

FLUID OVERLOAD MODIFIES HEMODYNAMIC IMPACT OF CONTINUOUS RENAL REPLACEMENT THERAPY: EVIDENCE OF A COVERT CARDIORENAL SYNDROME?

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ABSTRACT—Background: Fluid overload (FO) in critically ill children correlates with higher morbidity and mortality rates. Continuous renal replacement therapy (CRRT) is commonly employed to manage FO. In adults, both FO and CRRT adversely affect myocardial function. It remains unclear if children experience similar cardiovascular effects. **Methods:** Observational single-center study on children (<18 years) receiving CRRT at Texas Children's Hospital from 11/2019 to 3/2021. Excluded were those with end-stage renal disease, pacemakers, extracorporeal membrane oxygenation, ventricular assist devices, apheresis, or without an arterial line. Electrocardiometry (ICON Osypka Medical GmbH, Berlin, Germany) which is noninvasive and utilizes bioimpedance, was applied to obtain hemodynamic data over the first 48 h of CRRT. Our aim was to identify how FO >15% affects hemodynamics in children receiving CRRT. **Results:** Seventeen children, median age 43 months (interquartile range [IQR] 12–124), were included. The median FO at CRRT initiation was 14.4% (2.4%–25.6%), with 9 (53%) patients having FO >15%. Differences were noted in systemic vascular resistance index (1,277 [IQR 1088–1,666] vs. 1,030 [IQR 868–1,181] dynes/s/cm⁵/m², $P < 0.01$), and cardiac index (3.90 [IQR 3.23–4.75] vs. 5.68 [IQR 4.65–6.32] L/min/m², $P < 0.01$), with no differences in heart rate or mean arterial pressure between children with and without FO. **Conclusion:** FO affects the hemodynamic profile of children on CRRT, with those having FO >15% showing higher systemic vascular resistance index and lower cardiac index, despite heart rate and mean arterial pressure remaining unchanged. Our study illustrates the feasibility and utility of electrocardiometry in these patients, suggesting future research employ this technology to further explore the hemodynamic effects of dialysis in children.

KEYWORDS—Continuous renal replacement therapy; hemodynamics; critical illness; fluid overload; cardiorenal syndrome

INTRODUCTION

Critically ill children receive large volumes of intravenous fluid to maintain intravascular volume and provide obligate medical therapies (antibiotics, nutrition, etc.) (1). Even with optimized fluid prescription, several pathophysiological states put critically ill children at high risk for the development of fluid overload (FO). Innate immunity and complement activation leads to capillary leakage (2), while the renin-angiotensin-aldosterone system and antidiuretic hormone lead to salt and fluid retention both contributing to fluid accumulation (3–5). When fluid accumulation leads to organ edema and reduced tissue oxygen delivery, pathological FO ensues, which can potentiate progressive injury and nonrecovery (6). The etiology of FO in critically ill children is complex, and the two major drivers are the maladaptive physiological

changes, and obligate fluid exposure to deliver medications, in which sicker patients who require more medications are exposed to greater amounts of fluid (7). It is not surprising that FO in critically ill children is associated with adverse outcomes such as prolonged length of hospital admission, fewer ventilator-free days, and increased risk of mortality (8–13). Renal replacement therapy (RRT) for mechanical fluid removal is frequently necessary to assist in the management of severe and medically refractory FO (14).

Continuous renal replacement therapy (CRRT) is the support of choice for critically ill children, as it enables dynamic ultrafiltration rates in response to changing hemodynamics and fluid kinetics (15). In critically ill children requiring CRRT, every 1% increase in FO is associated with a 3% increase in mortality (8). An often underappreciated and unmeasured impact of FO is the resultant strain on the cardiovascular system due to altered preload, afterload, reduced contractility, and unfavorable myocardial energetics (16). Along with the negative impact of FO, dialytic therapies themselves can be independently associated with cardiovascular dysfunction and hemodynamic perturbations (17).

Myocardial stunning and regional wall motion abnormalities have been demonstrated in critically ill adults receiving intermittent

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hemodialysis (iHD) and CRRT (18–20). Children receiving chronic iHD, despite a preserved ejection fraction, also experience asymptomatic global, systolic, and diastolic myocardial strain identified through echocardiography. We have previously investigated the hemodynamic impact of CRRT in children in the hour following connection (21). We observed relative hypotension in 27% of connections (defined as a >20% drop in mean arterial pressure from baseline). Given the relatively high incidence of hemodynamic perturbation, further investigations over a longer time frame are needed to understand the hemodynamic impact of CRRT. Although echocardiography has been used to assess regional wall motion abnormalities and myocardial function in critically ill adults on CRRT, it is intermittent in nature and unlikely to optimally capture dynamic cardiovascular changes associated with fluctuations in the clinical state of the patient and CRRT prescription (20). Noninvasive hemodynamic monitoring devices, such as electrocardiometry can allow clinicians to avoid invasive techniques and obtain advanced hemodynamic measurements.

ICON (Osypka Medical GmbH, Berlin, Germany) is a noninvasive electrocardiometry device that utilizes changes in bioimpedance between systole and diastole to derive stroke volume (SV). Using the derived SV, the ICON can calculate other hemodynamic parameters, including, but not limited to, the cardiac index (CI), systemic vascular resistance index (SVRI), and stroke volume variability (SVV) (22). This technology allows clinicians noninvasive access to hemodynamic measurements that are not readily available using the current standard bedside cardiopulmonary monitors. Hemodynamic measurements obtained *via* electrocardiometry have been validated against gold standard thermodilution *via* cardiac catheterization as well as measurements obtained by echocardiogram (23–25). This technology has been utilized to identify significant hemodynamic changes associated with ultrafiltration in children receiving maintenance iHD (26). Electrocardiometry has the potential to characterize the hemodynamic profile and reveal the hemodynamic impact of CRRT in critically ill children.

Building on our previous work and given the known negative association between FO, dialysis, and cardiovascular dysfunction, we sought to use electrocardiometry to explore the hemodynamic profile of critically ill children undergoing CRRT. We aimed to identify differences in the hemodynamic profiles of children requiring CRRT with and without FO. We hypothesized that children with FO >15% will have a different hemodynamic profile compared to those without.

METHODS

We conducted a single-center, prospective, observational pilot study at Texas Children's Hospital involving children admitted to the pediatric or cardiac intensive care units between 11/2019 and 3/2021. Because of the COVID-19 pandemic, recruitment was suspended between 4/2020 and 11/2020. We excluded patients who required extracorporeal membrane oxygenation, ventricular assist devices, pacemakers, or apheresis as well as those without an arterial line and/or previously diagnosed end-stage renal disease. This study was approved by the Baylor College of Medicine Institutional Review Board (H-43712) and all researchers involved with this study adhered to the Declaration of Helsinki. Informed consent was obtained from the parents/guardians, and in patients who were not sedated and >8 years of age, assent was obtained prior to placement of the study monitors.

Demographic data were collected from the electronic health record, including patient characteristics such as age, weight, height, body surface area, primary indication for ICU admission, primary comorbid condition, history of organ transplantation, date of admission, and date of CRRT initiation. The indication of CRRT was

extracted from the nephrology consultation note. We prescribed CRRT in continuous venovenous hemodiafiltration (CVVHDF) mode using HF1000 polyarylethylsulfone filters (Baxter Deerfield, IL) with regional citrate anticoagulation for all patients. Illness severity was measured daily using the Pediatric Logistic Organ Dysfunction 2 score (PELOD-2) (27,28). Vasoactive inotropic score (VIS) was calculated at 1-hour intervals across the observation period (29). Percent FO was calculated using the formula [(fluid in – fluid out)/ICU admission weight (kg)] (30). A threshold of >15% was used to group patients into those with and without FO. Hypotension was defined using the Pediatric Advanced Life Support guidelines as follows: for infants 1 month –1 year of age, systolic BP (SBP) <70 mm Hg; for children 1 year –10 years of age, SBP <70 + 2 × age (in years) mm Hg; and for children >10 years of age, SBP <90 mm Hg (31). The baseline estimated glomerular filtration rate (eGFR) was calculated using the lowest serum creatinine level within 90 days prior to CRRT initiation. If no creatinine was available, the patient was assigned a baseline eGFR of 100 mL/min/1.73 m² as previously described (32). Data on mortality was collected and censored 30 days after CRRT initiation.

We used the ICON Osypka Medical GmbH (Berlin, Germany) device to obtain hemodynamic data until CRRT day 10 or liberation from CRRT, whichever came first. To better understand the initial impact of CRRT on hemodynamics the first 48 h of hemodynamic data collected *via* electrocardiometry was utilized for this analysis. Patients were connected to the ICON device in accordance with the manufacturer's instructions. Hemodynamic variables, including CI, heart rate (HR), thoracic fluid content, SV, SVV, a measure of the variation in arterial blood pressure associated with the change in intrathoracic pressure throughout the respiratory cycle (33), and systemic vascular resistance index (SVRI), were measured at 1-min intervals using the ICON device. These measurements were subsequently aggregated into 1-h epochs using medians. If a central venous pressure (CVP) measurement was not obtained within the designated period, it was set to 10 mm Hg and used to calculate the SVRI. Mean arterial pressure (MAP) was collected using high resolution archived physiological data (Sickbay Medical Informatics Corporation, Houston, TX). Similar to the advanced hemodynamic variables, MAP values were aggregated into 1-hour epochs using medians.

Statistical analysis

Descriptive statistics included medians with interquartile range (IQR) for continuous variables and counts with percentages (%) for categorical variables. To assess the differences between FO groups across multiple time points and to control for within-group variations, we employed a repeated-measures ANOVA. Missing data were imputed using multiple imputation with chained random forest models using the “missRanger” package in R version 4.3.1. The number of trees used was chosen by verifying the clinical appropriateness of the numbers as well as considering the imputed dataset that was closest to the median of the original dataset. Significance was considered a two-sided $\alpha < 0.05$. R version 4.3.1 with packages compiler_4.3.1, survey_4.2-1, tools_4.3.1, mitools2.4, and lattice_0.21-8 were utilized for statistical analysis.

RESULTS

A total of 41 children received CRRT during the study period. A total of 41 children received CRRT during the study period. Twenty-four patients were excluded, 17 (71%) received CRRT during the COVID-19 pandemic during which time consent for this study was on hold and 7 (29%) did not consent (Supplemental Fig. 1, <http://links.lww.com/SHK/C147>). Therefore a total of 17 children with a median age of 43 months (IQR 12–124) were included in the analysis. Ten (59%) were female. The median weight and height were 13.9 (IQR 8.79–29.80) kg and 94 (IQR 77.00–124.40) cm, respectively, with a median body surface area (BSA) of 0.63 (IQR 0.43–1.01) m². Six (35.3%) patients were admitted with sepsis/shock and the most common indication for CRRT was FO (94.1%) followed by AKI (88.2%). The median FO% at CRRT initiation was 14.4% (2.4%–25.6%) and 9 (53%) patients had FO (>15%) at CRRT start (Supplemental Table 1, <http://links.lww.com/SHK/C150>). The median time between ICON connection and CRRT start was 24.5 h (IQR 21.50–41.00). At ICON connection, the median PELOD-2 score was 7 (IQR 5.5–8.5) (Table 1).

Over the first 48 h of ICON connection the median CI was 4.65 (3.53–5.98) L/min/m² with a SVRI 1153.03 (959.87–1384.74) dyne*s/m²/cm⁵. The median HR and stroke volume index (SVI) were

117 beats/min (102–128) and 39.23 mL/beat/m² (30.56–49.60). The median MAP was 78 (66–90) mm Hg and the median VIS 4 (2–8) (Table 2 and Supplemental Figs. 2–3, <http://links.lww.com/SHK/C148>, <http://links.lww.com/SHK/C149>).

Fluid overload and hemodynamic profile utilizing electrocardiometry

Over the entirety of the 48-h observation period, we noted significant differences in hemodynamic measurements obtained *via* the electrocardiometry when stratified by FO status. Patients with FO (FO% > 15) had higher SVRI (1,277 [IQR 1088–1,666] vs. 1,030 [IQR 868–1,181] dyne*s/m²/cm⁵, $P < 0.01$) and lower CI (3.90 [IQR 3.23–4.75] vs. 5.68 [IQR 4.65–6.32]), $P < 0.01$) compared to those without FO (Table 2, Figs. 1–4). There was no difference in HR (118 [IQR 98–132] vs. 116 [IQR 104–124], $P = 0.11$). Additionally, patients with FO had higher SVV and lower SVI (SV indexed to body surface area) (18% [IQR 15–20] vs. 11% [IQR 8–14], $P < 0.01$) and (34 [IQR 29–42] vs. 45 [IQR 37–56], $P < 0.01$), respectively. There was no difference in VIS between the two groups (Table 2). None of the patients experienced hypotension during the observational period.

DISCUSSION

In this prospective, single-center, observational pilot study, we evaluated the effects of FO on the cardiovascular system using electrocardiometry to measure hemodynamic parameters in children undergoing CRRT. To the best of our knowledge, this is the first pediatric study to use electrocardiometry to identify distinct hemodynamic profiles associated with FO in children undergoing CRRT. We identified significant differences in CI, SVRI, SVV, and SVI in patients with FO >15% compared to those without,

despite similar patient demographics, CRRT characteristics, and VIS. Additionally there was no difference in mortality between the groups.

FO in critically ill pediatric patients has been associated with an increased risk of morbidity and mortality (34–37), conferring a 4.3-fold increase in mortality and fewer ventilator-free days, an increased incidence of AKI, and longer ICU and hospital stays (38). In critical illness, FO likely arises as a consequence of disruptions in the glycocalyx layer and an increase in capillary hydrostatic pressure, resulting in capillary leakage and interstitial fluid accumulation, contributing to organ edema and impaired perfusion (6,8,12). Recent consensus guidelines have suggested that patients with an FO > 20% meet criteria for renal failure/dysfunction in addition to the Kidney Disease Improving Global Outcomes creatinine and urine output AKI criteria (39,40). Our findings suggest that FO >15% adversely impacts cardiovascular performance in patients undergoing CRRT.

Dialysis can induce cardiac dysfunction. In adults without a previous cardiac history requiring iHD, positron emission tomography showed a decrease in myocardial blood flow, a decrease in CO, and a > 30% decrease in left ventricular end-diastolic and systolic volumes (19,41). Myocardial stunning starts within 4 h of CRRT initiation and persists for up to 24 h in critically ill adults, despite unchanged blood pressure or HR (20). In children on iHD, our group previously demonstrated worsening global and diastolic longitudinal strain on echocardiography that persisted post-iHD treatment, despite preserved ejection fraction (42). Pediatric patients undergoing chronic iHD experience a decrease in CI and SV and an increase in SVV and HR, even without initiation of ultrafiltration (26). These findings indicate that dialytic therapies themselves independently increase myocardial strain. Our findings confirm our hypothesis that children with FO

TABLE 1. Demographics of the fluid overload <15% cohort, the fluid overload >15% cohort, and the overall cohort

Variable	Fluid overload < 15% (n = 8)*	Fluid overload > 15% (n = 9)*	Total (n = 17)*	P value
Sex (male)	2 (25%)	5 (56%)	7 (41%)	0.11
Age at ICU admission (months)	74 (4–175)	43 (15–85)	43 (12–124)	0.47
Weight at ICU admission (kg)	36 (7–54)	14 (9–27)	14 (9–35)	0.27
Height at ICU admission (cm)	112 (59–155)	94(78–112)	94 (72–131)	0.61
Body surface area	0.92 (0.34–1.52)	0.63 (0.45–0.91)	0.63 (0.42–1.15)	0.37
History of organ transplant	2 (25%)	0 (0%)	2(12%)	0.17
Indication for ICU admission				0.71
Shock	4 (50%)	4 (45%)	8 (47%)	
Cardiovascular	0 (0%)	1 (11%)	1 (6%)	
Respiratory	3 (38%)	3 (33%)	6 (35%)	
Central nervous system	1 (12%)	1 (11%)	2 (12%)	
Time between CRRT initiation and ICON connection (hours)	27 (22–43)	22 (1–45)	24 (12–45)	0.82
Weight at ICON connection (kg)	26 (7–55)	17 (11–31)	17 (11–37)	0.41
Fluid administered prior to CRRT start (mL/kg)	23 (–48–101)	307 (216–559)	171 (23–315)	0.04
Percent fluid accumulation at CRRT start	2.3 (–4.8–9.8)	24.4 (19.5–45.5)	14.4 (2.4–25.6)	0.03
Indication for CRRT				
Acute kidney injury	7 (88%)	8 (89%)	15 (88%)	0.93
Fluid overload	7 (88%)	9 (100%)	16 (94%)	0.35
Elevated ammonia	2 (25%)	0 (0%)	2 (12%)	0.17
Location of HD line (internal jugular)	5 (63%)	5 (56%)	10 (59%)	0.52
PELOD-2 score at ICON connection	6 (5–8)	8 (5–10)	7 (6–9)	0.40
Gauge of HD line	9 (8–12)	10 (8–10)	10 (8–10)	0.60
Initial CRRT clearance mL/h/1.73 m ²	2000 (2000–2000)	2000 (2000–2000)	2000 (2000–2000)	0.35
Hemoglobin at ICON connection (g/dL)	9 (8.5–9.8)	8.2 (7.8–9.6)	8.5 (8–9.8)	0.82
Death at 30 days	4 (50%)	3 (33%)	7 (41%)	0.22

*Values presented as n (%) or median (IQR).

TABLE 2. Medians of hemodynamic variables by fluid overload status

Hemodynamic parameter	Fluid overload < 15% (n = 8)*	Fluid overload > 15% (n = 9)*	Total (n = 17)*	P value
Systemic vascular resistance index	1030.18 (868.98–1181.45)	1277.77 (1088.15–1666.65)	1153.03 (959.87–1384.74)	<0.01
Cardiac index	5.68 (4.65–6.32)	3.90 (3.23–4.75)	4.65 (3.53–5.98)	<0.01
Stroke volume variability	10.70 (8.49–13.70)	18.01 (14.64–20.20)	14.63 (10.28–19.29)	<0.01
Stroke volume index	44.65 (36.55–55.56)	34.04 (29.13–41.57)	39.23 (30.56–49.60)	<0.01
Heart rate	116 (104–124)	118 (98–132)	117 (102–128)	0.11
Mean arterial pressure	81 (63–91)	74 (66–89)	78 (66–90)	0.07
Vasoactive inotropic score	2 (2–6.75)	5 (2–8.33)	4 (2–8)	0.99

*Values presented as median (IQR).

compared to those without receiving CRRT demonstrate a different hemodynamic profile, and we theorize this is due to higher circulatory strain as well as other patient-related factors.

Our findings support the adverse impact of FO on cardiovascular performance and might be congruent with type 3 cardiorenal syndrome. This pathology occurs when an acute worsening in renal function leads to fluid, electrolyte, and inflammatory dysregulation, potentiating mitochondrial uncoupling and dysregulation of normal homeostasis inducing cardiac dysfunction (16,43). It is in this setting when the myocardium is likely extremely sensitive to changes in the delivery of oxygen. It has been reported that up to 50% of CRRT initiations in critically ill children are associated with hypotension (21,44). Repeated bouts of hemodynamic perturbations during CRRT in the setting of type 3 cardiorenal syndrome may potentiate myocardial dysfunction and, with enough progressive cardiovascular strain, end-organ recovery may be adversely affected.

We also identified significant differences in SVV between groups. SVV is a measure of the change in SV that occurs during

the respiratory cycle and can indicate an intravascular deplete state when the value exceeds 10% (33). In our FO group, the median SVV was 18.01%, which far exceeded this threshold. We theorize that despite their fluid overloaded state these patients might be intravascularly depleted secondary to the majority of fluid retained in the interstitial or third space. Therefore, these patients are total body fluid overloaded but behave in a preload dependent fashion. Therefore, slow ultrafiltration/fluid removal might be essential to maintain intravascular volume and prevent augmentation of organ hypoperfusion.

In adult patients, ultrafiltration thresholds surpassing >13 mL/kg/h on iHD and >1.75 mL/kg/h on CRRT have been associated with mortality (6). These discrete thresholds are theorized to be the hinge point at which ultrafiltration rate (UFR) exceeds the intravascular refill rate leading to end-organ ischemia. Electrocardiometry has the potential to allow clinicians to elucidate the hemodynamic profiles of children on CRRT and could be utilized to identify UFR thresholds associated with dialytrauma prior to onset of end-organ damage.

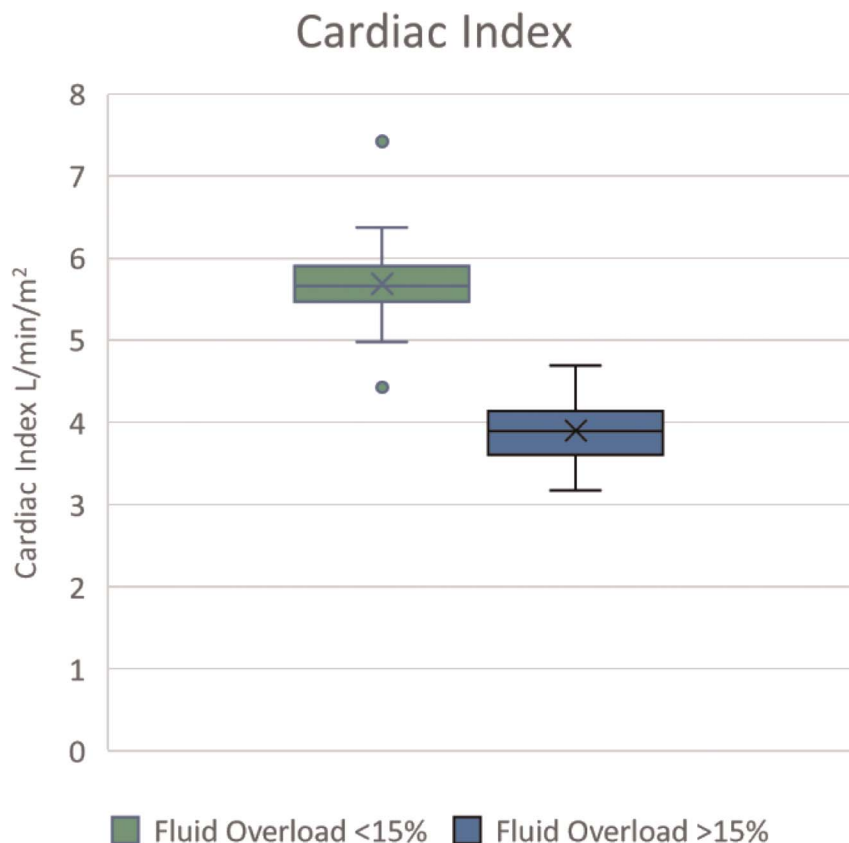


FIG. 1. Box and whisker plots of the cardiac index of those patients with a fluid overload < 15% (green) and those with a fluid overload > 15% (blue).

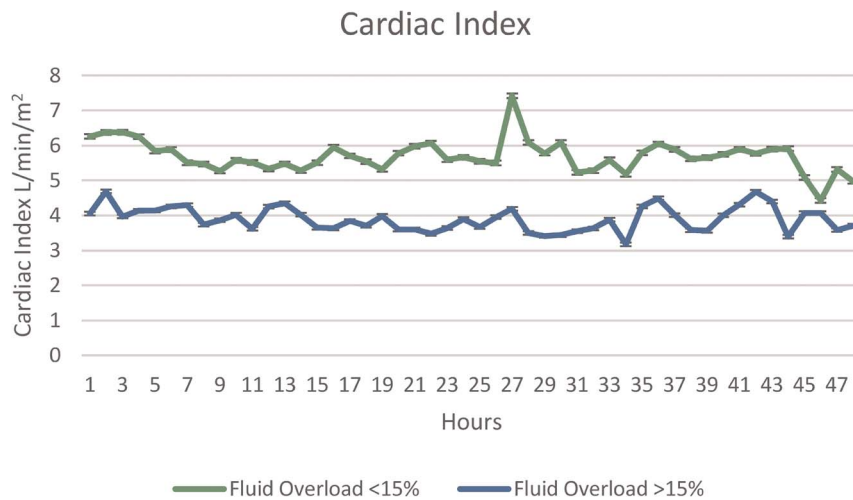


FIG. 2. Cardiac index over the first 48 h of ICON connection. Fluid overload <15% (green) and fluid overload >15% (blue).

Within our observational period, we were unable to capture any bouts of hypotension as defined by the Pediatric Advanced Life Support criteria. Evidence suggests that in the hour after connection to CRRT at least 27% of children have relative hypotension (>20% decrease from MAP 1 h prior to CRRT connection) (21). Despite the absence of overt hypotension and similar illness severity, we found differences in the CI, SVRI, and SVI between our groups. Given no differences were observed in HR and MAP, we propose that these conventional hemodynamic measurements in children requiring CRRT are insufficient to capture the true hemodynamic burden in vulnerable populations. Further understanding of the hemodynamic profile of children receiving CRRT has the potential to lead to a more personalized approach to resuscitation and fluid management, and may ultimately improve outcomes.

Our study has several limitations. First, generalizability is limited as it was a single-center study with a small sample size, which

may not fully capture the heterogeneity of pediatric CRRT patients. Therefore, our findings should be interpreted with caution, and validated in larger multicenter studies. Second, our results from this prospective study do not establish causation, and it is possible that patient-related factors that were not captured in our study could have influenced the differences in hemodynamic parameters observed between FO groups. Third, we aggregated data into 1-hour intervals, which could result in the loss of granularity and failure to capture dynamic hemodynamic perturbations. Fourth, our illness severity score, PELOD-2, did not account for hepatic dysfunction. Fifth, 4.4% of the data were missing, which required imputation. We expected this missingness due to patient activities such as bathing/imaging/transportation, but the missing data may have prevented us from capturing other notable hemodynamic perturbations. We were underpowered to identify a difference in VIS. Lastly, during the beginning of the COVID-19

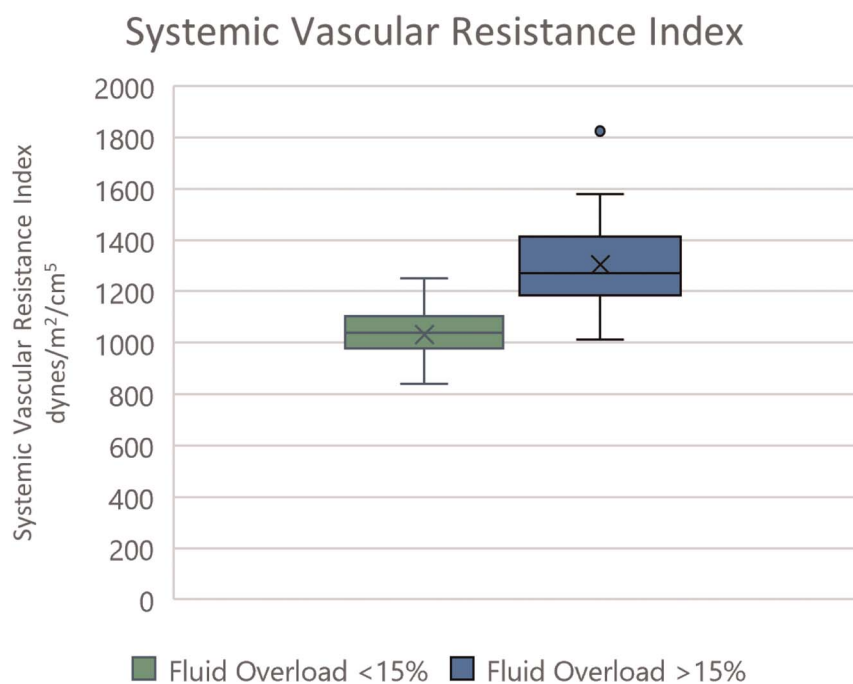


FIG. 3. Box and whisker plots of the systemic vascular resistance index of those patients with a fluid overload < 15% (green) and those with a fluid overload > 15% (blue).

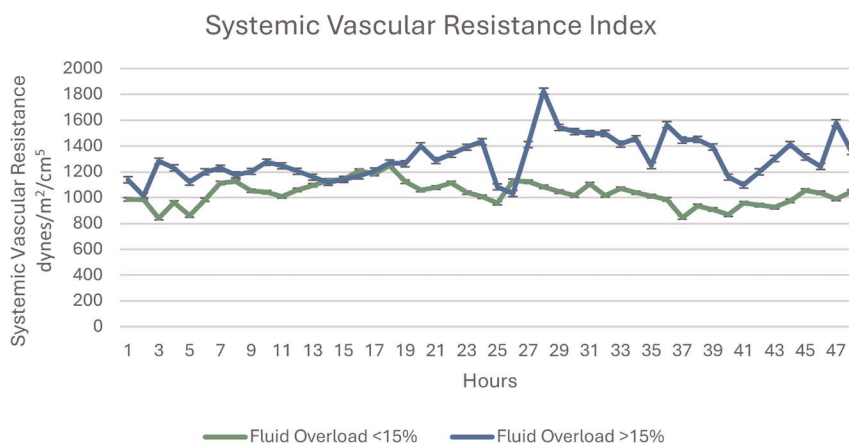


FIG. 4. Systemic vascular resistance index over the first 48 h of ICON connection. Fluid overload <15% (green) and fluid overload >15% (blue).

pandemic study recruitment was paused, and we were unable to capture hemodynamics in patients with COVID-19 requiring CRRT during this time.

CONCLUSIONS

Utilizing electrocardiometry, we were able to quantify changes in SVRI, SVV, and CI in children on CRRT and discovered novel differences in the hemodynamic profile in children with and without FO. Those with FO had a lower CI and SVI with an increase in SVRI and SVV. Conventional measures of cardiovascular function did not demonstrate a difference between the two groups. Our findings suggest that the current approach to hemodynamic monitoring in children undergoing CRRT might be inadequate. Measures obtained *via* electrocardiometry may precede hypotension and, if validated, may allow clinicians to intervene prior to hemodynamic compromise within this population.

REFERENCES

- Van Regenmortel N, Verbrugge W, Roelant E, et al. Maintenance fluid therapy and fluid creep impose more significant fluid, sodium, and chloride burdens than resuscitation fluids in critically ill patients: a retrospective study in a tertiary mixed ICU population. *Intensive Care Med.* 2018;44:409–417.
- Siddall E, Khatri M, Radhakrishnan J. Capillary leak syndrome: etiologies, pathophysiology, and management. *Kidney Int.* 2017;92:37–46.
- Lote C. The renin-angiotensin system and regulation of fluid volume. *Surg Oxf.* 2006;24:154–159.
- Zarbock A, Chawla L, Bellomo R. Why the renin-angiotensin-aldosterone system (RAAS) in critically ill patients can no longer be ignored. *Crit Care.* 2021;25:389.
- Stanski NL, Pode Shakked N, Zhang B, et al. Serum renin and prorenin concentrations predict severe persistent acute kidney injury and mortality in pediatric septic shock. *Pediatr Nephrol.* 2023;38:3099–3108.
- Murugan R, Bellomo R, Palevsky PM, et al. Ultrafiltration in critically ill patients treated with kidney replacement therapy. *Nat Rev Nephrol.* 2021;17:262–276.
- Selewski DT, Barhight MF, Bjornstad EC, et al. Fluid assessment, fluid balance, and fluid overload in sick children: a report from the Pediatric Acute Disease Quality Initiative (ADQI) conference. *Pediatr Nephrol.* 2024;39:955–979.
- Sutherland SM, Zappitelli M, Alexander SR, 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;55:316–325.
- Michael M, Kuehnl I, Goldstein SL. Fluid overload and acute renal failure in pediatric stem cell transplant patients. *Pediatr Nephrol.* 2004;19:91–95.
- Kaddourah A, Basu RK, Goldstein SL, et al. Assessment of Worldwide Acute Kidney Injury, Renal Angina and, Epidemiology (AWARE) Investigators. Oliguria and acute kidney injury in critically ill children: implications for diagnosis and outcomes. *Pediatr Crit Care Med.* 2019;20:332–339.
- Ker GL, Gangadharan S. Management of fluid overload in the pediatric ICU. In: Mastropietro CW, Valentine KM, eds. *Pediatric Critical Care.* Cham: Springer International Publishing, 2019:193–209.
- Selewski DT, Gist KM, Basu RK, et al. Impact of the magnitude and timing of fluid overload on outcomes in critically ill children: a report from the Multicenter International Assessment of Worldwide Acute Kidney Injury, Renal Angina, and Epidemiology (AWARE) Study. *Crit Care Med.* 2023;51:606–618.
- Sethi SK, Raghunathan V, Shah S, et al. Fluid overload and renal angina index at admission are associated with worse outcomes in critically ill children. *Front Pediatr.* 2018;6:118.
- Tandukar S, Palevsky PM. Continuous renal replacement therapy. *Chest.* 2019;155:626–638.
- Guzzo I, De Galasso L, Mir S, et al. Acute dialysis in children: results of a European survey. *J Nephrol.* 2019;32:445–451.
- Prastaro M, Nardi E, Paolillo S, et al. Cardiorenal syndrome: pathophysiology as a key to the therapeutic approach in an under-diagnosed disease. *J Clin Ultrasound.* 2022;50:1110–1124.
- Selby NM, McIntyre CW. The acute cardiac effects of dialysis. *Semin Dial.* 2007;20:220–228.
- McIntyre CW. Recurrent circulatory stress: the dark side of dialysis. *Semin Dial.* 2010;23:449–451.
- Dasselaar JJ, Slart RHJA, Knip M, et al. Haemodialysis is associated with a pronounced fall in myocardial perfusion. *Nephrol Dial Transplant.* 2009;24:604–610.
- Slessarev M, Salerno F, Ball IM, et al. Continuous renal replacement therapy is associated with acute cardiac stunning in critically ill patients. *Hemodial Int.* 2019;23:325–332.
- Thadani S, Fogarty T, Mottes T, et al. Hemodynamic instability during connection to continuous kidney replacement therapy in critically ill pediatric patients. *Pediatr Nephrol.* 2022;37:2167–2177.
- Osycka MJ, Bernstein DP. Electrophysiologic principles and theory of stroke volume determination by thoracic electrical bioimpedance. *AACN Clin Issues.* 1999;10:385–399.
- Malik V, Subramanian A, Chauhan S, et al. Correlation of electric cardiometry and continuous thermomodulation cardiac output monitoring systems. *World J Cardiovasc Surg.* 2014;04:101–108.
- Blohm ME, Obrecht D, Hartwich J, et al. Impedance cardiography (electrical velocimetry) and transthoracic echocardiography for non-invasive cardiac output monitoring in pediatric intensive care patients: a prospective single-center observational study. *Crit Care.* 2014;18:603.
- Rauch R, Welisch E, Lansdell N, et al. Non-invasive measurement of cardiac output in obese children and adolescents: comparison of electrical cardiometry and transthoracic Doppler echocardiography. *J Clin Monit Comput.* 2013;27:187–193.
- Wilken M, Oh J, Pinn Schmidt HO, et al. Effect of hemodialysis on impedance cardiography (electrical velocimetry) parameters in children. *Pediatr Nephrol.* 2020;35:669–676.
- Leteurtre S, Duhamel A, Deken V, et al. Daily estimation of the severity of organ dysfunctions in critically ill children by using the PELOD-2 score. *Crit Care.* 2015;19:324.
- Leteurtre S, Duhamel A, Salleron J, et al. PELOD-2: an update of the Pediatric Logistic Organ Dysfunction score. *Crit Care Med.* 2013;41:1761–1773.
- Gaies MG, Gurney JG, Yen AH, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass*. *Pediatr Crit Care Med.* 2010;11:234–238.
- Goldstein SL, Currier H, Graf JM, et al. Outcome in children receiving continuous venovenous hemofiltration. *PEDIATRICS.* 2001;107:1309–1312.

31. (2000) Part 10: Pediatric Advanced Life Support. *Circulation* 102. doi: 10.1161/circ.102.suppl_1.1-291
32. Batte A, Starr MC, Schwaderer AL, et al. Methods to estimate baseline creatinine and define acute kidney injury in lean Ugandan children with severe malaria: a prospective cohort study. *BMC Nephrol.* 2020;21:417.
33. Zhang Z, Lu B, Sheng X, et al. Accuracy of stroke volume variation in predicting fluid responsiveness: a systematic review and meta-analysis. *J Anesth.* 2011;25:904–916.
34. Lopes CLS, Piva JP. Fluid overload in children undergoing mechanical ventilation. *Rev Bras Ter Intensiva.* 2017;29:346–353. doi:https://doi.org/10.5935/0103-507X.20170045.
35. Leow EH, Wong JJ, Mok YH, et al. Fluid overload in children with pediatric acute respiratory distress syndrome: A retrospective cohort study. *Pediatr Pulmonol.* 2022;57:300–307.
36. Claire-Del Granado R, Mehta RL. Fluid overload in the ICU: evaluation and management. *BMC Nephrol.* 2016;17:109.
37. Vaara ST, Korhonen A-M, Kaukonen K-M, et al. Fluid overload is associated with an increased risk for 90-day mortality in critically ill patients with renal replacement therapy: data from the prospective FINNAKI study. *Crit Care.* 2012;16:R197.
38. Alobaidi R, Anton N, Burkholder S, et al. Association between acute kidney injury duration and outcomes in critically ill children*. *Pediatr Crit Care Med.* 2021;22:642–650.
39. Bembea MM, Agus M, Akcan-Arikan A, et al. Pediatric Organ Dysfunction Information Update Mandate (PODIUM) contemporary organ dysfunction criteria: executive summary. *Pediatrics.* 2022;149:S1–S12.
40. Section 2: AKI definition. *Kidney Int Suppl.* 2011;2:19–36.
41. Burton JO, Jefferies HJ, Selby NM, et al. Hemodialysis-induced cardiac injury: determinants and associated outcomes. *Clin J Am Soc Nephrol.* 2009;4:914–920.
42. Idrovo A, Pignatelli R, Loar R, et al. Preserved cerebral oxygenation with worsening global myocardial strain during pediatric chronic hemodialysis. *J Am Soc Nephrol.* 2021;32:2912–2919.
43. Rangaswami J, Bhalla V, Blair JEA, et al. Cardiorenal syndrome: classification, pathophysiology, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. *Circulation.* 2019;139:e840–e878. doi:10.1161/CIR.0000000000000664.
44. Fernandez Lafever SN, Santiago MJ, Lopez J, et al. Hemodynamic effects of connection to continuous renal replacement therapy in a pediatric animal model. *Artif Organs.* 2018;42:640–646.

