Boletín Médico del
Hospital Infantil de México

PERMANYER

Check for updates

RESEARCH ARTICLE

Fluid overload as a predictor of morbidity and mortality in pediatric patients following congenital heart surgery

Violeta Castañuela-Sánchez[1], Alfredo Hernández-Suárez[1], Luis García-Benítez[2], Luisa Díaz-García[3], Guadalupe Martínez-Jasso[4], and Alexis Palacios Macedo-Quenot[2]*

[1]Unidad de Cuidados Intensivos Cardiovasculares, Instituto Nacional de Pediatría, Mexico City; [2]División de Cirugía Cardiovascular, Instituto Nacional de Pediatría, Mexico City; [3]Departamento de Metodología de Investigación, Instituto Nacional de Pediatría, Mexico City; [4]Unidad de Cuidados Intensivos Pediátricos, Hospital Regional de Alta Especialidad de Ixtapaluca, Ixtapaluca, Estado de México. Mexico

Abstract

Background: *Patients undergoing congenital heart surgery with cardiopulmonary bypass frequently require the administration of intravenous fluids and blood products due to hemodynamic instability. Correctly performed fluid resuscitation can revert the state of tissue hypoperfusion in the different organs. However, excessive fluid administration and acute kidney injury may promote fluid overload (FO) and increase the risk of complications, hospital stay, and mortality.* **Methods:** *We conducted a prospective longitudinal study of pediatric patients with congenital heart surgery and cardiopulmonary bypass in the Pediatric Cardiac Intensive Care Unit (PCICU), Instituto Nacional de Pediatría, from July 2018 to December 2019. Fluid overload was quantified every 24 hours during the first 3 days of stay at the PCICU and expressed as a percentage. We recorded PCICU stay, days of mechanical ventilation, and mortality as outcome variables.* **Results:** *We included 130 patients. The main factors associated with fluid overload were age < 1 year ($p < 0.001$), weight < 5 kg ($p < 0.001$), and longer cardiopulmonary bypass time ($p = 0.003$). Patients with fluid overload ≥ 5% had higher inotropic score ($p < 0.001$), higher oxygenation index ($p < 0.001$), and longer mechanical ventilation time ($p < 0.001$). Fluid overload ≥ 5% was associated with higher postoperative mortality (odds ratio 89, $p = 0.004$).* **Conclusions:** *Fluid overload can be used as a prognostic factor in the evolution of pediatric patients undergoing congenital heart surgery since it is associated with increased morbidity and mortality.*

Keywords: *Congenital heart disease. Fluid overload. Oxygenation index.*

Sobrecarga hídrica como predictor de morbilidad y mortalidad en pacientes pediátricos operados de corazón

Resumen

Introducción: *Los pacientes con cirugía cardiaca congénita en la que se emplea una bomba de circulación extracorpórea frecuentemente requieren la administración de líquidos intravenosos y hemoderivados por inestabilidad hemodinámica. La resucitación con volumen realizada adecuadamente puede revertir el estado de hipoperfusión tisular en los diferentes órganos. Sin embargo, el ingreso excesivo de líquidos y la falla renal aguda pueden favorecer la sobrecarga hídrica (SH) e incrementar el riesgo de complicaciones, la estancia hospitalaria y la mortalidad.* **Métodos:** *Se llevó a cabo un estudio prospectivo longitudinal de pacientes pediátricos con cirugía del corazón y empleo de bomba de circulación extracorpórea*

Correspondence:
*Violeta Castañuela-Sánchez
E-mail: violeta_castanuela@yahoo.com.mx

Date of reception: 02-09-2021
Date of acceptance: 02-01-2022
DOI: 10.24875/BMHIM.21000183

Available online: 13-07-2022
Bol Med Hosp Infant Mex. 2022;79(3):187-192
www.bmhim.com

en la Unidad de Cuidados Intensivos Cardiovasculares (UCICV), Instituto Nacional de Pediatría, de julio 2018 a diciembre 2019. La SH, registrada como porcentaje, fue cuantificada cada 24 horas durante los primeros 3 días de estancia en UCICV. Como variables de desenlace se registraron la estancia en UCICV, el tiempo de ventilación mecánica y la mortalidad. **Resultados:** *Se incluyeron 130 pacientes. Los principales factores asociados con la SH fueron la edad < 1 año (p < 0.001), peso < 5 kg (p < 0.001) y mayor tiempo de circulación extracorpórea (p = 0.003). Los pacientes con SH ≥ 5% presentaron mayor puntaje inotrópico (p < 0.001), mayor índice de oxigenación (p < 0.001) y mayor tiempo de ventilación mecánica (p < 0.001). La SH ≥ 5% se asoció con una mayor probabilidad de muerte en el periodo posoperatorio (razón de momios: 89, p = 0.004).* **Conclusiones:** *La SH puede utilizarse como factor pronóstico en la evolución de los pacientes pediátricos operados de corazón, ya que se asocia con una mayor morbimortalidad.*

Palabras clave: *Cardiopatías congénitas. Sobrecarga hídrica. Índice de oxigenación.*

Introduction

The administration of intravenous fluids is a common practice in intensive care. In critically ill patients, adequate volume administration can improve systemic perfusion in different organs and tissues, thus preventing multiorgan dysfunction and death. However, this practice is often prolonged for extended periods without apparent benefit to the patient[1]. The cause of fluid overload (FO) in critically ill patients is often multifactorial. Sepsis, postoperative states, burns, or ischemia-reperfusion injury increase vascular permeability, capillary leakage, and interstitial edema.

Patients undergoing cardiac surgery with extracorporeal circulation frequently present hemodynamic instability, requiring acute administration of intravenous fluids to prevent and correct arterial hypotension. Low cardiac output syndrome and capillary leak syndromes produce interstitial edema and relative hypovolemia. Furthermore, hypovolemia may result from excessive ultrafiltration during extracorporeal circulation or postoperative bleeding. On many occasions, the administration of solutions and blood products in large quantities is required[2].

Moreover, cardiac surgery patients also present increased vascular permeability secondary to the presence of endothelial inflammation. This inflammation is due to the release of cytokines and interleukins produced by the passage of blood through a circuit without endothelium during extracorporeal circulation, predisposing the patient to develop FO easily[3].

Acute kidney injury occurs in 30% of patients and increases to 50% in neonates. This complication is mainly due to acute tubular injury and activation of the renin-angiotensin-aldosterone axis. Activation of this axis increases the release of antidiuretic hormone, producing sodium and water retention in the tissues with secondary hypervolemia. Angiotensin produces renal vasoconstriction, compromising renal perfusion and significantly decreasing glomerular filtration. All these factors predispose to the development of FO, impairing patient prognosis[4,5]. Some studies associate FO (> 7% in the first 48 hours) with increased intensive care unit stay[6,7].

Similarly, excess fluids negatively affect patient oxygenation, increasing the oxygenation index (OI), a marker of restrictive pulmonary physiology. An elevated OI influences the duration of mechanical ventilation[8,9].

The main objective of this study was to identify the frequency and degree of FO in patients undergoing cardiovascular surgery with extracorporeal circulation, as well as the association between the degree of FO and OI, days of mechanical ventilation, hospital stay, and mortality.

Methods

Study design

We conducted a longitudinal study of pediatric patients undergoing heart surgery with extracorporeal circulation. The study was conducted in the Pediatric Cardiac Intensive Care Unit (PCICU), Instituto Nacional de Pediatría, from July 2018 to December 2019. Before surgery, patients with the following conditions were excluded: clinical data of FO (manifested by soft-tissue edema, pleural effusion, or ascites), assisted mechanical ventilation, and presence of acute kidney injury (AKI).

Surgery was performed by median sternotomy and extracorporeal circulation pump in all cases. A Tenckhoff catheter was placed for fluid management at the end of surgery. All patients received the same fluid management protocol, consisting of 30% of Holliday Segar requirements in the first 48 to 72 hours[10], followed by total parenteral nutrition of 40-80 ml/kg. Peritoneal dialysis at 1.5% was started at 10 ml/kg with inflow-by-outflow baths from admission.

Data collection

Data were collected in Microsoft Office 2016 Excel format. Demographic data collected were age, sex, procedure, and surgical complexity (RACHS classification)[11]. Intraoperative data collected were extracorporeal circulation time, aortic clamp time, circulatory arrest time, and temperature (°C). Postoperatively, data collected were the weight on admission, daily weight over the following 72 hours, and the percentage of FO accumulated every 24 hours during the 72 hours after surgery.

The percentage of FO was calculated with the following formula[12]:

$$\%FO = \frac{\text{fluid input (L) - fluid output (L)}}{\text{weight at patient admission (kg) x 100}}$$

Other variables collected every 24 hours were OI (mean airway pressure x inspiratory oxygen fraction x 100 divided by arterial oxygen pressure), inotropic score[13], and AKI (AKI classification)[14]. In addition, the following outcome variables were collected: days of PCICU stay, days of mechanical ventilation, and mortality, both within the unit and 30 days postoperatively.

Statistical analysis

Analyses were performed with the statistical package STATA version 17.0 (StataCorp). Qualitative variables were presented as frequencies and proportions, while quantitative variables were presented as median and interquartile ranges. For the analysis, the population was divided into two groups according to the FO level: patients who presented FO ≥ 5% in any of the three measurements during the first 72 postoperative hours and patients with no FO or FO ≤ 4%.

The χ^2 and Mantel-Henzell tests were used to identify associations between qualitative variables. The Kruskal-Wallis nonparametric test was used to identify differences between medians. Spearman's test was used in the case of correlations between quantitative variables. In all cases, a *p*-value < 0.05 was considered statistically significant. Outcome variables were dichotomized to identify confounding factors by multivariate analysis with logistic regression, for which odds ratio (OR) and 95% confidence intervals (CI) were presented.

Results

We included 130 patients who underwent heart surgery with extracorporeal circulation from July 2018 to December 2019. Sixty-one patients (47%) were female, and 69 (53%) were male. Twenty-one patients (16%) had FO ≥ 5% during the study period. Patients with FO ≥ 5% were younger and weighed less than those with FO < 5%. More than two-thirds of patients with FO ≥ 5% had high surgical complexity (RACHS ≥ 3). Also, extracorporeal circulation time was longer in the group with FO ≥ 5% (159 min vs. 109 min, p = 0.003) (Table 1).

Patients with FO ≥ 5% were 11.6 times more likely to require a high inotropic score (≥ 10) during the study period, regardless of the RACHS-1 surgical risk scale. Concerning respiratory variables such as OI, patients with FO ≥ 5% showed 3.5 times higher odds of an OI ≥ 8. Consequently, their stay in the PCICU was longer, and they required more mechanical ventilation time. Mortality in the study population was 5%, representing seven patients, six of whom had an overload > 5%. Patients with significant FO were 89 times more likely to die than patients with no or < 4% overload (Table 2).

A positive correlation was found between inotropic score, OI, and maximum peak FO in the first 72 hours. The top peak FO during the study was 5 ± 4.3%, lower in the first 24 hours (3.3 ± 2.1%) and higher at 72 hours (5.3 ± 4.8%) (Table 3). Similarly, an increase in the inotropic score at 24 hours was observed parallel to the rise in FO (Figure 1).

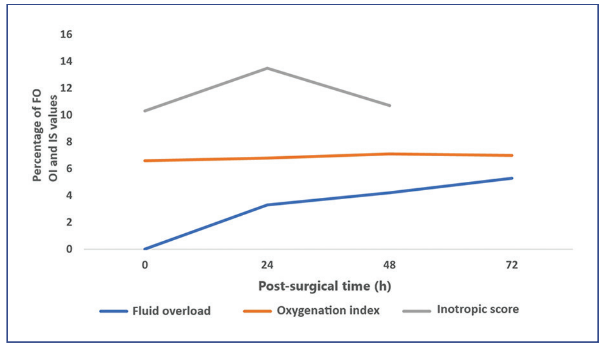

Figure 1. Changes in fluid overload (FO) levels, oxygenation index (OI), and inotropic score (IS) in the postoperative period. As FO increases, the IS increases after 24 hours, while the OI increases subtly.

Discussion

FO in critically ill patients remains a concern for critical care physicians due to its association with a less favorable outcome. Excessive fluid intake and AKI, frequently present in critically ill patients, lead to excessive fluid accumulation in the tissues, increasing the risk of FO.

Table 1. Sociodemographic and surgical characteristics

	Total (n = 130)	FO ≥ 5%* (n = 21)	FO < 5% (n = 109)	*p*-value
Male	69 (53%)	12 (57%)	57 (52%)	0.683
Female	61 (47%)	9 (43%)	52 (48%)	
Age in months, median (IQR)	16 (6-55)	4 (1-11)	22 (8-59)	< 0.001
Weight in kg, median (IQR)	8 (4.4-14)	3.4 (3-4.8)	9.5 (5.4-15)	< 0.001
Age group				
< 30 days	3 (2.3%)	2 (67%)	1 (33%)	0.035
1-11 months	54 (42%)	15 (28%)	39 (72%)	0.026
1-4 years	44 (34%)	2 (5%)	42 (95%)	0.666
≥ 5 years	29 (22%)	2 (7%)	27 (93%)	___**
RACHS ≥ 3	51 (39%)	16 (76%)	35 (32%)	< 0.001
RACHS				
1	21 (16%)	0 (0%)	21 (100%)	0.317
2	58 (44%)	5 (9%)	53 (91%)	___**
3	19 (15%)	4 (21%)	15 (79%)	0.212
4	28 (22%)	10 (36%)	18 (64%)	0.005
5-6	4 (3%)	2 (50%)	2 (50%)	0.059
Extracorporeal circulation time (min)	119 (77-171)	159 (122-213)	109 (72-164)	0.003

FO, fluid overload; IQR, interquartile range; RACHS, risk adjustment for congenital heart surgery.
*Includes patients with FO ≥ 5% in any of the three measurements taken during the first 72 hours postoperatively.
**Reference group.

Table 2. Postoperative evolution and FO

	Total (n = 130)	FO ≥ 5% (n = 21)	FP < 5% (n = 109)	*p*-value	Raw OR (95% CI)	Adjusted OR* (95% CI)
PCICU stay (days) median (IQR)	7 (4-13)	23 (13-31)	6 (4-9)	< 0.001	—	—
PCICU stay (≥ 7 days)	—	20 (95%)	49 (45%)	< 0.001	24.5 (3-189)	16.6 (2-135)
VMS time (days) median (IQR)	6 (2-10)	15 (9-20)	4 (1-7)	< 0.001	—	—
VMS time (≥ 7 days) (n = 78)	—	17 (85%)	16 (28%)	< 0.001	14.8 (3.8-57)	11.5 (2.7-48)
Inotropic score median (IQR)	8 (4-20)	28 (14-56)	6.5 (3-14)	< 0.001	—	—
Inotropic score (≥ 10, n = 105)	—	19 (91%)	32 (38%)	< 0.001	15.4 (3.4-70)	11.6 (2.3-58)
Oxygenation index median (IQR)	6.5 (4.5-8)	7 (6-13)	5 (4-8)	< 0.001	—	—
Oxygenation index (≥ 8, n = 72)	—	65% (13)	27% (14)	0.006	5 (1.6-15)	3.5 (1.07-11.7)
Mortality	7 (5%)	6 (29%)	1 (0.9%)	< 0.001	43 (4.8-384)	89 (4.3-1813)

CI, confidence interval; FO, fluid overload; IQR, interquartile range; OR, odds ratio; PCICU, Pediatric Cardiac Intensive Care Unit; VMS, ventilatory mechanical support.
*Adjusted for age in months, sex, and RACHS (risk adjustment for congenital heart surgery).

Our study found an incidence of FO of some level in 44% and FO ≥ 5% in 16%, consistent with other authors such as Seguin et al.[6], who found FO in 33.6%.

In the present study, the mean maximum peak of FO was 5% in the first 72 hours postoperatively. Seguin et al. reported a mean maximum peak of 7.4 ± 11.2%

Table 3. Correlation of fluid overload with oxygenation index and inotropic score.

Fluid overload	Peak overload (mean ± SD)	Oxygenation index		Inotropic score	
		Spearman's coefficient	p-value	Spearman's coefficient	p-value
General	5 ± 4.3%	0.45	0.001	0.63	< 0.001
24 h	3.3 ± 2.1%	0.11	0.473	0.59	< 0.001
48 h	4.2 ± 3.4%	0.35	0.056	0.53	0.001
72 h	5.3 ± 4.8%	0.51	0.004	—	—

FO, fluid overload; SD, standard deviation.

during the first 24 hours[6], whereas we found 3.3 ± 2.1%. Furthermore, the mean FO at 72 hours was 5.3 ± 4.7%, lower than that described by Valentine et al.[15] (8.5 ± 10.5%) or by Sinitsky et al.[9] (7.2%) at 48 hours. In another study, Hassinger et al. found that the FO was 5% in the first 24 hours[16]. These differences can be explained by the use of early dialysis in the first 24 hours of the postoperative period as part of the PCICU fluid management protocol, especially in patients with complex heart disease.

Here, we also observed that age < 10 months and weight < 5 kg were factors associated with FO, as well as high surgical complexity (RACHS-1 ≥ 3). Sinitsky et al. also detected age as a risk factor and the severity scale using PIM2 (pediatric mortality index)[9]. This relationship between age, surgical complexity, and FO can be explained because the more complex the heart disease, the earlier the surgery. Hence, patients usually have greater hemodynamic instability and a higher risk of bleeding, requiring the administration of intravenous fluids to restore systemic perfusion. Other studies suggest the presence of cyanogenic heart disease ($p = 0.03$) and the administration of excess fluids in the first 6 hours ($p = 0.0001$) as risk factors[6].

Pumping time was also longer in patients with FO ≥ 5%, with a median of 159 min (122-213), similar to those published by Seguin et al. of 138.9 ± 62.1 min (median of 134 min)[6]. These findings support the fact that the longer the extracorporeal circulation time, the greater the release of inflammatory mediators that produce increased vascular permeability and, consequently, the greater the need for intravenous fluid administration.

The inotropic score was also higher (> 10) in patients with FO ≥ 5%, similar to those reported in the meta-analysis conducted by Bellos et al. in 3111 patients[17]. In this meta-analysis, patients with cumulative FO rapidly developed cardiac dysfunction with a higher need for inotropic support (r = 0.7, $p < 0.01$)[18]. Volume overload negatively affects cardiac function in a heart stunned by using an extracorporeal circulation pump, requiring higher doses of inotropic drugs to preserve cardiac output.

Regarding respiratory variables, we found a significant correlation between OI and the percentage of FO ≥ 5% ($p = 0.001$) and between the maximum cumulative percentage of FO (coefficient = 0.45, $p = 0.001$), similar to that reported by Sinitsky et al. at 48 hours (coefficient = 0.318, $p < 0.001$)[9].

In our population, patients who spent more time on mechanical ventilation had a higher percentage of cumulative FO ($p = 0.001$), a result similar to that reported by Bellos et al.[17], showing a direct relationship between the overload index and days on mechanical ventilation (coefficient = 0.53, $p = 0.001$). Sampaio et al. also reported a direct relationship (coefficient = 0.54, 95%CI 0.38-0.66, $p = 0.001$) between peak FO and days of mechanical ventilation and soft tissue edema or pleural effusions on chest X-rays (p = 0.03)[18].

Intensive Care Unit stay was longer in patients with FO ≥ 5% ($p < 0.001$), while Arikan et al. reported that FO > 15% was a risk factor for more extended ICU stay ($p = 0.008$)[8]. In the multicenter study by Bellos et al., a significant correlation was reported between ICU stay ($\chi^2 = 63.69$, $p = 0.0001$) and hospital stay ($\chi^2 = 18.84$, $p = 0.0001$).[17]

Several studies in critically ill pediatric patients have found FO to be an independent risk factor for mortality. For example, Goldstein et al. studied 116 patients with multiorgan dysfunction secondary to sepsis or cardiogenic shock. These authors found a higher survival ($p < 0.03$) in patients with a lower %FO (14.2 ± 15.9) than those with a higher %FO (25.4 ± 32.9)[19].

In neonatal cardiac surgery patients, FO ≥ 16% on the third postoperative day was an independent risk factor for an undesirable outcome, such as cardiac arrest (p = 0.0001), increased hospital stay (p = 0.04), and the need for surgical re-exploration (p = 0.0001)[20].

In our study, seven patients died, representing 5% of the total; six belonged to the FO ≥ 5% group (p < 0.0001). Sutherland et al. and Hayes et al. showed a direct relationship between FO and mortality[21,22]. The former found that for each 1% increase in FO, mortality increased by 3% (OR 1.03, 95%CI 1.01-1.05). When patients showed %FO > 20, the OR for mortality was 8.5 (95%CI 2.8-25.7).[21]

Some strategies to reduce systemic inflammation after extracorporeal circulation are steroids and ultrafiltration. Both aim to reduce interleukins and cytokines that act as inflammatory mediators and are responsible for the increased vascular permeability that results in significant interstitial edema. Other strategies used in the ICU, such as water restriction of up to 25% of maintenance fluids in the first 24 hours and diuretics and kidney replacement therapies, such as early peritoneal dialysis, may decrease the incidence of FO[23]. In our study, 36 patients (27.6%) had AKI. Patients with FO ≥ 5% detected presented up to 71.4% (p < 0.001).

Age, weight, surgical complexity, and extracorporeal circulation time are associated with higher FO. Patients with FO ≥ 5% or a maximum FO peak show a higher OI and inotropic score and higher mortality. The presence of FO ≥ 5% increases days of mechanical ventilation and hospital stay.

Ethical disclosures

Protection of human and animal subjects. The authors declare that no experiments were performed on humans or animals for this study.

Confidentiality of data. The authors declare that they have followed the protocols of their work center on the publication of patient data.

Right to privacy and informed consent. The authors have obtained the written informed consent of the patients or subjects mentioned in the article. The corresponding author has this document.

Conflicts of interest

The authors declare no conflict of interest.

Funding

None.

References

1. O'Connor M, Prowle JR. Fluid overload. Crit Care Clin. 2015;31:803-21.
2. Raina R, Sethi SK, Wadwani N, Vemuganti M, Krishnappa V, Bansal SB. Fluid overload in critically ill children. Front Pediatr. 2018;6:306.
3. Hanot J, Dingankar AR, Sivarajan VB, Sheppard C, Cave D, Garcia GG. Fluid management practices after surgery for congenital heart disease: a worldwide survey. Pediatr Crit Care Med. 2019;20:357-64.
4. Zeng Z, Li Y, Dong Y, Li M. Correlation between fluid overload and acute kidney injury after congenital cardiac surgery in infants. Int J Clin Exp Med. 2018;11:932-8.
5. Blinder JJ, Goldstein SL, Lee VV, Baycroft A, Fraser CD, Nelson D, et al. Congenital heart surgery in infants: effects of acute kidney injury on outcomes. J Thorac Cardiovasc Surg. 2012;143:368-74.
6. Seguin J, Albright B, Vertullo L, Lai P, Dancea A, Bernier PL, et al. Extent risk factor, and outcome of fluid overload after pediatric heart surgery*. Crit Care Med. 2014;42:2591-9.
7. Mah KE, Hao S, Sutherland SM, Kwiatkowski DM, Axelrod DM, Almond CS, et al. Fluid overload independent of acute kidney injury predicts poor outcome in neonates following congenital heart surgery. Pediatr Nephrol. 2018;33:511-20.
8. Arikan AA, Zappitelli M, Goldstein SL, Naipaul A, Jefferson LS, Loftis LL. Fluid overload is associated with impaired oxygenation and morbidity in critically ill children. Pediatr Crit Care Med. 2012;13:253-8.
9. Sinitsky L, Walls D, Nadel S, Inwald DP. Fluid overload at 48 hours is associated with respiratory morbidity but not mortality in a general PICU: retrospective cohort study. Pediatr Crit Care Med. 2015;16:205-9.
10. Fuchs J, Adams ST, Byerley J. Current issues in intravenous fluid use in hospitalized children. Rev Recent Clin Trials. 2017;12:284-9.
11. Jenkins KJ, Gauvreau K, Newburger JW, Spray TL, Moller JH, Iezzoni LI. Consensus-base method for risk adjustment for surgery for congenital heart disease. J Thorac Cardiovasc Surg. 2002;123:110-8.
12. Lombei RM, Kommareddi M, Mottes T, Selewki DT, Han YY, Gipson DS, et al. Implications of different fluid overload definitions in pediatric stem cell transplant patients requiring continuous renal replacement therapy. Intensive Care Med. 2021;38:663-9.
13. Gaies MG, Gurney JG, Yen AH, Napoli ML, Gajarski RJ, Ohye RG, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. Pediatric Crit Care Med. 2010;11:234-8.
14. Bellomo R, Kellum JA, Ronco C. Acute kidney injury. Lancet. 2012; 380:756-66.
15. Valentine SL, Sapru A, Higgerson RA, Spinella PC, Flori HR, Graham DA, et al., Pediatric Acute Lung Injury and Sepsis Investigators (PALISI) Network, Acute Respiratory Distress Syndrome Clinical Research Network (ARDSNet). Fluid balance in critically ill children with acute lung injury. Crit Care Med. 2012;40:2883-9.
16. Hassinger AB, Wald EL, Goodman DM. Early postoperative fluid overload precedes acute kidney injury and is associated with higher morbidity in pediatric cardiac surgery patients. Pediatr Crit Care Med. 2014;15:131-8.
17. Bellos I, Iliopoulus DC, Perrea DN. Association of postoperative fluid overload with adverse outcome after congenital heart surgery: a systematic review and dose-response meta-analysis. Pediatr Nephrol. 2020;35:1109-19.
18. Sampaio TZAL, O'Hearn K, Reddy D, Menon K. The influence of fluid overload on the length of mechanical ventilation in pediatric congenital heart surgery. Pediatr Cardiol. 2015;36:1692-9.
19. Goldstein SL, Somers MJG, Baum MA, Symons JM, Brophy PD, Blowey D, et al. Pediatric patients with multi-organ dysfunction syndrome receiving continuous renal replacement therapy. Kidney Int. 2005;67:653-8.
20. Wilder Ns, Yu S, Donohue JE, Goldberg CS, Blatt NB. Fluid overload is associated with late poor outcomes in neonates following cardiac surgery. Pediatric Crit Care Med. 2016;17:420-7.
21. Sutherland SM, Zappitelli M, Alexander SR, Chua AN, Brophy PD, Bunchman TE, et al. Fluid overload and mortality in children receiving continuous renal replacement therapy: the prospective pediatric continuous renal replacement therapy registry. Am J Kidney Dis. 2010;55:316-25.
22. Hayes LW, Oster RA, Tofil NM, Tolwani AJ. Outcomes of critically ill children requiring continuous renal replacement therapy. J Crit Care. 2009;24:394-400.
23. Barhight MF, Soranno D, Faubel S, Gist KM. Fluid management with peritoneal dialysis after pediatric cardiac surgery. World J Pediatr Congenit Heart Surg. 2018;9:696-704.