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Impact of early versus delayed enteral nutrition on ICU outcomes: a comparative study on mortality, ventilator dependence, and length of stay

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Abstract

Background and Objective The timing of enteral nutrition initiation in critically ill patients in the intensive care unit (ICU) plays a crucial role in clinical outcomes. This study aimed to evaluate the impact of early (within 48 h of ICU admission) versus delayed enteral feeding on 28-day mortality, ventilator dependency, and ICU length of stay.

Methods A retrospective cohort study was conducted involving 295 patients across four ICUs in two Tehran hospitals, admitted between 2017 and 2018. Participants were grouped into early (n = 161) and delayed (n = 134) enteral feeding categories. Baseline characteristics were analyzed using the Mann–Whitney and Chi-Square tests. Mortality was assessed using Kaplan–Meier survival analysis and Cox proportional hazards models, while logistic and linear regression models were applied to examine associations with ventilator dependency and ICU length of stay, respectively.

Results Early enteral feeding (EEF) was significantly associated with reduced 28-day mortality (25.5% vs. 50.0%, $p < 0.001$), lower incidence of mechanical ventilation (66.5% vs. 80.6%, $p = 0.007$), and a shorter ICU stay (13.07 ± 16.44 days vs. 16.23 ± 13.57 days, $p < 0.001$). Kaplan–Meier analysis revealed a higher survival probability at 28 days in the early feeding group (log-rank test, $p < 0.001$). However, after adjusting for potential confounders (age, gender, BMI, baseline APACHEII, baseline SOFA score, number of comorbid, primary diagnosis and admission category), the relationships between delayed feeding and mortality (HR: 1.49, 95% CI 0.98, 2.26, $p = 0.062$), ventilator dependency (OR: 1.28, 95% CI 0.59, 2.70, $p = 0.558$), and ICU length of stay (LOS) (β : 1.96, 95% CI – 1.52, 5.45, $p = 0.268$) were not statistically significant. Subgroup analyses revealed that delayed enteral feeding was significantly associated with higher mortality risk in surgical patients (adjusted HR: 1.85, 95% CI 1.02, 3.35, $p = 0.043$) and prolonged ICU stay (β : 3.75, 95% CI 0.27, 7.23, $p = 0.035$), whereas no significant associations were observed in medical patients.

Conclusion Initiating enteral feeding within 48 h of ICU admission is associated with improved clinical outcomes, although these benefits may be influenced by individual patient factors and disease severity. Future studies should focus on tailoring enteral feeding strategies to optimize outcomes across varied ICU populations.

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Keywords Early enteral nutrition, ICU outcomes, 28-day mortality, Mechanical ventilation, ICU length of stay, Critical care

Introduction

Early enteral feeding (EEF) within 48 h of ICU admission significantly improves patient outcomes, including reduced infections, enhanced gastrointestinal function, and decreased mortality rates. Studies, including those on COVID-19 patients, have shown that this approach can shorten ICU stays and boost overall recovery by up to 38%. [1]. However, the timing of enteral feeding remains a topic of debate. Delayed initiation, often due to concerns about feeding tolerance or ongoing resuscitation efforts, may lead to increased complications and prolonged ICU stays. Evidence suggests that early feeding may be harmful in certain critically ill patients, particularly those on mechanical ventilation [2, 3]. These findings highlight the need for clear guidelines and protocols to optimize the timing of enteral nutrition across various ICU populations.

While the literature generally supports the benefits of early enteral feeding, its impact on certain clinical outcomes such as 28-day mortality, duration of mechanical ventilation, and length of ICU stay remains unclear. Early enteral nutrition has been shown to reduce the risk of infectious complications and improve survival, especially in patients with severe conditions like sepsis or major trauma [2, 3]. However, other studies have found no significant differences between early and late enteral feeding in these outcomes, suggesting that factors such as underlying disease, nutritional status, and illness severity may play a crucial role in determining its effectiveness [4]. Additionally, concerns about feeding intolerance, the risk of aspiration pneumonia, and the condition of critically ill patients add further complexity to interpreting the benefits of early enteral nutrition [1]. This variability highlights the need for more research to determine the optimal timing of enteral feeding, particularly in the diverse ICU populations with different indications.

Given the uncertainty and variability surrounding the timing of enteral feeding in the ICU, more research is urgently needed to clarify its effects. Recent 2024 studies have provided new insights, indicating that EEF may particularly benefit certain ICU patient populations, such as those with sepsis, by improving outcomes like mortality rates and reducing the duration of mechanical ventilation [5, 6]. However, evidence also suggests that these benefits are not universal and that the optimal timing of feeding should be tailored to individual patients based on their nutritional status and disease

severity [7]. Additionally, potential risks associated with both early and delayed enteral feeding, such as issues with gastric residuals and the need for strict glucose control, have been highlighted [8, 9]. This study aims to contribute to the growing body of literature by providing a more nuanced understanding of the timing of enteral nutrition, which could help in developing personalized nutritional strategies to better meet the needs of diverse ICU populations.

This research aims to compare early versus delayed enteral feeding in ICU patients, focusing on 28-day mortality, ventilator dependence, and ICU length of stay. Despite mixed results in recent literature, we hypothesize that initiating feeding within 48 h of ICU admission leads to better outcomes. By studying a diverse ICU population, the findings are expected to be more generalizable and could inform clinical guidelines. The study will also examine whether the benefits of early feeding vary based on nutritional status and illness severity, with the goal of optimizing enteral feeding protocols to enhance patient care.

Material and methods

Patients

The current research, conducted between 2017 and 2018, focused on patients within the intensive care units (ICUs) of Shohadaye-Tajrish and Taleghani hospitals in Tehran, Iran. The study spanned one year and included a total of four distinct ICUs: medical, neurosurgery, surgery, and general ICUs, across two educational institutions, with Shohadaye-Tajrish housing 26 beds and Taleghani 18. With ethics approval granted by the Tehran University of Medical Sciences (Approval No: IR.TUMS.VCR.REC.1395.602), the study's retrospective design justified the waiver of informed consent to safeguard patient anonymity. Adhering strictly to the STROBE guidelines, the clinical team, aided by a dietitian's input, provided tailored nutritional support based on individual energy requirements, preferred administration routes, and appropriate commercial formulas, without altering existing practices. Participants were selected with inclusion criteria, focusing only on those aged 18 years and older. Patients were excluded if they were on oral feeding or parenteral nutrition, had received enteral feeding prior to ICU admission, had incomplete NRS-2002 data, were transferred or readmitted to the ICU, or experienced discharge or death within the first 24 h of ICU admission.

Demographic assessment

A comprehensive demographic evaluation was conducted within the first 24 h of ICU admission to gather crucial details that could influence patient care and outcomes. This assessment included recording the patient's age and gender directly from their medical records, followed by a thorough review of their medical history to identify any pre-existing conditions or comorbidities. Additionally, the primary reason for ICU admission was documented, categorizing the condition that necessitated critical care. Patients were then classified as either medical or surgical based on the nature of their admission. Finally, the length of the patient's hospital stay prior to ICU admission was recorded, providing a complete overview of their status before entering the critical care unit.

Nutritional assessment

In parallel with the demographic evaluation, a detailed nutritional assessment was carried out within the first 24 h using the NRS-2002 tool. This assessment was pivotal in identifying patients at nutritional risk, and ensuring they received the appropriate support during their ICU stay. The nutritional assessment involved measuring the patient's height, weight, and body mass index (BMI). These measurements gathered through interviews with the patient or their family, were cross-referenced with medical records maintained by dietitians and nurses to ensure accuracy. Furthermore, data related to unintentional weight loss over the previous 3 to 6 months, as well as dietary intake in the 5 days leading up to ICU admission, were collected to assess the patient's nutritional status. The NRS-2002 scoring system, which includes four key components BMI, reduced food intake, weight loss, and illness severity was then applied. A score above 3 on this system indicated a high level of nutritional risk, guiding early nutritional intervention for those who needed it [10].

Assessments using SOFA and APACHE II

To further evaluate the severity of the patient's condition, two critical scoring systems were employed: the SOFA (Sequential Organ Failure Assessment) score and the APACHE II (Acute Physiology and Chronic Health Evaluation II) score.

The SOFA score monitored the function of six organ systems: respiratory, cardiovascular, hepatic, coagulation, renal, and neurological with each system being scored from 0 to 4. The total SOFA score, ranging from 0 to 24, provided a measure of organ dysfunction, with higher scores indicating more severe dysfunction and a

higher risk of mortality. This score was first documented at baseline upon ICU admission [11].

Similarly, the APACHE II score, which quantifies the severity of illness based on acute physiology, chronic health conditions, and age, was calculated. This score, ranging from 0 to 71, helped assess the initial severity of the patient's condition and provided insights into their prognosis, with higher scores correlating with increased mortality risk [12].

Classification of patients based on enteral feeding status

Based on the timing of enteral feeding initiation, patients were classified into two distinct groups. The EEF Group included those who began receiving enteral nutrition within the first 48 h of ICU admission, ensuring timely nutritional support. In contrast, the Late Enteral Feeding Group comprised patients who started enteral feeding after 48 h of ICU admission.

Sample size determination

The sample size for the current study was determined based on the primary outcome of 28-day mortality among ICU patients, comparing EEF (initiated within 48 h of ICU admission) with delayed enteral feeding (initiated after 48 h). The sample size was calculated using the formula for comparing two independent proportions, considering an expected difference in mortality rates of 15% between the two groups. This expected difference was informed by previous studies that have observed significant mortality benefits associated with EEF. With a power of 80% and a significance level (alpha) of 0.05, a sample size of 268 patients was required. To account for potential attrition or loss to follow-up, the sample size was increased by 10%, resulting in a final target sample size of 295 patients. The calculation was performed using G*Power 3.1 software, which is widely recognized for its accuracy in determining sample sizes for clinical research [13].

Statistical and analytical methods

All statistical analyses were performed using IBM SPSS Statistics for Windows, Version 26.0 (IBM Corp., Armonk, NY, USA). Descriptive statistics were utilized to summarize the baseline characteristics of the study participants. Continuous variables, including age, BMI, and length of stay (LOS) before ICU admission, were presented as means and standard deviations (SD). The normality of continuous variables was assessed using the Kolmogorov–Smirnov test. Since some variables did not follow a normal distribution, non-parametric tests were employed for further analysis. Categorical variables, such as gender, age class, primary diagnosis, and

admission category, were summarized using frequencies and percentages.

Comparative analyses between the early enteral and delayed enteral feeding groups were conducted using the Mann–Whitney U test for continuous variables, due to their non-normal distribution, and the Chi-Square test for categorical variables to determine any significant differences in proportions.

Survival analysis was conducted using the Kaplan–Meier method to estimate the probability of survival at 28 days after ICU admission across the two groups. Survival curves were compared using the log-rank test. To further explore the relationship between feeding strategy and mortality risk, a Cox proportional hazards model was utilized. This model was applied in stages: initially, without adjustments (crude model), followed by models adjusted for age and gender (Model 1), BMI, baseline APACHE II and SOFA scores (Model 2), and finally including the number of comorbidities, primary diagnosis, and admission category (Model 3).

To evaluate the association between delayed enteral feeding and outcomes such as dependency on mechanical ventilation and the length of ICU stay, logistic and linear regression models were respectively employed. The results for mechanical ventilation dependency were expressed as Odds Ratios (OR) with 95% confidence intervals, while for ICU stay length, beta coefficients (β) with 95% confidence intervals were reported. These models were adjusted in a stepwise manner, similar to the survival analysis models. A p-value of less than 0.05 was considered indicative of statistical significance for all tests. Additionally, subgroup analyses were conducted based on admission category (surgical vs. medical) to explore potential differences in outcomes.

Results

Comparison of baseline characteristics between early and delayed enteral feeding

Table 1 summarizes the baseline characteristics of 295 participants, divided into the EEF group (N = 161) and the delayed enteral feeding group (N = 134). This comparison highlights key differences that may influence the effect of feeding timing on patient outcomes.

Participants' ages averaged 61.64 years, with the early group slightly younger at 60.22 years compared to 63.34 years in the delayed group. However, this difference was not statistically significant (P = 0.233). A notable difference was seen in gender distribution: 64.0% of the early group were male, compared to 50.7% in the delayed group, a statistically significant disparity (P = 0.022).

Age distribution was almost equal between those under 64 and those over 65. The early group had more participants under 64 years (57.8% vs. 47.8%), though this was

not statistically significant (P = 0.086). BMI was similar between groups, with mean BMI of 24.37 kg/m² for the early group and 24.69 kg/m² for the delayed group (P = 0.292), suggesting BMI is not a differentiating factor between these groups.

The primary diagnosis categories revealed significant differences (P = 0.015). The early group had more neurological and cardiovascular conditions, while the delayed group had higher incidences of gastrointestinal/liver and endocrine/metabolic issues, indicating that the type of underlying condition may influence feeding timing.

Most participants were surgical patients, with a slightly higher proportion in the delayed group (67.2% vs. 61.5%). However, this difference was not statistically significant (P = 0.312). The majority of participants were at high nutritional risk (89.2%), with a slightly higher percentage in the delayed group (92.5% vs. 86.3%), nearing statistical significance (P = 0.088).

Baseline severity scores, measured by APACHE II and SOFA, were significantly higher in the delayed group, indicating worse initial conditions (P = 0.001 and P = 0.018, respectively). The delayed group also had a higher number of comorbidities (2.19 vs. 1.73, P = 0.009), suggesting more complex health issues. LOS before ICU admission was slightly longer in the early group (7.36 days vs. 4.96 days), but this difference was not statistically significant (P = 0.102).

Comparison of early versus delayed enteral feeding groups on outcomes

Table 2 specifies the comparison between patients' outcomes in the ICU among early and delayed enteral feeding. The total mean LOS in the ICU was 14.45 ± 15.20 days. Among patients who received early enteral feeding, the mean length of stay was significantly lower (p < 0.001), at 13.07 ± 16.44 days, than for those on delayed enteral feeding at: 16.23 ± 13.57 days. When stratified by admission category, the surgical subgroup showed a significantly lower mean ICU stay for early enteral feeding patients (10.10 ± 13.30 days) compared to the delayed group (14.44 ± 10.36 days) (p < 0.001), whereas no significant difference was found in the medical subgroup (17.81 ± 19.68 vs. 19.89 ± 18.08 days, p = 0.404).

The overall 28-day mortality was found to be 36.6% (108/295). For the early feeding enteral group, it was 25.5% (41/161), significantly low compared to that observed in the delayed feeding enteral group, which was 50.0% (67/134) (p < 0.001). Stratification by admission category revealed a significant difference in mortality among surgical patients, where the early enteral group had a mortality rate of 29.15% (18/62) versus 70.5% (43/90) in the delayed group (p < 0.001). However, in the medical subgroup, the

Table 1 The baseline characteristics of participants

Variable	Total (N = 295)	Early enteral (N = 161)	Delay enteral (N = 134)	P-value
Age (Years)	61.64 (19.74)	60.22 (20.52)	63.34 (18.70)	0.233
Gender				0.022
Male	171 (58.0%)	103 (64.0%)	68 (50.7%)	
Female	124 (42.0%)	58 (36.0%)	66 (49.3%)	
Age Class				0.086
Up to 64	157 (53.2%)	93 (57.8%)	64 (47.8%)	
> 65	138 (46.8%)	68 (42.2%)	70 (52.2%)	
BMI (kg/m ²)	24.51 (3.72)	24.37 (3.82)	24.69 (3.61)	0.292
Primary diagnosis				0.015
Respiratory	25 (8.5%)	12 (7.5%)	13 (9.7%)	
Sepsis	10 (3.4%)	7 (4.3%)	3 (2.2%)	
Trauma	32 (10.8%)	20 (12.4%)	12 (9.0%)	
Post operative condition	18 (6.1%)	6 (3.7%)	12 (9.0%)	
Cardiovascular/vascular	39 (13.2%)	25 (15.5%)	14 (10.4%)	
Neuralgic	83 (28.1%)	51 (31.7%)	32 (23.9%)	
Gastrointestinal/liver	32 (10.8%)	13 (8.1%)	19 (14.2%)	
Endocrine & metabolic	18 (6.1%)	4 (2.5%)	14 (10.4%)	
Renal	1 (0.3%)	1 (0.6%)	0 (0.0%)	
Malignant	33 (11.2%)	21 (13.0%)	12 (9.0%)	
Other	4 (1.4%)	1 (0.6%)	3 (2.2%)	
Admission category				0.312
Surgical	189 (64.1%)	99 (61.5%)	90 (67.2%)	
Medical	106 (35.9%)	62 (38.5%)	44 (32.8%)	
NRS 2002				0.088
Low risk	32 (10.8%)	22 (13.7%)	10 (7.5%)	
High risk	263 (89.2%)	139 (86.3%)	124 (92.5%)	
Baseline APACHE II	18.24 (6.75)	17.02 (6.51)	19.69 (6.76)	0.001
Baseline SOFA score	7.17 (2.60)	6.78 (2.27)	7.63 (2.88)	0.018
Number of comorbidities	1.94 (1.65)	1.73 (1.50)	2.19 (1.79)	0.009
Length of Stay Before ICU (days)	6.27 (12.53)	7.36 (15.23)	4.96 (8.06)	0.102

Data are presented as mean (SD) for continuous variables and n (%) for categorical variables

P-values are calculated using the Mann–Whitney U test for continuous variables and the Chi-Square test for categorical variables

difference was not statistically significant (early: 48.9% (23/47) vs. delayed: 51.1% (24/47), $p = 0.075$).

The patients in the early group of enteral feeding reported a far lower mechanical ventilation requirement, 66.5% (107/161) than those in the delayed group of enteral feeding: 80.6% (108/134) ($p = 0.007$). Subgroup analysis indicated that this difference was significant in the surgical group (early: 44.4% (56/126) vs. delayed: 55.6% (70/126), $p = 0.002$), but not in the medical subgroup (early: 57.3% (51/89) vs. delayed: 42.7% (38/89), $p = 0.570$).

Impact of early versus delayed enteral feeding on survival: a Kaplan–Meier analysis

Survival outcomes for patients in the ICU were represented in this study using time-to-event data through

Kaplan–Meier survival analysis. Figure 1 demonstrates the probability of overall survival (OS) at 28 days from ICU admission based on whether or not the patient received EEF or whether there was a delay in time to feeding initiation.

The mean survival time for these patients was 24.07 days (95% CI 22.87, 25.27). On the other hand, delayed enteral feeding led to a mean survival time of 21.55 days (95% CI 20.09, 23.00).

The statistical significance for this difference in survival between these two groups was also identified by a log-rank test. Testing indicated there was a significant difference in survival probability among patients who had EEF compared to the late-feeding group (P log rank < 0.001).

Table 2 Comparison of study outcomes among early versus delayed enteral feeding

Variable	Total	Early Enteral	Delay Enteral	P-value
Length of Stay (days)				
Overall (N = 295)	14.45 (15.20)	13.07 (16.44)	16.23 (13.57)	< 0.001
Surgical (N = 189)	12.17 (12.16)	10.10 (13.30)	14.44 (10.36)	< 0.001
Medical (N = 106)	18.67 (18.97)	17.81 (19.68)	19.89 (18.08)	0.404
Mortality at 28 days				
Overall (N = 295)				
No	187 (63.4%)	120 (74.5%)	67 (50.0%)	< 0.001
Yes	108 (36.6%)	41 (25.5%)	67 (50.0%)	
Surgical (N = 189)				
No	128 (67.7%)	81 (63.3%)	47 (36.7%)	< 0.001
Yes	61 (32.3%)	18 (29.15%)	43 (70.5%)	
Medical (N = 106)				
No	59 (55.7%)	39 (66.1%)	20 (33.9%)	0.075
Yes	47 (44.3%)	23 (48.9%)	24 (51.1%)	
Mechanical ventilation				
Overall (N = 295)				
No	80 (27.1%)	54 (33.5%)	26 (19.4%)	0.007
Yes	215 (72.9%)	107 (66.5%)	108 (80.6%)	
Surgical (N = 189)				
No	63 (33.3%)	43 (68.3%)	20 (31.7%)	0.002
Yes	126 (66.7%)	56 (44.4%)	70 (55.6%)	
Medical (N = 106)				
No	17 (16%)	11 (64.7%)	6 (35.3%)	0.570
Yes	89 (84%)	51 (57.3%)	38 (42.7%)	

Data are presented as mean (SD) for continuous variables and n (%) for categorical variables
 P-values are calculated using the Mann–Whitney U test for continuous variables and the Chi-Square test for categorical variables

Comparing the hazard of mortality between EEF and delayed enteral feeding at 28 days after admitted to the ICU

Table 3 presents the results of the Cox proportional hazards model assessing the hazard of mortality at 28 days in ICU patients receiving early versus delayed enteral feeding. The crude analysis shows a significantly higher mortality risk in the delayed enteral feeding group (HR: 2.22, 95% CI 1.51, 3.28, $p < 0.001$). After adjusting for age and gender (Model 1), the hazard ratio remains significant (HR: 2.05, 95% CI 1.39, 3.04, $p < 0.001$). Further adjustments incorporating BMI, baseline APACHE II, and baseline SOFA score (Model 2) reduce the hazard ratio to 1.50 (95% CI 0.99, 2.25, $p = 0.052$), with the association losing statistical significance. Model 3, which includes additional adjustments for comorbidities, primary diagnosis, and admission category, yields a similar result (HR: 1.49, 95% CI 0.98, 2.26, $p = 0.062$). When analyzed by subgroup, surgical patients exhibit a consistently

significant association between delayed enteral feeding and higher mortality risk. In contrast, the medical subgroup does not show a statistically significant association in any model. These findings suggest that delayed enteral feeding is associated with an increased hazard of mortality in ICU patients, particularly in surgical cases.

Association of delayed enteral nutrition in ICU patients with mechanical ventilation dependency and long ICU stay

In Table 4, the association between delayed enteral nutrition in ICU patients and two outcomes, mechanical ventilation dependency (MV) and length of ICU stay (LOS) is presented across various models. For MV dependency, the crude analysis shows that delayed enteral nutrition is associated with more than double the odds of requiring mechanical ventilation (OR: 2.01, 95% CI 1.22, 3.59, $p = 0.007$). However, after adjusting for age and gender (Model 1), the odds decrease (OR: 1.85, 95% CI: 1.06, 3.23, $p = 0.030$). Further adjustments for BMI, baseline APACHE II, and SOFA scores (Model 2) reduce the odds ratio to 1.40 (95% CI 0.69, 2.83), making the association non-significant ($p = 0.347$). In the fully adjusted model (Model 3), which includes additional factors like comorbidities and diagnosis details, the odds ratio decreases further to 1.28 (95% CI 0.59, 2.70, $p = 0.558$), indicating no significant association.

Subgroup analysis reveals that the association remains significant in surgical patients, with a crude OR of 2.69 (95% CI: 1.42, 5.08, $p = 0.002$). This effect remains significant in Model 1 (OR: 2.33, 95% CI 1.21, 4.49, $p = 0.011$) but becomes non-significant in Model 2 (OR: 1.65, 95% CI 0.71, 3.86, $p = 0.244$) and Model 3 (OR: 1.77, 95% CI 0.74, 4.19, $p = 0.197$). In medical patients, there is no significant association between delayed enteral nutrition and MV in any model.

For LOS, the crude analysis suggests a non-significant trend towards a longer ICU stay with delayed enteral nutrition (β : 3.16, 95% CI - 0.34, 6.66, $p = 0.076$). After adjusting for age and gender (Model 1), the effect size decreases (β : 2.43, 95% CI - 1.05, 5.91, $p = 0.171$). Further adjustments in Model 2 reduce the effect size further (β : 1.41, 95% CI - 2.05, 4.87, $p = 0.422$), and in the fully adjusted Model 3, the association remains non-significant (β : 1.96, 95% CI - 1.52 to 5.45, $p = 0.268$). However, subgroup analysis indicates a significant association between delayed enteral nutrition and prolonged ICU stay in surgical patients. The crude analysis shows an effect size of β : 4.34 (95% CI 0.90, 7.79, $p = 0.014$), which remains significant in Model 1 (β : 3.75, 95% CI 0.27, 7.23, $p = 0.035$). In Models 2 and 3, the association is no longer significant (Model 2: β : 1.68, 95% CI - 1.73, 5.10, $p = 0.332$; Model 3: β : 1.86, 95% CI - 1.56, 5.29, $p = 0.284$).

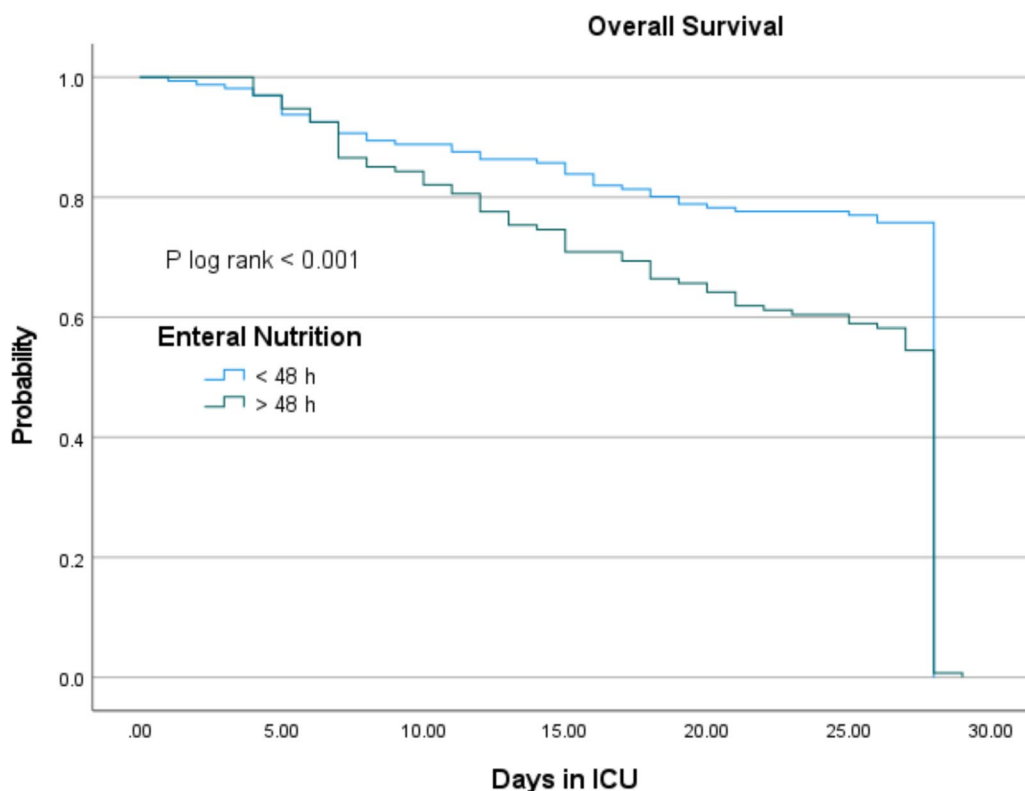


Fig. 1 Probability of OS at 28 days after ICU admitted in the early and delay enteral feeding

Table 3 Cox proportional model comparing the hazard of mortality between early enteral feeding and delay enteral feeding at 28 days after admitted to ICU

Subgroup	Model	HR (95% CI)	P-value
Overall	Crude	2.22 (1.51, 3.28)	< 0.001
	Model 1	2.05 (1.39, 3.04)	< 0.001
	Model 2	1.50 (0.99, 2.25)	0.052
	Model 3	1.49 (0.98, 2.26)	0.062
Surgical	Crude	3.01 (1.77, 5.32)	< 0.001
	Model 1	2.52 (1.44, 4.41)	0.001
	Model 2	1.83 (1.01, 3.31)	0.046
	Model 3*	1.85 (1.02, 3.35)	0.043
Medical	Crude	1.60 (0.90, 2.84)	0.107
	Model 1	1.68 (0.94, 3.01)	0.413
	Model 2	1.23 (0.67, 2.28)	0.501
	Model 3*	1.30 (0.69, 2.41)	0.419

The data are presented as Hazard Ratio (95%Confidence Interval)

Model 1 adjusted by age and gender

Model 2adjusted by age, gender, BMI, baseline APACHEII and baseline SOFA score

Model 3 adjusted by age, gender, BMI, baseline APACHEII, baseline SOFA score, number of comorbid, primary diagnosis and admission category

* Adjusted by age, gender, BMI, baseline APACHEII, baseline SOFA score, number of comorbid and primary diagnosis

No significant association is found in medical patients across any model.

Discussion

This study demonstrates that EEF in ICU patients significantly improves outcomes, reducing mortality risk and mechanical ventilation dependency. However, after adjusting for confounders, these associations were no longer statistically significant in the overall population. Subgroup analysis revealed that delayed enteral feeding in surgical patients was associated with a higher risk of mortality, mechanical ventilation dependency and prolonged ICU stay, whereas no such associations were observed in medical patients. These findings emphasize the importance of initiating enteral nutrition within 48 h of ICU admission, particularly for surgical patients, to improve survival and recovery.

In critically ill patients admitted to the ICU, starting enteral feeding is a vital part of supportive care. Evidence-based guidelines recommend beginning enteral nutrition within 24 to 48 h of ICU admission, provided the patient is hemodynamically stable [14]. EEN has been linked to better clinical outcomes, including lower infection rates, shorter ICU stays, and reduced overall mortality [14, 15].

Table 4 Association of delay enteral nutrition in ICU patients with mechanical ventilation dependency and longs of ICU stay

Subgroup	Variable	Effect size ¹ (95% CI)	P-value
MV			
Overall	Crude	2.01 (1.22, 3.59)	0.007
	Model 1	1.85 (1.06, 3.23)	0.030
	Model 2	1.40 (0.69, 2.83)	0.347
	Model 3	1.28 (0.59, 2.70)	0.558
Surgical	Crude	2.69 (1.42, 5.08)	0.002
	Model 1	2.33 (1.21, 4.49)	0.011
	Model 2	1.65 (0.71, 3.86)	0.244
	Model 3*	1.77 (0.74, 4.19)	0.197
Medical	Crude	1.37 (0.46, 4.02)	0.571
	Model 1	1.14 (0.37, 3.50)	0.813
	Model 2	0.91 (0.25, 3.29)	0.884
	Model 3*	1.12 (0.26, 4.79)	0.883
LOS			
Overall	Crude	3.16 (− 0.34, 6.66)	0.076
	Model 1	2.43 (− 1.05, 5.91)	0.171
	Model 2	1.41 (− 2.05, 4.87)	0.422
	Model 3	1.96 (− 1.52, 5.45)	0.268
Surgical	Crude	4.34 (0.90, 7.79)	0.014
	Model 1	3.75 (0.27, 7.23)	0.035
	Model 2	1.68 (− 1.73, 5.10)	0.332
	Model 3*	1.86 (− 1.56, 5.29)	0.284
Medical	Crude	2.08 (− 5.36, 9.52)	0.581
	Model 1	1.24 (− 6.25, 8.73)	0.744
	Model 2	0.65 (− 6.81, 8.11)	0.863
	Model 3*	0.56 (− 6.99, 8.11)	0.884

MV/Mechanical Ventilation, LOS/Longs of ICU Stay

¹ The data are presented as Odds Ratio (95%Confidence Interval) for MV and β (95%Confidence Interval) for LOS Model 1 adjusted by age and gender

Model 2 adjusted by age, gender, BMI, baseline APACHEII and baseline SOFA score

Model 3 adjusted by age, gender, BMI, baseline APACHEII, baseline SOFA score, number of comorbid, primary diagnosis and admission category

* Adjusted by age, gender, BMI, baseline APACHEII, baseline SOFA score, number of comorbid and primary diagnosis

However, it's crucial to ensure that the patient is not in shock or requiring increasing doses of vasopressors, as these conditions can elevate the risk of gastrointestinal ischemia, making early feeding potentially harmful [15]. For patients who are hemodynamically unstable, enteral feeding should be delayed until stabilization. Once feeding begins, it's generally recommended to start with a low volume, known as trophic or "trickle" feeds, and gradually increase the rate as tolerated [16]. This approach helps minimize complications like aspiration, which is a common concern in critically ill patients [15].

The observed reduction in 28-day mortality among patients receiving EEF (25.5% vs. 50.0%) aligns with

findings from previous studies, including those by Doig et al. and Khalid et al., which also demonstrated lower mortality rates associated with early feeding [17, 18]. This outcome highlights the critical role of early nutritional support in improving survival, particularly among critically ill patients. However, it is important to recognize that not all studies have reported this benefit. For example, Casaer et al. and Arabi et al. found no significant difference in mortality between early and delayed feeding [19, 20].

The significant reduction in the need for mechanical ventilation in the early feeding group (66.5% vs. 80.6%) underscores the potential of early enteral nutrition to enhance respiratory outcomes. This result aligns with findings from studies such as Khalid et al., which also observed decreased ventilator dependence with early feeding [18]. However, it contrasts with the outcomes reported by Casaer et al. and Rice et al., where early feeding did not significantly affect ventilator days [19, 21].

The reduction in ICU LOS associated with EEF (13.07 \pm 16.44 days vs. 16.23 \pm 13.57 days) is consistent with the findings of Doig et al., who reported similar results in trauma patients [17]. However, our findings contrast with studies like those by Casaer et al. and Dhaliwal et al., which found no significant differences in ICU stay with early feeding [16, 19].

The variability in results across the three outcomes can be attributed to several factors. First, patient heterogeneity, including differences in underlying conditions, illness severity, and nutritional status, influences responses to EEF [20]. Second, variations in study design and methodologies, such as intervention timing, criteria for early versus delayed feeding, and ICU settings, contribute to discrepancies [22]. Third, nutritional risk and baseline health status affect outcomes, with lower-risk patients deriving less benefit from early feeding [14]. Lastly, differences in ICU clinical practices, including enteral nutrition formulas and monitoring protocols, further explain inconsistencies across studies [23]. These factors highlight the complexity of evaluating EEF effects.

The current study's findings offer valuable insights but may not be universally applicable due to variations in healthcare settings. ESPEN and ASPEN recommend early enteral nutrition [14, 15], but adherence depends on institutional policies and resource availability. In lower-resource settings, delayed feeding is more common due to limited specialized formulas, staffing, and monitoring capabilities [19, 20]. Cultural preferences and financial factors also influence feeding practices. Future research should examine how these differences affect clinical outcomes and the feasibility of adapting standardized guidelines in diverse ICU environments.

This study has several strengths that enhance its validity and applicability. The inclusion of a diverse ICU population across multiple units in two major hospitals strengthens the generalizability of the results. The rigorous methodology, utilizing validated tools like the NRS-2002 for nutritional assessment and SOFA and APACHE II scores for illness severity, ensures a comprehensive evaluation of baseline conditions and nutritional risks. Additionally, the study employs advanced statistical techniques, including survival analysis and Cox proportional hazards modeling, allowing for robust adjustments for potential confounders and increasing the reliability of the findings.

However, the study also has limitations. The retrospective design introduces potential biases in data collection and patient selection, affecting internal validity. Despite adjustments, residual confounding remains due to the complexity of ICU care. The study's setting in Tehran, Iran, may limit external validity to other healthcare contexts. Selection bias may have occurred as certain patient groups were excluded, potentially underrepresenting the sickest patients. Long-term outcomes beyond the ICU, such as post-discharge morbidity and quality of life, were not assessed. Socioeconomic factors, known predictors of ICU prognosis, were not collected, limiting generalizability. Future research should incorporate these variables to enhance the applicability of findings across diverse settings.

Conclusion

In conclusion, the current study shows that starting enteral feeding within 48 h of ICU admission significantly improves clinical outcomes, including reduced 28-day mortality, decreased ventilator dependence, and shorter LOS. While initial analyses suggested that delayed feeding was associated with higher mortality and greater ventilator dependence, these links became non-significant after adjusting for confounding factors. These findings emphasize the importance of early nutritional intervention in critically ill patients and highlight the need to consider multiple variables when assessing outcomes. Although the study has its strengths, the retrospective design and potential biases mean the results should be interpreted with caution. Future research should focus on refining feeding protocols and exploring long-term outcomes across various healthcare settings to optimize ICU patient care.

Acknowledgements

We thank the school of Nutritional and Dietetics at Tehran University of medical sciences and participants in this investigation.

Author contributions

The authors contributed to this study as follows: V.H. led the conceptualization and methodology, managed data curation, and drafted the original

manuscript. R.A. conducted the investigation, data collection, and formal analysis. H.I. handled data validation and contributed to editing the manuscript. B.J. supervised the project, managed administration, and secured funding. K.M. was in charge of software, data visualization, and analysis. F.K. provided resources and assisted with data curation and manuscript editing. S.H. oversaw the entire project, supported the conceptualization and methodology, secured funding, and is the corresponding author.

Funding

The project was funded by the Tehran University of Medical Sciences (code: IR.TUMS.VCR.REC.1395.602).

Availability of data and materials

No datasets were generated or analysed during the current study.

Declarations

Ethics approval and consent to participate

This research has been supported by the Tehran University of Medical Sciences (TUMS) (Ethics No. IR.TUMS.VCR.REC.1395.602). All methods were performed following the relevant guidelines and regulations. All participants provided informed consent before the investigation.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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Received: 9 September 2024 Accepted: 10 April 2025

Published online: 22 April 2025

References

- Dainelli L, Delgado-Aros S, Lagravinese R, Paradiso GM, Perlini M. Early versus late enteral nutrition in US COVID-19 patients: a systematic literature review and meta-analysis. *Clin Nutr Open Sci*. 2023;52:128–35.
- Kasotakis G, Whitmore C. Fat malabsorption in critical illness. *Nutr Clin Pract*. 2024;39(Suppl 1):S29–s34.
- Golubykh K, Calderon-Martinez E, Zarandi N, Singh H, Singh J, Kovalenko I, Amhaz H, Ramesh N. Preventing the delay in enteral feeding initiation in critically ill mechanically ventilated patients: The quality improvement project. *Chest*. 2023;164(4):A1537–8.
- Powers J, Bourgault A, Aguirre L. Safe placement of feeding tubes. *Am J Critical Care*. 2023;32(5):324–5.
- O'Brien J: Medical nutritional therapy of paediatric burns patients: a retrospective audit. ResearchSpace@ Auckland; 2024.
- Xu F, Xu J, Ma J, Xu W, Gu S, Lu G, Wang J. Early versus delayed enteral nutrition in ICU patients with sepsis: a propensity score-matched analysis based on the MIMIC-IV database. *Front Nutr*. 2024;11:1370472.
- Mohammadzadeh F, Bilondi S, Sahebanmaleki M, Asari Sani Mend J, Tavakolizadeh M, Aalami H, Noghabi AD. The effect of *Mentha spicata* essential oil (supermint oral drops) on gastric residual volume in mechanically ventilated intensive care unit patients: a parallel-group, triple-blinded, randomised placebo-controlled trial. *J Herbal Med*. 2024;45: 100886.
- Dubois J: The impact of software-guided tight glucose control on outcome of critical illness, in relation to nutrition and circulating insulin. 2024.

9. Isaza-Lopez MC, Jimenez JC, Arbeláez EV, Rios JV, Ortiz-Muñoz LE: Oropharyngeal impregnation with maternal colostrum to reduce adverse perinatal outcomes. Evidence-based decision making after a prioritization process. 2024.
10. Kondrup J, Allison SP, Elia M, Vellas B, Plauth M. ESPEN guidelines for nutrition screening 2002. *Clin Nutr.* 2003;22(4):415–21.
11. Vincent J-L, Moreno R, Takala J, Willatts S, De Mendonça A, Bruining H, Reinhart C, Suter P, Thijs LG. The SOFA (Sepsis-related Organ Failure Assessment) score to describe organ dysfunction/failure: on behalf of the working group on sepsis-related problems of the European society of intensive care medicine (see contributors to the project in the appendix). In.: Springer-Verlag; 1996.
12. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. *Crit Care Med.* 1985;13(10):818–29.
13. Faul F, Erdfelder E, Buchner A, Lang A-G. Statistical power analyses using G* power 31: tests for correlation and regression analyses. *Behavior Res Meth.* 2009;41(4):1149–60.
14. McClave SA, Taylor BE, Martindale RG, Warren MM, Johnson DR, Braunschweig C, McCarthy MS, Davanos E, Rice TW, Cresci GA, 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.). *JPEN.* 2016;40(2):159–211.
15. Reintam Blaser A, Malbrain ML, Starkopf J, Fruhwald S, Jakob SM, De Waele J, Braun JP, Poeze M, Spies C. Gastrointestinal function in intensive care patients: terminology, definitions and management. Recommendations of the ESICM working group on abdominal problems. *Inten Care Med.* 2012;38(3):384–94.
16. Dhaliwal R, Cahill N, Lemieux M, Heyland DK. The Canadian critical care nutrition guidelines in 2013: an update on current recommendations and implementation strategies. *Nutr Clin Prac.* 2014;29(1):29–43.
17. Doig GS, Heighes PT, Simpson F, Sweetman EA. Early enteral nutrition reduces mortality in trauma patients requiring intensive care: a meta-analysis of randomised controlled trials. *Injury.* 2011;42(1):50–6.
18. Khalid I, Doshi P, DiGiovine B. Early enteral nutrition and outcomes of critically ill patients treated with vasopressors and mechanical ventilation. *Am J Critical Care.* 2010;19(3):261–8.
19. Casaer MP, Mesotten D, Hermans G, Wouters PJ, Schetz M, Meyfroidt G, Van Cromphaut S, Ingels C, Meersseman P, Muller J, et al. Early versus late parenteral nutrition in critically ill adults. *N Engl J Med.* 2011;365(6):506–17.
20. Arabi YM, Aldawood AS, Haddad SH, Al-Dorzi HM, Tamim HM, Jones G, Mehta S, McIntyre L, Solaiman O, Sakkijha MH, et al. Permissive under-feeding or standard enteral feeding in critically ill adults. *N Engl J Med.* 2015;372(25):2398–408.
21. Rice TW, Wheeler AP, Thompson BT, Steingrub J, Hite RD, Moss M, Morris A, Dong N, Rock P. Initial trophic vs full enteral feeding in patients with acute lung injury: the EDEN randomized trial. *JAMA.* 2012;307(8):795–803.
22. Elke G, van Zanten AR, Lemieux M, McCall M, Jeejeebhoy KN, Kott M, Jiang X, Day AG, Heyland DK. Enteral versus parenteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. *Critical care (London, England).* 2016;20(1):117.
23. Bateman RM, Sharpe MD, Jagger JE, Ellis CG, Solé-Violán J, López-Rodríguez M, Herrera-Ramos E, Ruíz-Hernández J, Borderías L, Horcajada J, et al. 36th International symposium on intensive care and emergency medicine: Brussels, Belgium. 15–18 March 2016. *Critical care (London, England).* 2016;20(Suppl 2):94.

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