

# Near-Infrared Spectroscopy (NIRS) Monitoring in Pediatric Shock, and The Effect of Fluid Resuscitation on Multisite NIRS Values

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## ABSTRACT

**Objective:** To study the effects of fluid resuscitation on cerebral (cSO<sub>2</sub>) and renal tissue oxygenation (rSO<sub>2</sub>) in pediatric shock patients.

**Methods:** Prospective, observational study in a tertiary PICU (January- September 2016). We monitored bilateral cSO<sub>2</sub> and rSO<sub>2</sub> via NIRS during fluid resuscitation.

**Results:** Twenty-five patients (56% female) with compensated shock were included. Median age was 19 months (IQR 10-85). Median weight was 12 kg (IQR 5.9-20). The mean left and right brain tissue oxygenation (cSO<sub>2</sub>) of the patients participating was 57.7±16.4 and 54.1±16.7, mean left and right kidney tissue oxygenation (rSO<sub>2</sub>) was 63.1±14.1, and 62.8±14.8. Tissue oxygen saturation increased significantly after fluid resuscitation. The decline in lactate level and the increase in systolic and diastolic blood pressures was statistically significant. The median absolute differences between R-L cSO<sub>2</sub> and rSO<sub>2</sub> at time 0 were 5 (IQR 4-7), and 4 (IQR 1-9) respectively, but the difference was significant only for the brain (p=0.046). Bilateral cSO<sub>2</sub> and rSO<sub>2</sub> increased significantly after fluid bolus in survivors, whereas in non-survivors (n=9, 36%), there was no significant change. The mortality scores of the non survivors were higher than survivors (p<0.005).

**Conclusions:** This study provides insights into laterality and pediatric cerebral and renal NIRS measurements in critically ill children and may facilitate the interpretation of NIRS data in critically ill patients. Further research with a larger cohort of healthy and critically ill patients is needed to confirm these findings.

**Keywords:** Near infrared spectroscopy, shock, tissue oxygen saturation, fluid resuscitation

## INTRODUCTION

Shock is a critical medical condition characterized by severe disruption of the circulatory system, where tissues cannot meet their oxygen and other nutrient needs. A unifying factor among all types of shock is disruption of cellular metabolism and energy production, which ultimately result in reduced blood flow to vital organs (1). In the initial phase of shock, blood flow to critical organs like the brain, heart, and kidneys is preserved by reducing blood flow to the skin, muscles, stomach, and intestines. This adjustment helps maintain cardiac output at a nearly normal level, thereby preventing the development of hypotension (2). In children, systemic vascular resistance and vasoactive capacity are elevated to prevent rapid and easy decreases in blood pressure. Consequently, hypotension in children is a late indicator of shock that can complicate early diagnosis (3). The objective of shock treatment is to enhance oxygen delivery to tissues. In the event of failure of

compensation mechanisms during a state of shock, hypoxia in tissues will worsen, resulting in the development of multiple organ failure and ultimately leading to death. Implementing early recognition and intervention strategies in the context of shock can potentially enhance prognosis (4-5). It has been demonstrated that the parameters used during standard monitoring, including peak heart rate, mean arterial pressure, and arterial oxygen saturation, are insufficient for the detection of early-stage tissue oxygenation. Clinical examinations and laboratory tests (base deficit, lactate) only reveal perfusion abnormalities after a certain period has elapsed. However, there is a lack of complete coherence between macro- and microcirculation in shock (6-7-8-9). In order to address this monitoring gap, studies have introduced the evaluation of tissue oxygenation using near-infrared spectroscopy (NIRS).

The NIRS method can continuously and noninvasively assess tissue oxygenation and indirectly assess hemodynamics

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by measuring changes in oxy-deoxyhemoglobin (ODH) concentrations in the blood. The NIRS value should accurately reflect the mixed venous saturation (~20% arterial, ~5% capillary, and ~75% venous blood) (10). In pediatric patients, NIRS is a commonly preferred method for monitoring tissue oxygenation status, particularly before cardiac surgery, during cardiopulmonary bypass, and in intensive care units. In general, it is expected that healthy children and adults have NIRS values between 60 and 80 per the cent. Cerebral perfusion may be 5%–20% lower than that of somatic perfusion because of higher oxygen extraction in the brain. Clinical data from both children and adults suggest that cerebral  $cSO_2$  levels 40 % to 50% or a reduction of >20% from baseline, are linked to hypoxic-ischemic neural injury (11-12-13). The manufacturer recommends monitoring regional saturation on both sides, although clinical studies almost exclusively report data collected from one side only. The non-invasive nature of the NIRS method, the portability of the devices used, and their ability to provide immediate, cost-effective, and continuous tissue perfusion parameters without the need for invasive procedures have made it a frequent choice in clinical research and patient monitoring. NIRS offers a non-invasive, continuous, and approximate insight into regional oxygenation based on physiological principles. However, the most optimal approach is to base decisions on the analysis of trends exhibited in the graphs over time instead of relying exclusively on the assessment of instantaneous values (14).

The current study aimed to assess the effects of fluid resuscitation on cerebral and renal tissue oxygenation via double-sided (bilateral) NIRS monitoring along with hemodynamic and laboratory parameters (lactate and base deficit) in pediatric patients with shock.

## MATERIALS AND METHODS

This was a prospective, observational study with institutional ethics approval (09.2016186) and intramural grant support (BAPKO SAG-C-TUP-131216-0524). The study included 25 patients aged between 1 month and 18 years who required fluid resuscitation support due to compensated shock, from January 2016 to September 2016, at a tertiary Pediatric Intensive Care Unit. Patients with decompensated shock who were receiving inotrope and those with a wound dressing on which the NIRS probe was to make contact were excluded from the study. We compared the vital signs, blood gas parameters, mortality scores, and cerebral and renal NIRS before and after fluid resuscitation. During fluid bolus administration, the INVOS 5100 C Cerebral/Somatic Oximeter (Medtronic) device, which is routinely used in our unit, was used. Demographic and clinical characteristics of the patients, NIRS data (brain-kidney), fluid bolus duration, mortality scoring, and routine laboratory data (blood gas, blood count, biochemical values) were recorded. Two NIRS probes were placed on the frontal region of the patient in a state of shock, and two probes were placed on the T10-L2 kidney level. Patients received a bolus of crystalloid solution at a dose of at least 20 cc/kg within 15-20 minutes. In the event of continued clinical indications for fluid boluses

(i.e., prolonged capillary refill, weakened peripheral pulses, tachycardia), repeated boluses were administered.

All hemodynamic parameters and NIRS values were recorded in the central system developed and made ready for use in the project "Centralization of Alarms in the Pediatric Intensive Care Unit and Examination of Smart Alarm Algorithms (Scientific Research Projects Unit Commission, Project No: SAG-A-100713-0297)". The system automatically transferred all relevant data, as measured from the patient monitor, NIRS screen, and ventilator (if connected), to a desktop computer in Excel file format. Measurements were also manually recorded at 5-min intervals.

Frequency tables (n.%) were used for categorical variables, and descriptive statistics (mean, median, standard deviation, etc.) were used for numerical variables. If numerical variables were not distributed normally, analyses were performed using non-parametric statistical methods. The Mann–Whitney U test was used for group comparisons between the two groups. Before-after comparisons were performed using the Wilcoxon test. The threshold of statistical significance was taken as  $p < 0.05$ . SPSS 21 software was used for the analyses.

## RESULTS

Twenty-five patients with compensated shock (56% female) were included. Median age was 19 months (IQR 10-85). Median weight was 12 kg (IQR 5.9-20). Most patients had comorbidities (84%). Comorbidities included oncologic malignancies (n=8), severe neurologic problems (n=7), hemolytic anemia (n=1), combined immune deficiency (n=1), mitochondrial disease (n=1), achondroplasia (n=1), prune belly syndrome (n=1), and anal and esophageal atresia (n=1). Shock occurred due to hypovolemia (72%) and sepsis (28%). Fluid bolus was initiated on the basis of clinical criteria of inadequate perfusion based on tachycardia, prolonged capillary refill, diminished pulses, and changes in mental status. Four patients required a second fluid bolus.

The mean left and right brain tissue oxygenation ( $cSO_2$ ) of the patients participating in the study was  $57.7 \pm 16.4$  and

**Table 1. Tissue oxygenation before and after fluid resuscitation**

		Mean (SD)	Median (IQR)	Min-Max	p
$cSO_2$ (L)	Before	57.7±16.4	58 (47.5-72)	24-92	0.027*
	After	62.6±18	65 (51.5-71.5)	15-91	
$cSO_2$ (R)	Before	54.1±16.7	55 (44-65)	16-95	0.004*
	After	58.6±17.2	58 (44.5-72.5)	15-95	
$rSO_2$ (L)	Before	63.1±14.1	61 (50-74)	43-91	0.004*
	After	69.4±19.3	73 (57-84.5)	15-95	
$rSO_2$ (R)	Before	62.8±14.8	62 (51-74.5)	31-95	0.010*
	After	69.4±18	71 (57.5-86.5)	15-93	

$cSO_2$  (L): left cerebral oxygen saturation,  $cSO_2$  (R): right cerebral oxygen saturation;  $rSO_2$  (L): left renal oxygen saturation,  $rSO_2$  (R): right renal oxygen saturation

54.1±16.7, mean left and right kidney tissue oxygenation (rSO<sub>2</sub>) was 63.1±14.1, and 62.8±14.8. The median absolute differences between R-L cSO<sub>2</sub> and rSO<sub>2</sub> at time 0 were 5 (IQR 4-7), and 4 (IQR 1-9) respectively, but the difference was significant only for the brain (p = 0.046). Renal tissue oxygen saturation was higher than brain oxygen saturation in 64% (n=16) of patients. Tissue oxygen saturation increased significantly after fluid resuscitation (Table 1), but the absolute difference between the right and left cSO<sub>2</sub> and rSO<sub>2</sub> remained unchanged (p=0.94, p=0.84). The mean cSO<sub>2</sub> and rSO<sub>2</sub> of survivors trended higher than those of non-survivors before the fluid bolus, but the difference was not significant (p>0.05).

The decline in lactate levels and the increase in systolic and diastolic blood pressures were statistically significant after the bolus. There were no significant differences in base excess, respiratory rate, SpO<sub>2</sub>, and heart rate before and after resuscitation (Table 2). Bilateral cSO<sub>2</sub> and rSO<sub>2</sub> increased significantly after fluid bolus in survivors, whereas in nonsurvivors (n:9, 36%), there was no significant change (Table 3A-3B). The mortality scores of non-survivors were higher than survivors (p<0.005).

**Table 2. Vital and blood gas levels before and after fluid resuscitation**

		n	Mean±Std Dev.	Median	Min-Max	p
SpO <sub>2</sub>	Before	25	95,1±7,7	98	66-100	0,147
	After	25	93,2±19,9	99	0-100	
HR	Before	25	142,8±40,1	152	56-203	0,078
	After	25	137,8±33,9	139	71-197	
SBP	Before	25	84,4±23,3	85	45-136	0,001*
	After	25	97,4±19,8	94	68-139	
DBP	Before	25	45,8±21,5	49	13-96	0,004*
	After	25	55,4±15,6	55	25-96	
BE	Before	25	-4,03±6,91	-1,8	-18,6-6,7	0,809
	After	25	-3,32±5,95	-3,6	-13,8-9,1	
Lactate	Before	25	3,38±2,4	2,7	0,6-8,7	0,009*
	After	25	2,29±1,65	1,6	0,7-7,4	
RR	Before	25	37,3±16,2	32	12-77	0,893
	After	25	36,8±14,3	35	15-63	

SpO<sub>2</sub>: pulse oximetry, HR: heart Rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, BE: baz excess RR: respiratory rate

**DISCUSSION**

Shock is a leading cause of mortality and morbidity in children. Time is critical in shock management because early diagnosis and targeted treatment significantly reduce mortality and morbidity rates. Currently, there are no specific or sensitive methods to aid in the early recognition of sepsis. To address this gap, previous studies have explored the use of NIRS to evaluate tissue oxygenation. Recognizing that trends and changes in tissue oxygenation are more significant than

**Table 3A. Tissue oxygenation values before and after fluid resuscitation in survivors**

	Survivors	n	Mean±Std Dev	Median	Min-Max	p
cSO <sub>2</sub> (L)	Before	16	62±16,5	66	28-92	0,024*
	After	16	69,3±13,3	69,5	44-91	
cSO <sub>2</sub> (R)	Before	16	59,5±14,3	61	34-95	0,013*
	After	16	65,1±14,2	65,5	43-95	
rSO <sub>2</sub> (L)	Before	16	65,1±15	62	43-91	0,003*
	After	16	73±15,3	75,5	45-95	
rSO <sub>2</sub> (R)	Before	16	63,5±17	62	31-95	0,008*
	After	16	73,2±14,1	73,5	51-92	

cSO<sub>2</sub> (L): left cerebral oxygen saturation, cSO<sub>2</sub> (R): right cerebral oxygen saturation; rSO<sub>2</sub> (L): left renal oxygen saturation, rSO<sub>2</sub> (R): right renal oxygen saturation

**Table 3B. Tissue oxygenation values before and after fluid resuscitation in non-surviving patients**

	Non-survivors	n	Mean±Std Dev	Median	Min-Max	p
cSO <sub>2</sub> (L)	Before	9	50±14	48	24-73	0,575
	After	9	50,7±19,9	54	15-75	
cSO <sub>2</sub> (R)	Before	9	44,4±16,9	44	16-70	0,435
	After	9	47,1±16,7	45	15-71	
rSO <sub>2</sub> (L)	Before	9	59,6±12,4	57	44-83	0,4
	After	9	63±24,7	59	15-95	
rSO <sub>2</sub> (R)	Before	9	61,7±10,9	58	48-75	0,4
	After	9	62,6±22,8	61	15-93	

cSO<sub>2</sub> (L): left cerebral oxygen saturation, cSO<sub>2</sub> (R): right cerebral oxygen saturation; rSO<sub>2</sub> (L): left renal oxygen saturation, rSO<sub>2</sub> (R): right renal oxygen saturation

the absolute values. A reduction in the NIRS value indicates impaired tissue perfusion. In our study, the mean left and right brain tissue oxygenation (cSO<sub>2</sub>) of the patients participating in the study was 57.7±16.4 and 54.1±16.7, mean left and right kidney tissue oxygenation (rSO<sub>2</sub>) was 63.1±14.1, and 62.8±14.8. Bilateral cerebral and renal perfusion increased significantly after fluid resuscitation. The kidney tissue saturation values of 64% of patients were higher than the brain saturation values, which is consistent with the findings of previous research in this area. In the literature, Hanson et al. demonstrated that brain perfusion was preserved in children presenting with acute dehydration, whereas renal perfusion increased following fluid resuscitation in the emergency department (15). In an animal study, piglets were experimentally placed in hypovolemic shock. They observed that cerebral and renal perfusion increased significantly after resuscitation (16).

Blood lactate level is a biochemical marker frequently used to evaluate tissue hypoxia resulting from compromised oxygen delivery or use during shock management. In our study, the decline in lactate levels and the increase in systolic and diastolic blood

pressures after fluid resuscitation were statistically significant. In a similar study, Tayar et al. identified a significant negative correlation between cerebral tissue perfusion and lactic acid as well as a positive correlation with mean arterial pressure (17).

A study investigating the effect of cerebral perfusion on predicting prognosis in shock patients found a significant difference in regional cerebral oxygen saturation between survivors and non-survivors after 72 hours in the intensive care unit. ( $52.58\% \pm 7.33\%$  and  $44.75\% \pm 9.44\%$  ( $p=0.049$ )) (17). Balakrishnan et al. reported that children with cerebral tissue oxygen saturation  $<70\%$  in the first 4 hours after arrival to the pediatric intensive care unit had significantly higher PRISM 3 and PELOD scores compared to NIRS  $>70\%$  (18). Alexandre et al. found SOFA and APACHE II scores were significantly higher in adult patients admitted to the intensive care unit with baseline tissue oxygen saturation below 70% who continued low saturation after resuscitation (19). Vorwerk and Coates found that a persistent low  $StO_2$  (muscle tissue oxygenation) level (below 75%) following resuscitation in patients with septic shock had a double risk of mortality (RR 2.1%, 95% CI 1.2% to 3.5%;  $p=0.008$ ) (20). In our study, the mortality scores of the surviving patients were significantly lower than those of the non-surviving patients. The mean cerebral and renal oxygen saturation values of the surviving patients were higher than those of the non-surviving patients, but the differences were not statistically significant due to the limited number of patients.

In the literature, because it is easier to collect data, many NIRS studies of patients in shock tend to use the thenar muscle. There are only a few studies using bilateral measurements. However, these have primarily been used to assess brain tissue oxygen saturation in pediatric cardiovascular and interventional cardiology. Although typically used unilaterally, studies have shown that localized neuronal activation can cause regional changes in cerebral blood flow and oxygenation (21-22-23). There is currently a lack of clarity regarding the difference in right-left brain and kidney tissue oxygen saturation in both healthy and shock persons. Although there are not many studies, it is generally accepted in pediatric cardiac practice that the difference between hemispheres is 5-10% at stable systemic oxygenation. Lemmers et al. demonstrated a strong correlation between the oxygenation values of the right and left cerebral tissues in a cohort of 36 very-low-birth-weight preterm infants ( $r=0.89$ ;  $p < 0.01$ ). Furthermore, premature infants with unstable arterial saturation may demonstrate discrepancies between the right and left sides (24). Kussman et al. reported that bihemispheric measurements were similar during pediatric cardiac surgery ( $\leq 2$  percentage points/absolute scale units) (25). The present study included 12 patients with a right-left brain difference of more than 10%. Five patients died during the follow-up period. There were 9 patients with a right-left kidney difference of  $>10\%$  and 4 of them died during follow-up. Our study is the only one to use NIRS to evaluate four regions (right-left brain, kidney) in children in shock with short-term recordings in the pediatric age group.

The discrepancy between right and left differences among patients may not be solely attributable to saturation ( $SpO_2$ ).

Regional blood flow, false-positive measurements, and intra- and inter-patient variation can also contribute to the observed differences between the right and left sides. The presence of right-left differences indicates that unilateral measurements may not be sufficient for patient monitoring. Further studies with larger numbers of patients are necessary for evaluating the left-right difference as a prognostic factor.

It is noteworthy that in healthy children without shock, no significant difference was observed between the right and left sides. In our previous study, we demonstrated no discernible differences in cerebral and renal NIRS values between the right and left sides in healthy children (26). The findings of our study support the notion that multisite NIRS monitoring could have prognostic importance in critically ill pediatric patients. However, further studies are needed to define the differences between the right and left sides.

This study has several limitations. The sample size of 25 was relatively small. Moreover, the positioning of renal probes was based on anatomical landmarks without the use of ultrasound scans to verify the position. Despite its limitations, this study provides insights into laterality and pediatric cerebral and renal NIRS measurements in critically ill children and may facilitate the interpretation of NIRS data in critically ill patients. Further research with a larger cohort of healthy and critically ill patients is needed to confirm these findings.

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**Ethics Committee Approval:** This study was approved by the ethics committee of Marmara University (09.2016186) and intramural grant support (BAPKO SAG-C-TUP-131216-0524).

**Informed Consent:** Written consent was obtained from the participants.

**Peer Review:** Externally peer-reviewed.

**Author Contributions:** Conception/Design of Study- B.A., N.Y.Ö.; Data Acquisition- B.A.; Data Analysis/Interpretation- B.A., F.G.İ., E.U., N.Y.Ö.; Drafting Manuscript- B.A., N.Y.Ö.; Critical Revision of Manuscript- B.A., F.G.İ., E.U., N.Y.Ö.; Final Approval and Accountability- B.A., F.G.İ., E.U., N.Y.Ö.

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