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ORIGINAL ARTICLE

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Gastrostomy tube placement among infants with hypoplastic left heart syndrome undergoing stage 1 palliation

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Abstract

Objective: Different feeding strategies have been suggested to improve growth and survival of infants with hypoplastic left heart syndrome following stage 1 palliation. The study objective was to assess hospital mortality following stage 1 palliation among infants with hypoplastic left heart syndrome who had two feeding modalities, gastrostomy tube vs no gastrostomy tube.

Design: Retrospective study design.

Setting: Multicenter pediatric heath information system database.

Patient: About 4287 patients with hypoplastic left heart syndrome who underwent stage 1 Norwood procedure from 2004 through 2013. Infants who had gastrostomy tube with or without fundoplication procedure were identified and their clinical characteristics were compared.

Intervention: None.

Outcomes Measures: The primary outcome was discharge hospital mortality following stage 1 palliation.

Results: About 1214 patients who underwent stage 1 palliation had gastrostomy tube placement prior to hospital discharge. About 881 only had this procedure, while 333 patients also underwent fundoplication. Infants who had a gastrostomy tube placement vs no gastrostomy procedure had longer hospital stay, but significantly lower hospital mortality (5% vs 19%, $P < .001$). Hospital mortality was lower in infants who had only gastrostomy vs gastrostomy with fundoplication procedure (4% vs 8%, $P = .004$). In the multivariable analysis, gastrostomy procedure was associated with a higher likelihood of survival to hospital discharge (HR: 0.06, CI [0.04, 0.1]), whereas additional fundoplication procedure increased the risk of mortality (HR: 2.77, CI [1.52, 5.04]).

Conclusions: The gastrostomy procedure did not place infants with hypoplastic left heart syndrome at higher risk of mortality. These infants should be considered for gastrostomy tube placement if they had persistent difficulty in oral feeding following stage 1 palliation.

KEYWORDS
gastrostomy tube, hypoplastic left heart syndrome, outcomes

Abbreviations: CHCA, Child Health Corporation of America; CI, confidence interval; CPT, correct procedures terminology; CTC, Clinical Transaction Classification; d, days; ECMO, extracorporeal membrane oxygenation; FP, Nissen fundoplication; GERD, gastroesophageal reflux disease; GT, gastrostomy tube; HLHS, hypoplastic left heart syndrome; ICD-9, International Classification of Diseases, Ninth Revision; NEC, necrotizing enterocolitis; PHIS, Pediatric Health Information System.

*This study was first presented (poster) in 2015 at the Society of Pediatric Research, San Diego, USA.

1 | INTRODUCTION

The survival of infants with hypoplastic left heart syndrome (HLHS) post–stage 1 Norwood procedure has drastically improved over the last decade.[1,2] Despite improved survival, these patients remain at significant risk for various morbidities.[2,3] Appropriate nutrition and growth are critical elements for improved outcomes post–stage 1 palliation and are linked with better neurodevelopment and decreased late mortality.[4,5] Thus, varied approaches for dietary intervention to optimize growth have been adopted.[6] Some centers reported good results with preemptive gastrostomy tube placement (GT),[7] while others described increased morbidities in infants who had a GT with/without Nissen fundoplication procedure (GT ± FP).[6]

A study from the National Pediatric Cardiology Quality Improvement Collaborative data registry examined the effect of feeding modality on inter-stage growth and found that appropriate growth can be reached regardless of feeding modality, concluding that complication risks are the most critical factors for deciding on specific feeding practices.[8] Although the literature generally indicates increased risk of hospital morbidities and inter-stage mortality in infants who underwent GT ± FP procedure, none of these studies specifically evaluated discharge hospital mortality following stage 1 palliation.[6,9]

We utilized a multicenter validated database, the Pediatric Health Information System (PHIS), to examine variation over time and across hospitals in post–stage 1 Norwood procedure feeding modalities. We evaluated mortality among infants with two different feeding modalities (GT ± FP vs No GT). We hypothesized a priori that while infants in the GT ± FP group might have longer hospital stay, the incidence of mortality is lower in this high-risk population.

2 | METHODS

This study received The University of Arkansas for Medical Sciences Institutional Board Review approval.

2.1 | Data source

We conducted a retrospective cohort study of infants with HLHS using PHIS, an administrative database that contains inpatient data from 43 US not-for-profit, tertiary care children's hospitals in North America.[10] Institutions are affiliated with the Child Health Corporation (CHCA, Shawnee Mission, KS) and account for 20% of all tertiary care children's hospitals. Institutions are labeled within the database but cannot be identified in public reporting. Participating hospitals provide discharge data and diagnoses coded with the International Classification of Diseases, Ninth Revision (ICD-9). Billing data are available and are coded under the Clinical Transaction Classification (CTC) system. Other codes reported include Correct Procedures Terminology (CPT) for procedures and V codes used to describe encounters with circumstances other than disease. Data are de-identified at the time of submission and are subjected to a number of reliability and validity checks before being processed into quality reports. The diagnoses, procedures, and corresponding codes applied in this study are summarized in Supporting Information Table S1.

2.2 | Study population

We evaluated all patients who were discharged from a PHIS participating hospital between January 1, 2004 and December 31, 2013 and had a diagnosis code of HLHS. All patients underwent stage 1 Norwood operation during that hospitalization and were then discharged from the hospital or died during the hospitalization. Determination of stage 1 Norwood surgery was based on identifying patients with HLHS who had extracorporeal circulation auxiliary to open heart surgery and either creation of a conduit between the right ventricle and pulmonary artery [Sano] or systemic to pulmonary artery shunt [Shunt]. Infants who had a hybrid procedure or heart transplant were excluded.

Infants who had open or percutaneous GT placement were then identified. Some patients also underwent open or laparoscopic FP. FP is typically completed concurrently with GT placement when there is an additional diagnosis risk of gastroesophageal reflux disease (GERD). We thus excluded patients ($n = 23$) who had only a code for FP without a supplementary code for GT placement or had unclear diagnosis of GERD with corresponding codes indicative of placement of GT with or without FP. Our final study population included 4287 infants with HLHS (Supporting Information Figure S1).

The study population was divided in two groups: HLHS patients who underwent stage 1 Norwood procedure and had GT placement with or without FP (GT ± FP) and those who did not undergo a GT (No GT) procedure during the same hospitalization. Infants in the GT ± FP group were further allocated in two separate subgroups: Only GT and GT + FP.

2.3 | Variables queried (Supporting Information Table S1)

Demographics and clinical characteristics were collected. We gathered data on various diagnoses and different procedures (pre– and post–stage 1 palliation). Pharmacological data were also abstracted and included antiarrhythmic and inotropic medications use as well as nitric oxide administration.

2.4 | Outcomes measures

The primary outcome measure was discharge hospital mortality. Discharge hospital mortality following stage 1 Norwood procedure was evaluated over time among the study groups and subgroups. The count of Norwood cases and the number of GT and FP procedures were assessed across centers. Discharge hospital mortality per study groups were then calculated across centers. Since gastrostomy procedure was typically offered later than the first month of life (>30 days), we also evaluated mortality among infants who survived or remained hospitalized beyond thirty days of life to exclude potentially confounding effect of early discharges or deaths. In addition, we assessed length of hospital stay as a secondary outcome among the different study groups and subgroups.

2.5 | Gastrostomy tube group

We tabulated the incidence of various diagnoses, procedures, and use of pharmacological agents among infants in in the GT ± FP group. These variables were considered comorbidities as they can possibly be associated with a more complex and prolonged hospital stay. Clinical data and hospital mortality were compared between infants in the GT ± FP group who had any comorbidity vs no comorbidities.

2.6 | Statistical analysis

All statistical analyses were generated using SAS/STAT software, version 9.4 of the SAS System for Windows 7 (SAS Institute, Inc., Cary, NC). Plots were generated using the ggplot2 package in R (R Core Team, Vienna, Austria). All tests were 2-sided assuming a P value of .05. Descriptive statistics were reported as medians and interquartile ranges for continuous variables and percentages and frequencies for categorical variables. Two Cox regression models were fitted to investigate the impact of multiple risk factors on time to death for the overall study cohort and for infants who survived or remained in the hospital beyond the first month of life, respectively. Another Cox regression model was also fitted to evaluate predictors for prolonged hospital stay among the study population. A prolonged hospital stay was defined as >52 days (>75th percentile of the hospital stay of the overall study cohort). The clustering effect of patients from different centers was accounted for by including the hospital median annual cardiopulmonary bypass cases as a variable in both the univariable and multivariable models. Variables were selected for the multivariable models, if they had a $P < .2$ on the univariable analysis or were considered a priori as clinically important. Variables (birth weight and race) with >20% missing values were excluded. The model results were expressed in terms of hazard ratios (HR) for time to death with corresponding 95% confidence intervals (CI) and P values.

3 | RESULTS

3.1 | Cohort description

Supporting Information Figure S1 provides a description of the cohort. From January 1, 2004 through December 31, 2013, a total of 5721 infants with HLHS were discharged from PHIS affiliated hospitals. About 41 hospitals performed stage 1 Norwood procedures in the PHIS dataset. One hospital performed only two Norwood procedures with 100% mortality during the study period and was excluded. About 4287 patients in 40 hospitals met our inclusion criteria.

The characteristics of the study population are presented in Table 1. About 28.3% (1214 infants) underwent a GT placement including 333 infants who also had FP procedure. Gestational age, birth weight and race were comparable between the two study groups. Infants in the GT ± FP vs No GT group had longer intensive care unit stay [35 vs 18 days (d), $P < .001$], duration of mechanical ventilation (13 vs 8 d, $P < .001$) and parenteral nutrition (12 vs 7 d, $P < .001$), larger percentage of congenital anomalies, higher incidence of necrotizing enterocolitis (NEC) (6.9% vs 4.4%, $P < .001$), vocal cord paralysis (19% vs 6%, $P < .001$), and septicemia (10.3% vs 6.3%, $P < .001$), and more frequent use of antiarrhythmic medications post–stage 1 palliation. The majority of the study cohort (77.3%) underwent only the shunt procedure. A larger percentage of patients in the GT ± FP compared with the No GT group had multiple cardiac procedures (19.6% vs 15.6%). Age of death (134 vs 26 d, $P < .001$) and length of hospital stay (51 vs 25 d, $P < .001$) were significantly lower in the No GT group. Infants in the GT + FP vs Only GT subgroup had longer hospital stay (62 vs 47 d, $P < .001$), though they died at a younger age (101 vs 166 d, $P = .16$). They also required longer intensive care unit stay (47 vs 28 d, $P < .001$), duration of mechanical ventilation (18 vs 11 d, $P < .001$) and parenteral nutrition (17 vs 10 d, $P < .001$), and had a higher incidence of NEC (9.9% vs 5.8%, $P = .012$), and septicemia (12.6% vs 9.4%, $P < .001$).

3.2 | Mortality

3.2.1 | Mortality over time

Mortality data over the study period are summarized in Table 2 and Supporting Information Table S2. The mortality at hospital discharge over the 10-year study period was consistently and significantly lower in the GT ± FP compared with the No GT group (5% vs 19%, $P < .001$). Hospital mortality was also significantly lower in the Only GT vs the GT + FP subgroup (4% vs 8%, $P = .004$). The discharge hospital mortality outcomes among infants who survived or remained hospitalized at one month of life were comparable to mortality outcomes in the overall study cohort (Supporting Information Table S2).

3.2.2 | Norwood cases count and mortality across centers

The number of HLHS infants undergoing stage 1 Norwood procedure was tabulated per center over the study period (Supporting Information Figure S2). The number of stage 1 Norwood procedure varied among centers and ranged from 2 to 386 cases (median, 94; IQR [48–128]). The percentage of GT ± FP procedures among the study population ranged from 0% to 60% per center (median, 24%; IQR [0%-70%]. The discharge mortality was higher in the No GT group among 38 centers. The median mortality per center in the GT ± FP and the No GT groups was 4% [IQR: 0–7] and 19%, respectively [IQR: 11–30]. About 34 centers that placed GT also performed FP procedure. About 10 centers performed FP in ≤2 patients, while 13 centers completed FP in ≥10 patients. The mortality per center in infants in the Only GT vs the GT + FP subgroup was not calculated secondary to the small count of infants having FP procedure in some centers.

3.2.3 | Gastrostomy tube group

Infants in the GT ± FP group who had any comorbidity (Supporting Information Table S3) compared with infants with no additional morbidities had longer hospital stay, duration of mechanical ventilation and parenteral nutrition, and higher discharge hospital mortality (Supporting Information Table S4).

TABLE 1 Clinical and demographic characteristics of the study cohort

Patient characteristics	All patients (N = 4287)	No GT (N = 3073)	GT ± FP (N = 1214)	P value for comparing No GT to GT ± FP	GT + FP (N = 333)	Only GT (N = 881)	P value for comparing GT + FP to Only GT
*Gestational age (N = 2621)	39 (37–39)	39 (37–39)	39 (37–39)	.7	39 (38–39)	39 (37–39)	.12
*Birth weight (g) (N = 3846)	3120 (2780–3458)	3135 (2800–3460)	3090 (2747–3436)	.077	3170 (2780–3500)	3052 (2720–3400)	.005
*Race (N = 1761)				.57			.47
White	1291 (73.3%)	931 (72.5%)	360 (75.6%)		100 (71.9%)	260 (77.2%)	
Black	219 (12.4%)	163 (12.7%)	56 (11.8%)		18 (12.9%)	38 (11.3%)	
Asian	36 (2.0%)	25 (1.9%)	11 (2.3%)		2 (1.4%)	9 (2.7%)	
American Indian	10 (0.6%)	8 (0.6%)	2 (0.4%)		1 (0.7%)	1 (0.3%)	
Other	205 (11.6%)	158 (12.3%)	47 (9.9%)		18 (12.9%)	29 (8.6%)	
Gender is male	2621 (61%)	1916 (62%)	705 (58%)	.01	194 (58%)	511 (58%)	.95
Clinical data							
Hospital length of stay	30 (19–52)	25 (17–39)	51 (34–79)	<.001	62 (43–94)	47 (30–75)	<.001
Age at death (days) (N = 653)	29 (14–64)	26 (13–53)	134 (66–233)	<.001	101 (84–150)	166 (48–272)	.16
Age at first Norwood	7 (5–10)	7 (5–10)	7 (5–13)	<.001	7 (5–12)	7 (5–13)	.2
Age at gastrostomy tube placement (days)	NA	NA	45 (32–65)	NA	44 (31–65)	46 (32–66)	.44
Days in intensive care unit	21 (12–38)	18 (11–29)	35 (19–63)	<.001	47 (28–2)	28 (17–57)	<.001
Pre-Norwood	4 (2–7)	4 (2–6)	5 (2–7)	<.001	5 (3–8)	4 (2–7)	.077
Post-Norwood	15 (8–31)	12 (7–23)	28 (14–53)	<.001	42 (24–66)	23 (12–48)	<.001
Days on parenteral nutrition	8 (1–15)	7 (0 −13)	12 (3–23)	<.001	17 (6–31)	10 (3–19)	<.001
Days on mechanical ventilation	9 (4–7)	8 (4–4)	13 (6–25)	<.001	18 (10–35)	11 (5–22)	<.001
Pre-Norwood	0 (0–3)	0 (0–3)	0 (0–3)	<.001	1 (0–5)	0 (0–3)	.004
Post-Norwood	7 (4–3)	6 (3–11)	10 (5–22)	<.001	15 (7–9)	9 (4–18)	<.001
Other diagnoses							
Chromosomal abnormalities	181 (4.2%)	115 (3.7%)	66 (5.4%)	.013	15 (4.5%)	51 (5.8%)	.38
Congenital anomalies							
Tracheoesophageal fistula/anomalies of esophagus	22 (0.5%)	4 (0.1%)	18 (1.5%)	<.001	1 (0.3%)	17 (1.9%)	.036
Cleft lip or palate	41 (1.0%)	19 (0.6%)	22 (1.8%)	<.001	8 (2.4%)	14 (1.6%)	.34
Anomalies of larynx	160 (3.7%)	68 (2.2%)	92 (7.6%)	<.001	31 (9.3%)	61 (6.9%)	.16
Vocal cord paralysis	424 (10%)	193 (6%)	231 (19%)	<.001	87 (26%)	144 (16%)	<.001
Anomalies of the urinary system	248 (5.8%)	159 (5.2%)	89 (7.3%)	.007	28 (8.4%)	61 (6.9%)	.38
Anomalies of the nervous system	95 (5.8%)	49 (1.6%)	46 (3.8%)	<.001	14 (4.2%)	32 (3.6%)	.64
Extracorporeal membrane oxygenation (ECMO)	576 (13%)	432 (14%)	144 (12%)	.056	47 (14%)	9 (11%)	.14
Necrotizing enterocolitis	220 (5.1%)	136 (4.4%)	84 (6.9%)	<.001	33 (9.9%)	51 (5.8%)	.012
Septicemia	320 (7.5%)	195 (6.3%)	125 (10.3%)	<.001	42 (12.6%)	83 (9.4%)	.1
Cardiopulmonary resuscitation	272 (6.3%)	200 (6.5%)	72 (5.9%)	.55	25 (7.5%)	47 (5.3%)	.15

(Continues)

TABLE 1 (Continued)

Patient characteristics	All patients (N = 4287)	No GT (N = 3073)	GT ± FP (N = 1214)	*P* value for comparing No GT to GT ± FP	GT + FP (N = 333)	Only GT (N = 881)	*P* value for comparing GT + FP to Only GT
Procedures				.01			.01
Cardiac procedure							
Sano only	252 (5.9%)	183 (6.0%)	69 (5.7%)		8 (2.4%)	61 (6.9%)	
Shunt only	3316 (77.3%)	2409 (78.4%)	907 (74.7%)		253 (76.0%)	654 (74.2%)	
Sano + Shunt	719 (16.8%)	481 (15.6%)	238 (19.6%)		72 (21.6%)	166 (18.9%)	
(Pre-Norwood procedure)							
Ventricular assist device	1 (0%)	1 (0%)	0 (0%)	.53	0 (0%)	0 (0%)	NA
Hemodialysis	2 (0.0%)	2 (0.1%)	0 (0.0%)	.37	0 (0.0%)	0 (0%)	NA
Peritoneal dialysis	8 (0.2%)	6 (0.2%)	2 (0.2%)	.83	0 (0.0%)	2 (0.2%)	.38
Pericardiocentesis	13 (0.3%)	7 (0.2%)	6 (0.5%)	.15	0 (0.0%)	6 (0.7%)	.13
Cardiopulmonary bypass	114 (2.7%)	90 (2.9%)	24 (2.0%)	.081	8 (2.4%)	16 (1.8%)	.51
Tracheostomy	2 (0.0%)	1 (0.0%)	1 (0.1%)	.5	1 (0.3%)	0 (0.0%)	.1
Cardiac catheterization	390 (9.1%)	261 (8.5%)	129 (10.6%)	.029	36 (11%)	93 (11%)	.9
ECMO	299 (7.0%)	224 (7.3%)	75 (6.2%)	.2	20 (6.0%)	55 (6.2%)	.88
Procedures (Post-Norwood procedure)							
Ventricular assist device	8 (0.2%)	7 (0.2%)	1 (0.1%)	.32	0 (0.0%)	1 (0.1%)	.54
Hemodialysis	46 (1.1%)	38 (1.2%)	8 (0.7%)	.098	2 (0.6%)	6 (0.7%)	.88
Peritoneal dialysis	240 (5.6%)	197 (6.4%)	43 (3.5%)	<.001	8 (2.4%)	35 (4.0%)	.19
Pericardiocentesis	57 (1.3%)	35 (1.1%)	22 (1.8%)	.083	6 (1.8%)	16 (1.8%)	.99
Cardiopulmonary bypass	274 (6.4%)	153 (5.0%)	121 (10.0%)	<.001	38 (11.4%)	83 (9.4%)	.3
Tracheostomy	75 (1.7%)	14 (0.5%)	61 (5.0%)	<.001	19 (5.7%)	42 (4.8%)	.5
Cardiac catheterization	627 (15%)	374 (12%)	253 (21%)	<.001	81 (24%)	172 (20%)	.066
ECMO	329 (7.7%)	245 (8.0%)	84 (6.9%)	.24	33 (9.9%)	51 (5.8%)	.012
Medications (Pre-Norwood procedure)							
Use of antiarrhythmics	274 (6.4%)	184 (6.0%)	90 (7.4%)	.086	19 (5.7%)	71 (8.1%)	.16
Use of pressors	2145 (50%)	1506 (49%)	639 (53%)	.032	178 (54%)	461 (52%)	.73
Use of Nitric Oxide	29 (0.7%)	20 (0.7%)	9 (0.7%)	.74	4 (1.2%)	5 (0.6%)	.25
Medication (Post-Norwood procedure)							
Use of antiarrhythmics	2147 (50%)	1456 (47%)	691 (57%)	<.001	214 (64%)	477 (54%)	.001
Use of pressors	4133 (96.4%)	2962 (96.4%)	1171 (96.5%)	.91	326 (97.9%)	845 (95.9%)	.095
Use of Nitric oxide	216 (5.0%)	135 (4.4%)	81 (6.7%)	.002	18 (5.4%)	63 (7.2%)	.28

*There were incomplete data on gestational age, birth weight, and race; More than 20% of values on gestational age and race variables were missing; Continuous variables were summarized as median (IQR); Categorical variables were summarized as N (%); Mann–Whitney U tests were used to compare continuous variables; chi-square tests were used to test categorical variables. $P \leq .05$ is considered statistically significant.

TABLE 2 Discharge hospital mortality for the overall study cohort

Discharge hospital mortality by time era	No GT $N = 3037$	GT ± FP Total $N = 1214$	Only GT $N = 881$	GT + FP $N = 333$	P value	P value No GT vs GT ± FP
2004 – 2006	21% (206/981)	6% (18/313)	5% (11/236)	9% (7/77)	.24	<.001
2007 – 2009	18% (188/1020)	5% (20/405)	3% (7/270)	10% (13/135)	.005	<.001
2010 – 2013	19% (201/1072)	4% (20/496)	4% (14/375)	5% (6/121)	.74	<.001
2004 – 2013	**19% (595/3073)**	**5% (58/1214)**	**4% (32/881)**	**8% (26/333)**	**.004**	**<.001**

GT, gastrostomy tube; FP, Nissan fundoplication.
Mortality data were summarized as N (%).
Chi-square tests were used to compare mortality among different groups; $P \leq .05$ was considered statistical significant.

3.2.4 | Risk factor analysis

Both univariable and multivariable analysis were completed to assess risk factors for hospital mortality for the entire study cohort (Table 3). Multivariable analysis indicated that a GT placement was associated with a significantly higher likelihood of survival to hospital discharge (HR, 0.06, CI [0.04-0.1]), whereas additional FP placement was associated with a higher risk of mortality (HR, 2.77; CI [1.52, 5.04]). Hospitals with a larger median annual cardiopulmonary bypass had better survival. The presence of vocal cord paralysis, cardiopulmonary bypass post-Norwood, and a more recent time era were linked with a better likelihood of survival. On the other hand, patients who had chromosomal abnormalities, needed extracorporeal membrane oxygenation (ECMO), or underwent the Shunt procedure were at higher risk of mortality prior to hospital discharge. These results were very consistent in the models for hospital survival at 1 month of life till hospital discharge (Supporting Information Table S5).

In addition, GT or FP procedure, chromosomal abnormalities, anomalies of the larynx or the urinary system, and the need for ECMO or cardiopulmonary resuscitation prior or post–stage 1 Norwood procedure (cardiac catheterization or cardiopulmonary bypass) were identified as significant predictors for prolonged hospital stay (Supporting Information Table S6).

4 | DISCUSSION

This study specifically investigates *in-hospital mortality* among infants with HLHS who had GT ± FP procedure following stage 1 palliation. In this large multicenter retrospective cohort study, we observed that infants in the GT ± FP vs the No GT group had higher survival while still hospitalized after the stage 1 Norwood operation. Interestingly, this improved survival was noted consistently across the 10-year study period and across centers even though this high-risk population had longer hospital stay. In addition, infants in the GT + FP vs Only GT subgroup had higher mortality. In the multivariable analysis, a GT placement was associated with a higher likelihood of survival to hospital discharge, whereas additional FP was associated with a higher risk of mortality.

In contrast to our study endpoint of in-hospital mortality, previous studies have mainly focused on inter-stage mortality post–hospital discharge.[9,11–13] Furthermore, unlike previous reports which included patients with diverse heart lesions and single ventricle physiology, our study specifically examined infants with HLHS.[9,11–13] Literature on inter-stage mortality for infants with single ventricular physiology generally indicated that infants who underwent a GT placement have higher mortality rate. Hebson et al conducted a single center retrospective review of patients undergoing single-ventricle palliation and reported a higher mortality in the GT group.[9] Ghanayem et al completed a secondary analysis of the Single Ventricle Reconstruction Trial cohort and also showed that the inability to feed orally at time of first discharge was associated with higher mortality.[12] In addition, Keating et al noted higher mortality in patients with single ventricle physiology who had a GT placement.[13] In contrast, Di Maria et al concluded that a GT procedure after the initial palliation is linked with longer hospital stay, though is not associated with an increase in the inter-stage mortality.[11] The above studies speculated that infants in the GT group had a more complicated hospital course. As such, the GT procedure was a surrogate for a significant disease burden rather than a contributing factor for increased mortality. Our study confirmed that infants in the GT ± FP group are the sicker cohort and had longer hospital stay. However, our analysis also revealed that these infants did not have higher hospital mortality. In contrast to our study, previous reports have excluded infants who died prior to their first hospital discharge. An analysis that calculated an aggregate mortality rate (ie, discharge hospital mortality and inter-stage mortality) might have a different conclusion. The limitations of the database preclude us from further delineating the causes for the differences in mortality between the study groups post–hospital discharge. Nevertheless, our results clearly point to the need for a prospective study with a robust follow-up design to further examine this question.

The association of GERD and congenital heart disease has been well described.[14] Earlier studies evaluated surgical correction of reflux symptoms in infants with HLHS and concluded that FP procedure can be safely performed following stage 1 palliation.[15–17] Though, this procedure is not without associated risks.[16] Garey et al reviewed their single center experience of FP during the inter-stage period and determined that the procedure carried a high morbidity and mortality.[18]

TABLE 3 Univariable and multivariable Cox regression for time-to-death for the overall study cohort

Variable	Univariable HR (95% CI)	Univariable *P* value	Multivariable HR (95% CI)	Multivariable *P* value
Gastrostomy tube placement	0.11 (0.08, 0.15)	<.001	0.06 (0.04, 0.1)	<.001
Birth weight (kg)				
0.5 kg increase	0.79 (0.74, 0.85)	<.001	0.81 (0.75, 0.86)	<.001
Male	0.84 (0.72, 0.98)	.028	1 (0.85, 1.18)	.999
Age at Norwood (days)				
30 day increase	0.99 (0.98, 1.01)	.266		
Chromosomal abnormalities	1.36 (1.01, 1.84)	.046	1.63 (1.17, 2.26)	.004
Tracheoesophageal fistula/anomalies of esophagus	1.30 (0.58, 2.92)	.52		
Cleft lip or palate	0.86 (0.42, 1.74)	.67		
Anomalies of larynx	0.30 (0.18, 0.50)	<.001	0.45 (0.25, 0.78)	.005
Anomalies of urinary system	1.27 (0.96, 1.68)	.096	1.52 (1.13, 2.03)	.005
Vocal cords paralysis	0.20 (0.13, 0.32)	<.001	0.45 (0.28, 0.72)	<.001
Extracorporeal membrane oxygenation (ECMO) pre-Norwood	3.77 (3.17, 4.48)	<.001	3.07 (2.53, 3.71)	<.001
ECMO post-Norwood	4.58 (3.87, 5.43)	<.001	4.09 (3.4, 4.92)	<.001
Cardiopulmonary bypass post-Norwood	0.74 (0.57, 0.95)	.017	0.72 (0.55, 0.94)	.015
Cardiac catheterization post-Norwood	0.88 (0.73, 1.06)	.19	0.82 (0.67, 1.01)	.063
Cardiopulmonary resuscitation (CPR) pre-Norwood	2.85 (2.31, 3.51)	<.001	1.72 (1.36, 2.17)	<.001
CPR post-Norwood	3.38 (2.37, 4.82)	<.001	1.35 (0.9, 2.02)	.153
Cardiac procedure				
Shunt only	1.69 (1.14, 2.51)	.009	1.67 (1.07, 2.6)	.023
Sano + Shunt	1.38 (0.9, 2.13)	.14	1.24 (0.76, 2.01)	.394
Sano only	Reference		Reference	
Nissen fundoplication	0.24 (0.16, 0.36)	<.001	2.77 (1.52, 5.04)	<.001
Hospital median annual cardiac bypass cases				
100 unit increase	0.89 (0.85, 0.94)	<.001	0.89 (0.84, 0.95)	<.001
Era				
2004 to 2006	1.73 (1.43, 2.09)	<.001	1.6 (1.3, 1.97)	<.001
2007 to 2009	1.24 (1.02, 1.50)	.029	0.92 (0.74, 1.13)	.417
2010 to 2013	Reference		Reference	

Gestational age and race variables were not included in the model since they were missing ≥20% of data points.

Watkin et al also indicated that GT with FP procedure was associated with increased intraoperative and immediate postoperative morbidity.[16] In addition, Berman et al evaluated 1289 pediatric patients that who underwent GT placement in the 2012 National Surgical Quality Improvement Program.[19] The authors concluded that concomitant fundoplication was an independent risk factor for 30-day postoperative morbidity.[19] Our multivariable analysis showed that FP procedure increased the risk of mortality prior to hospital discharge. Though, our study was limited by the retrospective design. Thus, were unable to carefully assess the preoperative workup for FP procedure, including swallow study or reflux evaluation. Concomitant FP along with GT procedure is controversial and varies greatly across centers. Despite its purported advantage in preventing severe GERD, FP is a more invasive procedure compared with only GT placement and is not without additional morbidity. This may explain the reluctance of some centers in our study cohort to consider FP.

The overall hospital mortality of 15% following stage 1 Norwood was comparable to earlier reports.[20] In addition to the GT and FP procedures, our study evaluated multiple risk factors for mortality prior to hospital discharge. Patients who underwent the Shunt vs the Sano procedure were at higher risk of mortality. This finding was previously shown in a randomized multicenter trial comparing the 12-months transplantation free survival among the shunt types in the Norwood Procedure.[21] The authors attributed their finding to a better coronary flow with the Sano procedure.[21] A trend of decreasing mortality across the different eras was anticipated and well documented as the field of cardiology progressed over time.[20] In addition, higher center volume was previously linked with better outcomes.[22] Surprisingly, vocal cord paralysis and anomalies of the larynx variables were associated with better survival prior to hospital discharge. We speculate that this result is possibly due to an earlier GT placement in this group as the median time for GT placement was earlier in infants with vocal cord paralysis and [35.5 d; IQR 28, 49.5 d] and among those with anomalies of larynx was [36 d; IQR 28, 67.5 d], compared with 45 d [IQR 32, 66] in the overall study cohort. In addition, post-Norwood use of cardiopulmonary bypass variable was also associated with higher survival. We can only speculate that this variable could be a surrogate for a more diligent postoperative care and an aggressive proactive approach to diagnosing and treating arch obstruction or shunt malfunction.

Our study also identified significant predictors of prolonged hospital stay following stage 1 including a GT placement and congenital anomalies. While prior studies evaluating feeding practices post–stage 1 palliation differ on mortality rates among infants who had GT placement, they consistently prolonged hospitalization among these infants.[6,11]

Our study has limitations since it is a retrospective evaluation of multi-institutional pediatric administrative database. The use of administrative database in outcome research offers the advantage of a large samples size, though is limited by the unavailability of specific data points.[23] As such, our study lacked specific anthropometric data including weight gain and nutritional practices such as the details of specific feeding strategies, the amount of oral, nasogastric, or GT feedings, and the type of feeding (breast milk or formula) or its caloric content. We could not gather for GT and/or FP procedure. We were also unable to collect some known risk factors for mortality such as the anatomic and operative variables[24] or identify the exact etiology for reoperation or death in our patient population. In addition, we could not follow our study cohort post the primary hospitalization given the significant loss of follow up of patients across multiple hospitalizations in the PHIS database. Though, this study still provides the distinctive advantage of national level, pediatric data from the majority of US metropolitan areas and clearly points to the imperative need to further investigate this question in a prospective study design or by data linkage with other national databases.

In conclusion, GT procedure did not place infants with HLHS at higher risk for mortality even though these infants had prolonged hospital stay. Patients with HLHS who had difficulty reaching goal oral feeding post stage 1 palliation should be considered for a GT placement. Although we do not advocate preemptive GT placement in patients with HLHS following stage 1 palliation, the findings of this analysis emphasize the need to conduct a multicenter prospective study evaluating the impact of GT placement following stage 1 Norwood procedure.

CONFLICT OF INTEREST

None.

AUTHOR CONTRIBUTIONS

Research design, acquisition, interpretation of data, drafting of manuscript, approval of article: Parthak Prodhan

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REFERENCES

[1] Azakie T, Merklinger SL, McCrindle BW, et al. Evolving strategies and improving outcomes of the modified norwood procedure: a 10-year single-institution experience. *Ann Thorac Surg.* 2001;72(4):1349–1353.

[2] Furck AK, Uebing A, Hansen JH, et al. Outcome of the Norwood operation in patients with hypoplastic left heart syndrome: a 12-year single-center survey. *J Thorac Cardiovasc Surg.* 2010;139(2):359–365.

[3] Anderson JB, Beekman RH, 3rd, Border WL, et al. Lower weight-for-age z score adversely affects hospital length of stay after the bidirectional Glenn procedure in 100 infants with a single ventricle. *J Thorac Cardiovasc Surg.* 2009;138(2):397–404.

[4] Eskedal LT, Hagemo PS, Seem E, et al. Impaired weight gain predicts risk of late death after surgery for congenital heart defects. *Arch Dis Child.* 2008;93(6):495–501.

[5] Newburger JW, Wypij D, Bellinger DC, et al. Length of stay after infant heart surgery is related to cognitive outcome at age 8 years. *J Pediatr.* 2003;143(1):67–73.

[6] Lambert LM, Pike NA, Medoff-Cooper B, et al. Variation in feeding practices following the Norwood procedure. *J Pediatr.* 2014;164(2):237–242.

[7] Garcia X, Jaquiss RD, Imamura M, Swearingen CJ, Dassinger MS, 3rd, Sachdeva R. Preemptive gastrostomy tube placement after Norwood operation. *J Pediatr.* 2011;159(4):602–607.

[8] Hill GD, Hehir DA, Bartz PJ, et al. Effect of feeding modality on interstage growth after stage I palliation: a report from the National Pediatric Cardiology Quality Improvement Collaborative. *J Thorac Cardiovasc Surg.* 2014;148(4):1534–1539.

[9] Hebson CL, Oster ME, Kirshbom PM, Clabby ML, Wulkan ML, Simsic JM. Association of feeding modality with interstage mortality after single-ventricle palliation. *J Thorac Cardiovasc Surg.* 2012;144(1):173–177.

[10] Fletcher DM. Achieving data quality. How data from a pediatric health information system earns the trust of its users. *J Ahima.* 2004;75(10):22–26.

[11] Di Maria MV, Glatz AC, Ravishankar C, et al. Supplemental tube feeding does not mitigate weight loss in infants with shunt-dependent single-ventricle physiology. *Pediatr Cardiol.* 2013;34(6):1350–1356.

[12] Ghanayem NS, Allen KR, Tabbutt S, et al. Interstage mortality after the Norwood procedure: results of the multicenter Single Ventricle

Reconstruction trial. *J Thorac Cardiovasc Surg*. 2012;144(4): 896–906.

[13] Keating JJ, Simsic JM, Kogon BE, et al. Impact of early fundoplication or gastrostomy tube on midterm outcomes for patients with single ventricle. *J Thorac Cardiovasc Surg*. 2012;143(4): 891–895.

[14] Weesner KM, Rosenthal A. Gastroesophageal reflux in association with congenital heart disease. *Clin Pediatr(Phila)*. 1983;22(6): 424–426.

[15] Cribbs RK, Heiss KF, Clabby ML, Wulkan ML. Gastric fundoplication is effective in promoting weight gain in children with severe congenital heart defects. *J Pediatr Surg*. 2008;43(2):283–289.

[16] Watkins S, Morrow SE, McNew BS, Donahue BS. Perioperative management of infants undergoing fundoplication and gastrostomy after stage I palliation of hypoplastic left heart syndrome. *Pediatr Cardiol*. 2012;33(5):697–704.

[17] Slater B, Rangel S, Ramamoorthy C, Abrajano C, Albanese CT. Outcomes after laparoscopic surgery in neonates with hypoplastic heart left heart syndrome. *J Pediatr Surg*. 2007;42(6): 1118–1121.

[18] Garey CL, Laituri CA, Aguayo P, et al. Outcomes in children with hypoplastic left heart syndrome undergoing open fundoplication. *J Pediatr Surg*. 2011;46(5):859–862.

[19] Berman L, Sharif I, Rothstein D, Hossain J, Vinocur C. Concomitant fundoplication increased morbidity of gastrostomy tube placement. *J Pediatr Surg*. 2015;50(7):1104–1108.

[20] Czosek RJ, Anderson JB, Heaton PC, Cassedy A, Schnell B, Cnota JF. Staged palliation of hypoplastic left heart syndrome: trends in mortality, cost, and length of stay using a national database from 2000 through 2009. *Am J Cardiol*. 2013;111(12): 1792–1799.

[21] Ohye RG, Sleeper LA, Mahony L, et al. Comparison of shunt types in the Norwood procedure for single-ventricle lesions. *N Engl J Med*. 2010;362(21):1980–1992.

[22] Hornik CP, He X, Jacobs JP, et al. Relative impact of surgeon and center volume on early mortality after the Norwood operation. *Ann Thorac Surg*. 2012;93(6):1992–1997.

[23] Gandhi S, Salmon JW, Kong SX, Zhao SZ. Administrative databases and outcomes assessment. An overview of issues and potential utility. *J Managed Care Pharm*. 1999;5(3):215–222.

[24] Alsoufi B, Mori M, Gillespie S, et al. Impact of patient characteristics and anatomy on results of Norwood operation for hypoplastic left heart syndrome. *Ann Thorac Surg*. 2015;100(2):591–598.

SUPPORTING INFORMATION

Additional Supporting Information may be found online in the supporting information tab for this article.

Figure S1. Flow diagram showing description of the study cohort.

Figure S2. Center variation for case count (GT ± FP and No GT) (upper graph) and discharge hospital mortality (GT ± FP and No GT) (lower graph).

Table S1. Diagnosis, procedures, and pharmacological agents, and corresponding codes.

Table S2. Discharge hospital mortality among infants who survived or remained hospitalized beyond the first month of life.

Table S3. Tabulation of comorbidities among infants who had a gastrostomy procedure.

Table S4. Comparison of outcomes among infants in the gastrostomy tube feeding group who had any comorbidity versus no comorbidity.

Table S5. Univariate and multivariable Cox regression for time-to-death for infants who remained hospitalized or survived at one month of life.

Table S6. Univariate and multivariable logistic regression for evaluation of predictors of prolonged length of hospital stay (LOS>52 days).

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