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Postnatal Weight Gain in Preterm Infants with Severe Bronchopulmonary Dysplasia

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Abstract

Objectives—To characterize postnatal growth failure (PGF), defined as weight < 10th percentile for postmenstrual age (PMA) in preterm (< 27 weeks' gestation) infants with severe

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Disclosures

Jeanette Asselin and Isabella Zaniletti are employees of the Children's Hospital Association. The Children's Hospital Association had no role in the study design, data interpretation, drafting the manuscript, or the decision to submit the manuscript. The data analysis was performed by Dr Zaniletti, a statistician employed by the Children's Hospital Association.

bronchopulmonary dysplasia (sBPD) at specified time points during hospitalization, and to compare these in subgroups of infants who died/underwent tracheostomy and others.

Study Design—Retrospective review of data from the multicenter Children’s Hospital Neonatal Database (CHND).

Results—Our cohort ($n = 375$) had a mean $\pm$ standard deviation gestation of 25 ± 1.2 weeks and birth weight of 744 ± 196 g. At birth, 20% of infants were small for gestational age (SGA); age at referral to the CHND neonatal intensive care unit (NICU) was 46 ± 50 days. PGF rates at admission and at 36, 40, 44, and 48 weeks’ PMA were 33, 53, 67, 66, and 79% of infants, respectively. Tube feedings were administered to $> 70\%$ and parenteral nutrition to a third of infants between 36 and 44 weeks’ PMA. At discharge, 34% of infants required tube feedings and 50% had PGF. A significantly greater (38 versus 17%) proportion of infants who died/underwent tracheostomy ($n = 69$) were SGA, compared with those who did not ($n = 306$; $p < 0.01$).

Conclusions—Infants with sBPD commonly had progressive PGF during their NICU hospitalization. Fetal growth restriction may be a marker of adverse outcomes in this population.

Keywords

nutrition; tracheostomy; growth; bronchopulmonary dysplasia

Sustaining optimal postnatal growth remains an important component of management of preterm infants. Prior studies have demonstrated the inherent challenges in maintaining growth velocities approximate to intrauterine growth rates in preterm infants.^{1,2} In a large multicenter cohort of very low-birth-weight infants born between 24 and 29 weeks’ gestation, most had not achieved the median birth weight of the reference fetus at the same postmenstrual age (PMA).³ This was despite a postnatal weight gain approximating intrauterine rates of between 14 and 16 g/kg/d, once birth weight was regained.³ Infants who survived to hospital discharge without morbidities gained weight faster than those with major morbidities, defined as chronic lung disease, severe intraventricular hemorrhage (IVH), necrotizing enterocolitis (NEC), or late-onset sepsis.³ In another recent multicenter study involving 1,187 extremely low-birth-weight infants born between 23 and 27 weeks’ gestation, median growth velocity exceeded the current guideline of 15 g/kg/d, with the highest growth velocities in the most immature infants who had birth weights > 1 standard deviation (SD) below the expected median.² Despite having average or higher growth velocities, growth restriction (< 10 th percentile of weight for gestation) at 28 days was noted in 75% of infants.² The authors had speculated that current recommendations to approximate intrauterine growth rates may be too low to achieve sustained postnatal weight gain for most extremely low-gestational-age neonates. Many factors influence postnatal growth velocity including the provision of nutritional support, adjunctive treatments, as well as the presence and severity of comorbidities such as NEC and bronchopulmonary dysplasia (BPD).

BPD remains a major morbidity among extremely preterm infants, with a reported incidence of 42% in those born at 22 to 28 weeks’ gestational age.⁴ The National Institutes of Health (NIH) consensus definition of BPD includes a severity-based classification based on duration and extent of supplemental oxygen and positive pressure ventilation need.⁵ Optimal growth may be particularly problematic in infants with severe BPD (sBPD), who have

increased work of breathing and chronic lung injury. Our goal was to assess growth trajectories and rates of postnatal growth failure (PGF) at specified PMAs in a multicenter cohort of extremely preterm infants with sBPD. The specific aims of the current study were to describe the in-hospital weights at specified time points in a multicenter cohort of extremely preterm (< 27 weeks' gestation) infants with sBPD, by a modified NIH definition, referred to any of the Children's Hospitals Neonatal Consortium neonatal intensive care units (NICUs). We further sought to compare the rates of PGF, defined as weight < 10th gender-specific percentile for PMA at specified times in groups of infants with sBPD who died or underwent tracheostomy and those who did not.

Materials and Methods

This was an analysis of data from the Children's Hospital Neonatal Database (CHND), a database of all admissions to 24 participating tertiary- and quaternary-level NICUs in the United States. The CHND was accessed to identify all extremely preterm (born < 27 weeks' gestational age) infants with sBPD who were cared for at any of the participating NICUs over a 16-month period in 2010 to 2011. sBPD was defined by a modified NICHD definition as any positive pressure ventilation (including nasal intermittent mandatory ventilation or nasal continuous positive airway pressure) or nasal cannula > 2 L per minute or supplemental effective fraction of inspired oxygen ≥ 0.3 at 36 weeks' PMA. Infants were excluded if their gestational age at birth or respiratory status at 36 weeks' PMA was not known.

The CHND was designed to capture the care and outcomes of infants referred to the participating NICUs. All participating sites obtained Institutional Review Board approval for participation in the database and for waiver of parental consent. The Children's Memorial Research Center Institutional Review Board exempted this analysis from review. Nearly all patients cared for in the CHND NICUs were born outside the CHND sites, and the timing and reasons for referral to the participating CHND NICUs varied. When their illnesses or management allowed, infants may have been transported back to their referring NICU/institution. The final status (death or discharge) and date of discharge were ascertained in all cases for the database. Data for each participating infant were obtained by data abstractors, based on a manual of operations with precise data point definitions. Quality control was ensured by monthly data abstractor conference calls and an interrater agreement of > 90% (scored by the central data center) between the physician sponsor and data abstractor at each site on two cases before the start of data collection and biannually thereafter.⁶

The composite primary outcome measure for our cohort of infants with sBPD was chosen as death or tracheostomy prior to discharge. This measure was selected because tracheostomy insertion was thought to potentially compete with death and be a surrogate of severity of BPD. Gestational age was based on a hierarchy of best obstetric estimate (last menstrual period, obstetric parameters, or prenatal ultrasound) or neonatologist estimate (physical, neurologic examinations, or a combination using Ballard or Dubowitz scoring). Small for gestational age (SGA) was defined as birth weight less < 10th percentile based on gender and gestational age-specific Olsen growth curves.⁶ Birth weight was recorded as the weight in the obstetric record if available and judged to be accurate. If unavailable or judged to be

inaccurate, the weight on admission to the neonatal unit or last, the weight obtained on autopsy (if the infant expired within 24 hours of birth) were used. Similarly, admission weights (in grams) were taken as the first weights within 72 hours of admission to the NICU or the weight obtained on autopsy (if the infant expired within 24 hours). To assess growth over time during the hospitalization, weights were recorded at 36, 40, 44, and 48 weeks' PMA and at discharge home for infants still in the participating CHND NICUs. Weights were taken from the weight measured on the specific date or the closest weight within a 5-day period from the desired specific date. PGF was defined as < 10th centile for the PMA using published standards.^{7,8} Nutritional support data were collected at the same specified key dates. The type of nutrition received during the majority of the specific day, for each time point, was abstracted. Similarly, the mode of enteral nutrition was recorded as oral, gastric, or transpyloric, based on mode of feeding for the majority of the feedings on the specific day. Parenteral nutrition was defined as any intravenous fluid that contains two or more of protein, lipid, or dextrose components. Inhospital weight gain was calculated as the difference in weights between discharge home/death and birth (total in-hospital weight gain), death/discharge/transfer from the CHND NICU and CHND admission weight (CHND weight gain) and the difference between CHND admission weight and birth weight (prereferral weight gain). These differences were then indexed to initial weight and divided by the duration between the two time points, in days.

Maternal characteristics collected included race/ethnicity, chorioamnionitis, diabetes, pregnancy-induced hypertension, and mode of delivery. Infant characteristics included interventions prior to admission such as surfactant therapy, comorbidities such as patent ductus arteriosus (PDA), IVH, NEC, and central line-associated bloodstream infection (CLABSI). PDA was defined as echocardiographic evidence of left-to-right or bidirectional shunt or clinical evidence of left-to-right PDA shunt as documented by a murmur with hyperdynamic precordium, bounding pulses, wide pulse pressure, or congestive heart failure, as evidence by increased pulmonary vascular markings or cardiomegaly by chest radiograph, and/or increased oxygen requirements. NEC was defined as NEC diagnosed at surgery or at postmortem examination or diagnosed clinically and radiographically with one or more clinical signs (bilious gastric aspirate or emesis, abdominal distention, occult or gross blood in stool with no apparent rectal fissure) and one or more radiographic findings (pneumatosis intestinalis, hepatobiliary gas, or pneumoperitoneum). IVH grading was based on standard definitions.^{9,10} CLABSI was defined by standard National Healthcare Safety Network definitions. Other measures such as length of stay and selected surgical interventions such as gastrostomy tube insertion were also described.

Statistical Analysis

Descriptive statistics included mean (SD) or median (range) as appropriate. Comparisons between groups of infants who died or underwent tracheostomy during initial hospitalization and those who did not were performed using Fisher exact test for proportions for categorical variables and non-parametric Wilcoxon rank sum test for continuous variables. The interaction between PGF, defined as weight < 10th gender-specific percentile for specified key dates and the dichotomous primary outcome (death/tracheostomy) was examined and a *p* value < 0.01 for the test of heterogeneity was considered a significant subgroup effect. All

statistical tests were two-tailed and, due to the multiple comparisons, $p < 0.01$ was used to define statistical significance. Analyses were performed with SAS software 9.3 (SAS Institute Inc., Cary, North Carolina, United States).

Results

A total of 375 infants born at 27 weeks' gestation were eligible for the analysis. A flowchart of the study cohort ($n = 375$) is shown in Fig. 1. The mean $\pm$ SD gestational age was 25 ± 1.2 weeks and birth weight was 744 ± 196 g. Non-Hispanic whites comprised 43.5%, females 37.1%, and multiples 22.4% of the cohort. SGA status at birth was noted in 20.5% of the cohort. Of the cohort, 96% were born outside the CHND hospital, and the postnatal time and PMA at the time of referral to the CHND NICU were 46 ± 50 days and 31.6 ± 7.3 weeks, respectively. The most common primary reasons for referral to a CHND NICU were for respiratory and surgical evaluations (26% each). Mechanical ventilation was required at the time of referral in 73% and at some time during CHND hospitalization in 91.5% of cases. Surgical NEC was diagnosed in 1.4% of the cohort.

Nutritional Support and In-Hospital Weight Gain

Table 1 describes the weights, rates of PGF, and nutritional support at 36, 40, 44, and 48 weeks' PMA and at discharge to home or foster care. On admission to the CHND site at a mean $\pm$ SD PMA of 32 ± 7 weeks, 33% had PGF. Parenteral nutrition was administered to the majority (72%) of infants, and gastric (24.6%) or transpyloric (5.2%) tube feedings were quite frequent. Only 5.6% infants were on oral feeds. A surgical feeding tube was in place in 4 (1.1%) infants at the time of admission and 88 (23.5%) infants underwent gastrostomy tube insertion after referral. At the time of discharge home or foster care ($n = 242$), only 1 (0.4%) infant received parenteral nutrition, 82 (33.9%) received either transpyloric or gastric gavage feedings, and 159 (65.7%) were entirely on oral feeds. Only 2.4% of infants were exclusively on breast milk and 18.1% of infants received both breast milk and formula. At discharge, the mean $\pm$ SD postnatal age was 146 ± 51 days and PMA was 45.9 ± 7.1 weeks. The head circumference at discharge was 35.5 ± 5.4 cm. Total in-hospital weight gain indexed to birth weight was 30 ± 10 g/kg/d; prereferral weight gain (50 SD; 25 g/kg/d) and CHND weight gain (20 SD; 10 g/kg/d) were not significantly different.

Comparison of PGF between Groups of Infants Who Died or Underwent Tracheostomy and Others

A total of 46 (12.3%) infants required tracheostomy; 27 (7.2%) infants died and 69 (18.4%) infants died or underwent tracheostomy. Table 2 shows the comparison of clinical characteristics of infants who died or needed tracheostomy and those who did not. A significantly greater proportion of those who died or underwent tracheostomy were SGA at birth and were born by cesarean delivery. At 48 weeks' PMA, infants who died or underwent a tracheostomy had significantly less PGF than those infants who were still hospitalized but without a tracheostomy, although the numbers were small. A significant interaction between weight < 10 th gender-specific percentile for the specified key date and primary outcome (death/tracheostomy) was noted at birth ($p = 0.0001$), admission ($p = 0.007$), and at 48 weeks' PMA ($p = 0.006$).

Discussion

We performed an analysis of weight gain and selected nutritional practices in a large multicenter cohort of extremely preterm infants with sBPD referred to NICUs in children's hospitals participating in the CHND. Our results reveal that PGF during the NICU hospitalization is strikingly common, despite a mean in-hospital weight gain of 30 g/kg/d. About a third of infants with sBPD received parenteral nutrition beyond 36 weeks' PMA. In addition, a significantly greater proportion of infants with sBPD who died or underwent tracheostomy were SGA at birth, compared with those who survived without tracheostomy. Infants with death/tracheostomy had PGF significantly less often than those without but still hospitalized at 48 weeks' PMA.

PGF occurred in more than half the cohort with severe chronic lung disease (sCLD) at 36 weeks' PMA and rates continued to increase in those hospitalized beyond 36 weeks' PMA, despite a reasonable in-hospital mean daily weight gain. These data are consistent with the limited previous studies in preterm infants with BPD.^{3,11} Ehrenkranz and colleagues demonstrated slower growth curves in infants with birth weights between 701 and 1,500 g, who developed chronic lung disease, defined as oxygen administration at 36 weeks' PMA, compared with those who did not.³ A body weight of 2,000 g was achieved 1 to 2 weeks later than the control birth weight cohort without chronic lung disease. In a recent retrospective analysis of 88 extremely low-birth-weight infants with BPD, 25 of whom had severe BPD, growth restriction at discharge was noted in 45 (51%) infants, a rate very similar to ours.¹¹ There are several plausible mechanisms of growth failure in infants with sBPD: increased caloric expenditure in the work of breathing, intermittent hypoxia, restricted fluids, diuretic and postnatal steroid therapy, and comorbidities such as sepsis and pneumonia.¹¹ In our data set, approximately 25% of infants with sBPD required surgical feeding tubes, a third of hospitalized infants were administered parenteral nutrition at 36 weeks' PMA and beyond, and a third were on tube feeds at discharge. These findings suggest that the severity of respiratory illness precluded oral feeding for prolonged periods or that feeding difficulties contributed to PGF in this population.

We found a significantly higher rate of SGA at birth in those who died or underwent tracheostomy. Although relatively underinvestigated, a few previous animal studies have shown that intrauterine growth restriction may result in structural changes in the lung, decreased total gas exchange surface density, decreased pulmonary alveolar and vessel growth, and pulmonary artery endothelial cell dysfunction.^{12,13} In a large cohort of preterm (< 28 weeks' gestation) infants, fetal growth restriction was found to be the only prenatal or maternal characteristic that was highly predictive of chronic lung disease, after adjustment for other factors.¹⁴ Several smaller studies have found an association between fetal growth restriction and BPD.^{15–18} Some experts have suggested that the BPD associated with antecedent intrauterine growth restriction may represent the subgroup of BPD complicated by pulmonary hypertension.¹⁹ Our results amplify these findings and suggest that SGA status at birth may be associated with worse clinical outcomes (death or tracheostomy) among those with sBPD.

In a previous study, extremely low-birth-weight infants who were “critically ill,” defined as receiving mechanical ventilation for the first 7 days of life, were found to have received less total nutritional support for the first 3 weeks of life, compared with those less critically ill.¹ The less critically ill infants had improved growth velocities, less frequent moderate or severe BPD, lower death rate, and superior neurodevelopmental outcomes at 18 to 22 months’ corrected age.¹ Based on regression analysis, the authors suggested that the effect of severity of illness on adverse outcomes was mediated by the energy intake during the first week of life.¹ In our population of preterm infants with sBPD, the rates of major morbidities such as PDA, IVH, and NEC did not differ between those who died or underwent tracheostomy and those who did not. However, we did not have data on early severity of illness indices. Whether early aggressive nutritional support in “more sick” infants would ameliorate outcomes related to sBPD, such as need for tracheostomy, remains to be determined. In addition, it is not possible to elucidate if SGA at birth or early PGF are causal or simply covariates in the pathway to death or tracheostomy in those with sBPD. We also found a higher rate of PGF at 48 weeks’ PMA and a trend toward a higher rate at 44 weeks’ PMA among those who survived without tracheostomy. This is not surprising, because infants still hospitalized at 48 weeks’ PMA are a subset of infants with major comorbidities; in addition, a tracheostomy may actually allow oral feeds, optimize nutrition, and improve ventilation.

We recognize the limitations of our study. Our cohort comprised preterm infants with sBPD who were referred to the CHND sites at varying ages for varying indications and in many cases were transferred back to the referral sites. Therefore, we did not have data for all time points for all infants. In addition, these were infants referred to the higher-level children’s hospital NICUs and likely comprised the “sickest” preterm infants or those with complex medical issues. This limits the generalizability of our findings. Moreover, the temporal relationship of variables is difficult to ascertain. We assessed PGF based on clinically documented weights at specified time points. True growth is the biological acquisition of tissue and organ growth; however, we did not evaluate changes in lengths or head circumferences. Data on exact causes of feeding difficulties, composition of parenteral nutrition, details of caloric and protein intake, and timing of initiation of enteral feeds were not available. SGA status at birth was collected but data on intrauterine growth restriction were not available. We measured weight gain as the difference between weights at two time points divided by the starting weight and the intervening duration. This measure, although simple to use, cannot be directly compared with recommended daily weight gains indexed to current weight and has been previously shown to vary widely compared with actual growth velocity and to be inferior to the exponential model method.²⁰ As in all multicenter databases, coding errors are certainly possible, although unlikely, given the prospective efforts dedicated to quality control of data abstraction.

Nonetheless, our results are derived from a large, unique, and recent multicenter cohort of infants with sBPD who often suffered additional comorbidities and were cared for at NICUs in children’s hospitals. The data were prospectively collected, consistently defined, and rigorously quality-controlled. Our data are potentially important to base further studies on early nutritional strategies to improve outcomes in extremely preterm infants with sBPD.

References

1. Ehrenkranz RA, Das A, Wrage LA, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Early nutrition mediates the influence of severity of illness on extremely LBW infants. *Pediatr Res*. 2011; 69:522–529. [PubMed: 21378596]
2. Martin CR, Brown YF, Ehrenkranz RA, et al. Extremely Low Gestational Age Newborns Study Investigators. Nutritional practices and growth velocity in the first month of life in extremely premature infants. *Pediatrics*. 2009; 124:649–657. [PubMed: 19651583]
3. Ehrenkranz RA, Younes N, Lemons JA, et al. Longitudinal growth of hospitalized very low birth weight infants. *Pediatrics*. 1999; 104(2 Pt 1):280–289. [PubMed: 10429008]
4. Stoll BJ, Hansen NI, Bell EF, et al. Eunice Kennedy Shriver National Institute of Child Health and Human Development Neonatal Research Network. Neonatal outcomes of extremely preterm infants from the NICHD Neonatal Research Network. *Pediatrics*. 2010; 126:443–456. [PubMed: 20732945]
5. Jobe AH, Bancalari E. Bronchopulmonary dysplasia. *Am J Respir Crit Care Med*. 2001; 163:1723–1729. [PubMed: 11401896]
6. Murthy, K.; Hall, M. The Children's Hospitals Neonatal Database (CHND): An Assessment of Inter-Rater Agreement (IRA) [abstract #751047]. Pediatric Academic Societies/Society of Pediatric Research Annual Conference; Boston, MA. 2012; p. 751047E-PAS
7. Olsen IE, Groveman SA, Lawson ML, Clark RH, Zemel BS. New intrauterine growth curves based on United States data. *Pediatrics*. 2010; 125:e214–e224. [PubMed: 20100760]
8. Van den Broeck J, Willie D, Younger N. The World Health Organization child growth standards: expected implications for clinical and epidemiological research. *Eur J Pediatr*. 2009; 168:247–251. [PubMed: 18670787]
9. Papile LA, Burstein J, Burstein R, Koffler H. Incidence and evolution of subependymal and intraventricular hemorrhage: a study of infants with birth weights less than 1,500 gm. *J Pediatr*. 1978; 92:529–534. [PubMed: 305471]
10. Early Treatment For Retinopathy Of Prematurity Cooperative Group. Revised indications for the treatment of retinopathy of prematurity: results of the early treatment for retinopathy of prematurity randomized trial. *Arch Ophthalmol*. 2003; 121:1684–1694. [PubMed: 14662586]
11. Theile AR, Radmacher PG, Anschutz TW, Davis DW, Adamkin DH. Nutritional strategies and growth in extremely low birth weight infants with bronchopulmonary dysplasia over the past 10 years. *J Perinatol*. 2012; 32:117–122. [PubMed: 21617642]
12. Lipsett J, Tamblyn M, Madigan K, et al. Restricted fetal growth and lung development: a morphometric analysis of pulmonary structure. *Pediatr Pulmonol*. 2006; 41:1138–1145. [PubMed: 17063475]
13. Rozance PJ, Seedorf GJ, Brown A, et al. Intrauterine growth restriction decreases pulmonary alveolar and vessel growth and causes pulmonary artery endothelial cell dysfunction in vitro in fetal sheep. *Am J Physiol Lung Cell Mol Physiol*. 2011; 301:L860–L871. [PubMed: 21873446]
14. Bose C, Van Marter LJ, Laughon M, et al. Extremely Low Gestational Age Newborn Study Investigators. Fetal growth restriction and chronic lung disease among infants born before the 28th week of gestation. *Pediatrics*. 2009; 124:e450–e458. [PubMed: 19706590]
15. Bardin C, Zelkowitz P, Papageorgiou A. Outcome of small-for-gestational age and appropriate-for-gestational age infants born before 27 weeks of gestation. *Pediatrics*. 1997; 100:E4. [PubMed: 9233975]
16. Garite TJ, Clark R, Thorp JA. Intrauterine growth restriction increases morbidity and mortality among premature neonates. *Am J Obstet Gynecol*. 2004; 191:481–487. [PubMed: 15343225]
17. Lal MK, Manktelow BN, Draper ES, Field DJ. Population-based study. Chronic lung disease of prematurity and intrauterine growth retardation: a population-based study. *Pediatrics*. 2003; 111:483–487. [PubMed: 12612225]
18. Reiss I, Landmann E, Heckmann M, Misselwitz B, Gortner L. Increased risk of bronchopulmonary dysplasia and increased mortality in very preterm infants being small for gestational age. *Arch Gynecol Obstet*. 2003; 269:40–44. [PubMed: 12682849]

19. Mestan KK, Steinhorn RH. Fetal origins of neonatal lung disease: understanding the pathogenesis of bronchopulmonary dysplasia. *Am J Physiol Lung Cell Mol Physiol*. 2011; 301:L858–L859. [PubMed: 21964401]
20. Patel AL, Engstrom JL, Meier PP, Kimura RE. Accuracy of methods for calculating postnatal growth velocity for extremely low birth weight infants. *Pediatrics*. 2005; 116:1466–1473. [PubMed: 16322172]

Fig. 1. Flowchart for study cohort and outcomes. Abbreviation: sBPD, severe bronchopulmonary dysplasia.

Table 1
Nutritional Support and Longitudinal In-hospital Weights Among Infants with sBPD

Mean (SD) or %	PMA (wk)				Discharge home
	36	40	44	48	
<i>n</i>	270	242	183	164	242
PMA (wk)	36 (0)	40 (0)	44 (0)	48 (0)	46 (7.1)
Weight (g)	2,055 (390)	2,731 (496)	3,345 (623)	3,477 (1,173)	4,000 (1,437)
< 10th percentile for PMA (%)	53	67	66	79	50
Nutritional support					
Parenteral (%)	40.7	29.3	32.2	28.7	0.4
Transpyloric (%)	4.4	7.4	13.1	9.8	3
Gastric (%)	67.4	64	58	67.1	43.2
Oral (%)	17.8	34.3	34.4	25.6	65.7

Abbreviations: PMA, postmenstrual age; sBPD, severe bronchopulmonary dysplasia; SD, standard deviation.

Table 2

Characteristics Among Infants with sBPD, Stratified by Primary outcome Measure

Variable, mean (SD) or %	Survival without tracheostomy (<i>n</i> = 306)	Death or tracheostomy (<i>n</i> = 69)	<i>p</i>
Gestational age (wk)	27.5 ± 4.3	26.6 ± 3.3	0.13
Birth weight (g)	1,113 ± 777	938 ± 548	0.11
SGA < 10th percentile (%)	16.7	37.7	< 0.001
Female gender (%)	35.9	26.1	0.12
Black race (%)	23.5	36.2	0.03
Multiple gestation (%)	21.2	27.5	0.26
Pregnancy-associated hypertension (%)	18.9	17.4	0.76
Maternal diabetes mellitus (%)	4.9	8.7	0.22
Cesarean delivery (%)	66.0	73.9	0.001
Apgar 3 at 5 min (%)	16.0	24.6	0.09
Chorioamnionitis (%)	8.2	7.2	0.80
Antenatal steroids (%)	61.4	60.9	0.93
Any surfactant (%)	84.3	87.0	0.58
PDA (%)	21.2	23.2	0.72
IVH grades 3 or 4 (%)	3.3	4.3	0.66
CLABSI (%)	5.9	4.3	0.62
NEC (%)			
Medical	5.6	8.7	0.33
Medical-surgical	0	1.45	0.03
Postnatal steroids for CLD (%)	30.7	36.2	0.37
PMA 36 wk			
< 10th percentile	56.6	61.5	0.63
TPN administration	40	43.5	0.63
PMA 40 wk			
< 10th percentile	68.7	61.3	0.41
TPN need	29.2	29.3	0.83
PMA 44 wk			
< 10th percentile	72.7	59.1	0.09
TPN need	32.5	31.0	0.94

Variable, mean (SD) or %	Survival without tracheostomy (<i>n</i> = 306)	Death or tracheostomy (<i>n</i> = 69)	<i>p</i>
PMA 48 wk			
< 10th percentile	85.7	66.7	0.006
TPN need	31.1	46.4	0.16
Weight gain (g/kg/d)	25 ± 11	27 ± 11	0.22
Total length of stay	105 ± 60	105 ± 51	0.72
PMA at discharge (wk)	47.3 ± 8.8	46.7 ± 8.0	0.77

Abbreviations: CLABSI, central line–associated bloodstream infection; CLD, chronic lung disease; PDA, patent ductus arteriosus; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; PMA, postmenstrual age; sBPD, severe bronchopulmonary dysplasia; SD, standard deviation; SGA, small for gestational age; TPN, total parenteral nutrition.