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Early Enteral Nutrition And Clinical Outcomes In Critically Ill Medical And Post-Surgical ICU Patients: A Prospective Cohort Study From A South Asian ICU

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Abstract

Early Enteral nutrition (EEN) is recommended for critically ill patients with a functional gastrointestinal tract, but its effects on ICU length of stay and mortality remain uncertain, and evidence from South Asian ICUs is limited. This study was conducted to determine whether the use of Enteral nutrition started within 48 hours of admission to ICU is associated with shorter ICU length of stay (LOS) and lower in-ICU mortality. A prospective observational cohort study was conducted in the ICU of RIMS Trauma Hospital, Karachi. Critically ill adults aged 18 years and older who required enteral tube feeding during their ICU stay were eligible for inclusion. early Enteral nutrition (EEN, ≤48 hours after ICU admission) or late Enteral nutrition (LEN, >48 hours after ICU admission). Patients on parenteral nutrition, mechanically ventilated, or with major trauma-related conditions were excluded. The primary outcomes were ICU length of stay (days) and in-ICU mortality. Groups were compared using the independent-samples t test for ICU length of stay and Fisher's exact test for mortality. A total of 110 participants were included (55 EEN, 55 LEN). Baseline nutritional risk was similar (NRS-2002: 2.5±0.9 vs 2.3±0.8). ICU LOS was shorter in EEN than LEN (3.5±0.6 vs 5.0±0.3 days; $p<0.01$), corresponding to a mean difference of −1.50 days (95% CI −1.68 to −1.32). In-ICU mortality was 3.6% (2/55) in EEN versus 16.4% (9/55) in LEN (risk ratio 0.22, 95% CI 0.05 to 0.98; $p=0.05$). In this South Asian ICU cohort, EEN within 48 hours was associated with shorter ICU LOS. Lower observed in-ICU mortality was also noted in the EEN group, but this finding should be interpreted cautiously because mortality events were limited. However, because of the observational design, baseline imbalances, limited mortality events, and unavailable data on APACHE II/SOFA scores, vasopressor use, sepsis status, and comorbidities, these findings should be interpreted as associations rather than causal effects.

Introduction

Early Enteral nutrition (EEN), typically defined as initiation within 24–48h of ICU admission, is recommended in major international critical care nutrition guidelines for patients with a functional gastrointestinal tract. The 2023 ESPEN practical guideline advises starting Enteral nutrition within 48h in hemodynamically stable critically ill adults, emphasizing the preferential use of the enteral route over parenteral nutrition

when feasible (Singer et al., 2023). Likewise, ASPEN/SCCM guidelines suggest early Enteral feeding in the appropriately resuscitated patient without contraindications (McClave et al., 2016). The recommendations are based on physiological reasoning as well as a body of clinical evidence.

Enteral feeding is preferred as it helps to maintain integrity of gut mucosa, splanchnic perfusion, and may reduce the risk of bacterial translocation and infection when compared with exclusive parenteral nutrition. Meta-analyses of studies that compared enteral and parenteral nutrition have demonstrated reduced infectious complications with enteral nutrition in specific groups of critically ill patients, but the effects on mortality have been inconsistent (Gramlich et al., 2004; Casaer et al., 2011). A Cochrane review comparing early (<48h) and delayed Enteral nutrition found that early feeding is feasible and generally safe in stable patients, but that there are limited numbers of events and heterogeneity in the data, making it uncertain whether early feeding improves mortality (Fuentes Padilla et al., 2019).

Recent reviews highlight the need for individualization and phase-specific nutrition therapy in the ICU. The 2024 Intensive Care Medicine review by de Man et al. (2024) highlights that early nutrition must focus on tolerance and physiological stability, especially in the acute stage of the disease, and not on high calorie intake. Similarly, a 2025 review article published in BMJ, on nutritional support in the ICU, confirms the use of EEN in stable patients, but also warns against a uniform high dose approach in the unstable or shock state (Reignier et al., 2025). All these sources are consistent with the idea that EEN is recommended practice in patients who are appropriately resuscitated, but its impact on definitive clinical outcomes is context dependent.

The clinical benefit of early Enteral nutrition in terms of length of stay in the ICU and mortality is unclear despite international guideline recommendations. The results of early nutritional strategies on mortality and other clinical outcomes have been inconsistent in large, randomized trials, which may be attributed to differences in illness severity, route of feeding, shock status, and patient selection (Harvey et al., 2014; Reignier et al., 2018). Data from South Asian ICUs is still scarce, but delayed feeding could be due to practice variation, fear of hemodynamic instability, feeding intolerance and resource limitations. Therefore, region-specific observational data are needed to evaluate whether EEN is associated with clinically meaningful outcomes in routine ICU practice.

Therefore, the aim of this study was to determine whether initiation of Enteral nutrition within 48 hours of ICU admission was associated with ICU length of stay and in-ICU mortality among critically ill medical and post-surgical adults in a South Asian ICU. We hypothesized that patients receiving EEN would experience shorter ICU stays and lower mortality than those receiving delayed Enteral nutrition.

Methods

This prospective observational cohort study was conducted in the adult intensive care unit (ICU) of RIMS Trauma Hospital, Karachi, Pakistan. The ICU is a tertiary-care facility providing medical and post-surgical critical care services. Data were collected consecutively from eligible patients admitted between 15 Sep 2023 and 15 Mar 2024.

Critically ill adults aged 18–71 years who required enteral tube feeding during their ICU stay were eligible for inclusion. Enteral nutrition was initiated according to the treating physician's assessment of clinical stability and absence of contraindications to Enteral feeding. Detailed vasopressor dose, lactate, and perfusion data at the exact time of feeding initiation were not systematically collected. Patients receiving parenteral nutrition, those mechanically ventilated at admission, and individuals admitted with major trauma-related conditions, including burns, road traffic injuries, or gunshot wounds, were excluded. Mechanically ventilated patients were excluded to reduce clinical heterogeneity because feeding protocols, aspiration risk, and severity

of illness may differ substantially in ventilated ICU populations. A total of 110 participants met the eligibility criteria and were included in the final analysis.

The sample size was based on consecutive enrollment of all eligible patients during the study period chosen for feasibility given the fixed recruitment window and single-center setting rather than a probability-based sampling design. No formal priori sample-size calculation was performed. Therefore, analyses of mortality were considered exploratory, particularly because of the limited number of mortality events. Participants were categorized according to the timing of Enteral nutrition (EN) initiation following ICU admission. EEN was defined as administration of the first Enteral feeding formula through a feeding tube within 2-48 hours of ICU admission, independent of achieved caloric or protein targets (de Man et al., 2024). Allocation to exposure groups was determined by routine clinical practice and not influenced by the investigators.

Baseline demographic and clinical data were collected from medical records using a standardized data collection form. Variables included age, sex, residential background, body mass index (BMI), primary admission diagnosis, and severity of illness assessed using the quick Sequential Organ Failure Assessment (qSOFA) score. Nutritional risk was evaluated at ICU admission using the Nutritional Risk Screening 2002 (NRS-2002) tool. Feeding-related variables, including route of administration and formula type, were also recorded.

Primary outcomes included length of stay (LOS) in days from ICU admission to discharge or death and in-ICU mortality. ICU LOS was considered a continuous variable and mortality was considered a binary variable (alive or dead at the time of ICU discharge).

Continuous variables were presented as mean ± standard deviation (SD) and categorical variables as frequencies and percentages. Independent-samples t test was used for approximately normally distributed continuous variables and χ^2 test or Fisher's exact test was used for categorical variables for between-group comparisons. As a sensitivity analysis, median and interquartile range of the length of stay in the ICU were also summarized and compared using the Mann–Whitney U test.

Multivariable regression analyses were conducted to evaluate independent associations of timing of EN initiation with clinical outcomes. Linear regression was used to evaluate the association between EEN and ICU LOS, and logistic regression was used to examine the association between EEN and in-ICU mortality. Both models were adjusted for age, sex, body mass index, admission diagnosis category, baseline qSOFA score, and NRS-2002 score. Data on vasopressor dose, sepsis status, major comorbidities, APACHE II score, and full SOFA score were not available; therefore, these variables could not be included in the adjusted models. Because only 11 mortality events occurred, the adjusted mortality model was considered exploratory and interpreted cautiously because of the risk of overfitting (Peduzzi et al., 1996). Results are presented as adjusted β coefficients with 95% confidence intervals (CI) for ICU LOS and adjusted odds ratios (OR) with 95% CI for mortality. Missing data were assessed for each variable. Analyses were conducted using available cases, and Missing data were assessed for each variable and were minimal (affecting a single participant for feeding-route/formula documentation; Table 2). A two-sided p value <0.05 was considered statistically significant. Statistical analyses were performed using SPSS software (version 26; IBM Corp., Armonk, NY, USA).

Ethical considerations

The study was approved by the Institutional Ethics Committee of RIMS Trauma Hospital, Karachi. Written informed consent was obtained from all participants or their legally authorized representatives prior to enrollment. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Results

A total of 110 critically ill adults were included and classified according to timing of Enteral nutrition initiation: early Enteral nutrition (EEN ≤48h; n=55) and late Enteral nutrition (LEN >48h; n=55).

Table 1. Baseline characteristics of participants by Enteral nutrition timing (N = 110)

Values are **n (%)** unless otherwise stated.

Characteristic	EEN ≤48h (n = 55)	LEN >48h (n = 55)	p-value
Age group (years)			0.032
18–35	10 (18.2)	10 (18.2)	
36–53	14 (25.5)	22 (40.0)	
54–71	24 (43.6)	23 (41.8)	
>71	7 (12.7)	0 (0.0)	
Sex			0.034
Male	37 (67.3)	26 (47.3)	
Female	18 (32.7)	29 (52.7)	
Residential background			0.42
Urban	33 (60.0)	37 (67.3)	
Rural	22 (40.0)	18 (32.7)	
BMI (kg/m²), mean (SD)	23.2 (3.3)	24.5 (7.2)	0.36
NRS-2002 score, mean (SD)	2.5 (0.9)	2.3 (0.8)	0.32

Note. *BMI, body mass index; EEN, early Enteral nutrition; LEN, late Enteral nutrition; NRS-2002, Nutritional Risk Screening 2002. Statistical tests: chi-square or Fisher's exact test for categorical variables and independent-samples t test for continuous variables.*

Baseline characteristics are presented in Table 1. Age distribution differed between groups (p = 0.032), with a higher proportion of participants aged 36–53 years in the LEN group and a small subgroup aged >71 years in the EEN group. Sex distribution also differed (p = 0.034), with males more frequently represented in the EEN group. Residential background and body mass index were similar between groups. Baseline nutritional risk, assessed using NRS-2002, did not differ significantly between EEN and LEN (mean ± SD: 2.5 ± 0.9 vs 2.3 ± 0.8; p = 0.32).

Table 2. Primary clinical outcomes by Enteral nutrition timing

Outcome	EEN ≤48h (n = 55)	LEN >48h (n = 55)	Crude effect estimate	p-value	Adjusted effect estimate†	p-value
ICU length of stay (days), mean ± SD	3.5 ± 0.6	5.0 ± 0.3	Mean difference = −1.50 (95% CI −1.68 to −1.32)	<0.01	β = −1.43 days (95% CI −1.63 to −1.22)	<0.001
In-ICU mortality, n (%)	2 (3.6)	9 (16.4)	Risk ratio = 0.22 (95% CI 0.05 to 0.98)	0.05	OR = 0.19 (95% CI 0.04 to 0.92)	0.039

Note*. †Adjusted for age, sex, body mass index, admission diagnosis category, baseline qSOFA score, and NRS-2002 score. The adjusted mortality model should be interpreted cautiously because only 11 mortality events occurred.*

Primary clinical outcomes are summarized in Table 2. Mean ICU length of stay was shorter in the EEN group than in the LEN group (3.5 ± 0.6 vs 5.0 ± 0.3 days), corresponding to a crude mean difference of −1.50 days (95% CI −1.68 to −1.32; p < 0.01). In multivariable linear regression adjusted for age, sex, body mass index, admission diagnosis category, baseline qSOFA score, and NRS-2002, EEN remained

associated with a shorter ICU length of stay (adjusted β = −1.43 days; 95% CI −1.63 to −1.22; p < 0.001). In-ICU mortality occurred in 2 of 55 patients (3.6%) in the EEN group and 9 of 55 patients (16.4%) in the LEN group, yielding a crude risk ratio of 0.22 (95% CI 0.05 to 0.98; Fisher's exact p = 0.05). In exploratory adjusted logistic regression, EEN was associated with lower odds of in-ICU mortality (adjusted OR = 0.19; 95% CI 0.04 to 0.92; p = 0.039); however, this estimate should be interpreted cautiously because only 11 mortality events occurred.

Table 3. Feeding route and formula type by Enteral nutrition timing among patients with available feeding data

Variable	EEN ≤48h (n = 55)	LEN >48h (n = 55)	p-value
Formula type			**0.01**
Non-diabetic formula	35 (63.6)	21 (38.9)	
Diabetic formula	20 (36.4)	33 (61.1)	
Feeding route			**0.001**
Nasogastric (NG)	47 (85.5)	34 (63.0)	
Percutaneous endoscopic gastrostomy (PEG)	5 (9.1)	20 (37.0)	
Percutaneous endoscopic jejunostomy (PEJ)	3 (5.5)	0 (0.0)	

Note. *Percentages for formula type and feeding route were calculated using non-missing data. One participant in the LEN group had missing feeding-route/formula documentation. EEN, early Enteral nutrition; LEN, late Enteral nutrition; NG, nasogastric; PEG, percutaneous endoscopic gastrostomy; PEJ, percutaneous endoscopic jejunostomy.*

Feeding characteristics are presented in Table 3. The route of Enteral feeding differed between groups (p = 0.001). Nasogastric feeding was more frequent in the EEN group, whereas PEG feeding was more frequent in the LEN group. Formula type also differed between groups (p = 0.01), with diabetic formulations more frequently used in the LEN group.

Discussion

In this prospective cohort study of critically ill medical and post-surgical adults in a South Asian ICU, initiation of Enteral nutrition within 2-48 hours was associated with shorter ICU length of stay compared with later initiation. Lower observed in-ICU mortality was also found in the EEN group, although this association should be interpreted cautiously because mortality events were few and residual confounding remains likely. These associations persisted after adjustment for measured covariates; however, residual confounding remains likely because feeding timing was determined by routine clinical practice rather than randomization.

The biological plausibility of the association between EEN and decreased ICU LOS is that EEN could help preserve gut mucosal integrity, improve immune function, and minimize cumulative energy deficits during critical illness. But this observation could also be due to early clinical stabilization of patients selected for earlier feeding. Current ESPEN and other expert guidelines advocate early enteral nutrition (EN) when possible, highlighting its importance for maintaining gastrointestinal function and aiding recovery (Singer et al., 2023; Wischmeyer et al., 2023). Recent reviews also emphasize the continued importance of EEN as a key component of supportive care in the ICU, with careful consideration of patient stability and tolerance (Reignier et al., 2025).

The mortality result should be interpreted with caution. Although lower mortality was observed in the EEN group, the number of deaths was small, and the adjusted logistic regression model may be overfitted. In addition, unmeasured differences in illness severity, vasopressor use, sepsis status, comorbidities, feeding route, and clinician decision-making may have influenced both the timing of EN initiation and mortality. Therefore, the mortality result should be considered exploratory rather than confirmatory. Evidence regarding mortality benefits of early feeding remains inconsistent across heterogeneous ICU populations. A Cochrane review and subsequent analyses have reported uncertainty in mortality effects due to variations in patient selection, feeding protocols, and illness severity (Fuentes Padilla et al., 2019). More recent literature underscores the importance of individualized and phase-specific nutritional strategies, particularly during the acute phase of critical illness, when overly aggressive feeding may not confer additional benefit (de Man et al., 2024; Reignier et al., 2025). In this context, the lower mortality observed in our cohort may reflect earlier stabilization, improved nutritional delivery, or differences in case mix, rather than a direct causal effect of EEN.

Importantly, this study provides evidence from a South Asian ICU, a region underrepresented in critical care nutrition research. Resource limitations, variability in feeding practices, and differences in case mix may influence both the timing and impact of nutritional interventions in low- and middle-income settings. In such environments, even modest reductions in ICU length of stay may have substantial implications for resource utilization and patient throughput. Our findings therefore contribute region-specific evidence supporting the feasibility and potential benefits of EEN in this context.

From a local practice perspective, these findings support the need for standardized Enteral feeding protocols in Pakistani ICUs, particularly protocols that document eligibility for EN, hemodynamic stability, feeding intolerance, reasons for delay, and daily nutritional delivery. Such protocols may improve consistency of care and allow future studies to better distinguish the effect of feeding timing from differences in baseline illness severity.

Strengths and Limitations

This study has several strengths. It was prospective, conducted in a real-world ICU setting, and focused on clinically meaningful outcomes including ICU length of stay and in-ICU mortality. Using a standardized nutritional risk assessment (NRS-2002) and accounting for available clinical covariates increases the strength of the analysis, but residual confounding is possible. Further, the study provides data from the South Asian population, which is a gap in the literature on critical care nutrition.

A number of limitations should be taken into account. First, the observational design does not allow for causal inference and the possibility of residual confounding by indication cannot be excluded (Harvey et al., 2014). Second, there was no documentation of the reasons why EN was not initiated. Third, severity was assessed using qSOFA and not APACHE II or SOFA scores (Vincent et al., 1996; Knaus et al., 1985). Fourth, information on caloric adequacy, protein delivery, feeding tolerance and gastrointestinal complications was not available. Fifth, there is uncertainty about adjusted estimates due to small sample size and limited mortality events (Reignier et al., 2018). Lastly, the single-center design may have a restricted generalizability.

Conclusion

In a prospective single-center cohort in a South Asian ICU, early EN (within 2-48 hours of ICU admission) was linked to a shorter length of stay in the ICU in non-ventilated, critically ill medical and post-surgical adults. This was also observed for in-ICU mortality in the EEN group, but this finding should be interpreted as exploratory given limited mortality events and the possibility of residual confounding.

Due to the observational nature of this study, the imbalances at baseline and the inability to fully adjust for illness severity, vasopressor exposure, sepsis status, co-morbidities and nutrition-delivery variables, the results should be interpreted as associations and not causal effects. These findings need to be confirmed in South Asian ICUs with larger multicenter studies that utilize standardized severity assessment, feeding protocols, and detailed nutrition-delivery data.

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