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Brain Magnetic Resonance Immediately Prior To Surgery In Single Ventricles and Surgical Postponement

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Abstract

Background—Single ventricle patients undergoing surgical reconstruction experience a high rate of brain injury; incidental findings on pre-operative brain scans may result in safety considerations involving hemorrhage extension during cardiopulmonary bypass that result in surgical postponement.

Methods—Single ventricle patients were studied with brain scans immediately preoperatively as part of a National Institute of Health study and were reviewed by neuroradiology immediately prior to cardiopulmonary bypass.

Results—One hundred and thirty four consecutive subjects recruited into the project were studied: 33 prior to stage I (3.7 ± 1.8 days), 34 prior to bidirectional Glenn (5.8 ± 3.5 months) and 67

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prior to Fontan (3.3 ± 1.1 years). Six (4.5%) surgeries were postponed because of concerning imaging findings on brain MRI; 2 prior to stage I, 3 prior to bidirectional Glenn and 1 prior to Fontan. Five were due to unexpected incidental findings of acute intracranial hemorrhage and one due to diffuse cerebellar cytotoxic edema; none who proceeded to surgery had these lesions. Prematurity as well as genetic syndromes were not present in any with postponed surgery. Four of 4 prior to bidirectional Glenn/Fontan with surgical delays had hypoplastic left heart syndrome compared with 44/97 who did not ($P=0.048$). After observation and follow up, all eventually had successful surgeries with bypass.

Conclusion—Preoperative brain MRI performed in children with single ventricles disclosed injuries in 4.5% leading to surgical delay; hemorrhagic lesions were most common and raised concerns for extension during surgery. The true risk of progression and need for delay of surgery due to heparinization associated with these lesions remains uncertain.

Keywords

CHD, Fontan; CHD, hypoplastic left heart syndrome; Brain, anatomy, function, injury, etc; Magnetic resonance imaging, MRI

Introduction

Patients with single ventricle who undergo staged surgical reconstruction culminating in the Fontan procedure face a high risk of mortality and may suffer adverse outcomes such as cardiac transplantation [1], decreased ventricular performance [2], poor somatic growth [3] and development of pulmonary arterial venous malformation [4]. There exists well-known concerns for poor neurologic outcome in patients with single ventricle due to both brain injury and delayed maturation [5,6,7,8,9]. This has presumably led to the findings of poor neurodevelopmental outcome in this patient population [10,11,12,13].

In the course of discovering causes of neurodevelopmental challenges seen in this population, incidental findings on research brain MRIs such as structural malformations or tumors are discovered that require further work up, new medical therapies or modifying clinical care. Here we report a secondary analysis on the timing of surgery in patients who participated in an NIH sponsored research project that demonstrated brain lesions on immediate preoperative brain MRIs with the potential to be adversely affected by anticoagulation required for cardiopulmonary bypass. MRI findings were reviewed by a neuroradiologist, neurologist and surgeon while the patient was still in the scanner and a decision made whether to proceed to surgery or postpone the operative date. Whether these previously occult findings contribute to poor outcomes in patients who do not receive preoperative brain MRIs or surgical postponement prevents harm is not known [14].

Material and Methods

Patients

This was a single center, retrospective secondary analysis of a prospective study of cerebral blood flow in single ventricle patients throughout staged surgical reconstruction. All patients were enrolled in either one of two National Institutes of Health protocols; all were enrolled

from April 2009 – March 2012. The inclusion criteria included any patient < 10 years of age with single ventricle physiology undergoing surgery at our institution. The patient needed to be stable enough to undergo an approximately 1-hour magnetic resonance imaging scan under general anesthesia. Exclusion criteria included any contraindication to magnetic resonance imaging. Demographics obtained included age, body surface area, gestational age, genetic disorders, diagnosis and stage of surgical reconstruction. Informed consent for participation in the larger study was obtained from all participants' families. The hospital's Institutional Review Board has approved both prospective studies.

Study procedure

Patients underwent a magnetic resonance imaging immediately prior to heart surgery. The patient was prepared in the operating room with intravenous and arterial line placement; all participants were administered general anesthesia that varied according to age (eg those who were at Stage I or at the bidirectional Glenn/hemiFontan stage received nitrous oxide and sevoflourane of 1 MAC or less), were paralyzed, endotracheally intubated and mechanically ventilated using a minute ventilation to achieve a PaCO_2 of 40 ± 2 mm Hg. The patient was then transported via stretcher to the adjacent scanner which was a Siemens Avanto 1.5 Tesla whole body MRI system (Siemens Medical Solutions, Malvern, PA). The patient was placed in the supine position, head first into the scanner utilizing the 6-channel head coil and 8-channel body array coil; all imaging was performed at isocenter. Studies lasted approximately one hour; afterwards, the patient was immediately removed from the scan room and transported either to the operative suite where surgery was performed or to the hospital floor. On completion of the MRI, the study was read by a staff neuroradiologist and a determination made to proceed to surgery or to wake child in discussions with the neurologist and surgeon.

Magnetic Resonance Imaging Protocol

A stack of static steady state free precession images were obtained from the diaphragm to the neck to assess cardiovascular anatomy. Gradient localizers were used to locate the brain and were used as a basis to perform the following anatomic brain imaging:

1. 3D volumetric T1-weighted MPRAGE (Magnetization Prepared Rapid Acquisition Gradient Echo: TR/TE/TI = 1980/2.65/1100, flip angle = 15 degree, slice thickness 1.5 mm, matrix 256×256)
2. 3D volumetric T2-weighted SPACE (Sampling Perfection with Application optimized Contrasts using different flip angle Evolution: TR/TE = 3200/453, slice thickness 2 mm, matrix 256×254)
3. 3D susceptibility-weighted imaging (SWI: TR/TE = 49/40, slice thickness 2 mm, matrix 256×177)
4. Diffusion-weighted imaging (TR/TE = 2903/86 ms, slice thickness = 4 mm, three b values of 0, 500, and 100 mm^2/s , matrix 128×128)
5. 2D T2-weighted coronal imaging (TR/TE = 6000/112, slice thickness 4 mm, no gap, matrix 448×336).

Imaging Review

All images in native form and multiplanar reformat were immediately reviewed by a pediatric neuroradiologist while the patient was in the scanner. Any concerning abnormalities or injuries identified were brought to attention and the decision to proceed or delay with surgery was made following discussions between neuroradiologist (AV), pediatric neurologist (DJL) and cardiothoracic surgeon (TLS, JWG, SF).

There are no well-established protocols or previous studies to delineate the exact contraindications to surgery in this setting, but the abnormalities of concern were those with concerning features that would increase the risk of intracranial hemorrhage as a result of anticoagulation in other relevant scenarios [15,16,17,18,19,20]. These included acute brain parenchymal hemorrhage, acute subarachnoid hemorrhage, acute or sizeable intraventricular hemorrhage beyond simple grade I intraventricular hemorrhage, acute subdural hemorrhage beyond the neonatal period, and large territories of acute infarct or cytotoxic edema (restricted diffusion on diffusion-weighted imaging). The presence of small amounts of posterior convexity, tentorial, and posterior fossa subdural blood in patients being operated upon in the first week of life was not considered a contraindication since these findings are very common in the perinatal period subsequent to normal vaginal delivery as a result of the birthing process, and have been reported to be seen in up to 62% of patients before neonatal heart surgery [21,22]. Determination of recent hemorrhage was based on a combination of hyperintensity on T1-weighted images, hypointensity on T2-weighted images, and susceptibility blooming on susceptibility-weighted images. Tiny punctate foci of susceptibility without T1- or T2-weighted signal abnormalities were not considered a contraindication.

Statistics

Descriptive statistics were used and recorded as mean $\pm$ standard deviation. A Fisher's Exact Test was used to assess categorical variables. A P-value ≤ 0.05 was considered significant.

Results

Population

One hundred and thirty four single ventricle patients comprise the study population. During the study period, the entire cardiac center performed 92 Stage I, 76 bidirectional Glenn/hemiFontan and 154 Fontan surgeries; the recruitment rate for the Stage I patients was 68% and for the bidirectional Glenn/hemiFontan and Fontan patients was 48%. Reasons for not being able to approach all patients included exclusion criteria, insufficient manpower, contraindication to MRI and scanner availability. Figure 1 graphically demonstrates the distribution of all patients by surgical stage as well as by age.

Postponement of Surgery

Tables 1 and 2 list data on those patients that incurred a delay in surgery due to brain injury demonstrated on MRI; a total of 6 (4.5%) had their operative date postponed. Of these, two patients were prior stage I (1% of the total, 6% of patients prior to Stage I), 3 prior to bidirectional Glenn or hemiFontan (2% of the total, 9% of Stage I patients) and one prior to

Fontan (1% of the total, 1% of bidirectional Glenn/hemiFontan patients) had delay of surgical intervention. The age at the time of MRI was typical for the respective operative stage (table 1). Surgery for those patients prior to Stage I was delayed one week compared to a delay of that ranged from 7 to 105 days for those prior to bidirectional Glenn / hemiFontan and Fontan. All patients whose surgical date was delayed eventually had successful operations with bypass and without neurological injury. Demographic and surgical data for all patients are listed in table 2. Because of the small numbers, a comparison of cardiopulmonary bypass, circulatory arrest and cross clamp times between groups precluded a definitive analysis.

MRI findings incurring a delay in surgical intervention were unexpected intracranial hemorrhage in 5 patients. These included acute temporal lobe parenchymal and subpial hemorrhage in 1, acute subarachnoid hemorrhage in 1, sizeable acute intraventricular and choroid plexus hemorrhage in 1, and non-neonatal acute subdural hemorrhage in 2. Two patients also had small foci of cerebellar hemorrhage (some patients had more than one focus of bleeding). The other patient had an unusual diffuse cerebellar cytotoxic edema and restricted diffusion involving nearly the entirety of the bilateral cerebellar hemispheres. No patients with surgical delay were on anticoagulation pre-operatively. In addition, none of the patients without surgical delay had any of the lesions described above and all patients with the lesions described above incurred a surgical delay. Figure 2 demonstrates representative MRI findings in two of these patients.

The five patients with intracranial hemorrhage had follow-up imaging after the initial MRI study which showed decrease or resolution of the initially detected lesions. Follow-up MRI of the patient with cytotoxic cerebellar edema demonstrated resolution.

No patient who experienced a postponement of their surgical date had a genetic syndrome or had premature birth. To determine whether hypoplastic left heart syndrome was a risk factor for surgical postponement in those who were in the Stage I or bidirectional Glenn / hemiFontan stage, a contingency table was utilized (table 3). The 4 patients with surgical delays in this subgroup had hypoplastic left heart syndrome (100%) compared to 44/97 (45%) with hypoplastic left heart syndrome without surgical postponement ($P=0.048$).

Comment

This study was a secondary analysis reviewing our experience from 2 prospective studies of cerebral blood flow that involved preoperative brain magnetic resonance imaging immediately prior to surgery in patients with single ventricle throughout staged reconstruction; this is one of the first studies to address incidental brain findings and the timing of surgery. Overall, 4.5% of single ventricle surgeries were rescheduled to a later date because of unexpected intracranial hemorrhage or diffuse cerebellar cytotoxic edema with a significant percentage prior to the bidirectional Glenn / hemiFontan stage. Prematurity and genetic syndromes were not present in subjects whose surgery was delayed, however, hypoplastic left heart syndrome at Stage I and the bidirectional Glenn/hemiFontan stages was found to be a risk factor for surgical postponement.

It is known that hemorrhagic brain lesions, usually local, appear in a significant proportion of neonates and infants with congenital heart disease undergoing magnetic resonance studies before [23] and after operations [24]. One risk factor is pre-existing lesions and there may be good reason to be cautious in deciding to undergo cardiothoracic surgery in patients with preexisting hemorrhagic lesions; cardiopulmonary bypass and hypothermic circulatory arrest could increase the cerebral damage by heparinization causing expansion and progression of cerebral hemorrhage [25].

A number of studies have demonstrated the development of new lesions post-operatively associated with various risk factors, a few of which were preexisting hemorrhagic lesions [7,24]. Tavani et al. [7] studied full term newborns with congenital heart disease before and after surgery with brain magnetic resonance imaging; of patients with intracranial hemorrhage, 43% worsened after the operation. Dent et al's investigation [24] concentrated on patients with hypoplastic left heart syndrome who underwent the Norwood procedure and found 53% with either new or worsened focal ischemic or hemorrhagic brain lesions by comparing pre- and post-operative brain MRIs.

There are a few dissenting investigations, one of which was published by Block et al. [14] who studied patients with transposition of the great arteries and single ventricle physiology undergoing neonatal operations. This group did not find preoperative injury worsening after surgery. In addition, the relative risk of new post-operative lesions for patients with pre-operative brain lesions compared to those without was not significant. This study, however, combined small and large brain lesions into one group, their statistical analysis combined both transposition of the great arteries and single ventricle patient together and combined all brain lesions into one group (all white matter injury and stroke for example) making their study inapplicable to the neonatal population presented in the current study. Beca et al. [26] recently studied 153 infants before and after congenital heart surgery for varied congenital heart lesions and also did not find cardiopulmonary bypass a risk factor for extension of pre-existing hemorrhage or stroke.

Limitations

Our study cannot make a recommendation on the routine use of preoperative brain MRI throughout staged surgical reconstruction because of a lack of knowledge on whether these previously occult findings are associated with a risk of extension and further injury during surgery, contribute to poor outcomes in patients who do not receive preoperative brain MRIs, or whether surgical postponement prevents harm. Although this study suggests that the strategy of delaying the operation after imaging the brain by MRI preoperatively may be useful and have clinical implications, further investigation is needed to be able to make a definitive statement.

Conclusion

Preoperative brain magnetic resonance imaging in children with single ventricle congenital heart disease throughout surgical reconstruction disclosed incidental findings which generated clinical concern (abnormalities that would increase the risk of intracranial hemorrhage as a result of anticoagulation) leading to surgical postponement in 4.5%;

hypoplastic left heart syndrome was a risk factor for this delay. The true risk of progression and need for delay of surgery associated with these lesions remains uncertain. Additional studies are needed to determine which patients are risk and therefore should undergo preoperative MRI.

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Figure 1. Pie chart with distribution of patients at the various stages of surgical reconstruction
Ages are at time of magnetic resonance imaging.

Hemorrhage

**Cerebellar
Cytotoxic
Edema**

Figure 2. Examples of 2 brain lesions leading to the decision to postpone surgery

The top 2 images are an example of hemorrhage from a patient with hypoplastic left heart syndrome. On the top left is an axial view utilizing susceptibility imaging while the top right is a coronal view utilizing T1 weighted imaging; red arrows point to the hemorrhage. The bottom 2 axial images are examples from a patient with cerebellar cytotoxic edema using diffusion weighted (left) and apparent diffusion coefficient (ADC) imaging; red arrows point to the lesion.

Table 1

Patients who experienced surgical postponement because of brain magnetic resonance findings

Prior to Stage I	Age @ Surgery	Delay	Time from last surgery	Gestational Age
1	10 days	7 days	-	40 wks
2	12 days	7 days	-	39 wks
Pre-BDG/HF				
3	5.6 mo	1.6 mo	0.59 yr	37 wks
4	4.6 mo	0.73 mo	0.44 yr	39 wks
5	4.2 mo	0.23 mo	0.37 yr	39 wks
Pre-Fontan				
6	2.8 yr	3.5 mo	2.66 yr	39 wks

BDG=bidirectional Glenn, HF=hemiFontan, mo=months, wks=weeks, yr=years

Table 2
Demographics and Surgical Variables of Patients Experiencing Surgical Postponement and Those Who Did Not

	Pre-Stage I		Pre-BDG or Hemi		Pre-Fontan	
	Delay	No Delay*	Delay	No Delay*	Delay	No Delay*
Male/female	0/2	13/18	2/1	20/11	0/1	40/26
Birth weight (kg)	4.1±0.1	3.1±0.52	3.4 ± 0.4	3.1 ± 0.7	3.4	3.2 ± 0.7
Estimated gestational age (wks)	39.6±0.6	38.86±0.85	38.5 ± 1.4	38.56 ± 1.3	39.1	38.3± 2.7
Weight at MRI (kg)	4.1±0.1	3.1±0.52	5.8 ± 0.8	6.2 ± 1.2	10.9	14.0 ± 2.3
Age at MRI	4±1.41 days	3.58±1.74 days	0.40 ± 0.06 years	0.50 ± 0.30 years	2.84 years	3.33 ± 1.07 years
Delay of Surgery	7 days	N/A	0.86 ± 0.69 months	N/A	3.50 months	N/A
Stage I CPB Time (min)	-	-	121.7 ± 35.57	87.41 ± 28.50	76.00	84.89 ± 34.65
Stage I Circulatory Arrest time (min)	-	-	56.33 ± 17.21	41.95 ± 19.99	22.00	37.65 ± 21.18
Stage I Cross-Clamp Time (min)	-	-	56.33 ± 17.21	39.91 ± 21.49	33.00	41.29 ± 20.22
BDG/Hemi CPB Time (min)	-	-	-	-	74.00	59.60 ± 20.37
BDG/Hemi Circulatory Arrest time (min)	-	-	-	-	27.00	15.43 ± 14.31
BDG/Hemi Cross-Clamp Time (min)	-	-	-	-	29.00	20.40 ± 15.01
HLHS	1	30	3	19	1	25
Other single RVs	1	1	-	9	-	32
Single LVs	0	0	-	3	-	9

* none had the hemorrhagic lesions or cerebellar cytotoxic edema described in the patients who incurred a surgical postponement. BDG=bidirectional Glenn, CPB=cardiopulmonary bypass, HF=hemiFontan, HLHS=hypoplastic left heart syndrome, LV=left ventricle, min=minutes, mo=months, RV=right ventricle, wks=weeks, yr=years

Table 3

Hypoplastic left heart syndrome and surgical delay

Pre-Bidirectional Glenn/HemiFontan or Pre-Fontan	Surgical Delay	No Surgical Delay	Total
HLHS (N)	4	44	48
Non-HLHS (N)	0	53	53
Total	4	97	101

HLHS=hypoplastic left heart syndrome