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EARLY ENTERAL NUTRITION AND SHORT-TERM LABORATORY DYNAMICS IN ACUTE STROKE WITH DYSPHAGIA: HEMORHEOLOGY, INFLAMMATORY CYTOKINES, AND INTESTINAL BARRIER BIOMARKERS

RANA ENTERALNA ISHRANA I KRATKOROČNA LABORATORIJSKA DINAMIKA KOD AKUTNOG MOŽDANOG UDARA SA DISFAGIJOM: HEMOREOLOGIJA, INFLAMATORNI CITOKINI I BIOMARKERI CREVNE BARIJERE

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Summary

Background: We hypothesized that early enteral nutrition support could synergistically regulate three biomarker domains (hemorheology, inflammatory stress, intestinal barrier) by improving nutritional metabolism in patients with acute cerebral stroke (CS) complicated by swallowing disorders (SD). This study aimed to verify the hypothesis by examining the dynamic changes of the three domains, and to explore the biochemical correlations among these changes.
Methods: This retrospective cohort study included 126 patients with acute CS complicated by SD admitted to our hospital from August 2022 to August 2025. According to the intervention plan, patients were assigned to an observation group (68 cases; enteral nutrition support) or a control group (58 cases; routine fluid replacement therapy). Fasting venous blood was collected before intervention (T0), at 7 days (T1), and at 14 days (T2). Hemorheological parameters and red blood cell functional indices were measured with an automatic hemorheology analyzer; inflammatory/stress-related mediators, and intestinal barrier–related indicators were quantified by enzyme-linked immunosorbent assay; nutrition metabolism–related indices were determined using an automatic biochemical analyzer.
Results: In the observation group, hemorheological parameters improved progressively after intervention. Compared with T0, whole-blood high-shear viscosity (W-Vis-H), whole-blood low-shear viscosity (W-Vis-L), and fibrinogen were lower at T1 and further reduced at T2, while the red

Kratak sadržaj

Uvod: Pretpostavili smo da rana enteralna nutritivna podrška može sinergistički regulisati tri domena biomarkera (hemoreologiju, inflamatorni stres, crevnu barijeru) poboljšanjem nutritivnog metabolizma kod pacijenata sa akutnim cerebralnim moždanim udarom (CMU) komplikovanim poremećajima gutanja (PG). Cilj ove studije je bio da se potvrdi hipoteza ispitivanjem dinamičkih promena tri domena i da se ispitaju biohemijske korelacije između ovih promena.
Metode: Ova retrospektivna kohortna studija obuhvatila je 126 pacijenata sa akutnim komplikovanim sindromom depresije (SD) primljenim u našu bolnicu od avgusta 2022. do avgusta 2025. godine. Prema planu intervencije, pacijenti su raspoređeni u grupu za posmatranje (68 slučajeva; enteralna nutritivna podrška) ili kontrolnu grupu (58 slučajeva; rutinska terapija nadoknade tečnosti). Venska krv na gladno je prikupljena pre intervencije (T0), nakon 7 dana (T1) i nakon 14 dana (T2). Hemorološki parametri i funkcionalni indeksi crvenih krvnih zrnaca mereni su automatskim hemorološkim analizatorom; inflamatorni/stres-povezani medijatori i indikatori povezani sa crevnom barijerom kvantifikovani su imunosorbentnim testom; indeksi povezani sa metabolizmom ishrane određeni su pomoću auto
Rezultati: U posmatračkoj grupi, hemoreološki parametri su se progresivno poboljšavali nakon intervencije. U poređenju sa T0, viskozitet pune krvi pri visokom smicanju (W-Vis-H), viskozitet pune krvi pri niskom smicanju (W-Vis-L) i fibrinogen bili su niži u T1 i dodatno smanjeni u

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blood cell deformation index (RDI) increased (P<0.05). Inflammatory/stress-related mediators, and intestinal barrier indicators declined in parallel. By T2, tumor necrosis factor-α, interleukin-6, high-sensitivity C-reactive protein, and endotoxin each decreased by more than 35% versus T0 (P<0.05). Nutrition metabolism indices increased gradually: prealbumin (PA) and transferrin (TRF) increased at T1, and six indicators (including albumin [ALB] and hemoglobin [Hb]) showed statistically significant improvements at T2 (P<0.05). No significant changes were observed in these indices at any time point in the control group (P>0.05). Between-group comparisons showed more favorable values in the observation group at T1 and T2 (P<0.05).

Conclusion: In patients with acute CS complicated by SD, enteral nutrition support was associated with short-term favorable changes in multiple biochemical indicators, suppression of excessive inflammatory/stress responses, and reinforcement of nutritional reserves.

Keywords: acute stroke, dysphagia, enteral nutrition support, blood microcirculation, inflammatory/stress-related mediators, nutritional metabolism

T2, dok se indeks deformacije crvenih krvnih zrnaca (RDI) povećao (P<0,05). Inflamatorni/stres-povezani medijatori i indikatori crevne barijere su se paralelno smanjivali. Do T2, faktor tumorske nekroze-a, interleukin-6, C-reaktivni protein visoke osetljivosti i endotoksin su se smanjili za više od 35% u odnosu na T0 (P<0,05). Indeksi metabolizma ishrane su se postepeno povećavali: prealbumin (PA) i transferin (TRF) su se povećali u T1, a šest indikatora (uključujući albumin [ALB] i hemoglobin [Hb]) pokazalo je statistički značajna poboljšanja u T2 (P<0,05). Nisu primećene značajne promene u ovim indeksima ni u jednom trenutku u kontrolnoj grupi (P>0,05). Poređenja između grupa pokazala su povoljnije vrednosti u posmatranoj grupi na T1 i T2 (P<0,05).

Zaključak: Kod pacijenata sa akutnim komplikovanim sindromom začepljenja pluća (SD), enteralna nutritivna podrška bila je povezana sa kratkoročnim povoljnim promenama u višestrukim biohemijskim pokazateljima, suzbijanjem prekomernih inflamatornih/stresnih odgovora i jačanjem nutritivnih rezervi.

Ključne reči: akutni moždani udar, disfagija, enteralna nutritivna podrška, mikrocirkulacija krvi, inflamatorni/stresni medijatori, nutritivni metabolizam

Introduction

Cerebral stroke (CS), specifically acute ischemic cerebral stroke (AIS) in this study, is a neurological emergency with substantial disability and mortality worldwide, and outcomes are strongly shaped by complications arising in the acute phase (1). Swallowing disorders (SD) are frequent after acute CS (reported incidence 30%–65%) and can precipitate malnutrition, aspiration pneumonia, and related secondary problems, thereby worsening the overall clinical course (2). Enteral nutrition is a cornerstone intervention for acute CS complicated by SD, providing energy substrates and helping preserve intestinal barrier integrity; however, how this support translates into changes in microcirculation and stress cytokine expression has not been fully characterized (3). Disrupted microcirculation is a core feature of CS-related injury and may intensify cerebral ischemia and hypoxia (4). Meanwhile, excessive activation of inflammatory/stress-related mediators (e.g., tumor necrosis factor-α, interleukin-6, and C-reactive protein) can amplify inflammatory cascades and aggravate neurological injury (5). Together, these processes are closely tied to disease progression and prognosis and represent key biochemical nodes in the pathophysiology of CS (6).

Existing clinical studies have largely focused on the macroscopic effects of enteral nutrition in CS, such as nutritional indices and clinical outcomes. Although some reports describe changes in inflammatory factors, few have tracked microcirculation-related indicators (including hemorheology and perfusion surrogates) in parallel with stress cytokine dynamics, making it difficult to interpret their temporal coupling. Mechanistic insight into how these domains interact under enteral nutrition also remains limited (7, 8). In addition, much of the available evidence comes from small prospective cohorts, whereas retrospective evaluations in populations managed under updated CS diagnostic and treatment standards since 2022 are relatively scarce (9). As a result, the regulatory patterns of enteral nutrition on microcirculation and inflammatory/stress-related mediators within current care pathways remain insufficiently defined, limiting the biochemical basis for more precise nutritional interventions.

Accordingly, this study characterizes the dynamic trajectories of key microcirculation parameters and inflammatory/stress-related mediators before and after enteral nutrition support in patients with acute CS complicated by SD. The analysis emphasizes biochemical coherence across systems, aiming to clarify how enteral nutrition reshapes short-term microenvironmental homeostasis. These data may strengthen laboratory evidence for optimizing nutritional strategies and support the use of microcirculation- and cytokine-related indices as adjunct markers for condition assessment and prognosis appraisal.

Materials and Methods

Study Subjects

A total of 126 patients with acute CS complicated by SD treated in our hospital from August 2022 to August 2025 were retrospectively enrolled. This study was approved by the Medical Ethics Committee of our hospital. Among them,

68 patients received enteral nutrition support (observation group), whereas 58 did not receive enteral nutrition support (control group). This study will be conducted in strict compliance with the Declaration of Helsinki, and written informed consent was waived due to retrospective analysis. Patients in the control group were unable to take oral food due to dysphagia, did not receive EN, PN support, and did not receive standardized swallowing diet intervention. Only routine rehydration (glucose and electrolyte injection) was given to maintain basic fluid balance, and the volume of rehydration was 1500–2000 mL/d. The observation group only received enteral nutrition, without additional oral feeding and parenteral nutrition.

Inclusion and Exclusion Criteria

Inclusion criteria ① Conforming to the diagnostic criteria for acute ischemic AIS (10), confirmed by cranial CT/MRI imaging, with the time from onset to admission ≤ 72 h; ② SD assessment: grade III–V in Kubota Water Swallowing Test (11), or swallowing dysfunction indicated by videofluoroscopic swallowing study (VFSS); ③ Patients in the observation group received enteral nutrition support with a continuous treatment duration ≥ 14 d, and the nutrition plan was fully traceable; ④ Complete laboratory data were available, including blood microcirculation, inflammatory/stress-related mediators, and related biochemical indices at each time point; ⑤ Aged 18–80 years, with clear consciousness and able to cooperate with basic assessment.

Exclusion criteria ① Severe hepatic or renal insufficiency, malignant tumors, sepsis, or autoimmune diseases; ② History of chronic SD, intestinal failure, or contraindications to enteral nutrition; ③ Use of glucocorticoids, immunosuppressants, anticoagulant, or thrombolytic drugs within the recent month; ④ Hematological diseases or coagulation dysfunction (INR>1.5); ⑤ Missing medical records or incomplete key laboratory test data.

Enteral Nutrition Support Scheme and Implementation Standards

Enteral nutrition was administered via a nasogastric tube (12F silicone catheter), with radiographic confirmation – performed at the bedside using abdominal X-ray – that the distal tip was positioned within the gastric body. Initiation occurred at an infusion rate of 20 mL/h; this rate was incrementally increased by 10 mL/h every 24 hours, contingent upon gastrointestinal tolerance, up to a maximum of 50 mL/h. The nutritional targets were set at 30–35 kcal/kg/day for energy and 1.2–1.5 g/kg/day for protein. Advancement to higher caloric delivery was permitted only in the absence of intolerance signs – including vomiting, abdominal distension, or diarrhea – and provided gastric residual volume remained below 200 mL over any 4-hour period. Enteral nutrition support was initiated within 24–72 h after admission. Intermittent nasogastric tube infusion was adopted, with an initial calorie supply of 15–20 kcal·kg/d and an increase of 5 kcal·kg/d every 3 d. The enteral nutrition preparation used in this study was the whole protein high-nutrition formula powder (trade name: Nengquansu, Nutricia Pharmaceutical Co., LTD.). The following ingredients are the standard solution concentrations after the preparation was adjusted according to the instructions: containing 35% whey protein and 25% soybean protein, with 5 g dietary fiber per 100 mL and vitamin B group content ≥ 2.5 mg per 100 mL.

Clinical data collection

Demographic information, vascular risk factors, stroke severity at admission (NIHSS), imaging findings, and relevant comorbidities were extracted from electronic medical records. Concomitant therapies during hospitalization (e.g., antiplatelet agents, statins, thrombolysis/thrombectomy when applicable) were recorded.

Detection Time Points and Sample Processing

Fasting elbow venous blood (8 mL) was collected at three time points: before enteral nutrition support (T0, within 24 h after admission), at 7 d after support (T1), and at 14 d after support (T2). Samples were divided into four parts: ① Two milliliters of EDTA solution (1.8 mg/mL) were added to an EDTA-coated anticoagulant tube, and plasma was subsequently separated for hemorheological analysis. ② Two milliliters of blood were collected into a plain (non-additive) dry tube; serum was isolated after centrifugation and used for quantification of stress-related cytokines. ③ Two milliliters of blood were collected into a heparin-coated anticoagulant tube; plasma was separated and utilized for assessment of oxidative stress markers. The colorimetric assay kit employed was validated for use with heparinized plasma. ④ Two milliliters of blood were collected into a non-anticoagulant (serum-separation) tube; serum was obtained following clot formation and centrifugation, and used for measurement of biochemical indicators associated with intestinal barrier function. Centrifugation was performed at 3500×g (4 °C) for 15 min. All separated plasma and serum samples were stored at -80 °C, with repeated freeze–thaw cycles limited to ≤ 3 times, and batch testing was performed centrally. To minimize pre-analytical variability, all samples were collected

under standardized conditions, processed within the same predefined time window, and stored under identical conditions. Whenever feasible, samples from different time points of the same patient were analyzed within the same analytical batch to reduce inter-run variation. Samples showing visible hemolysis or clotting were excluded from analysis.

Laboratory measurements

All laboratory testing was performed in the central clinical laboratory accredited according to ISO 15189. Assays were carried out by experienced technicians blinded to group allocation whenever feasible. Calibration and internal quality control (IQC) followed the manufacturer's instructions and laboratory standard operating procedures. All laboratory analyses were performed in the central clinical laboratory using routine, fully automated platforms under standardized operating procedures. Hemorheological parameters were measured using an automatic hemorheology analyzer (rotational viscometry-based system) with instrument-matched reagents. Routine biochemical indices were determined on an automated clinical chemistry analyzer, and enzyme-linked immunosorbent assays were conducted using a microplate reader compatible with the corresponding commercial kits. All instruments were operated according to the manufacturers' instructions and underwent regular calibration and maintenance.

Assay performance characteristics were evaluated according to routine laboratory verification procedures. For automated biochemical assays, the analytical measuring range, limit of detection, and imprecision (intra- and inter-assay coefficients of variation) were consistent with the manufacturers' specifications and verified by internal quality control records. For ELISA-based measurements, standard curves demonstrated good linearity across the analytical range (coefficient of determination $R^2 \geq 0.99$). Recovery rates ranged from 95% to 105%, and intra-assay coefficients of variation were controlled within 5%. Hemorheological parameters showed analytical coefficients of variation ≤3% based on repeated measurements of quality control materials.

Information of instruments and supporting reagents used in this research: ① Automatic hemorheology instrument: Chongqing Tianhai Medical Equipment Co., LTD., model TH-MS9000, supporting reagent item No. TH-202207; ② Automatic biochemical analyzer: Hitachi Hi-Tech Co., LTD., model 7600-020, supporting nutrient protein detection reagent item No. 7600-S01; ③ Microplate reader: Thermo Fisher Scientific (China) Co., LTD., model Multiskan FC, detection wavelength 450 nm, reference wavelength 630 nm, ELISA kit item numbers are all Shanghai enzyme-linked Biology E-BC-2022 series; ④ Oxidative stress colorimetric assay kit: Nanjing Jiancheng Bioengineering Institute.

Blood Microcirculation Indicators

Hemorheological measurements were performed using an automatic hemorheology analyzer based on rotational viscosity measurement. Instrument-matched special kits were used (batch No. 20220715). The following indicators were measured: ① Whole-blood high-shear viscosity (W-Vis-H) (200 s^{-1}, reflecting biochemical characteristics related to red blood cell deformability); ② Whole-blood low-shear viscosity (W-Vis-L) (5 s^{-1}, reflecting biochemical state related to red blood cell aggregation); ③ Plasma viscosity (PV) (capillary method–derived); ④ Red blood cell aggregation index (RAI); ⑤ Red blood cell deformation index (RDI); ⑥ Fibrinogen (FIB) (coagulation method). Blank controls and calibrators were included to ensure an analytical coefficient of variation (CV) ≤3%. The RAI and RDI were automatically calculated by the automatic hemorheology meter (Chongqing Tianhai TH-MS9000) with its own special algorithm, based on the raw data such as high/low shear viscosity detected by the instrument, without manual calculation.

Inflammatory/Stress-related Mediators and Cytokines

Detection was carried out using enzyme-linked immunosorbent assay (ELISA), following routine clinical laboratory quality-control specifications. Kits were purchased from Shanghai Enzyme-linked Biotechnology Co., Ltd., including tumor necrosis factor-α (TNF-α), interleukin-6 (IL-6), interleukin-1β (IL-1β), high-sensitivity C-reactive protein (hs-CRP), and monocyte chemoattractant protein-1 (MCP-1). An automatic microplate reader was used (450 nm detection wavelength; 630 nm reference). Concentrations were calculated from standard curves ($R^2 \geq 0.995$). Each sample was run in triplicate wells, and the mean value was used as the final result.

Oxidative Stress and Intestinal Barrier Function Biochemical Indicators

Oxidative stress indicators Detection was performed by colorimetric methods using kits from Nanjing Jiancheng Bioengineering Institute, including superoxide dismutase (SOD), malondialdehyde (MDA), and glutathione peroxidase (GSH-P). Intestinal barrier function indicators Intestinal fatty acid binding protein (I-FABP) and endotoxin (ET) were detected by ELISA using the same general procedure as above, with replicate-well CV controlled at ≤ 5%.

Nutritional Proteins

Nutritional proteins were detected using an automatic biochemical analyzer, including serum albumin (ALB), total protein (TP), prealbumin (PA), transferrin (TRF), and hemoglobin (Hb). After turning on the instrument, the reagent kits for each assay were equilibrated to room temperature and loaded into the designated reagent positions. The corresponding test items were selected on the operation interface, and the detection wavelengths were set (ALB 628 nm, TP 546 nm, PA 340 nm, TRF 340 nm, Hb 540 nm), with the detection mode confirmed as double-well detection. Sample numbers and target items were entered, and the instrument then automatically completed aspiration, reagent addition, reaction, absorbance reading, and concentration calculation. For each batch, blank controls, calibrators, and quality-control materials at three concentration levels (high, medium, and low) were included. Each sample was measured in parallel wells; if the relative deviation between the two wells exceeded 5%, the sample was re-tested.

Laboratory Test Quality Control Measures

1. Instrument Calibration: All instruments underwent metrological certification and were calibrated daily using certified calibrators. Weekly maintenance and performance verification were conducted. Calibration acceptance was determined according to the Westgard multirule criteria (1-2S/1-3S).

2. Reagent Management: All reagents were stored at –20 °C and used within their stated expiration dates. Assays were initiated within 2 hours of reagent reconstitution.

3. Sample Quality Control: Specimens were processed within 2 hours of venipuncture. Hemolyzed samples (hemoglobin concentration >5 g/L) were excluded from analysis and recollected.

4. Methodology Verification: In ELISA assays, a standard curve was generated in triplicate per run, with an $R^2 \geq 0.995$ required for acceptance. Three concentration levels (low, medium, high) of quality control materials were analyzed five times each; recovery rates were required to fall within 95–105%. For hemorheological parameters, two levels of internal quality control materials were tested daily over 20 consecutive days; the within-run coefficient of variation (CV) was ≤3%. Acceptance criteria for assay precision were defined as intra-assay CV ≤5% and inter-assay CV ≤8%, evaluated in accordance with Westgard multirule principles.

Statistical Methods

SPSS 26.0 statistical software was used for data processing. Measurement data were assessed for normality using the Shapiro–Wilk test. Variables conforming to normal distribution were expressed as mean ± standard deviation ($\bar{\chi} \pm s$). In order to control the type I error caused by multiple testing, the Holm-Bonferroni method was used to correct the results of inter-group and intra-group comparisons of all biomarkers. The prespecified primary endpoints of this study were whole blood high shear viscosity (W-Vis-H), tumor necrosis factor-α (TNF-α), and prealbumin (PA) at 14 days of intervention (T2). Only LSD-t test was used for pairwise comparison of the primary endpoints within the group. All secondary end points were tested with the use of adjusted methods, and P values of less than 0.05 were considered to indicate statistical significance. Non-normally distributed variables were expressed as median (interquartile range) [M (Q1, Q3)] and compared using the Friedman M test. Count data were expressed as n (%) and compared using the χ^2 test. A two-tailed P value<0.05 was considered statistically significant.

Results

Comparison of Baseline Data

Baseline characteristics, including age, sex, and CS type, did not differ significantly between the observation and control groups (P>0.05, *Table I*).

Table I Comparison of baseline clinical characteristics between the two groups.

Groups	n	Gender	Age	Duration of illness (h)	Underlying diseases			Smoking	Drinking
		Male/female			Hypertension	Diabetes mellitus	Coronary heart disease	Yes/no	Yes/no
Control	58	30/28	65.40±8.40	47.07±11.93	34 (58.62)	24 (41.38)	20 (34.48)	38/20	26/32
Observation	68	39/29	64.59±8.71	48.88±9.97	45 (66.18)	35 (51.47)	20 (29.41)	51/17	26/42
		0.400	0.528	0.930	0.764	1.280	0.372	1.357	0.561
		0.527	0.599	0.354	0.382	0.258	0.542	0.244	0.454

Changes in Core Hemorheological Biochemical Indicators

There were no significant fluctuations in W-Vis-H, W-Vis-L, or PV in the control group from T0 to T2 (P>0.05). In the observation group, all three indices declined over time; compared with T0, values were lower at T1 and further reduced at T2 (P<0.05). At T2, W-Vis-H decreased to (4.82±0.35) mPa·s and W-Vis-L to (9.79±0.75) mPa·s. Between-group values were comparable at T0 (P>0.05). After intervention (T1 and T2), W-Vis-H, W-Vis-L, and PV were lower in the observation group than in the control group, and the between-group differences were more pronounced at T2 (P<0.05, *Figure 1*).

Changes in Red Blood Cell Function and Fibrinogen Indicators

Similarly, the levels of RAI, RDI, and fibrinogen in the control group remained stable at all time points (P>0.05). In the observation group, RAI and fibrinogen decreased continuously, whereas RDI increased at T1 and T2 compared with T0 (P<0.05). At T2, RDI increased to (0.66±0.07) (reference range: 0.60–0.80) and fibrinogen decreased to (3.06±0.37) g/L (reference range: 2.00-4.00 g/L), which were within the normal reference ranges. Between-group comparison showed no significant differences at T0 (P>0.05). At T1 and T2, RAI and fibrinogen were lower in the observation group than in the control group, while RDI was higher (P<0.05, *Figure 2*).

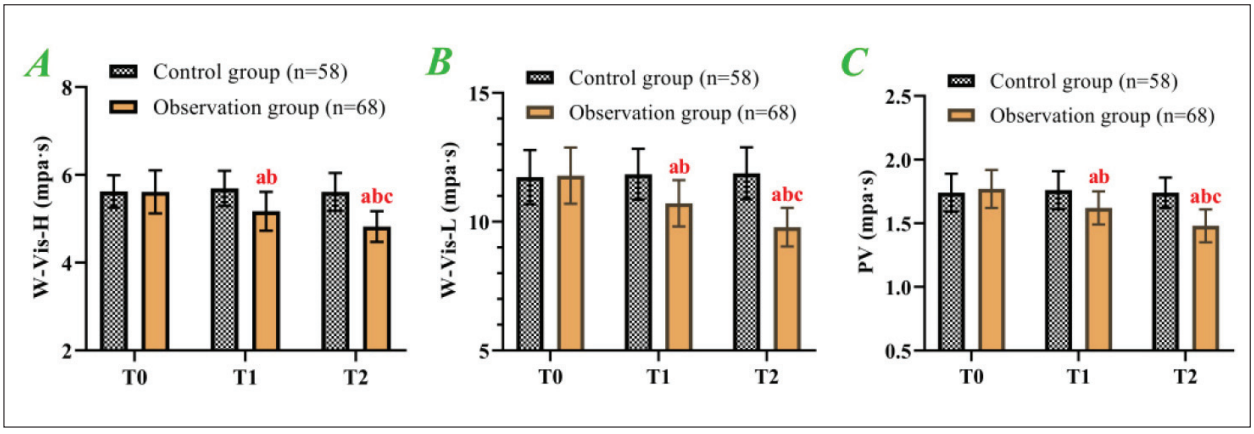

Figure 1 Dynamic changes in core hemorheological indicators of the two groups at different time points.

A; Changes in whole-blood high-shear viscosity (W-Vis-H); B: Changes in whole-blood low-shear viscosity (W-Vis-L); C: Changes in plasma viscosity (PV). Note: Compared with the control group (between groups), $^{a}P<0.05$, compared with T1 (within groups), $^{a}P<0.05$, compared with T2 (within groups), $^{c}P<0.05$.

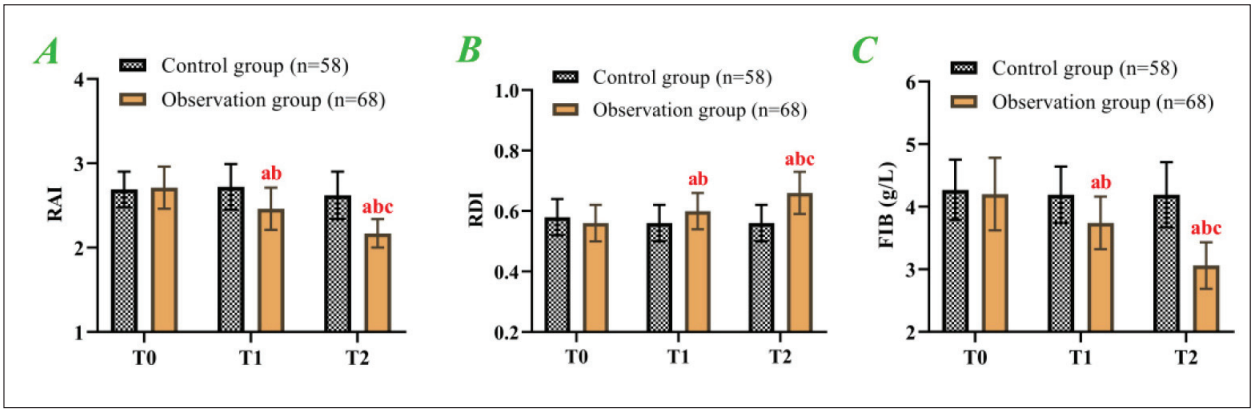

Figure 2 Dynamic changes in red blood cell function and fibrinogen indicators of the two groups at different time points.

A; Changes in whole-blood high-shear viscosity (W-Vis-H); B: Changes in whole-blood low-shear viscosity (W-Vis-L); C: Changes in plasma viscosity (PV). Note: Compared with the control group (between groups), $^{a}P<0.05$, compared with T1 (within groups), $^{a}P<0.05$, compared with T2 (within groups), $^{c}P<0.05$.

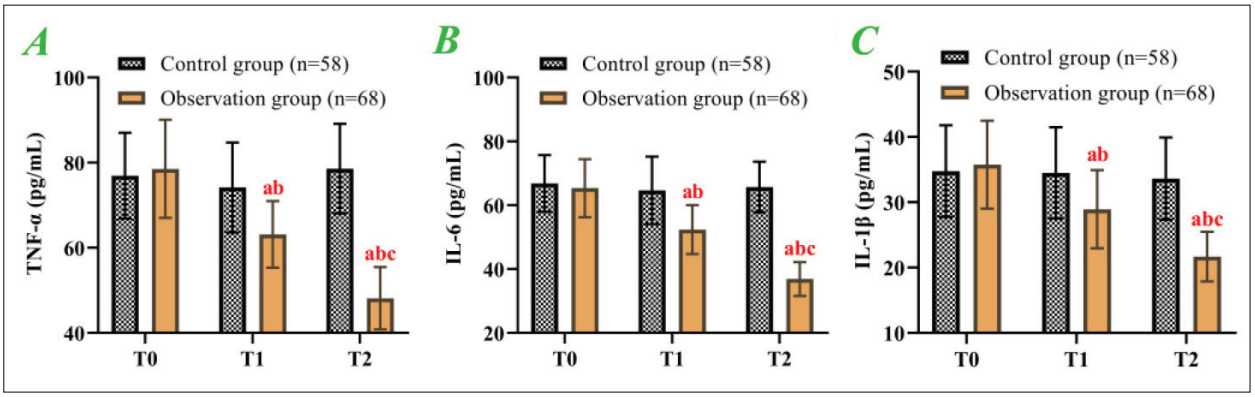

Figure 3 Dynamic changes in key inflammatory/stress-related mediators of the two groups at different time points.

A: Changes in tumor necrosis factor-α (TNF-α) level; B: Changes in interleukin-6 (IL-6) level; C: Changes in interleukin-1β (IL-1β) level. Note: Compared with the control group (between groups), $^{a}P<0.05$, compared with T1 (within groups), $^{a}P<0.05$, compared with T2 (within groups), $^{c}P<0.05$.

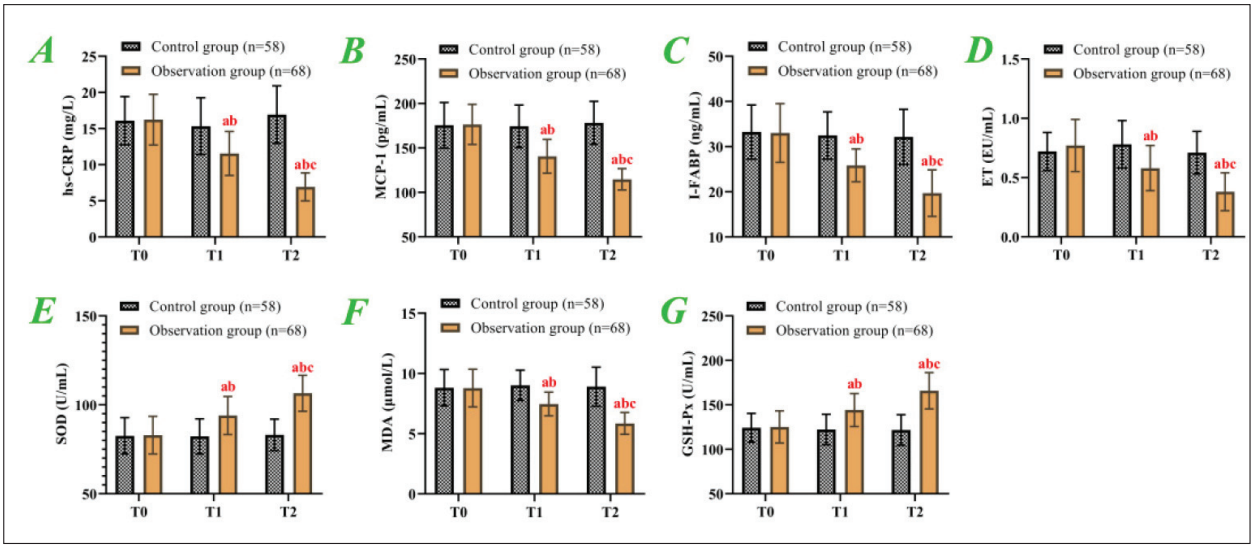

Figure 4 Dynamic changes in inflammatory, intestinal barrier and oxidative stress-related indicators of the two groups at different time points.

A: Changes in high-sensitivity C-reactive protein (hs-CRP) level; B: Changes in monocyte chemoattractant protein-1 (MCP-1) level; C: Changes in intestinal fatty acid binding protein (I-FABP) level; D: Changes in endotoxin (ET) level; E: Changes in malondialdehyde (MDA) level; F: Changes in superoxide dismutase (SOD) activity; G: Changes in glutathione peroxidase (GSH-Px) activity. Note: Compared with the control group (between groups), $^{a}P<0.05$, compared with T1 (within groups), $^{a}P<0.05$, compared with T2 (within groups), $^{c}P<0.05$

Changes in Key Inflammatory/Stress-related Mediators

TNF-α, IL-6, and IL-1β showed no significant fluctuations in the control group during follow-up, and within-group differences across time points were not significant ($P > 0.05$). In the observation group, all three cytokines decreased continuously ($P<0.05$). The two groups were comparable at T0 ($P>0.05$); at T1 and T2, cytokine levels were lower in the observation group than in the control group, with the most pronounced between-group contrast at T2 ($P<0.01$, *Figure 3*).

Changes in Inflammatory, Intestinal Barrier and Oxidative Stress-related Biochemical Indicators

The levels of hs-CRP, MCP-1, I-FABP, ET, and MDA in the observation group showed a clear decreasing pattern; compared with T0, each marker was reduced at T1 and further reduced at T2, with statistically significant differences ($P < 0.05$). At T2, hs-CRP decreased to (6.92±1.94) mg/L and ET to (0.38±0.16) EU/mL, representing reductions of more than 40% versus T0. Between-group comparisons showed no significant differences at T0

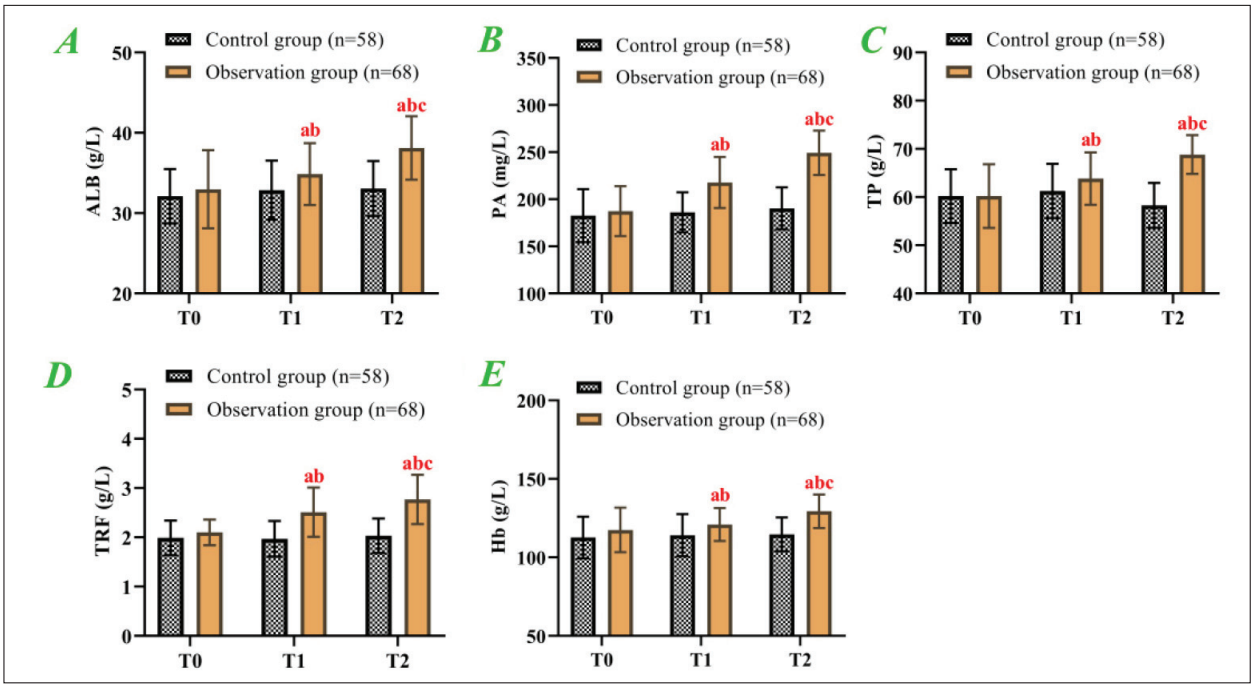

Figure 5 Dynamic changes in nutritional protein indicators of the two groups at different time points.

A: Changes in serum albumin (ALB) level; B: Changes in prealbumin (PA) level; C: Changes in total protein (TP) level; D: Changes in transferrin (TRF) level; E: Changes in hemoglobin (Hb) level. Note: Compared with the control group (between groups), $^{a}P<0.05$, compared with T1 (within groups), $^{a}P<0.05$, compared with T2 (within groups), $^{c}P<0.05$.

(P>0.05); at T1 and T2, these indices were lower in the observation group than in the control group (P<0.05). In contrast, SOD and GSH-Px increased with treatment progression, peaked at T2, and were higher than those in the control group (P<0.05, *Figure 4*).

Changes in Nutritional Protein Indicators

Finally, nutritional protein indices showed no significant variation in the control group from T0 to T2 (P>0.05), suggesting that routine fluid replacement alone did not improve short-term nutritional and metabolic imbalance in patients with acute CS complicated by SD. In the observation group, PA and TRF increased at T1 (P<0.05). At T2, all five indicators increased significantly (P<0.05). At T1 and T2, PA, TRF, ALB, and other nutritional indices were higher in the observation group than in the control group, and the between-group differences were more evident at T2 (P<0.05, *Figure 5*).

Discussion

The results of this study suggest that enteral nutrition support in acute CS complicated by SD is accompanied by coordinated short-term improvements across multiple biochemical domains. Hemorheological parameters and red blood cell function moved toward more favorable ranges, inflammatory/stress-related mediators and inflammatory mediators declined, intestinal barrier–related indicators decreased, and nutrition/metabolism indices increased over time. In contrast, in patients who did not receive enteral nutrition support, these laboratory indices stayed close to baseline throughout follow-up. Overall, the data point to a multi-system laboratory response after enteral nutrition support in the acute stage.

These findings can be explained by two interrelated biochemical mechanisms. ① At the nutrition and metabolism level, the high-quality protein delivered by enteral nutrition is digested and absorbed into essential amino acids, including leucine and glutamine. In this study, PA in the observation group was increased at T1, suggesting that leucine may activate the mammalian target of rapamycin (mTOR) pathway and promote hepatic synthesis of albumin, PA, and TRF (12). Glutamine is an important energy substrate of intestinal epithelial cells. In this study, I-FABP and ET decreased in the observation group, suggesting that glutamine may improve the metabolic state of intestinal mucosa. and help sustain nutrient absorption capacity (13). In addition, iron provided through nutritional formulations may bind TRF and be taken up by hematopoietic precursors to support Hb synthesis, which may contrib-

ute to correction of nutrition-related anemia in the acute phase (14). ② Improvements in nutritional substrates may also couple to microcirculation and inflammatory regulation. Adequate energy and amino acids may temper stress-related catabolism, limit excessive protein breakdown in skeletal muscle, and reduce immune activation linked to substrate imbalance (15, 16). In the present study, the increase in trophins occurred synchronously with the decrease in inflammatory mediators in the observation group, suggesting that mTOR pathway activation may inhibit the transcription of proinflammatory factors such as TNF-α and IL-6, partly through reducing nuclear translocation of nuclear factor-κB (NF-κB) (17), which aligns with the concurrent rise in nutritional proteins and fall in inflammatory mediators observed here. On the rheological side, in the present study, RDI was significantly increased in the observation group, suggesting that improved protein synthesis may contribute to the maintenance and repair of erythrocyte membrane skeleton proteins, reducing membrane rigidity and enhancing deformability (18). This could lower aggregation and help correct hemorheological abnormalities (19). Better microcirculatory flow may, in turn, improve perfusion to metabolic organs such as the intestine and liver, facilitating nutrient utilization, forming a benign regulatory relationship among nutritional metabolism, microcirculation and inflammation (20). Similar clinical observations have been described by Suzuki et al in CS patients receiving enteral nutrition (21). Notably, PA improved earlier than albumin, which is consistent with the shorter half-life of PA (2–3 d) and supports its use as an earlier laboratory readout during nutritional intervention (22).

However, several limitations should be acknowledged. First, the biomarker panel was limited to routine peripheral blood and serum indices, and deeper mechanistic markers – such as intestinal mucosal tight-junction proteins – were not assessed, which restricts interpretation of barrier-related mechanisms. Second, laboratory methods were primarily ELISA and hemorheology analysis; additional verification using techniques such as Western blotting or RT-qPCR was not performed, so protein and transcription-level corroboration is lacking. Third, the study used a single-center retrospective design with a modest sample size (126 cases), and group allocation was influenced by refusal of enteral nutrition, which may introduce selection bias. Moreover, stratified analyses by stroke etiology, infarct location, or severity were not performed, and different enteral formulas were not compared. Finally, follow-up was limited to 14 d; without longer laboratory tracking, the durability of the observed biochemical changes cannot be determined.

Conclusion

Enteral nutrition support can improve short-term nutritional reserves, microcirculation-related hemorheology, and inflammation/stress-related laboratory indices in patients with acute CS complicated by SD. These findings provide objective laboratory evidence for the application of early enteral nutrition in the acute phase of this population. Future studies should expand sample size, adopt multicenter designs, extend follow-up, and incorporate deeper mechanistic markers and multi-method verification to refine the understanding of how enteral nutrition reshapes biochemical homeostasis and to optimize timing and indicator panels for laboratory monitoring.

Availability of data and materials

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

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Conflict of interest statement

All the authors declare that they have no conflict of interest in this work.

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