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ORIGINAL ARTICLE

Clinical Outcomes and Resource Use for Infants With Hypoplastic Left Heart Syndrome During Bidirectional Glenn: Summary From the Joint Council for Congenital Heart Disease National Pediatric Cardiology Quality Improvement Collaborative Registry

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Abstract The National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC) registry captures information on interstage management of infants with hypoplastic left heart syndrome (HLHS). The purpose of this study was to identify interstage risk factors for increased resource use and adverse outcomes during bidirectional Glenn (BDG) hospitalization. All infants in the NPC-QIC registry (31 United States hospitals) undergoing BDG surgery were included (December 2009 to August 2010). Patient demographics, interstage variables, operative procedures, and complications were recorded. Days of hospitalization, ventilation, inotrope use, and complications were surrogates of resource use. Logistic regression analysis determined the associations between predictor variables and resource use. Of 162 infants, 105 (65 %) were males. At BDG, the median age was 155 days (range 78–128), mean weight-for-age z-score was -1.6 ± 1.1, mean length-for-age z-score was -1.5 ± 1.7, and mean preoperative oxygen saturation was 78 % ± 7 %. Caloric recommendations were met in 60 % of patients, and 85 % of patients participated in a home-surveillance program. Median days of intubation, inotrope use, and hospitalization were 1, 2, and 7, respectively. There were 4 post-BDG deaths and 55 complications. In multivariate analysis, lower weight-for-age z-score, female sex, and aortic atresia with mitral stenosis were associated with a higher risk of BDG complications. Meeting caloric recommendations before BDG was associated with fewer hospitalization days. Lower weight-for-age z-score was an independent and potentially modifiable risk factor for BDG complications. HLHS infants who met caloric recommendations before BDG had a lower duration of hospitalization at BDG. These data justify targeting nutrition in interstage strategies to improve outcomes and decrease costs for patients with HLHS.

Keywords Bidirectional Glenn · Hypoplastic left heart syndrome · Outcome · Resource use · Second stage · Superior cavopulmonary anastomosis

This study is conducted on behalf of the Joint Council for Congenital Heart Disease National Pediatric Cardiology Quality Improvement Collaborative.

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Introduction

The bidirectional Glenn (BDG) procedure is the second of three stages in the surgical palliation of hypoplastic left heart syndrome (HLHS) [11]. This stage includes take-down of the right ventricle-to-pulmonary artery shunt or modified Blalock–Taussig shunt and anastomosis of the superior vena cava to the pulmonary artery and is typically performed when the patient is between 3 and 6 months of age [12]. Risk factors for poor BDG outcomes remain poorly defined. Some centers report an association between poor interstage growth

and younger age at BDG and longer duration of hospitalization [1], but others have failed to verify this finding [8, 13]. During the last decade, single-center studies have reported improved early and intermediate survival for HLHS patients using a surveillance strategy that includes home monitoring of oxygen saturation and growth velocity [5, 6, 16], but this has not been studied in a multicenter setting.

The National Pediatric Cardiology Quality Improvement Collaborative (NPC-QIC) is the first quality-improvement collaborative in pediatric cardiology, and its registry captures information on interstage care and outcomes of infants after the Norwood procedure [14]. To be eligible for inclusion in the registry, the infant must have HLHS or complex single ventricle undergoing a Norwood or Norwood-variant procedure and must be discharged home after surgery. The purpose of this study was to identify interstage risk factors for greater resource use as well as adverse outcomes during hospitalization for BDG in infants with HLHS or complex single ventricle who underwent a Norwood or Norwood-variant procedure.

Methods

NPC-QIC

The NPC-QIC registry (31 United States hospitals contributed data during the study period) captures data from HLHS or other complex single-ventricle patients discharged home after undergoing a Norwood procedure. All infants in the NPC-QIC registry who underwent BDG procedure between December 2009 and August 2010 were included in this study. Infants with chromosomal defects, syndromes, and major extracardiac malformations were excluded from the study. Deidentified patient data—including patient demographics, cardiac diagnosis, clinical care processes, interstage surveillance and anthropometric measurements, surgical interventions, postoperative complications, and outcomes—were entered by participating centers into a secure central online data repository. Institutional Review Board approval was obtained by the University of Utah and the Primary Children's Medical Center for contributing data to this registry.

NPC-QIC and Study Definitions

- *Interstage*: Interstage included the time between hospital discharge after the Norwood procedure and admission for the BDG procedure.
- *Met caloric requirement:* "Met caloric requirement" was defined as infants who met their target caloric recommendation as determined by the individual center at the last hospital/clinic visit before BDG. Specific caloric amounts were not collected.
- *Home surveillance*: Home surveillance included home monitoring of oxygen saturation and/or weight.
- *HLHS subgroups*: To study the effect of anatomical cardiac diagnosis on outcome, HLHS anatomic variants were divided into three groups: aortic and mitral atresia, aortic atresia and mitral stenosis (patients likely to have a hypoplastic and hypertensive left ventricle), and others (e.g., aortic stenosis and mitral stenosis, unbalanced atrioventricular septal defect).
- *Complications*: Complications were defined as any deviation from the normal postoperative course that required intervention. Complications were treated as a dichotomized variable (i.e., yes or no).
- *Resource use*: Days of hospitalization, ventilation, and inotrope use, as well as postoperative complications (yes/no), were used as surrogates of resource use.
- *Potential risk factors included in the analysis*: The pre-BDG variables considered as potential risk factors for adverse outcome included birth weight, sex, ethnicity, race, cardiac anatomical diagnosis, type of Norwood palliation (Sano vs. modified Blalock–Taussig shunt), home surveillance (yes/no), met center-defined target recommended caloric intake at the most recent hospital discharge or clinic visit before BDG (yes/no), age at BDG, weight-for-age z-score at BDG, length-for-age Z-score at BDG, oxygen saturation at BDG, and type of BDG. Death or cardiac transplantation during the first 30 postoperative days or before discharge from BDG hospitalization was noted. To study the differences in BDG hospitalization resource use between centers, centers were divided into two groups: centers with <10 patients in the registry and centers with ≥ 10 patients in the registry.

Statistical Analysis

All continuous variables were described, and the data distribution was tested for normality. Normally distributed continuous variables were expressed as mean $\pm$ SD, and nonnormally distributed data are expressed as median and range. Categorical data were analyzed using Chi-square or Fisher's exact test as appropriate. Continuous variables were analyzed using Student *t* test. Bivariate analyses of potential risk factors for adverse outcome were performed using parametric tests for normally distributed data and nonparametric tests for nonnormally distributed data to determine the effects of pre-BDG and BDG predictor variables on parameters of resource use and complications. Nonparametric tests for two independent samples were performed using Mann–Whitney U-test. Variables with $p < 0.05$ were included in the multivariate logistic regression analysis. All analyses were performed using SAS 9.2 software (SPSS, Cary, NC).

Results

Patient Population

The study cohorts consisted of 162 patients from 31 centers (5 centers had $\geq$ 10 patients). Birth weight ranged from 1.9 to 5.0 kg (median 3.2) with 70 % of patients being white and 65 % of patients being male (Table 1). The most common anatomic diagnosis was aortic and mitral atresia (33 %). Of the 162 patients, 71 had no information entered into the database regarding center-defined target caloric intake at the most recent hospital discharge or clinic visit before BDG. Of the 91 patients with this information, 55 (60 %) met target caloric intake. Of the 162 patients, 134 (83 %) had home surveillance during interstage, and in 5 (3 %) this information was not entered.

Table 1 Patient demographics

Variables	Sub category	*N*	%
Birth weight (kg)	Mean ± SD (range) 3.2 ± 0.48 (1.9–5.0)	162	100
	Category		
Sex	Female	57	35
	Male	105	65
Ethnicity	Non-Hispanic/Non-Latino	100	62
	Hispanic/Latino	37	23
	Missing	25	15
Race	White	114	70
	Black African American	21	13
	American Indian or Alaska Native	2	1
	Asian	1	1
	Other	20	12
	Missing	4	3
HLHS-grouped categories	Aortic and mitral atresia	57	35
	Aortic atresia and mitral stenosis	43	27
	Other defects	62	38
Major syndrome	Yes	12	7
Other chromosome abnormality	Yes	6	4
Organ system anomaly	Yes	19	12
Met caloric requirements	Yes	55	34
	No	36	22
Home surveillance	Yes	134	83
	No	23	14

BDG Hospitalization

Age at BDG (Table 2) ranged from 2.6 to 12.8 months (median 5.2), weight-for-age z-score ranged from −5.2 to 0.9 (median −1.6), and oxygen saturation ranged from 60 % to 93 % (median 78 %). The majority (114 [70 %]) of patients underwent unilateral BDG. Bilateral BDG was performed in 35 (22 %) patients, and 11 (7 %) patients underwent a hemi-Fontan procedure. Ventilation duration (Table 2) ranged from 0 to 106 days (median 1), inotrope use ranged from 0 to 64 days (median 2), and hospitalization ranged from 2 to 200 days (median 7). Postoperative complications occurred in 55 of 162 (34 %) patients (Table 3). There were 4 (3 %) post-BDG deaths, and 1 patient required extracorporeal membrane oxygenation (ECMO).

Risk Factors for Complications After BDG

In multivariate analysis, higher weight-for-age z-score at BDG ($p = 0.03$, hazard ratio [HR] 0.68, 95 % confidence interval [CI] 0.48–0.96) was associated with a lower risk of complications (Table 4). For each one point increase in weight-for-age z-score, the probability of having postoperative complications decreased by 32 %. Female sex ($p = 0.028$, HR 2.31, 95 % CI 1.09–4.92) and cardiac diagnosis of aortic atresia with mitral stenosis ($p = 0.002$, HR 3.67, 95 % CI 1.45–9.31) were associated with an

Table 2 Patient characteristics and resource use after BDG

Characteristics and resources used	Mean	SD	Median	Minimum	P25	P75	Maximum
Age at BDG (d)	163	54	155	78	128	183	384
Weight at BDG (kg)	6.2	1.1	6.2	3.5	5.4	6.8	9.3
Weight-for-age z-score at BDG	−1.6	1.1	−1.6	−5.2	−2.2	−0.8	0.9
Length-for-age z-score at BDG	−1.5	1.7	−1.3	−8.0	−2.3	−0.3	1.7
Oxygen saturation at BDG	78	7	78	60	75	82	93
Days intubated	3.2	11.6	1.0	0.0	0.0	2.0	106
Days on inotropes	4.4	9.6	2.0	0.0	1.0	3.0	64
Days of hospitalization	16.9	34.5	7.0	2.0	5.0	11.0	200

Min minimum, *Max* maximum, *P25* 25th percentile, *P75* 75th percentile

Table 3 Frequency distribution of postoperative complications

Complications	*N*	%
Postoperative complications[a]	55	34
ECMO	1	0.6
Unplanned cardiac catheterization	15	9
Reoperation	9	6
Cardiac arrest	4	3
Death	4	3
New neurological deficit	2	1
New-onset seizures	2	1
Fundoplication	2	1
Gastric-tube placement	7	4
Discharge with feeding tube	20	12

[a] Patients may have more than one complication

increased risk of complications. The risk of having any postoperative complication after BDG was greater for those with aortic atresia and mitral stenosis *versus* those with aortic and mitral atresia by a factor of 3.7 and in girls by a factor of 2.3 (Table 4). There was no difference in complication risk between Sano or modified Blalock–Taussig shunt cohort, infants on or not on home surveillance, centers with <10 or ≥ 10 patients in the registry, and other potential risk factors studied. None of the other previously specified potential target predictors were associated with a risk of complications after BDG.

Risk Factors for Increased Resource Use During BDG Hospitalization

In univariate analysis, infants who failed to meet target caloric recommendations and those on home surveillance had longer hospitalization days ($p = 0.004$, HR 1.97, CI 1.28–3.02; $p = 0.050$, HR 1.55, CI 0.99–2.42, respectively). In multivariate analysis, however, failure to meet target caloric recommendations was the only variable associated with more hospitalization days ($p = 0.013$, HR 1.81, 95 % CI 1.13–2.87). None of the other previously specified potential target predictors were associated with days of ventilation or inotrope use.

Discussion

This multi-institutional cohort study of HLHS patients found that meeting caloric recommendations at the most recent hospital discharge or clinic visit before BDG was the sole factor associated with decreased hospitalization days. In previous single-center studies of single-ventricle patients with mixed cardiac diagnosis, younger age (< 4 months) [13], and lower weight-for-age z-score [1] at BDG were associated with longer hospitalization after BDG. Previous single-center study failed to show an association between younger age at BDG and increased duration and amount of chest tube drainage, duration of mechanical ventilation, and hospital stay [8]. The conflicting results among these single-center studies may partially be explained by the heterogeneity of the study populations. In this multi-institutional study, only those with HLHS or HLHS variants who underwent a Norwood procedure was included, and we found no association between age, weight- or length-for-age z-scores or oxygen saturation at BDG and hospitalization days, mechanical ventilation days, or inotrope use days. Neither did we find any association between birth weight, cardiac diagnosis, and type of Norwood palliation (Sano vs. modified Blalock–Taussig shunt) and resource use at BDG. Although beneficial effects of weight gain on BDG hospitalization have been reported, this study shows a beneficial effect of meeting center-specific caloric recommendations on BDG resource use. It is likely that adequate caloric intake resulted in positive nitrogen balance and provides an indicator of improved nutrition that occurs before actual weight gain is achieved. This may improve the infant's

Table 4 Multivariate logistic regression analysis showing variables associated with risk of complications and longer days of hospitalization after BDG

Effect	*N*	*p*	HR	Lower CL	Upper CL
Risk of complication					
Weight-for-age z-score at BDG[a]	159	0.028	0.68	0.48	0.96
Cardiac diagnosis (group 2 vs. group 1)[b]	162	0.002	3.67	1.45	9.31
Sex (female vs. male)	162	0.028	2.31	1.09	4.92
Longer hospitalization days					
Caloric recommendation met (no vs. yes)	160	0.013	1.81	1.13	2.87

CL confidence limit

[a] For each one point increase in weight-for-age z-score, the probability of having postoperative complications decreased by 31.5 %

[b] Group 1 = aortic and mitral atresia, and group 2 = aortic atresia and mitral stenosis. Variables included in the univariate analysis are discussed in the Methods section

ability to adapt to stress as manifested by decreased incidence of postoperative sepsis, fewer hospitalization days, and cost of hospitalization [15].

Although not associated with increased hospital days, lower weight-for-age z-score was associated with increased postoperative complications, thus supporting findings from previous single-center reports [8]. The increased risk of complications after BDG in girls and in infants with mitral stenosis and aortic atresia has not been previously reported. Although the role that sex plays in HLHS outcomes has not been explored, female sex has been reported as a risk factor for mortality after surgical repair of other forms of congenital heart disease [3, 10]. Mitral stenosis and aortic atresia have been implicated as a risk factors for decreased survival during Norwood surgery and may be related to coronary abnormalities that occur in this HLHS subtype [2, 4, 7], which may lead to ischemia, ventricular dysfunction, and fatal arrhythmias [7]. We speculate that coronary abnormalities that occur in mitral stenosis and aortic atresia may play a role in perioperative outcomes not only after Norwood surgery but also after BDG and Fontan surgeries. Data regarding ventricular function are not available in the NPC-QIC database, so this remains speculative. We did not find any association between risk factors, such as birth weight, ethnicity, race, type of BDG, and type of Norwood palliation (Sano vs. modified Blalock–Taussig shunt) and post-BDG complications. The positive association between home surveillance and increased duration of hospitalization at BDG may be attributed to the increased use of this strategy in high- risk patients. Although single-center studies have shown clear benefits of home surveillance in decreasing interstage mortality in HLHS [5, 6], the critical components of home surveillance that decrease morbidity and mortality in high-risk post-Norwood patients warrants further investigation. Although previous studies showed that younger age at the time of BDG was associated with longer hospital length of stay [1, 9], that was not the case in this multicenter study and, similar to other single-center reports, younger age had no association with duration and amount of chest tube drainage, duration of mechanical ventilation, and hospital length of stay [8]. These differences might be again be partly explained by the heterogeneity of the subject's' cardiac diagnoses in the previous reports and by center practice variation. Center volume does not appear to be a factor because there were no differences in post-BDG resource use between centers with $\geq$ 10 patients *versus* other centers.

Limitations

This study is limited by the use of prespecified data entered into the NPC-QIC database. Echocardiographic findings were not included in the database, and the relationship between right-ventricular systolic function or severity of tricuspid regurgitation and resource use could not be analyzed [1]. The registry cohort is limited to patients who were discharged home after the Norwood procedure and whose parents gave consent for them to participate in the study. Long-term outcome data on this cohort of patients were not available in NPC-QIC database. The caloric recommendation guidelines were not standardized but rather determined by each center. and the exact calories per kilogram per day were not entered. Finally, the various components of home surveillance were not uniform among centers, so we were unable to determine which component was associated with adverse BDG outcomes. The NPC-QIC continues to expand the data collection, thus allowing these questions be better addressed in future studies.

Conclusion

The Joint Council for Congenital Heart Disease NPC-QIC is a multi-institutional quality-improvement collaborative that targets intervention strategies to improve outcomes in HLHS infants. Lower weight-for-age z-score, although not associated with duration of ventilation, inotrope use, or hospitalization, was associated with an increased risk of postoperative BDG complications. This is the first study to demonstrate a beneficial effect of meeting caloric recommendations on BDG resource use. We speculate that adequate caloric intake creates positive nitrogen balance and is an early marker of improved nutrition. These data from the NPC-QIC registry justify targeting nutrition in interstage strategies to improve interstage care and outcome of patients with HLHS.

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