Renal Oxygen Saturation as an Early Indicator of Shock in Children

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Background: Shock is a life-threatening syndrome in which tissue perfusion and oxygen delivery are inadequate. Near-infrared spectroscopy (NIRS) has been suggested as a noninvasive tool for monitoring and detecting the state of inadequate tissue perfusion. Renal and mesenteric oximetry show decreased cardiac output earlier than systemic or global parameters of tissue oxygenation or cerebral oximetry. However, until now there has been no study on the validity of regional renal oxygen saturation (rRSO2) by NIRS for diagnosing shock in children.

Purpose: To analyze the validity of rRSO2 by NIRS to diagnose shock in children.

Patients and Methods: This cross-sectional study was conducted in critically ill children (aged 1 month–18 years) who were admitted to the pediatric intensive care unit (PICU), from September to November 2020, consecutively. Patients were classified into two groups: shock and non-shock. The diagnosis of shock is based on clinical criteria (tachycardia, sign of hypoperfusion and decrease systolic blood pressure <P5 according to age). Measurement of rRSO2 by NIRS was performed by the doctor in charge when the patient came to PICU. The baseline rRSO2 value (%) made a receiver operating characteristic (ROC) curve and was used to find the optimal cut-off value and calculated sensitivity and specificity.

Results: We enrolled 20 critically ill patients. The baseline rRSO2 in the shock (n=10) and non-shock (n=10) groups were, 44.00±4.95 vs 78.70±4.52 (p 0.003). The optimal cutoff value of the baseline rRSO2 to predict shock is less than 58.5% with area under the curve (AUC) value is 94.4% (95% CI of 84.4–100%), p 0.001, sensitivity 90% and specificity 90% in critically ill children.

Conclusion: The rRSO2 value by NIRS can differentiate between shock and non-shock in critically ill patients accurately.

Keywords: critically ill children, regional renal oxygen saturation, NIRS, shock

Introduction

Shock is an emergency problem in the emergency room and pediatric intensive care unit (PICU) because it’s one of the common cause of cardiac arrest in children.1,2 Shock is a life-threatening syndrome due to inadequate tissue perfusion to meet metabolic demands and tissue oxygenation.3,4 Prompt treatments to fulfill the oxygen debt will improve outcomes.2,5,6 Delayed recognition and treatment of oxygen deficiency can increase morbidity and mortality.2,6

Frequently used physiological parameters cannot predict the level of circulatory failure and often underestimate the amount of oxygen deficiency.2,7 The laboratory examination for organ hypoperfusion—such as blood lactate is correlated with the severity of oxygen deprivation and mortality,2,8 but it’s unsustainable measured and lags circulatory changes. Monitoring of systemic venous oxygen saturation (SvO2) from pulmonary artery catheter (PAC) can estimate the global oxygen balance to guide resuscitation, because it represents the average amount of every organ saturation and it will improve outcomes in shock. However, it can not show the maldistribution of regional blood flow, so SvO2 can not detect the regional ischemia until organ dysfunction occurs and it will increase mortality and morbidity.2,5,7 Besides that the monitoring of SvO2 is invasive and technically challenging in infants and small children and can delay assessment and therapy.2 Because technical limitations constitute important limits for its widespread use, so mixed vein saturation (ScvO2) is used to surrogate SVO2 which describes...
the oxygen level in the superior vena cava, although it is technically easier, but the insertion of a catheter in the superior vena cava still requires special skills.

Infrared spectroscopy is a tool that we can use to monitor organ-specific perfusion continuously. A 20% reduction from the recommended baseline normal rSO\(_2\) of 70% has been shown to predict the risk of organ injury. Several studies have investigated the utility of NIRS in children. One small study showed that an average of less than 65% brain and renal rSO\(_2\) measured by NIRS correlated with an increase in serum lactate—a marker of poor perfusion globally.

A commonly use technology that is completely non-invasive to measure regional tissue oxygenation and perfusion is called NIRS. A combination of regional oxygen saturation (rSO\(_2\)) that approximates regional venous saturation, with arterial oxygen saturation can be used to estimate the regional oxygen condition.

To our knowledge, until now there have been no studies on the validity of regional renal oxygen saturation (rRSO\(_2\)) by NIRS for diagnosing shock in children.

**Materials and Methods**

**Patient Population and Methods**

Ethical clearance letters with approval number 0069/KEPK/IX/2020 were obtained from the Ethics Committee of Soetomo General Hospital, a tertiary teaching hospital. All procedures performed in this study which involved human participants were in accordance with the ethical standards of the institutional research committee and conducted in accordance with the most recent version of the Declaration of Helsinki. All the parents/guardians of the children were well informed about the purpose of the study and gave consent. Critically ill children between 1 month - ≤ 18 years of age who were admitted to the Pediatric Intensive Care Unit (PICU) of Soetomo General Hospital from September – November 2020 were included. In this study, the subjects were divided into two groups based on the presence of shock or no shock from the diagnosis by the pediatric intensivist in charge. The diagnosis of shock is based on clinical criteria (tachycardia, the sign of hypoperfusion (i.e the quality of the central pulse is greater than the peripheral, clammy extremities or mottled skin, capillary refill time > 2 second, narrowing pulse pressure <20 mmHg, decrease urine production < 1 mL/kgbw/hours, decrease or altered mental status) and decrease systolic blood pressure <P5 according to the age.

Patients with congenital heart disease, chronic kidney disease, the disease that obstruct the renal blood flow, and no sufficient data were excluded.

We calculated sample size from this following formula for unpaired \(t\)-test (two-tailed test):

\[
N = \frac{2\sigma^2 (Z_{1-\alpha/2} \pm Z_{1-\beta})^2}{(\mu_1 - \mu_2)^2}
\]

with \(Z_{1-\alpha/2} = 95\%\) confidence interval =1.96, \(Z_{1-\beta} = \) Power = 0.84, \(\sigma = \) pooled variant, according to study by Crookes, et al, 2005, \(\mu_1 - \mu_2\) = estimated the difference in means of NIRS value between shock and non shock population, according to study by Crookes, et al, 2005.

A minimum of seven subjects in each group were needed according to the statistical calculation.

**Data Collection and Methods of Measurement**

All the critically ill children admitted to the PICU were assessed by the attending physician (and confirmed by the pediatric intensivist in charge) regarding their diagnosis of shock. We used medical charts to record the identity, working diagnosis, vital signs (hemodynamic measurement non-invasively) using a GE B40 patient monitor, number and types of fluid, and type and dosage of vasoactive agent that were given during the assessment period.

The children were laid in a supine position, and NIRS probes were attached above the left and right kidneys. Blood was drawn from the central vein catheter (standard procedure in all critically ill patients admitted to our PICU) to check lactate, SeVO\(_2\), and hemoglobin levels. In addition, blood gas analysis was taken from the arterial line that had been inserted by the pediatric intensivist in charge (or via direct puncture for no shock subjects).
At the same time, the pediatric cardiologist on duty in the PICU took SV measurements using echocardiography. The echocardiography was performed using GE Vivid-q. All procedures were conducted simultaneously.

**Near-Infrared Spectroscopy (NIRS)**

After turning on the NIRS device and entering the patient’s data, the proper probe according to the patient’s weight (for infants/children, 5–40 kg) was selected. After identifying the correct probe position above the kidney and cleaning and drying the site, the probe cover was removed and the sensor was placed on the skin from the center of the probe to the side, making sure the edges of the probe were firmly connected to the skin. A baseline was set after placing the probe, and the device then recorded the $rRSO_2$ from the renal. After the $rRSO_2$ was calculated, it was calculated for a second time manually for tissue oxygen extraction ($rFTOE$) using the formula $(SaO_2 - rSO_2)/SaO_2$.

**Stroke Volume (SV) Measurement Using Echocardiography**

First, the left ventricular outflow tract (LVOT) area are measured along with the amount of blood flow to the area (VTI). The system in the echocardiography device then calculates the stroke volume. We then used the calculated stroke volume to calculate cardiac output, cardiac index and stroke volume index with specific calculator (https://www.omnicalculator.com/health/stroke-volume).

**Data Analysis**

The collected data were analyzed using SPSS for Windows 20.0 software (IBM, Armonk, NY, USA). Numerical data were tested for normality with Kolmogorov–Smirnov, where data with normal distribution were presented in the mean and standard deviation (SD). The two means that are normally distributed were analyzed using a t-test, and those that are not normal were analyzed using the Mann–Whitney test. Correlation between variables was made with bivariate analysis, data with normal distribution was analyzed using the Pearson correlation, while data that are not normal were analyzed using Spearman correlation.

The $rRSO_2$ minimal value made a receiver operating characteristic (ROC) curve and was used to find the optimal cut-off value and calculated sensitivity and specificity.

**Results**

Fifty-two critically ill children were admitted to the PICU from September through November 2020. Thirty-two children were excluded consisting of 7 children with cyanotic congenital heart disease, 12 chronic kidney disease children, 7 patients died ≤ 2 hours and 6 children with intra-abdominal mass. Twenty patients were subjects of the study, consisting of 10 shock and 10 non-shock subjects, which is the most type of shock in this study are septic shock (Table 1). Clinical characteristics are summarized in Table 1. Sex, nutritional status, hemoglobin levels and glomerular filtration rate between patients with shock and non-shock did not differ. The initial conventional hemodynamic parameter that was used as the basis for the diagnosis of shock in this study showed significant differences in all variables. Children with shock had a higher mean HR (156.80±5.48), a lower mean value arterial pressure (MAP) (52.91±2.34), and lower systolic blood pressure (SBP) (mean value of 78.20±1.59) than non-shock children, and most had a prolonged capillary refill time (90%). Meanwhile, when viewed from the patients’ outcomes, there was no significant difference between shock and non-shock patients.

The macrohemodynamics parameter in shock and non-shock patients differed significantly in the mean values of stroke volumes index (SVI), cardiac index, and SVRI. All the mean values were lower in the shock patient than in non-shock patients (Table 2). Likewise, lactate levels in patients with shock showed a higher mean than those in non-shock 4.83±0.65 vs 1.24±0.12.

The $rRSO_2$ baseline value was much lower in patients with shock compared to non-shock patients (44.00±4.95 vs 78.70±4.52) with p 0.001, as well as $rFTOE$ values were higher in shock patients (Table 3).

There were no correlation between SVRI and DO$_2$ with $rRSO_2$, r 0.349; p 0.131, and r 0.344; p 0.137, respectively. There were a moderate to good correlation between MAP, SBP, SVI, CI, and SpO$_2$ with $rRSO_2$ baseline, r 0.599; p 0.005, r 0.567; p 0.009, r 0.592; p 0.006, r 0.636; p 0.003 and r 0.609; p 0.004, respectively (Figure 1A–E). Lactate and $rRSO_2$
baseline have negative correlation with $r \sim 0.603$ (Figure 1G). The ScVO2 have a strong correlation with rRSO2 baseline with $r 0.728$ (Figure 1F) and negative correlation with rFTOE, $r \sim 0.641$ (Figure 2).

The area under the curve (AUC) value for baseline rRSO2 is 94.4% (95% CI of 84.4–100%), p 0.001 (Figure 3). The optimal cutoff value of the baseline rRSO2 in children with shock is < 58.5% (Figure 4), with the sensitivity 90% and specificity 90% (Table 4).

### Table 1 Characteristics of the Sample

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Shock (n=10)</th>
<th>Non-Shock (n=10)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>117 (24.51)</td>
<td>31.90 (13.21)</td>
<td>0.011</td>
</tr>
<tr>
<td>Sex (boy/girl)</td>
<td>6/4</td>
<td>5/5</td>
<td>1.000</td>
</tr>
<tr>
<td>Nutritional status (malnourished) (%)</td>
<td>5 (50%)</td>
<td>6 (60%)</td>
<td>0.053</td>
</tr>
<tr>
<td>Hb (mean, SD)</td>
<td>9.4 (0.73)</td>
<td>11.34 (0.66)</td>
<td>0.198</td>
</tr>
<tr>
<td>RR (tpm) (mean, SD)</td>
<td>38.80 (2.05)</td>
<td>28.40 (2.39)</td>
<td>0.008</td>
</tr>
<tr>
<td>Temperature (°C) (mean, SD)</td>
<td>38.24 (0.28)</td>
<td>37.77 (0.31)</td>
<td>0.400</td>
</tr>
<tr>
<td>GCS (&lt;8) (%)</td>
<td>3 (30)</td>
<td>3 (30)</td>
<td>0.558</td>
</tr>
<tr>
<td>Type of shock</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypovolemic (%)</td>
<td>4 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septic (%)</td>
<td>6 (60)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Inotropic/vasoactive agent</td>
<td>7 (70)</td>
<td>1 (10)</td>
<td>0.016</td>
</tr>
<tr>
<td>Mechanical ventilation (%)</td>
<td>7 (70)</td>
<td>8 (80)</td>
<td>1.000</td>
</tr>
<tr>
<td>Outcome (death) (%)</td>
<td>4 (40)</td>
<td>1 (10)</td>
<td>0.303</td>
</tr>
<tr>
<td>HR (bpm) (mean, SD)</td>
<td>156.80 (5.48)</td>
<td>126.50 (7.84)</td>
<td>0.015</td>
</tr>
<tr>
<td>MAP (mmHg) (low) (n,%)</td>
<td>52.91 (2.34)</td>
<td>67.95 (2.49)</td>
<td>0.015</td>
</tr>
<tr>
<td>SBP (mmHg) (low) (n,%)</td>
<td>78.20 (1.59)</td>
<td>92.90 (3.26)</td>
<td>0.003</td>
</tr>
<tr>
<td>CRT (&gt;2 second) (%)</td>
<td>9 (90)</td>
<td>1 (10)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diuresis (&lt;1mL/kgBW/hour) (%)</td>
<td>6 (60)</td>
<td>1 (10)</td>
<td>0.019</td>
</tr>
<tr>
<td>Glomerular filtration rate (mL/min/1.73m²) (mean, SD)</td>
<td>81.71 (8.5)</td>
<td>84.09 (14.29)</td>
<td>0.112</td>
</tr>
</tbody>
</table>

*Note: Significant if p<0.05.*

### Table 2 Macrohemodynamic Dan Microhemodynamic Parameter

<table>
<thead>
<tr>
<th>Variable</th>
<th>Shock (Mean, SD)</th>
<th>Non-Shock (Mean, SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SVI (mL/m²)</td>
<td>36.05 (2.98)</td>
<td>57.15 (4.45)</td>
<td>0.003</td>
</tr>
<tr>
<td>CI (l/min/m²)</td>
<td>2.84 (0.32)</td>
<td>9.79 (1.51)</td>
<td>0.001</td>
</tr>
<tr>
<td>DO₂ (mL/min)</td>
<td>700.80 (121.20)</td>
<td>403.47 (61.19)</td>
<td>0.164</td>
</tr>
<tr>
<td>SVRI (dyn*sec/cm⁵)</td>
<td>738.87 (89.13)</td>
<td>1372.02 (138.79)</td>
<td>0.001</td>
</tr>
<tr>
<td>SpO₂ (%)</td>
<td>94.50 (1.66)</td>
<td>99.30 (0.30)</td>
<td>0.007</td>
</tr>
<tr>
<td>ScVO₂ (%)</td>
<td>58.60 (5.96)</td>
<td>76.10 (2.59)</td>
<td>0.015</td>
</tr>
<tr>
<td>Lactate (mmol/L)</td>
<td>4.83 (0.65)</td>
<td>1.24 (0.12)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Note: Significant if p<0.05.*

### Table 3 Comparison of Regional Oxygen Saturation and Tissue Oxygen Extraction in Shock and Non-Shock Patients

<table>
<thead>
<tr>
<th>NIRS</th>
<th>Shock (Mean, SD)</th>
<th>Non Shock (Mean, SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>rRSO₂ baseline</td>
<td>44.00 (4.95)</td>
<td>78.70 (4.52)</td>
<td>0.003</td>
</tr>
<tr>
<td>rRSO₂ after resuscitation</td>
<td>68.10 (4.72)</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td>rFTOE</td>
<td>0.52 (0.04)</td>
<td>0.13 (0.02)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

*Note: Significant if p<0.05.*
Discussion

In shock, there is impaired tissue perfusion and oxygen delivery, and delays in recognizing and providing therapy for oxygen-deprived tissue can lead to high rates of mortality and morbidity. It is a challenge to identify bedside tissue hypoperfusion. In clinical practice, tissue perfusion is usually assessed on the basis of global hemodynamic parameters. There are several methods that commonly used to measure the adequacy of tissue oxygen delivery in this critical period, including clinical and biochemical. The clinical methods that includes monitoring are vital sign and physical examination, and for biochemical usually uses laboratory examination (ie lactate and ScVO₂). Each of these methods has limitations, because it may be subjective, operator dependent/need high expertise, invasive or unsustainable.

In this study, the percentage of patients with high HR, low MAP, low systolic blood pressure, prolonged CRT, and diuresis was significantly different between the shock and non-shock groups, and the mean RR value was higher in shock patients. These vital signs form the basis for the diagnosis of shock in this study. These results are in accordance with the theory of how to recognize shock. That theory states that the first response of our body to increase the cardiac output in shock are tachycardia, and other clinical sign that found in shock are prolonged CRT and weak peripheral pulses, it’s due to increased of SVR, and when the body fails to compensate, hypotension will occur. The decompensated shock stage will show signs of inadequate end-organ perfusion, including decreased mental status, decreased urine output, metabolic acidosis, tachypnea, weak central pulse, and worsening peripheral perfusion. In this study there was no difference in

Figure 1 Scatter plot correlation between macrohemodynamic parameters and microhemodynamic; (A) MAP and rRSO₂ baseline r=0.599; p=0.005, (B) SBP and rRSO₂ baseline r=0.567; p=0.009, (C) SVI and rRSO₂ baseline r=0.592; p=0.006, (D) CI and rRSO₂ baseline r=0.636; p=0.003, (E) SpO₂ and rRSO₂ baseline r=0.609; p=0.004, (F) ScVO₂ and rRSO₂ baseline r=0.728; p=0.001, (G) lactate and rRSO₂ baseline r=−0.603; p=0.005.
mental status between patients with shock and non-shock. This could be because all of the participants in this study were critically ill patients who could have a decrease in mental performance caused by their underlying disease.

On the macrohemodynamic parameter, the mean values of SVI, CI, SVRI, SpO\textsubscript{2}, and ScVO\textsubscript{2} in the shock group were lower compared to the non-shock group (36.05±2.98 vs 57.15±4.45; 2.84± 0.32 vs 9.79±1.51; 738.87± 89.13 vs 1372.02 ±138.79; 94.50±1.66 vs 99.30±0.30 and 58.60±5.96 vs 76.10±2.59, respectively). These results are aligned with the pathophysiology of patients with shock. In the compensation phase, if hypoperfusion is obtained, there is a decrease in the stroke volume which a cause a decrease in cardiac output. As compensation, heart rate and SVR increase\textsuperscript{13–15} whereas on laboratory examination in tissue hypoperfusion conditions, a decrease in ScVO\textsubscript{2} will be seen due to low oxygen delivery.\textsuperscript{16}

Blood lactate levels are often measured to detect poor global tissue perfusion. Elevated lactate levels often indicate anaerobic metabolism, which occurs with an imbalance of oxygen delivery and oxygen consumption or impaired oxygen utilization in the tissues.\textsuperscript{11} In accordance with the results of this study, the mean lactate value of the shock group was higher than that of the non-shock group (4.83± 0.65 vs 1.24±0.12, p 0.001).

Compared to current bedside non-invasive monitoring devices (a device that can assess microperfusion and can monitor microcirculation disorders from several existing tools), NIRS has several advantages. As well as being non-invasive and easy to use, this method is operator-independent and is a continuous method that provides continuous charts and trends. Recently, NIRS has been widely used in critically ill conditions such as severe trauma, hemorrhagic shock, cardiogenic shock, severe heart failure, and septic shock in adult patients.\textsuperscript{17} Most studies of children were conducted on neonatal patients and almost all only assessed regional cerebraltissue oxygen saturation (cRSO\textsubscript{2}). A study by McQuillen of pediatric cardiac surgery patients (which also assessed cerebral oximeter using NIRS versus central venous saturation) showed that cRSO\textsubscript{2} values obtained by NIRS correlated with SvO\textsubscript{2} obtained through invasive monitoring.\textsuperscript{18} To our knowledge, until now there has been no study on the use of NIRS in children with shock.

Assessment of renal and mesenteric regional oxygen saturation indicates a decrease in cardiac output earlier than systemic or global parameters of tissue oxygenation or cerebral oximetry.\textsuperscript{2,19} This study showed that the regional oxygen saturation values in the renal as measured using NIRS can be used to quickly and noninvasively detect/diagnose the incidence of tissue hypoperfusion that occurs in pediatric patients with and without shock, as well as the rFTOE values. The results of this study are also in line with a study of trauma patients conducted by Crookes. That study assessed whether a patient was in shock or not based on regional oxygen saturation values in the thenar muscle using NIRS.
Figure 3 The ROC of the baseline rRSO₂ to predict shock in critically ill children.

Figure 4 The optimal cutoff value of the baseline rRSO₂ to predict shock in critically ill children.
compared with conventional physiological parameters. The study showed that decreased thenar muscle tissue oxygen saturation reflects severe hypoperfusion.20

The new finding in this study is that a mean baseline rRSO\textsuperscript{2} value in critically ill children is different significantly in shock and non-shock patients, so it helps to diagnose shock. Regarding an optimal cut-off rRSO\textsuperscript{2} to predict shock in critically ill children is less than 58.5% (p = 0.001), with the AUC value was 94.4, and has sensitivity at 90% and specificity at 90%. In Balaguru et al’s 2018 study of 168 children with and without heart disease, the normal mean rRSO\textsuperscript{2} value for children <1 year old was 67.8±12 and for children >1 year old was 71.6±11.21

The other new finding in this study is that the mean baseline rRSO\textsuperscript{2} value is associated with changes in macro-hemodynamic values in study subjects. The lower the rRSO\textsuperscript{2} value in the NIRS, the lower the MAP, systolic blood pressure, SVI, and CI values. Meanwhile, when associated with oxygen extraction, the higher the rFTOE value in the NIRS, the lower the ScVO\textsubscript{2} value, which indicates inadequate tissue perfusion and oxygenation.

From this study we also found that although the SpO\textsubscript{2} level was still about 94%, the other macro hemodynamic parameter and renal oximetry were already low and indicated hypoperfusion in a patient.

A study conducted by Chakravarti of pediatric patients after cardiac surgery showed a mean cerebral and renal rSO\textsubscript{2} value of less than 65% as measured by NIRS, predicting hyperlactatemia (>3 mmol/L) in acyanotic children after congenital heart surgery and identifying global hypoperfusion caused by low cardiac output syndrome in this population.11

In line with the results of Chakravarti’s research, this study shows that the rRSO\textsuperscript{2} value correlates with the lactate value, where a lower rRSO\textsuperscript{2} value correlates with a higher lactate value in research subjects.

The limitation of this study is subject heterogenous in the type of shock and the number of samples in each type of shock is uneven, that’s why the result for the macrohemodynamic parameter profile is influenced by the most type of shock in the sample. For further research, it is necessary to conduct research on patients with homogenous shock types to determine the macrohemodynamic correlation of each type of shock with the value of rRSO\textsuperscript{2} by NIRS.

**Conclusion**

Based on this study rRSO\textsuperscript{2} value have good sensitivity and specificity, so we can use this as a tool to diagnose shock in critically ill children. The low RSO\textsubscript{2} value also indicates the presence of tissue hypoperfusion, because it has a moderate to good correlation with macro and microhemodynamic status. Further study is needed to evaluate the applicability of these values in a specific type of shock.

**Disclosure**

The authors report no conflicts of interest in this work.

**References**


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