The Impact of Enteral Nutritional Support on Surgical Complications and Clinical Efficacy in Children With Neuroblastoma With Moderate or High Nutritional Risk

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AIM: This study aims to investigate the association between enteral nutritional support, surgical complication rates, and the nutritional improvement effect in pediatric neuroblastoma (NB) patients.
METHODS: This retrospective cohort study enrolled 94 neuroblastoma patients (≤14 years old) with moderate or high nutritional risk who underwent treatment at Hunan Children's Hospital between August 2019 and October 2021. Patients were assigned to a control group (n = 45), who received routine dietary guidance, and an experimental group (n = 49), who received enteral nutritional support along with routine dietary guidance. Group assignment indicated clinical decision-making by the treating clinicians, taking into account various parameters such as the children's tolerance to oral intake, the severity of digestive tract symptoms, the Nutrition Screening Tool for Childhood Cancer (SCAN) score, and caregivers' preferences. These clinical considerations were combined with input from caregivers when determining the nutritional protocol. The nutritional status, daily energy intake, and incidence of complications after surgery and chemotherapy were compared between groups.
RESULTS: Before treatment, no statistically meaningful variations in all indicators were observed between groups ($p > 0.05$). After surgery and chemotherapy, the experimental group showed substantially higher levels of physical indicators (mid-upper arm circumference [MUAC], triceps skinfold thickness [TSFT] and biochemical indicators (hemoglobin [Hb] and prealbumin [Pre-Alb]) than the control group ($p < 0.05$)). After surgery and chemotherapy, the experimental group exhibited substantially higher average daily energy and protein intake levels compared with the control group ($p < 0.05$). Additionally, the experimental group had significantly lower rates of postoperative complications (4.1% versus 24.4%, risk ratio [RR] = 0.168, 95% confidence interval [CI]: 0.041–0.690) and post-chemotherapy complications (2.0% versus 15.6%, RR = 0.128, 95% CI: 0.017–0.967) than the control group ($p < 0.05$). No adverse events related to enteral nutritional support occurred in the experimental group during the intervention period.
CONCLUSIONS: Enteral nutritional support can substantially improve the nutritional status and daily energy intake in neuroblastoma patients with moderate or high nutritional risk. This intervention can further decrease the likelihood of complications after surgery and chemotherapy.

Keywords: enteral nutritional support; neuroblastoma; moderate or high nutritional risk; surgical complications; nutritional improvement effect

Introduction

Neuroblastoma (NB) is an embryonal tumor that arises from immature precursor cells of the adrenal medulla or the paravertebral sympathetic ganglia. It primarily affects children, most commonly between 1 and 5 years of age, and accounts for approximately 14.6% of cancer-related mortalities [1]. Current treatment approaches for NB include surgery, chemotherapy, radiotherapy, and immunotherapy. Although advances over the past few decades have improved outcomes, with five-year survival rates in metastatic neuroblastoma cases rising from <20% to >50%, the overall prognosis for affected children remains unsatisfactory [2].

Management of neuroblastoma often requires a multimodal strategy, which can severely disrupt nutritional status and eventually affect normal growth and development [3]. Evidence indicates that a significant proportion of NB patients are already at nutritional risk, and their condition often worsens gradually after surgery, chemotherapy, and other treatments [4]. Children with moderate or high nutritional risk tend to exhibit relatively compromised immune function, predisposing them to a higher risk of treatment-related complications. These conditions reduce their tolerance and responsiveness to treatment, thereby impairing therapeutic

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efficacy and adversely affecting survival outcomes [5].

Enteral nutritional support therapy is a structured intervention to optimize nutritional status in these patients. It has been found to effectively lower the occurrence of complications, enhance the overall therapeutic effect, and improve the overall survival outcomes, while reducing the mortality rate [6]. Despite the moderate or high nutritional risk in children with NB, the role of enteral nutritional support therapy remains under-recognized in both clinical practice and by caregivers [7].

This study focuses on children with NB combined who are at moderate or high nutritional risk and are treated using a unified therapeutic pathway consisting of surgery followed by chemotherapy. It systematically evaluates the effect of enteral nutritional support, particularly short peptide or hydrolyzed formula, on short-term nutritional outcomes and the incidence of perioperative and chemotherapy-associated complications. Given the limited availability of population-specific data, our findings aim to provide clinical evidence for the development of standardized nutritional interventions in pediatric NB patients. This study further seeks to analyze the association between enteral nutritional support, postoperative complications, and improvement in nutritional status among this high nutritional patient group.

Methods

Patient Recruitment and Baseline Characteristics

This retrospective cohort study enrolled 94 children with neuroblastoma who were at moderate or high nutritional risk and underwent treatment at the Hunan Children's Hospital between August 2019 and October 2021. Based on the clinical treatment strategy selected during routine clinical management, patients were assigned to a control group (n = 45), who received routine dietary guidance, and an experimental group (n = 49), who received routine dietary guidance along with enteral nutritional support. Group assignments indicated clinical decision-making by the treating clinicians, taking into account various parameters such as the children's tolerance to oral intake, the severity of digestive tract symptoms, the Nutrition Screening Tool for Childhood Cancer (SCAN) score, and caregivers' preferences. These clinical considerations were combined with input from the caregiver when determining the nutritional protocol.

Baseline clinical characteristics such as gender, age, clinical stage, and risk stratification were comparable between the two groups, minimizing the risk of selection bias. The study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and obtained ethical approval from the Ethics Committee of Hunan Children's Hospital (approval number: 2023-003-07). Given the retrospective study design, the requirement for informed consent was waived by the Ethics Committee. All patient data were de-identified before analysis. No participants were dropped or lost during the follow-up period.

Inclusion and Exclusion Criteria

Inclusion criteria for patient selection were as follows: ① a confirmed diagnosis of neuroblastoma based on clinical and pathological evaluation; ② children with moderate or high nutritional risk using the SCAN [8]; ③ patients aged ≤14 years; ④ no evidence of major organ dysfunction; and ⑤ all children received a standardized treatment strategy consisting of complete or partial surgical resection of the tumor followed by 4 cycles of chemotherapy, in line with the standardized institutional clinical treatment protocol for pediatric NB adopted during 2019–2021 across different risk categories such as low/intermediate/high-risk NB.

Patients were excluded if they ① coexisted with severe systemic disease; ② had a known family history of psychiatric illness; ③ had undergone treatment for recurrent disease; ④ had an acute infectious disease; and ⑤ were unable to complete the planned course of treatment.

Nutrition Risk Screening

The SCAN was utilized to assess nutritional risk. This tool consists of 6 items, each with a score ranging from 1 to 2 points, giving a total of 10 points. A SCAN score of 3 or higher indicates a moderate or high nutritional risk in these patients. Further details of the SCAN assessment are shown in Table 1.

Treatment Protocols

All neuroblastoma patients (n = 94) with moderate or high nutritional risk underwent complete or partial surgical resection of the tumor, followed by 4 cycles of standard chemotherapy. According to the *Diagnosis and Treatment Standards for Childhood Neuroblastoma* [9] issued by the National Health Commission, the chemotherapy regimens were as follows: etoposide + cisplatin (EP) regimen — cyclophosphamide + doxorubicin + vincristine (CAV) regimen — etoposide + cisplatin (EP) regimen — cyclophosphamide + doxorubicin + vincristine (CAV) regimen (EP-CAV-EP-CAV). Each treatment cycle lasted 21 days.

Clinical evaluations were performed at three key time points of initial diagnosis, after tumor resection but before the initiation of the first chemotherapy cycle, and upon the completion of the fourth postoperative chemotherapy cycle. During the study, patients received chemotherapy according to the institutional treatment protocol for pediatric NB.

Nutritional Assessment and Intervention Procedures

(1) Before initiating nutritional intervention, dietary intake was evaluated using a structured, self-designed questionnaire consisting of 12 items. The tools assessed information on daily food type, quantity of intake, feeding frequency, and tolerance to oral intake, and were completed by caregivers under the guidance of nursing staff. To obtain more reliable information on habitual intake, a three-day dietary record was documented. Based on these data, dietary composition was evaluated, and individual energy

Table 1. Details of SCAN assessment scores.

Content	Yes	No
Does the child have a high-risk tumor?	1	0
Is the child receiving intensive treatment?	1	0
Does the child have digestive tract-related symptoms?	2	0
Was the child's oral nutrient intake insufficient in the past week?	2	0
Did the child experience weight loss in the past month?	2	0
Does the child have clinical manifestations related to malnutrition?	2	0

SCAN, Nutrition Screening Tool for Childhood Cancer.

and protein requirements were determined using the Recommended Nutrient Intake (RNI) guidelines [10]. Adjustments in daily intake were made according to body weight, with daily targets of 30–35 kcal/kg for energy and 1.5–2.0g/kg for protein, considering the increased metabolic demands associated with malignancy.

(2) Both study groups received standardized dietary guidance aligned with RNI recommendations for pediatric cancer patients. The guidance focused on a diet that was high in protein and calories, easily digestible, and administered in regular, measured amounts, while avoiding food likely to irritate the gastrointestinal tract. Furthermore, the dietary plan was individualized based on age, tolerance to oral intake, and gastrointestinal symptoms. An experienced nutritionist provided tailored advice during hospitalization and continued support after discharge.

(3) In addition to standard dietary guidance, patients in the experimental group received enteral nutrition (EN) intervention [11]. During neoadjuvant chemotherapy and postoperative chemotherapy phases, children aged ≥1 year were given a short peptide formula enriched with high medium-chain triglycerides (Xiaobaitai, 4.184 kJ/mL; nutrient content, 1 kcal/mL; protein, 3.6 g/100 mL; fat, 4.2 g/100 mL; carbohydrate, 10.8 g/100 mL). Whereas those aged <1 year received an extensively hydrolyzed formula (Aiershu, 4.184 kJ/mL; nutrient content, 1 kcal/mL; protein, 2.0 g/100 mL; fat, 3.8 g/100 mL; carbohydrate, 11.2 g/100 mL). The selection of enteral formulas was based on age and gastrointestinal tolerance according to clinical nutritional assessment.

The dosage of enteral nutrition was approximately one-quarter of the total daily energy requirement. This approach was based on the principle of gradual nutritional supplementation recommended for malnourished pediatric cancer patients in the "Expert Recommendations on the Standardized Process for Nutritional Management of Children with Hematological/Oncological Diseases" [11] and Tume et al. (2020) [6], aiming to reduce digestive tract intolerance associated with rapid or excessive feeding. The duration of the support lasted for 1–2 weeks: one week for children with good oral intake tolerance and up to two weeks for children with poor oral intake tolerance, based on clinical evaluation by nutritionists and pediatricians [12]. Adherence to nutritional support was monitored through documented intake of the enteral nutrition formula and caregiver feedback during follow-up. The remaining child's nutritional needs were provided through regular oral feeding. The control group received conventional oral dietary management according to routine clinical practice.

Observation Indicators

Nutritional Outcomes: Nutritional improvement was assessed through both physical and biochemical indicators. Physical indicators included body weight, height, body mass index (BMI), mid-upper arm circumference (MUAC), and triceps skinfold thickness (TSFT). The short-term changes in height largely reflect minor measurement fluctuations associated with variations in body composition rather than actual linear growth. BMI was calculated using the standard formula (weight kg/height m^2) to ensure consistency with weight and height data. Corrected-BMI (cBMI) was calculated to mitigate bias from tumour-associated fluid retention. Raw weight was adjusted by subtracting clinically-estimated excess fluid mass, while raw height remained unchanged for computation (cBMI = $\text{weight}_{\text{corrected}}/\text{height}^2$). Raw body weight and height plotted in Fig. 1 represent unadjusted bedside measurements. MUAC and TSFT served as primary nutritional markers owing to their low susceptibility to fluid shifts.

Biochemical indicators included hemoglobin (Hb), albumin (Alb), and prealbumin (Pre-Alb). Fasting venous blood samples (2 mL) were collected in the early morning at three time points, such as at initial diagnosis, after surgery, and after completion of chemotherapy. After centrifugation, the biochemical indicators were analyzed using standardized clinical assays: hemoglobin (Hb) by SLS spectrophotometry (Mindray Medical), albumin (Alb) by BCP method (Roche), and prealbumin (Pre-Alb) by immunoturbidimetry (UpingBio). All procedures followed the routine protocols of the hospital laboratory.

The primary indicators for evaluating nutritional status used in this study were MUAC and TSFT, as these measurements are less affected by tumor burden or fluid shifts and therefore provide a more reliable indication of the nutritional status of children with tumors [13]. Other indicators were used as supportive reference indicators.

We did not convert height and weight measurements into age- and sex-standardized Z-scores in the present study

for two main reasons. First, enrolled patients covered a wide age span from neonates up to 14 years old, and local Chinese pediatric growth standard Z-score databases lack unified, mature reference criteria for pediatric cancer children complicated by tumor-induced edema and cachexia, which would cause biased Z-score calculation. Second, this research focused on short-term perioperative and post-chemotherapy dynamic changes of nutritional status within individual patients rather than population-based normative comparison against healthy children; raw measured values were sufficient to reflect intergroup short-term anthropometric variations, while MUAC and TSFT were prioritized as core stable nutritional markers to avoid calculation bias from Z-score normalization.

Daily Energy Intake: Nutritional intake was evaluated in terms of energy and protein consumption. For each assessment point, the average daily intake was calculated based on 3 consecutive days of dietary record (one week after surgery and at the end of the fourth chemotherapy cycle). These data were recorded and analyzed by trained medical staff.

Complications: Both surgical and chemotherapy-associated complications were documented. Postoperative complications included wound dehiscence, infection, and exudation. Additional recovery-related indicators, including time to first oral intake and duration of postoperative hospital stay, were recorded and analyzed as supplementary outcomes. Chemotherapy-related complications included myelosuppression, organ dysfunction, and gastrointestinal adverse reactions. The severity of all complications was graded according to the Common Terminology Criteria for Adverse Events (CTCAE), version 5.0 (National Cancer Institute, Bethesda, MD, USA).

Statistical Analysis

Statistical analysis was conducted using SPSS version 22.0 (IBM Corp, Armonk, NY, USA). Before analysis, the normality of measurement data was assessed using the Shapiro-Wilk test, and homogeneity of variance was evaluated using Levene's test. For repeated measurements of nutritional indicators across the three time points (baseline, postoperative, and post-chemotherapy), repeated measures analysis of variance was used to determine time effects, group effects, and time × group interactions. When the assumption of sphericity was violated, the Greenhouse–Geisser correction was applied. When multiple comparisons were required, the Bonferroni correction method was used.

Measurement variables that met the assumption of normal distribution and homogeneity of variance were expressed as mean ± standard deviation ($\bar{x}\pm s$) and analyzed using an independent samples *t*-test for inter-group comparisons and a paired samples *t*-test for intra-group comparisons. Categorical variables were presented as frequencies and percentages and compared using the chi-square test.

To account for potential confounding, multivariate logistic regression analysis was performed for key outcome indicators, such as postoperative and chemotherapy-associated complications, with adjustment for age, clinical stage, and risk stratification. GraphPad Prism 8.0 (GraphPad Software, Inc., San Diego, CA, USA) was used to generate graphical outputs, and a *p*-value of <0.05 was considered statistically significant. Risk ratios (RRs) and 95% confidence intervals (CIs) were calculated to estimate the relative risk of postoperative and chemotherapy-associated complications between groups. Missing data were minimal (<3%) and were appropriately handled during analysis. Given the retrospective study design, neither clinicians nor evaluators were blinded to the nutritional intervention during complication evaluation.

Results

Comparison of Baseline Information Between Groups

The control group consisted of 45 patients, including 32 males and 13 females. Of these, 10 children were younger than 1 year, and 35 were aged 1 year or older. Regarding clinical staging, 2 cases were classified as Stage I, 11 as Stage II, 12 as Stage III, 17 as Stage IV, and 3 as Stage IVs. Based on risk stratification, 12 cases were classified as low-risk, 10 as intermediate-risk, and 23 as high-risk.

In the experimental group, there were 35 males and 14 females. Among them, 14 children were under 1 year of age, and 35 were ≥1 year old. Clinical staging revealed 3 cases in Stage I, 12 in Stage II, 15 in Stage III, 17 in Stage IV, and 2 in Stage IVs. For risk stratification, 13 cases were in the low-risk group, 12 in the intermediate-risk group, and 24 in the high-risk group.

Comparative analysis demonstrated no significant differences between the two groups in terms of baseline characteristics, including sex, age, clinical stage, or risk stratification ($p > 0.05$). These findings indicate the two groups were well balanced at baseline (Table 2).

Comparison of Nutritional Status Between Groups

Repeated-measures analysis of variance (ANOVA) showed significant effects of group, time, and group × time interaction across all nutritional indicators ($p < 0.05$). At the baseline, there were no statistically significant differences between groups for any measured indicator ($p > 0.05$), indicating comparable baseline conditions.

Bonferroni post-hoc analysis demonstrated that after surgery, corrected BMI showed a numerical trend toward higher values in the experimental group (18.74 ± 3.26 kg/m^2) relative to the control group (17.55 ± 2.41 kg/m^2), without reaching statistical significance. By contrast, MUAC (9.52 ± 2.21 cm) and TSFT (6.23 ± 1.62 mm) were substantially higher in the experimental group compared with the control group (6.53 ± 1.42 cm, 4.49 ± 1.21 mm) ($p < 0.05$). The coexistence of relatively higher BMI, TSFT, and biochemical indicators was due to the tumor-associated fluid retention affecting BMI, along with early improvement in fat stores and biochemical status fol-

Table 2. Comparison of baseline characteristics between the two groups [n (%)].

	Control group (n = 45)	Experimental group (n = 49)	χ^2	*p*-value
Gender			0.001	0.973
Male	32	35		
Female	13	14		
Age (years)			0.497	0.481
<1	10	14		
≥1	35	35		
Clinical stage			–	0.980
Stage I	2	3		
Stage II	11	12		
Stage III	12	15		
Stage IV	17	17		
Stage IVs	3	2		
Risk stratification			0.073	0.964
Low risk	12	13		
Intermediate risk	10	12		
High risk	23	24		

Note: Risk stratification refers to disease/tumor risk stratification of neuroblastoma. – indicates that Fisher's exact test was used.

lowing nutritional intervention.

Bonferroni post-hoc test further indicated that following chemotherapy, body weight (17.42 ± 7.74 kg), height (93.52 ± 18.23 cm), and corrected-BMI (19.90 ± 3.82 kg/m^2) showed higher numerical values in the experimental group versus the control group (13.42 ± 5.32 kg, 83.35 ± 16.21 cm, 19.30 ± 2.51 kg/m^2), only the difference in corrected-BMI was not statistically significant. However, MUAC (9.82 ± 2.04 cm) and TSFT (6.43 ± 1.52 mm) remained significantly higher in the experimental group than in the control group (6.52 ± 1.23 cm, 4.61 ± 1.11 mm) ($p < 0.05$). Of note, the observed between-group height discrepancy was attributable to short-term body water shift, posture and measurement error instead of true longitudinal skeletal growth over the brief treatment period.

Biochemical parameters followed a similar pattern. After surgery, the levels of Hb (118.11 ± 18.62 g/L), Alb (42.92 ± 7.11 g/L), and Pre-Alb (171.42 ± 48.21 g/L) were significantly higher in the experimental group compared with the control group (109.21 ± 15.04 g/L, 38.32 ± 5.83 g/L, 145.32 ± 46.51 g/L) ($p < 0.05$). Following chemotherapy, the levels of Hb (121.43 ± 16.72 g/L) and Pre-Alb (175.04 ± 49.32 g/L) remained significantly higher in the experimental group than in the control group (108.12 ± 14.04 g/L, 143.52 ± 48.04 g/L) ($p < 0.05$).

Significant group × time interactions were observed for MUAC, TSFT, Hb, Alb, and Pre-Alb ($p < 0.05$), but not for corrected-BMI ($p > 0.05$). These findings indicated that the nutritional improvement observed in the experimental group was time-dependent and more evident than in the control group for primary anthropometric and biochemical nutritional markers. These results are illustrated in Fig. 1.

Comparison of Daily Energy Intake Between Groups

Repeated-measures ANOVA showed significant effects of group, time, and group × time interaction for both daily energy intake and daily protein intake ($p < 0.05$). At baseline, no statistically significant differences were observed between groups in daily energy and protein intake ($p > 0.05$). Bonferroni-adjusted post-hoc analysis showed that during the early postoperative recovery phase (one week after surgery), patients in the experimental group had substantially higher average daily energy intake (2320.40 ± 326.20 kJ/d) and protein intake (33.42 ± 9.21 g/d) compared with those in the control group (1802.50 ± 363.50 kJ/d, 24.77 ± 6.12 g/d) ($p < 0.05$). Bonferroni post-hoc test further indicated that after completion of chemotherapy (at the end of the fourth chemotherapy cycle), the experimental group maintained higher average daily energy intake (2410.60 ± 472.10 kJ/d) and average daily protein intake (42.93 ± 6.40 g/d) compared to the control group (1820.30 ± 290.40 kJ/d, 22.94 ± 3.89 g/d) ($p < 0.05$). Significant group × time interactions were observed for both energy intake and protein intake ($p < 0.05$), indicating that improvement in dietary intake in the experimental group increased over time and was consistently greater than that reported in the control group. These results are presented in Fig. 2.

Comparison of Postoperative Complication Rates Between the Two Groups

In the experimental group, postoperative complications were relatively less frequent: 1 case of wound dehiscence, no wound infection, and 1 case of wound oozing were observed, yielding an overall complication rate of 4.1% (2/49). In contrast, the control group had a higher incidence of postoperative complications, with 4 cases of wound de-

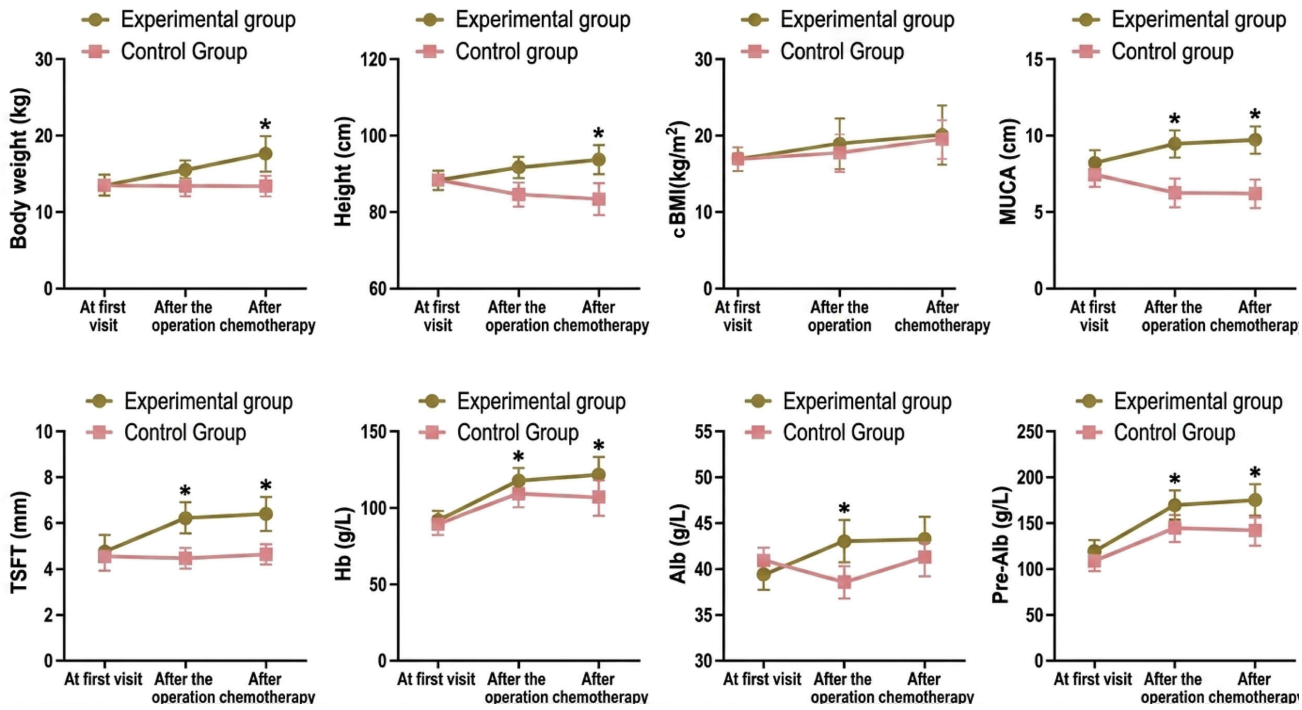

Fig. 1. Comparison of nutritional status ($\bar{x} \pm s$) in children with neuroblastoma before and after treatment. Note: * indicates $p < 0.05$ vs. control group at the same time point. Abbreviations: cBMI, corrected body mass index; MUAC, mid-upper arm circumference; TSFT, triceps skinfold thickness; Hb, hemoglobin; Alb, albumin; Pre-Alb, prealbumin; ANOVA, analysis of variance.

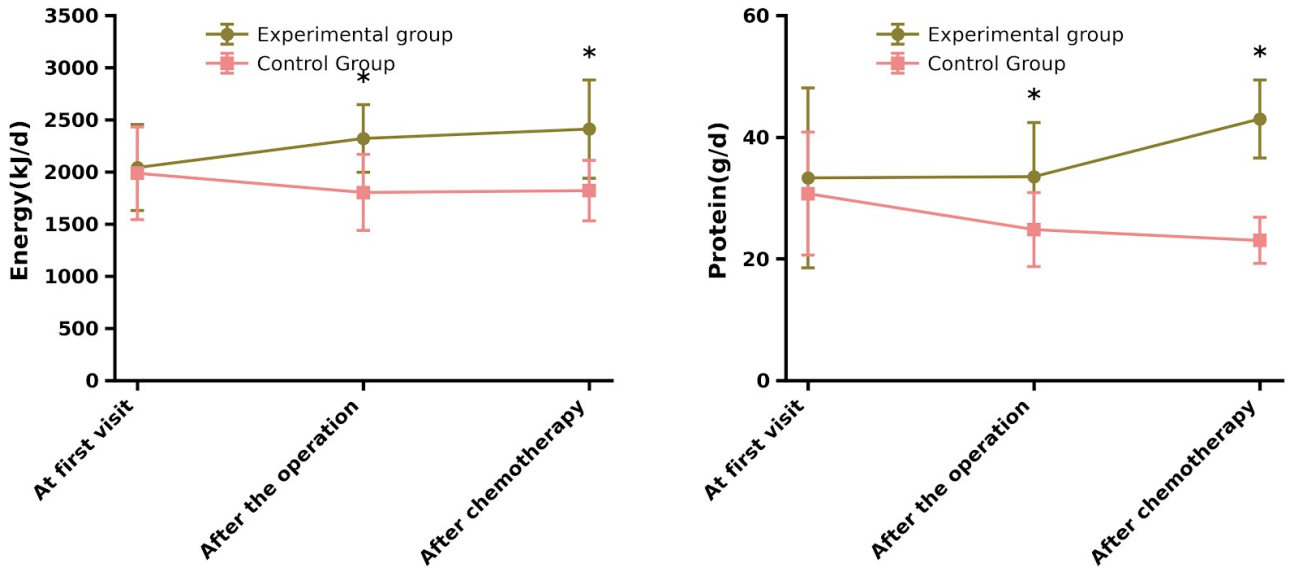

Fig. 2. Comparison of daily energy intake ($\bar{x} \pm s$) in children with neuroblastoma before and after treatment. Note: * indicates $p < 0.05$ vs. control group at the same time point. Abbreviations: kJ/d = kilojoules per day, g/d = grams per day. Intake values represent the average of 3 consecutive days of dietary records.

hiscence, 2 cases of wound infection, and 5 cases of wound oozing, giving a total complication rate of 24.4% (11/45). The incidence of postoperative complications was significantly lower in the experimental group than in the control group ($p < 0.05$, RR = 0.168, 95% CI: 0.041–0.690), as shown in Table 3.

Multivariate logistic regression analysis adjusted for age, clinical stage, and risk stratification showed that enteral nutritional support was associated with a reduced risk of postoperative complications (odds ratio [OR] = 0.152, 95% CI: 0.036–0.645, $p = 0.010$; the OR value is for reference only due to the small number of complication events).

Table 3. Comparison of postoperative complication rates between the groups [n (%)].

Group	Number of cases	Wound dehiscence	Wound infection	Wound oozing	Total incidence (%)	RR (95%CI)	χ^2	*p*-value
Experimental group	49	1	0	1	4.1% (2/49)	0.168 (0.041–0.690)	8.162	0.004
Control group	45	4	2	5	24.4% (11/45)	–		

RR, risk ratio; CI, confidence interval.

Table 4. Comparison of post-chemotherapy complication rates between groups [n (%)].

Group	Number of cases	Myelosuppression	Organ function damage	Gastrointestinal reaction	Total incidence (%)	RR (95%CI)	χ^2	*p*-value
Experimental group	49	0	0	1	2.0% (1/49)	0.128 (0.017–0.967)	–	0.026
Control group	45	1	2	4	15.6% (7/45)			

Fisher's exact test was used when expected frequencies were small; "–" indicates that the χ^2 value was not applicable.

Additional parameters of postoperative surgical recovery also favored the experimental group. The time to first oral intake was significantly shorter (24.5 ± 6.2 h vs. 36.8 ± 8.5 h, $p < 0.05$), and the length of postoperative hospital stay was reduced (7.2 ± 1.5 d vs. 10.5 ± 2.3 d, $p < 0.05$) in the experimental group than in the control group.

All recorded complications were mild to moderate in severity (CTCAE v5.0 Grade 1–2), and no severe (Grade 3–4) complications occurred in either group. Notably, no adverse events related to enteral nutrition support were found in the experimental group.

Analysis of Post-Chemotherapy Complication Rates Across Groups

The experimental group reported very few postoperative complications after chemotherapy, with no cases of myelosuppression or organ dysfunction and only one case of gastrointestinal reaction, yielding an overall complication rate of 2.0% (1/49). In contrast, the control group demonstrated a higher complication rate, with one 1 case of myelosuppression, 2 cases of organ function impairment, and 4 cases of gastrointestinal reaction, giving a total complication rate of 15.6% (7/45). The incidence of post-chemotherapy complications was significantly lower in the experimental group than in the control group ($p < 0.05$, RR = 0.128, 95% CI: 0.017–0.967), as shown in Table 4.

Multivariate logistic regression analysis adjusted for age, clinical stage, and risk stratification showed that enteral nutritional support was associated with a reduced risk of post-chemotherapy complications (OR = 0.119, 95% CI: 0.015–0.927, $p = 0.042$; the OR value is for reference only due to the small number of complication events).

All reported complications were graded as mild to moderate (CTCAE v5.0 Grade 1–2), and no severe (Grade 3–4) adverse events were found in either group.

Discussion

Children with neuroblastoma often present with moderate or high nutritional risk, which can adversely affect treatment outcomes. Poor nutritional status can reduce response to treatment, increase the risk of complications during surgery and chemotherapy, and ultimately affect the overall survival [14]. Compared with adult cancer patients, children have additional nutritional demands for growth and development, making them particularly vulnerable to malnutrition during cancer treatment [15]. Currently, therapeutic strategies often focus on tumor-directed therapies, while the impact of malnutritional status is relatively underrecognized by clinicians and caregivers [16]. Therefore, this study recruited 94 children with neuroblastoma and moderate or high nutritional risk who received a standardized surgery followed by a chemotherapy regimen, and assessed the association between enteral nutritional support, surgical complications, and short-term nutritional recovery. The aim was to explore the clinical relevance of structured nutritional intervention in these patients.

Initially, dietary assessment, based on questionnaire data, revealed that both energy intake and protein intake in these patients were below pre-illness levels and did not meet recommended standards such as the Swedish Nutrition Recommendations (SNR) [17]. This underscores the significance of early and precise nutritional evaluation in guiding intervention approaches [18]. However, there are various clinical methods for assessing nutritional status, and to date, no universally accepted gold standard exists for the nutritional evaluation of pediatric tumor patients [19]. In the present study, nutritional assessment indicators were selected based on clinical relevance and the distinct characteristics of children with neuroblastoma.

Anthropometric parameters such as body weight, height, and NMI may be affected by tumor burden, fluid retention, and hormonal factors, restricting their reliability in indicating true nutritional status. In contrast, MUAC and TSFT are less affected by these factors and provide a more stable estimate of the true nutritional status of children with tumors. Therefore, this study used MUAC and TSFT levels as the primary indicators for assessing nutritional risk, while biochemical indicators were interpreted as supportive measures.

Our findings indicated that patients receiving enteral nutritional support showed consistent improvements in both physical and biochemical indicators after surgery and chemotherapy. Post-surgery, the experimental group exhibited higher levels of BMI, MUAC, TSFT, Hb, Alb, and Pre-Alb compared to the control group. After chemotherapy, the experimental group maintained the same higher levels for these variables. These improvements may be due to adequate provision of energy, resulting in improved metabolic functions, enhanced protein synthesis, and broader immune competence, as evidenced by increases in albumin and prealbumin levels [6,13]. At the molecular level, nutritional support may also help regulate inflammatory signaling pathways, including cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), and improve immune cell function (such as lymphocytes), thereby alleviating the risk of complications. In addition, the individualized energy and protein calculation based on body weight and age, tailored to the high metabolic demands of these patients, likely contributed to these outcomes.

Previous studies have shown that nutritional risk tends to worsen as treatment progresses in children with neuroblastoma [4,20], especially when surgical intervention is followed by immediate chemotherapy. This combined physiological effect causes damage to the children's health and greatly increases the risk of complications [21]. Barr et al. [22] found that the prevalence of nutritional risk in children with cancer is as high as 95%, and nutritional support can significantly improve clinical outcomes. This study's outcomes are in agreement with their conclusions, which further confirms that enteral nutritional support therapy is associated with a significant reduction in the probability of complications from surgery and chemotherapy in children. In addition, the experimental group had a shorter time to first oral intake and shorter postoperative hospital stay, which is consistent with the conclusion of Joffe et al. (2020) [16] that nutritional support can improve the treatment tolerance of children with tumors. Regrettably, we were unable to analyze the correlation between improved nutritional status and chemotherapy dose reduction or treatment delay rates in the current retrospective analysis due to incomplete archived medical record documentation of planned versus actual chemotherapy dosing and scheduling; further prospective research is needed to verify whether optimized enteral nutrition could lower the incidence of chemotherapy dose adjustments or treatment postponement.

Despite these promising findings, this study has several limitations that should be acknowledged before interpreting these findings. First, as a retrospective cohort study, the grouping was based on clinicians' and caregivers' preferences (according to oral intake tolerance, digestive tract symptoms, and SCAN score), which may introduce potential selection bias. Although baseline characteristics were balanced and multivariate regression adjusted for confounding factors (age, clinical stage, risk stratification), other confounders such as tumor location/size, surgical complexity, chemotherapy toxicity risk factors and other indicators were not included in the adjustment due to the lack of standardized recording in the retrospective study. Second, this study was performed at a single center with a relatively small sample size, which may limit the generalizability of the findings. In addition, the wide age range of the enrolled children and the use of raw height measurements rather than age- and sex-standardized values may have contributed to the observed between-group difference in height; therefore, height should be interpreted only as a supportive anthropometric indicator. Third, follow-up duration was short; therefore, it was challenging to conduct an accurate assessment and evaluation of the long-term prognostic outcomes (e.g., 5-year survival rate, treatment completion rate and relapse rate). This study analyzed short-term nutritional outcomes and complication rate, and the long-term effect needs to be further verified through extended follow-up. Fourth, the nutritional support duration (1–2 weeks) was relatively short, and the impact of long-term support remains unclear. Fifth, due to the retrospective study design, the clinicians and evaluators were not blinded to the nutritional intervention, which may lead to assessment bias. Finally, the relatively small number of complication events in this study reduces the stability of regression estimates, and the reported associations should be interpreted with caution. Future studies should follow prospective, randomized controlled trials, ideally multicenter with larger cohorts, and extended follow-up, to better explore the causal effect of enteral nutritional support in pediatric neuroblastoma patients with moderate or high nutritional risk. Future investigations should also clarify the underlying molecular mechanisms and establish an optimized, individualized nutritional support protocol based on patient age, risk profile, and treatment stage.

Conclusions

In children with neuroblastoma and moderate or high nutritional risk undergoing unified surgery followed by chemotherapy, the implementation of enteral nutritional support was associated with improved nutritional status, increased energy intake, and significantly reduced treatment-related complications. These improvements may effectively enhance tolerance to treatment without causing additional safety concerns. However, due to the retrospective study design, these findings only indicate an association, and larger, prospective randomized controlled trials are required to confirm the causal relationship. Standardized and individualized enteral nutritional support protocols should be developed for pediatric NB patients with moderate or high nutritional risk through multi-center, extended follow-up approaches.

Availability of Data and Materials

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions

QZ conceived and designed the research, performed the data collection and statistical analysis, and drafted the manuscript. HXY contributed to the data extraction and verified the accuracy of clinical data. MCZ and BSZ contributed to the patient follow-up, collated observation indicator data, and provided technical support for data organization. WYK and WLL contributed to the data analysis and interpretation. PW supervised the entire research process, designed the research, provided guidance on study design and data analysis. All authors contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was conducted in compliance with the ethical principles outlined in the Declaration of Helsinki and obtained ethical approval from the Ethics Committee of Hunan Children's Hospital (approval number: 2023-003-07). Given the retrospective study design, the requirement for informed consent was waived by the Ethics Committee. All patient data were de-identified before analysis.

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Conflict of Interest

The authors declare no conflict of interest.

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