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Analyzing Continuous Physiologic Data to Find Hemodynamic Signatures Associated With New Brain Injury After Congenital Heart Surgery

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IMPORTANCE: Continuous data capture technology is becoming more common. Establishing analytic approaches for continuous data could aid in understanding the relationship between physiology and clinical outcomes.

OBJECTIVES: Our objective was to design a retrospective analysis for continuous physiologic measurements and their relationship with new brain injury over time after cardiac surgery.

DESIGN, SETTING, AND PARTICIPANTS: Retrospective cohort study in the Cardiac Critical Care Unit at the Hospital for Sick Children in patients after repair of transposition of the great arteries (TGA) or single ventricle (SV) lesions.

MAIN OUTCOMES AND MEASURES: Continuously acquired physiologic measurements for up to 72 hours after cardiac surgery were analyzed for association with new brain injury by MRI. Distributions of heart rate (HR), systolic blood pressure (BP), and oxygen saturation (Spo_2) for SV and TGA were analyzed graphically and with descriptive statistics over postoperative time for data-driven variable selection. Mixed-effects regression analyses characterized relationships between HR, BP, and Spo_2 and new brain injury over time while accounting for variation between patients, measurement heterogeneity, and missingness.

RESULTS: Seventy-seven patients (60 TGA; 17 SV) were included. New brain injury was seen in 26 (34%). In SV patients, with and without new brain injury, respectively, in the first 24 hours after cardiac surgery, the median (interquartile range) HR was 172.0 beats/min (bpm) (169.7–176.0 bpm) versus 159.6 bpm (145.0–167.0 bpm); systolic BP 74.8 (67.9–78.5 mm Hg) versus 68.9 mm Hg (61.6–70.9 mm Hg). Higher postoperative HR (parameter estimate, 19.4; 95% CI, 7.8–31; $p = 0.003$ and BP, 8.6; 1.3–15.8; $p = 0.024$) were associated with new brain injury in SV patients. The strength of this relationship decreased with time.

CONCLUSIONS AND RELEVANCE: Retrospective analysis of continuous physiologic measurements can provide insight into changes in postoperative physiology over time and their relationship with new brain injury. This technique could be applied to assess relationships between physiologic data and many patient interventions or outcomes.

KEY WORDS: brain injuries; congenital heart disease; imaging; pediatric cardiac surgery; statistical model

With improved survival for patients with critical congenital heart disease, active research priorities include describing, predicting, and improving neurodevelopmental sequelae (1–7). Preoperative and postoperative brain injury have been reported on brain MRI studies of children with critical congenital heart disease, including both transposition of the great arteries (TGA) and single ventricle (SV) defects (5, 8). Postoperative brain injury, particularly white matter injury (WMI), has been associated

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with adverse neurodevelopmental outcomes (3–5, 9). Neurologic injuries in patients with TGA and SV have been associated with longer, more complicated stays in the ICU and low cardiac output (1, 2, 10, 11). Postoperative strategies to modify the risk of neurologic injury are desirable and understanding the relationship between postoperative physiology and new brain injury may help with this aim. Although multimodal physiologic monitoring is the standard of care in the ICU, the ability to store and retrospectively analyze these data has been limited (12). Newer data capture techniques have changed how millions of continuous physiologic data points per patient can be retrospectively analyzed in granular detail (12). This may help us to better characterize the relationship between postoperative physiology and clinically meaningful outcomes, such as new brain injury detected by MRI. Defining these associations, however, will require new analytic approaches if continuous physiologic data are to be used to create clinically actionable information at the bedside.

Using routinely monitored continuous physiologic data collected in the first 72 hours after cardiac surgery for infants with either TGA or SV, our primary objective was to design an analytic approach to retrospectively characterizing the relationship between physiologic data and either new brain injury or WMI over postoperative time. We hypothesized that this analysis might reveal insights into the associations between physiologic states and new brain injury and could be used as a basis for ongoing research into the use of continuous physiologic data as a way to understand clinical outcomes.

MATERIALS AND METHODS

Study Setting and Design

This retrospective cohort study was undertaken in the Cardiac Critical Care Unit (CCCU) at the Hospital for Sick Children, Toronto, ON, Canada, from January 1, 2013, to December 31, 2018. Prior to study initiation, the protocol was approved by SickKids Research Ethics Board with waived consent (REB Number 1000062143, first approved October 31, 2018). The procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional or regional) and with the Helsinki Declaration of 1975, as most recently amended (https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/).

Participants

We included infants with either TGA or SV who underwent surgical repair on cardiopulmonary bypass (CPB) in the first 10 weeks of life, had both pre and postoperative brain MRI studies and postoperative Tracking, Trajectory, and Triggering (T3) application data for up to 72 hours after surgery (Etiometry, Boston, MA). T3 is a web-based program that allows for acquisition, storage, and visualization of physiologic data at 5-second intervals. Included patients represent a subset of children prospectively enrolled in the Cardiovascular Physiology and Brain Development in Neonates with Congenital Heart Disease (CND) longitudinal cohort study at the Hospital for Sick Children. Exclusion criteria were conditions known to affect brain development including congenital syndromes, less than 32 weeks gestational age, infections, intrauterine growth restriction, or maternal comorbidities associated with placental dysfunction. Patients received routine clinical care at the discretion of CCCU physicians. All neonates undergoing CPB received methylprednisolone 30 mg/kg preoperatively and in the CPB circuit. Milrinone, epinephrine, and other vasoactive agents were used as needed to obtain the best possible indices of perfusion based on examination, vital signs, and mixed venous saturation monitoring. Brain MRI studies for TGA and SV patients are routinely performed preoperatively and postoperatively. However, preoperative brain MRI was occasionally omitted due to logistical issues or patient stability. The timing of the postoperative MRI was based on patient clinical status. This CND cohort is not scheduled to undergo neurodevelopmental testing until later in life.

Outcomes

Our primary aim was to develop a method of retrospectively analyzing continuous physiologic data to characterize the relationship between postoperative physiology and new brain injury over time. New brain injury was defined as injury detected on postoperative but not preoperative MRI and was separate from evolution of previous pathology. New brain injury was operationalized as any stroke, intraventricular

hemorrhages (IVHs), or WMI. We examined both brain injury overall and isolated new WMI. Our secondary outcomes were 1) the qualitative prevalence of concurrent high blood pressure (BP), heart rate (HR), and low oxygen saturation (Spo_2) occurring in SV patient in the first 24 hours after surgery and 2) the relationship between lactate, mixed venous oxygen saturation, and arterial and mixed venous oxygen saturations differences in SV patients with and without new postoperative brain injury.

Data Collection

We collected patient demographics at operative day, surgical data, and CCCU stay data from medical records. Operative day patient demographics included age, sex, weight, and prematurity (32–36 wk gestation). Surgical data included CPB, cross-clamp, and deep hypothermic circulatory arrest times. CCCU data included delayed sternal closure, cardiac arrest between the preoperative and postoperative brain MRI, CCCU, and hospital length of stay (LOS). Postoperative laboratory values included lactate, arterial, and mixed venous oxygen saturation. Delayed sternal closure indicates that the patient's sternum was left open after surgery and was subsequently closed in the CCCU. MRI scans, including diffusion-weighted imaging and T1 and T2 weighted sequences, were performed using a 1.5T Avanto MRI scanner. Institutional brain MRI protocols did not change significantly during the study period. Brain injury on MRI was scored by a staff neurologist as previously described (13). Brain volume *z* scores were calculated using age and sex (13).

We obtained patient physiologic data at 5-second intervals including HR, arterial BP, Spo_2, and central venous pressure (CVP), using T3. Postoperative physiologic data measurements were reviewed for up to 72 hours to reflect the early postoperative course (14). Time zero (t0) was the time the patient arrived in the CCCU postoperatively.

Statistical Analysis

The analysis was stratified by anatomy due to differences in physiology, surgery, and postoperative courses. We performed descriptive statistics for patient, surgical, CCCU, and MRI characteristics.

Physiologic Variable Selection for Primary Analysis. We first performed an exploratory analysis of HR, systolic BP, Spo_2, and CVP data in TGA and SV patients stratified by presence of new brain injury. To visualize the physiologic data over time, we smoothed the data using a simple rolling mean (**Fig. 1**). The duration of the time window used for the mean reflects a tradeoff between how smooth the line will be and preservation of the original signal. We then compared the distributions of each physiologic data type in 6-hour blocks in the first 24 hours and three 24-hour blocks in the first 72 hours after surgery. We reported the medians (interquartile range [IQR]) for each physiologic data type stratified by the presence of anatomy and new brain injury (**Table e1**, http://links.lww.com/CCX/B50). Based on the review of these data distributions (**Fig. 2**), we hypothesized that there could be clinically relevant differences in HR, systolic BP, and Spo_2 between SV patients with new brain injury and selected these data to pilot our primary analysis.

Primary Analysis: Mixed-Effects Regression Analyses. To use all measurements for each patient, we modeled the continuous physiologic data directly and used the presence of either new brain injury (overall injury or new WMI), a third degree polynomial for postoperative time and injury-time interaction terms as predictors in a mixed-effects regression model. By including postoperative time as a continuous variable, we were able to include all data points from each patient at different times and naturally accommodated for missing points. To account for inter-patient variation, we included random intercept and slope terms. We performed a simple denoising by taking the mean over nonoverlapping 15-minute windows, resulting in four samples per hour over 72 hours, totaling 288 points per patient. The model was fit via Restricted Maximum Likelihood using R (R: A language and environment for statistical computing. R Foundation for Statistical Computing, Vienna, Austria; https://www.R-project.org/) (15). The resulting parameter estimates for injury and the injury-time interaction provided clinically interpretable estimates of the change in physiology between the two groups. For example, the parameter estimates for injury and the injury-time interaction for HR are in units of bpm and bpm per hour, respectively. Model fit was assessed by plotting residuals and actual versus predicted values per patient (**Fig. 3**). We performed a sensitivity analysis where we refit the model excluding patients who did not have complete data for all 72 hours. As this did not affect the physiologic measurements achieving

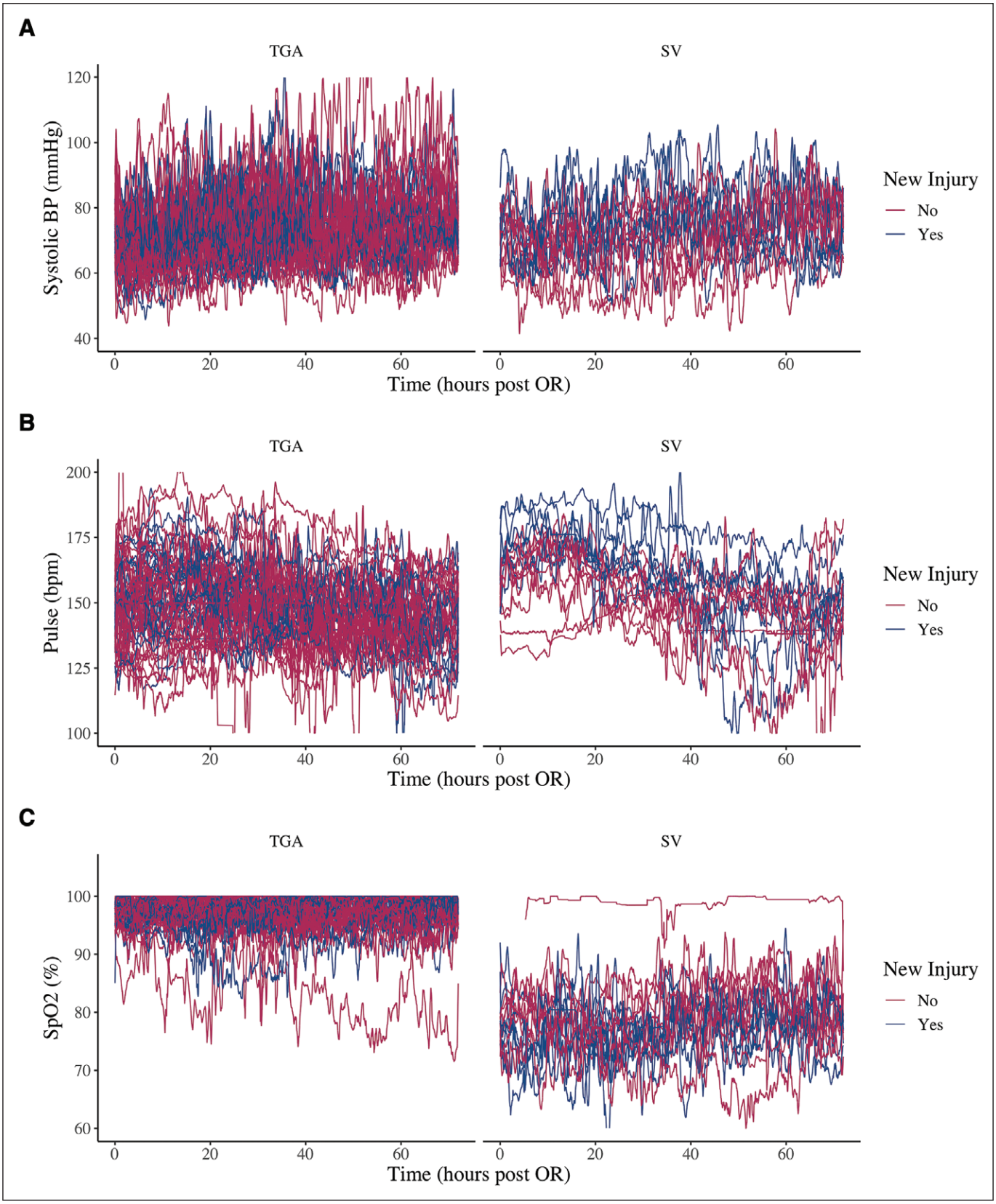

Figure 1. Visualization of physiologic data for transposition of the great arteries (TGA) and single ventricle (SV) patients over time. Mean systolic blood pressure (BP) (**A**), heart rate (**B**), and oxygen saturation (Spo_2) (**C**) over an 18-min time window for each patient graphed over the 72 hr after surgery. Patients with new brain injury are labeled *blue* and those without new brain injury are labeled *red*. bpm = beats/min.

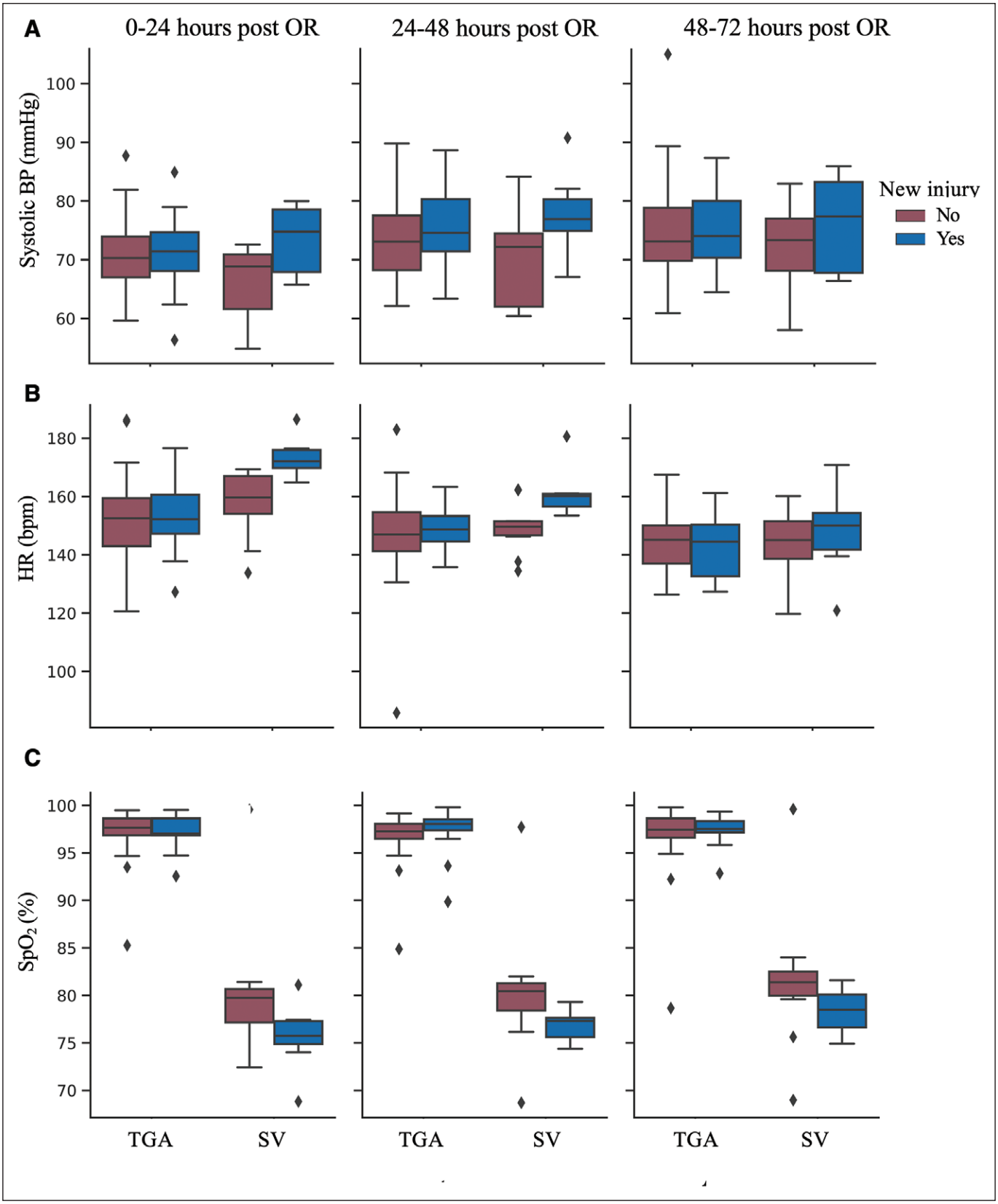

Figure 2. Physiologic data distribution in transposition of the great arteries (TGA) and single ventricle (SV) patients. Median (interquartile range) systolic blood pressure (BP) (**A**), heart rate (HR) (**B**), and oxygen saturation (Spo_2) (**C**). Patients with new brain injury are labeled *blue* and those without new brain injury are labeled *red*. bpm = beats/min.

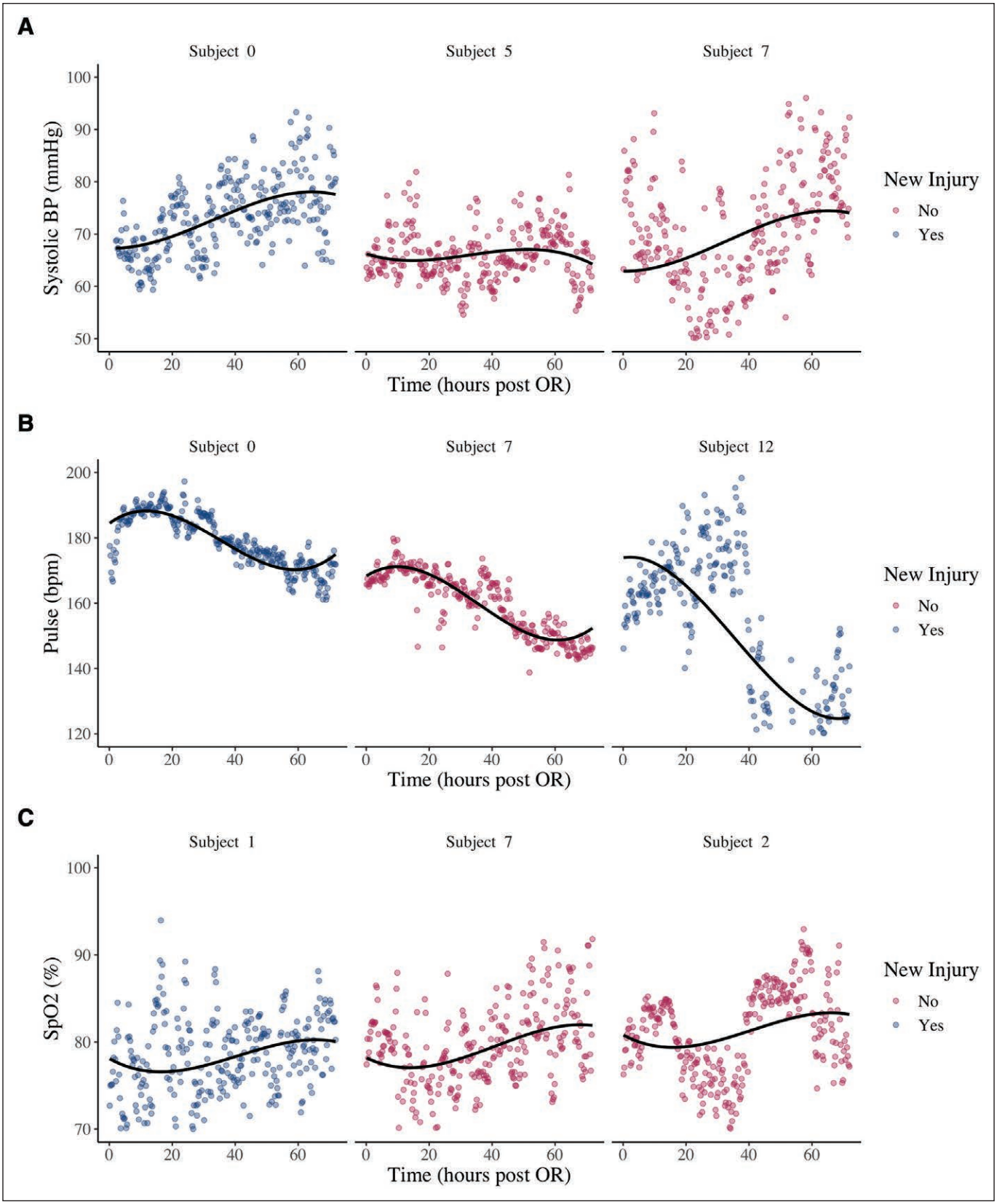

Figure 3. Regression model fit in sample of single ventricle patient with and without new injury. Patient data points for systolic blood pressure (BP) (**A**), heart rate (**B**), and oxygen saturation (Spo_2) (**C**) shown relative to the line predicted by the model. The patients selected in **A** illustrate a good model fit in a patient with new brain injury (*blue*). The patients selected in **B** illustrates a good model fit in patients without new brain injury (*red*). The patients selected in **C** illustrates relatively poor model fit in patients with (*blue*) or without (*red*) new brain injury. bpm = beats/min.

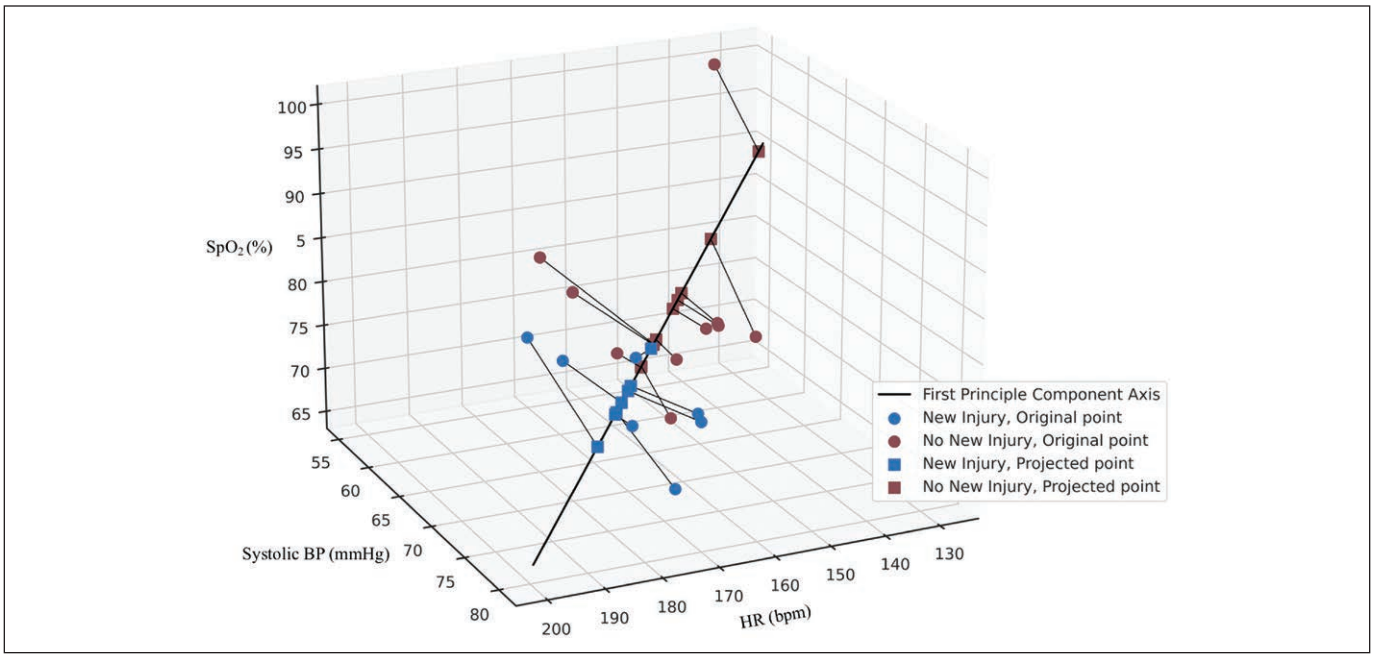

Figure 4. Principal component axis of postoperative physiology in single ventricle patients. Three-dimensional illustration of the 24-hr mean heart rate (HR), oxygen saturation (Spo_2), and systolic blood pressure (BP) reduced into an axis that maximizes the variance of the projected data using principal component analysis. Patients with new postoperative brain injury are labeled *blue* and those without new postoperative brain injury are labeled *red*. The *circle* indicates patient data and the *square* demonstrates the projected point on the first principal component axis. The resulting axis shows points with high BP, HR, and low Spo_2 on one end and points with low BP, HR, and high Spo_2 on the other. The separation along the axis between patients with and without new brain injury qualitatively suggests that patients varied primarily according to the degree in which they express the phenotype of high BP, HR, and low Spo_2. bpm = beats/min.

statistical significance, we reported the model including all SV patients.

Secondary Outcome Analyses. To understand physiologic variability between patients in the first 24 hours after surgery, we reduced mean HR, Spo_2, and systolic BP in SV patients into an axis that maximizes the variance of the projected data using principal component analysis (PCA) (16). We plotted the mean HR, Spo_2, and systolic BP in all SV patients during the first 24 hours and the projected points generated using the PCA analysis (**Fig. 4**). We then chose different colors in the plot to identify patients with and without new brain injury to qualitatively assess if they plotted separately along the axis in the first 24 hours after surgery.

We calculated median (IQR) lactates, mixed venous oxygen saturations, and arterial-mixed venous oxygen saturation differences in SV with and without new postoperative brain injury and compared these medians using Wilcoxon rank-sum tests.

Statistical analysis was performed using R (R Foundation for Statistical Computing, Vienna, Austria). We used an α value of less than or equal to 0.05 as the threshold for statistical significance.

RESULTS

Cohort Characteristics

There were 77 infants in the cohort, 60 TGA patients (77%) and 17 (23%) SV patients (**Table 1**). TGA infants were a median (IQR) 7 days old (6–14 d old) and had a mean (SD) weight of 3.5 kg (0.5 kg) at the time of surgery. Their median (IQR) CPB time was 139 min (114–167 min) and 18 (30%) had delayed sternal closure. Median (IQR) TGA CCCU and hospital LOS were 5.4 days (3–12.6 d) and 19.2 days (14.9–28.3 d), respectively. Postoperative MRI was done a median (IQR) of 9 days (6–17 d) after arterial switch operation. Preoperative brain injury was noted in 28 (46.7%) TGA patients and 19 (32%) had new postoperative brain injury. SV patients were median (IQR) of 4 days old (4–9 d old) at the time of surgery. Their CPB and cross-clamp times were a median (IQR) of 108 minutes (99–129 min) and 67 minutes (64–74 min), respectively. CCCU and hospital LOS were a median (IQR) of 20 days (15.2–43 d) and 45.2 days (25.8–76.3 d), respectively. Of the 17 SV patients, preoperative brain injury was noted

TABLE 1.
Patient Characteristics Stratified by Anatomy and Presence of New Brain Injury

Characteristics	Transposition of the Great Arteries ($n = 60$)		Single Ventricle ($n = 17$)	
	No New Postoperative Injury ($n = 41$)	New Postoperative Injury ($n = 19$)	No New Postoperative Injury ($n = 10$)	New Postoperative Injury ($n = 7$)
Demographic				
Age, median (IQR), d	7 (6–15)	7 (6–14)	4.5 (4–9)	4 (3–15)
Female sex, *n* (%)	12 (29)	4 (21)	4 (40)	1 (14)
Weight, mean (SD), kg	3.46 (0.5)	3.48 (0.38)	3.38 (0.62)	3.32 (0.49)
Prematurity, *n* (%)	0	0	1 (10)	1 (14)
Surgical				
Cardiopulmonary bypass time median (IQR), min	147 (135–172)	140 (120–164)	109.5 (99–125)	106 (92–129)
Cross-clamp time median (IQR), min	90 (80–113)	99 (70–115)	66.5 (64–74)	67 (63–75)
Circulatory arrest time median (IQR), min	0	0	24 (19–25)	33 (20–39)
CCCU				
Delayed sternal closure, *n* (%)	12 (29.3)	6 (31.6)	5 (50)	4 (57)
Cardiac arrest, *n* (%)	1 (2.4)	0	1 (10)	0
CCCU LOS, median (IQR), d	5.9 (3.0–13.9)	4.1 (2.0–6.0)	16.5 (12.4–35.7)	35.7 (16.2–56.7)
Hospital LOS, median (IQR), d	19.6 (14–28.2)	16.3 (15.1–28.3)	31 (19.5–76.3)	70 (37.3–90.6)
Days between Operating Room and MRI, median (IQR), d	12 (7–17)	6 (6–8)	15 (13–32)	24 (19–40)

CCCU = cardiac critical care unit, IQR = interquartile range, LOS = length of stay, *n* = number.

in 6 (35%) and new postoperative brain injury was seen in 7 (41%) patients.

MRI Findings

In the 60 TGA patients, WMI was the most prevalent injury type on preoperative (n = 20 [33%]) and postoperative (n = 14 [23%]) MR images. Half of the new postoperative WMI was mild (n = 7) and only 2 (14%) patients had severe WMI. IVH was noted preoperatively in 10 (17%) and new IVH was seen postoperatively in 3 (5%) TGA patients. New strokes were noted preoperatively in 9 (15%) and postoperatively in 2 (3%) TGA patients. Median (IQR) preoperative and postoperative brain volume z scores in TGA patients with new brain injury were –0.05 (–0.3 to 0.1) and –0.3 (–0.6 to –0.02), respectively, in patients with new brain injury versus –0.2 (–0.5 to 0.3) and –0.6 (–0.96 to –0.05) in patients without new brain injury. Of the 17 SV patients, new WMI injury was reported preoperatively in 2 (12%) and postoperatively in 4 (24%), all of which were characterized as mild WMI. IVH was reported preoperatively in 17 (24%) SV patients and not seen postoperatively. Strokes were reported in 1 (6%) preoperative and 1 (6%) postoperative SV patient, respectively. Median (IQR) preoperative and postoperative brain volume z scores in SV patients with new brain injury were –0.1 (–0.4 to 0) and 1.7 (–2.2 to –1.0), respectively, versus 0.2 (–0.3 to 0.3) and –1.2 (–0.6 to –0.2), respectively, in patients without new brain injury.

Postoperative Physiologic Data

In the first 24 hours after surgery, the median (IQR) physiologic measurements for TGA patients, with and without new brain injury, respectively, were HR 152.1 beats/min (bpm) (147.2–160.6 bpm) and 152.6 bpm (143.0–159.4 bpm); systolic BP 71.4 mm Hg (68.1–74.7 mm Hg) and 70.3 mm Hg (67.0–73.9 mm Hg);

TABLE 2.
Mixed-Effect Regression of Physiologic Parameters Over Time in Single Ventricle Patients With and Without New Brain Injury

Physiologic Parameter	Covariate	Parameter Estimate (95% CI)	*p*
SV and new brain injury			
Heart rate	New postoperative injury	19.4 (7.8–31)	0.003
	New injury-time interaction	−0.25 (−0.55 to 0.05)	0.097
Systolic BP	New postoperative injury	8.6 (1.3–15.8)	0.024
	New injury-time interaction	−0.03 (−0.16 to 0.10)	0.579
Spo_2	New postoperative injury	−4.93 (−11.37 to 1.52)	0.124
	New injury-time interaction	0.03 (−0.026 to 0.08)	0.275
SV and new WMI			
Heart rate	New WMI	18.1 (2.8–33.4)	0.024
	New injury-time interaction	−0.015 (−0.52 to 0.22)	0.39
Systolic BP	New WMI	4.6 (−5.1 to 14.4)	0.32
	New injury-time interaction	−0.05 (−0.19 to 0.1)	0.5
Spo_2	New WMI	−2.7 (−10.7 to 5.3)	0.48
	New injury-time interaction	0.02 (−0.04 to 0.09)	0.46

BP = blood pressure, Spo_2 = oxygen saturation, SV = single ventricle, WMI = white matter injury.

CVP 10.3 mm Hg (8.3–10.8 mm Hg) and 9.6 mm Hg (8.3–11.3 mm Hg); and Spo_2 97.0% (96.9–98.6%) and 97.6% (96.9–98.6%). (IQR) physiologic measurements for SV patients with and without new brain injury, respectively, were HR 172.0 bpm (169.7–176.0 bpm) and 159.6 bpm (145.0–167.0 bpm); systolic BP 74.8 mm Hg (67.9–78.5 mm Hg) and 68.9 mm Hg (61.6–70.9 mm Hg); and Spo_2 75.7% (74.9–77.3%) and 79.7% (77.2–80.7%).

Mixed-Effects Regression Analyses

We described the parameter estimates generated with the mixed-effects model (**Table 2**). In SV patients within the first 72 hours after surgery, new brain injury was independently associated with statistically significant elevations in HR (parameter estimate, 19.4 bpm; 95% CI, 7.8–31 bpm; $p = 0.003$) and systolic BP (8.6 mm Hg [1.3–15.8 mm Hg]; $p = 0.02$) and new WMI was independently associated with higher HR (8.1 bpm [2.8–33.4 bpm]; $p = 0.02$). In this model, the differences in physiologic measurements are greatest in the immediate postoperative period and decreased with time (Table 2). The model residuals were normally distributed, and patient data clustered around the physiologic parameter values predicted by the model (Fig. 3).

Secondary Outcome Analyses

Using PCA, we saw that during the first 24 hours after surgery, the physiologic data collected from SV patients varied in the extent to which they expressed the phenotype of concurrent high systolic BP, high HR, and low Spo_2. SV patients with and without new brain injury were separated on the emerging axis generated with PCA (Fig. 4). This qualitatively suggests that patients with new brain injury more commonly had the phenotype of concurrent high systolic BP, high HR, and low Spo_2 in the first 24 hours after surgery.

In the first 24 hours after surgery, there were no significant differences in median (IQR) mixed venous oxygen saturation (49 [41–61] vs 53 [44–61]; $p = 0.25$), arterial-mixed venous oxygen saturation difference (22 [13.5–27] vs 21 [12–28]; $p = 0.85$), or lactate (4.5 [2.4–7.3] vs 4.05 [2.5–6.3]; $p = 0.69$) in SV patients with and without new brain injury, respectively.

DISCUSSION

We developed an approach to retrospective analysis of continuous physiologic data acquired early after congenital heart surgery, which allowed us to examine changes in physiology over time and examine possible associations with new brain injury. This methodology offers clinically interpretable parameter estimates, a principled way to account for variability between patients, heterogeneity in measurement number and timing and missing data. This method could also be broadly applied to characterize the relationship between physiologic data and other interventions or outcomes over time. Although commercial physiologic data storage software is not present in every unit, its use is increasing and the insights gained by retrospective analysis of continuous cardiorespiratory and hemodynamic monitoring are widely generalizable.

We found a statistically significant differences in HR and systolic BP in SV patients with and without new brain injury that decreased with the time from surgery. The clinical significance of this association should be cautiously interpreted as the precise time frame where the insult or insults leading to new brain injury occur cannot be determined. Our cohort examined only 17 SV patients. However, the proportions of postoperative WMIs, strokes and IVHs in our cohort are similar to those reported in other studies (8, 10, 17, 18). The physiologic associations are hypothesis generating and suggest that the first 24 hours after surgery may be relevant in further study to better understanding new brain injury.

Qualitatively, our PCA analysis suggests that SV patients with new brain injury more commonly had the phenotype of concurrent high systolic BP, high HR, and low Spo_2 in the first 24 hours after surgery. The postoperative phenotype of high HR, high BP, and low Spo_2 in SV patients included in our model may reflect marginal cardiac output. This finding is in keeping with other studies illustrating a relationship between low cardiac output state and new postoperative brain injury (10, 11). However, our study sample was small and underpowered to detect any differences in clinical indicators of cardiac output such as central venous oxygen saturation/arterial-venous oxygen saturation difference or lactic acid levels. Our approach to analyzing continuous physiologic data and recognizing phenotypes associated with new brain injury could also be applied to understanding the relationship between physiologic data and clinical indicators of low cardiac output or other organ injury over time. Physiologic data patterns that identify patients at risk for these types of outcomes would have considerable clinical value in guiding real-time targets and therapeutic decisions. More work is needed in larger cohorts across institutions to establish these integrated physiologic phenotypes.

We did not include TGA patients in our regression models as postoperative physiologic data were qualitatively similar in TGA infants with and without new postoperative brain injury. This may support the hypothesis that the timing and mechanism of new postoperative brain injury in TGA patients may be different that SV patients (19).

Our study has several limitations. The statistically significant associations in our model should cautiously interpreted as it is not possible to determine the exact time frames during which brain injury occurred. Further study is needed as our small sample of 17 patients may not be representative of the entire population of SV patients. Our study population was limited to patients well enough to have a preoperative MRI and those who survived to have a postoperative brain MRI. Therefore, our findings may not reflect patients with more unstable SV phenotypes. As a next step, our model could be applied in a larger cohort of patients with preoperative, intraoperative, and postoperative continuous physiologic data to potentially identify differences in physiologic measurements in patients with and without new brain injury. The goal of our study was to design an analytic approach to retrospectively characterizing the relationship between physiologic data points and new brain injury over postoperative time. Studies aiming to uncover additional risk factors for new brain injury or adverse neurodevelopmental outcomes over time would require the addition of patient pharmacotherapy, continuous electroencephalogram monitoring, patient, surgical and ICU characteristics, and long-term neurodevelopmental follow-up data.

CONCLUSIONS

Retrospective analysis of continuous physiologic measurements using a PCA approach can provide insight into changes in postoperative physiology over time and their relationship with new brain injury. Our principled approach used all physiologic measurements from each patient and derived clinically interpretable measurement estimates. This technique could be applied to

assess the relationship between physiologic data and many patient interventions or outcomes over time.

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