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Cohort Study

Characteristics of hemodynamic parameters after fluid resuscitation and vasoactive drugs administration in pediatric shock: A prospective observational study

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ABSTRACT

Background: Prior studies have shown that septic shock survivors had a normal cardiac index (CI) and systemic vascular resistance index (SVRI). However, this feature seems to be questionable in other-caused shock, since several factors are associated with the hemodynamic profile. This study aims to describe hemodynamic profiles (preload, inotropy, afterload, stroke volume, and cardiac output) after fluid resuscitation and vasoactive therapy in children with shock.

Methods: Children aged 1 month to 18 years old with shock conditions were included in this study. Fluid resuscitation was administered following the American College of Critical Care Medicine (ACCM) protocol. Hemodynamic profiles were assessed at 1 and 6 h from the start of fluid resuscitation. Grouping of the subjects was determined by the USCOM examination in 1st hour until the end of the study and we divided into 3 groups.

Results: At 1 h, group 1 (low CI) was 14% (CI:2.5[1.2–3.2]L/min/m^2), group 2 (normal CI) was 66% (CI:4.2 [3.4–5.8]L/min/m^2), and group 3 (high CI) was 20% (CI:7.1[6.1–9.4]L/min/m^2). SVRI was higher in groups 1 and 2 compared to group 3 ($p < 0.05$). Group 1 and 2 revealed fluid-refractory shock (SVV:25[12–34]% and 29 (13–58)%, respectively), lower Smith-Madigan Inotropy Index (SMII) and higher Potential to Kinetic Ratio (PKR) compared to group 3 ($p < 0.05$). Group 3 revealed fluid-responsive shock (Stroke Volume Variation (SVV):32 [18–158]%), higher SMII and lower PKR. At 6th hour, CI in all groups were normal (group 1:3.5[1.2–7.5]; group 2:4.0[1.7–6.1]; group 3:6.0[3.1–6.2]). However, 71.4% and 54.5% of subjects in groups 1 and 2, respectively, still revealed low inotropy. Group 3 revealed a significant increase in SVRI and PKR ($p < 0.01$).

Conclusions: Most pediatric shock patients were hypodynamic. Even when the CI was normal, the preload, inotropy, and afterload may still be abnormal. It represented the inotropy as a key to hemodynamic.

1. Introduction

Shock is a clinical syndrome caused by the circulation system's failure to fulfill the nutrition and oxygen tissue demand, which causes cell dysfunction and dying. Shock is common in pediatric critical care; with the highest incidence of septic shock (49–65%) and hypovolemic shock (17–31%). The mortality rate ranges from 38 to 55% [1].and can be reduced to 8–22% by adequate treatment. Delay of restoring the shock condition is associated with a 2-fold increase in mortality odds for every hour [2].

An observational study demonstrated higher sepsis survivors having normal cardiac index (CI) and systemic vascular resistance index (SVRI) [3]. CI 3.3–6.0 L/min/m^2 is a therapeutic goal in septic shock and has to be achieved in 6 h [4,5]. However, its relevance is questionable in other forms of shock. Targeting only the CI can be misleading since it is influenced by many factors, namely: stroke volume (SV) and heart rate (HR). As such, SV is regulated by preload, inotropy, and afterload [6].

These basic parameters (preload, inotropy, afterload) seem more reasonable for guiding therapy, instead of the cardiac output. Basically, fluid resuscitation and vasopressor are designated to expand preload, while vasoactive agents increase inotropy and afterload [6].The clinical sign does not always represent the component of hemodynamic disturbance, making clinical-based management tend to be inaccurate. Therefore, the device informing all hemodynamic parameters is

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necessary to guide shock management optimally. Unfortunately, preload, inotropy, and afterload data in children with shock are still lacking. Some CI and SVRI data are provided, but only in the septic shock population [7,8]. We hypothesize the shock condition in children is tend to be hypodynamic and can not be predicted using one certain parameter; thus in this study, we aim to define hemodynamic profiles (preload, inotropy, and afterload level in pediatric shock), after completing fluid resuscitation and vasoactive agents therapy.

2. Methods

2.1. Design, period, and study area

A prospective observational study was conducted from January to September 2014 in an emergency department (ED) and pediatric intensive care unit (PICU), at Dr. Cipto Mangunkusumo General Hospital. Our hospital is located in Jakarta City, Indonesia which is a national referral center and tertiary level pediatric critical care. The study was approved by the institutional ethics committee and all participants' parents or guardians provided an informed written consent. The Research Registry number was stated as 7743. This study has been reported in line with the STROCSS criteria [9].

2.2. Inclusion and exclusion criteria

Inclusion criteria were children, ages 1 month to 18 years old, who have shock condition with any causation. The exclusion criteria were shock children who previously had fluid resuscitation in the last 24 h or had congenital heart disease with a shunt. All children who fulfilled the inclusion criteria were consecutively recruited. Clinical data, including age, gender, anthropometric status, clinical type of shock, and diagnosis, were recorded at the time of entry.

2.3. Sample size determination

Power analysis for one sample *t*-test was conducted in G-POWER to determine a sufficient sample size using an alpha of 0.05, a power of 0.80, a medium effect size (d = 0.5), and two tails [10]. Based on the aforementioned assumption, the desired sample size is 50.

2.4. Description of processes and measurements

Shock was defined as: (1) hypotension or (2) tachycardia with poor perfusion (cold extremities, capillary refill time >2 s, weak peripheral pulses, altered mental status, or oliguria). Hypotension and tachycardia were defined based on pediatric advance life support (PALS) criteria [11]. Oliguria was defined as urine output <1 ml/kgBW/hour for body weight (BW) < 30 kg or <0.5 ml/kgBW/hour for BW > 30 kg.

The therapy was based on hospital protocol, under the provision of the physician, who was not involved in this study. The hospital protocol was adopted from the American College of Critical Care Medicine (ACCM) Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. The recommendation was fluid bolus 20 mL/kg for 5–15 min, could be repeated to 60 mL/kg to achieve therapeutic goals (normal heart/pulse rate and blood pressure according to age, normal perfusion [capillary refill test (CRT), urine output, mental status], serum lactate <2.0 mmol/L, CI 3.3–6.0 L/min/m^2, and SVRI 800–1600 d s/cm^5/m^2). Fluid bolus must be discontinued either if therapeutic goals are achieved, total fluid is 60 ml/kg, or the patient reveals liver enlargement and rales. In persistent shock following ≥60 mL/kg, vasoactive agents are administered. Inotropes (dopamine 5–10 mcg/kg/min, dobutamine 5–20 mcg/kg/min, or epinephrine 0.05–0.3 mcg/kg/min) given in low CI – high SVRI case, can be combined with vasodilator (milrinone 0.5–0.75 mcg/kg/min) if blood pressure is normal. Vasopressor (norepinephrine 0.05–1 mcg/kg/min or epinephrine >0.3 mcg/kg/min) given in high CI – low SVRI case. Inotropes and vasopressors are combined in low CI – low SVRI cases.

Two-time measurements were defined to represent the completion of fluid resuscitation (1st-time point) and vasoactive agent therapy (2nd-time point). The 1st time point was about 1 h after shock recognition and 2nd time point was 6 h after presentation. At the 1st time point, fluid amount and hemodynamic parameters were recorded. At the 2nd time point, the type and dose of vasoactive agent, as well as hemodynamic parameters and clinical outcome were recorded. The baseline (zero hour) value was not recorded due to ethical issues about preventing the delay of therapy. We also recorded mortality at the time of PICU discharge.

2.5. Hemodynamic measurement

We measured hemodynamic parameters by ultrasound hemodynamic monitor (USCOM 1 A, USCOM Pvt Ltd, Coffs Harbor, NSW, Australia), using a suprasternal approach (aortic flow view). Three measurements were performed to obtain the mean value of stroke volume variation (SVV), Smith-Madigan Inotropy Index (SMII), potential to kinetic ratio (PKR), stroke volume index (SVI), CI, and SVRI. Preload was represented by SVV, inotropy by SMII, and afterload by SVRI and PKR. SVV ≤30% was defined as a fluid-refractory, and >30% as fluid-responsive shock. Each parameter of SMII, PKR, and SVI was divided into 3 levels: low, normal, and high, based on normal value for age [12]. Normal CI and SVRI were 3.3–6.0 L/min/m^2 and 800–1600 dyne s.cm^{-5} m^{-2}, respectively; a below-normal value was categorized as low, while an above normal as high [3,5]. A pediatric emergency and intensive care consultant or trained senior-trainee performed all measurements.

3. Statistical analyses

Patient characteristics were described using a frequency table. The subjects were divided into 3 groups of CI: low, normal, and high. In each group, profiles and proportion of preload, inotropy, and afterload, were also analyzed. Data of SVV, SVI, PKR, CI, and SVRI were presented as median (IQR). The alteration of hemodynamic profiles between the 1st and 6th hour was analyzed using Wilcoxon signed-rank test. The differences of hemodynamic profiles between groups were analyzed using the Kruskal-Wallis test, followed by Dunn-Bonferroni nonparametric comparison for the post hoc test. A p-value <0.05 was considered statistically significant. All of the statistical analysis performed with SPSS software version 21 (IBM®, New York, United States).

4. Results

4.1. Subjects characteristic

Fifty patients were included with 25 of them are male. The median age was 35 months (1 month–18 years old). Septic shock was the most (60%) clinical type of shock, due to pneumonia, meningitis, malignancy, and post-surgery condition. The survival rate at PICU discharge was 74% (Table 1). The fluid amount was similar between groups (p = 0.72). The median fluid volume was <40 mL/kg to achieve fluid-refractory condition. There were variations of vasoactive used in each group (Table 1). The most common vasoactive agents in this study were inotropes (dopamine, dobutamine, epinephrine, and milrinone), especially in groups 1 and 2. Vasopressor (norepinephrine) was used in groups 2 and 3. Some combination of inotropes was administered in groups 1 and 2. Grouping of the subjects was determined by the USCOM examination in 1st hour until the end of the study and we divided into 3 groups.

4.2. Hemodynamic profiles after fluid resuscitation and vasoactive drugs administration

Analysis of preload, inotropy, and afterload in each group at the 1st hour, groups 1 and 2 revealed fluid-refractory shock (SVV 25 [12–34]%

Table 1
Subject characteristics.

Characteristics	Proportion
Age, *month median (min - max)*	35 (1–219)
Gender, *n (%)*	
Boys	25 (50)
Girls	25 (50)
Clinical type of shock, *n (%)*	
Septic	32 (64)
Hypovolemic	15 (30)
Cardiogenic	3 (6)
Diagnosis, *n (%)*	
Pneumonia	13 (26)
Diarrhea and enterocolitis	10 (20)
Post-surgical	8 (16)
CNS infection	6 (12)
Malignancy	4 (8)
Dengue Shock Syndrome	3 (6)
Cardiac disease (Kawasaki, myocarditis)	2 (4)
Burn injury	2 (4)
Diabetic Ketoacidosis	1 (2)
Trauma with massive bleeding	1 (2)
Fluid-responsiveness	
Fluid-responsive	21
Fluid-refractory	29
Fluid amount, *ml, median (IQR)*	
Group 1 (low CI)	20 (0–40)
Group 2 (normal CI)	20 (0–60)
Group 3 (high CI)	30 (0–40)
Vasoactive types in non-fluid responder (n = 29), *n (%)*	
Dopamine	4
Dobutamine	7
Milrinone	2
Norepinephrine	4
Combination of inotropes	10
No drugs	2
Outcome of PICU discharge, *n (%)*	
Survivor	37 (74)
Non-survivor	13 (26)

and 29 (13–58]%, respectively), whereas group 3 revealed fluid-responsive shock (SVV 32 [18–158]%). As well, SMII and SVI were lower, and PKR was higher in groups 1 and 2 compared to group 3 ($p < 0.05$). The HR was higher in group 3 compared to group 1 ($p < 0.05$) (Table 2). At the 6th hour, fluid-responsiveness status was not altered in all groups. The CI's in all groups were in normal level (group 1: 3.5 [1.2–7.5]; group 2: 4.0 [1.7–6.1]; group 3: 6.0 [3.1–6.2]). There was an insignificant increase in SMII and SVI in groups 1 and 2. Only group 3 revealed a significant reduction of SVI ($p < 0.01$) along with the increase of SVRI and PKR ($p < 0.01$) (Table 2).

4.3. Various hemodynamic alteration

Based on normal hemodynamic values for age, at 1st hour, all of low CI patients had low SMII, while 6/7 were in fluid-refractory shock and high afterload. In the normal CI group, the majority (19/33) were in fluid-refractory shock; more than half (10/19) had low SMII. In the high CI group, the majority (6/10) were in fluid-responsive shock, and most of them (4/6) had normal SMII. At the 6th hour, 5/7 and 18/33 subjects in groups 1 and 2, respectively, still revealed low SMII (with various afterload levels). Conversely, most subjects in group 3 (6/10) revealed normal SMII along with various afterload levels (Table 3).

5. Discussion

Our study revealed only a few subjects had either low or high CI, while most subjects had normal CI and SVRI following fluid resuscitation. Furthermore, the inotropy level was low in most subjects of the low and normal CI group, which indicated hypodynamic condition in the majority of the pediatric shock population. At the 6th hour, all groups had normal CI; however, in low and normal CI groups, the inotropy was still low or depressed. Only a high CI group revealed normal inotropy (with various levels of afterload).

Table 2
Hemodynamic profiles in each group at 1st and 6th hour after fluid resuscitation and vasoactive drugs administration Data are presented as median (IQR).

Group	Parameters	1st hour	6th hour	p value
Group 1 – Low CI (n = 7)	HR, *per minute*	120 (61–162)[c]	122 (90–165)[c]	0.40
	CI, L/mnt/m^2	2.5 (1.2–3.2)[b]	3.5 (1.2–7.5)[b]	0.52
	SVRI, d.s/cm^5	2579 (1081–4873)[b]	1707 (557–5135)[b]	0.87
	Preload SVV, %	25 (12–34)	32 (18–89)	0.24
	Inotropy SMII, W/m^2 SVI, ml/m^2	1.0 (0.4–1.4)[b] 21 (10–41)[b]	1.2 (0.4–3.7) 24 (14–51)[c]	0.67 0.80
	Afterload PKR	32 (25–128)[b]	31 (12–193)	0.55
Group 2 – Normal CI (n = 33)	HR, *per minute*	140 (91–199)	141 (107–182)	0.70
	CI, L/mnt/m^2	4.2 (3.4–5.8)[b]	4.0 (1.7–6.1)[b]	0.12
	SVRI, d.s/cm^5	1285 (789–2295)[b]	1492 (788–4850)[b]	0.03[a]
	Preload SVV, %	29 (13–58)	25 (13–122)	0.23
	Inotropy SMII, *W/m* SVI, ml/m^2	1.2 (0.8–2.0)[b] 30 (20–49)[b]	1.3 (0.4–2.4) 31 (13–46)	0.99 0.09
	Afterload PKR	31 (11–74)[b]	36 (10–218)	0.14
Group 3 – High CI (n = 10)	HR, *per minute*	170 (133–187)[c]	163 (126–182)[c]	0.50
	CI, L/mnt/m^2	7.1 (6.1–9.4)[b]	6.0 (3.1–6.2)[b]	<0.01[a]
	SVRI, d.s/cm^5	704 (535–1000)[b]	944 (624–1670)[b]	<0.01[a]
	Preload SVV, %	32 (18–158)	33 (22–36)	0.51
	Inotropy SMII, *W/m* SVI, ml/m^2	1.5 (1.2–3.3)[b] 45 (34–60)[b]	1.8 (0.8–2.5) 35 (21–48)[c]	0.20 0.01[a]
	Afterload PKR	16 (9–22)[b]	27 (12–78)	<0.01[a]

[a] Statistically significant between 1st and 6th hour.
[b] Statistically significant between group 1 and 3, also group 2 and 3.
[c] Statistically significant between group 1 and 3, CI = cardiac index, SVV = stroke volume variation, SMII= Smith-Madigan Inotropic Index, SVI = stroke volume index, PKR = potential to kinetic ratio, HR = heart rate.

The results indicated most subjects were hypodynamic, represented the inotropy as a key to hemodynamic. Besides myocardial contractility, inotropy level also influences fluid-responsiveness based on the Frank-Starling curve. The higher inotropy (steeper curve) will give higher stroke volume at the same cardiac preload. The low inotropy is related to impaired myocardial contractility. In pediatric patients, primary myocardial disorders can be found in congenital or acquired heart defects. Meanwhile, secondary myocardial depression is the most existing case due to metabolic disorders, sepsis/infection (including Dengue) [13–18], immune response, or reperfusion injury [19,20].

In our study, most cases needed volume expansion of less than 40 mL/kg (Table 1). It was smaller than recommended by the American College of Critical Care Medicine Task Force Committee Member for the pediatric septic shock [5] and the previous study [21,22]. Using $ScvO_2$ goal-directed therapy, de Olivera et al. revealed less volume is needed to achieve the therapeutic goals at the 6th hour, i.e. 28 (20–40) ml/kg [23]. It indicated therapeutic goals based on advanced hemodynamic measurement may reduce the fluid volume to avoid fluid overload.

One of the therapeutic endpoints is CI 3.3–6.0 L/min/m^2 [4,5] thus, we classified the subjects into three groups: (1) low CI (<3.3 L/min/m^2), (2) normal CI (3.3–6.0 L/min/m^2), and (3) high CI (>6.0 L/min/m^2).

Table 3
Various hemodynamic alteration at 1st and 6th hour after fluid resuscitation and vasoactive drugs administration, according to cardiac index (CI) level at 1st hour. Data are presented as n (%).

1st hour			6th hour	
Cardiac Index (CI)	Fluid responsiveness	Inotropy-Afterload	Fluid responsiveness	Inotropy Afterload
Low (n = 7)	Fluid -refractory (n = 6)	• Low inotropy – high afterload (n = 5) • Low inotropy – normal afterload (n = 1)	Fluid-refractory (n = 3)	• Low inotropy – high afterload (n = 2) • Low inotropy – normal afterload (n = 1)
	Fluid-responsive (n = 1)	• Low inotropy – normal afterload (n = 1)	Fluid-responsive (n = 4)	• Low inotropy – high afterload (n = 2) • Normal inotropy – normal afterload (n = 1) • High inotropy – low afterload (n = 1)
Normal (n = 33)	Fluid -refractory (n = 19)	• Low inotropy – high afterload (n = 5) • Low inotropy – normal afterload (n = 5) • Normal inotropy – low afterload (n = 1) • Normal inotropy – normal afterload (n = 5) • Normal inotropy – high afterload (n = 2) • High inotropy – normal afterload (n = 1)	Fluid-refractory (n = 23)	• Low inotropy – high afterload (n = 11) • Low inotropy – normal afterload (n = 2)
	Fluid-responsive (n = 14)	• Low inotropy – high afterload (n = 9) • Low inotropy – normal afterload (n = 1) • Normal inotropy – high	Fluid-responsive (n = 10)	• Low inotropy – high afterload (n = 4) • Low inotropy – normal afterload (n = 1) • Normal inotropy – normal

Table 3 (*continued*)

1st hour			6th hour	
Cardiac Index (CI)	Fluid responsiveness	Inotropy-Afterload	Fluid responsiveness	Inotropy Afterload
		afterload (n = 1) • Normal inotropy – normal afterload (n = 2) • High inotropy – high afterload (n = 1)		afterload (n = 1) • Normal inotropy – high afterload (n = 2) • High inotropy – low afterload (n = 1) • High inotropy – normal afterload (n = 1)
High (n = 10)	Fluid -refractory (n = 4)	• Normal inotropy – normal afterload (n = 1) • High inotropy – normal afterload (n = 3)	Fluid -refractory (n = 4)	• Low inotropy – high afterload (n = 1) • Normal inotropy – normal afterload (n = 2) • High inotropy – normal afterload (n = 1)
	Fluid-responsive (n = 6)	• Normal inotropy – normal afterload (n = 4) • High inotropy – low afterload (n = 2)	Fluid-responsive (n = 6)	• Low inotropy – high afterload (n = 1) • Normal inotropy – low afterload (n = 1) • Normal inotropy – normal afterload (n = 2) • Normal inotropy – high afterload (n = 1) • High inotropy – high afterload (n = 1)

The majority (66%) of subjects had normal CI and SVRI at the first hour, whereas 20% had high CI - low SVRI, and 14% had low CI - high SVRI (Table 2). A previous observational study in fluid-refractory pediatric septic shock, revealed 80% of children were hypodynamic (low CI - high SVRI), and only 20% were hyperdynamic (high CI - low SVRI) [24]. Similarly, in the septic shock due to community-acquired infection, 83–86% of patients revealed CI < 3.3 L/min/m^2 [24,25].

As expected, at the 1st hour, subgroup analysis of group 1 revealed lower SVV and inotropy, but higher afterload than group 3 (Table 2). Moreover, according to the normal value of age, 85.7% of subjects were non-fluid responders and all patients had low inotropy (Table 3). This group showed myocardial depression, that fluid restriction and

inotropes will be the appropriate treatments [6,26]. Most of the low inotropy conditions are followed by high afterload as a response to CI decrease, through the catecholamines response lead to vasoconstriction or increased SVR. It will maintain blood pressure and distribute blood flow to vital organs (brain, heart, lung, and kidney). This compensation is so effective in children that hypotension often emerges in advanced stages of shock [8,20].

On the contrary, in group 3, SVV and inotropy were higher and afterload was lower than group 1 and 2 (Table 2). Also, the median heart rate was 170 times *per* minute, which is higher than other groups ($p < 0.05$). This group revealed a vasodilatory mechanisms that leads to relative hypovolemia condition. Tachycardia was compensation to increase CI and maintain blood pressure. Moreover, the higher inotropy preserves the optimal stroke volume. Since SVV was higher (indicating fluid-responder) and afterload was lower, fluid bolus and vasopressor will be the appropriate treatment in this group [26].

Remarkably, sub-group analysis of group 2 revealed 57.6% of subjects were non-fluid responder and 60.6% had low inotropy with high or normal afterload (Table 2). It could be explained that in low inotropy and stroke volume, cardiac output is maintained by the increase of heart rate in order to preserve oxygen delivery (DO_2) [8,20]. Hence, fluid and vasoactive therapy should be adjusted to normalizing cardiac preload, inotropy, and afterload, instead of simply normalize cardiac output.

At the 6th hour, all groups had achieved CI and SVRI targets. Nevertheless, inotropy and SVI insignificantly increase in groups 1 and 2 (Table 2). Most subjects (71% and 54.5% in groups 1 and 2, respectively) still revealed low inotropy (Table 3). Only group 3 revealed a significant reduction of SVI and CI along with the increase of afterload (Table 2), which most (60%) subjects in this group revealed normal inotropy along with various afterload levels (Table 3). These results indicated normal CI does not necessarily reflect normal hemodynamics. Therefore, using CI as a therapeutic goal in pediatric shock needs to be re-evaluated, since it neither describes the normal preload, inotropy, nor afterload status.

Preferably, afterload is the guidance for selecting and adjusting vasoactive agents. PKR is a parameter for afterload or vascular impedance that reflects the ratio of the energy of arterial pressure to blood flow. It also reflects ventriculo-aortic coupling, where the vascular impedance is optimally matching with transfer energy from the heart. If the vascular impedance is too low (vasodilation), there is high blood flow but arterial pressure is inadequate for tissue perfusion; on the contrary, if it is too high (vasoconstriction), then there is insufficient blood flow in the peripheral circulation [16,17,27].

While the vascular impedance (PKR) was predictable high in group 1 and low in group 3, however, various afterload level was found in group 2. Only 7 cases had normal inotropy and afterload, and it might be the most appropriate therapeutic goal (Table 3). These reflect the limitation of SVRI for guiding vasoactive therapy. A physician must be aware of the persistent hemodynamic disturbance, even if the patient has normal CI and SVRI. Selecting vasoactive only based on CI and SVRI may lead to inappropriate management.

USCOM is a non-invasive tool, which is comparable with the gold standard. The previous study showed a difference of 9% [28], $r = 0.89$ and the mean error of 29% between USCOM and pulmonary artery catheter (PAC) [29]. A study in children showed a low bias (−0.13) and intraobserver variation of only 5.7% compared to the PAC [30]. It showed USCOM is a reliable tool for hemodynamic monitoring. Limitations in this study include the difficulty of keeping the USCOM Doppler probe in a steady position on a critically ill pediatric patient, data were collected in a single center, and the subjects were heterogeneous in etiology and shock stage. It caused variations in hemodynamic features and patient outcomes, so care must be taken in generalizing our results.

The study showed the majority of shocks in children were hypodynamic (low inotropy). Most subjects were non-fluid responders and had high resistance. Only a few were low resistance, and there was due to the vasodilatory shock.

6. Conclusion

The study concluded that even if CI was normal, either after fluid or vasoactive administration, some preload, inotropy, and afterload abnormalities still persist. It indicated CI could describe neither complete hemodynamic features nor successful shock treatment. Analysis of preload, inotropy, and afterload was required to guide appropriate management.

Ethical approval

This study was approved by the Ethical Commission of Medical/Health Researches, Faculty of Medicine, University of Indonesia, Dr. Cipto Mangunkusumo General Hospital (Approval # 753/H2·F1/ETIK/2012; Approval date December 17th, 2013).

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Authors contribution

Saptadi Yuliarto: design the study concept, collect & summarize the associated references, review the manuscript, **Antonius H. Pudjiadi:** design the study concept, collect & summarize the associated references, review the manuscript, **Abdul Latief:** collect & summarize the associated references, writing the paper.

Trial registry number

1. Name of the registry: research registry Unique Identifying number or registration ID: 7743.
2. Hyperlink to your specific registration (must be publicly accessible and will be checked):https://researchregistry.knack.com/research-registry#user-researchregistry/registerresearchdetails/6231867210775200 1ef34214/

Guarantor

The guarantor of this study is Saptadi Yuliarto as the corresponding author.

Consent

Informed consents were obtained from patient's parents or guardians.

Provenance and peer review

Not commissioned, externally peer-reviewed.

Declaration of competing interest

None of the authors have a conflict of interest to disclosure.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2022.103521.

Acronyms and abbreviations

BW	Body Weight
CI	Cardiac Index
HR	Heart Rate
PKR	Potential to Kinetic Ratio
SMII	Smith-Madigan Inotropy Index
SV	Stroke Volume
SVV	Stroke Volume Variation
SVRI	Systemic Vascular Resistence Index
SVI	Stroke Volume Index
USCOM	Ultrasound Hemodynamic Monitor

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