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

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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 (z) 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 of 230 subjects for period 1 and 173 of 197 subjects for period 2. For period 1, greater gestational age, younger age at study enrollment, tube feeding at neonatal hospitalization discharge, and clinical center were associated with a greater negative z (poorer growth) in multivariable modeling (adjusted R^2 = 0.39, $P < .001$). For period 2, younger age at SCPC and greater daily caloric intake were associated with greater positive z (better growth; R^2 = 0.10, P = .002).

Conclusions Aggressive nutritional support and earlier SCPC are modifiable factors associated with a favorable change in weight-for-age z-score. *(J Pediatr 2011;159:1017-22).*

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 reference range.[3] Poor growth is an important problem in infants with single ventricle (ISV) physiology,[5-9] particularly before 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 affect 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 ISV physiology.[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 ISV 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] In brief, ISV physiology between 1 week and 45 days of age with stable systemic and pulmonary blood flow in whom an SCPC (bidirectional Glenn anastamosis,

ISV	Infants with single ventricle
PHN	Pediatric Heart Network
SCPC	Superior cavopulmonary connection

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 7 points: study enrollment, 4 days after study enrollment, 2 weeks after enrollment, pre-SCPC, 7 days after restarting study drug after 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 by 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 when the first two were not in agreement (within 0.1 kg for weight, within 1.0 cm for height).

Nutritional data collected at these points included method of feeding (tube, breast, bottle) and total daily caloric intake. Daily caloric intake was determined on the basis of caloric density of formula or breast milk (fortified or non-fortified [assumed 20 kcal/oz], given via feeding tube or bottle) and the estimated volume consumed on the day before the study visit as reported by the caregiver. Method of feeding was defined as: patients with any type of tube feeding (nasojejunal, nasogastric, gastrostomy) were classified as tube fed; patients with any breastfeeding (actual breastfeeding rather than receiving breast milk via a feeding tube or bottle) were classified as breast fed, and all other patients were classified as bottle fed. Total calories per day were also collected at the time of discharge after 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, postoperative 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 ISV 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 after 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 at 14 months was performed with 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 by 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 25th and 75th percentile values, and means with SDs 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 subjects 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 with SAS statistical software version 9.2 (SAS Institute, Cary, North Carolina).

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% of subjects had a diagnosis of hypoplastic left heart syndrome. Of the 230 subjects, 28 were withdrawn from the study before the pre-SCPC visit, and two did not have a pre-SCPC visit. Reasons for withdrawal included death in 15 subjects, transplant in two subjects, family choice in 8 subjects, physician choice in one subject, loss to follow-up in one subject, and other reason in one subject. Of the remaining 200 subjects, 197 had an available weight at the pre-SCPC

visit and formed the cohort for analysis of 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 patients without an available weight.

Of the 202 subjects not withdrawn from the study before the pre-SCPC visit, 17 were withdrawn from the study before the final 14-month visit. Reasons for withdrawal included death in 8 subjects, transplant in 5 subjects, family choice in one subject, physician choice in one subject, loss to follow-up in one subject, and other reason in one subject. All the remaining 185 subjects had weight measurements at the final 14-month visit, and 183 subjects had an available weight measurement at the pre-SCPC visit. There were 173 subjects who underwent an SCPC. The remaining 10 subjects 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 period 2. Of these subjects, 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 subjects included in the model and those not included.

Values for weight and height at birth and for all 7 study 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 on the basis of data available for each of the seven points is shown graphically in **Figure 1** (locally weighted scatterplot smoothing Lowess curves). Average weight-for-age z-score decreased by one SD 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 of 219 patients (37%) 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 ($P < .001$ 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 ($P < .01$ for each paired comparison). The mean change in weight-for-age z-score for period 1 was -0.37 ± 1.15 (n = 197), and the mean change for period 2 was 1.12 ± 0.89 (n = 173). The change in weight and height growth for each of the two periods were significantly associated (Pearson correlation coefficient 0.49 for period 1 and 0.47 for period 2, $P < .001$ for each).
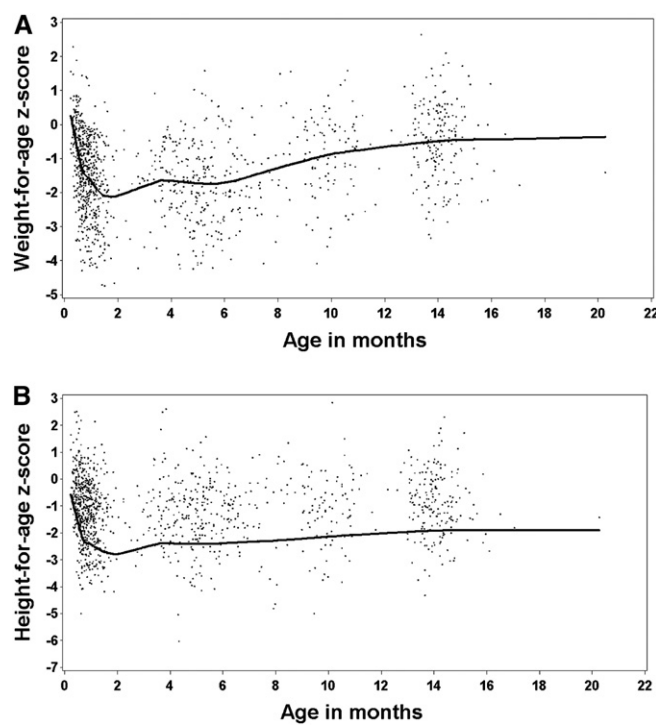

Figure 1. A, Lowess-smoothed curve and scatterplot of weight-for-age z-score versus age in months. **B,** Lowess-smoothed curve and scatterplot of height-for-age z-score versus age in months.

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 period (study enrollment) was negatively associated with the change in weight-for-age z-score (R = -0.57, $P < .01$). 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 $R^2 = 0.39$, $P < .001$). 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 breastfeeding 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 period 2 are shown in **Table IV**. Weight-for-age z-score at the beginning of this period (pre-SCPC) was negatively associated with the change in weight-for-age z-score (R = -0.43, $P < .01$). In the final multivariable model (**Table IV**), only 2 predictor variables were selected with

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

1019

*Paired t-test comparing means of growth z-scores at pre-SCPC visit and baseline (n=197)

**Paired t-test comparing means of growth z-scores at 14 month and pre-SCPC visits (n=183)
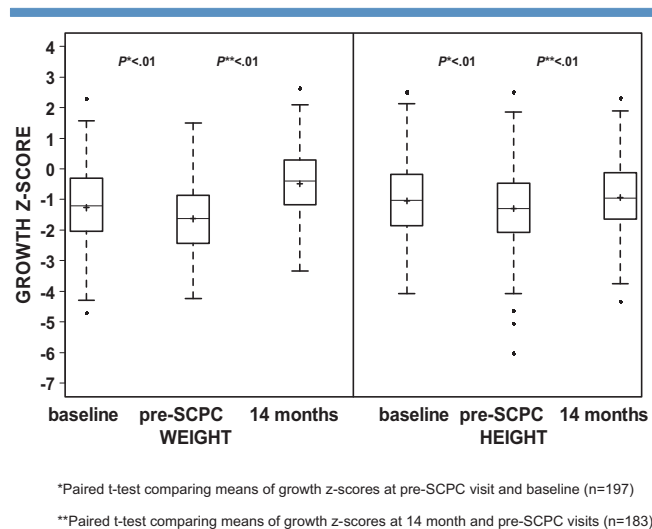
Figure 2. Boxplots of weight- and height-for-age z-scores at baseline (median age, 0.6 months; n = 229), pre-SCPC (median age, 4.8 months; n = 197), and at 14 months (median age, 14.0 months; n = 185). The lower, middle, and upper edges of the box represent the 25th, 50th, and 75th percentiles, respectively. The "+" symbol represents the mean.

stepwise regression: age at SCPC and daily caloric intake per kilogram of body weight at the pre-SCPC visit ($R^2 = 0.10$, $P = .002$). The increase in weight-for-age z-score was greater (better growth) in subjects undergoing the SCPC at an earlier age and in subjects 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. Optimizing nutritional status has been targeted as a key component in improving interstage 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 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 period. Growth during this interstage period is important because

poor growth and nutrition during early infancy may adversely affect neurodevelopment[21] and surgical outcome after the SCPC.[7] At the 2-week post-enrollment study visit, approximately one-third of patients were still hospitalized, indicating a potential opportunity for intensive nutritional intervention.

Earlier single center, retrospective studies have investigated the predictors of poor weight gain in ISV physiology before 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 re-admissions, 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 our multicenter study, multivariable modeling demonstrated that there was less of a decrease in weight-for-age z-score before the SCPC in those patients who were of younger gestational age, older at the time of study enrollment, and receiving nutrition via breastfeeding or bottlefeeding rather than tube-feeding. The clinical center also was significant in the multivariable analysis. The greatest decline in weight-for-age z-score is seen early during the neonatal period, likely explaining the first two findings. Those patients who were older at the time of enrollment likely had a decrease in weight-for-age z-score before 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 caused by inadequate adjustment of feeding volume during follow-up, or a combination of both. Approaches to nutritional support in this population vary in 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. A diagnosis of hypoplastic left heart syndrome, ventricular dysfunction, and severity of atrioventricular valve regurgitation were not associated with the change in z-score before the SCPC in multivariable analysis.

Table III. 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 value	Parameter estimate	P value
Age at enrollment, days	0.05	<.001	0.05	<.001
Gestational age, weeks	−0.27	<.001	−0.21	<.001
Clinical center		.038		.002
Feeding group		.004		<.001
Tube	Reference		Reference	
Bottle	0.54		0.55	
Breast	0.58		0.81	
Birth weight, kg	−0.89	<.001		
Birth weight adjusted for gestational age		<.001		
Low (percentile <30)	Reference			
Medium (percentile 30-70)	−0.25			
High (percentile >70)	−0.88			
Race		.008		
White	Reference			
Black	0.45			
Other	−0.74			
Hypoplastic left heart syndrome	−0.33	.049		
Predominant ventricular morphology		.269		
Left	−0.13			
Right	−0.37			
Mixed	Reference			
Sex, male	−0.13	.457		
Hispanic	−0.11	.639		
Baseline AVVR, none or mild	−0.06	.748		
Baseline systemic ventricular dysfunction, none	0.06	.787		
Palliative surgery				
Daily calories per kg, Kcal/day/kg[‡]	0.01	.002		
Number of discharge medications		.005		
Low (<3)	0.91			
Medium (3-5)	0.54			
High (>5)	Reference			
Circulatory arrest	−0.42	.045		
Age at palliative surgery, days	0.02	.126		
Length of hospital stay, days[§]	0.18	.241		
Length of ICU stay, days[§]	0.13	.239		
Concurrent procedures, n	−0.05	.585		
Palliative surgery: crossclamp time, minutes	−0.00	.763		
Palliative surgery: bypass time, minutes	0.00	.794		
Discharge oxygen saturation, %	−0.00	.924		
Type of Norwood surgery	0.02	.916		

AVVR, atrioventricular valve regurgitation; *ICU*, intensive care unit.
*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), $P < .001$, n = 197.
[‡]4 days after randomization.
[§]After logarithmic transformation.

Table IV. 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 value	Parameter estimate	P value
Birth weight, kg	−0.46	<.001		
Birth weight adjusted for gestational age		.048		
Low (percentile <30)	Reference			
Medium (percentile 30-70)	−0.20			
High (percentile >70)	−0.44			
Race		.008		
White	Reference			
Black	−0.43			
Other	0.04			
Gestational age, weeks	−0.12	.009		
Hypoplastic left heart syndrome	0.28	.048		
Hispanic	0.17	.378		
Predominant ventricular morphology		.399		
Left	0.02			
Right	0.22			
Mixed	Reference			
Clinical center		.662		
Sex, male	0.05	.744		
SCPC surgery				
Daily calories per kg, Kcal/day/kg[‡]	0.006	.010	0.005	.027
Age at SCPC surgery, days	−0.004	.005	−0.003	.014
Feeding group[‡]		.004		
Tube	Reference			
Bottle	0.08			
Breast	−0.93			
Postoperative arrhythmia	0.49	.027		
Total days of ventilatory support[§]	−0.18	.133		
AVVR,[‡] none or mild	−0.23	.151		
Discharge oxygen saturation, %	−0.02	.210		
Number of interventional cardiac catheterizations	0.13	.311		
Ejection fraction, %[‡]	−0.01	.327		
Number of discharge medications		.338		
Low (<3)	−0.19			
Medium (3-5)	−0.26			
High (>5)	Reference			
Length of ICU stay, days[§]	−0.09	.398		
Number of concurrent cardiac surgical procedures	0.05	.430		
Total days until last chest tube removed[§]	−0.11	.488		
Chylous drainage	−0.08	.732		
Number of significant anatomic diagnoses	−0.01	.861		
Length of hospital stay, days[§]	0.01	.915		
Number of other cardiac surgical procedures	0.00	.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), $P = .002$, n = 130.
[‡]At pre-SCPC visit.
[§]After logarithmic transformation.

After the SCPC, there was a gradual increase in the mean weight-for-age z-score with a mean improvement of >1 SD 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 patients who underwent SCPC at a younger age, although this model explained only approximately 10% of the variance in change in z-score for this period. A likely explanation for the low variance explained

with 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.

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

1021

Higher average daily caloric intake per kilogram of body weight pre-SCPC was also an important predictor of improved weight gain after 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 of patients remained at risk for poor growth.

This study has some important limitations. Only patients who fulfilled the inclusion criteria, specifically those ISV 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 infants 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 ISV 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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Appendix

Investigators for the Pediatrc Heart Network Infant Single Ventricle Trial include: National Heart, Lung, and Blood Institute: Gail Pearson, Victoria Pemberton, Mario Stylianou, Marsha Mathis; Network chair: Lynn Mahony, University of Texas Southwestern Medical Center; Data Coordinating Center: New England Research Institutes, Lynn Sleeper (principal investigator), Steven Colan, Lisa Virzi, Lisa Wruck, Victor Zak, David F. Teitel; Core Clinical Site Investigators: Children's Hospital Boston, Jane Newburger (principal investigator), Roger Breitbart, Jami Levine, Ellen McGrath, Carolyn Dunbar-Masterson; Children's Hospital of New York, Daphne Hsu (study chair), William Hellenbrand (principal investigator), Ashwin Prakash, Darlene Servedio; Children's Hospital of Philadelphia, Victoria L. Vetter (principal investigator), Sarah Tabbutt, Katherine Lee, Marisa Nolan, Stephanie Piacentino; Cincinnati Children's Medical Center, D. Woodrow Benson (principal investigator), Catherine Dent, Lois Bogenschutz, Teresa Barnard, Steven Schwartz, David Nelson; North Carolina Consortium: Duke University, East Carolina University, Wake Forest University, Page A. W. Anderson (principal investigator), Wesley Covitz, Kari Crawford, Michael Hines, James Jaggers, Theodore Koutlas, Jennifer Li, Charlie Sang Jr, Lori Jo Sutton, Mingfen Xu; Medical University of South Carolina, J. Philip Saul (principal investigator), Andrew Atz, Girish Shirali, Teresa Atz; Primary Children's Medical Center, Salt Lake City, Utah, LuAnn Minich (principal investigator), Richard Williams, Linda Lambert, John Hawkins,, Marian Sharrow; Hospital for Sick Children, Toronto, Brian McCrindle (principal investigator), Elizabeth Radojewski, Nancy Slater, Svetlana Khaikin, Susan McIntyre; Auxiliary sites: Children's Hospital of Wisconsin, Nancy Ghanayem, Kathy Mussatto, Michele Frommelt, Lisa Young-Borkowski; University of Michigan, Albert Rocchini, Laurie Rodgers-Augustyniak Echocardiography Core Laboratory: Children's Hospital Boston: Steven Colan, Renee Margossian; Genetics Core Laboratory: Children's Hospital of New York: Wendy Chung, Liyong Deng, Patricia Lanzano; Protocol Review Committee: Michael Artman, chair, Judith Massicot-Fisher, executive secretary; Timothy Feltes, Julie Johnson, Thomas Klitzner, Jeffrey Krischer, G. Paul Matherne; Data and Safety Monitoring Board: John Kugler, chair, Rae-Ellen Kavey, executive secretary, David J. Driscoll, Mark Galantowicz, Sally A. Hunsberger, Thomas J. Knight, Holly Taylor, Catherine L. Webb.

Table I. Patient and medical characteristics of 230 patients enrolled in 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)
Postoperative arrhythmia	21	11%
Cavopulmonary anastamosis type of SCPC surgery	188	95%

AV, atrioventricular; *ICU*, intensive care unit.
*n represents sample size for continuous variables or number of subjects with attribute for categorical variables.
†%, mean ± SD, or median (IQR).

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

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Table II. Weight and height from birth to age 14 months

Point	n	Age (months)	Weight kg	Weight z score*	n	Height cm	Height 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 World Health Organization standards.