The correlation between vasoactive-inotropic score with mortality and the use of mechanical ventilation in pediatric shock admitted to the PICU in Dr. Soetomo General Hospital, Surabaya

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Abstract

***Objective*: To evaluate and to assess the correlation between the vasoactive-inotropic score (VIS) with mortality and the used of mechanical ventilation in pediatric shock.**

***Design*: A retrospective cross-sectional study.**

***Setting*: The study was conducted in the Pediatric Intensive Care Unit (PICU) at Dr. Soetomo General Hospital, Surabaya from November 1st, 2017 until April 30th, 2018.**

***Patients and participants*: All children <18 years old with shock who were admitted to the PICU.**

***Interventions*: None.**

***Measurement and results*: Eighty children with shock were admitted in PICU using minimal one vasoactive-inotropic treatment in the first 48 hours were included. Fifty-nine patients were eligible and met the inclusion criteria such as age <18-year-old, has one or more types of shock (hypovolemic shock, cardiogenic shock, obstructive shock, distributive shock), and received at least one vasoactive-inotropic drug ≤48 hours. We used Chi-square and Fisher's Exact test and Receiver Operating Characteristic (ROC) curve analysis. The children consisted of 31 males (52.5%) and 28 females (47.5%). The median age was 36 ranging from 2-216 months. Fifty-four used mechanical ventilation. The mean of VIS was 10±6 and the mortality rate was 47.5%. The cut-off value of the ROC curve of VIS in relation to mortality was 6 with sensitivity 82.1% and specificity 64.5%. We divided our subjects into two groups based on the cut-off value of 6 as High VIS (>6) and Low VIS (≤6). The High VIS group consisted of 34 subjects, in which 68% of them died and 59% of them needed mechanical ventilation. VIS had a correlation with mortality (r=-0.472, p<0.001).**

***Conclusion*: VIS had a moderately correlation with mortality, but had no correlation with the used of mechanical ventilation. Nevertheless, VIS may be a better screening tool for pediatric shock in our setting.**

Key words: Children, shock, vasoactive-inotropic score, mortality, mechanical ventilation.

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Introduction

Critical illness in children greatly affects the life of a child, parents, family, and health care workers. The mortality of children admitted to Pediatric Intensive Care Units (PICU) due to critical illnesses with various etiologies in one year reached 33.1%. (1) Shock provides the largest percentage of diagnosing children with critical illness. Shock is a hemodynamic disorder that can include decreased systemic vascular resistance, especially in the arteries, reduced back blood flow, decreased ventric-

ular filling, and low cardiac output. The management of hemodynamic disorders requires blood volume expansion and the help of vasoactive and inotropic drugs according to the patient's hemodynamic status. Vasoactive and inotropic drugs are routinely given to patients with both septic and cardiogenic shock to maintain cardiovascular function and tissue perfusion. (2)

A research in India reported the prevalence of shock in children admitted to the PICU was 28/1000 patients, where 49.2% of 57 children with shock needed inotropic assistance and 43.9% of 57 patients died. (3) Kutko, et al (2003) (4) in United States stated that of 96 septic shock patients admitted to the PICU, 36 required one type of vasoactive or inotropic drug and 28 required more than one vasoactive or inotropic type. The mortality in patients with one vasoactive or inotropic type was 0% whereas in patients with multiple vasoactive or inotropic drugs was 42.9%. (4) A study in Yogyakarta, Indonesia reported 239 shock patients who were treated in the PICU from November 2011 - June 2014, of which 136 experienced septic shock. A total of 47 patients received more than one inotropic, but only one patient survived while 46 others died. (1) A reliable tool for monitoring vasoactive inotropic administration and predictors of mortality is urgently needed. Several countries have used the vasoactive-inotropic score as an objective aid for hemodynamic monitoring, measuring the need for cardiovascular assistance in children after cardiac surgery, and as a predictor of mortality and morbidity. A validated score accurately describes cardiovascular dysfunction and correlates with other clinical relevant conditions such as the use of mechanical ventilation, length of stay in the PICU, and also can be used to identify high-risk patients and as a result of research and quality improvement. (2)

Various studies have used the vasoactive-inotropic score (VIS) formula proposed by Gaies, et al (2010) (5) to describe inotropic and vasoactive support for cases of cardiogenic shock, septic shock, and cardiac surgery. The outcomes measured from these studies also varied, including morbidity, mortality, use of mechanical ventilation, duration of mechanical ventilation, length of stay in the PICU, and myocardial dysfunction. (2,6-8)

The use of a vasoactive-inotropic score at PICU Dr. Soetomo General Hospital has yet to be implemented. VIS can be used as a predictor of mortality and the use of mechanical ventilation in shock patients admitted to the PICU Dr. Soetomo General Hospital Surabaya. Therefore, we could prevent the mortality rate and the number of uses of mechanical ventilation can be reduced. In that regard, this study aims to assessed the association between VIS with mortality and the use of mechanical ventilation.

Material and methods

This retrospective cross-sectional study was performed in Dr. Soetomo General Hospital, Surabaya, Indonesia from November 1st, 2017 until April 30th, 2018. This study was approved by Ethical Committee of Clinical Research Unit Dr. Soetomo General Hospital (Number 0159/KEPK/IV/2018). All parents have signed the informed consent prior to admitting their children to the PICU. The samples of this research were all children who admitted in the PICU. The study size of this research was estimated using total sampling by Lemeshow, et al (1990) (9) formulation, used confidence interval 95% with the proportion 0.5 resulting minimum of samples 43 patients. The inclusion criteria of this study were children under 18 years old who had any type of shock e.g. hypovolemic shock, cardiogenic shock, obstructive shock, distributive shock, and received at least one vasoactive-inotropic drug ≤48 hours. We excluded patients due to incomplete data of medical records and who received vasoactive-inotropic drug >48 hours in the PICU. In this study, we collected data from medical records as follows: gender of patients, age, length of stay, Pediatric Logistic Organ Dysfunction (PELOD) score, vasoactive-inotropic score, the use of mechanical ventilation and mortality.

Data analysis

The data were analyzed using Microsoft Office Excel 2013, IBM SPSS Statistic version 25. Kolmogorov-Smirnov test was used to obtained the normality value. Then we used T-test or Mann Whitney U test to derive the difference between variables. We performed the receiver operating characteristic (ROC) curve analysis to determine the cut-off value of VIS and classified into two groups as Low VIS and High VIS. In addition, we also calculated the sensitivity and specificity of VIS to predict the cut-off value of mortality and the used of mechanical ventilation. Chi-square and Fisher's Exact test were used to compare the VIS to mortality and the used of mechanical ventilation. The coefficient correlation between variables were analyzed using Spearman correlation test. A p value <0.05 was considered statistically significant.

Results

Eighty children with shock were admitted to the PICU during the study period. Out of 80 patients,

72 of them received vasoactive and inotropic drugs. Of 72 patients, we excluded 13 of them due to the admission of vasoactive inotropic drugs for more than 48 hours. Fifty-nine patient were eligible samples and met the inclusion criteria. The mean of age in this study was 60±61.16 (2-216) months. Out of 59 children, 47.5 % of them did not survived. The median age of non-survived children was 9 months, with a mean of 46±60.7 months. Meanwhile, the median age of survived children was 48 months, with a mean of 72±60 months. The demographic and clinical characteristic are further presented in **Table 1**.

In **Figure 1** we analyzed the vasoactive-inotropic score in relation to mortality and used of mechanical ventilation with ROC curve analysis. Area under the curve (AUC) of VIS and the used of mechanical ventilation was 62.9% (95% CI 48.6-77.2) (**Figure 1A**). The sensitivity and specificity were 62.5% and 55.6%, respectively, with a cut-off value of 9 (**Table 2**). Whereas, the AUC of VIS and mortality was 77.8% (95% CI 65.5-90) (**Figure 1B**). The sensitivity and specificity were 82.1% and 64.5%, respectively (**Table 3**). The cut-off value of VIS in accordance with mortality was 6. Therefore, we classified VIS into two groups as Low VIS with VIS≤6, and High VIS with VIS>6. The cut-off values were chosen based on the high value of sensitivity and specificity.

The correlation between VIS and mortality was correlated statistically (p=0.001), with a negative correlation coefficient (r=-0.472). On the other hand, the used of mechanical ventilation and VIS were not correlated statistically (p=0.440, r=-0.107) (**Table 4**). Thirty-four children have high VIS (>6), of which 68% of them did not survive during treatment and 59% of them need ventilator support. Twenty-five children who categorized as low VIS, 80% of them were survived and have better clinical outcome.

Discussion

This study shows the proportion of male children (52.5%) is slightly higher than the female ones. In other research by Haque, et al whereas 71 children who included in the study, 47 of them were male. (2) Other studies also stated that the number of male patients enrolled in cases of shock were slightly higher by 54% (6) and 53.3%. (7) All these studies reported the number of male patients were slightly higher than female patients. These results caused by postmenopausal in male and female experience increased levels of dihydrotestosterone and decreased levels of 17β-estradiol, which resulting in the release of pro-inflammatory cytokines and the incidence of apoptosis. Based on this statement, sex hormones were most likely affecting the proportion of male in these studies. (10) PELOD score was included into the characteristics of the children in our study because this score was routinely calculated in patients who were admitted to the PICU in our hospital. Since 2003, PELOD score was introduced and has undergone several validations. (11) The advantages of this PELOD score include that it can describe various disturbed organ systems and its use is free of charge. (12)

Approximately 90% of the pediatric shock received vasoactive inotropic therapy. This showed that the majority of pediatric shock required vasoactive inotropic therapy. In other case, Musick, et al (2018) reported that patients in critical condition who required vasoactive inotropic therapy were 17.4%. This was because the number of samples in this study was very large. This may be due to the large number of samples in that study. (13)

Wernovsky, et al created an inotropic score for hemodynamic support after surgery. (14) Gaies, et al (15) updated the quantitative index of cardiovascular support as a vasoactive-inotropic score to calculate hemodynamic support in the first 48 hours after cardiac surgery in an infant intensive care unit as a predictor of morbidity and mortality. The VIS is very simple, easy to use, and based on hemodynamic parameters to monitor cardiovascular support in critically ill children. Therefore, this score can be used as a predictor outcome, especially in countries with limited health care facilities. (5) In this study, we used the VIS proposed by Gaies, et al. (15)

We calculated the correlation of VIS and length of stay (LOS) and the used of mechanical ventilation in the PICU. It turned out in this study, LOS and the used of mechanical ventilation were not correlated significantly. Different from our study, Davidson, et al concluded that there was a strong association between VIS and ventilator use. This can be caused by the presence of positive pressure ventilation reducing the energy expended by the patient to breathe. (16) Haque, et al showed that VIS in the first 48 hours after ICU admission was associated with the LOS in the ICU and used of a ventilator. (2) A study by McIntosh, et al indicated that persistent vasoactive and inotropic administration within the first 48 hours was closely associated with length of critical care. Patients with a high VIS in the first 48 hours exhibited ongoing cardiovascular dysfunction and were at high risk of adverse outcomes. (6) A research by Butts, et al also stated that high VIS was associated with the used of mechanical ventilation, LOS in the ICU, and

cost of care. (17)

We obtained the cut-off value for VIS of 6 based on the ROC curve. Several other studies obtained cut-off values that varied according to their statistical analysis. Our study indicated that high VIS (>6) might have a poor clinical outcome in pediatric shock as might lead to death. Our result of VIS was moderately correlated to mortality and showed a negative correlation which indicated that low VIS patients would have a better clinical outcome and higher chance of life. These results were in line with a study by Haque, et al in 2015 who exhibited that high VIS were associated with poor clinical outcome of children with shock in the PICU especially in developing countries. The results of this study found that children who were in the High VIS group (VIS>20), all subjects (100%) experienced death. Whereas children in the Low VIS group (VIS≤20), 44% experienced death. Haque's research used a cut-off value of 20. (2)

Sanil and Aggarwal calculated the peak of VIS at 24- and 48-hour baseline after 51 consecutive open-heart transplants. VIS was calculated using the formula proposed by Gaies, et al. VIS≥15 at two or more of the 8 readings was defined as high inotropic requirement (24-hour high VIS). VIS<15 at all observation times defined as low inotropic requirement (24-hour low VIS). The cut-off value for VIS in this study was 15. Patients with VIS≥15 was in the High VIS group and these patients stayed in the ICU longer, used inotropes and ventilation and had higher morbidity rates. Mortality tended to be higher in patients with high VIS for up to 48 hours, although this was not statistically significant. (18) The cut-off value of VIS from the study by Dilli, et al resulting in 15.5 as high VIS (>15.5) within 72 hour indicated that the infant continued to be at risk of poor outcomes. (7)

A study by Kumar, et al (19) regarding the correlation of VIS with clinical outcome in neonatal after cardiac surgery. This retrospective study was conducted to 208 patients who underwent the cardiac surgery in ICU. There was a significant relationship between VIS with several variables such as age, weight <10 kg, time of cardiopulmonary bypass (CPB), pump failure, and postoperative variables such as sepsis, hematological complications, hepatic dysfunction, acute renal failure during treatment, mortality, need for ventilators, CPB time, and LOS. The cut-off value of VIS in this study was 10. The study concluded that the inotropic score and its adaptation were excellent tools in helping to measure disease severity, decide on interventions and during parental counselling in the Pediatric Cardiac Surgery ICU. (19) The cut-off value obtained in each study was not always the same. The cut-off value showed specificity and high negative predictive value for predicting outcomes. (20)

We believed that VIS at 48 hours were appropriate to be implemented in the limited resources setting to help clinicians be more aware of patient outcome who suffer from pediatric shock. Our study might have limitations because our data only taken by medical records and concentrated only in one hospital. Further study is needed especially in more centre hospitals in Indonesia. We also encourage to study regarding septic shock considering it is the most common type of shock in pediatric patients in our hospital.

Conclusion

Vasoactive-inotropic score clearly had a good correlation with mortality of pediatric shock. However, the use of mechanical ventilation was not correlated to VIS. We cannot draw a quick conclusion. It is worthwhile to remain alert to other possibilities. The existence of a scoring system or screening to prevent mortality must be done more frequently so that mortality can be reduced. This vasoactive-inotropic score needs to be validated internally and externally so that it can be adjusted for use in the PICU of our hospital settings.

Table 1. The clinical characteristic of patients

Characteristic of patients (n=59)	Value
Age (months), mean±SD (range)	60±61.16 (2-216)
Gender, n (%) - Male - Female	 31 (52.5) 28 (47.5)
Type of shock, n (%) - Hypovolemic - Cardiogenic - Sepsis	 10 (16.9) 21 (35.6) 28 (47.5)
Vasoactive-inotropic score, mean±SD (range)	10±6 (3-25)
Mortality, n (%) - Survived - Non-survived	 31 (52.5) 28 (47.5)
Use of mechanical ventilation, n (%) - Yes - No	 32 (54.2) 27 (45.8)
Duration of mechanical ventilation (days), mean±SD (range) - 0 day, n (%) - 1-7 days, n (%) - >7 days, n (%)	8.2±12.86 (0-54) 27 (45.8) 14 (23.7) 18 (30.5)
Length of stay in PICU (days), mean±SD (range) - 1-7 days, n (%) - >7 days, n (%)	15.34±13.34 (1-56) 22 (37.3) 37 (62.7)
PELOD score, mean±SD (range)	6.2±3.26 (2-14)

Legend: SD=standard deviation; PICU=Pediatric Intensive Care Unit; PELOD=Pediatric Logistic Organ Dysfunction.

Table 2. The coordinates of the ROC curve (cut-off value) between VIS and the use of mechanical ventilation

Cut-off value of VIS	Sensitivity (%)	Specificity (%)
2	100.0	0.0
4	96.9	11.1
6	62.5	48.1
7.25	62.5	51.9
8.75	62.5	55.6
11	43.8	85.2
12.5	37.5	85.2
14	34.4	85.2
16.5	18.8	85.2
19	18.8	88.9
22.5	6.3	100.0
26	0.0	100.0

Legend: ROC=receiver operating characteristic; VIS=vasoactive-inotropic score. Data were analyzed by ROC curved.

Table 3. The coordinates of the ROC curve (cut-off value) between VIS and mortality

Cut-off value of VIS	Sensitivity (%)	Specificity (%)
2	100.0	0.0
4	96.4	9.7
6	82.1	64.5
7	78.6	64.5
8	78.6	67.7
11	53.6	90.3
12.5	46.4	90.3
14	42.9	90.3
16.5	25.0	90.3
19	25.0	93.5
22.5	7.1	100.0
26	0.0	100.0

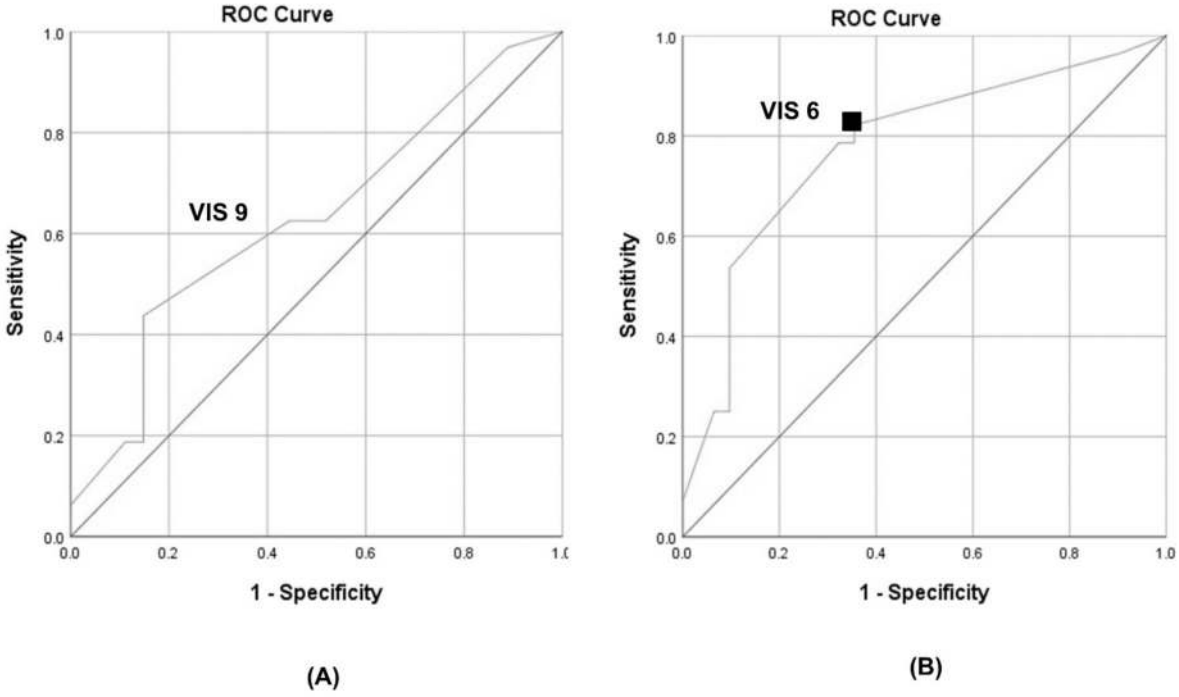
Legend: ROC=receiver operating characteristic; VIS=vasoactive-inotropic score. Data were analyzed by ROC curved.

Table 4. The proportion of mortality and the use of mechanical ventilation according to classified group of VIS

VIS	Mortality, n (%)		p value	Mechanical ventilation, n (%)		p value
	Non-survived	Survived		Yes	No	
Low VIS (≤6)	5 (8.5)	20 (33.9)	0.001*	12 (20.3)	13 (22)	0.440
High VIS (>6)	23 (39)	11 (18.6)		20 (33.9)	14 (23.7)	
Total	28 (47.5)	31 (52.5)		32 (54.2)	27 (45.7)	

Legend: VIS=vasoactive-inotropic score. *Data were calculated using Chi-square test.

Figure 1. Vasoactive-inotropic score to predict the cut-off value for the use of mechanical ventilation (A) and mortality (B)



Legends: ROC=receiver operating characteristic; VIS=vasoactive-inotropic score. ROC curve analysis for the use of mechanical ventilation (A) and mortality (B). Straight line is line of identity, while diagonal line represents classifiers ROC points results.

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