Conventional ultrafiltration with technical modification in congenital heart defect surgery

Ultrafiltração convencional com modificação técnica no tratamento cirúrgico dos defeitos cardíacos congênitos

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Abstract

Objective: To compare patients submitted to conventional ultrafiltration (CUF) with and without a technical modification that allows the use of residual blood from the circuit tubes and oxygenator.

Method: From March 2002 to January 2005, 301 patients undergoing congenital heart defect surgery with cardiopulmonary bypass (CPB) were retrospectively analyzed and divided into two groups: Group A - 130 submitted to CUF and Group B, 171 patients submitted to CUF with a technical modification that uses residual blood. Demographic data, diagnosis, surgical treatment, intra-operative and postoperative data, the need and amount of blood transfusions, laboratorial results and length of hospital stay were compared between the groups.

Results: There was no differences in the initial hematocrit

before CPB (p = 0.06), but in Group B, the values after ultrafiltration were higher (p <0.0001). Group B patients received more transfusions in the first 48 hours of the postoperative period (p <0.0001). There was no significant difference in the time of mechanical ventilation (p = 0.34), but the inotropic support (p <0.0001), antibiotic therapy (p = 0.0006), length of stay in the intensive care unit (p <0.0001) and length of hospital stay (p <0.0001) were greater for Group B.

Conclusions: CUF with the technical modification was not better than conventional CUF, because in spite of elevating the hematocrit after CBP, it caused greater postoperative bleeding with a greater need of blood transfusions and longer hospital stays.

Descriptors: Ultrafiltration. Extracorporeal circulation. Heart defects, congenital.

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Resumo

Objetivo: Comparar pacientes submetidos à ultrafiltração convencional (UFC), sem e com modificação técnica que permite aproveitamento do sangue residual do circuito de tubos e do oxigenador.

Método: No período de março de 2002 a janeiro de 2005, 301 pacientes submetidos à correção de cardiopatias congênitas com circulação extracorpórea (CEC) foram analisados, retrospectivamente, e divididos em dois grupos: A – constituído de 130 pacientes submetidos à UFC clássica e grupo B - constituído de 171 pacientes submetidos à UFC com modificação técnica para aproveitamento do sangue residual. Foram comparadas variáveis demográficas, diagnóstico, tratamento cirúrgico, dados do período intra-operatório e pósoperatório, necessidade e volume de transfusões, exames laboratoriais e permanência hospitalar.

Resultados: Não houve diferença no valor inicial de hematócrito antes da CEC (p = 0,06), mas no grupo B, os

valores após a ultrafiltração foram maiores (p < 0,0001). O grupo B foi mais transfundido nas primeiras 48 horas do pósoperatório (p < 0,0001). Não houve diferença no tempo de ventilação mecânica (p = 0,34), mas o tempo de uso de drogas vasoativas (p < 0,0001), tempo de uso de antibióticos (p = 0,0006), tempo de internação na unidade de terapia intensiva (p < 0,0001) e o tempo total de internação no pós-operatório (p < 0,0001) foram maiores no grupo B.

Conclusões: A UFC com a modificação técnica não apresentou resultados superiores aos da UFC clássica, pois, apesar de elevar o hematócrito após a circulação extracorpórea, proporcionou maior sangramento no pósoperatório com maior necessidade de transfusão de hemoderivados e prolongamento do tempo de permanência hospitalar.

Descritores: Ultrafiltração. Circulação extracorpórea. Cardiopatias congênitas.

INTRODUCTION

Ultrafiltration (UF) is a common procedure performed during cardiac surgeries with cardiopulmonary bypasses (CPB) with the aim of removing inflammatory mediators [1-5], as well as to reduce fluid overload [1,3] and to decrease the need for transfusions [1,6,7]. In neonates and children, systemic inflammatory response after CPB results in increased capillary permeability, which leads to increased morbidity and mortality rates [8]. This process can cause fluid overload, making gas exchange more difficult and delaying weaning from mechanic ventilation. In addition, hemodilution of platelets and coagulation factors related to CPB aggravates hemostasis, a situation often observed in children [9].

When UF is performed during CPB it is named conventional UF (CUF). In this context, UF of the perfusate is performed while the patient is still being assisted by the lung-heart machine and the hemoconcentrator is connected to the recirculation line between the oxygenator and the venous reservoir [1]. Currently a technically modified method of CUF is being used, which enables residual blood from the tube and oxygenator circuit to be used after CPB without interfering with the patient's hemodynamic performance [10].

The objective of this study is to compare patients who were submitted to CUF, with and without this technical modification, reviewing laboratorial data, the necessities of transfusions and clinical outcomes in the immediate postoperative period.

METHOD

From March, 2002 to January 2005, 301 patients undergoing surgical corrections for congenital heart diseases, exclusively with CUF, were studied retrospectively. The patients were divided into two groups: Group A, consisting of 130 patients for whom the traditional CUF procedure was used (operated from March 2002 to March 2003) and Group B, consisting of 171 patients in which the technically modified method of CUF was used, enabling residual blood from the tubes and oxygenator to be used (operated from April 2003 to January 2005).

Description of cardiopulmonary bypass

The circuit used for CPB consisted of a membrane oxygenator with tubes made of polyvinyl chloride (PVC), a cardiotomy reservoir, an arterial line filter capable of filtering particles larger than 40 micrometers (μ), a sanguineous cardioplegia system and a hemoconcentrator (*). Oxygenators were used depending on the patients' weight: neonate oxygenator – up to 8 kg with 3/16' tubes; infant oxygenator – from 8 to 22 kg with 1/4' tubing and two 3/8' caval cannulae; pediatric oxygenator – from 22 to 50 kg with 3/8' arterial tubing and two 3/8' caval cannulae; and adult oxygenator – over 50 kg with 3/8' arterial tubing and two 3/8' caval cannulae.

A BEC 2000 pump with one arterial module and three suction modules and a cardioplegia pump including one impulsion module and one heat exchange unit were used in the CPB system (*).

Prior to the perfusate composition, all circuits were previously rinsed using from 800 mL for neonates to 2000 mL for adults of Ringer lactate solution. For the perfusate composition, total or partial hemodilution was based on the following formula:

 $[(W \times 0.08 + PV) \times Htt) - (W \times 0.08 \times Htp)] / AVPRC$

Where:

W - weight;

0.08 – blood volume factor;

VP – perfusate volume;

Htt – desired hematocrit concentration in CPB;

Htp – patient's hematocrit concentration before CPB;

AVPRC – Arithmetic mean of Ht in concentrated red blood cells.

Full heparinization was achieved using non-fractioned heparin at 400 IU/kg of body weight, which was administered directly into right atrium by the surgeon.

Perfusion flows varied according to the following scale:

< 5 kg - 150 to 200 mL/kg/min;

6 to 10 kg - 100 to 150 mL/kg/min;

11 to 20 kg - 80 to 100 mL/kg/min;

21 to 40 kg - 60 to 80 mL/kg/min;

40 kg - 40 to 60 mL/kg/min

Myocardial protection was obtained using cooled blood cardioplegia and St. Thomas cardioplegia solution, which was infused at 30 mL/kg after aortic clamping and repeated with 20 to 30-mL/kg at 15-minute intervals.

UF was initiated while the patient was being warmed using a pressure of 150 to 250 mmHg across the membranes giving a filtration rate of 10 to 15 mL/min. The pressure across the membranes was increased to between 350 and 450 mmHg by the end of CPB and during residual blood UF, with a filtration rate of 40 to 75 mL/min.

On removal of CPB, the non-fractioned heparin was neutralized using protamine. The dose used was 1.0 to 1.5 mg of protamine per 100 IU of heparin.

Description of ultrafiltration techniques

In Group A (traditional CUF), the hemoconcentrator was coupled to the recirculation line, which connects the oxygenator to the venous reservoir. After the heating procedure is initiated, the hemoconcentrator line (recirculation) was unclamped and, afterwards, it was partially clamped in order to restrict the blood flow across the hemoconcentrator. This type of hemoconcentration was concluded with the removal of the arterial cannulae and all the blood remaining in the CPB circuit was discarded (Figure 1).

In Group B (technically modified CUF), the utilization of the residual blood was achieved by the cardioplegia system, which was connected in parallel using a 1/8" tube and two "Y-shaped" connectors of 1/8" x 1/8" x 1/8" at the exit of the cardioplegia pump and entrance of the hemoconcentrator. After removing the CPB, the volume inside the caval cannulae was calculated and 500 mL of Ringer lactate solution was transferred to the venous reservoir to impel the residual volume towards the cardioplegia reservoir through the arterial line filter bypass. This volume was again ultrafiltered removing 40% to 50% of water and the concentrate was infused into the patient by a peripheral vein (Figures 2A, 2B and 2C).

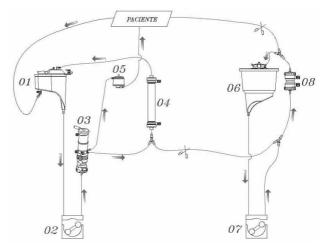


Fig. 1 - Conventional ultrafiltration diagram (UFC) using the luer of the oxygenator to return blood to the venous reservoir 01-venous reservoir, 02- arterial pump, 03- oxygenator, 04-hemoconcentrator, 05- arterial filter, 06- cardioplegia reservoir, 07- cardioplegia pump, 08- heat exchanger

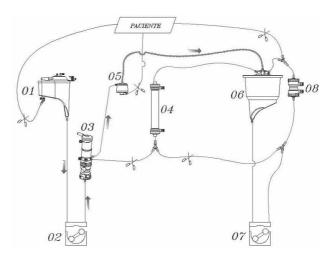


Fig. 2A - Residual volume transportation from the circuit to cardioplegia reservoir, with blood impelled by 500 mL Ringer lactate solution across the arterial filter bypass. 01- venous reservoir, 02- arterial pump, 03- oxygenator, 04-hemoconcentrator, 05- arterial filter, 06- cardioplegia reservoir, 07- cardioplegia pump, 08- heat exchanger

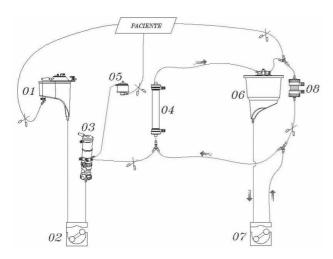


Fig. 2B - Ultrafiltration of the residual volume from the oxygenator transported to the cardioplegia reservoir. 01- venous reservoir, 02- arterial pump, 03- oxygenator, 04- hemoconcentrator, 05- arterial filter, 06- cardioplegia reservoir, 07- cardioplegia pump, 08- heat exchanger

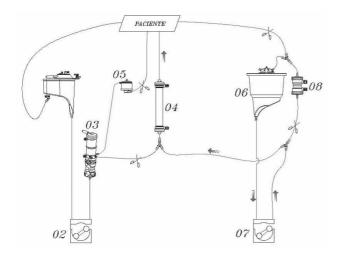


Fig. 2C - Concentrated blood infusion to patient into peripheral vein 01- venous reservoir, 02- arterial pump, 03- oxygenator, 04-hemoconcentrator, 05- arterial filter, 06- cardioplegia reservoir, 07- cardioplegia pump, 08- heat exchanger

Variables related to demographic data, heart disease diagnosis, surgical procedure, peri- and postoperative data, transfusion requirements, laboratorial tests (hematocrit, prothrombin activity and activated thromboplastin time, INR - International Normalized Ratio, platelet count and creatinine level) and time of hospital stay were compared.

The diseases were grouped and classified as follows:

- Atrial septal defect (ASD), including ASD and ASD associated with patent ductus arteriosus (PDA);
 - Ventricular septal defects (VSD), concerning VSD,

VSD with PDA and VSD with ASD;

- Left or right ventricular physiological diseases, partial (PAVSD) and total (TAVSD) atrioventricular septum defects, tetralogy of Fallot (TF), transposition of the Great Arteries (TGA);
- Other diagnoses, heart valve diseases, aortopulmonary window, and abnormal coronary artery, Shone syndrome and left ventricular-aortic tunnel.

The surgical procedures performed were: atrioseptoplasty, closed by direct suture or using a bovine pericardial patch, either with or without ductus arteriosus ligature. For ventriculoseptoplasty, the defect was closed by direct sutures or, more often, using a bovine pericardial patch, either with or without ductus arteriosus ligature or ASD closure, if present. For PAVSD, the left atrioventricular valve cleft was closed and for the ostium primum ASD type, a bovine pericardial patch was utilized. For TAVSD correction, the double patch technique was used in all patients. For TF, the ASD was closed using a bovine pericardial patch and the right ventricle outflow tract, pulmonary valve and trunk were enlarged when required. Jatene and Senning operations were the alternatives to treat TGA. The Glenn operation (bidirectional upper cavopulmonary shunt) was either associated or not with pulmonary trunk ligature, atrioseptectomy or pulmonary branch enlargement, as required. Less frequent diseases, included as other diagnosis, were corrected according to traditional standard surgical procedures.

The preoperative diagnoses (in some cases combined), as well as surgical procedures performed, are listed in Tables 1 and 2.

Table 1. Preoperative diagnoses.

Diagnosis	Gro	up A	Gro	up B	p-value
	130		1	71	
	n	%	n	%	
ASD	43	33.1	43	25.1	0.15
VSD	25	19.2	45	26.3	0.17
PAVSD	5	3.8	6	3.5	>0.99
TAVSD	8	6.2	6	3.5	0.4
TF	16	12.3	22	12.9	>0.99
TGA	4	3.1	8	4.7	0.56
Univentricular heart	0	0.0	4	2.3	0.13
Other diagnoses	29	22.3	37	21.6	0.89

ASD – Atrial septal defect, VSD – ventricular septal defect, PAVSD – partial atrioventricular septal defect, TAVSD – total atrioventricular septal defect, PDA – patent ductus arteriosus, TF – tetralogy of Fallot, TGA – transposition of great arteries.

Table 2. Surgical procedures

Diagnosis	Group A		Gro	up B	p-value
	130		1	71	
	n	%	n	%	
Atrioseptoplasty	43	33.1	43	25.1	0.15
Ventriculoseptoplasty	25	19.2	45	26.3	0.17
TAVSD complete correctio	n 5	3.8	6	3.5	>0.99
PAVSD complete correction	n 8	6.2	6	3.5	0.4
TF complete correction	16	12.3	22	12.9	>0.99
Jatene operation	4	3.1	6	3.5	>0.99
Senning operation	0	0.0	2	1.2	0.5
Glenn operation	0	0.0	4	2.3	0.13
Other procedures	29	22.3	37	21.6	0.89

TAVSD – Total atrioventricular septal defect, PAVSD – partial atrioventricular septal defect, TF – tetralogy of Fallot

Intraoperative data were collected from the perfusion records, which provide details of the patient weight, height, body surface, initial hematocrit concentration and after CPB, red blood cell transfusions added to the perfusate prior to CPB, perfusion and ischemia times, total blood volume, UF total volume and water concentration at the end of the CPB.

Identification of the patients (name and enrollment number) and their date of birth, gender, preoperative diagnosis, type of surgery performed, and pre- and postoperative coagulation and creatinine profiles were taken from their computer records. Blood losses through drains, amounts of blood component transfusions, diuresis and dialysis needs were monitored during the initial 48 postoperative hours. The time of antibiotic therapy, the use of vasoactive drugs (intravenous inotropic, antihypertensive and antiarrhythmic drugs), time of stay in the intensive care unit and in the hospital were also checked.

Statistical analysis of categorical data are presented as absolute numbers and percentages and continuous variables are shown as medians (minimum and maximum values), when applicable. For univariant comparisons among categorical variables, the Fisher exact test was used and for continuous variables, the non-parametric Mann-Whitney test was employed. Simple linear regression analyses were carried out, if applicable. All p-values were two-tailed and values lower than 0.05 were considered to be statistically significant. The GraphPad Instat v. 3.00 and Stats Direct Statistics Software v. 1.617 computer programs were used.

The study was approved by the Research Ethics Committee of the Medicine School in São José do Rio Preto.

RESULTS

Among the 301 patients included in the study, 136 (45.2%) were male and the median age was 3 years and 9

months old, ranging from 1 day old to 49 years and 2 months old. When the groups were compared, no statistically significant differences were observed in relation to gender (p-value = 0.55), age (1460 days vs. 1175 days; p-value = 0.45), weight (15.2 kg vs. 12.6 kg; p-value = 0.30), body surface (0.64 m² vs. 0.55 m^2 ; p-value = 0.25) and time of preoperative stay in hospital (1 day vs. 1 day; p-value = 0.89).

The initial hematocrit values were 35% vs. 36% (p-value = 0.06); the values after UF were 26% vs. 34% (p < 0.0001). The INR of Group A was higher, both before CPB (1.1 vs. 1.0; p < 0.0001) and after UF (1.5 vs. 1.4; p < 0.0001) when compared to Group B. The platelet counts before CPB were 295 x 10^3 /mm³ vs. 287 x 10^3 /mm³ (p-value = 0.18), and after UF they were 168 x 10^3 /mm³ vs. 153 x 10^3 /mm³ (p-value = 0.10).

Variables analyzed during the operative procedure were similar between the groups in respect of perfusion time (80 min vs. 75 min; p-value = 0.27), ischemia time (57.5 min vs. 56 min; p-value = 0.23), CPB minimum temperature (28° C vs. 27.6° C; p-value = 0.79), initial perfusate volume (102.8 mL/kg vs. 103.4 mL/kg; p-value = 0.87), patient blood volume (80 mL/kg vs. 80 mL/kg; p-value = 0.62), final water balance (- 1.8 mL/kg vs. 2.3 mL/kg; p-value = 0.09) and UF total volume (45.6 mL/kg vs. 50.4 mL/kg; p-value = 0.06).

In respect to the use of blood components, there was a greater proportion of patients requiring transfusion within the initial 48 postoperative hours in Group B (66.2% vs. 86.5%; p < 0.0001), and a higher infused volume (10.0 mL/kg vs. 10.2 mL/kg; p-value = 0.02) compared to Group A. The fresh plasma transfusion rate was also higher in Group B than in Group A (62.3% vs. 83.6%; p < 0.0001), with higher infused volume (9.8 mL/kg vs. 13.9 mL/kg; p-value = 0.0006) and number of patients who received cryoprecipitate transfusions was also higher in this group (10.8% vs. 27.5%; p-value = 0.0004), as shown in Figure 3.

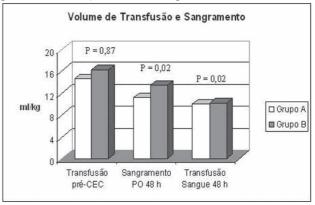


Fig.3 - Comparison between Groups A and B in relation to concentrated red blood cell transfusion requirements before cardiopulmonary bypass (CPB), postoperative bleeding (PO) and transfusion requirements after the surgical procedure

Group B patients had higher creatinine levels in the preoperative period (0.5 mg/dL vs. 0.5 mg/dL - 95% CI - 0.1 to 0; p-value = 0.0018), however, on the second postoperative day, the creatinine level was higher in Group A (0.6 vs. 0.5 - 95% CI - 0.2 to - 0.1; p < 0.0001). Diuresis volumes during the initial 48 postoperative hours were 3.3 mL/kg/h vs. 4.8 mL/kg/h (p < 0.0001). The mean use of mechanical ventilation lasted 8 vs. 8 hours (p-value = 0.34), and the time required for vasoactive drugs were 2 days vs. 3 days (p < 0.0001). The time required for antibiotic use (2 days vs. 2 days - 95% CI - 0 to 0; p-value = 0.0006), time of intensive care unit stay (4 days vs. 5 days; p < 0.0001) and the total time of stay at hospital in the postoperative period (6 days vs. 8 days; p < 0.0001) were longer in Group B compared to Group A.

DISCUSSION

The use of CUF in on-pump cardiac surgeries is an established procedure, providing an important contribution to patient management during the intraoperative period. UF prevents excess of body fluids and enables the removal of inflammatory agents such as C3a and C5a [2,3,5], TNF-á and IL-6 and 8[3], particularly during the warming phase. It is well-known that increases in body water are a very important factor in low-weight children undergoing prolonged low-temperature CPB. As the hemodilution effects are more evident in children, due to the unproportional perfusate volume in the CPB circuit, potential benefits of UF are even more significant in these patients. This knowledge provided the basis for a comparative study on congenital heart disease patients undergoing on-pump surgical treatment. In this study, most of the patients were children with an average age of 39.2 months, similar to previous studies, which compared UF techniques, showing the great interest in CUF beneficial effect studies on lowweight patients [11,12].

Surgical complexity seen in preoperative diagnosis must be considered as an important factor in the outcomes of these patients [13]. Pulmonary hypertension, cyanosis and malnutrition represent increased surgical and postoperative risks for complications. Congenital heart diseases with moderate to severe pulmonary hypertension, where the ratio between pulmonary and systemic pressures is greater than or equal to 60%, prolongs the stay in the intensive care unit and the need for mechanically assisted ventilation. Surgical interventions in children who suffer from complex congenital heart diseases require longer times on CPB and lower temperatures, prolonging perfusion and ischemia times, thereby increasing the risk of water retention [1]. In both groups assessed in this study, perfusion and ischemia times were similar, reflecting the homogeneity of patient distribution in relation to the complexity of the heart diseases.

As hypothermia is known to increase blood viscosity, hemodilution is necessary to enhance oxygen transportation to tissues, since this is reversely proportional to blood viscosity. Therefore, a low hematocrit rate is more seen at lower temperatures than high ones; this can be achieved with hemodilution [14]. Considering 80 mL/kg blood volume, the initial perfusate volume was similar in both groups (102.8 mL/kg vs. 103.4 mL/kg, p-value = 0.87), remembering that the ratio between patient blood volume and perfusate volume in children is different from adults; it must always be maintained at less than 1 [1].

The total liquid volume added to the perfusate, the total ultrafiltrate volume and the final water balance are proportionally interrelated [14]. In our study, the addition of fluids to the perfusate (concentrated blood red cells, albumin, mannitol and sodium bicarbonate) followed technical standards and were equivalent in Groups A and B, in respect to weight and body surface. This was reflected in the total ultrafiltrate quantity and the final water balance; statistical differences were not evidenced among the studied patients.

CUF enables hemodynamic and ventilatory stabilization, reducing generalized edema and diminishing the need of peritoneal dialysis. Thus, liquid management before the surgery has a direct influence on the immediate postoperative hemodynamic balance, with consequences on the cardiac, renal and respiratory functions and hemostasis [14].

Kidney immaturity seen in low-weight children may delay water balance, the reason that diuretics and peritoneal dialysis are frequently necessary in this process [15]. In our series, which was not only limited to low-weight children, no statistical difference in the indication of dialysis was observed. Creatinine levels at admission were higher in Group B than in Group A, but on the second day following surgery the level was higher in Group A.

Improvement in the tissue oxygenation, particularly in pulmonary hypertension patients, is achieved by the removal of fluid overload and inflammatory mediators, optimizing the pulmonary function as well as decreasing the time of mechanical ventilation and of stay in the intensive care unit [3]. It is known that pulmonary endothelium lesions mediated by neutrophils and increased pulmonary vascular permeability participate in changing the functioning of this organ [16]. It is also likely that CUF during CPB has a beneficial effect on reducing edema and on the myocardial function, as well as on pulmonary function [2]. The systemic inflammatory response that occurs in neonates and infants after CPB results in increased capillary permeability, leading to increased morbidity and mortality rates [8]. This process can lead to volume overload, making gas exchange more difficult and delaying weaning from mechanical ventilation. In the patients assessed in our study, no differences in the time of mechanical ventilation were observed.

Considering that hemodilution is responsible for decreases by as much as 50% in coagulation factors and for decreased by as much as 70% in platelet counts after CPB is initiated [9], CUF is able to attenuate such harmful effects at the end of the procedure. The relevance of hemoconcentration with the aim of minimizing the blood component use, with better reutilization of the blood remaining in the oxygenator, was described by Souza and Braile [10] giving additional advantages such as a reduction of the demands from blood banks and diseases in risk related to diseases (such as hepatitis, AIDS etc.), adverse transfusional reactions and coagulation disorders.

A decrease in hematocrit due to postoperative bleeding is harmful to the body, causing reduced left ventricle function, in addition to diminishing the supply of oxygen to tissues, which may prolong the use of vasoactive drugs. Besides, postoperative bleeding leads to more blood components being transfused which is related to an increased risk in bacterial and viral infections, increasing the need for antibiotic therapy and prolonging hospital stay, as well as increasing the mortality rate [17,18].

In our study, Group B patients had greater bleeding during the initial 48 hours after surgery, requiring a larger number of red blood cell, plasma and cryoprecipitate transfusions than in Group A, and consequently prolonging the use of vasoactive drugs and requiring longer stays in the intensive care unit. Although giving a higher hematocrit level at the end of the surgical procedure, the modified technique of CUF that enabled the reutilization of residual blood from the tubes and oxygenator was not efficient to reduce the necessity of blood component transfusions, which was seen by the use of more vasoactive drugs and a longer stay at the intensive care unit in the postoperative period. This may have several explanations, among which is the possibility that the reutilization of the blood in the circuit (which was submitted to increased concentration causing more destruction of elements of the coagulation system) could lead to an excessive blood quantity without coagulation properties and with the adverse factor of containing heparin, which had then already been fully reverted by protamine.

In the simple linear regression analysis, CUF with the technical modification for reusing residual blood from the tubes and oxygenator was an independent predictor for prolonged use of vasoactive drugs and antibiotic therapy and also prolonged time in the intensive care unit and in hospital after the surgery.

CONCLUSIONS

Considering all studied variables, CUF technically modified to reutilize residual blood from tubes and the

oxygenator circuit, gave worse results when compared to the traditional CUF, as, although effective to increase the hematocrit level after CPB, it lead, in this study group, to higher postoperative bleeding, requiring more blood component transfusions and a longer stay at hospital than the other group.

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