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RESEARCH ARTICLE

Comparison of Modified and Conventional Ultrafiltration in Pediatric Patients Undergoing Open-Heart Surgery: Single-Center, Early Outcomes

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ABSTRACT

Objectives: The use of cardiopulmonary bypass (CPB) in pediatric patients during open-heart surgery is associated with excessive inflammation, fluid leakage, and end-organ dysfunction. To reduce these effects, various ultrafiltration (UF) techniques are utilized. In this study, we aimed to compare the effect and early outcomes of modified UF (MUF) and conventional UF (CUF) in infants undergoing pediatric cardiac surgery.

Methods: A total of 232 infants who underwent open-heart surgery with CPB between February 2018 and January 2020 were retrospectively reviewed. Fifty-six patients weighing ≤15 kg with a history of any UF technique use were included. Patients were stratified into CUF (n=23) and MUF (n=33) groups. Preoperative patient characteristics and intraoperative and postoperative outcomes were recorded.

Results: The MUF group had a lower patient size (height, weight, and body surface area), with no statistical difference. Intraoperative parameters (CPB and cross-clamp time) and prime solution components were similar between groups. MUF significantly shortened the mechanical ventilation (MV) time (p=0.048) in contrast to intensive care unit stay, which showed no significant difference.

Conclusion: In our series, we demonstrated that the MV duration was shorter in the MUF group, which is consistent with prior literature. Additionally, although the lower weight of the patients in the MUF group showed no statistical significance, early hemodynamic effect and low mortality in this group support the potential benefits of MUF. With its cost-efficiency and early benefits, MUF is an effective UF method with a good safety profile, especially in low-weight infants.

Keywords: Cardiopulmonary bypass, ultrafiltration, ventilator weaning

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Introduction

The use of cardiopulmonary bypass (CPB) is associated with remarkable inflammation, third-space fluid leakage, and end-organ dysfunction, particularly within the pediatric patient population.[1] To mitigate the adverse effects of inflammation and improve postoperative outcomes, various ultrafiltration (UF) techniques are routinely employed by several centers. The superiority among these UF methods remains a controversial discourse. The modified ultrafiltration (MUF) technique, introduced by Naik et al. [2] in 1991 for pediatric cardiac surgery patients, has been speculated to offer potential advantages over conventional ultrafiltration (CUF). While MUF use has gained popularity in pediatric cases, a consensus has not yet been reached regarding the specific patient profiles and protocols for its application. Our study aimed to investigate the impact of two different UF strategies on early phase outcomes in pediatric heart surgery cases.

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Methods

In the study, all patients (232 patients) who underwent cardiac surgery under CPB in the Department of Pediatric Cardiovascular Surgery at Diyarbakır Gazi Yaşargil Education and Research Hospital between February 2018 and January 2020 were retrospectively reviewed.

Infants weighing 15 kg or less who underwent any type of UF during open-heart surgery were included in the study. In this study, neonates were excluded owing to the more complex underlying cardiac pathologies and the predominant use of MUF in nearly all cases. Written informed consent was obtained from all parents of each patient prior to the study initiation. The Ethics Committee of our Hospital approved the research protocol (Date: 13.01.2023 No: 317). The study was conducted in accordance to the guidelines outlined in the Declaration of Helsinki. According to the applied filtration strategy, patients were divided into two groups: CUF (23 patients) and MUF group (33 patients). Conventional UF was conducted by passing the blood via a hemofilter (Fresenius, FX Paed) connected to the arterial line before the oxygenator during the warming phase. The ultrafiltered blood was returned to the patient through the venous line. MUF was employed after weaning from CPB, with a fluid withdrawal rate of 3–5 mL/kg/min for 10 min, considering the patient's overall fluid balance. During MUF, blood from the arterial line was passed through the oxygenator and heater, filtered through a hemofilter (Fresenius, FX Paed) by a roller pump, and returned to the right atrium via the venous line. The preoperative, intraoperative, and early hemodynamic parameters and postoperative outcomes of all patients were recorded.

Table 1. Patient characteristics and preoperative findings

Variables (%, median (IQR))	CUF group (n=23)		MUF group (n=33)		All patients (n=56)		p
	n	%	n	%	n	%	
Gender							0.47
Male	11	47.8	19	57.6	30	53.6	
Female	12	52.2	14	42.4	26	46.4	
Height (cm)	70 (65–75)		66 (64–74)		67 (64–74)		0.20
Weight (kg)	7.3 (5.7–9.0)		5.8 (5.3–7.8)		6.4 (5.4–8.4)		0.10
BSA (m^2)	0.38 (0.31–0.43)		0.32 (0.30–0.40)		0.35 (0.31–0.41)		0.12
Syndrome	4	17.4	3	9.1	7	12.5	0.36
Redo cardiac surgery**	0	0	1	3.0	1	1.8	0.30
Preoperative status							0.77
Active pneumonia	1	4.3	1	3.0	2	3.6	
Pulmonary hypertension	3	13.0	4	12.1	7	12.5	
Hypoxic spell	0	0	1	3.0	1	1.8	
Diagnosis							0.13
VSD	13	56.5	9	27.3	22	39.3	
CAVSD	4	17.4	10	30.3	14	25.0	
TOF	6	26.1	12	36.4	18	32.1	
TAPVR	0	0	2	6.1	2	3.6	
Laboratory findings							
Urea (mg/dL)	19 (15–23)		20 (15–23)		19 (15–23)		0.91
Creatinine (mg/dL)	0.40 (0.40–0.45)		0.41 (0.40–0.48)		0.41 (0.40–0.46)		0.49
Albumin (g/L)	42 (36–48)		43 (40–44)		43 (39–45)		0.73
AST (IU/L)	35 (30–44)		41 (31–44)		38 (30–44)		0.58
ALT (IU/L)	17 (13–27)		18 (14–28)		17 (13–27)		0.58
INR	1.17 (1.10–1.26)		1.25 (1.10–1.31)		1.21 (1.10–1.29)		0.23
Leukocyte (10^3/µL)	10.5 (8.9–12.9)		10.5 (8.1–14.7)		10.5 (8.4–13.2)		0.99
Hemoglobin (g/dL)	12.3 (10.9–13.2)		12.3 (11.9–14.7)		12.3 (11.4–13.6)		0.20
Platelet(10^3/µL)	360±93		378±110		370±103		0.42
CRP (mg/L)	2.0 (2.0–2.0)		2.0 (2.0–2.0)		2.0 (2.0–2.0)		0.59

**: Pulmonary banding operation. IQR: Inter quartile range; CUF: Conventional ultrafiltration; MUF: Modified ultrafiltration; BSA: Body surface area; VSD: Ventricular septal defect; CAVSD: Complete atrioventricular septal defect; TOF: Tetralogy of fallot; TAPVD: Total anomalous pulmonary venous return; AST: Aspartate transaminase; ALT: Alanine transaminase; INR: International normalized ratio; CRP: C-reactive protein.

Table 2. Intraoperative findings

Variables (%, med (IQR))	CUF group (n=23)		MUF group (n=33)		All patients (n=56)		p
	n	%	n	%	n	%	
Urgent surgery	1	4.3	5	15.2	6	10.7	0.18
Additional cardiac procedure							0.15
RV-PA conduit implantation	0	0	1	3.0	1	1.8	
Monocusp implantation	0	0	2	6.1	2	3.6	
Mitral valve repair	1	4.3	0	0	1	1.8	
Pulmonary banding	1	4.3	0	0	1	1.8	
CPB parameters							
Temperature (°C)	28 (28–32)		28 (28–28)		28 (28–28)		0.06
Cross clamp time (min)	92±35		91±29		92±31		0.06
CPB time (min)	128±42		141±44		136±44		0.39
Pre-CPB mean ABP (mmHg)	52±12		57±12		55±12		0.98
Lowest ABP during CPB (mmHg)	35 (30–40)		40 (35–40)		40 (35–40)		0.19
Post-CPB mean ABP (mmHg)	74±9		78±10		76±10		0.66
CPB fluid balance							
Prime volume of ES (ml)	150 (150–190)		150(145–150)		150 (150–160)		0.06
Prime volume of FFP (ml)	50 (30–85)		50 (39–70)		50 (31–70)		0.98
Prime volume of albumin (ml)	40 (30–50)		50 (35–50)		50 (35–50)		0.52
Cardioplegia volume (ml/kg)	40 (21–60)		20 (20–50)		30 (20–51)		0.14
Filtration volume (ml)	153±74		132±30		135±47		0.14
Negative fluid balance (ml)	80 (20–170)		100 (25–160)		95 (21–169)		0.59

IQR: Inter quartile range; CUF: Conventional ultrafiltration; MUF: Modified ultrafiltration; RV-PA: Right ventricle-pulmonary artery; CPB: Cardiopulmonary bypass; ABP: Arterial blood pressure; ES: Erythrocyte suspension; FFP: Fresh frozen plasma

Statistical Analysis

The Statistical Package for the Social Sciences software was used for the statistical analyses. For descriptive analyses, categorical variables were presented as frequencies (percentages), while normally distributed numerical variables were expressed as mean±standard deviation, and non-normally distributed numerical variables were presented as median (interquartile range). For group comparisons, the "chi-square Fisher's exact test" was used for the categorical variables, the "independent sample T-test" was used for normally distributed numerical variables, and the "Mann–Whitney U test" was used for non-normally distributed numerical variables. Statistical significance was set at a $p<0.05$.

Results

A total of 56 patients were included in the study, with 23 in the UF group and 33 in the MUF group. The patient characteristics such as height, weight, and body surface area (BSA) were relatively lower in the MUF group; however, no statistically significant difference was found between the two groups. Similarly, the presence of syndromes and a prior history of cardiac surgery did not reveal significant differences between the groups. No statistically significant differences were observed in terms of preoperative conditions (active pneumonia, pulmonary hypertension, and hypoxic spell) and diagnoses (ventricular septal defect, complete atrio-ventricular septal defect, tetralogy of Fallot [TOF], and total anomalous pulmonary venous return). Patient characteristics and preoperative findings are presented in Table 1.

In the intraoperative finding evaluation, there were no significant differences between the groups in terms of CPB parameters, cross-clamp time, CPB time, and arterial blood pressure (ABP) values. The amount of prime solution components (red blood cell suspension, fresh frozen plasma, and albumin) and cardioplegia volume were also similar between the groups. Moreover, the amount of filtration employed during CPB did not reveal a significant difference between the groups ($p>0.05$). The intraoperative parameters are detailed in Table 2.

In the postoperative finding evaluation, no statistically significant differences were observed between the groups in terms of vasoactive inotrope score and first-day laboratory results. When examining complications (such as wound infection rate, pacemaker implantation, sepsis, chylothorax, bleeding, and low cardiac output), no significant differences were found between the groups. The median mechan-

Table 3. Postoperative laboratory findings, complications and outcomes

Variables (%, med (IQR))	CUF group (n=23)		MUF group (n=33)		All patients (n=56)		p
	n	%	n	%	n	%	
Laboratory findings (1st day)							
Urea (mg/dL)	21 (18–27)		20 (16–29)		20 (16–28)		0.44
Creatinine (mg/dL)	0.40 (0.39–0.50)		0.42 (0.40–0.50)		0.41 (0.40–0.50)		0.72
Albumin (g/L)	34 (30–38)		34 (31–37)		34 (31–37)		0.96
AST (IU/L)	137 (116–224)		169 (120– 246)		148 (118–232)		0.34
ALT (IU/L)	20 (14–26)		21 (17–24)		21 (16–25)		0.58
INR	1.40 (1.31–1.58)		1.53 (1.41–1.66)		1.46 (1.35–1.64)		0.08
Leukocyte (10^3/µL)	15.9 (11.7–18.2)		14.8 (11.9–20.4)		15.8 (11.9–19.5)		0.98
Hemoglobin (g/dL)	11.6±1.7		11.3±1.5		11.4±1.6		0.95
Platelet(10^3/µL)	136 (107–188)		138 (92–186)		137 (99–188)		0.89
CRP (mg/L)	47±18		46±20		46±19		0.63
Vasoactive inotrope score	17±9.5		19.7±8.7		18.6±8.5		0.28
Complications							
Infection	3	13.0	2	6.1	5	8.9	0.37
Temporary pacemaker	0	0	1	3.0	1	1.8	0.30
Permanent pacemaker	2	8.7	2	6.1	4	7.1	0.71
Sepsis	1	4.3	1	3.0	2	3.6	0.79
JET	0	0	1	3.0	1	1.8	0.30
Gastrointestinal bleeding	1	4.3	0	0	1	1.8	0.18
Chylothorax	0	0	1	3.0	1	1.8	0.30
Re-exploration for bleeding	1	4.3	1	3.0	2	3.6	0.79
Low cardiac output	1	4.3	1	3.0	2	3.6	0.79
Peritoneal dialysis	1	4.3	1	3.0	2	3.6	0.79
MV time (hour)	24 (18–59)		14 (12–30)		20 (12–44)		0.048*
ICU stay (day)	5 (3–6)		5 (3–6)		5 (3–6)		0.91
Hospital stay (day)	13 (11–24)		15 (11–18)		15 (11–19)		0.65
Mortality	3 (13)		2 (6.1)		5 (8.9)		0.37

*: Statistically significant parameter. IQR: Inter quartile range; CUF: Conventional ultrafiltration; MUF: Modified ultrafiltration; AST: Aspartate transaminase; ALT: Alanine transaminase; INR: International normalized ratio; CRP: C-reactive protein; JET: Junctional ectopic tachycardia; MV: Mechanical ventilation; ICU: Intensive care unit

ical ventilation (MV) time was noted to be significantly shorter in the MUF group, with 14 (12–30) h, compared to the UF group (p:0.048). The median MV time was 24 (18–59) h in the UF group. The median time of intensive care unit stay was 5 (3–6) days in both groups, with no significant difference. The mortality rate was found to be 13% in the UF group and 6.1% in the MUF group, which was remarkable but with no statistically significant difference. Postoperative findings and outcomes are presented in Table 3.

Discussion

As the BSA decreases, the adverse effect of inflammation secondary to extracorporeal circulation increases.[3] In our study, parameters such as height, body weight, and BSA were lower in the MUF group, which was noteworthy. Accordingly, it can be inferred that the MUF group is composed of relatively more vulnerable patients, although with no statistical significance. When exploring intraoperative and postoperative outcomes, although the results of the UF group appear to be comparable to the MUF group, the MV time was shorter in the MUF group, with statistical significance.

Numerous studies[4,5] have reported similar results regarding MV time. In a prospective study by Talwar et al.[4] involving infants undergoing surgery for TOF, patients who received MUF exhibited lower peak airway pressure and shorter MV times. This could be attributed to MUF's potential to increase pulmonary compliance (both dynamic and static),[6] reduce lung injury,[7] and rapidly enhance pulmonary function in the early period.[8] Another experimental study performed on piglets[9] showed that MUF reduced pulmonary inflammation and pulmonary hypertension. Likewise, in another study involving single-ventricle patients, indirect indicators of pulmonary function, such as chest tube drainage and pleural effusion, were significantly lower in patients who received MUF.[10] Considering all these findings, it can be concluded that the most discernible and early positive effect of MUF is on pulmonary function improvement.

Another notable effect of MUF is its contribution to early hemodynamics and myocardial function. Initially, Naik and colleagues[11] showed that MUF increases ABP. This effect has been elucidated in various studies over the years.[12–14] In a 2009 study by Yokoyama et al.,[13] they suggested that this effect could be attributed to Prostaglandin E2 (PGE-2) level reduction after MUF, leading to a more pronounced hemodynamic improvement in low-weight infants. Furthermore, many studies also suggested that MUF fosters myocardial function improvement.[15,16] In our study, although it can be postulated that the MUF group has demonstrated better performance when examining the ABP during and after CPB, the difference was not statistically significant. In a larger and more homogeneous series of patients, clearly observing and demonstrating the positive impact of MUF on hemodynamics and ventricular function might be possible, which corroborate with our clinical experiences and existing literature.

However, literature on the effect of MUF regarding postoperative bleeding is contradictory. Particularly, in publications from the 1990s when MUF gained popularity[2,17–19] it was highlighted that MUF reduced the requirement for postoperative blood replacement and the incidence of postoperative bleeding. However, in recent studies, this effect has not been consistently demonstrated. In fact, in a study by Abbas et al.,[20] it was revealed that MUF had a negative effect on thromboelastogram parameters, which improved again after protamine administration. In our series, no statistically significant difference was found in the reoperation rates due to bleeding between the two groups.

Fluid load reduction is another remarkable benefit of both UF methods. In our study, a similar negative fluid balance can be achieved with both techniques while maintaining comparable hemodynamic values. Considering early albumin, hematocrit, and ABP values, both methods seem to be equally efficacious in the reversal of hemodilution.

Limitations

The retrospective design and the limited number of patients are among the study's limitations. Moreover, the fact that the groups were not perfectly matched contributed to the study constraints.

Conclusion

In many centers, UF is routinely employed in pediatric open-heart surgery cases to reduce fluid overload and inflammatory mediators. In our series, it has been shown that MUF significantly shortened the MV time, consistent with the literature. While no significant differences were found among other parameters, the results of the MUF group, comprising more vulnerable patients with a lower BSA, support the potential benefits of MUF. In conclusion, MUF can be considered an easily applicable, low-cost, and potentially more efficacious method in certain aspects compared to CUF in infants undergoing pediatric cardiac surgery.

Disclosures

Ethics Committee Approval: The study was approved by The University of Health Sciences Gazi Yaşargil Training and Research Hospital Clinical Research Ethics Committee (Date: 13/01/2023, No: 317).

Informed Consent: Written informed consent was obtained from all patients.

Peer-review: Externally peer-reviewed.

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