Cardiac Intensive Care

An Elevated Low Cardiac Output Syndrome Score Is Associated With Morbidity in Infants After Congenital Heart Surgery*

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Objectives: To evaluate an empirically derived Low Cardiac Output Syndrome Score as a clinical assessment tool for the presence and severity of Low Cardiac Output Syndrome and to examine its association with clinical outcomes in infants who underwent surgical repair or palliation of congenital heart defects.

Design: Prospective observational cohort study.

Setting: Cardiac ICU at Seattle Children's Hospital.

Patients: Infants undergoing surgical repair or palliation of congenital heart defects.

Interventions: None.

Measurements and Main Results: Clinical and laboratory data were recorded hourly for the first 24 hours after surgery. A Low Cardiac Output Syndrome Score was calculated by assigning one point for each of the following: tachycardia, oliguria, toe temperature less than 30°C, need for volume administration in excess of 30 mL/kg/d, decreased near infrared spectrometry measurements, hyperlactatemia, and need for vasoactive/inotropes in excess of milrinone at 0.5 μg/kg/min. A cumulative Low Cardiac Output Syndrome Score was determined by summation of Low Cardiac Output Syndrome Score on arrival to cardiac ICU, and 8, 12, and 24 hours postoperatively. Scores were analyzed for association with composite morbidity (prolonged mechanical ventilation, new infection, cardiopulmonary arrest, neurologic event, renal dysfunction, necrotizing enterocolitis, and extracorporeal life support) and resource utilization. Fifty-four patients were included. Overall composite morbidity was 33.3%. Median peak Low Cardiac Output Syndrome Score and cumulative Low Cardiac Output Syndrome Score were higher in patients with composite morbidity (3 [2–5] vs 2 [1–3]; $p = 0.003$ and 8 [5–10] vs 2.5 [1–5]; $p < 0.001$)]. Area under the receiver operating characteristic curve for cumulative Low Cardiac Output Syndrome Score versus composite morbidity was 0.83, optimal cutoff of greater than 6. Patients with cumulative Low Cardiac Output Syndrome Score greater than or equal to 7 had higher morbidity, longer duration of mechanical ventilation, cardiac ICU, and hospital length of stay (all $p \leq 0.001$). After adjusting for other relevant variables, peak Low Cardiac Output Syndrome Score and cumulative Low Cardiac Output Syndrome Score were independently associated with composite morbidity (odds ratio, 2.57; 95% CI, 1.12–5.9 and odds ratio, 1.35; 95% CI, 1.09–1.67, respectively).

Conclusion: Higher peak Low Cardiac Output Syndrome Score and cumulative Low Cardiac Output Syndrome Score were associated with increased morbidity and resource utilization among infants following surgery for congenital heart defects and might be a useful tools in future cardiac intensive care research. Independent validation is required. (*Pediatr Crit Care Med* 2017; 18:26–33)

Key Words: cardiac surgery; low cardiac output syndrome; morbidity; pediatric; score

*See also p. 85.

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Low cardiac output syndrome (LCOS) occurs in as many as 25% of children undergoing surgical repair or palliation of congenital heart defects (CHDs) (1), and its occurrence contributes to significant morbidity and mortality (2).

Because invasive procedures and/or echocardiography have limitations (3) for postoperative determination of LCOS, researchers have derived their own clinical definitions of LCOS (1, 4–6), but no consensus definition exists. Use of inconsistent definitions among studies makes comparisons of associations, therapeutic effects, and meta-analysis difficult.

The Vasoactive-Inotropic Score (VIS) has been demonstrated to correlate with clinical outcomes (7, 8), and has previously been used as a surrogate measure of LCOS. However, it is dependent on individual physician and institutional practices regarding escalation and weaning, only considers contractility and afterload as potential causes of LCOS, and does not take clinical signs of LCOS into consideration.

Accordingly, the purpose of this investigation was to empirically derive a LCOS measure with biological plausibility that takes into account clinical manifestations as well as therapeutic maneuvers necessary to optimize preload, contractility, and afterload. We developed a LCOS Score (LCOSS) and hypothesized that a higher peak LCOSS (pLCOSS) and cumulative LCOSS (cLCOSS) would be associated with worse outcomes and greater cardiac ICU (CICU) resource utilization in infants undergoing surgical repair or palliation of CHDs.

MATERIALS AND METHODS

We recruited infants admitted to the CICU at Seattle Children's Hospital, a tertiary care children's hospital staffed 24 hr/d by pediatric cardiac intensivists, in addition to pediatric critical care, cardiology, and anesthesiology fellows. The CICU has approximately 550 admissions every year, with postoperative cardiac patients generally representing 70% of this total. At the time of this investigation, approximately 200 cardiac surgeries were performed annually in infants.

This study was approved by the Institutional Review Board of Seattle Children's Hospital, an affiliate of the University of Washington. We conducted a prospective observational cohort study of infants who underwent surgical repair or palliation of CHDs at Seattle Children's Hospital from January 1, 2011, to January 1, 2012, and who required admission to the CICU after their operation. Potential subjects were identified through the weekly surgical schedule screening, and informed consent was obtained from their parents or legal guardian prior to their child's surgery. Patients who were born prematurely (< 37 wk) and were less than 40 weeks corrected gestational age at the time of surgery, weighed less than 2.5 kg at the time of surgery, had a preexisting diagnosis of necrotizing enterocolitis, preexisting evidence of documented or highly suspected infection, preoperative requirement of extracorporeal membrane oxygenation, or whose parents could not communicate in English or Spanish were excluded from the study. Baseline demographic information including age, weight at the time of surgery, gender, diagnosis, type of repair (univentricular/biventricular), and surgical procedure was obtained from the medical record. Patients were classified into risk categories according to the consensus-based method of risk adjustment for surgery for CHDs (RACHS-1) (9). Preoperative data collected included need for vasoactive-inotropic support and/or mechanical ventilation (MV). Operative course data obtained from the anesthesia and operating room records included cardiopulmonary bypass (CPB) time, aortic cross clamp time (AoX), and circulatory arrest time. Hourly vasoactive-inotropic drug dosage and hourly crystalloid and colloid (including blood products) administration for the first 3 days were recorded. Dosages of vasoactive-inotropic drugs were used to derive a VIS as described by Gaies et al (8): (1 × dopamine [μg/kg/min] + 1 × dobutamine [μg/kg/min] + 100 × epinephrine [μg/kg/min] + 100 × norepinephrine [μg/kg/min] + 10 × milrinone [μg/kg/min] + 10,000 × vasopressin [U/kg/min]). Peak VIS during the first 24 hours after surgery was recorded. Mean VIS was obtained by averaging hourly VIS over the first 24 hours postoperatively. Heart rate, toe temperatures, near infrared spectroscopy (NIRS) measurements, pulse oximetry, and urine output in the first 72 hours were also recorded hourly. All arterial lactate levels for the first three postoperative days, daily peak creatinine levels, and all blood, urine, and tracheal cultures for the first five postoperative days were recorded.

Development of the Score

We empirically developed a LCOSS taking into account clinical manifestations of decreased perfusion, such as tachycardia, decreased urine output, cool extremities, increased lactate, and therapies to treat LCOS such as augmenting preload and/or administering vasoactive-inotropic medication. Altered mental status, although clinically important as a manifestation of low cardiac output, was not included in the score as patients are generally provided sedation and analgesic medications that alter sensorium. Cerebral and renal NIRS have been used as surrogate indicators of CNS and renal perfusion, respectively (10–12), and were included as part of our score as surrogates of Svo_2 and to aid in the recognition of decreased perfusion in the early postoperative period.

The score was calculated by assigning one point for each of the following: 1) tachycardia, 2) oliguria, 3) low toe temperature, 4) need for volume administration (on top of maintenance IV fluids), 5) decreased NIRS measurements, 6) elevated arterial lactate, and 7) need for vasoactive-inotropic infusions in excess of milrinone at 0.5 μg/kg/min (**Table 1**). If a patient was being actively cooled, a point was not assigned for a low toe temperature. If staff had begun measuring urine output every 2 hours instead of every 1 hour, urine output was calculated by averaging the urine output over the preceding 2 hours. If the Foley catheter was removed, a point was not assigned for oliguria. If a patient received more than 30 mL/kg in boluses (colloid or crystalloid) in the first 24 hours, a point was assigned for volume every hour from the time the 30 mL/kg/d were met. LCOSS was recorded hourly, and we prospectively defined a pLCOSS as the highest LCOSS in a patient during the first 24 hours following surgery, and also defined a cLCOSS as the sum of LCOSS on arrival to the CICU, and scores obtained at 8, 12, and 24 hours after surgery, as a comprehensive measure of the severity and duration of LCOS during the first postoperative day.

TABLE 1. Low Cardiac Output Syndrome Score Components

Variable	Assign One Point If:
HR	> 20% above postinduction HR in operating room
Urine output	< 1 mL/kg/hr
Toe temperature	< 30°C
Vasoactive/inotrope requirement	In excess of milrinone 0.5 μg/kg/min
Volume administration (crystalloid and colloid)	> 30 mL/kg/d
Decreased NIRS measurement	Cerebral and renal NIRS < 50% and 75% of arterial saturations, respectively
Arterial lactate	> 2 mmol/L Texto

HR = heart rate, NIRS = near infrared spectroscopy.

Outcome Variables

Variables relating to hospital course included duration of MV, CICU, and hospital length of stay (LOS). We identified indicators of early morbidity as clinically meaningful, patient-centered outcomes. These morbidities included prolonged duration of postoperative MV (defined as a duration of MV above the 75th percentile for the cohort), occurrence of a new infection (positive blood, urine, or tracheal cultures that prompted surveillance cultures and the initiation or change of antimicrobial therapy), cardiopulmonary arrest, adverse CNS events (intracranial hemorrhage, stroke, or seizures), renal dysfunction (defined by Renal Injury, Failure, Loss of Kidney Function, End-stage kidney disease criteria [13] utilizing the upper limit of normal creatinine ranges for age as the definition of a baseline creatinine [14, 15]), occurrence of necrotizing enterocolitis, and need for extracorporeal life support (ECLS) in the postoperative period. Composite morbidity and mortality was defined as the occurrence of mortality, an individual morbidity or any permutation of the aforementioned morbidities in a single subject, and it was selected a priori to be our primary outcome variable. However, as only one death was recorded for this cohort, the primary outcome variable was collapsed to occurrence of one or more new morbidities. Prolonged CICU LOS was defined as a postoperative CICU stay greater than 5 days.

Statistical Analysis

Data are presented as means and SDs or medians and interquartile ranges for normally and nonnormally distributed continuous variables, respectively, and as proportions for categoric variables. Categoric variables were analyzed with the chi-square test or the Fisher exact test. Normally distributed continuous variables were analyzed with the Student *t* test. Nonnormally distributed continuous data were analyzed with the Wilcoxon signed rank test. Receiver operating characteristic (ROC) curves were used to assess the predictive ability of peak and cLCOSS for morbidity and prolonged CICU stay. Although the purpose of this study was not a comparison between VIS and LCOSS, the same analyses were performed with peak and mean VIS to evaluate performance of an adequately validated score in our sample and offer a point of reference for analysis of LCOSS performance. Multivariate logistic regression was used to test the relationship between LCOSS and composite morbidity adjusting for clinically relevant variables that were found to be significantly associated with morbidity on univariate analysis. Statistical significance was taken at two sided *p* value less than 0.05. Analyses were performed with dedicated statistical software (SigmaStat version 2.03: SPSS, Chicago, IL; and MedCalc Statistical Software version 13.3.1: MedCalc Software bvba, Ostend, Belgium).

RESULTS

A total of 55 patients met eligibility criteria for the study. However, one patient was excluded from the analysis as his stay in the CICU was more than 700 days and the duration of MV was several SDs above the mean for the cohort and it would have skewed results. The demographic and baseline clinical characteristics of the 54 patients included in the study are shown in **Table 2**. A list of all the procedures performed in our cohort is shown in **Supplemental Digital Content 1** (http://links.lww.com/PCC/A317).

There was one death in our cohort. Eighteen patients (33.3%) developed morbidity. Three patients (5.6%) developed renal dysfunction. Two patients (3.7%) developed a hospital-acquired infection. Two patients (3.7%) suffered an adverse neurologic event. Fourteen patients (26%) required prolonged duration of MV which in our cohort was more than 68.4 hours. Two patients (3.7%) suffered a cardiopulmonary arrest and both required ECLS. Patients with composite morbidity had a significantly lower age and weight, a higher RACHS-1 score, and required preoperative MV more frequently when compared with patients without morbidity (Table 2). However, when comparing weight utilizing *z* score for age, there was no difference between the groups. Gender, CPB use, type of repair (univentricular or biventricular), and need for vasoactive-inotropic support prior to surgery were not different between the groups. The duration of CPB and AoX was significantly longer in the morbidity group.

Resource utilization and scores for the cohort are summarized in **Table 3**. The duration of MV was significantly longer in patients with morbidity as would be expected given the inclusion of prolonged MV in the definition of morbidity. Patients with morbidity had significantly longer CICU and hospital LOS. Both pLCOSS and cLCOSS were significantly greater among patients with morbidity. VISs were also significantly higher in this group. Two patients had a peak VIS score greater than 20: one underwent a right ventricle to pulmonary

TABLE 2. Patient Demographics and Baseline Characteristics by Morbidity Status

Characteristics	No Morbidity (*n* = 36)	Morbidity (*n* = 18)	*p*[a]
Surgery with CPB, *n* (%)	34 (94.4)	16 (88.9)	NS
Male gender, *n* (%)	17 (47.2)	14 (77.8)	NS
Age, mo[b]	6.06 ± 3.37	2.94 ± 2.86	0.001
Neonates	4 (11.1)	8 (44.4)	0.012
Weight, kg[b]	5.78 ± 1.74	4.30 ± 1.60	0.004
Weight, *z* score for age[b]	−1.94 ± 1.43	−1.42 ± 1.39	NS
Risk Adjustment for Congenital Heart Surgery-1 category[c], *n* (%)	2 (2–3)	3 (3–4)	0.003
1	1 (2.8)	1 (5.6)	
2	25 (69.4)	3 (16.7)	
3	8 (22.2)	9 (50)	
4	2 (5.6)	2 (11.1)	
5	0 (0)	0 (0)	
6	0 (0)	3 (16.7)	
Preoperative mechanical ventilation use, *n* (%)	0 (0)	4 (22.2)	0.01
Preoperative inotrope use, *n* (%)	0 (0)	1 (5.6)	NS
Type of repair, *n* (%)			
Univentricular	8/36 (22.2)	4/18 (22.2)	NS
Biventricular	28/36 (77.8)	14/18 (77.8)	
CPB times, min			
Total CPB time[b]	69.4 ± 33.5	100.0 ± 57.1	0.016
Cross clamp time[b]	42.8 ± 31.0	71.3 ± 52.0	0.015
Circulatory arrest time[b]	5.2 (3.8–27.5)	6.0 (4.3–25.0)	NS

CBP = cardiopulmonary bypass, NS = not significant.
[a]Comparison between patients with and without morbidity.
[b]Mean ± SD.
[c]Median and interquartile range.

artery conduit for a tetralogy of Fallot with pulmonary atresia and the other had an arterial switch operation.

The total number of times a component of the LCOSS score was met over the 24 hours and across the four different time points is shown as **Supplemental Digital Content 2** (http://links.lww.com/PCC/A318). The most frequently encountered components in the first 24 hours were vasoactive/inotropic support and decreased urine output. Forty-nine percent of the all the occurrences of any component of the LCOSS over the four time points for cLCOSS calculation were secondary to volume administration or vasoactive/inotropic drug administration. The remaining 51% were secondary to clinical criteria being met.

Performance Characteristics of LCOSS and VIS

A summary of these characteristics is shown in **Table 4**. The area under the ROC curve (AUROC) for each of the scores entered in relation to morbidity was not significantly different from each other with the exception of cLCOSS having a significantly higher AUROC than pLCOSS with an AUROC of 0.83 (95% CI, 0.70–0.92). The optimal cutoff points were a pLCOSS greater than 3 (sensitivity, 44%; specificity, 97%), a cLCOSS greater than 6 (sensitivity, 67%; specificity, 86%), and a peak VIS greater than 8 (sensitivity, 78%; specificity, 72%). **Figure 1** displays ROC curves for pLCOSS and cLCOSS versus morbidity. ROC curves for peak and mean VIS versus morbidity are displayed in **Supplemental Figure 1** (Supplemental Digital Content 3, http://links.lww.com/PCC/A319; **legend**, Supplemental Digital Content 5, http://links.lww.com/PCC/A321).

When scores were tested against prolonged CICU LOS, all scores performed well and were not statistically different. pLCOSS and cLCOSS performed almost identically to each other with an AUROC of 0.85 (95% CI, 0.73–0.93) and 0.87 (95% CI, 0.75–0.95), respectively. Optimum cutoff points were greater than 3 for pLCOSS (sensitivity, 62%; specificity, 93%)

TABLE 3. Resource Utilization and Scores by Morbidity Status

Variable	No Morbidity ($n = 36$)	Morbidity ($n = 18$)	p[a]
Hospital LOS, d[b]	5 (4–7)	20 (14–50)	< 0.001
Cardiac ICU LOS, d[b]	2 (1–3)	8 (5–17)	< 0.001
Duration of mechanical ventilation, d[b,c]	0.4 (0.2–0.8)	5.8 (2.9–7.1)	< 0.001
Peak Vasoactive-Inotropic Score[b]	7 (5–10)	11(10–13)	0.001
Mean Vasoactive-Inotropic Score[b]	4.4 (2.7–5.3)	8 (5.6–10.0)	0.001
Peak LCOSS[b]	2 (1–3)	3 (2–5)	0.003
Cumulative LCOSS[b]	2.5 (1–5)	8 (5–10)	< 0.001

LCOSS = Low Cardiac Output Syndrome Score, LOS = length of stay.
[a]Comparison between patients with and without morbidity.
[b]Median and interquartile range.
[c]Prolonged mechanical ventilation is included in the definition of composite morbidity.

TABLE 4. Performance Characteristics of Low Cardiac Output Syndrome Score and Vasoactive-Inotropic Score

Scores and Outcome	Area Under the Curve	SE	95% CI
Morbidity			
Peak VIS	0.77	0.09	0.64–0.88
Mean VIS	0.73	0.09	0.59–0.89
Peak LCOSS	0.75	0.07	0.61–0.86
Cumulative LCOSS	0.83	0.06	0.70–0.92
Cardiac ICU length of stay > 5 d			
Peak VIS	0.81	0.08	0.67–0.90
Mean VIS	0.82	0.08	0.69–0.91
Peak LCOSS	0.85	0.09	0.73–0.93
Cumulative LCOSS	0.87	0.05	0.70–0.95

LCOSS = Low Cardiac Output Syndrome Score, VIS = Vasoactive-Inotropic Score.

and greater than 7 for cLCOSS (sensitivity, 69%; specificity, 88%). Peak VIS had an AUROC of 0.81 (95% CI, 0.67–0.90) with an optimum cutoff point of greater than 10 for peak VIS (sensitivity, 62%; specificity, 90%).

pLCOSS and cLCOSS as a Dichotomous Outcome Measures

We used the cutoff points derived from the ROC curve analysis of pLCOSS and cLCOSS versus morbidity to separate our cohort dichotomously. Those with a pLCOSS greater than or equal to 4 and those with cLCOSS greater than or equal to 7 had highly significantly elevated occurrence rate of morbidity, CICU LOS, hospital LOS, as well as a significantly higher VIS. (**Table 5**).

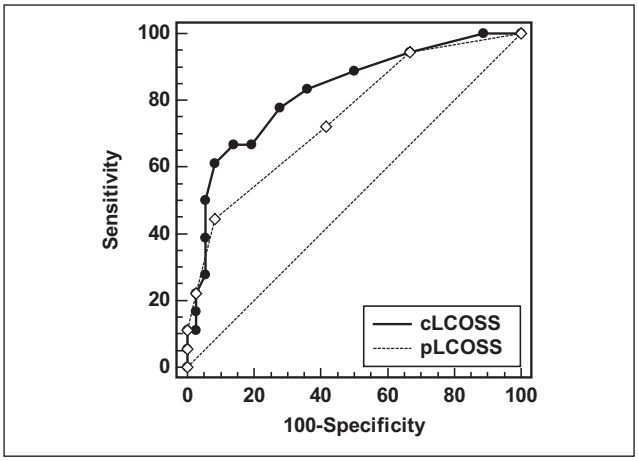

Figure 1. Receiver operator characteristic curve for Low Cardiac Output Syndrome Score versus morbidity. cLCOSS = cumulative Low Cardiac Output Syndrome Score, pLCOSS = peak Low Cardiac Output Syndrome Score.

Regression Analyses

When adjusted for other relevant variables (age, preoperative MV, CPB time, and RACHS-1 score) by multivariate logistic regression, pLCOSS and cLCOSS were independently associated with morbidity (odds ratio [OR], 2.57; 95% CI, 1.12–5.9 and OR, 1.35; 95% CI, 1.09–1.67, respectively). Aortic cross clamp duration was not entered because of collinearity with CPB time. Weight was not included in the models because of collinearity with age and because weight *z* score for age was not significant in univariate analysis.

Post Hoc Analyses

The majority of patients with composite morbidity was in that outcome group solely because they required prolonged MV, and one patient was in the composite morbidity group solely because of a new infection. Both of these variables could conceivably be related to other factors aside from LCOS (e.g., surgical complexity, care of central catheters, and tubes). Therefore, we undertook separate post hoc analyses of a new "unfavorable

TABLE 5. Outcomes Comparing Children With Peak Low Cardiac Output Syndrome Score Less Than 4 Versus Peak Low Cardiac Output Syndrome Score Greater Than or Equal to 4; and Cumulative Low Cardiac Output Syndrome Score Less Than 7 Versus Cumulative Low Cardiac Output Syndrome Score Greater Than or Equal to 7

Variable	pLCOSS < 4 (*n* = 45)	pLCOSS ≥ 4 (*n* = 9)	*p*[a]	cLCOSS < 7 (*n* = 39)	cLCOSS ≥ 7 (*n* = 17)	*p*[b]
Duration of mechanical ventilation, days[c]	0.5 (0.2–1)	6.7 (4.4–9.3)	< 0.001	0.38 (0.1–0.8)	3.8 (2.2–7.0)	< 0.001
Cardiac ICU LOS, d[c]	2 (1–3)	9 (6.8–22.3)	< 0.001	2 (1–3)	7 (4.5–13.8)	< 0.001
Hospital LOS, d[c]	7 (4–10.3)	16 (14–30.5)	0.001	6 (4–9.3)	14 (8–19.3)	0.001
Peak Vasoactive-Inotropic Score[c]	8 (5–10)	13 (10.4–40)	< 0.001	5 (5–8.5)	10.5 (10–13)	< 0.001
Morbidity, *n* (%)	10 (22.2)	8 (88.8)	< 0.001	6 (15.4)	12 (70.6)	< 0.001
Unfavorable outcome, *n* (%)	2 (4.4)	4 (44.4)	< 0.01	1 (2.7)	5 (29.4)	< 0.01

cLCOSS = cumulative Low Cardiac Output Syndrome Score, LOS = length of stay, pLCOSS = peak Low Cardiac Output Syndrome Score.
[a]Comparison between patients with peak Low Cardiac Output Syndrome Score (LCOSS) < 4 and ≥ 4.
[b]Comparison between patients with cumulative LCOSS < 7 and ≥ 7.
[c]Median and interquartile range.

TABLE 6. Resource Utilization and Scores by Unfavorable Outcome Status–Post Hoc Analysis

Variable	No Morbidity (*n* = 48)	Unfavorable Outcome (*n* = 6)	*p*[a]
Cardiac ICU LOS, d[b]	2 (1–4.5)	12.5 (5–20)	0.002
Hospital LOS, d[b]	7 (4–14)	16 (9–50)	0.02
Duration of mechanical ventilation, d[b]	0.6 (0.2–2.3)	6.9 (2.8–12.8)	0.02
Peak VIS[b]	8 (5–10)	14 (10–15)	0.004
Mean VIS[b]	4.7 (3–7.2)	6.5 (5.6–50.4)	Not significant
Peak LCOSS[b]	2 (1–3)	4.5 (3–5)	0.01
Cumulative LCOSS[b]	3 (1–6.5)	9.5 (7–16)	0.008

LCOSS = Low Cardiac Output Syndrome Score, LOS = length of stay, VIS = Vasoactive-Inotropic Score.
[a]Comparison between patients with and without morbidity.
[b]Median and interquartile range.

outcome group," only including patients with cardiopulmonary arrest, adverse CNS events, occurrence of necrotizing enterocolitis, renal dysfunction, and need for ECLS in the postoperative period. Patients with unfavorable outcome had significantly longer duration of MV, and CICU and hospital LOS. pLCOSS and cLCOSS were significantly higher in patients with unfavorable outcome as well. Resource utilization and scores by unfavorable outcome status are displayed in **Table 6**.

On ROC curve analyses, both pLCOSS and cLCOSS had exactly the same optimal cutoff points, yet performed better than in previous analyses. AUROC for pLCOSS, cLCOSS, and peak VIS versus unfavorable outcome and their optimal cutoff points are displayed in **Table 7**. There was no statistically significant difference between the curves. **Figure 2** displays ROC curves for peak and cLCOSS versus unfavorable outcome. ROC curves for peak and mean VIS versus unfavorable are displayed as **Supplemental Figure 2** (Supplemental Digital Content 4, http://links.lww.com/PCC/A320; legend, Supplemental Digital Content 5, http://links.lww.com/PCC/A321).

Patients with a pLCOSS greater than or equal to 4 and those with cLCOSS greater than or equal to 7 had a significantly higher incidence of unfavorable outcome when compared with those with lower scores. pLCOSS and cLCOSS were again independently associated with unfavorable outcome with similar odds as in the previous multivariate analysis which included the same covariates (OR, 2.54; 95% CI, 1.04–6.2 and OR, 1.32; 95% CI, 1.04–1.69, respectively).

DISCUSSION

We developed and tested the performance of the LCOSS, a proposed new scoring system for infants following cardiac surgery, meant to identify and quantify a low cardiac output state, that

TABLE 7. Performance Characteristics of Scores Versus Unfavorable Outcome–Post Hoc Analysis

Score	Area Under the Curve	95% CI	Cutoff Point	Sensitivity, %	Specificity, %
Peak LCOSS	0.82	0.69–0.91	> 3	67	89
Cumulative LCOSS	0.85	0.73–0.93	> 6	83	75
Peak Vasoactive-Inotropic Score	0.87	0.75–0.95	> 12.5	67	94

LCOSS = Low Cardiac Output Syndrome Score.

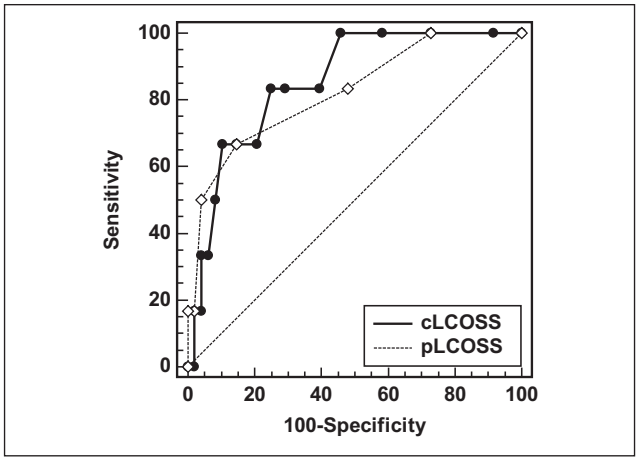

Figure 2. Receiver operator characteristic curve for Low Cardiac Output Syndrome Score versus unfavorable outcome. cLCOSS = cumulative Low Cardiac Output Syndrome Score, pLCOSS = peak Low Cardiac Output Syndrome Score.

can be easily calculated at bedside and takes into account both clinical and therapeutic variables. We found that cLCOSS and pLCOSS were strongly associated with new morbidity as well as increased CICU resource utilization.

In the 6 decades since the first clinical severity scoring system was introduced in 1953 by Apgar (16), many other scoring systems have been developed taking into account clinical criteria alone (17, 18), a combination of clinical and therapeutic criteria (19), and therapy metrics alone (20, 21). These scores have proven to be useful assessment, prognostic and triage tools, and some are useful in clinical practice guidelines, as is the case of Glasgow Coma Scale for trauma. Scores such as these provide for a common language, allowing for meaningful comparisons to be made across institutions, including quality of care comparisons. In some situations, such scores make it easier to convey patient status in our communications. Very few scoring tools have been developed with the pediatric cardiac patient in mind or have been validated in this population (22). Existing scores that can be applied to critically ill children with heart disease only take therapeutic criteria into consideration (8, 21).

Although commonly encountered after pediatric cardiac surgery, there is to this date no pathognomonic sign of LCOS and pulmonary artery catheters are impractical for every day clinical use or for research purposes. The diagnosis of LCOS in pediatric patients has frequently been made by gestalt. This has complicated its use as a reproducible outcome measure, even more so a quantifiable one.

In our analysis, a high LCOSS was significantly associated with a variety of clinically meaningful adverse outcomes. Both the intensity and duration of LCOS, as measured by pLCOSS and cLCOSS, were significantly associated with increased morbidity as well as CICU and hospital LOS. cLCOSS had moderate discriminative ability in predicting composite morbidity and CICU LOS greater than 5 days for our population. When applied dichotomously using the optimal cutoff point derived from the ROC curve analysis of LCOSS versus morbidity, a pLCOSS greater than or equal to 4 and cLCOSS greater than or equal to 7 were strongly associated with worse outcomes. Even though the predictive ability of pLCOSS was lower than cLCOSS in our original analysis, it proved to be similar to cLCOSS in our post hoc analysis. pLCOSS also has the advantage over cLCOSS that its cutoff can be applied in real time, instead of waiting 24 hours for its computation. Thus, an on the spot LCOSS could be more useful as a study trigger point, for example, where an intervention versus placebo is started for an LCOSS greater than or equal to 4.

Therapy-based metrics are entirely practice dependant. Although LCOSS is not completely practice independent, our score offers a combination of therapeutic and clinical criteria. Both types of criteria occurred in roughly the same frequency in our population. Because each therapy metric was assigned the same weight on the score—one point each—physician preference for optimization of preload or contractility and afterload is less likely to skew the score.

Practice variation will diminish as standardized approaches to prescribing and adjusting vasoactive-inotropic support are developed as a result of clinical trials. A standardized definition of LCOS is necessary for such studies to be feasible. This is demonstrated by the recent systematic review by Burkhardt et al (23) reporting insufficient evidence to support standard postoperative milrinone use in the early postoperative period partly due to inconsistent definitions of LCOS across studies. Our study suggests LCOSS could help fill the clinical metrics gap existing in pediatric cardiac critical care today and offer a way to quantitatively describe LCOS in future research.

Our research has the inherent limitations of being a single center study with a small sample size. Ideally, this study would have compared LCOSS with invasive monitoring or echocardiography to determine its true capacity for predicting occurrence of LCOS. However, ethical considerations, cost, and likely difficulties in obtaining institutional review board approval for such a study prevented us from doing so. In addition, because

pLCOSS and cLCOSS were tested on the same cohort from whom it was derived, its discriminative ability mandates validation in an independent cohort. Further, as this study was performed in infants, it is unclear whether the LCOSS will have the same predictive ability if applied to an older pediatric population and may not be generalizable to places where certain components of the score are not obtainable, for example, lack of NIRS measurements.

Finally, the VIS score was utilized as a framework to better understand our patient population by using a marker of illness severity that has been adequately validated. Our study does not imply superiority over VIS. They are two different types of metrics that could become valuable companions in pediatric cardiac surgery research.

CONCLUSIONS

It is important to define LCOS for CICU clinical research. We present one approach that appears to be related to clinically meaningful outcomes. Higher peak and cLCOSS are associated with increased morbidity among children undergoing surgical repair or palliation of CHDs. After adjusting for other clinically relevant variables, high cLCOSS is independently associated with morbidity. A pLCOSS of 4 and a cLCOSS of 7 or greater in the first 24 hours are strongly associated with combined morbidity, increased CICU and hospital LOS.

Results derived from the current derivation cohort require prospective validation in an independent cohort. However, LCOSS as a surrogate clinical measure for the intensity and duration of LCOS and predictor of poor outcome may be a useful quantitative tool for future descriptive and interventional research in cardiac intensive care.

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