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Assessment of Growth Six Years after the Norwood Procedure

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Abstract

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At age 6 years, patients with hypoplastic left heart syndrome had mean age-adjusted z-scores for weight (WAZ) and height (HAZ) below and body mass index (BMIZ) similar to the normative population. Higher birth weight infants had the greatest decrease in WAZ and HAZ. Males had the greatest increase in BMIZ.

Trial registration ClinicalTrials.gov: NCT00115934

Keywords

Hypoplastic left heart syndrome; pediatrics; growth; risk factors

Growth failure among infants with hypoplastic left heart syndrome (HLHS) 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 HLHS or a related single morphologic right ventricular (RV) 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 age 6 years.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; available at www.jpeds.com) on subjects from birth to age 6 years. To assess the effect of the Fontan procedure, we analyzed measurements obtained between the pre-Fontan visit and age 6 years. We included growth data up to death (N=153), transplant (n=21) or biventricular repair (N=3). The shunt type in place when the subject left the operating room following the Norwood procedure was used for this analysis.

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

Analyses were performed between birth and age 6 years and between pre-Fontan and age 6 years with subgroup analyses for those subjects with WAZ <−2 at Norwood discharge. A one-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 $p < 0.20$ were used as candidate predictors for multivariable modeling. For variables with $> 5\%$ missing data, mean imputation was performed prior to 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 $p < 0.15$ and $p < 0.05$, respectively. All terms in the final multivariable models have a reliability $> 50\%$ and $p < 0.05$. Separate models were constructed adjusting, and not adjusting, for center.

Results

Birth to age 6 years

The analysis of anthropometric measurements at age 6 years included 265 subjects enrolled between May 2005 and July 2008 (Figure 1; available at www.jpeds.com). At age 6 years, 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 ($p < 0.001$ for both). WAZ was less impaired than HAZ ($p < 0.001$). 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 ($p = 0.17$) with 13% of subjects having BMIZ < -1 and 3% with BMIZ < -2 .

Mean WAZ and mean HAZ decreased between birth and age 6 years ($p < 0.001$ for both) (Table II; available at www.jpeds.com). WAZ decreased 0.5 SD in 49% of subjects and HAZ decreased by 0.5 SD in 61%. In contrast to WAZ and HAZ, mean BMIZ increased between birth and age 6 years. 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 $p < 0.05$) are shown in Table III (available at www.jpeds.com). Higher birth weight ($p < 0.001$), longer cumulative length of stay (LOS) for all admissions ($p = 0.001$) and being white/non-Hispanic ($p = 0.02$) were independently associated with a greater decrease in WAZ (Table IV). Higher birth weight was the only factor independently associated with a greater decrease in HAZ ($p < 0.001$). 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 Age 6 Years

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 age 6 years. At the pre-Fontan

visit, mean WAZ (-0.51 ± 0.97) and HAZ (-0.96 ± 1.19) were significantly below the normative mean ($p < 0.001$). WAZ was < -1 in 31% of subjects and < -2 in 5%. Mean WAZ decreased between the pre-Fontan visit and age 6 years (Table II), but compared with the Norwood 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.

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 age 6 years (Table II) with a decrease of 0.5 SD in 26% of subjects. In contrast to WAZ and HAZ, at the pre-Fontan visit, mean BMIZ was similar to the normative population; 16% were < -1 and 2% were < -2 . Overall, mean BMIZ increased between Fontan and age 6 years. 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 independently associated with change in WAZ ($p = 0.03$). With center removed from the model, being white/non-Hispanic was independently associated with a decrease in WAZ. Longer 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 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 ($p = 0.002$). The type of shunt in place after the Norwood procedure had no association with change in any anthropometric measurement.

Age 6 Years Anthropometric Measurements 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%, $p = 0.72$). 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 , $p < 0.001$). RV area change at the pre-Norwood echocardiogram had a non-linear association with increased weight gain between Norwood discharge and age 6 years. Multiple births and low birth weight were also independently associated with better weight gain between Norwood and age 6 years in this subgroup. Between the Fontan and age 6 years, being black non-Hispanic and oral feeding at 13–24 months of age were associated with better weight gain. At age 6 years, HAZ was similar between those discharged with and those without WAZ < -2 ($p = 0.25$). BMIZ was 0.26 SD below normal in those discharged with WAZ < -2 and 0.34 SD above normal in those with WAZ ≥ -2 ($p < 0.001$). Of those discharged with WAZ < -2 , BMIZ was > 1.5 in 5% and none had BMIZ > 2.0 at age 6 years.

Discussion

This longitudinal assessment of growth from birth to age 6 years in a well characterized cohort of subjects with HLHS and related single RV anomalies enrolled in the SVR trial demonstrated that the Fontan procedure had little effect on growth at age 6 years. Similar to our findings at age 3 years³, both mean WAZ and HAZ for this study population remained

below mean values for the normative population, with HAZ more impaired than WAZ at age 6 years. Despite the drop in both mean WAZ and HAZ, mean BMIZ increased >0.5 SD in over 50% of the SVR survivors. These data highlight both the trends and the variance in growth for 6 years old transplant-free survivors of the Norwood procedure.

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. Shorter total LOS for all hospitalizations correlated with a greater increase in growth between Fontan and age 6 years 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 age 6 years. 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, as HAZ remains more impaired than WAZ and no association was found between birth weight and BMIZ at age 6 years.

Feeding predictor variables were not associated with growth. Tube feeding at any time was associated with a greater decrease in BMIZ between birth and age 6 years. Being fed a caloric-supplemented diet at any time was associated with a greater decrease in HAZ between pre-Fontan and age 6 years 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 age 6 years 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 Fontan patients,^{3, 6} height has not historically been the focus of efforts to improve early growth. 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 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 environment⁸ 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 typically carefully obtained in this vulnerable population. Because height is known to be unreliable in infants³, 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 transplant-free survivors. 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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Abbreviations

SVR	Single Ventricle Reconstruction trial
RV	right ventricle
WAZ	weight-for-age z-score
HAZ	height-for-age z-score
BMIZ	body mass index-for-age z-score
HLHS	hypoplastic left heart syndrome
LOS	length of stay

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Appendix

Additional Pediatric Heart Network Investigators include (*no longer at the institution listed): National Heart, Lung, and Blood Institute--Gail Pearson, Victoria Pemberton, Kristin Burns, Jonathan Kaltman, Mario Stylianou, Frank Evans.

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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.

FIGURE 1.

on line: Flow diagram showing the study sample used for the growth analysis from birth to age 6 years (without intermediate time points).

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 standard deviation. Age at surgery (months): Norwood 0.2 ± 0.4 ; stage II 4.7 ± 1.8 ; Fontan 33.8 ± 9.6 .

Table 1

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

A. Between Birth and age 6 years

General

Center

Socioeconomic status and Hollingshead scores at birth

Percentage of residents below federal poverty level

Gender

Gestational age

Race/ethnicity

Anatomy subtype

Obstructed pulmonary venous return

Birth weight

Birth weight <2,500 grams

Multiple birth

Maternal age

Paternal age

History of consanguinity

Exposures during pregnancy

Smoking

Prescription drugs or general anesthesia Recreational drugs

Number of complications during pregnancy

Number of infections during pregnancy

Number of miscarriages or stillbirths

Number of terminations for a cardiac defect

Number of full and half siblings deaths Shunt type

Type of Fontan (extracardiac vs. lateral tunnel)

Genetics

Diagnosed with a genetic syndrome or genetic abnormalities

APOE genotype

Interventional catheterizations

Cumulative number

Concomitant surgeries

Cumulative number

Total number of non-cardiac surgeries**Total number of adverse events****Age at procedure**

Age at Norwood

Age at stage II

Urgency of stage II (elective/non-elective)

Age at Fontan

Feeding method

Any enteral feedings pre-Norwood
 Oral feeding at all times
 Oral feeding with tube feeding supplementation at any time
 Tube feeding at all times
 Tube feeding at any time

Feeding issues

Feeding issues at any time

Therapy for feeding issues

Therapy for feeding issues at any time

Diet

Increased caloric density at Norwood discharge
 Solid foods 13–36 months
 Caloric-supplemented diet at any time

Digoxin use at any time**Monitoring or early intervention services (speech/language/occupational therapy) at any time****NYHA Heart failure classification >Class 1 at age 5 or 6 years****Arrhythmias**

Arrhythmias treated with medications or implantable cardioverter defibrillator(ICD) at any time
 Arrhythmias treated with medications at any time
 Arrhythmias treated with ICD at any time

Echocardiography

Right ventricular area change
 Tricuspid regurgitation mild 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****Length of hospital stay**

Cumulative length of stay for all admissions
 Unplanned readmissions
 Number of unplanned readmissions

B. Between Fontan and age 6 years**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 <2,500 grams
 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 OR
 Length 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 (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 (yes/no)

Pre-Fontan catheterization

Pulmonary artery abnormalities
 Systemic ventricular end-diastolic pressure

Pre-Norwood to 6 years

Cumulative cardiac surgeries
 Cumulative non-cardiac 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 length of stay all hospitalizations
 Unplanned readmissions
 Number of unplanned hospital readmissions
 Digoxin use at any time
 Tricuspid regurgitation moderate 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/non-elective)

Age

Length of stay

12 or 14 months to 3 years

Number of medications

Feeding method 13–24 months (oral, oral with tube supplementation)

Feeding method 25–36 months

Solid foods at 2 years

Solid foods at 3 years

Pre-Fontan echocardiogram

Right ventricular area change

Tricuspid regurgitation moderate

Pre-Norwood to 6 years (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 (yes/no)

NYHA Heart failure classification >Class 1 at age 5 or 6 years (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

Length of stay

Readmission within 30 days post-Fontan

Readmission length of stay

Table 2**Changes in Anthropometric Measurements for Each Time Period**

Time period	Time between measurements (months)	Change in Z-score			P-value comparing shunts**
		Mean $\pm$ Standard Deviation (n)			
		All subjects*	MBTS	RVPAS	
		Weight-for-age Z-score			
Birth to 6 years	70.0 $\pm$ 3.5	-0.34 $\pm$ 1.30 (265)	-0.38 $\pm$ 1.37 (125)	-0.30 $\pm$ 1.23 (140)	0.62
Pre-Fontan to 6 years	36.0 $\pm$ 10.3	-0.07 $\pm$ 0.82 (237)	-0.01 $\pm$ 0.89 (114)	-0.11 $\pm$ 0.76 (123)	0.36
		Height-for-age Z-score			
Birth to 6 years	70.0 $\pm$ 3.5	-1.04 $\pm$ 1.65 (259)	-1.03 $\pm$ 1.59 (120)	-1.05 $\pm$ 1.71 (139)	0.91
Pre-Fontan to 6 years	36.1 $\pm$ 10.3	-0.09 $\pm$ 1.10 (231)	0.00 $\pm$ 1.18 (109)	-0.18 $\pm$ 1.01 (122)	0.20
		Body Mass Index-for-age Z-score			
Birth to 6 years	70.0 $\pm$ 3.6	0.54 $\pm$ 1.72 (246)	0.43 $\pm$ 1.55 (115)	0.64 $\pm$ 1.85 (131)	0.34
Pre-Fontan to 6 years	36.1 $\pm$ 10.3	0.04 $\pm$ 1.12 (231)	0.07 $\pm$ 1.16 (109)	0.02 $\pm$ 1.10 (122)	0.76

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 two-sample t-test

Table 3

Univariable Regression Results for Change in Anthropometric Z-score¹

	Change in Z-scores Between Birth and Age 6 Years					
	Weight-for-age			Length-for-age		
	N	Mean ± SD	P-value	N	Mean ± SD	P-value
Hollingshead category			0.11			0.42
3.0–27.0	63	−0.13±1.29		60	−0.80±1.22	
>27.0–43.0	54	−0.63±1.37		52	−1.22±1.71	
>43.0–54.5	70	−0.27±1.09		69	−1.25±1.96	
>54.5–66.0	54	−0.55±1.27		54	−1.06±1.49	
Missing	24	0.02±1.63		24	−0.60±1.79	
Sex			0.77			0.25
Male	165	−0.32±1.32		163	−1.13±1.72	
Female	100	−0.37±1.27		96	−0.89±1.53	
Race/ethnicity			0.02			0.02
Hispanic	48	−0.16±1.28		45	−0.86±1.33	
Non-Hispanic white	181	−0.50±1.30		178	−1.24±1.61	
Non-Hispanic black	26	0.26±1.16		26	−0.37±1.62	
Non-Hispanic other	6	0.21±0.99		6	−0.25±1.27	
Missing	4	0.01±1.57		4	0.25±4.52	
Birth weight						
Slope ± SE	265	−0.0015±0.0001	<0.001	259	−0.0015±0.0002	<0.001
Low birth weight (<2,500 grams)			<0.001			<0.001
Yes	18	1.48±0.98		18	1.00±1.84	
No	247	−0.47±1.21		241	−1.19±1.53	
Multiple birth			0.009			0.03
Yes	4	1.33±0.76		4	0.70±1.38	
No	261	−0.36±1.29		255	−1.07±1.64	
Cumulative length of stay for all admissions			0.02			0.39
1–30 days	31	0.34±1.12		31	−0.67±1.92	
31–44 days	89	−0.36±1.27		84	−0.95±1.52	
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Change in Z-scores Between Birth and Age 6 Years									
	Weight-for-age			Length-for-age			BMI-for-age		
	N	Mean ± SD	P-value	N	Mean ± SD	P-value	N	Mean ± SD	P-value
45–67 days	75	−0.43±1.12		75	−1.24±1.26		73	0.63±1.61	
>67 days	70	−0.51±1.49		69	−1.10±2.01		64	0.42±1.71	
Tube feeding at any time point			0.004			0.54			0.008
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 age 6 years			0.42			0.97			0.37
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			0.04			0.10			0.46
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	
Change in Z-scores Between Pre-Fontan and Age 6 Years									
	Weight-for-age			Length-for-age			BMI-for-age		
	N	Mean ± SD	P-value	N	Mean ± SD	P-value	N	Mean ± SD	P-value
Length of hospital stay at Stage II procedure²			0.01			0.13			0.17
6 days	66	0.10±0.76		64	0.17±0.93		64	0.03±1.09	
7–8 days	70	−0.21±0.76		67	−0.23±1.02		67	−0.07±1.05	
9–14 days	55	−0.25±0.77		54	−0.23±1.14		54	−0.08±1.00	
>14 days	46	0.15±0.98		46	−0.09±1.32		46	0.36±1.37	
Feeding method 13–24 months²			<0.001			0.07			0.08
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	

²Unless otherwise indicated, all means and standard deviations are based on the subjects with 6 year growth measurements and available data on the change from birth to age 6 years. Continuous variables were categorized into groups based on the quartiles of the distribution using all available data.

Means and standard deviations are based on the subjects with 9 year growth measurements and available data on the change from pre-Fontan to age 6 years.

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Table 4

Multivariable Models for Change in Anthropometric Z-scores from Birth to Age 6 Years. *

Weight-for-age Z-score (n=261, adjusted R ² =0.34)				
Variable	Estimate	Standard Error	P-value	Reliability (%)
Birth weight, kg	−0.001	0.0001	<0.001	82
Cumulative length of stay: all admissions (days)			0.001	64
30	0.914	0.229		
31–44	0.351	0.170		
45–67	0.242	0.179		
>67	Reference			
Race/ethnicity			0.02	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)				
Variable	Estimate	Standard Error	P-value	Reliability (%)
Birth weight, kg	−0.002	0.0002	<0.001	85
Body Mass Index-for-age Z-score (n=246, adjusted R ² =0.07)				
Variable	Estimate	Standard Error	P-value	Reliability (%)
Hollingshead score			0.014	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			0.003	59
Yes	−0.700	0.232		
No	Reference			
Sex			0.040	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.