World Journal for Pediatric and Congenital Heart Surgery
2016, Vol. 7(2) 180-184
© The Author(s) 2015
Reprints and permission:
sagepub.com/journalsPermissions.nav
DOI: 10.1177/2150135115618939
pch.sagepub.com

Postoperative Abdominal NIRS Values Predict Low Cardiac Output Syndrome in Neonates

Rhiannon L. Hickok, MD[1], Michael C. Spaeder, MD, MS[2], John T. Berger, MD[2,3], Jennifer J. Schuette, MD, MS[3], and Darren Klugman, MD, MS[2,3]

Abstract

Background: The development of low cardiac output syndrome (LCOS) after cardiopulmonary bypass (CPB) occurs in up to 25% of neonates and is associated with increased morbidity. Invasive cardiac output monitors such as pulmonary artery catheters have limited availability and are costly. Near-infrared spectroscopy (NIRS) is a noninvasive tool for monitoring regional oxygenation in neonates in the cardiac intensive care unit (CICU). We hypothesize that anterior abdominal NIRS may aid in the early identification of LCOS after cardiac surgery. **Methods:** Prospective observational study from October 2013 to October 2014 of all neonates with congenital heart disease admitted to the CICU following CPB. Abdominal NIRS values were continuously recorded upon CICU admission and for the subsequent 24-hour period. The primary outcome was the development of LCOS. Low cardiac output syndrome was defined as the presence of metabolic lactic acidosis (pH < 7.3 and lactate > 4) or addition of a new vasoactive agent or a vasoactive inotropic score > 15. Autoregressive time series models were constructed for each patient based on the continuously recorded NIRS values, and patients were stratified by development of LCOS. **Results:** Twenty-seven neonates met inclusion criteria, of whom 11 developed LCOS. Neonates who developed LCOS had lower constant NIRS values (49% vs 66%, $P < .001$). Constant NIRS values less than 58% best predicted development of LCOS with a sensitivity of 100% and specificity of 69%. **Conclusion:** Lower constant anterior abdominal NIRS values in the early postoperative period may allow early identification of neonates at risk for LCOS.

Keywords
congenital heart surgery, intensive care, postoperative care, congenital heart disease, neonate

Submitted June 18, 2015; Accepted October 19, 2015.

Introduction

The development of low cardiac output syndrome (LCOS) following cardiopulmonary bypass (CPB) occurs in approximately 25% of neonatal cardiac surgery patients[1-3] and has been associated with significant morbidity and mortality.[4] Low cardiac output syndrome has been attributed to many factors[3,5,6] and is typically seen 6 to 12 hours postoperatively.[3,7]

Although this drop in cardiac output is well documented, studies evaluating tools to predict or prevent LCOS have not identified the ideal noninvasive monitor. Near-infrared spectroscopy (NIRS) is a noninvasive monitoring tool that has been studied both intraoperatively and postoperatively to assess regional tissue oxygenation and thus potentially assess the adequacy of end-organ perfusion. Chakravarti et al[8] showed that multisite NIRS monitoring in the operating room correlated with rising lactate levels after bypass. Postoperatively, a decrease in somatic NIRS values has been associated with extubation failure[9] and with acute kidney injury[10] in the cardiac intensive care unit (CICU).

A recent report has highlighted the potential advantage of abdominal site NIRS monitoring in children after cardiac surgery.[11] Changes in abdominal site NIRS may precede other clinical signs of LCOS as cardiac output is shunted to the vital organs in a state of low cardiac output. We hypothesize that decreased anterior abdominal NIRS values in the first 24 hours after cardiac surgery are associated with the development of LCOS in neonates.

[1] Division of Critical Care Medicine, Texas Children's Hospital, Houston, TX, USA
[2] Division of Critical Care Medicine, Children's National Health System, Washington, DC, USA
[3] Division of Cardiology, Children's National Health System, Washington, DC, USA

Current address for Dr. Spaeder: Division of Pediatric Critical Care, University of Virginia School of Medicine, Charlottesville, VA, USA.

Current address for Dr. Schuette: Division of Pediatric Anesthesia and Critical Care Medicine, Johns Hopkins Medical Institutions, Baltimore, MD, USA

Corresponding Author:
Rhiannon Hickok, Department of Critical Care, Texas Children's Hospital, 6621 Fannin St, Ste W6006 Houston, TX 77030, USA.
Email: lynaerhi@gmail.com

Abbreviations and Acronyms

CICU	cardiac intensive care unit
CPB	cardiopulmonary bypass
ICU	intensive care unit
LCOS	low cardiac output syndrome
NIRS	near-infrared spectroscopy
RMSSDs	root mean square of successive differences
ROC	receiver–operating characteristic
RACHS-1	risk adjustment for congenital heart surgery
NEC	necrotizing enterocolitis
SvO_2	mixed venous oxygen saturation
TOF	Tetralogy of Fallot
TGA	Transposition of the great arteries
VIS	vasoactive inotropic score

Materials and Methods

Neonates (<30 days of age) admitted to the CICU after congenital cardiac surgery requiring CPB between October 2013 and October 2014 were included. This was a subset of data within a larger prospective observational study examining the association between abdominal NIRS values and postoperative morbidity in neonates after cardiac surgery. The primary goal of this analysis was to examine the association between abdominal NIRS values and the development of LCOS; patients were excluded from analysis if they had LCOS on admission without resolution in the first four hours postoperatively. This study was approved by the institutional review board at the Children's National Health System with a waiver of documentation of written informed consent.

On arrival to the CICU from the operating room, a pediatric NIRS probe (INVOS; Covidien, Mansfield, Massachusetts) was placed on the anterior abdomen in the left lower quadrant. The left lower quadrant location was chosen to avoid interference from the liver, except in one patient with heterotaxy where the abdominal NIRS probe was placed on the right lower quadrant. The NIRS values were recorded every 30 seconds in a blinded fashion for the first 24 hours after admission. In addition to the NIRS data, additional data collected included patient demographics (including age, weight, and cardiac diagnosis), CPB and circulatory arrest time, laboratory data, and information related to vasoactive medications.

The primary outcome was the development of LCOS. Low cardiac output syndrome was defined as the presence of metabolic lactic acidosis (pH < 7.3 and lactate > 4 mmol/L) or addition of a new vasoactive agent or a vasoactive inotropic score > 15.[12,13] Secondary outcomes analyzed were length of mechanical ventilation, length of CICU stay, length of hospital stay, need for extracorporeal membrane oxygenation in the first 24 postoperative hours, and hospital mortality.

We employed a time series modeling approach to analyze the relationship between NIRS values and the development of LCOS using traditional time series methods.[14] For each patient, NIRS values were plotted over time. In the cohort of patients who developed LCOS, we included NIRS values from CICU admission until development of LCOS. In the cohort of patients who did not develop LCOS, we included NIRS values from CICU admission to 24 hours following CICU admission. Each time series was assessed for stationarity using the Augmented Dickey-Fuller test for unit root.[14] The autocorrelation and partial autocorrelation functions were calculated for each time series and plotted to aid in the initial identification of a base Box-Jenkins model.[14] Initial identification suggested that an autoregressive model of order two would best explain the behavior of NIRS values over time for all included patients, represented as:

$$Z_t = \varnothing_1 Z_{t-1} + \varnothing_2 Z_{t-2} + Z_0 + a_t,$$

where Z_t = NIRS value for time period t,
Z_{t-1} = NIRS value for time period t−1,
$\varnothing_1$ = weighted coefficient of NIRS value for time period t−1,
Z_{t-2} = NIRS value for time period t−2,
$\varnothing_2$ = weighted coefficient of NIRS value for time period t−2,
Z_0 = constant NIRS value over time,
a_t = white noise term for time period t.

For the purposes of simplicity, we termed Z_0 as the *constant NIRS value* as this constant best represents the value around which NIRS oscillates over time for each patient. Model coefficients were calculated using maximum likelihood estimation. Patients were stratified by the development of LCOS in the first 24 hours, and model variables were compared using Wilcoxon rank-sum testing. Receiver–operating characteristic (ROC) curve analysis was performed to assess discriminatory ability of the models to predict the development of LCOS.

To examine the relationship between NIRS variability and the development of LCOS, we calculated the root mean square of successive differences (RMSSDs) of subsequent NIRS values, similar to the methods used in the assessment of heart rate variability.[15] In the subset of patients who developed LCOS, we calculated the RMSSD for both (a) the time period from CICU postoperative admission to the development of LCOS and (b) the hour preceding the development of LCOS.

Continuous variables were tested for normality using the Wilk-Shapiro test. Continuous variables were analyzed using Student *t* test or Wilcoxon rank-sum testing as appropriate. Categorical variables were assessed using chi-square or Fisher exact testing as appropriate. Type I error was set at .05. All calculations were performed using Stata/IC 12.1 (Stata Corporation, College Station, Texas).

Results

There were 35 neonates who underwent cardiac surgery with CPB during the period of study. Three neonates were not enrolled due to parental refusal and one was excluded because an abdominal monitor was not placed due to the development of necrotizing enterocolitis (NEC) prior to cardiac surgery. Of the 31 remaining neonates, 4 were excluded due to low cardiac output states on admission to the CICU that persisted beyond the first four hours following admission. The demographics of the 27 neonates included in the study are illustrated in Table 1. The median age

Table 1. Patient Demographics Data Stratified by Development of LCOS.

Characteristics	LCOS (n = 11)	No LCOS (n = 16)	*P* Value
Age at surgery, days	6 (IQR 5-11)	6.5 (IQR 5-11)	.82
Male gender	7 (64%)	10 (63%)	1.0
Weight, kg	3.3 (SD 0.6)	3.2 (SD 0.8)	.43
RACHS-1	6 (IQR 3-6)	3 (IQR 3-4)	.048
Diagnosis			.24
Single ventricle (%)	5 (45)	2 (12.5)	
Tetralogy of Fallot (%)	2 (18)	2 (12.5)	
TGA (%)	3 (27)	8 (50)	
Other	1 (10)	4 (25)	

Abbreviations: LCOS, low cardiac output syndrome; IQR, interquartile range; kg, kilogram; SD, standard deviation; RACHS-1, risk adjustment for congenital heart surgery; TGA, transposition of the great arteries.

Table 2. Patient Clinical and Surgical Data.

Variables	LCOS (n = 11)	No LCOS (n = 16)	*P* Value
Type of repair			.03
Univentricular (%)	6 (55%)	2 (13%)	
Biventricular (%)	5 (45%)	14 (87%)	
Bypass time, minutes	139 (SD 36)	159 (SD 50)	.25
Peak 24-hour lactate level	6.1 (IQR 4.8-8.8)	3.6 (IQR 3.1-4.4)	.007
24-Hour change in creatinine (mg/dL)	0.18 (SD 0.15)	0.02 (SD 0.14)	.01
First hour VIS score	13 (IQR 5-18)	5 (IQR 5-10)	.23
Ventilator days	12 (IQR 6-17)	4.5 (IQR 2-7)	.006
ICU LOS (days)	24 (IQR 15-33)	15 (IQR 11-25)	.08
Mortality (%)	2 (18%)	0	.16

Abbreviations: LCOS, low cardiac output syndrome; SD, standard deviation; IQR, interquartile range; VIS, vasoactive inotropic score; ICU, intensive care unit; LOS, length of stay.

at the time of surgery was six days. The most common cardiac diagnosis was transposition of the great arteries (41%), single-ventricle anatomy (26%), and tetralogy of Fallot (TOF; 15%). Those neonates with TOF underwent primary repair, which is preferred at our institution. Nineteen neonates (70%) underwent a two-ventricle repair.

Eleven neonates (40%) developed LCOS. Single-ventricle palliation and the Risk Adjustment for Congenital Heart Surgery (RACHS-1) score were associated with the development of LCOS ($P = .03$ and .048, respectively). Neonates with LCOS had a higher peak 24-hour lactate level when compared to those who did not develop LCOS (6.1 mmol/L vs 3.6 mmol/L, $P = .007$; Table 2). The LCOS group also had increased ventilator days (12 vs 4.5, $P = .006$), although intensive care unit (ICU) length of stay and mortality were not different between the two groups.

The constant abdominal NIRS value for the entire cohort was 58% (standard deviation $\pm$13%) and did not differ between single-ventricle and two-ventricle repairs (53% vs 61%, $P = .12$). Neonates who developed LCOS had a lower constant abdominal NIRS value (49% vs 66%, $P < .001$). The time series plots for two representative neonates are shown in Figure 1. The variability of abdominal NIRS values did not differ over the entire time period from CICU admission to the development of LCOS (RMSSD = 1.3% in no LCOS group vs 1.0% in LCOS group); however, in the hour prior to the development of LCOS, abdominal NIRS variability decreased to 0.8%, which was lower than the no LCOS group ($P = .03$). By ROC analysis, a constant abdominal NIRS value of less than 58% (sensitivity = 100% and specificity = 69%) and NIRS variability of less than 0.8% (sensitivity = 55% and specificity = 94%) best predicted the development of LCOS (Figure 2). Median cerebral and renal NIRS values obtained during the first hour following ICU admission were 61% (interquartile range [IQR] 49%-70%) and 82% (IQR 68%-89%) in patients who did not develop LCOS, and 42% (IQR 38%-59%) and 53% (IQR 49%-58%) in patients who did develop LCOS. Among the group of patients who developed LCOS, the median cerebral and renal NIRS values at the time of LCOS diagnosis were 48% (IQR 33%-58%) and 50% (IQR 46%-54%), respectively.

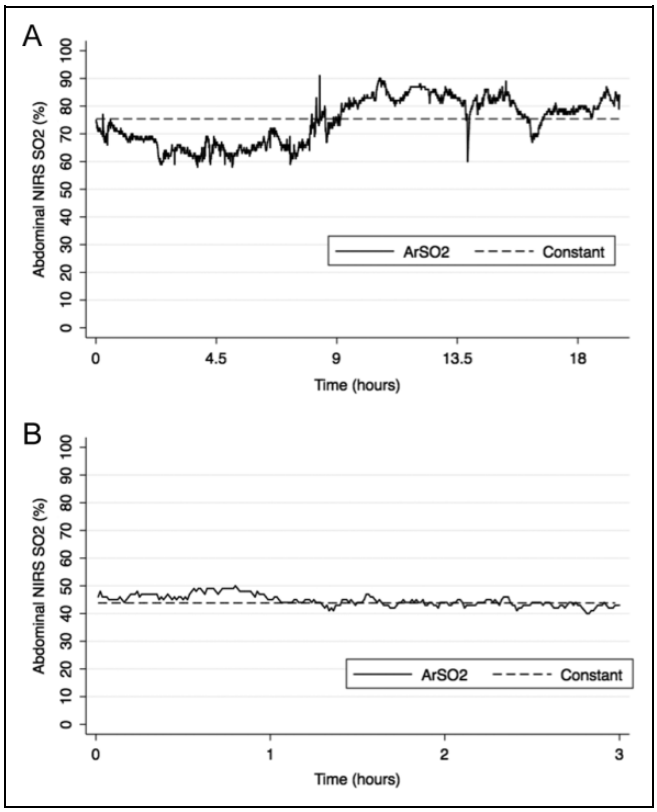

Figure 1. Example of individual patient autoregressive time series model. A, TGA s/p arterial switch operation—no LCOS and (B) TGA s/p arterial switch operation—LCOS.

Comment

Our study shows that neonates who developed LCOS had a lower constant abdominal NIRS value and that NIRS variability decreased in the hour preceding clinical signs of LCOS.

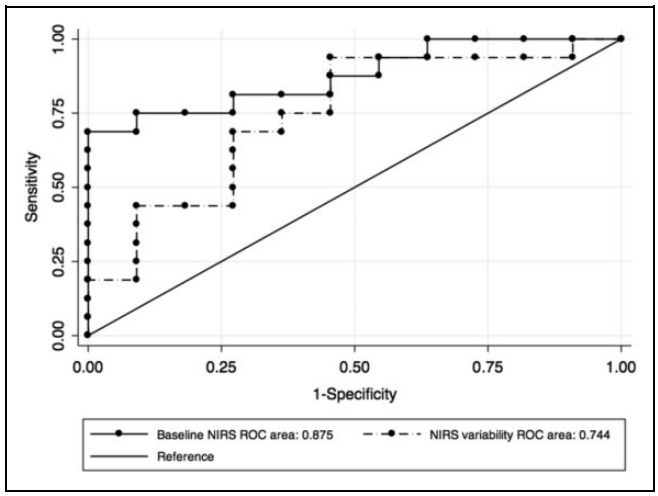

Figure 2. Receiver–operating characteristics (ROC) curve.

Although some studies fail to demonstrate an association between abdominal NIRS values and LCOS in children after cardiac surgery,[16] our results mirror other reports of the utility of abdominal NIRS values in the early identification of LCOS.[8,11] In the operating room, Kim et al showed that abdominal oxygen saturation immediately after weaning from CPB best predicted vasoactive inotrope requirement, duration of mechanical ventilation, and postoperative hospital stay in children after congenital heart surgery.[17] These varied results are likely multifactorial, including the various definitions of LCOS and the different abdominal NIRS monitoring techniques.[3,16,18]

Another potential explanation for the varied results is the approach to NIRS data analysis. Our findings suggest that time series modeling and variability might be more predictive of LCOS than percentage change in postoperative NIRS. We chose to employ a time series analysis approach as it better describes the behavior of frequently sampled time-sensitive data in comparison to previously employed measures, such as hourly means. This approach has shown promise in the modeling of continuous physiologic data for predictions.[19-21]

Within our cohort, the constant NIRS value did not differ between patients with single-ventricle and two-ventricle repairs, however, was significantly lower in those who developed LCOS. This suggests that lower constant abdominal NIRS values are not attributable to the physiologic difference between single-ventricle and two-ventricle repairs but rather to clinical changes such as increased oxygen consumption, decreased regional perfusion, or decreased oxygen delivery. The neonates who developed LCOS also had a decrease in abdominal NIRS variability in the hour prior to the development of LCOS. Although loss of variability can be attributed to many factors (such as edema, ascites, or poor lead adhesion), the lack of NIRS variability in our study may be attributable to changes in cardiac output and oxygen delivery as neonates with LCOS had decreased constant NIRS values and higher lactate levels. The loss of physiologic variability has been suggested in other studies as an early sign of clinical deterioration. A loss of heart rate variability has been seen in neonates with sepsis[22] or NEC.[23] Likewise, decreased abdominal NIRS variability has been shown in preterm neonates prior to the development of NEC.[24]

Our study has several limitations. This is a prospective observational single-center study with a small sample size that only includes neonates. Applying our findings to older children requires further investigation, as abdominal site monitoring may be less accurate in children older than six years or weighing over 25 kg. Additionally, our definition of LCOS depends in part on practitioner clinical decision making regarding inotrope use, and future studies may include other nonpractitioner-dependent physiologic parameters, such as mixed venous oxygen saturation (SvO_2) monitoring, in the definition of LCOS. While we do not use mixed venous oxygen saturations, others have shown similarities between NIRS values and mixed venous oxygen measurements. Mixed venous oxygen saturation is another surrogate for oxygen delivery and consumption; however, this might not be sensitive to regional changes in oxygen delivery.[25] The NIRS monitoring provides information on regional oxygen delivery, which might be important for early recognition of changes in regional blood flow and potential end-organ injury.

Another important question that arises from this work is whether abdominal NIRS values are more predictive than the standard cerebral and renal measurements, which are standard of care in our CICU. When retrospectively examining the data, the cerebral and renal NIRS data were only recorded every hour and thus a comparison between cerebral or renal NIRS and abdominal NIRS in the setting of LCOS in this patient cohort was not feasible. Comparing abdominal NIRS values with the traditional cerebral and renal NIRS is an important step, and future studies should be done to evaluate the relationship between these various measurements.

Increasingly, there has been a newfound appreciation for the value of predictive monitoring tools of clinical deterioration.[20] The primary goal of these tools is to get the practitioner to the bedside of the patient at high risk of clinical deterioration to allow for interventions at the earliest possible opportunity. Predictive tools utilizing continuous monitor data will require different methodology for analysis, such as time series modeling. We envision our findings as a first step in the development of a predictive, noninvasive monitoring tool for LCOS in the postoperative management of children following cardiac surgery. Future studies should focus on the prospective applicability of this model to patients with various ages and diagnosis including comparisons to other noninvasive cardiac output monitors.

Our study results demonstrate that lower constant anterior abdominal NIRS and loss of variability may aid in the identification of neonates at increased risk for developing postoperative LCOS.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding

The author(s) received no financial support for the research, authorship, and/or publication of this article.

References

1. Parr GV, Blackstone EH, Kirklin JW. Cardiac performance and mortality early after intracardiac surgery in infants and young children. *Circulation*. 1975;51(5): 867-874.
2. Burrows FA, Williams WG, Teoh KH, et al. Myocardial performance after repair of congenital cardiac defects in infants and children. response to volume loading. *J Thorac Cardiovasc Surg*. 1988;96(4): 548-556.
3. Hoffman TM, Wernovsky G, Atz AM, et al. Efficacy and safety of milrinone in preventing low cardiac output syndrome in infants and children after corrective surgery for congenital heart disease. *Circulation*. 2003;107(7): 996-1002.
4. De Oliveira NC, Ashburn DA, Khalid F, et al. Prevention of early sudden circulatory collapse after the norwood operation. *Circulation*. 2004;110(11 suppl 1): II133-II138.
5. Wessel DL. Managing low cardiac output syndrome after congenital heart surgery. *Crit Care Med*. 2001;29(10 suppl): s220-s230.
6. Van Saet A, De Wildt SN. Prevention of low cardiac output syndrome in children: where is the evidence? *Paediatr Anaesth*. 2011;21(12): 1173-1175.
7. Wernovsky G, Wypij D, Jonas RA, et al. Postoperative course and hemodynamic profile after the arterial switch operation in neonates and infants. A comparison of low-flow cardiopulmonary bypass and circulatory arrest. *Circulation*. 1995;92(8): 2226-2235.
8. Chakravarti SB, Mittnacht AJ, Katz JC, Nguyen K, Joashi U, Srivastava S. Multisite near-infrared spectroscopy predicts elevated blood lactate level in children after cardiac surgery. *J Cardiothorac Vasc Anesth*. 2009;23(5): 663-667.
9. Foster CB, Spaeder MC, McCarter RJ, Cheng YI, Berger JT. The use of near-infrared spectroscopy during an extubation readiness trial as a predictor of extubation outcome. *Pediatr Crit Care Med*. 2013;14(6): 587-592.
10. Owens GE, King K, Gurney JG, Charpie JR. Low renal oximetry correlates with acute kidney injury after infant cardiac surgery. *Pediatr Cardiol*. 2011;32(2): 183-188.
11. Kaufman J, Almodovar MC, Zuk J, Friesen RH. Correlation of abdominal site near-infrared spectroscopy with gastric tonometry in infants following surgery for congenital heart disease. *Pediatr Crit Care Med*. 2008;9(1): 62-68.
12. Gaies MG, Gurney JG, Yen AH, et al. Vasoactive-inotropic score as a predictor of morbidity and mortality in infants after cardiopulmonary bypass. *Pediatr Crit Care Med*. 2010;11(2): 234-238.
13. Gaies M, Cooper DS, Tabbutt S, et al. Collaborative quality improvement in the cardiac intensive care unit: development of the paediatric cardiac critical care consortium (PC4). *Cardiol Young*. 2015;25(5): 951-957.
14. Wei W. *Time Series Analysis: Univariate and Multivariate Methods*. 1st Edition. Reading, MA: Addison Wesley; 1990.
15. Heart rate variability. standards of measurement, physiological interpretation, and clinical use. task force of the european society of cardiology and the North American society of pacing and electrophysiology. *Eur Heart J*. 1996;17(3): 354-381.
16. Bhalala US, Nishisaki A, McQueen D, et al. Change in regional (somatic) near-infrared spectroscopy is not a useful indicator of clinically detectable low cardiac output in children after surgery for congenital heart defects. *Pediatr Crit Care Med*. 2012;13(5): 529-534.
17. Kim JW, Shin WJ, Park I, Chung IS, Gwak M, Hwang GS. Splanchnic oxygen saturation immediately after weaning from cardiopulmonary bypass can predict early postoperative outcomes in children undergoing congenital heart surgery. *Pediatr Cardiol*. 2014;35(4): 587-595.
18. Zulueta JL, Vida VL, Perisinotto E, Pittarello D, Stellin G. Role of intraoperative regional oxygen saturation using near infrared spectroscopy in the prediction of low output syndrome after pediatric heart surgery. *J Card Surg*. 2013;28(4): 446-452.
19. Imhoff M, Bauer M, Gather U, Löhlein D. Statistical pattern detection in univariate time series of intensive care on-line monitoring data. *Intensive Care Med*. 1998;24(12): 1305-1314.
20. Leuthold AC, Langheim FJ, Lewis SM, Georgopoulos AP. Time series analysis of agnetoencephalographic data during copying. *Exp Brain Res*. 2005;164(4): 411-422.
21. Yien HW, Hseu SS, Lee LC, Kuo TB, Lee TY, Chan SH. Spectral analysis of systemic arterial pressure and heart rate signals as a prognostic tool for the prediction of patient outcome in the intensive care unit. *Crit Care Med*. 1997;25(2): 258-266.
22. Griffin MP, Moorman JR. Toward the early diagnosis of neonatal sepsis and sepsis-like illness using novel heart rate analysis. *Pediatrics*. 2001;107(1): 97-104.
23. Stone ML, Tatum PM, Weitkamp JH, et al. Abnormal heart rate characteristics before clinical diagnosis of necrotizing enterocolitis. *J Perinatol*. 2013;33(11): 847-850.
24. Cortez J, Gupta M, Amaram A, Pizzino J, Sawhney M, Sood BG. Noninvasive evaluation of splanchnic tissue oxygenation using near-infrared spectroscopy in preterm neonates. *J Matern Fetal Neonatal Med*. 2011;24(4): 574-582.
25. Tweddell JS, Ghanayem NS, Mussatto KA, et al. Mixed venous oxygen saturation monitoring after stage 1 palliation for hypoplastic left heart syndrome. *Ann Thorac Surg*. 2007;84(4): 1301-1310;discussion 1310-1311.