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Pei Zhao
Wuhan Children's Hospital, Huazhong University of Science &Technology
Qiong Fang
Wuhan Children's Hospital, Huazhong University of Science &Technology
Ting Gao
Wuhan Children's Hospital, Huazhong University of Science &Technology
Linling Gui
guilinling815@163.com
Wuhan Children's Hospital, Huazhong University of Science &Technology

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Pei Zhao[1, 3], Qiong Fang[2, 3], Ting Gao[2], Linling Gui[2,*]

[1] Department of Child Health Care, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science &Technology, Wuhan, China.

[2] Department of Neonatal Surgery, Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science &Technology, Wuhan, China.

[3] These authors contributed equally: Pei Zhao, Qiong Fang

*Corresponding author. Tel:+86 18163511982, email: guilinling815@163.com

BACKGROUND: To investigate changes in neuropsychological development in preterm infants with a temporary small intestinal stoma before and after stoma closure, and to examine the influence of nutritional status on developmental levels, in order to guide early clinical intervention.

METHODS: A total of 38 preterm infants with a temporary small intestinal stoma were enrolled. A self-controlled comparison was conducted to assess differences in neurodevelopment before stoma closure and at 6 months post-closure. Additionally, 49 preterm infants without a stoma during the same period were recruited as a control group. Developmental quotients (DQs) across five major neurofunctional domains were compared among the groups, and the correlation between DQ and nutritional status was analyzed.

RESULTS: At 6 months after stoma closure, DQs in all domains were significantly improved compared with pre-closure values ($P < 0.05$). DQ showed a weak positive correlation with nutritional level ($r = 0.401$, $P < 0.05$). At 6 months post-closure, neurodevelopmental parameters in the stoma group remained slightly but significantly lower than those in the control group ($P < 0.05$).

CONCLUSION: A temporary small intestinal stoma delays early neuropsychological development in preterm infants. Stoma closure effectively reverses this developmental lag. Clinical practice should incorporate long-term neurodevelopmental follow-up after stoma closure, along with nutritional management and early rehabilitation interventions, to support catch-up growth in neurodevelopment.

IMPACT:

- This study clarifies the adverse effect of temporary small intestinal stoma on early neurodevelopment in preterm infants, confirming that stoma closure contributes to the catch-up of neuropsychological development.
- Nutritional status is a modifiable factor correlated with neurodevelopmental outcomes of preterm infants with intestinal stoma, which provides a targeted regulatory direction for clinical nursing.
- This finding emphasizes the necessity of combined nutritional optimization and early neurorehabilitation for preterm infants after stoma closure to improve their long-term neurological prognosis.

INTRODUCTION

With the continuous improvement of neonatal intensive care technology and perioperative management systems in pediatric surgery, the clinical survival rate of preterm infants with critical digestive system diseases, including congenital gastrointestinal malformations and necrotizing enterocolitis (NEC), has significantly increased. Enterostomy is a core emergency surgical procedure that saves the lives of these critically ill infants. It effectively diverts intestinal contents, relieves high intestinal pressure, and promotes the repair of diseased intestinal segments, and has now been widely applied in neonatal surgery[1]. However, small intestinal enterostomy interrupts the physiological continuity of the intestine, reduces the effective intestinal absorption surface area, and disrupts the homeostatic regulatory mechanism of gastrointestinal hormones. Consequently, affected infants are highly prone to complications such as intractable diarrhea, recurrent electrolyte imbalances, and intestinal nutrient malabsorption[2]. As the organs of preterm infants are not yet fully developed, their compensatory capacity and tolerance are far lower than those of full-

term infants. They are therefore more significantly affected by the aforementioned postoperative complications, which predisposes them to various short-term adverse outcomes, including physical growth retardation, immune dysfunction, and an increased risk of infection[3].

A meta-analysis has indicated that most survivors of NEC experience neurodevelopmental impairments. These infants have a higher risk of developing intraventricular hemorrhage and periventricular leukomalacia than preterm infants without NEC. Furthermore, the severity of neurodevelopmental impairment correlates with the severity of intestinal injury, and among NEC patients, those who require surgery demonstrate more severe neurodevelopmental impairments than those managed non-surgically[4-7]. The period from birth to 6 months of corrected age is a critical window for neuronal proliferation, differentiation, and myelination in preterm infants. During this period, brain tissue exhibits strong plasticity but is also highly sensitive to adverse stimuli, including nutritional imbalance, chronic inflammation, and internal environmental disturbances. Infants following small intestinal enterostomy are in a prolonged state of negative nitrogen balance. Coupled with multiple stressors such as persistent chronic inflammation and recurrent electrolyte imbalances, this imposes a "second hit" on the developing central nervous system. This process impairs normal neuronal proliferation, migration, and myelination, thereby increasing the risk of multidimensional neurodevelopmental delays, including in motor function, language, cognition, and social behavior.

Based on the above, this study enrolled preterm infants with a temporary small intestinal stoma as the research subjects and employed the Neuropsychological Development Scale for Children Aged 0–6 Years to conduct a multidimensional neurodevelopmental assessment. The aim is to provide an objective clinical basis for early screening of preterm infants at high risk for neurodevelopmental delay, the development of individualized nutritional support protocols, and the formulation of early neurorehabilitation intervention strategies. Ultimately, this study seeks to advance the philosophy of neonatal surgical care—from simply ensuring patient survival to

integrating quality of life and long-term neurodevelopmental outcomes—thereby comprehensively optimizing the long-term recovery and outcomes of preterm infants with a small intestinal stoma.

MATERIALS AND METHODS

General information

A retrospective analysis was conducted on preterm infants who underwent small intestinal enterostomy at Wuhan Children's Hospital affiliated with Tongji Medical College, Huazhong University of Science and Technology, from January 2024 to January 2026. These infants were enrolled as the study subjects (Stoma Group). Inclusion criteria: ① Gestational age < 37 weeks; ② Underwent small intestinal enterostomy due to conditions such as necrotizing enterocolitis, intestinal atresia, or meconium peritonitis. Exclusion criteria: ① Death during hospitalization or follow-up period; ② Missing or incomplete clinical data. Additionally, preterm infants hospitalized during the same period with similar corrected gestational ages were selected as the control group. Inclusion criteria for the control group: ① Gestational age < 37 weeks; ② No history of enterostomy surgery; ③ No severe neurological disorders. Exclusion criteria were the same as those for the stoma group.

Assessment methods

General information including name, sex, gestational age, corrected gestational age, birth weight, enrollment weight, and corrected age was recorded for all infants. The Neuropsychological Development Scale for Children Aged 0–6 Years was used for assessment. The stoma group was evaluated once before stoma closure and again at 6 months after closure. The control group was evaluated at enrollment and again at 6 months later. The assessment covered five functional domains: gross motor, fine motor, adaptive ability, language, and social behavior, and the developmental quotient (DQ) was calculated.

A self-controlled before-and-after study design was employed to compare changes in neurodevelopmental levels in the stoma group before and after stoma closure.

Additionally, using matched preterm infants from the same period as controls, the study compared developmental levels between the stoma group at 6 months after closure and the control group at the same corrected age. No intervention was applied to the control group.

The WHO Child Growth Standards Z-score was used to calculate the weight Z-score for each subject using the formula: $Z = (X - \text{Median}) / SD$, where X represents the measured weight, Median is the median weight for children of the same age and sex (WHO standards), and SD is the standard deviation of weight for children of the same age and sex (WHO standards). The Z-score was used to evaluate the long-term/chronic nutritional status of the infants, and correlation analysis was performed between the Z-score and the developmental quotient (DQ).

Ethical approval

This study was approved by the Ethics Committee of Wuhan Children's Hospital, Tongji Medical College, Huazhong University of Science and Technology (Approval No.: 2026R046-E01). Clinical trial number: not applicable.

Statistical analysis

Statistical analysis was performed using SPSS 24.0 software. For normally distributed continuous data, independent samples t-test was used for between-group comparisons, and paired t-test was used for before-and-after comparisons within the same group. Data were expressed as mean ± standard deviation (x±s). For non-normally distributed continuous data, the Mann-Whitney U test was used, and data were expressed as median (interquartile range) [M (P25, P75)]. Categorical data were analyzed using the $\chi 2$ test and expressed as frequencies and percentages (%). A *P*-value < 0.05 was considered statistically significant.

RESULTS

General characteristics of infants with small intestinal enterostomy

A total of 88 preterm infants were enrolled in this study, including 39 cases in the enterostomy group and 49 cases in the non-enterostomy group. There were no significant between-group differences in gender distribution, gestational age at birth, corrected gestational age at enrollment, twin pregnancy rate and mode of delivery (P>0.05), indicating comparable baseline data (Table 1). The birth weight and body weight at enrollment were significantly lower in the enterostomy group than in the non-enterostomy group (P<0.05). These baseline differences will be adjusted for in subsequent analyses of neurodevelopmental outcomes.

Comparison of neurodevelopmental levels before and after intervention

Before intervention, the total DQ and scores in all five domains (gross motor, fine motor, adaptive ability, language, and social behavior) of the Neuropsychological Development Scale for Children Aged 0–6 Years were significantly lower in the stoma group than in the control group (Table 2), and all differences were statistically significant ($P < 0.001$).In terms of the magnitude of improvement across domains, the stoma group showed the greatest improvement in the adaptive ability domain, with the median score increasing from 45.0 to 75.0 (an increase of 30 points), followed by the language domain, with the median score increasing from 47.0 to 72.0 (an increase of 25 points). In contrast, the control group showed relatively balanced improvements across all domains, with the median total DQ increasing by 11 points. At 6 months after intervention, all domain scores and the total DQ in the stoma group were significantly improved compared with pre-intervention levels ($P < 0.05$), but remained slightly lower than those of the control group at the same time point ($P < 0.05$)..

Given the imbalance in baseline birth weight and weight at enrollment between the two groups, rank-transformed analysis of covariance (ANCOVA) was performed to adjust for birth weight and weight at enrollment, in order to eliminate the confounding effect of weight on neurodevelopmental outcomes. The results showed that after adjusting for baseline weight confounders, all neurodevelopmental scores in the stoma group remained significantly lower than those in the control group both before and after intervention, and the differences between groups remained statistically significant ($P <$

0.05). These findings suggest that even after removing the effect of weight differences, the neurodevelopmental level of preterm infants with an enterostomy continues to lag behind that of normal preterm infants, and that enterostomy is an independent risk factor affecting neurodevelopment in preterm infants.

Correlation analysis between nutritional status and developmental quotient

Spearman rank correlation analysis and linear regression fitting were used to compare the correlation between nutritional Z-score at enrollment and DQ between the two groups（Fig.1）. The results showed that in the control group, nutritional Z-score was significantly and strongly positively correlated with DQ ($r = 0.719$, $P < 0.001$, $R^2 = 0.517$). In the stoma group, nutritional Z-score showed a weak positive correlation with DQ ($r = 0.401$, $P < 0.05$, $R^2 = 0.161$). The difference in regression slopes between the two groups suggests that enterostomy may attenuate the impact of nutritional status on neurodevelopment.

DISCUSSION

The brain tissue of preterm infants is not yet fully developed, making them highly susceptible to various external factors such as disease-related trauma, insufficient nutritional intake, physical pain, and hospitalization stress. Consequently, they are at increased risk of long-term adverse outcomes, including neurodevelopmental delay and lag in motor and language function development [8-10]. Studies have shown that preterm infants have physiological vulnerabilities during the stage of brain development, which serve as the neurological basis for poor neurodevelopmental outcomes. These vulnerabilities are mainly attributed to impaired synaptogenesis and myelination [11]. For preterm infants with an enterostomy, in addition to the inherent developmental deficits of prematurity, they are also exposed to additional stressors including organic gastrointestinal lesions, surgical trauma, and long-term postoperative stoma care-related stimulation. Consequently, their risk of neurodevelopmental disorders is further increased [4, 12].

The results of this study showed that before intervention, the stoma group had significantly lower scores than the control group in all six neurodevelopmental domains: DQ, gross motor, fine motor, adaptive ability, language, and social behavior. After stoma closure intervention, the neurodevelopmental level of the stoma group improved significantly; however, scores in all domains remained significantly lower than those of the control group. In the baseline comparison between the two groups, the stoma group had lower birth weight and lower weight at enrollment than the control group. Low birth weight itself is a well-established risk factor for adverse neurodevelopmental outcomes in preterm infants. Notably, preterm infants with lower birth weight are more likely to develop NEC and subsequently require enterostomy. To eliminate the confounding effect of baseline weight differences on the study results, rank-transformed analysis of ANCOVA was used to adjust for these two confounding variables. After adjustment, the between-group differences remained statistically significant. These findings confirm that, even after removing the effect of weight differences, enterostomy remains an independent risk factor affecting neurodevelopment in preterm infants. The neurodevelopmental delay observed in preterm infants with an enterostomy is not solely attributable to low birth weight; rather, enterostomy-related diseases and traumatic stress play a critical negative role.

Based on the findings of this study and a review of the relevant literature, the comprehensive neurodevelopmental delay observed in preterm infants with an enterostomy is primarily attributable to the following factors: First, surgical trauma and persistent pain stress. The surgical procedure itself (including anesthetics, antibiotics, etc.) may exert negative effects on the developing brain [13]. Persistent pain from postoperative wound pain, daily stoma appliance changes, and fecal irritation activates the infant's hypothalamic-pituitary-adrenal (HPA) axis, leading to sustained excessive secretion of stress hormones such as cortisol. This damages immature brain neurons, impedes neuronal proliferation and differentiation, and consequently inhibits the development of motor, language, and other multidimensional neurological functions. Second, nutritional absorption disorders. Enterostomy results in substantial loss of

intestinal fluid, leading to inadequate intake and absorption of essential nutrients for neurodevelopment, including proteins, fatty acids, and vitamins. This insufficiency fails to meet the rapid developmental demands of brain tissue. Third, hospitalization isolation and lack of parent-child interaction. Preterm infants with an enterostomy have longer hospital stays and remain in the closed environment of the neonatal intensive care unit (NICU) for extended periods. They lack beneficial sensory stimuli such as maternal holding, breastfeeding, and parental soothing, which directly affects the development of social behavior, language, and adaptive abilities.

The results of this study also showed that after stoma closure and return to the home environment, both the stoma group and the control group demonstrated significant improvements in all neurodevelopmental scores compared with pre-intervention levels. This indicates that early rehabilitation interventions—including tactile stimulation, motor function training, audiovisual intervention, and parent-child touching—have a positive promoting effect on neurodevelopment in preterm infants. However, it is noteworthy that even with the same interventions, the rate of neurodevelopmental catch-up growth in the surgical preterm infants remained slower than that in normal preterm infants. The reason is that standard, uniform early intervention protocols cannot fully offset the neurodevelopmental damage caused by intestinal resection or underlying gastrointestinal malformations.

Furthermore, the nutritional Z-score showed a strong positive correlation with DQ in the control group, whereas only a weak positive correlation was observed in the stoma group, with the coefficient of determination (R^2) decreasing from 0.517 to 0.161. This finding suggests that after enterostomy, neurodevelopment in affected infants is no longer primarily determined by nutritional status, but rather is influenced by multiple interacting factors.

Therefore, for preterm infants with an enterostomy, the intervention model used for general preterm infants cannot be directly applied. Instead, a tailored intervention strategy integrating pain management, enteral nutrition support, and individualized neurorehabilitation should be developed. Emphasis should be placed on alleviating

postoperative pain and optimizing enteral nutrition supply. Only on this basis can neurodevelopmental rehabilitation training be implemented to effectively narrow the developmental gap between these infants and healthy preterm infants. Studies have shown that vitamin D supplementation (800 IU/day) in preterm infants improves mineral absorption and bone formation, and provides neuroprotective effects through anti-inflammatory and antioxidant mechanisms [14]. Kangaroo mother care is a simple and cost-effective intervention that effectively reduces neonatal mortality and the risk of infection in low-birth-weight infants, and the earlier it is initiated, the better [15]. Furthermore, breastfeeding in preterm infants has a positive effect on cognitive development and may reduce the risk of neurodevelopmental disorders [16].

In summary, the neurodevelopmental management of infants with an enterostomy should not be limited to nutritional support alone. Comprehensive intervention measures are necessary, including optimizing perioperative management, reducing complications, strengthening early neurodevelopmental stimulation, and providing family support, in order to maximize the improvement of long-term outcomes in these infants.

Future research should include multicenter, large-sample prospective studies with extended follow-up until 24 months of corrected age to further investigate the long-term neurodevelopmental prognosis of preterm infants with an enterostomy. At the same time, individualized intervention protocols should be optimized, focusing on the two core challenges of pain management and nutritional support, and developing tailored early rehabilitation models specifically for preterm infants with an enterostomy, so as to maximally improve the neurodevelopmental outcomes of this high-risk population.

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AUTHOR CONTRIBUTOONS

P.Z was involved with: conceptualization, methodology, data curation, and writing-original draft preparation. Q.F was involved with the conceptualization, project administration, writing-review and editing. T.G were involved with investigation, data curation. L.G was involved with conceptualization, funding acquisition, writing-review and editing, and supervision.

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COMPETING INTERESTS

The authors declare no competing interests.

INFORMED CONSENT STATEMENT

Individual patient informed consent was waived for this study. All clinical data adopted in this study were fully anonymized and de-identified, with no personal identifiable information retained. The data are untraceable to specific patients and will not infringe patient rights. This study was conducted in accordance with the ethical principles stated in the Declaration of Helsinki and relevant institutional ethical guidelines.

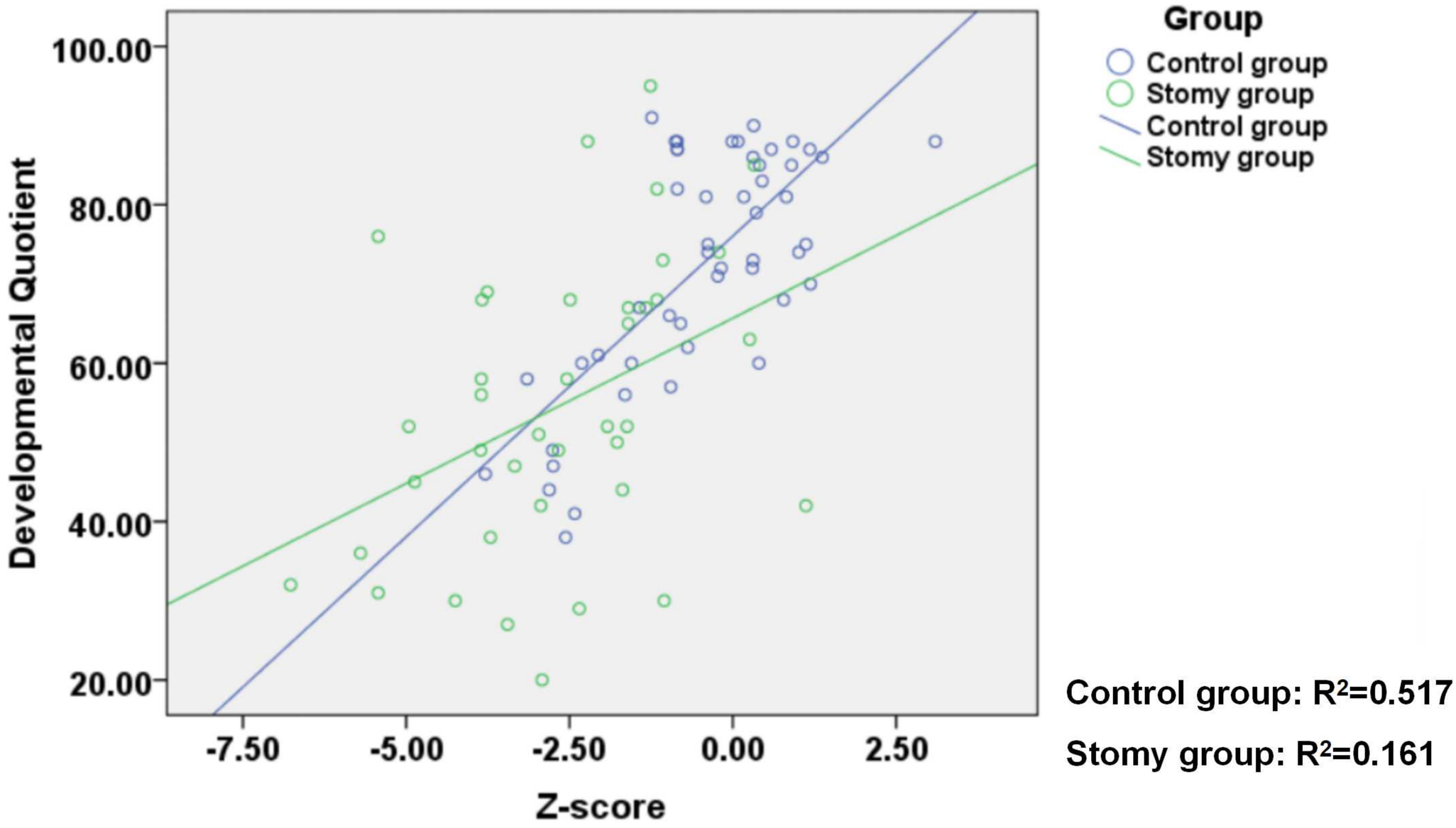


Figure 1. Correlation between nutritional Z-scores and DQ in the control group and stoma group.

Table 1 Comparison of general characteristics between enterostomy group and control group

Item	Item	Enterostomy group	Control group	Statistical value	*P* value
Gender	Male	22 (56.41%)	30 (61.22%)	0.208[a]	0.648
	Female	17 (43.59%)	19 (38.78%)		
Twin pregnancy	Yes	4 (10.53%)	11 (22.45%)	1.378[a]	0.240
	No	34 (89.47%)	38 (77.55%)		
Delivery mode	Cesarean section	34 (89.47%)	40 (81.63%)	0.510[a]	0.475
	Vaginal delivery	4 (10.53%)	9 (18.37%)		
Corrected age (months)		3.281±0.619	3.217±0.726	0.438[b]	0.663
Gestational age at birth (weeks)		32.00 (30.86, 34.86)	33.86 (30.86, 35.00)	727.5[c]	0.055
Birth weight (kg)		1.70 (1.40, 2.32)	2.00 (1.65, 2.51)	667.0[c]	0.023
Body weight at enrollment (kg)		4.924±0.763	6.314±1.084	6.783[b]	0.001

Note: b indicates t-test; c indicates Mann-Whitney U test; a indicates χ^2 test.

Table 1 Comparison of neurodevelopmental indicators between enterostomy group and control group before and after intervention

Item	Time point	Enterostomy group	Control group	U value	*P* value	Adjusted *P* value
Developmental Quotient (DQ)	Before intervention	52.0 (42.0, 68.0)	74.0 (60.5, 86.5)	443	<0.001	0.001
	After intervention	71.0 (66.0, 79.0)	85.0 (74.5, 86.0)	478.5	<0.001	0.001
Gross Motor	Before intervention	47.0 (33.0, 63.0)	65.0 (56.5, 77.0)	508.5	<0.001	0.048
	After intervention	69.0 (62.0, 77.0)	77.0 (70.5, 85.0)	543.5	<0.001	0.010
Fine Motor	Before intervention	61.0 (39.0, 74.0)	82.0 (67.5, 90.5)	413	<0.001	0.004
	After intervention	71.0 (63.0, 78.0)	82.0 (74.0, 84.5)	487	<0.001	0.001
Adaptive Ability	Before intervention	45.0 (32.0, 71.0)	66.0 (47.0, 77.0)	650	<0.001	0.001
	After intervention	75.0 (68.0, 83.0)	85.0 (76.5, 89.0)	504.5	<0.001	0.001
Language	Before intervention	47.0 (30.0, 67.0)	77.0 (62.0, 97.0)	425	<0.001	0.000
	After intervention	72.0 (66.0, 83.0)	82.0 (73.0, 87.5)	529.5	<0.001	0.002
Social Behavior	Before intervention	61.0 (41.0, 76.0)	78.0 (64.5, 93.0)	517.5	<0.001	0.001
	After intervention	75.0 (70.0, 83.0)	83.0 (79.5, 90.0)	516.5	<0.001	0.008

Note: Adjusted factors included birth weight and weight at enrollment.