Early growth of preterm infants with prolonged hospitalisation

Xi-Fang Ru[1], MD, *Qi Feng*[1], MD, PhD, *Ying Wang*[1], MB, *Xin Zhang*[1], MD, *Xing Li*[1], MMed, *Jing-Wen Meng*[1], BM, *Zai-Chen Guo*[1], MMed

INTRODUCTION This study aimed to determine the early growth patterns of preterm infants who required prolonged hospitalisation in terms of body weight Z-score, and to explore the influencing factors and predictors of their growth.
METHODS The criteria of enrolment included preterm birth, singleton pregnancy, hospitalisation within the first 24 hours of life, hospital stay ≥ 28 days and clinical follow-up beyond 91 days of corrected age. Body weight Z-scores and the incidence of underweight infants were reviewed periodically, and the influencing factors and possible predictors of growth analysed.
RESULTS Body weight Z-scores of all infants of gestational age (GA) groups kept decreasing, with a trough seen at 36 weeks corrected gestational age (CGA). At corrected full-term, body weight Z-scores for all birth weight groups achieved birth level and were higher than that at 36 weeks CGA. Body weight Z-scores at 61 days corrected age was (−0.300 × GA [weeks] + 0.210 × birth weight [g] + 0.682 × body weight Z-score) at 40 weeks CGA. The cut-off values for body weight Z-score at birth (cut-off, −1.79; sensitivity, 100%; specificity, 91.3%) and 61 days corrected age (cut-off, −1.95; sensitivity, 100%; specificity, 97.1%) were selected to predict the risk of being underweight at 183 days corrected age.
CONCLUSION Early growth restriction is a practical problem in preterm infants with prolonged hospitalisation. Body weight Z-scores at 40 weeks CGA and 61 days corrected age can be used to predict body weight gain prior to 183 days corrected age in these infants.

INTRODUCTION

Premature delivery is a worldwide problem.[1] Catch-up growth after birth is crucial for preterm infant development. However, preterm infants are at high risk for growth delay[2-10] and some have inevitable postnatal growth failure.[11-13] The more immature the infant, the worse the postnatal growth restriction is.[11] Although there is controversy about the viability of duplicating intrauterine growth on an extrauterine basis, intrauterine growth pattern remains the gold standard for preterm infant postnatal growth.[14]

If the obstruction of intrauterine and postnatal growth exists during key periods of human development, it may have long-term implications on adult health.[6] It has been hypothesised that accommodations made in metabolism, hormonal output and distribution of cardiac output result in central obesity, hypertension, type II diabetes mellitus and cardiovascular disease in adult life.[6,15-24] Animal studies have also demonstrated that poor intrauterine or infantile nutrition can produce lifetime effects on growth and metabolism as well as manifest as diabetes mellitus, hypertension, neurodevelopment, atherosclerosis and obesity.[25] There is also evidence that infants who have rapid growth are at risk for these sequelae.[16-18,26-28] Apart from this, some studies have demonstrated that early nutrition and growth have an impact on later cognition and motor development.[29]

There is a limited number of literature on the weight gain patterns of high-risk preterm infants from the Chinese mainland, especially with regard to their body weight Z-scores. In this study, we focused on the changing patterns of body weight Z-scores in preterm infants with prolonged hospitalisation during the inpatient and early post-discharge periods. We also sought to identify risk factors of body weight Z-scores at early age and to explore the predictive value of early body weight Z-score for later growth.

METHODS

All preterm infants admitted to our neonatal intensive care unit (NICU) from January 2002 to April 2009 were selected for inclusion in our study. The criteria for enrolment included: (a) gestational age (GA) < 37 weeks; (b) singleton pregnancy; (c) hospitalisation within the first 24 hours of life; (d) hospitalisation period ≥ 28 days; and (e) clinical follow-up beyond 91 days (three months) of corrected age. The discharge criteria included stable vital signs, body weight ≥ 2,000 g and full enteral feeding.

The GA of preterm infants was estimated based on the last maternal menstrual period and obstetric examination as well as physical examination of the preterm infant. Age was adjusted by corrected gestational age (CGA) in weeks until 40 weeks CGA and by corrected age in days after 40 weeks CGA. The patients' clinical information was collected from inpatient and outpatient medical records. All data was input into a computer and verified by the project's principal investigator. Data collection was completed at 274 days (nine months) corrected age and the summarisation deadline was set at 183 days (six months) corrected age.

In the hospital, the infant's fluid and energy requirements were met via parenteral nutrition, if enteral nutrition could not

[1]Department of Paediatrics, Peking University First Hospital, Beijing, China
Correspondence: Dr Feng Qi, Chief Physician, Department of Paediatrics, Peking University First Hospital, Beijing 100034, China. fengqizf@yahoo.com

fulfil daily requirements. Amino acid and lipid emulsion were discontinued if enteral intake was over 80 kcal/kg/day. Breast-feeding was encouraged, and preterm formula milk was used if there was no breast milk or breast milk was insufficient. Breast milk fortifier was rarely used. Post-discharge, breast-feeding, mixed feeding or formula feeding was recommended. Preterm formula milk was switched to standard formula if body weight was 2.0–2.5 kg or more. Parents or caregivers were instructed to give complementary food according to the infant's condition and recommendations. Generally, infant cereal foods and fruits were given at 4–6 months corrected age.

Body weight was taken daily in the hospital and during each outpatient visit by nurses. Scales were regularly calibrated and were accurate to 0.1 kg. Data on body weight were collected and analysed each week in the first four weeks, and then at 36, 38 and 40 weeks CGA, and subsequently at 28 days (one month), 61 days (two months), 91 days (three months), 122 days (four months), 152 days (five months) and 183 days (six months) corrected age. In accordance with the World Health Organization (WHO) Child Growth Standards 2006,[30] data was corrected to target age. The maximum tolerable difference in days between planned and actual age at measurement was 3 and 5 days at 0–6 months and 6–12 months, respectively.

Parents of preterm infants were encouraged to participate in the follow-up programme. Clinical examination was carried out by experienced neonatologists, and subspecialists were consulted when necessary. An NICU nurse, who was involved in the regular follow-up of infants, recorded all the anthropometric data. First hospital visit was scheduled at two weeks post-discharge, and subsequently at three, six and nine months corrected age, or longer. Frequent visits were requested by physicians if there were any indications.

The absolute value of body weight was normalised as body weight Z-scores by using age- and gender-matched anthropometric data. The reference for < 40 weeks CGA was the birth weight of newborns of different gestational ages from 15 cities in China.[31] After correcting to full-term, reference data was obtained from the WHO Child Growth Standards and growth charts for Chinese children.[32] Body weight Z-scores were calculated by subtracting the mean value of the reference population from the observed value and divided by the standard deviation (SD). Preterm infants were categorised into three groups according to GA (< 30 weeks, 30–32 weeks and ≥ 32 weeks) or birth weight (< 1,250 g, 1,250–1,500 g, and ≥ 1,500 g). Body weight Z-scores below −2 were defined as underweight[33,34] or subnormal weight.[6,35,36]

Results were analysed using the Statistical Package for the Social Sciences (SPSS) for Windows version 14.0 (SPSS Inc, Chicago, IL, USA). Data with normal distribution were expressed as mean ± SD. Univariate analysis of variance was used to compare the various continuous parameters, following which Bonferroni analysis was used to compare any two groups. Chi-square test was used to compare discrete variables that met

conditions, otherwise, Fisher's exact test was used. Mixed model analysis was used to compare the various continuous parameters at each time point within each GA or birth weight group, and Bonferroni analysis was used to compare any two data. A p-value < 0.05 was considered statistically significant. Multiple linear regression analysis was used to calculate regression coefficients. Receiver operating characteristic curves were drawn using SPSS to explore the predictive value of body weight Z-scores at birth and 61 days (two months) corrected age for the incidence of being underweight at 183 days (six months) corrected age.

RESULTS

91 infants (52.7% male) were enrolled in the study. The mean GA was 30.9 ± 1.9 (range of 27–36) weeks, mean birth weight was 1,392 ± 312 (range of 850–2,450) g and mean body weight Z-score at birth was −1.08 ± 0.77 (range of −4.15 to −0.97). Pregnancy-induced hypertension (PIH) syndrome and gestational diabetes mellitus were seen in 39 and 5 pregnant women, respectively. The critical clinical conditions observed among our preterm infants included asphyxia (n = 26), respiratory distress syndrome (RDS; n = 37), late-onset sepsis (n = 3), necrotising enterocolitis (NEC; n = 4), chronic lung disease (n = 3) and blood exchange transfusion (n = 1). Table I and Fig. 1 present the findings based on GA of the preterm infants.

Prior to correcting to full-term (40 weeks CGA), no difference was observed in the body weight Z-scores of infants from the different GA groups at birth, and the Z-scores were all < 0 (F = 2.030; p = 0.137). Body weight Z-score kept declining, and a trough was observed at 36 weeks CGA in all the infants. However, no significant difference was observed in the body weight Z-scores among the various groups at 36 weeks CGA (F = 2.804; p = 0.066). Further analysis showed that the decline in body weight Z-scores was more marked in the first three weeks of life in infants with higher GA, and that the decline in body weight Z-scores lasted longer in preterm infants with lower GAs.

Each GA group had the same incidence of underweight infants at birth (p = 0.245). In parallel with the dynamic shift of body weight Z-scores, the incidence of underweight infants reached a peak at 36 weeks CGA, with 23.8%, 38.2% and 59.4% infants in the groups with GA < 30 weeks, GA 30–32 weeks and GA ≥ 32 weeks, respectively, being underweight. The differences among these groups at 36 weeks CGA were statistically significant (χ^2 = 6.983; p = 0.030). Except for the GA < 30 weeks group, the incidence of underweight was higher in the other groups than at birth, especially in the GA ≥ 32 weeks group.

After correction to full-term, gradual recovery of mean body weight Z-scores was noticed in early age following the decline seen earlier, and infants from all groups had significantly raised body weight Z-scores compared to those at 36 weeks CGA. Infants from groups other than those with GA ≥ 32 weeks demonstrated some catch-up growth. This same trend was seen in the incidence of underweight infants as well. The incidence of underweight infants remained at levels seen at birth until 183

Table I. Body weight Z-scores and incidence of underweight infants among preterm infants of various gestational ages.

Parameter	Gestational age at birth (wks)			F	χ²	p-value
	< 30	**30–32**	**≥ 32**			
At birth	22 (100)	36 (100)	33 (100)			
Birth weight Z-score	−0.88 ± 0.64	−1.02 ± 0.52	−1.28 ± 1.01	2.030		0.137
Underweight infants	1 (4.5)	1 (2.8)*	5 (15.2)*		-	0.245‡
Three weeks after birth	22 (100)	36 (100)	33 (100)			
Body weight Z-score	−1.28 ± 0.53	−1.60 ± 0.89	−2.17 ± 1.09†	7.090		0.001
Underweight infants	1 (4.5)	7 (19.4)	20 (60.6)†		23.061	< 0.001
36 weeks CGA	21 (95.5)	34 (94.4)	32 (97.0)			
Body weight Z-score	−1.43 ± 1.00	−1.64 ± 0.89	−2.01 ± 0.89	2.804		0.066
Underweight infants	5 (23.8)	13 (38.2)†	19 (59.4)†		6.983	0.030
40 weeks CGA (full-term)	18 (81.8)	23 (63.9)	24 (72.7)			
Body weight Z-score	−0.26 ± 1.34*	−0.48 ± 1.62*	−1.15 ± 1.11	2.462		0.094
Underweight infants	2 (11.1)	4 (17.4)	5 (20.8)*		-	0.846‡
61 days corrected age	13 (59.1)	25 (69.4)	24 (72.7)			
Body weight Z-score	0.27 ± 0.93*,†	−0.22 ± 1.44*,†	−0.89 ± 1.40*	3.406		0.040
Underweight infants	0 (0.0)	2 (8.0)	5 (20.8)*		-	0.110‡
122 days corrected age	15 (68.2)	16 (44.4)	16 (48.5)			
Body weight Z-score	−0.41 ± 0.84*	−0.22 ± 1.57*	−0.85 ± 1.33*	0.985		0.381
Underweight infants	0 (0.0)	2 (12.5)	3 (18.8)		-	0.345‡
183 days corrected age	14 (63.6)	15 (41.7)	21 (63.6)			
Body weight Z-score	0.05 ± 0.93*,†	−0.26 ± 1.09*	−0.78 ± 1.44*	2.071		0.137
Underweight infants	0 (0.0)	0 (0.0)	4 (19.0)*		-	0.060‡

Note: Data is presented as number of infants (%) or mean ± standard deviation.
*Comparisons of all parameters for body weight Z-scores (mixed model analysis; p < 0.05) and the incidence of underweight infants (p < 0.0045; 0.05/11) were based on measurements obtained at 36 weeks CGA and other times.
†Comparisons of all parameters for body weight Z-scores (mixed model analysis; p < 0.05) and the incidence of underweight infants (p < 0.0045; 0.05/11) were based on measurements obtained at birth and other times.
‡ Fisher's exact test.
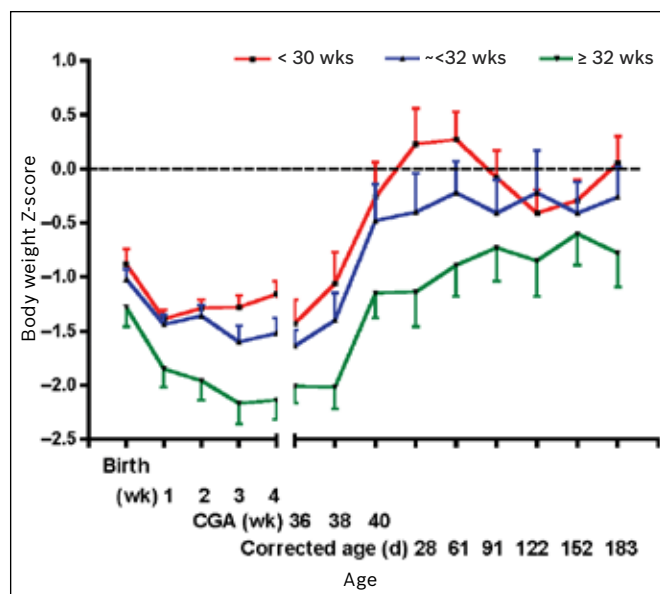χ²: chi-square; CGA: corrected gestational age

Fig. 1 Body weight Z-score pattern according to gestational age among preterm infants.

days corrected age. Table II and Fig. 2 present the findings based on the birth weights of the preterm infants.

Prior to correction to full-term (40 weeks CGA), the mean birth weight Z-scores of infants from the different body weight groups were < 0 at birth and there were differences among the various groups at birth (F = 12.790; p < 0.001). In general, it was observed that the lower the birth weight, the lower was the body weight Z-score. The body weight Z-score for very low birth weight (VLBW; birth weight < 1,500 g) infants was −1.30 at birth. As seen in the infant groups based on GA, the body weight Z-scores in infants from the various birth weight groups declined until a trough appeared at 36 weeks CGA. Different body weight Z-scores among the various birth weight groups persisted until 36 weeks CGA (F = 6.357; p = 0.003).

The incidence of underweight infants at birth was the same in each birth weight group (p = 0.220; VLBW, 8.1%). Increased incidence of underweight infants was seen at 36 weeks CGA, when 60.0%, 51.5% and 17.2% infants in the groups with birth weights < 1,250 g, 1,250–1,500 g and ≥ 1,500 g, respectively, were underweight. The incidence of underweight infants was higher among VLBW infants than non-VLBW infants (55.2% vs. 17.2%). After correction to full-term, body weight Z-scores for VLBW infants were −0.38 at 40 weeks CGA and −0.50 at 183 days corrected age. During the infantile period, the body weight Z-scores of VLBW infants increased and were higher than at birth, although the trend was slower in babies with birth weights < 1,250 g. The incidence of underweight infants among VLBW infants remained at the same level as at birth, and was 20.8%, 12.2% and 9.1% at 40 weeks CGA, 61 days corrected age and 183 days corrected age, respectively.

Multiple linear regression analysis was used to determine the predictors and risk factors of growth during the developing period (Table III). Prior to correcting to full-term (40 weeks CGA), the independent variables that were included in the analysis for three weeks after birth and 36 weeks CGA included GA, birth weight, birth weight Z-score, early complications (such as sepsis, RDS and NEC), maternal complications, duration of invasive or

Table II. Body weight Z-scores and incidence of underweight infants among preterm infants of various birth weights.

Parameter	Birth weight (g)			F	χ²	p-value
	< 1,250	1,250–1,500	≥ 1,500			
At birth	27 (100)	35 (100)	29 (100)			
Birth weight Z-score	−1.53 ± 0.74	−1.12 ± 0.53	−0.60 ± 0.79	12.790		< 0.001
Underweight infants	4 (14.8)*	1 (2.9)*	2 (6.9)		-	0.220‡
Three weeks after birth	27 (100)	35 (100)	29 (100)			
Body weight Z-score	−2.00 ± 0.85	−1.72 ± 0.78†	−1.48 ± 1.20	2.118		0.126
Underweight infants	9 (33.3)	14 (40.0)†	5 (17.2)		3.975	0.142
36 weeks CGA	25 (92.6)	33 (94.3)	29 (100)			
Body weight Z-score	−2.20 ± 0.76	−1.71 ± 1.00	−1.34 ± 0.84	6.357		0.003
Underweight infants	15 (60.0)†	17 (51.5)†	5 (17.2)		11.800	0.003
40 weeks CGA (term)	20 (74.1)	28 (80.0)	17 (58.6)			
Body weight Z-score	−1.16 ± 1.32	−0.53 ± 1.35*	−0.32 ± 1.50	1.959		0.150
Underweight infants	7 (35.0)	3 (10.7)*	1 (5.9)		-	0.051‡
61 days corrected age	17 (63.0)	24 (68.6)	21 (72.4)			
Body weight Z-score	−0.79 ± 1.66*	−0.34 ± 1.23*	−0.08 ± 1.31*	1.264		0.290
Underweight infants	4 (23.5)	1 (4.2)*	2 (9.5)		-	0.157‡
122 days corrected age	19 (70.4)	14 (40.0)	14 (48.3)			
Body weight Z-score	−1.02 ± 1.39*	−0.22 ± 1.05*,†	−0.06 ± 1.21	2.882		0.067
Underweight infants	4 (21.1)	0 (0.0)*	1 (7.1)		-	0.167‡
183 days corrected age	15 (55.6)	18 (51.4)	17 (58.6)			
Body weight Z-score	−0.47 ± 1.45*	−0.52 ± 1.18*	−0.17 ± 1.15	0.394		0.677
Underweight infants	2 (13.3)*	1 (5.6)*	1 (5.9)		-	0.671‡

Note: Data is presented as number of infants (%) or mean ± standard deviation.
* Comparisons of all parameters for body weight Z-scores (mixed model analysis; p < 0.05) and the incidence of underweight infants (p < 0.0045; 0.05/11) were based on measurements obtained at 36 weeks CGA and other times.
† Comparisons of all parameters for body weight Z-scores (mixed model analysis; p < 0.05) and the incidence of underweight infants (p < 0.0045; 0.05/11) were based on measurements obtained at birth and other times.
‡ Fisher's exact test.
χ²: chi-square; CGA: corrected gestational age

noninvasive ventilation (hours), weight loss percentage, the lowest body weight, duration of weight loss, duration of weight gain (days), duration of total enteral feeding (days) and duration of intravenous (IV) intake < 50% of the daily requirement (days). Body weight Z-score at three weeks after birth was positively associated with the lowest body weight and duration of IV intake < 50% of daily requirement, but negatively associated with GA and duration of total enteral feeding (p < 0.05). Body weight Z-score at 36 weeks CGA was positively associated with birth weight, duration of total enteral feeding and duration of weight gain, but negatively so with duration of invasive ventilation (p < 0.05; Table III). After correction to full-term, the independent variables included body weight Z-score at 36 weeks CGA in addition to the variables described above. The duration of invasive ventilation was a negative factor while the duration of IV intake < 50% of daily requirement and body weight Z-score at 36 weeks CGA were positive factors (p < 0.05). After correction to full-term, the independent variables included for analysis at 61 days corrected age were GA, birth weight, and body weight Z-scores at birth, 36 weeks and 40 weeks CGA. Birth weight and body weight Z-score at 40 weeks CGA were positively associated with body weight Z-score at 61 days corrected age, while GA showed a negative correlation (p < 0.05). The standard regression equation for body weight Z-score at 61 days corrected age was as follows:

Body weight Z-score (at 61 days corrected age) = −0.300 × GA (weeks) + 0.210 × birth weight (g) + 0.682 × body weight Z-score at 40 weeks CGA, where r^2 was 0.807 and adjusted r^2 was 0.792.
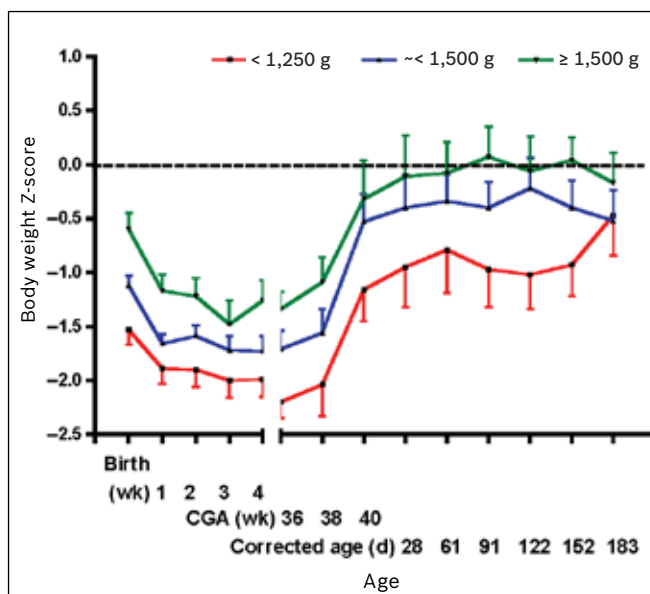

Fig. 2 Body weight Z-score pattern according to birth weight among preterm infants.

In addition to the factors included in the analysis at 61 days corrected age, body weight Z-score at 61 days corrected age was added as an independent variable during the analysis for 122 days corrected age while body weight Z-scores at 61 days and 122 days corrected age were added during the analysis for 183 days corrected age. Body weight Z-score at 61 days corrected age was a positive predictor of body weight Z-scores at 122 days and 183 days corrected age (p < 0.05).

Table III. Multiple linear regression analysis of body weight Z-scores in growing infants.

Parameter	Standard error	β	T	p-value
Preterm				
Three weeks after birth				
Gestational age (wks)	0.034	−0.927	−14.019	< 0.001
Duration of intravenous intake < 50% of daily requirement (days)	0.013	0.150	2.001	0.048
Duration of total enteral feeding (days)	0.025	−0.145	−2.040	0.044
Lowest body weight	0.212	0.808	12.670	< 0.001
36 weeks CGA				
Birth weight	0.205	0.920	13.390	< 0.001
Duration of invasive ventilation (days)	0.001	−0.155	−2.680	0.009
Duration of total enteral feeding (days)	0.007	0.152	2.184	0.032
Duration of weight gain (days)	0.006	0.734	9.122	< 0.001
Full-term				
40 weeks CGA				
Duration of invasive ventilation (days)	0.001	−0.162	−2.288	0.026
Duration of intravenous intake < 50% of daily requirement (days)	0.008	0.217	2.841	0.006
Body weight Z-score at 36 weeks CGA	0.111	0.697	8.985	< 0.001
Infantile				
61 days corrected age				
Gestational age (wks)	0.074	−0.300	−2.959	0.005
Birth weight	0.406	0.210	2.078	0.045
Body weight Z-score at 40 weeks CGA	0.097	0.682	6.898	< 0.001
122 days corrected age				
Body weight Z-score at 61 days corrected age	0.167	1.193	6.862	< 0.001
183 days corrected age				
Body weight Z-score at 40 weeks CGA	0.220	−0.488	−2.045	0.058
Body weight Z-score at 61 days corrected age	0.243	1.255	5.256	< 0.001

CGA: corrected gestational age
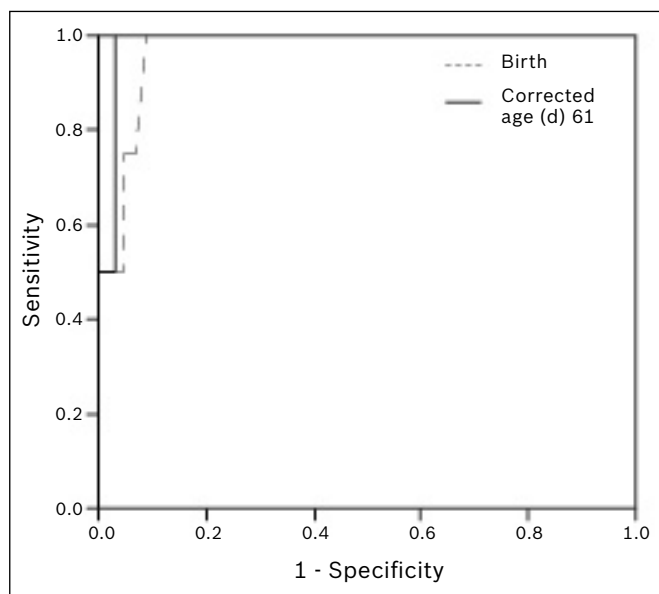
Fig. 3 Receiver operating characteristic curve to predict the incidence of underweight infants at 183 days corrected age.

Table IV. Predictors of underweight infants at 183 days corrected age.

Parameter	At birth	61 days corrected age
Body weight Z-score		
Area under the curve	0.970	0.985
Standard error	0.025	0.018
P_b*	0.002	0.002
Asymptomatic 95% CI	0.922–1.018	0.950–1.020
Cut-off value	−1.79	−1.95
Sensitivity (%)	100	100
Specificity (%)	91.3	97.1

CI: confidence interval
*P_b null hypothesis: true area = 0.5.

The cut-off values for body weight Z-score at birth (cut-off, −1.79; sensitivity, 100%; specificity, 91.3%; positive predictive value [PPV], 50%; negative predictive value [NPV], 100%) and 61 days corrected age (cut-off, −1.95; sensitivity, 100%; specificity, 97.1%; PPV, 80%; NPV, 100%) were selected to predict the risk of underweight infants at 183 days corrected age (Fig. 3 and Table IV).

DISCUSSION

Body weight Z-score is an index that is useful for illustrating systemic development. It reflects the personal status of the subject in a related population and can eliminate any potential bias arising from age and gender. Body weight is not only a variable that can be determined easily and accurately but also a very good index of early growth and development. While Knops et al found that early weight gain was an important prognostic factor for predicting childhood growth,[37] Belfort et al reported that for preterm infants, the neurodevelopmental advantages of more rapid weight gain in the first year of life seems modest.[38] Franz et al meanwhile suggested that early neonatal weight gain was associated with the long-term motor development and cognitive development of extremely preterm infants.[39]

Our research focused on preterm infants with prolonged hospitalisation. Irrespective of the GA or birth weight of infants, long hospital stays imply that infants are exposed to a much higher number of risk factors early in life. However, as prolonged hospitalisation enables accurate data collection, systemic follow-up of such preterm infants allows for: (i) their growth outcomes under current clinical management protocols

to be determined; (ii) the prediction of growth patterns of inpatients; (iii) ascertaining special working points for such high-risk infants; and (iv) improvement of the systemic management of preterm infants.

In our study, the body weight Z-scores of infants from all GA and birth weight groups were < 0 at birth, following which the scores kept declining until a trough was reached at 36 weeks CGA. Generally, the lower the birth weight, the lower was the birth weight Z-score recorded for our cohort. We found that the decline of body weight Z-score was more marked in the first three weeks of life among infants with higher GAs. However, this decline in Z-scores lasted for a longer time in infants with lower GAs. These results are in agreement with those of Sun et al who, in a study of 439 preterm infants (mean GA, 31.3 ± 1.4 weeks), found that body weight Z-score < 0 (mean Z-score, −0.60 ± 0.68) at birth tended to decline during hospital stay and reached −1.44 ± 0.95 at discharge (mean GA, 35.6 ± 1.8 weeks).[40] Our data showed that, at corrected full-term (40 weeks CGA), the body weight Z-scores of infants from all groups had regained the levels seen at birth and remained at or were higher than these levels at later periods. Early regain and maintenance of body weight in preterm infants provide a good foundation for further development and catch-up growth. In keeping with this, catch-up growth was observed to start earlier in our study than in other reports.[41] Some studies have also proposed that catch-up growth in preterm infants begins from discharge (mean GA, 39.2 ± 3 weeks),[35] 40 weeks,[36] 18 months[41] or eight years.[6]

GA is an important factor that indicates the maturity of preterm infants. Dodrill et al reported that the mean body weight Z-scores of 64 preterm infants who were appropriate for GA during the infantile period changed between −1.0 and 0.[24] These authors found that infants with higher GAs had higher body weight Z-scores, although no significant differences were found between the mean Z-scores of the three subgroups selected in their study (GA < 28.0 weeks, GA 28.0–31.6 weeks, GA 32.0–36.6 weeks).[24] We found that the mean body weight Z-scores of infants with GA ≥ 32 weeks at birth and during the infantile period were lower than that among other GA and body weight groups in our study, as well as that reported by Dodrill et al. This may indicate that there were more infants with higher GAs in our study who were small for GA (SGA). It is also possible that our inclusion criteria of at least four weeks of hospitalisation may have contributed to this result. Earlier evaluation at 36 weeks CGA may give rise to some bias due to invisible water loss in infants with higher GAs even as lower GA infants benefit from aggressive parenteral nutrition.

Birth weight is a very good index for predicting subsequent weight gain in preterm infants. Body weight relates not only to GA but also to the intrauterine development of the foetus. In our study, lower body weight Z-scores were seen among VLBW infants, especially among those with body weight < 1,250 g, which indicates that there were more SGA infants or intrauterine growth restriction (IUGR) infants in this group. SGA infants have

lasting low body weight Z-scores and are a high-risk population for growth restriction.[40,42] Studies have also suggested that IUGR does affect development to a certain extent, especially in critical restricted conditions.[25,43] Hack et al reported that among male VLBW infants, body weight Z-scores at birth, 40 weeks and eight years were −0.7, −1.8 and −0.5, respectively, while for female VLBW infants the corresponding scores were −1.1, −2.0, and −0.2, respectively.[6] In our study, body weight Z-scores for VLBW infants were −1.30 at birth, −0.38 at 40 weeks CGA and −0.50 at 183 days corrected age. Compared to Hack et al's report, infants in our study had lower body weight Z-scores at birth, but higher Z-scores at 40 weeks CGA. The VLBW infants in our study also had better catch-up growth in the subsequent development period.

In our study, the incidence of underweight infants was relative higher in infants with higher GA and lower birth weight (< 1,500 g). This finding may be related to the development of Chinese perinatal medicine as well as the criteria used in our study. Peak incidence of underweight infants was seen at 36 weeks CGA, with 23.8%, 38.2% and 59.4% infants in the groups with GAs < 30 weeks, 30–32 weeks and ≥ 32 weeks, respectively, and 60.0%, 51.5% and 17.2% infants in the groups with birth weights < 1,250 g, 1,250–1,500 g and ≥ 1,500 g, respectively, being underweight. The incidence of underweight infants among VLBW infants was 8.1% at birth, 55.2% at 36 weeks CGA, 20.8% at 40 weeks CGA, 12.2% at 61 days corrected age and 9.1% at 183 days corrected age (data not shown).

Santos et al found that infants of late preterm births (GA 34/0–36/6 weeks) were at increased risk of being underweight in the first two years of life when compared to term children, with the incidence of underweight infants being 3.4% and 3.0% at 12 months and 24 months, respectively.[33] Meanwhile, Hack et al reported that 18% of male VLBW infants and 22% of female VLBW infants were of subnormal weight at birth, and the incidence of underweight infants increased to 57% and 50%, respectively, at 40 weeks CGA but decreased to 38% and 21%, respectively, at eight months corrected age.[6] The incidence of underweight infants among VLBW infants in our study during the infantile period were lower than that reported by Hack et al. Similarly, Sices et al also reported that 7%, 49%, 24% and 38% of extremely low birth weight (ELBW; birth weight < 1,000 g) infants had subnormal weight at birth, 40 weeks CGA, and at four and eight months corrected age, respectively.[35] Growth in our infants was better than that reported in these studies. However, although early decline in growth rates may recover prior to 61 days corrected age in preterm infants, long-term catch-up growth in these infants needs longer observation.

Birth weight is recognised as an important predictor of weight gain in preterm infants.[18,10,42] Our results indicated that greater attention should be paid to infants with lower birth weight Z-scores. In Hack et al's study, birth weight Z-score was included as a predictor during multivariate analysis of 20-year growth attainment.[6] Morley et al also reported that birth weight ratio

(infant's birth weight divided by reference median birth weight for the infant's gestation) was strongly and linearly related to body weight at 18 months corrected age.[44]

We also found that weight gain was influenced by nutrition and the duration of invasive ventilation. Martin et al, for instance, reported that early (day 7) nutritional practices were positively associated with growth velocity measured between days 7 and 28, and that early provision of nutrients was an important determinant of postnatal growth.[45] According to Madden et al[36] and Radmacher et al,[46] prolonged duration of mechanical ventilation is associated with poor growth in VLBW populations. Neonatal growth failure in VLBW and ELBW infants related to NEC, late-onset sepsis, postnatal steroid therapy, neurodevelopmental disability, bronchopulmonary dysplasia and feeding problems have also been reported.[47,48]

We found, as did previous studies,[49] that regular follow-up of preterm infants post-discharge was not easy to enforce, especially in big cities with a large immigrant population. Therefore, establishing appropriate key check-up time points or indexes that can used to predict a reasonable period of development for such infants would prove beneficial for all concerned, be it the infants, parents or clinicians. The growth of tiny preterm infants or those with critical long hospital stays could be predicted based on data obtained during earlier follow-ups. Such information could also help in evaluating the condition of infants who cannot be followed up as frequently as necessary. Our results show that predictive cut-off values for body weight Z-scores at birth and 61 days corrected age for high-risk preterm infants were very useful for estimating weight gain in these infants during the infantile period.

This present study had some limitations. First, although the follow-up rate in our study was 100% in the first four weeks and close to two-thirds at most other time points, there were several points that were still lower, which may have led to some bias. Second, growth is not only related to early nutrition but also affected by later nutrition and health condition, especially in infants with critical or chronic diseases in early life. This aspect of growth was not addressed in this study. Third, although body length and head circumference are good parameters of growth and development in addition to body weight, only body weight was selected for this study, as it could be measured easily and accurately. Fourth, as our study was carried out in a tertiary university teaching hospital, it is possible that the conclusions drawn from it may only be appropriate for other similar hospitals.

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