# Association of immediate postoperative hemodynamic and laboratory values in predicting Norwood admission outcomes

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**Article**

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# Abstract

## Background

The primary objective of this study was to determine whether or not hemodynamic parameters and laboratory values at the time of admission to the pediatric cardiac intensive care unit after the Norwood operation were associated with a composite outcome of either need for extracorporeal membrane oxygenation or inpatient mortality.

## Methods

This was a single-center retrospective study of infants with functionally univentricular hearts admitted to intensive care after the Norwood procedure from January 2011 to January 2020. Data were obtained at a single point(after a Norwood procedure) and then compared between two subsets of patients based on the presence or not of the composite outcome of interest. In univariate and multiple regression analyses, a series of receiver operator curves were generated to assess the relationship between the variables of interest and the composite outcome.

## Results

Eight(7.6%) experienced the composite outcome out of a total of 104 patients. Those who experienced the composite endpoint had significantly higher oxygen extraction ratio (0.43 vs. 0.31, $p = 0.01$), lower systemic blood flow (2.5 L/min versus 3.1 L/min, $p = 0.01$), and higher systemic vascular resistance (20.2 indexed woods units versus 14.8 indexed woods units, $p = 0.01$). Those with systemic blood flow of less than 2.5 L/min/m$^2$ had a 17% risk of experiencing the composite endpoint AUC = 0.79. Those with systemic vascular resistance of greater than 19 indexed woods units had a 22% risk of experiencing the composite endpoint AUC 0.80.

## Conclusion

Systemic blood flow and systemic vascular resistance are independently associated with this composite outcome.

# Introduction

Functionally univentricular hearts represent a subset of cyanotic congenital malformations of the heart (1). Parallel circulation, defined as the physiological construct in which the pulmonary and systemic circulation is getting equally saturated blood, is a hallmark of the early period of those with a functionally univentricular heart[1]. Children with functionally univentricular hearts will need to undergo a Norwood procedure. They will continue to have parallel circulation until a superior cavopulmonary anastomosis is performed later in life.

Despite a better understanding of anatomic variants, physiologic considerations, and clinical monitoring nuances, there is still relatively high morbidity and mortality after the Norwood procedure (2–6). Several factors for suboptimal outcomes, including postoperative cardiac arrest, need for extracorporeal membrane oxygenation, and organ dysfunction, have been implicated in mediating inpatient mortality after the Norwood procedure[2, 3].

Identification of hypoplastic left hearts patients at increased risk for the need for extracorporeal membrane oxygenation or inpatient mortality after the Norwood operation at the time of admission to the pediatric cardiac intensive care unit (PCICU) could help identify those patients requiring more vigilance. The primary objective of this study was to determine whether or not hemodynamic parameters and laboratory values at the time of admission to the PCICU after undergoing a Norwood operation were associated with the composite outcome.

## Methods

## Study design

This was a single-center, retrospective study. Data were obtained from a review of patient data from the institution's electronic health record. Data were obtained at a single timepoint and then compared two subsets of patients based on a composite endpoint of interest. The study was approved by the institutional review board and was in concordance with the Helsinki Declaration.

## Variables of interest

Several variables of interest were identified. Admission characteristics with the need for extracorporeal membrane oxygenation, postoperative duration of mechanical ventilation, postoperative length of hospital stay, and inpatient mortality. Hemodynamic variables collected were as follows: heart rate, systolic blood pressure, diastolic blood pressure, mean arterial blood pressure, central venous pressure, renal near-infrared spectroscopy, and cerebral near-infrared spectroscopy. These hemodynamic variables were collected as recorded in the electronic health record. These first recorded values were collected upon admission to the cardiac intensive care unit. All patients had an arterial line, and the arterial line obtained all collected blood pressures.

Arterial blood gas values were also collected: hydrogen ion concentration (pH), partial pressure of carbon dioxide (pCO2), oxygen saturation, base excess, serum lactate, and hemoglobin. The first recorded values for these upon admission were collected. All blood gas samples at the institution are annotated with the unit in which they were drawn, allowing for easy identification of gases drawn in the operating room versus the cardiac intensive care unit.

Next, there were a series of calculated values. The average of the renal and cerebral near-infrared spectroscopy values was calculated. The somato-cerebral gradient was calculated as the renal near-infrared spectroscopy and cerebral near-infrared spectroscopy values. The bedside pulmonary to systemic blood flow ratio was calculated using the following equation: (arterial oxygen saturation – venous saturation)/(pulmonary venous saturation – pulmonary artery saturation). Since all the patients had parallel circulation, arterial oxygen saturation was also used for pulmonary artery saturation. The average near-infrared spectroscopy value was used for the venous saturation, and the pulmonary venous saturation was assumed to be 100.

Additionally, clinical values were also calculated. Rate pressure product was calculated as the heart rate x systolic blood pressure, while shock index was calculated as the heart rate/systolic blood pressure. Systemic blood flow was calculated as oxygen consumption/(arterial saturation – venous saturation). For this calculation, oxygen consumption was estimated using the LaFarge equation, and the venous saturation utilized was the average near-infrared spectroscopy value. Pulmonary blood flow was calculated as oxygen consumption/(pulmonary venous saturation – venous saturation). Total cardiac output was calculated as the sum of the systemic and pulmonary blood flows. Systemic vascular resistance was calculated as (mean arterial blood pressure – central venous pressure)/systemic blood flow. Due to the lack of routine pulmonary artery pressure monitoring, pulmonary vascular resistance was not calculated. The oxygen extraction ratio was calculated as (arterial oxygen saturation – average near-infrared spectroscopy)/arterial oxygen saturation. There are limitations to all the calculations used above. Using these calculated values wasn’t to establish absolute values for these parameters but rather to use them to establish trends.

## Patient identification

Patients who underwent the Norwood operation at our institution from January 1, 2011, to January 1, 2020, were identified using our surgical database. Patients before 2013 were not included due to a lack of electronic health records, and after 2020, due to changes in the electronic medical record. For inclusion in the study, patients must have been admitted to the cardiac intensive care unit after their Norwood operation, must have had an arterial line in place, must have had an arterial blood gas within the first 20 minutes of admission, and could not have been on extracorporeal membrane oxygenation upon entry to the cardiac intensive care unit. Furthermore, those on extracorporeal membrane oxygenation going into the operating room were excluded.

## Statistical analyses

Patients were divided into two groups based on a composite endpoint of postoperative need for extracorporeal membrane oxygenation or inpatient mortality after the Norwood operation but during the Norwood admission. The normalcy of the distribution of data was assessed using skewness and kurtosis. As data were not normally distributed, non-parametric statistical tests were utilized. Continuous variables are reported as median and range, while descriptive variables are reported as absolute count and percentage.

Variables between the two groups were compared in a univariate fashion using Mann-Whitney-U tests for continuous variables and Fisher-exact tests for descriptive variables. Following these univariate analyses, a series of receiver operator curves were generated to assess further the accuracy of the variables of interest in predicting the composite outcome.

Next, a series of regressions were conducted. The first was a stepwise linear regression with the duration of postoperative mechanical ventilation as the dependent variable. The independent variables included the following: heart rate, systolic blood pressure, mean blood pressure, diastolic blood pressure, renal near-infrared spectroscopy, cerebral near-infrared spectroscopy, pulmonary blood flow, systemic blood flow, total cardiac output, oxygen extraction ratio, and arterial saturation. Next, a stepwise linear regression was conducted with the postoperative length of stay as the dependent variable. The same independent variables as the previous linear regression were utilized. Finally, a stepwise logistic regression was conducted with the composite outcome as the dependent variable. The same independent variables were entered as with the previously described regressions.

Next, correlation analyses within the variables of interest were conducted to determine how they correlated with one another. The primary focus was on identifying parameters that significantly correlated with systemic blood flow.

Next, the frequency of the composite endpoint at various values of the variables of interest with an area under the curve of 0.70 or greater for predicting the composite endpoint was quantified.

Finally, the correlation of variables of interest with systemic blood flow was assessed using Spearman correlation analyses. This analysis was done to help clarify any impact of covariance that may be present in the regression analyses.

All statistical analyses were conducted using SPSS Version 23.0. A p-value of less than 0.05 was considered statistically significant. Any use of the word “significant,” “significantly,” or “significance” implies statistical significance unless explicitly stated otherwise.

## Results

## Cohort characteristics

A total of 104 patients were included in the final analyses. Of these, 8 (7.6%) experienced the composite outcome. The median age at Norwood was ten days, and the median weight was 3.3 kg. The median duration of delayed sternal closure was 3.8 days, the postoperative period of mechanical ventilation was 9.2 days, and the postoperative hospital length of stay was 30 days. The most frequent congenital malformation of the heart was hypoplastic left heart syndrome in 68 (65%).

## Univariate analyses

A genetic anomaly was present in 12% of patients, with an equal proportion of patients in both groups. A significantly smaller proportion of patients in the composite endpoint group had a Sano shunt versus a Blalock-Taussig-Thomas shunt when compared to the group that did not experience the composite endpoint (75% versus 90%, $p < 0.01$). Acute kidney injury did not differ between the two groups (Table 1).

Hemodynamic data demonstrated few significant differences between the two groups. Those who experienced the composite endpoint had significantly lower cerebral near-infrared spectroscopy, lower renal near-infrared spectroscopy, and lower average near-infrared spectroscopy values (table 2). No significant difference was present in arterial blood gas values between the two groups (Table 3).

Concerning the calculated values, those who experienced the composite endpoint had significantly higher oxygen extraction ratio (0.43 vs. 0.31, $p = 0.01$), lower systemic blood flow (2.5 L/min versus 3.1 L/min, $p = 0.01$), and higher systemic vascular resistance (20.2 indexed woods units versus 14.8 indexed woods units, $p = 0.01$) (table 4).

## Receiver operator curve analyses

Receiver operator curves were created to assess the accuracy of cerebral near-infrared spectroscopy, renal near-infrared spectroscopy, average near-infrared spectroscopy, systemic blood flow, oxygen extraction ratio, systemic vascular resistance, lactate, and vasoinotrope score in predicting the composite endpoint (Table 5).

Cerebral near-infrared spectroscopy demonstrated good accuracy with an area under the curve of 0.75 with an optimal cutoff of 47. Those with a cerebral near-infrared spectroscopy value less than 47 had a 12% risk of experiencing the composite endpoint. Near-infrared spectroscopy demonstrated good accuracy with an area under the curve of 0.73 with an optimal cutoff of 57. Those with a renal near-infrared spectroscopy value of less than 57 had a 14% risk of experiencing the composite endpoint. The average near-infrared spectroscopy had good accuracy with an area under the curve of 0.79 with an optimal cutoff of 49. Those with an average near-infrared spectroscopy value of less than 49 had a 17% risk of experiencing the composite endpoint (Table 5).

Systemic blood flow demonstrated good accuracy with an area under the curve of 0.79 with an optimal cutoff of 2.5 L/min/$m^2$. Those with systemic blood flow of less than 2.5 L/min/$m^2$ had a 17% risk of experiencing the composite endpoint (Table 5).

Systemic vascular resistance demonstrated excellent accuracy with an area under the curve of 0.80 with an optimal cutoff of 19 indexed woods units. Those with systemic vascular resistance of greater than 19 indexed woods units had a 22% risk of experiencing the composite endpoint (Table 5). Lactate and vasoinotrope scores had poor accuracy with an area under the curve of 0.56 and 0.59, respectively, due to their poor overall accuracy (table 5).

## Regression analyses

Regression analyses demonstrated that the following factors were associated with a longer duration of mechanical ventilation in days: higher lactate, higher hemoglobin, and lower average near-infrared spectroscopy. For each increase in lactate of 1, there was an increase in the duration of mechanical ventilation by 0.5 days. For each increase in hemoglobin by one, there was an increase in mechanical ventilation time by 0.9 days. For each decrease in average near-infrared spectroscopy value by one, there was an increase in mechanical ventilation by 0.3 days (table 6).

Regression analyses demonstrated that the following factors were associated with a longer post-Norwood hospital length of stay: higher lactate, lower central venous pressure, and higher hemoglobin. For each increase in lactate of 1, there was an increase in post-Norwood hospital length of stay by 2.5 days. For each decrease in central venous pressure by 1, there was an increase in post-Norwood hospital length of stay by 2.0 days. For each increase in hemoglobin by 1, there was an increase in post-Norwood hospital length of stay by 1.9 days (table 6).

Regression analyses demonstrated that systemic blood flow was significantly associated with the composite endpoint. For each decrease in systemic blood by 1 L/min, there was a 70% decrease in the odds of the composite endpoint (Table 6).

## Quantifying the risk of the composite endpoint

As the average near-infrared spectroscopy, systemic vascular resistance, and oxygen extraction ratio had a high area under the curve values; those metrics were utilized to quantify the risk of the composite endpoint (Table 7).

Concerning systemic vascular resistance, a systemic vascular resistance of fewer than 12 hours was associated with a 0% risk of the composite endpoint, systemic vascular resistance between 12 and 19 hours was associated with a 3% risk of the composite endpoint, and systemic vascular resistance greater than 19 hours was associated with an 18% risk of the composite endpoint (Table 7).

Concerning the average of near-infrared spectroscopy, an average of greater than 57 was associated with a 0% risk of the composite endpoint, an average between 49 and 57 was associated with a 6% risk of the composite endpoint, and an average of less than 49 was associated with a 17% risk of the composite endpoint (Table 7).

Concerning oxygen extraction ratio, an oxygen extraction ratio of less than 0.27 was associated with a 0% risk of the composite endpoint, between 0.27 and 0.37 was associated with a 3% risk of the composite endpoint, and greater than 0.37 was associated with a 15% risk of the composite endpoint (Table 7).

## Correlation of variables of interest with systemic blood flow

The systemic blood flows significantly correlated with pH and total cardiac output. The systemic blood flow had a significant, moderate correlation with pCO2, arterial oxygen saturation, and renal near-infrared spectroscopy. The systemic blood flow had a robust, strong correlation with cerebral near-infrared spectroscopy, average near-infrared spectroscopy, and estimated pulmonary to systemic blood flow ratio. The systemic blood flow had a significant, strong correlation with oxygen extraction ratio and systemic vascular resistance (table 8).

# Discussion

The current study highlights factors related to outcomes in single ventricles patients who undergo the Norwood operation. Concerning a composite endpoint of need for extracorporeal membrane oxygenation and inpatient mortality, only systemic blood flow was independently associated with this composite outcome for the duration of mechanical ventilation and post-Norwood hospital length of stay. Other factors such as average near-infrared spectroscopy, hemoglobin, central venous pressure, and lactate were also found to be independently associated.

Parallel circulation, wherein the saturation of blood going to the pulmonary and systemic circulations is equal, is a unique physiological construct. In this circulation, the systemic saturation is a weighted average of the pulmonary venous and systemic venous saturation, with the weights of each being dictated by the pulmonary to systemic blood flow ratio. Additionally, in this circulation, all the blood is either pumped by a single ventricle and then distributes itself to either the pulmonary or systemic circulation based on the relative resistances of the two circulations. If total cardiac output remains the same, an increase in pulmonary or systemic blood flow must be met with a decrease in the flow to the other circulation by an equal but opposite amount. Thus, parallel circulation represents a unique circulation with dynamic systemic arterial saturation, dynamic systemic venous saturation, dynamic pulmonary blood flow, and dynamic systemic blood flow. This vulnerable physiologic results in an increased risk of morbidity and mortality as systemic oxygen delivery is more likely to be insufficient in such a circulation [4–6].

The current analyses demonstrate that the risk of requiring extracorporeal membrane oxygenation or experiencing inpatient mortality is independently associated with systemic blood flow and no other variables of interest. This finding should come as little surprise as systemic oxygen delivery is required for life. Systemic oxygen delivery is equal to the product of oxygen content and systemic blood flow. While hemoglobin and fraction of inspired oxygen can module oxygen content, heart rate, preload, afterload, and contractility modulate cardiac output. Correlation analyses in the current study identified several variables that had moderate or more significant correlation with systemic blood flow, of which systemic vascular resistance had the strongest correlation.

Although not synonymous with afterload, systemic vascular resistance does contribute to systemic ventricular afterload. Previous studies have demonstrated that higher systemic vascular resistance is associated with lower systemic blood flow and increased morbidity and mortality [7]. Clinical and modeling studies have shown that a high systemic blood flow and low systemic vascular resistance state decreases the risk of morbidity and mortality, findings consistent with those of the current study [8–10]. Increased systemic vascular resistance may lead to increased blood flow to the pulmonary rather than systemic circulation. It may also increase myocardial oxygen consumption, which can decrease systemic oxygen delivery. A systemic vascular resistance of over 19 indexed wood units was associated with an increased risk of the composite endpoint.

The current study identifies metrics of systemic oxygen delivery. As calculated using near-infrared spectroscopy, the oxygen extraction ratio had a high accuracy in identifying those at risk for the composite endpoint. Both renal and cerebral near-infrared spectroscopy were helpful in this regard, and the average of two was found to be perhaps the most accurate in predictive value. Near-infrared spectroscopy allows for the monitoring of regional venous saturation. While its absolute correlation to the regional venous saturation is not perfect, its trend with the underlying regional venous saturation is strong. The average of the cerebral and renal near-infrared spectroscopy values more closely represents the mixed systemic venous saturation, which may have subsequently increased predictive value. Although it is important to note that the value for the area under the curve of cerebral, renal, and average near-infrared spectroscopy ranged from 0.73 to 0.79, ultimately, they were pretty similar. This indicates that monitoring trends in any regional venous saturation can be helpful, a finding that has been described in the literature in the parallel circulation [1, 11–20]. More importantly, the current data reinforce that near-infrared spectroscopy is a valuable tool to predict adverse events in those with parallel circulation [19, 21–25]. An average near-infrared spectroscopy value of under 49 was associated with an increased risk of the composite endpoint.

An oxygen extraction ratio can be calculated using the near-infrared spectroscopy values. The average near-infrared spectroscopy values were utilized in the study to do this calculation. It demonstrated that the oxygen extraction ratio had an excellent predictive value for the composite endpoint, with an area under the curve equal to the average near-infrared spectroscopy value. The value of the oxygen extraction ratio in estimating changes in systemic blood flow and subsequently oxygen delivery is implicit in the Fick equation, which demonstrates that systemic cardiac output is equal to oxygen consumption divided by the arteriovenous oxygen content difference. The current data highlight its utility in this unique population. Previous studies have demonstrated that oxygen extraction ratios of 0.35 or greater are associated with increased morbidity and mortality. Need citation

We also show multiples factors not associated with morbidity and mortality. More conventional hemodynamic variables such as heart rate, systolic blood pressure, diastolic blood pressure, and mean arterial blood pressure were not significant in any of the analyses. This finding is important to highlight as anecdotally; clinical care is often titrated to blood pressure targets in the cardiac intensive care unit. Such titration is ill-advised as mean arterial blood pressure is the product of systemic vascular resistance and cardiac output. Thus arterial blood pressure can be increased by increasing systemic vascular resistance while cardiac output is maintained or decreased. This offers no benefit to systemic blood flow or systemic oxygen delivery and is likely detrimental. Thus, the current data demonstrate the shortcomings of blood pressure as a clinical target due to its lack of effect on discrete clinical events. Lactate, often used to guide clinical care, was not found to be independently associated with morbidity and mortality. This should not be particularly surprising as lactate can be influenced by many systemic factors, including hyperglycemia, and is not always modulated by systemic oxygen delivery.

These findings in the clinical setting imply that they may help guide clinical management. The data highlight that minimization of systemic vascular resistance and optimizing systemic blood flow are of the utmost importance. The data also demonstrate that near-infrared spectroscopy can be used to titrate care and evaluate the impact of interventions while also highlighting that blood pressure is not a particularly helpful target to titrate clinical care. This all indicates that an inodilator strategy may help optimize systemic oxygen delivery in those with parallel circulation [10, 26–29]. Any interventions that increase systemic vascular resistance out of proportion to any increase in cardiac output are unlikely to be helpful.

In contrast, interventions that increase cardiac output more than systemic vascular resistance may benefit [26, 30, 31]. The current study also presents some data on hemoglobin. It indicates that increasing hemoglobin was independently associated with the duration of mechanical ventilation and hospital length of stay without impacting the composite endpoint. Firm conclusions about packed red blood cell transfusions in the management of patients with parallel circulation cannot be made from the current data. Other studies have demonstrated conflicting findings [32–36].

Overall, it is interesting to note the strength in the predictive value of systemic oxygen delivery metrics at admission for overall postoperative morbidity and mortality. This allows for identifying those at higher risk for adverse events when access to the PCICU immediately after the Norwood operation. This allows for more heightened awareness for the clinical team and the preparation of resources, such as extracorporeal membrane oxygenation, to be employed quickly to help abate organ dysfunction.

While these data are sourced from a large sample size and are helpful and additive, they are not without their limitations. First, this is a single-center study, meaning center-specific practices may influence data. The influence of this bias in the current study may be minimized because the focus of this study was on general physiologic states and not specific interventions. Second, the cutoffs here may be influenced by particular monitoring equipment, specifically the near-infrared spectroscopy data. This equipment-related cutoff does not mean that this data cannot be applied to those using other devices. The data should demonstrate general physiologic associations and that the absolute cutoff values may differ across different devices.

## Conclusion

Monitoring and clinical data upon admission to the cardiac intensive care unit immediately after the Norwood operation may help predict the risk of the need for extracorporeal membrane oxygenation or inpatient mortality. Systemic blood flow is independently associated with this composite endpoint and is modulated by systemic vascular resistance, and can be monitored accurately with either cerebral or renal near-infrared spectroscopy.

# Declarations

### Author contributions statements

R.L., S.F., U.D., and J.W. conceptualized the study, analyzed the data, and prepared parts of the draft. E.V. and J.F. contributed to the interpretation of the results and critically reviewed the manuscript. F.S and S.A. contributed to the interpretation of the results, wrote parts of the draft and critically reviewed the manuscript. All authors reviewed the manuscript and accepted its final version.

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# Tables

## Table 1

| | **No ECMO or mortality (n=96)** | **ECMO or mortality (n=8)** | **p-value** |
|---|---|---|---|
| ***Extracorporeal membrane oxygenation*** | 0 (0%) | 5 (62%) | – |
| ***Inpatient mortality*** | 0 (0%) | 6 (75%) | – |
| ***Acute kidney injury*** | 42 (43%) | 2 (25%) | 0.30 |
| ***Genetic anomaly*** | 12 (12%) | 1 (12%) | 0.99 |
| ***Sano (versus BT)*** | 87 (90%) | 6 (75%) | 0.01 |

## Table 2

| | **No ECMO or mortality** | **ECMO or mortality** | **p-value** |
|---|---|---|---|
| ***Heart rate*** | 175 (130 to 213) | 185 (168 to 201) | 0.12 |
| ***Systolic blood pressure*** | 81 (49 to 142) | 74 (67 to 92) | 0.24 |
| ***Diastolic blood pressure*** | 48 (24 to 67) | 47 (40 to 64) | 0.98 |
| ***Mean arterial blood pressure*** | 58 (39 to 92) | 56 (50 to 73) | 0.57 |
| ***Pulse pressure*** | 34 (5 to 77) | 29 (16 to 45) | 0.19 |
| ***Rate pressure product*** | 14,315 (8,424 to 24,992) | 13,472 (11,256 to 17,848) | 0.80 |
| ***Shock index*** | 2.17 (1.23 to 3.65) | 2.42 (2.10 to 2.67) | 0.05 |
| ***Central venous pressure*** | 9 (3 to 19) | 8 (7 to 13) | 0.26 |
| ***Cerebral near infrared spectroscopy*** | 47 (24 to 71) | 36 (31 to 47) | 0.02 |
| ***Renal near infrared spectroscopy*** | 61 (30 to 82) | 54 (44 to 59) | 0.04 |
| ***Average near infrared spectroscopy*** | 52 (30 to 72) | 45 (39 to 53) | 0.01 |
| ***Somato-cerebral gardient*** | 11 (-16 to 52) | 15 (3 to 26) | 0.41 |
| ***Vasoinotrope score*** | 18 (10 to 30) | 19 (13 to 26) | 0.27 |

**Table 3**

| | **No ECMO or mortality** | **ECMO or mortality** | **p-value** |
|---|---|---|---|
| ***pH*** | 7.41 (7.22 to 7.57) | 7.40 (7.32 to 7.51) | 0.77 |
| ***pCO2*** | 38 (20 to 58) | 40 (31 to 49) | 0.67 |
| ***Oxygen saturation*** | 81 (47 to 96) | 80 (59 to 94) | 0.65 |
| ***HCO3*** | 24 (4 to 66) | 25 (21 to 28) | 0.15 |
| ***Base excess*** | -1 (-17 to 6) | 80 (59 to 94) | 0.15 |
| ***lactate*** | 6.8 (2.6 to 14.0) | 7.1 (4.8 to 12.1) | 0.53 |
| ***Ionized calcium*** | 1.4 (0.6 to 5.7) | 1.7 (1.3 to 1.9) | 0.06 |
| ***Hemoglobin*** | 12.0 (7.7 to 19.3) | 13.0 (9.0 to 17.5) | 0.42 |

pH- hydrogen ion concentration, pCO2- partial pressure of carbon dioxide, HCO3- bicarbonate

## Table 4

| | No ECMO or mortality | ECMO or mortality | p-value |
|---|---|---|---|
| *Estimated pulmonary to systemic blood flow ratio* | 1.26 (0.09 to 13.37) | 1.80 (0.48 to 7.58) | 0.21 |
| *Oxygen extraction ratio* | 0.31 (0.04 to 0.66) | 0.43 (0.33 to 0.48) | 0.01 |
| *Pulmonary blood flow (l/min/m$^2$)* | 4.7 (1.8 to 6.8) | 4.6 (1.5 to 8.5) | 0.87 |
| *Systemic blood flow l/min/m$^2$)* | 3.1 (1.2 to 4.9) | 2.5 (1.7 to 2.9) | 0.01 |
| *Total cardiac output (l/min/m$^2$)* | 8.4 (5.1 to 12.9) | 7.0 (4.4 to 11.1) | 0.14 |
| *Systemic vascular resistance (Woods units*m$^2$)* | 14.8 (2.1 to 45.3) | 20.2 (15.6 to 23.5) | 0.01 |

## Table 5

| | Optimal cutoff | Area under the curve | Frequency of ECMO or mortality |
|---|---|---|---|
| *Cerebral near infrared spectroscopy* | 47 | 0.75 | 12% |
| *Renal near infrared spectroscopy* | 57 | 0.73 | 14% |
| *Average of near infrared spectroscopy* | 49 | 0.79 | 17% |
| *Systemic blood flow* | 2.5 | 0.79 | 17% |
| *Oxygen extraction ratio* | 37 | 0.79 | 17% |
| *Systemic vascular resistance* | 19 | 0.80 | 22% |
| *Systolic blood pressure* | – | 0.59 | – |
| *Diastolic blood pressure* | – | 0.49 | – |
| *Mean arterial blood pressure* | – | 0.56 | – |
| *Lactate* | – | 0.56 | – |
| *Vasoinotrope score* | – | 0.59 | – |

## Table 6

| | Beta-coefficient | Odds ratio with 95% confidence interval) |
|---|---|---|
| | | |
| **ECMO or mortality** | | |
| Systemic blood flow | -1.1 | 0.3  (0.1 to 0.6) |
| | | |
| **Mechanical ventilation days** | | |
| Average near infrared spectroscopy | -0.3 | – |
| Hemoglobin | 0.9 | – |
| Lactate | 0.5 | – |
| | | |
| **Post-Norwood length of stay** | | |
| Lactate | 2.5 | – |
| Central venous pressure | -2.0 | – |
| Hemoglobin | 1.9 | – |

## Table 7

| **Systemic vascular resistance** | **Less than 12** | **Between 12 and 19** | **Over 19** |
|---|---|---|---|
| | 0% | 3% | 18% |
| | | | |
| **Average of near infrared spectroscopy** | **Over 57** | **Between 49 and 57** | **Less than 49** |
| | 0% | 6% | 17% |
| | | | |
| **Oxygen extraction ratio** | **Under 0.27** | **Between 0,27 and 0.37** | **Over 0.37** |
| | 0% | 3% | 15% |

## Table 8

| | Correlation coefficient | Clinical interpretation | p-value |
|---|---|---|---|
| ***pH*** | -0.38 | Weak | < 0.01 |
| ***pCO2*** | 0.44 | Moderate | < 0.01 |
| ***Arterial oxygen saturation*** | -0.43 | Moderate | < 0.01 |
| ***Cerebral near infrared spectroscopy*** | 0.62 | Strong | < 0.01 |
| ***Renal near infrared spectroscopy*** | 0.42 | Moderate | < 0.01 |
| ***Average of near infrared spectroscopy*** | 0.60 | Strong | < 0.01 |
| ***Oxygen extraction ratio*** | -0.88 | Very strong | < 0.01 |
| ***Estimated pulmonary to systemic blood flow ratio*** | -0.77 | Strong | < 0.01 |
| ***Systemic vascular resistance*** | -0.89 | Very strong | < 0.01 |
| ***Total cardiac output*** | 0.31 | Weak | < 0.01 |

Correlation of various markers with systemic blood flow (only statistically significant correlations outlined here)