Optic nerve ultrasound and cardiopulmonary bypass: A pilot study

ABSTRACT

Introduction: Despite advances in surgical, anesthetic, perfusion, and postoperative care, adverse neurological consequences may occur following cardiac surgery and cardiopulmonary bypass (CPB). Consequences of the physiologic effects of CPB may alter the blood–brain barrier, autoregulation, and intracranial pressure (ICP) in the immediate postoperative period.

Methods: We evaluated the effects of cardiac surgery and CPB on the central nervous system by measuring the optic nerve sheath diameter (ONSD) by using ultrasound as a surrogate marker of ICP. ONSD was measured after anesthetic induction and endotracheal intubation (time 1), after separation from CPB (time 2), and at the completion of the surgical procedure prior to leaving the OR (time 3).

Results: The study cohort included 14 patients, ranging in age from newborn to 6 years. When comparing the Fontan group (n = 5) to the non-Fontan group (*n* = 9), four elevated ONSD observations were recorded for the Fontan patients during the study period, including one at time 1, one at time 2, and two at time 3. In Fontan versus non-Fontan patients, ONSD was greater at all three time points compared to non-Fontan. The change in the ONSD from time 1 to time 2 was greater (+0.2 mm vs. −0.1 mm), and the mean value at time 2 was significantly higher (4.2 vs. 3.5 mm, $P = 0.048$).

Conclusions: Patients with Fontan physiology may be more prone to higher levels of baseline intracranial pressure due to elevated systemic venous pressure and decreased cardiac output. Alternatively, the chronically high central venous pressures may artificially elevate ONSD without clinical changes in ICP, necessitating the development of separate normative values based on the type of congenital heart disease.

Keywords: Cardiopulmonary bypass, intracranial pressure, point-of-care ultrasound, optic nerve sheath diameter

Introduction

Despite advances in surgical, anesthetic, perfusion, and postoperative intensive care unit (ICU) care, adverse neurological consequences may occur following surgery for congenital heart disease (CHD) and cardiopulmonary bypass (CPB).[1-3] These adverse neurologic outcomes may

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be related to embolic effects, hypoxic-ischemic events, changes in autoregulation, alterations in the blood − brain barrier (BBB), and changes in intracranial pressure (ICP).[4-6] The potential for changes in ICP during the immediate postoperative period may be particularly prevalent following CPB which has the potential to alter the integrity of the BBB.[7-9] Changes in ICP may be proportionately greater in patients subjected to higher than normal physiologic central venous pressures, such as those who undergo procedures involving a direct anastomosis of the superior vena cava to the pulmonary artery (Glenn shunt).

Invasive intracranial pressure monitoring using intraventricular catheters or intraparenchymal microtransducers remains standard care for patients following severe traumatic brain injury or to monitor ICP.[10,11] However, the invasiveness of these procedures increases the risk of complications, including hemorrhage and infection.[12-14] The potential for complications may be even greater in the presence of coagulation disturbances following CPB. As an alternative to invasive ICP monitoring, bedside point-of-care ultrasound has been used to measure optic nerve sheath diameter (ONSD) as a surrogate measure of ICP.[15-18] The current study measures ONSD during cardiac surgery using CPB in patients with and without single ventricle (Fontan) physiology.

Methods

This study was approved by the Institutional Review Board of Nationwide Children's Hospital (#IRB18-01209) and was registered at clinicaltrials.gov (NCT#03757312) the study was approved by our IRB on 11/23/2018. The study population included patients ranging in age from newborn to 18 years presenting for surgery for congenital heart disease necessitating the use of CPB. Written informed consent was obtained from a parent or legal guardian. Patients with preexisting ophthalmic disease, a history of ophthalmic surgery, or affected by any type of neurological disorder were excluded. Standard demographics were obtained, including the age, weight, gender, type of CHD, and surgical procedure.

All ultrasound measurements were performed by or conducted under the direct supervision of one of the co-investigators with experience in using an ocular sonographer. Sonographic examinations were conducted using a SonoSite X-Porte Fuji Film SonoSite Inc., Bothell, WA, USA) equipped with a 6–13-MHz linear probe. All patients were examined in the supine position. The patients' eyes were closed and covered by a bio-occlusive dressing (Tegaderm®; 3M™ Healthcare). A thick layer of ultrasound gel was applied over the Tegaderm®. The ultrasound probe was placed gently on the gel overlying the eye. The position of the probe was adjusted to obtain the appropriate images. Bilateral ONSD was measured 3 mm posterior to the papilla. Two measurements were taken for each optic nerve: one in the transverse plane, with the probe being horizontal, and one in the sagittal plane, with the probe being vertical. The final ONSD was the mean of these measurements. We defined elevated ONSD as greater than 4.0 mm at age <1 year and greater than 4.5 mm at age 1–18 years by referring to previous reports.[15-18]

The ONSD was recorded at three time points during the surgical and anesthetic course, including time 1 immediately after the induction of anesthesia and endotracheal intubation; time 2 after separation from CPB; and time 3 following completion of surgical procedure, after wound closure, before tracheal extubation, prior to leaving the operating room. At these time points, the following physiologic data were obtained: heart rate (HR), diastolic blood pressure (dBP), systolic blood pressure (sBP), central venous pressure (CVP), end-tidal carbon dioxide ($ETCO_2$), and cerebral oxygenation assessed using near-infrared spectroscopy (rSO_2). Total CPB was considered short in duration if patients were under CPB for less than 100 min, while patients who had CPB for ≥100 mins were considered to have a long total bypass duration.

The mean and the range were calculated for continuous variables. Number and percentages were calculated for continuous variables. Characteristics of Fontan and non-Fontan patients were compared using the Wilcoxon rank-sum test or Fisher's exact test depending on the type of data. The mean and range were calculated for the ONSD, hemodynamic, and respiratory variables at the three time points. Differences between Fontan and non-Fontan patients were tested using student's *t* test. The number of patients with optic nerve sheath diameter above normal was calculated. A Chi-squared analysis with a 2 × 2 table was used to compare the number of ONSD values that were above the normal value for age in Fontan and non-Fontan patients during the study protocol. Finally, mean ONSDs were calculated for short and long CPB time, and differences between the two groups were tested using student's *t* test. SAS 9.4 was used to complete all data analysis (Cary, NC).

Results

The study cohort included 14 patients ranging in age from newborn to 6 years weighing 3.7–20.3 kg, undergoing surgery for congenital heart disease using CPB [Table 1]. The study cohort included seven males and seven females with an average weight of 10.8 kg and an average height of 79.2 cm. Two patients were ASA physical status III, while the remaining 12 patients were ASA physical status IV. There were five patients with single ventricle physiology who underwent

Table 1: Demographics of the study cohort

Variable	All (n=14)	Fontan (n=5)	Non-Fontan (n=9)	P
Age at time of procedure (years)	1.8 (0, 6)	2.6 (1, 3)	1.3 (0, 6)	0.105
Weight (kg)	10.8 (3.7, 20.2)	13.5 (7.9, 16.6)	9.3 (3.7, 20.2)	0.099
Height (cm)	79.2 (53, 114.6)	88.2 (63, 97.1)	74.3 (53, 114.6)	0.172
Gender, female	7 (50%)	3 (60%)	4 (44%)	1.000
ASA physical status (III or IV)	2, 12	0, 5	2, 7	0.056

Data are presented as the mean (range) or number (%) ASA=American Society of Anesthesiology.

Fontan surgery on the day of the study and nine patients for non-Fontan surgery [Table 2].

Table 2: Non-Fontan procedures

- Atrial septal defect closure
- Atrioventricular septal defect repair
- Aortic arch repair and ventricular septal defect repair
- Tetralogy of Fallot repair
- Ventricular septal defect closure
- Right ventricle muscle bundle resection
- Right ventricle to pulmonary artery conduit placement

The ONSD measurements during the study protocol are listed in Table 3. In the cohort as a whole, no changes were noted in ONSD during the course of the study protocol. When comparing Fontan versus non-Fontan patients, ONSD was greater at all three times points in Fontan patients. The change in the ONSD from time 1 to time 2 was greater (+0.2 mm vs. −0.1 mm) and the value at time 2 was significantly higher (4.2 vs. 3.5 mm, $P = 0.048$) in Fontan patients. Four elevated ONSD observations were recorded for the single ventricle patients having Fontan surgery during the study period, including one at time 1, one at time 2, and two at time 3, while only one elevated ONSD value was noted in non-Fontan patients [Table 4]. Overall, four of 15 ONSD values were elevated in Fontan patients versus one of 27 values in non-Fontan patients ($P = 0.015$) [Table 4]. No difference in ONSD values was noted based on the duration of CPB [Table 5].

Hemodynamic and respiratory data are listed in Table 6. When comparing Fontan versus non-Fontan patients, HR was lower at all three time points in Fontan patients; however, no difference was noted in the other physiologic parameters, including systolic BP, diastolic BP, CVP, ETCO2, and rSO2 [Table 6].

Discussion

The optic nerve is a central nervous system white matter tract that is wrapped from deep to superficial by the pia, arachnoid, and dura mater, forming the optic nerve sheath. The subarachnoid space (SAS) covers the brain, lying between the pia and arachnoid mater. It is filled with cerebrospinal fluid and is continuous with the optic nerve perineural space.[19] The same pressure changes that impact the intracranial SAS extend to the intraorbital SAS and the optic nerve sheath. When ICP increases, the pressure is transmitted to and distends the optic nerve sheath, increasing its diameter.[20,21]

Various investigators have demonstrated a clinically useful correlation between ONSD and ICP in children.[22-26] Beare *et al*.[23] compared the findings of optic ultrasound (ONSD) in children with acute neurological diseases, comparing those with and without clinical signs of increased ICP. In 14 children with clinical signs of increased ICP, the mean ONSD was 5.4 mm (range: 4.3–6.2 mm). In seven children with clinical signs of increased ICP, the mean ONSD was 3.6 mm (range: 2.8–4.4 mm). By using 4.2 mm as the upper limit of normal for ONSD, the sensitivity and specificity of ONSD for increased ICP were noted as 100% and 86%, respectively.

Subsequently, other investigators have suggested higher cut-offs for the ONSD that may be associated with increased ICP. Kerscher *et al*.[24] compared ultrasound ONSD measurements with invasive ICP measurements in 72 neurosurgical children. In the entire study cohort, the correlation between ONSD and ICP was good (r = 0.52, $P < 0.01$). However, the correlation was better in children more than 1 year of age compared to those ≤1 year of age (r = 0.63 vs. 0.21). There was no correlation noted in infants with an open fontanelle. The authors suggested that the best ONSD cut-off value for detecting an ICP of ≥15 and ≥20 mm Hg was 5.28 and 5.57 mm (OR: 22.5 and 7.2, area under the curve 0.782 and 0.733, respectively). A similar study that investigated the relationship between ultrasound ONSD and ICP in 174 pediatric patients concluded that ocular ultrasound measurement of the ONSD was a reliable and highly accurate diagnostic tool to evaluate ICP in children.[25,26] The authors compared the mean binocular ONSD measurement to the ICP. An ONSD measurement greater than 5.5 mm had the greatest diagnostic accuracy for detecting an ICP of ≥20 mmHg (sensitivity: 93.2%, specificity: 74%, and odds ratio: 39.3).

In our study, we noted that the ONSD was higher than previously reported normal values (ONSD greater than 4.0 mm

Table 3: Optic nerve sheath diameter

Time	All (*n*=14)	Fontan (*n*=5)	Non-Fontan (*n*=9)	*P*[1]
Post induction of anesthesia (Time 1)	3.7 (3.0, 4.6)	4.0 (3.0, 4.6)	3.6 (3.1, 3.9)	0.169
Following CPB (Time 2)	3.7 (3.1, 5.1)	4.2 (3.5, 5.1)	3.5 (3.1, 3.9)	0.048
Prior to tracheal extubation in the OR (Time 3)	3.8 (3.0, 5.3)	4.2 (3.2, 5.3)	3.7 (3.0, 4.3)	0.202

Values listed in mm. Data are presented as the mean (range). CPB=cardiopulmonary bypass; OR=operating room. [1]Difference tested by t-test, Fontan versus non-Fontan.

Table 4: Patients with above normal optic nerve values based on age and procedure

Variable and time	Fontan (*n*=5)		Non-Fontan (*n*=9)	
	<1 year (*n*=1)	≥1 year (*n*=4)	<1 year (*n*=4)	≥1 year (*n*=5)
Post-induction of anesthesia (Time 1)	0	1	0	0
Following CPB (Time 2)	0	1	0	0
Prior to tracheal extubation in the OR (Time 3)	0	2	1	0

Optic nerve sheath diameter normal values: ≤4.0 mm for patients <1 year and ≤4.5 mm used for patients ≥1 year of age. CPB=cardiopulmonary bypass; OR=operating room.

Table 5: Optic nerve sheath diameter: short versus long cardiopulmonary bypass time[1]

Variable and time	Short CPB time (*n*=7)	Long CPB time (*n*=7)	*P*[2]
Post-induction of anesthesia (Time 1)	3.8 (3.6, 4.0)	3.6 (3.0, 4.6)	0.450
Following CPB (Time 2)	3.6 (3.5, 3.9)	3.8 (3.1, 5.1)	0.658
Prior to tracheal extubation in the OR (Time 3)	3.8 (3.5, 4.3)	3.8 (3.0, 5.3)	0.989

CPB=cardiopulmonary bypass; OR=operating room. [1]Short CPB time defined as <100 min. Long CPB time defined as ≥100 min Data are presented as the mean (range).

Table 6: Perioperative vital signs

Time	Variable	All (*n*=14)	Fontan (*n*=5)	Non-Fontan (*n*=9)	*P*[1]
Baseline	HR	131 (92, 161)	121 (101, 137)	137 (92, 161)	0.198
	dBP	82 (48, 109)	73 (48, 87)	86 (73, 109)	0.094
	sBP	51 (31, 73)	49 (31, 60)	52 (38, 73)	0.582
	ETCO$_2$	34 (7, 49)	29 (7, 43)	36 (8, 49)	0.398
	rSO$_2$	89 (71, 100)	87 (81, 91)	91 (71, 100)	0.385
Post induction of anesthesia (Time 1)	HR	130 (93, 166)	112 (93, 136)	140 (103, 166)	0.030
	dBP	74 (34, 93)	72 (54, 80)	75 (34, 93)	0.766
	sBP	45 (16, 74)	42 (32, 56)	47 (16, 74)	0.587
	ETCO$_2$	37 (28, 47)	33 (28, 40)	40 (30, 47)	0.077
	rSO$_2$	92 (79, 100)	89 (87, 91)	94 (79, 100)	0.097
Following CPB (Time 2)	HR	119 (83, 171)	101 (83, 133)	129 (92, 171)	0.032
	dBP	75 (52, 99)	71 (52, 88)	78 (56, 99)	0.450
	sBP	48 (37, 66)	46 (37, 57)	49 (40, 66)	0.483
	CVP$_2$	11 (4, 24)	13 (7, 24)	10 (4, 16)	0.285
	ETCO$_2$	36 (27, 55)	34 (29, 42)	37 (27, 55)	0.523
	rSO$_2$	97 (69, 100)	93 (69, 100)	99 (96, 100)	0.384
Prior to tracheal extubation in the OR (Time 3)	HR	118 (81, 156)	107 (81, 140)	123 (82, 156)	0.269
	dBP	78 (45, 111)	70 (57, 88)	82 (45, 111)	0.248
	sBP	48 (33, 63)	45 (36, 58)	50 (33, 63)	0.306
	CVP	11 (5, 20)	12 (5, 20)	11 (5, 16)	0.811
	ETCO$_2$	42 (29, 53)	43 (32, 51)	42 (29, 53)	0.844
	rSO$_2$	97 (77, 100)	94 (77, 100)	98 (94, 100)	0.412

Data presented as mean (range). HR is listed as beats/minute. sBP, dBP, and ETCO2 are listed in mmHg. ONSD is listed in mm. CPB=cardiopulmonary bypass; dBP=diastolic blood pressure; HR=heart rate; ONSD=optic nerve sheath diameter; OR=operating room; sBP=systolic blood pressure; CVP=central venous pressure; rSO2=cerebral oxygenation; ETCO2=end-tidal carbon dioxide [1]Differences tested using *t*-test

at age <1 year and greater than 4.5 mm at age 1–18 years), at five of the 42 measurement points. However, the value was not above those previously reported to be associated with increased ICP by either Kerscher *et al.* or Padayachy *et al.*[24,25] Furthermore, none of the patients in our cohort had clinical signs of increased ICP during the postoperative period after emerging from anesthesia when clinical evaluation was feasible. At one evaluation point in our study cohort, the ONSD was 5.3 mm, which is only slightly above the value (5.3 mm) suggested by Kerscher *et al*. to correlate with an ICP of ≥15 mmHg, but less than the value (5.57 mm) suggested to correlate with an ICP ≥20 mmHg.

Our study is the first to use ONSD prior to and following CPB. As noted above, several factors may be responsible for neurologic injury and increased ICP following CPB and surgery for CHD. Additionally, it may be that the type of CHD impacts ONSD findings. In our study cohort, ONSD was higher at the three evaluation points in patients with single ventricle physiology and the increase in ONSD was greater following CPB. Four elevated ONSD observations were recorded for the Fontan patients during the study compared to one in patients with two ventricle anatomy. Patients with single ventricle and Fontan physiology lack the pump (right ventricle) to drive blood into the pulmonary arteries due to the direct connection of the systemic veins to the pulmonary arteries.[27,28] As such, these patients may be exposed to chronic elevations in central venous pressure with venous congestion and decreased cardiac output. Chronic venous congestion may alter CNS dynamics at baseline and following CPB. The potential for increased ICP related to chronic venous congestion and elevated CVP may be exacerbated by inflammatory and hemodynamic changes following CPB with disruption of the BBB, especially in patients with single ventricle physiology.[29-31]

Limitations of our current study include a small study size. As a pilot study, our population size was limited. The study attempted to evaluate the utility of ONSD in this patient population, including the feasibility of ocular sonography intraoperatively and following tracheal extubation in patients undergoing surgery for CHD by using CPB. Ocular sonography was performed without technical concerns in all the patients without impacting patient flow or care in the intraoperative setting. Given the limited size of the study cohort, larger trials are needed to confirm our findings.

In summary, by using ONSD, we noted that there were differences in baseline values and those following CPB when comparing patients with single and two ventricle physiology. Although values were slightly elevated in single ventricle (Fontan) patients, none of the patients had clinical signs suggestive of increased ICP. It is possible that chronic venous congestion which may be present in patients with single ventricle physiology prior to Fontan surgery results in higher ONSD values than patients with two ventricle physiology even in the absence of increased ICP. This raises the question of whether the normative values for two ventricle patients can be applied to single ventricle (Fontan) patients. Additionally, as the ONSD values were higher following CPB in single ventricle patients, it may also be that patients with chronic venous congestion are at a greater risk of experiencing subclinical elevations of ICP following CPB given its impact on CNS dynamics and the BBB.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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