Pediatric cardiac surgery without homologous blood transfusion, using a miniaturized bypass system in infants with lower body weight

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Objective: We have established a low-priming volume cardiopulmonary bypass system for pediatric heart surgery to avoid homologous blood transfusion. The priming volume of our system is down to 140 mL for patients weighing less than 7 kg. We can prime the bypass circuits without blood products for patients weighing more than 4 kg.

Methods: Seventy consecutive patients weighing 4 to 7 kg underwent heart surgery with a bloodless prime from October 2003 to September 2006. The type of procedures (Risk Adjustment in Congenital Heart Surgery category) included the following: category 1: atrial septal defect (n = 3); category 2: ventricular septal defect, tetralogy of Fallot, bidirectional Glenn shunt, and others (n = 55); category 3: atrioventricular septal defect, double-outlet right ventricle, and others (n = 8); category 4: Rastelli procedure for transposition of the great arteries (n = 3); and category 6, Damus-Kaye-Stansel procedure (n = 1). Transfusion criteria were hematocrit less than 20%, mixed venous oxygen saturation less than 70%, regional cerebral oxygenation less than 50%, and plasma lactate level greater than 4.0 mmol/L during bypass.

Results: The mean age and body weight were 7.3 ± 5.4 months and 5.4 ± 0.8 kg, respectively. Forty-five patients (64%) underwent transfusion-free procedures. Preoperative hematocrit, age, body weight, complexity of procedure and cardiopulmonary bypass time were compared between patients with and without transfusion. Bypass time and Risk Adjustment in Congenital Heart Surgery risk category in patients with transfusion were significantly greater than those in patients without ($P < .0001$, and $P < .05$, respectively). Body weight in patients without transfusion was significantly greater than that in patients with ($P < .01$). In multiple regression analysis, the determinants of blood transfusion were the bypass time and body weight (odds ratio 1.026, 95% confidence interval 1.011–.040, $P < .0001$, and odds ratio 0.366, 95% confidence interval 0.171–0.785, $P < .01$).

Conclusions: It is possible to do complex transfusion-free procedures safely for patients weighing more than 4 kg by using the low-priming volume circuit. The limiting factors of bloodless heart surgery are not preoperative hematocrit and complexity of procedure but the cardiopulmonary bypass time and the patient's body weight.

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Abbreviations and Acronyms

CPB	= cardiopulmonary bypass
MUF	= modified ultrafiltration
RACHS	= Risk Adjustment in Congenital Heart Surgery
rSO ₂	= regional cerebral oxygenation
Svo ₂	= mixed venous oxygen saturation

In infants and children, anemia is one of the primary problems observed during and after heart surgery. Because of the small circulating volume of blood, extreme hemodilution occurs when a large cardiopulmonary bypass (CPB) circuit is used. In that event, a homologous blood transfusion is required during CPB. However, a blood transfusion can potentially cause a variety of complications, such as an immunologic reaction that causes organ dysfunction and infectious transmissions.^{1,2} To eliminate these risks, we developed a low-priming volume CPB system for pediatric heart surgery to avoid the need of a blood transfusion. The priming volume of our system is as low as 140 mL. We can prime the bypass circuits without blood products for patients weighing more than 4 kg and less than 7 kg. In this article we retrospectively reviewed our experience with bloodless cardiac surgery for patients weighing between 4 and 7 kg to determine the factors best predicting blood transfusion in the extremely low-priming CPB system.

Patients and Methods

Seventy consecutive patients weighing 4 to 7 kg underwent heart surgery with a bloodless prime from October 2003 to September 2006 in the Kitasato University Hospital. The mean age and body weight were 7.3 ± 5.4 months (range 1.6–28.6 months) and 5.4 ± 0.8 kg (range 4.0–6.9 kg), respectively. There were 29 boys and 41 girls. The type of procedures and the Risk Adjustment in Congenital Heart Surgery (RACHS) risk category^{3,4} are shown in Table 1. There were 60 patients with biventricular repair and 10 with univentricular repair (bidirectional Glenn shunt, 8; Damus–Kaye–Stansel anastomosis, 1; and aortoplasty, 1).

Criteria for red blood cell transfusion included anemia with a hematocrit level of less than 20% during CPB for patients who had undergone biventricular repair and less than 25% during CPB for those who had undergone univentricular repair. After modified ultrafiltration (MUF), the autologous transfusion was performed to keep the hematocrit level of 25% for patients with biventricular repair and 35% of those with univentricular repair.

We monitored mixed venous oxygen saturation (Svo₂) and regional cerebral oxygenation (rSO₂) using near-infrared spectroscopy (INVOS 5100; Somanetics, Inc, Troy, Mich) during CPB and maintained the values above 70% and 50%, respectively. If we had difficulty maintaining the Svo₂ above 70% and rSO₂ above 50%, despite increasing the pump flow or oxygen concentration during CPB, we decided to transfuse the allogeneic blood. The plasma lactate level (micromoles per liter) was also monitored during

TABLE 1. Type of procedures and RACHS risk category

RACHS risk category	Procedure	No. of patients
Category 1	ASD closure	3
Category 2	VSD closure	32
	TOF repair	10
	BCPS	8
	RVOTR	3
	MVR/MVP	2
Category 3	AVSD repair	4
	DORV repair	2
	TOF/PA repair	1
	Aortoplasty	1
Category 4	Rastelli operation	3
Category 6	DKS	1
Total		70

RACHS, Risk Adjustment in Congenital Heart Surgery; ASD, atrial septal defect; VSD, ventricular septal defect; TOF, tetralogy of Fallot; BCPC, bidirectional cavopulmonary shunt; RVOTR, right ventricular outflow tract reconstruction; MVR, mitral valve replacement; MVP, mitral valvuloplasty; AVSD, atrioventricular septal defect; DORV, double-outlet right ventricle; PA, pulmonary atresia; DKS, Damus–Kaye–Stansel procedure.

bypass, and when the lactate increased above 4.0 mmol/L, we decided to transfuse the allogeneic blood. If postoperative hemodynamic instability persisted despite sufficient inotropic support, we decided to transfuse red blood cells even when the hematocrit level was above 25%. We did not transfuse platelets or fresh frozen plasma before red blood cell transfusion in the present study. Erythropoietin was not used preoperatively or postoperatively.

The Miniaturized CPB System

To achieve a low-priming volume CPB system, we needed a low-prime oxygenator and reservoir (priming volume, 40 mL; Baby RX; Terumo Inc, Tokyo, Japan), arterial filters (15 mL; Filtia; JMS Inc, Hiroshima, Japan), and a smaller and shortened extracorporeal circuit. The oxygenator, reservoir, and circuits were coated with biocompatible poly 2-methoxyethylacrylate. To shorten the circuit, we placed the CPB roller pump close enough to the operative field to minimize tubing length. Our CPB system consisted of a distant roller-pump head, a remote-controlled unit, and a sterilized sheet. The distant roller pump and remote-controlled unit (TONOKURA Compo III; Tonokura Medical Inc, Tokyo, Japan) allows maximal proximity to the operative field (Figure 1). The sterilized sheet (50 × 100 mm, SteriSheet; Tonokura Medical Inc, Tokyo, Japan), made of polyvinyl chloride, acts as a protective barrier between the first assistant and the CPB unit (Figure 2). The arterial, venous, and suction tubes are attached to the sheet and then covered by an unwoven, polypropylene sheet. The tubes were 3/16 inch in diameter at the pump heads, and the rest of the tubes were 5/32 inch in diameter. With this system, the total length of the circuit was reduced to about 280 cm, and its priming volume was reduced to 65 mL. The minimum priming volume of this system is currently 140 mL with 15 mL of the reservoir level. Albumin or any other colloid was not used in the CPB prime.

Figure 1. System of low-priming extracorporeal circulation (Tonokura Component System III). The distant roller pump and remote-controlled unit allows maximal proximity to the operative field.

CPB Techniques

Blood gas management was performed with the pH-stat strategy. A high-flow ($150 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) normal to mildly hypothermic (32°C) CPB was used. Crystalloid cardioplegic solution (10 mL/kg) was given every 20 minutes. After termination of the bypass, MUF was performed with a polymethylmethacrylate hemofilter in all patients. MUF was started with an ultrafiltration rate of 5 to $10 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ for 5 to 10 minutes. The heparinization was neutralized by protamine sulfate until the activated coagulation time had normalized. A cell salvage device was used during the procedure, and the remaining blood in the CPB circuit was returned to the patient within the operative day. Aprotinin was not used in the present study.

Study Protocol

Data collected from all the patients included age, sex, body weight, types of procedure, re sternotomy, CPB time, the lowest SvO_2 ,

rSO_2 , and highest plasma lactate level during CPB, preoperative hematocrit levels, the lowest hematocrit levels during CPB, the hematocrit level, the dose of the inotropic agent (dopamine) that was used at the separation from CPB, and usage and volume of blood product transfused. Data collection was performed according to the guidelines of the institutional review board. Seventy patients were divided into two groups: the transfusion group (group 1) and the nontransfusion group (group 2). Age, sex, body weight, the RACHS risk category, re sternotomy, CPB time, and preoperative hematocrit levels were analyzed as risk factors for blood transfusion in both groups. Multiple logistic regression analysis was used to determine the factors that best predicted the blood transfusion using a low-priming volume CPB system.

Statistical Analysis

Differences in patient characteristics between the transfusion group and the nontransfusion group were examined by Mann-Whitney-Wilcoxon tests and rank sum tests for continuous variables and by the Fisher exact tests for dichotomous variables. Then the bivariate relationships among these variables were examined by calculating the Spearman rank correlation coefficients for continuous variables. Multiple logistic regression analysis was used to investigate which of the factors best predicted the need for a blood transfusion. All of the factors were entered and removed at a significance level of $P < .05$ by either forward multiple logistic or backward stepwise regression analysis. Sex, re sternotomy, and RACHS risk category were modeled with binary dummy variables, whereas body weight, age, preoperative hematocrit, and perfusion time were examined as continuous variables.

Results

CPB was begun with crystalloid (bloodless) prime in all patients. There was 1 operative death. A patient with a double-outlet of the right ventricle and a Taussig-Bing anomaly, who underwent a Rastelli operation, died of pulmonary hypertension crisis. This patient received an intraoperative transfusion.

The mean follow-up period was 621 days (range 86–1283 days), and no postoperative neurologic deficits, in-

Figure 2. Arrangement of the operating room and the sterilized polyvinyl chloride sheet is close to the first assistant's right elbow and functions as a protective barrier between the patient and the unsterilized CPB unit. The arterial, venous, and suction circuits are attached to the sheet.

TABLE 2. Clinical characteristics and surgical data

	Group 1 (n = 25)	Group 2 (n = 45)	Difference (<i>P</i> values)
Age (mo)	6.5 ± 5.2	7.7 ± 5.4	.362
Sex (male/female)	15/10	26/19	.364
Body weight (kg)	5.0 ± 0.8	5.6 ± 0.8	.006
Preoperative Hct (%)	37.1 ± 8.2	38.7 ± 5.8	.349
Resternotomy	10/15	9/36	.071
RACHS risk category	2.6 ± 1.0	2.1 ± 0.5	.006
CPB time (min)	141.2 ± 46.2	92.5 ± 41.4	.0001
Inotropic agent (dopamine: μg · mL ⁻¹ · kg ⁻¹)	5.1 ± 1.7	3.8 ± 1.8	.004
Hct (%) at separation from CPB	28.1 ± 3.0	21.8 ± 3.6	.0001
Lowest Hct (%)	22.9 ± 3.4	21.7 ± 3.5	.14
Lowest Svo ₂ (%)	71.4 ± 7.8	72.2 ± 3.3	.51
Lowest rSo ₂ (%)	52.7 ± 10.4	53.8 ± 7.5	.639
Highest plasma lactate (mmol/L)	2.8 ± 1.8	2.1 ± 0.5	.012

Hct, Hematocrit; RACHS, Risk Adjustment in Congenital Heart Surgery; CPB, cardiopulmonary bypass; Svo₂, mixed venous oxygen saturation; rSo₂, regional cerebral oxygenation. An inotropic agent was needed for separation from CPB.

cluding seizure activity, delirium or delusion, or significant motor dysfunction, were found by the cardiologists or the parents. All patients are being followed up by pediatric cardiologists at our outpatient clinic. No mortalities or neurologic sequelae have been reported. As a part of follow-up, the Japanese infant developmental scale (Enjoji Scale of Infant Analytical Development)⁵ was used for patients without mental retardation diagnosed before surgery (4 patients) or chromosomal abnormality (14 patients). Pediatric cardiologists at our outpatient clinic performed the tests when the patients were from 1 to 3 years old. There were no neurodevelopmental deficits in these patients.

The lowest hematocrit level was 22.2% ± 3.5% (range 15.7%-30.4%), and the hematocrit level at separation from CPB was 24.0% ± 4.6% (range 19.8%-35.4%). The lowest Svo₂ and rSo₂ were 71.9% ± 5.3% (range 56%-84%) and 53.4% ± 8.6% (range 27%-70%), respectively. The highest plasma lactate level during CPB was 2.3 ± 1.2 mmol/L (range 0.9-9.2 mmol/L). The dose of dopamine required for weaning from CPB was 4.2 ± 1.9 μg · mL⁻¹ · kg⁻¹ (range 0-10 μg · mL⁻¹ · kg⁻¹). All the patients were separated from CPB easily without any other inotropic agents, such as epinephrine or norepinephrine. In patients with univentricular repair, the hematocrit level at separation from CPB was 27.7% ± 2.3% (range 23.7%-30.7%), and the dose of dopamine required for weaning from CPB was 4.7 ± 2.7 μg · mL⁻¹ · kg⁻¹ (range 0-10 μg · mL⁻¹ · kg⁻¹). There were no significant differences in the dose of inotropic agents between patients with biventricular repair and univentricular repair (4.2 ± 1.7 vs 4.7 ± 2.7 μg · mL⁻¹ · kg⁻¹; *P* = .40). There

TABLE 3. Clinical characteristics and surgical data

Selected variables	Odds ratios (95% CI)	<i>P</i> values
CPB time (min)	1.026 (1.019-1.033)	.0001
Body weight (kg)	0.366 (0.224-0.508)	.010

CI, Confidence interval; CPB, cardiopulmonary bypass.

were no correlations between the hematocrit level and the dose of dopamine at separation from CPB (Pearson correlation coefficient = 0.20; *P* = .10).

Twenty-five of 70 (35.7%) patients received a transfusion during their operation or stay in the intensive care unit. Of the 25 patients who received a transfusion, 21 patients required blood to maintain hematocrit level, Svo₂, rSo₂ or plasma lactate level during CPB and 4 patients required blood because of hemodynamic instability after the termination of CPB. The fresh frozen plasma was transfused in 2 patients, and platelets were transfused in 5 patients after red blood cell transfusion. The clinical characteristics and surgical data in the patients with transfusion (group 1) and without transfusion (group 2) are shown in Table 2. Significant differences were observed in body weight, RACHS risk category, CPB time, hematocrit level and dose of inotropic agents at separation from CPB, and highest plasma lactate level (*P* = 0.006, *P* = 0.027, *P* = 0.0001, *P* = 0.0001, *P* = 0.004, and *P* = 0.006, respectively).

We used multiple logistic regression analysis to discover the explanatory variable that could best predict the need for a blood transfusion (Table 3). Our results reveal that a combination of CPB time and body weight best predicts the need for a blood transfusion: odds ratios 1.026 (95% confidence interval, 1.019-1.033) (*P* = .0001) and 0.366 (95% confidence interval, 0.224-0.508) (*P* = 0.01). Age, sex, resternotomy, RACHS risk category, and preoperative hematocrit were not selected as significant predictors of the need for a blood transfusion.

Discussion

A large amount of blood products is needed in cardiac surgery for neonates and small infants to avoid hemodilution. Efforts have been made to minimize the unnecessary use of homologous blood in the pediatric population.⁶⁻⁸ The miniaturized CPB system may allow transfusion-free heart surgery for small infants and children⁹ and sometimes for neonates.¹⁰ In our institution, we have developed a priming volume CPB system with the minimal volume of 140 mL for patients weighing more than 4 and less than 7 kg. Using this system, we can prime the CPB circuit without blood products for patients weighing more than 4 kg but less than 7 kg. Of 70 patients weighing between 4 and 7 kg, 45 (64%) patients underwent heart surgery without blood transfusion. This patient group included complex procedures, such as

tetralogy of Fallot repair, atrioventricular septal defect repair, and the Rastelli operation.

One of the most potentially limiting factors to bloodless heart surgery is the patient's preoperative hematocrit level. Reduction of the priming volume can reduce this limiting factor. The present study revealed that the CPB time and the patient's body weight best predicted the need for a blood transfusion, instead of the patient's age, procedure complexity, re sternotomy, and preoperative hematocrit value in the miniaturized CPB circuit. The miniaturized CPB circuit also reduces the surface contact of the circulating blood and, thus, is expected to reduce the overall inflammatory responses.¹¹⁻¹³

Many investigators^{6,9,10} reported that low-hematocrit bypass was effective in avoiding the need for allogeneic transfusion. Kurth and associates¹⁴ also reported that the lowest safe hematocrit level was approximately 15%. Croughwell and colleagues¹⁵ reported that there was a marked increase in cognitive impairment when jugular venous oxygen saturation was less than 50%. Therefore, to prevent neurologic sequelae, our transfusion criteria during bypass were hematocrit less than 20%, Svo₂ less than 70%, rSo₂ less than 50%, and plasma lactate level greater than 4.0 mmol/L. On the other hand, recent reports have addressed concern for adverse effects of hemodilution during CPB on neurologic outcome. Jonas and coworkers¹⁶ reported, in a study including newborns, those who required profound hypothermia and/or circulatory arrest, that the use of a lower hematocrit level during CPB (22%) resulted in lower psychomotor development than did the use of a higher hematocrit. Ando and coworkers⁹ reported that no neurologic sequelae were seen and psychomotor development appeared normal despite the low hematocrit level (approximately 15%) observed during CPB. In their study, the infant psychomotor scale assessment questionnaire was used to assess overall mental and motor developments of the individual compared with that of the normal population. This assessment is considered reliable and valid in the age range of between 1 and 3 years. However, the patient group investigated included only acyanotic patients with a simple heart lesion—ventricular septal defect.

Several investigators reported the importance and usefulness of cerebral monitoring during cardiac surgery,¹⁷⁻¹⁹ especially during low-hematocrit bypass.²⁰ In the present study, Svo₂, hematocrit values, and rSo₂ were continuously monitored during CPB. In all patients, we monitored rSo₂ using near-infrared spectroscopy, in which two probes were placed on the forehead bilaterally. With this system, changes in intracranial oxygenation were recorded every second during the operation. The rSo₂ was used as an indicator of trends in cerebral oxygenation.²¹

The most important parameter during CPB is organ oxygen delivery, not hematocrit level, Svo₂, and rSo₂. There-

fore, we monitored plasma lactate level every 30 minutes during and after bypass for all patients. The highest lactate level in patients with transfusion was significantly greater than that in patients without ($P < .05$), although there were no significant differences in hematocrit level, Svo₂, and rSo₂, between two groups. These results supported that the plasma lactate level is one of the most sensitive indexes of vital organ oxygen delivery.^{22,23}

More inotropic agent was needed for separation from CPB in patients with a transfusion than in those without one ($P < .01$), even though the hematocrit level at separation from CPB in the transfused group was significantly greater than that in the bloodless heart surgery group, because the transfused group underwent more complicated procedures and required a longer CPB time. There was no tendency that more inotropes were required in patients with lower hematocrit levels in our study.

In summary, of 70 patients weighing between 4 and 7 kg, 45 (64%) patients underwent transfusion-free procedures. With the low-priming volume circuit, it is possible to do complex transfusion-free procedures safely for patients weighing more than 4 kg and less than 7 kg. The limiting factors of bloodless heart surgery are not preoperative hematocrit or complexity of procedure, but CPB time and body weight, despite using a miniaturized bypass system. Further investigation and follow-up studies are warranted to determine a safe, low-hematocrit strategy in transfusion-free procedures for uneventful neurologic development.

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