the patient from the ECC.

A search of the literature revealed no studies relating the techniques of centrifugation and ultrafiltration specifically to the pediatric patient undergoing CPB. The results of many comparative centrifugation and ultrafiltration studies performed on adult patients[4-7] should not be directly applied to pediatric patients. The CPB pediatric patient group is physiologically unique from adult CPB patients. The disease processes of each are very dissimilar, requiring adherence to different protocols for hemodynamic and pharmacologic management. Direct application of clinical and theoretical practice from an adult to a child is not always possible and could even be considered danger-

ous.

Centrifugation, utilized first for postoperative CPB blood salvage by Moran in 1978[8], involves the use of a centrifugal pump to separate the red blood cell layer from the plasma layer. Packed red blood cells are washed with 0.9% normal saline to remove plasma and debris. Administration of the resultant normal saline and pRBC suspension, which has a sodium ion (Na+) concentration of 154 mEq/L, is a concern to a child whose normal blood Na+ concentration is 134-145 mmol/L[9]. The pediatric kidney is less capable of handling large electrolyte and serum concentration changes than the adult kidney. Elevated sodium levels lead to an increase in potassium ion (K+) depletion in pediatric patients[10]. Since pediatric renal Na+ clearance is lower than adult Na+ clearance, a sudden increase in blood Na+ concentrations may not be followed by a corresponding increase in Na+ excretion.(11) Imposing sudden electrolyte imbalances places additional stress on pediatric kidneys to provide adequate and prompt homeostatic restoration. The inability to adjust may lead to nephrotic impairment.

Acute renal failure in the pediatric patient can be defined as a decrease in normal renal function resulting in the buildup of nitrogenous waste in the blood.[12] Normal plasma blood urea nitrogen (BUN) and creatinine levels for a child are 5-18 mg/dl and 0.3-0.7 mg/dl respectively.[9] Plasma-free hemoglobin (PFH) has been recognized as a substance capable of producing acute renal failure[13,14] and nephrotoxicity[15]. Hemoglobin, the primary oxygen carrier of the blood, is liberated into the plasma upon rupture of a red blood cell. Under normal daily conditions, less than 1 mg/dl of hemoglobin is released into the plasma. Once free in the plasma, hemoglobin is removed by one of two physiologic processes: hepatic parenchymal breakdown or renal excretion. Haptoglobin, a glycoprotein in the plasma, binds to free hemoglobin to form a complex which prevents leakage of hemoglobin through the glomeruli. Haptoglobin is present in sufficient concentrations to bind 50-200 mg/dl of hemoglobin; excessive hemoglobin concentrations in the plasma can result in haptoglobin depletion. Hemoglobin is subsequently filtered by the kidneys to produce hemoglobinuria. Following a large deposit of hemoglobin in the glomerulus, casts may develop causing impairment of nephrotic function[16] The centrifugation technique has been shown to result in incomplete removal of PFH from the blood in various adult surgical cases[13], but PFH removal specific to pediatric open heart patients has yet to be established.

Sodium heparin, a heterogenous material of molecular weight 6,000-22,000 daltons[17], acts pharmacologically as a catalyst in the presence of an anticoagulant plasma cofactor called antithrombin III. This heparin-antithrombin III complex blocks the coagulation cascade by binding thrombin and the activated forms of coagulation factors 9,10,11, and 12. Heparin has little anticoagulant activity both below a molecular weight of 6-7,000 and in instances of antithrombin III depletion. The reinfusion bag volume should be optimally free of heparin and contain pure pRBCs in normal saline. Anticoagulant removal by centrifugation has been shown to be almost complete in adult surgical cases, with levels of 0.1-0.2 units of heparin per milliliter of reinfused blood considered adequate washout.[13]

First used by Darup in 1979 during CPB[18], ultrafiltration involves removal of substances from the blood smaller than the hollow fiber pores such as plasma water, electrolytes, and crystalloid. A negative suction pressure applied across hollow fiber membranes plus the positive pressure produced by blood flow through the hemoconcentrator create an ultrafiltration transmembrane pressure gradient. Solutes removed from the blood in the ultrafiltrate have a molecular weight size less than the pore size of the membrane. All larger solutes are retained in the blood. The protein-bound heparin molecule is thought to be too large to pass through the hollow fiber pores and remains in the blood returned to the patient.[5] Protamine sulfate effectively combines with and neutralizes heparin in the blood. Therefore, an additional dose of protamine is required when reinfusing ultrafiltrated blood.

Studies have shown PFH also to be concentrated in the ultrafiltrated reinfused blood due to its large molecular size[15]. A sudden increase in PFH levels has been shown to be toxic to the pediatric kidney leading to impaired postoperative renal function[13,14]

The outcome of this comparison of concentrated autologous post-CPB blood for administration to the pediatric cardiac surgery patient is of great importance in determining the utility and safety of pediatric blood processing practices on postoperative recovery and optimal pediatric patient care.

The purpose of this study is to show the superiority of either ultrafiltration or centrifugation as utilized during intraoperative and postoperative autologous blood conservation.

Materials and Methods

Twenty-two patients (<25 kilograms) undergoing surgical repair of various congenital heart defects with CPB were prospectively assigned to either the ultrafiltration (UF) (n=11) or the centrifugation (CF) (n=11) group. The circuit assembly for both groups consisted of a filtered cardiotomy[a], continuous membrane oxygenator with soft-shell venous reservoir and heat exchanger[b], arterial line filter[c], arterial roller pump[d], and custom tubing pack[e]. Intraoperatively, similar alpha stat hypothermic blood gas management was used for both groups. Cold crystalloid cardioplegia solution provided necessary myocardial protection. Activated clotting times were measured with an automated system[f]. The prime consisted of a varied mixture of pRBCs, FFP, SPA, and Plasma-Lyte A solution[g]. According to Medical University of South Carolina (MUSC) surgeon's CPB protocol, pRBCs were added to the prime to raise the calculated post-dilutional hematocrit to a mini-

mum level of 25%. FFP was added to the prime also according to protocol to maintain the fibrinogen level above 100 mg/dl. Blood products, crystalloid, colloids, and heparin were added to the circuit as required during the case.

In the UF group, blood processing was performed parallel to the arterial side of the ECC by a connection from the sampling manifold to the cardiotomy. An Amicon Diafilter 10 or 20[h], flushed with 1000 ml 0.9% normal saline, was used as the hemoconcentrator after CPB (and during CPB if required) in all UF cases. The Amicon Diafilter was chosen due to its small priming volume (25 to 38 ml) and surface area (0.2-0.4 m^2), as compared to other hemofilters commonly used on adults. After CPB, the ECC blood volume was ultrafiltrated, pumped into a transfer bag, and administered through a peripheral intravenous line. The protamine dosage was given through a separate line. Protamine dose was calculated based on the following equation:

$$\frac{\text{Post-CPB patient protamine dose}}{\text{Patient blood volume}} = \text{x} \frac{\text{(protamine dose post-UF)}}{\text{Pre-UF Circuit volume}}$$

The CF group circuit was set up by attaching the Cell Saver device[i] to the cardiotomy drainline. During CPB, CF was permitted; however, a wash cycle was not performed. After CPB, each 125cc bowl was washed with at least 375cc 0.9% normal saline and then administered to the patient through a peripheral intravenous line.

The following data was recorded for evaluation for both groups (unless otherwise specified):

Preoperatively

Group, patient number, age, height, weight, body surface area, heparin dose, patient volume, prime pRBC volume, prime FFP volume , prime 25% salt poor albumin (12.5 grams/50 ml) volume, prime Plasmalyte A volume, hematocrit, white blood cell count, platelet count, Na+, K+, BUN, creatinine, prothrombin time (PT), and partial thromboplastin time (PTT).

Intraoperative Samples:

Na+ sample before rewarming

Immediate Post-CPB:

Total cardioplegia volume, anesthesia volume, CPB time, circulatory arrest time, cross-clamp time, patient protamine dose, intraoperative fluid volume additions (pRBCs, FFP, SPA, Plasmalyte A, heparin), last hematocrit recorded on CPB, and reinfusion bag volume.

CF: Spillover volume in waste bag if centrifugated during CPB, 0.9% normal saline volume used to wash the reinfusion volume post-CPB, PFH sample from the ECC before centrifugation, and heparin and PFH levels from the reinfusion bag after processing and before administering to the patient.

UF: Ultrafiltrate during the post-CPB ultrafiltration process, ultrafiltration protamine dose, heparin and PFH level from ECC before ultrafiltration, and heparin and PFH level from the reinfusion bag after processing and before administering to the patient.

Post-CPB Administration of Reinfusion Blood - 30 minutes & 12 Hours

Platelet count, Na+, white blood cell count, hematocrit, BUN, creatinine, K+, PT, and PTT.

The laboratory values were measured as follows by the MUSC Laboratory:

Chemistry 7 Profile: BUN, Na+, K+, Creatinine

Hematology Panel: White blood cell count, Hematocrit

Platelet analysis: Platelet count

Coagulation Profile: PT, PTT

The PFH sample was analyzed by the Routine Coagulation Department of the MUSC laboratory by two methods: spectro-photometrically and the chlorpromazine method. The absorbance spectrum band for oxyhemoglobin is 528nm measured spectro-photometrically and 577nm measured by the chlorpromazine method. The PFH values were recorded using the chlorpromazine method, which has been shown to block interference of serum bilirubin with PFH[19]. The heparin assay was analyzed by the Coagulation and Chemistry Department of MUSC on the ACA discrete clinical analyzer[j].

Sixty-one variables were compared using analysis of variance, analysis of covariance, and correlation from a computerized statistics package[k]. All p values <0.05 were considered to be significant.

Results

The two test groups were found to be similar with regard to age, weight, height, body surface area, and patient blood volume. Tables 1 and 2 summarize the remaining variable data. The parameters, as listed in Table 2, found to be significant between the two groups were the hematocrit values recorded just before termination of bypass, the 30 minute postoperative hematocrit values, the heparin and PFH levels measured in the reinfusion bag, and the total pRBC volume addition.

The reinfusion bag volume of both groups was ana-

a CR Bard Inc., Billerica, MA 01821
b SCIMED, Life Systems, Inc., Minneapolis, MN 55441
c Pall Biomedical Products Corp., Glen Cove, NY 11542
d Shiley Laboratories, Irvine, CA 92714
e Baxter Bentley Laboratories Inc., Irvine, CA 92714
f International Technidyne, Edison, NJ 08820
g Baxter Healthcare Corp., Deerfield, IL 60015
h Amicon Division, Beverly, MA 01915
i Haemonetics Corporation, Braintree, MA 02184
j DuPont Company, Biomedical Products Dept., Wilmington, DE, 19898
k BMDP Statistical Software, Inc., Los Angeles, CA 90025

lyzed for heparin and PFH levels. The UF group was found to have significantly more heparin than the CF group. PFH levels were also found to be significantly higher in the UF group than the CF group.

Hematocrit values just prior to ECC termination and 30 minutes postoperatively were found to be significantly higher in the CF group than in the UF group. A significantly higher total pRBC volume was given to the CF group.

PFH levels in the reinfusion bags for both groups showed significant positive correlation to 12 hour postoperative creatinine levels ($r = +.4029$, $p < .05$), but significant negative correlation to postoperative 30 minute hematocrit levels ($r = .4548$, $p < .05$).

The 0.9% normal saline wash volume used in the CF group was found to have a significant positive correlation with 30 minute postoperative Na+ levels ($r = +0.4006$, $p < .05$). No significant difference was found between preoperative and postoperative Na+ or K+ levels ($p > 0.05$).

PFH levels in the ECC before blood processing showed a significant positive correlation ($r = +.5339$, $p < 0.05$) to the PFH in the reinfusion bag after processing in both groups. Heparin levels in the ECC before blood processing showed significant positive correlation ($r = +.8025$, $p < 0.05$) to heparin levels in the reinfusion bag after processing.

Discussion

In choosing a blood conservation process to be used during and after bypass, the specific needs of the patient should be considered carefully. There are important differences in the final reinfusion product with each method that could directly affect a patient's postoperative progress. The pediatric patient is no exception. Analysis of the data from this study revealed that CF was the treatment of choice for post-CPB blood processing in the pediatric patient due to higher postoperative hematocrit levels, lower heparin and PFH levels in the reinfused blood, and near total anticoagulant removal requiring no additional protamine. UF was found to be superior to CF when used during CPB in pediatric patients due to a lower required total pRBC volume addition before and during bypass as well as plasma component preservation during CPB. These results differ from similar comparative studies on adult patients in that UF was found to be the preferred method for intraoperative[4] and post-CPB blood processing[4-6].

Total pRBC volume is defined as priming pRBC volume plus intraoperative pRBC volume addition. UF patients received less total pRBC volume than CF patients. (Figure 1) The intraoperative difference in pRBC addition can most likely be attributed to the way the perfusionist chooses to raise the hematocrit during CPB given the blood conservation process at hand. If centrifugation is the chosen method of blood processing during CPB, the perfusionist may be more inclined to add donor blood to raise the hematocrit rather than lose a substantial amount of circuit volume to the centrifugation bowl at one time while the blood volume is washed and then returned to the circuit. When the ultrafiltrator is employed during CPB, the perfusionist may delay the addition of donor blood to the circuit since extra volume can be concentrated quite conveniently without large circuit volume depletion or ultrafiltrator holdup volume. The CF group had significantly higher hematocrit values at the cost of increased pRBC volume addition just prior to CPB termination. However, the difference in the mean hematocrit values of the groups at CPB termination was 2.36%. (Figure 2) This small difference in the hematocrit values does not substantiate the increased use of donor blood volume associated with the CF process. Clearly, this reduced exposure to blood transfusion, is an advantage of the intraoperative use of the UF technique.

Post-CPB ECC heparin levels were found to be significantly and positively correlated to heparin levels in the reinfusion blood for the UF group. Most of the heparin in the ECC did not pass through the ultrafiltrator hollow fibers and became concentrated by an average of 314% in the reinfusion blood. Heparin in the blood is bound to plasma antithrombin III. When an antithrombin III deficiency is present, as in cases of acute venous thrombosis, disseminated intravascular coagulation, inherited tendencies, and liver cirrhosis, heparin circulates freely unbound in the plasma. The hollow fibers of the ultrafiltrator have an average molecular weight restriction size of >20,000 daltons for proteins and >54,000 daltons for linear molecules, such as heparin (Amicon Division specifications) The average molecular weight of unbound heparin (6,000-22,000 daltons[17]) is small enough to pass through the membrane pores. The average molecular weight of the antithrombin III protein molecule (60,000-65,000 daltons[20]) combined with the molecular weight of heparin gives a complex much too large to cross the membrane. Therefore, most of the heparin is concentrated in the blood, not the ultrafiltrate, after UF.

The UF technique resulted in more heparin concentrated in the reinfused blood than the CF technique. (Figure 3) Residual heparin is known to cause substantial postoperative bleeding in CPB patients.[17] To counteract the heparin in the reinfused blood, additional protamine must be given with the UF reinfusion blood based on the post-CPB protamine dose after activated clotting times have returned to baseline. Excessive protamine administration for heparin reversal should be monitored closely for potential patient anaphylactic reaction.[21] The CF technique was shown to leave only traces of heparin in the reinfused blood as compared to the UF technique. An adult study by Bolt(6) also found heparin to be higher in the UF group. No additional protamine was required for the CF group.

Post-CPB PFH levels in the circuit showed a significant positive correlation to PFH levels in the reinfused blood for both groups. The concentration of PFH in the reinfusion blood is dependent on the concentration in the ECC prior to blood processing. Based on these data, neither the ultrafiltration or centrifugation processes cause significant gen-

eration of additional PFH. These findings concur with those of Hopeck[22] who concluded that the UF process does not cause an increase in hemolysis.

PFH levels prior to blood processing were not found to be significantly different, whereas PFH levels in the reinfusion bag volume were found to be significantly higher in the UF group. (Figure 4) These data suggests PFH to be concentrated by approximately 538% with the UF process and by approximately 262% with the CF process. Thus, PFH is not reduced by 1/3 in the CF process in children as Solem[7] suggested in a similar adult study. PFH was concentrated with both processes, but to a greater extent with the UF process.

Large quantities of PFH have been shown to lead to decreased renal function in the pediatric patient.[13,14] High postoperative blood creatinine levels correlated well to high PFH levels in the reinfused blood in both groups. (Figure 5) CPB time was also shown to have a significant positive correlation to postoperative blood creatinine levels in both groups. Since longer CPB times are known to be associated with increased hemolysis and PFH levels[23-24], the higher postoperative creatinine levels can most likely be attributed to PFH generation from damaged red blood cells. These associations suggest the presence of potential postoperative renal dysfunction in both groups, with the UF group having the higher reinfusion PFH and postoperative creatinine levels. PFH-induced renal dysfunction is potentially irreversible in patients exhibiting a prior preoperative history of renal problems or who experience a prolonged hemolytic episode (as caused by prolonged CPB times).[15] Since the plasma half-life of heparin is prolonged in renal dysfunction[17], high PFH levels in the reinfused blood may increase the risk of postoperative bleeding. The higher PFH levels in the UF group in this data is similar to findings of adult studies by Solem[7] and Bolt[6], but differ from adult findings by Sutton[4] where there was no significant difference between groups for PFH levels.

The autologous blood returned after CPB contributed an average of 54.45% of the patient's preoperative circulating blood volume. In both groups, the higher the PFH levels in the reinfused blood, the lower the postoperative patient hematocrit. Often, pediatric patients with cyanotic heart defects become polycythemic during their preoperative disease course[25] to compensate for hypoxemia and require a higher than normal hematocrit post-CPB. It is advantageous for this patient population group, as well as the acyanotic group, to receive non-hemolyzed blood post-CPB with a maximized hematocrit to help support tissue oxygenation post-CPB and decrease renal dysfunction.

The CF technique resulted in a significantly higher hematocrit 30 minutes postoperatively than the UF technique, with the mean difference being 7.66%. (Figure 2) The reinfusion bag volumes were not significantly different between groups. The blood processing technique of CF used post-CPB does result in substantial increases in initial postoperative patient hematocrit values. Both postoperative intensive care blood loss and intensive care pRBC addition volumes were not recorded as data in this study; these variables most likely had an influence on postoperative 12 hour hematocrit levels. Adult patient studies by Solem[7] and Bolt[6] also found postoperative hematocrits to be higher in the centrifugation group; whereas Sutton[4] and Brickley[5] found them to be not significantly different.

One concern of the CF technique was higher postoperative Na+ levels causing K+ depletion. This study showed that total wash volumes greater than three times the reinfusion bag volumes resulted in higher postoperative patient blood Na+ levels in the CF group. Similarly, studies by Solem[7] and Bolt[6] found increased Na+ levels in the reinfusion blood volume after CF. Hypernatremia secondary to Na+ excess is associated with significant intracranial pathological changes and central nervous system dysfunction. Rapid correction of hypernatremia can cause seizures and even death in pediatric patients.[26] This might generate concern for the volume of wash solution used for CF in pediatric patients; however, postoperative patient Na+ and K+ levels were not found to be significantly different from preoperative and intraoperative Na+ and preoperative K+ levels respectively in both groups. From these data, the 0.9% normal saline solution used in the CF technique appears to be a safe and effective way to wash red blood cells prior to pediatric patient administration. Five of the eleven CF patients had postoperative blood Na+ levels elevated above the normal range for pediatric patients. All eleven CF patients' reinfusion bag volumes were washed with an average of 5.67 times the reinfusion bag volume itself. Pediatric patients with poor or questionable renal function would probably benefit from a CF wash volume of exactly three times the bowl volume and no greater. The manufacturer recommends a wash volume of no less than three times the bowl volume.

The process of UF allows for plasma salvage in the reinfused blood.[27] The postoperative return of plasma in hemoconcentrated blood to the pediatric patient was shown to be of no significant advantage over the CF process, which causes plasma separation from the reinfused blood[8] with subsequent loss of protein and clotting factors. No significant difference was found between the two groups for postoperative PT and PTT values at 30 minutes and 12 hours; thus, the clotting factor deficiency present in the reinfused blood volume of the CF group appeared to be a nonsignificant disadvantage. Platelet counts were not significantly different at preoperative, 30 minute postoperative, or 12 hour postoperative time periods. Neither plasma protein levels or the postoperative addition of FFP, cryoprecipitate, albumin, or platelet volumes were analyzed in this study. The CF process can cause severe depletion of plasma proteins and blood components when used during CPB.[15] The UF technique is a known method of conserving plasma proteins in adults.[4-7] If used intraoperatively, UF would allow plasma proteins and clotting factors to be sufficiently concentrated and returned to the patient upon

termination of CPB without the added expense of plasma replacement volume. Postoperative CF would allow the pediatric patient to receive the washed RBCs needed to increase the hematocrit.

Conclusion

1) Centrifugation was found to be superior for post-CPB ECC blood processing in the pediatric patient due to a higher 30 minute postoperative hematocrit, lower heparin and PFH levels in the reinfused blood, and the near total removal of anticoagulant, requiring no additional protamine.

2) Ultrafiltration was found to be superior for blood processing during CPB due to a lower required total pRBC volume addition before and during bypass as well as plasma preservation during CPB.

References

1. Minifee PK, Daeschner CW II, Griffin MP, Allison PL, Zwischenberger JB. Decreasing blood donor exposure in neonates on extracorporeal membrane oxygenation. J Pediatr Surg. Jan 1990;25(1):38-42.
2. Adler SP. Neonatal cytomegalovirus infections due to blood. Crit Rev Clin Lab Sci. 1986;23:1-14.
3. Sanders MR, Graeber JE. Post-transfusion graftversus-host disease in infancy. J Pediatr. July 1990;117(1 Pt 1):159-163.
4. Sutton RG, Yates BS, Borg SP, et al. A Comparison of three blood processing treatments during and after cardiopulmonary bypass. AmSECT Proceedings, 1990.
5. Brickley JM, Kalshoven JD, Wilds SL, Dearing JP. A comparison of two methods of post-bypass hemoconcentration. JECT. 1982;14(5):431-436.
6. Bolt J, Kling D, von Bormann B, Zuge M, Scheld H, Hempelmann G. Blood conservation in cardiac operations: cell separation versus hemofiltration. J Thorac Cardiovasc Surg. 1989;97:832-840.
7. Solem JO, Tengborn L, Steen S, Luhrs C. Cell saver versus hemofilter for concentration of oxygenator blood after cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1987;35:42-47.
8. Moran JM, Babka R, Silberman S, et al. Immediate centrifugation of oxygenator contents after cardiopulmonary bypass. J Thorac Cardiovasc Surg. 1978;76(4): 510-517.
9. Hendricks KM, Walker WA. Manual of Pediatric Nutrition. B.C. Decker Incorporated:Ontario, Canada;1990:44.
10. Gamble JL, Wallace WM, Eliel L, et al. Effects of large loads of electrolytes. Pediatrics. 1951;7:305.
11. McCance RA, Widdowson EM. Physiology of the newborn infant. Lancet. 1957;2:585.
12. Feld LG, Springate JE, Fildes RD. Acute renal failure: pathophysiology and diagnosis. J Pediatr. Sep 1986;109(3):401-408.
13. Hatlestad D, Wesel R. Characteristics of washed human erythrocytes in the clinical setting. Shiley Incorporated First Annual Symposium on Blood Conservation and Autologous Blood Transfusion, Irvine, CA, June 1990.
14. Savitsky JP, Doczi J, Black J, Arnold JD. A clinical safety trial of stroma-free hemoglobin. Clin Pharmacol Ther. Jan 1978; 23(1):73-80.
15. Yuichirou N, Munetaka M, Yoshihiro T. Comparative study of cell saver and ultrafiltration nontransfusion in cardiac surgery. Ann Thorac Surg. 1990;49:973-980.
16. Jandl JH. Blood: textbook of hematology. Little, Brown & Co.:Boston/Toronto;1987:87-88.
17. Gallus A, Engel G. Heparin. The Society of Hospital Pharmacists of Australia, 1978.
18. Darup J, Bleese N, Kalmer P, Lute G, Pokar A, Polonius MJ. Hemofiltration during extracorporeal circulation. J Thorac Cardiovasc Surg. 1979;27:227-230.
19. Nyyssonen K, Parviainen MT, Penttila IM. Plasma hemoglobin determination using chlorpromazine as a non-carcinogenie reagent. J Clin Chem Clin Biochem. 1988;26:219-222.
20. Collen D, Wiman B, Verstraete M: The Physiological Inhibitors of Blood Coagulation and FibrinolYsis. Proceedings of the Round-Table Conference, University of Leuven;Biomedical Press:Belgium;1979:40.
21. Lowenstein E, Johnston WE, Lappas DG, et al. Catastrophic pulmonary vasoconstriction associated with protamine reversal of heparin. Anesthesiology 1983;59:470-473.
22. Hopeck JM, Lane RS, Schroeder JW. Oxygenator volume control by parallel ultrafiltration to remove plasma water. JECT 1981;13(6):267-271.
23. Lohrer RM, Trammer AR, Dietrich W, Hagl S, Linderkamp O. The Influence of extracorporeal circulation and hemoseparation on red cell deformability and membrane proteins in coronary artery disease. J Thorac Cardiovasc Surg. April 1990;99(4):735-740.
24. Hirayama T, Yamaguchi H, Allers M, Roberts D. Evaluation of red cell damage during cardiopulmonary bypass. Scand J Thor Cardiovasc Surg. 1985;19:263-265.
25. Haga P, Cotes PM, Till JA, Minty BD, Shinebourne EA. Serum immunoreactive erythropoietin in children with cyanotie and aeyanotie eongenital heart disease. Blood. Sep 1987;70(3):822-826.
26. Tune BM, Mendoza SA. Pediatric Nephrology. Churchhill Livingstone:New York, New York; 1984:12:138-143.
27. Hakim M, Wheeldon D, Bethune DW, Milstein BB, Tah English, Wallwork J. Haemodialysis and haemofiltration on cardiopulmonary bypass. Thorax 1985;40:101-106.

Table 1
Results are expressed as mean±standard deviation; p>0.05 for all variables; RBC (red blood cell); FFP)fresh frozen plasma); SPA (25% albumin; WBC (white blood cell); BUN (blood urea nitrogen); PT (prothrombin time); PTT (partial thromboplastin time).

Table 1. Not Significant Variables for Both Groups

Variable	UF	CF
Age (yr)	2.49 ± 2.49	1.34 ± 1.12
Weight (kg)	10.17 ± 5.45	9.80 ± 3.20
Height (cm)	76.27 ± 19.03	74.15 ± 9.81
Body Surface Area (m^2)	0.45 ± 0.19	0.43 ± 0.09
Blood Volume (ml)	825.73 ± 425.74	777.64 ± 274.62
Heparin Dose (units)	3275.22 ± 1568.46	3004.55 ± 971.20
Prime:		
RBC (ml)	227.27 ± 75.38	295.45 ± 101.13
FFP (ml)	243.64 ± 93.09	197.73 ± 142.49
SPA (ml)	90.91 ± 49.08	109.09 ± 37.54
Plasmalyte-A (ml)	417.73 ± 256.08	265.00 ± 118.39
Preoperative:		
Hematocrit (%)	37.37 ± 7.72	36.91 ± 6.08
WBC (K/Cumm)	10.65 ± 4.90	11.30 ± 3.97
Platelets (K/Cumm)	356.91 ± 57.96	418.45 ± 162.28
Na^+ (mmol/L)	139.45 ± 1.86	138.09 ± 2.02
K^+ (mmol/L)	4.58 ± 0.63	4.81 ± 0.95
BUN (mg/dl)	13.82 ± 6.15	12.36 ± 7.97
Creatinine (mg/dl)	0.53 ± 0.11	0.46 ± 0.16
PT (seconds)	12.13 ± 0.55	12.09 ± 0.57
PTT (seconds)	28.64 ± 2.85	28.10 ± 3.07
During CPB:		
RBC (ml)	204.55 ± 150.78	238.64 ± 162.54
FFP (ml)	0.00	0.00
SPA (ml)	4.55 ± 15.08	27.27 ± 64.67

Table 1. continued

Variable	UF	CF
Plasmalyte-A (ml)	20.00 ± 60.00	0.00
Heparin (units)	727.27 ± 1506.05	386.36 ± 861.42
Na^+ (mmol/L)	145.45 ± 2.91	146.27 ± 4.36
Immediate Post-CPB:		
Cardioplegia (ml)	245.45 ± 251.41	429.18 ± 287.26
Anesthesia (ml)	142.09 ± 152.63	314.55 ± 316.70
CPB Time (minutes)	100.55 ± 36.01	121.73 ± 38.74
Cross-Clamp (min)	59.73 ± 35.00	74.27 ± 25.88
Protamine Dose (mg)	41.00 ± 22.34	45.55 ± 20.55
ECC PFH Before UF/CF (mg/dl)	30.70 ± 20.29	23.98 ± 9.26
Reinfusion Bag Volume (ml)	357.27 ± 40.89	356.73 ± 44.78
30 Minute Postoperative:		
WBC (K/Cumm)	10.67 ± 3.67	9.73 ± 3.76
Platelets (K/Cumm)	126.64 ± 65.93	114.80 ± 61.99
Na^+ (mmol/L)	145.36 ± 4.20	145.73 ± 3.55
K^+ (mmol/L)	3.74 ± 0.55	3.55 ± 0.25
BUN (mg/dl)	10.45 ± 2.58	9.82 ± 3.76
Creatinine (mg/dl)	0.65 ± 0.10	0.62 ± 0.13
PT (seconds)	10.01 ± 1.75	16.05 ± 1.32
PTT (seconds)	45.77 ± 20.78	47.75 ± 11.12
12 Hour Postoperative:		
Hematocrit (%)	39.00 ± 2.67	40.81 ± 3.75
WBC (K/Cumm)	13.67 ± 3.65	13.96 ± 5.05
Platelets (K/Cumm)	115.30 ± 44.04	121.20 ± 58.93
Na^+ (mmol/L)	138.50 ± 4.79	141.90 ± 5.36
K^+ (mmol/L)	3.49 ± 0.41	3.70 ± 0.63
BUN (mg/dl)	12.89 ± 6.31	12.80 ± 6.31
Creatinine (mg/dl)	0.58 ± 0.02	0.58 ± 0.16
PT (seconds)	13.02 ± 0.91	13.73 ± 0.99
PTT (seconds)	23.68 ± 5.29	35.27 ± 7.38

Table 2

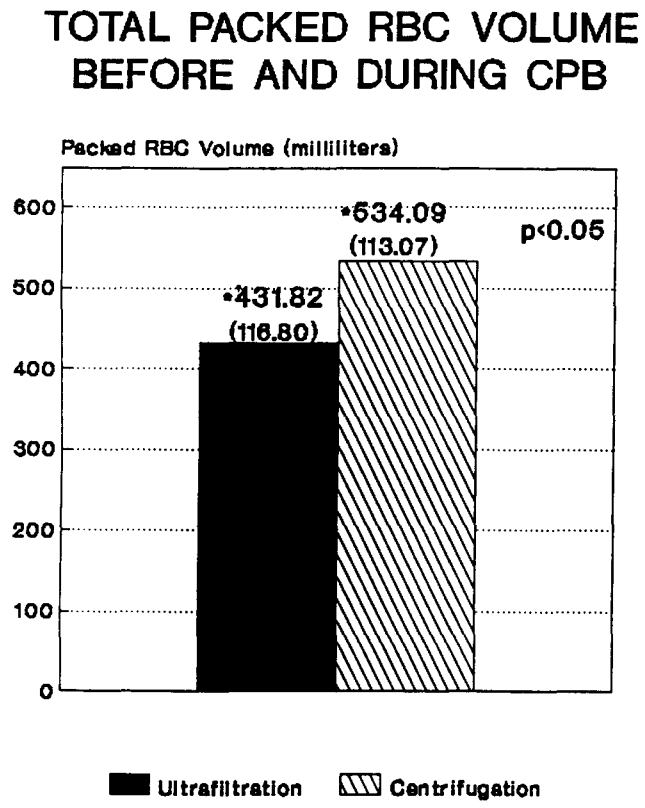
A. in reinfusion bag; B. in reinfusion bag; C. just before CPB termination; D. 30 minutes postoperatively; E. total packed RBC volume addition = prime RBC volume + RBC volume during CPB; Results are expressed as mean±standard deviation; *p<0.01; **p<0.05; p relates to sign of the difference between UF and CF.

Table 2. Significant Variables for Both Groups

Variable	UF	CF
A. Heparin Level (units/ml)*	5.41 ± 2.93	0.01 ± 0.00
B. PFH Level (mg/dl)*	165.34 ± 52.93	62.87 ± 38.86
C. Hematocrit (%)**	27.09 ± 2.21	29.45 ± 2.84
D. Hematocrit (%)*	31.23 ± 5.46	38.89 ± 6.36
E. Total pRBC Volume (ml)**	431.82 ± 116.80	534.09 ± 113.07

Figure 1

Total pRBC volume addition is equal to the prime pRBC volume plus the intraoperative pRBC volume added. Use of the CF technique resulted in a significantly greater reliance on donor blood products to concentrate circuit volume during CPB. Results are expressed as *mean (standard deviation).



Questions and Comments

Q. I would like to congratulate you on this nice paper. I have one comment. I think you didn't mention the advantage of using ultrafiltration during bypass. In addition to all of the things you did mention, it reduces the extracellular water content of the body and probably water edema. We have been able to show that and presented at one of these meetings in 1984, and so did Megiligan in the United States. I think that is a very important point, doing ultrafiltration during bypass. The other is a question. WOuld you now advise, on your results, that you would use ultrafiltration during the case and the centrifugation cell-saver after the case?

A. Yes, I would advise them to be used that way.

Jerry Sterns, Providence, R.I.

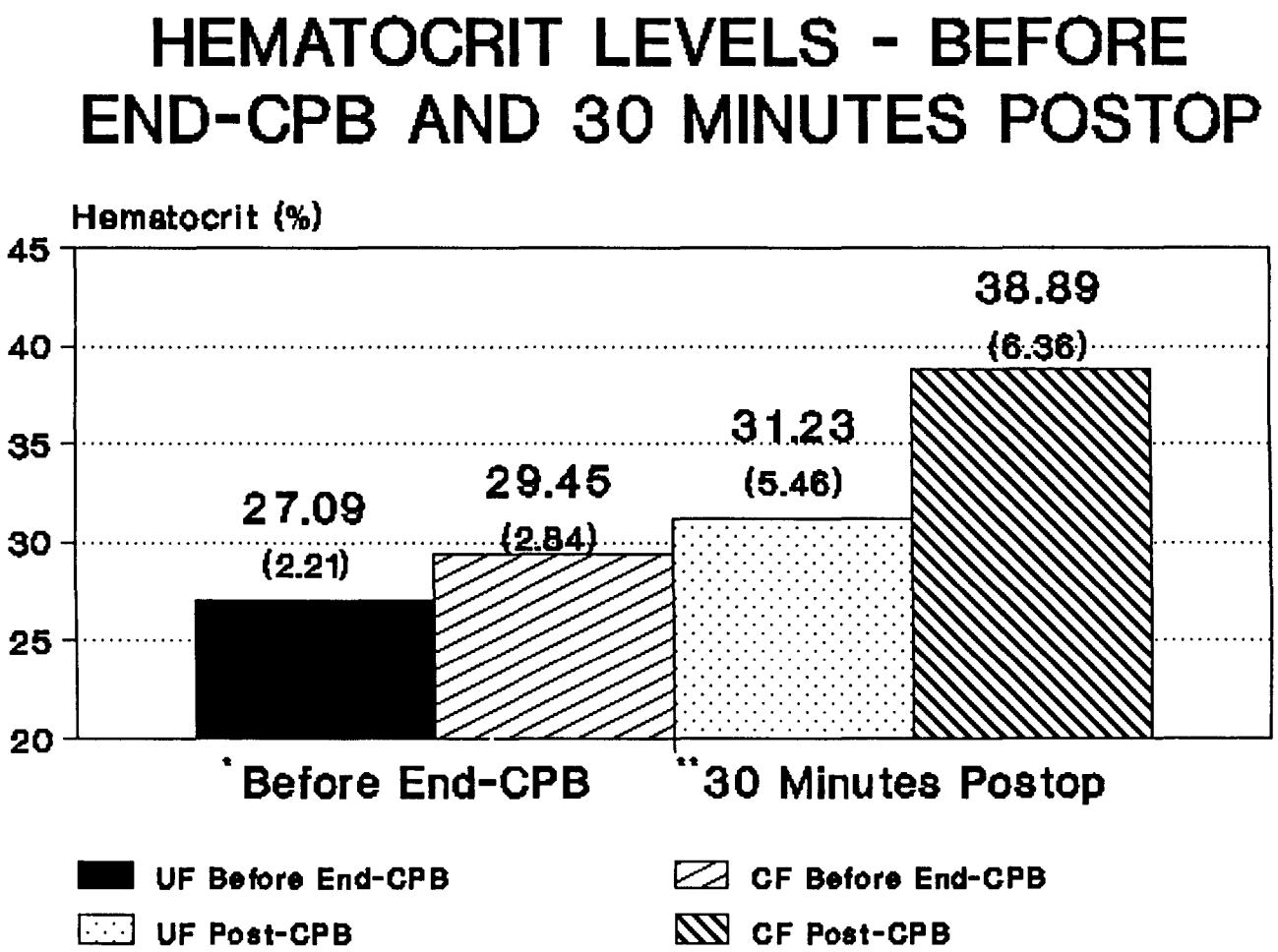
Q. Did you at any time measure colloidal oncotic pressures during bypass, particularly with cell-savers? And did your perfusionists reinfuse the patients with crystalloids as volume replacement for the system with cell-saver rather that have to do it with the hemoconcentrator?

A. We measured total protein. They were found not to be significantly different between the two groups before bypass or after bypass.

Q. In the patients that you were removing proteins with the cell-savers during the perfusion, did your perfusionists reinfuse with crystalloid while on bypass if they needed extra fluid to maintain their system volume?

A. During centrifugation with the volume you don't want to let it drop too low. There was crystalloid

Figure 2
Hematocrit values were much greater 30 minutes postoperatively when CF was used as the postoperative blood processing technique over UF. When CF was used during CPB, the hematocrit was slightly higher. This small difference in hematocrit was attributed to an increased use of donor blood products before and during CPB with the CF technique. Results are expressed as mean (standard deviation). *p<0.05; **p<0.01 with p<0.05 considered significant.



added to both groups during bypass. I would imagine that they added more crystalloid to the centrifugation group but I am not sure about that.

Al Stammers, Charleston, S.C.

Q. I have a question in regard to some recent literature on use of ultrafiltration in complement activation of leukopenia. By any chance did you look at white cell count or leukopenia with any of these patients and perhaps even complements with C3A?

A. There was found to be no significant complement activation with the centrifugation group or the ultrafiltration group. Probably due to no significant difference between the platelets or the white cell counts before or after bypass.

Q. Just following up on another question that was asked about the colloid onconic pressure, did you find that these patients received greater colloids during the post-operative period or did you look in the ICU to see if they received additional colloids or even albumin or FFP?

A. No, we did not keep track of post-operative fluid additions.

Figure 3
The UF technique causes heparin to be significantly concentrated in the circuit for post-CPB blood processing. The CF technique results in an autologous blood product virtually free of anticoagulants. Results are expressed as mean (standard deviation).

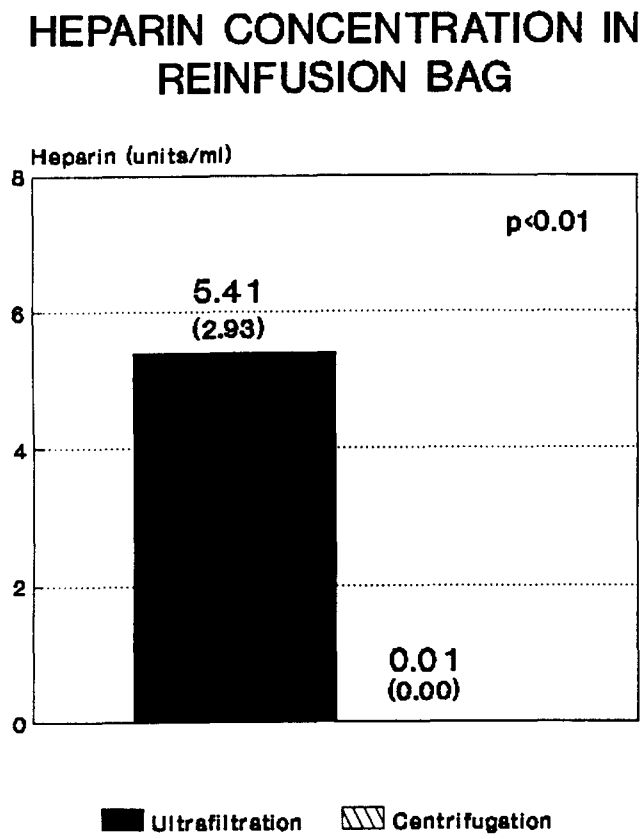


Figure 5
Plasma free hemoglobin (PFH) in the reinfusion bag after blood processing is shown to be significantly positively correlated with 12 hour postoperative creatinine levels. The UF technique resulted in high reinfusion bag PFH levels and greater creatinine levels as compared with the CF technique.

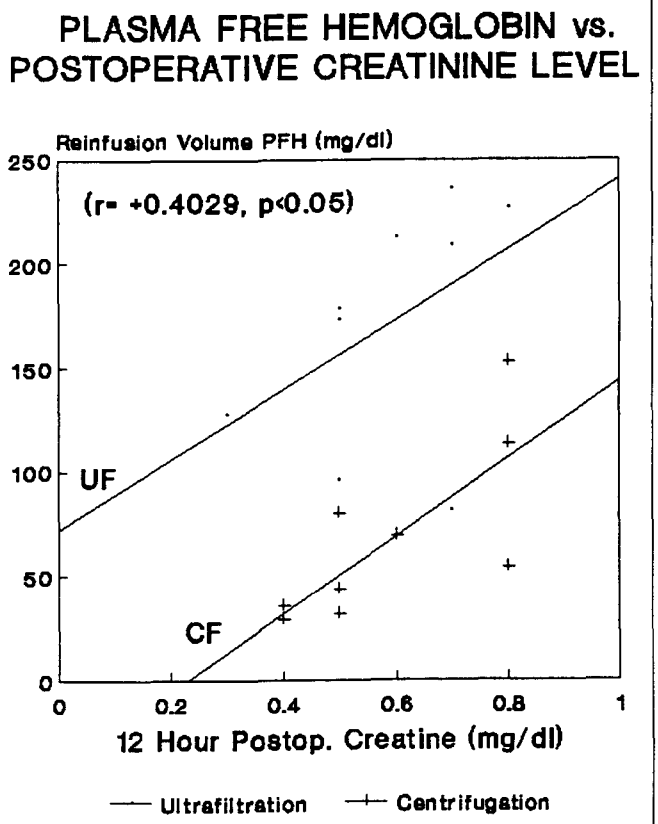


Figure 4
Plasma free hemoglobin (PFH) levels in the circuit before blood processing were not significantly different between the two groups (*p>0.05). Post-CPB blood processing with the UF technique resulted in the concentration of a significantly greater (**p<0.01) level of PFH in the reinfusion bag. Results are expressed as mean (standard deviation).