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Original Article

Comparative effects of enteral nutrition strategies on nutritional indices, inflammatory factors, and clinical outcomes in patients with severe traumatic brain injury

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Abstract: Objective: To evaluate the effects of different enteral nutrition (EN) strategies on nutritional status, inflammatory factors, immune markers, coagulation function, and clinical outcomes in patients with severe traumatic brain injury (sTBI). Methods: A retrospective analysis was conducted on 121 sTBI patients treated at Yiwu Central Hospital between January 2023 and January 2025. Among them, 58 received early EN alone (control group) and 63 received early EN with probiotics (study group). Pre- and post-treatment comparisons between the two groups included: nutritional indices (total protein [TP], albumin [ALB], and prealbumin [PA]), inflammatory factors (interleukin-6 [IL-6], C-reactive protein [CRP], and tumor necrosis factor-α [TNF-α]), immune-related markers (immunoglobulin A [IgA], IgG, and IgM), coagulation indicators (fibrinogen [Fib] and D-dimer [D-D]) and clinical outcomes (Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores, Glasgow Coma Scale (GCS) scores, incidence of complications, time to first defecation, and time to target feeding volume [TFV]). Results: Following treatment, the study group demonstrated significantly smaller reductions in TP and ALB, greater increases in PA, and more pronounced decreases in IL-6, CRP, and TNF-α (all $P<0.05$). IgA, IgG, and IgM rose more significantly, and Fib and D-D decreased more in the study group (all $P<0.05$). Clinical outcomes improved significantly, including better APACHE II and GCS scores, earlier defecation and TFV times, and fewer intestinal complications (4.76% *vs.* 17.24%, $P=0.015$), with no significant difference in infectious complications. Conclusion: Early EN combined with probiotics significantly improved nutrition, reduced inflammation, enhanced immune and coagulation function, and improved recovery in sTBI patients.

Keywords: Enteral nutrition, severe traumatic brain injury, nutritional indices, inflammatory factors, immune markers, coagulation function, clinical outcome

Introduction

Traumatic brain injury (TBI) is a critical neurosurgical condition associated with high rates of disability and mortality, typically presenting with sudden onset and rapid progression [1, 2]. Patients with severe TBI (sTBI) are often comatose in the early stages and commonly present with profound metabolic disturbances, dysphagia, nausea, and vomiting, all of which significantly impair enteral nutrition (EN) intake [3, 4]. Furthermore, the combined effect of trauma and surgical stress induces a hypermetabolic state that accelerates protein and fat catabolism, increases energy expenditure, and disrupts metabolic homeostasis. This dysregulation not only contributes to malnutrition and elevates the risk of hypoproteinemia, but also may impair immune function [5]. Therefore, maintaining adequate nutritional support is essential for patients with sTBI. Nutritional therapy addresses caloric and nutrient deficiencies in critically ill patients by providing sufficient protein and energy intake, thereby reducing infection risk, enhancing immune function, improving nitrogen balance, and promoting better clinical outcomes [6]. Two primary approaches are employed: parenteral nutrition (PN) and EN. PN delivers nutrients intravenously, while EN provides nutrients via the gastrointestinal tract - typically through a nasogastric tube or oral feeding - to maintain metabolic homeostasis [7, 8]. Clinical evidence, particularly from Elke et al. [9], indicates that EN demonstrates

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superior clinical benefits over PN, including a lower incidence of infectious complications and shorter intensive care unit stays. By delivering nutrients through the gastrointestinal tract, EN helps preserve the integrity of the intestinal mucosal barrier, prevents bacterial translocation, reduces infection risks, and facilitates neurological recovery [10, 11]. Probiotics, as key constituents of the intestinal microbiota, colonize the gut mucosa to form a biological barrier that inhibits pathogenic bacteria, mitigates inflammatory damage, and maintains intestinal barrier integrity [11]. Nevertheless, current evidence supporting the combined use of EN and probiotics remains limited.

Accordingly, this study conducted a comparative analysis of the effects of EN with probiotic supplementation on nutritional and inflammatory factors, immune markers, coagulation function, and clinical outcomes in sTBI patients, as detailed below.

Materials and methods

Patient selection

This retrospective study analyzed the clinical records of 140 patients with sTBI who received treatment at Yiwu Central Hospital between January 2023 and January 2025. Based on predefined inclusion and exclusion criteria, 121 eligible patients were enrolled. Among them, 58 patients received early EN alone (control group), while 63 received early EN combined with probiotics (study group). The study protocol was reviewed and approved by the Ethics Committee of Yiwu Central Hospital prior to implementation.

Inclusion and exclusion criteria

Inclusion criteria: (1) diagnosis of TBI confirmed by magnetic resonance imaging or computed tomography, including intracranial hematoma, acute subdural hematoma, cerebral contusion or laceration, or brainstem hemorrhage; (2) age between 18 and 70 years; (3) Glasgow Coma Scale (GCS) score between 3 and 8; (4) expected survival time of ≥15 days; (5) no pre-existing significant gastrointestinal disorders, metabolic diseases, or major organ dysfunction (i.e., cardiac, hepatic, pulmonary, or renal).

Exclusion criteria: (1) presence of comorbidities such as diabetes mellitus, malignancy or immunosuppressive disorders; (2) pregnancy or lactation; (3) use of corticosteroids or immunosuppressants within the past 3 months; (4) body mass index >30 kg/m^2; (5) contraindications to EN, such as intestinal obstruction.

Methods

All patients received condition-specific emergency interventions upon admission, including standard surgical treatment and intracranial pressure-lowering therapy. EN was initiated by nasogastric tube using enteral feeding pumps after hemodynamic stabilization, defined as a mean arterial pressure ≥65 mmHg maintained for over 2 hours.

Patients in the control group received standard EN, starting with a low-fat, peptide-based formula (1.0 kcal/mL) for the first two days. If tolerated - defined as a gastric residual volume <300 mL and no vomiting - the regimen was transitioned to a balanced polymeric formula (1.0 kcal/mL) from day 3 onward. The target caloric intake (25-30 kcal/kg/day) was calculated individually using the Penn State equation. EN was initiated at 20-30 mL/h via continuous 24-hour infusion, with the rate increased by 20 mL/h every 12 hours up to a maximum of 80-100 mL/h. Gastric residual volume was monitored every 4 hours. All feeding solutions were maintained at 37-42°C using in-line warmers. Blood glucose was monitored every 4-6 hours, with a target range of 6.1-8.3 mmol/L. Intravenous insulin was administered if blood glucose levels remained above 8.3 mmol/L [12].

Patients in the study group received the same EN regimen with additional supplementation of Bifidobacterium-Lactobacillus-Enterococcus Triple Viable Tablets (Inner Mongolia Shuangqi Pharmaceutical Co., Ltd., National Medicine Approval No.: S19980004). Each 3.5 g tablet contained ≥1.0×10^7 colony-forming units (CFU) of Bifidobacterium longum, ≥1.0×10^7 CFU of Lactobacillus acidophilus, and ≥1.0×10^7 CFU of Enterococcus faecalis. The tablets were crushed, suspended in 20 mL of sterile water, and administered by nasogastric tube three times daily (08:00, 16:00, and 24:00), providing a total daily bacterial count of ≥3.0×10^8 CFU over 14 consecutive days [13].

Data collection

Clinical baseline data were collected for all patients, including age, sex, disease duration,

cause of injury, and place of residence, National Institutes of Health Stroke Scale (NIHSS) score. Laboratory indicators included nutritional indices (total protein [TP], albumin [ALB], and prealbumin [PA]), inflammatory factors (interleukin-6 [IL-6], C-reactive protein [CRP], and tumor necrosis factor-alpha [TNF-α]), immune-related markers (immunoglobulin [Ig] A, IgG, and IgM), and coagulation parameters (fibrinogen [Fib], D-dimer [D-D]). Clinical outcomes included Acute Physiology and Chronic Health Evaluation II (APACHE-II) score, GCS scores, occurrence of complications, time to first defecation, and time to reach target feeding volume (TFV).

Outcome measures

Primary outcome measures: (1) Nutritional indices: A 20 mL venous blood sample was collected from each patient before treatment and on day 14 post-treatment. Samples were divided into four aliquots, one of which was used to assess levels of TP, ALB, and PA using an automated blood chemistry analyzer. (2) Inflammatory factors: Levels of IL-6, CRP, and TNF-α were measured from 5 mL of venous blood using a biochemical analyzer. All assay kits were obtained from Wuhan Boster Biological Technology Co., Ltd., and tests were conducted in accordance with the manufacturer's protocols. (3) Immune-related indices: Serum levels of IgA, IgG and IgM were determined from 5 mL of venous blood using a protein analyzer (Beckman, USA) with corresponding commercial reagent kits. (4) Coagulation function indices: Fibrinogen (Fib) levels were measured using the clotting method, while D-D levels were quantified by immunoturbidimetry.

Secondary outcome measures: (1) Clinical baseline characteristics: Clinical baseline data were collected for both groups, including age, sex, disease duration, cause of injury, NIHSS score at admission, and place of residence. (2) Treatment-related complications: All complications occurring during the treatment period were recorded, including intestinal complications (diarrhea, abdominal distension, gastric retention, and reflux) and infectious complications (pulmonary infections, urinary tract infections, intracranial infections, and gastrointestinal bleeding). (3) ACHE-II scores: The APACHE-II scoring system (maximum score: 71; higher scores indicate greater disease severity) was used to assess before treatment and on day 14 post-treatment [14]. (4) GCS scores: Before treatment and 14 days after treatment: The GCS, comprising eye opening, verbal response, and motor response components, was used to evaluate the level of consciousness before and 14 days after treatment. The total GCS score ranges from 3 to 15, with higher scores indicating better neurological function. (5) Time to first defecation and the time to TFV: These two gastrointestinal recovery indices were compared between the two groups.

Statistical analyses

All statistical analyses were performed using SPSS version 20.0 (IBM Corp., Armonk, NY, USA), and graphical representations were generated with GraphPad Prism version 7 (GraphPad Software Inc., San Diego, CA, USA). Categorical variables were presented as counts and percentages [n (%)], and between-group comparisons were conducted using the chi-square test (χ^2 test). Continuous variables were assessed for normality and expressed as mean ± standard deviation ($\bar{x} \pm s$). Between-group comparisons of continuous variables were analyzed using independent sample *t*-tests, while within-group comparisons (pre- and post-treatment) were evaluated using paired *t*-tests. A P value <0.05 was considered significant. To control for multiple comparisons across outcome domains (nutritional, inflammatory, immune, coagulation, and clinical factors), the Benjamini-Hochberg false discovery rate correction was applied independently within each outcome category. Adjusted P values (i.e., q-values) <0.05 were considered statistically significant.

Results

Comparison of clinical baseline characteristics

There were no statistically significant differences between the two groups with respect to baseline characteristics, including age, sex, disease duration, cause of injury, NIHSS score at admission, or place of residence (all P>0.05, **Table 1**).

Changes in nutritional indices before and after treatment in both groups

Before treatment, there were no significant differences between the study and control groups in TP (71.16±10.39 *vs.* 73.70±11.46

Table 1. Comparison of clinical baseline characteristics

	Age (year)	Sex		Course of disease (h)	Cause of injury			NIHSS score at admission	Place of residence	
		Male	Female		Car accident	Falling accident	Strike		Rural areas	Urban areas
Control group (n=58)	39.39±5.55	33	25	3.85±1.04	20	17	21	14.53±2.57	35	23
Study group (n=63)	40.57±5.46	40	23	3.68±0.84	27	21	15	14.16±2.58	43	20
χ^2/t	1.177	0.549		0.988	2.261			0.773	0.825	
P	0.242	0.459		0.325	0.323			0.441	0.364	

Note: NIHSS: National Institutes of Health Stroke Scale.

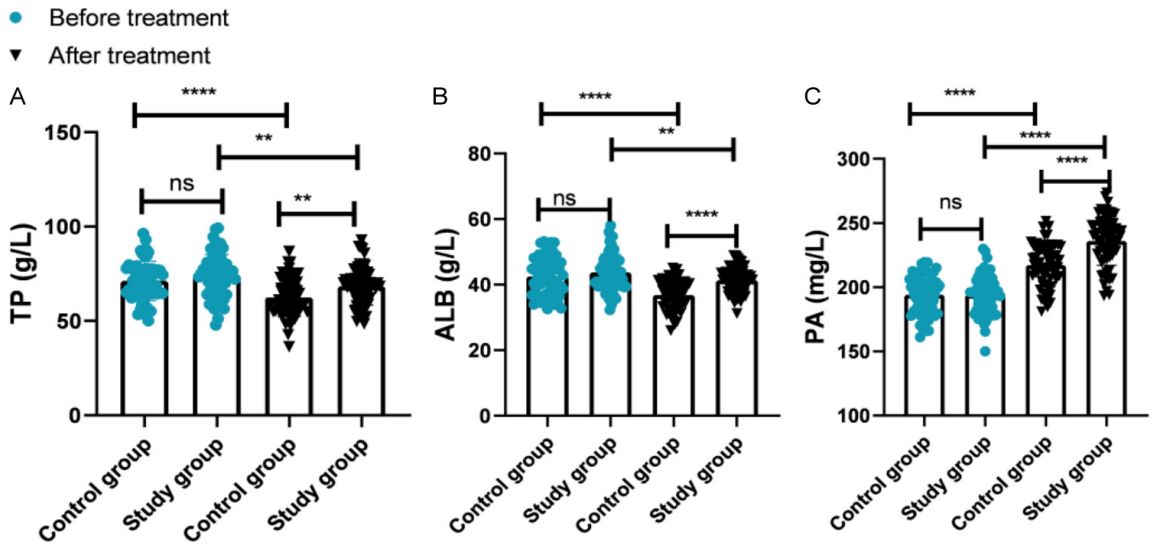

Figure 1. Comparison of TP (A), ALB (B), and PA (C) levels between the two groups before and after treatment. Notes: ns: non-significant; **P<0.01; ****P<0.0001 after false discovery rate correction. TP: Total protein; ALB: Albumin; PA: Prealbumin.

g/L), ALB (42.50±5.97 *vs.* 43.72±5.51 g/L), or PA (194.10±15.16 *vs.* 194.03±15.23 mg/L) levels (all *P*>0.05). After treatment, both groups showed significant reductions in TP and ALB (all *P*<0.05); however, the declines were significantly more pronounced in the control group compared to the study group (TP: 62.43±10.01 *vs.* 68.43±10.04 g/L; ALB: 36.81±4.41 *vs.* 41.36±3.91 g/L; both *P*<0.05). Conversely, PA levels increased significantly in both groups (both *P*<0.05), with the study group showing a significantly greater increase than the control group (236.14±19.13 *vs.* 217.25±16.71 mg/L, *P*<0.05) (**Figure 1** and Supplementary Table 1).

Changes in inflammatory factors before and after treatment in both groups

At baseline, there were no significant differences between the study and control groups in IL-6 (62.00±5.23 *vs.* 63.35±5.20 pg/mL), CRP (79.31±11.74 *vs.* 80.16±9.39 mg/L), or TNF-α (42.21±5.07 *vs.* 43.67±4.50 pg/mL) levels (all *P*>0.05). After treatment, both groups exhibited significant reductions in all three inflammatory markers (all *P*<0.05). Notably, the reductions were more pronounced in the study group compared to the control group (IL-6: 32.54±3.82 pg/mL *vs.* 41.92±4.61 pg/mL; CRP: 53.55±7.19 mg/L *vs.* 61.47±8.98 mg/L; TNF-α: 24.54±3.51 pg/mL *vs.* 34.32±3.75 pg/mL; all *P*<0.05) (**Figure 2** and Supplementary Table 2).

Changes in immune-related indices before and after treatment in both groups

Prior to treatment, no significant differences were observed between the study and control groups in IgG (7.44±1.17 *vs.* 7.10±1.07 g/L), IgM (1.04±0.23 vs. 1.11±0.19 g/L), or IgA (1.03±0.14 *vs.* 1.06±0.24 g/L) levels (all *P*>0.05). Following treatment, both groups showed significant increases in all Ig levels (all *P*<0.05). Notably, the study group demonstrat-

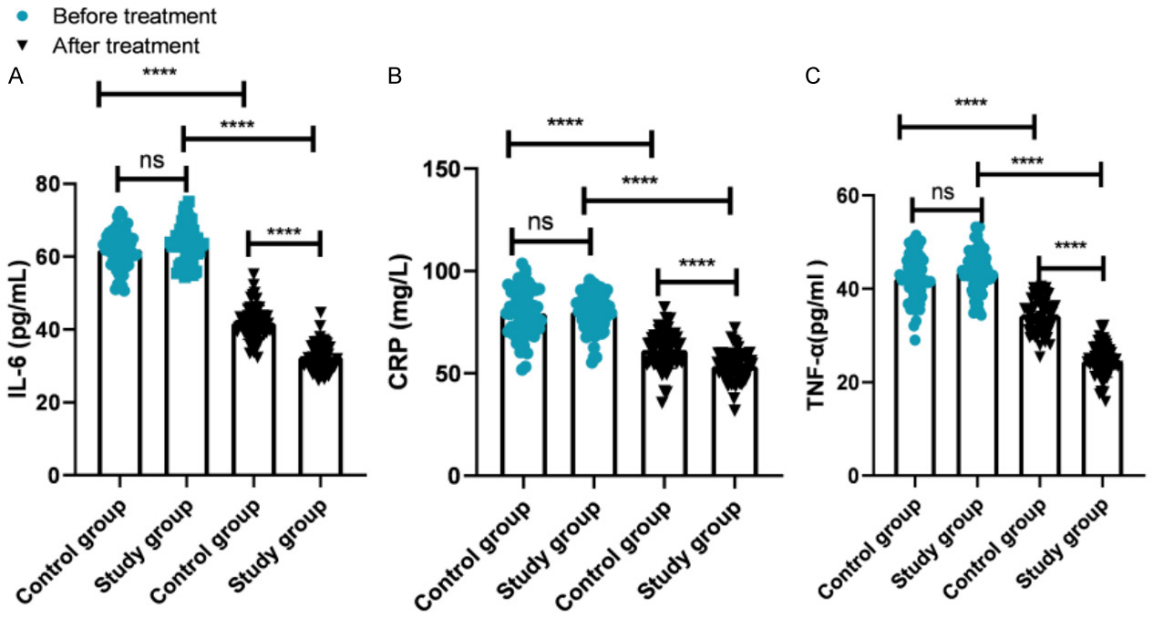

Figure 2. Comparation of IL-6 (A), CRP (B), and TNF-α (C) levels between the two groups before and after treatment. Notes: ns: non-significant; ****P<0.0001 after false discovery rate correction. IL-6: Interleukin-6; CRP: C-reactive protein; TNF-α: Tumor necrosis factor-alpha.

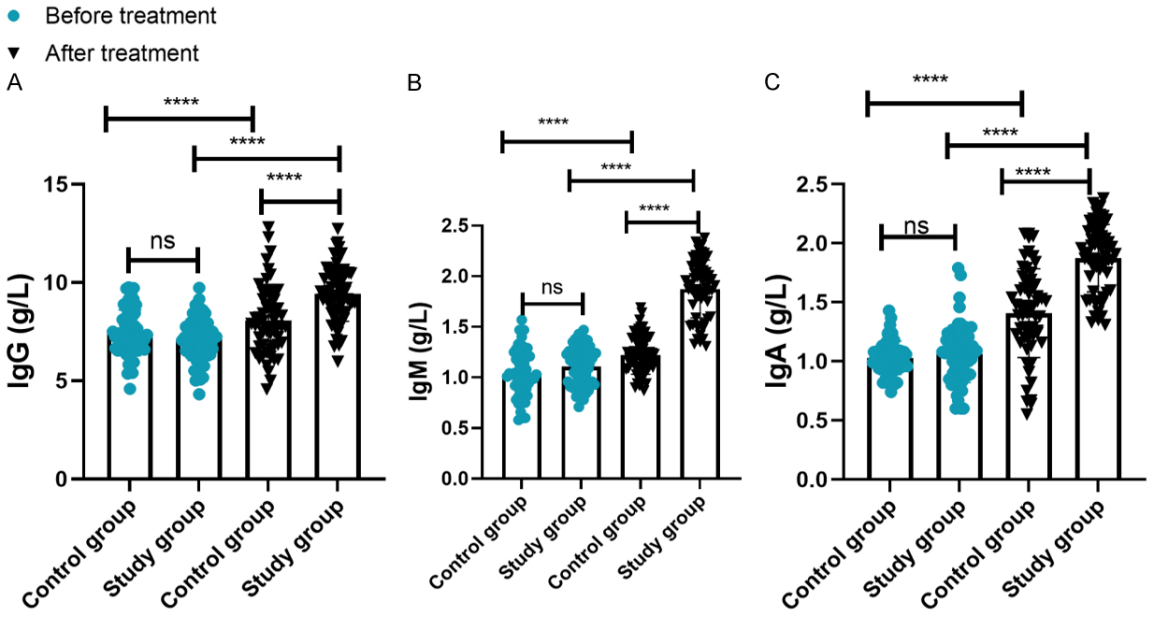

Figure 3. Comparation of IgG (A), IgM (B), and IgA (C) levels between the two groups before and after treatment. Notes: ns: non-significant; ****P<0.0001 after false discovery rate correction. IgG: Immunoglobulin G; IgM: Immunoglobulin M; IgA: Immunoglobulin A.

ed more pronounced improvements compared to the control group (IgG: 9.43±1.39 g/L *vs.* 8.08±1.73 g/L; IgM: 1.47±0.25 g/L *vs.* 1.22±0.19 g/L; IgA: 1.87±0.28 g/L *vs.* 1.41±0.38 g/L; all *P*<0.05) (**Figure 3** and Supplementary Table 3).

Changes in coagulation values before and after treatment in both groups

Prior to treatment, no significant differences were observed between the control and study groups in Fib levels (3.67±0.82 *vs.* 3.57±0.78

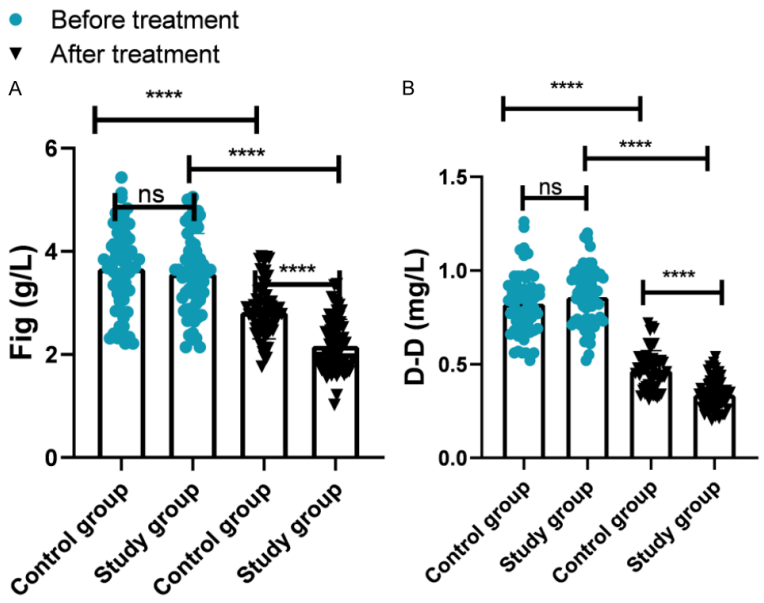

Figure 4. Comparation of Fib (A) and D-D (B) levels between the two groups before and after treatment. Notes: ns: non-significant; ****P<0.0001 after false discovery rate correction. Fib: Fibrinogen; D-D: D-Dimer.

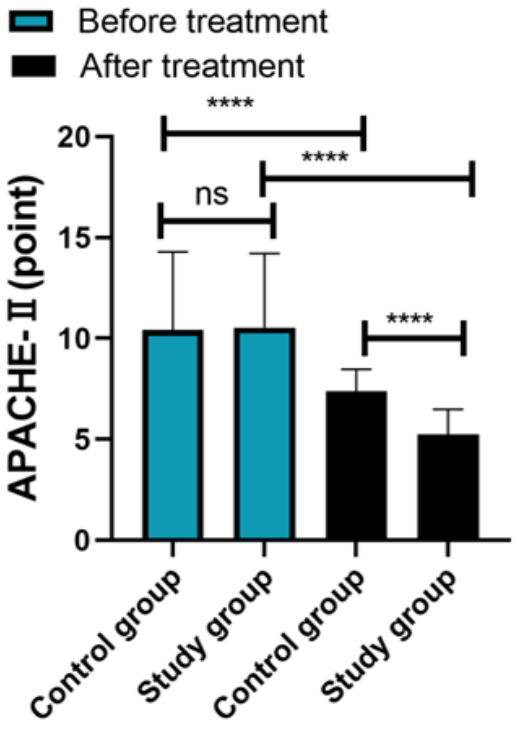

Figure 5. Comparison of APACHE-II scores between the two groups before and after treatment. Notes: ns: non-significant; ****P<0.0001 after false discovery rate correction. APACHE-II: Acute Physiology and Chronic Health Evaluation II.

g/L) or D-D levels (0.82±0.17 *vs.* 0.86±0.15 mg/L) (both P>0.05). Following treatment, both groups exhibited significant reductions in coagulation parameters (all *P*<0.05). However, the reductions were more pronounced in the study group compared to the control group (Fib: 2.17±0.52 g/L *vs.* 2.82±0.52 g/L; D-D: 0.34±0.08 mg/L *vs.* 0.47±0.10 mg/L; both *P*<0.05) (**Figure 4** and Supplementary Table 4).

Changes in APACHE-II scores before and after treatment in both groups

No significant difference was observed in APACHE-II scores between the study and control groups prior to treatment (10.58±3.70 *vs.* 10.41±3.88; *P*>0.05). After treatment, both groups showed significant reductions in APACHE-II scores (both *P*<0.05), and the study group showed a more pronounced decline, with scores decreasing to 5.27±1.22 compared to 7.35±1.05 in the control group (*P*<0.05) (**Figure 5** and Supplementary Table 5).

Changes in GCS scores before and after treatment in both groups

No significant difference was observed in GCS scores between the study and control groups prior to treatment (5.91±1.54 *vs.* 5.86±1.45; *P*>0.05). After treatment, both groups showed significant increases in GCS scores (both *P*<0.05), and the study group demonstrated superior neurological recovery, achieving a mean GCS score of 13.14±1.45 compared to 11.47±1.26 in the control group (*P*<0.05) (**Figure 6** and Supplementary Table 6).

Comparison of first defecation time and time to achieve TFV

The study group experienced significantly earlier first defecation time (4.23±0.48 h *vs.* 6.83±0.94 h) and shorter time to achieve TFV (4.07±0.44 h *vs.* 5.66±0.51 h) compared to the

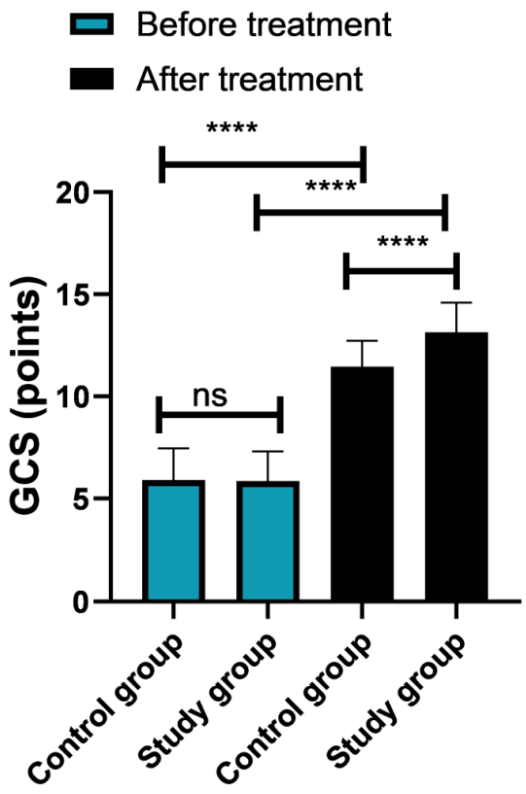

Figure 6. Comparison of GCS scores between the two groups before and after treatment. Notes: ns: non-significant; ****P<0.0001 after false discovery rate correction. GCS: Glasgow Coma Scale.

control group (both *P*<0.05) (**Figure 7** and Supplementary Table 7).

Comparison of the incidence of treatment-related complications

The study group and the control group had a total complication rate of 4.76% (3/63) and 18.97% (11/58), respectively. Intestinal complications showed a downward trend after in the study group, which approached statistical significance after false discovery rate correction (χ^2=4.904, P=0.015, q=0.015). In addition, the incidence of infectious complications did not differ significantly between groups (15.87% *vs.* 18.97%; χ^2=0.201, *P*=0.654, q=0.721). Detailed results are presented in **Table 2**.

Discussion

Patients with severe traumatic brain injury (sTBI) frequently experience severe nutritional deficits and increased susceptibility to infections, primarily due to a hypermetabolic state, exaggerated systemic inflammatory responses, and compromised gastrointestinal function [15]. While EN remains the preferred modality of nutritional support in sTBI patients, conventional EN alone is limited in its capacity to modulate the gut microbiota and mitigate infectious complications [16]. In recent years, probiotics have garnered increasing attention for their multifaceted roles in modulating the gut microbiota, enhancing host immune responses, and attenuating systemic inflammation. This study investigated the therapeutic efficacy of standard EN versus EN supplemented with probiotics, with the goal of identifying an optimal nutritional support strategy for sTBI patients. The findings revealed that patients receiving probiotic-supplemented EN exhibited significantly better clinical outcomes compared to those receiving standard EN alone, as evidenced by improved nutritional parameters, enhanced modulation of systemic inflammation, more robust immune function recovery, and overall better clinical prognosis.

Specifically, the study group showed a significantly attenuated decline in TP and ALB levels, alongside a more pronounced increase in PA. These benefits are likely attributable to the multifaceted actions of probiotics. Bifidobacterium and Lactobacillus strains have been shown to enhance intestinal barrier integrity, thereby reducing protein loss, and to modulate the gut-liver axis, promoting hepatic protein synthesis [17, 18]. The study group exhibited significantly earlier first defecation and shorter time to reach TFV, indicating that probiotic supplementation enhances intestinal motility and reduces the incidence of ileus, thereby improving nutrient absorption efficiency and facilitating earlier restoration of gastrointestinal function. Furthermore, under the hypermetabolic conditions following TBI, probiotics may optimize gut microbiota metabolism, thereby reducing inefficient energy expenditure and facilitating the allocation of more nutritional substrates toward protein synthesis [19]. The study further revealed notably lower post-treatment levels of IL-6, CRP, and TNF-α in the study group compared to the control group, suggesting that probiotic supplementation may effectively attenuate systemic inflammatory responses in sTBI patients. In cases of sTBI, probiotics appear to exert anti-inflammatory effects through multiple mechanisms, notably by up-

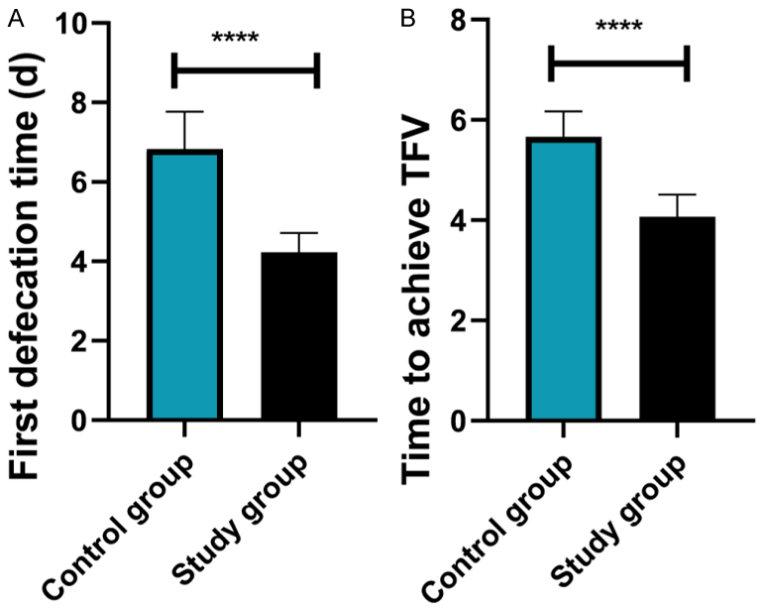

Figure 7. Comparison of first defecation time (A) and time to achieve TFV (B) between the two groups. Note: ****P<0.0001 after false discovery rate correction. TFV: Target feeding volume.

regulating intestinal tight junction proteins to reduce bacterial and endotoxin translocation secondary to stress-induced mucosal injury, thereby limiting the release of gut-derived inflammatory mediators [20, 21]. Additionally, Bifidobacterium promotes regulatory T cell differentiation, thereby suppressing excessive inflammatory responses [22], while Lactobacillus activates dendritic cells to enhance the secretion of anti-inflammatory cytokines, together exerting a synergistic immunomodulatory effect [23]. Through competitive colonization and the secretion of antimicrobial peptides, probiotics effectively suppress the growth of pathogenic bacteria such as Escherichia coli and Klebsiella, potentially reducing infection risks [24]. sTBI can activate the intrinsic coagulation pathway in response to hypoxia, acidosis, infection, or shock, thereby contributing to coagulopathy. Moreover, the severity of the injury is positively correlated with the extent of coagulation abnormalities [25]. Fib serves as a key biomarker for thrombosis formation [26], whereas D-D reflects the dynamic balance between coagulation and fibrinolysis. Both indicators are closely associated with the severity and prognosis of TBI [26]. This study demonstrated that the group receiving probiotic-supplemented EN exhibited significantly lower post-treatment Fib and D-D levels compared to the control group, suggesting that probiotic supplementation may contribute to improved coagulation function in sTBI patients. Moreover, while both groups showed comparable rates of infectious complications, the probiotic group exhibited a significantly lower rate of intestinal complications. This reduction may be attributed to improved gut microbiota homeostasis and enhanced enteral feeding tolerance mediated by probiotics through modulation of intestinal motility and reinforcement of mucosal barrier integrity. Although no significant difference was observed in overall complication rates between the two groups, the probiotic group showed a favorable trend toward lower incidences of pulmonary infections and intracranial infections. These findings are consistent with those of Yi et al. [27], who reported that probiotic supplementation in patients with severe head injuries effectively reduced the risk of infections and gastrointestinal complications. Similarly, Du et al. demonstrated that probiotic-supplemented EN effectively reduced gastrointestinal complications and infection rates in patients with sTBI, further corroborating the present study's results [28].

Notably, the study group exhibited significant post-treatment increases in IgG, IgM, and IgA levels, highlighting the immunomodulatory benefits of probiotic supplementation. The underlying mechanisms may involve: (1) stimulation of B-cell differentiation within Peyer's patches, leading to activattion of gut-associated lymphoid tissue and enhanced IgA secretion for improved mucosal immunity [29]; and (2) modulation of the Th1/Th2 balance, whereby Bifidobacterium promotes Th1-mediated anti-infective responses, while Lactobacillus induces Th2 activity to attenuate excessive inflammation [30]. Importantly, the improved nutritional status in the study group provided adequate protein substrates for immunoglobulin synthesis, establishing a positive feedback loop between nutrition and immune function. The significant improvements in APACHE-II and GCS scores further aligned with the enhanced

Table 2. Incidence of complications during treatment in both groups

Complication Type	Control (n=58)	Study (n=63)	χ^2	*P*-value	Adjusted q-value
Intestinal					
Diarrhea	4 (6.90%)	1 (1.59%)			
Abdominal distension	2 (3.45%)	0 (0.00%)			
Gastric retention	2 (3.45%)	1 (1.59%)			
Reflux	3 (5.17%)	1 (1.59%)			
Total incidence	11 (18.97%)	3 (4.76%)	5.954	0.015	0.015
Infectious					
Pulmonary	3 (5.17%)	2 (3.17%)			
Urinary tract	2 (3.45%)	4 (6.35%)			
Intracranial	3 (5.17%)	1 (1.59%)			
Gastrointestinal	3 (5.17%)	3 (4.76%)			
Total incidence	11 (18.97%)	10 (15.87%)	0.201	0.654	0.721

immunological indices, suggesting a comprehensive therapeutic benefit.

This study suggests that probiotic supplementation combined with EN may improve nutritional metabolism, attenuate inflammatory responses, and enhance immune function in patients with sTBI. However, its retrospective design precludes definitive causal inferences. These findings should therefore be interpreted with caution given the inherent limitations of observational studies in establishing causality. Several additional limitations should be acknowledged: (1) the moderate sample size may have limited statistical power; (2) the short observation period precluded evaluation of long-term outcomes; (3) the absence of gut microbiota analysis limited direct assessment of probiotic-induced microbial changes, although previous studies have confirmed that similar formulations significantly altered intestinal flora composition [31, 32]; and (4) the single-center design may restrict generalizability. Future studies should address these limitations by enrolling larger cohorts, extending follow-up durations, incorporating standardized fecal sampling with 16S rRNA sequencing to track microbiota dynamics, and conducting multicenter trials to validate and generalize these findings.

In conclusion, probiotic-enriched EN emerges as a promising therapeutic adjunctive strategy for patients with sTBI, effectively enhancing nutritional status, mitigating systemic inflammation, and improving immune and coagulation functions, all while maintaining a favorable safety profile. These findings offer a novel, multifaceted approach to the comprehensive management of severe neurotrauma and warrant further investigation and clinical translation.

Disclosure of conflict of interest

None.

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Supplementary Table 1. Changes in nutritional indices before and after treatment in both groups

	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
TP (g/L)	71.16±10.39	62.43±10.01	73.70±11.46	68.43±10.04
ALB (g/L)	42.50±5.97	36.81±4.41	43.72±5.51	41.36±3.91
PA (mg/L)	194.10±15.16	217.25±16.71	194.03±15.23	236.14±19.13

Notes: TP: Total protein; ALB: Albumin; PA: Prealbumin.

Supplementary Table 2. Changes in inflammatory factors before and after treatment in both groups

	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
IL-6 (pg/mL)	62.00±5.23	41.92±4.61	63.35±5.20	32.54±3.82
CRP (mg/L)	79.31±11.74	61.47±8.98	80.16±9.39	53.55±7.19
TNF-α (pg/mL)	42.21±5.07	34.32±3.75	43.67±4.50	24.54±3.51

Notes: IL-6: Interleukin-6; CRP: C-reactive protein; TNF-α: Tumor necrosis factor-alpha.

Supplementary Table 3. Changes in immune-related indexes before and after treatment in both groups

	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
IgG (g/L)	7.44±1.17	8.08±1.73	7.10±1.07	9.43±1.39
IgM (g/L)	1.04±0.23	1.22±0.19	1.11±0.19	1.47±0.25
IgA (g/L)	1.03±0.14	1.41±0.38	1.06±0.24	1.87±0.28

Notes: IgG: Immunoglobulin G; IgM: Immunoglobulin M; IgA: Immunoglobulin A.

Supplementary Table 4. Changes in coagulation indices before and after treatment in both groups

	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
Fib (g/L)	3.67±0.82	2.82±0.52	3.57±0.78	2.17±0.52
D-D (mg/L)	0.82±0.17	0.47±0.10	0.86±0.15	0.34±0.08

Notes: Fib: Fibrinogen; D-D: D-dimer.

Supplementary Table 5. Changes in APACHE-II scores before and after treatment in both groups

	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
APACHE-II	10.41±3.88	7.35±1.05	10.58±3.70	5.27±1.22

Note: APACHE-II: Acute Physiology and Chronic Health Evaluation II.

Supplementary Table 6. Changes in GCS scores before and after treatment in both groups

	Control group		Study group	
	Before treatment	After treatment	Before treatment	After treatment
GCS	5.91±1.54	11.47±1.26	5.86±1.45	13.14±1.45

Note: GCS: Glasgow Coma Scale.

Supplementary Table 7. Comparison of first defecation time and time to achieve target feeding volume between groups

	Control group	Study group
First Defecation Time	6.83±0.94	4.23±0.48
Time to Achieve Target Feeding Volume	5.66±0.51	4.07±0.44