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Higher mortality rate in postoperative icu patients is associated with combination of early enteral and parenteral nutrition

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ABSTRACT

Introduction: Postoperative intensive care unit (ICU) patients often experience increased metabolic demands and are at risk of malnutrition, making early nutritional support crucial for recovery. Despite the existing body of literature, the impact of different modes of early nutrition on mortality in postoperative ICU patients remains unclear. Previous studies have produced mixed results, with some suggesting that early parenteral nutrition is associated with worse outcomes, while others have found no significant differences between the different modes of nutrition. This study aims to examine the impact of early nutrition on mortality in postoperative ICU patients. The study also seeks to explore the impact of early nutrition on other clinical outcomes.

Methods: This retrospective observational study included 361 postoperative ICU patients and divided by four groups based on their early nutritional support (early enteral, early parenteral, early mixed enteral and parenteral, and no early nutrition). Baseline characteristics, nutritional intake was assessed using 24hours food recall, length of stay in ICU, hospital LOS, duration of mechanical ventilation, and mortality were evaluated. Statistical analyses included univariate and multivariate models to assess the relationship between early nutrition and clinical outcomes.

Result: The early PN and EN & PN groups had higher ICU mortality rates (33.6% and 26.5%, respectively) compared to the EN group (19.1%) and no early nutrition group (11.1%). Early PN was associated with an increased odds ratio for mortality (OR = 3.03, 95% CI = 0.83, 11.09). The EN & PN group also showed increased odds (OR = 4.82, 95% CI = 1.10, 21.11). The highest median calorie intake was in the PN group, while the longest ICU LOS was in the EN & PN group.

Conclusion: Early supplemental parenteral nutrition, particularly when combined with enteral nutrition, is associated with higher mortality in postoperative ICU patients. Early enteral nutrition appears to be a safer option, and careful consideration should be given to the risks and benefits of different nutritional interventions in this patient population.

KEYWORDS

Early nutrition, critical illness, surgical patients, hospital mortality.

INTRODUCTION

Postoperative care in intensive care units (ICUs) presents challenges and opportunities for improving patient outcomes. In the critical phase following surgery, patients experience increased metabolic demands and are at risk of malnutrition. Nutrition support is a fundamental component of postoperative care, aiming to meet the metabolic needs of critically ill patients, enhance recovery, reduce the risk of infections, and shorten the length of hospital stay[1,2]. The timing and optimal route of nutrition remains a topic of debate. Enteral nutrition, delivered directly into the gastrointestinal tract, is often favored due to its physiological benefits, including maintaining gut integrity and function. Parenteral nutrition, delivered intravenously, is reserved for patients who cannot tolerate or adequately receive enteral feeding. Despite its benefits, par-

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enteral nutrition has been associated with an increased risk of complications, such as infections, metabolic disturbances, and liver dysfunction, leading to concerns about its routine use in ICU patients. Given these issues, clinicians often employ a combination of enteral and parenteral nutrition (EN & PN) to achieve optimal nutrient delivery, particularly in patients with complex nutritional needs[3,4].

Despite the existing body of literature, the impact of different modes of early nutrition on mortality in postoperative ICU patients remains unclear. Previous studies have produced mixed results, with some suggesting that early parenteral nutrition is associated with worse outcomes, while others have found no significant differences between the different modes of nutrition. The existing guidelines are often based on mixed evidence, leading to variations in clinical practice and uncertainty among healthcare providers about the best approach to nutritional support in postoperative ICU patients[5,6].

Given the uncertainties and gaps in the current literature, this study aims to examine the impact of early nutrition on mortality in postoperative ICU patients[7,8]. The specific objectives of the study are to evaluate the association between early enteral, parenteral, and combined enteral and parenteral nutrition and mortality, and to identify potential predictors of mortality in this patient population. The study also seeks to explore the impact of early nutrition on other clinical outcomes, such as ICU and hospital length of stay and duration of mechanical ventilation, to provide a more comprehensive understanding of the effects of different modes of early nutrition.

METHODS

Study Design

Retrospective observational study was conducted in the intensive care unit (ICU) of Wahidin Sudirohusodo Hospital, Makassar, Indonesia. The study was conducted over a 12-month period, from April 2022 to March 2023, and aimed to evaluate the association between different types of early nutrition and clinical outcomes, particularly mortality. The study adhered to the ethical guidelines of the institutional review board, which approved the study protocol and ensured that patient confidentiality was maintained throughout the research process. The Ethic protocol number is 966/UN4.6.4.5.31/PP36/2023.

Patient Selection

The study population included all postoperative patients admitted to the ICU during the study period. Exclusion criteria for the study were, patients below 18 years old, patients who died within 48 hours of ICU admission and patients who were discharged from the ICU within 48 hours.

Data Collection

Data for the study were collected from medical records, which provided detailed information on patient demographics, clinical characteristics, nutritional intake, and clinical outcomes. Demographic data included age, sex, height, weight, and body mass index (BMI). The clinical characteristics collected included the type of surgery, severity of illness, and nutritional risk. The type of surgery was categorized based on the primary surgical procedure performed, while the severity of illness was assessed using the APACHE II and SOFA scores, both of which are widely used tools for evaluating the severity of illness in ICU patients. The nutritional risk was assessed using the mNutric score, which is a validated tool for identifying ICU patients who may benefit from nutritional support. Nutritional intake was assessed based on the average calorie and protein intake during ICU stay. The clinical outcomes assessed included ICU and hospital length of stay (LOS), duration of mechanical ventilation, and ICU mortality.

Statistical Analysis

The normality of continuous data was assessed using the Shapiro-Wilk test, which is a statistical test that evaluates whether a dataset follows a normal distribution. Depending on the distribution, continuous variables were expressed as either mean ± standard deviation (SD) or median and interquartile range (IQR). Categorical variables were presented as numbers and percentages. For continuous variables, the Student's t-test or Mann-Whitney U test was used for two-group comparisons, while one-way ANOVA or Kruskal-Wallis test was used for more than two groups. For categorical variables, the chi-square test or Fisher's exact test was used, depending on the sample size and distribution of the categories. To identify independent predictors of mortality, a multivariate logistic regression analysis was performed. Unadjusted and Adjusted odds ratios (ORs) and 95% confidence intervals (CIs) were reported to measure the strength and precision of the association between early nutrition and mortality. A p-value of < 0.05 was considered statistically significant. Statistical analysis for the study was performed using SPSS 25.0 (IBM Corp., Armonk, NY).

RESULTS

A total of 889 postoperative patients were admitted to the ICU from April 2022 to March 2023. Among these patients, 677 were excluded due to various reasons, including being under 18 years of age (n = 83), death within 48 hours of admission (n = 49), and discharge from the ICU less than 48 hours (n = 516). The final analysis included 361 patients, divided into four groups based on their early nutrition intake: no early nutrition (n = 36), early enteral nutrition (n = 89), early parenteral nutrition (n = 134), and early enteral and parenteral nutrition (n = 102). The me-

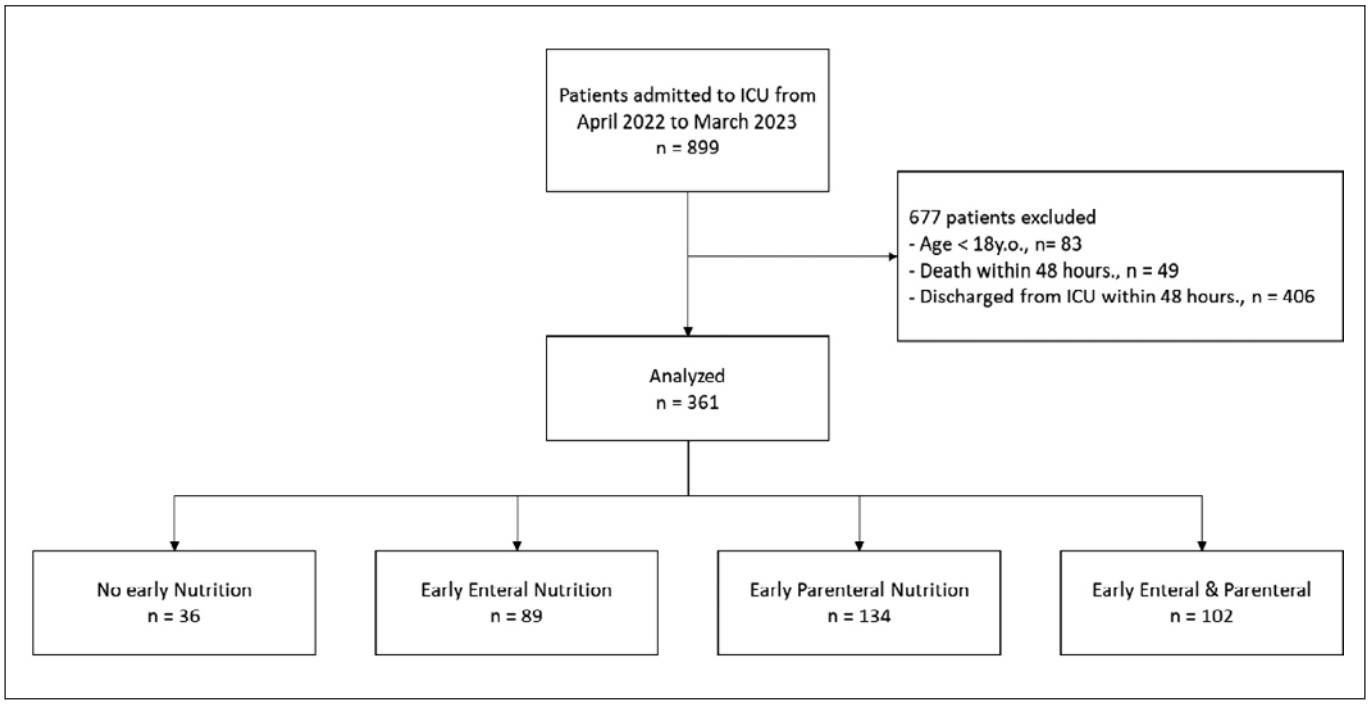

Figure 1. Flowchart of the study patients

dian age of the patients across the groups was similar, with no significant differences observed (p = 0.293). Likewise, the gender distribution was comparable across all groups (p = 0.474). Additionally, the height (p = 0.895), weight (p = 0.552), and BMI (p = 0.34) were not significantly different among the groups. The majority of patients had a BMI in the range of 18.5 to 29.9, with no significant differences in BMI distribution across the groups (p = 0.538). However, significant differences were observed in the types of surgeries performed among the groups (p < 0.001). Significant differences were also found in the APACHE II score, SOFA score, and mNutric score among the groups (all p < 0.05). The Early Parenteral group had the highest median APACHE II score (8 [6, 10]) and SOFA score (7 [5, 9]), indicating a higher severity of illness in this group. Conversely, the No Early Nutrition group had the highest median mNutric score (5 [3, 6]), suggesting a higher risk of malnutrition in this group.

The median calorie intake significantly differed among the groups (p < 0.001). The Early Parenteral group had the highest median calorie intake (12.2 [7.15, 16.8]), while the Early Enteral group had the lowest (5.5 [3.2, 9.25]). Protein intake also varied significantly among the groups (p < 0.001), with the Early Parenteral group having the highest median protein intake (0.6 [0.4, 0.8]) and the Early Enteral group having the lowest (0.3 [0.2, 0.5]). The ICU length of stay (ICU LOS) differed significantly across the groups (p = 0.032). The Early Parenteral group had the longest median ICU LOS (6 [3, 11]), while the No Early Nutrition group had the shortest (3 [1, 6.75]). However, there were no significant differences in the hospital length of stay (Hospital LOS) among the groups (p = 0.348). The duration of mechanical ventilation was significantly different among the groups (p = 0.051). The Early Parenteral group had the longest median duration (2.5 [1, 7]), while the No Early Nutrition group had the shortest (1 [1, 3.5]). Finally, ICU mortality rates were significantly different among the groups (p = 0.015). The Early Parenteral group had the highest ICU mortality rate (33.6%), followed by the Early Enteral & Parenteral group (26.5%). The Early Enteral group had the lowest ICU mortality rate (19.1%), while the No Early Nutrition group had a rate of 11.1%.

In the unadjusted analysis, early parenteral nutrition was associated with a significantly higher odds ratio (OR) for mortality (1.88 [95% CI: 0.58, 6.062], p = 0.163) compared to early enteral nutrition, but the result was not statistically significant. The combined early enteral and parenteral nutrition group had a similarly high OR for mortality (4.04 [95% CI: 1.34, 12.41], p = 0.013), which was statistically significant. The adjusted analysis, which considered potential confounders, provided a clearer picture. After adjustment, early parenteral nutrition remained associated with an increased odds ratio for mortality (1.73 [95% CI: 1.026, 10.48], p = 0.376), while the early enteral and parenteral nutrition also showed an increased odd ratio for mortality (3.28 [95% CI: 1.02, 10.48], p = 0.045).

Table 1. Baseline characteristics of the study patients

	Early Enteral (n=89)	Early Parenteral (n=134)	Early Enteral & Parenteral (n=102)	No Early Nutrition (n=36)	p Value
Age, year	51 [38, 59.5]	51 [39, 62.65]	49 [36, 57]	48 [30.25, 60.5]	0,293
Sex					0,474
Men	43 (48.3)	65 (48.5)	59 (57.8)	19 (52.8)	
Woman	46 (51.7)	69 (51.5)	43 (42.2)	17 (47.2)	
Height, cm	160 [155, 165]	160 [155, 165]	160 [155, 165]	160 [155, 161.75]	0,895
Weight, kg	60 [50, 65]	60 [50, 65]	58 [50, 65]	57.5 [50.5, 64.5]	0,552
BMI, kg/m2	22.8 [20.7, 24.8]	22.0 [20.6, 23.8]	22.6 [20.7, 24.5]	22.8 [21.1, 24.9]	0,34
BMI Category					0,538
<18.5	8 (9)	12 (9)	7 (6.9)	3 (8.3)	
18.5 - 22.9	37 (41.6)	69 (51.5)	49 (48)	17 (47.2)	
23 - 24.9	22 (24.7)	30 (22.4)	23 (22.5)	6 (16.7)	
25 - 29.9	22 (24.7)	21 (15.7)	19 (18.6)	10 (27.8)	
>30	0 (0)	2 (1.5)	4 (3.9)	0 (0)	
Type of Surgery					<0,001
Digestive	5 (5.6)	77 (57.5)	18 (17.6)	9 (25)	
Brain	35 (39.3)	26 (19.4)	38 (37.3)	10 (27.8)	
Orthopedic	22 (24.7)	9 (6.7)	20 (19.6)	4 (11.1)	
Oncology	14 (15.7)	4 (3)	10 (9.8)	4 (11.1)	
Urology	3 (3.4)	2 (1.5)	2 (2)	1 (2.8)	
ENT	7 (7.9)	2 (1.5)	3 (2.9)	1 (2.8)	
Plastic	1 (1.1)	1 (0.7)	0 (0)	0 (0)	
Vaskular	0 (0)	0 (0)	1 (1)	0 (0)	
Ophtalmology	1 (1.1)	0 (0)	0 (0)	0 (0)	
Obstetric	1 (1.1)	13 (9.7)	10 (9.8)	7 (19.4)	
APACHE II Score	7 [5, 8.5]	8 [6, 10]	6 [5, 8]	5 [2.75, 6]	<0,001
SOFA Score	7 [5, 9]	7 [5, 9]	5 [5, 7]	5 [3.5, 6]	<0,001
mNutric Score					0,029
Low Risk	80 (89.9)	111 (82.8)	96 (94.1)	34 (94.4)	
High Risk	9 (10.1)	23 (17.2)	6 (5.9)	2 (5.6)	

Data are presented as n (%) or median (interquartile range).
BMI, Body Mass Index; ENT, Ear Nose Throat; APACHE II, Acute Physiology and Chronic Health Evaluation II ; SOFA, Sequential Organ Failure Assessment ; mNutric, modified Nutrition Risk in the Critically III.

Table 2. Intake and clinical outcome according to initiation of nutrition

	Early Enteral (n=89)	Early Parenteral (n=134)	Early Enteral & Parenteral (n=102)	No Early Nutrition (n=36)	p Value
Calorie Intake, kcal/kg/d	5.5 [3.2, 9.25]	12.2 [7.15, 16.8]	9 [5.6, 13,92]	6.6 [5.72, 8.52]	<0.001
Protein Intake, kcal/kg/d	0.3 [0.2, 0.5]	0.6 [0.4, 0.8]	0.45 [0.3, 0.7]	0.4 [0.3, 0.4]	<0.001
ICU LOS, days	4 [3, 8]	6 [3, 11]	6 [3, 11]	5 [3, 6.75]	0.032
Hospital LOS, days	15 [9, 27.5]	15.5 [10, 28]	19 [11, 31.25]	18.5 [10, 29.75]	0.348
Mechanical Ventilation, days	2 [1, 5.5]	2.5 [1, 7]	2 [1, 8.25]	3 [1, 7.9]	0.051
ICU Mortality, n(%)	17 (19.1)	45 (33.6)	27 (26.5)	4 (11.1)	0,015

Data are presented as n (%) or median (interquartile range).
ICU, Intensive Care Unit; LOS, Length of stay.

Table 3. Relationship between early nutrition and mortality

	Unadjusted			Adjusted*		
	Hazard ratio	95% CI	p Value	Hazard ratio	95% CI	p Value
Early Enteral (n=89)						
Early Parenteral (n=134)	1.889	0.589 - 6.062	0.285	1.738	0.511 - 5.908	0.376
Early Enteral & Parenteral (n=102)	4.045	1.347 - 12.416	0.013	3.280	1.026 - 10.482	0.045
No Early Nutrition (n=36)	2.880	0.932 - 8.904	0.066	3.070	0.943 - 9.992	0.062
Energy Intake, kcal/kg/d	1.045	1.010 - 1.080	0.011	1.046	1.009 - 1.084	0.014
Protein Intake, kcal/kg/d	1.910	1.088 - 3.352	0.024	2.019	1.115 - 3.656	0.020

*Adjusted for age, sex, BMI, Type of Surgery, and mNutric Score.

DISCUSSION

The results of this study provide important insights into the association between early nutritional interventions and clinical outcomes in postoperative ICU patients. The key finding that early parenteral nutrition, particularly when used as a supplement to enteral nutrition, is associated with higher ICU mortality[9-11]. In contrast, early enteral nutrition appears to be associated with better outcomes, supporting the notion that enteral feeding should be the preferred mode of early nutrition in critically ill postoperative patients[11-13]. These results align with the concept that the gastrointestinal tract plays a crucial role in immune function and metabolic regulation, and that preserving its integrity through enteral feeding can have beneficial effects on patient outcomes[14]. The increased mortality observed in the early parenteral nutrition group, even when combined with enteral nutrition, suggests that the risks associated with parenteral feeding may outweigh the benefits in certain patient populations[7,15,16]. The reasons for this increased mortality are likely multifactorial, including the risk of infections, metabolic complications, and liver dysfunction associated with parenteral nutrition[10,17,18]. Additionally, the potential for overfeeding or inappropriate nutrient composition in parenteral solutions could contribute to adverse outcomes[18-20]. The findings of this study highlight the need for careful consideration of the risks and benefits of parenteral nutrition in postoperative ICU patients, and suggest that early enteral feeding should be prioritized whenever possible[21].

The findings of this study are consistent with some previous studies that have suggested an association between early parenteral nutrition and worse outcomes in critically ill patients. For example, several randomized controlled trials have shown that early parenteral nutrition, compared with enteral nutrition or delayed parenteral nutrition, is associated with an increased risk of infections and other complications[9-11,19]. However, other studies have found no significant difference between the modes of nutrition, highlighting the heterogene-

ity of the critically ill population and the potential for patient-specific factors to influence outcomes[15,20]. The current study adds to the existing literature by specifically focusing on postoperative ICU patients, a population that is often excluded from broader studies of nutritional support in critical illness. The focus on surgical patients allows for a more nuanced understanding of the impact of early nutrition in this population, which may have different nutritional needs and risks compared with medical ICU patients[11,18,21]. The findings also align with guidelines from organizations such as the American Society for Parenteral and Enteral Nutrition (ASPEN), which recommend early enteral nutrition as the preferred mode of feeding in critically ill patients[17].

The findings of this study have important implications for clinical practice and future research. The increased mortality associated with early parenteral nutrition suggests that this mode of feeding should be used with caution in postoperative ICU patients, and that early enteral feeding should be prioritized whenever possible[22,23]. The results also highlight the potential risks of combined enteral and parenteral nutrition, suggesting that this approach should be reserved for patients who cannot meet their nutritional needs with enteral feeding alone[23,24]. The study also highlights the importance of individualized nutritional support in critically ill patients. While early enteral feeding appears to be beneficial for most postoperative ICU patients, there may be cases where parenteral nutrition is necessary or where combined enteral and parenteral feeding is appropriate[11,14,17]. Clinicians should carefully consider the risks and benefits of different nutritional interventions and tailor their approach to the individual needs and preferences of their patients.

There are several limitations that should be acknowledged. First, the retrospective observational design limits the ability to establish causality between early nutritional interventions and outcomes. While the study identified associations between early parenteral nutrition and increased mortality, other factors such as patient severity of illness or preexisting comorbidities could also contribute to these outcomes. Future prospective studies or randomized controlled trials are needed to confirm these findings and establish causality. Second, the study relied on medical records for data collection, which may be subject to inaccuracies or missing data. While the researchers took steps to validate the data, the potential for errors in documentation or coding could affect the results. Third, the study population consisted of postoperative ICU patients, which may limit the generalizability of the findings to other patient populations. While the focus on surgical patients is a strength of the study, it also means that the results may not apply to medical ICU patients or other critically ill populations. Future studies should examine the impact of early nutrition in different patient populations to determine whether the findings are consistent across different types of critical illness.

CONCLUSION

In conclusion, this study provides important insights into the association between early nutritional interventions and clinical outcomes in postoperative ICU patients. The findings suggest that early parenteral nutrition, particularly when used as a supplement to enteral nutrition, is associated with higher ICU mortality, while early enteral feeding is associated with better outcomes. These results support the prioritization of enteral nutrition in postoperative ICU patients and highlight the need for careful consideration of the risks and benefits of parenteral nutrition in this population. Future research should focus on prospective studies or randomized controlled trials to confirm these findings and establish causality, as well as exploring the impact of early nutrition in different patient populations and subgroups.

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