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Carrie Ciccotello January 30, 2018

Role and Utility of Cranial and Abdominal Ultrasound Screening in Patients Undergoing Cardiac Surgery

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Abstract

Role and Utility of Cranial and Abdominal Ultrasound Screening in Patients Undergoing Cardiac Surgery

By Carrie Ciccotello

Background: Ultrasound is commonly used as a screening tool for extracardiac anomalies in infants undergoing cardiac surgery. The goal of our study was to assess the utility of cranial ultrasound (CUS) and abdominal ultrasound (AUS) as a screening tool by determining the prevalence of intracranial anomalies in the Congenital Heart Disease (CHD) population and evaluating the cost associated with screening.

Methods: Both cranial and abdominal ultrasounds were performed at our center using a standardized protocol. We performed a retrospective study between 2006-2014 to obtain demographic, diagnostic, procedural and outcomes data to assess for cranial and renal pathologies.

Results: Of 1045 patients, 92 (8.3%) were found to have minor anomalies (no clinical significance) on the CUS while only 11 (~1%) were found to have major abnormalities. Of those with major pathologies, 5 had a follow-up CT and 8 had follow-up MRI. All advanced imaging confirmed CUS findings and thus suggests CUS has 100% specificity for major anomalies. Follow-up studies were performed as clinically indicated and resulted in slightly higher detection of major abnormalities via CUS (6-7%).

881 screening AUS were performed resulting in diagnosis of 247 (28%) minor abnormalities (no clinical significance) and 49 major (5.6%) renal morbidities.

Lastly, cost analysis using average hospital Medicaid fees showed that the cost of detecting one major anomaly using screen CUS is $10,835.57 and using screening AUS is $2,464.29.

Conclusion: In a large study of infants receiving screening cranial and abdominal ultrasounds, prevalence of extracardiac anomalies was very low. Of the ~1% with major cranial anomalies detected by ultrasound, all diagnoses were confirmed by CT or MRI. Thus, the CUS specificity is 100% in our experience. We also determined prevalence of major renal abnormalities to be 5.6%. We concluded that there is a major cost associated with using ultrasound as a screening test and the low yield may not justify its routine use. We suggest a strategy of directed screening and comprehensive follow up program to ameliorate added morbidity and mortality as caused by extra-cardiac abnormalities.

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Background:

Presence of extra-cardiac anomalies in newborns and infants with significant congenital heart disease is an important determinate of outcome (1). Twenty-two to forty-five percent of infants with Congenital Heart Disease (CHD) are found to have cranial, renal, pulmonary or gastrointestinal extracardiac abnormalities (2-4). These comorbidities result in significantly higher morbidity and mortality in CHD patients (1).

One of the most important long-term morbidities effecting patients with CHD has to do with more common diagnosis of cerebral atrophy, linear echodensities and intraventricular hemorrhage. These abnormal cranial diagnoses often result in long term neurodevelopmental delay, learning disability or motor deficits (4). Pre-operative assessments show that that altered cardiovascular flow patterns in utero could be responsible for some structural brain abnormalities present at birth. Postnatal hypoxia, acidosis, circulatory arrest or cardiopulmonary bypass during surgery can result in additional insults to the brain. In 1996, Van Houten et a performed a comparison of cranial ultrasound screening results between 49 CHD patients and 42 healthy normal infants to assess for prevalence of cranial abnormalities in the two populations. They found the incidence of cranial abnormalities to be 59% in CHD individuals as compared with a significantly lower incidence of 14% found in the control cohort ($p<0.001$). Due to the seemingly larger prevalence of cranial abnormalities, Van Houten et al recommended that a cranial ultrasound be a standard of care for all CHD infants (4). Similar routine screening recommendations for CHD patients were made as a result of a study performed by Te Pas et al. In this study, 50 neonates admitted to the NICU with major congenital heart diseases were assessed. They found 21 (42%) to have abnormalities on the CUS. These and multiple other studies emphasize the necessity of cranial screening due to a higher than normal prevalence of cranial abnormalities. When compared to 7% of the normal population (5), published studies show that prevalence among the CHD in anywhere between 22 to 45% based on small cohorts of 30 to 70 CHD patients (1-5)

In addition to the cranial anomalies, renal anomalies appear to present co-morbid burden on patients with congenital heart disease and seem to be me prevalent (2,3,6). Proposed mechanisms for the increased prevalence of renal abnormalities such as solitary kidney, cystic disease and congenital hydropnehrosis have to do with reduced renal blood flow (due to low cardiac output) and renal venous congestion. Cardiothoracic surgery and cardiopulmonary bypass, similar to cranial abnormalities, also impose an increased risk for renal injury (8). The incidence of such morbidities, as observed in pediatric congenital heart disease population, has been reported to be anywhere between 4.7% to 39.1% (1,6,7). One study regarding extra-cardiac manifestations in adult CHD cases by Gaeta et al concluded that CHD individuals have a 35-fold higher prevalence than the general population. In their study, they determined that 50% of their cohort had mild renal dysfunction, and 9.3% had severe dysfunction as compared to less than 5% of the normal population. Their study emphasizes the importance of screening since renal dysfunction can result in poorer long-term outcomes in addition to effecting medical and surgical treatment options (9). Similarly, Akita et al found occurrence of renal tubular dysfunction in 14 of 16 patients ages 3 to 28 (10).

The previously mentioned studies repeatedly show a higher than normal prevalence of these renal and cranial anomalies. Additionally, the study by Gonzales et al indicates strong association between impaired renal and cardiac function and mortality in CHD (3). Therefore, extracardiac abnormalities have many implications for medical and surgical intervention in CHD as well as implications for long term care. Diagnosis of structural abnormalities are important to understand premorbid burden while other significant findings such as high-grade hemorrhage may dictate surgical candidacy. Especially as surgical interventions improve, addressing long term major morbidities, perhaps by focusing on these comorbidities, has become an important focus (10). Structural renal and cranial anomalies can be easily detected using basic ultrasound imaging as has been done in many previous studies. Both cranial and abdominal ultrasounds are a non-invasive, safe and convenient imaging technique to assess structure of the brain and organs in newborns and infants.

At the cardiac intensive care unit (CICU) at Children's Healthcare of Atlanta, we perform routine surveillance ultrasounds in our pediatric heart congenital heart disease patients to assess for such cranial or renal malformations based on the conclusions of previous studies. However, the small sample sizes and varying results of previous studies calls to question if we truly understand the prevalence of cranial and renal abnormalities and the usefulness of ultrasound as a screening tool. Additionally, repeated normal findings on screenings indicates prevalence may be lower than determined in these studies. Determining the true prevalence of cranial and renal abnormalities in the CHD population is important to set expectations as well as to guide appropriate screening (3,4,11,12).

The goal of this study was largely to assess prevalence of cranial and renal anomalies in a large, representative cohort of newborns undergoing cardiac surgery in the CICU at Children's Healthcare of Atlanta. Using cranial ultrasound, we assessed prevalence of brain abnormalities in newborn and infants undergoing cardiac surgery. Additionally, we evaluated any clinically relevant cranial follow-up imaging. Secondly, using abdominal ultrasound, infants undergoing cardiac surgery were assessed for the incidence of renal anomalies. Both cranial and renal ultrasound cohorts were than evaluated to determine utility and cost-effectiveness of routine surveillance ultrasounds and the current appropriateness of use.

Methods:

The Cardiac Intensive Care Unit (CICU) at Children's Healthcare of Atlanta (CHOA) receives a large number of admitted patients for cardiac surgeries requiring cardiopulmonary bypass. As a standard of practice, newborns and neonates less than 30 days old admitted for surgeries requiring cardiopulmonary bypass received routine cranial and renal ultrasounds. Relevant patients were identified from CHOA's institutional surgical database between January 2006 and January 2014 after approval from the Institutional Review Board. There was a change of practice in 2015, thus inclusion was stopped in 2014. At CHOA, cranial ultrasounds are performed using the Phillips iE33 system®(Philips Medical Systems, Bothell, WA, USA) following standard protocol prescribed by the American Institute of Ultrasound in Medicine (AIUM) and American College of Radiography.

Regarding cranial ultrasounds (CUS), basic demographic data, diagnostic data and procedural data was collected for the included patients. Data was also collected from cranial ultrasound reports found in the electronic medical and radiology records. These tests had been reviewed by the pediatric radiologists. Recorded observations were then classified into four categories: 1) normal 2) variation of normal 3) minor abnormality and 4) major abnormality. Observations that were considered variations of normal were asymmetric appearance of ventricles or mild prominence of extra-axial fluid/space. Minor abnormalities included grade I hemorrhage, choroid plexus cysts, simple cysts and mild enlargement of ventricles. Dysgenesis or agenesis of corpus callosum, grade II or higher grade intraventricular hemorrhage, intracranial hemorrhage, Dandy-Walker malformation and significant calcifications were considered to be major abnormalities. For any comparisons in diagnosis classifications, previously published normative data was used as reference (5). Abnormal ultrasounds may have triggered follow-up studies such as a computerized tomography (CT) or magnetic resonance imaging (MRI). Data regarding these tests was recorded as well. This decision was based on the discretion of the attending physician's interpretation and on clinical assessment by radiologist or neurologist.

Patients who were included in the prior cohort were also reviewed for the abdominal ultrasound study. Basic demographic data and clinical data was collected for included patients. Abdominal ultrasound data was also collected from ultrasound reports found within the Electronic Medical Records System (EPIC). Abdominal Ultrasound results were collected and classified based on previously set standards by Gonzalez et al (3). Those of major clinical significance were defined as "a diagnosis that would generally result in changes of treatment." For example, Grade II hydronephrosis, ectopic kidney, horseshoe, multi cystic or absent kidney were considered major. Other diagnosis' such as Grade I hydronephrosis, ascites, minimal cysts and dilation were classified as minor (3). Outcome information was collected for all included patients.

Cost-utility analyses were performed using data from CHOA's hospital billing department for average Medicaid technical fees and professional fees. Cost was estimated for a cranial ultrasound (CPT 76506) as $119.67 and as $138 for abdominal ultrasound based on 2017 Medicaid fee schedule. Statistical analysis was performed using SPSS ™(IBM, Armonk, New York) version 21 for Windows ® statistical software. Descriptive statistics were used to describe demographics and categorical findings and are reported as frequencies (percentages) and totals.

Results:

Demographics:

Patient characteristics of the 1045 individuals included in the Cranial Ultrasound (CUS) study are shown in Table 1. The wide range of diagnoses evident in our study is representative of the population at Children's Healthcare of Atlanta. Almost 60% of the individuals were males. The overall sample had mean age of 8.2 days (median of 6.0 days, range 1-30 days) and a mean weight of 3.1 kg (range 1.3 -5.6 kg). The race distribution shown in Table 1 is representative of the area, with Caucasian and African American as the largest subgroups. The most common cardiac diagnoses were systemic obstructive lesions (including HLHS) with a prevalence of 39%. Other common diagnosis' included pulmonary obstructive lesions and transposition of the great arteries (19%). Average length of stay in the CICU was 12.1 days, and hospital stay was 21.6 days. Total hospital mortality was 7.6% (80 patients).

During the study period, 881 total AUS were performed. The demographics for AUS patients is shown in Table 2. The range of diagnoses in this cohort of patients receiving AUS is also representative of the population at Children's Healthcare of Atlanta with the most common cardiac diagnosis being HLHS. In the cohort of 881 patients, the average age at operation was 6 days (median of 8.1 days, range 0-30). Length of stay in the CICU was an average of 12.6, and total hospital mortality was 9% (80 patients).

Ultrasound:

Results of the CUS screening are shown in Table 3. Of 1045 neonates included in the study, 966 (92.4%) received preoperative screening ultrasounds. An additional 79 patients who did not have a screening ultrasound prior to surgery but had one after their surgery were included due to clinical relevance and are discussed below. The screening cranial ultrasound was found to be consistent with normal variations in 857 (82%) patients. Of those remaining who received ultrasound screening, minor or major anomaly was found. We defined minor anomaly as those with no clinical significance. Those considered to be a major anomaly were as follows:

dysgenesis or agenesis of corpus callosum, grade II or greater hemorrhage, intracranial hemorrhage, Dandy-Walker malformation or variant and scattered calcifications. (2, 12, 13) Of the remaining individuals, 92 (8.8%) were classified as having minor anomalies, and 11 (1.05%) were found to have major anomalies. The distribution of major anomaly and associated cardiac defects is shown in Table 4. There were no particular associations between cranial anomaly and cardiac defect. The major abnormalities did not prevent cardiac intervention, and all of these patients underwent surgical intervention as planned. Ten of eleven were discharged alive while one patient died of unrelated reasons two weeks post-operatively. Of note, the study population included 201 (out of 996) patients with diagnosis of hypoplastic left heart syndrome which is representative of the normal population. Of these patients with hypoplastic left heart syndrome, 182 had a normal CUS, 18 showed minor abnormalities and only 1 showed major abnormality (dysgenesis of corpus callosum setting of Heterotaxy and hypoplastic left sided structures).

A total of 881 screening abdominal ultrasounds were performed, and results are shown in Table 5. Of the 880 abdominal ultrasounds, 585 (66%) were reported to be normal. The remaining 296 abnormal ultrasounds were then classified as either a minor or major abnormality. Those considered to be minor were grade 1 hydronephrosis, ascites, minimal cysts, increased echogenicity and kidney dilation. Major abnormalitties were grade II hydronephrosis, ectopic kidney, horseshoe kidney, multicystic or absent kidney (12). Of the remaining 296 individuals, 247 (28%) were classified as minor, and 49 (5.6%) were classified as major. Among those diagnosed with major renal anomaly, there was no single dominant lesion, and the distribution of CHD diagnosis was representative of the cohort as a whole. Distribution of cardiac diagnosis among these 49 patients can be found in Table 6.

Cranial Ultrasound Follow Up Studies:

In our cohort of cranial ultrasound patients, a portion received follow up study for reasons such as a need for an extracorporeal membrane oxygenator, resuscitation event, abnormal neurologic examination or concern for bleeding indicated by a drop in hematocrit. Of the 857

with an initial normal ultrasound, 232 had additional ultrasound performed post-surgery based on clinical indications. Of these, 55 (23.7%) were classified as abnormal. When further classified according to our same initial categories, 39/55 were categorized as minor abnormality and 14/55 were major abnormalities (Figure 1). Thus, for patients with a previous normal ultrasound, clinically indicated follow up ultrasounds show a 6.1% (14/232) likelihood of demonstrating a major abnormality,

Of the 109 patients with initially abnormal cranial ultrasounds, 43 received follow up ultrasounds either as a follow up to the screening study or due to new clinical indication, and 66 patients had no further follow-up ultrasounds. The 43 follow-up ultrasounds resulted in 13 (30.2%) normal, 24 (56%) minor abnormality and 6 (13.9%) major abnormalities (Figure 1). Therefore, in a cohort of patients with initially abnormal screening cranial ultrasounds, the incidence of major abnormalities on a clinically indicated follow-up ultrasound was 13.9% (6/43).

No initial screening ultrasound was performed for 79 patients as they did not require cardiopulmonary bypass for their surgeries. Patients in this group primarily underwent placement of Blalock –Taussig shunt, coarctation of aorta repair or pulmonary artery band placement. They did not otherwise differ from the larger cohort in terms of age, weight or timing of surgery. These 79 patients had ultrasound performed after their surgery due to clinical indications or concerns. Most common indications for performing ultrasound were need for extracorporeal membrane oxygenator support, cardiac arrest, abnormal neurologic examination and unexplained acute anemia. Figure 2 summarizes the findings in these patients. Of these patients, 19/79 (24.1%) were abnormal and 60/79 (75.9%) were normal. The abnormal ultrasounds were then further classified into three groups: variations of normal (2/79, 2.5%), minor abnormality (11/79, 13.9%), and major abnormality (6/79 patients, 7.6%). This frequency of major abnormalities (7.6%) is similar to the frequency noted in the patients with normal screening CUS who had a clinically indicated follow up study done (6.1%).

Advanced Neuroimaging:

Further advanced imaging such as CT scan or MRI was performed on 9 of the 11 patients with major findings on the cranial ultrasound. Each of the 5 CT scans performed showed significant abnormalities and thus confirmed the ultrasound diagnosis. 8 of the 11 patients received a follow up MRI. These also all were abnormal and confirmed the cranial ultrasound findings. These findings are listed in Table 4.

Cost Analysis:

Cost analysis was performed using the published Medicaid fee schedule for conservative estimates on the analysis. We used procedural code for cranial ultrasound (CPT 76506) to obtain the 2017 Medicaid fee schedule of $119.67. Using the yield of 1.1% for major abnormalities on screening ultrasound, the cost to detect one major anomaly using screen CUS is $10,879.10. The same estimate for clinically indicated ultrasounds, with an average yield of 6 to 7% for major abnormalities, is $1805.92, and therefore a substantially improved cost-yield. For abdominal ultrasound, 2017 Medicaid fee schedule indicated an estimated cost of $138. Using the yield of 5.6% for major anomalies, the cost to detect one major renal abnormality is $2,464.29. It is important to note that these are based on the lowest possible denomination of the Medicaid fees schedule and do not actually reflect either the cost or the hospital charges, which are significantly higher.

Discussion:

Among this large cohort of neonates undergoing cardiac surgery, major intracranial abnormalities occurred at a prevalence of ~1% as assessed by a screening preoperative cranial ultrasound. This is a significantly lower prevalence finding than previous publications. For example, our results found a much lower prevalence than an early study done to recognize the relationship between cranial abnormalities and congenital heart disease. This study, by Glauser et al, assessed 41 newborns with hypoplastic left heart syndrome and reported that 29% of the 41 infants had either minor or major abnormalities. Four of the infants, or 10%, were classified as having major abnormalities with 3 cases of agenesis of the corpus callosum and 1 case of holoprosencephaly. Additionally, 27% were found to have micrencephaly or an autopsy brain weight greater than 2 SD below the age mean (15). Our study, in comparison, included a much larger proportion of 201 total patients with hypoplastic left heart syndrome. Of our large cohort, only 1 was found to have a major abnormality on the screening cranial ultrasound (<1%).

In comparison to the study by van Houten et al, our study consisted of a much larger, more representative cohort of 966 infants that underwent ultrasound before their surgeries as was the practice at CHOA. Van Houten et al found the incidence of cranial ultrasound abnormalities to be 59% in a cohort of 28 CHD individuals. This was significantly higher than the 14% of cranial anomalies found in their control cohort (4). Another notable fact is that the 14% incidence of abnormalities in the van Houten et al normal cohort was higher than the 7% incidence of cranial abnormalities in significantly larger studies of solely normal infants (14). They, in addition to the study performed by Te Pas et al, recommended routine cranial ultrasound for all CHD infants in addition to neurodevelopmental follow-up. Te Pas et al, who found 21/50 (42%) infants to have abnormalities on the CUS, also found more frequent abnormalities in neonates with hypoplastic left heart syndrome (63%) than in those with transposition of the great arteries (5). Other studies contradict Te Pas et al in that there is any association of cerebral anomalies with left sided lesions. For example, Dittrich et al performed a meta-analysis to

quantify the prevalence of prenatal brain abnormalities in fetuses with CHD. In a total of 221 cases, the analysis showed no clear associations between particular types of CHD and occurrence of brain abnormality (16). In our view, associations of particular heart defects with major cerebral abnormality by Te Pas et al may represent a type I error due to the small sample size (5). In our much larger study, we did not identify any associations between particular cardiac defects and the CNS abnormalities.

Another study by Rios et al set out to compare the utility CUS versus MRI for preoperative imaging in patients with CHD. They found 5/167 (3%) patients to have an abnormal cranial ultrasound. Of these, 4 had intraventricular hemorrhage and 1 had periventricular leukomalacia. The 4 patients with intraventricular hemorrhage on ultrasound did not show intraventricular hemorrhage on MRI, representing an 80% false positive rate. They report MRI abnormalities in 44/167 (26%) patients of which 32/44 were white matter injury. This study was significant in demonstrating the extent of white matter injury present preoperatively in patients with congenital heart disease. However, the findings of significant errors with ultrasound are in contrast to other studies that have shown validity of the tool (3,4,6). The study findings of an 80% false positive rate for ultrasound diagnosed intraventricular hemorrhage is in stark contrast to well accepted neonatal literature that supports the use of ultrasound for cranial assessment and documents high degree of sensitivity and specificity when compared to MRI (17-19). It is also important to note that they excluded any patients with potential genetic or malformation syndromes associated with neurodevelopmental impairment or any one with abnormality of neurologic assessment as well as patients that were not undergoing cardiac surgery. Our retrospective study, contrastingly, was not designed to answer the question about sensitivity or specificity of CUS. However, all of our 11 patients with significant abnormalities on screening ultrasound did have confirmation with advanced imaging in the form of CT scan or MRI. In each of our cases, the advanced imaging confirmed the ultrasound findings therefore yielding no false positives in patients with a major CNS abnormality (100% specificity). Additionally, unlike the Rios study, our goal was not focused on assessing for white matter

injury which necessitates an MRI, but rather the established diagnostic capabilities of cranial ultrasound using a much larger cohort of one thousand patients undergoing cardiac surgery.

Abnormalities detected through cranial ultrasound, as shown by many studies, often include abnormalities of corpus callosum, Dandy-Walker malformations, intraventricular hemorrhages and ventricular enlargement (or micrencephaly). Certain hypotheses that show commonalities between these abnormalities have been proposed. The findings of ventriculomegaly, enlargement of the subarachnoid space, or micrencephaly (reduction in brain size) may be a result of reduced brain growth during the prenatal developmental phase in patients with CHD. Fetal ultrasound studies as well as pre-and post-natal MRI studies have reported on such brain growth patterns in patients with CHD (20,21). Observed patterns in white matter development among CHD patients are proposedly due to hemodynamic and metabolic alterations (4,16,21). Metabolic stressors such as relative hypoxia and glucose deprivation as a result of lactic acid accumulation in the brain are suggested mechanisms leading to Encephaloclastic injury. Developmental delays and abnormalities can also be further contributed to by genetic abnormalities and secondary disruptions. For example, patients with left sided obstructive lesions have a substantially lower antegrade flow from the aorta which leads to hypoperfusion of the brain (20-21). Although there is retrograde perfusion from the ductus arteriosus in these situations, the altered flow patterns may significantly affect the brain perfusion and development in a fetus. Masoller et al have shown that fetuses with CHD demonstrated significantly lower middle cerebral artery pulstaility index and cerebro-placental ration Z scores compared to controls. These findings were even more evident in cases of CHD associated with compromised oxygenated blood delivery to the brain (left outflow tract obstruction and transposition of the great arteries). Thus, Masoller et al suggest longitudinal follow up with ultrasound Doppler studies as a possible way of identifying higher risk patients at an earlier time (20-21). However, it is currently unclear if identification of these higher risk patients early in fetal life would allow for interventions that would alter brain development in these patients.

Post-natal events can also play a significant role in brain injury. White matter injury, for example, correlates with post-natal hypoxia and acidosis. Interventions such as balloon atrial septostomy and cardiopulmonary bypass (especially with long circulatory arrest, prolonged hypothermic arrest), can independently cause both grey and white matter injury that has long standing impact (12,20,22,23,26). Prolonged hospitalization and mechanical support or cardiopulmonary resuscitation during this time have also been shown to contribute to function or structural brain abnormalities and neurodevelopmental delay. Although relationships between CUS abnormalities and CHD are difficult to determine, perinatal stressors such as significant hemodynamic swings, hypoxia and reperfusion injury are certainly plausible mechanisms for CUS findings such as intraventricular hemorrhages.

Similarly, congenital heart lesions, tricuspid regurgitation, atrial septal defects, pulmonary hypertension and pulmonic regurgitation are all heart lesions that have been previously associated with renal dysfunction. Our retrospective study found major renal abnormalities occurring in CHD infants at a prevalence of ~5% as assessed by a screening preoperative abdominal ultrasound. Compared to the studies by Gaeta et al and Akita et al, our prevalence finding was much smaller. Gaeta et al, while assessing adult CHD cases, concluded that CHD individuals have a 35-fold higher prevalence than the general population (9). Akita et al found occurrence of renal tubular dysfunction in 14 of 16 patients ages 3 to 28 (10). Our study consisted of a cohort (n=881) of solely neonates and thus is a larger, more representative sample. Other factors influencing the seemingly high prevalence of renal anomalies in these previously published studies may be due to the presence of additional extracardiac anomalies. In a study by Murugasu et al, the prevalence of renal tract anomalies in a cohort of 109 patients with isolated CHD was 4.7%. While this value does not significantly differ from our conclusion, they found that individuals with associated extracardiac morbidities had a 39.1% incidence of renal tract anomalies indicating the need for screening in those with multiple congenital defects (24). However, based on our study and that of Voisin et al, there seems to be no particular associations with cardiomyopathy and prevalence or type of renal tract morbidity (25).

There are no other large-scale studies to compare the cost-yield related to routine cranial ultrasound screening prior to cardiac surgery. Nor are there large scale abdominal ultrasound incidence and usefulness studies. Our cost to yield for detection of major abnormality was very high even when using very conservative Medicaid fee schedule. Hospital charges for these, as well as follow-up studies, amount to a significant burden on healthcare cost with an associated low diagnostic yield.

Limitations:

The cranial and abdominal aspects of this study are limited by the retrospective study design. However, due to the completeness of the data, the goals of the study were met.

Follow-up imaging with CT or MRI was performed as indicated by cranial ultrasound, on clinical need or on radiologists' recommendations and thus introduces some inconsistency. The study was focused on patients undergoing cardiac surgery only and not designed to answer a question about incidence of abnormal brain and abdominal imaging in all patients with congenital heart disease or about neurodevelopmental assessment in these patients. Similarly, the cost-analysis is presented primarily to drive the notion of healthcare expense and not to perform a cost-benefit or cost-effectiveness analysis neither of which can be appropriately performed in our population.

When multiple abnormalities are present, patients are very likely to have underlying chromosomal abnormalities. This study did not address this aspect although genetic testing may have been performed. When available, data regarding genetic tests was collected but not analyzed for the cohort.

Conclusion:

Based on our large, single center study, there is a low utility of performing routine preoperative cranial and abdominal ultrasounds on neonates with congenital heart disease due to a very low yield. However, when major anomaly is detected by the cranial ultrasound, the specificity is 100% in our experience. This low yield of major cranial and abdominal diagnoses results in a major cost to perform a regular pre-operative screening test and may not justify its routine use for screening. However, because comorbidities do present long term effects, we recommend that money spent on prescreening be reallocated to implement comprehensive neurologic and renal assessment and monitoring program to improve long term outcomes.

Tables and Figures:

Table 1: Patient Characteristics for Neonates Undergoing Cranial Ultrasound Screening

Age at Operation	1-30 days
Median	6.0 days
Mean	1-30 days
Gender	
Male	623 (59.6%)
Female	422 (40.4%)
Race	
Caucasian	577 (55.21%)
African American	303 (28.99%)
Hispanic	99 (9.47%)
Asian/Other	66 (6.31%)
Weight (mean, range)	3.1 (1.3-5.6) kg
Height (mean, range)	49.1 (32-59) cm
Diagnosis	
Systemic obstructive lesions (including HLHS)	410 (39.23%)
Pulmonary obstructive lesions	186 (17.79%)
Transposition of great arteries	200 (19.13%)
Single Ventricle, complex	72 (6.88%)
Total anomalous pulmonary venous return	64 (6.12%)
Truncus arteriosus	48 (4.59%)
Septal defects (including AVSD, VSD, AP window)	28 (2.67%)
Congenitally corrected transposition of great arteries	9 (0.86%)
Miscellaneous	28 (2.67%)
Total	**1045**
Procedural Details	
Cross clamp time (mean)	55.57 min
Perfusion time (mean)	143 min
ICU length of stay (mean, range)	12.17 (2-282) days
Total length of stay (mean, range)	21.61 (2-289) days
Mortality	80 (7.6%)

Table 2: Patient Characteristics for Neonates Undergoing Abdominal Ultrasound Screening

Age at Operation	(0-30 days)
Median	6
Mean	8.1
Total	**881**
Procedural Details	
Cross clamp time (mean)	55.4
Perfusion time (mean)	144.3
Total length of stay (mean,)	21.5
Mortality	80 (9%)

Table 3: Findings of Cranial Ultrasound Screening

Normal/ Normal Variant (Asymmetric appearance of ventricles, Mild prominence of extra-axial fluid /spaces)	863 (82.57%)
Minor Findings (Grade I hemorrhage**,** Choroid plexus cysts, Simple cysts / echogenic focus**,** Mild enlargement of the ventricles	92 (8.80%)
Major Findings (Dysgenesis / agenesis of corpus callosum**,** Grade II or greater intraventricular hemorrhage**,** Intracranial hemorrhage**,** Dandy-Walker malformation**,** Significant calcifications suggestive of infection	11 (1.05%)
No screening CUS*	79 (7.55%)

*Patients undergoing cardiac surgery within 30 days of life without an initial CUS were included if they had a follow-up CUS postoperatively that was abnormal due to clinical relevance.

Table 4: Major abnormalities on screening cranial ultrasound and associated cardiac defects

Cranial Ultrasound Findings	Follow-up Imaging (CT/MRI)	Cardiac Defect	Extracardiac Defect (if present)	Age at Surgery (days)	Outcome
Agenesis of corpus callosum	Complete agenesis of the corpus callosum with associated colpocephaly	Truncus Arteriosus		21	Died 2 weeks post-surgery
Dandy- Walker variant	Inferior vermian hypogenesis	Transposition of great arteries with VSD	Hydronephrosis	4	Alive at discharge
Significant hydrocephalus and thinning of corpus callosum	Trilateral ventricular enlargement	Transposition of great arteries		15	Alive at discharge
Right occipital hemorrhage	Chronic and early to late subacute blood in the right occipital lobe corresponding to area of hemorrhage on cranial ultrasound	VSD + Aortic arch hypoplasia		25	Alive at discharge
Grade III intraventricular hemorrhage (bilateral)	Bilateral grade 3 germinal matrix hemorrhages, with intraventricular hemorrhage and mild hydrocephalus	VSD + Coarctation of aorta		7	Alive at discharge
Dandy-Walker variant	None performed	VSD + Coarctation of aorta		6	Alive at discharge
Parallel configuration of the ventricular system with partial agenesis of corpus callosum	Callosal dysgenesis and small bilateral colobomas suggestive of CHARGE syndrome	Aortic arch hypoplasia	CHARGE syndrome	4	Alive at discharge
Scattered parenchymal	None performed	Pulmonary atresia, VSD		18	Alive at discharge

calcifications and lenticulostriate vasculopathy					
Cystic, echogenic area within left anterior frontal lobe representing resolving hemorrhage or infarct. Additionally, mild dilatation of the bilateral frontal horns and moderate dilatation of the left lateral ventricle	Abnormal sulcation in the bilateral frontal lobes and ateromedial left frontal lobe and posteromedial right parietal lobe intraparenchymal hemorrhages.	Double outlet right ventricle	Ascites	29	Alive at discharge
Dysgenesis of corpus callosum	Extensive gray matter heterotopia with mega cisterna magna and eye abnormalities suggestive of filamin A gene mutation#	Single ventricle, Heterotaxy syndrome		3	Alive at discharge
Dandy-Walker variant	Consistent with CHARGE syndrome,Dandy-Walker malformation and atretic right globe	Vascular ring	CHARGE syndrome, absent left kidney	13	Alive at discharge

- Full gene sequencing did not detect any pathogenic variant for filamin gene related disorders

Table 5: Findings of Abdominal Ultrasound Screening

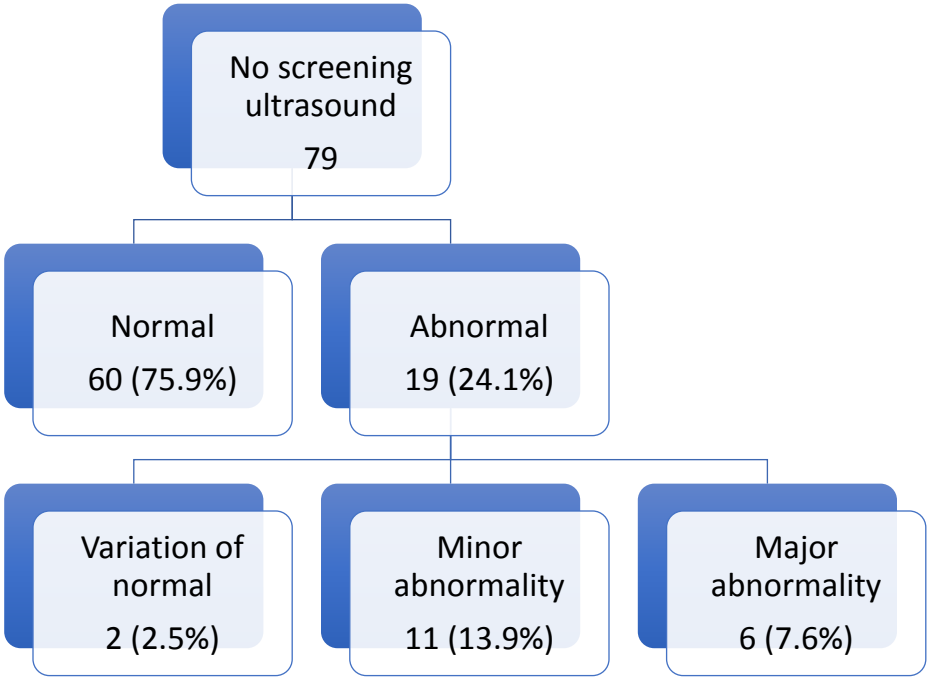
Normal	585 (66%)
Minor Findings (Grade 1 hydronephrosis (minimal dilation), ascites, minimal cysts, increased echogenicity, kidney dilation	247 (28%)
Major Findings (Grade 2 hydronephrosis, ectopic kidney, horseshoe, multi cystic, absent kidney)	49 (5.6%)
Total	881

Table 6: : Major abnormalities detected on screening abdominal ultrasound and cardiac defect distribution

Cardiac Defect	
Aortic Arch Hyopolasia	2 (4%)
Coarctation of Aorta	5 (10.2%)
DORV	6 (12.2%)
Hypoplastic Left Heart Syndrome	3 (6.2%)
Interrupted Aortic Arch	2 (4%)
Interrupted Aortic Arch +VSD	6 (12.2%)
Pulmonary Atresia + VSD	4 (8.2%)
TGA + IVS	4 (8.2%)
TGA + VSD	3 (6.2%)
Truncus arteriosis	2 (4%)
VSD + Coarctation of aorta	3 (6.2%)
Other	9 (18.4%)

Figure 1: Follow-up Studies for Screening Cranial Ultrasounds

Figure 2: Follow-up studies for patients without screening cranial ultrasounds



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