Impact of Prenatal Diagnosis in Survivors of Initial Palliation of Single Ventricle Heart Disease

Subtitle: Analysis of the National Pediatric Cardiology Quality Improvement Collaborative Database

Short title: Impact of Prenatal Diagnosis in NPCQIC Database
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David W. Brown, MD[1], Katie E. Cohen, BA[1], Patricia O'Brien, CPNP [1], Kimberlee Gauvreau, ScD[1], Thomas S. Klitzner, MD-PhD[2], Robert H. Beekman III, MD[3], John D. Kugler, MD[4], Gerard R. Martin, MD[5], Steven R. Neish, MD[6], Geoffrey L. Rosenthal, MD-PhD[7], Carole Lannon, MD, MPH[3], Kathy J. Jenkins, MD[1], on behalf of the JCCHD National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC)

[1]Departments of Cardiology and Cardiac Surgery, Boston Children's Hospital, Boston MA; [2]Mattel Children's Hospital UCLA, Los Angeles CA; [3]Cincinnati Children's Hospital Medical Center, Cincinnati OH; [4]University of Nebraska Medical Center, Omaha NE; [5]Children's National Medical Center, Washington, DC; [6]Texas Children's Hospital, Houston, TX; [7]University of Maryland School of Medicine, Department of Pediatrics, Baltimore, MD.

Address for correspondence: David W. Brown, MD, Department of Cardiology, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, Tel: (617) 355-6429, Fax: (617) 739-6282, Email: david.brown@cardio.chboston.org

Abbreviations: CHD, congenital heart disease**;** BDG, bidirectional Glenn operation**;** HLHS, hypoplastic left heart syndrome**;** JCCHD, Joint Council on Congenital Heart Disease**;** NPCQIC, National Pediatric Cardiology Quality Improvement Collaborative**;** PD, prenatal diagnosis**;** RVPA, right ventricle to pulmonary artery conduit; S1P, Stage 1 Norwood operation or equivalent; SVD, single ventricle heart disease

Key words: Cardiovascular Disorders, Cardiovascular Surgery, Quality Improvement; Congenital Heart Disease

Abstract

Background: Among infants with single ventricle congenital heart disease (SVD) requiring Stage I palliation (S1P), the impact of prenatal diagnosis (PD) on outcomes has been variably characterized. We investigated the impact of PD in a large multi-center cohort of survivors of S1P in the National Pediatric Cardiology Quality Improvement Collaborative (NPCQIC) registry.

Methods: Retrospective analysis of demographic and outcomes data among infants enrolled in the NPCQIC database; eligibility includes SVD requiring S1P and survival to discharge.

Results: From 43 contributing surgical centers, 591 infants had data available through time of BDG (519) or interstage death (55). Median gestational age was 39 weeks (31-46), and 66% had variants of hypoplastic left heart syndrome. PD was made in 445 (75%), with significant variation by center (p=0.004). While infants with PD had slightly lower gestational age at birth (p<0.001), there were no differences in birth weight, presence of major syndromes or other organ system anomalies. Those without PD were more likely to have atrioventricular valve regurgitation (p=.002), ventricular dysfunction (p=0.06), and pre-operative risk factors including acidosis (p<0.001), renal insufficiency (p=0.007), and shock (p=0.05). Post-operative ventilation was shorter in the PD group (9 vs. 12 d, p=0.002). Other early post-operative outcomes, interstage course and outcomes at BDG were similar between groups.

Conclusions: In a large cohort of infants with SVD surviving to hospital discharge after S1P, PD showed significant inter-site variation and was associated with improved preoperative status and shorter duration of mechanical ventilation. The significance of such associations merits further study.

Introduction

      Approximately 4000 infants with single ventricle congenital heart disease (SVD) are born in the United States each year[1]. Among congenital cardiac defects, those with SVD physiology remain the most complex and have the highest rates of associated morbidity and mortality. Children with hypoplastic left heart syndrome (HLHS) and other forms of left heart hypoplasia face the highest mortality rates, up to 30-45% in their first four years of life, with typical mortality rates of 15-20% occurring around the Stage 1 palliation (S1P), and "interstage" mortality rates of 10-15% prior to bidirectional Glenn operation (BDG)[2,3]. In addition to mortality, associated morbidities include poor growth, feeding difficulties, vocal cord paralysis, phrenic nerve injury, renal dysfunction, seizures and developmental delay, and frequent, often prolonged, hospitalizations[4].

      Neonates with unrecognized HLHS and other forms of SVD are frequently critically ill upon presentation, and often require resuscitation and intensive medical stabilization before S1P can be performed. With dramatic improvements in ultrasound technology and widespread availability, one prospect for improved outcomes for infants with SVD requiring S1P is prenatal diagnosis (PD) by fetal echocardiography. Recently, detection rates as high as 75% for SVD have been reported with prenatal ultrasound[5]. However, the reported impact of PD for infants with HLHS and other forms of SVD on outcomes has been mixed, with variable results in retrospective studies. Data from the Pediatric Heart Network Investigators demonstrated that PD was not associated with a reduction in pre-operative death in a large cohort of infants[5]. One single-center study of HLHS patients demonstrated improved pre-operative clinical status including less acidosis, tricuspid regurgitation, and ventricular dysfunction among those with PD, as well as improved short-term survival after S1P[6]. However, no other studies have found a survival benefit from PD in this setting. Indeed, a follow-up study from the same center a decade later[7] found that PD of HLHS was no longer associated with improved survival, and was not associated with post-operative morbidity, duration of ventilation, or hospital length of stay (LOS);

in that study and others, PD has been associated with lower birth weight and gestational age, two risk factors for worse outcomes from congenital heart surgery[8-10].

The National Pediatric Cardiology Quality Improvement Collaborative (NPCQIC) was established in 2008, with goals of the first project to reduce mortality and improve the quality of life of infants with HLHS and SVD variants discharged to home during the interstage period between discharge from S1P and BDG. The NPCQIC has expanded into a nation-wide data collection network of over 50 participating surgical centers in North America. A previous review of the first 100 infants in the NPCQIC registry demonstrated an association of PD with improved measures of peri-operative morbidity, although not the focus of that study[11]. We therefore sought to further explore the association of PD with outcomes including pre-operative risk factors, post-operative hospital course, and outcomes through time of BDG in the first 591 patients enrolled in the NPCQIC registry.

Methods

All infants followed at participating centers and meeting the criteria for enrollment into the NPCQIC registry were identified for potential enrollment. Inclusion criteria for entry into this registry required 1) diagnosis of SVD such as HLHS requiring S1P operation or similar variant, and 2) survival to and discharge from the hospital prior to BDG. After verification of eligibility, consent was obtained and patients' data included in the registry. All data collection was performed after obtaining IRB approval at each participating institution. The first 591 patients entered into the database include those born between June 2008 and June 2012. The NPCQIC registry database was developed by JCCHD Task Force members using Vanderbilt University's REDCap software to manage the data. De-identified data was entered by each participating site into the web-based REDCap database. Each institution had access to only their patients' data in REDCap, but data from all the participating sites can be aggregated there.

Multiple data elements were collected from the time of the patient's birth through their discharge from their BDG operation. The current study utilized data that included the presence

of PD, patient demographic and anatomic factors including chromosomal anomalies and other associated organ system abnormalities, the presence of pre-operative risk factors, and characterizations of post-operative hospitalization such as choice of initial palliation, length of intubation, significant post-op rhythm abnormalities, requirement of ECMO, major post-operative procedures, post-operative complications, and any necessary cardiac reoperation. These data points were collected during the initial hospitalization for S1P surgery, as well as during interstage clinic visits and readmissions, and finally, during the hospitalization for patients' second stage palliative surgery, the bidirectional Glenn procedure. In addition, interstage data on readmissions, unscheduled readmissions and death were examined.

Data for the first 591 patients entered into the database was analyzed. Categorical variables were summarized using frequencies and percents, and compared for subjects with and without a prenatal diagnosis using Fisher's exact test. Continuous variables were summarized using medians with either 25th and 75th percentiles or the range as specified, and compared using the Wilcoxon rank sum test. To examine center-specific variability, we only considered sites entering ≥10 patients in the NPCQIC registry over the 48-month time period of the study.

This study was performed according to a protocol approved by the internal review boards of all participating institutions, including the Committee for Clinical Investigation at Boston Children's Hospital. The authors had full access to the data and take full responsibility for its integrity. All authors have read and agree to the manuscript as written.

Results

Patient Characteristics

A total of 592 patients from 43 participating collaborative sites met inclusion criteria and were entered into the NPCQIC REDCap database registry during the study period from June 2008-June 2012. Summary demographic information is listed in Table 1. Patients were predominantly male (61%), with a median birth weight of 3.2 kg; the majority of patients had a subtype

of HLHS (66%). Syndromes or genetic disorders were present in 9% and major non-cardiac or-

gan system anomalies in 8%. Pre-operative risk factors were present in the majority (53%) of

patients, including mechanical ventilatory support, acidosis, arrhythmia requiring therapy, renal

insufficiency and shock.

Congenital heart disease was diagnosed prenatally in 445 (75%) patients, with missing

data on timing of diagnosis in only 1 patient; PD did not vary by race or ethnicity. There was

significant variation among contributing centers in the frequency of PD (p=0.004); Figure 1 de-

picts the center-to-center variation among those 16 sites entering ≥10 patients in the registry,

which varied from 40% at Site I to 100% at Site J.

PD and Pre-operative Status

Pre-operative characteristics analyzed by the presence or absence of a PD are shown in

Table 2. PD was associated with younger gestational age (Table 2, Figure 2, p<0.001). A pri-

mary cardiac diagnosis of HLHS variant was more common in the PD group (p=0.05). Those

infants without PD had a higher incidence of ≥ moderate ventricular dysfunction (p=0.002) and a

strong trend for ≥ moderate systemic AV valve regurgitation (p=0.06). The prevalence of syn-

dromes or genetic abnormalities as well as major non-cardiac organ anomalies did not differ

between groups.

Pre-operative risk factors were more common in those infants without PD (68% vs. 48%,

p<0.001). While absolute lowest pH prior to intervention was similar between groups, acidosis

was more common in those without PD (34% vs. 14%, p<0.001). Pre-operative mechanical ven-

tilator support was more common in those without PD (51% vs. 29%, p<0.001), as well as renal

insufficiency (12% vs. 5%, p=0.007) and shock (2% vs. <1%, p=0.05).

Neonatal Surgery and Subsequent Hospitalization

While median age at S1P was lower in those with PD (5 days vs. 8 days, p<0.001), median

weight at S1P did not differ by group and the type of S1P performed was similar between

groups (Table 3), the most common being the Stage I with right ventricle to pulmonary artery

conduit. Post-operative length of intubation was significantly longer in those without PD (12 vs. 9 days, p=0.002), although total hospital length of stay was similar.

Following S1P, post-operative complications occurred in the majority of both groups (65% entire cohort) but did not differ by PD status (Table 3). The most common complications included arrhythmia requiring treatment (96 patients, 16%), respiratory insufficiency requiring mechanical ventilation >14 days (76, 13%), chylothorax (65, 11%), recurrent laryngeal nerve injury/vocal cord paresis (59, 10%), necrotizing enterocolitis (32, 5%), and central line infection (32, 5%).

Cardiac reoperation, post-operative catheterizations, and non-cardiac post-operative procedures were also relatively common in both groups. Cardiac re-operations were necessary in 19% of the entire cohort and did not differ by PD. The most common cardiac reoperations included chest exploration for bleeding or tamponade (59 patients, 10%), ECMO cannulation/decannulation (49, 8%), mediastinal or sternal debridement (16, 3%), BT shunt revision (12, 2%), RV-PA conduit revision (10, 2%), conversion to alternative palliation type (7, 1%), and aortic arch repair (5, 1%). While post-operative catheterizations were slightly more common in the PD group (23% vs. 14%, p=0.04), major non-cardiac post-operative procedures were similar between groups (32% vs 33%, p=0.92).

Interstage Period and Glenn Surgery

At discharge after S1P, patients with and without PD had similar median weights (3.5 kg vs. 3.6 kg, p=0.27, see Table 4) and similar cutaneous oxygen saturation levels (83% for both groups, p=0.20). The interstage period was notable for a similar frequent rate of readmissions in both groups (72% PD vs. 71% no PD), with similar rate of unscheduled readmissions (51% PD vs. 50% no PD). There were 55 interstage deaths (9%) prior to BDG, with no statistically significant difference between groups (9% PD vs. 11% no PD, p=0.42).

Survivors to BDG (n=519, 88% cohort) underwent surgery with younger age at BDG in the PD group (4.9 mos vs. 5.3 mos, p=0.007), although no significant difference in weight (6.1

vs 6.2 kg, p=0.08) or oxygen saturation at BDG (79% vs. 78%, p=0.20).   PD status was not as-
sociated with prevalence of complications after BDG (40% PD vs. 35% no PD, p=0.34) or medi-
an hospital LOS (8 days PD vs. 7 days no PD, p=0.48).

Discussion

This study of the impact of PD in a large, multi-center cohort of infants with SVD discharged
to home after S1P from the NPCQIC database demonstrates several findings. First, PD of SVD
is common, occurring in 75% of our cohort; this finding is similar to that from the Pediatric Heart
Network Investigators[5], and places SVD among congenital heart lesions most frequently
detected by fetal echocardiography[12], most likely due to severity of the abnormality resulting
in improved detection[9]. Despite this, we found marked variation in the rate of PD across
centers, even when considering only those sites with higher enrollment in the registry (≥10
patients) as a proxy for center volume (Figure 1), with PD rates as low as 40% in some sites
and 100% in others. While the rate of PD did not vary by race or ethnicity, such differences in
PD rates are likely attributable to complex differences in multiple patient factors such as
geographic proximity to medical services, socioeconomic status, and insurance coverage[12],
as well as variation in the availability of and expertise in fetal echocardiography. Regardless,
this marked variation in PD across enrolling sites represents a target for further quality
improvement efforts.

This study also demonstrated significant associations between PD and a reduction in a
number of important measures of pre-operative morbidity and risk, including significant AV valve
regurgitation, ventricular dysfunction, acidosis, pre-operative mechanical ventilation, renal
insufficiency, and shock. As noted previously, several studies have demonstrated an
association of PD with some measures of improved pre-operative status in this patient
population[6,7], although generally single-center studies over large time periods. While most
studies have failed to find a significant association with PD and short-term post-operative

outcomes, we did find a significantly shorter duration of post-operative mechanical ventilation in those with PD (9 vs 12 days). However, this did not result in shorter hospital LOS, and most other measures of outcomes including post-operative complications, interstage course including death, and course at BDG were similar between groups. Presumably, the shorter duration of mechanical ventilation in PD infants was related to the reduction in pre-operative risk factors such as pre-operative mechanical ventilation, acidosis, renal insufficiency, and shock. While the impact of reduced pre-operative risk factors and shorter duration of mechanical ventilation associated with PD may not manifest in short-term hard outcomes such as length of stay or 30-day mortality, there may be other long-term benefits such as improved neurodevelopment that require further evaluation and study, and are beyond the scope of the current investigation. Indeed, several studies have found longer length of mechanical ventilation after Norwood to be an independent risk factor for worse neurodevelopmental outcomes on formalized testing in HLHS patients (particularly cognitive function)[13,14]; one major role for PD in this group of infants may be to allow for the mitigation of this and other similar factors that may impact subsequent neurodevelopment.

Finally, several studies have shown lower birth weight and reduced gestational age in infants with PD, including those with HLHS[7,9]. This is particularly important as birth weight has been demonstrated in multiple studies including one prospective randomized multi-center trial[15] to be an independent risk factor for 30-day and hospital mortality. While our analysis also showed that while infants with PD had a lower gestational age than non-PD infants (Table 2 and Figure 2), the differences in gestational age were small compared to previous studies, and there was no difference in birth weight. Our findings may be reflective of a recent trend to avoid "early-term" (37-38 weeks gestation) elective deliveries of infants with known SVD, given recently published research demonstrating increased morbidity and mortality after heart surgery for critical congenital heart disease associated with early-term infants[8]. As the trend away from

earlier elective delivery for patients with PD continues, the positive effect of PD on pre- and post-operative outcomes is likely to become more significant.

Study Limitations

There are several limitations to this study. Most importantly, because study eligibility and inclusion in the registry requires survival to hospital discharge after S1P, infants with SVD who either die in the hospital before or after S1P, or stay in the hospital until BDG, are not included in the NPCQIC database. Thus we are unable to analyze any data regarding the association of PD with outcomes in these groups of patients, who likely represent a more severely ill and less stable population of SVD infants in whom PD could be postulated to have more demonstrable short-term impact on outcomes including hospital mortality. Secondly, as informed consent is required for inclusion in the database, selection bias may have occurred, although as this is a non-interventional study the consent rate for eligible patients among participating centers is high; recent audit of participating sites reported 95% consent rate for eligible patients. Additionally, the registry does not collect information on surgical technical performance, which has been correlated with short-term surgical outcomes in this population[16,17], and may be an important confounder. Finally, as it is currently organized, the registry does not collect data on other outcomes that may be associated with PD, such as parental stress, which are therefore not addressed in this study.

Conclusions

In summary, in this study of a large, multi-center cohort of infants with SVD surviving to hospital discharge after S1P, PD was common but showed significant inter-site variation. PD was associated with reduced preoperative risk factors and shorter duration of mechanical ventilation after S1P, but not interstage course or outcomes at BDG. The significance of such associations on other outcomes including neurodevelopment merits further study. Additional

investigation of variables affected by PD, such as parental stress, may help to fully understand the impact of PD in this high-risk group of infants and improve long-term outcomes for patients and families during and after the interstage period.

Funding Sources

Disclosures

There are no disclosures to report.

Table 1. Patient Enrollment Summary Information (n=592)

Demographic Information	Number (%), Median	IQR	Range
Male	364 (61%)		
Birth weight (kg) [n=585]	3.2	2.9, 3.5	1.4-5.0
Gestational age (wks)	39	38,39	31-46
Primary Cardiac Diagnosis [n=590]			
Hypoplastic left heart syndrome	388 (66%)		
HLHS with MA/AA	211 (36%)		
HLHS with MS/AS	80 (14%)		
HLHS with MS/AA	80 (14%)		
HLHS with MA/AS	17 (3%)		
Double outlet right ventricle with left sided hypoplasia	33 (6%)		
Double inlet left ventricle	23 (4%)		
Unbalanced AV canal	23 (4%)		
Double inlet right ventricle	2 (<1%)		
Other	121 (20%)		
Secondary Diagnoses			
Restrictive atrial septum	98 (17%)		
AV valve regurgitation*	17 (3%)		
Ventricular dysfunction*	15 (3%)		
Arrhythmia requiring therapy	6 (1%)		
Other	111 (19%)		

Lowest pH Pre- Intervention [n=564]	7.29	7.23,7.34	6.62-7.79
Any Major Syndrome	52 (9%)		
Heterotaxy	13 (2%)		
Turner	5 (1%)		
Down Syndrome	4 (1%)		
Other Chromosomal Anomaly	24 (4%)		
Other	8 (1%)		
Any Major Anomaly of Organ System	50 (8%)		
Renal/GU	19 (3%)		
CNS	13 (2%)		
GI	14 (2%)		
Endocrine	9 (2%)		
ENT	8 (1%)		
Musculoskeletal	7 (1%)		
Pulmonary	7 (1%)		
Prenatal Cardiac Diagnosis	445 (75%)		

*Defined as ≥moderate

IQR, intraquartile range; HLHS, hypoplastic left heart syndrome; AA, aortic atresia; MA, mitral atresia; AS, aortic stenosis; MS, mitral stenosis; AV, atrioventricular; GU, genitourinary; CNS, central nervous system; GI, gastrointestinal; ENT, ear/nose/throat.

Table 2. Comparison of Patient Characteristics By Prenatal Cardiac Diagnosis (PD, n=591)

Baseline Patient Information	PD, n=445 Median [IQR], or number (%)	No PD, n=146 Median [IQR], or number (%)	P-value
Birth weight (kg) [n=443, 141]	3.1 [2.9,3.5]	3.2 [2.9, 3.5]	0.72
Gestational age (wks) [n=439, 146]	39 [38,39]	39 [38,40]	<0.001
APGAR score - 1 min [n=436, 125]	8 [8,8]	8 [8,9]	0.15
APGAR score - 5 min [n=436, 125]	9 [8,9]	9 [9,9]	<0.001
Age at presentation (days) [n=434, 146]	0 [0,0]	1 [0,4]	<0.001
Lowest pH pre-intervention [n=424, 139]	7.30 [7.24,7.34]	7.29 [7.19,7.35]	0.35
Primary cardiac diagnosis (n=444,145)			0.53
Hypoplastic left heart syndrome	295 (68%)	92 (64%)	
HLHS with MA/AA	*171 (39%)*	*40 (28%)*	
HLHS with MS/AA	*60 (14%)*	*19 (13%)*	
HLHS with MS/AS	*56 (13%)*	*24 (17%)*	
HLHS with MA/AS	*8 (2%)*	*9 (6%)*	
DORV with left sided hypoplasia	21 (5%)	12 (8%)	
Double inlet left ventricle	19 (4%)	4 (3%)	
Unbalanced AV canal	16 (4%)	7 (5%)	
Double inlet right ventricle	2 (<1%)	0 (0%)	
Other	91 (20%)	30 (21%)	
Secondary Diagnoses			
Restrictive atrial septum	76 (17%)	22 (15%)	0.61

AV valve regurgitation*	7 (2%)	10 (7%)	0.002
Ventricular dysfunction*	8 (2%)	7 (5%)	0.06
Any major syndrome	35 (8%)	17 (12%)	0.18
Any major non-cardiac organ anomaly	34 (8%)	16 (11%)	0.23
Age at admission to ICU (days)	0 [0,0]	1 [0,4]	<0.001
Age at initial intubation (days) [n=442,146]	3 [0,5]	3 [1,8]	0.02
Any preoperative risk factors	218 (48%)	99 (68%)	<0.001
Mechanical ventilatory support	128 (29%)	75 (51%)	<0.001
Acidosis	61 (14%)	49 (34%)	<0.001
Renal insufficiency	22 (5%)	17 (12%)	0.007
Arrhythmia	17 (4%)	3 (2%)	0.43
Shock, resolved or persistent	1 (<1%)	3 (2%)	0.05
Pre-operative cath performed [n=436, 145]	46 (11%)	15 (10%)	1
Surgical septostomy [n=442, 146]	26 (6%)	8 (5%)	1

*Defined as ≥moderate

IQR, intraquartile range; HLHS, hypoplastic left heart syndrome; AA, aortic atresia; MA, mitral atresia; AS, aortic stenosis; MS, mitral stenosis; DORV, double outlet right ventricle; AV, atrioventricular; ICU, intensive care unit.

Table 3. Neonatal Surgery Summary Comparisons by Prenatal Cardiac Diagnosis (PD)

Neonatal Surgery Summary	PD, n=445 Median	No PD,n=146	P-value

	[IQR], or number (%)	Median [IQR], or number (%)	
Age at Norwood (days) [n=444, 146]	5 [3,7]	8 [5,13]	<0.001
Weight at Norwood (kg) [n=442, 143]	3.2 [2.9, 3.5]	3.3 [3.0, 3.7]	0.11
Type of Norwood equivalent [n= 442, 146]			0.09
Norwood RV-PA conduit	238 (54%)	72 (49%)	
Norwood BT shunt	142 (32%)	55 (38%)	
Hybrid Norwood	39 (9%)	6 (4%)	
DKS with BT shunt	15 (3%)	7 (5%)	
Other	8 (2%)	6 (4%)	
ECMO required [n=443, 145]	12 (3%)	7 (5%)	0.28
Length of intubation (days) [n=437, 145]	9 [5,17]	12 [8,17]	0.002
Post-operative arrhythmia requiring treatment	128 (29%)	33 (23%)	0.16
Cardiac reoperation performed *	99 (22%)	23 (16%)	0.12
Post-operative complications‡	305 (69%)	89 (61%)	0.11
Other major post-operative procedures	143 (32%)	48 (33%)	0.92
Post-operative cath performed [n=436, 138]	100 (23%)	20 (14%)	0.04
Hospital LOS [n= 443, 146]	27 [17,46]	27 [18,42]	0.61
Weight at discharge (kg) [n=444, 145]	3.5 [3.2,4.0]	3.6 [3.2,4.0]	0.27

Discharge O2 saturation [n=441,145]	83 [80,86]	83 [79,86]	0.46

* Not including delayed chest closure, see Results section for details.

‡ See Results section for details.

RV-PA, right ventricle to pulmonary artery shunt; BT, Blalock-Taussig shunt; DKS, Damus-Kaye-Stansel anastomosis; ECMO, extra-corporeal membrane oxygenator; LOS, length of stay; 02, oxygen.

Table 4. Interstage Period and Bi-directional Glenn Surgery Course by Prenatal Cardiac Diagnosis (PD)

	PD, n=445 Median [IQR], or number (%)	No PD,n=146 Median [IQR], or number (%)	P-value
Interstage Period (n=591)			
Any subsequent readmission	322 (72%)	104 (71%)	0.83
Any unscheduled readmission	228 (51%)	73 (50%)	0.85
Interstage death	39 (9%)	16 (11%)	0.42
BDG Surgery Summary (n=519)			
Underwent BDG Surgery	396 (89%)	123 (84%)	0.14
Age at surgery (mos) [n=395, 123]	4.9 [4.0,5.6]	5.3 [4.3,6.2]	0.007
Weight (kg) [n=394,122]	6.1 [5.4, 6.8]	6.2 [5.6,7.0]	0.08
O2 saturation [n=384, 117]	79 [75,82]	78 [74,81]	0.2
Post-operative complication	158 (40%)	43 (35%)	0.34
Hospital LOS (days) [n=389, 119]	8 [5, 14]	7 [6,12]	0.46

BDG, bi-directional Glenn operation;02, oxygen; LOS, length of stay.

FIGURE LEGENDS

Fig. 1 Center Variation in PD. Figure 1 depicts the inter-center variation in PD for patients with SVD discharged home after S1P and enrolled in the NPCQIC registry. The figure bars represent percent of patients with PD among 16 sites (Sites A-P) entering ≥10 patients in the NPCQIC registry

Fig. 2 Gestational Age at Birth by PD. Gestational age at birth from 591 patients with SVD discharged home after S1P and enrolled in the NPCQIC registry. Those with a PD (blue bars, n=445) versus those with no PD (red bars, n=146) had younger gestational ages at birth (p<0.001)

References

1   Hoffman JI, Kaplan S (2002) The incidence of congenital heart disease. J AmCollCardiol 39: 1890-1900
2   Krasemann T, Fenge H, Kehl HG, Rukosujew A, Schmid C, Scheld HH, Tjan TD, Vogt J (2005) A decade of staged Norwood palliation in hypoplastic left heart syndrome in a midsized cardiosurgical center. Pediatr Cardiol 26: 751-755
3   McGuirk SP, Griselli M, Stumper OF, Rumball EM, Miller P, Dhillon R, de Giovanni JV, Wright JG, Barron DJ, Brawn WJ (2006) Staged surgical management of hypoplastic left heart syndrome: a single institution 12 year experience. Heart 92: 364-370
4   Dooley KJ, Bishop L (2002) Medical management of the cardiac infant and child after surgical discharge. Crit Care Nurs Q 25: 98-104
5   Atz AM, Travison TG, Williams IA, Pearson GD, Laussen PC, Mahle WT, Cook AL, Kirsh JA, Sklansky M, Khaikin S, Goldberg C, Frommelt M, Krawczeski C, Puchalski MD, Jacobs JP, Baffa JM, Rychik J, Ohye RG, Pediatric Heart Network I (2010) Prenatal diagnosis and risk factors for preoperative death in neonates with single right ventricle and systemic outflow obstruction: screening data from the Pediatric Heart Network Single Ventricle Reconstruction Trial(*). J Thorac Cardiovasc Surg 140: 1245-1250
6   Tworetzky W, McElhinney DB, Reddy VM, Brook MM, Hanley FL, Silverman NH (2001) Improved surgical outcome after fetal diagnosis of hypoplastic left heart syndrome. Circulation 103: 1269-1273

7   Kipps AK, Feuille C, Azakie A, Hoffman JI, Tabbutt S, Brook MM, Moon-Grady AJ (2011) Prenatal diagnosis of hypoplastic left heart syndrome in current era. Am J Cardiol 108: 421-427

8   Costello JM, Polito A, Brown DW, McElrath TF, Graham DA, Thiagarajan RR, Bacha EA, Allan CK, Cohen JN, Laussen PC (2010) Birth before 39 weeks' gestation is associated with worse outcomes in neonates with heart disease. Pediatrics 126: 277-284

9   Levey A, Glickstein JS, Kleinman CS, Levasseur SM, Chen J, Gersony WM, Williams IA (2010) The impact of prenatal diagnosis of complex congenital heart disease on neonatal outcomes. Pediatr Cardiol 31: 587-597

10 Landis BJ, Levey A, Levasseur SM, Glickstein JS, Kleinman CS, Simpson LL, Williams IA (2013) Prenatal diagnosis of congenital heart disease and birth outcomes. Pediatr Cardiol 34: 597-605

11 Brown DW, Connor JA, Pigula FA, Usmani K, Klitzner TS, Beekman RH, 3rd, Kugler JD, Martin GR, Neish SR, Rosenthal GL, Lannon C, Jenkins KJ, Joint Council on Congenital Heart Disease National Pediatric Cardiology Quality Improvement C (2011) Variation in preoperative and intraoperative care for first-stage palliation of single-ventricle heart disease: a report from the Joint Council on Congenital Heart Disease National Quality Improvement Collaborative. Congenital heart disease 6: 108-115

12 Peiris V, Singh TP, Tworetzky W, Chong EC, Gauvreau K, Brown DW (2009) Association of Socioeconomic Position and Medical Insurance With Fetal Diagnosis of Critical Congenital Heart Disease. Circ Cardiovasc Qual Outcomes: 354-360

13 Knirsch W, Liamlahi R, Hug MI, Hoop R, von Rhein M, Pretre R, Kretschmar O, Latal B (2012) Mortality and neurodevelopmental outcome at 1 year of age comparing hybrid and Norwood procedures. Eur J Cardiothorac Surg 42: 33-39

14 Newburger JW, Sleeper LA, Bellinger DC, Goldberg CS, Tabbutt S, Lu M, Mussatto KA, Williams IA, Gustafson KE, Mital S, Pike N, Sood E, Mahle WT, Cooper DS, Dunbar-Masterson C, Krawczeski CD, Lewis A, Menon SC, Pemberton VL, Ravishankar C, Atz TW, Ohye RG, Gaynor JW, Pediatric Heart Network I (2012) Early developmental outcome in children with hypoplastic left heart syndrome and related anomalies: the single ventricle reconstruction trial. Circulation 125: 2081-2091

15 Tabbutt S, Ghanayem N, Ravishankar C, Sleeper LA, Cooper DS, Frank DU, Lu M, Pizarro C, Frommelt P, Goldberg CS, Graham EM, Krawczeski CD, Lai WW, Lewis A, Kirsh JA, Mahony L, Ohye RG, Simsic J, Lodge AJ, Spurrier E, Stylianou M, Laussen P, Pediatric Heart Network I (2012) Risk factors for hospital morbidity and mortality after the Norwood procedure: A report from the Pediatric Heart Network Single Ventricle Reconstruction trial. J Thorac Cardiovasc Surg 144: 882-895

16 Nathan M, Karamichalis JM, Liu H, Emani S, Baird C, Pigula F, Colan S, Thiagarajan RR, Bacha EA, Del Nido P (2012) Surgical technical performance scores are predictors of late mortality and unplanned reinterventions in infants after cardiac surgery. J Thorac Cardiovasc Surg 144: 1095-1101 e1097

17 Nathan M, Karamichalis J, Liu H, Gauvreau K, Colan S, Saia M, Pigula F, Fynn-Thompson F, Emani S, Baird C, Mayer JE, del Nido PJ (2014) Technical Performance Scores are strongly associated with early mortality, postoperative adverse events, and intensive care unit length of stay-analysis of consecutive discharges for 2 years. J Thorac Cardiovasc Surg 147: 389-394, 396 e381-396 e383