Fluid overload is associated with impaired oxygenation and morbidity in critically ill children*

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Rationale: **Fluid overload is common in the critically ill and is thought to contribute to oxygenation failure and mortality. Since increasing disease severity often requires more fluid for resuscitation, it is unclear whether fluid overload is a causative factor in morbidity or is simply an indicator of disease severity.**

Objective: **Investigate the association between fluid overload and oxygenation while controlling for severity of illness by daily Pediatric Logistic Organ Dysfunction scores.**

Design and Setting: **Retrospective chart review, tertiary children's hospital.**

Patients and Methods: **The oxygenation index, fluid overload percent, and daily Pediatric Logistic Organ Dysfunction scores were obtained in a retrospective chart review of 80 patients (mean age 58.7 ± 73.0 months) with respiratory failure. Univariate and multivariate approaches were used to assess the independent relation between fluid overload percent and duration of stay and ventilation.**

Interventions: **None.**

Main Results: **Higher peak fluid overload percent predicted higher peak oxygenation index, independent of age, gender, and Pediatric Logistic Organ Dysfunction ($p = .009$). Fluid overload percent ≥15% on any given day was also independently associated with that day's oxygenation index, controlled for age, gender, and Pediatric Logistic Organ Dysfunction ($p < .05$). Peak fluid overload percent and severe fluid overload percent (≥15%) were both independently associated with longer duration of ventilation ($p = .004$, $p = .01$), and pediatric intensive care unit ($p = .008$, $p = .01$) and hospital length of stay ($p = .02$, $p = .04$), controlled for age, gender, Pediatric Logistic Organ Dysfunction, and in the case of ventilation, respiratory admission.**

Conclusion: **This is the first study to report that positive fluid balance adversely affected the pediatric intensive care unit course in children who did *not* receive renal replacement therapy. While timely administration of fluids is lifesaving, positive fluid balance after hemodynamic stabilization may impact organ function and negatively influence important outcomes in critically ill patients. (Pediatr Crit Care Med 2012; 13:253–258)**

Key Words: children; critical illness; fluid management; respiratory failure

The requirement for ongoing fluid resuscitation in conditions associated with underlying endothelial dysfunction often leads to the development of significant fluid overload (FO) in the critically ill patient. However, recent data has underlined the detrimental effect positive fluid balance plays in the recovery phase after hemodynamic stabilization is reached by negatively impacting organ function (1, 2). Specifically, a causal relationship between positive fluid balance and respiratory morbidity has been postulated (3, 4). A dose-response relationship between cardiopulmonary complications and increasing degrees of FO was demonstrated in adult critical care patients; those with less fluid gain and lower lung water had more ventilator free days and shorter intensive care unit (ICU) and hospital length of stays (LOS) (5, 6). Additionally, diuresis with albumin-furosemide infusions has been shown to lead to rapid and persistent improvements in oxygenation (7). More recently, in adult patients with acute lung injury (ALI), an oxygenation benefit and shortened length of ventilation and ICU stay was demonstrated in those patients managed with a conservative fluid strategy (8). In the pediatric patient population, data on the impact of fluid balance on pulmonary mechanics and oxygenation is scarce. Randolph et al (9) found that patients with the highest degree of cumulative FO at the time of weaning had a significantly longer period of time to extubation. Association between the need for renal replacement therapy (RRT) and increased duration of mechanical ventilation has been reported previously, suggesting a relationship between FO and lung mechanics (10–12). Since those patients who are more critically ill at presentation require more initial fluid resuscitation (13, 14), it is unclear whether fluid balance is an independent risk factor for worse outcome in critically ill pediatric patients, or simply a result of underlying severity of illness.

We hypothesized that the degree of positive fluid balance is associated with impaired oxygenation and increased morbidity in critically ill children with respiratory failure. Our main objective was to determine whether a higher degree of FO was associated with impaired oxygenation independent of severity of illness. Our secondary aims were to investigate the association between degree of FO and clinically important outcome measures, such as survival, duration of ventilation, and LOS in the pediatric ICU (PICU) and the hospital.

***See also p. 348.**

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METHODS

Design, Setting, and Patients

This single-center retrospective study was conducted on patients admitted to the PICU of Texas Children's Hospital between September 2004 and May 2005. Inclusion criteria were the need for invasive mechanical ventilation for >24 hrs and the presence of an indwelling arterial catheter. Patients with congenital heart disease, known right-to-left shunts (e.g., hepatopulmonary syndrome), or those who received RRT were excluded. The Institutional Review Board of Baylor College of Medicine approved the study protocol and waived the informed consent requirement.

Data Collection

Daily data collection included ventilatory parameters (ventilator rate, tidal volume, peak inspiratory pressure, positive end expiratory pressure, F_{IO_2}, mean airway pressure), arterial blood gas measurements (pH, P_{CO_2}, P_{O_2}, $HCO_3^{[minus]}$), and daily fluid intake and output (in mL) beginning at PICU admission and continued for up to 14 days. Additional data collected included demographic characteristics, admission diagnoses, admission Pediatric Risk of Mortality score, and outcomes (28-day mortality, duration of mechanical ventilation, and PICU and hospital LOS).

FO Assessment

Fluid intake included all enterally or parenterally administered fluids, including blood products and intravenous medications. Fluid output included urine, stool, nasogastric output, blood loss, or any other output from surgical drains. Insensible losses were assumed to be negligible since all patients were ventilated with humidified gases.

The fluid balance on each day of PICU admission for each patient was recorded based on previously reported formulae (15).

FO percent (FO%), expressing the cumulative FO% from the day of PICU admission to the given study day was calculated as: FO% = (mL fluid in – mL fluid out from PICU admission)/PICU admission weight in kg ´ 100%.

We elected to use the term "fluid overload percent" term in lieu of "positive fluid balance" since it has been used previously to report fluid balance in relation to weight (15, 12, 17).

Oxygenation Assessment

The oxygenation index (OI) (mean airway pressure × F_{IO_2} × 100/Pa_{O_2}) was calculated daily as a surrogate measure of pulmonary dysfunction, with higher OI values denoting worsening oxygenation. The worst OI for a given day was calculated using the lowest Pa_{O_2}, the mean airway pressure, and F_{IO_2} recorded closest in time to that particular Pa_{O_2} measurement. The mean and peak OI values during PICU admission for each patient were recorded as summary measures.

Assessment of Severity of Illness

Pediatric Logistic Organ Dysfunction (PELOD) is an organ dysfunction score developed and validated for daily measurement in pediatric patients, and includes a total of 12 variables for six key organ dysfunctions (cardiovascular, respiratory, hematologic, neurologic, renal, and hepatic) (16). All clinical and laboratory parameters required for calculation of the PELOD score were collected and the scores were calculated at admission and daily thereafter. The neurologic assessment includes calculation of Glasgow Coma Scores. For the sedated patients, the Glasgow Coma Scores calculated before administration of sedation was used.

Data Management

Our primary relationship of interest was that between FO% and OI, and we examined this relationship in two ways.

We first derived summary measures of these two variables over the study period, namely, peak FO% (highest FO% occurring throughout the study period) and peak OI (the highest OI recorded during the study period). We examined the association between these two summary measures using multivariate analyses and controlling for confounders, such as age, gender, and admission PELOD score.

We next examined the relationship between each study day's FO% and OI using repeated-measures multivariate analyses adjusting for the same potential confounders, which provides information on whether FO% was associated with OI on a given day.

Previous studies have revealed that FO% above a certain percentage varying from 10% to 20% may be associated with increased mortality in specific critically ill pediatric populations (12, 17–19). Cutoff values for FO% ranging from 2.5% to 20% were generated and then used in repeated-measures multivariate analyses to determine whether the independent relationship between FO% and OI became stronger with increasing cutoff values.

Statistical Analysis

Continuous variables were presented as mean ± SD and median (interquartile range). Categorical variables were presented as proportions (%). Non-normally distributed variables were transformed to their natural logarithms for inclusion in multivariate analyses and/or parametric tests of significance. Continuous variables were compared using *t* tests and analysis of variance. Proportions were compared using chi-squared and Fisher's exact tests or z-tests. A p value of $< .05$ was considered statistically significant. Backward stepwise multiple linear regression was used to evaluate the independent association between peak FO% and peak OI, controlling for confounders (p value for exit was .2). Multiple linear regressions with generalized estimating equations were used to evaluate the repeated-measures daily association between FO% and daily OI, controlling for other daily confounding variables. Generalized estimating equations allows for the analysis of repeated measures on individuals, while accounting for the presence of correlated values occurring within each individual, and also prevents skewing of results in favor of patients with the most number of observations (20). Backward stepwise multiple logistic regression analysis was used to determine the association between peak FO% with mortality, controlling for age, gender, admission PELOD score, and admission OI (p value for exit was .2). Multiple Cox regression was used to evaluate the independent effect of peak FO% on LOS (hospital and PICU) and length of mechanical ventilation to censor for death. In analyses evaluating the relationship between peak FO% and length of mechanical ventilation, we additionally controlled for the presence/absence of a respiratory diagnosis for primary reason of PICU admission. All analyses were conducted using Intercooled STATA statistical software package (College Station, TX).

RESULTS

Descriptive Statistics

Eighty patients met inclusion criteria. Males comprised 56% of the sample, and mean age was 58.7 ± 73.0 months (Table 1). The most common admission diagnosis was respiratory failure (63%) followed by nonpulmonary infections (16%). Mean ± SD admission day Pediatric Risk of Mortality and PELOD scores were 15.4 ± 7.5 and 21.2 ± 13.8, respectively. The patients were ventilated for an average of 12.9 ± 10.7 days. Mean PICU and hospital LOS were 13.9 ± 9.6 days and 25.4 ± 22.5 days, respectively. Six patients (7%) received high-frequency oscillatory ventilation, and the remaining 74 were on conventional ventilation. PICU mortality was 17.5% (14 of 80). Mean OI at admission was 11.9 ± 12.3, and peak OI during the study period was 19.2 ± 20.7 (median [interquartile range] = 11.5 [17.6]). Seventy-four percent of all patients reached peak FO% on or earlier than day 7 or admission (Fig. 1).

Table 1. Demographic characteristics and outcome variables of the cohort

	Mean ± SD, Median (Interquartile Range)
Continuous variables at pediatric intensive care unit admission	
Age (months)	58.7 ± 73.0, 15.5 (95.5)
Weight (kg)	18.3 ± 18.3, 10.0 (15.2)
Pediatric Logistic Organ Dysfunction score	21.2 ± 13.8, 20 (20)
Serum creatinine (mg/dL)	0.6 ± 0.5, 0.4 (0.4)
Total fluid overload %a	5.0 ± 6.1, 4.3 (5.3)
FIO_2 (%)	67.3 ± 19.8, 60.0 (20)
Mean airway pressure (mm Hg)	12.1 ± 6.7, 10.5 (5.0)
Pao_2 (mm Hg)	97.4 ± 56.7, 78.0 (48.0)
Oxygenation index	11.9 ± 12.3, 7.7 (10.8)
Continuous variables, outcome	
Pediatric intensive care unit length of stay (days)	13.9 ± 9.6, 11.5 (10)
Hospital length of stay (days)	25.4 ± 22.5, 18 (24.5)
Days ventilated	12.9 ± 10.7, 10 (9.5)
High-frequency oscillatory ventilation	6 of 80 (7.5%)
28-day mortality	14 of 8 (17.5%)
Categorical Variables	n/Total (%)
Gender, male	45 of 80 (56%)
Ethnicity	
Caucasian	21 of 80 (26%)
African-American	17 of 80 (21%)
Hispanic	32 of 80 (40%)
Other	7 of 80 (9%)
Unknown	3 of 80 (4%)
Admission diagnosis	
Respiratory	50 of 80 (62.5%)
Cardiac	2 of 80 (2.5 %)
Infection (nonpulmonary)	13 of 80 (16.3%)
Hepatic/gastrointestinal	3 of 80 (3.8%)
Neurological	3 of 80 (3.8%)
Hematologic/oncologic	3 of 80 (3.8%)
Toxicity	3 of 80 (3.8%)
Trauma	2 of 80 (2.5%)
Other	1 of 80 (1.3%)

[a]Total fluid overload as a percentage of body weight.

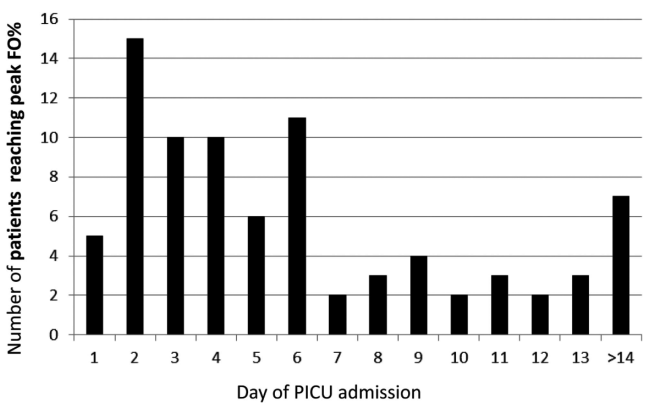

Figure 1. Timeline of occurrence of peak fluid overload percent (*FO%*) during the pediatric intensive care unit (*PICU*) admission. On average, peak FO% was first achieved on day 5.7 ± 4.2, median 4.5, 74%, or patients reached peak cumulative fluid overload on day 7 or earlier.

FO and Oxygenation Failure

Peak FO% during the study period correlated significantly with peak OI ($r = .26$, $p < .02$) and with PELOD score ($r = .31$, $p = .05$) (Fig. 2). Higher peak FO% was an independent predictor of higher peak OI ($p = .009$), even when controlled for age, gender, and PELOD in multivariate analyses ($p = .027$) (Table 2).

To determine whether FO% was associated with OI on a given day, all 14 days of observation were included in a repeated-measures multivariate analysis that accounted for correlation between the within-subject repeated measures. On any given day, FO% was associated with that day's OI ($p = .036$), independent of age, gender, and that day's PELOD score (Table 2).

When examining the relationship between increasing daily cutoff values of FO% and OI, we found that FO% ⩾15% (severe FO%) on a given day was independently associated with that day's OI, controlled for age, gender, and daily PELOD score. We also observed a dose-response relationship where, as the FO % cutoff percentage increased, the regression coefficient and significance progressively increased (Table 3). Severe FO% also happened early; 81% of patients with severe FO% had reached peak FO% ⩾15% in the first week of the PICU admission.

FO and Mortality/LOS

Peak FO% was independently associated with longer LOS both in the PICU (hazard ratio [HR] 0.96, 95% confidence interval [CI] 0.93–0.99, $p = .008$) and hospital (HR 0.97, 95% CI 0.95–0.99, $p = .02$), controlled for PELOD, age, and gender. Peak FO%, when controlled for admission and respiratory diagnosis, was also independently associated with longer duration of ventilation (HR 0.95, 95% CI 0.92–0.98, $p = .004$). When peak FO% was made binary, based on our repeated-measures analyses above, peak FO% >15% was more strongly associated with a longer PICU stay (HR 0.46, 95% CI 0.25–0.85, $p = .01$), longer hospital stay (HR 0.55, 95% CI 0.30–0.98, $p = .04$), and longer duration of ventilation (HR 0.35, 95% CI 0.19–0.66, $p = .001$), controlling for the same variables.

Patients who died had higher peak OI values (nonsurvivors: 31.5 ± 29.6 vs. survivors: 16.6 ± 17.6, $p < .05$). Although FO values were also higher in nonsurvivors, this difference did not reach statistical significance (Table 4). In multivariate analyses, PELOD score was the only independent predictor of mortality.

DISCUSSION

This is the first study examining the negative effects of FO in critically ill children *not* requiring RRT. We investigated the impact of FO on pulmonary dysfunction as measured by severity of hypoxemia in a tertiary care PICU setting. We demonstrated that increasing FO during

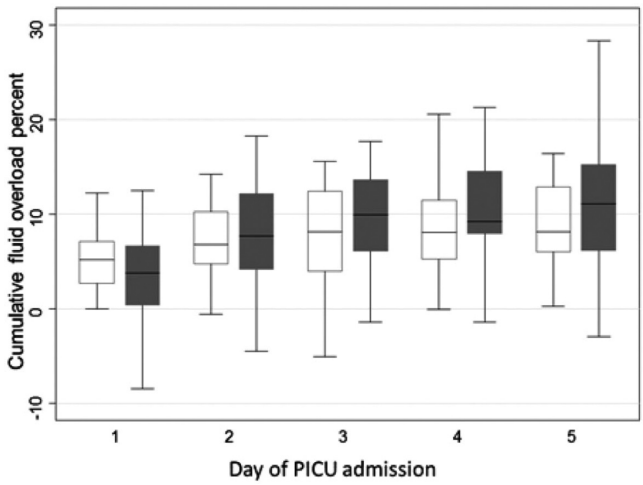

Figure 2. A representative graph of total fluid overload percent in the first 5 days of pediatric intensive care unit (*PICU*) admission stratified by oxygenation index (OI). Graph only includes data from the patients who had data for all 5 days. *Open boxes* represent patients with OI less than the median OI of the cohort (OI <11.5), while *gray boxes* represent patients with OI >11.5. Graph excludes outside values.

Table 2. Univariate and multivariate regression analyzing the association between our major outcomes of interest

Variable	Univariate, Peak OI	Multivariate, Peak OI	Daily Repeated Measures Analysis, Daily OI[a]
Total fluid overload %	$r = .26, p < .02$	$p = .03$	$p = .009$
Pediatric Logistic Organ Dysfunction score	$r = .31, p < .001$	$p = .162$	$p < .001$

OI, oxygenation index.

[a]Examines the association between a particular day's OI and fluid overload, Pediatric Logistic Organ Dysfunction (*daily*) values.

Table 3. Relationship between total fluid overload percent and oxygenation index

Total Fluid Overload %	Regression Coefficient	*p*
2.5%	0.05	.76
5%	0.05	.92
7.5%	0.05	.56
10%	0.08	.38
12.5%	0.10	.16
15%	0.12	.004
17.5%	0.20	<.001
20%	0.31	<.001

As total fluid overload as a percentage of body weight increases, the association with oxygenation index becomes stronger, demonstrating a dose-response relationship. All analyses are controlled for gender, age, Pediatric Logistic Organ Dysfunction score, and respiratory admission. Pediatric Logistic Organ Dysfunction score and female gender remained significantly associated with oxygenation index for all fluid overload percentage cutoff values.

the PICU stay was associated with worsening oxygenation. As predicted, severity of illness also correlated with increased FO. However, when controlled for illness severity using PELOD scores, increasing fluid balance was an independent predictor of worse oxygenation, longer time on the ventilator, and longer length of ICU and hospital stay. While survivors had less pulmonary dysfunction, we were not able to demonstrate an association between mortality and FO.

Our cohort is quite representative of other children with respiratory failure reported in the literature in terms of respiratory parameters and oxygenation failure (21, 22). Our reported mortality rate of 17.5%, although fairly high, is very similar to others reported in children with respiratory failure (23-25). Not surprisingly, we found that FO is common in children with respiratory failure. Patients gained an average of 10% of their initial body weight in the first week of PICU stay, which is comparable to that reported in adults with ALI (7, 8). Fluid balance becomes positive quickly in the critically ill, likely due to initial required resuscitation and increased capillary leak leading to interstitial FO in organs. Patients who are sicker at presentation require more volume for stabilization (13), and early aggressive fluid administration is lifesaving (14, 26, 27). As expected, in our cohort, fluid balance became positive early in the PICU course, and more severely ill patients had greater degrees of FO. Sicker patients stayed in the ICU longer and required longer ventilation. Severity of illness also correlated with oxygenation, with sicker patients having greater impairment in oxygenation.

Many studies have attempted to predict respiratory morbidity and outcome based on the OI, which takes into account mean airway pressure utilized as opposed to Pao_2/Fio_2 ratio and correlates better with mortality (28). In pediatric patients with ALI, OI at admission predicted death and length of mechanical ventilation, with high specificity and sensitivity (10, 29), as well as predicting the development of chronic lung disease in neonates (30). Similarly, in our cohort, peak OI values were two-fold higher in nonsurvivors compared to survivors. Since worsening oxygenation is likely related to underlying severity of illness, we examined this relationship and found that PELOD was associated with OI. However, the significant association between increased FO and worse oxygenation persisted when controlled for PELOD score, suggesting that oxygenation will be impacted negatively by FO regardless of severity of illness.

Several single-center and multicentered pediatric studies have demonstrated that greater degrees of fluid overload at continuous RRT initiation are associated with higher morbidity and mortality (11, 12, 15, 17, 19, 31). Positive fluid balance is thought to contribute to organ dysfunction in different organ systems. Restrictive fluid management strategy in ALI improves oxygenation and lung function without adversely affecting resolution of shock (8). Positive fluid balance also adversely affects survival in critically ill adult patient populations (5, 6, 32–34). Few data exist to determine the effect of fluid balance on pediatric respiratory morbidity. In a pediatric ALI population, Trachsel et al (10) found that the need for RRT was independently associated with a longer time to extubation. Randolph et al (9) reported that cumulative FO was not associated with duration of weaning in pediatric patients. However, patients on the ventilator more than 7 days (the "high-risk" group) weaned from mechanical ventilation without a specified protocol, had significantly greater positive fluid balance and significantly longer times to extubation (9). Our

Table 4. Comparison of survivors versus nonsurvivors

Variables	Survivors, n = 66 Mean ± SD	Nonsurvivors, n = 14 Mean ± SD	*p*
Peak total fluid overload %	13.7 ± 10.0	15.9 ± 10.3	.45
Peak oxygenation index	16.6 ± 17.6	31.5 ± 29.6	<.05
Admission Pediatric Logistic Organ Dysfunction Score	18.2 ± 7.6	20.9 ± 9.5	.01

study population was similar to that "high-risk" group in that most patients required mechanical ventilation for greater than 7 days and no weaning protocols were used, and similar to what was reported by Randolph et al (9), we found that positive fluid balance was associated with duration of ventilation and PICU and hospital LOS. In a more clinically relevant context, total FO%, assessed daily, predicted the OI for that day. Furthermore, a dose-response relationship was observed where, as FO% increased to 15% and greater, the association became stronger, suggesting that there is a threshold value beyond which implementation of interventions to reduce or prevent further FO might be beneficial for improving patient outcome (12, 19). Although severity of illness was also correlated with OI, we are the first to report that the association between positive fluid balance and worsening oxygenation was independent of severity of illness.

In all of the pediatric acute kidney injury (AKI) studies referred to above, increased mortality and/or morbidity was observed when FO crossed the 10%–20% threshold before initiating continuous RRT. As a result, a novel concept has been proposed where worsening FO ⩾15% itself is viewed as a marker of severe AKI, which should guide initiation of RRT to prevent worsening fluid accumulation (36). The current guidelines for management of septic shock in children call for intervention for fluid removal beyond 10% fluid overload with diuretics or intra- or extracorporeal RRTs (37). Our study's finding of an association of worsening OI with FO [mtequ]15% offers, for the first time, a potential physiologic rationale for using FO to guide RRT initiation irrespective of presence AKI or conservative fluid management in children. FO has emerged as a preventable or treatable risk factor for critically ill patients who have recovered hemodynamic stability. In all reported studies, the association between increased FO and worse outcomes is independent of severity of illness, suggesting that FO is an independent contributor to pathogenesis of multiorgan dysfunction as opposed to simply a marker of disease severity. Currently, neither severity of illness nor mortality predictor scoring systems has fluid balance incorporated into their calculation. We suggest that fluid balance, especially when measured by objective parameters, could become another outcome predictor for the critically ill patient.

Our study differs from the other published pediatric studies in the daily evaluation of severity of illness using the PELOD score which, in contrast to the Pediatric Risk of Mortality score (35), has been designed and validated to be a daily indicator of changing severity of illness throughout the PICU course (16). However, since the score itself contains two of the variables used in computing OI and we were not able to investigate potential interactions due to our small sample size, it should be remembered that OI is not completely independent of PELOD, and using PELOD scores to stratify severity of illness is imperfect at its best.

Another strength of our study was the inclusion of all patients with respiratory failure instead of restricting enrollment to those with ALI. The underlying pathogenesis of ALI involves noncardiogenic pulmonary edema and endothelial dysfunction, which by definition makes the fluid management integral to disease management and improved outcome (8). As mentioned, pediatric data regarding the relationship between FO and mortality/morbidity mostly come from studies in patients with multiorgan dysfunction requiring RRT. We chose not to include patients who required RRT and instead to focus on a general PICU population, making our findings more pertinent for any critically ill pediatric patient. We believe that demonstration of a negative impact of fluid balance on pulmonary morbidity in a general population of critically ill patients underscores our findings, making them more applicable to general ICU practice.

We do interpret our findings with caution, since reestablishment of adequate intravascular volume is crucial for successful resuscitation in the face of ongoing intravascular depletion and is necessary for improved patient outcome. The increased morbidity demonstrated with FO in the critically ill refers to the period after stabilization. When that period is achieved could be patient dependent. The question arises then of when to intervene. Based on the available literature and data from the current study, we suggest that a positive fluid balance ⩾15% increases the risk for increased morbidity and pulmonary dysfunction in a general pediatric ICU population. We also realize that there were some patients in our cohort who might have had AKI, since AKI is common and under-recognized in the PICU due to the absence of a widely accepted standardized definition (38); however, our current study was not designed to distinguish this comorbidity. We must be cautious as well, since all reported studies on FO are retrospective or observational and thus clinical management was not standardized. Better tracking of fluid balance with objective parameters that are practical and suitable to use in daily PICU routine and further studies exploring the effect of standardized liberal vs. conservative regimens are needed to answer these questions. Further studies should perhaps prospectively compare restrictive fluid management after stabilization to intervention after a critical value is reached.

There are several limitations to our study. We were not able to ascertain the fluid balance before PICU admission, although this omission would only likely serve to underestimate the degree of FO. Fluid balance, recorded as daily fluid intake and output during the ICU stay, is not very sensitive and can be prone to errors, as has been suggested previously (39-41). Due to the critical condition of many of these patients, tracking an objective parameter like changes in body weight is not always possible. Potential future methods such as electrical bioimpedance measurements, which have been shown to correlate closely with changes in body weight assumed to be due to fluid shifts in critically ill patients, could be a useful tool as an objective measure if validated in children (42–44).

Increasing FO in mechanically ventilated pediatric patients is associated with worsened oxygenation, and lengthened course of mechanical ventilation and PICU and hospital stay, independent of severity of illness. The early *goal* of achieving adequate perfusion through

liberal fluid resuscitation might need to be shifted to the *goal* of attaining or maintaining euvolemia once hemodynamic stability is achieved. Future studies randomizing patients into liberal vs. conservative fluid management strategies may help delineate whether FO truly is a causative factor in oxygenation failure and outcome. Meanwhile, day-to-day bedside practice should include assessment of fluid status as a new vital sign/risk parameter.

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