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ORIGINAL RESEARCH

Impact of Low-Energy and High-Energy Early Enteral Nutrition Strategies on Patient Outcomes in Acute Kidney Injury

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Objective: To investigate the impact of different early enteral nutrition (EEN) strategies on nutritional indicators and immune function in patients with acute kidney injury (AKI) undergoing continuous renal replacement therapy (CRRT).

Methods: A retrospective analysis was conducted on 60 CRRT-treated AKI patients from January 2020 to March 2024, divided into a control group (high-energy EEN) and an observation group (low-energy EEN). Nutritional indicators (albumin, prealbumin, hemoglobin), immune function indicators (CD4+, CD8+, immunoglobulin A, G, M), and clinical outcomes (ICU stay duration, CRRT duration, gastric retention) were compared.

Results: Before treatment, there were no significant differences in nutritional indicators between the two groups ($P > 0.05$). After 7 days of treatment, the observation group showed significantly greater improvements in all nutritional indicators ($P < 0.05$). Immune function indicators also improved significantly in the observation group ($P < 0.05$). Additionally, the observation group had significantly shorter ICU and CRRT durations compared to the control group ($P < 0.05$).

Conclusion: Compared to high-energy EEN guidance, low-energy EEN guidance significantly improves nutritional status and enhances immune function in CRRT-treated AKI patients.

Keywords: acute renal failure, early enteral nutrition, EEN, nutritional indicators, immune function

Introduction

Renal failure (RF) is a metabolic disease caused by decreased glomerular filtration rate, typically resulting from kidney disease or systemic diseases that progressively damage the kidneys, ultimately leading to renal failure. *Acute kidney injury* (AKI) is a sudden loss of kidney function characterized by an abrupt decline or loss of renal physiological function, marked by a rapid increase in blood urea nitrogen and serum creatinine levels, and electrolyte imbalances.[1,2] Currently, clinical diagnosis and treatment of AKI primarily rely on renal function tests, including serum creatinine and blood urea nitrogen measurements, which are crucial for assessing the patient's renal function and disease severity.[3–5] Continuous renal replacement therapy (CRRT) is a blood purification treatment that removes toxic substances from the kidneys, maintains internal environment stability, and significantly supports organ function. In recent years, it has been widely used in the treatment of sepsis.[6] However, despite the use of CRRT in patients with severe AKI and sepsis,[7] the mortality rate among these patients has not decreased.

Nutritional support has always been a focus of clinical research, especially early enteral nutrition (EEN). EEN not only provides essential energy but also protects the intestinal barrier function and regulates the immune system, having a significant positive impact on patient prognosis.[8] AKI and critically ill patients are the primary groups that require artificial nutrition.[9] For AKI patients induced by sepsis, early nutritional support can rapidly improve nutritional levels and promote the recovery of gastrointestinal and immune system functions. Studies have indicated that improper enteral nutrition support can lead to gastric retention in patients.[10] In the early stages of sepsis complicated by AKI, patients are usually in a stress state, and the goal of EEN should be to maintain nutritional status without increasing metabolic

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burden. Although moderately increasing energy supply helps improve the condition, there is no consensus on the optimal energy requirement,[11–13] and studies on EEN energy requirements are still rare. In this study, "high-energy" enteral nutrition refers to a regimen that provides a greater caloric density, typically involving a higher proportion of carbohydrates and proteins, designed to meet the increased metabolic demands of critically ill patients. Conversely, "low-energy" enteral nutrition involves a lower caloric density, focusing on providing sufficient nutrition without over-whelming the patient's compromised metabolic state, which can help avoid gastrointestinal complications.

In summary, this study retrospectively analyzed the clinical data of 60 CRRT-treated AKI patients in our hospital from January 2020 to March 2024. It explored the impact of different early enteral nutrition guidance strategies on nutritional indicators and immune function in CRRT-treated AKI patients.

Materials and Methods

Study Design

This study was conducted at a single institution, Xianyang Central Hospital. This study selected the clinical data of 60 AKI patients treated with CRRT in our hospital from January 2020 to March 2024. Patients were divided into control and observation groups, with 30 patients in each group. Inclusion criteria: (1) met KDIGO guidelines for the definition of AKI;[14] (2) patients met the criteria for CRRT treatment. Exclusion criteria: 1) Mental or cognitive impairment that would hinder informed consent. 2) Major organ dysfunction (excluding renal failure) complicating the patient's condition. 3) Unwillingness to cooperate with treatment. 4) Patients with end-stage kidney disease (ESKD) already on CRRT were excluded to focus specifically on ARF cases. Additionally, patients diagnosed with COVID-19 during the study period were excluded due to potential confounding factors related to the pandemic. The study flowchart is shown in Figure 1.

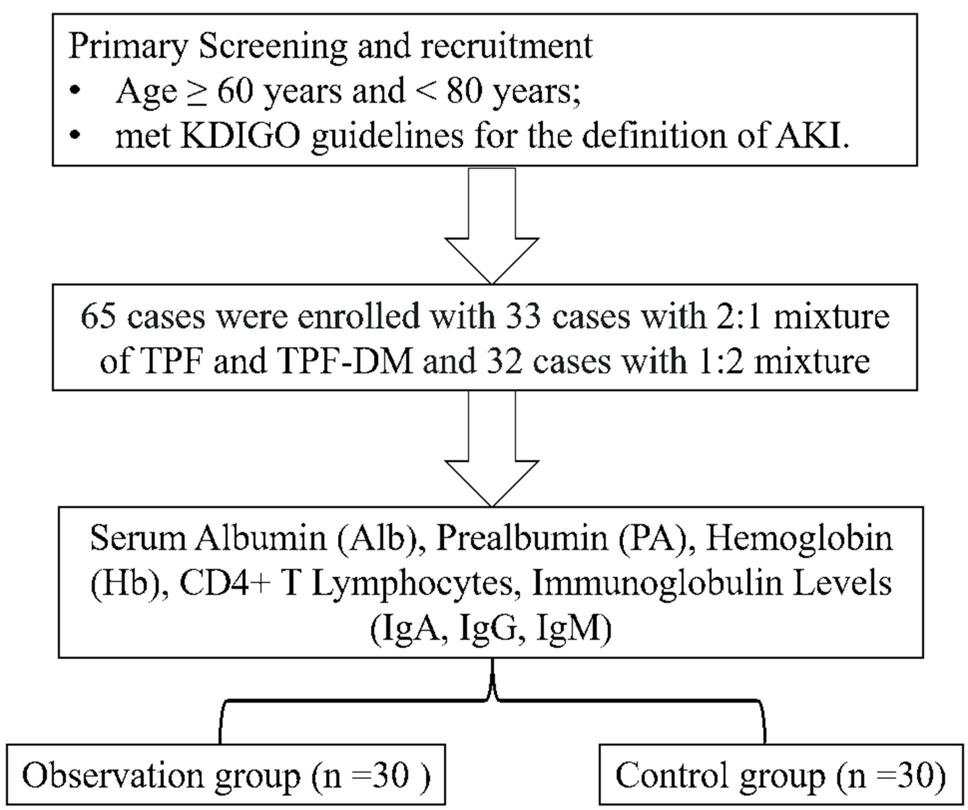

Figure 1 Study flowchart.

Methods

After admission, all patients received routine symptomatic treatment, including antibiotics, glucocorticoids, and regulation of water, electrolytes, and acid-base balance. According to the "Guidelines for the Evaluation and Implementation of Nutritional Support Therapy for Adult Critical Patients" by the American Society for Parenteral and Enteral Nutrition (2016), all patients were required to receive enteral nutrition suspension (TPF, Nutricia Pharmaceutical Co., Ltd.) or enteral nutrition suspension (TPF-DM, Nutricia Pharmaceutical Co., Ltd.) via nasogastric tube within 48 hours of admission for EEN. TPF: Provides approximately 1.5 kcal/mL with a macronutrient composition of 60% carbohydrates, 20% protein, and 20% fat. TPF-DM: Provides approximately 1.2 kcal/mL with a composition of 50% carbohydrates, 30% protein, and 20% fat, specifically designed for patients with diabetes to manage blood sugar levels effectively.

The control group used a 2:1 mixture of TPF and TPF-DM, while the observation group used a 1:2 mixture. On the first day, both groups received 500 mL of nutritional solution, which increased to 550 mL on the second day, and from the third to the seventh day, 800 mL per day. Gastric retention was monitored every 4–6 hours during these 7 days, and adjustments were made based on patient response. If gastric retention exceeded 200 mL, the enteral nutrition infusion was stopped.

The rationale for these ratios was based on the metabolic demands of the patients and the need to balance caloric density with nutritional adequacy. The higher proportion of TPF in the control group aimed to meet the increased caloric and protein requirements of critically ill patients, while the lower ratio of TPF in the observation group was intended to minimize metabolic stress and gastrointestinal complications, allowing for better tolerance of enteral nutrition.

Outcomes

Primary Outcomes

The primary outcomes of the study included several nutritional and immune function indicators. Nutritional status was assessed by measuring serum albumin (Alb), prealbumin (PA), and hemoglobin (Hb) levels. Albumin, a protein synthesized by the liver, indicates nutritional status and liver function, while prealbumin serves as a more sensitive marker for short-term nutritional changes. Hemoglobin levels reflect the oxygen-carrying capacity of the blood and can indicate anemia. Blood samples were collected before treatment and after 7 days of treatment, followed by analysis using an automatic biochemical analyzer. The 7-day timeframe for assessing nutritional and immune outcomes was selected based on clinical guidelines and previous studies indicating that significant changes in nutritional status and immune function typically become apparent within this period in critically ill patients. During this time, enteral nutrition is expected to exert its effects on metabolic parameters, which allows for a meaningful evaluation of the interventions. Furthermore, this duration aligns with the typical monitoring period for patients undergoing CRRT, facilitating the assessment of both immediate and short-term impacts of nutritional strategies.

Immune function was evaluated through the measurement of CD4+ T lymphocytes, which are crucial for immune response, and immunoglobulin levels (IgA, IgG, IgM). These measurements provide insight into the body's immune response to infections. Blood samples were analyzed using flow cytometry for T lymphocyte subsets and enzyme-linked immunosorbent assay (ELISA) for immunoglobulin levels.

Secondary Outcomes

Secondary outcomes encompassed various clinical indicators. ICU stay duration was defined as the total number of days each patient remained in the intensive care unit, providing insight into the severity of the patient's condition and treatment effectiveness. CRRT duration reflected the total number of days patients underwent continuous renal replacement therapy, indicating the intensity and duration of renal support required for recovery. Gastric retention was measured by assessing the volume of gastric contents retained, evaluated every 4–6 hours. If gastric retention exceeded 200 mL, adjustments in nutritional support strategies were implemented to enhance tolerance to enteral nutrition. Gastric retention was defined as the volume of gastric contents remaining in the stomach after a specified feeding period. It was quantified using a gastric residual volume (GRV) measurement, which involved aspirating gastric contents through a nasogastric tube prior to each feeding. Retention was considered significant if the GRV exceeded 200 mL or if the volume was greater than 50% of the total infused volume. This method was validated against clinical outcomes, including the occurrence of aspiration and gastrointestinal intolerance.

Additionally, data collected included weight to monitor changes in nutritional status, hematocrit (HCT) to indicate the proportion of blood volume occupied by red blood cells, and serum creatinine (Cr) and blood urea nitrogen (BUN) levels to assess kidney function. Electrolytes, including potassium (K), phosphorus (Phos), and magnesium (Mg), were measured to evaluate metabolic balance and the effectiveness of renal support.

Statistical Analysis

Statistical analysis was performed using SPSS 23.0. Descriptive statistics summarized demographic and clinical characteristics. Differences between groups were assessed using *t*-tests for continuous variables and χ^2-tests for categorical variables. To address potential confounding factors, multivariable analysis was conducted, adjusting for variables such as age, gender, and baseline comorbidities. To control for the risk of Type I error due to multiple comparisons, we utilized the Bonferroni correction method. This approach involved adjusting the significance level for each hypothesis tested by dividing the overall alpha level (0.05) by the number of comparisons made. Statistical significance was determined at $P < 0.05$, indicating meaningful differences between the treatment groups.

Results

Comparison of General Information Between the Two Groups

There were no statistically significant differences in age, gender, and 24-hour urine output between the control and observation groups ($P > 0.05$), indicating comparability. The clinical data of the patients are shown in Table 1.

Comparison of Nutritional Indicators Between the Two Groups

Before treatment, there were no statistically significant differences in Alb, PA, and Hb levels between the two groups ($P > 0.05$). However, after 7 days of treatment, both groups showed significant improvements in Alb, PA, and Hb levels compared to before treatment. The observation group showed significantly greater improvements than the control group

Table 1 Comparison of General Data Between the Two Groups ($\bar{x} \pm s$)

Variable	Observation Group (n=30)	Control Group (n=30)	t/χ^2	p
Gender (n)				
Male	18	17	0.0686	0.7934
Female	12	13		
Age (years)	61.32 ± 4.93	62.16 ± 5.02	0.6539	0.5158
Body Weight (kg)	67.58 ± 12.34	66.87 ± 11.56	0.325	0.745
Hematocrit (HCT) (%)	36.5 ± 4.5	36.1 ± 4.3	0.408	0.684
Serum Creatinine (Cr) (mg/dL)	2.1 ± 0.9	2.2 ± 0.8	0.45	0.652
Blood Urea Nitrogen (BUN) (mg/dL)	45.3 ± 12.1	47.2 ± 11.7	0.4	0.69
Potassium (K) (mEq/L)	4.6 ± 0.7	4.7 ± 0.8	0.5	0.63
Phosphorus (Phos) (mg/dL)	3.8 ± 0.6	4.0 ± 0.7	0.25	0.8
Magnesium (Mg) (mg/dL)	2.2 ± 0.4	2.3 ± 0.5	0.3	0.76
24-Hour Urine Output (mL)	322.57 ± 91.29	321.62 ± 89.75	0.0406	0.9677
ICU Stay Duration (days)	12.6 ± 3.4	13.1 ± 3.7	0.62	0.535
CRRT Duration (days)	8.4 ± 2.1	8.7 ± 2.3	0.4	0.69
Gastric Retention (mL)	180 ± 50	190 ± 55	0.5	0.62
Albumin (g/dL)	2.8 ± 0.5	2.7 ± 0.4	0.4	0.69
Prealbumin (g/dL)	15.2 ± 3.1	14.8 ± 3.0	0.3	0.76
Hemoglobin (g/dL)	10.5 ± 1.2	10.3 ± 1.1	0.45	0.652
CD4+ T Lymphocytes (cells/μL)	550 ± 150	530 ± 140	0.4	0.69
IgA (mg/dL)	150 ± 30	145 ± 28	0.35	0.73
IgG (mg/dL)	900 ± 100	875 ± 95	0.25	0.8
IgM (mg/dL)	80 ± 20	78 ± 18	0.4	0.69

(P < 0.05), as detailed in Figure 2. This trend suggests that low-energy nutrition may enhance protein synthesis and contribute to improved nutritional status, which is crucial for recovery in critically ill patients.

Comparison of Immune Function Indicators Between the Two Groups

As shown in Figures 3 and 4, there were no statistically significant differences in immune function indicators between the two groups before treatment (P > 0.05). After 7 days of treatment, both groups showed improvements in immune function indicators. The observation group exhibited significantly higher improvements in CD4+, IgA, IgG, and IgM levels compared to before treatment and the control group, with statistically significant differences (P < 0.05). This increase in CD4+ T cells is clinically significant, as it indicates a potential enhancement in the immune response, which is vital for combating infections in vulnerable patients. The increase in immunoglobulin levels further supports this trend, suggesting that the low-energy enteral nutrition strategy may bolster immune function.

Comparison of Clinical Indicators Between the Two Groups

Urinary retention refers to the inability to completely empty the bladder, leading to the accumulation of urine. In this study, urinary retention is assessed through 24-hour urine output measurements, which serve as vital indicators of renal function and overall fluid balance in critically ill patients. High levels of urinary retention may suggest impaired renal function or urinary tract obstruction, necessitating adjustments in fluid management strategies. This is particularly significant for patients undergoing Continuous Renal Replacement Therapy (CRRT), as it can affect fluid balance and electrolyte levels. Additionally, urinary retention may correlate with gastric retention, impacting the tolerance to enteral

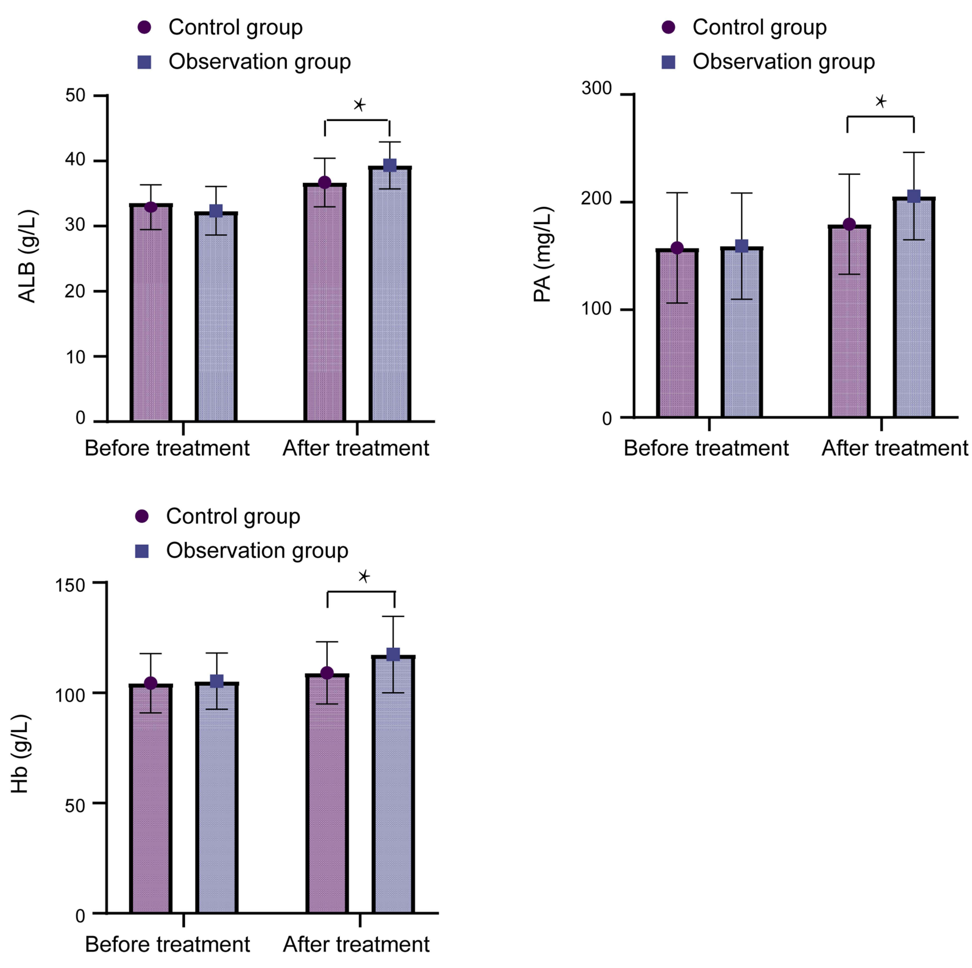

Figure 2 Comparison of Nutritional Indicator Changes Between the Two Groups. *Represent P<0.05.

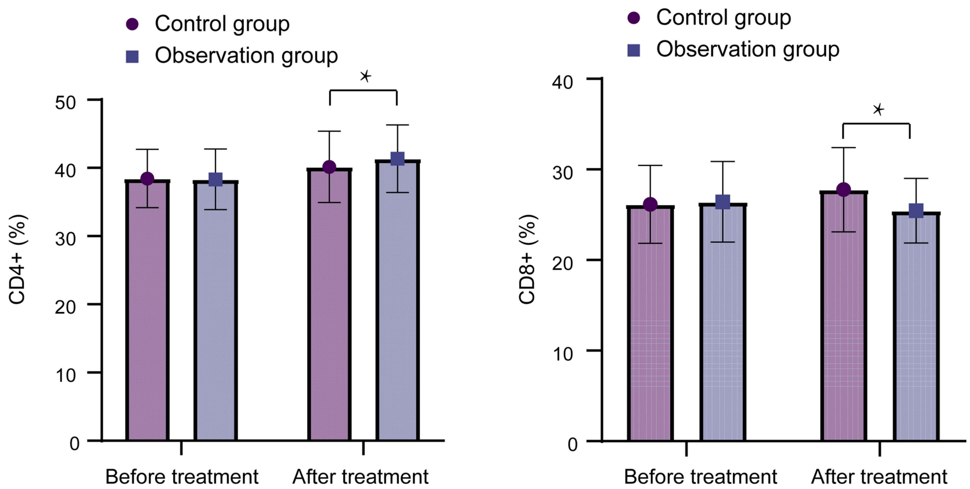

Figure 3 Comparison of Changes in Immune T-Cell Subset Indicators Between the Two Groups. *Represent P<0.05.

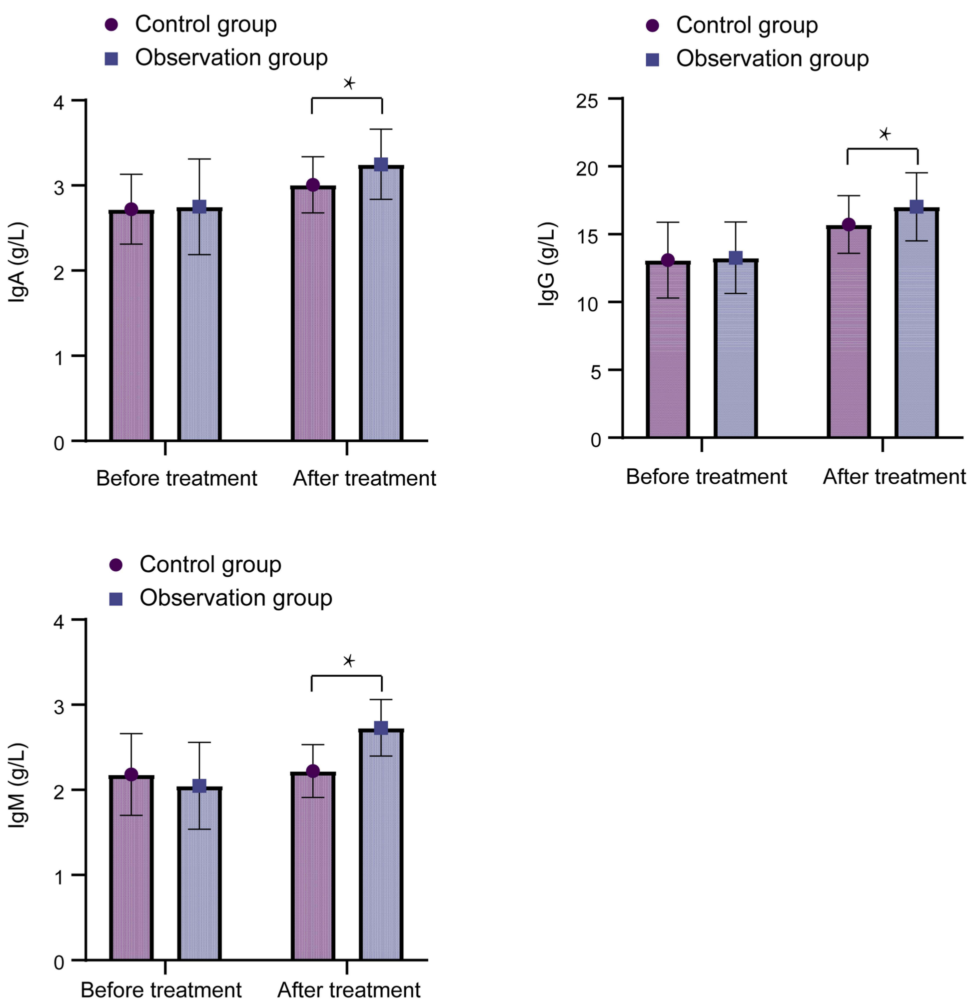

Figure 4 Immunoglobulin-related immune indexes. *Represent P<0.05.

Table 2 Levels of Clinical and Prognostic Indicators

Group	Case	ICU Length of Stay (d)	CRRT Time (d)	Retention of Urine (Case, %)
Observation group	30	4.23±1.56	5.81±1.13	1
Control group	30	5.37±2.13	6.03±2.41	3
t/χ^2		2.365	2.0745	0.2044
P		0.0214	0.0425	0.6512

nutrition. Therefore, understanding urinary retention is crucial for interpreting treatment outcomes and managing patient care effectively. Compared to the control group, the observation group had significantly shorter ICU stay durations and CRRT durations, with statistically significant differences ($P < 0.05$). There was no statistically significant difference in urinary retention between the two groups ($P > 0.05$), as shown in Table 2. This reduction is clinically relevant, as shorter ICU stays can lead to decreased healthcare costs and reduced patient exposure to potential hospital-acquired infections. Additionally, the observation group had a significantly lower gastric retention rate, suggesting better tolerance of enteral feeds, which is essential for maintaining nutritional intake in critically ill patients.

Discussion

AKI is an independent risk factor for patients with end-stage renal disease, significantly impacting their quality of life and survival.[15] In this study, 60 AKI patients undergoing CRRT were guided with different EEN protocols. It was found that compared to high-energy EEN guidance, low-energy EEN guidance significantly improved the nutritional status and immune function of patients, promoting disease recovery.

The results of this study showed that Alb, PA, and Hb levels in both groups significantly increased, but the improvement was significantly greater in the observation group compared to the control group ($P < 0.05$). This indicates that EEN guidance can effectively alleviate the nutritional depletion of AKI patients during CRRT treatment and improve their nutritional status. The superior effect of early low-energy EEN support may be related to the weakened gastrointestinal motility and decreased intestinal absorption function in early-stage patients.[16] Additionally, high-energy EEN guidance includes a large amount of maltodextrin and hydrolyzed whey protein. Studies have shown that extensive use of these substances can lead to gastrointestinal adverse reactions in patients.[17]

Further analysis revealed that the immune function of AKI patients is influenced as the disease progresses. After 7 days of treatment, the improvement in immune function with low-energy EEN guidance was superior to the high-energy group ($P < 0.05$), indicating that low-energy EEN support can better enhance the immune function of patients.[17] Studies have shown that the levels of CD4+ T lymphocyte subsets fluctuate significantly with physiological changes, with higher levels indicating stronger immune function. AKI patients typically exhibit immunological characteristics of high catabolic metabolism and poor immune function.[18] While this provides favorable conditions for disease treatment, adjustments to energy requirements in the later stages still require further exploration.

Compared to the control group, the observation group showed significantly reduced ICU stay duration and CRRT duration, with statistically significant differences ($P < 0.05$). There was no statistically significant difference between the two groups in terms of urinary retention ($P > 0.05$). Ji et al[19] reported that the ICU stay duration of AKI patients with sepsis guided by low-energy EEN was shorter than that of patients guided by high-energy EEN. Studies have shown that ICU patients are at higher risk of gastric retention after receiving EEN guidance, which may be associated with stress status, gastrointestinal dysfunction, and intolerance to nutritional fluids.[20]

In this study, we explore the implications of varying energy levels in total parenteral nutrition (TPN) formulations, emphasizing the balance between macronutrients—specifically proteins, lipids, and carbohydrates. High-energy TPN compositions typically feature increased protein content to support tissue repair and muscle maintenance, crucial for critically ill patients. These formulations often have a higher lipid ratio, providing concentrated energy while minimizing fluid volume, which is essential in cases of fluid restriction. Conversely, low-energy TPN formulations tend to have a greater carbohydrate concentration, offering a more straightforward energy source but might lack sufficient protein for muscle preservation. This study highlights that an optimal TPN composition should be tailored to individual patient needs, considering factors such as metabolic demands, the presence of comorbidities, and tolerance to specific macronutrients. Understanding these nuances allows for more effective nutritional management, ultimately improving patient outcomes in the critical care setting.

This study has several limitations that should be acknowledged. Firstly, it is a single-center study, which may affect the applicability of the results to broader populations. The small sample size further limits the generalizability of the findings, making it difficult to draw robust conclusions. Additionally, the specific demographic and clinical characteristics of patients at our institution may not reflect those seen in other hospitals or regions. Future research should involve multi-center trials with larger cohorts to validate these findings and explore the effects of different EEN strategies across diverse patient populations. Regarding urinary retention, its relevance to the study hinges on its potential link to remaining kidney function. Urinary retention can occur when there is compromised kidney performance, leading to an inability to adequately excrete waste products. In patients receiving total parenteral nutrition (TPN), any changes in kidney function could be reflected in urinary output, which might influence fluid balance and overall metabolic status. However, the study did not delve deeply into these relationships, leaving a gap in understanding how urinary retention might impact clinical outcomes in TPN patients. Thus, further investigation is necessary to clarify how urinary retention relates to kidney function and TPN formulations. Understanding this relationship could provide valuable insights into optimizing TPN strategies for patients with varying levels of kidney health.

Conclusion

In conclusion, while this study provides preliminary insights into the impacts of TPN compositions on patient outcomes, the limitations in statistical analysis and sample size highlight the need for further research. Future studies should aim to utilize more advanced statistical techniques and larger cohorts to better understand the relationships between urinary retention, kidney function, and TPN formulations. A more comprehensive approach will enhance the applicability of findings in clinical settings.

Data Sharing Statement

All data generated or analysed during this study are included in this published article.

Ethics and Consent Statements

This study was approved by the ethics committee of Xianyang Central Hospital. Informed consent was obtained from all study participants. All the methods were carried out in accordance with the Declaration of Helsinki.

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Disclosure

The authors declare that they have no competing interests in this work.

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