The Role of Focused Echocardiography in Optimizing Lactate Clearance in the First 3 h of Pediatric Sepsis Resuscitation

by Yos Kowara

Original Article

The Role of Focused Echocardiography in Optimizing Lactate Clearance in the First 3 h of Pediatric Sepsis Resuscitation

Yos Kowara, Arie Utariani, Bambang Pujo Semedi, Elizeus Hanindito

Department of Anesthesiology and Intensive Care, Faculty of Medicine, Universitas Airlangga – Dr Soetomo General Hospital, Surabaya, East Java, Indonesia

Abstract

Background: Sepsis causes high morbidity and mortality in pediatric patients globally. Early shock diagnosis and management are important to determine patient survival. Fluid boluses, early inotropic, and vasopressor usage are the keys to improve lactate clearance. Echocardiography helps both determining the type of shock and selecting the hemodynamic therapies. **Patients and Methods:** A quasi-experimental with one group posttest only design was conducted on 23 pediatric patients who were treated in the resuscitation room of Dr. Soetomo Hospital Surabaya. Patients who met the inclusion and exclusion criteria became the research sample and resuscitated, according to the 1-h sepsis bundle. Patients' hemodynamic status was assessed by echocardiography, and their early blood lactate was checked. Therapies such as fluid adequacy maintenance, cardiac contractility optimization, and vasopressor administration were given according to the type of shock. On the 3rd h, evaluation of clinical improvement, lactate level, and the posttherapy echocardiography were done. **Results:** As many as 39% of the patients suffered normotension cold shock, 26% with hypotension cold shock, 9% with normotension warm shock, and the rest 26% with hypotension warm shock. Echocardiographic-guided hemodynamic therapy statistically significantly improved the patient's volume status, contractility, and vascular resistance ($P < 0.05$). Reversal of shock within the first 3 h, which were derived from clinical improvement and echocardiography measurement, was statistically significantly correlated with >10% lactate clearance ($P = 0.001$; $r = 0.558$). **Conclusion:** Focused echocardiography was effective in evaluating the hemodynamics and lowering the clearance of lactate of pediatric patients with septic shock.

Keywords: Echocardiography, hemodynamic, lactate clearance, pediatric, septic shock

Introduction

Sepsis causes high morbidity and mortality rate in pediatric patients. The prevalence of septic shock and severe sepsis among hospitalized pediatric patients varies from 1% to 26%, with a 5% mortality rate in the developed countries, and up to 35% in the developing countries.[1] A global study that compared hospitals with adequate and limited resources showed no difference in mortality rate (25%).[2] Among them, 67% of sepsis patients experienced multi-organ dysfunction, and 17% of those who survived had moderate disabilities. In 2015, Cipto Mangunkusumo Hospital in Indonesia reported that as many as 19.3% of the 502 pediatric sepsis patients had a mortality rate of 54%, with the highest incidence at the 1st year of age.[3]

Early recognition, adequate fluid resuscitation, and administration of antibiotics are a series of actions that must be carried out within the 1st h of sepsis.[4,5] The 2017 American College of Critical Care Medicine/Pediatric Advanced Life Support (ACCM/PALS) guidelines are still in line with the 2014 targets: Central venous oxygen saturation and Cardiac Index (CI) goals need to be achieved in this golden period.[6] Normalization of blood pressure and returning capillary refill time to <3 s in the early hours using vasoactive drugs have succeeded in reducing the mortality rate from 39% to 12%.[7]

Initial standard therapy in pediatric patients with sepsis is based on the data from adult studies. Patients in a state of shock receive 60 ml/kg of fluid in the first 15 min. The Fluid

Address for correspondence: Dr. Arie Utariani,
Department of Anesthesiology and Intensive Care, Faculty of Medicine,
Universitas Airlangga – Dr Soetomo General Hospital,
Mayjend Prof. Dr. Moestopo Street No. 6-8, Airlangga, Gubeng,
Surabaya, East Java 60285, Indonesia.
E-mail: arie.utariani@fk.unair.ac.id

Submitted: 07-Apr-2020 **Revised:** 02-May-2020
Accepted: 23-May-2020 **Published:** 18-Jul-2020

How to cite this article: Kowara Y, Utariani A, Semedi BP, Hanindito E. The role of focused echocardiography in optimizing lactate clearance in the first 3 h of pediatric sepsis resuscitation. Bali J Anaesthesiol 2020;4:109-14.

Access this article online

Quick Response Code:

Website: www.bjoaonline.com

DOI: 10.4103/BJOA.BJOA_43_20

Expansion As Supportive Therapy (FEAST) study showed a higher mortality rate within 48 h of fluid administration in critically ill children with poor perfusion.[8] Gelbart *et al.*[9] showed the results of a systematic study in both randomized and nonrandomized studies and did not reveal reliable evidence to recommend aggressive fluid therapy. Some practitioners believe that the guidelines which have been used so far can be used in developed countries with strict and invasive monitoring.[10]

Additional hemodynamic examinations will certainly help to guide practitioners to be more precise in establishing the diagnosis and providing appropriate management. However, reports on the effectiveness of echocardiography are still minimal.[10,11] Echocardiography, which is conducted simultaneously with resuscitation, is an important noninvasive tool to overcome the limitations of clinical examination in diagnosing the various categories of septic shock in pediatrics.

Through echocardiography-guided volume infusion, 96% of patients survived from shock condition, and 91% were discharged from the hospital.[12] In pediatric patients with sepsis, the focused bedside echocardiography usage provides crucial information that is not apparent by the clinical assessment. Focused echocardiography also helps the clinicians in determining the cause of low cardiac output in patients with intractable shock conditions despite rigorous fluid administration and inotropic support.

Patients and Methods

This was a quasi-experimental with one group posttest only design, which evaluated all pediatric patients who were admitted to the resuscitation room of Dr. Soetomo General Hospital (Surabaya, Indonesia) from February to April 2019. All patients who were admitted in this unit were classified into blue triage tags according to Canadian triage criteria. The Hospital Ethics Commission of Dr. Soetomo General Hospital has approved this study.

The inclusion criteria include age 2 months to 18 years with sepsis suspicion who met 3 out of 8 clinical signs criteria of the 2017 ACCCM-PALS standard.[6] During the 1st h, the patient received standard oxygenation therapy, either with oxygen supplementation or endotracheal intubation with controlled ventilation for patients who were prone to have respiratory failure. They also had empiric antibiotic therapy and rapid crystalloid fluid infusion through intravenous or intraosseous route, with dosing based on their body weight. Complete blood count and lactate level ($lactate_1$) were also measured within the 1st h. The patients would receive vasoactive agents when they show the signs of fluid-resistant shock to raise their blood pressure. The exclusion criteria include major congenital cardiac abnormalities, intracardiac shunt, pediatric logistic organ dysfunction score <10, initial lactate level <2 mmol/L, and history of other underlying diseases such as dengue shock syndrome, intoxication, malaria, or malignancy.

After the 1st h, a focused echocardiographic examination was performed to assess the patient's fluid adequacy, cardiac contractility, and systemic vascular resistance (SVR). Fluid adequacy was assessed based on the inferior vena cava (IVC) diameter and its collapsibility, which is useful to estimate the right atrial pressure (RAP). Contractility was measured by calculating CI through the diameter of the aorta and the velocity-time integral calculation of the aortic output. Systemic Vascular Resistant Index (SVRI) calculation was conducted with a formula: $(80 \times [MAP - RAP])/CI$.

Based on the results of focused echocardiography and the patient's clinical condition, septic shock was divided into four categories: (1) cold shock with normotension, (2) cold shock with hypotension, (3) warm shock with normotension, or (4) warm shock with hypotension. This classification would determine whether the patient still needed more fluids, inotropic, or vasoconstrictor. Finally, lactate was taken again at the 3rd h ($lactate_3$) to calculate the lactate clearance using this formula: $([Lactate_1 - Lactate_3)/Lactate_1) \times 100\%$. This study outcome was the lactate clearance improvement, which was achieved when the lactate clearance was >10% of the initial lactate.

Statistical analysis was performed using the The IBM SPSS® software SPSS software version 20. Samples distribution was carried out by the Kolmogorov–Smirnov test. Continuous variables were written in the mean ± standard deviation, and categorical variables were expressed in absolute numbers and percentages (%). A comparison between improved lactate clearance group and not improved lactate clearance group was performed with the Mann–Whitney test or simple *t*-test for continuous variables, and Chi-square test or Fisher's exact test for categorical variables. Two-tailed $P < 0.05$ was set as a standard of significance.

Results

Table 1 described subjects based on shock classification (cold or warm) along with normal blood pressure or with low blood pressure. The highest frequency was found in cold shock with normal blood pressure, followed by cold shock with low blood pressure and warm shock with low blood pressure. The highest frequency based on the age group was in the range of 2 months to 1 year (52.2%), with the lowest frequency was on the age group of 12 years–18 years. The average volume of crystalloid given in the group with nonimproving lactate clearance was 18 ml/kg body weight, whereas in the improved lactate clearance group was 26 ml/kg body weight [Table 2].

Echocardiographic utilization was important to measure whether there was an improvement in echocardiographic results between the initial examination at the 1st h and the final examination at the end of resuscitation hours. In this case, focused echocardiographic examination will observe three conditions: Volume adequacy [Table 3], cardiac contractility [Table 4], and SVR [Table 5]. The echocardiography analysis result of these three parameters was combined with the

Table 1. Profile of resuscitative efforts, echocardiography results and patient outcome based on shock profile

Parameters observed	Cold Shock, *n*(%)		Warm Shock *n*(%)	
	Low BP	Normal BP	Low BP	Normal BP
Incidence	9	6	2	6
Echo Results after First Hour Resuscitation				
Inferior vena cava				
Collapse	7 (78.8)	4 (66.7)	0 (0)	3 (50)
Normal	0 (0)	2 (33.3)	2 (100)	2 (33.3)
Overload	2 (21.2)	0 (0)	0 (0)	1 (16.7)
Systolic				
Normal	5 (55.6)	2 (33.3)	1 (50)	3 (50)
Dysfunction	4 (44.4)	4 (66.7)	1 (50)	3 (50)
Peripheral vascular resistance				
Low	0 (0)	0 (0)	1 (50)	6 (100)
Normal	5 (55.6)	6 (100)	1 (50)	0 (0)
High	3 (44.4)	0 (0)	0 (0)	0 (0)
Post-resuscitation echo recommendation				
Fluid bolus	7 (77.8)	5 (83.3)	0 (0)	3 (50)
Inotropic	7 (77.8)	5 (83.3)	1 (50)	4 (66.7)
Vasopressor	0 (0)	1 (16.7)	0 (0)	6 (100)
Outcome				
Clinical improvement	9 (100)	5 (83.3)	1 (50)	6 (100)
48-hours survival	7 (77.8)	5 (83.3)	1 (50)	2 (33.3)

BP: blood pressure

patient's clinical condition (the warmth of extremities, cardiac resynchronization therapy, pulse, systolic pressure, awareness, urine production according to age and weight) to conclude whether there was an overall improvement or not. The combined analysis results were then compared with lactate clearance improvement to analyze the impact of focused echocardiography utilization and the serum lactate clearance improvement [Table 6].

Shock improvement is defined as the improvement of clinical condition (warmth of extremities, CRT, pulse, systolic pressure, consciousness, urine production based on age and body weight) and echocardiographic improvement.

Discussion

The incidence of cold shock was higher than the warm shock, which corresponds to the pathophysiological stages of sepsis in pediatrics.[13] The early stage of pediatric sepsis begins with impaired perfusion, which is caused by relative hypovolemia due to the reduction of the Stroke Volume Index and CI. The second stage of pediatric sepsis is marked with myocardial dysfunction, without any sign of decrease SVRI. At this stage, the condition may vary on the occurrence of peripheral vasodilation. However, a good cardiac contractility is capable of compensating for this condition. At the advanced stage, cardiac contractility disorders and severe peripheral vascular disorder occur.[14] This is in line with the survival rate in the first 48 h, which got worse (33.3%) at the stage of warm shock with hypotension. The 48-h survival rate in patients with cold shock was quite high (77.8%–83.3%) because they were still in the early stages of sepsis.

Exogenous administration of catecholamines was the lowest in cold-shock patients (20%) and highest in warm-shock patients (62.5%). This condition might happen because patients with warm shock and hypotension do not respond to a fluid bolus. Most crystalloid boluses were given at 20–40 ml/kg.[15] These were certainly different from the ACCM standard. ACCM recommends fluid administration of 60 ml/kg in the 1st h if there are neither rhonchi in the lungs nor enlarging liver.[16]

As many as 13%–25% of patients were not given fluid bolus due to the presence of fluid overload signs (frothy pink sputum and bilateral rhonchi). The fluid administration variation is basically caused by the "zero" point that varies for each patient.[15] This study was in line with the FEAST study that administered as much as 20–40 ml/kg, either using crystalloid boluses or albumin.[8]

Echocardiography results focused on four main signs: IVC diameter and collapsibility, systolic dysfunction on both left and right ventricles, diastolic dysfunction, and peripheral vascular dysfunction.[17] In cold shock, there were 66.7%–78.8% of patients with collapsed IVC. In contrast to patients with cold shock, there was no collapsed IVC in normotension patients with warm shock, and there were 50% collapsed IVC incidence in hypotension patients with warm shock.

The incidence of fluid overload was 16.7%–22.2%. Previous studies also revealed a very different variation in IVC collapsibility, namely 25% in cold shock with normotension and 83% in cold shock with hypotension, and 29% in warm shock with normotension and 80% in warm shock with hypotension.[16] The great variation shows how important it is to use echocardiography to decide on the administration of fluid

Table 2: Patient demographics based on lactate clearance

Parameter	Variable	Lactate clearance not improved (%)	Lactate clearance improved (%)	*P*
Sex	Male	1 (4.3)	12 (52.2)	0.281*
	Female	3 (13.0)	7 (30.4)	
Age	Mean (months)	50.5±48.47	42.89±55.16	0.371**
BSA	Mean (m^2)	0.47±0.13	0.54±0.33	0.903**
Initial diagnosis	Respiratory infection	3 (13.0)	12 (52.2)	0.453*
	Postarrest/near arrest	1 (4.3)	2 (8.7)	
	Meningo/encephalitis	2 (8.7)	8 (34.8)	
	Abdominal infection	2 (8.7)	9 (39.1)	
	Urinary tract infection	1 (4.3)	2 (8.7)	
Initial clinical parameters	Heart rate (x/minute)	180±42.43	162.58±29.41	0.328*
	Systolic BP (mmHg)	58.75±22.11	85.58±33.61	0.145*
	MAP (mmHg)	31±26.15	57.63±23.88	0.059*
Shock type	Cold - Normotensive	1 (4.3)	8 (34.8)	0.892*
	Cold - Hypotensive	2 (8.7)	5 (21.7)	
	Warm - Normotensive	0 (0)	1 (4.3)	
	Warm - Hypotensive	1 (4.3)	5 (21.7)	
First-hour resuscitation	Intubation	3 (13.0)	18 (78.3)	0.324*
	Antibiotics	1 (4.3)	18 (78.3)	0.067*
	Vasopressor	2 (8.7)	5 (21.7)	0.557*
Fluid administration	Volume in first hour (ml/kg)	17.5±20.62	26.32±14.23	0.502**
Initial prognosis	PELOD score	34±14.90	25.74±9.29	0.159*
	Initial lactate (mmol/L)	2.08±2.25	3.62±3.71	0.224**
Echocardiography measurements	IVC (cm)	0.65±0.24	0.54±0.44	0.136**
	Collapsibility (%)	53.5±24.35	68.5±32.57	0.284**
	SI (ml/m^2)	26.17±9.57	30.39±10.00	0.449*
	CI (ml/m^2/mnt)	3.88±0.85	4.36±1.33	0.598**
	SVRI (d.s/cm^5/m^2)	949.68±248.71	1134.98±400.99	0.389*

**t*-test, **Mann–Whitney test. SVRI: Systemic Vascular Resistant Index, CI: Cardiac Index, SI: Stroke Index, IVC: Inferior vena cava, MAP: Mean arterial pressure, BP: Blood pressure, BSA: Body surface area, PELOD: Pediatric logistic organ dysfunction

Table 3: Volume adequacy test based on echocardiography results

Volume status 1 h resuscitation	Volume status after 3 h resuscitation (%)			*P**
	Inadequate	Adequate	Overload	
Inadequate	2 (13.3)	13 (86.7)	0	0.001
Adequate	0	4 (80)	1 (20)	
Overload	0	0	3 (100)	

*Chi-square test. Inadequate volume status: Estimated RAP <5 mmHg, Adequate: Estimated RAP 5–15 mmHg, Overload: Estimated RAP >15 mmHg. RAP: Right atrial pressure

Table 4: Contractility test based on echocardiography results

Contractility after 1 h resuscitation	Contractility 3 h after resuscitation (%)		*P**
	Inadequate	Adequate	
Inadequate	6 (40)	9 (60)	0.004
Adequate	0	8 (100)	

*McNemar test. Inadequate contractility: SVI <40 ml/m^2 or CI <3.3 ml/m^2/min, Adequate: SVI ≥40 ml/m^2 and CI 3.3–6.0 ml/m^2/min. SVI: Stroke volume index

bolus in the following hours. The IVC collapsibility rate found by previous studies varies between 21.1% and 41.4% with the assumption of giving crystalloid fluid in the 1st h as much as 50 ml/kg.[16] Therefore, the Surviving Sepsis Campaign (SSC) Pediatrics recommends giving a maximum of 40 ml/kg with bolus titration of 10–20 ml/kg, but the recommendation grade is still weak, and the level of evidence is low.[15]

In contractility disorders, the average of SI was 29.66 ± 9.85 ml/m^2, which was slightly below the normal value (40–60 ml/m^2). The average of CI was 4.27 ± 1.26 ml/m^2/min, which was still within the normal range (3.3–6.0 ml/m^2/min). This result showed that in pediatric patients, a low SI would be compensated with significant tachycardia to meet the need for CI.[18]

In our study, the SVRI results were within the normal limit (1102.76 ± 380.98 ds/cm^5/m^2). Therefore, inotropic (dobutamine) without any addition of vasopressor was enough to treat our patients. Kawasaki reported that in general, most of the children with community-acquired septic shock presented in cold shock conditions, whereas all the children with hospital-acquired septic shock manifested in warm shock conditions. However, some of the patients in cold shock who were initially commenced on adrenaline would require noradrenaline or

Table 5: Vascular resistance test based on echocardiography results

Vascular resistance 1 h after resuscitation	Vascular resistance 3 h after resuscitation (%)		P*
	Low	Normal	
Low	3 (30)	7 (70)	0.016
Normal	0	13 (100)	

*McNemar test. Low vascular resistance: SVRI <800 ds/cm^5/m^2; normal vascular resistance: SVRI 800–1600 ds/cm^5/m^2. SVRI: Systemic vascular resistant index

Table 6: Correlation between shock improvement and lactate clearance

Shock improvement	Lactate clearance ≤10% (%)	Lactate clearance >10% (%)	P*
Absence	2 (8.7)	0	0.001
Presence	2 (8.7)	19 (82.6)	

*Chi-square test. R=0.558. Shock improvement is defined as improvement of clinical condition (warmth of extremities, CRT, pulse, systolic pressure, consciousness, urine production based on age and body weight) and echocardiographic improvement. CRT: Cardiac resynchronization therapy

milrinone later on. Meanwhile, some of the patients with warm shock who initially responded to noradrenaline would subsequently develop a decrease in the cardiac output.[19] This was in line with various studies in each group of sepsis.[20,21] El-Nawawy used dobutamine and milrinone as an alternative inotropic and combined it with norepinephrine or epinephrine for vasopressors.[11]

Ranjit *et al*. used dobutamine in combination with norepinephrine for patients with cold shock and used dopamine in combination with adrenaline for the warm shock.[12] ACCCM/PALS standard used adrenaline or dopamine as an initial exogenous catecholamine for patients with unclassified and unconfirmed shock conditions.[22] By the use of focused echocardiography, clinicians could choose the most suitable and individualized inotropic or vasopressor for the patient.[23]

Echocardiographic assessment is conducted before and after the resuscitation process. In evaluating fluid adequacy, significant positive results were achieved with the use of echocardiographic guidance ($P = 0.001$). Measurement of IVC and collapsibility index was easy to do and very helpful in assessing whether the patients still needed to take more fluid boluses or even fluid restriction. This finding was in line with the previous study. A total of 12 of 22 patients had uncorrected hypovolemia despite the 60 ml/kg fluid resuscitation protocol, either accompanied by myocardial dysfunction or not.[16] Fluid overload also increased the patient's morbidity and mortality rate. The use of echocardiography will be very helpful in guiding the administration of fluid therapy of pediatric patients with sepsis. Studies conducted in 90% of pediatrics with sepsis showed fewer fluid overload events in echocardiographic-guided patients (11%) compared to the standard therapy group (44%).[11]

Significant contractility assessment using echocardiographic was very helpful in improving the patient's CI ($P = 0.004$). The CI results were also used to calculate the SVRI representing the patient's vascular system. Vascular comparisons of patients before and after the resuscitation process, with the help of echocardiography, showed significant results ($P = 0.016$). Classification of cold or warm shock based on the clinical course only causes bias results and errors in determining the most appropriate therapy. A study reported that echocardiography use led to an earlier administration of dobutamine, which in turn led to a better outcome compared to those whose echocardiography was not performed.[11]

Ranjit *et al*.[16] showed that 7 of 10 patients with cardiac dysfunction had significantly better cardiac function with echocardiography guided treatment. Raj *et al*.[20] found that 37% of pediatric patients with sepsis had systolic dysfunction, whereas 33% of them had diastolic dysfunction, and the other 17% of them had both.

This study showed clinical improvement of 91% patients based on the echocardiography evaluation, clinical improvement of the five sepsis signs, and urine production. The results were in line with what was done in the previous studies using echocardiography, which showed a high percentage of recovery patients (94.7%–96.6%).[16] Statistical analysis showed a significant correlation between the improvement of shock guided by echocardiography on lactate clearance >10% with a value of sufficient correlation. Of course, improvement in lactate clearance was not only caused by hemodynamic improvement, but also improvement in hypoxemia, administration of antibiotics, and actions to reduce oxygen consumption (reducing fever and sedation). Previous studies showed a survival rate of 73% in all 12 patients. With the use of focused echocardiography, it has been shown to produce a high survival rate and rapid recovery from shock (<3 h).[11] Focused echocardiography also provides objective data to determine detailed hemodynamic conditions that cannot be assessed only by physical examination (perfusion, pulsation, and peripheral blood pressure).

The study has some limitations. The pathophysiology of sepsis certainly develops based on the age groups. More specific age classification will correspond better with the pathophysiology of shock based on the pediatric category. Another limitation is the ethical problem, which makes it inappropriate to divide the sample population into two groups where echocardiography was not performed in one group. This study contributes as an initial study whether the use of focused echocardiography is useful for reducing lactate clearance.

Conclusion

Focused echocardiography usage helps clinicians in analyzing hemodynamic parameters (IVC diameter and collapsibility, stroke index and CI, and calculation of SVRI) and determining the type of septic shock which could help in choosing the most appropriate therapeutic approach in pediatric sepsis patient.

Effective usage of focused echocardiography also improved the patient's lactate clearance after the 3-h initial resuscitation.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

References

1. de Souza DC, Machado FR. Epidemiology of pediatric septic shock. J Pediatr Intensive Care 2019;8:3-10.
2. Weiss SL, Fitzgerald JC, Pappachan J, Wheeler D, Jaramillo-Bustamante JC, Salloo A, *et al*. Global epidemiology of pediatric severe sepsis: The sepsis prevalence, outcomes, and therapies study. Am J Respir Crit Care Med 2015;191:1147-57.
3. Wardhana A, Djan R, Halim Z. Bacterial and antimicrobial susceptibility profile and the prevalence of sepsis among burn patients at the burn unit of Cipto Mangunkusumo Hospital. Ann Burns Fire Disasters 2017;30:107-15.
4. Loncarica DK, Fustiñana A, Jabornisky R. Recommendations for the management of pediatric septic shock in the first hour. Arch Argent Pediatr 2019;117:e24-33.
5. Chong SL, Ong GY, Venkataraman A, Chan YH. The golden hours in paediatric septic shock – Current updates and recommendations. Ann Acad Med Singapore 2014;43:267-74.
6. Davis AL, Carcillo JA, Aneja RK, Deymann AJ, Lin JC, Nguyen TC. American College of critical care medicine clinical practice parameters for hemodynamic support of pediatric and neonatal septic shock. Crit Care Med 2017;45:1061-92.
7. Carcillo JA, Han YY, Kissoon N. Sepsis guidelines and the global pediatric sepsis initiative: Implications for treatment. Therapy 2008;5:391-4.
8. Maitland K, Kiguli S, Opoka RO, Engoru C, Olupot-Olupot P, Akech SO, *et al*. Mortality after fluid bolus in African children with severe infection. N Engl J Med 2011;364:2483-95.
9. Gelbart B, Glassford NJ, Bellomo R. Fluid bolus therapy-based resuscitation for severe sepsis in hospitalized children: A systematic review. Pediatr Crit Care Med 2015;16:e297-307.
10. Frazier WJ, Muszynski JA. Fluid resuscitation in pediatric sepsis: Lack of data versus lack of equipoise. Pediatr Crit Care Med 2015;16:789-90.
11. El-Nawawy AA, Abdelmohsen AM, Hassouna HM. Role of echocardiography in reducing shock reversal time in pediatric septic shock: A randomized controlled trial. J Pediatr (Rio J) 2018;94:31-9.
12. Ranjit S, Aram G, Kissoon N, Ali K, Natraj R, Shresti S, *et al*. Multimodal monitoring for hemodynamic categorization and management of pediatric septic shock: A pilot observational study. Pediatr Crit Care Med 2013;15:17-26.
13. Martin K, Weiss SL. Initial resuscitation and management of pediatric septic shock. Minerva Pediatr 2015;67:141-58.
14. Deep A, Goonasekera CD, Wang Y, Brierley J. Evolution of haemodynamics and outcome of fluid-refractory septic shock in children. Intensive Care Med 2013;39:1602-9.
15. Weiss SL, Peters MJ, Alhazzani W, Agus MS, Flori HR, Inwald DP, *et al*. Surviving sepsis campaign international guidelines for the management of septic shock and sepsis-associated organ dysfunction in children. Intensive Care Med 2020;46:10-67.
16. Ranjit S, Kissoon N. Bedside echocardiography is useful in assessing children with fluid and inotrope resistant septic shock. Indian J Crit Care Med 2013;17:224-30.
17. Perera P, Mailhot T, Riley D, Mandavia D. The RUSH Exam: Rapid ultrasound in shock in the evaluation of critically ill. Emerg Med Clin North Am 2010;28:29-56.
18. Irawan A, Pradhana AP, Senapathi TG. EGDT modifications using IVC diameter and IVC collapsibility index to provide intravascular adequacy for sepsis management in remote areas. Bali J Anesthesiol 2018;2:1-2.
19. Kawasaki T. Update on pediatric sepsis: A review. J Intensive Care 2017;5:47.
20. Raj S, Killinger JS, Gonzalez JA, Lopez L. Myocardial dysfunction in pediatric septic shock. J Pediatr 2014;164:72-7.
21. Vincent JL, Rhodes A, Perel A, Martin GS, Della Rocca G, Vallet B, *et al*. Clinical review: Update on hemodynamic monitoring – A consensus of 16. Crit Care 2011;15:229.
22. Plunkett A, Tong J. Sepsis in children. BMJ 2015;350:h3017.
23. Seif D, Perera P, Mailhot T, Riley D, Mandavia D. Bedside ultrasound in resuscitation and the rapid ultrasound in shock protocol. Crit Care Res Pract 2012;2012:503254.

The Role of Focused Echocardiography in Optimizing Lactate Clearance in the First 3 h of Pediatric Sepsis Resuscitation

ORIGINALITY REPORT

13%	10%	11%	2%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	eprints.kaums.ac.ir Internet Source	2%
2	Submitted to Universitas Airlangga Student Paper	2%
3	preview-jintensivecare.biomedcentral.com Internet Source	1%
4	Pediatric and Congenital Cardiology Cardiac Surgery and Intensive Care, 2014. Publication	1%
5	ecommons.aku.edu Internet Source	1%
6	link.springer.com Internet Source	1%
7	colorectalresearch.com Internet Source	<1%
8	Prihatma Kriswidyatomo, Maharani Pradnya Paramitha. "Rapid sequence	<1%

induction/intubation controversies", Hong Kong Journal of Emergency Medicine, 2020
Publication

9	bookstore.acep.org Internet Source	<1%
10	www.frontiersin.org Internet Source	<1%
11	"Full Issue PDF", JACC: Cardiovascular Imaging, 2019 Publication	<1%
12	digitalcommons.wustl.edu Internet Source	<1%
13	bjoa.balijournals.org Internet Source	<1%
14	www.ajol.info Internet Source	<1%
15	Alqahtani, Mashael F., Craig M. Smith, Scott L. Weiss, Susan Dawson, Hantamalala Ralay Ranaivo, and Mark S. Wainwright. "Evaluation of New Diagnostic Biomarkers in Pediatric Sepsis: Matrix Metalloproteinase-9, Tissue Inhibitor of Metalloproteinase-1, Mid-Regional Pro-Atrial Natriuretic Peptide, and Adipocyte Fatty-Acid Binding Protein", PLoS ONE, 2016. Publication	<1%
16	bmcpediatr.biomedcentral.com Internet Source	

		<1%
17	vuir.vu.edu.au Internet Source	<1%
18	"1-B2: Respiratory Infections (Non-Tuberculosis) 2 : Poster Sessions", Respirology, 2013. Publication	<1%
19	Christoph E. Schwarz, Eugene M. Dempsey. "Management of Neonatal Hypotension and Shock", Seminars in Fetal and Neonatal Medicine, 2020 Publication	<1%
20	Joseph A Carcillo. "Sepsis guidelines and the global pediatric sepsis initiative: implications for treatment", Therapy, 07/2008 Publication	<1%
21	jped.elsevier.es Internet Source	<1%
22	pesquisa.bvsalud.org Internet Source	<1%
23	www.ahcmedia.com Internet Source	<1%
24	www.rbti.org.br Internet Source	<1%

25	Gaston N. King, Claire M. Healy, Mary T. Glover, Jonathan T.C. Kwan et al. "Increased Prevalence of Dysplastic and Malignant Lip Lesions in Renal-Transplant Recipients", New England Journal of Medicine, 1995 Publication	<1 %
26	Martin W. Dünser. "Recommendations for sepsis management in resource-limited settings", Intensive Care Medicine, 02/14/2012 Publication	<1 %
27	Ranjit, Suchitra, Gnanam Aram, Niranjan Kissoon, Mhd Kashif Ali, Rajeshwari Natraj, Sharad Shresti, Indira Jayakumar, and Deepika Gandhi. "Multimodal Monitoring for Hemodynamic Categorization and Management of Pediatric Septic Shock : A Pilot Observational Study*", Pediatric Critical Care Medicine, 2014. Publication	<1 %

Exclude quotes	On	Exclude matches	Off
Exclude bibliography	On		

The Role of Focused Echocardiography in Optimizing Lactate Clearance in the First 3 h of Pediatric Sepsis Resuscitation

GRADEMARK REPORT

FINAL GRADE

/100

GENERAL COMMENTS

Instructor

PAGE 1

PAGE 2

PAGE 3

PAGE 4

PAGE 5

PAGE 6