The Association among Feeding Mode, Growth, and Developmental Outcomes in Infants with Complex Congenital Heart Disease at 6 and 12 Months of Age

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Objective To assess the association between early anthropometric measurements, device-assisted feeding, and early neurodevelopment in infants with complex congenital heart diseases (CHDs).

Study design Bayley Scales of Infant Development II were used to assess cognitive and motor skills in 72 infants with CHD at 6 and 12 months of age. Linear regression models were used to assess the association between mode of feeding and anthropometric measurements with neurodevelopment at 6 and 12 months of age.

Results Of the 72 infants enrolled in the study, 34 (47%) had single-ventricle physiology. The mean Mental Developmental Index (MDI) and Psychomotor Developmental Index (PDI) scores at 6 months of age were 92 ± 10 and 81 ± 14, respectively. At 12 months of age, the mean MDI and PDI scores were 94 ± 12 and 80 ± 16, respectively. Lower length-for-age z score ($P < .01$) and head circumference-for-age z score ($P < .05$) were independently associated with lower MDI at 6 months, and both increased hospital length of stay ($P < .01$) and lower length-for-age z score ($P = .04$) were associated independently with lower MDI at 12 months. Device-assisted feeding at 3 months ($P = .04$) and lower length-for-age z score ($P < .05$) were independently associated with lower PDI at 6 months. Both lower weight-for-age z score ($P = .04$) and lower length-for-age z score ($P = .04$) were associated independently with PDI at 12 months.

Conclusion Neonates with complex CHD who required device-assisted feeding and those with lower weight and length and head circumference z scores at 3 months were at risk for neurodevelopmental delay at 6 and 12 months of age. *(J Pediatr 2016;169:154-9).*

Congenital heart disease (CHD) is the most common congenital defect in neonates,[1] affecting some 40 000 births each year. Advances in surgical, medical, and nursing care for infants with complex CHD have resulted in an increase in survival and a growing population of infants with morbidities related to their underlying defect, surgical intervention, and/or residual anatomic or hemodynamic abnormalities. Current literature suggests infants with complex CHD are at increased risk for worse neurodevelopmental outcomes in both cognitive and motor domains in late infancy and early childhood.[2,3] Various factors that influence neurodevelopmental outcomes in infants with complex CHD have been identified; these include genetic abnormalities and syndromes, prematurity, postsurgical physiology, length of stay (LOS), history of cardiac arrest, use of extracorporeal membrane oxygenation or ventricular assist device, postoperative stroke, seizures, or abnormalities on neuroimaging.[4-6] The etiology of abnormal cognitive and motor neurodevelopment in these infants appears to be multifactorial and is not well understood.[7] Most recently, there is new interest in nutritional factors such as feeding mode or growth status as predictors of neurodevelopmental outcomes.[4,8]

There are several reports of growth failure and feeding dysfunction in children with complex CHD.[9-11] Early sucking and swallowing difficulties have been shown to be a significant predictor of worse neurodevelopmental outcomes in premature infants[12] and in children with brain injury.[13] Although many infants with CHD are born full term, evidence suggests they may be neurologically immature and suffer neurologic insult early in life.[14] We reported previously an association between poor oral feeding skills and growth failure at hospital discharge[15] in children with CHD. Despite a history of early growth faltering, most infants with complex CHD demonstrate adequate catch-up growth during the first

2V	2 Ventricles
CHD	Congenital heart disease
LOS	Length of stay
MDI	Mental Developmental Index
PDI	Psychomotor Developmental Index
SV	Single-ventricle

year of life, and few require supplemental tube feedings after 3 months of age.[16] Given the importance of nutrition in assuring optimal brain growth during the first months of life, we hypothesized that poor early growth and device assisted feeding will be associated with worse neurodevelopmental outcomes at 6 and 12 months of age.

Methods

This study was a prospective cohort study of growth and development in the first year of life in infants who had undergone neonatal cardiac surgery during the first month of life. The Institutional Review Board at the Children's Hospital of Philadelphia approved the project. Informed consent was obtained from a parent or legal guardian before the enrollment of each infant.

Neonates with CHD who underwent cardiac surgical intervention within 30 days of birth were screened for enrollment. Neonates were eligible if they had a postmenstrual age ≥36 weeks at birth and were discharged to home after surgical intervention. Neonates with multiple congenital, facial, and/or complex gastrointestinal anomalies; chromosomal abnormalities; and/or congenital or acquired neurologic insult were excluded because these factors are known to be associated with poor growth.

Data collection was performed prospectively throughout the hospitalization, and included intraoperative support times, total hours of ventilation, history of infections, LOS, and mode of feeding at discharge. Research procedures included anthropometric measurements at 3, 6, 9, and 12 months completed by research staff in the Growth and Nutrition Laboratory of the Clinical Translational Research Center at Children's Hospital of Philadelphia. Feeding mode (bottle or breast only, bottle or breast combined with tube-assisted feeding with nasogastric tube or gastrostomy tube, and nasogastric tube or gastrostomy tube only) was recorded at discharge and at 3 months of age. Neurodevelopment was assessed at 6 and 12 months with the Bayley Scales of Infant Development II in the Behavioral Neuroscience Core of the Clinical Translational Research Center by

research psychometricians under the supervision of a licensed psychologist. The Bayley Scales of Infant Development II yield 2 scores: the Psychomotor Developmental Index (PDI), which is used to assess gross motor and fine motor skills; and the Mental Developmental Index (MDI), which is used to evaluate cognitive, memory, problem-solving, generalization, vocalizations, and social skills. The mean MDI and PDI score for the normal population is 100, with a SD of 15.[17]

Statistical Analyses

Measures of central tendency and variation (means and SDs, medians, and ranges) for continuous variables, as well as frequencies and percentages for categorical variables, were used to describe the study sample. Bivariate general linear regression models were created to assess the association between predictors (feeding mode at discharge and 3 months of age; 3-month anthropometric measurements [weight, length, head circumference]) and developmental outcomes (MDI and PDI at 6 and 12 months of age, separately). Multivariable models were generated for each outcome, separately, and included variables significant at the .05 level in bivariate models, along with postoperative physiology classified as single-ventricle (SV) or 2 ventricles (2V) and LOS. To avoid multicollinearity between feeding mode at discharge and 3 months, as well as among the 3 growth measures observed at 3 months, individual models were generated for the different combinations of these predictors. Finally, neurodevelopmental outcomes were described and compared by physiology group (SV vs 2V) and feeding mode (oral vs device assisted) by the use of 2-sample *t* tests. Significance was set at .05 for all analyses. A post hoc analysis based upon our group of 72 participants achieves 80% power to detect an R^2 increase of 7% attributed to a single predictor of interest with a 0.05 level of significance, adjusting for 3 additional covariates that demonstrate a total R^2 of 0.30. The statistical analysis section was revised. All analyses were performed by the STATA software package, V.11.0 (Stata-Corp, College Station, Texas).

Table II. Descriptive statistics and comparisons for neurodevelopment by physiology and feeding mode at DC and 3 mo

	MDI at 6 mo, mean (SD)	MDI at 12 mo, mean (SD)	PDI at 6 mo, mean (SD)	PDI at 12 mo, mean (SD)
Physiology				
SV	90.53 (8.78)	91.18 (10.33)	76.58 (14.77)	73.94 (15.78)
2V	92.81 (10.56)	97.05 (12.60)	83.97 (13.47)	84.58 (15.33)
Subsample *P* value	.435	.035	.074	.005
Feeding mode at DC				
Orally fed	94.62 (10.25)	96.16 (12.68)	85.70 (11.58)	80.47 (15.36)
Tube-assisted	89.04 (8.79)	92.18 (10.70)	76.17 (15.54)	78.53 (17.54)
Subsample *P* value	.045	.157	.016	.618
Feeding mode at 3 mo				
Orally fed	93.18 (9.14)	94.98 (12.15)	83.43 (12.85)	81.84 (15.36)
Tube-assisted	80.8 (10.33)	89.9 (9.35)	60.8 (10.71)	65.4 (15.75)
Subsample *P* value	.007	.211	<.001	.003

DC, discharge.
P values from 2-samples *t* test.