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Longitudinal growth in patients with single ventricle cardiac disease receiving tube-assisted feeds

Arene Butto MD[1] | Laura Mercer-Rosa MD, MSCE[1] | Christopher Teng MD[1] | Carrie Daymont MD, MSCE[2] | Jonathan Edelson MD[1] | Jennifer Faerber PhD[1] | Erika Mejia MD[1] | Chitra Ravishankar MD[1] | Meryl S. Cohen MD[1]

[1]Division of Cardiology, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania

[2]Departments of Pediatrics and Public Health Sciences, Penn State College of Medicine, Hershey, Pennsylvania

Correspondence
Arene Butto, Children's Hospital of Philadelphia, 3401 Civic Center Blvd., Philadelphia, PA, 19104.
Email: buttoa@email.chop.edu

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Abstract

Objective: Children with single ventricle cardiac disease (SVCD) have poor growth in early life. Tube-assisted feeding (TF) is used to improve weight gain, but its impact on long-term growth remains unknown. We sought to compare the longitudinal growth of SVCD patients receiving TF after initial cardiac surgery with those fed entirely by mouth.

Design: We conducted a retrospective cohort study of SVCD patients who underwent initial surgical palliation between 1999 and 2009. We defined TF as the use of nasogastric, gastrostomy, or jejunostomy TF. We compared maximal attained growth z-scores for each year of life between TF and non-TF patients. A secondary analysis compared surgical and clinical factors between groups.

Results: A total of 134 patients were included; 64% were male and 68% underwent the Norwood operation. One third of patients (44) received TF. Adjusting for age, TF patients had an average of 0.56 lower weight-for-age z-score (WAZ) than non-TF patients ($P = 0.007$) through the age of 6 years. Longitudinal height was not affected by TF status ($P = 0.15$). In a subanalysis of Norwood patients, TF patients had lower WAZ at initial hospital discharge despite longer LOS. TF patients had diminished WAZ after adjusting for complications, interstage hospitalizations, and timing of subsequent operations.

Conclusions: In this single-center study, patients with SVCD requiring TF at discharge from initial surgical palliation had diminished WAZ at discharge and on long-term follow-up, despite controlling for other identifiable risk factors. Further investigation is needed to understand the mechanisms underlying this phenomenon and to risk stratify infants who go home on TF.

KEYWORDS
growth, Norwood, single ventricle, tube-assisted feeds

1 | INTRODUCTION

Children with congenital heart disease have decreased growth parameters in the first 3 years of life compared to healthy peers.[1] Patients with single ventricle cardiac disease (SVCD) are at particular risk for early growth impairment after their initial surgical palliation. Poor growth in this population is likely related to several factors including the hemodynamic consequences of shunt-dependent pulmonary blood flow, long length of stay after initial surgery, and feeding issues, such as vocal cord paralysis and oral aversion.[2,3] The issue cannot be entirely related to the surgical shunt because SVCD patients have persistently limited weight gain and linear growth even after the second and third stages of surgical palliation, when the increased metabolic demand of shunt dependence is resolved.[4,5]

This population often has difficulty in eating sufficient calories by mouth, possibly due to congestive heart failure, recurrent laryngeal nerve damage, poor oral coordination after intubation, neurodevelopmental abnormalities, or prolonged illness. With the advent of standardized nutrition protocols and interstage home monitoring programs, there has been increasing use of tube-assisted feeding (TF) in these patients to promote weight gain.[6-8] Prior studies have shown that TF is associated with poor weight gain soon after neonatal surgery in patients with SVCD.[9,10] However, little is known about the effects of TF on long-term growth in this population.[7,11,12]

We sought to compare the longitudinal growth of all SVCD patients receiving TF at the time of hospital discharge after initial cardiac surgery with those who were fed entirely by mouth. We hypothesized that patients discharged on TF would have a different pattern of growth than those who were fed by mouth.

2 | METHODS

We conducted a longitudinal retrospective cohort study comparing attained growth in SVCD patients requiring TF to those fed by mouth at the time of discharge from the first surgical hospitalization. We extracted discrete data, including diagnostic codes and growth parameters, from our institution's electronic health records (Epic and CardioIMS). We performed manual chart review in these systems, as well as scanned paper charts in a separate system, ChartMaxx. The study was approved by the Institutional Review Board at our institution.

2.1 | Patient selection

Between February 1999 and March 2009, we identified children with *International Classification of Diseases*, *Ninth Revision* (ICD-9) codes for CHD. Patients who underwent surgical palliation for SVCD were identified via diagnostic codes and confirmed with chart review. Initial SVCD surgeries included the Norwood operation, Blalock-Taussig shunt only, Blalock-Taussig shunt with atrial septectomy, or pulmonary arterial banding. Patients were also included if their first surgical palliation was a superior cavopulmonary anastomosis (typically considered the second stage of SVCD palliation) or total cavopulmonary anastomosis (Fontan) (typically the third stage). SVCD patients were included if they had at least two outpatient visits between ages 2 and 7 years, occurring approximately 6-12 months apart, in which weight and height were recorded.

Patients were excluded if they were born prematurely (<37 weeks gestation) or if they had other known noncardiac chronic conditions, as defined by Feudtner et al[13]. Patients who underwent initial surgical palliation for SVCD at another center were also excluded, as were those who underwent heart transplantation during the study period.

We compared growth in children receiving TF to those receiving oral feeds at the time of hospital discharge from the initial surgical palliation for SVCD. TF was defined as feeds delivered by nasogastric tube (NGT), gastrostomy tube (GT), or gastrojejunostomy tube (GJT), either for primary or supplementary nutrition. During the study period, patients were not enrolled in an interstage monitoring program (it did not yet exist); feeds were therefore managed by the patients' primary care physician and/or cardiologist, typically in conjunction with a nutritionist. Exposed subjects had documentation of TF in the hospital discharge summary or in an outpatient clinic letter. Patients who were not receiving TF at the time of hospital discharge were identified as the control group. Those who did not have documentation of the route of feeding at the time of discharge were assumed to be fed entirely by mouth and were included in the control group.

2.2 | Measures

We obtained the maximal attained weight and height at age 6-12 months and 12-24 months. Weight, height, and body mass index (BMI, kg/m^2) were collected for each year of life between ages 2 and 6 years that were available from outpatient records. We defined the time frame for each year-of-life encounter as the 12 months following the subject's birthday and used the visit with the highest height to represent the maximal growth achieved during that year of life. Weight-for-age (WAZ) and height-for-age (HAZ) z-scores were calculated by each child's sex and age (in months) using the 2000 SAS macro available from the Centers for Disease Control.[14]

Demographic and clinical information collected included birth weight and underlying cardiac diagnosis. Operative reports were reviewed to obtain factors related to the initial SVCD surgical palliation, including the type of operation, age at the time of surgery, and the use and duration of cardiopulmonary bypass. Hospital length of stay (LOS) and WAZ at the time of discharge were obtained, along with postoperative complications and rehospitalizations prior to the second stage of surgery (cavopulmonary anastomosis). Postoperative complications were defined as cardiopulmonary resuscitation (CPR), extracorporeal membrane oxygenation (ECMO), mediastinitis, unplanned or urgent reoperations, or cardiac catheterizations. Echocardiographic measures of ventricular function and atrioventricular valve regurgitation (AVVR) at the time of discharge were abstracted from echocardiographic reports.

In the exposure group, additional data on TF were obtained where available, including the modality of TF and feeding schedule (bolus, continuous, or combination). The use of TF as primary vs supplemental nutrition was also recorded. As there is great practice variability for diagnosing vocal cord paralysis or feeding disorders, such as oromotor dysfunction or food aversion, these diagnoses were extracted from the patient's documented problem list in Epic. Few patients had documentation regarding TF schedule and duration of time that TF feeds were administered; thus, these variables were not included in the analysis.

2.3 | Primary analysis

We used a mixed effects fractional polynomial regression approach to separately model the longitudinal trajectories of WAZ, HAZ, and BMIZ as a function of TF status (TF vs non-TF) and a polynomial function of age. This model accounted for each individual's growth trajectory. Each model used all available measurements of the outcome per child up through the age of 6 years. The fractional polynomial approach examines all possible pairs of polynomial functions of age and used model deviance to select the best-fitting model. For each outcome (WAZ, HAZ, and BMIZ), we considered if the effect of TF varied across age and included any significant age-by-TF interaction in the final model. To adjust the model for patient heterogeneity in the outcomes, we included a random intercept for each patient and a random slope for age, and we allowed for the random intercept and slope to be correlated. Surgery type and number of postoperative complications from the initial surgery were examined as covariates and retained in the model if associated with the outcome. In all three outcome models, Norwood status (Norwood vs other single ventricle surgery) and number of postoperative complications were examined as potential covariates and retained in the model if associated with the outcome or confounders of the TF-outcome relationship.

2.4 | Secondary analysis

A secondary objective was to compare demographic, surgical, and clinical characteristics between TF and non-TF patients in the entire SVCD cohort. To address the heterogeneity of the SVCD population, we performed a separate subgroup analysis in Norwood patients, a more homogenous population. Demographic characteristics in both groups were summarized by standard descriptive summaries with continuous characteristic variables expressed as means with standard deviations or medians with interquartile ranges, depending on the distribution, and the values were compared using standard *t* tests (or Wilcoxon regression models). Categorical variables were expressed as frequency counts and percentage. Chi-square tests (or the Fisher's exact test, if there were any sparse cells) were used to test if the distribution of categorical variables differed significantly across TF and non-TF groups. The proportion of children undergoing Norwood vs another surgery was also compared across the two feeding groups.

3 | RESULTS

A total of 203 SVCD patients were identified. Of those, 57 patients had initial surgical palliation performed outside our institution and were excluded. Additionally, 12 patients were excluded due to prematurity. The final cohort included 134 patients. The median number of growth assessments per patient for the full cohort was 6 (interquartile range 4-7) between ages 6 months and 6 years. The median number of years between the first and last growth measurements was 5 (IQR 4-6).

3.1 | Baseline characteristics

Patient demographics and baseline characteristics are shown in Table 1. The subjects were predominantly white and male. The most common cardiac diagnosis was hypoplastic left heart syndrome (HLHS) in 51% (n = 68). A total of 68% (n = 91) underwent the Norwood operation. At the time of discharge, 33% of patients (n = 44) received TF. There was no difference in birth weight between the TF and non-TF groups. HLHS patients represented a majority of the TF group (n = 29, 66%).

In the TF group, the majority of patients received NGT feeds (86%); four received GT and two received GJT feeds. Three of the GT patients remained on TF for at least the first 4 years of childhood. One patient with a GJT transitioned to exclusively oral feeds before Stage 2 palliation and the other used GJT feeds through age of 30 months. Only two patients used TF as the sole source of nutrition, one with a GT and one with GJT. Feeding disorders were diagnosed in seven TF patients only. There were seven patients with vocal cord paralysis in the TF group and only one in the non-TF group (P = 0.017).

3.2 | Growth related to surgical and hospitalization characteristics

As shown in Table 2, a greater percentage of patients who received TF underwent the Norwood operation compared to controls (84% vs 60%; P = 0.0078). Cardiopulmonary bypass and deep hypothermic circulatory arrest times were longer in the TF group. TF patients had significantly longer median LOS (28 vs 12 days, P < 0.0001) and a higher incidence of postoperative complications (32% vs 16%, P = 0.03). However, there was no significant difference in the degree of ventricular dysfunction or amount of AVVR at the time of discharge between groups. Median WAZ at the time of initial hospitalization discharge was significantly lower in the TF group but was within two standard deviations of normal for both groups.

3.3 | Longitudinal growth after discharge

There were no significant differences in the number of interstage hospitalizations after discharge among patients who underwent a surgical repair prior to Stage 2 palliation (Table 3). The age at which patients underwent second and third stages of single ventricle palliation were also similar between groups. In the full SVCD cohort,

TABLE 1 Baseline characteristics

	All single ventricle (*n* = 134)			Norwood only (*n* = 91)		
	TF (*n* = 44)	No TF (*n* = 90)	*p*	TF (*n* = 37)	No TF (*n* = 54)	*p*
Gender, *n* (%)						
Male	27 (61.4)	59 (65.6)	0.63	23 (62.2)	35 (64.8)	0.80
Female	17 (38.6)	31 (34.4)		14 (37.8)	19 (35.2)	
Race, n (%)						
White/Caucasian	32 (72.7)	69 (76.7)	0.7	30 (81.1)	47 (87.0)	0.46
Black/African American	6 (13.6)	13 (14.4)		3 (8.1)	5 (9.3)	
Other	6 (13.6)	8 (8.9)		4 (10.8)	2 (3.7)	
Cardiac diagnosis, n (%)						
HLHS and variants	29 (65.9)	39 (43.3)	0.17	29 (78.4%)	38 (70.4)	0.56
Unbalanced AV canal	1 (2.3)	10 (11.1)		1 (2.7%)	3 (5.6)	
Tricuspid atresia	6 (13.6)	12 (13.3)		3 (8.1%)	4 (7.4)	
Pulmonary atresia	2 (4.5)	5 (5.6)		0	0	
Complex single dominant LV	4 (9.1)	16 (17.8)		3 (8.1)	9 (16.6)	
Complex single dominant RV	2 (4.5)	8 (8.9)		1 (2.7)	0	
Heterotaxy syndrome, *n* (%)	0	8 (8.9)	0.05	0	1 (1.9)	1
Birth weight (kg)[a]	3.4 (2.9-3.7)	3.4 (2.9-3.6)	0.45	3.4 (2.9-3.7)	3.4 (3.1-3.7)	0.33

[a]Median (interquartile range).

TABLE 2 Surgical and hospitalization characteristics

	All single ventricle (*n* = 134)			Norwood only (*n* = 91)		
	TF (*n* = 44)	No TF (*n* = 90)	*p*	TF (*n* = 37)	No TF (*n* = 54)	*p*
Type of single ventricle surgery, *n* (%)						
Norwood[a]	37 (84)	54 (60)	0.0078			
Other[b]	7 (16)	36 (40)				
Surgical times (minutes)[c]						
Cardiopulmonary bypass	87.5 (74.5, 106)	75 (38, 84)	0.0039	95 (79, 106)	82 (75, 103)	0.15
Deep hypothermic circulatory arrest	41.5 (30, 53.5)	35 (4, 43)	0.008	47 (37, 54)	41 (37, 45)	0.18
Any postoperative complications, *n* (%)[d]	14 (31.8)	14 (15.6)	0.03	14 (37.8)	11 (20.4)	0.067
Length of stay for index admission (days)[c]	27.5 (18.5, 39)	12 (10, 16)	<0.0001	30 (21, 41)	13.5 (10, 16)	<0.0001
Ventricular function at discharge, *n* (%)						
Normal or low normal	38 (86.4)	68 (86.1)	0.96	32 (86.5)	43 (89.6)	0.74
Mildly diminished or greater	6 (13.6)	11 (13.9)		5 (13.5)	5 (10.4)	
AV valve regurgitation at discharge, *n* (%)						
None, trivial, or mild	33 (80.5)	65 (84.4)	0.59	28 (77.8)	39 (83.0)	0.58
Mild or greater	8 (19.5)	12 (15.6)		8 (22.2)	8 (17.0)	
WAZ at time of hospital discharge (kg)[c]	−1.7 (−2.5, −0.5)	−0.9 (−1.9, −0.1)	0.04	−1.7 (−2.5, −0.4)	−0.8 (−1.7, −0.1)	0.02

[a]Norwood surgery: includes patients with shunt or with Sano modification.
[b]Other single ventricle surgery: shunt only (*n* = 20); shunt with atrial septectomy (*n* = 4); pulmonary artery (PA) bands (*n* = 2); other combination of shunt, atrial septectomy, and PA band (*n* = 7); initial Glenn (*n* = 9); and initial Fontan 3 (*n* = 1).
[c]Median (interquartile range).
[d]CPR, ECMO, mediastinitis, unplanned/urgent reoperations, unplanned/urgent catheterizations.

there was no difference in median attained WAZ or HAZ at two earlier time points, between 6-12 months and 12-24 months of life (Table 4). Among the 44 patients who received TF at the time of discharge, TF status for 36 patients was recorded at the time of the second stage of surgical palliation. In that group, 15 patients (42%) still required TF; the remaining 21 patients were not receiving TF.

Multivariable mixed effects models for WAZ, HAZ, and BMIZ with fractional polynomial modeling of age were used to estimate

TABLE 3 Postdischarge characteristics

	All single ventricle (*n* = 134)			Norwood only (*n* = 91)		
	TF (*n* = 44)	No TF (*n* = 90)	*p*	TF (*n* = 37)	No TF (*n* = 54)	*p*
Interstage period						
One or more interstage hospitalizations, *n* (%)	22 (50.0)	34 (37.8)	0.20	19 (51.4)	24 (44.4)	0.52
Number of interstage hospitalizations[a]	1.4 (0.67)	1.6 (0.99)	0.91	1.5 (0.70)	1.5 (0.83)	0.87
Glenn or Stage 2						
Age at the time of Glenn or Stage 2 (months)[b]	5.5 (4.8-6.3)	5.6 (4.6-6.7)	0.68	5.5 (4.8-6.2)	5.6 (4.0-6.8)	0.48
LOS at the time of Glenn or Stage 2 (days)[b]	7 (5-18)	5 (4-6)	<0.0001	7 (4.5-19)	5 (4-6)	<0.0001
Fontan or Stage 3						
Age at time of Fontan or Stage 3 (months)[b]	35.0 (25.2-43.1)	30.8 (26.5-39.1)	0.31	33.3 (25.1-42.5)	30.4 (25.0-36.9)	0.18
LOS at the time of Fontan or Stage 3 (days)[b]	8 (6-13)	8 (6-11)	0.39	8 (7-12.5)	7 (5-11)	0.27

[a]Mean (standard deviation).
[b]Median (interquartile range).

TABLE 4 Growth measurements prior to age 24 months

	All single ventricle (*n* = 134)			Norwood only (*n* = 91)		
	TF (*n* = 44)	No TF (*n* = 90)	*p*	TF (*n* = 37)	No TF (*n* = 54)	*p*
Growth at 6-12 months, median (IQR)						
WAZ	−1.4 (−2.2, −0.8)	−1.0 (−2.1, −0.2)	0.064	−1.3 (−1.8, −0.8)	−0.9 (−1.8, −0.02)	0.1
HAZ	−0.9 (−1.6, 0.04)	−0.6 (−1.4, 0.2)	0.62	−0.8 (−1.4, 0.1)	−0.6 (−1.3, 0.3)	0.58
Growth at 12-24 months, median (IQR)						
WAZ	−0.8 (−2.2, −0.2)	−0.6 (−1.4, 0.1)	0.067	−0.7 (−2.2. −0.2)	−0.4 (−1.3, 0.1)	0.06
HAZ	−0.8 (−1.3, −0.04)	−0.5 (−1.3, 0.3)	0.27	−0.8 (−1.2, 0.07)	−0.6 (−1.1, 0.4)	0.37

the effect of TF on longitudinal growth between ages 2 and 6 years, adjusting for age and Norwood status (Figure 1). TF patients had lower WAZ than non-TF patients [z-score difference = −0.56 (95% CI: −0.96, −0.15), *P* = 0.007]. The number of postoperative complications was not associated with WAZ. HAZ in TF patients was not found to be significantly lower than in non-TF patients [z-score difference = −0.23, 95% CI: (−0.62, 0.15), *P* = 0.23]. In the HAZ model (Figure 2), there were no significant interactions by Norwood operation or number of postoperative complications. Similar to the WAZ, TF patients had significantly lower BMIZ compared to non-TF patients [z-score difference = −0.58 (95% CI: −0.95, −0.21), *P* = 0.002].

3.4 | Norwood subgroup analysis

A separate analysis was performed on patients undergoing the Norwood operation. Similar to the full cohort, these patients were predominantly white and male, with overall normal birth weights (Table 1). There was no difference in perioperative variables between the TF and non-TF patients (Table 2). There was no significant difference in the degree of ventricular dysfunction or in the amount of AVVR between groups. However, the median hospital LOS in the TF group was more than twice that in the non-TF group (*P* < 0.0001), similar to the difference seen in the full SVCD cohort. Similarly, median WAZ at discharge was significantly lower in the TF group [−1.7, (95% CI: −0.25, 0.4) vs −0.8 (95% CI: −1.7, −0.1), *P* = 0.02]. There was no difference in the number of interstage hospitalizations or in the timing of subsequent surgical palliations between groups (Table 3). In both the full SVCD cohort and the Norwood subgroup, the TF patients had a longer LOS compared to the non-TF group at the second surgical palliation (median 7 (IQR 5-18) vs 5 (IQR 4-6) days, *P* < 0.0001), but not the third.

4 | DISCUSSION

To our knowledge, this is the first study to assess the association of TF with long-term growth in patients with CHD. Overall, we found that children with SVCD have longitudinal growth that falls in the low-normal range compared to normal peers. With regard to the groups, we found that patients with SVCD who require TF after their initial surgical palliation have consistently lower WAZ and BMIZ compared to non-TF patients until at least 7 years of age. Despite this difference in growth parameters, the growth in the TF patients on average was in the low-normal range.

Multiple factors, including surgical complexity and complications, increased caloric demands, neurodevelopmental disability, and abnormal energy expenditure may influence early growth in this vulnerable population.[4,7,15,16] Prior studies have identified

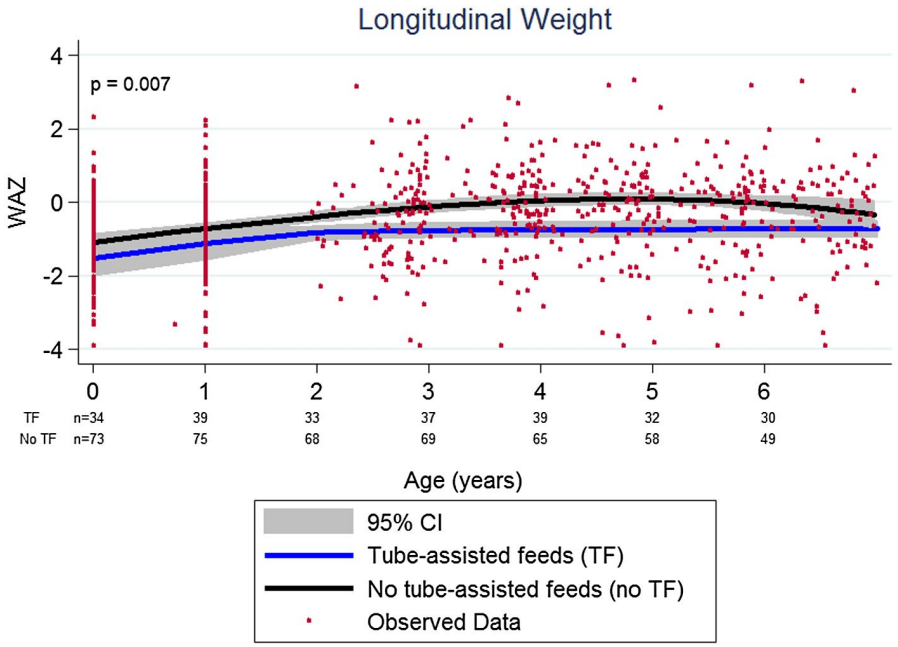

FIGURE 1 Differences in weight z-scores by tube-assisted feeding status. Legend: fractional polynomial regression of WAZ over time, adjusted for age. Time point 0 indicates maximal WAZ at age 6-12 months. Time point 1 reflects maximal WAZ at age 12-24 months

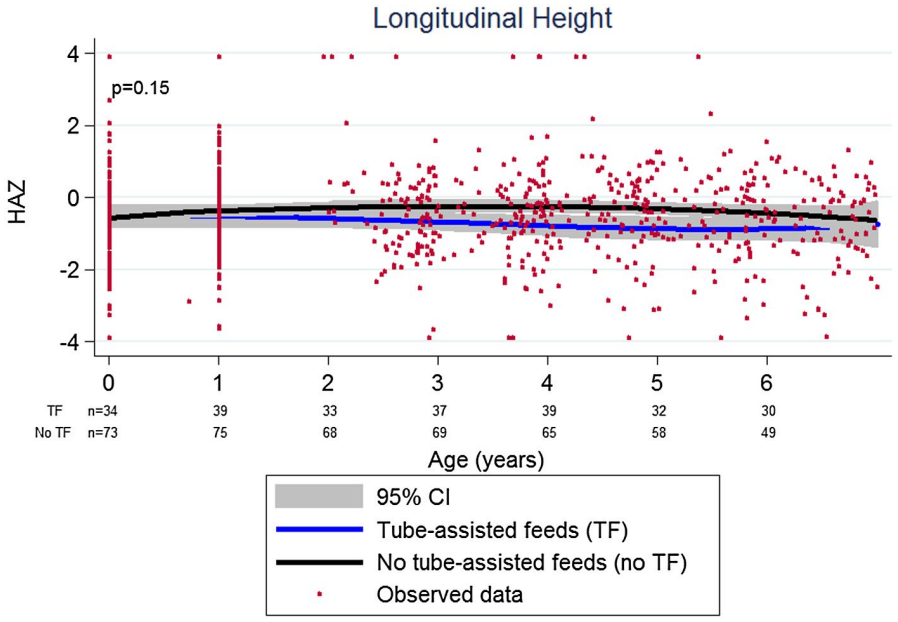

FIGURE 2 Differences in height z-scores by tube-assisted feeding status. Legend: fractional polynomial regression of HAZ over time, adjusted for age. Time point 0 indicates maximal HAZ at age 6-12 months. Time point 1 reflects maximal HAZ at age 12-24 months

hemodynamic factors, such as ventricular dysfunction and increased arterial saturation, which correlate with poor growth in the early postoperative period.[2,3] In our study, patients in both groups had comparable degrees of ventricular dysfunction and AVVR. The TF group had significantly more postoperative complications in the total cohort, with a trend toward more complications in the TF group among Norwood patients. It is possible that these complications contributed to the greater LOS in the TF group. Despite the longer LOS in the TF group, patients requiring TF had significantly lower WAZ at the time of hospital discharge, which persisted over time. Thus, the trajectory of growth in the TF group may be related to illness severity at the time of discharge rather than be related to the TF itself. In theory, TF guarantees caloric intake in this population and these patients are monitored frequently for growth. It might, therefore, be expected that the TF group would have had better longitudinal growth than their counterparts who are fed exclusively by mouth.

Previous studies have shown that SVCD patients requiring TF have diminished short-term growth. The Pediatric Heart Network Infant Single Ventricle Trial demonstrated a marked decrease in WAZ between hospital discharge and a 2-week follow-up visit in a majority of patients.[10] This decline was less severe in patients receiving feeds entirely by mouth. One can surmise that this may be related to underlying illness in those who require TF at discharge from the hospital. Similarly, a retrospective single-center study demonstrated lower WAZ at hospital discharge in SVCD patients who received

TF.[9] WAZ in TF patients remained lower than the non-TF patients at the time of the second surgical palliation despite the prescription of higher calorie feeds in this group. Lower WAZ at the time of superior cavopulmonary anastomosis was also associated with longer surgical LOS.[9]

In our study, the TF and non-TF groups had similar median attained WAZ or HAZ between ages 6 and 24 months, suggesting that the TF group had catch-up growth after the superior cavopulmonary anastomosis operation (second surgical palliation). Our findings are consistent with reports of catch-up growth during this time period.[4,10,15] The reason for the convergence of the growth curves at this age is unclear but may be related to the volume-unloading nature of the second surgical palliation, decreasing metabolic demand and the relative stability of this circulation. Moreover, it is common that TF has ended by the time of superior cavopulmonary anastomosis; in our study, 58% of patients were no longer on TF at the time of their second surgical palliation. The impact of TF may therefore be greatest during the vulnerable interstage period.

After the age of 24 months, the TF group had lower WAZ compared to those fed by mouth, with WAZ more than half a standard deviation lower than the non-TF group over time. This finding was independent of the Norwood procedure and independent of the number of postoperative complications after the initial surgical palliation. Given that the TF and non-TF groups had similar timing of their later stages of surgical palliation, it is unlikely that growth differences were primarily driven by hemodynamic factors that could have affected the timing of later stages of surgery.

This hypothesis is also supported by the results of the Norwood subgroup analysis, which demonstrated significantly longer LOS in TF patients than non-TF patients. The TF patients were ultimately discharged with lower WAZ than the non-TF patients, despite their longer hospitalizations. The consistency of this finding in the more homogeneous Norwood group suggests that surgical complexity is not the sole driver of the lower WAZ in these patients over time. It may be that children who required TF early in life continue to have poor oral intake later in childhood that may be quite subtle. The endocrine effects of TF remain unknown, but such issues as natural satiety and hunger are likely affected by TF; this issue requires more exploration.

Recent studies have demonstrated decreased height, abnormal bone mineralization, deficient skeletal muscle mass, and delayed puberty in SVCD patients in late childhood and adolescence that have undergone the Fontan operation.[17,18] In a large cross-sectional study of Fontan patients, there was a 23% prevalence of short stature, which was associated with worse functional outcomes as measured by the Child Health Questionnaire.[19] These problems are likely related to the physiology of the Fontan circulation, but have also been correlated with deficiencies in vitamin D and insulin-like growth factor-1.[17] Our data are consistent with these findings; we demonstrated that HAZ for both groups was below zero throughout the time of analysis. While the individual time points were within two standard deviations of normal, this finding suggests that the SVCD population is at risk for overall lower height as compared to healthy patients.

It is difficult to compare the SVCD population to other groups, as limited longitudinal growth data are available in noncardiac patients or patients with biventricular circulations using TF. In children with cerebral palsy and oromotor dysfunction, TF has been shown to increase short-term growth, but is associated with higher fat mass than patients fed by mouth.[20,21] One prospective study showed rapid weight gain after 12 months of GT feeds, but there were no long-term data to determine if the trend led to obesity.[22] In a study of children with chronic kidney disease, TF was associated with significantly increased weight and BMI for age, but there was no significant change in these parameters 5 years after GT removal.[23] We certainly did not find any significant obesity in this cohort of patients receiving TF, which is likely related to the underlying physiology of their CHD.

5 | LIMITATIONS

This study was performed at a single center; thus, these data may not be generalizable, as the indication for TF was not known and the use of TF at may reflect an institutional practice. Further, this study assessed growth in a relatively heterogeneous SVCD patient population, but it was our purpose to assess all-comers. Notably, however, the findings of the Norwood group subanalysis were consistent with that seen in the overall SVCD cohort, suggesting that different initial surgical strategy did not impact the findings.

Because of the retrospective nature of this study, it is possible that the prevalence of feeding disorders was underreported, as we relied on the problem list in the electronic medical record to identify these diagnoses. We also were unable to accurately capture a diagnosis of necrotizing enterocolitis (NEC) in this study because of the subjective nature of the diagnosis (no patient had abdominal surgery for NEC).

Importantly, we were unable to assess the duration that patients in the exposure group received TF, which may have affected long-term growth. We do know that the majority of children receiving TF were on full oral feeds by the time of superior cavopulmonary anastomosis surgery, which does not explain their lower WAZ over time.

6 | CONCLUSIONS

In children with SVCD, the need for TF at hospital discharge appears to be a marker for lower longitudinal weight in childhood when compared to non-TF peers up to the age of 7 years. Despite this lower weight, these patients on average maintain a WAZ in the low-normal range. There are no obvious perioperative risk factors for this difference between the groups, suggesting that TF may be a surrogate for patient fragility or illness severity. Further study of the growth trajectory of these patients will be important, as their growth patterns may remain abnormal throughout childhood and adolescence.[24-26] These findings warrant elucidation of potential physiologic perturbations as a result of TF, particularly its effect on satiety and hunger.

CONFLICT OF INTEREST

Dr. Ravishankar has served as a consultant for Nutricia. The other authors have indicated they have no potential conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conceptualized and designed the study: Butto, Mercer-Rosa, Cohen, and Ravishankar

Designed the data collection instruments: Butto and Mercer-Rosa

Drafted the initial manuscript: Butto and Mercer-Rosa

Reviewed and revised the manuscript: Butto, Mercer-Rosa, Teng, Edelson, Daymont, Faerber, and Mejia

Collected, and aided with the initial analyses: Teng, Edelson, Daymont, and Mejia

Aided with the initial analyses: Daymont and Faerber

Supervised data collection: Cohen and Ravishankar

Critically reviewed the manuscript for important intellectual content: Cohen and Ravishankar

ORCID

Arene Butto https://orcid.org/0000-0002-8633-5420

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