Impact of postoperative nutrition on weight gain in infants with hypoplastic left heart syndrome

Borah J. Hong, MD,^a Brady Moffett, PharmD, MPH,^b William Payne, BS,^a Sundae Rich, MS, RD,^c Elena C. Ocampo, MD,^a and Christopher J. Petit, MD^d

Objective: The study objective was to evaluate risk factors for poor weight gain in infants with hypoplastic left heart syndrome after stage 1 palliation.

Methods: We reviewed all term infants with hypoplastic left heart syndrome who had stage 1 palliation and stage 2 palliation at Texas Children's Hospital between 2000 and 2011 (n = 120). Predictor variables included age at stage 1 palliation, intensive care unit factors, calories delivered, and echocardiographic findings. Outcome variables included weight for age Z scores at hospital discharge, stage 2 palliation, and change in weight for age Z scores between stage 1 palliation and hospital discharge.

Results: Complete nutritional data were available for 47 of 120 patients. Median total parenteral nutrition duration was 6 days (range, 1-43 days), and median intensive care unit calories delivered was 53.9 kcal/kg/d (range, 22.3-119.6 kcal/kg/d). Before hospital discharge, the median caloric intake was 106.7 kcal/kg/d (range, 70.0-152.0 kcal/kg/d). Median weight for age Z scores was -0.59 (range, -3.6 to 0.5) at stage 1 palliation, -1.62 (range, -4.5 to -0.1) at intensive care unit transfer, and -1.81 (range, -4.9 to -0.5) at hospital discharge. A total of 46 of 47 patients had a negative change in weight for age Z scores between stage 1 palliation and hospital discharge, with a median change of -1.14 (range, -2.3 to 0.6). Change in weight for age Z scores from stage 1 palliation to discharge was directly associated with calories delivered and indirectly associated with hospital length of stay and moderate tricuspid regurgitation ($P < .001$).

Conclusions: Postoperative nutrition fails to meet the needs of infants with hypoplastic left heart syndrome despite increased focus on nutritional support. Modifiable factors (eg, nutritional intake) and hemodynamic factors (eg, tricuspid regurgitation) may play roles in the poor weight gain of these infants. (J Thorac Cardiovasc Surg 2014;147:1319-25)

Infants with complex congenital heart disease are at increased risk of failure to thrive because of several factors, including chronic cyanosis, decreased mesenteric perfusion from low cardiac output, and increased energy expenditure from congestive heart failure.^{1,2} Infants with hypoplastic left heart syndrome (HLHS) are at particular risk of poor weight gain between stage 1 surgical palliation (S1P) and stage 2 surgical palliation (S2P).^{3,4} A low weight-for-age Z score at the time of S2P has been associated with poor clinical outcomes at S2P.⁵ Mesenteric perfusion seems to be altered in infants after the Norwood operation.⁶ Whether poor interstage somatic growth belies poor cardiovascular

efficiency and somatic perfusion or is due to inadequate caloric intake is unclear.^{3,7} A number of studies have shown that increasing caloric density of infant formula during the interstage outpatient period results in improved growth.^{3,8} Thus, identifying any modifiable risk factors for poor weight gain may result in better short-term surgical outcomes and long-term neurodevelopmental outcomes.⁹

To date, there has been little focus on the in-hospital nutrition and calorie administration in infants with single-ventricle physiology. The hospital course surrounding the Norwood operation often is as long as 4 to 8 weeks.⁸ Neonates with HLHS may be undernourished preoperatively for several reasons, including concern for mesenteric ischemia.¹⁰ In the postoperative period, these neonates are often unstable, requiring inotropic support and mechanical ventilation. Total parenteral nutrition (TPN) often is used in place of enteral nutrition in the immediate postoperative period. We hypothesize that the early postoperative period is associated with significant under-nutrition, that TPN is not used fully to achieve adequate nutrition, and that this postoperative period provides an opportunity to improve nutritional delivery to these at-risk neonates.

From the Lillie Frank Abercrombie Section of Cardiology,^a Department of Pediatrics, Texas Children's Hospital, Baylor College of Medicine, Houston, Tex; Department of Pharmacy,^b Texas Children's Hospital, Houston, Tex; Department of Food and Nutrition Services,^c Texas Children's Hospital, Houston, Tex; and Division of Pediatric Cardiology,^d Department of Pediatrics, Children's Healthcare of Atlanta Sibley Heart Center, Emory University School of Medicine, Atlanta, Ga.

Disclosures: Authors have nothing to disclose with regard to commercial support. Received for publication Nov 8, 2012; revisions received May 18, 2013; accepted for publication June 26, 2013; available ahead of print Sept 3, 2013.

Address for reprints: Borah J. Hong, MD, 6621 Fannin St, MC-19345-C, Houston, TX 77030 (E-mail: bjhong@texaschildrens.org).

0022-5223/\$36.00

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<http://dx.doi.org/10.1016/j.jtcvs.2013.06.044>

Abbreviations and Acronyms

HLHS	= hypoplastic left heart syndrome
ICU	= intensive care unit
S1P	= stage 1 surgical palliation
S2P	= stage 2 surgical palliation
TPN	= total parenteral nutrition
WAZ	= weight for age Z scores
Δ WAZ	= change in weight for age Z scores

MATERIALS AND METHODS**Patient Data**

We performed a retrospective study of all term neonates (gestation >36 weeks at birth) born with the diagnosis of HLHS from 2000 to 2011 at Texas Children's Hospital who underwent the Norwood operation as their S1P with a modified Blalock-Taussig shunt or Sano right ventricular to pulmonary artery conduit and who survived to S2P with a Glenn operation consisting of a superior cavopulmonary anastomosis. The institutional review board of our institution approved this study. We excluded infants of preterm gestation (<36 weeks) and those with chromosomal abnormalities, metabolic abnormalities, or gastrointestinal abnormalities. Infants who did not survive to S2P also were excluded.

Patient demographic data were obtained, including gestational age at birth, gender, and age at S1P and discharge from hospital after S1P. Weight at various points for each patient was recorded, including weight at admission, S1P, discharge from intensive care unit (ICU), hospital discharge, and S2P. Weight for age Z scores (WAZ) were calculated using World Health Organization Anthro software, version 3.2.2. Medical data were noted, including total length of hospital stay after S1P, duration of ICU stay, and duration of intubation after S1P. Echocardiogram reports for each patient were reviewed for the presence of moderate or greater tricuspid valve regurgitation and moderate or greater right ventricular systolic dysfunction before S1P, at ICU discharge, and before hospital discharge.

Nutritional Data

Nutritional data, including postoperative TPN duration and caloric density after S1P, and postoperative day of enteral feed initiation, and volume and caloric density of enteral feeds were obtained. At our institution, neonates who undergo S1P are initially placed on intravenous fluids for the first postoperative day and then started on TPN after the initial 24-hour postoperative period. Enteral feeds are generally not started until the patients are off all inotropes, and a significant number do not start enteral feeds before extubation. The total caloric intake was calculated for each patient for each postoperative day up to the day of discharge from S1P hospitalization. Total caloric intake included calories from both TPN and enteral formula. The inpatient pharmacy records were reviewed to calculate the total intravenous daily caloric delivery via TPN for each patient. For enteral nutrition, the daily nursing flow sheets of each patient were reviewed to obtain daily enteral formula volume given, as well as the daily caloric density during the postoperative inpatient period after S1P. Intravenous fluids with dextrose (not ordered with TPN) were not included in calculating the average calories per kilogram per patient.

Data Analysis

The primary outcome variable was change in WAZ (Δ WAZ) from S1P to hospital discharge. All statistical analysis was performed using IBM SPSS Statistics Version 18.0 (Somers, NY). Continuous variables are expressed as mean $\pm$ standard deviation or median (range) where appropriate. Student *t* test was performed to compare continuous variables, and Fisher exact test was used to compare categorical variables where appropriate.

We evaluated both the actual WAZ (at S1P, at ICU discharge, at hospital discharge, and at S2P) and the Δ WAZ between S1P and hospital discharge. Univariate analysis of potential risk factors associated with the continuous outcome of Δ WAZ was performed, and those variables found on univariate analysis to have an association with the primary outcome were selected for the multivariate analysis. The multivariate analysis was performed with backward regression.

RESULTS

From 2000 to 2011, 170 neonates born with HLHS were treated at our institution. Excluded patients included 12 preterm infants defined as gestational age less than 36 weeks, 5 infants with chromosomal abnormalities, and 33 patients who underwent cardiac transplant or died before S2P. Medical records were reviewed for the cohort of 120 patients. Of these 120 patients, 47 had complete nutritional records and ICU records available for review. The complete clinical characteristics of this patient population described next are summarized in Table 1.

Somatic Growth Measurement

Of the 47 patients for whom there were complete nutritional data, there was a decrease in WAZ between S1P and hospital discharge in all but 1 of the patients (98%). The median Δ WAZ from S1P to hospital discharge was -1.14 (range, -2.3 to 0.6) (Figure 1). The median absolute weight at S1P was 3.10 kg (range, 2.17-4.75 kg), with a WAZ of -0.59 (range, -3.56 to 0.5). At cardiac ICU transfer to the medical floor, the median weight was 3.10 kg (range, 2.18-4.89 kg) with a corresponding decrease in WAZ to -1.62 (range, -4.5 to -0.1). At hospital discharge, the median weight was 3.39 kg (range, 2.37-5.02 kg), with a further decrease in WAZ to -1.81 (range, -4.9 to -0.5). The median daily weight gain was 12 g/d (range, -18 to 36 g/d) from S1P to hospital discharge. At S2P, the median weight in the cohort of 47 patients was 5.75 kg (range, 4.0-9.0 kg), with a median WAZ of -1.51 (-4.0 to 1.4).

Comparison of the excluded 73 patients with the included 47 patients in this study cohort found no differences in absolute weight or WAZ at both S1P ($P = .718$ for absolute weight and $P = .540$ for WAZ) and S2P ($P = .791$ for absolute weight and $P = .083$). The median weight of the excluded patients at S1P was 3.10 kg (range, 2.30-4.10 kg) with a median WAZ of -0.51 (range, -2.38 to 1.09). The median weight of the excluded patients at S2P was 5.80 kg (range, 3.40-8.72 kg) with a median WAZ of -2.07 (-4.30 to -0.04).

Intensive Care Unit Management

The median age of the 47 patients at S1P was 6 days (range, 2-34 days). All the patients were managed in the cardiac ICU after initial surgical palliation. All the patients returned from the operating room intubated and ventilated with median length of intubation of 4 days

TABLE 1. Patient characteristics (n = 47)

	Median (range)
Age at S1P (d)	6 (2-34)
Weight at S1P (kg)	3.10 (2.17-4.75)
Duration of intubation (d)	4 (2-70)
Gestational age at birth (wk)	38.4 (36.0-39.7)
Duration of TPN (d)	6 (1-43)
Caloric intake in the ICU (kcal/kg/d)	53.9 (22.3-119.6)
Postoperative ICU length of stay (d)	10 (5-101)
Caloric intake after ICU transfer (kcal/kg/d)	106.7 (70.0-152.0)
Total postoperative length of stay (d)	22 (11-118)
Age at hospital discharge (d)	28 (14-123)
Average daily weight gain (g)	12 (−18-36)
Age at S2P (d)	148 (91-239)
Weight at S2P (kg)	5.75 (4.0-9.0)

ICU, Intensive care unit; S1P, stage 1 surgical palliation; S2P, stage 2 surgical palliation; TPN, total parenteral nutrition.

(range, 2-70 days). The median length of stay in the cardiac ICU was 10 days (range, 5-101 days). The patient with the ICU length of stay of 101 days remained in the ICU until S2P. Three other patients remained in the hospital through S2P but were able to transfer to the medical floor before S2P.

The median TPN duration in the ICU was 6 days (range, 1-43 days). The median postoperative day for initiation of enteral nutrition was day 4 (range, postoperative day 1-12). Of the 47 patients for whom complete nutritional data were available, 28 (60%) had enteral feeds started before extubation. The median caloric intake including TPN and enteral feeds during the postoperative ICU stay was 53.9 kcal/kg/d (range, 22.3-119.6 kcal/kg/d).

FIGURE 1. Boxplot of WAZ at S1P (Norwood operation), ICU discharge, hospital discharge, and S2P (Glenn operation). The lower, middle, and upper edges of the box represent the first quartile, median, and third quartile, respectively.

Nutritional Data

All infants were started on enteral feeds before transfer from the cardiac ICU to the medical floor. Once the patients were on the medical floor, enteral feed volumes were increased along with increasing caloric density to 24 to 27 kilocalories/ounce. A median caloric intake of 70 calories/kg/d was achieved on postoperative day 6, and a median caloric intake of 100 calories/kg/d was achieved at postoperative day 12 (Figure 2). The median average caloric intake on the medical floor was 106.7 kcal/kg/d (range, 70.0-152.0 kcal/kg/d).

Echocardiographic Data

All the neonates underwent echocardiographic evaluation before surgery and before hospital discharge. Of the 120 patients, 15 (12.5%) had moderate to severe tricuspid valve regurgitation preoperatively. Twelve of those patients had resolution of their tricuspid regurgitation after S1P. In addition to the 3 of the 15 patients who continued to have moderate to severe tricuspid regurgitation postoperatively, 13 additional patients developed moderate to severe tricuspid regurgitation by hospital discharge. Of the 120 patients, 6 (5%) had moderate to severe right ventricular dysfunction at ICU transfer to the medical floor. Five of those 6 patients had resolution of their dysfunction before discharge. The single patient who continued to have moderate to severe right ventricular dysfunction remained in the ICU until S2P. Postoperatively, 6 patients (5%) who had normal or mild right ventricular dysfunction at ICU transfer to the medical floor went on to develop moderate to severe dysfunction by hospital discharge.

Patients who had moderate to severe tricuspid regurgitation by hospital discharge (n = 16) had significantly decreased WAZ at S2P (−2.42 vs −1.73, P = .028) compared with those patients who had no significant regurgitation (n = 104). Patients who had moderate to severe right ventricular dysfunction at hospital discharge (n = 7) had decreased WAZ at S2P (−2.45 vs −1.78) compared with those patients who had mild to no right ventricular dysfunction (n = 113), although the difference was not statistically significant (P = .086).

Univariate and Multivariate Analyses

The results of the univariate analysis of the association between risk factors and the ΔWAZ from S1P to hospital discharge are shown in Table 2. A decrease in WAZ from S1P to hospital discharge was associated with lower caloric intake delivered via enteral feeds after ICU transfer to the medical floor (P = .005) (Figure 3, A). The average daily weight gain also was directly associated with the caloric intake delivered by enteral feeds (P = .001) (Figure 3, B). However, the duration of TPN supplementation (P = .43), postoperative day of enteral feed initiation (P = .85), and

FIGURE 2. Caloric intake delivered by postoperative day. The solid line represents the median, and the lower and upper dashed lines represent the first and third quartiles, respectively.

average calories delivered in the ICU ($P = .683$) were not associated with the decrease in WAZ scores from S1P to hospital discharge. The length of cardiac ICU stay was associated with decrease in WAZ from S1P to hospital discharge ($P = .049$) (Figure 4), and the duration of intubation was suggestive of an association ($P = .056$). Univariate analysis of the echocardiographic findings demonstrated an association between having moderate to severe tricuspid regurgitation and a decrease in WAZ from S1P to hospital discharge ($P = .011$), whereas having moderate to severe right ventricular dysfunction did not seem to have an association ($P = .778$). Last, of the 47 patients in this cohort, 40 (85%) underwent S1P with a modified Blalock–Taussig shunt, whereas the other 7 had placement of a right ventricle to pulmonary artery conduit. The type of shunt used in S1P did not seem to be associated with a decrease in WAZ from S1P to hospital discharge ($P = .506$).

Multivariate modeling using backward linear regression demonstrated that a lower average caloric intake after ICU transfer, having moderate to severe tricuspid regurgitation at hospital discharge, and an increased length of hospital stay were significantly associated with a decrease in WAZ scores from S1P to hospital discharge (Table 2) with an R^2 of 0.475 and P value less than .001.

For S1P postoperative factors affecting S2P, only 2 factors were found to be significantly associated with

WAZ at S2P: duration of TPN in the ICU and average calories delivered via TPN in the ICU. The longer the duration of TPN, the lower the WAZ at S2P ($P = .009$), whereas the higher the TPN calories, the higher the WAZ at S2P ($P = .026$) by linear regression analysis. Factors that did not seem to be significantly associated with WAZ at S2P included ICU duration, average calories before discharge, duration of intubation, and postoperative day of enteral feed initiation.

In addition, multiple linear regression analysis of postoperative weight variables, including WAZ at S1P, WAZ at ICU discharge, WAZ at hospital discharge, and average daily in-hospital weight gain as they relate to WAZ at S2P, found that WAZ at hospital discharge was significantly associated with WAZ at S2P ($P = .006$), whereas the other variables were not significant.

DISCUSSION

Neonates with HLHS start life with low normal birth weights,¹¹ and after the Norwood operation, they experience poor weight gain.^{3,4} The present study demonstrates poor in-hospital weight gain after S1P with a progressive decrease in Δ WAZ from the time of the Norwood operation until discharge. Our study is novel in that actual daily caloric intake during the postoperative hospitalization after S1P was measured and found to have an impact on early

TABLE 2. Univariate and multivariate variables as predictors of weight gain

Variable	Univariate P value	Multivariate P value	B-coefficient (95% CI)
Age at Norwood	.175	NS	
Modified Blalock–Taussig shunt	.506		
Average caloric intake in ICU	.683		
Duration of TPN	.43		
Postoperative day of feed initiation	.85		
ICU length of stay	.049	NS	
Duration of intubation	.056	NS	
Moderate to severe tricuspid regurgitation at hospital discharge	.011	<.001	1.19 (0.66-1.73)
Moderate to severe right ventricular dysfunction at hospital discharge	.778		
Average caloric intake before hospital discharge	.005	<.001	0.015 (0.008-0.022)
Total postoperative length of stay	.142	<.001	−0.010 (−0.015 to −0.005)

CI, Confidence interval; ICU, intensive care unit; TPN, total parenteral nutrition; NS, not significant.

FIGURE 3. A, The association between caloric intake before hospital discharge and Δ WAZ from S1P to hospital discharge with an $R^2 = 0.16$ and $P = .005$. B, The direct association between caloric intake before hospital discharge with average daily weight gain with an $R^2 = 0.209$ and $P = .001$. S1P, Stage 1 surgical palliation; WAZ, weight for age Z scores.

weight gain. This poor early weight gain, as evidenced by lower WAZ at hospital discharge compared with WAZ at S1P, also seems to have sustaining effects because there seems to be an association with lower WAZ at S2P. Although a number of studies have shown that neonates with HLHS often require fortified formula and higher calories to achieve adequate somatic growth, it is striking that a significant portion of our patients never achieved the recommended neonatal caloric intake of 110 to 120 kcal/kg/d.^{8,12} The median caloric intake was 106.7 kcal/kg/d after transfer to the medical floor, which was achieved only at postoperative day 17.

There are a number of factors that impede the delivery of adequate enteral nutrition in neonates after the Norwood operation. Vocal cord dysmotility, poor oral coordination, frequent emesis, and feeding intolerance are common in this population. In addition, these infants are at risk for

FIGURE 4. The association between ICU length of stay and Δ WAZ from S1P to hospital discharge with an $R^2 = 0.158$ and $P = .049$. S1P, Stage 1 surgical palliation; WAZ, weight for age Z scores; ICU, intensive care unit.

mesenteric ischemia and merit caution with enteral feeding. It may be difficult to provide adequate calories immediately postoperatively because these neonates often are on multiple inotropes and mechanically ventilated as evidenced by a median ICU caloric intake of 53.9 kcal/kg/d. The concern with feeding patients on inotropes is warranted given the risk of decreased splanchnic perfusion with inotrope use,¹³ which places these patients with HLHS who are already at higher risk of developing necrotizing enterocolitis compared with other patients with congenital heart disease at even higher risk.¹⁰ However, those concerns often subside by the time these patients are transferred to the medical floor, yet they still manage to receive inadequate calories. The role of parenteral nutrition as an adjuvant while enteral feeds are in progress should be explored.

Despite having a median ICU caloric intake of 54 kcal/kg/d via TPN administration and enteral feeds, there was no association between caloric intake in the ICU with the decrease in WAZ from S1P to hospital discharge. It is likely that the short duration of the ICU stay does not allow for the nutrition in the intensive care setting to significantly contribute to the overall calorie delivery during the first hospitalization. Although the nutrition delivered in the ICU does not seem to affect the weight gain during the first hospitalization, it does seem that longer duration of intubation and ICU stay may be associated with poorer weight gain by univariate analysis. It is likely that those patients who remain in the ICU longer are at greater nutritional risk. Complications resulting in prolonged ICU stays also may result in delays to enteral feed initiation and feed advancement. Nevertheless, these neonates spend significant time in the ICU postoperatively, and strategies to optimize calorie administration may well result in improved growth.¹⁴

The present study also revealed an association between having moderate to severe tricuspid regurgitation at hospital discharge with a greater decrease in WAZ from S1P to hospital discharge by both univariate and multivariate analyses. Tricuspid regurgitation may relate to somatic growth because of the associated ventricular volume load, low cardiac output, or relative atrial hypertension. However, no such association could be found in those patients who had moderate to severe right ventricular dysfunction. The lack of an association between having significant right ventricular dysfunction and the Δ WAZ could be due to the small cohort of patients with this characteristic. Our finding of an association of moderate to severe tricuspid regurgitation with a greater negative Δ WAZ from S1P to hospital discharge differs from a prior similarly sized cohort, which found no such association.³ This finding, along with a prolonged hospital length of stay and average caloric intake, seems to be associated independently with a greater decrease in WAZ from S1P to hospital discharge.

Before the current study, few studies have looked at actual calories delivered during the neonatal hospitalization for cardiac surgery. A study from Children's Hospital of Philadelphia looked at 100 neonates who underwent cardiac surgery with cardiopulmonary bypass for biventricular and single ventricle repair.¹⁵ Their study demonstrated similarly suboptimal caloric intake with their median caloric intake of 93 kcal/kg in patients with single ventricle or biventricular repair in the ICU. Compared with patients with biventricular repair, patients with single ventricle had a significantly longer length of ICU stay, started enteral feeds later, and spent more time in the ICU with enteral feeds. They also looked at factors causing interruption of feeds, which occurred on 21% of total feeding days within their cohort. Factors included procedure preparation, deterioration in clinical status, planned extubation, or feeding intolerance with emesis, abdominal distension, and bloody stools. Another study demonstrated that continuous feeds improved WAZ and achieved higher caloric delivery compared with those infants who were fed orally.¹⁶

The present study demonstrates that in addition to factors that are difficult to modify (eg, tricuspid regurgitation on interstage somatic growth in neonates with HLHS), there are modifiable factors (eg, caloric intake) that should be addressed as early as the immediate postoperative period. The Pediatric Heart Network Single Ventricle Trial demonstrated that in the interstage period between S1P and S2P, the only factors that were associated with worse weight gain were younger age at study enrollment, being born at higher gestational age, and tube feedings at hospital discharge.¹⁷ That study also found that average daily calories as estimated by caregivers were associated with the Δ WAZ. Ultimately, it seems that nutritional intake during the interstage period between S1P and S2P, and in

particular, the in-hospital nutrition after the Norwood operation, may result in improved growth and recovery after later palliation surgery.

Study Limitations

This is a single-center retrospective study of a small patient cohort, and a significant portion of the patients had missing medical charts. However, comparison of the included and excluded patients found no differences in WAZ at S1P and S2P, which confirms that there were no differences in the growth pattern of the included and excluded patients. We demonstrated that in-hospital nutrition has an important effect on WAZ scores. Selection bias is an issue given that we included only those patients who survived to S2P. We intentionally excluded premature infants and those with metabolic, chromosomal, gastrointestinal, or neurologic abnormalities. In addition, given that the patients included in this cohort were born between 2000 and 2011, shifts in perioperative medical management may have slightly contributed to the weight outcomes.

CONCLUSIONS

Patients with HLHS have poor weight gain after S1P, and both modifiable factors (eg, parenteral and enteral nutrition) and intrinsic hemodynamic factors (eg, degree of tricuspid regurgitation) play significant roles in the early weight gain of these infants. Efforts to optimize early calorie administration should be used in this population, who are nutritionally at risk and have been found to have poor growth. However, caution in advancing volume and density of enteral feeds may limit the ability of the clinician to delivery early optimal nutrition.

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