2-1-2014

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Recommended Citation

Lambert, L. M., Pike, N. A., Medoff-Cooper, B., Zak, V., Pemberton, V. L., Young-Borkowski, L., Clabby, M. L., Nelson, K. N., Ohye, R. G., Trainor, B., Uzark, K., Rudd, N., Bannister, L., Korsin, R., Cooper, D. S., Pizarro, C., Zyblewski, S. C., Bartle, B. H., Williams, R. V., ., Shirali, G. S. Variation in feeding practices following the Norwood procedure. *The Journal of pediatrics* 164, 237-242 (2014).

Published in final edited form as:
J Pediatr. 2014 February ; 164(2): 237–242.e1. doi:10.1016/j.jpeds.2013.09.042.

Variation in Feeding Practices Following the Norwood Procedure

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Abstract

Objectives—To assess variation in feeding practice at Norwood discharge, factors associated with tube feeding, and associations between site, feeding mode, and growth prior to stage II.

Study design—From May 2005 to July 2008, 555 subjects from 15 centers were enrolled in the Pediatric Heart Network Single Ventricle Reconstruction Trial; 432 survivors with Norwood discharge feeding data were analyzed.

Results—Demographic and clinical variables were compared among 4 feeding modes: oral only (n=140), oral/tube (n=195), nasogastric tube (N-tube) only (n=40), and gastrostomy tube (G-tube) only (n=57). There was significant variation in feeding mode among sites (oral only 0–81% and G-tube only 0–56%, $p<0.01$). After adjusting for site, multivariable modeling showed G-tube feeding at discharge was associated with longer hospitalization, and N-tube feeding was associated with greater number of discharge medications ($R^2=0.65$, $p<0.01$). After adjusting for site, mean pre-stage II weight-for-age z-score (WAZ) was significantly higher in the oral only group (−1.4) vs. the N-tube only (−2.2) and G-tube only (−2.1) groups ($p=0.04$ and 0.02, respectively).

Conclusions—Feeding mode at Norwood discharge varied among sites. Prolonged hospitalization and greater number of medications at the time of Norwood discharge were associated with tube feeding. Infants exclusively fed orally had a higher WAZ pre-stage II than those fed exclusively by tube. Exploring strategies to prevent morbidities and promote oral feeding in this highest risk population is warranted.

Keywords

hypoplastic left heart syndrome; growth; nutrition; practice variation

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Despite improvements in survival of infants with hypoplastic left heart syndrome (HLHS) following the Norwood procedure, this population remains at risk for a number of medical morbidities. One of the most difficult to manage medical problems in these infants following surgical palliation is poor growth. The pattern of poor growth following the Norwood procedure has been well described (1–4) with the poorest growth occurring during the early post-operative period and the interstage period, the time between hospital discharge following the Norwood procedure, and the performance of the volume unloading superior cavopulmonary anastomosis (stage II procedure). Both poor growth during early infancy and longer hospitalizations are risk factors for poor neurodevelopmental outcome (6–8) and increased late mortality (9).

Although many feeding strategies have been proposed in neonates with HLHS, including standardized feeding protocols (10, 11) and preemptive gastrostomy tube placement (12), none have resulted in dramatic improvement in weight gain during the interstage period or become “standard care” to promote growth in this population. Because of this, there is significant center variation in feeding practice and growth outcomes in these high risk infants (3, 13).

The National Heart, Lung, and Blood Institute sponsored Pediatric Heart Network Single Ventricle Reconstruction (SVR) trial was a multicenter, randomized trial of shunt type (modified Blalock-Taussig shunt vs. right ventricle-to-pulmonary artery shunt) in neonates with HLHS and other single right ventricular anomalies undergoing a Norwood procedure (15). The purposes of this analysis were to assess differences in feeding practices at the time of Norwood hospital discharge among participating centers, identify factors associated with tube feeding, and to assess associations between site, mode of feeding, and growth prior to the stage II procedure.

Methods

Subjects who were consented and enrolled in the SVR Trial from May 2005 through July 2008 at the 15 participating North American centers and who had feeding data recorded at the time of Norwood hospitalization discharge were included in this post hoc analysis. Institutional review board approval was obtained at each individual site. Briefly, inclusion criteria for the SVR trial included a diagnosis of HLHS or a related single right ventricular anomaly and a planned Norwood procedure. Exclusion criteria included preoperative identification of an anatomic abnormality that would render either a modified Blalock-Taussig shunt or a right ventricle-to-pulmonary artery shunt technically impossible, and any major congenital abnormality (e.g. congenital diaphragmatic hernia, tracheoesophageal fistula, trisomy 13, and trisomy 18) or acquired extra-cardiac disorder (e.g. meconium aspiration with need for high frequency ventilation, persistent renal failure requiring dialysis) that, in the opinion of the investigator, could independently affect the likelihood of the subject meeting the primary endpoint (15). Subjects who were not discharged from the hospital prior to their stage II procedure were not included in this analysis.

Subject data collected during the SVR trial included sex, gestational age, birth weight, specific anatomic diagnosis, and the presence or absence of a genetic syndrome. Norwood hospitalization data collected included pre-Norwood intubation, number of discharge medications, number of additional surgical or catheter-based procedures, and Norwood hospitalization length of stay. Mode of feeding at Norwood discharge was classified into 4 groups as follows: (1) oral only: all nutrition provided via oral route(breast or bottle feeding); (2) oral/tube: nutrition provided via oral feeding and supplemented by enteral tube feeding; (3) nasogastric/jejunal tube feeding only (N-tube): all nutrition received via a nasogastric or nasojejunal tube; and (4) gastrostomy tube only (G-tube): all nutrition received via a gastrostomy or gastrojejunostomy tube Information regarding the specific type of nutritional support (type of formula, caloric density, total calories per day, bolus vs. continuous feedings) was not collected during the SVR trial.

As part of the SVR trial subject weights were obtained at the time of study enrollment (prior to the Norwood procedure), at the time of Norwood hospitalization discharge, and weight at admission for the stage II procedure. Weight-for-age z-scores (WAZ) were calculated using the World Health Organization standard.

Statistical Analyses

Associations between weight-for-age z-score and feeding mode at Norwood discharge and clinical site were assessed using ANOVA modeling. Univariate and multivariable logistic regression were used to examine patient and clinical factors associated with tube feeding.

Continuous variables included gestational age, total cardiopulmonary bypass time, total deep hypothermic circulatory arrest time, oxygen saturation at Norwood discharge, number of medications at Norwood discharge, number of adverse events, and log-transformed length of Norwood hospital stay, length of intensive care unit stay and days of ventilator support. Categorical variables included sex, ethnicity, prematurity (gestational age <37 weeks), confirmed genetic syndrome, diagnosis of hypoplastic left heart syndrome, shunt type (modified Blalock-Taussig shunt vs. right ventricle to pulmonary artery shunt), associated diagnosis, pre-Norwood intubation, extracorporeal membrane oxygenation support, and whether the patient was discharged on oxygen following the Norwood procedure.

Because the outcome (mode of feeding) is a nominal variable with 4 unordered categories, and it is not clinically clear how to convert feeding mode into ordered categories (especially for G-tube vs. N-tube), a multinomial logit model was used to analyze associations between the outcome and each of the potential predictors. Therefore, the results are presented as odds ratios (and estimates) for each of 3 feeding categories vs. a reference one (pure N-tube, or pure G-tube). To inform selection of the final multivariable model, multinomial logit stepwise regression (with p-value for entry =0.15 and p-value for staying =0.05) was used. Multivariable modeling was limited to the predictors which demonstrated reasonably strong univariate associations ($p < 0.2$). Tukey test was used for post hoc multiple comparisons. Missing values presented only a minor issue in these analyses, and imputation was not performed.

Results

Of the 555 subjects enrolled in the SVR trial, 467survived to discharge and 435 had feeding data recorded at the time of Norwood discharge. Three subjects receiving only total parenteral nutrition were excluded leaving a cohort of 432 for the analysis. There were 140 subjects in the oral only group, 195 in the oral/tube group, 40 in the N-tube group, and 57 in the G-tube group. Weight-for-age z-scores were available prior to the stage II procedure in 377 of 432 subjects (87%). Data were missing due to death or heart transplant in 48/55 (87%) cases. Those subjects with missing weight-for-age z-scores prior to the stage II procedure had lower weight-for-age z-scores at Norwood discharge (−2.3±1.2 vs. −1.8±1.2, p=0.008).

Clinical characteristics of the study subjects by feeding mode are shown in Table I. Sex, specific diagnosis, and birth weight were similar among the 4 feeding groups. Subjects in the oral only group were less likely to have required intubation prior to the Norwood procedure. They also appear less likely to have a genetic syndrome (although overall only 4% of subjects had a genetic syndrome). Subjects in the oral only group had a shorter length of stay following the Norwood procedure and were receiving fewer medications at the time of Norwood discharge. Subjects who were exclusively tube fed (N-tube or G-tube group) at the time of Norwood discharge were receiving a greater number of total medications including anti-reflux medications. Necrotizing enterocolitis, tricuspid regurgitation and right ventricular function were not associated with feeding mode. A minority of patients was followed using some form of a home monitoring program during the SVR trial and therefore this variable was not included in the analysis.

There was significant variability among participating centers in the percentage of subjects receiving each mode of feeding at the time of Norwood hospitalization discharge ($p<0.001$). The range across centers for the oral only group was 0 to 81% with a median of 28%, 13 to 86% with a median of 48% for oral/tube group, 0 to 43% with a median of 5% for the N-tube group, and 0 to 56% with a median of 12% for the G-tube group.

There was no significant difference in weight-for-age z-score at baseline, Norwood discharge or prior to the stage II procedure among enrolling sites. However, there were significant differences by site in the change in weight-for-age z-score from baseline to Norwood discharge and from Norwood discharge to the stage II procedure ($p \leq 0.001$).

There was no difference in weight-for-age z-score at baseline by mode of feeding (range −0.8 to −0.4, $R^2=0.01$, $p=0.18$). However, significant differences in the weight-forage z-score by mode of feeding at Norwood discharge (range −2.5 to −1.6, $R^2=0.06$, $p<0.001$) and prior to the stage II procedure (range −2.1 to −1.5, $R^2=0.03$, $p=0.01$) was seen (Figure). The changes in weight-for-age z-score also differed by feeding mode with the change from baseline to Norwood discharge ranging from −1.9 to −1.2 ($R^2=0.08$, $p<0.001$) and the change from Norwood discharge to the stage II procedure ranging from −0.2 to 0.3 ($R^2=0.02$, $p=0.03$). Subjects in the oral only feeding group had the least decline in mean weight-for-age z-score from baseline to Norwood discharge (mean change −1.2±0.5), and those in the G-tube group had the greatest decline (mean change −1.9±0.9). Those subjects in the G-tube group demonstrated the greatest increase in mean weight-for-age z-score between Norwood discharge and the stage II procedure (mean change 0.3 vs. 0.1 for the oral only group).

There was significant variability in weight-for-age z-score by feeding mode at Norwood discharge and prior to the stage II procedure. After adjustment for clinical site variability in weight-for-age z-scores by feeding mode remained significant at Norwood discharge ($R^2=0.09$, $p<0.001$) and prior to the stage II procedure ($R^2=0.08$, $p=0.01$). Clinical site and feeding mode combined explained 21% of the variation in the change in z-score from baseline to Norwood discharge ($R^2=0.21$, $p<0.001$). Comparisons of weight-for-age z-scores for each feeding mode after adjusting for clinical site and for post-hoc multiple comparisons (Tukey) are shown in Table II, which reports adjusted means and pairwise p-values. Subjects in the oral only feeding group generally had the highest adjusted mean weight-for-age z-score and had the lowest decline in weight-forage z-score from baseline to Norwood discharge.

Univariate analysis revealed a number of significant associations with feeding mode at Norwood discharge. Higher odds of being in the oral only or oral/tube vs. N-tube feeding groups were associated with some positive clinic factors including: not receiving supplemental oxygen at Norwood discharge (odds ratio [OR] and 95% confidence intervals 8.6 (2.5, 30.5) for oral only, 3.6 (1.4, 9.6) for oral/tube) and absence of significant pre-Norwood complications (OR 2.6 (1.2, 5.7) for oral only). Similarly, lower odds were associated with some negative clinical factors including increased log-transformed length of ventilation (OR 0.3 (0.2, 0.5) for both), intensive care unit stay (OR 0.3 (0.2, 0.5)for oral only; 0.4 (0.3, 0.7) for oral/tube), and hospital stay (OR 0.3 (0.2, 0.7) for oral only); number of Norwood discharge medications (OR 0.5 (0.4, 0.6) for oral only, 0.7 (0.6, 0.9) for oral/tube); and number of post-Norwood complications (OR 0.8 (0.6, 0.9) for oral only OR 0.8 (0.7, 0.96) for oral/tube). Similarly, higher odds of being in the oral only or oral/tube groups vs. G-tube feeding groups were associated with positive clinical factors including decreased post-Norwood complications (OR 0.7 (0.6, 0.8) for oral only and 0.8 (0.7, 0.8) for oral/tube), and lower odds were associated with negative clinical factors including increased number of discharge medications (OR 0.5 (0.4, 0.6) for oral only and 0.7 (0.6, 0.9) for oral/tube), and

log-transformed length of intensive care unit stay (OR 0.1 (0.06, 0.2) for oral only and 0.2 (0.1, 0.3) for oral/tube).

The final multivariable model for predicting feeding mode at the time of Norwood discharge included the number of post-Norwood medications, log-transformed length of Norwood hospitalization, and clinical site (R^2=0.65, p<0.001). When clinical site was not included in the model the number of post-Norwood medications and log-transformed length of Norwood hospitalization explained 30% of the variation in feeding mode (R^2=0.30, p<0.001). When anti-reflux medications were excluded from the analysis, total number of medications remained an independent predictor of feeding mode. The odds ratio of being in a particular feeding category vs. N-tube or G-tube (p<0.05) at the time of Norwood discharge is shown in Table III.

Discussion

Despite improvements in surgical techniques and medical management of infants with HLHS who undergo Norwood procedure (16), these infants remain at high risk for major morbidities including growth failure (1–3, 13). In other studies of growth in infants following cardiac surgery, increasing caloric intake has resulted in improved weight gain (17), however, similar studies are not available in infants with HLHS. Inadequate caloric intake in this population may be due to a number of factors including oral-motor dysfunction, vocal cord paralysis and gastroesophageal reflux. (18–21). These infants are also at increased risk for the development of necrotizing enterocolitis (21–23), which may result in multiple interruptions in feeding.

For these reasons, one would hypothesize that enteral feeding tubes would be helpful in infants who have poor feeding and growth, yet the data are mixed in regards to feeding tubes resulting in improved growth (2, 13), and failure to feed orally prior to Norwood discharge is associated with interstage mortality (24). Our results suggest that this may be due to the fact that those subjects with feeding tubes are a sicker cohort and suffer other medical morbidities, such as longer length of hospital stay and increased medication use, which may contribute to poor growth. These findings are similar to those of DiMaria et al (4) who demonstrated associations between tube feeding and disease complexity in a single center report in a heterogenous population of infants with shunt dependent congenital heart disease. Alternatively, growth failure in the tube feeding groups may be due to lack of advancement of daily caloric intake as the child grows. In our study only a minority of subjects were involved in a home monitoring program. Home monitoring may allow for increased nutritional surveillance promoting growth as has been shown in other studies (25–27).

Although subjects at all sites had a decline in mean weight-for-age z-scores from baseline to Norwood discharge, subjects at some centers had less of a decline than subjects at others. Our results, which demonstrate that 21% of the variability in the change in weight-for-age z-score from baseline to Norwood discharge is explained by clinical center and feeding mode suggests that there are center specific practices that may result in better growth during this time period.

The National Pediatric Cardiology Quality Improvement Collaborative HLHS registry database revealed significant variability in feeding mode at Norwood discharge, as well as interstage growth. Centers using a growth bundle including standardized feeding evaluation prior to Norwood discharge, use of red flags for weight gain/loss and an interstage home monitoring program had the best interstage growth (13). However, feeding mode and its impact on center variability in growth was not analyzed.

Those subjects who were feeding orally at the time of Norwood discharge demonstrated the lowest decline in weight-for-age z-score from baseline to Norwood discharge and had stable weight-for-age z-scores during the interstage period. Subjects who were feeding orally but receiving some supplemental tube feedings had a higher weight-for-age z-score at the time of Norwood discharge. Subjects who were receiving exclusively enteral tube feedings at the time of Norwood discharge were receiving a greater number of medications and had a longer hospital stay suggesting this group was generally more ill than the subset of subjects receiving at least some oral feedings. Those subjects who were G-tube fed at the time of Norwood discharge demonstrated the poorest growth during the Norwood hospitalization, but did demonstrate some catch-up growth during the interstage period. This finding suggests that these patients may benefit most from the G-tube feedings and would have had poor outcomes with only oral alimentation. Although it is not clear which center specific practices might lead to a greater proportion of orally fed infants following the Norwood procedure or if those subjects receiving nutrition via enteral tubes are simply too ill to tolerate oral feedings, further exploration of these factors may lead to improved nutritional and feeding recommendations in these patients.

Our study has important limitations. Detailed nutritional data, including pre-operative nutrition practices, specific formula, caloric density of the formula, and daily caloric intake were not collected as part of the SVR trial. Details regarding the specifics of gastrointestinal disorders including gastroesophageal reflux or necrotizing enterocolitis were not collected. Other anthropometric data including length and head circumference were not collected at every time point, therefore, evaluation of growth was limited to weight only. There may be center specific practices other than feeding mode that affect growth which were not analyzed. The mode of feeding at Norwood discharge was not necessarily the mode of feeding throughout the entire interstage period.

Our findings suggest that understanding center-specific practices that improve growth may result in better outcomes in this high risk population and potentially other complex congenital heart disease populations at risk for growth failure. These practices are likely multifactorial and may be impacted by the development of feeding protocols and best practice guidelines to promote oral feeding, as well as standardization of postoperative care through a collaborative approach.

Acknowledgments

Supported by the National Heart, Lung, and Blood Institute (NHLBI; HL068269, HL068270, HL068279, HL068281, HL068285, HL068292, HL068290, HL068288, HL085057, HL109781, HL109737). Its contents are solely the responsibility of the authors and do not necessarily represent the official views of NHLBI or the National Institutes of Health. The authors declare no conflicts of interest.

Abbreviations

G-tube	gastrostomy tube
HLHS	hypoplastic left heart
N-tube	nasojejunal or nasogastric tube
SVR Trial	single ventricle reconstruction trial
WAZ	Weight for age Z-score

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APPENDIX

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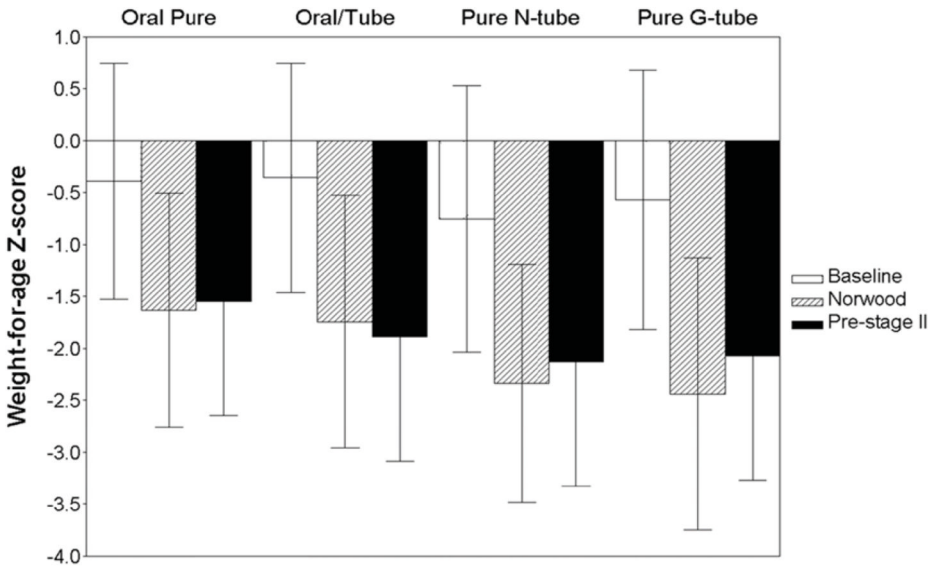

Figure.
Weigh-for-Age Z-scores at Baseline, Norwood Discharge, and Prior to Stage

Table 1

Associations of Clinical Characteristics with Feeding Mode at Norwood Discharge

Characteristic	Oral Only	Oral/Tube	N-Tube Only	G-Tube Only	Site Adjusted p-value*
N	140	195	40	57	
Sex					0.40
Male	82 (59%)	137 (70%)	24 (60%)	32 (56%)	
Female	58 (41%)	58 (30%)	16 (40%)	25 (44%)	
HLHS					0.35
Yes	123 (88%)	176 (90%)	34 (85%)	53(93%)	
No	17 (12%)	19 (10%)	6 (15%)	4 (7%)	
Birth Weight <2.5 kg					0.10
Yes	12 (9%)	20 (10%)	7 (18%)	8 (14%)	
No	128 (91%)	175 (90%)	33 (83%)	49 (86%)	
Pre-Norwood Intubation					**0.001**
Yes	44 (31%)	99 (51%)	24 (62%)	33 (58%)	
No	96 (69%)	95 (49%)	15 (38%)	24 (42%)	
Genetic Syndrome					**0.01**
Yes	3 (3%)	8 (6%)	3 (12%)	4 (10%)	
No	115 (98%)	137 (94%)	21 (88%)	36 (90%)	
Gestational Age (wks)	38.3±1.4	38.4±1.5	38.3±1.8	37.7±1.7	**0.02**
Number of Discharge Medications	4.2±1.6	5.1±1.5	6.4±3.0	6.3±2.7	**<0.01**
Medians	4	5	6	6	

Characteristic	Oral Only	Oral/Tube	N-Tube Only	G-Tube Only	Site Adjusted p-value*
Log Length of Norwood Hospitalization (days)	3.0±0.4	3.2±0.5	3.3±0.7	3.9±0.6	**<0.01**

*Wald Chi-square or ANOVA test, HLHS – Hypoplastic left heart syndrome.

Table 2

Post Hoc Multiple Comparison Tests (Tukey) for Mean Weight-for-age Z-scores by Feeding Mode at Norwood discharge (Adjusted for Clinical Site)

Outcome	Feeding Mode	Adjusted Mean	Pure Oral	Oral/Tube	N-tube	G-tube
Weight-for-age Z-score at Norwood Discharge	Pure Oral	−1.53		0.5	**0.002**	**<0.001**
	Oral/Tube	−1.75	0.5		**0.02**	**0.003**
	N-Tube	−2.43	**0.002**	0.2		0.99
	G-Tube	−2.5	**<0.001**	**0.003**	0.99	
Change in Weight-for-age Z-score from Baseline to Norwood Discharge	Pure Oral	−1.24		0.06	0.03	<0.001
	Oral/Tube	−1.47	0.06		0.64	**<0.001**
	N-Tube	−1.62	**0.03**	0.64		**0.04**
	G-Tube	−2.01	**<0.001**	**<0.001**	**0.04**	
Weight-for-age Z-score Prior to Stage II Procedure	Pure Oral	−1.44		0.17	**0.04**	**0.02**
	Oral/Tube	−1.77	0.17		0.36	0.49
	N-Tube	−2.23	**0.04**	0.36		0.95
	G-Tube	−2.06	**0.02**	0.49	0.95	

Table 3

Final multivariable model for feeding mode at Norwood discharge (N=432, R^2=0.65)

Reference Category	Effect	N	Response	Odds Ratio	95%CL		P-value**	P-value§
					Lower	Upper		
N-Tube	**Number of discharge medications (post-Norwood)**							<.001
		140	Oral Pure	0.56	0.42	0.75	<.01	
		195	Oral/Tube	0.64	0.50	0.82	<.01	
		57	Pure G-tube	0.66	0.50	0.88	<.01	
	Log-transformed length of hospital stay*							<.001
		140	Oral Pure	0.26	0.09	0.73	0.01	
		195	Oral/Tube	1.14	0.48	2.70	0.76	
		57	Pure G-tube	12.76	4.36	37.36	<.01	
	Clinical site							<.001
G-Tube	**Number of discharge medications (post-Norwood)**							<.001
		140	Oral Pure	0.85	0.64	1.12	0.25	
		195	Oral/Tube	0.97	0.77	1.24	0.83	
		40	Pure N-tube	1.51	1.14	2.01	<.01	
	Log-transformed length of hospital stay*							<.001
		140	Oral Pure	0.02	0.01	0.06	<.01	
		195	Oral/Tube	0.09	0.04	0.21	<.01	
		40	Pure N-tube	0.08	0.03	0.23	<.01	
	Clinical site							<.001

* over the course of the Norwood surgery hospitalization

** Wald chi-sq test for the null hypothesis that this coefficient is equal to 0 (i.e. has no effect on the outcome variable). We reject the null hypothesis if p-value <0.05. This p-value should be ignored if overall p is > 0.05.

§ Wald chi-sq test for the null hypothesis that all coefficients are equal to 0. We reject the null hypothesis if p-value <0.05.

N-Tube – nasogastric or jejunal tube, G-Tube – gastrostomy tube.