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Intracranial Pressure and Cerebral Hemodynamics in Infants Before and After Glenn Procedure

OBJECTIVES: This prospective cohort study aimed to investigate changes in intracranial pressure (ICP) and cerebral hemodynamics in infants with congenital heart disease undergoing the Glenn procedure, focusing on the relationship between superior vena cava pressure and estimated ICP.

DESIGN: A single-center prospective cohort study.

SETTING: The study was conducted in a cardiac center over 4 years (2019–2022).

PATIENTS: Twenty-seven infants with congenital heart disease scheduled for the Glenn procedure were included in the study, and detailed patient demographics and primary diagnoses were recorded.

INTERVENTIONS: Transcranial Doppler (TCD) ultrasound examinations were performed at three time points: baseline (preoperatively), postoperative while ventilated (within 24–48 hr), and at discharge. TCD parameters, blood pressure, and pulmonary artery pressure were measured.

MEASUREMENTS AND MAIN RESULTS: TCD parameters included systolic flow velocity, diastolic flow velocity (dFV), mean flow velocity (mFV), pulsatility index (PI), and resistance index. Estimated ICP and cerebral perfusion pressure (CPP) were calculated using established formulas. There was a significant post-operative increase in estimated ICP from 11 mm Hg (interquartile range [IQR], 10–16 mm Hg) to 15 mm Hg (IQR, 12–21 mm Hg) postoperatively (p = 0.002) with a trend toward higher CPP from 22 mm Hg (IQR, 14–30 mm Hg) to 28 mm Hg (IQR, 22–38 mm Hg) postoperatively (p = 0.1). TCD indices reflected alterations in cerebral hemodynamics, including decreased dFV and mFV and increased PI. Intracranial hemodynamics while on positive airway pressure and after extubation were similar.

CONCLUSIONS: Glenn procedure substantially increases estimated ICP while showing a trend toward higher CPP. These findings underscore the intricate interaction between venous pressure and cerebral hemodynamics in infants undergoing the Glenn procedure. They also highlight the remarkable complexity of cerebrovascular autoregulation in maintaining stable brain perfusion under these circumstances.

KEYWORDS: cerebral blood flow; congenital heart defects; Glenn procedure; intracranial pressure; superior vena cava; transcranial Doppler sonography

The human cardiovascular system relies on the synchronized functioning of the systemic and pulmonary circulations. However, infants born with congenital heart conditions, such as hypoplastic left heart syndrome, cannot maintain these dual blood circulations. Instead, they require palliative surgical procedures to ensure an adequate pulmonary blood supply while operating with only a single ventricle physiology. One of the palliative procedures involves redirecting blood from the superior vena cava (SVC) to the Abdulraouf M. Z. Jijeh, MD^{1,2,3} AnisFatima, MD¹ Mohammad A.Faraji, MD⁴ Hussam K. Hamadah, MD¹ Ghassan A. Shaath, MD^{1,2,3}

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RESEARCH IN CONTEXT

- After Glenn procedure, the superior vena cava (SVC) pressure becomes reflective of pulmonary artery pressure, which typically exceeds the right atrial pressure.
- We used transcranial Doppler before and after Glenn to estimate intracranial pressure (ICP) and cerebral perfusion pressure (CPP) using established verified formulas.
- After Glenn procedure, there was a significant increase in ICP with a trend toward higher CPP.

right pulmonary artery (PA), a technique known as the cavopulmonary connection or "Glenn" procedure (1).

In normal anatomy, SVC pressure is equal to right atrial pressure. However, following the Glenn procedure, SVC pressure becomes reflective of PA pressure, which typically exceeds right atrial pressure. Consequently, the elevation in venous pressure, as indicated by the increase in SVC pressure, leads to a rise in intracranial pressure (ICP) (2, 3). Adult literature demonstrated a clear association between increased ICP and elevated venous pressure or venous obstruction (2, 3). Similarly, adult patients with elevated right atrial pressure had significantly higher cerebral pulsatility index (PI) than patients with normal right atrial pressure (4). Building on this knowledge, we postulated that the increased pressure in the SVC following the Glenn procedure might similarly lead to elevated ICP. So, we aimed in this study to explore this hypothesis clinically in infants going for the Glenn procedure.

Transcranial Doppler (TCD) ultrasonography is a valuable tool for assessing cerebral blood flow in major intracranial arteries. It was introduced by Aaslid et al (5) in 1982 for monitoring cerebral hemodynamics. Detailed guidelines for conducting TCD ultrasound examinations are well-documented in the literature (6–8), including normal values for TCD indices in both adults (9, 10) and children (11).

The PI, introduced in the 1970s (12), is the most commonly used formula today (13), defined as PI = (sFV-dFV)/mFV, where sFV represents systolic flow velocity, dFV represents diastolic flow velocity, and mFV represents mean flow velocity. Notably, PI and resistance index (RI) are advantageous because they are ratios and not affected by the angle of insonation (14).

Numerous studies have demonstrated a strong correlation between TCD parameters and ICP in pediatric populations (15–23) and adults (24–27). However, it is worth noting that this correlation may become less reliable when ICP exceeds 20 mm Hg (28).

MATERIALS AND METHODS

This prospective cohort study was conducted at a single cardiac center. Over 4 years (2019–2022), all infants admitted with congenital heart disease and scheduled for Glenn procedure were screened after obtaining parental consent. We excluded paying (Business) patients and those who were ventilated before the Glenn procedure. The study was approved by the Institutional Review Board (IRB) at the King Abdullah International Medical Research Center (KAIMRC) on January 30, 2017, with the study number RC16/028/R. All procedures followed the approved protocol from the IRB at KAIMRC and adhered to the Helsinki Declaration of 1975.

TCD was performed at three distinct time points:

- 1) Baseline: Before the Glenn procedure, the first TCD was conducted preoperatively.
- 2) Postoperative: The second TCD was performed within 24–48 hours after the Glenn procedure while the patient was still intubated and ventilated.
- 3) At discharge: The third and final TCD was conducted after extubation before discharging the patient home.

TCD was performed by ICU team members trained in point-of-care ultrasound, including TCD. A lowfrequency (2–4 MHz) phased-array probe (cardiac probe) was applied to the temporal area to obtain the middle cerebral artery pulse Doppler and record the following parameters: Peak systolic flow velocity (sFV), diastolic flow velocity (dFV), mean flow velocity (mFV), PI, and RI, all of which were calculated by the ultrasound machine. The radiologist reviewed the images and calculated parameters. Blood pressure, heart rate, arterial blood gas measurements, hemoglobin, and hematocrit were measured at the time of each TCD. Examples of TCD images after Glenn are shown in **Figure 1**. PA pressure measurements were recorded when cardiac catheterization was done preoperatively.

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Figure 1. Transcranial Doppler (TCD) images of the middle cerebral artery (the *red flow*) in two patients after the Glenn procedure. **A**, Normal diastolic flow and pulsatility index (PI). **B**, Decreased diastolic flow and increased PI. This flow pattern of TCD indicates an elevation in intracranial pressure and reduced perfusion, mainly when the end-diastolic velocity (EDV) falls below 20 cm/s and the PI exceeds 1.4 (9). PSV = peak systolic velocity, RI = resistance index, S/D = systolic/diastolic velocity ratio, TAP = time-averaged pulsatility (or time-averaged mean velocity).

We used the following verified formulas to estimate ICP and cerebral perfusion pressure (CPP):

 $ICP = (10.972 \times PI) - 1.284$ by Bellner et al (29, 30).

 $CPP = mFV/(mFV-dFV) \times (mBP-dBP)$ by Edouard et al (31), where mBP and dBP are mean and diastolic blood pressures, respectively.

After data cleaning, continuous variables were reported as mean \pm sD for normally distributed data and median and interquartile range for skewed data. Categorical variables were presented as counts (percentages). Means were compared using a paired *t* test, while medians of paired variables were compared using the Wilcoxon signed-rank test. A *p* value of less than or equal to 0.05 was considered statistically significant.

RESULTS

Patients' Demographics

In total, 44 cases were screened. Seventeen were excluded for various reasons: one refused consent, three were paying patients, four had canceled Glenn procedures, eight did not have the oppor-

tunity to undergo preoperative TCD, and one lost follow-up. The study included the remaining 27 cases that underwent the Glenn procedure. The median age was 8 months (6.3-12.3 mo), and the median weight was 6.7 kg (5.8-8.4 kg) (Table 1). The patients' primary diagnoses are detailed in Table 2. Twenty-four patients (89%) underwent cardiac catheterization before the Glenn procedure. The mean PA pressure was 14 mm Hg (11.3-16.8 mm Hg). Blood pressure, heart rate, blood gas measurements, and hemoglobin were compared between the three time points in Table 3. Systolic blood pressure, oxygen saturation, PH, PCO₂, bicarbonate, and hemoglobin were similar at all time points. In contrast, mean blood pressure and hematocrit were lower postoperatively.

Transcranial Doppler Indices

sFV remained relatively stable postoperatively, with no significant alteration. dFV and mFV decreased significantly after the Glenn procedure. dFV decreased from 34 mm Hg (13–43 mm Hg) to 22 mm Hg (17–28 mm Hg; p = 0.04), whereas mFV dropped from 63 mm

TABLE 1.

Demographics of the 27 Cases That Underwent Glenn Procedure

Variables	Median (IQR) or <i>n</i> (%)
Age (mo)	8 (6.3–12.3)
Sex (males), <i>n</i> (%)	15 (56)
Weight (kg)	6.7 (6-8.4)
Height (cm)	68 (63–75)
Cardiac catheterization, mm Hg	
Systolic PA pressure	16.5 (13.7–20.3)
Diastolic PA pressure	11 (8.7–13.3)
Mean PA pressure	14 (11.3–16.8)

IQR = interquartile range, PA = pulmonary artery.

TABLE 2.

Diagnoses of the 27 Cases That Underwent Glenn Procedure

Diagnosis	n (%)
Tricuspid atresia	8 (29.6)
Pulmonary atresia/critical pulmonary stenosis	6 (22.2)
DORV, remote VSD	4 (14.8)
Double inlet left ventricle	3 (11.1)
DORV, hypoplastic mitral valve	2 (7.4)
Hypoplastic left heart syndrome	2 (7.4)
Congenitally corrected transposition of great arteries, VSD	1 (3.7)
Unbalanced atrioventricular septal defect	1 (3.7)
Total	27

DORV = double outlet right ventricle, VSD = ventricular septal defect.

Hg (50–71 mm Hg) to 46 mm Hg (32–56 mm Hg; p=0.008).

The PI showed an increase from the initial measurement of 1.08 (1–1.6) to 1.5 (1.2–2) after the operation (p = 0.005). This elevated level persisted after extubation, measuring 1.37 (1.8–1.1, p = 0.1) (**Fig. 2**). During ventilation, the RI tended to rise. Initially, RI was 0.67 (0.63–0.77), increased to 0.73 (0.67–0.86) postoperatively (p = 0.08).

Estimated Cerebral Hemodynamics

The estimated ICP at the baseline was 11 mm Hg (10–16 mm Hg) and significantly increased to 15 mm Hg



- Considering increased ICP following the Glenn procedure can guide the clinical management of these patients, particularly when there are signs of elevated SVC pressure.
- Irritability, facial edema, or increased SVC pressure are indicators of increased ICP, warranting proper sedation and pain management and the avoidance of medications that could raise ICP.
- Reduced end-diastolic flow velocity below 20 cm/s, and elevated pulsatility index above 1.4, are indicators of increased ICP and decreased brain perfusion, which would warrant further investigation.
- Diuresis, pulmonary vasodilation (e.g., oxygen, inhaled nitric oxide), avoiding hypocapnia, and optimizing mean arterial pressure may improve brain perfusion.

(12–21 mm Hg) postoperatively (p = 0.002). Upon discharge, it remained elevated at 14 mm Hg (11–18 mm Hg; p = 0.1) (Fig. 2). This elevation in ICP was associated with a tendency to increase in the estimated CPP, which rose from 22 mm Hg (14–30 mm Hg) at baseline to 28 mm Hg (22–38 mm Hg) postoperatively (p = 0.1). At discharge, the CPP remained on the higher side at 28 mm Hg (19–37 mm Hg; p = 0.9) (**Table 4**). There was no correlation between the preoperative PA pressure or central venous pressure (CVP) (postoperative PA pressure) and the estimated ICP or CPP.

DISCUSSION

This study represents the first attempt to describe the estimated ICP dynamics following the Glenn procedure in infants with congenital heart disease. Our investigation sheds new light on the intricate relationship between intracranial hemodynamics and Glenn procedure. Estimated ICP increased after the Glenn procedure and remained high at discharge.

Despite the importance of understanding cerebral hemodynamics in children with congenital heart disease, the literature in this area remains limited (32). In a previous study of 24 cases undergoing Glenn procedure (33), it was observed that dFV remained constant,

TABLE 3. Hemodynamic Parameters, Arterial Blood Gases, and Hemoglobin at Three Time Points^a

Parameters	Baseline Preoperative	After Glenn (Ventilated)	At Discharge	ρ ^ь
Systolic BP (mm Hg)	93±9	86±13	93±15	0.22
Diastolic BP (mm Hg)	61±9	47±9	54±12	0.001
Mean BP (mm Hg)	71±9	61±10	67±12	0.02
Heart rate (beats/min)	137 ± 14	128±18	128±18	0.2
O_{2} saturation (%)	74±6	79±6	79±7	0.14
рН	7.36 ± 0.03	7.38 ± 0.04	7.41 ± 0.03	0.16
Pco ₂ (mm Hg)	40±4	44±9	42±5	0.83
Bicarbonate (mm Hg)	22 ± 2.2	25 ± 2.5	26±3	0.28
Hemoglobin (g/L)	154±23	137±21	130±18	0.06
Hematocrit (%)	49±7	40±7	39±6	0.007

BP = blood pressure.

^aResults are presented as mean \pm sp.

^bAnalysis of variance test.



Figure 2. Compares findings at three time points: preoperatively (baseline), postoperatively while ventilated (Glenn), and before discharge (discharge). Each *boxplot* represents the median (the *middle line*), the 25th quartile (the *lower edge of the box*), and the 75th quartile (the *upper edge of the box*). *Lines* extending out of the *box* represent the range. CPP = cerebral perfusion pressure, ICP = intracranial pressure, PI = pulsatility index.

whereas sFV and mFV decreased after Glenn. In this series, they did not report PI or an estimate of ICP or CPP. However, our findings revealed a different pattern: dFV and mFV decreased simultaneously with the rise in ICP. This decline in dFV and mFV resulted in an increase in PI as a compensatory response to counter the elevated ICP.

A case report highlighted the rise of ICP in the context of irritability after the Glenn procedure,

confirmed by brain MRI, fundal examination, and elevated opening pressure in lumbar puncture (34). Furthermore, brain imaging in 24 patients before and after the Glenn procedure revealed ventriculomegaly linked to higher CVP (35). These cases align with our findings regarding the elevation of ICP following Glenn procedure. In nine ventilated patients after the Glenn procedure, sFV and mFV increased with higher PCO₂ levels (45 and 55 mm Hg) (36). There was no

TABLE 4.

Transcranial Doppler Parameters and Estimated Intracranial Pressure and Cerebral Perfusion Pressure at Three Time Pointsa

Parameters	Baseline Preoperative	After Glenn (Ventilated)	At Discharge	P ^b	p ℃
Central venous pressure (mm Hg)	-	15 (13–18)	13 (10–21)	-	0.4
Systolic flow velocity (cm/s)	104 (80–134)	97 (62–121)	108 (77–127)	0.15	0.4
Diastolic flow velocity (cm/s)	34 (13–43)	22 (17–28)	29 (17–36)	0.04	0.1
Mean flow velocity (cm/s)	63 (50–71)	46 (32–56)	54 (36–67)	0.008	0.1
Pulsatility index	1.08 (1–1.6)	1.5 (1.2–2)	1.37 (1.8–1.1)	0.005	0.1
Resistance index	0.67 (0.64–0.77)	0.73 (0.67–0.86)	0.72 (0.66–0.79)	0.08	0.04
Estimated intracranial pressure (mm Hg)	11 (10–16)	15 (12–21)	14 (11–18)	0.002	0.1
Estimated cerebral perfusion pressure (mm Hg)	22 (14–30)	28 (22–38)	28 (19–37)	0.1	0.9

^aResults are presented as medians (interquartile range).

^bThe p value compares the medians of preoperative and postoperative findings during ventilation.

^cThe *p* value compares the medians between postoperative findings and those observed before discharge.

Dashes indicate data not available.

comparison of brain perfusion before and after Glenn. In our cohort, the PCO_2 level was the same at all the time points (Table 3).

Interestingly, in contrast to our expectations, our study revealed that eliminating the positive airway pressure did not significantly affect the estimated ICP and CPP in children who underwent the Glenn procedure. This finding echoes a similar observation in a cohort of 14 pediatric patients with traumatic brain injuries, where incremental increases in positive end-expiratory pressure, from 0 to 4 and then 8, failed to elicit changes in directly measured ICP and CPP (37). These findings highlight the complexity of the intracranial dynamics.

Under normal conditions, cerebral blood flow remains relatively stable across a range of CPPs, a phenomenon called cerebrovascular autoregulation (38). This mechanism helps elucidate our observation of an increase in CPP to overcome the elevation in the ICP as the system strives to sustain cerebral blood flow within normal parameters. One study highlighted this regulation in nine mechanically ventilated patients after the Glenn procedure, infused with sodium nitroprusside, which reduced systemic blood pressure but did not decrease cerebral blood flow velocity or brain perfusion (39). We could not find a correlation between the preoperative and postoperative PA pressure and the ICP. This may be explained by the small sample size or suggest other factors playing a role in determining the ICP.

The primary limitation of our study is the relatively small sample size. While our findings provide valuable insights, the generalizability of our results to a larger population may be limited. Future studies with larger cohorts could confirm the relationship between intracranial hemodynamics and Glenn procedure. Another notable limitation inherent to TCD ultrasonography is the potential variability in the values it provides. These values can be influenced by operatordependent factors, such as the ability to identify an acoustic window and capture a strong pulse signal. Ensuring consistency in TCD measurements is essential for accurate interpretation and clinical decision-making. Furthermore, it is essential to acknowledge that our analysis was based on estimating ICP and CPP rather than direct measurements. Direct measurement of these parameters in normal children is not feasible due to ethical and practical constraints. Therefore, the estimated values should be interpreted cautiously and considered as surrogate markers of intracranial hemodynamics.

CONCLUSIONS

Our study provides evidence that the Glenn procedure leads to a substantial increase in estimated ICP

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while showing a trend toward higher CPP. These findings underscore the intricate interplay between venous pressure and cerebral hemodynamics in infants undergoing the Glenn procedure. They also highlight the remarkable complexity of cerebrovascular autoregulation in maintaining stable brain perfusion under these circumstances.

Understanding the dynamics of ICP and CPP in this context is essential for clinicians caring for infants with congenital heart disease. This knowledge may inform more precise management strategies, ultimately improving patient outcomes. While our study has limitations, including a relatively small sample size and the use of estimated ICP and CPP, it represents a valuable step toward enhancing our understanding of the neurologic implications of the Glenn procedure. Further research with larger cohorts is warranted to confirm and build upon these findings.

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