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The Effect of Fluid Therapy on the Development of Metabolic Disturbances and ICU Length of Stay in Pediatric Patients Undergoing Surgery for Congenital Heart Defects

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Summary

Aim: to compare the effects of restrictive versus liberal fluid therapy on the duration of mechanical ventilation (MV), total intensive care unit (ICU) stay, and the need for inotropic and vasopressor support during the post-perfusion period and the first 24 hours after surgery in young children undergoing surgical correction of congenital heart defects (CHD).

Materials and Methods. A prospective, randomized, single-center study included pediatric patients (toddlers) with CHD who were assigned to one of two groups. Group 1 received fluid therapy according to a restrictive protocol (RP group, *N*=65) at 8 mL/kg/h, while group 2 received therapy according to a liberal protocol (LP group, *N*=67) at 16 mL/kg/h. The study evaluated the dynamics of metabolic disturbances, duration of ventilatory support, postoperative weight gain, and total ICU stay.

Results. Mechanical ventilation time and total ICU stay were longer in the RP group compared to the LP group: 14±5 hours vs. 10±3 hours (*P*=0.035) and 27±4 hours vs. 23±2 hours (*P*=0.036), respectively. Mean postoperative weight gain in the LP group was 2.00% vs 0.32% in the RP group (*P*=0.001). No clinically significant metabolic or electrolyte disturbances were observed in either group, except for elevated K^+ ion levels in the LP group.

Conclusion. These findings contradict previously reported data in adult population with CHD. In toddlers, a liberal approach to fluid therapy resulted in shorter duration of ventilation and ICU stay compared to a restrictive approach. Toddlers are more sensitive to fluid volume and their preload requirements are higher than those of adults.

Keywords: fluid therapy; intensive care; pediatric cardiac surgery; cardiopulmonary bypass; congenital heart defects

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Introduction

Recent studies have demonstrated the significant impact of fluid therapy on immediate surgical outcomes and overall clinical outcomes in various surgical disciplines [1–3]. Currently, three main strategies of perioperative fluid management are recognized: restrictive (limiting intravenous fluid volume), liberal (no strict fluid limits), and goal-directed therapy aimed at avoiding both hypovolemia and hypervolemia [4, 5].

Each of these approaches has limitations. The restrictive strategy often requires the use of vasopressors, which, as several studies have shown, may impair peripheral circulation and in some cases lead to anastomotic dysfunction [6, 7]. The liberal strategy does not take into account individual tol-

erance to anemia and increases the risk of iatrogenic edema due to fluid overload [8]. Goal-directed fluid therapy requires the use of invasive monitoring techniques (e. g., PiCCO, Swan–Ganz catheters, or left atrial catheters, CVP monitoring) or specialized noninvasive tools (e. g., USCOM), all of which require a high level of expertise on the part of the anesthesiologist. These considerations remain the subject of ongoing debate and represent an ever persisting challenge in anesthesiology and critical care [9, 10].

International guidelines recommend the use of instrumental methods to assess volume status, primarily based on linear or volumetric flow rate measurements, with the caveat «when technically feasible» [11]. Especially in infants and young children, the applicability of such methods, especially invasive ones, is limited. Studies suggest that there are discrepancies of at least 30% between values obtained by invasive monitoring and echocardiography [12]. At the same time, simpler physical methods, such as serial weighing and careful recording of fluid balance, may offer practical alternatives for assessing volemic status. While a substantial body of research focuses on fluid therapy in neonatology and general pediatrics, early childhood remains relatively understudied. This age group surpasses neonates in metabolic requirements, but is still below the age typically included in pediatric studies.

The aim of the study was to compare the effects of restrictive versus liberal fluid therapy on the duration of mechanical ventilation, total length of stay in the pediatric intensive care unit (PICU), and the need for inotropic and vasopressor support during the postperfusion period and the first 24 hours after surgery in young children undergoing correction of congenital heart defects (CHDs).

Materials and Methods

A single-center, prospective, randomized trial was conducted after approval by the local ethics committee (Protocol No. 001 dated January 30, 2020). The study was not preregistered on ClinicalTrials.gov.

This was a prospective, randomized, observational study that enrolled young children who underwent surgical correction of septal congenital heart defects at the Early Childhood Department of the A. N. Bakulev National Medical Research Center for Cardiovascular Surgery, Ministry of Health of the Russian Federation from February 2020 to February 2022.

The analysis was performed using a per-protocol (PP) approach. All patients had an American Society of Anesthesiologists (ASA) physical status of III–IV, NYHA functional class I–II, Aristotle Basic Complexity score of 1–2 out of 6, and an expected PICU stay of 1–3 days.

Patients enrolled underwent radical correction of CHDs: patch closure or direct suture repair of atrial septal defects (ASD) and/or ventricular septal defects (VSD).

The inclusion criteria were as follows:

- age between 11 and 36 months;
- absence of significant comorbidities;
- written informed consent obtained from the parent or legal guardian;
- congenital heart defect requiring surgical correction under cardiopulmonary bypass (CPB);
- no previous open heart surgery (e. g., no previous pulmonary artery banding [Müller procedure] prior to VSD closure; no history of attempted transcatheter defect closure).

Exclusion criteria were as follows:

- severe genetic syndromes;
- massive intraoperative blood loss;
- emergency surgery;
- severe comorbidities;
- re-sternotomy within the first postoperative day;
- reinitiation of CPB due to low cardiac output in the postperfusion period.

The authors hypothesized that a liberal fluid therapy strategy would be no less effective than a restrictive strategy. Patients were randomized into two groups according to the volume of fluid administered intraoperatively.

Group 1 received restrictive fluid therapy at 8 mL/kg/h (restrictive protocol, RP group, *N*=65), while group 2 received liberal fluid therapy at 16 mL/kg/h (liberal protocol, LP group, *N*=67) (see Fig. 1). Randomization was performed using sealed opaque envelopes one day prior to surgery.

During the study, eight patients were excluded for the following reasons: need for epinephrine infusion (*N*=4), arrhythmia after sternal closure (*N*=2), complete atrioventricular block requiring temporary pacing after CPB (*N*=1), and anaphylactic reaction to protamine (*N*=1).

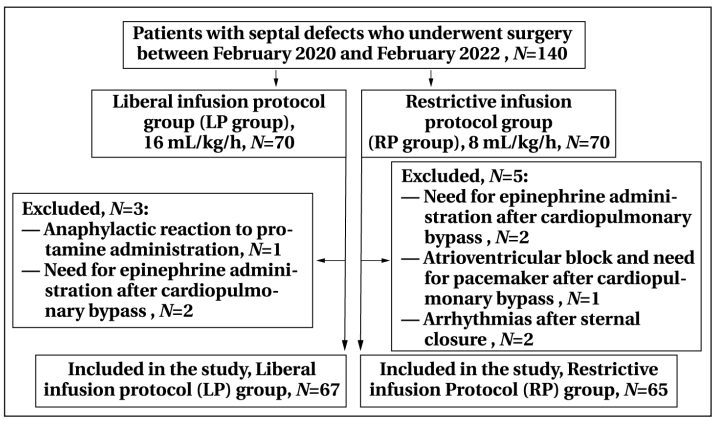

Fig. 1. Study flowchart.

Hemodynamic stabilization after termination of cardiopulmonary bypass (CPB) was achieved by adequate volume loading and titration of inotropic support. Dopamine was administered at doses ranging from 3 to 6 μg/kg/min. In the RP group, all patients required post-CPB norepinephrine infusion at doses ranging from 0.03 to 0.05 μg/kg/min. In 31% of cases, vasopressor support was continued until admission to the ICU.

Anesthesia management was standardized in both groups according to institutional protocol:

- Induction of anesthesia: midazolam 0.2 mg/kg, propofol 2 mg/kg, rocuronium 1 mg/kg, fentanyl 5 μg/kg;
- Maintenance of anesthesia: sevoflurane 1.0–1.2 MAC, fentanyl 5 μg/kg/h, rocuronium 0.5 mg/kg/h;
- Pre-perfusion: All patients received sodium oxybate at a dose of 80–120 mg/kg;
- During CPB: isoflurane was insufflated into the CPB circuit at a concentration of 2 vol%, with continuous fentanyl infusion at 3 μg/kg/h and rocuronium at 0.5 mg/kg/h.

Cardiopulmonary bypass was performed according to institutional protocol. Perfusion was maintained at an index of 2.8–3.2 L/min/m² under normothermic conditions (36°C). Blood cardioplegia was used to induce cardiac arrest and provide myocardial protection.

Arterial blood samples were taken at the following time points: after tracheal intubation, after initiation and termination of extracorporeal circulation, after sternal closure, upon admission to the ICU, and then every 3 hours for the first 12 postoperative hours, at 18 hours, and at the end of the first postoperative day. The following parameters were evaluated: blood glucose, lactate, acid-base balance (pH, base excess, HCO_3^-), electrolytes (Na^+, K^+, Cl^-), and blood gas levels (pO_2, pCO_2, SO_2).

To assess fluid balance, all patients underwent triple body weight measurements. The mean was used for analysis. Weighing was performed in the operating room before skin incision, after tracheal intubation and catheter placement, and again before transfer to the ICU. The first intraoperative weight measurement was compared with the preoperative body weight recorded in the medical record.

Data were analyzed using SPSS software version 11.5 for Windows (SPSS Inc., Chicago, IL) and analysis tools available in Microsoft Excel 2016. No a priori sample size calculation was performed. The Shapiro–Wilk test was used to assess the normality of the data distribution.

Descriptive statistics were presented as means with standard deviations (SD). The independent samples Student's *t*-test was used for comparisons between two independent groups. The paired samples Student's *t*-test was used for related samples, and the one-sample Student's *t*-test was used to compare group values with reference norms. The Mann–Whitney *U* test was used for nonparametric comparisons between two independent groups. Repeated measures were analyzed with the Friedman test. Categorical variables (e. g. sex) were compared using Pearson's chi-squared test.

A $P \leqslant 0.05$ was considered statistically significant. Results were visualized using graphs and charts.

Results

Patients in both groups were comparable with respect to sex, duration of cardiopulmonary bypass, aortic cross-clamp time, surgical complexity, and time to recovery of cardiac function in the postperfusion period (Tables 1 and 2).

Table 1. Comparative characteristics of patients in the two groups by sex.

Sex, *N* (%)	RP (*N*=65)	LP (*N*=67)	*P* (χ^2 test)
Male	32 (49)	33 (49)	0.876
Female	33 (51)	34 (51)	

In the postperfusion and early postoperative periods, acid-base balance (pH<7.36, BE<–2.5 mmol/L, HCO_3^-<22 mmol/L) was assessed. Intergroup comparisons at all time points showed no statistically significant differences in the incidence of metabolic abnormalities (P>0.05). Differences in blood metabolite and electrolyte levels, except for potassium ions (K^+), were also not statistically significant between groups at any time point (P>0.05). However, significant differences in blood K^+ concentrations were observed between the RP and LP groups at baseline (P=0.007) and at ICU admission (P=0.002) (Table 3).

Thus, the use of Sterofundin to maintain the blood electrolyte balance may be sufficient, provided that blood products are used to prime the CPB circuit, as its electrolyte profile is fully balanced. This is supported by previous studies [13–14]. In

Table 2. Comparative characteristics of patients in the two groups.

Parameters	Values in groups		*P* value
	RP (*N*=65)	LP (*N*=67)	
Age, months	19.4±8.6	19.8±8.8	0.920
Height, cm	82.5±7.9	80.5±7.0	0.903
Body weight, kg (according to medical history)	10.17±1.9	10.7±2.1	0.518
Body weight, kg (intraoperatively)	10.1±1.7	9.8±1.7	0.801
Duration of CPB, min	48.12±3.15	43.07±10.2	0.735
Duration of aortic clamping, min	23.6±8.7	20.06±8.1	0.013**
Blood loss, mL	148.1±27.2	150.2±31.2	0.638

Note. ** — Significant differences at $P \leqslant 0.01$ (Mann–Whitney test).

the LP group, a significant dynamic change in the PO_2/FiO_2 ratio was observed (P=0.002): the lowest values were recorded immediately after CPB (3.8), while the highest values were recorded at baseline (4.3) and three hours after admission to the ICU (4.23). In the RP group, changes in the PO_2/FiO_2 ratio were not significant (P=0.289). Comparisons between groups also showed no significant differences (Table 4).

Moderate hypervolemia did not compromise pulmonary oxygenation despite the twofold difference in infusion rates between groups (8 mL/kg/h vs. 16 mL/kg/h). Ventilation modes and parameters were identical in both groups. Duration of mechanical ventilation and total ICU length of stay were significantly longer in the RP group compared to the LP group: 14±5 hours versus 10.3±4 hours (P=0.022) and 27.5±4 hours versus 23±2 hours (P=0.036), respectively (Mann–Whitney test).

Special attention should be paid to accurate weight determination in this patient population (Table 4). Infants and young children should be weighed in the operating room to avoid discrepancies between actual body weight and the weight recorded in the medical chart. Body weight is used to calculate ventilatory volume, doses of inotropes, muscle relaxants, opioid analgesics, antibiotics, and other medications, as well as to determine perfusion and infusion rates, urine output, and blood loss. The mean percentage weight gain was significantly higher in the LP group than in the RP group: 2.00% vs. 0.32% (P=0.001) (Table 5).

Table 3. Analysis of differences and changes in metabolite and electrolyte levels in arterial blood.

Parameter	Group	Values at study stages				**P value
		Baseline	After CPB	In the ICU	After 3 h in the ICU	
pH	RP	7.44±0.05	7.41±0.15	7.44±0.08	7.39±0.09	1.1×10^{-5}**
	LP	7.39±0.06	7.41±0.05	7.45±0.06	7.40±0.05	1.1×10^{-5}**
*P value		0.375*	0.681*	0.458*	0.301*	
HCO_3^-, mmol/L	RP	20.94±2.46	23.49±2.40	23.76±2.96	22.59±2.50	1.3×10^{-12}**
	LP	20.90±2.65	24.56±2.50	24.53±2.59	23.07±2.75	5.6×10^{-13}**
*P value		0.875*	0.116*	0.305*	0.477*	
Osmolality	RP	283.55±35.65	294.28±6.00	296.43±6.60	296.63±6.71	6.4×10^{-13}**
	LP	288.18±4.90	293.07±7.02	295.85±7.13	297.38±15.55	6.8×10^{-10}**
*P value		0.766*	0.436*	0.608*	0.311*	
BE, mmol/L	RP	–3.2±1.8	–0.3±2.1	0.5±2.3	–1.3±0.7	1.2×10^{-15}**
	LP	–3.1±0.17	–0.3±0.19	1.18±0.4	–0.7±0.19	1.2×10^{-11}
*P value		0.982*	0.338*	0.309*	0.104*	
Na^+, mmol/L	RP	135.68±18.32	139.67±3.10	141.31±3.53	140.46±3.70	3.9×10^{-7}**
	LP	135.11±5.19	137.16±2.07	139.13±2.19	138.21±3.16	1.8×10^{-10}**
*P value		0.940*	0.647*	0.809*	0.395*	
K^+, mmol/L	RP	3.82±0.39	4.1±0.31	3.77±0.35	3.78±0.28	3.0×10^{-6}**
	LP	3.65±0.29	4.16±0.29	4.04±0.36	3.51±0.29	9.4×10^{-7}**
*P value		0.007**	0.246*	0.002**	0.568*	
Cl^-, mmol/L	RP	113.23±3.97	111.06±2.68	111.76±3.77	110.19±2.90	3.6×10^{-8}**
	LP	112.35±3.08	110.57±3.47	110.98±3.35	110.33±3.00	7.6×10^{-4}**
*P value		0.395*	0.480*	0.377*	0.579*	
Lactate, mmol/L	RP	1.01±0.30	1.69±0.64	1.49±0.73	1.70±1.02	3.5×10^{-13}**
	LP	0.94±0.30	1.60±0.57	1.32±0.61	1.55±0.89	3.7×10^{-15}**
*P value		0.198*	0.351*	0.238*	0.426*	
Glucose, mmol/L	RP	4.54±0.92	6.72±1.28	6.24±1.57	8.14±2.60	1.2×10^{-22}**
	LP	4.61±0.89	6.72±1.22	6.00±1.31	9.34±3.91	5.2×10^{-18}**
*P value		0.651*	0.936*	0.445*	0.065*	

Note. Differences are statistically significant at $P\leqslant0.05$ (* — Mann–Whitney U test; ** — Friedman test).

Table 4. Changes in PO_2/FiO_2 ratio in arterial blood between groups.

Parameter	Group	Values at study stages				P value
		Baseline	After CPB	In the ICU	After 3 h in the ICU	
PO_2/FiO_2	RP	4.60±0.82	4.05±0.53	4.14±0.4	4.23±0.41	0.289
	LP	4.30±1.10	3.80±0.41	4.10±0.42	4.21±0.45	0.002**
P value		0.174*	0.307*	0.280*	0.151*	

Note. * — Mann–Whitney U test; ** — Friedman test

Table 5. Postoperative weight gain in the two groups.

Parameters	Values in groups		P value
	RP (N=65)	LP (N=67)	
Preoperative weight, kg	11.22±2.80	11.04±2.89	0.396
Postoperative weight, kg	11.26±2.89	11.26±2.92	0.704
P value (Wilcoxon test)	0.332	3.1×10^{-7}**	—
Absolute weight gain, kg	0.05±0.03	0.22±0.03	0.002**
Weight gain, %	0.32±0.29	2.00±0.27	0.001**

Note. $P\leqslant0.01$ indicates statistical significance (Mann–Whitney U test). RP — restrictive protocol; LP — liberal protocol.

Table 6. Association between postoperative weight gain and duration of mechanical ventilation and ICU stay.

Parameter during ICU stay	Statistical test	Weight gain (kg)	Weight gain (%)
Duration of mechanical ventilation, h	Spearman's *R*	–0.160*	–0.119
	P value	0.039	0.128
Total ICU stay, h	Spearman's *R*	0.047	0.041
	P value	0.551	0.603

Note. * — correlation is significant at $P \leqslant 0.05$.

A negative linear correlation was found only between the difference in body weight and the duration of mechanical ventilation in the ICU (R=–0.160; P=0.039): as weight increased, the duration of mechanical ventilation in the ICU decreased (Table 6).

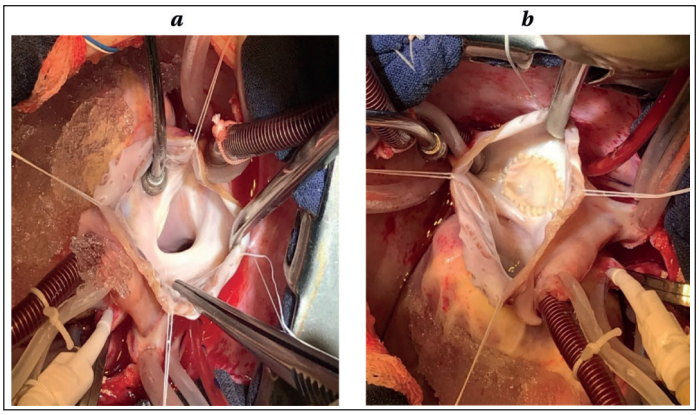

Fig. 2. Atrial septal defect (*a*) before correction and (*b*) after patch closure.

Discussion

Patients with septal defects were selected for this study because these defects are highly prevalent in individuals with congenital heart disease. They are typically associated with hemodynamic stability and can be successfully treated with radical surgical correction in the vast majority of cases (Fig. 2).

Changes in fluid status — particularly hypovolemia — are a major cause of hemodynamic instability in patients undergoing surgery for septal and other congenital heart defects. Because open heart surgery is associated with significant fluctuations in blood volume and vascular tone, optimization of perioperative fluid therapy and accurate assessment of blood loss are critical responsibilities of the anesthesiologist-intensivist. Both fluid overload and hypovolemia increase the risk of postoperative complications. In addition, fluid deficits may occur in the absence of apparent losses due to vasodilation, sweating, and hemodilution.

The study showed that liberal fluid management reduced the length of stay in the pediatric ICU. In this age group, compensatory physiological mechanisms are not fully developed, which may explain the discrepancy with findings from studies of infusion strategies in patients with acquired heart disease (AHD), where more restrictive approaches are often favored due to the severity of the underlying pathology. In one retrospective study [15], patients received restrictive fluid therapy due to the presence of edema and congestive heart failure.

Pulmonary oxygenation function did not differ significantly between the two fluid management strategies, while ventilatory parameters remained consistent in both groups. Based on the present findings, liberal fluid therapy does not compromise pulmonary oxygenation or preclude early mobilization or tracheal extubation in this patient population.

There is ongoing debate regarding the optimal fluid management strategy in young children. In the postoperative period, children with CHD are always at risk for fluid overload, which is known to be associated with adverse outcomes. Several studies have reported that a positive fluid balance greater than 10% of baseline body weight after cardiac surgery is associated with adverse outcomes [16–19]. For example, a single-center study by Hudkins et al. [20] found that early postoperative fluid accumulation in the PICU was associated with increased mortality and prolonged mechanical ventilation. Similarly, a meta-analysis by Bellos [21], which included 12 studies from electronic databases such as Medline, Scopus, CENTRAL, ClinicalTrials.gov, and Google Scholar (a total of 3,111 pediatric patients), yielded comparable results.

In the study by Delpachitra [21], of 1,996 children with a positive fluid balance, 46 (2.3%) died, and of these, 45 (98%) had a fatal outcome associated with prolonged cardiopulmonary bypass time. A 10-minute increase in bypass time was associated with an odds ratio [95% CI] of 1.06 [1.00–1.12]; P=0.03, and with the need for extracorporeal membrane oxygenation in the early postoperative period. Therefore, while early fluid overload was not directly associated with mortality, it was associated with longer duration of mechanical ventilation and prolonged ICU stay.

In a multicenter study involving 2,223 patients [22], the time to first negative 24-hour fluid balance (but not the percentage of fluid overload) was associated with better postoperative outcomes in children after cardiac surgery. Specific management strategies aimed at reducing fluid overload may shorten the duration of postoperative ICU observation in these patients. All authors agree that daily patient weighing is critical for early detection

of fluid overload after cardiac surgery. However, patient weighing practices vary widely among medical centers. Patients with more severe conditions are weighed less frequently [23]. Key recommendations include the use of isotonic balanced solutions and regular monitoring of plasma electrolyte and glucose levels and fluid balance [24].

Conclusion

In patients with congenital heart defects receiving liberal infusion therapy, pulmonary oxygenation function remains unaffected in the postperfusion and early postoperative periods. In addition, there are no significant metabolic or electrolyte disturbances compared to the group receiving restrictive infusion therapy. Weight gain does not prolong the duration of mechanical ventilation or the total ICU stay in patients after radical correction of septal defects.

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