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Original Article

Fluid overload and length of mechanical ventilation in pediatric sepsis

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Abstract

Background A hospital-based cancer registry can be used as Background Children with sepsis often experience hemodynamic failure and would benefit from fluid resuscitation. On the other hand, critically ill children with sepsis have a higher risk of fluid accumulation due to increased capillary hydrostatic pressure and permeability. Therefore, fluid overload may result in higher morbidity and mortality during pediatric intensive care unit (PICU) hospitalization.

Objective To evaluate the correlation between fluid overload and the length of mechanical ventilation in children with sepsis admitted to the PICU.

Methods Our retrospective cohort study included children aged 1 month-18 years with sepsis who were admitted to the PICU between January 2013 and June 2018 and mechanically-ventilated. Secondary data was extracted from subjects' medical records. Data analyses used were independent T-test and survival analysis.

Results Of 444 children admitted to the PICU, 166 initially met the inclusion criteria. Of those, 17 children were excluded due to congenital heart disease. Subjects' median age was 19 months and median PELOD-2 score was 8. Eighteen children (12.1%) had positive fluid balance in the first 48 hours. Median mechanical ventilation duration was 5 days. Fluid overload was significantly correlated with length of mechanical ventilation (P=0.01) and PICU mortality (RR=2.06; 95%CI 2.56 to 166; P=0.001). Neither length of PICU stay nor extubation failure were significantly correlated to fluid overload.

Conclusion Fluid overload was significantly correlated with length of mechanical ventilation and may be a predictor of mortality in children with sepsis in the PICU. **[Paediatr Indones. 2019;59:211-6; doi: http://dx.doi.org/10.14238/pi59.4.2019.211-6]**.

Keywords: *fluid overload; sepsis; length of mechanical ventilation*

Sepsis is a life-threatening clinical condition frequently faced by PICU pediatricians.[1] The prevalence of sepsis was reported to be 8.2% globally in 2013, with a 15.3% prevalence in Asia.[2,3] Therapeutic approaches to sepsis are comprised of resucitation (including fluid), pathogen eradication, maintaining oxygen delivery, and inflammatory response modification.[4] Increased capillary permeability and changes in oncotic gradient pressure are pitfalls in sepsis management that lead to fluid overload.[5,6] Therefore, fluid administration to sepsis patients either for resucitation or maintenance necessitates careful attention by the physician. Fluid may accumulate in various organs, inducing organ dysfunction. Fluid accumulation in the lung interstitium and alveoli may induce lung edema and ventilation perfusion mismatch. In patients on mechanical ventilation, these conditions may result in prolonged ventilation. Previous studies by Vidal *et al.*[7] and Arikan *et al.*[8] found that fluid overload could extend the length of mechanical ventilation and PICU stay. Fluid overload was also related to

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increased mortality rate in adult sepsis.[9] Hence, we aimed to evaluate for a possible correlation between fluid overload and mechanical ventilation duration in a pediatric sepsis population.

Methods

We conducted a retrospective cohort study and reviewed all children admitted to the PICU of Dr. Sardjito Hospital, Yogyakarta, from January 2013 to June 2018. Children with sepsis who required mechanical ventilation (MV) within the first 24 hours of care and were hospitalized in the PICU for more than 48 hours were included in the study. Those with brainstem death, end-stage renal disease on routine hemodialysis, suspected or confirmed congenital heart disease, or whole body (anasarca) edema were excluded. Subjects were included using consecutive sampling and data regarding basic characteristics, fluid balance, length of MV, length of PICU stay, and mortality were collected from medical records. All children's medical records were reassessed using the Indonesian Pediatric Society criteria for sepsis.[10] The primary outcome in our study was fluid overload percentage (%FO), defined as percentage of fluid balance (difference between fluid input and output) in the first 48 hours divided by body weight on admission. Secondary outcomes were PICU mortality and length of PICU stay. Data analyses were performed with *SPSS 24* software.

This study was approved by the Medical Ethics Committee at Universitas Gadjah Mada.

Results

A total of 444 children with sepsis required mechanical ventilation from January 2013 to June 2018. One hundred and sixty six children met the inclusion

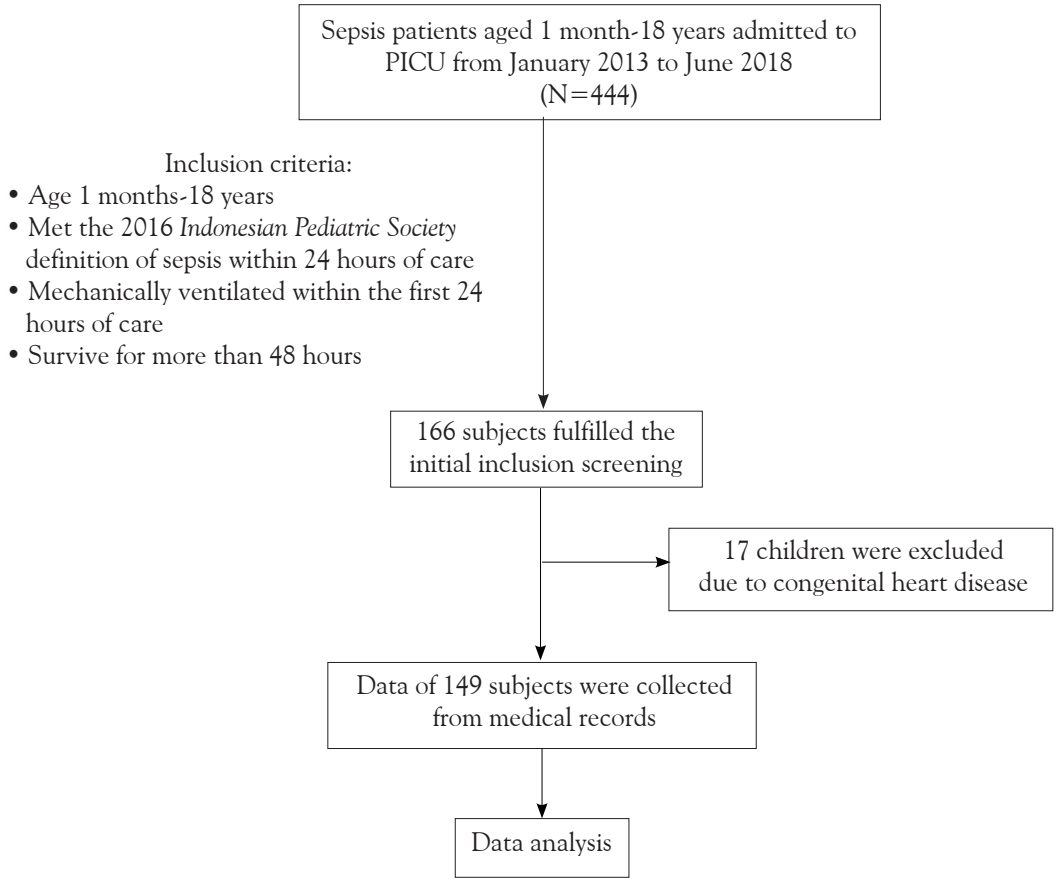

Figure 1. Study plot and sample collection steps

criteria upon initial screening. Of these, 17 children were excluded due to echocardiographically-confirmed congenital heart disease (**Figure 1**). We calculated the first 48 hours cumulative fluid balance and %FO based on fluid administration data and admission weight in subjects' medical records. Basic characteristics of subjects are presented in **Table 1**. Subjects' median age was 19 months, with males predominating (59.7%). Underlying diseases were classified into 9 categories as shown in **Table 1**. Of 33 patients with acute kidney injury, 22 (67%) died. Nevertheless, acute kidney injury was not significantly correlated with mortality in our study (P=0.051). Seventy-six (51%) subjects had chronic illness comorbidities and 45 (59.2)% of them died.

Table 1. Basic characteristics of subjects

Characteristics	(N=149)
Median age (IQR), months	19 (7-84.5)
Median body weight (IQR), kg	9.3 (6.9-18.5)
Median PELOD-2 score (IQR),	8 (7-9)
Male sex, n (%)	89 (59.7)
Underlying disease, n (%)	
Respiratory	54 (36.2)
Neurologic	35 (23.5)
Gastrointestinal	3 (2.0)
Tropical disease	26 (17.4)
Hematooncologic	8 (5.4)
Cardiovascular	2 (1,3)
Immunological	5 (3.4)
Surgical	14 (9.4)
Others	2 (1.3)
Acute kidney injury, n (%)	33 (22.1)
Chronic illness, n (%)	76 (51)

Table 2 presents the outcomes of our study. Many more subjects had <10% FO (131 subjects; 87.9%) than ≥ 10% FO (18 subjects; 12.1%). Median length of mechanical ventilation was 5 days, with the longest duration of 60 days. More than half the patients died in the PICU (77 subjects; 51.7%), mostly from septic shock.

Independent T-test revealed no significant mean difference in mechanical ventilation duration between the two %FO groups (P=0.85) (**Table 3**). Other factors such as age, PELOD-2 score, and types of underlying disease also did not significantly correlate with mechanical ventilation duration.

Survival analysis was performed to analyze the relationship between %FO value and length of mechanical ventilation (**Figure 2**). Subjects who eventually died and those whose actual duration of MV could not be calculated were censored. Mean duration of MV in the ≥ 10% FO group was longer than that of the <10% FO group (56.72 *vs.* 13.41 days) and log rank test revealed a significant mean difference (P=0.01). In the ≥ 10%

Table 2. Outcomes of the study

	(N=149)
% FO	
FO <10%, n (%)	131 (87.9)
FO ≥ 10% body weight, n (%)	18 (12.1)
Median duration of MV, days (IQR)	5 (3.5-9)
Median length of PICU stay, days (IQR)	7 (5-13.5)
Mortality in the PICU, n (%)	77 (51.7)

Table 3. Bivariate analysis of %FO and length of mechanical ventilation

	Mean length of mechanical ventilation, days (SD)	95%CI	P value
% FO		-4.01 to 3.28	0.85
≥ 10%	8 (13)		
< 10%	8 (6)		
Age		-0.50 to 5.16	0.11
< 12 months	9 (10)		
≥12 months	7 (5)		
PELOD-2 score	8 (7)		0.49
Underlying diseases			0.411
Respiratory	9 (9)		
Neurologic	8 (5)		
Gastrointestinal	7 (1)		
Tropical disease	6 (4)		
Hematooncologic	5 (3)		
Cardiovascular	6 (2)		
Immunological	6 (3)		
Surgical	11(10)		
Others	7 (6)		

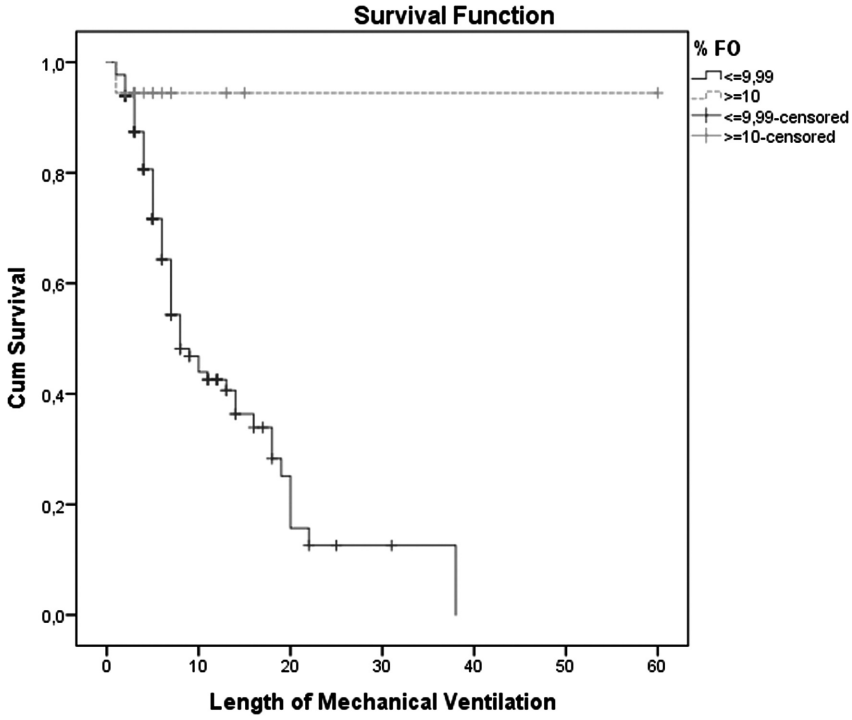

Figure 2. Survival analysis of %FO and MV duration

Table 4. Bivariate analysis of %FO and length of PICU stay

	Mean length of PICU stay, days (SD)	95%CI	P value
% FO		-3.71 to 6.20	0.62
≥ 10%	10 (17)		
< 10%	11 (9)		
Age		0.08 to 6.26	0.04
< 12 months	13 (11)		
≥12 months	9 (8)		
PELOD-2 score	11 (9)		0.46
Underlying diseases			0.52
Respiratory	12 (11)		
Neurologic	11 (10)		
Gastrointestinal	12 (20		
Tropical disease	9 (5)		
Hematooncologic	5 (3)		
Cardiovascular	6 (2)		
Immunological	6 (3)		
Surgical	13 (13)		
Others	11 (11)		

FO group, all but one subject died in the PICU, therefore, the actual total MV duration could not be calculated.

Table 4 shows the bivariate analysis results of %FO and length of PICU stay. Age of <12 months was the only factor significantly correlated to length of PICU stay (P=0.04).

Table 5 presents the whole PICU mortality among subjects based on fluid status, age, PELOD-2 score and underlying disease. Mortality was significantly higher in the ≥ 10% FO group and affected by type of underlying disease. However, which underlying disease that mostly contribute to the mortality could not be furtherly determined.

Table 5. Bivariate analysis of %FO and PICU mortality

	Non-survivor (n=77)	Survivor (n=72)	RR	95%CI	P value
% FO, n(%)			2.06	1.66 to 2.56	0.001
≥ 10%	17 (22)	1 (1.4)			
< 10%	60 (78)	71 (98.6)			
Age, n(%)			0.85	0.61 to 1.19	0.32
< 12 months	26 (33.8)	30 (41.7)			
≥12 months	51 (66.2)	42 (58.3)			
Mean PELOD-2 score (SD)	9 (2)	9 (2)		-0.68 to 0.71	0.96
Underlying diseases					
Respiratory	26 (33.7)	28 (38.9)			0.009
Neurologic	18 (23.4)	17 ((23.6)			
Gastrointestinal	0 (0)	3 (4.2)			
Tropical disease	8 (10.4)	18 (25.0)			
Hematooncologic	6 (7.8)	2 (2.8)			
Cardiovascular	2 (2.6)	0 (0)			
Immunological	5 (6.5)	0 (0)			
Surgical	10 (13.0)	4 (5.5)			
Others	2 (2.6)	0 (0)			

Discussion

Patients in the PICU are susceptible to fluid overload following intravenous fluid administration or deterioration during critical illness. Sepsis and multiple organ failure increase the risk of fluid overload-related complications due to glycocalyx breakdown and pre-existing organ dysfunction.[5]

We studied children aged 1 month to 18 years with sepsis and who were mechanically ventilated. Their median age was 19 months, with male predominance (89 males; 59.7%). The main underlying diseases found in our subjects were respiratory, especially community-acquired pneumonia (36.2%), followed by neurological problems and tropical infections (23.5% and 17.4%, respectively). The respiratory system is the most common infection site found in pediatric sepsis globally.[2] A total of 76 (51%) subjects had chronic illness comorbidities, of whom 59.2% eventually died. Unsurprisingly, previous study by Hartman et al. also figured out that septic children with pre-existing chronic illness had higher risk of mortality compared to previously healthy children (10.5% vs. 8.1%, respectively; P<0.001).[1]

Survival analysis revealed a significant mean difference in mechanical ventilation duration between the two %FO groups, with log rank P value of 0.01 (**Figure 2**). The longest duration of mechanical ventilation was in the ≥10% FO group. This finding was consistent with previous study witheld by Arikan *et al.*[8] which showed that fluid overload was independently correlated with longer duration of MV in children with critical illness (HR 0.95; 95%CI 0.92 to 0.98; P=0.004). Other factors such as age, PELOD-2 score, and underlying disease had no significant correlations with MV duration.

A previous study reported a significant correlation between fluid overload in the first 24 hours of care and mortality in 202 subjects (OR 1.22; 95%CI 1.12 to 1.33; P<0.001).[11] Fluid overload of ≥ 10% was also significantly predictive of mortality in our subjects. Although the length of PICU stay seemed shorter in ≥10% FO group, independent T-test revealed no significant difference between the 2% FO groups. On the contrary, Arikan et al. found that fluid overload >15% was strongly related with longer PICU stay.[8] Koonrangsesomboon *et al.*[12] also found that mean fluid balance in the first 72 hours after septic shock was independently related to ICU length of stay and mortality. In our study, age was the only independent factor predictive of length of PICU stay, with longer duration in the <12-month age group. This finding was consistent with a study by Nupen *et al.*[13] which found that younger age was significantly related to longer duration of PICU stay (P=0.03).

Various studies have been performed to identify correlations between fluid overload and length of mechanical ventilation in critically ill patients.[7,8] Our study

measured similar variables in a more specific population, i.e., critically ill patients who were clinically proven to have sepsis. The limited sample size and risk of inaccurate recording of fluid input and output during PICU admission bias were limitations of our study. However, all fluid administration data collected from medical records were recalculated to minimize any risk of bias. In conclusion, fluid overload in pediatric sepsis significantly correlates with length of mechanical ventilation and PICU mortality, but not with length of PICU stay.

Conflict of Interest

None declared.

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