Evaluation of Cerebral Oxygenation and Perfusion With Conversion From an Arterial-to-Systemic Shunt Circulation to the Bidirectional Glenn Circulation in Patients With Univentricular Cardiac Abnormalities

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Objective: Superior vena cava pressure after the bidirectional Glenn operation usually is higher than that associated with the preceding shunt-dependent circulation. The aim of the present study was to determine whether the acute elevation in central venous pressure was associated with changes in cerebral oxygenation and perfusion.

Design: Single-center prospective, observational cohort study.

Setting: Academic children's hospital.

Participants: Infants with single-ventricle lesions and surgically placed systemic-to-pulmonary artery shunts undergoing the bidirectional Glenn operation.

Interventions: Near-infrared spectroscopy and transcranial Doppler sonography were used to measure regional cerebral oxygen saturation and cerebral blood flow velocity.

Measurements and Main Results: Mean differences in regional cerebral oxygen saturation and cerebral blood flow velocity before anesthetic induction and shortly before hospital discharge were compared using the F-test in repeated measures analysis of variance. In the 24 infants studied, mean cerebral oxygen saturation increased from 49% ± 2% to 57% ± 2% ($p = 0.007$), mean cerebral blood flow velocity decreased from 57 ± 4 cm/s to 47 ± 4 cm/s ($p = 0.026$), and peak systolic cerebral blood flow velocity decreased from 111 ± 6 cm/s to 99 ± 6 cm/s ($p = 0.046$) after the bidirectional Glenn operation. Mean central venous pressure was 8 ± 2 mmHg postinduction of anesthesia and 14 ± 4 mmHg on the first postoperative day and was not associated with a change in cerebral perfusion pressure ($p = 0.35$).

Conclusions: The bidirectional Glenn operation in infants with a shunt-dependent circulation is associated with an improvement in cerebral oxygenation, and the lower cerebral blood flow velocity is likely a response of intact cerebral autoregulation.

***KEY WORDS:** congenital heart defect, near-infrared spectroscopy, transcranial Doppler sonography, modified Blalock-Taussig shunt, bidirectional Glenn shunt, hypoplastic left-heart syndrome, single ventricle*

NEURODEVELOPMENTAL IMPAIRMENT is a frequent finding in survivors of the Norwood operation for hypoplastic left-heart syndrome (HLHS) or other single-ventricle variants requiring aortic arch reconstruction.[1–4] Although many independent risk factors for adverse neurologic outcome are not modifiable, potentially modifiable risk factors are improvements in cerebral oxygenation and perfusion during the perioperative period.

In the first stage of palliation to a Fontan circulation, pulmonary blood flow is reestablished by creation of a shunt between the systemic circulation and the pulmonary artery, typically a modified Blalock-Taussig (MBT) shunt or a right ventricle-to-pulmonary artery (RV-PA) conduit. Despite a higher diastolic blood pressure with an RV-PA conduit, systemic oxygen delivery, regional cerebral oxygen saturation (rSO_2), and cerebral blood flow velocity (CBFV) have been found to be similar between the 2 shunt types in the early postoperative period.[5–7] Between 3 to 6 months of age, a bidirectional Glenn (BDG) or hemi-Fontan operation is performed in which the shunt is taken down and pulmonary blood flow is provided by an anastomosis of the superior vena cava to the pulmonary artery. The pressure in the superior vena cava after the BDG operation usually is higher than the common atrial pressure associated with the shunt-dependent circulation.[8,9] Because the impact of this acute elevation of central venous pressure on cerebral oxygenation and blood flow in this population has not been investigated, it is unknown whether transition from an arterial-to-systemic shunt circulation to a circulation with a cavopulmonary anastomosis is associated with changes in cerebral oxygenation and perfusion. The primary aim of this study was to evaluate cerebral oxygenation and blood flow immediately before and after the BDG operation. Because the dominant mechanism of cerebral autoregulation is metabolic rather than myogenic[10] and because arterial oxygen saturation generally increases in the initial period after the BDG operation,[11] it was hypothesized that cerebral oxygen saturation would increase and cerebral blood flow would decrease in the early postoperative period.

METHODS

After approval by the Committee on Clinical Investigation and parental written informed consent, infants undergoing elective BDG at Boston Children's Hospital were enrolled in the study. Subject enrollment was determined solely by the schedule of the investigators able to perform perioperative transcranial Doppler (TCD) sonography. It was not feasible for investigators to be blinded to the patient's pre-BDG physiology. Inclusion criteria were single-ventricle lesions previously palliated with either an MBT shunt or RV-PA conduit. Exclusion criteria were known intracranial pathology, neurologic disease, or craniofacial anomalies.

After premedication with oral midazolam (0.5 mg/kg) and ketamine (5 mg/kg), baseline measurements were performed in the

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operating room before induction of general anesthesia. Supplemental midazolam and/or ketamine were administered as necessary to ensure a sedated and calm infant. Patients breathed room air and were monitored clinically and with standard ASA monitors. Anesthetic technique was not controlled specifically but was conducted according to institutional practice. An intravenous induction with ketamine and/or opioid generally was performed. After intravenous line placement, it was normal practice to administer albumin 5%, 10 to 15 mL/kg, to counteract patient dehydration. The F_IO_2 was decreased to 0.21 after endotracheal intubation and patients ventilated to normocapnia or mild hypercapnia. Opioid-based anesthesia (fentanyl ~50 μg/kg) was supplemented with isoflurane and midazolam as tolerated, and neuromuscular blockade achieved with pancuronium. The head was turned to just off the midline to prevent pressure or movement on the endotracheal tube by the surgical team while avoiding the possible effects of extremes of lateral head position on cerebral blood flow and venous drainage. In addition to routine monitoring, a central venous catheter was placed via the internal jugular vein for perioperative monitoring of central venous pressure (CVP).

A BDG procedure was performed on cardiopulmonary bypass (CPB) in all patients with a beating heart, except in those infants requiring concomitant intracardiac procedures for which an aortic cross-clamp and cardioplegia were necessary. Reconstituted whole blood was added to the bypass prime to achieve a hematocrit of at least 30% at the initiation of CPB. Mild hypothermic bypass (32°C) with an alpha-stat strategy was used for all patients, with no changes in anesthetic technique, surgical technique, or perfusion strategy over the time period of the study. Cardiac index was maintained at 2-2.4 L/m^2 with a mean arterial pressure between 35 and 45 mmHg, and modified ultrafiltration was used. Bihemispheric cerebral tissue oxygen saturation was measured by near-infrared spectroscopy (NIRS) using the INVOS 5100B (Somanetics, Troy, MI). In early 2009, the INVOS 5100B was replaced with the 5100C (same measurement technology and algorithm per the manufacturer). Pediatric SomaSensors (Somanetics, Troy, MI) were placed on the right and left forehead according to the manufacturer's guidelines before induction of anesthesia. After an accommodation period, data collection was begun and downloaded to storage disk every 10 seconds throughout the case for further analysis. The scale unit for the regional saturation of oxygen (rSO_2) is percent (%).

A 2-Mz, range-gated, pulsed-wave transcranial Doppler ultrasonographic probe (Multi-Dop T, DWL Elektronische Systeme GmbH, Sipplingen, Germany) was placed over the temporal window to measure middle cerebral artery blood flow velocity in the proximal (M1) segment of the middle cerebral artery. After 19 subjects had been studied, the Multi-Dop T stopped working and was replaced by a similar 2-Mz, range-gated, pulsed-wave TCD system (Sonara, Viasys Healthcare, Madison, WI). To ensure a reproducible window, the signal from the artery was adjusted to be accompanied by retrograde anterior cerebral artery flow (A1 segment). After achieving an acceptable waveform, the insonation depth was documented and the probe position noted to ensure constancy of measurement technique. The sample volume, gain, and power of ultrasound were kept constant for all measurements. Peak systolic flow velocity (V_S), mean flow velocity (V_M), and peak end-diastolic flow velocity (V_D) were measured during hemodynamically stable intervals, with constant recordings of at least 15 seconds' duration. The Pourcelot Resistance Index (RI) was used as a qualitative measure of cerebral vascular resistance and calculated according to the formula $RI=[V_S\text{-}V_D]/V_S$[12]

Intraoperative and postoperative data were collected and analyzed at the following time points: Baseline (sedated, calm, nonintubated infant), postinduction (after endotracheal intubation, placement of all invasive monitors, and before surgical stimulation), and pre-discharge (on the ward usually after a feeding on the day before hospital discharge). All the pre-discharge measurements were performed in room air while the infant was calm, with the Doppler probe and NIRS sensors held in place by hand.

Regional cerebral oxygen saturation and CBFV were assessed between baseline and discharge using the F-test in repeated measures analysis of variance with two-tailed p value of 0.05 for significance testing. A secondary aim was to evalute whether the RV-PA and MBT groups differed in rSO_2 and CBFV in transitioning from shunt circulation to BDG circulation. Additionally, the effect of anesthesia on rSO_2 and CBFV was assessed by comparing the baseline and postinduction values. Because there were no significant differences in rSO_2 and CBFVs between the right and left sides of the head, measurements from the right side are presented and analyzed. Physiologic variables such as arterial oxygen saturation (SaO_2), systolic blood pressure (SBP), mean arterial blood pressure (MAP), diastolic blood pressure (DBP), and hematocrit also were analyzed. Variables that necessitated an invasive measurement (CVP, cerebral perfusion pressure (CPP; MAP−CVP), PaO_2, $PaCO_2$, SvO_2) were collected only after induction of anesthesia and on postoperative day (POD) 1.

Assuming a pre-Glenn baseline NIRS of 42[13] and a standard deviation of 9.6,[13] the study was powered to detect an absolute difference of 10% in rSO_2 during the transition to BDG circulation (this difference having been reported as possibly clinically significant[14–16]). A minimum estimated sample size of 20 children was required, based on the formula for a paired *t* test with a normal distribution and assuming a two-sided type-I error of 0.05 and a power of 80%. The Kolmogorov-Smirnov goodness-of-fit test was used to assess normality of the TCD and rSO_2 variables and did not identify any significant departures from a normal Gaussian distribution for any variable at any time point, including postinduction and pre-discharge.

Statistical analysis was conducted using the IBM SPSS Statistics (version 21.0, IBM, Armonk, NY). Two-tailed values of $p < 0.05$ were considered statistically significant. Power calculations were determined using nQuery Advisor software (version 7.0, Statistical Solution, Saugus, MA).

RESULTS

Twenty-four patients were enrolled between September 2006 and November 2010. Median age was 5.6 (range: 3.0-8.2) months and weight 6.4 (range; 5.1-8.1) kg, with a male: female ratio of 2:1 (16 males, 8 females). There were 15 subjects with HLHS, 3 with tricuspid atresia, 3 with single right

Table 1. Demographic Data

Age (months)	5.6 (3.0–8.2)
Weight (kg)	6.4 (5.1–8.1)
CPB time (min)	87 (40–162)
Male:female	16:8
Lesions:	
Hypoplastic left-heart syndrome (HLHS)	15
Tricuspid atresia (TA)	3
Single right ventricle	3
Double-inlet left ventricle (DILV)	2
Transposition of the great arteries (TGA) with single left ventricle	1
Shunt type:	
MBT shunt	14
RV-PA conduit	10

Data are presented as median (range) or number of patients.
Abbreviations: CPB, cardiopulmonary bypass; MBT shunt, modified Blalock-Taussig shunt; RV-PA conduit, right ventricle-to-pulmonary artery conduit.