Predictors of Poor Weight Gain in Infants with a Single Ventricle

Jeffrey B. Anderson, MD, MPH, Robert H. Beekman, III, MD, Pirooz Eghtesady, MD, PhD, Heidi J. Kalkwarf, PhD, Karen Uzark, PhD, Jack E. Kehl, BS, and Bradley S. Marino, MD, MPP, MSCE

Objective To assess growth from the time of neonatal discharge to the time of performance of the bidirectional Glenn (BDG) procedure in infants with a single ventricle and determine predictors of poor growth.

Study design We performed a retrospective case series of infants who underwent the BDG procedure at our institution between January 2001 and December 2007 (n = 102). Anthropometric and clinical data were recorded during neonatal hospitalization and before BDG. Outcome variables included weight-for-age *z*-score (WAZ) at the time of BDG and average daily weight gain between neonatal discharge and BDG.

Results Median age at the time of BDG was 5.1 months (range, 2.4-10 months), and median WAZ was -0.4 (range, -2.6 to 3.2) at neonatal admission and -1.3 (range, -3.9 to 0.6) at the time of BDG. Non-Caucasian infants ($P = .03$) and those with lower WAZ at neonatal discharge ($P < .0001$) had a lower WAZ at BDG. Being formula-fed at neonatal discharge ($P = .04$), and having higher mean pulmonary arterial pressure ($P = .04$) and systemic oxygen saturation ($P = .006$) were associated with lower average daily weight gain between neonatal discharge and BDG.

Conclusions Infants with a single ventricle have poor weight gain between neonatal discharge and BDG. Non-Caucasian infants and those with evidence of increased pulmonary blood flow are at particular risk for growth failure. *(J Pediatr 2010;157:407-13)*.

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Failure to thrive (FTT) occurs when rate of growth is below expectations based on age- and sex-specific growth charts.[1] Specifically, FTT is diagnosed when growth is below the 5th percentile, the growth-for-age *z*-score is <-2.0, or when growth has crossed 2 major age-indexed percentiles or *z*-scores.[2,3] Most children who have FTT as infants experience adequate catch-up growth by the time they reach school age;[4] however, several studies have reported long-term growth and cognitive deficiencies in children with FTT early in life, including increased vulnerability to short stature and poor arithmetic performance,[5] increased incidence of attention problems and aggressive behavior,[6] and increased risk of poor overall emotional, social, and cognitive development.[1]

FTT is common in infants with congenital heart disease (CHD)[7-9] and is especially prevalent in those with a single ventricle.[10-13] These patients, who typically undergo a series of palliative surgical procedures[14-16] have difficulty achieving adequate weight gain goals between surgical stages.[11] The etiology of growth failure is poorly understood; it is known that infants with a single ventricle have a lower-than-desired total caloric intake, and that their growth improves with the introduction of high-caloric enteral feedings.[11] Pulmonary hypertension has been associated with poor growth in infants with cyanotic CHD, but not specifically in infants with a single ventricle.[17] Compared with infants with other types of CHD, those with a single ventricle also demonstrate more oral-motor feeding difficulties, have a higher incidence of gastroesophageal reflux, and are slower to reach goal feedings after surgery infants.[10]

Although the long-term effects of FTT in infants with a single ventricle have not been studied, we recently reported an association between lower weight-for-age *z*-score (WAZ) and increased length of hospital stay in infants with a single ventricle who underwent the bidirectional Glenn (BDG) procedure.[18] FTT and its effects on development and cognitive function might be even more deleterious in this high-risk population of infants with CHD than in the general pediatric population.

Identifying predictors of poor growth in this high-risk population will help us better understand their growth failure and inform efforts to design strategies that might improve their nutrition and growth. The present study was designed to identify specific nutritional and physiological risk factors that predict poor weight gain before the BDG procedure in infants with a single ventricle.

BDG	Bidirectional Glenn	FTT	Failure to thrive
BTS	Blalock-Taussig shunt	HLHS	Hypoplastic left heart syndrome
CCHMC	Cincinnati Children's Hospital Medical Center	NEC	Necrotizing enterocolitis
		NG	Nasogastric
CDC	Centers for Disease Control and Prevention	PVR	Pulmonary vascular resistance
		SGA	Small for gestational age
CHD	Congenital heart disease	WAZ	Weight-for-age *z*-score

From the Division of Cardiology (J.A., R.B., K.U., J.K., B.M), Division of Cardiothoracic Surgery (P.E.), Division of Critical Care Medicine (B.M.), and Division of General and Community Pediatrics (H.K.), Cincinnati Children's Hospital Medical Center, Cincinnati, OH

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Methods

This study was a retrospective case series including all patients who underwent BDG at Cincinnati Children's Hospital Medical Center (CCHMC) between July 2001 and December 2007. This study was approved by CCHMC's Institutional Review Board (06-10-30). Study data were collected from hospital medical records, Heart Institute outpatient records, and cardiac catheterization, echocardiography, and cardiac surgical databases. Exclusion criteria included preterm birth (defined as <35 weeks gestational age); chromosomal abnormalities; congenital anomalies of the central nervous, gastrointestinal and/or pulmonary systems; and age >12 months at the time of the BDG procedure.

Demographic data collected included sex, gestational age, race, and cardiac diagnoses. For analysis, cardiac diagnoses were separated into those with dominant right and left ventricles and further subgrouped into those with hypoplastic left heart syndrome (HLHS), hypoplastic left heart syndrome variant (HLHS, double-outlet right ventricle with mitral atresia, and right dominant atrioventricular canal defect), double-inlet left ventricle, tricuspid atresia, and pulmonary atresia with intact ventricular septum.

Information regarding medical and surgical management before the BDG procedure was recorded, including previous surgeries and hospital courses, history of necrotizing enterocolitis (NEC) or documented vocal cord paralysis, home medications used, and the use of supplemental oxygen before the BDG procedure. Feeding route, type of nutritional support, and the caloric density of formula or human milk were noted at the time of neonatal discharge and at the time of presentation for BDG.

Findings from the most recent echocardiogram performed before the BDG procedure were reviewed. Atrioventricular valve regurgitation and aortic or neo-aortic regurgitation were considered significant if graded as moderate or greater. Residual defects, including restrictive atrial septal defect (>2 mm Hg gradient) and aortic arch obstruction (>20 mm Hg peak corrected gradient), were noted. Depressed systolic ventricular function was defined as moderate or greater systolic dysfunction in either a right or left single ventricle or a shortening fraction <28% in a left ventricle. Data from the most recent cardiac catheterization performed before the BDG procedure were reviewed; measurements recorded included mean pulmonary artery pressure (PAP), transpulmonary gradient, pulmonary vascular resistance (PVR), ventricular end-diastolic pressure, aortic arch systolic pressure gradient, systemic arterial and mixed venous oxygen saturation (SaO_2 and SvO_2), and hemoglobin level.

Anthropometric measures included absolute weight and WAZ at initial neonatal hospital admission and discharge and at the time of presentation for the BDG procedure. Average daily weight gain during neonatal hospitalization and between neonatal discharge and the BDG procedure was calculated as well. WAZ values were determined using the Centers for Disease Control and Prevention's (CDC) Epi-Info program.

Statistical Analyses

The primary outcome variables were WAZ at the time of BDG and average daily weight gain between neonatal discharge and presentation for BDG. All statistical analyses were performed using Stata version 10.0 (StataCorp, College Station, Texas). All continuous variables were described, and the data distribution was tested for normality. Normally distributed continuous variables are expressed as mean ± standard deviation, and non-normally distributed data are expressed as median and range. Bivariate analyses of potential risk factors for adverse outcome were performed using parametric tests for normally distributed data and nonparametric tests for non-normally distributed data. Candidate predictor variables for multivariate modeling had a P value <.10 on bivariate analysis. Multivariate analyses were performed using linear regression and stepwise forward selection. Correlation coefficients were calculated to assess for colinearity among variables.

Results

During the study period, 120 patients underwent the BDG procedure at our institution. A total of 18 patients were excluded (4 due to preterm birth; 7 due to chromosomal anomalies; 3 due to other major central nervous system, gastrointestinal, or pulmonary anomalies; and 4 due to being over 12 months old at the time of BDG), leaving 102 patients for the analysis (Table I). All patients undergoing superior cavopulmonary anastomosis had a BDG; no hemi-Fontan procedures were performed. Eight patients with bilateral

Table I. Patient characteristics

Sex	Male	56%
	Female	44%
Median gestational age	40 weeks (35-40 weeks)	
Median birth weight	3.1 kg (2.2-4.4 kg)	
Race	Caucasian	82%
	African American	15%
	Other	3%
Neonatal surgery	No neonatal surgery	11%
	BTS alone	22%
	PA band alone	7%
	Arch reconstruction	60%
	With BTS	51%
	With Sano shunt	9%
Median age a neonatal discharge	23 days (3-100 days)	
Median age at BDG surgery	5.1 months (2.4-10 months)	
Cardiac diagnoses		
Dominant right ventricle	n = 56	
Hypoplastic left heart syndrome	n = 38	
Right dominant AV canal	n = 8	
Double-outlet RV/mitral atresia	n = 6	
RV to Ao/pulmonary atresia	n = 4	
Dominant left ventricle	n = 45	
Double-inlet left ventricle	n = 22	
Tricuspid atresia	n = 11	
Pulmonary atresia/IVS	n = 10	
Left dominant AV canal	n = 2	
Unknown ventricular morphology	n = 1	

PA, pulmonary artery; AV, atrioventricular; IVS. interventricular septum; RV, right ventricle.