Is there an association of near-infrared spectroscopy with low cardiac output and adverse outcomes in single-ventricle patients after stage 1 palliation?

Pezad Doctor[1], Sanjeev Aggarwal[2], Richard Garcia[3]

[1]Department of Pediatrics, Division of Cardiology, Children's Medical Center, University of Texas Southwestern Medical Center, Medical District, Dallas, Texas, USA, [2]Department of Pediatrics, Division of Cardiology, Children's Hospital of Michigan, Central Michigan University College of Medicine, Beaubien Blvd, Detroit, MI, USA, [3]Department of Pediatrics, Division of Critical Care Medicine, Children's Hospital of Michigan, Central Michigan University College of Medicine, Beaubien Blvd, Detroit, MI, USA

ABSTRACT

Objective : **Our primary objective study was to evaluate the association between near-infrared spectroscopy (NIRS) and low cardiac output (LCO) in patients with single-ventricle physiology after stage 1 palliation.**

Methods : **In this retrospective study, infants ≤6 months of age with single-ventricle physiology who underwent stage 1 palliation were included. Cerebral and renal NIRS values at various time intervals after surgery were compared between patients with low and normal cardiac output. LCO within the first 48 after surgery was defined as per the pediatric cardiac critical care consortium database. NIRS values were also compared with other adverse outcomes such as cardiac arrest, need for extracorporeal membrane oxygenation and mortality. The receiver operative characteristic curve was generated to determine an optimal cut-off NIRS value for detecting LCO.**

Results : **Ninety-one patients with median (Interquartile range) age of 10 days (6–26) and weight of 3.3 kg (3–3.5) were included in the study. Cerebral NIRS at 1 h (41.2 vs. 49.5; P = 0.002), 6 h (44 vs. 52.2; P < 0.001), and 12 h (51.8 vs. 56; P = 0.025) was significantly lower in the group with LCO compared to no LCO. Cerebral NIRS at 6 h was independently associated with LCO (P = 0.018), and cerebral NIRS at 6 h ≤57% had 91% sensitivity and 72% specificity to detect LCO.**

Conclusions : **Cerebral NIRS ≤57% at 6 h after surgery detected LCO after stage 1 palliation in single-ventricle patients. Cerebral or renal NIRS was not associated with adverse outcomes and therefore, may not be useful in predicting adverse outcomes in this population.**

Keywords : Adverse outcome, hypoplastic left heart syndrome, low cardiac output, near-infrared spectroscopy, single ventricle, stage 1 palliation

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Address for correspondence: Dr. Pezad Doctor, No. 2140 Medical District Dr, Apt: 2089, Dallas, Texas 75235, USA.
E-mail: pezaddoctor@gmail.com

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INTRODUCTION

Low cardiac output syndrome (LCO) is common in the early postoperative period after surgery for congenital heart disease (CHD) and is associated with increased morbidity and mortality.[1] The etiology of LCO is multifactorial, including the inflammatory cascade from cardiopulmonary bypass (CPB), myocardial ischemia from aortic cross-clamping, reperfusion injury, hypothermia, and pericardial tamponade.[2] In the early postoperative period following stage I surgical palliation for single ventricle physiology, a fine balance of blood flow in the systemic and pulmonary circulation is important to optimize tissue perfusion. There are several markers of low tissue perfusion: capillary refill time, urine output, core to peripheral temperature difference, blood pressure, heart rate, serum lactate, base deficit, and mixed venous saturation.[3] However, none of these clinical or laboratory markers are sensitive and specific for detecting LCO. Recently, near-infrared spectroscopy (NIRS) has been used for monitoring of LCO following various types of cardiac surgeries. NIRS is a noninvasive, continuous method of evaluating real-time regional oximetry based on the differential absorption of varying wavelengths of light by hemoglobin as it associates with oxygen.[4-6] As the name suggests, it uses near-infrared spectrum of light (700–900 nm wavelength) to detect fine variations in tissue oxygenation by measuring the capillary venous saturation by a sensor placed over the skin.[3] NIRS technology has been described in multiple clinical settings, including the pediatric and neonatal intensive care unit as well as operating room for predicting postoperative course.[6,7]

NIRS monitoring has shown to correlate with mixed venous oxygen saturation in a variety of clinical settings.[8-11] Kirshbom *et al.* reported that cerebral NIRS was independently associated with superior vena cava (SVC) saturations in awake patients with single-ventricle parallel circulation prior to routine cardiac catheterization ($P = 0.009$).[12] Ranucci *et al.* stated that cerebral NIRS correlated with SVC saturation in patients with CHD after surgical repair and the correlation was better in cyanotic patients.[9] Cerebral and renal NIRS values have also been shown to correlate with adverse postoperative outcomes in children after cardiac surgery such as acute kidney injury, need for extracorporeal membrane oxygenation (ECMO), acute neurological injury, and mortality.[10-15] NIRS monitoring for detecting low cardiac output (LCO) in infants with single ventricle lesions after stage 1 palliation is essential due to parallel circulation, risk of pulmonary over circulation at the expense of systemic perfusion as well as decreased myocardial contractility in the early postoperative period.[7,13,16] To the best of our knowledge, there are no reported studies correlating NIRS values with LCO state as defined by the Pediatric Cardiac Critical Care Consortium (PC4) database. The primary objective of the study was to determine if postoperative cerebral and renal NIRS values were associated with LCO state defined by the PC4 database in patients who underwent stage 1 palliation for single ventricle physiology. Our secondary aim was to evaluate the role of NIRS in predicting composite adverse outcomes and individual outcome variable; including, cardiac arrest, ECMO, and mortality in this patient population.

METHODS

This was a retrospective study approved by the Institutional Review Board of our center. Consecutive patients <6 months of age with single ventricle physiology who underwent stage 1 surgical palliation our center from January 2010 to December 2019 were included in the study. Patients older than 6 months of age at the time of stage one palliation, required ECMO support at arrival to the intensive care unit, and those undergoing hybrid procedures were excluded from the study. Demographic data at the time of surgery and perioperative variables such as hemodynamic, laboratory, and inotropic data were collected. Laboratory data include renal function test, arterial blood gas, and lactate performed preoperatively and at 1 h, 6 h, 12 h, 24 h, and 48 h after arrival to the cardiac intensive care unit. Serum lactate was measured from arterial blood sample obtained from an arterial line.

Near-infrared spectroscopy measurements

Cerebral and renal saturations were measured using the weight-appropriate Covidien SomaSensor oxygen saturation probe, and Somanetics INVOS Cerebral/Somatic oximeter. As per protocol, cerebral NIRS values were obtained by probes placed on the forehead whereas renal NIRS values were obtained by probes placed in the flank region between T10 and L1 level. We collected cerebral and renal NIRS values at 1 h, 6 h, 12 h, 24 h, and 48 h after arrival to the cardiac intensive care unit. NIRS difference referred to the arithmetic difference between the renal and cerebral NIRS values calculated at a specific point in time. The doses of various vasopressors and inotropes were collected along with the NIRS values for calculating the vasoactive inotropic score (VIS) as described by Gaies *et al.*[17]

Low cardiac output definition

We defined LCO during the first 48 postoperative h using the PC4 database definition: VIS ≥15 at any time, tripling of the VIS from the least value during a 48 h period, considering that after tripling, the VIS must be 10 or higher, arterial and venous oxygen saturation difference ($A\text{-}VO_2$) >40% by invasive measurement, or LCO documented in the attending physician note.[18] Due

to the variable location of the central venous catheter tip and lack of blood draw consistency between patients, mixed venous oxygen saturations were not collected. Therefore, the mixed venous saturation was not utilized to define LCO.

Composite outcome score

A composite adverse outcome variable included the presence of any one of the following within 30 days after surgery; cardiac arrest, need for ECMO or death. Acute kidney injury was defined by a decrease in the effective glomerular filtration rate by >50% from baseline as per pRIFLE criteria.[19,20] Acute neurological injury was considered if the patient's head imaging showed ischemic injury or intracranial bleeding.

Statistical analysis

Data were analyzed using SPSS software for PC version 22 (SPSS Inc., Chicago, Illinois, USA). Demographic data were presented as median and interquartile range (IQR). Other continuous data were presented as mean and standard deviation. Categorical data were presented as number and percentage. The entire cohort was divided into two groups by the presence of LCO. Student's *t*-test and Chi-square were used to compare the demographic, hemodynamic, laboratory, and NIRS data at various time points between the groups as appropriate. Binary logistic regression was used to identify the independent association between NIRS and LCO. Secondary analysis was performed between NIRS values and composite adverse outcomes. The cohort was also divided by type of primary surgical repair Norwood versus isolated aortopulmonary shunt. Receiver operative characteristic curve analysis was performed for assessing the optimal cutoff values for predicting the LCO. A $P < 0.05$ was considered statistically significant.

RESULTS

The study cohort included 91 patients. The median (IQR) age was 10 days,[6-26] weight was 3.3 kg (3–3.5), and length was 51 cm (48.35–53). The demographic data are depicted in Table 1. The primary cardiac diagnoses included 26 (28.6%) hypoplastic left heart syndrome (HLHS), 8 (8.8%) HLHS variants, and 57 (62.6%) hypoplastic right heart syndromes (HRHS). Sixteen patients underwent Norwood with Sano shunt and 18 patients underwent Norwood with right modified Blalock–Taussig shunt as per institutional preference. Fifty-seven patients with a diagnosis of HRHS underwent isolated aortopulmonary shunt [Table 2]. CPB was used in 79 (87%) patients and the remaining 12 (13%) who did not require CPB for placement of isolated aortopulmonary shunt. The primary outcome of LCO state was seen in 42 (46%) patients in the first 48 postoperative hours. Figure 1 illustrates the distribution of patients with the diagnosis of LCO at various time points in the first 48 h after surgery. The composite adverse outcome was noted in 25 (27.5%) of patients in the cohort. Postoperative adverse outcomes within 30 days include cardiac arrest in 20 (22%), venoarterial ECMO required in 15 (16.5%), and death in 15 (16.5%) patients. Table 3 illustrates all postoperative outcomes.

Table 1: Demographic variables for the entire cohort

Variables Median (IQR) or *n* %	Cohort *n*=91
Age at surgery (days)	10 (6-26)
Weight (kg)	3.3 (3-3.5)
Length (cm)	51 (48.4-53)
Gestation age (weeks)	38 (37-39)
Males	54 (59.3%)

Table 2: Primary cardiac diagnoses and surgical procedures

Variables (*n* (%))	Cohort (*n*=91)
Primary cardiac diagnoses	
HLHS	26 (28.6%)
HLHS Variants	8 (8.8%)
a. Heterotaxy syndrome + DILV	4 (4.4%)
b. TA with malposed great arteries	2 (2.2%)
c. Other	2 (2.2%)
HRHS	(62.6%)
a. PA, VSD±MAPCAs	18 (19.8%)
b. PA, IVS	10 (11.0%)
c. TA with normally related great arteries	8 (8.8%)
d. Unbalance left dominant AV canal	6 (6.4%)
e. Heterotaxy syndrome with hypoplastic RV	5 (5.5%)
f. DILV	5 (5.5%)
g. Crisscross ventricles	4 (4.4%)
h. Double outlet left ventricle with PA	1 (1.1%)
Surgical procedures	
Norwood + Sano modification	16 (17.6%)
Norwood + MBTS	18 (19.8%)
Aortopulmonary shunt	57 (62.6%)

HLHS: Hypoplastic left heart syndrome, DILV: Double inlet left ventricle, TA: tricuspid atresia, PA: pulmonary atresia, VSD: Ventricular septal defect, IVS: Intact ventricular septum. MAPCAs: major Aortopulmonary collateral arteries, HRHS: Hypoplastic right heart syndrome, AV canal: Atrioventricular canal

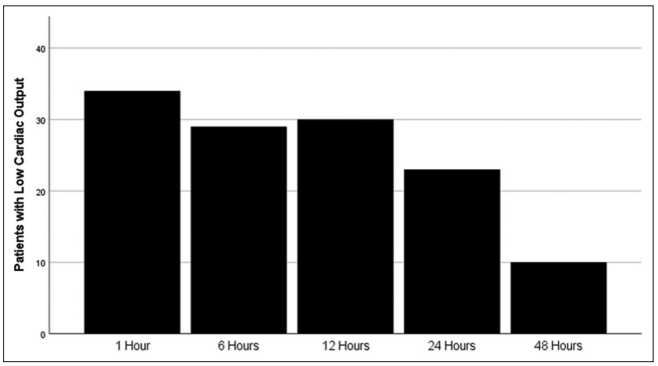

Figure 1: Histogram illustrating the number of patients with low cardiac output at various time points within the first 48 h after surgery

For the entire cohort, mean standard deviation (SD) cerebral NIRS values were significantly lower in the LCO group compared to the rest of the cohort at 1 h (41.2 vs. 49.5; $P = 0.002$), 6 h (44 vs. 52.2; $P < 0.001$), and 12 h (51.8 vs. 56; $P = 0.025$) after surgery [Figure 2]. The difference between renal and cerebral NIRS was significantly higher in the LCO group compared to normal cardiac output group at 1 h (26.7 vs. 18.2; $P = 0.008$), 6 h (22.1 vs. 14.7; $P = 0.03$), 12 h (15.6 vs. 10.3; $P = 0.036$), and 24 h (10.6 vs. 2; $P = 0.001$) [Table 4]. Table 5 portrays the comparison of various postoperative variables between the LCO group and the rest of the cohort. Using logistic regression analysis, cerebral NIRS at 6 h ($P = 0.018$), systolic blood pressure at 1 h ($P = 0.04$), and arterial lactate ($P = 0.024$) at 1 h remained independently associated with LCO. Receiver operating characteristic curve analysis was performed with factors that were significant in univariate analysis. NIRS at 6 h had the best area under the curve (AUC) and showed that a mean cerebral NIRS of ≤ 57% at 6 h had 91% sensitivity and 72% specificity to detect LCO (AUC: 0.72, $P < 0.001$). Patients with a mean cerebral NIRS of ≤ 55% during the first 24 h had a tendency toward higher risk for LCO, odds ratio (OR): 2.6 (0.99–6.80; $P = 0.05$).

Near-infrared spectroscopy and postoperative outcomes

Cerebral NIRS (37.63 vs. 47.23; $P = 0.007$) and NIRS difference (30.53 vs. 20.7; $P = 0.02$) at 1 h were associated with need for ECMO, although this difference did not remain significant after logistic regression analysis. There was no association between NIRS values and acute kidney injury, cardiac arrest, or mortality individually. Cerebral NIRS at 1 h (40.65 vs. 47.5; $P = 0.024$) and NIRS difference at 24 h (10.8 vs. 5.1; $P = 0.048$) were associated with our composite adverse outcome, although did not remain significant after logistic regression analysis.

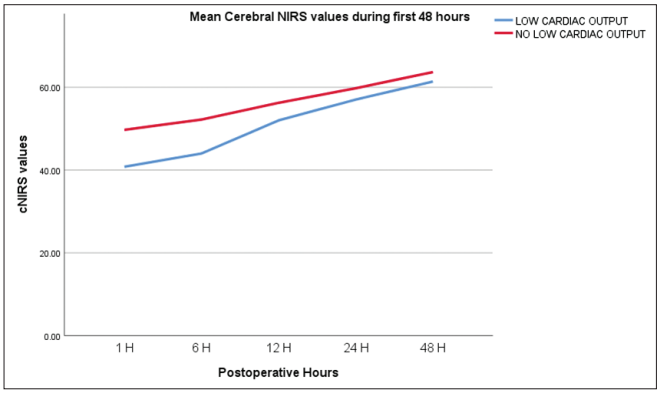

Figure 2: Mean cerebral NIRS values during first 48 h after surgery. NIRS: Near-infrared spectroscopy

Table 3: Post operative outcomes

Variables (Median (IQR) or *n* %)*	Cohort (*n*=91)
Low cardiac output	42 (46%)
Duration on MV (days)	8 (3-24)
Duration of hospital stay (days)	26 (15-69)
Acute kidney injury	30 (33%)
Acute neurological injury	8 (8.6%)
Cardiac arrest	20 (22%)
VA ECMO	15 (16.5%)
Mortality	15 (16.5%)
Composite adverse outcome	25 (27.5%)

MV: mechanical ventilation, VA ECMO: Veno-arterial extracorporeal membrane oxygenation

Table 4: Comparison of demographic variables and NIRS values in Low cardiac output vs. normal cardiac output groups

Variables Mean (SD)	Low Cardiac Output		
	Yes (*n*=42)	No (*n*=49)	*P*
Age, days	14 (21.2)	30.6 (43)	0.025
Weight, kg	3.3 (0.68)	3.4 (0.58)	0.512
Length, cm	51.2 (3.3)	50.8 (2.9)	0.568
Gestational age, weeks	38.3 (1.8)	3.7 (1.9)	0.142
cNIRS at 1 hour	41.2 (13.5)	49.5 (11.4)	0.002
cNIRS at 6 hours	44 (9.8)	52.2 (9.6)	< 0.001
cNIRS at 12 hours	51.8 (8.3)	56.2 (9.7)	0.025
cNIRS at 24 hours	57.2 (7.2)	59.9 (6.6)	0.098
rNIRS at 1hour	67.7 (12.7)	67 (11)	0.78
rNIRS at 6 hours	66.1 (15.1)	66.4 (10.4)	0.92
rNIRS at 12 hours	67.2 (9.3)	65.6 (11.6)	0.5
rNIRS at 24 hours	67.3 (9.9)	62 (10.8)	0.039
NIRS difference at 1 hour	26.7 (14)	18.2 (14)	0.008
NIRS difference at 6 hours	22.1 (18.3)	14.7 (12.6)	0.03
NIRS difference at 12 hours	15.6 (10.3)	10.3 (11.7)	0.036
NIRS difference at 24 hours	10.6 (9.3)	2 (10.3)	0.001

cNIRS: Cerebral near Infrared spectroscopy, rNIRS: renal near infrared spectroscopy values, NIRS difference refers to the difference between the somatic and cerebral NIRS values

Table 5: Comparison of clinical and laboratory variables in Low cardiac output vs. normal cardiac output groups

Perioperative Variables Mean (SD)	Low Cardiac Output		
	Yes (*n*=42)	No (*n*=49)	*P*
SBP at 1 hour (mmHg)	81 (14.6)	88 (14.5)	0.036
SBP at 6 hour (mmHg)	78 (13.1)	81 (11.8)	0.23
SBP at 12 hour (mmHg)	75 (11.1)	78 (10.1)	0.21
SBP at 24 hour (mmHg)	77 (10.9)	83 (9.9)	0.013
DBP at 1 hour (mmHg)	43 (7.2)	44 (8.7)	0.72
DBP at 6 hour (mmHg)	42 (7.1)	39 (6.7)	0.063
DBP at 12 hour (mmHg)	40 (6.9)	38 (4.7)	0.19
DBP at 24 hour (mmHg)	42 (8.6)	40 (5.8)	0.19
Heart rate at 1 hour (bpm)	168 (17.2)	160 (16.7)	0.72
Heart rate at 6 hours (bpm)	167 (14)	156 (15.4)	<0.001
Heart rate at 12 hours (bpm)	166 (14)	155 (16.7)	<0.001
Heart rate at 24 hours (bpm)	166 (16.4)	156 (18.1)	0.016
Initial arrival Lactate (mmol/L)	7.7 (3.8)	4.2 (2.5)	<0.001
Lactate at 6 hours (mmol/L)	6.8 (6.6)	2.9 (1.9)	<0.001
Lactate at 24 hours (mmol/L)	2.3 (1.5)	1.6 (0.8)	0.013
CPB time (min)	216 (110.9)	122 (95.1)	<0.001
ACC time (min)	66.1 (53.4)	21.5 (38.6)	<0.001

SBP: systolic blood pressure, SaO_2: Arterial oxygen saturation, CPB: Cardiopulmonary bypass, ACC: Aortic cross-clamp time

Table 6: Norwood procedure vs Aortopulmonary shunt

Perioperative Variables Mean (SD)	Low Cardiac Output		
	Yes (*n*=42)	No (*n*=49)	*P*
SBP at 1 hour (mmHg)	81 (14.6)	88 (14.5)	0.036
SBP at 6 hour (mmHg)	78 (13.1)	81 (11.8)	0.23
SBP at 12 hour (mmHg)	75 (11.1)	78 (10.1)	0.21
SBP at 24 hour (mmHg)	77 (10.9)	83 (9.9)	0.013
DBP at 1 hour (mmHg)	43 (7.2)	44 (8.7)	0.72
DBP at 6 hour (mmHg)	42 (7.1)	39 (6.7)	0.063
DBP at 12 hour (mmHg)	40 (6.9)	38 (4.7)	0.19
DBP at 24 hour (mmHg)	42 (8.6)	40 (5.8)	0.19
Heart rate at 1 hour (bpm)	168 (17.2)	160 (16.7)	0.72
Heart rate at 6 hours (bpm)	167 (14)	156 (15.4)	<0.001
Heart rate at 12 hours (bpm)	166 (14)	155 (16.7)	<0.001
Heart rate at 24 hours (bpm)	166 (16.4)	156 (18.1)	0.016
Initial arrival Lactate (mmol/L)	7.7 (3.8)	4.2 (2.5)	<0.001
Lactate at 6 hours (mmol/L)	6.8 (6.6)	2.9 (1.9)	<0.001
Lactate at 24 hours (mmol/L)	2.3 (1.5)	1.6 (0.8)	0.013
CPB time (min)	216 (110.9)	122 (95.1)	<0.001
ACC time (min)	66.1 (53.4)	21.5 (38.6)	<0.001

Footnote: CPB: Cardiopulmonary bypass time, MV: mechanical ventilation, VA ECMO: Veno-arterial extracorporeal membrane oxygenation

Table 7: NIRS and low cardiac output in patients after the Norwood procedure

NIRS values mean (SD)	Low Cardiac Output		
	Yes (*n*=26)	No (*n*=8)	*P*
cNIRS at 1 hour	38.70 (14.87)	48.89 (10.7)	0.67
cNIRS at 6 hours	43.15 (10.58)	54.11 (7.77)	0.007
cNIRS at 12 hours	51.32 (8.67)	58.11 (13.64)	0.095
cNIRS at 24 hours	56.56 (7.11)	57.13 (7.22)	0.85
rNIRS at 1 hour	65.85 (12.47)	66.88 (9.67)	0.83
rNIRS at 6 hours	65.44 (18.27)	69.5 (7.6)	0.55
rNIRS at 12 hours	67.67 (10.85)	68.50 (8.18)	0.84
rNIRS at 24 hours	66.54 (9.76)	62.43 10.83)	0.35
NIRS difference at 1 hr	27.15 (12.98)	19.88 (14.07)	0.18
NIRS difference at 6 hr	22.30 (21.28)	17.25 (10.99)	0.52
NIRS difference at 12 hr	16.71 (10.27)	14.25 (13.10)	0.58
NIRS difference at 24 hr	10.63 (9.71)	6.71 (10.07)	0.36

Table 8: NIRS and low cardiac output after Aortopulmonary shunt

NIRS values mean (SD)	Low Cardiac Output		
	Yes (*n*=16)	No (*n*=41)	*P*
cNIRS at 1 hr	44.31 (11.1)	49.88 (11.62)	0.106
cNIRS at 6 hr	45.50 (8.13)	51.80 (9.9)	0.028
cNIRS at 12 hr	53.06 (7.81)	55.83 (8.6)	0.27
cNIRS at 24 hr	57.92 (7.7)	60.5 (6.43)	0.27
rNIRS at 1 hr	71.8 (12.27)	67 (11.33)	0.195
rNIRS at 6 hr	69.36 (7.88)	65.76 (10.74)	0.25
rNIRS at 12 hr	68 (8.3)	64.84 (12.16)	0.37
rNIRS at 24 hr	69.64 (10.4)	61.43 (11.04)	0.041
NIRS difference at 1 hr	27.57 (18.27)	17.63 (14.12)	0.043
NIRS difference at 6 hr	23.64 (12.53)	14.24 (12.91)	0.023
NIRS difference at 12 hr	14.57 (10.81)	9.22 (11.32)	0.13
NIRS difference at 24 hr	12 (9.4)	1.11 (10.15)	0.004

Norwood versus Aortopulmonary shunt

Patients who underwent the Norwood procedure had a significant higher incidence of LCO compared to aortopulmonary shunt (26/34 [76.5%] vs. 16/57 [28%] $P < 0.001$). Other postoperative outcomes such as need for ECMO ($P = 0.007$), mortality ($P = 0.001$), and composite adverse outcomes ($P = 0.005$) were significantly higher in Norwood patients as well. Table 6 describes the difference in perioperative variables and outcomes between these two groups.

In the Norwood group, only cerebral NIRS values at 6 h after admission to the cardiac intensive care unit were associated with LCO; $P = 0.007$. However, logistic regression did not show independent association between NIRS values and LCO at 6 h. Similarly, in the aortopulmonary shunt group, cerebral NIRS values at 6 h were associated with LCO, $P = 0.028$. In addition, the arithmetic NIRS difference was associated to LCO at 1 h ($P = 0.043$), 6 h ($P = 0.023$), and at 24 h ($P = 0.004$). Renal NIRS was associated to LCO at 24 h; $P = 0.041$. Binary logistic regression did not show independent association to LCO for any of the above variables in the aortopulmonary shunt group. The relationship of NIRS values in patients with and without LCO at various time points post operatively are illustrated in Table 7 and 8.

DISCUSSION

In our study, cerebral NIRS values at 6 h were independently associated with LCO in the early postoperative period in patients with single ventricle physiology. Mean cerebral NIRS at 6 h ≤57% was highly sensitive in detecting LCO within the first 48 postoperative h. This is the first study to use the LCO definition developed by the PC4 database. This definition is useful in assessing LCO in patients with single ventricle physiology when mixed venous saturation is not reliable due to central catheter position or intra-atrial mixing for blood. Zulueta *et al.* reported the use of NIRS in 22 patients with mean (SD) age of 2.7 (3.6) months undergoing cardiac surgery for CHD, and showed intraoperative cerebral oxygen desaturation by NIRS were associated with lower central venous saturations ($P = 0.002$), cardiac index ($P = 0.004$), oxygen availability index ($P = 0.0004$), and higher oxygen extraction ($P = 0.0005$) suggesting LCO.[21] In a prospective study by Gil-Anton *et al.* in 15 infants with CHD, postoperative combined cerebral and renal NIRS monitoring correlated with LCO assessed by the thermodilution method.[22] Similarly, we report an association between cerebral NIRS and LCO, although no association between renal NIRS values and LCO was noted in our cohort. This differs from the study by Hoffman *et al.*, who reported that renal NIRS values below 70.5% at 6 h were associated with LCO (OR: 1.06 ± 0.03; $P = 0.048$).[13] In a study by Hickok *et al.*, of 27 neonates who underwent CPB reported that renal NIRS values <58% predicted the development of LCO with 100% sensitivity and 69% specificity.[23] On the other hand, an observational study by Bhalala *et al.*, of 17 children after cardiac surgery reported that renal

NIRS (AUC: 0.51; confidence interval [CI]: 0.37–0.65) was not associated to LCO.[24] Our study uniformly comprises children with similar diagnoses (single-ventricle lesions) undergoing stage one palliation whereas other studies have a cohort of patients with varying diagnoses, surgical procedures, and postoperative hemodynamics. The lack of association between renal NIRS and LCO could be explained by regional variation in the distribution of blood flow after CPB accounting for the variable renal NIRS values. Hence, changes in renal regional saturation did not correlate with a true LCO state.

Arithmetic difference between cerebral near-infrared spectroscopy and renal near-infrared spectroscopy values

The difference between renal and cerebral NIRS in healthy newborns has been previously reported as mean (SD) of 8.9% (9.4%).[25] In our study, a higher difference between renal and cerebral NIRS values was observed in LCO patients. The higher difference was due to lower cerebral NIRS as the renal NIRS values remained similar between the LCO and no LCO groups. In a study by Hoffman *et al.*, of 79 patients with HLHS after stage 1 palliation, renal and cerebral NIRS difference of <10% in the first 48 h after surgery was associated with shock and postoperative complications.[26] We propose that the higher renal to cerebral NIRS difference could be due to redistribution of the limited blood flow and greater consumption of oxygen by the brain compared to kidneys leading to a regional tissue difference in oxygen delivery and consumption. Although using invasive blood samples, in a similar fashion, this concept was previously explained in a study by Barnea *et al.* that stated a higher arterialvenous oxygen saturation difference was associated to lower oxygen delivery to the tissues in patients with parallel single-ventricle circulation.[27]

Near-infrared spectroscopy and postoperative outcomes

Our data did not show statistically significant independent association between NIRS and cardiac arrest, need for ECMO, mortality, or composite adverse outcome. Phelps *et al.* studied 50 neonates with HLHS after the Norwood procedure and found that lower mean cerebral NIRS over the first 48 h postoperatively (52.8% ± 9.93% vs. 60.8% ± 5.91%; $P < 0.001$) was associated with subsequent adverse outcome defined as intensive care unit length of stay >30 days, need for ECMO or hospital death after 48 h. They reported mean cerebral NIRS value of <56% in the first 48 h after surgery was predictive of a subsequent adverse outcome with 75% sensitivity and 79.4% specificity.[16] A study by Hoffman *et al.* in 194 patients after the Norwood procedure found that cerebral NIRS at 6 h (OR: 0.94, CI: 0.86–0.99; $P < 0.038$), 48 h (OR: 0.91, CI: 0.86–0.96; $P < 0.001$), and somatic NIRS at 6 h (OR: 1.05, CI: 1.01–1.14; $P < 0.018$) predicted survival.[13] Interestingly, we did not find this association between NIRS values at various time points and mortality, either by univariate or logistic regression analysis. This could be due to the difference in management practices and increasing awareness about NIRS values in recent years leading to timely interventions, perhaps preventing some of these adverse outcomes.

In our cohort, there was no association of cerebral or renal NIRS values with postoperative acute kidney injury. In contrast, Flechet *et al.* reported a model combining cerebral NIRS monitoring along with other perioperative physiological variables that allowed early detection of acute kidney injury after pediatric cardiac surgery (AUC: 0.79; 95% CI, 0.79–0.80; $P < 0.001$).[8] Colasacco *et al.* reported that mean renal saturation <80% predicts renal insufficiency with a sensitivity of 100% and specificity of 75% ($P < 0.001$) in a cohort of patients after CHD surgery, including biventricular patients.[28]

In a cohort of single-ventricle patients after stage I surgical repair; Dent *et al.* outlined new or worsening ischemic lesions on postoperative magnetic resonance imaging associated with prolonged low cerebral NIRS (<45% for >180 min).[29] However, we did not find an association between acute neurological injury and cerebral NIRS values at any time point. This difference can be related to the small number of patients with acute neurological injury in our cohort since only symptomatic patients underwent neurological imaging in our institution.

Limitations

This was a single-center, retrospective chart review with a small sample size. No fixed protocol for discontinuation of NIRS monitoring was followed. No protocol was employed for the routine monitoring of cardiac output in the early postoperative period. The use of inotropes and other interventions was at the discretion of the intensive care team taking care of the patients that may have confounded the data. In the early postoperative period, low cerebral oxygen saturation is influenced by multiple competing physiological effects.

CONCLUSIONS

Lower cerebral NIRS values were associated with LCO defined as per the PC4 Database in single-ventricle patients after stage 1 palliation. Cerebral NIRS ≤57% at 6 h after surgery was indicative of LCO. Cerebral or renal NIRS were not independently associated to postoperative adverse outcomes such as cardiac arrest, need for ECMO, or mortality. This is the first study that has employed the PC4 Database definition of LCO to evaluate the association between NIRS values, LCO, and adverse outcomes, while previous studies

used mixed venous saturation to define LCO; making comparisons to previously reported studies difficult. Future prospective randomized controlled trials are essential to determine if NIRS-directed interventions can truly improve postoperative outcomes in this population.

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Conflicts of interest

There are no conflicts of interest.

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