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Intraventricular Hemorrhage in Moderate to Severe Congenital Heart Disease

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Abstract

Objective—Determine the incidence of intraventricular hemorrhage (IVH) in infants with moderate to severe congenital heart disease (CHD), investigate the impact of gestational age, cardiac diagnosis, and cardiac intervention on IVH, and compare IVH rates in preterm infants with and without CHD.

Methods—A retrospective review was performed from 2007–2012 of all infants admitted to St. Louis Children's Hospital with moderate to severe CHD requiring cardiac intervention in the first 90 days of life and all preterm infants without CHD or congenital anomalies/known genetic diagnoses admitted during the same time period. Cranial ultrasound (CUS) data were reviewed for presence/severity of IVH. Head computed tomography (CT) and brain magnetic resonance imaging (MRI) data were also reviewed in the CHD infants. Univariate analyses were undertaken to determine associations with IVH and a final multivariate logistic regression model was performed.

Results—There were 339 infants with CHD who met inclusion criteria and 25.4% were born preterm. IVH was identified on CUS in 13.3% of infants, with the majority of IVH being low-grade (Grade I/II). The incidence increased as gestational age decreased such that IVH was present in 8.7% of term infants, 19.2% of late preterm infants, 26.3% of moderately preterm infants, and 53.3% of very preterm infants. There was no difference in IVH rates between cardiac diagnoses. Additionally, the incidence of IVH did not increase after cardiac intervention, with only three infants demonstrating new/worsening high-grade (Grade III/IV) IVH after surgery. In a multivariate model, only gestational age at birth and African American race were predictors of IVH. In the subset of infants with CT/MRI data, there was good sensitivity and specificity of CUS for presence of IVH.

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Conclusion—Infants with CHD commonly develop IVH, particularly when born preterm. However, the vast majority of IVH is low-grade and is associated with gestational age and African American race.

Keywords

cerebral hemorrhage; brain imaging; heart defects; congenital; cardiac surgery; infant; newborn; infant; premature

Introduction

Neurological complications are recognized as a major adverse outcome in infants with moderate to severe forms of congenital heart disease (CHD). Recent literature describing brain abnormalities in this population have primarily focused on white matter injury, stroke, and alterations in brain development as key pathways for subsequent neurodevelopmental impairment (1–5). However, in clinical settings, intraventricular hemorrhage (IVH) is also commonly discussed, particularly when infants with CHD are born preterm. IVH can have significant ramifications for long-term neurodevelopmental outcomes (6, 7) and is potentially relevant to cardiac intervention for timing of surgery and conduct of cardiopulmonary bypass. Neuroimaging studies have reported IVH in 2–23% of patients with CHD. However, these reports are limited in number, often involve small sample sizes, and have varying inclusion criteria for cardiac diagnoses. In addition, there are minimal data investigating new or worsening IVH after cardiac intervention (8–11). Therefore, interpretation and application of the existing literature to the clinical setting can be challenging.

The effect of gestational age on development of IVH in infants with CHD has also not been fully characterized. Our understanding of the pathophysiology of IVH and the risk factors leading to development of this type of lesion have primarily evolved from the preterm infant literature and have identified an inverse relationship between presence/severity of IVH and gestational age (12). This correlation has not been reported in the CHD population. However, a small number of studies have described IVH in preterm infants with CHD, either as an independent outcome or part of a combined brain injury measure. Similar to the term data, reported incidence for IVH in preterm infants is wide-ranging (13–15). In addition, it is not clear whether preterm infants with CHD are at greater risk of IVH than the general preterm population.

While existing data provide an evolving understanding of IVH in CHD, further investigation is needed to characterize this neurological complication. Therefore, the aim of this study was to define the incidence of IVH in a large, single-center cohort of term and preterm infants with moderate to severe CHD requiring cardiac intervention, determine the effect of gestational age, cardiac diagnosis, and cardiac intervention on risk of IVH, and compare IVH in preterm infants with and without CHD.

Materials and Methods

A retrospective, single-center cohort study was undertaken of all infants with CHD admitted within the first two weeks of life to St. Louis Children's Hospital Neonatal Intensive Care Unit (NICU) or Cardiac Intensive Care Unit (CICU) from January 2007 to December 2012. Infants were included if they 1) had a preoperative cranial ultrasound (CUS) performed and 2) underwent cardiac surgical or catheter-based intervention by 90 days of age, or died before cardiac intervention but had a diagnosis that was anticipated to require a procedure within the first 90 days of life. Exclusion criteria included isolated patent ductus arteriosus, atrial septal defect (ASD), or ventricular septal defect (VSD); lack of CUS data; and inability to determine gestational age at birth. To determine whether preterm CHD infants were at increased risk of IVH compared to a general preterm population, preterm infants without CHD admitted to the NICU at St. Louis Children's Hospital during the same timeframe were also included if they underwent a CUS as part of routine clinical care and did not have congenital anomalies/known genetic diagnoses. The study was approved by the Institutional Review Board and need for informed consent was waived.

Subjects were identified using existing NICU and CICU databases and demographic and clinical data were extracted. Additional and/or missing data were collected by reviewing the infant and maternal medical records. Information regarding delivery and birth history, medical and surgical factors, and brain imaging (CUS, head computed tomography [CT], and brain magnetic resonance imaging [MRI]) were recorded. Gestational age was defined as completed weeks of gestation at birth and those born at <37 weeks were categorized as preterm. Cardiac diagnosis was determined from the written echocardiography report and surgical data were recorded from the procedure notes and anesthesia records. Presence of IVH was determined from clinical CUS data and categorized by Papile's grading system (16). At our institution, routine CUS is performed in preterm and CHD infants if they are born <32 weeks gestation or are <1800 grams at birth. For infants who do not meet these criteria, decisions regarding whether to acquire a CUS, as well as the timing of acquiring this imaging, is at the discretion of the clinical team. The timing of CUS was defined as preoperative if it was performed before a cardiac surgical or catheter-based intervention that was intended as the primary corrective or initial palliative procedure. CUS performed after balloon atrial septostomy, but before the primary procedure, were defined as preoperative. Postoperative CUS included any ultrasound performed after the primary procedure. Head CT and brain MRI data acquired preoperatively or within four weeks of intervention were also collected and reviewed for presence of IVH and other patterns of injury. CUS, head CT, and brain MRI findings were recorded from the written radiology reports. If the radiology report was unclear regarding presence of IVH and/or other patterns of injury, two authors (CO and CS) reviewed the raw images to characterize presence and pattern of injury for these subjects.

Statistical Analysis

Statistical analysis was undertaken using SPSS, version 24. Descriptive statistics for demographic and clinical data are reported using median and interquartile range (IQR) for continuous variables and frequency and percentage for categorical variables. Group

comparisons were performed with a Mann-Whitney U test for continuous variables and a chi-square test for categorical variables. To determine the impact of cardiac diagnosis on IVH, infants were categorized into one of the following: 1) single ventricle physiology, 2) transposition of the great arteries (TGA) and related transposition physiology, 3) systemic blood flow obstruction, 4) pulmonary blood flow obstruction, or 5) other.

Logistic regression analysis was performed to determine the association between IVH and clinical factors using IVH as a binary dependent variable (presence/absence). Analyses for gestational age were undertaken in two ways: 1) with gestational age as a continuous variable to determine the impact of each week of gestation on IVH risk and 2) with gestational age as a categorical variable using the following categories: term (≥ 37 weeks), late preterm (34–36 weeks), moderately preterm (32–33 weeks), and very preterm (<32 weeks). Analyses were not completed for IVH severity because of limitations in sample size for high-grade (Grade III/IV) IVH in this cohort. Clinical factors found to have a p value <0.2 were included in a final multivariate logistic regression model.

Results

Patient Population and Clinical Characteristics

There were 339 CHD infants who met inclusion criteria for the study. There were 104 infants excluded because of lack of CUS data (23.5% of moderate to severe CHD infants who otherwise met inclusion criteria). Infants who were excluded for lack of CUS data had a higher gestational age (mean 37.9 weeks, standard deviation [SD] 2.1 compared to 37.3 weeks, SD 2.7) and a larger head circumference (mean 33.4 cm, SD 2.1 compared to 32.8 cm, SD 2.5). They were also less likely to undergo a cesarean section (36% compared to 49%) and had lower rates of death (12% compared to 27%). Demographic and clinical variables for infants included in the study are displayed in Table 1. Infants ranged from 25 to 41 weeks gestation at birth, and preterm birth occurred in 25.4% (86/339) of all CHD infants. Of infants born preterm, 60.5% (52/86) were late preterm, 22.1% (19/86) were moderately preterm, and 17.4% (15/86) were very preterm. The most common cardiac lesions in the cohort were single ventricle and TGA physiology.

Intraventricular Hemorrhage on CUS

The overall incidence of IVH in the cohort was 13.3% (45/339), and the majority of lesions were low-grade: 77.7% (35/45) were grade I, 6.7% (3/45) were grade II, 8.9% (4/45) were grade III, and 6.7% (3/45) were grade IV. IVH was more common as gestational age decreased, with an incidence of 8.7% (22/253) in term infants, 19.2% (10/52) in late preterm infants, 26.3% (5/19) in moderately preterm infants, and 53.3% (8/15) in very preterm infants (Table 2). When gestational age was evaluated as a continuous variable, the odds of developing IVH were 1.3 times higher (95% confidence interval [CI] 1.2–1.4) per each week decrease in gestational age. Only seven infants had high-grade (Grade III/IV) IVH, therefore analysis could not be undertaken for IVH severity. Four of the infants with high-grade IVH were born at <34 weeks, two were born at 37 weeks, and one was born at 38 weeks gestation.

IVH was identified on preoperative CUS in 11.5% (39/339) of infants. Of those with IVH, 82.0% (32/39) were grade I, 7.7% (3/39) were grade II, 2.6 % (1/39) were grade III, and 7.7% (3/39) were grade IV. Thirty-six infants did not have cardiac intervention (34 died prior to intervention, one was discharged home on hospice, and one was lost to follow-up). The IVH rate for infants who died prior to cardiac intervention was 26.5% (9/34), including six with Grade I IVH and three with Grade IV IVH.

Of the 303 infants who underwent a cardiac intervention, 91 had CUS before and after intervention. IVH was present in 16.5% (15/91) of these infants preoperatively and 18.7% (17/91) postoperatively ($p = 0.75$, McNemar test). Only 8.8% (8/91) had a new or worsening IVH after cardiac intervention, three of which were high-grade IVH (Table 3). One infant was a 37-week male with coarctation/VSD, tracheoesophageal fistula, multiple vertebral anomalies and a hypoplastic thumb. His preoperative CUS on day of life 6 showed a grade I IVH on the right and a grade II IVH on the left. Repeat CUS on day of life 15, 3 days after pulmonary artery banding and coarctation repair, showed progression to a left grade III IVH. The second infant was a 32-week female with HLHS who had no IVH on preoperative CUS. She underwent a Norwood procedure with Sano modification on day of life 8 and was placed on ECMO on day of life 9 for hemodynamic instability and worsening metabolic acidosis. CUS that day demonstrated new bilateral grade III IVH. She died on day of life 13, after significant deterioration attributed to sepsis. The final infant was a 33-week male with HLHS born in the setting of placental abruption. His preoperative CUS was negative for IVH. He underwent a Norwood procedure with Sano modification on day of life 23, and CUS on day of life 25 showed new bilateral grade III IVH and parenchymal hemorrhages, which were confirmed as multiple bilateral hemorrhagic infarcts on head CT. He died on day of life 26 after an acute cardiopulmonary arrest.

Clinical Factors and IVH in CHD

Infants with IVH were more likely to have a lower gestational age at birth, a lower birthweight, a smaller head circumference, be African American, be delivered for maternal or fetal indications, have a lower 5-minute Apgar score, have surgery at a later day of life, require extracorporeal membrane oxygenation (ECMO), and have a higher rate of mortality. Cardiac diagnostic category was not associated with presence of IVH. The type of cardiac intervention was also not associated with presence of IVH, although infants with IVH trended toward less use of cardiopulmonary bypass and higher catheter-based interventions (Table 1). Clinical factors with a p value < 0.2 were included in a multivariate logistic regression model to determine their association with IVH. Birthweight and OFC at birth were not included because of collinearity with gestational age at birth. In the final model, only gestational age at birth and African American race remained significant predictors of IVH (Table 4).

Intraventricular Hemorrhage in “Typical” Preterm versus Preterm CHD Infants

There were 330 late preterm infants, 242 moderately preterm infants, and 1033 very preterm infants without CHD who met inclusion criteria for comparison. IVH rates did not differ between “typical” (*i.e.*, non-CHD) preterm and CHD preterm infants (Table 5).

Head CT and Brain MRI Data

Sixty infants in the cohort had a head CT or brain MRI performed preoperatively or within four weeks of intervention. Two MRIs were performed as part of a research study, with the remainder of the CT and MRI data obtained for clinical indications at the discretion of the primary ICU teams. Brain injury was present in 45% (27/60) of infants, with some infants displaying multiple forms of injury. IVH was identified in 22% (13/60), infarct (ischemic or hemorrhagic) in 25% (15/60), white matter injury in 23% (14/60), and other parenchymal hemorrhage (*i.e.* cerebellar hemorrhage) in 5% (3/60) of infants. Of the 60 infants with head CT or brain MRI data, 56 had a corresponding CUS in the same period. Comparison of CUS and CT/MRI data are displayed in Table 6. The timing between acquisition of CUS and CT/MRI for the preoperative images was a median of one day (IQR 0–4 days) and for the postoperative images was a median of one day (IQR 0–3 days). Specific to the IVH findings, CUS had three false positives (all with grade I IVH) and three false negatives. Therefore, the sensitivity of CUS for detecting IVH was 82%, specificity was 93%, positive predictive value was 82%, and the negative predictive value was 93%.

With regards to the false positives, one infant had a preoperative CUS that demonstrated a right grade I IVH with diffuse echogenicity in the left cerebral hemisphere and scattered foci of echogenicity in the right cerebral hemisphere, concerning for infarct. MRI on the same day demonstrated a large ischemic infarct with Wallerian degeneration and patchy areas of diffusion restriction in the right cerebral hemisphere, but no IVH. A second infant had bilateral grade I IVH preoperatively that was resolving on repeat CUS two days prior to the preoperative CT scan, which did not demonstrate IVH. The third infant had bilateral grade I IVH on preoperative CUS that resolved to unilateral grade I IVH postoperatively. Postoperative brain MRI eight days later did not demonstrate IVH, which may be reflective of a fully resolved lesion.

For the false negative IVH data, one infant had a preoperative CUS on day of life 1 that was negative. An MRI performed the next day demonstrated bilateral germinal matrix hemorrhages with a small amount of intraventricular blood and two small acute right thalamic infarcts. The second infant had a postoperative CUS on day of life 21 that was negative. On day of life 23, she had an acute change in neurologic status while on ECMO and head CT demonstrated a new large IVH with marked hydrocephalus. The third infant did not have any abnormalities on pre- or post-operative CUS. On day of life 22, four days after the most recent postoperative CUS, he developed seizures and brain MRI demonstrated a hemorrhagic infarct in the left occipital lobe, bilateral white matter injury, and a small right IVH. Based on the available neuroimaging data, it is unclear when these injuries occurred.

CUS did not have good correlation with most other patterns of injury, with the exception of postoperative infarct, which was typically detected on CUS first and subsequently further characterized by CT or MRI.

Discussion

In this large, single-center study of over 330 infants with CHD undergoing cardiac intervention, IVH was identified on CUS in 13.3% of infants. The vast majority of IVH was

low-grade and, importantly, there were no differences in IVH rates between cardiac diagnoses or from pre- to post-operative imaging. To our knowledge, this is the largest study to date investigating the incidence of IVH in term and preterm CHD infants in relation to cardiac subgroups and cardiac intervention.

Data from previous CUS studies have described IVH in 2–16% of term CHD infants, whereas MRI data have reported rates of 2–23%. Within these cohorts, the majority of IVH was low-grade (9–11, 17, 18). Our finding of an 8.7% incidence of IVH (typically low-grade) in term CHD infants is within the range and pattern of previous reports. However, our data reflect a much larger sample size than many prior studies. Data evaluating CUS in healthy, term infants have identified IVH in 2.9–4% of infants (19, 20). With the lack of a concurrent term control population, we are unable to directly determine if IVH rates are higher in the CHD population, however, the existing literature suggest CHD may predispose to increased risk.

Specific to the preterm population, our study demonstrated increasing incidence of IVH as gestational age decreased. This began even in late preterm CHD infants, where the incidence of IVH was 19.2%, and increased to 53.3% in very preterm infants with CHD. Existing studies reporting IVH in the preterm CHD population frequently include isolated ASD or VSD diagnoses, which were excluded in our cohort, and often only report high-grade IVH or a combined brain injury outcome, making it challenging to compare our results to others (13–15). The incidence of IVH in our preterm CHD infants is higher than what is often reported in the general preterm literature (21). However, our comparison of CHD and non-CHD preterm infants did not demonstrate a difference between groups. This may be related to small sample size in the preterm CHD population, as there is a plausible pathogenic mechanism for increased rates of IVH in CHD infants. Alterations in cerebral blood flow in the context of a pressure-passive circulation and the vulnerability of the germinal matrix to hypoxia-ischemia are considered major contributors to IVH in the preterm population (22, 23). Therefore, it is possible that the hypoxia and impaired perfusion that often occur in CHD could potentiate these effects when infants with CHD are born preterm. In addition, our own data and others have demonstrated preoperative alterations in brain development that appear to begin *in utero*, even when born at term (24–28). It is not known how these alterations affect the germinal matrix, but changes in the typical developmental trajectory could theoretically contribute to IVH in the CHD population.

The timing of IVH is also an important clinical consideration because of the anticoagulation necessary for cardiopulmonary bypass and the concern for worsening hemorrhage. It is well known that neonates undergoing ECMO are at risk for progression of intracranial hemorrhage, particularly those born preterm and with lower birthweight. However, this appears to be independent of cardiac diagnosis and surgery (29–31). In addition, prior data evaluating pre- and post-operative MRIs in 92 neonates with CHD born at 36 weeks gestation demonstrated a low risk of progression or hemorrhagic transformation of stroke, white matter injury, or IVH after cardiac surgery (8). Our data also did not demonstrate a difference in IVH rates from pre- to postoperative CUS. It is important to note that not all infants in our cohort had imaging at both time points, which limited the sample size for comparison. Therefore, while our data suggest there is no increased risk of IVH after cardiac

intervention, a larger sample is needed to definitively make this conclusion. Importantly, cardiac diagnosis, preoperative catheterization, and cardiopulmonary bypass were also not associated with IVH. While ECMO was significant on univariate analyses, this effect did not remain after controlling for multiple clinical factors and, in the final model, only gestational age at birth and African American race remained predictors. Racial disparities have been demonstrated in the CHD population, with African American infants displaying increased mortality compared to white infants (32). In addition, preterm African American infants have been shown to have increased risk of IVH (33, 34). To our knowledge, our study is the first to report this in the CHD literature.

Finally, our study focused primarily on IVH identified on CUS. Prior work has demonstrated routine CUS to be insensitive and nonspecific in the CHD population (10). While only 56 infants in our study had CT/MRI data for direct comparison, CUS demonstrated good sensitivity and specificity for IVH in our cohort. The difference in findings between our data and that of Rios *et al* may relate to the use of clinical versus research quality imaging. Several studies have reported high rates of neuropathology in the absence of clinical signs or symptoms in infants with CHD undergoing research imaging (8, 26). Thus, it is possible higher resolution, research data may detect more subtle abnormalities, whereas data acquired for clinical indications may have a higher yield but may not identify more minor lesions, potentially affecting the sensitivity and specificity when comparing imaging modalities within cohorts.

One of the key limitations to our study is its retrospective nature, which limits our data to only those infants who underwent neuroimaging for clinical evaluation. Therefore, our reported rates of IVH may be an underestimate of the true incidence of this lesion. In addition, we do not have neurodevelopmental follow-up data to determine the long-term effects of low-grade IVH in this population. Prior work has demonstrated no association between preoperative CUS abnormalities and neurodevelopment at one year. However, there were only two infants with IVH in that cohort and the majority of abnormalities consisted of brain edema and white matter injury (17). Historically, low-grade IVH has been thought to have lesser effects on neurodevelopmental outcome. Recent data have begun to challenge this, suggesting that even less severe forms of IVH may predispose to developmental impairment (7, 35). These data need to be interpreted with caution as it is unclear whether the low-grade IVH or other clinical factors, such as severity of illness, are mediating the outcome. Nonetheless, this remains an important consideration for the clinician.

Conclusions

In summary, this study identified IVH to be common on CUS in the CHD population, particularly for infants <37 weeks gestation, with good sensitivity and specificity when compared to head CT and brain MRI data. While clinical factors such as cardiac diagnosis, preoperative catheterization, and cardiopulmonary bypass were not associated with IVH, gestational age and African American race remained strong predictors. Based on our results and in the context of existing literature, we would recommend routine screening with CUS in all preterm CHD infants, even those beyond 32 weeks gestation. In addition, CUS can be used as an initial imaging tool in infants who have clinical indications for neuroimaging,

such as acute decompensation or need for ECMO, with follow-up with higher resolution (*i.e.* MR) imaging once clinically stable to ensure full characterization of all patterns of injury. Finally, further prospective studies are needed to definitively determine the timing and progression of IVH in term and preterm infants with CHD and to investigate the relationship between IVH and long-term neurodevelopment.

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Table 1

Demographic and Clinical Characteristics of Infants With and Without Intraventricular Hemorrhage

Demographic/Clinical Characteristics	Infants with IVH n=45	Infants Without IVH n=294	p value
Cardiac Diagnosis, n (%)			0.58
Single ventricle physiology	15 (34)	103 (35)	
TGA or TGA physiology	10 (22)	58 (20)	
Systemic blood flow obstruction	6 (13)	43 (15)	
Pulmonary blood flow obstruction	8 (18)	31(10)	
Other	6 (13)	59 (20)	
GA at birth (weeks), median (IQR)	36.0 (32.5–38.0)	38.0 (37.0–39.0)	<0.001
Birthweight (kg), median (IQR)	2.61 (1.73–3.26)	3.08 (2.60–3.45)	<0.001
HC at birth (cm), median (IQR)	31.8 (29.0–34.0)	33.5 (32.0–34.5)	0.001
Sex, male, n (%)	30 (67)	182 (62)	0.54
Race, n (%)			0.007
Caucasian	34 (76)	213 (72)	
African American	9 (20)	25 (9)	
Ethnic Minority or Unknown	2 (4)	56 (19)	
Prenatal diagnosis, n (%)	23 (51)	156 (53)	0.76
Inborn, n (%)	17 (38)	119 (41)	0.73
Cesarean delivery, n (%)	24 (53)	135 (46)	0.48
Indication for Delivery, n (%)			0.05
Spontaneous labor	16 (36)	105 (36)	
Induction or scheduled cesarean delivery	10 (22)	80 (27)	
Maternal or fetal Indication	16 (36)	49 (17)	
Unknown	3 (6)	60 (20)	
5 minute Apgar score, median (IQR)	8 (7–9)	8 (8–9)	0.001
Extra-cardiac anomalies/chromosomal abnormalities, n (%)	13 (29)	59 (20)	0.18
Preoperative catheterization, n (%)	12 (27)	83 (28)	0.74
Type of Cardiac Intervention, n (%)			0.08 ^a
Cardiopulmonary bypass	20 (45)	178 (60)	
No cardiopulmonary bypass	11 (24)	81 (28)	
Catheter-based intervention	4 (9)	9 (3)	
No surgery	10 (22)	26 (9)	
Age at surgery (days), median (IQR)	9 (6–27)	7 (5–11)	.03

Demographic/Clinical Characteristics	Infants with IVH n=45	Infants Without IVH n=294	<i>p</i> value
Treatment with ECMO, n (%)	9 (20)	20 (7)	0.01
Death, n (%)	20 (44)	65 (22)	0.001

TGA = transposition of the great arteries, GA = gestational age, HC = head circumference, IQR = interquartile range, ECMO = extracorporeal membrane oxygenation.

^aRepresents the Chi-square *p* Value when comparing operative interventions, excluding those that did not have surgery, to determine the effect of the intervention.

Table 2

Risk of Intraventricular Hemorrhage by Gestational Age Category

Gestational Age Category	Odds Ratio (95% CI) of Any IVH
Term (reference group) (n = 253)	-
Late Preterm (n = 52)	2.5 (1.1 – 5.7)
Moderately Preterm (n = 19)	3.8 (1.2 – 11.4)
Very Preterm (n = 15)	12.0 (4.0 – 36.2)

CI = confidence interval

Table 3

Intraventricular Hemorrhage Before and After Cardiac Intervention

Postoperative CUS						
	Preoperative CUS	No IVH	Grade I	Grade II	Grade III	Grade IV
No IVH	76/91 (83.5)	70/76 (92)	4/76 (5.3)	0/76 (0)	2/76 (2.6)	0/76 (0)
Grade I	12/91 (13.2)	4/12 (33.3)	7/12 (58.3)	1/12 (8.3)	0/12 (0)	0/12 (0)
Grade II	2/91 (2.2)	0/2 (0)	1/2 (50)	0/2 (0)	1/2 (50)	0/2 (0)
Grade III	1/91 (1.1)	0/1 (0)	0/1 (0)	0/1 (0)	1/1(100)	0/1 (0)
Grade IV	0/91 (0)	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)	0/0 (0)

CUS = cranial ultrasound. Data are displayed as n (%). Shaded boxes represent new or worsening IVH postoperatively.

Table 4

Association of Clinical Factors with Intraventricular Hemorrhage

Clinical Factors	Unadjusted OR	Unadjusted 95% CI	Adjusted OR	Adjusted 95% CI
GA at birth	1.31 ^a	1.18–1.45	1.30 ^b	1.09–1.54
African American race	2.25	0.97–5.24	3.29 ^b	1.11–9.71
Maternal or fetal indication for delivery	2.32 ^b	1.16–4.67	1.55	0.61–3.96
5-minute Apgar score	1.31 ^b	1.08–1.59	0.88	0.61–1.28
Extra-cardiac anomalies/chromosomal abnormalities	1.62	0.80–3.28	2.16	0.82–5.66
Use of Cardiopulmonary Bypass	1.48	0.72–3.04	1.03	0.42–2.56
Age at surgery	1.02 ^b	1.00–1.03	1.01	0.98–1.03
Treatment with ECMO	2.94 ^b	1.24–6.98	3.26	0.88–11.94

^a p < 0.001,^b p < 0.05.

OR = odds ratio, CI = confidence interval, GA = gestational age, ECMO = extracorporeal membrane oxygenation. Gestational age and Apgar score data are displayed with higher values as the reference.

Table 5

Intraventricular Hemorrhage Rates in Preterm Infants

Presence of IVH			
Preterm Category	“Typical” Preterm	CHD Preterm	<i>p</i> value
Late Preterm, n (%)	59/330 (17.9)	10/52 (19.2)	0.81
Moderately Preterm, n (%)	61/242 (25.2)	5/19 (26.3)	0.92
Very Preterm, n (%)	339/1033 (32.8)	8/15 (53.3)	0.09

Analyses were undertaken using a chi-square test.

Table 6

Patterns of Injury on Cranial Ultrasound, Head Computed Tomography, and Brain Magnetic Resonance Imaging

	Preoperative Imaging (n=35)			Postoperative Imaging (n=21)		
	CUS Positive	MRI/CT Positive	Both Positive	CUS Positive	MRI/CT Positive	Both Positive
IVH	9	8	7	5	6	4
WMI	6	10	3	2	5	1
Infarct	4	7	4	7	8	7
Other Hemorrhage	2	1	1	1	2	0
Ventriculomegaly	2	2	0	6	6	4
LSV	2	0	0	1	0	0

Data represent results for the 56 infants who had a brain MRI or head CT that corresponded with a preoperative or postoperative CUS. One infant had both pre- and post-operative imaging that identified IVH. WMI = white matter injury, LSV = lenticulostriate vasculopathy.