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Assessment of Growth 6 Years after the Norwood Procedure

Phillip T. Burch, MD[1], Chitra Ravishankar, MD[3], Jane W. Newburger, MD[4], Linda M. Lambert, MSN[1], Victoria L. Pemberton, RNC, MS[5], Suzanne Granger, PhD[6], Alejandro A. Floh, MD[7], Jeffrey B. Anderson, MD[8], Garick D. Hill, MD[9], Kevin D. Hill, MD[10], Matthew E. Oster, MD[11], Alan B. Lewis, MD[12], Kurt R. Schumacher, MD[13], Sinai C. Zyblewski, MD[14], Ryan R. Davies, MD[15], Jeffrey P. Jacobs, MD[16], Wyman W. Lai, MD[17], and L. LuAnn Minich, MD[2], on behalf of the Pediatric Heart Network Investigators*

At 6 years of age, patients with hypoplastic left heart syndrome had mean age-adjusted *z*-scores for weight and height below the normative population, and body mass index was similar to the normative population. Males had the greatest increase in *z*-scores for body mass index. *(J Pediatr 2017;180:270-4).*

Trial registration ClinicalTrials.gov: NCT00115934.

Growth failure among infants with hypoplastic left heart syndrome is common.[1,2] We previously used the database from the National Heart, Lung, and Blood Institute-sponsored Pediatric Heart Network Single Ventricle Reconstruction (SVR) trial to assess growth patterns in the first 3 years after the Norwood procedure.[3] Because the factors contributing to impaired growth may change over time, particularly after the Fontan procedure, we sought to expand this analysis.

Methods

Neonates with hypoplastic left heart syndrome or a related single morphologic right ventricular anomaly were randomized to either a modified Blalock-Taussig shunt or right ventricle-to-pulmonary artery shunt in the SVR trial and follow-up was subsequently extended to 6 years of age.[4] Sociodemographic and clinical characteristics, medical and surgical variables, unanticipated procedures, complications, outcome data, and core laboratory analysis of echocardiographic images were collected.[3,4]

We extended our analysis of changes in *z*-scores-for-age for weight (WAZ), height (HAZ), and body mass index (BMIZ) using all available data (**Table I** and **Table II**; available at www.jpeds.com) on subjects from birth to 6 years of age. To assess the effect of the Fontan procedure, we analyzed measurements obtained between the pre-Fontan visit and 6 years of age. We included growth data up to death (n = 153), transplantation (n = 21), or biventricular repair (n = 3). The shunt type in place when the subject left the operating room after the Norwood procedure was used for this analysis.

The primary outcomes were the change in WAZ, HAZ, and BMIZ between birth and 6 years of age. Anthropometric measurements were obtained at study visits as previously described.[3] Reliable height data were available only at birth, pre-Fontan, and annually from 3-6 years of age.

Analyses were performed between birth and 6 years of age and between pre-Fontan and 6 years of age with subgroup analyses for those subjects with WAZ < −2 at Norwood discharge. A 1-sample *t* test was used to determine if the mean *z*-score for a growth of the study population differed from a *z*-score of 0 for the normative population. Simple linear regression was used to obtain initial estimates of association of each candidate predictor with change in WAZ, HAZ, and BMIZ. Nonlinear relationships with continuous outcomes were assessed by categorizing continuous variables into groups based on quartiles; in addition, relationships between the natural logarithm of predictors with skewed distributions and the outcomes were explored. Variables with unadjusted $P < .20$ were used as candidate predictors for multivariable modeling. For variables with >5% missing data, mean imputation was performed before conducting multivariable modeling. Stepwise linear regression was employed to develop multivariable models, in conjunction with bootstrapping (1000 samples) to obtain reliability estimates. The criteria to enter and remain in the model were $P < .15$ and $P < .05$, respectively. All terms in the

BMIZ	*z*-Scores-for-age for body mass index
HAZ	*z*-Scores-for-age for height
LOS	Length of stay
SVR	Single Ventricle Reconstruction
WAZ	*z*-Scores-for-age for weight

From the [1]Departments of Surgery; [2]Departments of Pediatrics, Primary Children's Hospital, University of Utah, Salt Lake City, UT; [3]The Children's Hospital of Philadelphia, Philadelphia, PA; [4]Boston Children's Hospital and Harvard Medical School, Boston, MA; [5]National Institutes of Health, Bethesda, MD; [6]New England Research Institutes, Watertown, MA; [7]The Hospital for Sick Children, Toronto, Ontario, Canada; [8]University of Cincinnati, Cincinnati, OH; [9]The Children's Hospital of Wisconsin, Milwaukee, WI; [10]Duke University Medical Center, Durham, NC; [11]Children's Healthcare of Atlanta and Emory University School of Medicine, Atlanta, GA; [12]Children's Hospital Los Angeles, Los Angeles, CA; [13]University of Michigan Medical School, Ann Arbor, MI; [14]Medical University of South Carolina, Charleston, SC; [15]Nemours/A.I. DuPont Hospital for Children, Wilmington, DE; [16]Johns Hopkins All Children's Heart Institute, Orlando, FL; and [17]Columbia University Medical Center, New York, NY

*List of additional Pediatric Heart Network Investigators is available at www.jpeds.com (**Appendix**).

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final multivariable models have a reliability >50% and $P < .05$. Separate models were constructed adjusting, and not adjusting, for center.

Results

Birth to 6 Years of Age

The analysis of anthropometric measurements at 6 years of age included 265 subjects enrolled between May 2005 and July 2008 (**Figure 1**; available at www.jpeds.com). At 6 years of age, 19 SVR transplant-free survivors had not undergone the Fontan procedure. Mean WAZ (−0.58 ± 1.13) and mean HAZ (−1.03 ± 1.18) were below the mean of the normative population ($P < .001$ for both). WAZ was less impaired than HAZ ($P < .001$). By 6 years of age, 37% of subjects had WAZ < −1 and 51% had HAZ < −1; WAZ was < −2 in 9% and HAZ was < −2 in 18%. Mean BMIZ (0.09 ± 1.11) was similar to the normative population ($P = .17$) with 13% of subjects having BMIZ < −1 and 3% with BMIZ < −2.

Mean WAZ and mean HAZ decreased between birth and 6 years of age ($P < .001$ for both) (**Table III**; available at www.jpeds.com). WAZ decreased by ≥0.5 SD in 49% of subjects and HAZ decreased by ≥0.5 SD in 61%. In contrast with WAZ and HAZ, mean BMIZ increased between birth and 6 years of age. During this time, BMIZ decreased by ≥0.5 SD in 28% of subjects and increased by ≥0.5 SD in 52%. At 6 years of age, 9% of SVR survivors had BMIZ > 1.5 and 4% had BMIZ > 2.

The univariable results for candidate predictors that remained significant in any of the final multivariable models presented (both reliability >50% and $P < .05$) are shown in **Table IV** (available at www.jpeds.com). Higher birth weight ($P < .001$), longer cumulative length of stay (LOS) for all admissions ($P = .001$), and being white/non-Hispanic ($P = .02$) were associated independently with a greater decrease in WAZ (**Table V**). Higher birth weight was the only factor independently associated with a greater decrease in HAZ ($P < .001$). Males had a greater increase in BMIZ over the 6-year study period. A Hollingshead score of >54.5 (highest socioeconomic status) was associated with the smallest increase in BMIZ, but the relationship was not linear. Tube feeding at any time point correlated with a greater decrease in BMIZ. Independent predictors were similar whether or not center was included in the model and explained only 11% of the variation in change in BMIZ. Shunt type was not associated with change in WAZ, HAZ, or BMIZ.

Relation of the Fontan Procedure to Anthropometric Measurements at 6 Years of Age

Among the 255 subjects who had a Fontan procedure (33.8 ± 9.6 months of age), 1 subject underwent cardiac transplantation and 12 subjects died before 6 years of age. At the pre-Fontan visit, the mean WAZ (−0.51 ± 0.97) and HAZ (−0.96 ± 1.19) were significantly below the normative mean ($P < .001$). The WAZ was <−1 in 31% of subjects and <−2 in 5%. The mean WAZ decreased between the pre-Fontan visit and 6 years of age (**Table III**), but compared with the Norwood

Table V. Multivariable models for change in anthropometric *Z*-scores from birth to 6 years of age*

	Estimate	Standard error	*P* value	Reliability (%)
Weight-for-age *Z*-score (n = 261; adjusted $R^2 = 0.34$)				
Birth weight (kg)	−0.001	0.0001	<.001	82
Cumulative duration of stay: all admissions (d)			.001	64
≤30	0.914	0.229		
31-44	0.351	0.170		
45-67	0.242	0.179		
>67	Reference			
Race/ethnicity			.02	56
Hispanic	−0.229	0.459		
White non-Hispanic	−0.471	0.440		
Black non-Hispanic	0.193	0.479		
Other non-Hispanic	Reference			
Height-for-age *Z*-score (n = 259; adjusted $R^2 = 0.20$)				
Birth weight (kg)	−0.002	0.0002	<.001	85
Body mass index-for-age *Z*-score (n = 246; adjusted $R^2 = 0.07$)				
Hollingshead score†			.014	69
<27.0	0.296	0.323		
27.0-43.0	0.158	0.302		
43.0-54.5	0.921	0.312		
>54.5	reference			
Tube feeding–any time			.003	59
Yes	−0.700	0.232		
No	Reference			
Sex			.040	54
Male	0.457	0.221		
Female	Reference			

*Results were similar with and without center included as a potential predictor in the model. Only those without center are presented.
†The Hollingshead Four Factor Index of Socioeconomic Status is a survey designed to measure social status of an individual based on four domains: marital status, retired/employed status, educational attainment, and occupational prestige.

and stage II procedures,[3] the Fontan procedure had the least impact on WAZ (**Figure 2**). During this time interval, WAZ decreased by ≥0.5 SD in 24% of subjects.

The HAZ was <–1 in 50% and <–2 in 15% at the pre-Fontan assessment. Similar to WAZ, HAZ decreased from the pre-Fontan visit to 6 years of age (**Table III**) with a decrease of ≥0.5 SD in 26% of subjects. In contrast with the WAZ and HAZ, at the pre-Fontan visit, the mean BMIZ was similar to the normative population; 16% were <–1 and 2% were <-2. Overall, the mean BMIZ increased between Fontan and 6 years of age. During this time, 29% of subjects had a decrease in BMIZ of ≥0.5 SD and 28% had an increase of ≥0.5 SD.

Center was associated independently with change in WAZ ($P = .03$). With center removed from the model, being white/non-Hispanic was associated independently with a decrease in WAZ. Greater LOS at the stage II hospitalization but shorter cumulative LOS at all hospitalizations correlated with a greater increase in WAZ. Being fed a caloric-supplemented diet at any time point was the only variable associated with a greater decrease in HAZ. Center was associated with change in BMIZ from pre-Fontan to 6 years of age, but explained only 14% of the variation. The mean change in BMIZ ranged from a decrease of 0.94 SD to an increase of 0.88 SD ($P = .002$). The type of shunt in place after the Norwood procedure had no association with change in any anthropometric measurement.

Anthropometric Measurements at 6 Years of Age for Subjects with WAZ <–2 at Norwood Discharge

Of the 445 subjects discharged from the Norwood hospitalization, 169 (38%) had WAZ < –2. The prevalence of WAZ < –2 was similar between the group of subjects who died or were transplanted (35/97, 36%) and the group who survived (134/348, 39%; $P = .72$). At 6 years of age, WAZ for these subjects was lower than the group discharged with WAZ ≥ -2 (-1.08 ± 1.01 vs –0.24 ± 1.08; $P < .001$). Right ventricular area change at the pre-Norwood echocardiogram had a nonlinear association with increased weight gain between Norwood discharge and 6 years of age. Multiple births and low birth weight were also associated independently with better weight gain between Norwood and 6 years of age in this subgroup. Between the Fontan and 6 years of age, being black non-Hispanic and oral feeding at 13-24 months of age were associated with better weight gain. At 6 years of age, HAZ was similar between those discharged with and those without WAZ < -2 ($P = .25$). BMIZ was 0.26 SD below normal in those discharged with WAZ < -2 and 0.34 SD above normal in those with WAZ ≥ –2 ($P < .001$). Of those discharged with WAZ < –2, BMIZ was >1.5 in 5% and none had BMIZ > 2.0 at 6 years of age.

Discussion

This longitudinal assessment of growth from birth to 6 years of age in a well-characterized cohort of subjects with hypoplastic left heart syndrome and related single right ventricular anomalies enrolled in the SVR trial demonstrated that the Fontan procedure had little effect on growth at 6 years of age. Similar to our findings at 3 years of age,[3] both mean WAZ and HAZ for this study population remained below mean values for the normative population, with HAZ more impaired than WAZ at 6 years of age. Despite the drop in both mean WAZ and HAZ, mean BMIZ increased by >0.5 SD in >50% of the SVR survivors. These data highlight both the trends of the Norwood procedure and the variance in growth for survivors who are 6 years of age and transplant free.

It is possible that the increase in BMIZ may be from increasing adipose rather than increasing lean body mass. Because of the strong associations reported between poor weight gain in infancy and increased morbidity, including prolonged hospitalization, and impaired neurodevelopment,[5,6] many centers have focused on improving weight gain by increasing caloric intake with varying degrees of success.[1,2,5] Increasing weight by adding adipose tissue without a proportional increase in height, however, may have long-term detrimental effects.

In this cohort, factors associated with better weight gain were inconsistent, varied by time interval and, at best, explained only a small percentage of the variability in growth over the first 6 years of life. A lesser total LOS for all hospitalizations correlated with a greater increase in growth between Fontan and 6 years of age likely reflecting better operative outcomes or less severe disease. Non-Hispanic black subjects had the greatest increase and higher birth weight resulted in a greater decline in growth between birth and 6 years of age. These findings are consistent with previous reports and have been thought to reflect a regression toward the mean.[3,5] This explanation may be too simplistic, however, because HAZ remains more impaired than WAZ and no association was found between birth weight and BMIZ at 6 years of age.

Feeding predictor variables were not associated with growth. Tube feeding at any time was associated with a greater decrease in BMIZ between birth and 6 years of age. Being fed a caloric-supplemented diet at any time was associated with a greater decrease in HAZ between pre-Fontan and 6 years of age and may indicate that increasing calories alone has little effect on height in this population. Because caloric intake was not collected in the SVR database, however, these associations are difficult to interpret beyond noting that feeding seems more associated with change in BMIZ rather than change in WAZ or HAZ alone.

It is noteworthy that infants with WAZ < –2 at Norwood discharge experienced increases in WAZ indicating that even the smallest subjects were capable of gaining weight if they survived. Mean HAZ at 6 years of age was similar between the group with WAZ < –2 and the group with WAZ ≥ 2 at Norwood discharge.

Although previous reports documented short stature in older patients receiving Fontan,[3,6] height has not been the focus of efforts to improve early growth historically. Height, not weight, has been associated with poorer socioeconomic and neurodevelopmental outcomes, however.[5,7,8] Impairment of linear growth is not readily modifiable by increasing caloric intake.

De novo mutations likely play a role in impairment of linear growth.[9] Genetic polymorphisms or pathologic copy number variants have been associated with short stature and worse

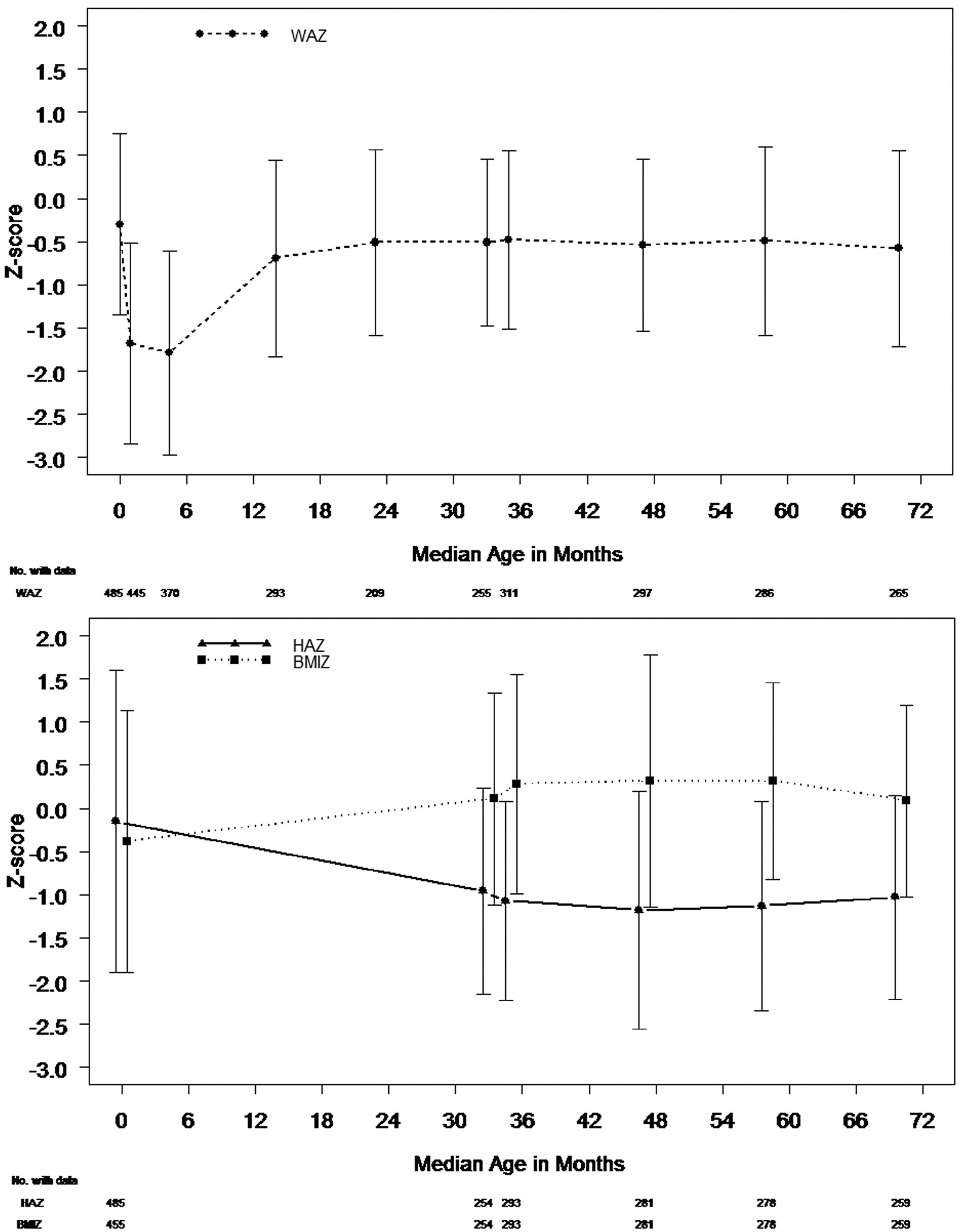

Figure 2. WAZ over all time periods (*top*). HAZ and BMIZ are demonstrated at birth, pre-Fontan, and annually between ages 3-6 years (*bottom*). Each mean is based on all data available at the respective time point. Error bars represent one SD. Age at surgery (months): Norwood 0.2 ± 0.4; stage II 4.7 ± 1.8; Fontan 33.8 ± 9.6.

neurodevelopmental outcomes in children with single ventricles, but the role of genetic factors is still being explored.[10] Disruption of the neuroendocrine growth axis,[11] and the long-term effects of an unfavorable fetal environment[8] are also being investigated.

This study has several limitations. Growth measurements were not standardized as outcome measurements in the SVR trial. These measurements were used for clinical care, however, and are obtained typically carefully in this vulnerable population. Because height is known to be unreliable in infants,[3] we included only birth length and height in older children. The anthropometric data are conditional on transplant-free survival to each respective time point, using all available data to maximize precision of our estimates. As a result, qualitative comparisons of the change in anthropometric measurements among the time intervals are based on diminishing cohort size and subject to survivor bias. Genotyping was not used to define genetic syndromes. Children with potentially pathogenic copy number variants or de novo mutations often have no obvious clinical findings,[9,10] potentially accounting for the failure to find an association between genetic syndrome and poor linear growth or weight gain in this study. Blood samples were stored for future genetic studies that may be enlightening.

Thus, at 6 years of age, height remained more impaired than weight for SVR survivors who are transplant free. Efforts to avoid excessive weight gain in these children warrant attention because they are particularly vulnerable to the morbidity associated with obesity. Future studies should consider the impact of other factors beyond caloric intake to improve height in this population. ■

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Reprint requests: Phillip T. Burch, MD, Department of Surgery, University of Utah, Salt Lake City, UT. E-mail: Phillip.Burch@hsc.utah.edu

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Appendix

Additional Pediatric Heart Network Investigators include (*no longer at the institution listed):

National Heart, Lung, and Blood Institute Bethesda, MD–Gail Pearson, MD, Victoria Pemberton, RN, Kristin Burns, MD, Jonathan Kaltman, MD, Mario Stylianou, PhD, Frank Evans, PhD.

Protocol Chair: University of Texas Southwestern Medical Center, Dallas, TX: Lynn Mahony MD.

Data Coordinating Center: New England Research Institutes, Waterton, MA: Lynn Sleeper, PhD*, Sharon Tennstedt, PhD*, Steven Colan, MD, Minmin Lu, PhD*, Shan Chen, Julie Schonbeck, APRN*, Melissa Lamberti, David F. Teitel, MD.

Core Clinical Site Investigators-Boston Children's Hospital, Boston, MA: Jane W. Newburger, MD (PI), Peter Laussen, MD*, Pedro del Nido, MD, Roger Breitbart, MD, Jami Levine, MD, Carolyn Dunbar-Masterson, RN, Bethany Trainor, MD; Children's Hospital of New York: Wyman Lai, MD (PI)*, Ismee Williams, MD*, Rosalind Korsin, RN; Children's Hospital of Philadelphia, Philadelphia, PA: J. William Gaynor, MD (Study Co-Chair), Chitra Ravishankar, MD, Tonia Morrison, MSM; Cincinnati Children's Medical Center, Cincinnati, OH: James Cnota, MD (PI), Catherine Dent Krawczeski, MD *, Kathryn Hogan, Teresa Barnard, RN, Kathleen Ash; North Carolina Consortium (Duke University, East Carolina University, Wake Forest University, Durham, NC): Jennifer Li, MD, Mingfen Xu; Medical University of South Carolina, Charleston, SC: Andrew Atz, MD, J. Philip Saul, MD (PI)*, Scott Bradley, MD, Eric Graham, MD, Teresa Atz, RN, Carolyn Taylor, Girish Shirali, MD*, Patricia Infinger; Primary Children's Hospital and the University of Utah, Salt Lake City, Utah: L. LuAnn Minich, MD (PI), Richard V. Williams, MD (PI), Phillip T. Burch, MD, Thomas A. Miller, DO, Linda M. Lambert, MSN-FNP, Marian E. Shearrow, RN, Michelle L. Robinson; Hospital for Sick Children, Toronto, Canada: Brian McCrindle, MD (PI), Seema Mital, MD, Elizabeth Radojewski, RN*, Patricia Walter, RN; University of Michigan, Ann Arbor, MI: Caren S. Goldberg, MD (PI), Richard G. Ohye, MD (PI), Suzanne Welch; Children's Hospital of Wisconsin and Medical College of Wisconsin, Milwaukee, WI: Nancy S. Ghanayem, MD (PI), James S. Tweddell, MD *, Kathleen A. Mussatto, PhD, Michele A. Frommelt, MD, Peter C. Frommelt, MD, Lisa Young-Borkowski, RN*. Auxiliary Sites -Children's Hospital Los Angeles, Los Angeles, CA: Alan Lewis, MD (PI), Hesham Mahmoud; Johns Hopkins All Children's Heart Institute, Orlando, FL: Jeffrey P. Jacobs, MD (PI), Tracey Cox, RN; Emory University, Atlanta, GA: William Mahle, MD (PI), Kirk Kanter, MD, Jeryl Huckaby; Nemours Cardiac Center, Wilmington, DE: Christian Pizarro, MD (PI), Carol Prospero, RN, Erica Sood, MD, Gina M. Baffa, Wolfgang A. Radtke, MD, Jane Vetter; University of Texas Southwestern Medical Center, Dallas, TX: Ilana Zeltzer, MD (PI), Deborah McElroy*. Echocardiography Core Laboratories-Children's Hospital of Wisconsin, Madison, WI: Peter C. Frommelt, MD.

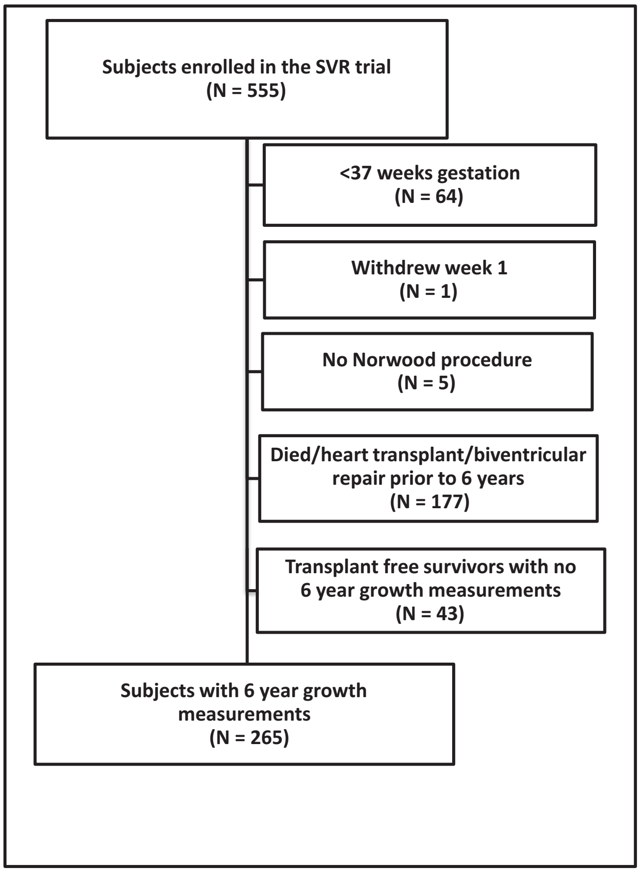

Figure 1. Flow diagram showing the study sample used for the growth analysis from birth to 6 years of age (without intermediate time points).

Table I. Candidate predictors considered in models predicting change in weight-for-age *Z*-score, height-for-age *Z*-score, and body mass index *z*-score for the designated time intervals

Between Birth and 6 Years of Age	
General	Age at procedure
Center	Age at Norwood
Socioeconomic status and Hollingshead scores at birth	Age at stage II
Percentage of residents below federal poverty level	Urgency of stage II (elective/nonelective)
Gender	Age at Fontan
Gestational age	
Race/ethnicity	Feeding method
Anatomy subtype	Any enteral feedings pre-Norwood
Obstructed pulmonary venous return	Oral feeding at all times
Birth weight	Oral feeding with tube feeding supplementation at any time
Birth weight < 2500 g	
Multiple birth	Tube feeding at all times
Maternal age	Tube feeding at any time
Paternal age	
History of consanguinity	Feeding issues
Exposures during pregnancy	Feeding issues at any time
Smoking	
Prescription drugs or general anesthesia	Therapy for feeding issues
Recreational drugs	Therapy for feeding issues at any time
Number of complications during pregnancy	
Number of infections during pregnancy	Diet
Number of miscarriages or stillbirths	Increased caloric density at Norwood discharge
Number of terminations for a cardiac defect	Solid foods at 13-36 months
Number of full and half siblings deaths	Caloric-supplemented diet at any time
Shunt type	
Type of Fontan (extracardiac vs lateral tunnel)	Digoxin use at any time
Genetics	Monitoring or early intervention services
Diagnosed with a genetic syndrome or genetic abnormalities	(speech/language/occupational therapy) at any time
APOE genotype	NYHA Heart failure classification greater than class 1 at 5 or 6 years of age
Interventional catheterizations	Arrhythmias
Cumulative number	Arrhythmias treated with medications or ICD at any time
Concomitant surgeries	Arrhythmias treated with medications at any time
Cumulative number	Arrhythmias treated with ICD at any time
Total number of noncardiac surgeries	Echocardiography
	Right ventricular area change
Total number of adverse events	Tricuspid regurgitation mild or greater at any time
Total number of complications	
Intraoperative variables	
Cumulative bypass support time	
Cumulative cross-clamp time	
Cumulative regional perfusion time	
Cumulative circulatory arrest time	
Extracorporeal membrane oxygenation at any hospitalization	
Cardiopulmonary resuscitation at any hospitalization	
Duration of hospital stay	
Cumulative duration of stay for all admissions	
Unplanned readmissions	
Number of unplanned readmissions	

APOE, apolipoprotein E; *ICD*, implantable cardioverter defibrillator; *NYHA*, New York Heart Association.

Table II. Candidate predictors considered in models predicting change in weight-for-age *Z*-score, height-for-age *Z*-score, and body mass index *z*-score for the designated time intervals

Between Fontan and 6 years of age
General
Center
Socioeconomic status and Hollingshead scores at birth
Percentage of residents below federal poverty level
Gender
Race/ethnicity
Anatomy subtype
Obstructed pulmonary venous return
Birth weight
Birth weight < 2500 g
Diagnosed with a genetic syndrome or genetic abnormalities
APOE genotype
Pre-Norwood
Enteral feedings before Norwood
Norwood hospitalization
Age at Norwood
Shunt type in place when leaving the operating room
Duration of hospital stay
At Norwood discharge
Feeding method (categorized as oral, oral with tube supplementation, tube)
Home monitoring (weight or oxygen) program (yes/no)
Post-Norwood echocardiogram
Right ventricular area change
Tricuspid valve regurgitation moderate or greater (yes/no)
Pre-stage II procedure
Feeding method (categorized as oral, oral with tube supplementation, tube)
End diastolic ventricular pressure
Right ventricular area change
Tricuspid valve regurgitation moderate or greater (yes/no)
Pre-Fontan catheterization
Pulmonary artery abnormalities
Systemic ventricular end-diastolic pressure
Pre-Norwood to 6 years
Cumulative cardiac surgeries
Cumulative noncardiac surgeries
Cumulative all surgeries
Cumulative serious adverse events
Cumulative complications
Cardiopulmonary resuscitation at any hospitalization
Extracorporeal membrane oxygenation at any hospitalization
Cumulative interventional catheterizations
Cumulative LOS all hospitalizations
Unplanned readmissions
Number of unplanned hospital readmissions
Digoxin use at any time
Tricuspid regurgitation moderate or greater at any time
Speech/language/occupational therapy at any time
Feeding issues at any time
Caloric-supplemented diet at any time point
Therapy for feeding issues at any time
Stage II hospitalization
Urgency (elective/nonelective)
Age
LOS
12 or 14 months to 3 years of age
Number of medications
Feeding method at 13-24 months of age (oral, oral with tube supplementation)
Feeding method at 25-36 months of age
Solid foods at 2 years of age
Solid foods at 3 years of age
Pre-Fontan echocardiogram
Right ventricular area change
Tricuspid regurgitation moderate or greater
Pre-Norwood to 6 years of age (continued)
Arrhythmia treated with medication, pacemaker or ICD at any time
Arrhythmia treated with medication at any time
Early intervention at any time
Oral feeding supplemented with tube at any time
Receiving only tube feedings at any data collection point between Norwood discharge and 6 years of age (yes/no)
NYHA Heart failure classification greater than class 1 at age 5 or 6 years of age (yes/no)
Fontan hospitalization
Age at Fontan
Type of Fontan
Use of cardiopulmonary bypass
Use of regional cerebral perfusion
Number of additional cardiac surgeries
Cardiopulmonary resuscitation
Extracorporeal membrane oxygenation
Number of interventional catheterization procedures
Number of other surgical procedures
ICD
Number of complications
Duration of stay
Readmission within 30 days post-Fontan
Readmission duration of stay

Table III. Changes in anthropometric measurements for each time period

Time period	Time between measurements (mo)	Change in *Z*-score Mean ± SD (n) All subjects*	MBTS	RVPAS	*P* value comparing shunts†
Weight-for-age *Z*-score					
Birth to 6 years of age	70.0 ± 3.5	–0.34 ± 1.30 (265)	–0.38 ± 1.37 (125)	–0.30 ± 1.23 (140)	.62
Pre-Fontan to 6 years of age	36.0 ± 10.3	–0.07 ± 0.82 (237)	–0.01 ± 0.89 (114)	–0.11 ± 0.76 (123)	.36
Height-for-age *Z*-score					
Birth to 6 years of age	70.0 ± 3.5	–1.04 ± 1.65 (259)	–1.03 ± 1.59 (120)	–1.05 ± 1.71 (139)	.91
Pre-Fontan to 6 years of age	36.1 ± 10.3	–0.09 ± 1.10 (231)	0.00 ± 1.18 (109)	–0.18 ± 1.01 (122)	.20
Body mass index-for-age *Z*-score					
Birth to 6 years of age	70.0 ± 3.6	0.54 ± 1.72 (246)	0.43 ± 1.55 (115)	0.64 ± 1.85 (131)	.34
Pre-Fontan to 6 years of age	36.1 ± 10.3	0.04 ± 1.12 (231)	0.07 ± 1.16 (109)	0.02 ± 1.10 (122)	.76

MBTS, modified Blalock Taussig shunt; *RVPAS*, right ventricle to pulmonary artery shunt.
*Each mean was based on data available at the respective time point.
†The *P* value used to compare shunts was derived from a 2-sample *t* test.

Table IV. Univariable regression results for change in anthropometric *Z*-score*

	Change in Z-scores between birth and 6 years of age								
	Weight-for-age			Length-for-age			BMI-for-age		
	N	Mean ± SD	*P* value	N	Mean ± SD	*P* value	N	Mean ± SD	*P* value
Hollingshead category			.11			.42			.04
3.0-27.0	63	−0.13 ± 1.29		60	−0.80 ± 1.22		56	0.53 ± 1.81	
>27.0-43.0	54	−0.63 ± 1.37		52	−1.22 ± 1.71		50	0.26 ± 1.53	
>43.0-54.5	70	−0.27 ± 1.09		69	−1.25 ± 1.96		65	1.04 ± 1.79	
>54.5-66.0	54	−0.55 ± 1.27		54	−1.06 ± 1.49		51	0.21 ± 1.72	
Missing	*24*	*0.02 ± 1.63*		*24*	*−0.60 ± 1.79*		*24*	*0.54 ± 1.42*	
Sex			.77			.25			.04
Male	165	−0.32 ± 1.32		163	−1.13 ± 1.72		156	0.71 ± 1.76	
Female	100	−0.37 ± 1.27		96	−0.89 ± 1.53		90	0.25 ± 1.61	
Race/ethnicity			.02			.02			.76
Hispanic	48	−0.16 ± 1.28		45	−0.86 ± 1.33		43	0.51 ± 1.77	
Non-Hispanic white	181	−0.50 ± 1.30		178	−1.24 ± 1.61		170	0.50 ± 1.75	
Non-Hispanic black	26	0.26 ± 1.16		26	−0.37 ± 1.62		25	0.69 ± 1.48	
Non-Hispanic other	6	0.21 ± 0.99		6	−0.25 ± 1.27		5	1.28 ± 1.64	
Missing	*4*	*0.01 ± 1.57*		*4*	*0.25 ± 4.52*		*3*	*0.85 ± 1.57*	
Birth weight									
Slope ± SE	265	−0.0015 ± 0.0001	<.001	259	−0.0015 ± 0.0002	<.001	246	−0.0007 ± 0.0002	.004
Low birth weight (<2500 g)			<.001			<.001			.009
Yes	18	1.48 ± 0.98		18	1.00 ± 1.84		11	1.86 ± 1.12	
No	247	−0.47 ± 1.21		241	−1.19 ± 1.53		235	0.48 ± 1.72	
Multiple birth			.009			.03			.38
Yes	4	1.33 ± 0.76		4	0.70 ± 1.38		2	1.61 ± 0.23	
No	261	−0.36 ± 1.29		255	−1.07 ± 1.64		244	0.54 ± 1.72	
Cumulative duration of stay for all admissions (d)			.02			.39			.30
1-30	31	0.34 ± 1.12		31	−0.67 ± 1.92		31	1.02 ± 2.12	
31-44	89	−0.36 ± 1.27		84	−0.95 ± 1.52		78	0.38 ± 1.64	
45-67	75	−0.43 ± 1.12		75	−1.24 ± 1.26		73	0.63 ± 1.61	
>67	70	−0.51 ± 1.49		69	−1.10 ± 2.01		64	0.42 ± 1.71	
Tube feeding at any time point			.004			.54			.008
Yes	97	−0.52 ± 1.44		95	−1.13 ± 1.81		86	0.44 ± 1.77	
No	168	−0.23 ± 1.20		164	−0.99 ± 1.56		160	0.60 ± 1.69	
Caloric supplemented diet at any time pre-Norwood to 6 years of age			.42			.97			.37
Yes	99	−0.42 ± 1.48		98	−1.05 ± 1.86		89	0.41 ± 1.78	
No	166	−0.29 ± 1.18		161	−1.04 ± 1.52		157	0.62 ± 1.69	
Right ventricular area change at baseline (%)			.04			.10			.46
9-29	65	−0.63 ± 1.32		63	−1.47 ± 1.52		62	0.52 ± 1.67	
>29-35	59	0.04 ± 1.27		57	−0.76 ± 1.39		55	0.78 ± 1.56	
>35-40	61	−0.33 ± 1.22		61	−0.89 ± 1.86		58	0.36 ± 1.91	
>40	63	−0.35 ± 1.26		61	−1.10 ± 1.78		56	0.78 ± 1.67	
Missing	*17*	*−0.52 ± 1.50*		*17*	*−0.68 ± 1.44*		*15*	*−0.38 ± 1.72*	
Duration of hospital stay at stage II procedure (d)†			.01			.13			.17
≤6	66	0.10 ± 0.76		64	0.17 ± 0.93		64	0.03 ± 1.09	
7-8	70	−0.21 ± 0.76		67	−0.23 ± 1.02		67	−0.07 ± 1.05	
9-14	55	−0.25 ± 0.77		54	−0.23 ± 1.14		54	−0.08 ± 1.00	
>14	46	0.15 ± 0.98		46	−0.09 ± 1.32		46	0.36 ± 1.37	
Feeding method at 13-24 months of age†			<.001			.07			.08
Oral	160	0.06 ± 0.78		156	−0.02 ± 0.97		156	0.14 ± 1.06	
Combination (oral + tube)	16	−0.66 ± 0.63		16	−0.41 ± 0.84		16	−0.51 ± 0.82	
Tube	16	−0.41 ± 1.04		15	−0.52 ± 1.15		15	−0.03 ± 1.59	
Missing	*45*	*−0.18 ± 0.82*		*44*	*−0.10 ± 1.50*		*44*	*−0.10 ± 1.20*	

*Unless otherwise indicated, all mean values and SDs are based on the subjects with 6-year growth measurements and available data on the change from birth to 6 years of age. Continuous variables were categorized into groups based on the quartiles of the distribution using all available data.

†Mean values and SDs are based on the subjects with 6-year growth measurements and available data on the change from pre-Fontan to 6 years of age.