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Factors Impacting Growth in Infants with Single Ventricle Physiology: A Report from Pediatric Heart Network Infant Single Ventricle Trial

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Abstract

Objectives—To describe growth patterns in infants with single ventricle physiology and determine factors influencing growth.

Study design—Data from 230 subjects enrolled in the Pediatric Heart Network Infant Single Ventricle Enalapril Trial were used to assess factors influencing change in weight-for-age z-score (Δz) from study enrollment (0.7 ± 0.4 months) to pre-superior cavopulmonary connection (SCPC) (5.1 ± 1.8 months, period 1), and pre-SCPC to final study visit (14.1 ± 0.9 months, period 2). Predictor variables included patient characteristics, feeding regimen, clinical center, and medical factors during neonatal (period 1) and SCPC hospitalizations (period 2). Univariate regression analysis was performed, followed by backward stepwise regression and bootstrapping reliability to inform a final multivariable model.

Results—Weights were available for 197/230 subjects for period 1 and 173/197 for period 2. For period 1, greater gestational age, younger age at study enrollment, tube feeding at neonatal discharge, and clinical center were associated with a greater negative Δz (poorer growth) in multivariable modeling (adjusted $R^2 = 0.39$, $p < 0.001$). For period 2, younger age at SCPC and greater daily caloric intake were associated with greater positive Δz (better growth) ($R^2 = 0.10$, $p = 0.002$).

Conclusions—Aggressive nutritional support and earlier SCPC are modifiable factors associated with a favorable change in weight-for-age z-score.

Growth impairment in infants with congenital heart disease is well documented, particularly in cyanotic forms of congenital heart disease including single ventricle physiology (1–4). Infants with cyanotic heart lesions are "stunted" with both weight and height below normal (3). Poor growth is an important problem in infants with single ventricle physiology (5–9), particularly prior to performance of the superior cavopulmonary connection (SCPC). Growth impairment during early infancy is associated with adverse developmental outcome, and increased surgical risk in this population requiring complex surgical interventions during the first year of life. Identifying modifiable factors that impact growth may result in improved outcomes.

The Pediatric Heart Network (PHN) completed a multicenter, randomized, placebo-controlled clinical trial of the angiotensin converting enzyme inhibitor enalapril in infants with single ventricle physiology (ISV Trial) (10). The primary outcome measure for this clinical trial was weight-for-age z-score at 14 months of age. Although no growth benefit was seen in infants treated with enalapril, clinical and growth data were collected systematically and prospectively in this large study. The purposes of this analysis were to use this well characterized cohort of infants with single ventricle physiology to describe growth patterns in the first 14 months of life, and to determine the influence of patient-related factors, feeding regimen, and medical factors on growth.

Methods

Details of the ISV Trial study design and main results have been published (10, 11). Briefly, infants with single ventricle physiology between 1 week and 45 days of age with stable systemic and pulmonary blood flow in whom an SCPC (bidirectional Glenn anastamosis, bilateral bidirectional Glenn anastamosis, or hemi-Fontan procedure) was planned were enrolled. Exclusion criteria included gestational age <35 weeks, small for gestational age (<10th percentile), a recognizable chromosomal or phenotypic syndromes associated with growth failure, hemodynamic instability or other contraindication to angiotensin converting enzyme inhibitors. Subjects were enrolled at 10 centers in North America between August 2003 and May 2007. The study protocol was approved by the Institutional Review or Ethics Board at each participating institution, and written informed consent was obtained from a parent/guardian. This clinical trial is registered at www.clinicaltrials.gov (NCT00113087).

Data collected at the time of study enrollment included a detailed anatomic diagnosis, age at study enrollment, gestational age, birth weight, sex, race, and ethnicity. Socioeconomic status (annual household income and highest grade of school completed by parent/guardian) was collected at the 14 month visit. Anthropometric measurements (weight and height) were made at seven time points: study enrollment, 4 days after study enrollment, 2 weeks after enrollment, pre-SCPC, 7 days after restarting study drug following SCPC, age 10 months, and age 14 months (11). All study coordinators performing anthropometric measurements at PHN centers underwent training specifically designed to ensure accurate and reliable measurements of weight and height using training modules from the Health Resources and Service Administration Maternal and Child Health Bureau (http://dept.washington.edu/growth/). All anthropometric measurements included in the analysis (study enrollment, pre-SCPC, and 14 months) were performed at PHN centers. Quality assurance measures included using dedicated, appropriately calibrated scales, duplicate measurements, and third measurements if the first two were not in agreement (within 0.1 kg for weight, with in 1.0 cm for height).

Nutritional data collected at these time points included method of feeding (tube, breast, bottle) and total daily caloric intake. Daily caloric intake was determined based on caloric density of formula or breast milk (fortified or nonfortified (assumed 20 kcal/oz), given via feeding tube or bottle) and the estimated volume consumed on the day prior to the study visit as reported by the caregiver. Method of feeding was defined as follows: patients with any type of tube feeding (nasojejunal, nasogastric, gastrostomy) were classified as tube fed; patients with any breast feeding (actual nursing rather than receiving breast milk via a feeding tube or bottle) were classified as breast fed, and all others were classified as bottle fed. Total calories per day were also collected at the time of discharge following neonatal hospitalization.

Medical and surgical data were collected from the neonatal and SCPC hospitalizations. Data collected included type of surgery, number of concurrent surgical procedures, length of ventilator support, length of intensive care unit stay, length of hospital stay, post-operative complications (arrhythmia, chylothorax, prolonged chest tube drainage and pacemaker placement), number of discharge medications, and discharge oxygen saturation. All echocardiograms were analyzed at a single core laboratory (12).

Statistical Analysis

Two distinct physiologic states are present in infants with single ventricle physiology during the first 14 months of life: before the SCPC when the volume-loaded single ventricle provides both the systemic and pulmonary blood flow, and following the SCPC when the single ventricle provides the systemic blood flow only. Comparison of the weight and height

z-scores at enrollment and pre-SCPC, and pre-SCPC and 14 months was performed using paired t-tests. The outcome variables assessed were change in weight-for-age z-scores: 1) pre-SCPC minus study enrollment (period 1), and 2) final study visit at 14 months of age minus pre-SCPC (period 2). The choice of the outcomes was informed by analyzing Lowess non-parametric curves. All z-scores were calculated using World Health Organization standards.

Because there were no differences in weight or height between the treatment groups in the ISV trial, growth data for both treatment groups, enalapril and placebo, were combined for this analysis. Data are described as frequencies, medians with 25^{th} and 75^{th} percentile values, and means with standard deviations as appropriate. Normalizing transformation was performed for skewed variables. Because weight and height were strongly collinear, only weight was used for regression analysis. The study population used for analysis was restricted to those subjects with non-missing weight-for-age z-scores. Subjects with missing weight were compared with those with non-missing weight. Univariate associations between the outcome and each of the potential predictors were investigated first. Multivariable linear regression analysis of each testing dataset was performed initially with all testing variables included, to determine overall adjusted R^2 for the number of included variables. Stepwise multivariable regression was performed for the outcome, with further testing for non-linear associations. Variable selection for final models was guided by bootstrap bagging (1000 random sample datasets) to assess reliability (percentage of random sample datasets for which the variable was selected) for inclusion. Interactions with the predictors were not assessed. Data analyses were performed using SAS statistical software version 9.2 (SAS Institute Inc., Cary, NC).

Results

The clinical characteristics of the 230 subjects enrolled in the ISV trial are shown in Table I (available at www.jpeds.com). Mean age at trial enrollment was 20.4 ± 9.0 days and 63% had a diagnosis of hypoplastic left heart syndrome. Of the 230 subjects, 28 were withdrawn prior to the pre-SCPC visit and 2 did not have a pre-SCPC visit. Reasons for withdrawal included death in 15, transplant in 2, family choice in 8, physician choice in 1, lost to follow up in 1, and other in 1. Of the remaining 200 subjects, 197 had an available weight at the pre-SCPC visit, and formed the cohort for analysis of time period 1. There were no differences in baseline characteristics between the 197 patients with an available weight at the pre-SCPC visit and the 33 without an available weight.

Of the 202 subjects not withdrawn prior to the pre-SCPC visit, 17 were withdrawn before the final 14 month visit. Reasons for withdrawal included death in 8, transplant in 5, family choice in 1, physician choice in 1, lost to follow up in 1, and other in 1. All of the remaining 185 subjects had weight measurements at the final 14 month visit, and 183 had an available weight measurement at the pre-SCPC visit. There were 173 subjects who underwent an SCPC. The remaining 10 underwent palliative procedures physiologically different from an SCPC and were excluded from the analysis (Kawashima procedure in 5, systemic to pulmonary artery shunt in 3, and no further palliation in 2). The 173 subjects undergoing an SCPC with an available weight measurement at the final study visit formed the cohort for time period 2. Of these, 130 were included in the final regression model. Patients not included had missing values for one of the key candidate predictors, caloric intake. There were no differences in baseline characteristics between those included in the model and those not included.

Values for weight and height at birth and for all seven study time points are shown in Table II (available at www.jpeds.com). The percentage of patients with weight-for-age z-score <

−2 was 26% at the time of study enrollment, 36% pre-SCPC, and 11% at 14 months. The pattern of growth z-scores for weight and height based on data available for each of the seven time points is shown graphically in Figure 1 (locally weighted scatter plot smoothing Lowess curves). Average weight-for-age z-score decreased by one standard deviation from birth to study enrollment at 20 ± 9 days from −0.15 ± 1.06 to −1.27 ± 1.27. There was also a decrease in weight-for-age z-score from study enrollment to the 2 week visit with no significant further decline in weight-for-age z-score between the 2 week visit and pre-SCPC visit. At the time of the 2 week visit 81/219 (37%) of patients were still hospitalized. Mean weight-for-age z-scores increased after the SCPC. The weight- and height-for-age z-scores were closely associated, with Pearson correlation coefficients of 0.78 at baseline, 0.69 at pre-SCPC, and 0.70 at 14 months ($p < 0.001$ for all associations).

Figure 2 demonstrates the z-scores for weight and height at baseline, pre-SCPC, and at 14 months of age. Weight-for-age and height-for-age z-scores decreased significantly from baseline to pre-SCPC, and then increased significantly from pre-SCPC to 14 months of age ($p < 0.01$ for each paired comparison). The mean change in weight-for-age z-score for time period 1 was −0.37 ± 1.15 (n = 197), and the mean change for time period 2 was +1.12 ± 0.89 (n = 173). The change in weight and height growth for each of the two time periods were significantly associated (Pearson correlation coefficient 0.49 for time period 1 and 0.47 for time period 2, $p < 0.001$ for each).

Period 1: Study Enrollment to Pre-SCPC

The results of univariate analysis of the relationship of predictor variables to the change in weight-for-age z-score for time period 1 are shown in Table III. Weight-for-age z-score at the beginning of this time period (study enrollment) was negatively associated with the change in weight-for-age z-score ($R = −0.57$, $p < 0.01$). Although a number of variables were associated with the outcome in univariate analysis, in the multivariable model (Table III), only age at study enrollment, gestational age, method of feeding and clinical center remained significant (adjusted $R^2 = 0.39$, $p < 0.001$). The change in weight-for-age z-score was less negative (better growth) in subjects who were older at the time of enrollment, born at lower gestational age, and who received nutrition via breast feeding or bottle feeding rather than tube feeding. There was no difference in age at enrollment among clinical centers.

Period 2: Pre-SCPC to Final Study Visit at 14 Months of Age

The results of univariate analysis of the relationship of predictor variables to the change in weight-for-age z-score for time period 2 are shown in Table IV. Weight-for-age z-score at the beginning of this time period (pre-SCPC) was negatively associated with the change in weight-for-age z-score ($R = −0.43$, $p < 0.01$). In the final multivariable model (Table IV) only 2 predictor variables were selected by stepwise regression: age at SCPC and daily caloric intake per kilogram of body weight at the pre-SCPC visit ($R^2 = 0.10$, $p = 0.002$). The increase in weight-for-age z-score was greater (better growth) in subjects undergoing the SCPC at an earlier age and in those receiving more calories per kilogram of body weight at the time of the pre-SCPC visit.

Discussion

Growth failure is common in infants with congenital heart disease, including those with single ventricle physiology (5, 6, 8, 9, 13). There are likely multiple mechanisms contributing to growth failure in this population including chronic cyanosis, alterations in energy expenditure (14, 15), inadequate caloric intake (16, 17), genetic factors (18), and alterations in serum growth factors and growth hormone (19). It can be difficult to achieve

adequate nutrition in neonates with single ventricle physiology who typically undergo complex surgical palliation within the first few days to weeks of life, with further surgical palliation within the first year of life. In fact, optimizing nutritional status has been targeted as a key component in improving inter stage outcome in infants with hypoplastic left heart syndrome in the Joint Council on Congenital Heart Disease Quality Improvement Task Force's quality improvement collaborative (20).

In our cohort the most dramatic change in weight-for-age z-score was from study enrollment (average age 3 weeks) to the 2 week visit, with a decrease in the mean z-score of −0.36 during this time period. From the 2 week visit to the pre-SCPC visit there was no change in mean weight-for-age z-score, suggesting growth velocity stabilized during this time period. Growth during this inter stage period is important because poor growth and nutrition during early infancy may adversely impact neurodevelopment (21) and surgical outcome following the SCPC (7). At the 2 week post-enrollment study visit approximately 1/3 of patients were still hospitalized, indicating a potential opportunity for intensive nutritional intervention.

Previous single center, retrospective studies have investigated the predictors of poor weight gain in infants with single ventricle physiology prior to the SCPC. In a study of 50 infants with hypoplastic left heart syndrome, Kelleher et al found that a lower weight-for-age z-score at the time of SCPC was associated with fewer calories/ounce of enteral feeds at the time of neonatal hospital discharge, worse right ventricular function, more frequent hospital readmissions, and higher oxygen saturations at the time of neonatal hospital discharge (5). Anderson et al (13) found that subjects with a lower weight-for-age z-score at neonatal hospital discharge and non-Caucasian race had a lower weight-for-age z-score at the time of the SCPC, and that lower average daily weight gain from neonatal discharge to SCPC was associated with formula feeding at neonatal discharge, a higher mean pulmonary arterial pressure, and higher systemic oxygen saturation. In both of these studies the absolute weight-for-age z-score was the outcome variable rather than the change in weight-for-age z-score used in our study.

In ourmulticenter study, multivariable modeling demonstrated that there was less of a decrease in weight-for-age z-score prior to the SCPC in those patients who were of younger gestational age, older at the time of study enrollment, and receiving nutrition via breast feeding or bottle feeding rather than tube feeding. The clinical center also was significant in the multivariable analysis. The fact that the greatest decline in weight-for-age z-score is seen early during the neonatal period is the likely explanation for the first two findings. Those patients who were older at the time of enrollment likely had a decrease in weight-for-age z-score prior to study enrollment, therefore, less of a change than those enrolled earlier, and those of younger gestational age were also likely smaller with less potential for decline in weight-for-age z-score. Growth failure was less prominent in breast or bottle fed infants, suggesting that they may have been healthier than the tube fed infants. Supplementation with tube feeds did not mitigate growth failure, suggesting either increased metabolic demand in this subset of patients, inadequate net caloric intake, perhaps due to inadequate adjustment of feeding volume during follow-up, or a combination of both. Approaches to nutritional support in this population vary among clinical centers, and our findings suggest that feeding and nutritional practices at some centers may result in better weight gain. Careful nutritional evaluation with a detailed history of caloric intake and appropriate adjustments in feeding, particularly in infants receiving supplemental nutrition via tube feeding, may result in improved growth in these patients. It is interesting to note that a diagnosis of hypoplastic left heart syndrome, ventricular dysfunction, and severity of atrioventricular valve regurgitation were not associated with the change in z-score prior to the SCPC in multivariable analysis.

Following the SCPC, there was a gradual increase in the mean weight-for-age z-score to a mean improvement of over one standard deviation in our cohort at 14 months of age. A greater increase in weight-for-age z-score was seen in those patients who were receiving a higher daily caloric intake per kilogram of body weight at the time of the pre-SCPC visit and those who underwent SCPC at a younger age, although this model explained only about 10% of the variance in change in z-score for this time period. A likely explanation for the low variance explained by this model is that the favorable change in hemodynamics that occurs with the decrease in volume load on the single ventricle overwhelms most other factors. We found a fairly strong negative association between the weight pre-SCPC and the increase in weight-for-age z-score suggesting those patients with the worst growth may benefit most from an earlier SCPC.

Higher average daily caloric intake per kilogram of body weight pre-SCPC was also an important predictor of improved weight gain following the SCPC. This finding highlights the importance of maintaining nutritional support in these patients after hospital discharge and throughout infancy. On average, the weight-for-age z-scores were much closer to the population mean at the 14 month visit (mean z-score −0.5); however, a significant subset remained at risk for poor growth.

This study has some important limitations. Only patients who fulfilled the inclusion criteria, specifically those infants with single ventricle physiology with stable systemic and pulmonary blood flow who were doing relatively well at less than 45 days of age, were approached for enrollment. Sicker, less stable patients who may be at the highest risk for growth failure were not included in this study. In addition, infants with a gestational age <35 weeks and those who were small for gestational age were excluded. Patients with recognizable genetic syndromes associated with growth failure were excluded from the ISV trial; therefore, the influence of genetic syndromes on growth in infants with single ventricle physiology could not be assessed. The greatest decline in weight-for-age z-score for the study population was from birth to 2 weeks after study enrollment; however, because the birth weight was not obtained according to our standard protocol, we chose to use the change in weight-for-age z-score from study enrollment to pre-SCPC for analysis. Additionally, only 130 of the 173 subjects who completed the trial had complete data and were included in the final regression model.

Aggressive nutritional support and performance of the SCPC at a younger age are modifiable factors associated with a favorable change in weight-for-age z-score during the first 14 months of life in this patient population.

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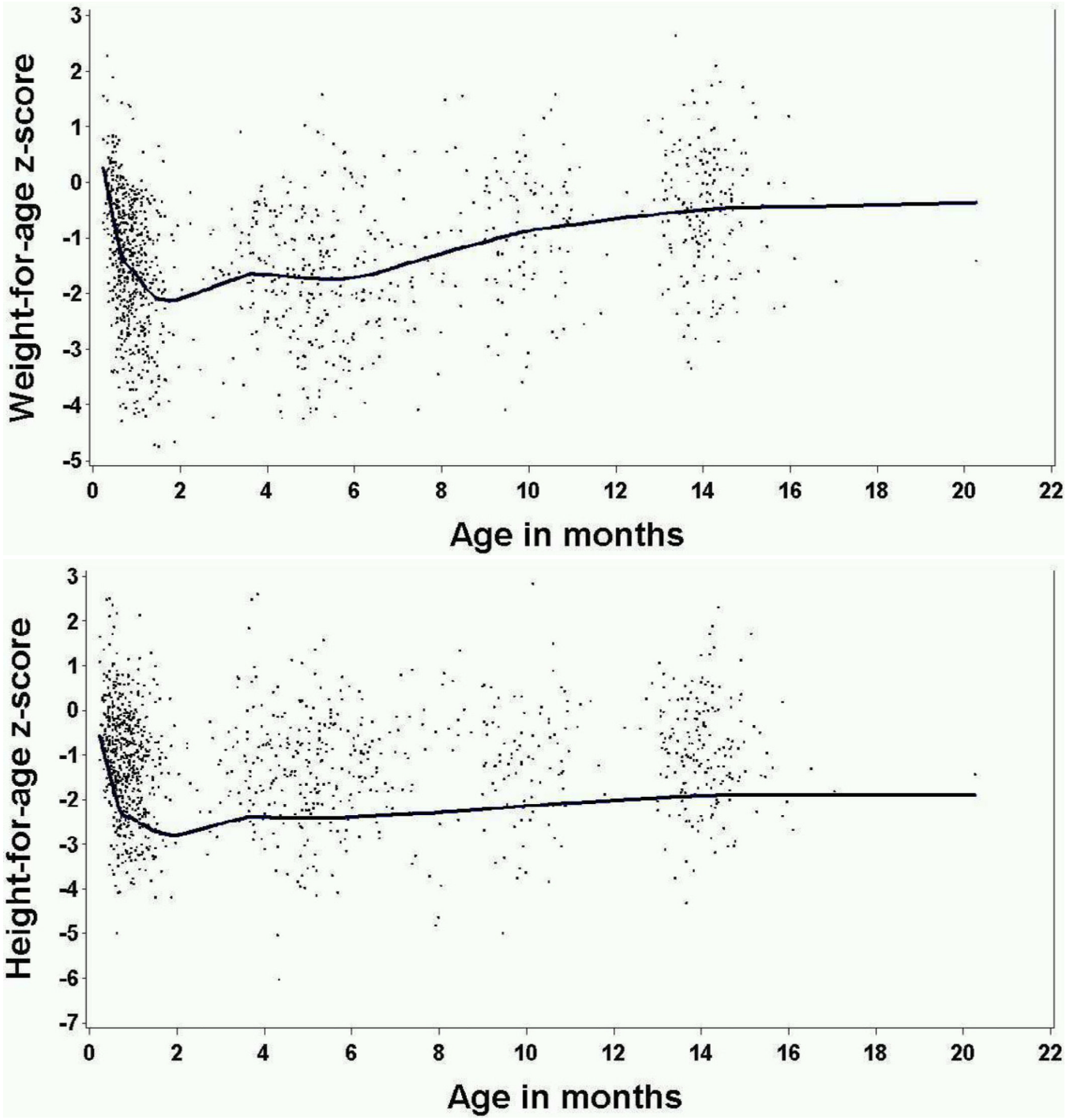

Figure 1.
A. Lowess-smoothed curve and scatter plot of weight-for-age z-score vs. age in months.
B. Lowess-smoothed curve and scatter plot of height-for-age z-score vs. age in months.

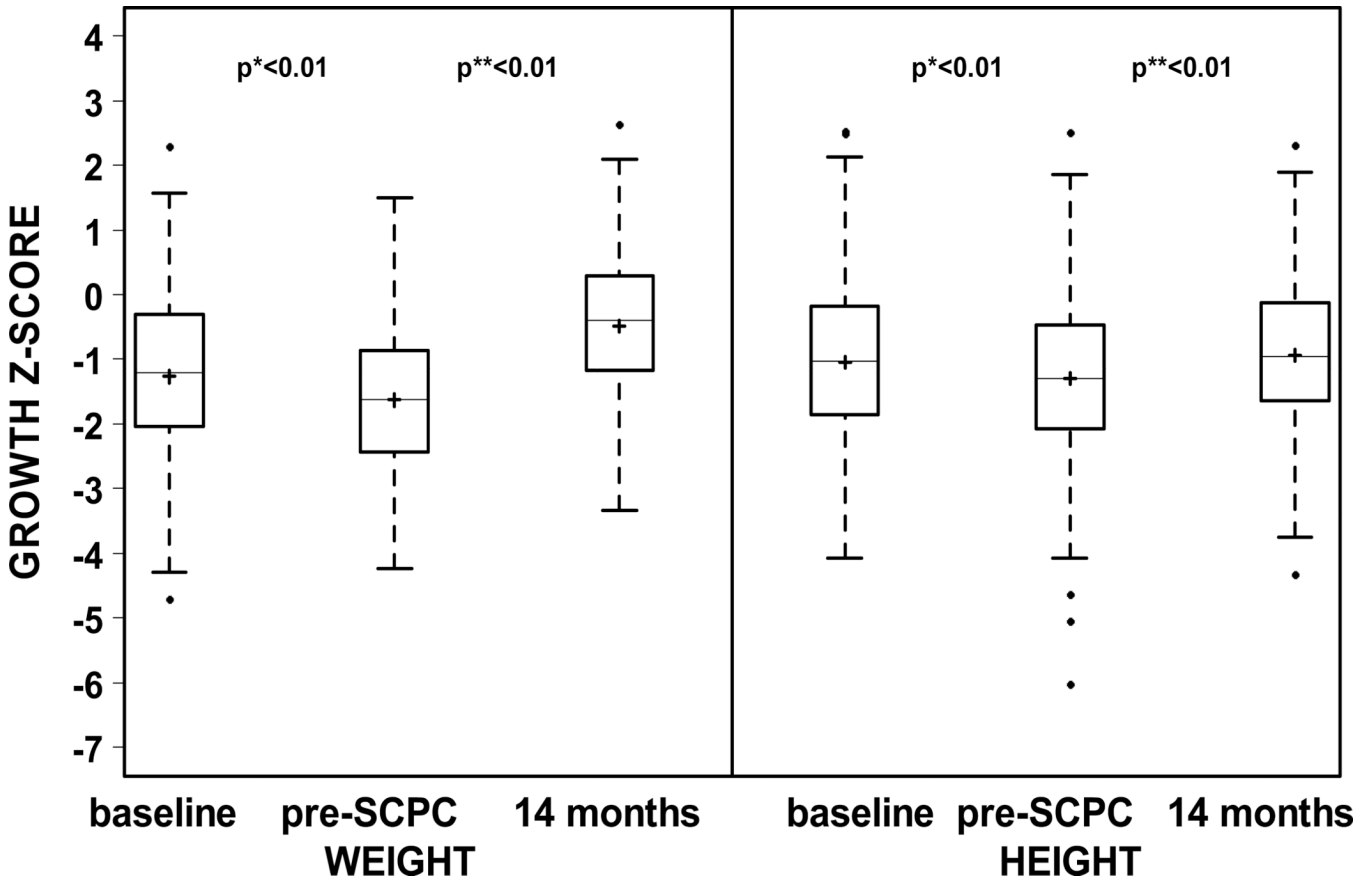

Figure 2.

Box plots of weight- and height-for-age z-scores at baseline (median age 0.6 months, n=229), pre-SCPC (median age 4.8 months, n=197), and at 14 months (median age 14.0 months, n=185). The lower, middle, and upper edges of the box represent the 25th, 50th, and 75th percentiles, respectively. The "+" symbol represents the mean. SCPC – superior cavopulmonary connection.

Table 1

Patient and Medical Characteristics of 230 Patients Enrolled into ISV trial.

Variable	N*	Value**
Age at enrollment (days)	230	20.4 ± 9.0
Sex, male	162	70%
Gestational age (weeks)	230	38 (37, 39)
Birth weight (kg)	230	3.3 ± 0.5
Race		
White	184	80%
Black	32	14%
Other	14	6%
Hispanic	34	15%
Predominant ventricular morphology		
Left	40	17%
Right	164	71%
Mixed	26	11%
Hypoplastic left heart syndrome	145	63%
Baseline AV valve regurgitation - none or mild	176	77%
Baseline systemic ventricular dysfunction - none	183	80%
Palliative surgery		
Norwood type of palliative surgery	166	74%
Length of stay at palliative surgery (days)	227	27.0 (21.0, 40.0)
Length of ICU stay at palliative surgery (days)	226	13.0 (9.0, 21.0)
Bypass time at palliative surgery (minutes)	223	122.9 ± 57.3
Circulatory arrest at palliative surgery	122	76%
Feeding type (at discharge after palliative surgery)		
Tube fed	119	53%
Bottle fed	97	43%
Breast fed	10	4%
Daily calories per kg (Kcal/day/kg, 4 days after randomization)	166	111.3 ± 28.0
SCPC surgery		
Pre-SCPC AV valve regurgitation - none or mild	144	73%
Daily calories per kg (Kcal/day/kg, at pre-SCPC visit)	151	108.0 ± 29.0
Age at SCPC surgery (days)	196	167.6 ± 55.0
Length of stay at SCPC surgery (days)	197	8.0 (6.0, 13.0)
Length of ICU stay at SCPC surgery (days)	197	4.0 (3.0, 5.0)
Post-operative arrhythmia	21	11%
Cavopulmonary anastamosis type of SCPC surgery	188	95%

* N represents sample size for continuous variables, or number of subjects with attribute for categorical variables

** %, mean ± sd, or median (iqr)

AV – atrioventricular; ICU – intensive care unit; SCPC – superior cavopulmonary connection.

Table 2

Weight and Height from Birth to Age 14 months

			Weight			Height	
Time Point	**n**	**Age (months)**	**kg**	**z score***	**n**	**cm**	**z score***
Birth	230	0	3.27 ± 0.50	−0.15 ± 1.06			
Baseline	229	0.7 ± 0.4	3.36 ± 0.54	−1.27 ± 1.27	229	51.1 ± 2.4	−1.05 ± 1.27
Day 4 study drug	211	0.8 ± 0.4	3.43 ± 0.54	−1.40 ± 1.23	209	51.4 ± 2.4	−1.17 ± 1.27
Week 2 study drug	161	1.2 ± 0.4	3.66 ± 0.54	−1.63 ± 1.07	160	52.5 ± 2.4	−1.29 ± 1.16
Pre-SCPC	197	5.1 ± 1.8	6.06 ± 1.05	−1.63 ± 1.14	197	62.4 ± 3.8	−1.29 ± 1.27
Restart (post-SCPC)	118	5.8 ± 1.6	6.34 ± 1.08	−1.64 ± 1.18	118	63.7 ± 3.6	−1.27 ± 1.22
Age 10 months	86	10.0 ± 0.7	8.22 ± 1.10	−0.81 ± 1.13	86	70.1 ± 3.4	−1.12 ± 1.30
Age 14 months	185	14.1 ± 0.9	9.45 ± 1.24	−0.49 ± 1.11	185	75.3 ± 3.1	−0.93 ± 1.16

All z-scores calculated using WHO standards. SCPC – superior cavopulmonary anastamosis.

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Table 3

Association between change in weight-for-age z-score from baseline to pre-SCPC* and patient and medical characteristics

	Univariate		Multivariable**	
Variable	**Parameter Estimate**	**p**	**Parameter Estimate**	**p**
Age at enrollment (days)	0.05	**<0.001**	0.05	**<0.001**
Gestational age (weeks)	−0.27	**<0.001**	−0.21	**<0.001**
Clinical center		**0.038**		**0.002**
Feeding group		**0.004**		**<0.001**
Tube	reference		reference	
Bottle	0.54		0.55	
Breast	0.58		0.81	
Birth weight (kg)	−0.89	**<0.001**		
Birth weight adjusted for gestational age		**<0.001**		
Low (percentile <30)	reference			
Medium (percentile 30–70)	−0.25			
High (percentile >70)	−0.88			
Race		**0.008**		
White	reference			
Black	0.45			
Other	−0.74			
Hypoplastic left heart syndrome	−0.33	**0.049**		
Predominant ventricular morphology		0.269		
Left	−0.13			
Right	−0.37			
Mixed	reference			
Gender, male	−0.13	0.457		
Hispanic	−0.11	0.639		
Baseline AVVR – none or mild	−0.06	0.748		
Baseline systemic ventricular dysfunction-none	0.06	0.787		
Palliative surgery				
Daily calories per kg (Kcal/day/kg) §	0.01	**0.002**		
Number of discharge medications		**0.005**		
Low (<3)	0.91			
Medium (3–5)	0.54			
High (>5)	reference			
Circulatory arrest	−0.42	**0.045**		
Age at palliative surgery (days)	0.02	0.126		
Length of hospital stay (days) †	0.18	0.241		
Length of ICU stay (days) †	0.13	0.239		
Concurrent procedures (number)	−0.05	0.585		

	Univariate		Multivariable**	
Variable	**Parameter Estimate**	**p**	**Parameter Estimate**	**p**
Palliative surgery: crossclamp time (min)	−0.00	0.763		
Palliative surgery: bypass time (min)	0.00	0.794		
Discharge oxygen saturation (%)	−0.00	0.924		
Type of Norwood surgery	0.02	0.916		

*Weight-for-age z-score at the pre-SCPC visit minus weight-for-age z-score at baseline

**R^2 = 0.31 (R^2 adjusted = 0.30), $p < 0.001$, n = 197

§4 days after randomization

†After logarithmic transformation

AVVR – atrioventricular valve regurgitation; ICU- intensive care unit.

Table 4

Association between change in weight-for-age z-score from pre-SCPC to 14 month visit* and patient and medical characteristics

	Univariate		Multivariable**	
Variable	**Parameter Estimate**	**p**	**Parameter Estimate**	**p**
Birth weight (kg)	−0.46	**<.001**		
Birth weight adjusted for gestational age		**0.048**		
Low (percentile <30)	reference			
Medium (percentile 30–70)	−0.20			
High (percentile >70)	−0.44			
Race		**0.008**		
White	reference			
Black	−0.43			
Other	0.04			
Gestational age (wks)	−0.12	**0.009**		
Hypoplastic left heart syndrome	0.28	**0.048**		
Hispanic	0.17	0.378		
Predominant ventricular morphology		0.399		
Left	0.02			
Right	0.22			
Mixed	reference			
Clinical center		0.662		
Sex, male	0.05	0.744		
SCPC surgery				
Daily calories per kg (Kcal/day/kg)§	0.006	**0.010**	0.005	**0.027**
Age at SCPC surgery (days)	−0.004	**0.005**	−0.003	**0.014**
Feeding group§		**0.004**		
Tube	reference			
Bottle	0.08			
Breast	−0.93			
Post-operative arrhythmia	0.49	**0.027**		
Total days of ventilatory support†	−0.18	0.133		
AVVR§ - none or mild	−0.23	0.151		
Discharge oxygen saturation (%)	−0.02	0.210		
Number of interventional cardiac catheterizations	0.13	0.311		
Ejection fraction, %§	−0.01	0.327		
Number of discharge medications		0.338		
Low (<3)	−0.19			
Medium (3–5)	−0.26			
High (>5)	reference			
Length of ICU stay (days) †	−0.09	0.398		

	Univariate		Multivariable**	
Variable	**Parameter Estimate**	**p**	**Parameter Estimate**	**p**
Number of concurrent cardiac surgical procedures	0.05	0.430		
Total days until last chest tube removed†	−0.11	0.488		
Chylous drainage	−0.08	0.732		
Number of significant anatomic diagnoses	−0.01	0.861		
Length of hospital stay (days)†	0.01	0.915		
Number of other cardiac surgical procedures	0.00	0.960		

*Weight-for-age z-score at the 14 month visit minus weight-for-age z-score at the pre-SCPC

**R^2 = 0.10 (R^2 adjusted = 0.08), p = 0.002, n = 130

§At pre-SCPC visit

†After logarithmic transformation

AVVR – overall atrioventricular valve regurgitation; SCPC – superior cavopulmonary anastamosis.