RESEARCH ARTICLE

Association between early enteral nutrition and clinical outcomes in critically ill obese Indian patients: An observational study

S. Ramya[1*], L. Uthira[2], R. Ebenezer[3]

ABSTRACT

Background: Guidelines for the critically ill obese recommend initiating nutrition support within 24-48 hours of intensive care unit (ICU) admission. However, very few studies have reported the effect of early enteral nutrition (EN) in this population. This study evaluated the impact of initiating EN within 12 hours of ICU admission on clinical outcomes in critically ill obese Indian patients. *Methods:* The study included 140 intubated critically ill obese patients (WHO-Asian obese BMI classification) with a minimum three-day ICU stay. Patients receiving EN within 12 hours (early EN, n=71) of admission were compared with patients initiated on EN after 12 hours (late EN, n=69). Key outcomes included the percentage of target calories and proteins achieved on day three, total calories and proteins delivered, mechanical ventilation days, ICU length of stay (LOS), LOS-hospital, and mortality. *Results:* The early EN group received significantly higher target calories (84% vs. 78%; p=0.05) and proteins (79% vs. 72%; p=0.05) on day three. The early EN was associated with significantly fewer mechanical ventilation days (6.5 ± 3.5 vs. 9.01 ± 6.1days; p=0.024), LOS-ICU (10 ± 3.5 vs. 14.2 ± 9 days; p=0.009) and LOS-Hospital (15.5 ± 8.1 vs. 24.9 ± 12.5 days; p=<0.001). Mortality rates were similar (18% vs 16%; p=0.71). *Conclusion:* In critically ill obese Indian patients, EN initiation within 12 hours of ICU admission leads to shorter mechanical ventilation days, LOS-ICU, and LOS-hospital.

Keywords: Critically ill obese, Indian patients, early enteral nutrition, clinical outcomes.

Indian Journal of Physiology and Allied Sciences (2024); DOI: 10.55184/ijpas.v76i04.352 **ISSN:** 0367-8350 (Print)

INTRODUCTION

Critically ill obese (CIO) patients exhibit distinct pathophysiological disturbances and endogenous macronutrient metabolism compared to non-obese patients. The acute phase of critical illness is marked by intense catabolic stress, leading to fat breakdown and loss of skeletal muscle proteins.[1] Additionally, starvation-induced severe stress causes metabolic maladaptation, resulting in protein catabolism and loss of lean body mass.[2] Consequently, nutrition support in the acute phase of critical illness is crucial for the obese to maintain nutritional status, prevent loss of lean body mass, and reduce complications such as infections and organ dysfunction.

Early enteral nutrition (EN) is preferred over parenteral nutrition since it promotes gut integrity by reducing bacterial translocation and gut barrier dysfunction.[3] European Society of Parenteral and Enteral Nutrition (ESPEN) and American Society of Parenteral and Enteral Nutrition (ASPEN)/Society of Critical Care Medicine (SCCM) guidelines recommend initiating nutrition support for the CIO within 24-48 hours of admission to the ICU.[4,5] Despite these recommendations, there is considerable confusion regarding the safety and practical application of early EN in the CIO. Several observational studies have reported that EN was typically not initiated early in obese and overweight patients.[1,6] Delay in initiating EN may be due to several factors, including the risk of reduced gut perfusion and ischemia related to hemodynamic instability, gastrointestinal complications such as delayed gastric emptying and ileus, and a higher risk of aspiration pneumonia due to reduced gastric motility and increased intra-abdominal pressure. Additionally, complications related to obesity, such as difficulties with airway management and intubation, metabolic issues like hyperglycemia, fluid and electrolyte imbalances, and pre-and post-operative care considerations, as well as the lack of appropriate feeding equipment for the obese, may contribute to these delays.[7-10] Haines et al. reported that initiating EN within three days of mechanical ventilation was associated with reduced mortality and shorter ICU and hospital stays in medical and surgical ICU patients.[11] Despite the growing body of evidence supporting early EN in diverse ICU populations, there is a significant gap in research concerning its application and outcomes, specifically in critically ill obese Indian patients. Most studies have focused on general ICU populations or specific

[1]Clinical Dietetics, Apollo Speciality Hospitals, Vanagaram, Chennai, India.

[2]Dept of Food Science & Nutrition, PSG College of Arts & Science, Coimbatore, India.

[3]Critical Care, Apollo Speciality Hospitals, Vanagaram, Chennai, India.

***Corresponding author:** S. Ramya, Clinical Dietetics, Apollo Speciality Hospitals, Vanagaram, Chennai, India, Email: ramyasubburaj@yahoo.com

How to cite this article: Ramya S, Uthira L, Ebenezer R. Association between early enteral nutrition and clinical outcomes in critically ill obese Indian patients: An observational study. *Indian J Physiol Allied Sci* 2024;76(4):60-65.

Conflict of interest: None

Submitted: 11/10/2024 **Accepted:** 13/10/2024 **Published:** 24/12/2024

subgroups, such as the non-obese or those from different geographic regions. Consequently, there is a lack of targeted research examining how early EN impacts clinical outcomes in the CIO Indian cohort. The CIO Indian group may present unique challenges and responses due to regional differences in healthcare practices, obesity-related complications, and nutritional needs.

Addressing this gap is critical for developing tailored nutritional strategies to improve outcomes in this specific patient population. Therefore, this study aimed to explore the effects of initiating EN within 12 hours of ICU admission on clinical outcomes in CIO Indian patients.

METHODS

Study Design

This single-center, prospective, observational study was conducted on CIO Indian adult patients admitted to a tertiary care hospital's multidisciplinary Intensive Care Unit (ICU) between November 2020 and October 2021. The study received approval from the Institutional Ethics Committee-Biomedical Research at Apollo Hospitals, Chennai. Before the commencement of the study, written informed consent was obtained from the patients' representatives.

Study Population

The study included critically ill patients identified as obese according to the WHO-Asian classification[12] (Table 1) who required mechanical ventilation within 48 hours of admission to the ICU and had a minimum ICU stay of three days. Exclusion criteria were non-obese patients (BMI less than 25), patients aged less than 18, patients admitted with burns, and pregnant women.

Study Procedure

Data were collected from 140 CIO patients consecutively admitted to the ICU. Patients were categorized based on the EN initiation time. The early EN group (EEN) included patients for whom EN was initiated within 12 hours (n=71), while the late EN group (LEN) consisted of patients for whom EN was initiated after 12 hours (n=69) of ICU admission. A hypocaloric, high-protein EN protocol was followed. Patients with a BMI between 25-29.9 kg/m^2 were prescribed 20-25 calories per kilogram of actual body weight, and patients with a BMI ≥30 received 15-20 calories per kilogram of actual body weight. All patients received 1.5 grams of protein per kilogram of ideal body weight per day.

A clinical Dietitian (CD) assessed the patients' nutritional status using the modified Subjective Global assessment (mSGA) tool.[13] The CD calculated the required calories and proteins according to the EN protocol, selected the appropriate EN formula, and prescribed it accordingly. Nurses initiated EN and recorded feed initiation, interruptions, and feed tolerance details in the patients' case records. The CD reviewed this documentation daily and followed up until the patients were discharged from the ICU or in the event of mortality.

Table 1: WHO classification of weight by BMI in adult Asians

Classification	*BMI (kg/m^2)*
Underweight	<18.5
Normal range	18.5-22.9
Overweight	23-24.9
Obese I	25-29.9
Obese II	≥30

Source: World Health Organization. Regional Office for the Western Pacific. (2000). The Asia-Pacific perspective: redefining obesity and its treatment.[12]

Data Collection

Basic demographic data, including age, sex, BMI, and admission diagnoses, were collected and recorded by the CD. The severity of illness was evaluated using the Acute Physiology and Chronic Health Evaluation II (APACHE II)[14], Sequential Organ Failure Assessment (SOFA) Score[15], and Nutrition Risk in the Critically Ill (NUTRIC) score.[16] Nutritional data recorded included the timing of EN initiation (within 12 hours or after 12 hours), target calories and proteins prescribed, and the percentage of target calories and proteins achieved on days three and five. Additionally, total calories and proteins delivered and all interruptions in feeding were documented.

Outcomes

The primary outcomes of interest were mechanical ventilator (MV) days, length of stay in ICU (LOS-ICU), and length of stay in hospital (LOS-Hospital). The secondary outcome was in-hospital mortality. Details on outcomes were collected from the patient's medical records and recorded by the CD.

Statistical Analysis

All study variables were summarized using descriptive statistics. For continuous variables, both the mean and standard deviation (SD) were calculated to describe central tendency and dispersion. The distribution of continuous variables was assessed for normality using the Shapiro-Wilk test. If a constant variable was normally distributed, the independent two-sample t-test was employed to compare the means of two independent groups. If the variable did not follow a normal distribution, the Mann-Whitney U test was used as a non-parametric alternative to compare the distributions between two independent groups. The Chi-Square test was utilized for categorical (qualitative) variables to examine relationships and assess whether there was a significant association between the variables by comparing observed frequencies with expected frequencies. All statistical analyses were performed using SPSS version 21.0.

RESULTS

The study included 140 CIO patients with a mean age of 67.4 ± 14.5 years, a BMI of 28.2 ± 3.6 kg/m^2, and a NUTRIC score of 4.6 ± 1.9. The cohort was 66% male and 34% female. Polymorbidity was observed in 53% of the patients, and 66% of the patients were classified as malnourished, according to mSGA. EN was initiated at a mean of 17.4 ± 15.7 hours after ICU admission.

Of the 140 patients, EN was started within 12 hours for 71 (51%) patients and after 12 hours for 69 (49%) patients. The mean EN initiation time was 6.7 ± 3.5 hours for the EEN group and 28.4 ± 15.7 hours for the LEN group. Patients in the EEN group were significantly (p = 0.001) older than those in the LEN group. The groups had similar distribution of BMI and polymorbidity, though the LEN group had a higher number of male patients. APACHE II scores (p=0.093), SOFA scores (p=0.298), and NUTRIC scores (p=0.081) were similar between the groups (Table 2). The proportion of patients undergoing tracheostomy was significantly lower in the EEN group (p=0.0004). Malnutrition rates were considerably higher in the EEN group (p=0.024).

On day three, the EEN group received significantly higher percentages of their target calories (84 vs. 78%; p=0.05) and proteins (79 vs. 72%; p=0.05) than the LEN group (Table 3). However, on day five, both groups received similar percentages of target calories (87% for both groups; p=0.884) and proteins (86 vs. 86%; p=0.875). There was no significant difference in the total percentage of target calories (89% vs. 90%; p=0.395) and proteins (87% vs. 88%; p=0.721) delivered. EN interruptions were more frequent in the LEN group, but the difference was insignificant.

Patients in the EEN group received EN for a significantly shorter duration in the ICU (9.4 ± 3.5 vs. 12.3 ± 8.5 days; p=0.009) and in the hospital (12.3 ± 8.3 vs. 18.2 ± 11.4 days; p=0.001) compared to the LEN group. Analysis of discharge diets revealed that a significantly smaller proportion of patients in the EEN group were on EN alone at discharge (61% vs. 76%; p=0.054). Conversely, more patients in the EEN group were discharged on a combination of EN and oral diets (17% vs. 13%) or oral diets alone (21% vs. 7%) (Figure 1).

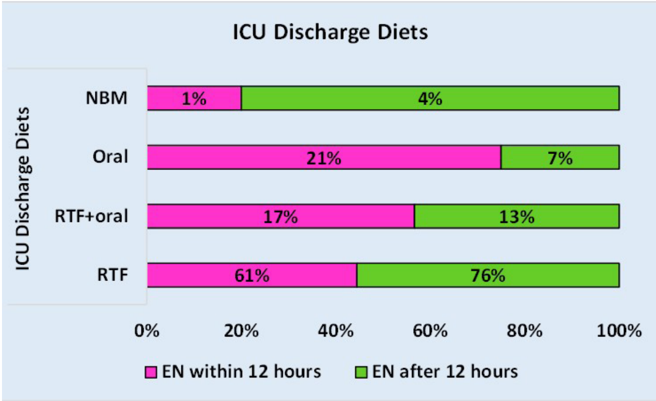

Figure 1: Distribution of different nutrition support routes of the EEN and LEN group patients at discharge from ICU.

Table 2: Baseline Characteristics of Study Population

Variables	*EN within 12 hours (n=71)*	*EN after 12 hours (n=69)*	*p-value*
Age, (years), mean ± SD	61.4 ± 13.4	53.2 ± 14.6	0.001
BMI, (kg/m^2), mean ± SD	28.5 ± 3.6	28 ± 3.6	0.262
Sex (Male), n (%)	40 (56%)	62 (66%)	0.018
APACHE II, mean ± SD	23.5 ± 6.4	21.6 ± 6.6	0.093
SOFA, mean ± SD	9.3 ± 2.5	8.9 ± 2.5	0.298
NUTRIC Score, mean ± SD	4.9 ± 1.8	4.3 ± 2	0.081
Polymorbidity, n (%)	39 (55%)	35 (51%)	0.618
Tracheostomy, n (%)	25 (35%)	45 (65%)	0.0004
EN Initiation time, (hours), mean ± SD	6.7 ± 3.5	28.4 ± 15.7	<0.0001

Table 3: Nutrition information

Variables	*EN within 12 hours (n=71), mean ± SD*	*EN after 12 hours (n = 69), mean ± SD*	*p-value*
% of target calories delivered on day 3	84 ± 18.5	77.5 ± 21.5	0.05
% of target proteins delivered on day 3	78.9 ± 20.7	72.2 ± 22.4	0.05
% of target calories delivered on day 5	86.9 ± 17.8	87.4 ± 22.8	0.884
% of target proteins delivered on day 5	85.5 ± 20.6	86.1 ± 23.1	0.875
% of total target calories delivered	89.1 ± 7.5	90.1 ± 7.5	0.395
% of total target proteins delivered	87.3 ± 12.0	87.9 ± 9.5	0.721

Table 4: Comparison of Outcomes between EEN and LEN groups

Variables	*EN within 12 hours (EEN) (n=71)*	*EN after 12 hours (LEN) (n=69)*	*p-value*
Mechanical Ventilation Days, [Mean ± SD]	6.5 ± 3.5	9.07 ± 6.1	0.024
LOS ICU, [Mean ± SD]	10.08 ± 3.5	14.2 ± 9.02	0.009
LOS Hospital, [Mean ± SD]	15.5 ± 8.1	24.9 ± 12.5	<0.001
LOSICU≤10 days, [Number (%)]	42 (59.2%)	30 (43.5%)	0.046
LOSHospital≤15 days, [Number (%)]	45 (63.4%)	19 (27.5%)	<0.001
Mortality, [Number (%)]	13 (18%)	11(16%)	0.710
Discharge,[Number (%)]	58 (82%)	58 (84%)	0.710

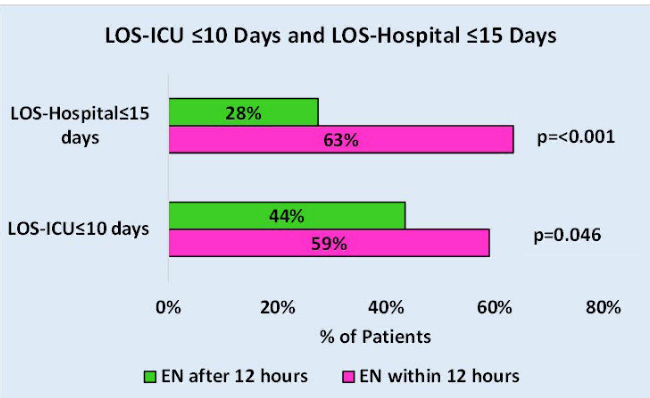

Figure 2: Percentage of Patients with LOS-ICU ≤10 Days and LOS-Hospital ≤15 Days in the EEN and LEN groups

Analysis of the primary outcomes showed (Table 4) that initiating EN within 12 hours significantly reduced mechanical ventilation days (p=0.024), LOS-ICU (p=0.009), and LOS-Hospital (p=<0.001). A notably higher percentage of patients in the EEN group experienced a significantly shorter stay in the ICU than those in the LEN group. Specifically, 59% of patients in the EEN group had an ICU stay of fewer than ten days, whereas only 44% of patients in the LEN group had an ICU stay of less than ten days (p=0.046) (Figure 2). Additionally, 63% of patients in the EEN group had a hospital stay of less than 15 days, compared to only 28% in the LEN group. This difference was statistically significant ($p < 0.001$), indicating a strong association between early EN and a reduction in the length of hospital stays.

The EEN group had a discharge rate of 82%, while 84% of the LEN group patients were discharged alive. Early EN did not significantly impact in-hospital mortality rates. Specifically, the mortality rate among patients who received early EN was 18%, while it was 16% in those who received EN after 12 hours (p=0.71).

DISCUSSION

The present study provides insight into the impact of early EN on clinical outcomes in CIO Indian patients, addressing a notable gap in the current literature. Our findings suggest that initiating EN within 12 hours of ICU admission is associated with improved outcomes, including reduced mechanical ventilator days, shorter ICU and hospital stays. However, early EN did not significantly impact in-hospital mortality rates.

Our results are consistent with previous studies demonstrating the benefits of early EN in critically ill patients. The EEN group in our study had a significantly shorter ICU and hospital stay than the LEN group. This finding is consistent with a meta-analysis by Thapa *et al*., which reported that early EN was associated with reduced ICU and hospital length of stay in critically ill patients.[17] Additionally, Haines *et al*. reported that early EN initiation was linked to reduced mortality and shorter ICU and hospital stays.[11] The benefits of early EN are thought to arise from its role in maintaining gut integrity and potentially improving overall clinical outcomes by enhancing metabolic response and reducing inflammatory markers.[3]

The observed reduction in mechanical ventilator days in the EEN group supports the hypothesis that early EN might help mitigate complications associated with mechanical ventilation. Reduced ventilator days are often linked to improved lung function and patient recovery.[11]

The increased percentage of target calories and proteins achieved in the EEN group on day three suggests that early EN might facilitate better nutritional support. This is consistent with findings from studies that highlight the importance of early EN in achieving nutritional goals more effectively.[18]

By day five, both groups had similar percentages of target calories and proteins achieved, suggesting that while early initiation of EN provides initial benefits, the long-term nutritional outcomes may decrease once EN is fully integrated into the patient's care. Interestingly, the EEN group had a higher discharge rate on oral or mixed diets than EN alone. This suggests that early EN might facilitate a faster transition to oral feeding, which is crucial for patient recovery and can reduce dependency on EN, a more complex and resource-intensive form of nutrition support.

Despite the clinical improvements, early EN did not significantly affect in-hospital mortality rates. This result aligns with some studies suggesting that while early EN can improve various clinical outcomes, its impact on mortality might be limited.[11,18-20] Mortality in critically ill patients is influenced by multiple factors, including the severity of illness, comorbidities, and overall treatment efficacy, which may overshadow the potential benefits of early nutritional interventions.

Our study contributes valuable data specifically concerning critically ill obese Indian patients, an area with limited prior research. Previous studies have generally focused on general ICU populations or specific subgroups, with less attention to obesity-related nuances in nutritional care.[21-23] The higher malnutrition rates observed in the EEN group could reflect the higher nutritional risk in this cohort, highlighting the need for tailored nutritional strategies in critically ill obese patients.

This study has several strengths. Its single-center design allowed a focused examination of CIO Indian patients in a real-world clinical setting. Detailed nutritional and clinical data enhanced the robustness of the outcome measures, providing a comprehensive view of patient status and treatment effects. The study's findings add important evidence to the literature, particularly in the context of early EN in CIO patients.

However, the study also has some limitations. As a single-center observational study, the findings may not be generalizable to other settings or populations. Variations in clinical practices, patient demographics, and healthcare infrastructure at other centers could affect the applicability of the results to broader populations. Additionally, observational studies' lack of randomization and control introduces potential biases. The sample size, while reasonable, may limit the ability to detect small but potentially clinically significant differences, especially concerning secondary outcomes like in-hospital mortality.

Future research should address these limitations by including multicentric trials with larger sample sizes and randomized controlled designs to validate the findings and minimize biases. Additionally, exploring the underlying mechanisms of how early EN influences recovery and clinical outcomes in CIO patients could provide deeper insights and help develop more targeted nutritional strategies. Investigating the impact of early EN across diverse patient populations and healthcare settings will be crucial for establishing broader applicability and optimizing critical care nutrition practices.

CONCLUSION

Initiating enteral nutrition within 12 hours of ICU admission in critically ill obese Indian patients is associated with improved clinical outcomes, including reduced mechanical ventilator days, shorter ICU and hospital stays. However, it does not significantly affect in-hospital mortality. These findings underscore the importance of timely nutritional support and suggest that early EN can be a beneficial component of critical care for obese patients. Further research is needed to validate these results and explore the broader implications for clinical practice.

ACKNOWLEDGMENTS

We wish to express our sincere appreciation to all the participants involved in this study.

CONFLICT OF INTEREST

The authors declare that they do not have conflicts of interest or financial relationships that could have influenced the work presented in this paper.

REFERENCES

1. Borel AL, Schwebel C, Planquette B, *et al*. Initiation of nutritional support is delayed in critically ill obese patients: a multicentre cohort study. *Am J Clin Nutr*. 2014;100(3):859-66. DOI: 10.3945/ajcn.114.088187.
2. Al-Dorzi HM, Stapleton RD, Arabi YM. Nutrition priorities in obese critically ill patients. *Curr Opin Clin Nutr Metab Care*. 2022;25(2):99-109. DOI: 10.1097/MCO.0000000000000803.
3. Zhang H, Wang Y, Sun S, *et al*. Early enteral nutrition versus delayed enteral nutrition in patients with gastrointestinal bleeding: A PRISMA-compliant meta-analysis. *Medicine (Baltimore)*. 2019;98(11):e14864. DOI: 10.1097/MD.0000000000014864.
4. Singer P, Blaser AR, Berger MM, *et al*. ESPEN guideline on clinical nutrition in the intensive care unit. *Clin Nutr*. 2019;38(1):48-79. DOI: 10.1016/j.clnu.2018.08.037.
5. Compher C, Bingham AL, McCall M, *et al*. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. *J Parenter Enteral Nutr*. 2022;46:12-41. DOI:10.1002/jpen.2267.
6. Alberda C, Gramlich L, Jones N, *et al*. The relationship between nutritional intake and clinical outcomes in critically ill patients: results of an international multicentre observational study. *Intensive Care Med*. 2009;35(10):1728-37. DOI: 10.1007/s00134-009-1567-4.
7. Taylor BE, McClave SA, Martindale RG, *et al*. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *Crit Care Med*. 2016;44(2):390-438. DOI: 10.1097/CCM.0000000000001525.
8. Martindale RG, McClave SA, Vanek VW, *et al*. Guideline for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition: Executive Summary. *Crit Care Med*. 2009;37(5):1757-61. DOI: 10.1097/CCM.0b013e3181a40116.
9. Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P; Canadian Critical Care Clinical Practice Guidelines Committee. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. *J Parenter Enteral Nutr*. 2003;27(5):355-73. DOI: 10.1177/0148607103027005355.
10. Bercault N, Boulain T. Mortality rate attributable to ventilator-associated nosocomial pneumonia in an adult intensive care unit: a prospective case-control study. *Crit Care Med*. 2001;29(12):2303-9. DOI: 10.1097/00003246-200112000-00012.
11. Haines KL, Ohnuma T, Grisel B, *et al*. Early enteral nutrition is associated with improved outcomes in critically ill mechanically ventilated medical and surgical patients. *Clin Nutr ESPEN*. 2023;57:311-17. DOI: 10.1016/j.clnesp.2023.07.001.
12. World Health Organization. Regional Office for the Western Pacific. (2000). The Asia-Pacific perspective: redefining obesity and its treatment. Sydney: Health Communications Australia. https://iris.who.int/handle/10665/206936.
13. Lovesley D, Sargunam S, Venkatesan B, *et al*. PT17- modified

subjective global assessment scoring system: is it reliable in hospital setting? *Clinical Nutrition ESPEN*, 54 (2023) 495-96. Available at https://clinicalnutritionespen.com/article/S2405-4577(22)00615-5/pdf
14. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med*. 1985;13(10):818-29. PMID: 3928249.
15. Vincent JL, de Mendonça A, Cantraine F, *et al*. Use of the SOFA score to assess the incidence of organ dysfunction/failure in intensive care units: results of a multicenter, prospective study. Working group on "sepsis-related problems" of the European Society of Intensive Care Medicine. *Crit Care Med*. 1998;26(11):1793-800. DOI: 10.1097/00003246-199811000-00016.
16. Heyland DK, Dhaliwal R, Jiang X, Day AG. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. *Crit Care*. 2011;15(6):R268. DOI: 10.1186/cc10546.
17. Thapa PB, Nagarkoti K, Lama T, Maharjan DK, Tuladhar M. Early enteral feeding in intestinal anastomosis. *J Nepal Health Res Counc*. 2011;9(1):1-5. PMID: 22929702.
18. Casaer MP, Mesotten D, Hermans G, *et al*. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med*. 2011;365(6):506-17. DOI: 10.1056/NEJMoa1102662.
19. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. *Crit Care Med*. 2001;29(12):2264-70. DOI: 10.1097/00003246-200112000-00005.
20. Moon SJ, Ko RE, Park CM, Suh GY, Hwang J, Chung CR. The effectiveness of early enteral nutrition on clinical outcomes in critically ill sepsis patients: A systematic review. Nutrients. 2023;15(14):3201. DOI: 10.3390/nu15143201.
21. Reignier J, Plantefeve G, Mira JP, *et al*. Low versus standard calorie and protein feeding in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group trial (NUTRIREA-3). *Lancet Respir Med*. 2023;11(7):602-12. DOI: 10.1016/S2213-2600(23)00092-9.
22. Pardo E, Lescot T, Preiser JC, *et al*. Association between early nutrition support and 28-day mortality in critically ill patients: the FRANS prospective nutrition cohort study. *Crit Care*. 2023;27(1):7. DOI: 10.1186/s13054-022-04298-1.
23. Reignier J, Boisramé-Helms J, Brisard L, *et al*. Enteral versus parenteral early nutrition in ventilated adults with shock: a randomised, controlled, multicentre, open-label, parallel-group study (NUTRIREA-2). *Lancet*. 2018;391(10116):133-43. DOI: 10.1016/S0140-6736(17)32146-3.

PEER-REVIEWED CERTIFICATION

During the review of this manuscript, a double-blind peer-review policy has been followed. The author(s) of this manuscript received review comments from a minimum of two peer-reviewers. Author(s) submitted revised manuscript as per the comments of the assigned reviewers. On the basis of revision(s) done by the author(s) and compliance to the Reviewers' comments on the manuscript, Editor(s) has approved the revised manuscript for final publication.