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Physical growth and brain MRI predict the neurodevelopmental outcomes in very low birth weight infants at 2-year-old

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Abstract

OBJECTIVE: The purpose of the current study was to determine the predictive effect of physical growth and brain magnetic resonance imaging (MRI) on neurodevelopmental outcomes in very low birth weight infants (VLBW) infants.
MATERIALS AND METHODS: A total of 85 VLBW infants were included in the current study. They were cared according to the guideline of preterm management during hospitalization, and to planned follow-up rules after discharged strictly. All patients enrolled in the present study had undergone measurement of weight, length and head circumference and reported on the infants' weight-for-age z-score (WAZ), height-for-age Z-score (HAZ), head circumference-for-age Z-score (HCZ), and weight-for-height Z score (WHZ).
RESULTS: At 29.38 ± 1.70 weeks old, the birth weight was 1240.06 ± 249.46g. MDI decreased gradually with the increase of corrective age ($p<0.001$), and MDI at 18 months of age decreased significantly compared to normal infants and young children of the same age ($p<0.05$), while at 24 months of age there was no significant difference between MDI and normal peers. Correcting PDI in 3, 6, 12, 18 and 24 months was significantly lower than that of normal infants and young children of the same age ($p<0.05$) and did not show a trend that changed with the correction of monthly age. WHZ gradually approaches normal as the age of the month increases ($p<0.05$), while HCZ decreases gradually with the correction of the age of the month ($p<0.05$).
CONCLUSION: VLBW has obvious motor development disorders, and there is no difference between intellectual development and healthy young children. MDI rises early and then gradually declines, eventually becoming 2 years old similar to that of healthy young children. PDI has consistently shown a significant decrease in infants and young children of the same age, and has not shown a trend that changes with the correction of monthly age. There is a great correlation between infancy physical development and long-term neurodevelopment, MRI at 12 months old is a valuable prediction method.

ORIGINAL ARTICLE

INTRODUCTION

Every year, approximately14.9 million neonates, representing a birth rate of 11.1%, are born preterm, globally (Blencowe *et al.* 2013). Though substantial advancement in medical care has led to an improved survival of preterm infants (Helenius *et al.* 2017), significant morbidity during the hospital stay and adverse long-term neurological consequences remain major areas of concern. In recent years, with the progress of perinatal medical technology, the survival rate of very low birth weight infants early premature infants has increased year by year (Hahn *et al.* 2011), VLBWI survival rates have reached over 90 per cent in some developed countries (Chung *et al.* 2017), China's VLBWI survival rate is also increasing year by year (Chen *et al.* 2016). However, there is a large gap between the growth and neurobehavioral development of these children and normal children (Oommen *et al.* 2019).

It has been reported that premature infants with lighter birth weight, younger gestational age, and lower Apgar score, the worse the prognosis for the development of the nervous system (Chen *et al.* 2013). The tissue and organ development of preterm infants is immature and lagging behind that of normal full-term newborns (Mathias *et al.* 2018). For example, their birth weight, body length, head circumference, chest circumference and other growth indicators are significantly worse than full-term newborns, and their physiological functions are relatively imperfect, resulting in the congenital deficiency of immune function of most preterm infants (Gu *et al.* 2017; Cao *et al.* 2018 ???). Additionally, these newborns are prone to complications such as respiratory distress, sucking and swallowing disorders. It is caused by that their organs and adaptability are poorer than those of healthy newborns, the brain is not mature enough, and the neural reflexes need to be perfected (Sharma *et al.* 2019).

In this study, we intend to analyze the parameters of standardized comprehensive management of very low birth weight infants early preterm infants in our hospital NICU, and evaluate the physical growth and nerve development within 2 years after birth. To explore the correlation and influencing factors between postnatal physical development and long-term neurodevelopment prognosis of very low birth weight infants / early preterm infants.

MATERIALS AND METHODS

Patients

The clinical study was approved by the Ethics committee of Guangdong Provincial People's Hospital (GUIJUAN0224). The extremely low birth weight (birth weight <1500 g) in our NICU from June 2015 to June 2017 was studied. All patients were excluded from genetic metabolic diseases, obvious congenital malformations, severe hypoxic-ischemic encephalopathy and bilirubin encephalopathy, which may affect brain development.

aEEG measurements

aEEG was monitored before cardiac surgery (24 hours) using an 8-channel EEG (NicoletOne monitor, CareFusion, San Diego, California). Eight disposable, self-adhesive, EEG scalp electrodes (Blue Sensor BRS-50 K AmbuTM ECG electrode; Medicotest A/S, Ølstykke, Denmark) were used in a reduced montage following the international 10-20 system. The expert who performed the main offline aEEG analyses was not involved in clinical care. The 8-channel cross-brain aEEG trace was derived and displayed at 6 cm/hour on paper using a semi logarithmic scale to assess and classify the aEEG background pattern. The channels were also used to record EEG data to describe episodes of EEG seizures in 10-second epochs. The 8-channel EEG recording was examined for the entire recording period for patients when necessary.

The interpretation of aEEG

The aEEG traces were classified by background voltage (al Naqeeb *et al.* 1999) and descriptive pattern. The aEEG recordings included background pattern, sleep -wake cycle (SWC) and electrographic seizure. The background pattern was categorized into normal, slightly abnormal, and severely abnormal. We classified SWC by occurrence: absent, immature or developed [813]????. An electrographic seizure was defined as an evolving repetitive, stereotyped waveform with a definite onset, peak, and end that lasted for ≥10 seconds on raw EEG data (Shah *et al.* 2015). Electrographic seizure activity (EA) was divided into no seizure; a single seizure (SS), in which the amplitude of a single waveform appeared suddenly and showed persistent cerebral cortex activity; and recurrent seizure (RS), in which a recurring amplitude showed sudden and persistent cerebral cortex activity. All the reports were examined by a neonatal neurological expert who was blinded from the patients' diagnosis.

Clinical characteristics

All subjects established neonatal records to record birth information, hospitalization and outpatient follow-up results after discharge. To inform the subjects of the follow-up contents and obtain informed consent, the subjects were required to follow up regularly in the child health clinic every month, and the preterm infants were followed up according to the age of correction. including physical measurement and evaluation, routine motor development assessment, intelligence test, feeding guidance, development assessment and early intervention based on physical development and neurodevelopmental examination, and regular infant feeding and early education training courses in parent schools.

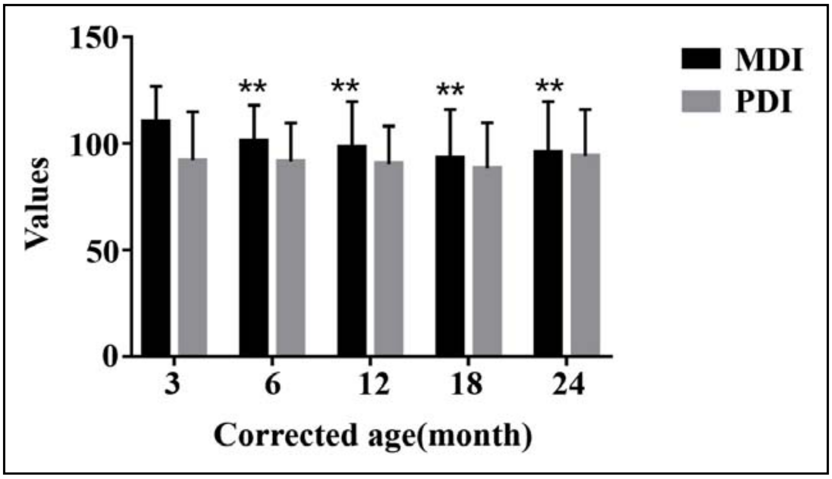

Fig. 1. Trends in MDI and PDI of preterm infants at different ages. Among MDI, there was significant difference in different ages (F = 23.54; *P* <0.01). Among PDI, there was not difference in different ages (F = 0.71; *P* = 0.40). **P* < 0.01. MDI, Mental developmental index; PDI, Psychomotor developmental index; VLBW, Very low birth weight.

Follow-up

The standardized Chinese city revised Bayley infant development scale (BSID) was used for neurodevelopmental assessment at corrected 6, 12, 18 and 24 months. The BSID includes two aspects: intelligence scale and exercise scale, including adaptive behavior, language and exploration activities ,163 items, expressed by intelligence development index (MDI), and 81 items, expressed by mental movement development index (PDI), including coarse movement and fine movement was assessed by professionally trained medical personnel under the same test conditions. Finally, according to the final results of BSID scale evaluation, the prognostic factors of neurodevelopment in very low birth weight infants were analyzed.

Growth and development evaluation using Z value (Zscore) evaluation, Growth criteria selected WHO 2006 growth criteria, WHO Anthro software calculated the age group mass Z (WAZ), age group length Z (HAZ), body length mass (WHZ) and head circumference Z (HCZ). The formula is: Z value =(measurement data-reference value median)/ reference value standard deviation. The criteria for the diagnosis of malnutrition by Z score were: WAZ<-2 was low weight, HAZ <-2 growth retardation, WHZ<-2 is divided into wasting. Unreasonable data of HAZ <-6 and HAZ >6, WAZ HAZ <-6 and WAZ HAZ >5 and WHZ HAZ <-5 and 5 were excluded.

Statistical analysis

Data were processed using SPSS 23.0 (SPSS, Inc.) software and presented as the mean ± SD. Comparisons between groups were performed using a student t-test and Bonferroni correction. Variance analysis or a signed-rank test was used for comparison of continuous variables and a $\chi 2$-test or Fisher's exact test for dichotomous variables. Comparisons with the grade data were performed using a Wilcoxon signed-rank test. Multiple linear regression analysis was used to determine the influencing factors of MDI and PDI. The β value or the regression coefficient, was applied for regression analysis. β>0, indicated a positive association between strain and independent variable, and β<0, indicated a negative association. The inspection standard was bilateral 0.05. *P*<0.05 was considered to indicate a statistically significant difference.

RESULTS

Clinical characteristics of infants

There were 85 premature infants <32 weeks of birth age, including 51 males and 34 females. artificial conception in 17 cases (20%). The gestational age was 29.38±1.70 weeks (range :25.71~31.86 weeks), and the birth weight was 1140.06±249.46 g (range: 780~1480). There are 8 pairs of twins. There were 23 cases (27.06%) with diabetes, hypertension, kidney disease and thyroid disease. Eighteen cases (21.18%) were delivered by cesarean section due to severe eclampsia. Thirty-four (40%) children were delivered by birth. Six (7.06%) children were diagnosed with severe asphyxia at birth and 21(24.71%) with mild asphyxia. Four children were born with III degree of amniotic fluid fecal stain, including 2 children with amniotic fluid stench and 1 child born with bloody amniotic fluid. Average length of stay 60.21 days (range: 18~141 days). Illness during hospitalization: 81 cases of neonatal hyaline membrane disease (95.29%), Septicemia 32, Meningitis in 4 cases, IVH6 example, PVL1 example, ROP20 example, Seven of them require surgical treatment, NEC20 example, Two of them require surgical treatment, VAP9 example, BPD32 example, Among them severe BPD3 cases, Four cases of pulmonary hemorrhage, Seven cases of apnea, Feeding intolerance in 11 cases, Anaemia 40,

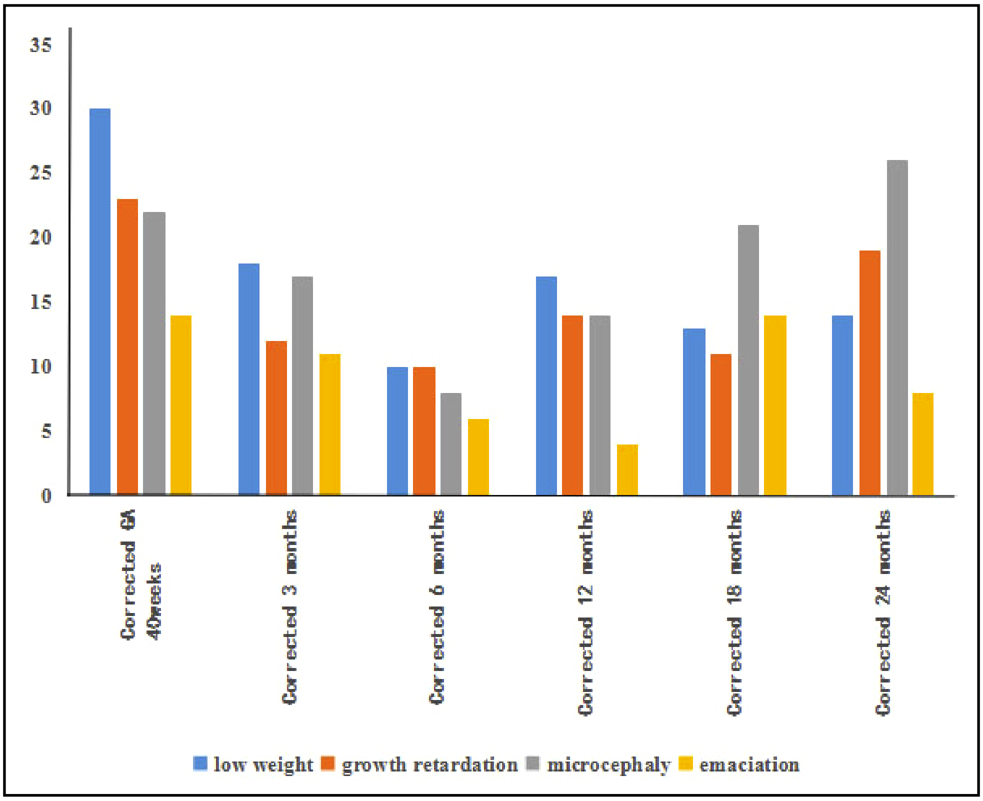

Fig. 2. Distribution of malnutrition types in different months

Hyperbilirubinemia 50 cases, PDA25 with symptoms, SGA15 example, 16 cases of surgical history during hospitalization, BPD8 cases of glucocorticoid therapy, EPO51 cases were used in hospital, citicoline in 7 cases. The average invasive ventilation time was 86.76 days (range: 0~696 days), the average non-invasive ventilation time was 162.36 days (range: 0~912 days), and the median NBNA of 3825 children was less than 38 points.

MDI and PDI in VLBW infants

The trend test showed (see Figure 1) that the MDI decreased gradually with the increase of corrected age (p<0.001), the MDI of 18 months was significantly lower than that of normal infants (p<0.05), but there was no significant difference between 24 months old and normal children of the same age. The PDI of correction age 3,6,12,18 and 24 were significantly lower than those of normal infants (p<0.05), and did not show the trend of change with the increase of correction age.

The MDI and PDI results were compared with the mean of 100 in the normal population at 3 months of age (p<0.05) and lower than in the healthy population at 18 months of age (p<0.05), and the PDI measured at all follow-up time points were significantly lower than those of normal infants of the same age. (Table 1 and Table 2)

Physical growth assessment

The weight-for-age z-score (WAZ), height-for-age Z-score (HAZ), head circumference-for-age Z-score (HCZ), and weight-for-height Z score (WHZ) were assessed in the cases at correct age of 3,6,12,18 and 24 months. The prevalence of malnutrition was assessed as shown in Figure 2.

The trend test showed (see Table 4) that the WHZ gradually approached normal with the increase of monthly age (p<0.05), while the HCZ gradually decreased with the increase of corrected monthly age (p<0.05). WAZ and HAZ did not show a trend that changes with the corrected age increase.

neuroimaging

Head ultrasound monitoring and head MRI scan were completed as planned. About 87–93% of cases were completely normal, and 78.82% and 90.50% were completely normal at 40 weeks and 12 months, respectively. Few cases had experienced significant neuroimagng abnormalities (Figure 3).

All children completed aEEG examination at 40 weeks of correction, 3 months and 6 months. The results showed mild abnormalities in very minor children. (Table 4)

Risk factors for abnormal MDI and PDI

According to univariate linear regression and multivariate linear regression, WAZ at corrected 40 weeks, PVL of brain MRI at 12 months old diagnosis is the risk factor of MDI at corrected 24 months old. There is a positive relationship between the WAZ at corrected 40 weeks old and MDI at corrected 24 months old

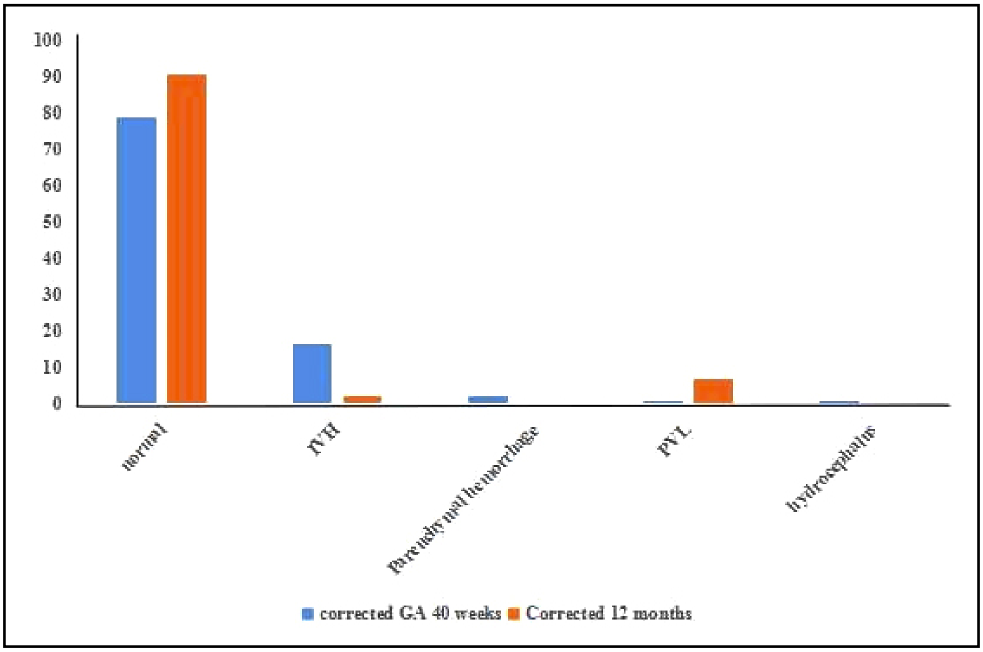

Fig. 3. Head ultrasound results of different days of age

(β=7.058, p=0.019). If the PVL diagnosed by brain MRI at 12-month-old, the MDI at corrected 24 months was lower (β=-27.686, p=0.006) (Table 5).

According to univariate linear regression and multivariate linear regression, ROPand NBNA score at 40 weeks and WAZ at corrected 6 months are the risk factors of the PDI at corrected 24 months old. The PDI of Children with ROP but needn't surgery was higher than others (β=17.716, p=0.013). There is a positive relationship between WAZ at corrected 6 months old and the PDI at corrected 24 months old (β=5.867, p=0.044). There is a positive relationship between NBNA score at 40 weeks and the PDI at corrected 24 months old (β=1.108, p=0.010). (Table 6)

DISCUSSION

Clinically, newborns with less than 1500 g of birth weight are called very low birth weight infants. According to the survey, about 15 million very low-birth-weight babies are born every year, accounting for more than a tenth of those born in the year, including 1.17 million in China (Montirosso *et al.* 2016). The survival rate of very low birth weight infants has improved significantly with the continuous progress of neonatal emergency medicine and reproductive medicine (Burke 2006). However, due to the poor organs and adaptability of healthy newborns, the brain is not mature, nerve reflex needs to be improved and other reasons, such as respiratory distress, sucking and swallowing disorders are prone to complications, resulting in malnutrition, behavioral state, decreased tissue capacity, stunting and other sequelae (Sharma *etal.* 2019). At present, the development trend of neonatal science is no longer only concerned with reducing the mortality rate of very low birth weight infants, and the physical and mental development of newborns is paid more and more attention by clinical first-line medical staff. Analysis of the parameters of very low birth weight infants admitted NICU our hospital, To assess physical and neurological

Tab. 1. Comparison of MDI and normal population mean (100) for preterm infants at different ages

Corrected age (month)	t	df	*p*-values	Mean Difference	95% CI of the difference	
					Lower	Upper
3	5.592	82	<0.001*	10.217	6.58	13.85
6	0.517	82	0.606	0.964	-2.74	4.67
12	-.767	82	0.445	-1.795	-6.45	2.86
18	-2.781	82	0.007*	-6.964	-11.95	-1.98
24	-1.636	82	0.106	-4.289	-9.50	0.92

*P<0.05. MDI, Mental developmental index; PDI, Psychomotor developmental index; VLBW, Very low birth weight; CI, Confidence interval.

Tab. 2. Comparison of PDI and normal population mean (100) for preterm infants at different ages

Corrected age (month)	t	df	*p*-values	Mean Difference	95% CI of the difference	
					Lower	Upper
3	-3.181	82	0.002*	-7.964	-12.94	-2.98
6	-4.304	82	<0.001*	-8.542	-12.49	-4.59
12	-4.919	82	<0.001*	-9.542	-13.40	-5.68
18	-4.955	82	<0.001*	-11.542	-16.18	-6.91
24	-2.403	82	0.019*	-5.747	-10.50	-0.99

*$P<0.05$.

development within 2 years of life, To explore the prognostic factors of neurodevelopment in very low birth weight infants. And it turns out that MDI rises early, And then gradually, The final age of 2 is similar to that of healthy children. And PDI has been showing a marked reduction from normal age, And did not show the trend of change with the correction of age growth. The correction of 40 weeks WAZ, 12 months old skull MRI abnormality is the influencing factor to correct 24 months old MDI. ROP correction of 6-month-old WAZ and NBNA is the influencing factor of 24-month-old PDI.

According to this study, the mental and intellectual development level of very low birth weight children increased first and then decreased with the increase of corrected age ($p<0.001$). The MDI of correcting 3 months old was significantly higher than that of normal infants ($p<0.05$). The level of intelligence development in the early postnatal period is significantly higher than that in healthy infants, which may be due to the soft stimulation of sound, light and touch after delivery of very low birth weight infants. The MDI of 18 months was significantly lower than that of normal children of the same age ($p<0.05$), but there was no significant difference between MDI and normal children of the same age at 24 months of age, indicating that the effect of this stimulation after early delivery led to the early development of intelligence gradually disappeared with the age of 1 and a half years, and reached the lowest point at 1 and a half years of age. With the early intervention of intensive training of, early intensive training, there was no significant difference between the level of intellectual development and healthy children at 2 years of age. Darlow, BA tested 229 VLBW adults and suggested VLBW adults have mean IQ scores 9 to 11 points below controls (Darlow *et al.* 2020).

The measured PDI at all follow-up time points (corrected age 3, 6, 12, 18, 24 months) were significantly lower than those of normal infants of the same age ($p<0.05$), and did not show a change trend with the corrected age. As most scholars at home and abroad conclude, the risk of VLBW motor dysfunction is much higher than that of ordinary newborns. Deng, Y (Deng *et al.* 2016) included of 61 VLBW preterm infants underwent a 12-month Denver development screening test (DDST). He found that within the first year after birth, the proportion of infants with abnormal DQ screened by DDST is high. Yaari (Yaari *et al.* 2018) tracked the neurodevelopment of preterm infants to varying degrees and found that extremely preterm and very preterm infants scored significantly lower in all areas of cognition, language and exercise than normal term infants. Kono, Y (Kono, 2020) analyzed of neurodevelopmental conditions of more than 40,000 VLBW born in Japan in the past decade shows that the impairment rates in the assessed infants were 7.1% for CP, 1.8% for blindness, 0.9% for hearing impairment, 15.9% for a DQ <70, and 19.1% for NDI. The NRNJ follow-up study results suggested that children born with a VLBW remained at high risk of NDI in early

Tab. 3. The results of the trend test of the parameters of body growth in different months

Corrected age (month)	WAZ	F	P	HAZ	F	P	HCZ	F	P	WHZ	F	P
40 weeks	-1.19±1.77	1.559	0.212	-0.78±1.80	1.163	0.281	-0.67±1.62	9.634	0.002*	-0.92±1.25	2.971	0.012*
3	-0.78±1.68			-0.57±1.69			-0.94±1.52			-0.37±1.29		
6	-0.42±1.34			-0.18±1.45			-0.59±1.33			-0.45±1.24		
12	-0.70±1.61			-0.57±1.94			-0.83±1.51			-0.22±1.10		
18	-0.50±1.47			-0.43±1.92			-1.12±1.62			-0.54±1.38		
24	-0.81±1.87			-1.04±2.66			-1.37±2.03			-0.28±1.30		

Tab. 4. Children completed aEEG examination at 40 weeks of correction, 3 months and 6 months

aEEG		Corrected 40 weeks (n=85)	Corrected 3 months (n=85)	Corrected 6 months (n=85)
Background pattern				
	Normal	85	85	85
	Mildly abnormal	0	0	0
	Severe abnormal	0	0	0
SWC				
	Developed SWC	5	81	82
	Immature SWC	80	4	3
	Absent SWC	0	0	0
Seizure				
	None	85	85	85
	Single attack	0	0	0
	Recurrent attack	0	0	0

childhood. Pascal, A (Pascal *et al.* 2020) analysis of more than 1,000 births from 2014 to 2016 VLBW, followed up to 2 years old. The results showed that 19.3%, 18.9% and 41.8% of infants had motor, cognitive and language delays, respectively. CP. diagnosed in 4.3% of infants. Nagy, BE (Nagy *et al.* 2021). The results of 305 BSID at age VLBW2, showing an increased risk of developmental delay in very low birth weight (ELBW) children:12.73 times exercise (95% CI =2.8–57.5), cognitive 9.81 times (95% CI =3.2–29.6) and language 3.91 times (95% CI =1.6–9.4) and social affective skills (95% CI =1.6–9.5).

The WHZ of the children in this group gradually approached normal with the increase of monthly age ($p<0.05$), while the HCZ gradually decreased with the increase of corrected monthly age ($p<0.05$). WAZ, HAZ does not show a trend that changes with the corrected age increase. As the age of the VLBW increases, the results show that the head circumference is smaller and more obvious. Deng Y, (Deng *et al.* 2016) included 61 VLBW preterm infants underwent 12 months of growth and development monitoring, and the results showed that peak body mass index Z scores (BAZ) and WHZ appeared at 1 month of the corrected age. At the corrected 40 weeks of age, the incidence of underweight, growth retardation, wasting, microcephaly, overweight and obesity was 15%, 16%, 11%, 13%, 20% and 10%, respectively. VLBW premature infants showed significant growth deviations within 3 months of the corrected age. Mackay, CA (Mackay *et al.* 2021) The physical development data of 151 VLBW at 40 weeks showed that the Z scores of men and women at 40 weeks were -2.5,-2.1 and -1.2, respectively.

The results of this study showed that only 40 weeks WAZ, 12 months old skull MRI were the influencing factors to correct 24 months old MDI. The correction of 40 weeks WAZ was positively correlated; When the 12-month-old skull MRI PVL diagnosed, to correct the low MDI. However, Fenton, TR (Fenton *et al.* 2021) suggests that preterm infant 36-week anthropometric measurements are not accurate predictors of cognitive impairment, consistent with the results of this study, brain injury and low maternal education are better predictors of cognitive impairment. However, the physical growth of very low birth weight infants is related to the prognosis of nerve development and is still widely supported. Darlow, BA tested 229 VLBW adults on the Wechsler Abbreviated Scale of Intelligence at 7 to 8 years and 26 to 30 years. Parental education and birthweight are the strongest predictors of IQ (Darlow *et al.* 2020). The single factor analysis of 24 months old MDI in this study also showed that the mother's education level was positively correlated with the MDI, but the inclusion of multivariate regression analysis showed that the correlation was not statistically significant continue to follow up or expand the sample size for further study. This study showed that the MDI of correcting 24-month-old skull MRI was lower when PVL was diagnosed, Consistent with the results of foreign scholars Inage (Inage *et al.* 2000; Kelly *et al.* 2016; Lin *et al.* 2020) periventricular leukomalacia in premature infants can lead to neurological sequelae and mental disorders. As early as 2014, Rose, J (Rose *et al.* 2014) noted structural brain abnormalities identified at near-term age have been recognized as potential predictors of neurodevelopment in children born preterm. The recent development of neuroimaging also proposes new examination methods and parameters that can be used for VLBW. Choi, YH (Choi *et al.* 2021) indicate the FA of MCP at near-term age may predict developmental outcomes of VLBW infants at 18 months of corrected age. Perhaps provide new directions for early MRI to predict neurodevelopmental outcomes. Groer, M (Groer *et al.* 2020) referred early growth patterns can

Tab. 5. Analysis of risk factors of MDI by univariate linear regression and multivariate linear regression

Variables		β	Standard error	t	P
ROP[a]	ROP but needn't surgery	-9.079	7.287	-1.250	0.217
	ROP and need surgery	-16.666	12.204	-1.370	0.177
Surgery history during hospitalization[b]	underwent surgery	14.234	9.589	1.480	0.142
MRI at corrected 12 months[c]	IVH	-22.147	20.845	-1.060	0.292
	PVL	-27.686	9.745	-2.840	0.006*
Invasive ventilation time		-0.013	0.020	-0.640	0.526
non-invasive positive pressure ventilation time		-0.009	0.014	-0.600	0.547
The rate of weight growth in 4 weeks after birth(g/kg/day)		1.102	0.572	1.930	0.058
WAZ at corrected 40 weeks		7.058	2.927	2.410	0.019*
HCZ at corrected 40 weeks		-3.865	3.043	-1.270	0.208
WAZ at corrected 6 months		3.181	2.385	1.330	0.187
length of stay		0.062	0.141	0.440	0.660
age at delivery		0.496	0.444	1.120	0.267

[a] reference group:no ROP group; [b] reference group:no surgery group; [c] no ROP group:MRI shows normal

affect later neurodevelopmental and anthropometric potentials. Ramel, SE (Ramel *et al.* 2020) indexed optimizing caloric intake, irrespective of illness is critical for enhancing body composition, and by extension, neurodevelopmental outcomes for preterm infants. The single - factor analysis of this study showed that the rate of weight gain within four weeks after life was positively associated with the 24-month age MDI, but not after a multifactor analysis.

The results of this study showed that ROP, correction of 6 months old WAZ and NBNA were the influencing factors of 24 months old PDI. Children who have reached ROP diagnosis but who do not need surgical treatment, the age of 24 months PDI higher (β=17.716, p=0.013); The correction of 6 month old WAZ was positively correlated (β=5.867, p=0.044); The correction NBNA score at 40 weeks was positively correlated (β=1.108, p=0.010). This study showed that the correction of 6 months old WAZ was positively correlated with the PDI level of 24 months old, which was consistent with the conclusions of foreign scholars. As if Blakstad, EW (Blakstad *et al.* 2015) Noting that optimal nutritional supply for infants with very low birth weight (VLBW: BW <1,500 g) is essential for growth and neurodevelopment, studies have shown that infants receiving enhanced nutrition respond more consistently to overall exercise. Medina-Alva, P (Medina-Alva *et al.* 2019) suggested that the combination of head circumference, cranial ultrasound and neurological examination at term age is useful to predict NDD in VLBW preterm infants through the prospective follow-up study of 132 VLBW infants. Consistent with the conclusion of this study, the correction NBNA score at 40 weeks was positively correlated with the PDI level at 24 months of age. Correction of term neurological examination can predict long-term motor development. Oommen, SP (Oommen *et al.* 2019) indexed that poor post-natal growth was an important determinant of the developmental outcome by analyzing 422 VLBW infants' follow-up results.

In recent years, with the improvement of neonatal treatment technology, the survival rate of premature infants under 34 weeks of gestational age is greatly improved, but the long-term quality of life is still worrying. Long hospital stays and high incidence of complications in early and middle-term preterm infants greatly increase the risk of long-term neurobehavioral abnormalities. All parameters during hospitalization were analyzed in order to find more convenient predictors for VLBW long-term poor prognosis. The results of this study showed that the VLBW gradually became symmetrical with the increase of age, but the head circumference was small and obvious; the intelligence level of the VLBW increased early and then gradually decreased to the average level of healthy children, while the exercise level was significantly lower than that of healthy children. The Z value of VLBW birth weight by age. However, due to the limitation of the number of cases, this study failed to carry out subgroup analysis of different degrees of abnormal clinical indicators. If more clinical samples can be collected in future studies, the prediction model of long-term neurodevelopmental outcome can be constructed by synthesizing clinical parameters VLBW neuroelectrophysiology and neuroimaging results.

Tab. 6. Analysis of risk factors of PDI by univariate linear regression and multivariate linear regression

Variables		*β*	Standard error	*t*	*P*
ROP [a]	1	17.716	6.940	2.550	0.013*
	2	-10.290	8.626	-1.190	0.237
non-invasive positive pressure ventilation time		-0.010	0.012	-0.800	0.429
WAZ at corrected 40 weeks		0.448	2.657	0.170	0.867
HCZ at corrected 40 weeks		-1.504	2.781	-0.540	0.591
WAZat corrected 6 months		5.867	2.851	2.060	0.044*
WHZ at corrected 6 months		-2.263	2.399	-0.940	0.349
NBNA score		1.108	0.420	2.640	0.010*
the educational background of mother [b]	1	3.918	23.208	0.170	0.866
	2	8.252	23.181	0.360	0.723
Brain MRI at corrected 40 weeks [c]	1	7.859	6.268	1.250	0.214
	2	-28.750	14.886	-1.930	0.058
	3	-15.223	19.382	-0.790	0.435
	4	-7.450	19.429	-0.380	0.703
Mother with pre-eclampsia [d]	1	-8.883	5.371	-1.650	

[a] reference group:no ROP group; [b] reference group:the educational background of mother-Junior high graduation below;
[c] reference group:MRI shows normal; [d] reference group:Mother without pre-eclampsia

With the change of fertility policy and the increase of elderly mothers, the number of premature infants may increase. Given the high risk of preterm infants in neurophysiological and psychological development, more attention, closer follow-up and more active early intervention are needed. In addition, it is necessary to improve the parenting ability and pay attention to their mental health, form a long-term follow-up monitoring system for the early development of premature infants, and then comprehensively analyze its influencing factors. Make full use of the protective factors of early development of premature infants to improve the quality of life of premature infants.

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