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# Superior blood-saving effect and postoperative recovery of comprehensive blood-saving strategy in infants undergoing open heart surgery under cardiopulmonary bypass

Ting Wu, MD[a,*], Jianshi Liu, MD[b], Qiang Wang, MD[b], Peijun Li, MD[c], Guoning Shi, MD[a]

**Abstract**

**Background:** Optimization of blood-saving strategies during open heart surgery in infants is still required. This study aimed to study a comprehensive blood-saving strategy during cardiopulmonary bypass (CPB) on postoperative recovery in low-weight infants undergoing open heart surgery.

**Methods:** This was a prospective study of 86 consecutive infants (weighing <5 kg) with acyanotic congenital heart disease treated at the Tianjin Chest Hospital between March and December 2016, and randomized to the control (traditional routine CPB) and comprehensive blood-saving strategy groups. The primary endpoints were blood saving and clinical prognosis. The secondary endpoints were safety and laboratory indicators, prior to CPB (T1), after 30 minutes of CPB (T2), after modified ultrafiltration (T3), and postoperative 12 (T4), 24 (T5), 48 (T6), and 72 h (T7).

**Results:** The total priming volume and banked red blood cells in the comprehensive strategy group were significantly lower than in the control group ($P = .009$ and $P = .04$, respectively). In the comprehensive strategy group, immediately after CPB, the amount of salvaged red blood cells exceeded the priming red blood cells by $40 \pm 11$ mL. Postoperatively, the comprehensive strategy group showed a significant decrease in the inotrope score ($P = .03$), ventilation time ($P = .03$), intensive care unit stay ($P = .04$), and hospital stay ($P = .03$) in comparison with the control group.

**Conclusion:** The comprehensive blood-saving strategies for CPB were associated with less blood use and favorable postoperative recovery in low-weight infants with congenital heart disease undergoing open heart surgery.

**Abbreviations:** COP = colloid osmotic pressure, CPB = cardiopulmonary bypass, ICU = intensive care unit, IL-6 = interleukin-6, LVEF = left ventricular ejection fraction, RBC = red blood cell, TNF-α = tumor necrosis factor-α.

**Keywords:** blood saving, cardiopulmonary bypass, comprehensive strategy, congenital heart disease, infant, neonates

## 1. Introduction

Neonates and infants undergoing open heart surgery present unique challenges in the management of cardiopulmonary bypass (CPB) due to their small body surface area and low body weight. In those pediatric patients, the CPB priming volume is often equivalent or even higher than their estimated blood volume. Consequently, these patients often require packed red blood cells (RBCs), whole blood, or component transfusion in the operating room and intensive care unit (ICU).

In addition, transfusion of stored bank blood may lead to inflammation and increased risk of organ dysfunction (especially pulmonary and right ventricular functions) and nosocomial infections.[1] Furthermore, transfusion of older blood increases the risk of serious complications and increases the ventilation time, because transfusion-related acute lung injury is one of the leading causes of transfusion-related morbidity and mortality.[1–3] Previous studies suggested that a restrictive transfusion strategy was associated with improved outcome by decreasing morbidity and mortality.[3]

In recent years, considerable progress has been made by using techniques that decrease the use of blood products or even allow surgery without the use of such products. These techniques involve a decrease in priming volume by downsizing the bypass circuit with the help of vacuum-assisted venous drainage, microplegia, autologous blood predonation (with or without infusion of recombinant erythropoietin), cell salvage, ultrafiltration, and retrograde autologous priming. Mast pumps, oxygenator with arterial filter, vacuum-assisted venous drainage, miniaturized circuits, minimal priming volume ultrafiltration, cell saver, and no plasma priming are now used routinely for low-weight neonates and infants with congenital heart disease.[4,5]

Nevertheless, optimization of this modified strategy is still required. This study aimed to describe our CPB strategy to reduce blood use. We report the postoperative recovery of pediatric patients with acyanotic congenital heart diseases.

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*[a] Department of Perfusion, [b] Department of Cardiac Surgery, [c] Intensive Care Unit, Tianjin Chest Hospital, Tianjin, China.*

*[*] Correspondence: Ting Wu, Department of Perfusion, Tianjin Chest Hospital, Tianjin, China (e-mail: ting_ting_wu@126.com).*



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## 2. Materials and methods

### 2.1. Study design and patients

This was a randomized prospective study of 86 consecutive neonates and infants with acyanotic congenital heart disease and who had receive surgery at the Department of Cardiac Surgery of Tianjin Chest Hospital between March and December 2016. Indication for open heart surgery was the need for radial correction.

The inclusion criteria were: <12 months of age; weighing <5 kg; and diagnosed with acyanotic congenital heart disease. The exclusion criteria were: reoperation; emergency operation; cyanotic disease; unstable hemodynamics; hematocrit <0.24; or palliative surgery. The study was approved by the institutional review board of Tianjin Chest Hospital. Written informed consent was obtained from the parents or legal guardians. This study was registered with the Chinese Clinical Trial Registry (ChiCTR-INN-16008019).

### 2.2. Randomization

The patients were equally randomized using sealed sequential envelopes prepared by an independent statistician using a computer-generated random number table.

### 2.3. Cardiopulmonary bypass strategies

All patients were operated by the same surgeon, who is a director of pediatric cardiac surgery. General anesthesia was induced with tracheal intubation. A Stockert S5 CPB machine (Stockert, Munich, Germany) was used in all patients. Routine (at the authors' hospital) traditional CPB techniques were used in the control group, including 5 pump positions (main, cardioplegia, ultrafiltration, vent, and suction pumps), Baby RX05 Terumo membrane oxygenator (Terumo, Tokyo, Japan), lower position of oxygenator, infant arterial filter (35 mL; Ningbo Fly Medical, Zhejiang, China), infant CPB circuit (6 mm in diameter), BLS 803 ultrafilter (Sorin Group, Mirandola, Italy, prime volume; 32 mL), and 4-mm connecting circuit. Priming was done with electrolytes, banked RBCs (120 mL), plasma (100 mL), and albumin (10 g).

In the comprehensive strategy group, we used 2 mast pumps (main pump and suction pump), 3 fixed pumps (vent, cardioplegia, and ultrafiltration), a Terumo FX05 membrane oxygenator (Terumo), elevation of oxygenator and pump to the level of the operative bed, and vacuum-assisted venous drainage on the reservoir of the oxygenator (negative pressure of −10 to −20 mm Hg, Medtronic pressure display 60000; Medtronic, Minneapolis, MN), customized miniaturized CPB circuit, Minntech ultrafiltration (Minntech HPH Junior, Minneapolis, MN; priming volume, 8 mL), a 2.5- to 3-mm connecting circuit, no plasma priming, and 55 mL of Sorin Electa cell saver (Sorin, Arvada, CO). Table 1 lists the differences between the 2 approaches.

A combination of conventional and modified ultrafiltration was used in both groups. The priming solution included compound sodium acetate electrolyte, 20% albumin, banked RBCs, plasma, 5% $NaHCO_3$ (20 mL), transamin (10 mL), and heparin (20 mg). In the control group, 500 mL of crystalloid was first used to prime the oxygenator, arterial filter, CPB circuit, and ultrafiltration system. One unit (approximately 120 mL) of banked RBCs, 100 mL of plasma, and 50 mL of 20% albumin were added in the oxygenator. Then, conventional ultrafiltration was performed to discharge the extra crystalloid. Finally, $NaHCO_3$, transamin, and heparin were added to fill the oxygenator from 150 to 200 mL. In the comprehensive strategy group, 180 mL of crystalloid was first used to prime the oxygenator, CPB circuit, and ultrafiltration system. Then, 110 mL of RBCs rinsed with cell saver and 50 mL of 20% albumin were added. Conventional ultrafiltration was performed to discharge the extra crystalloid. Finally, $NaHCO_3$, transamin, and heparin were added to fill the oxygenator from150 to 200 mL.

**Table 1**

**Cardiopulmonary bypass techniques in the comprehensive strategy and control groups.**

| | Comprehensive strategy group (n = 42) | Control group (n = 42) |
|---|---|---|
| Pump position | 2 mast, 3 fixed pump | Five fixed pump |
| Oxygenator with arterial filter | Yes (Terumo FX05) | No (Terumo RX05) |
| Elevation of oxygenator | Yes | No |
| Vacuum assisted venous drainage | Yes | No |
| Customized circuit | Yes | No |
| Miniaturized circuit | Yes (4 mm) | No (6 mm) |
| Ultrafiltration (priming volume) | Minntech HPH Junior (8 mL) | BLS803 (32 mL) |
| Ultrafiltration connecting circuit | 2.5–3 mm | 4 mm |
| Use of cell saver | Yes | No |
| Priming with plasma | No | Yes |

After bypass weaning, both groups received modified ultrafiltration until hemoglobin was >12 g/dL. In the control group, crystalloid was added to the reservoir for returning the remaining blood in the machine to the patient until hemoglobin levels were satisfying. The residual blood in the machine was discarded. In the comprehensive strategy group, all the residual machine blood after modified ultrafiltration was collected using the cell saver, and the cleaned RBCs were transfused to the patient when necessary.

An 8 Fr straight tip Medtronic DLP cannula (Medtronic) was used in the control group. In the comprehensive strategy group, an 8 to 10 Fr 1-piece pediatric Medtronic DLP arterial cannula (Medtronic) and single-stage venous cannula with right angle metal tip were used. During mild hypothermia (30–32°C) CPB, hemoglobin was maintained at 7 to 9 g/dL, mixed venous oxygen saturation ($SvO_2$) at >80%, flow rate at 150 to 250 mL/kg, perfusion pressure at 30 to 60 mm Hg, and activated clotting time (Hemochron Jr Signature, Accriva Diagnostics, Edison, NJ) at >400 seconds (heparin calcium 40 mg/kg for the first dose). St Thomas crystalloid cardioplegia ($K^+$ concentration: 16 mmol/L) was given every 30 minutes through the aortic root.

### 2.4. Study parameters

Temperature (nasopharyngeal and bladder), blood gas, and electrolytes were monitored before and after purifications. Priming volume, salvaged RBC, and use of blood products were recorded. Blood samples were taken through the oxygenator and the central venous catheter. The following parameters were evaluated and compared between the 2 groups prior to CPB (T1), after 30 minutes of CPB (T2), after modified ultrafiltration (T3), and postoperative 12 (T4), 24 (T5), 48 (T6), and 72 hours (T7): hemoglobin, $SvO_2$, lactate, free hemoglobin (Free Hemoglobin Colorimetric Assay kit; Leagene, Beijing, China), pump pressure (monitored on the top of the micro plug filter), colloid osmotic pressure (COP; through BMT923, Stahnsdorf, Germany),

interleukin-6 (IL-6, Raybiotech ELISA kit; RayBiotech, Beijing, China), tumor necrosis factor-α (TNF-α, Raybiotech ELISA kit, RayBiotech), inotrope score, ventilation time, left ventricular ejection fraction (LVEF, through UCG, PHILIPS ie33; Philips, Best, The Netherlands) 24 hours after surgery, amount of chest tube drainage over the first 24 hours, ICU stay, and hospital stay.

T1 is before CPB. T2 was selected because after 30 minutes, the administration of cardioplegic solution is completed. T3 is the final state of CPB after modified ultrafiltration. T4, T5, T6, and T7 are the early and stable states of postoperative monitoring.

The inotrope score was calculated as dopamine (×1) + dobutamine (×1) + amrinone (×1) + milrinone (×10) + adrenaline (×100) (μg/kg min).

### 2.5. Endpoints

The primary endpoints were blood-saving and clinical prognosis. The secondary endpoints were safety and the laboratory indicators described above.

### 2.6. Statistical analysis

All continuous variables were tested for normal distribution using the Kolmogorov–Smirnov test. Normally distributed continuous data were expressed as mean ± standard deviation and compared using the Student *t* test. Non-normally distributed data were presented as median (range) and analyzed with the Mann–Whitney *U* test. Categorical data were presented as proportion and analyzed with the Chi-square test or Fisher exact test, as appropriate. The variations in time of consecutively monitored parameters were evaluated using a mixed effect analysis of variance model (normal distribution) or the Kruskal–Wallis test (non-normal distribution). Statistical analysis was carried out using SPSS 17.0 for Windows (IBM, Armonk, NY). Two-sided *P*-values <.05 were considered statistically.

No power analysis was performed when designing the study and the sample size was determined arbitrarily based on the available patients and appropriate study duration. Nevertheless, a post hoc power analysis based on the length of stay at the ICU showed that using α = 0.05, n = 40/group, and the observed standard deviations (1.1 and 0.9 days, respectively), the power was 99% for detecting a difference of 0.98 days between the means. Since the difference in ICU length of stay was of 1.3 days, the study was sufficiently powered with 42 patients/group.

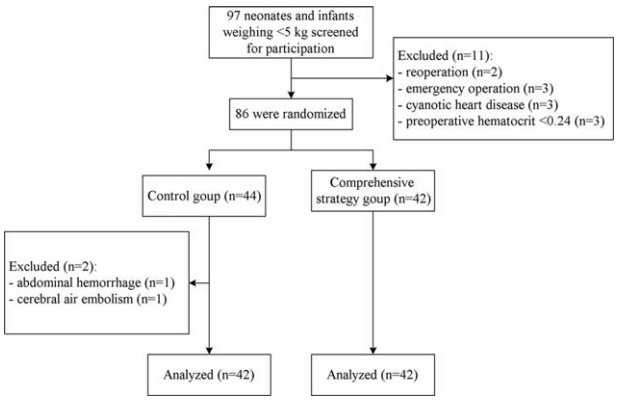


**Figure 1.** Patient flowchart.

## 3. Results

### 3.1. Characteristics of the patients

Figure 1 presents the patient flowchart. From 97 patients, 11 were excluded due to reoperation (n = 2), emergency operation (n = 3), cyanotic disease (n = 3), and preoperative hematocrit <0.24 (n = 3). Therefore, 86 patients were randomized: 44 in the control group and 42 in the comprehensive strategy group. In the control group, 2 patients were excluded from the analyses because of abdominal hemorrhage due to femoral artery puncture (n = 1) and cerebral air embolism (n = 1). Finally, there were 42 patients in each group.

Table 2 presents the characteristics of the patients. The 2 groups were similar. All analyses were performed as per protocol. The durations of CPB and aortic cross-clamp were 84.8 ± 25.7 versus 85.9 ± 23.1 minutes (*P* = .841), and 50.5 ± 15.8 versus 49.7 ± 17.6 minutes (*P* = .831) in the comprehensive strategy and control groups, respectively. Preoperative hemoglobin levels were 12.1 ± 0.9 versus 11.8 ± 1.1 g/L (*P* = .186).

**Table 2**

**Characteristics of the patients.**

| | Comprehensive strategy (n = 42) | Controls (n = 42) | *P* |
|---|---|---|---|
| Age, mo | 1.6 ± 0.8 | 1.5 ± 0.6 | .746 |
| Weight, kg | 3.8 ± 1.2 | 3.7 ± 1.3 | .700 |
| Gender | | | .899 |
| Male | 25 | 24 | |
| Female | 15 | 16 | |
| Surgical procedures | 40 | 40 | .834 |
| Atrial septal defect, ventricular septal defect, patent ductus arteriosus | 6 | 5 | |
| Ventricular septal defect | 10 | 11 | |
| Total anomalous pulmonary vein connection | 5 | 4 | |
| Pulmonary stenosis | 5 | 6 | |
| Double outlet right ventricle | 5 | 5 | |
| Aortic stenosis | 5 | 5 | |
| Interrupted aortic arch | 4 | 4 | |
| Cardiopulmonary bypass time, min | 84.8 ± 25.7 | 85.9 ± 23.1 | .841 |
| Blocking time, min | 50.5 ± 15.8 | 49.7 ± 17.6 | .831 |
| Preoperative hemoglobin, g/L | 12.1 ± 0.9 | 11.8 ± 1.1 | .186 |

**Table 3**

**Blood gas and electrolytes of banked blood before and after purification in the comprehensive strategy group.**

| Variables | Before purification | Immediately after purification | P |
|---|---|---|---|
| $PO_2$, mm Hg | 57.9±4.7 | 69.3±6.1 | .042 |
| $PCO_2$, mm Hg | 151.0±12.9 | 12.5±3.9 | .004 |
| pH | 6.4±1.2 | 6.5±1.1 | .791 |
| $SaO_2$, % | 62.1±2.1 | 75.8±2.6 | .042 |
| $K^+$, mmol/L | 20.9±5.1 | 1.7±0.7 | .006 |
| Glucose, mmol/L | 24.1±8.6 | 5.4±1.7 | .008 |
| Lactate, mmol/L | 25.0±7.7 | 8.7±3.9 | .023 |
| Hemoglobin, g/dL | 15.2±0.2 | 20.8±1.7 | .048 |

$PCO_2$=partial pressure of carbon dioxide, $PO_2$=partial pressure of oxygen, $SaO_2$=oxygen saturation.

### 3.2. Blood gas and electrolytes of banked blood before and after purification in the comprehensive strategy group

Table 3 presents the changes in blood gas and electrolytes of banked blood with purification. Only the patients in the comprehensive strategy group underwent blood purification. Following purification, the levels of potassium, glucose, and lactate in the banked blood were decreased ($P=.006$, $P=.008$, and $P=.023$, respectively). A significant decrease in the partial pressure of carbon dioxide ($PaCO_2$) ($P=.004$) and increase in partial pressure of oxygen ($PaO_2$) ($P=.042$) were observed after purification.

### 3.3. Priming volume, blood products, and salvaged red blood cells

The total priming volume and the use of banked RBCs in the comprehensive strategy group were significantly lower than in the control group (priming volume: 280±11 vs 450±16 mL, $P=.009$; banked RBCs: 110±18 vs 190±24 mL, $P=.04$). Immediately after CPB, the amount of salvaged RBCs in the comprehensive strategy group was 150±20 mL, which exceeded the amount of the banked RBCs used for priming by 40±11 mL, meaning that 40±11 mL of RBCs were actually recovered from the patients (Table 4). No fresh-frozen plasma was used in the comprehensive strategy group. Of course, no cell saving strategy was used in the control group, leading to a net use of RBCs of 190±24 mL.

**Table 4**

**Priming volume, blood products, and salvaged red blood cells.**

| | Comprehensive strategy group (n=42) | Control group (n=42) | P |
|---|---|---|---|
| Total priming volume, mL | 280±11 | 450±16 | .009 |
| Frozen fresh plasma, mL | No plasma | 100±5 | – |
| 20% albumin, mL | 50±2 | 50±2 | .99 |
| Banked red blood cells, mL | 110±18 | 190±24 | .040 |
| Rinsed red blood cells, mL | 150±20 | No cell saving | – |
| Actual use of blood products, mL* | −40±11 (rinsed blood volume exceed the blood volume used in priming) | 190±24 | <.001 |

* Calculated as (banked red blood cells) − (rinsed blood cells), which represents the net use of red blood cells.

### 3.4. Changes of study parameters in time

Table 5 presents the temporal changes of study parameters between the 2 groups. The levels of hemoglobin, $SvO_2$, COP, and pump pressure were similar between the 2 groups prior to, during, and after CPB (all $P>.05$). The levels of free hemoglobin peaked during CPB and decreased considerably after CPB in both groups. Because of the use of cell saver and ultrafiltration, the levels of free hemoglobin were significantly higher in the control group from T1 (before CPB) to T5 (postoperative 24 hours) ($P<.05$) compared with the comprehensive strategy group. Lactate levels started to increase upon initiation of CPB. Lactate levels in the comprehensive strategy group were significantly lower than in the control group from T1 (before CPB) to T5 (postoperative 24 hours) ($P<.05$). The levels of IL-6 and TNF-α in the comprehensive strategy group were significantly lower than in the control group from T2 (prior to initiation of CPB) to T6 (postoperative 48 hours) ($P<.05$).

### 3.5. Postoperative recovery

As shown in Table 6, the comprehensive strategy group showed a significant decrease in the inotrope score ($P=.032$), ventilation time ($P=.028$), ICU stay ($P=.039$), and hospital stay ($P=.033$) after surgery, but there were no significant differences for chest tube drainage ($P=.071$) and LVEF at 24 hours ($P=.089$) compared with the control group.

### 3.6. Adverse reactions and complications

In the control groups, there was 1 case with abdominal bleeding due to femoral puncture and 1 case of cerebral air embolism; they were excluded from the finale analyses because these complications were unrelated to CPB. In terms of postoperative complications, there was 1 case of difficult tracheal intubation removal due to pulmonary arterial hypertension in each arm. Moreover, 1 patient had a cerebral thrombus in the control group, and there was 1 death caused by cardiac arrest after surgery in the comprehensive strategy group.

## 4. Discussion

The optimization of blood-saving strategies during open heart surgery in infants is still required. This study aimed to study a comprehensive blood-saving strategy during CPB on the postoperative recovery of low-weight infants undergoing open heart surgery. The results showed that this comprehensive blood-saving strategy in CPB was associated with less blood use and favorable postoperative recovery in low-weight infants with congenital heart disease undergoing open heart surgery.

Since its introduction in the 1950s,[6] CPB has been playing an indispensable role in open heart surgery. During CPB, it is mandatory to remove all air from the oxygenator and circuits with crystalloids and colloids. Due to the low body weight and blood volume of infants and children, excessive hemodilution will lead to complications such as edema, hypoxia, and hemorrhage.[1–3] Transfusion of allogenic blood is an approach to reduce excessive hemodilution during open heart surgery under CPB for neonates and infants with congenital heart disease, but there is increasing evidence that the amount of blood transfused is associated with high fever, allergic reactions, postoperative infections,[7,8] and longer ventilation time and ICU stay,[9] probably because the organs are immature and immune functions are inadequate in pediatric patients. Several studies have shown

**Table 5**

**Temporal changes in parameters before and after cardiopulmonary bypass.**

| Variable | Group | T1 | T2 | T3 | T4 | T5 | T6 | T7 |
|---|---|---|---|---|---|---|---|---|
| Hemoglobin, g/dL | Comprehensive | 11.8±1.1 | 8.1±0.3 | 12.1±0.9 | 12.2±1.5 | 12.5±0.7 | 12.3±0.5 | 12.6±0.8 |
| | Control | 12.1±0.9 | 8.0±0.5 | 11,8±1.1 | 12.1±1.8 | 12.6±1.3 | 12.5±0.8 | 12.5±0.7 |
| $SvO_2$, % | Comprehensive | – | 99±0.2 | – | – | – | – | – |
| | Control | – | 99±0.2 | – | – | – | – | – |
| Colloid osmotic pressure, mm Hg | Comprehensive | 21.9±1.9 | 16.0±1.2 | 19.0±1.9 | 18.8±1.1 | 19.5±1.2 | 20.3±1.5 | 20.9±0.4 |
| | Control | 22.8±2.0 | 16.7±1.2 | 19.3±2.1 | 18.7±1.7 | 19.2±1.3 | 20.5±1.4 | 20.8±0.5 |
| Lactate, mmol/L | Comprehensive | 0.5±0.2* | 0.8±0.2* | 1.1±0.2* | 1.5±0.2* | 1.1±0.1* | 0.8±0.1 | 0.7±0.1 |
| | Control | 1.1±0.2 | 1.5±0.1 | 1.9±0.3 | 2.8±0.3 | 1.9±0.2 | 1.1±0.2 | 0.9±0.2 |
| Free hemoglobin, mg/L | Comprehensive | 59.2±8.7* | 123.6±34.9* | 113.9±28.6* | 81.9±10.1* | 55.9±6.5* | 50.6±7.1 | 50.0±6.2 |
| | Control | 77.3±10.2 | 209.0±40.8 | 197.3±30.3 | 109.1±10.5 | 67.9±8.8 | 58.3±9.0 | 52.9±7.7 |
| Pump pressure, mm Hg | Comprehensive | 31.3±6.1 | 128.1±19.4 | 54.5±6.2 | – | – | – | – |
| | Control | 30.0±5.4 | 120.8±20.9 | 50.3±7.8 | – | – | – | – |
| IL-6, ng/L | Comprehensive | 12.3±3.1 | 17.1±3.0* | 17.8±2.8* | 17.1±2.7* | 14.0±2.2* | 13.9±3.1* | 13.9±2.9 |
| | Control | 16.1±5.8 | 27.0±3.8 | 28.5±3.8 | 30.3±4.1 | 27.3±3.3 | 19.9±2.9 | 15.3±3.1 |
| TNF-α, pmol/L | Comprehensive | 1.8±0.3 | 2.1±0.5* | 2.4±0.4* | 1.8±0.3* | 1.7±0.3* | 1.6±0.2* | 1.6±0.2 |
| | Control | 2.2±0.3 | 5.7±0.6 | 6.5±0.5 | 4.0±0.6 | 3.1±0.3 | 2.6±0.3 | 2.2±0.3 |

T1 = prior to CPB, T2 = after 30 min of CPB, T3 = after modified ultrafiltration, T4 = postoperative 12 h, T5 = postoperative 24 h, T6 = postoperative 48 h, T7 = postoperative 72 h, $SvO_2$ = mixed venous oxygen saturation, IL-6 = interleukin 6, TNF-α = tumor necrosis factor-α.

* $P < .05$ between the comprehensive strategy and control groups (Student *t* test).

that allogenic blood transfusion may exacerbate the systemic inflammatory response associated with CPB[10] and directly affect operative outcomes.[11]

Shortage of blood products has greatly promoted the improvement of blood saving techniques and their safety.[12–14] Among the various improvements, 3 major techniques emerged as being simple, safe, efficient, and cost-effective: minimizing the priming volume, controlling the total volume of CPB, and increasing the blood salvaged from the circuit. Over the years, our team has developed a specific strategy that has been shown, by experience, to be effective and safe. This strategy encompasses mast pumps, oxygenator with arterial filter, vacuum-assisted venous drainage, miniaturized circuit, minimal priming volume, ultrafilter, cell saver, and no-plasma priming.

As discussed above, significant hemodilution and inflammatory response will occur in infants upon initiation of CPB. Important measures to counteract hemodilution and inflammation include minimizing the foreign-body contact area between blood and CPB circuits, decreasing the priming volume, and improving biocompatibility of surfaces entering into contact with the blood. In our practice, we switched to using a membrane oxygenator with high biocompatibility and minimal CPB circuits, reducing the CPB circuit priming volume considerably, as previously suggested.[15–17] We used 2 mast pumps to replace the conventional fixed pumps. This allowed the adjustment of the position of the pump head, thus allowing the main pump and suction pump to be close to the oxygenator, reducing tube length. When used in combination with the oxygenator equipped with a microplug filter, this method can save about 35 mL blood compared to using a microplug alone. In addition, this method can save another 25 mL of blood from the tube linking the microplug. The lifting up of the oxygenator is used in combination with the vacuum-assisted venous drainage negative-pressure-assisted drainage device. The specifically designed blood-saving tubes and suspended pump is used in addition; taken together, they can further save about 80 mL of blood. The application of ultrafiltration and different linking tubes can save about 30 mL of blood. The no plasma priming means the priming with crystalloid and protein, which does not reduce the volume of liquid, but can reduce the use of blood products.[4,18–20] The blood recycling system was used to recycle the blood during and after the operation. Therefore, from the descriptions above, the volume for priming can be reduced by 170 mL.

**Table 6**

**Postoperative recovery.**

| Variable | Comprehensive strategy group (n = 42) | Control group (n = 42) | *P* |
|---|---|---|---|
| Inotrope score | 6.1±2.3 | 8.4±1.9 | .032 |
| Left ventricular ejection fraction at 24 h, % | 60.2±3.1 | 54.8±7.5 | .089 |
| Chest tube drainage over first 24 h, mL | 185±40 | 190±54 | .071 |
| Ventilation time, h | 10.1±1.2 | 15.2±2.0 | .028 |
| Length of intensive care unit stay, days | 4.3±1.1 | 5.6±0.9 | .039 |
| Length of hospital stay, days | 12.1±2.1 | 15.3±3.3 | .033 |

The CPB is a known cause of systemic inflammatory response.[9,10,20] A number of different pro- and anti-inflammatory cytokines are released in response to CPB.[9,10,20] The production of cytokines such as IL-1β, IL-6, and TNF-α is stimulated by a variety of elicitors, which may lead to systemic inflammatory response syndrome and injury to the heart, lung, and brain.[5] In recent years, the improvements in extracorporeal technology and devices led to progressive miniaturization and modification of CPB circuits in an attempt to attenuate the inflammatory response. Apparently, efforts to reduce or avoid the use of blood products are indispensable to minimize the resultant hemolytic and consumptive effects on blood cells, especially in neonates and infants undergoing open heart surgery under CPB.

According to prior studies by Liu et al,[13,14] the safe limits of hemodilution during neonatal and infantile cardiac surgery is a hemoglobin level of ≥7 g/dL, below which RBCs should be transfused. We routinely maintained the COP at 16 to 18 mm Hg and continuously monitored the $SvO_2$, hematocrit, and blood gas. During CPB, after adjustment of the flow rate, temperature, and oxygen concentration, RBCs were transfused when the

lactate levels rose and $SvO_2$ decreased. As is widely agreed on, modified ultrafiltration after discontinuation of CPB facilitates reduction of hemodilution and tissue edema. In most studies, modified ultrafiltration has improved dilutional coagulopathy and reduced blood transfusion requirements,[21–23] thereby becoming an integral part of CPB in infants. Based on previous experience of transfusion during infant cardiac surgery,[13,14] we only used albumin to maintain the COP and achieved no-plasma priming for patients undergoing the comprehensive strategy in this study. Because all patients in this cohort weighed $<5$ kg, a small amount of banked RBCs was used for priming the system to maintain the hemoglobin concentration and satisfactory oxygenation and metabolic levels. In all patients, cell saver with a 55-mL centrifuge cup was used throughout the operative process. The preoperative use of cell saver can significantly reduce the concentrations of potassium, glucose, and acid, and improve the oxygen saturation of banked blood. Although washing removes platelets, coagulation factors, and other plasma proteins, the debris can also be eliminated, thereby reducing the risk of cerebral thromboembolism and improving neurologic outcomes. At the end of the procedures, the amount of salvaged RBCs exceeded that of banked RBCs transfused before and during CPB, which implies that RBC-free surgery has been achieved to some extent. The postoperative recovery was significantly better in patients in the comprehensive strategy group compared to the control group.

The present study is not without limitations. Only neonates and infants with acyanotic congenital heart disease were included; they had a relatively low operative risk compared to those with cyanotic congenital heart defects, limiting the generalizability of this study. Nevertheless, the results of this study could support the use of our comprehensive blood-saving strategy to improve the postoperative recovery and clinical outcomes in selected patients. In addition, some differences in blood parameters (eg, free hemoglobin, lactate, and cytokines) are probably due to the small sample size; it is unknown if these differences biased the results. Studies with larger sample size, broader inclusion criteria, and long-term outcomes are warranted to clarify the overall utility of this strategy for low-weight infants with congenital heart disease undergoing open surgical repair.

In conclusion, the present study strongly suggests that our comprehensive blood-saving strategy during CPB was associated with less blood product use and favorable postoperative recovery in low-weight infants with congenital heart disease undergoing open heart surgery.

## Author contributions

**Conceptualization:** Ting Wu, Jianshi Liu.
**Data curation:** Ting Wu, Jianshi Liu, Qiang Wang, Peijun Li, Guoning Shi.
**Formal analysis:** Ting Wu, Jianshi Liu, Qiang Wang, Peijun Li, Guoning Shi.
**Funding acquisition:** Ting Wu.
**Investigation:** Ting Wu, Jianshi Liu, Qiang Wang, Peijun Li, Guoning Shi.
**Methodology:** Ting Wu, Jianshi Liu, Peijun Li, Guoning Shi.
**Project administration:** Ting Wu.
**Resources:** Ting Wu.
**Software:** Ting Wu.
**Supervision:** Ting Wu.
**Validation:** Ting Wu.
**Visualization:** Ting Wu.
**Writing – original draft:** Ting Wu.
**Writing – review & editing:** Ting Wu, Jianshi Liu, Qiang Wang, Peijun Li, Guoning Shi.

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