Effects of early versus late enteral nutrition on the nutritional status of surgical intensive care unit patients: A retrospective observational study

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Pei-Chun Chao PhD[1,2,3], Frank Cheau-Feng Lin PhD[3,4,5], Hsien-Hua Liao PhD[4,5], Lu-Huan Chou MS[5], Chun-Fen Lee BS[3]

[1]School of Health Diet and Industry Management, Chung Shan Medical University, Taichung, R.O.C.
[2]Department of Nutrition, Chung Shan Medical University Hospital, Taichung, R.O.C.
[3]Department of Parenteral Nutrition, Chung Shan Medical University Hospital, Taichung, R.O.C.
[4]College of Medicine, Chung Shan Medical University, Taichung, R.O.C.
[5]Department of Surgery, Chung Shan Medical University Hospital, Taichung, R.O.C

Authors' email addresses and contributions:
P-CC: cshc029@csh.org.tw
Contribution: conceived the study question, and contributed to the study design, supervision of data collection, data analysis and interpretation, and writing the manuscript.
C-FL: frnklin@gmail.com
Contribution: undertook data collection and data analysis, and contributed to data interpretation.

C-FL: aqq3301@yahoo.com.tw
Contribution: undertook data collection and data analysis.

H-HL: cshyo11@csh.org.tw
Contribution: administrative support.

L-HC: cshe201@csh.org.tw
Contribution: collected the data.

Corresponding Author: Dr Pei-Chun Chao, School of Health Diet and Industry Management, Chung Shan Medical University, No. 110, Sec. 1, Jianguo N. Road, Taichung City 40201, Taiwan, R.O.C. Tel: 886-4-24739595 ext. 34303. Fax: 886-4-24739595 ext. 34301. Email: cshc029@csh.org.tw

ABSTRACT

Background and Objectives: We retrospectively evaluated the efficacy and safety of early enteral nutrition (within 48 h) and late enteral nutrition (after 48 h; control) in improving the nutritional status of surgical intensive care unit patients. **Methods and Study Design:** This single-center, retrospective, observational study was conducted using data from 82 patients (age > 18 years) who were admitted to surgical intensive care units between June and November 2019. Patients who received enteral nutrition for >7 days were included in this study, and those who received total parenteral nutrition or palliative care were excluded. **Results:** The early and late enteral nutrition groups comprised 41 patients each. Early enteral nutrition significantly increased the actual intake of calories and protein ($p < 0.0001$) as well as the length of stay in the surgical intensive care unit ($p = 0.047$) and hospital ($p = 0.028$). Late enteral nutrition significantly reduced albumin concentration ($p < 0.05$), hemoglobin concentration ($p < 0.05$), and lymphocyte count ($p < 0.05$) but significantly increased weight loss ($p < 0.05$). However, no significant between-group difference was observed in mortality rate. **Conclusions:** Early enteral nutrition improves the nutritional status of surgical intensive care unit patients. It shortens overall hospitalization duration and increases actual calorie and protein intake at discharge. Thus, early enteral nutrition is recommended for critically ill patients.

Key Words: early enteral nutrition, late enteral nutrition, surgical intensive care unit, nutritional status, clinical outcomes

INTRODUCTION

Intensive care units (ICUs) offer advanced facilities for the management of unstable patients.[1] Nutritional status is regarded as a key indicator of recovery in ICU patients because it plays a central role in ameliorating critical illnesses and adverse clinical outcomes.[2] Insufficient feeding is common among critically ill patients, particularly those with extended ICU stays.[3] Therefore, medical professionals should pay close attention to the nutritional status of ICU patients because of its prognostic value. However, to the best of our knowledge, no standard feeding strategy has been established for ICU patients.

A critical illness is a life-threatening condition characterized by infection, trauma, or any other medical problem. It involves a strong surge of proinflammatory mediators, which induce host catabolism.[4] To defend itself against pathogens and promote healing, the body exhibits a proinflammatory response to infection or trauma as an adaptive mechanism.

However, severe proinflammatory responses increase the rate of metabolism, which in turn increases catabolism, reduces fat storage in cases of calorie or protein deficits, and reduces muscle mass.[5] These conditions lead to protein–energy malnutrition, a major problem in critically ill hypercatabolic patients admitted to the ICU.[5,6]

The prevalence of malnutrition among ICU patients is approximately 78%.[7] Malnutrition is associated with poor clinical outcomes; it depletes health-care resources, increasing medical costs.[8] In critically ill patients, the priority is to provide adequate nutritional support to optimize organ function and host response.9 Enteral nutrition (EN) may regulate inflammation through several mechanisms—for example, by modulating the gut microbiome,[10] maintaining intestinal mucosal barrier function,[11] and restoring gut immunity.[11,12]

According to the available guidelines on nutritional support for ICU patients, early EN (EEN) is recommended for patients who cannot maintain adequate oral intake, are hemodynamically stable, and have a functioning gastrointestinal tract.[13,14] Many studies and guidelines have indicated that EEN (within 48 h of admission or injury) can substantially reduce the risk of mortality in critically ill patients.[13,14] Evidence suggests that EEN is beneficial for critically ill and trauma patients. Providing EEN is more difficult after emergency surgery than after elective surgery, particularly for patients with traumatic injuries.[15] In these patients, recovering bowel motility and function is challenging, which complicates EEN support.[16]

EN is an unstandardized intervention that necessitates individual assessment and management throughout the process of acute care. Although many guidelines recommend the use of EEN, contradictory findings have recently been published.[17] These findings indicate increased gastrointestinal complications and extended ICU stays among critically ill patients receiving EEN.[18] Moreover, whether the risk of infection-related complications differ between EEN and late EN (LEN) with supplemental parenteral nutrition remains to be confirmed.[17] Considering the lack of evidence regarding whether EEN can be safely administered to ICU patients, we conducted this retrospective cohort study to evaluate our nutritional practice for critically ill adults.

MATERIALS AND METHODS

Study cohort

This single-center, retrospective cohort study included 82 critically ill patients admitted to a surgical ICU (SICU). The patients were divided into two groups: EEN group (EN initiated

within 48 h of ICU admission, n = 41) and LEN group (EN initiated after 48 h of ICU admission, n = 41; control group). Their basic information, nutritional intakes, laboratory data, and clinical outcomes were compared before admission to the SICU and after transfer from the SICU. EN was provided with or without supplemental peripheral parenteral nutrition. Our ICU database was searched to identify eligible patients who were admitted to the SICU between June and December 2019. Details regarding ICU admission for EN support were obtained from the patients' medical records. Data extracted from the Hospital Information System of Chung Shan Medical University Hospital (CSMUH), Taiwan, were retrospectively analyzed. We integrated data from several hospital units, such as the information center, SICU, and management and nutrition departments.

Inclusion and exclusion criteria

This study included patients on enteral tube feeding (age > 18 years) admitted to the SICU of CSMUH between June and December 2019. Patients who received total parenteral nutrition, palliative care, or oral nutrition or stayed for <7 days were excluded from the analysis. In addition, patients with severe medical conditions that could affect the nutritional status or cause renal or hepatic failure were excluded from this study. Furthermore, patients who died within 48 h after SICU admission were excluded. Figure 1 depicts the process of patient selection.

ICU scoring systems

The Glasgow Coma Scale (GCS) is used to objectively determine the extent of impaired consciousness in patients with acute medical conditions or trauma. It is used to evaluate patients' visual, motor, and verbal responses. Each response is scored from 1 (no response) to 4 (visual response), 5 (verbal response), or 6 (motor response). The total score of the GCS ranges from 3 (lowest) and 15 (highest).[19]

Acute Physiology and Chronic Health Evaluation II (APACHE II) is a severity-of-disease classification system used for assessing ICU patients. It is usually administered within 24 h of ICU admission. An integer score ranging from 0 to 71 is calculated on the basis of several parameters. A higher APACHE II score indicates a higher severity of disease and a higher risk of mortality.[20]

Nutritional parameters

Body mass index (BMI) is widely used as a first-line biomarker of nutritional status. It is a simple, low-cost, noninvasive biomarker. BMI is calculated by dividing body mass (in kilograms) by the square of body height (in meters). In adults, a BMI of <18.5 kg/m^2 indicates underweight, a BMI of 18.5–24.9 kg/m^2 indicates normal weight, a BMI of 25–29.9 kg/m^2 indicates overweight, and a BMI of ≥30 kg/m^2 indicates obesity.[21]

Nutritional Risk Screening 2002 (NRS-2002) is a tool used for identifying patients susceptible to malnutrition. This tool helps determine patients' nutritional status (on the basis of weight loss, BMI, and general condition or food intake) and disease severity (on the basis of metabolic stress), which is associated with an increased risk of adverse outcomes. Each patient-related aspect is scored from 0 to 3 points, with an extra point awarded if the patient is aged ≥70 years. A total NRS-2002 score of ≥3 points indicates a high risk of malnutrition.[22]

The Subjective Global Assessment (SGA) survey is regarded as the gold standard for detecting malnutrition in patients. This tool comprises five nutritionally relevant items: nutrient intake, unintentional weight loss, symptoms affecting oral intake, functional capacity, and metabolic demand. It also involves a physical examination focused on assessing subcutaneous fat loss, muscle wasting, and fluid accumulation. On the basis of their SGA scores, patients are classified as well nourished, mildly or moderately malnourished, or severely malnourished.[23]

The Nutritional Risk Index (NRI) is an instrument based on optimal body weight designed to evaluate current body weight and serum albumin concentration. The NRI index value is calculated as follows: 1.519 × serum albumin (g/L) + 41.7 × (current weight / usual weight). Patients with NRI scores of >100, 97.5–100, 83.5–97.5, and <83.5 are considered to have no risk, a mild risk, a moderate risk, and a high risk of ICU mortality, respectively. Usual body weight is defined as stable body weight for the previous 6 months. Higher NRI scores indicate higher risks ICU mortality.[24]

Prognostic models

The modified Glasgow prognostic score (mGPS) is a score that considers both C-reactive protein (CRP) and albumin concentrations. This score indicates systemic inflammation and nutritional status, and it ranges from 0 to 2. Patients with a CRP concentration of >10 mg/L and an albumin concentration of <35 g/L receive a score of 2, those with a CRP concentration of >10 mg/L and an albumin concentration of ≥35 g/L receive a score of 1, and those with a

CRP concentration of ⩽10 mg/L receive a score of 0. For intensive care unit patients, a high mGPS is an independent predictor of mortality during hospital stay and follow-up. In summary, the mGPS is a simple and practical indicator of prognosis in intensive care unit patients.[25]

Biochemical parameters

Several biochemical indicators of the nutritional status and organ function of critically ill patients were evaluated. These indicators included albumin, CRP, glucose, blood urea nitrogen, creatinine, aspartate transaminase, alanine transaminase, sodium, and potassium. Routine blood analyses included hemoglobin concentrations, white blood cell count, and lymphocyte count. Changes in body weight were also measured.

Study design and ethical considerations

This single-center, retrospective, observational study was conducted using clinical dietetic data. According to the American Society for Parenteral and Enteral Nutrition guidelines,14 the target calorie intake and protein intake for ICU patients are 25–30 kcal/kg/day and 1.2–2.0 g/kg/day, respectively. Data pertaining to basic characteristics, nutritional intakes, laboratory results, and clinical outcomes were collected at admission to the SICU (T1) and at discharge from the SICU (T2). These data were compared between T1 and T2. The amount of food consumed was documented on the Hospital Information System by the nursing staff. The ICU team determined the timing of initial enteral feeding. Patients in both groups received EN support, assessed by a dietician who calculated calorie and protein intake. EN was initiated with a standard polymeric formula, providing trophic feeding (10–20 kcal/h or up to 500 kcal/d) within 48 hours, or after 48 hours, advancing to over 80% of the target energy goal within the first week. Feeding consisted of intermittent bag feeding with five meals per day. Because of the retrospective nature of this study, the requirement for informed consent was waived by the Ethical Committee of CSMUH (reference: CSH-2023-A-022). The present study adhered to the guidelines of the Declaration of Helsinki. The study protocol was approved by the Institutional Review Board of CSMUH (approval no. CS2-22139).

Statistical analysis

All statistical analyses were performed using PASW Statistics (SPSS Inc. Released 2009. PASW Statistics for Windows, Version 18.0. Chicago: SPSS Inc). Normally distributed

continuous data are presented in terms of mean ± standard deviation values. Categorical data are presented in terms of number and percentage values. Student's t test and the chi-square test were used for intergroup comparisons of continuous and categorical variables, respectively. Paired t tests were used for intragroup comparisons of continuous variables. Patient distributions per grade were compared between the EEN and LEN groups by using Fisher's exact test and between T1 and T2 by using McNemar's test. A two-sided *p* value of <0.05 indicated statistical significance.

RESULTS

Patient characteristics

A total of 156 potentially eligible patients were identified. From them, 82 met the inclusion criteria and thus were included in this study. The EEN and LEN groups comprised 41 patients each. Table 1 presents the characteristics of the two groups. No significant intergroup difference was observed in age, sex, ICU score, mechanical ventilation duration, comorbidity count, nutritional parameters, anthropometric parameters, NRS-2002 score, albumin concentration, daily protein requirements (g/day), or daily calorie requirements (kcal/day). However, significant intergroup differences were noted in the criteria for SICU admission. The rate of SICU admission among patients undergoing neurosurgery was significantly lower in the LEN group than in the EEN group ($p < 0.001$). By contrast, the rate of SICU admission among patients undergoing gastrointestinal or cardiothoracic surgery was significantly higher in the LEN group than in the EEN group (gastrointestinal surgery: $p = 0.003$; cardiothoracic surgery: $p = 0.018$).

Effects of EEN and LEN on blood parameters

Each patient's degree of compliance with the nutritional intervention was evaluated from their plasma nutritional markers (Table 2). No significant difference was observed between the two groups in CRP or potassium concentration. CRP concentration significantly decreased from T1 to T2 in both groups (EEN: −3.60 ± 7.68 mg/dL, $p < 0.05$; LEN: −2.82 ± 7.54 mg/dL, $p < 0.05$), whereas potassium concentration significantly increased (EEN: 0.37 ± 0.73 mEq/L, $p < 0.05$; LEN: 0.26 ± 0.63 mEq/L, $p < 0.05$).

In the EEN group, significant increases were observed in albumin concentration (0.29 ± 0.44 g/dL, $p < 0.05$) and lymphocyte count (4.67% ± 5.65%, $p < 0.05$) from T1 to T2. However, a significant reduction was noted in glucose concentration (−25.6 ± 58.1 mg/dL, $p < 0.05$). By contrast, in the LEN group, significant reductions were observed in albumin

concentration (−0.44 ± 0.67 g/dL, $p < 0.05$), hemoglobin concentration (−1.7 ± 1.35 g/dL, $p < 0.05$), sodium concentration (−2.05 ± 6.31 mEq/L, $p < 0.05$), and lymphocyte count (−3.41% ± 5.42%, $p < 0.05$). However, a significant increase was noted in blood urea nitrogen concentration (9.93 ± 16.0 mg/dL, $p < 0.05$).

After the intervention, the LEN group exhibited a lower albumin concentration, hemoglobin concentration, and lymphocyte count than did the EEN group (albumin: 2.92 ± 0.60 g/dL vs. 3.44 ± 0.62 g/dL, $p < 0.05$; hemoglobin: 10.3 ± 1.52 g/dL vs. 11.4 ± 2.02 g/dL, $p < 0.05$; lymphocytes: 9.80 ± 5.54 % vs. 15.0 ± 7.95 %, $p < 0.05$). By contrast, the LEN group exhibited a higher glucose concentration than did the EEN group (164 ± 71.2 mg/dL vs. 134 ± 58.2 mg/dL, $p < 0.05$).

Primary outcomes

The EEN group had a significantly shorter mean length of stay in the SICU, fasting duration before the initiation of EN therapy, and length of stay in the hospital than did the LEN group ($p = 0.047$, $p < 0.0001$, and $p = 0.028$, respectively). However, no significant between-group difference was observed in the average number of days spent on mechanical ventilation or the rate of mortality (Table 3).

On the third day of the intervention, the median calorie intake was significantly higher in the EEN group than in the LEN group. Specifically, the EN calorie intake and total calorie intake of the EEN group were 99% and 47% higher, respectively, than those of the LEN group (EN calorie intake: 1312 ± 155 vs. 656 ± 596 kcal/day, $p < 0.0001$; total calorie intake: 1325 ± 163 vs. 903 ± 400 kcal/day, $p < 0.0001$). At T2, the EN calorie intake and total calorie intake of the EEN group were 22% and 14% higher, respectively, than those of the LEN group (EN calorie intake: 1853 ± 271 vs. 1515 ± 276 kcal/day, $p < 0.0001$; total calorie intake: 1877 ± 258 vs. 1640 ± 235 kcal/day, $p < 0.0001$; Table 3).

On the third day of the intervention, the median protein intake of the EEN group was significantly higher than that of the LEN group. Specifically, the EN protein intake and total protein intake of the EEN group were 108% and 24% higher, respectively, than those of the LEN group (EN protein intake: 51.5 ± 9.19 vs. 24.7 ± 24.2 g/day, $p < 0.0001$; total protein intake: 51.5 ± 9.19 vs. 41.5 ± 13.3 g/day, $p < 0.0001$). At T2, the EN protein intake and total protein intake of the EEN group were 23% and 16% higher, respectively, than those of the LEN group (EN protein intake: 76.9 ± 13.3 vs. 62.7 ± 14.9 g/day, $p < 0.0001$; total protein intake: 78.8 ± 12.1 vs. 67.7 ± 13.6 g/day, $p < 0.0001$; Table 3).

Secondary outcomes

Changes in anthropometric parameters from T1 to T2—for example, significant reductions in body weight (−2.93 ± 4.14 kg, $p < 0.0001$) and BMI (−1.13 ± 1.61 kg/m^2, $p < 0.0001$)—were observed in the LEN group (Table 4).

Significant improvements were observed from T1 to T2 in the ICU scores of the two groups. Specifically, a significant increase was observed in the patients' GCS scores (EEN: 2.66 ± 2.60, $p < 0.0001$; LEN: 2.34 ± 4.78, $p = 0.003$), whereas a significant reduction was observed in their APACHE II scores (EEN: −5.12 ± 7.83, $p < 0.0001$; LEN: −3.49 ± 8.85, $p = 0.016$; Table 4).

At T2, the patients' NRI scores were significantly higher in the EEN group than in the LEN group (94.9 ± 9.05 vs. 85.0 ± 8.91, $p < 0.05$). From T1 to T2, the scores significantly increased in the EEN group (5.56 ± 7.28, $p < 0.05$) but significantly decreased in the LEN group (−8.54 ± 9.46, $p < 0.05$; Table 4).

At the end of the study, the distribution of patients per grade, as determined by their SGA scores, changed in the two groups from T1 to T2 (EEN: $p = 0.022$; LEN: $p = 0.001$). At T2, the distribution of patients per grade was better in the EEN group than in the LEN group ($p = 0.044$; Table 4).

Redistribution of patients depending on their mGPSs

From T1 to T2, the distribution of patients per grade, as determined by their mGPSs, changed in the two groups (EEN: $p = 0.086$; LEN: $p = 0.189$). At T2, the distribution of patients per grade was better in the EEN group than in the LEN group ($p = 0.007$; Table 5).

DISCUSSION

In this study, we explored the effects of EEN and LEN on the nutritional status of and clinical outcomes in SICU patients. Nutritional support is regarded as the cornerstone of therapy for critical illnesses. In the absence of EN, the disruption of mucosal integrity impairs the gut barrier.[26] Critical care guidelines typically recommend initiating EN within 24–48 h of ICU admission.[13] EEN improves the intake of nutrients and mitigates the risk of malnutrition and associated complications. Malnutrition is associated with poor patient outcomes.[27] Despite the benefits of EEN, it remains underutilized in clinical practice because it does not consistently yield meaningful clinical and financial outcomes (e.g., mortality and length of stay) compared with the outcomes of LEN.[28] Compared with our LEN group, the EEN group had an improved nutritional status (albumin, hemoglobin, and glucose concentrations and

lymphocyte count; Table 2). Furthermore, the time before the initiation of EN therapy was significantly shorter in the EEN group than in the LEN group, which effectively shortened the length of ICU stay and that of hospital stay in the EEN group (Table 3).

SICU patients typically lack energy and nutrition because of their inadequate food intake after surgery. Evidence suggests that nutritional status and food intake are strongly associated with patients' quality of life.[28] EN can be started early in hemodynamically stable patients who are intubated in the SICU. In this study, we identified an optimal care pathway for providing EEN to critically ill adults to improve their calorie and protein intake (Table 3).

Weight loss in ICU patients due to insufficient nutritional intake and malabsorption is a common symptom of postoperative malnutrition.[29,30] Durán Poveda et al.[31] highlighted insufficient nutritional intake as a reason for weight loss and malnutrition in surgical patients, even after discharge. A study unveiled various postoperative nutritional problems, characterized by malnutrition associated with considerable weight loss, and emphasized the importance of nutritional interventions for patients after discharge.[32] In our LEN group, significant reductions were observed in both body weight and BMI at discharge (Table 4).

Accurate assessment of nutritional status requires a validated and appropriate instrument. Several comprehensive nutritional assessment tools have been developed—for example, the SGA, NRS-2002, NRI, and Mini Nutritional Assessment tools. In this study, the EEN and LEN groups had the same NRS-2002 score at baseline, which indicated that both groups had similar risks of malnutrition (Table 1). Referencing a relevant study,[33] we used the SGA survey for assessing the nutritional status of critically ill adults and investigated the effects of the EEN and LEN interventions. Compared with LEN, EEN significantly improved the patients' nutritional status, as indicated by their SGA scores at discharge (Table 4). Therefore, the SGA survey can serve as a useful nutritional assessment tool for critically ill patients both before and after surgery and even during the convalescence period.[34]

The NRI is a simple screening tool that considers serum albumin concentration, current body weight, and optimal body weight. It is used to predict the risk of nutrition-related postoperative morbidity and mortality in critically ill patients.[35] Low albumin concentrations have been associated with short- and intermediate-term mortality.[36,37] In our study, the LEN group exhibited considerable deterioration in overall nutritional status, characterized by signs such as weight loss. By contrast, the EEN group maintained a good nutritional status, as indicated by the NRI and SGA scores (Table 4).

Predictive ICU scoring systems are tools that evaluate the extent of an ICU patient's illness and predict disease prognosis, usually in terms of mortality.[20] Currently, critically ill patients

admitted to the ICU are evaluated on the basis of their physiological state and the primary cause leading to a condition necessitating continuous monitoring. In this study, we used the GCS and the APACHE II system for patient evaluation. The GCS exhibits high accuracy in predicting in-hospital outcomes in trauma patients. Given its ease of use and calculation, the GCS can be regarded as the optimal predictive tool for this patient population.[38] In our study, both the EEN and LEN groups exhibited significant improvements in their APACHE II and GCS scores at discharge (Table 4).

The mGPS is independently associated with mortality in critically ill ICU patients.[39] Oh et al. reported that the mGPS calculated at ICU admission independently predicted both 28-day and 1-year mortality after admission.[40] In our study, the EEN group had a significantly better mGPS at discharge than did the LEN group (Table 5).

This study has some limitations. First, the sample size was relatively small. This may limit the risk of random variability and generalizability of the results. Second, because the retrospective nature of this study, we lacked comprehensive data on EEN and LEN—for example, information on drugs or antibiotics used during hospital stay. These factors may affect nutritional status and clinical outcomes. Retrospective studies have less control over variables and potential confounders since they rely on pre-existing data. We minimize information bias through standardized data collection, and we reduce selection bias by using inclusion and exclusion criteria. Including control groups also helps compare outcomes and further reduces selection bias. Finally, between-group differences in baseline characteristics might have influenced the clinical outcomes, such as in the criteria for admission to the SICU (Table 1). This may affect the interpretation of the results. For example, patients undergoing different types of surgery (such as neurosurgery, gastrointestinal surgery, etc.) may have different nutritional needs and recovery processes. Since the study was conducted at a single center with a small sample size, the generalizability of the results may be limited. Nutritional status and treatment responses may vary among different regions, different levels of medical care, and different patient groups. Despite these limitations, our study demonstrates the benefits of EEN. However, nutritional status and treatment responses may vary among different regions, levels of medical care, and patient groups; therefore, caution should be exercised when generalizing the results to other populations.

Conclusion

This study indicates that EEN improves the nutritional status of SICU patients. EEN shortens patients' SICU and hospital stays and increases their actual calorie and protein intake at

discharge. Despite its limitations and shortcomings, the study provides valuable insights into the application of early enteral nutrition in surgical intensive care unit patients and lays a foundation for further research. Future studies could consider using a larger-scale prospective design to better control variables and improve the reliability of the results. Additionally, long-term follow-up could enhance our understanding of the sustained impact of nutritional interventions on patient recovery and quality of life.

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CONFLICT OF INTEREST AND FUNDING DISCLOSURE

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Table 1. Baseline characteristics of the EEN and LEN groups

	EEN (n= 41)	LEN (n= 41)	*p* value
Age (years)	62.7±18.3[§]	67.8±14.0	0.162
Male (%)	27 (65.9)	25 (61.0)	0.647
APACHE II score[†]	20.7±4.45	19.4±6.91	0.299
GCS score[‡]	6.24±2.53	7.76±4.55	0.068
Mechanical ventilation(%)	40 (97.6)	36 (87.8)	0.090
ICU admission criteria (%)			
Neurosurgery	29 (70.7)	10 (24.4)	<0.001
Gastrointestinal surgery	0 (0)	8 (19.5)	0.003*
Cardiothoracic surgery	5 (12.2)	14 (34.1)	0.018
General Surgery	7 (17.1)	9 (22.0)	0.577
Number of comorbidities (%)			
0-1	21 (51.2)	19 (46.3)	0.659
≥2	20 (48.8)	22 (53.7)	0.659
Nutritional parameters			
Height (cm)	164±9.15	161±8.89	0.124
Weight (kg)	60.3±13.3	61.9±13.3	0.598
BMI (kg/m^2)	22.4±4.15	23.9±4.26	0.108
NRS 2002 score[§]	3.41±0.49	3.41±0.49	1.000
Albumin < 3 g/dL	13 (31.7)	11 (26.8)	0.627
Requirements			
Daily energy			
kcal/day	1798±197	1768±164	0.467
kcal/kg/day	30.8±5.30	29.6±5.75	0.339
Daily protein			
g/day	78.3±12.0	75.4±11.6	0.27
g/kg/day	1.33±0.23	1.25±0.20	0.071

EEN, early enteral nutrition; LEN, late enteral nutrition; APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Scale; ICU, intensive care unit; NRS 2002, Nutritional Risk Screening 2002; BMI, body mass index
Data are presented in terms of number (%) or mean ± standard deviation values
[†]The total score on the APACHE II system ranged from 0 to 71. A higher score indicated a higher severity of illness
[‡]The GCS was used to evaluate patients in a coma. A higher score indicated a higher level of consciousness. The total score ranged from 3 to 15 points
[§]The NRS 2002 instrument was used to detect undernutrition. Patients with a score of ≥3 points were classified as having a risk of malnutrition; these patients received nutritional care
[¶]Data are presented in terms of mean ± standard deviation values.
*$p < 0.05$

Table 2. Hematology and plasma biochemistry parameters of the EEN and LEN groups[†]

	EEN (n= 41)		LEN (n= 41)	
	At admission	At discharge	At admission	At discharge
Biochemical				
CRP (mg/dL)	8.03±7.24[§]	4.43±6.78[‡]	8.34±6.59	5.52±5.80[‡]
Albumin (g/dL)	3.15±0.49	3.44±0.62[‡]	3.36±0.65	2.92±0.60[‡]*
Glucose (mg/dL)	159±70.6	134±58.2[‡]	159±67.3	164±71.2*
BUN (mg/dL)	28.5±33.4	30.6±38.1	27.4±20.2	37.3±30.4[‡]
Creatinine (mg/dL)	1.39±1.36	1.32±1.42	1.59±1.34	1.90±1.92
AST (U/L)	34.5±17.4	33.5±16.4	40.5±61.1	42.7±47.9
ALT (U/L)	28.9±19.9	34.4±37.0	23.6±11.6	39.0±51.6
Sodium (mEq/L)	138±3.92	138±4.80	139±4.03	137±5.33[‡]
Potassium (mEq/L)	3.75±0.66	4.12±0.52[‡]	3.70±0.63	3.96±0.60[‡]
Blood routine				
Hemoglobin (g/dL)	11.3±2.24	11.4±2.02	12.0±2.10	10.3±1.52[‡]*
WBC count (10^3/mm)	9.88±4.39	9.24±3.56	9.66±4.57	12.0±10.1
Lymphocyte (%)	10.4±8.29	15.0±7.95[‡]	13.2±6.50	9.80±5.54[‡]*

EEN, early enteral nutrition; LEN, late enteral nutrition; CRP, C-reactive protein; BUN, blood urea nitrogen; AST, aspartate transaminase; ALT, alanine transaminase; WBC, white blood cell
[†]Data are presented in terms of mean ± standard deviation values
[‡]$p < 0.05$; admission vs discharge, paired t test
[§]$p< 0.05$; EEN vs LEN, unpaired t test

Table 3. Primary outcomes in the EEN and LEN groups

	EEN (n=41)	LEN (n=41)	Difference between mean (95% CI)	*p* value
Time before ENT (hours)	19.5±13.0§	75.5±13.9	-56.0 (-61.9 to -50.1)	<0.0001
ICU LOS (day)	15.1±9.44	20.0±18.2	-4.92 (-9.79 to -0.06)	0.047
Length of stay (day)	26.5±10.9	32.3±12.3	-5.75 (-10.9 to -0.64)	0.028
MV (day)	12.5±9.80	13.2±14.2	-0.63 (-5.99 to 4.72)	0.814
Mortality (n)	5(12)	8(19)		0.364
Energy (kcal/day)				
3rd EN	1312±155	656±596	655 (462 to 849)	<0.0001
% energy goals	73.8±11.8	37.5±34.4	36.4 (25.0 to 47.8)	<0.0001
3rd EN+PN	1325±163	903±400	67.5 (287 to 557)	<0.0001
% energy goals	74.6±11.9	51.4±23.4	23.1 (14.9 to 31.3)	<0.0001
At discharge EN	1853±271	1515±276	338 (218 to 458)	<0.0001
% energy goals	103±9.43	85.8±14.0	17.2 (11.9 to 22.5)	<0.0001
At discharge EN+PN	1877±258	1640±235	237 (129 to 346)	<0.0001
% energy goals	104±8.71	92.8±10.4	11.7 (7.46 to 15.9)	<0.0001
Protein (g/day)				
3rd EN	51.5±9.19	24.7±24.2	26.8 (18.6 to 34.9)	<0.0001
% protein goals	67.1±14.3	33.2±33.5	33.9 (22.5 to 45.3)	<0.0001
3rd EN+PN	51.5±9.19	41.5±13.3	9.98 (4.93 to 15.0)	<0.0001
% protein goals	67.1±14.3	56.0±19.4	11.1 (3.59 to 18.6)	0.004
At discharge EN	76.9±13.3	62.7±14.9	14.1 (7.91 to 20.3)	<0.0001
% protein goals	98.7±12.9	83.5±16.4	15.2 (8.69 to 21.7)	<0.0001
At discharge EN+PN	78.8±12.1	67.7±13.6	11.1 (5.41 to 16.7)	<0.0001
% protein goals	101±13.25	90.4±15.6	11.1 (4.73 to 17.4)	0.001

EEN, early enteral nutrition; ENT, enteral nutrition therapy; EN, enteral nutrition; PN, parenteral nutrition; ICU, intensive care unit; LEN, late enteral nutrition; LOS, length of stay; MV, mechanical ventilation

†Data are presented in terms of number (%) or mean ± standard deviation and 95% confidence interval values

‡Data are presented in terms of mean ± standard deviation values.

*$p < 0.05$

Table 4. Secondary outcomes in the EEN and LEN groups

	EEN (n= 41)		LEN (n= 41)	
	At admission	At discharge	At admission	At discharge
NRI	89.4±7.26§	94.9±9.05‡	93.6±9.74*	85.0±8.91‡*
Weight (kg)	60.3±13.3	61.4±12.1	61.9±13.3	59.0±12.4‡
BMI (kg/m^2)	22.4±4.15	22.9±3.81	23.9±4.26	22.8±4.01‡
APACHE II score	20.7±4.45	15.6±8.37‡	19.4±6.91	15.9±7.42‡
GCS score	6.24±2.53	8.9±3.60‡	7.76±4.55	10.1±4.01‡
Scored-SGA†				
Stage A	29	27	34	17
Stage B	3	11	4	14
Stage C	9	3	3	10

EEN, early enteral nutrition; LEN, late enteral nutrition; APACHE II, Acute Physiology and Chronic Health Evaluation II; GCS, Glasgow Coma Scale; SGA, Subjective Global Assessment; NRI, Nutritional risk Index; BMI, body mass index

†Data are presented in terms of the number of patients.

‡§Data are presented in terms of mean ± standard deviation values

§$p < 0.05$ (admission vs. discharge; paired t test)

¶$p < 0.05$ (EEN vs. LEN; unpaired t test)

††Patient distributions per grade were compared (using Fisher's exact test) between the two groups (EEN vs LEN) at admission ($p = 0.211$) and at discharge ($p = 0.044$). In addition, the distributions were compared (using McNemar's test) between admission and discharge for EEN ($p = 0.022$) and LEN ($p = 0.001$).

Table 5. Distribution of the mGPS in the study population[†‡§¶]

	EEN (n= 41)		LEN (n= 41)	
	At admission	At discharge	At admission	At discharge
Grade 0	29[a]	37	33	26
Grade 1	2	1	3	2
Grade 2	10	3	5	13

EEN, early enteral nutrition; LEN, late enteral nutrition; mGPS, modified Glasgow prognostic score

†The risk of malnutrition or inflammation was evaluated using the mGPS. A score of 0 points indicated a serum C-reactive protein (CRP) concentration of ≤10 mg/L. A score of 1 point indicated a serum CRP concentration of >10 mg/L and a serum albumin concentration of ≥35 g/L. A score of 2 points indicates a serum CRP concentration of >10 mg/L and a serum albumin concentration of <35g/L

‡Data are presented in terms of the number of patients

§Patient distributions per grade were compared (using Fisher's exact test) between the two groups (EEN vs LEN) at admission (p = 0.389) and at discharge (p = 0.007). In addition, the distributions were compared (using McNemar's test) between admission and discharge for EEN (p = 0.086) and LEN (p = 0.189)

¶Patients were stratified by the mGPS into three groups: a low-risk group (mGPS = 0 points), an intermediate-risk group (mGPS = 1 point), and a high-risk group (mGPS = 2 points)

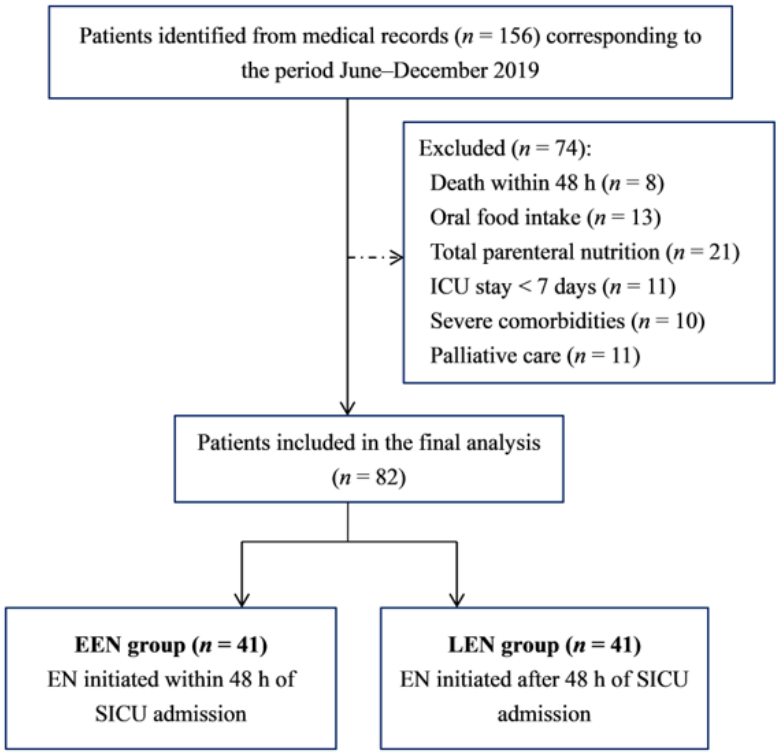

Figure 1. Flowchart depicting patient selection. ICU, intensive care unit; SICU, surgical intensive care unit; EN, enteral nutrition; EEN, early enteral nutrition; LEN, late enteral nutrition