Title: Vasoactive-Ventilation-Renal Score Reliably Predicts Hospital Length-of-Stay after Surgery for Congenital Heart Disease

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Funding: None

Conflicts of Interest: The authors have no conflicts of interest to disclose.

Word Count: 3173

Indiana University IRB Protocol #: 1412965128, approved 12/15/2014 – 12/14/2016

Glossary of Abbreviations

AUC: area under the receiver operating characteristic curve

CI: confidence interval

CPR: cardiopulmonary resuscitation

CVICU: cardiovascular intensive care unit

ΔCr: change in serum creatinine from baseline

ECMO: extracorporeal membrane oxygenation

FiO_2: fraction of inspired oxygen

ICU: intensive care unit

LOS: length of stay

IQR: interquartile range

MAP: mean airway pressure

OR: odds ratio

PEEP: positive end expiratory pressure

PIP: peak inspiratory pressure

ROC: receiver operating characteristic

RR: respiratory rate

STAT category: Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery mortality category

VI: ventilation index

VIS: vasoactive-inotrope score

VVR: vasoactive-ventilation-renal score

Abstract

Objectives: We aimed to further validate the vasoactive-ventilation-renal score (VVR) as a predictor of outcome in patients recovering from surgery for congenital heart disease. We also sought to determine the optimal time point within the early recovery period at which the VVR should be measured.

Methods: We prospectively reviewed consecutive patients recovering from cardiac surgery within our ICU between 1/2015 – 6/2015. The VVR was calculated at 6, 12, 24, and 48 hours postoperatively as follows: VVR = ventilation index + vasoactive-inotrope score + Δ creatinine [change in serum creatinine from baseline*10]. Primary outcome of interest was prolonged hospital length of stay (LOS), defined as LOS in the upper 25%. Receiver operating characteristic curves were generated and areas under the curve (AUC) with 95% confidence intervals (CI) were calculated for all time points. Multivariable logistic regression modelling was also performed.

Results: We reviewed 164 patients, median age 9.25 months (interquartile range: 2.6 - 58 months). Median LOS was 8 days (interquartile range: 5 - 17.5 days). The AUC value for the VVR as a predictor of prolonged LOS (>17.5 days) was greatest at 12 hours postoperatively, AUC=0.93 (95% CI: 0.89 - 0.97). On multivariable regression analysis, after adjustment for potential confounders, the 12-hour VVR remained a strong predictor of prolonged hospital LOS (OR: 1.15, 95% CI: 1.10, 1.20)

Conclusions: In a heterogeneous population of patients undergoing surgery for congenital heart disease, the novel VVR calculated in the early postoperative recovery period can be a strong predictor of prolonged hospital LOS.

Abstract Word Count: 249

Central Message

The vasoactive-ventilation-renal score is a novel measure that robustly predicts outcome after surgery for congenital heart disease.

Perspective Statement

In this prospective study of patients undergoing surgery for congenital heart disease, the vasoactive-ventilation-renal score obtained 12 hours after ICU arrival was a strong predictor of clinical outcome. This novel score could prove to be a powerful tool for bedside assessment of illness severity and prognosis, triage of ICU resources, and stratification of clinical research subjects.

Central Image

ROC curves for prolonged LOS and the multivariable model (solid) and its individual components (dashed).

Introduction

Scoring indices that can accurately reflect the severity of illness in critically-ill patients can be extremely valuable in contemporary medicine, providing guidance in patient care (e.g. triage, prognostication) and clinical research (e.g. stratification). The development of a disease severity index for children recovering from cardiac surgery however has been somewhat elusive, in large part due to the inherent heterogeneity of anatomy and pathophysiology within this patient population. To this end, the novel vasoactive-ventilation-renal (VVR) score has recently demonstrated promise [1,2]. Specifically, the VVR calculated at 48 hours postoperatively has been shown to be a robust predictor of short-term clinical outcomes and consistently outperformed the vasoactive inotrope score (VIS) and serum lactate, which have been used as more traditional measures of postoperative disease severity [3-8].

Our previous studies of the VVR have had notable limitations. These studies have been restricted to patients less than 18 years of age who have required cardiopulmonary bypass. Adults undergoing surgery for congenital heart disease and children undergoing cardiac surgery without cardiopulmonary bypass (e.g. systemic-to-pulmonary shunt, pulmonary artery banding, etc.) have been excluded. Additionally, these prior reports focused only on VVR measurements obtained at admission, peak and 48 hour measurements. Peak and 48-hour VVR measurements in particular were chosen for these initial studies because these measurements have been the focus of the majority of research on the VIS.[3-5] The clinical utility of measurements obtained at specific postoperative time points earlier in the postoperative course has not yet been determined. To address these gaps in what is known regarding the VVR, we sought to conduct a more inclusive prospective observational study examining the VVR score. We postulated that the VVR would continue to be more predictive of outcomes as compared

to the VIS and serum lactate in this broader population of patients recovering from surgery for congenital heart disease. We also sought to determine if the VVR obtained at distinct time points earlier in the postoperative period, which would have more practical clinical value, would be as predictive of postoperative outcomes as the VVR calculated at 48 hours.

Patients and Methods

Patient Population

This prospective observational validation study was approved by the Institutional Review Board within the Office of Research Compliance at Indiana University. Due to the observational nature of the study, consent was waived by the Institutional Review Board. All patients admitted to the cardiovascular intensive care unit (CVICU) at Riley Hospital for Children in Indianapolis, Indiana, from January 1, 2015 through June 30, 2015 were prospectively reviewed. Patients who required extracorporeal membrane oxygenation (ECMO) for the first 48 hours of CVICU admission were excluded, as their vasoactive medication regimens and ventilator requirements would not be reflective of their underlying disease severity but rather of the mechanical support provided by the extracorporeal circuit. All other patients were followed throughout their clinical courses and included in all analyses.

Data Collection

Pre- and perioperative data collected included: age, anthropometric measurements at time of surgery, anatomic diagnosis and procedure performed, Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery mortality category (STAT mortality category),[9] cardiopulmonary bypass duration, aortic cross-clamp duration, duration of hypothermic circulatory arrest if used, and preoperative

serum creatinine values. All arterial blood gas and lactate measurements (which are performed simultaneously using point-of-care testing) obtained during the first 48 postoperative hours were recorded daily by study personnel, along with the ventilator support at the time of each measurement, which included respiratory rate (RR), fraction of inspired oxygen (FiO_2), peak inspiratory pressure (PIP), positive end expiratory pressure (PEEP), and mean airway pressure (MAP). Patients at our institution are typically managed postoperatively with synchronized intermittent mandatory ventilation / pressure-regulated volume control, and typically extubated, at the discretion of the primary care team, from mechanical ventilator support when breathing comfortably with good gas exchange and without metabolic acidosis on the following ventilator settings: respiratory rate ≤ 10 breaths per minute, pressure support ≤ 10 cmH_2O, positive end-expiratory pressure ≤ 5 cmH2O, and fraction of inspired oxygen concentration ≤ 0.4. Doses of inotropic and vasopressor medications (e.g. dopamine, dobutamine, epinephrine, norepinephrine, milrinone, and vasopressin) at the time of each arterial blood gas measurement were also recorded. Lastly, serum creatinine values obtained on admission, postoperative day 1 and postoperative day 2 were recorded.

Derivation of the Vasoactive Ventilation Renal Score

Throughout each patient's hospital course, we calculated the patients' VIS at the time of each postoperative arterial blood gas measurement. The VIS was calculated in the following manner [3]:

VIS = dopamine dose (mcg/kg/min) + dobutamine dose (mcg/kg/min) + 100 * epinephrine dose (mcg/kg/min) + 10 * milrinone dose (mcg/kg/min) + 10,000 * vasopressin dose (U/kg/min) + 100 * norepinephrine dose (mcg/kg/min).

For patients on no vasoactive support at the time of blood gas measurement, VIS equaled zero. Secondly, the ventilation index (VI) was calculated for each postoperative arterial blood gas measurement as follows [10]:

$$VI = (\text{Ventilator RR}) * (PIP - PEEP) * PaCO_2 / 1000$$

Use of the VI, which incorporates $PaCO_2$ rather than PaO_2 into its formula, permits the inclusion of patients with mixing lesions and single ventricle anatomy in the study, as $PaCO_2$ is less affected by intra-cardiac shunting. For patients not requiring mechanical ventilation at the time of arterial blood gas measurement, VI equaled zero. Lastly, baseline preoperative serum creatinine was subtracted from each postoperative serum creatinine measurement (e.g. on admission, and postoperative days 1 and 2), which we labeled ΔCr. For patients in which postoperative serum creatinine measurements were less than or equal to baseline, we recorded ΔCr = 0. Creatinine was measured in mg/dL. (For centers where creatinine is measured in mmol/L, we recommend converting to mg/dL to calculate the score as follows: serum creatinine (mmol/dL) x 0.0113 = serum creatinine (mg/dL)).

Using each of these individual measurements, we then calculated the VVR at the time of each arterial blood gas measurement as follows:

$$VVR = VIS + VI + (\Delta Cr * 10)$$

VVR scores at 6, 12, 24, and 48 hours postoperatively were recorded.

Statistical Analyses

Descriptive statistics are provided as medians with interquartile ranges (IQR) for continuous variables and absolute counts with percentages for categorical variables. The primary outcome of interest was hospital length of stay (LOS). We opted to focus the study on hospital LOS because we deemed criteria for hospital discharge as compared to ICU discharge to likely be less inconsistent across centers. Hospital LOS is also inclusive of time spent in the ICU related to unplanned readmission after transfer to the cardiology ward. This outcome was dichotomized as upper (worst) 25th percentile versus lower 75th percentile. Patients in the upper 25% were defined as having prolonged LOS. Bivariate logistic regression analyses were performed to determine the individual contributions of VVR, VIS and serum lactate as predictors of LOS. This analysis was repeated for each of the four recorded time points. Receiver operative characteristic (ROC) curves were generated and the abilities of the predictors to correctly classify LOS were compared using area under the curve (AUC) values. AUC values for VVR at the study time points were compared using the method of DeLong, DeLong, and Clarke-Pearson as implemented by SAS.[11]

Bivariate comparisons were performed for demographic and surgical characteristics of patients with and without prolonged LOS using Wilcoxon rank-sum tests, X-square test, or Fisher's exact test as appropriate for individual variables. Variables that attained a bivariate significance of ≤ 0.30 and were of clinical relevance were considered for inclusion in a multivariable logistic regression model. Linearity in the logit was examined for continuous variables prior to model-building; those with evidence of non-linearity were converted to categorical variables. To obtain the best model, stepwise selection was used with a significance level of 0.3 for entry into the model, and 0.05 for staying. All statistical analyses were performed using STATA version 13 and SAS version 9.4.

Results

Study Population

During the study period, 168 unique patients were admitted to the cardiovascular ICU postoperatively. Four patients required ECMO support for the first 48 postoperative hours and were excluded from analysis. All other patients (*N*=164) were included in the analysis, median age 9.3 months (range: 1 day - 33 years). A summary of the demographic and clinical characteristics of the patient cohort are shown in Table 1. Median hospital LOS, our primary outcome variable, was 8 days (IQR: 5-17.5). Prolonged LOS was therefore defined as greater than 17.5 days. Three patients died before hospital discharge, all of which had prolonged hospital LOS prior to their deaths (range 29 - 148 days). In addition, the hospital LOS for the four excluded patients who required ECMO support for the first 48 hours ranged from 38 to 248 days, and none of these patients died prior to hospital discharge.

Median serum lactate, VIS, and VVR measurements with IQR and maximum values are presented in Table 2 for all study time points. We obtained ROC curves via bivariate logistic regression analysis for 6, 12, 24, and 48-hour serum lactate, VIS, and VVR as predictors of prolonged LOS. The AUC values for these models are also provided in Table 2. Similar to our prior studies [1,2], VVR performed well and had a greater AUC than the corresponding VIS and serum lactate at each time point ($P < 0.05$ for all comparisons). We also performed ROC analysis for age, weight, duration of cardiopulmonary bypass, and STAT category as predictors of prolonged LOS. The VVR at each of the four study time points was more predictive of prolonged LOS than any of these patient variables ($P < 0.05$ for all comparisons). The ROC curves for prolonged LOS and serum lactate, VIS, and VVR at 12 hours postoperatively, as well as STAT mortality category, are illustrated in Figure 2.

The AUCs for the VVR at 6, 12, 24, and 48 hours are statistically compared to each other in Supplemental Table 2. There were no statistical differences between the ROC curves for any of the VVR time points. In other words, the VVR at 6, 12, and 24 hours were, at the very least, as predictive as the VVR at 48 hours. Of the four VVR measurements, the 12-hour VVR had the highest AUC, 0.93 (95% CIs: 0.89-0.97). For this reason, the remainder of the analysis is focused on this time point.

Demographic and clinical variables for patients with and without prolonged hospital LOS are compared in Table 3. All variables with *P*-value <0.3 were considered for the multivariable model. On multivariable regression analysis, the 12-hour VVR remained a strong independent predictor of prolonged LOS. Specifically, with each increase of 1 in a patient's 12-hour VVR score, the odds of a prolonged LOS increased by 15% (OR: 1.15, 95% CI: 1.10, 1.20). Other variables that were independently associated with prolonged LOS were the presence of non-cardiac anatomic abnormalities and the use of inhaled nitric oxide. The remaining variables that were significant on bivariate analysis, namely age, weight, STAT category 4 or 5, duration of cardiopulmonary bypass, and admission lactate, were not significant on multivariable analysis and did not appreciably affect the model. Delayed sternal closure and the need for CPR were not included in the multivariable analysis because of the small number of patients within the study who had these postoperative complications. The best multivariable model for prolonged LOS including the 12-hour VVR, inhaled nitric oxide use, and non-cardiac anatomic abnormalities is presented in Table 4. The AUC for the model was 0.94 (95% CI: 0.91, 0.98). ROC curves for the model and its individual components are shown in Figure 2.

To simplify the interpretation and use of the 12-hour VVR, we dichotomized the variable into high and low. A 12-hour VVR cutoff value of 25 was chosen to maximize total accuracy and minimize weighted error ratios, and this cutoff correctly classified 90% of patients. Patients with 12-hour VVR greater than or equal to 25 were therefore defined as having a high VVR score. On multivariable logistic regression analysis, after adjustment for the presence of inhaled nitric oxide and non-cardiac anatomic abnormalities, high VVR at 12 hours remained strongly associated with prolonged LOS (odds ratio: 31; 95% CI: 10 - 90).

Comment

We have further validated the VVR as a multi-organ system severity of illness index for patients recovering from surgery for congenital heart disease. We have now demonstrated that the VVR strongly predicts hospital length of stay, more so than the VIS and serum lactate, in a patient population that not only includes children requiring cardiopulmonary bypass but also includes children undergoing procedures without cardiopulmonary bypass and adults with congenital heart disease. The patients included in this study reflect the postoperative patient populations at many centers, where adults undergoing surgery for congenital heart disease are commonly cared for within pediatric cardiovascular ICU's [12,13]. The greater heterogeneity of the patient population in this study has increased the strength and practicality of the VVR.

In our prior work, the VVR calculated at 48 hours was superior to admission and peak VVR measurements.[1,2] In fact, admission measurements performed poorly. This finding was not surprising, as vasoactive and ventilator support upon CVICU admission are likely less reflective of organ dysfunction and illness severity but rather more related to the dynamic processes that occur after cessation of cardiopulmonary bypass and

during transport to the CVICU. Likewise, the support upon admission may also be the peak support, which will negatively affect the strength of peak VVR measurements. We have now demonstrated that the VVR calculated at specific time points earlier in than 48 hours postoperatively can also reliably predict clinical outcome in children recovering from cardiac surgery. Specifically, patients with a VVR score greater than or equal to 25 at the 12 hours postoperatively were 31 times more likely to have a prolonged length of stay as compared to patients with lower VVR scores. This ability to provide important prognostic data earlier in the postoperative course further increases the functionality of the VVR.

The advantages of the VVR as compared to the VIS and serum lactate, as we have discussed in our prior work [1,2], should be intuitive to physicians caring for these children, as the VVR likely captures that subset of patients who have may have preserved hemodynamic integrity yet have significant burden of disease from postoperative lung or kidney injury. The additional components of the VVR, though on the surface may seem cumbersome to some, can be obtained from routinely available bedside data and the score can be quantitated with a simple calculator. Incorporation of VVR calculation into the electronic medical record could further enhance its utility. If available to physicians at the bedside, the 12-hour VVR has several potential clinical applications. The 12-hour VVR could provide a reliable estimate of illness severity, give parents and families realistic expectations of their child's postoperative course, or potentially assist with triage CVICU resources. Additionally, the 12-hour VVR could help stratify potential research subjects or assist with propensity score matching. Further validation in a multi-center data set should, however, be performed before widespread application is recommended.

This study also found that the use of inhaled nitric oxide and the presence of non-cardiac anatomic abnormalities had an effect on hospital LOS that was independent of the organ dysfunction quantitated by the 12-hour VVR. Use of inhaled nitric oxide, in many cases, represents an escalation of cardiopulmonary support beyond traditional vasoactive medications and ventilatory support. It is therefore somewhat intuitive that its use is associated with prolonged LOS, independent of the VVR. Likewise, the presence of non-cardiac anatomic abnormalities such as airway anomalies or gastrointestinal defects (e.g. intestinal malrotation, imperforate anus, Hirschsprung's disease) would not be accounted for by the VVR yet could surely prolong LOS, especially if surgical interventions were needed to address those abnormalities. Though the VVR at 12 hours in and of itself was a solid predictor of prolonged LOS, addition of these important variables further elevated the strength of our predictive model (Figure 2).

There are some limitations that must be noted. These data come from a single center, which limits their generalizability. The initial work on the VVR was however completed at a different center [1,2] and thus the VVR has now been validated as a predictor of postoperative outcome at two different institutions with different cardiac surgeons and varying practices. A multi-center validation study is the next step. Larger studies should also determine if the VVR has the ability to predict additional outcomes (most important of which is postoperative mortality), and whether other variables such as delayed sternal closure or the need for CPR have an effect on outcome independent of the VVR. We acknowledge that the VVR cannot reliably be calculated for patients requiring ECMO support, though the need for ECMO in these patients, in and of itself, is considered by most clinicians to be a reliable marker of disease severity. Indeed, all four patients who were excluded due to ECMO support would be characterized as having prolonged LOS. Also, no patients in our cohort required peritoneal dialysis or continuous renal

replacement therapy within the first 48 hours postoperatively, but either modalities could also affect the reliability of the score. Finally, the VVR remains affected by limitations previously noted in the VIS [3] - it does not assess the importance of the individual components of the VIS, and vasoactive medication administration as well as the degree of mechanical ventilator support were not under protocol and so may have been affected by variation in physician practice.

Conclusions

We have further validated the utility of the VVR score after surgery for congenital heart disease. The VVR calculated at 12 hours postoperatively could be a valuable and potentially powerful clinical tool to predict important postoperative outcomes in this patient population.

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Figure Legends

Figure 1: Receiver Operating Characteristic (ROC) curves for prolonged hospital length of stay and serum lactate (green), vasoactive-inotrope score (VIS) (red), vasoactive-ventilation-renal (VVR) score at 12 hours postoperatively (blue), along with STAT category (orange). The AUC was greatest for the VVR at 12 hours postoperatively, $P<0.001$ for all comparisons.

Figure 2: Receiver Operating Characteristic (ROC) curves for prolonged hospital length of stay and the multivariable model (solid blue line) and its individual components (dashed lines): vasoactive-ventilation-renal (VVR) score at 12 hours postoperatively (red), inhaled nitric oxide (purple), and non-cardiac anatomic abnormalities (green). Area under the curve for the multivariable model was 0.94 (95% CI: 0.91 – 0.98).

Video Legend

Video: Dr. Mastropietro explains the inception of the vasoactive-ventilation-renal score as an index of disease severity for infants and children who undergo cardiovascular surgery, and comments on the significance of the findings presented in their latest study.

Tables

Table 1: Patient Demographic Characteristics

Characteristic	All Patients (n=164)
Age (months)	9.3 (2.6 – 57.8)
Male (n)	102 (62%)
Weight (kg)	7.8 (4.6 – 17.8)
Race (n)	
Caucasian	131 (80%)
African American	23 (14%)
Asian	7 (4%)
Other	3 (2%)
Genetic / chromosomal abnormalities (n)	35 (21%)
Trisomy 21	17 (10%)
Other	18 (11%)
Non-cardiac anatomic abnormalities (n)	30 (18%)
STAT category (n)	
1	52 (32%)
2	41 (25%)
3	31 (19%)
4	31 (19%)
5	7 (4%)
Other	2 (1%)
Preoperative creatinine (mg/dL)	0.35 (0.29 - 0.50)
Cardiopulmonary bypass duration (min)	88 (59 -136)
Aortic cross clamp duration (min)	42 (15 – 66)
Delayed sternal closure (n)	16 (10%)
Postoperative inhaled nitric oxide use (n)	27 (16%)
Admission lactate (mg/dL)	2.0 (1.3 - 2.9)
Postoperative CPR (n)	6 (4%)

CPR: cardiopulmonary resuscitation; STAT: Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery mortality category

Data represented as absolute counts (%) or median (interquartile range)

Table 2: Relationship between postoperative measurements and prolonged LOS

Postoperative Variables	Median (IQR)	Maximum	AUC (95% CI)
6-hours:			
Lactate (mg/dL)	1.3 (0.8 - 2.6)	9.2	0.75 (0.67 - 0.84)
VIS	0 (0 - 5)	15.5	0.81 (0.74 - 0.88)
VVR	5.2 (0.6 - 24.3)	96	0.93 (0.89 - 0.97)
12-hours:			
Lactate (mg/dL)	1.1 (0.7 - 1.9)	9.7	0.78 (0.71 - 0.86)
VIS	0 (0 - 5)	16	0.81 (0.73 - 0.88)
VVR[a]	3.5 (0.2 - 24.6)	75	0.93 (0.89 - 0.97)
24-hours:			
Lactate (mg/dL)	0.9 (0.7 - 1.4)	5.4	0.61 (0.52 - 0.71)
VIS	0 (0 - 5)	17	0.84 (0.77 - 0.91)
VVR	1.7 (0 - 20.9)	64	0.91 (0.84 - 0.97)
48-hours:			
Lactate (mg/dL)	0.85 (0.6 - 1.3)	5.4	0.55 (0.45 - 0.65)
VIS	0 (0 - 4.5)	17.5	0.83 (0.76 - 0.91)
VVR	0.5 (0-11.1)	64	0.89 (0.81 - 0.96)
Age (months)	9.3 (2.6 - 57.8)	33 years	0.78 (0.70 - 0.87)
Weight (kg)	7.8 (4.6 -17.8)	100	0.80 (0.72 - 0.88)
STAT category	2 (1 - 3)	5	0.79 (0.72 - 0.87)
CPB duration (min)	87.5 (59 -136)	345	0.66 (0.55 - 0.77)

[a] AUC for VVR at 12 hours was 0.933, slightly greater than AUC for VVR at 6 hours of 0.929

AUC: Area under the receiver operating characteristic curve; CPB: cardiopulmonary bypass; CI: confidence interval; IQR: interquartile range; LOS: hospital length of stay; STAT: Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery mortality category; VIS: vasoactive inotrope score; VVR: vasoactive-ventilation-renal score

Table 3. Bivariate Analysis Comparing Patients With and Without Prolonged LOS

Characteristic	Prolonged LOS (n=41)	No Prolonged LOS (n=123)	P-value
Age (months)	1.5 (0.3 - 6.5)	11.5 (6.3 - 80)	<0.001
Male (n)	28 (68%)	74 (60%)	0.35
Weight (kg)	4.2 (3.4 - 5.5)	8.5 (6.1 - 22.3)	< 0.001
Genetic abnormalities (n)	7 (17%)	28 (23%)	0.44
NCAA (n)	13 (32%)	17 (14%)	0.01
STAT category 4 or 5 (n)	21 (51%)	17 (14%)	<0.001
Preoperative creatinine (mg/dL)	0.35 (0.29 - 0.48)	0.35 (0.29 - 0.51)	0.42
CPB Duration (min)	129 (78 - 173)	82 (56 - 122)	0.002
Aortic cross clamp duration (min)	53 (22 - 70)	36 (14 - 60)	0.13
Delayed sternal closure (n)	15 (37%)	1 (1%)	<0.001
Postoperative iNO use (n)	19 (46%)	8 (7%)	<0.001
Admission lactate (mg/dL)	2.3 (1.7 - 5)	1.9 (1.3 - 2.7)	0.004
VVR at 12 hours	31 (27 - 40)	1 (0 - 11)	<0.001

CPB: Cardiopulmonary bypass*; iNO*: inhaled nitric oxide; *NCAA*: non-cardiac anatomic abnormalities; *STAT*: Society of Thoracic Surgeons-European Association for Cardio-Thoracic Surgery Congenital Heart Surgery mortality category; *VVR*: vasoactive-ventilation-renal score

Data represented as absolute counts (%) or median (interquartile range)

Table 4. Multivariable Regression Analysis for Predictors of Prolonged LOS

Parameter	Estimate	SE	*P*-value	Odds Ratio (95% CI)
Intercept	-4.20	0.64	<0.0001	-
12-hour VVR	0.14	0.02	<0.0001	1.15 (1.10, 1.20)
Inhaled nitric oxide	1.50	0.71	0.033	4.50 (1.13, 17.99)
Non-cardiac anatomic abnormalities	1.54	0.73	0.034	4.67 (1.13, 19.34)

CI: Confidence interval; LOS: length of stay; SE: standard error; VVR: vasoactive-ventilation-renal score

Supplemental Table 1. Cardiovascular Surgical Procedures Organized by STAT Mortality Categories

Primary surgical procedure	All Patients (N=164)
STAT Category 1	**52 (32%)**
Repair, atrial septal defect	9
Repair, ventricular septal defect	13
Repair, Tetralogy of Fallot	9
Pulmonary valve replacement	7
Lateral tunnel Fontan operation	4
Repair, partial atrioventricular canal defect	3
Other	7
STAT Category 2	**41 (25%)**
Repair, coarctation of the aorta	8
Aortic valvuloplasty	6
Repair, Tetralogy of Fallot	4
Extracardiac Fontan operation	3
Bidirectional Glenn operation	3
Other	17
STAT Category 3	31 **(18%)**
Arterial Switch procedure (d-TGA w/IVS)	5
Hemi-Fontan operation	6
AV-Canal	5
Repair, pulmonary atresia w/VSD	5
Right ventricle-to-pulmonary artery conduit	4
Other	6
STAT Category 4	**31 (19%)**
Systemic-to-pulmonary artery shunt	7
Orthotopic heart transplant	5
Repair, total anomalous pulmonary venous return	5
Arterial switch procedure (d-TGA w/VSD)	2
Pulmonary artery banding	3
Other	9
STAT Category 5	**7 (4%)**
Norwood operation	6
Damus-Kaye Stanzel operation	1

d-TGA: d-transposition of the great arteries; IVS: intact ventricular septum; VSD: ventricular septal defect

Supplemental Table 2. Statistical Comparison for Area under the Curve Values for the Vasoactive-Ventilation-Renal (VVR) score and Prolonged Length of Stay at 6, 12, 24, and 48 hours.

Contrast	Estimate	SE	95% Wald CL		Chi-Square	*P*-value
VVR 6 hr - VVR 12 hr	-0.00366	0.0105	-0.0242	0.0169	0.1213	0.73
VVR 6 hr - VVR 24 hr	0.0210	0.0252	-0.0283	0.0704	0.6978	0.40
VVR 6 hr - VVR 48 hr	0.0403	0.0280	-0.0145	0.0952	2.0787	0.15
VVR 12 hr - VVR 24 hr	0.0247	0.0232	-0.0208	0.0702	1.1335	0.29
VVR 12 hr - VVR 48 hr	0.0440	0.0282	-0.0112	0.0992	2.4421	0.12
VVR 24 hr - VVR 48 hr	0.0193	0.0197	-0.0192	0.0578	0.9656	0.33