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RESEARCH

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# A randomized study on the impact of optimized modified ultrafiltration on the physiological parameters of infants and children undergoing a cardiopulmonary bypass

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## Abstract

**Background** The aim of this study is to assess the impact of optimized modified ultrafiltration (OMUF) on the physiological parameters of infants and children undergoing cardiopulmonary bypass (CPB).

**Methods** In this randomized clinical trial, 30 pediatric patients were recruited and allocated into the experimental and control groups, each comprising of 15 patients. The experimental group underwent OMUF prior to the termination of CPB and extubation, while the control group received conventional modified ultrafiltration (MUF).

**Results** In the experimental group, post-ultrafiltration levels of Na+, Ca++, hemoglobin (Hb), and hematocrit (HCT) exhibited a statistically significant increase compared to pre-ultrafiltration levels ($p < 0.05$), whereas no statistically significant differences were observed in the control group.

**Conclusion** The optimization of conventional MUF led to a significant enhancement in ultrafiltration efficacy, thereby exerting a beneficial impact on improving the physiological parameters of pediatric patients during CPB, surpassing conventional practices.

**Keywords** Cardiopulmonary bypass, Infants and children, Modified ultrafiltration, Physiological parameters

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## Background

Cardiopulmonary bypass (CPB) is a critical life-support technology that involves the use of specialized artificial devices to temporarily divert venous blood from the body, facilitate gas exchange through artificial means, regulate temperature, and filter the blood before reintroducing it into the arterial system. Its primary objective is to sustain adequate blood flow to organs and tissues during open-heart surgery. Originally used in cardiac, hepatic, renal, pulmonary, and other major vascular surgeries, CPB has also demonstrated notable efficacy in tumor treatment and life support for patients facing cardiopulmonary failure, thus assuming a pivotal role in clinical medicine [1]. The technique of modified ultrafiltration (MUF) was pioneered by Naik in 1991 [1–4]. MUF serves to elevate the concentration of active components in the blood, reduce lung injury to a certain extent, and enhance cardiopulmonary function. Given the prevalence of postoperative complications among infants and children with underdeveloped organ systems, refining techniques for pediatric patients holds significance [5–8]. As MUF is usually beneficial to the discharge of excess water after operation, which can reduce postoperative complications and blood transfusion, it is suitable for infants with small weight, large hemodilution and CPB for a long time. However, due to its initiation post-CPB completion and the requisite approximately 15-minute duration at a flow rate of 15 ml/kg to achieve optimal outcomes, this method inadvertently prolongs surgical duration and entails associated adverse effects such as decreased body temperature, air embolism, thrombosis, hemolysis, hypokalemia, hemodynamic instability, and cerebral ischemia [2–4]. Therefore, traditional MUF was further refined for the patients in this study, to investigate the impact of OMUF on arterial blood gas (ABG), electrolytes, and other indicators during CPB. In this study, we introduce optimized modified ultrafiltration (OMUF) as an advancement over conventional MUF and compare its effects with those of conventional intraoperative balanced ultrafiltration (BUF) and conventional MUF prior to the cessation of CPB and extubation. The aim is to investigate the effects of OMUF on ABG and electrolytes during CPB in infants and children.

## Materials and methods

### Clinical material and grouping

This prospective randomized controlled study involved 30 children weighing ≤ 12 kg who underwent surgical correction of congenital heart disease. Sample size was calculated based on ABG and electrolytes data during CPB from our previous studies. Surgeons were blinded. They were allocated into an experimental group and a control group, with 15 cases in each group. The clinical data of both groups of patients are presented in Table 1. The experimental groups were given OMUF while the control group were given conventional MUF, and other procedures were the same in the 2 groups.

The selection of surgical procedures was tailored to the specific heart conditions of the patients:

- For those diagnosed with both a ventricular septal defect (VSD) and patent foramen ovale (PFO), surgeries to repair the VSD and PFO were performed.
- Patients with a VSD and pulmonary artery stenosis (PAS) underwent VSD repair and PAS correction.
- In cases of VSD combined with patent ductus arteriosus (PDA), the treatment involved VSD repair and ligation of the PDA.
- For patients with an atrial septal defect (ASD) and PDA, the surgical approach included ASD repair and PDA ligation.
- Patients diagnosed with an ASD and PAS received surgeries for ASD repair and PAS correction.
- When a patient presented with both an ASD and a VSD without additional complications, the surgical intervention involved repairs of both defects.

There was no hepatic or renal insufficiency nor any endocrine system disease prior to surgery in any of the

**Table 1** The general characteristics in pediatric patients in the two groups

| Clinical Data | Experimental group | Control group | *P* |
|---|---|---|---|
| Age (m) (Mean ± SD) | 12.24 ± 7.89 | 13.74 ± 7.27 | 0.728 |
| Weight (kg) (Mean ± SD) | 8.55 ± 1.66 | 9.73 ± 2.02 | 0.104 |
| Gender (Male/Female) (Number) | 7/8 | 6/9 | |
| Ventricular septal defect with patent foramen ovale (PFO) (Number (percentage)) | 5 (33.3%) | 4 (26.7%) | |
| Ventricular septal defect with pulmonary artery stenosis (PAS) (Number (percentage)) | 0 | 1 (6.7%) | |
| Ventricular septal defect with patent ductus arteriosus (PDA) (Number (percentage)) | 1 (6.7%) | 0 | |
| Ventricular septal defect (VSD) (Number (percentage)) | 6 (40%) | 6 (40%) | |
| Atrial septal defect (ASD) (Number (percentage)) | 2 (13.3%) | 3 (20%) | |
| Atrial septal defect with patent ductus arteriosus (ASD with PDA) (Number (percentage)) | 1 (6.7%) | 0 | |
| Atrial septal defect with pulmonary artery stenosis (ASD with PAS) (Number (percentage)) | 0 | 1 (6.7%) | |

Note: Age and weight were analyzed by t-test; other data were analyzed by Wilcoxon signed-rank test patients. Those with severe pneumonia, heart failure, and blood coagulation disorders were excluded from the present study.

### CPB

During the CPB procedure utilizing conventional MUF, BUF is integrated after CPB. Conversely, when OMUF is utilized in the CPB procedure, an optimized and enhanced ultrafiltration process is adopted in conjunction with BUF. BUF utilizes a zero-balance approach, wherein the volume of fluid filtered during extracorporeal circulation is equivalent to the volume of fluid infused, akin to a washout mechanism.

The optimized and enhanced ultrafiltration method requires the utilization of improved ultrafiltration devices (as depicted in Fig. 1A). These devices are characterized by an infusion tube with a 2 mm diameter that connects the right atrium to the ultrafilter. Additionally, approximately 70 mL of blood is recirculated from the vena cava to disrupt the original vena cava circuit (as illustrated in Fig. 1B). Conversely, the outlet is connected to the venous return tube, enabling the return of blood to the right atrium. This ultrafiltration process can be executed both during and after CPB.

The CPB circuit components utilized for the two groups of infants encompass a specific circuit tubing configuration, ¼-inch diameter tube, a CapioxRx05 membrane oxygenator, the Stocker C5 cardiopulmonary bypass machine, an infant blood ultrafiltration device manufactured by the Ningbo Filar Medical Supplies Co., Ltd., and a matching extracorporeal ¼-inch diameter tube. Figure 1 illustrates the connection methods for the traditional MUF tube (A) and OMUF tube (B). In Fig. 1B, the ¼-inch diameter CPB tube that connects to the vena cava is substituted with a 2-mm diameter infusion tube, establishing a link between the right atrium and the ultrafiltration device. This substitution does not lead to an increase in the outlet pressure of the ultrafiltration device, as both the conventional MUF and OMUF protocols sustain ultrafiltration rates at 15 ml/kg/min, albeit with distinct pump settings. The infusion flow rates for both groups are maintained within the range of 100–120 ml/kg/min.

### ABG and electrolyte measurements

Arterial blood samples were obtained 10 min following the release of the aortic cross-clamp and subsequently after MUF upon completion of CPB. Immediate analysis of all blood samples was performed with a GEM Premier 3000 blood gas analyzer. The parameters measured included serum pH, arterial partial pressure of oxygen, arterial partial pressure of carbon dioxide, base excess, $Na^+$, $K^+$, $Ca^{++}$, Lactic acid (Lac), glucose (Glu), hemoglobin (Hb), and hematocrit (HCT).

### Statistical analysis

Statistical analysis was conducted using SPSS 19.0 software. The results are presented as means ± standard

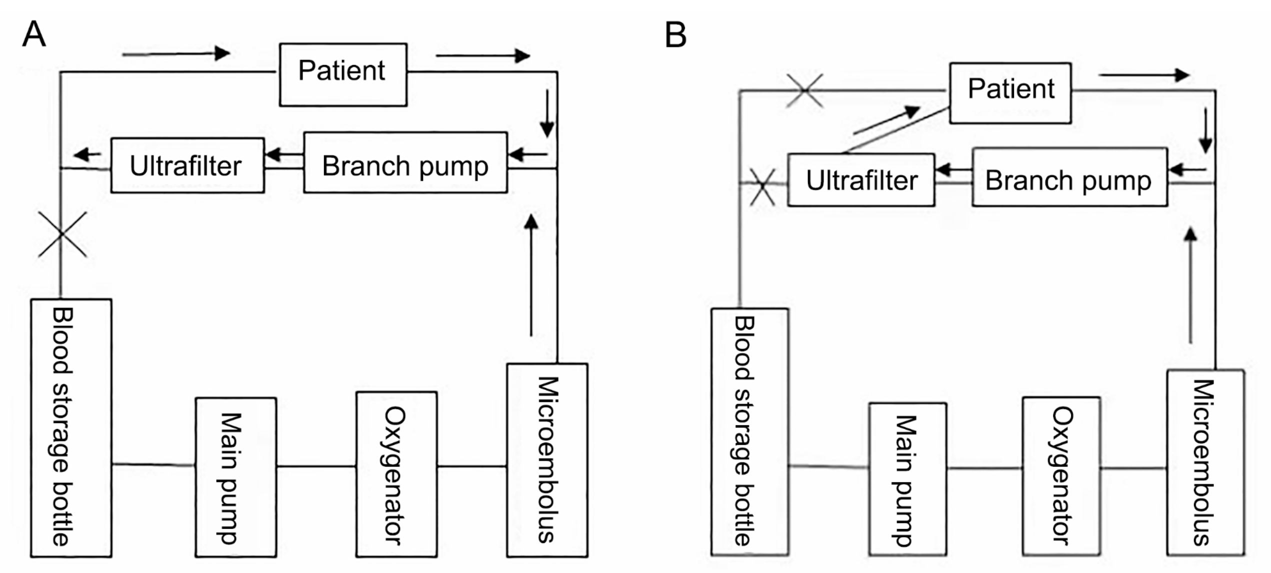


**Fig. 1** The conventional modified ultrafiltration (**A**) and the modern optimized modified ultrafiltration (**B**) are illustrated in the ultrafiltration pipeline connection diagrams. (**A**) depicts the connection mode diagram of the traditional improved ultrafiltration pipeline, while (**B**) showcases the diagram of the optimized and improved connection mode of the ultrafiltration pipeline. Additionally, as depicted in (**B**), a 2-mm diameter perfusion tube was used to replace the 1/4 CBP pipe connected to the vena cava, linking the right atrium to the ultrafiltration device. Notably, this change did not elevate the outlet pressure of the ultrafiltration device, as the ultrafiltration speed for both traditional MUF and OMUF remained at 15 ml/kg/min (with separate pump settings). The perfusion flow rate for both groups ranged from 100–120 ml/kg/min

**Table 2** The comparison of CPB duration and aortic cross-clamp duration during the operation between the two groups of pediatric patients

| Groups | CPB duration (min) | Aortic Cross-Clamp Duration (min) |
|---|---|---|
| Experimental group | 50.00 ± 8.62 | 26.08 ± 5.90 |
| Control group | 50.00 ± 9.27 | 28.25 ± 9.22 |
| P (Compared between the 2 groups) | 1.000 | 0.473 |

Note: Data were analyzed by t-test; CPB: cardiopulmonary bypass

deviations (x±s). Paired or grouped t-tests were used for data conforming to normal distribution, while the Wilcoxon signed-rank test was applied for non-normally distributed data. A significance level of $p<0.05$ was considered statistically significant.

## Results

### Clinical outcome

There were no fatalities reported in either group, and all patients were discharged following successful recovery. Statistical analysis revealed there were no significant differences between the experimental and control groups in terms of both CPB duration and aortic artery-blocking duration, as depicted in Table 2.

### Levels of ABG and electrolytes before and after MUF

In the experimental group, post-ultrafiltration levels of Na+, Ca++, Hb, and HCT were significantly higher than pre-ultrafiltration levels ($p<0.05$). Furthermore, statistically significant differences were observed between the two groups in terms of Hb and HCT ($p<0.01$). Conversely, post-ultrafiltration concentrations of K+, Lac, and Glu in the experimental group were lower compared to pre-ultrafiltration levels, with significant differences noted in K+and Lac ($p<0.05$). However, no significant differences were observed when compared to the control group ($p>0.05$). Detailed results are presented in Table 3.

### Hb and HCT levels at 10 and 15 min with MUF

The levels of Hb and HCT at 10 min post-OMUF were notably lower than those at 15 min post-OMUF ($p<0.01$). However, no significant difference was observed when compared to levels at 15 min post-conventional MUF ($p>0.05$), as illustrated in Table 4.

During CBP, 500 ml of compound electrolyte injection was administered gradually, resulting in the ultrafilter exceeding 500 ml of filtrate. After the cessation of CBP, the ultrafilter flow was maintained at 15 mL/kg/min. The ultrafiltration volumes were as follows: For conventional improved ultrafiltration at 15 min, the volume was 927 mL +/- 205 ml; no statistically significant difference was

**Table 3** The results of arterial blood gas analysis and electrolytes before and after modified ultrafiltration in the two groups

| Index | Groups | 10 min after release of aortic cross-clamp (before the modified ultrafiltration) | With the completion of CPB (15 min after the modified ultrafiltration) |
|---|---|---|---|
| pH | Experimental group | 7.47 ± 0.05 | 7.41 ± 0.05 |
| | Control group | 7.45 ± 0.06 | 7.41 ± 0.06 |
| PO2 (mmHg) | Experimental group | 277.10 ± 105.91 | 305.80 ± 55.06 |
| | Control group | 256.60 ± 139.79 | 280.20 ± 51.38 |
| PCO2 (mmHg) | Experimental group | 36.45 ± 5.08 | 39.98 ± 5.27 |
| | Control group | 35.08 ± 5.20 | 39.90 ± 5.58 |
| BE (mmol/L) | Experimental group | 0.83 ± 1.66 | 1.15 ± 1.70 |
| | Control group | 0.59 ± 2.23 | 1.53 ± 1.72 |
| $NA^+$ (mmol/L) | Experimental group | 141.00 ± 2.98 | 145.50 ± 1.84# |
| | Control group | 141.10 ± 2.99 | 142.70 ± 3.16 |
| $K^+$ (mmol/L) | Experimental group | 4.20 ± 0.65 | 3.71 ± 0.49# |
| | Control group | 4.35 ± 0.49 | 3.92 ± 0.29 |
| $Ca^{++}$ (mmol/L) | Experimental group | 0.96 ± 0.25 | 1.33 ± 0.15# |
| | Control group | 0.92 ± 0.32 | 1.26 ± 0.14 |
| Lac (mmol/L) | Experimental group | 1.47 ± 0.37 | 1.16 ± 0.16# |
| | Control group | 1.54 ± 0.77 | 1.43 ± 0.25 |
| Glu (mmol/L) | Experimental group | 5.98 ± 0.66 | 5.43 ± 0.85 |
| | Control group | 5.99 ± 0.91 | 5.48 ± 0.87 |
| HB (g/L) | Experimental group | 8.73 ± 1.11 | 12.42 ± 1.02** |
| | Control group | 8.70 ± 1.15 | 10.70 ± 0.58** |
| HCT (%) | Experimental group | 26.80 ± 3.42 | 38.06 ± 3.11** |
| | Control group | 25.71 ± 1.91 | 32.51 ± 1.32** |

Note: Data were analyzed by t-test; Compared with pre-ultrafiltration in the same group: #$P<0.05$; Comparison between the 2 groups post-ultrafiltration: P**<0.01

**Table 4** The results of indicators including hb and hct before modified ultrafiltration, 10 min, and 15 min after modified ultrafiltration in the two groups

| Index | The experimental group/The control group (10 min after release of aortic cross-clamp) | 10 min after the optimized modified ultrafiltration/15 min after the conventional modified ultrafiltration | 15 min after the optimized modified ultrafiltration |
|---|---|---|---|
| Hb | 8.73 ± 1.11/8.70 ± 1.15 | 10.53 ± 0.55/10.70 ± 0.58 | 12.42 ± 1.02** |
| HCT | 26.80 ± 3.42/25.71 ± 1.91 | 32.03 ± 2.35/32.51 ± 1.32 | 38.06 ± 3.11** |

Note: Data were analyzed by t-test; P**<0.01, compared with pre-ultrafiltration in the same group

**Table 5** Blood pressure at different time points

| Time Point (minutes post-bypass) | Systolic blood pressure | Diastolic blood pressure |
|---|---|---|
| T0 | 87 ± 15mmHg | 44 ± 9mmHg |
| T2 | 101 ± 14mmHg | 54 ± 10mmHg |
| T5 | 106 ± 13mmHg | 56 ± 10mmHg |
| T10 | 108 ± 15mmHg | 57 ± 10mmHg |
| T12 | 107 ± 13mmHg | 58 ± 14mmHg |

Note: Data were analyzed by t-test; T0: 0 min post-bypass; T2: 2 min post-bypass; T5: 5 min post-bypass; T10: 10 min post-bypass; T12:12 min post-bypass

observed between this and the optimized and improved ultrafiltration at 10 min, with a volume of 886 mL +/- 126 mL. However, for optimized ultrafiltration at 15 min, the volume was 1285 mL +/- 155 mL, which presented a statistically significant difference compared to the former two (Table 5).

## Discussion

With the introduction of conventional MUF and ongoing research efforts, ultrafiltration has emerged as a therapeutic intervention capable of enhancing prognoses and pulmonary function. Our previous studies demonstrated that MUF usage in low-birth-weight infants during CPB significantly increased postoperative hypervolemia [9–12].

Lac levels may signify an imbalance between oxygen supply and demand and impaired cell metabolism. Lac concentration in serum serves as an indirect marker reflecting this imbalance and is indicative of oxygen debt. Prior studies have indicated that post-CPB increases in Lac concentration or the anion gap are associated with surgical prognosis, indicating that effective reduction of Lac concentration may potentially improve outcomes [13, 14]. However, it is noteworthy that in our study, extensive ultrafiltration led to heightened lactate clearance, potentially resulting in lower lactate levels. Therefore, lower lactate levels may not necessarily indicate improved perfusion during surgery. Conversely, our findings indicate that OMUF effectively reduces concentrations of $K^+$ and Glu in the body at the conclusion of CPB, while elevating levels of $Na^+$ and $Ca^{++}$. The ultrafilter used was constructed from a polyarylsulfone membrane, which exhibits a filtration coefficient close to 1 for substances with a molecular weight of < 1000. Consequently, Glu and $K^+$ in plasma can be filtered into the filtrate at equivalent concentrations, thereby reducing overall levels of Glu and $K^+$.

The Hb and HCT levels at 10 min in the OMUF group exhibited a significant reduction compared to those at 15 min; however, there was no notable difference when compared to the conventional MUF group at 15 min. Consequently, this indicates that OMUF can substantially expedite the attainment of optimal oxygen-carrying capacity in pediatric patients' post-surgery (HCT > 30%). This accelerated process potentially facilitates quicker and more effective resolution of tissue oxygen debt, thereby enhancing postoperative cardiopulmonary function. The findings suggest that OMUF can reduce the duration of ultrafiltration compared to conventional MUF when achieving the same satisfactory levels of colloid osmotic pressure and HCT. This reduction in ultrafiltration time may decrease the associated adverse effects, including lower body temperature, air embolism, hemolysis, hypokalemia, hemodynamic instability, and cerebral ischemia in pediatric patients. Additionally, OMUF has the potential to lower the overall costs involved. A new aspect of this study involves the replacement of a broader CPB line connected to the vena cava with a 2 mm infusion line linked to the right atrium. This modification increases outlet pressure in the hemofilter, consequently increasing the filtration pressure and enabling the attainment of sufficient ultrafiltration within 10 min, as opposed to the standard 15-minute timeframe. However, it is pertinent to acknowledge a limitation of our study, which is the relatively small sample size. lso, we saw a wide range of congenital heart defects in our participants. Therefore, the goal of future studies should be to corroborate these findings in a larger study population.

## Conclusion

The optimization of conventional MUF led to a significant enhancement in ultrafiltration efficacy, thereby exerting a beneficial impact on improving the physiological parameters of pediatric patients during CPB, surpassing conventional practices.

**Abbreviations**

OMUF Optimized modified ultrafiltration
CPB Cardiopulmonary bypass

| | |
|---|---|
| BUF | Balanced ultrafiltration |
| MUF | Modified Ultrafiltration |
| Hb | Hemoglobin |
| HCT | Hematocrit |
| ABG | Arterial blood gas |
| VSD | Ventricular septal defect |
| PAS | Pulmonary artery stenosis |
| ASD | Atrial septal defect |
| Lac | Lactic acid |
| Glu | Glucose |

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**Author contributions**
Conception and design of the research: Jianhong Niu; Acquisition of data: Juanying Zhou, Guangdi Zhai, Wei Zhang, Shengqi Jiang, Jianping Ma, Aibin Zheng; Analysis and interpretation of the data: Juanying Zhou, Guangdi Zhai, Wei Zhang, Shengqi Jiang, Jianping Ma, Aibin Zheng; Statistical analysis: Juanying Zhou, Guangdi Zhai, Wei Zhang, Shengqi Jiang, Jianping Ma, Aibin Zheng; Obtaining financing: Jianhong Niu; Writing of the manuscript: Jianhong Niu; Critical revision of the manuscript for intellectual content: Jianhong Niu; All authors read and approved the final draft.

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**Data availability**
All data generated or analysed during this study are included in this article. Further enquiries can be directed to the corresponding author.

## Declarations

**Ethics approval and consent to participate**
The study was conducted in accordance with the Declaration of Helsinki(as was revised in 2013). The study was approved by Ethics Committee of the Changzhou Children's Hospital, Nantong University (NO.2017-022). The written informed consent has been provided by the legal guardian.

**Consent to publish**
Not applicable.

**Competing interests**
The authors declare no competing interests.

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