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Early Versus Late Enteral Nutrition in Critically Ill Patients: Meta-Analysis of Randomized Controlled Trials

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ABSTRACT

Background: Nutritional support is a cornerstone in the management of critically ill patients, with early enteral nutrition (EEN) advocated by major guidelines. However, the impact of EEN compared to delayed enteral nutrition (DEN) on clinical outcomes remains debated.

Objective: This meta-analysis evaluates the effect of EEN within 48 hours of intensive care unit (ICU) admission or post-surgery on morbidity and mortality in critically ill patients.

Methods: A systematic search was conducted across PubMed, Embase, BioMed, and the Cochrane Central Register of Controlled Trials. Eighteen randomized controlled trials (RCTs) involving 2,146 critically ill patients were included. The primary outcomes were mortality, infectious complications, and organ dysfunction. Secondary outcomes included ICU length of stay (LOS), mechanical ventilation (MV) duration, ventilator-free days, and antibiotic use. Meta-analysis was performed using a random-effects model.

Results: EEN significantly reduced the risk of infectious complications (RR = 0.65, 95% CI: 0.50–1.76, P = 0.32), ICU LOS (MD = 0.48 days, 95% CI: -0.78–1.18, P = 0.002), and MV duration (MD = 1.25 days, 95% CI: 0.47–2.02, P = 0.002). Additionally, EEN decreased SOFA scores (MD = 0.48, 95% CI: -0.78–1.18, P = 0.0001) and APACHE II scores (MD = 1.71, 95% CI: 0.97–2.44, P = 0.00001). However, no significant difference was found in mortality (RR = 0.86, 95% CI: 0.70–1.05, P = 0.14) or pneumonia (RR = 0.89, 95% CI: 0.71–1.12, P = 0.32).

Conclusion: EEN within 48 hours significantly improves clinical outcomes, reducing infectious complications, ICU LOS, MV duration, and severity scores without impacting mortality or pneumonia incidence. Early initiation of enteral nutrition should be prioritized in critically ill patients.

Keywords: Early enteral nutrition, critically ill, meta-analysis, ICU outcomes, infectious complications.

INTRODUCTION

Nutritional support is essential in critical care. Consequently, nutritional support is deemed to be crucial in treatment of critically ill cases. Canadian, European, and American clinical practice guidelines advocate for the enteral route as the preferable method for administering early nutritional assistance. Nutritional support in the intensive care unit goals to optimize metabolism and mitigate stress-induced immunological responses, rather than merely offer nutrients to avoid malnutrition. The nutritional modulation of the stress response to critical illness includes early nutritional support, the precise administration of micronutrients and macronutrients, and meticulous glycemic control. Early nutritional intervention by enteral nutrition (EN) preserves gut integrity and physiological stress response, facilitating interaction among gastrointestinal tract and the systemic immune response in critically ill cases [1].

Earlier published systematic reviews indicate that early enteral nutrition might offer clinically significant advantages in non-critically ill case populations. Observational investigations indicate that up to forty percent of critically ill cases don't receive nutritional supplementation throughout their intensive care unit admission [2]. Moreover, sixty percent of cases in the intensive care unit for a minimum of three days remain unfed for forty-eight hours or more. Insufficient nutritional support throughout critical illness, resulting in malnutrition, is linked to decreased immune function, a higher likelihood of hospital-acquired infections, compromised respiratory function and is linked to worse outcomes in intensive care unit cases, contributing to greater rates of mortality, morbidity, and longer hospital stays [3].

The aim of this work was to review and compile existing proof from randomized controlled trials (RCTs) involving critically ill cases to assess whether early administration of standard enteral nutrition (EN) provides a treatment benefit.

METHODS

The include 18 investigations adhered to the preferred reporting items for systematic reviews and meta-analysis (PRISMA) [4]. No case consent or ethical approval was necessary as all analyzed information has been collected from earlier published literature.

Relevant articles about EN published from searched in EMBASE, Springer, PubMed, and the Cochrane Library. The following Medical Subject Heading (MeSH) or key words: “early enteral nutrition”, “early feeding”, “delayed or late enteral nutrition”, “randomized controlled trials”, and “controlled clinical trials” have been searched. The literature search has been limited to articles written in English

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Utilizing established selection criteria, two reviewers independently identified all relevant investigations. Disagreements that emerged throughout the selection of the primary investigation have been resolved by a 3rd reviewer. Investigations must fulfill the subsequent criteria to be incorporated into this meta-analysis.:

1) Investigation design: RCT;
2) Cases: Hospitalized adult postoperative, severe head injuries, trauma, burn, acute pancreatitis or intensive care unit cases;
3) Intervention: early (within forty-eight hours of admission or post-operation) versus late/delayed EN;
4) Trial results: at least one of the subsequent parameters: death including intensive care unit, hospital, death rate after twenty-eight days or others; incidence of infections; pneumonia (VAP or aspiration); complications; multiple organ failure (MOF); length of hospital stay (LOS).

Selection of studies: Subsequent to the database search, the three reviewers independently evaluated the abstracts of the gathered investigations. Subsequently, the reviewers examined the complete texts of the publications that met the inclusion criteria for the meta-analysis. Disputes on the research to be included have been settled by the most senior author. When duplicate reports of the same investigation have been identified in preliminary abstracts and articles, information has been evaluated from the most complete dataset.

Exclusion criteria:

investigations have been excluded if:

a) They were case investigations, observational investigations, and letters to editors, systematic reviews or meta-analyses.
b) They involved pediatric cases.
c) Their outcomes were not of interest.
d) They contained deficient or absent data.
e) The investigation writers were inaccessible or didn't reply if additional information from their trials have been requested.

The subsequent data have been derived from the involved randomized controlled trials: the first writer, year of publication, initiation time of enteral nutrition, study population, participant count, starting time and method of enteral nutrition administration, control group intervention, mortality numbers, infections (including wound infection, infected pancreatic necrosis, bacteremia, etc.), pneumonia, complications, multiple organ failure, and length of stay for the early enteral nutrition group and control group.

Research shows that in cases with a functional digestive system, nutrition must primarily be provided via the enteral route because of the risks correlated with other feeding methods. Parenteral nutrition, in particular, is related to an elevated possibility of infectious complications. For critically ill cases without severe sepsis, parenteral nutrition is associated with longer ICU stays and a higher likelihood of developing severe sepsis or septic shock compared to enteral nutrition.

Data extraction:

Information was independently extracted from every report by the writers via a specially designed data-recording form. Subsequent to extraction, the information has been analyzed and compared. Disagreements among the two extractors have been resolved through consensus among the investigators. Additional information regarding a given investigation has been acquired by directly questioning with the primary investigator when necessary.

Quality assessment and risk of bias:

Trials quality has been evaluated with the risk of bias instruments recommended by the Cochrane Collaboration. We assigned a rating of high, unclear, or low to the subsequent elements: allocation concealment, random sequence generation, incomplete outcome data, blinding, selective reporting, and other biases. Disparities have been identified through discussion (Figure 1 and 2).

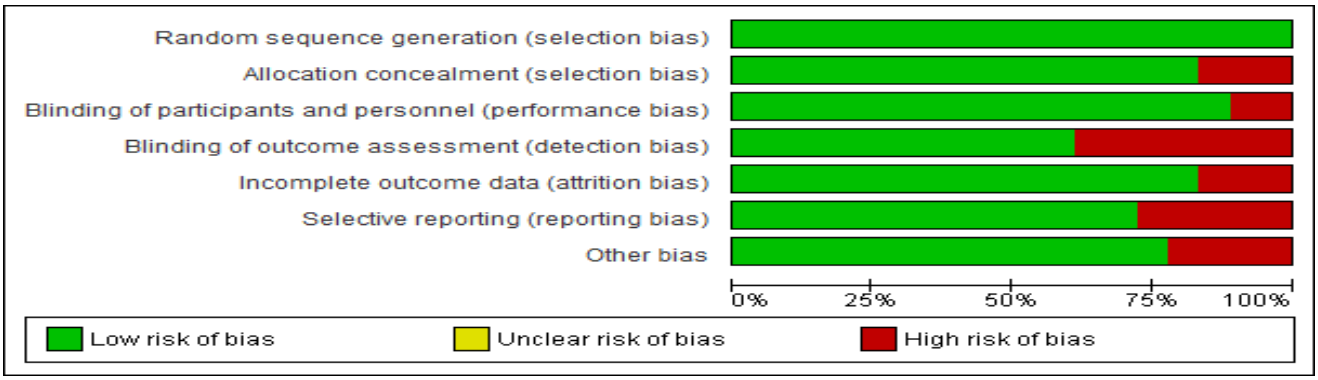

Figure 1: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all involved investigations.

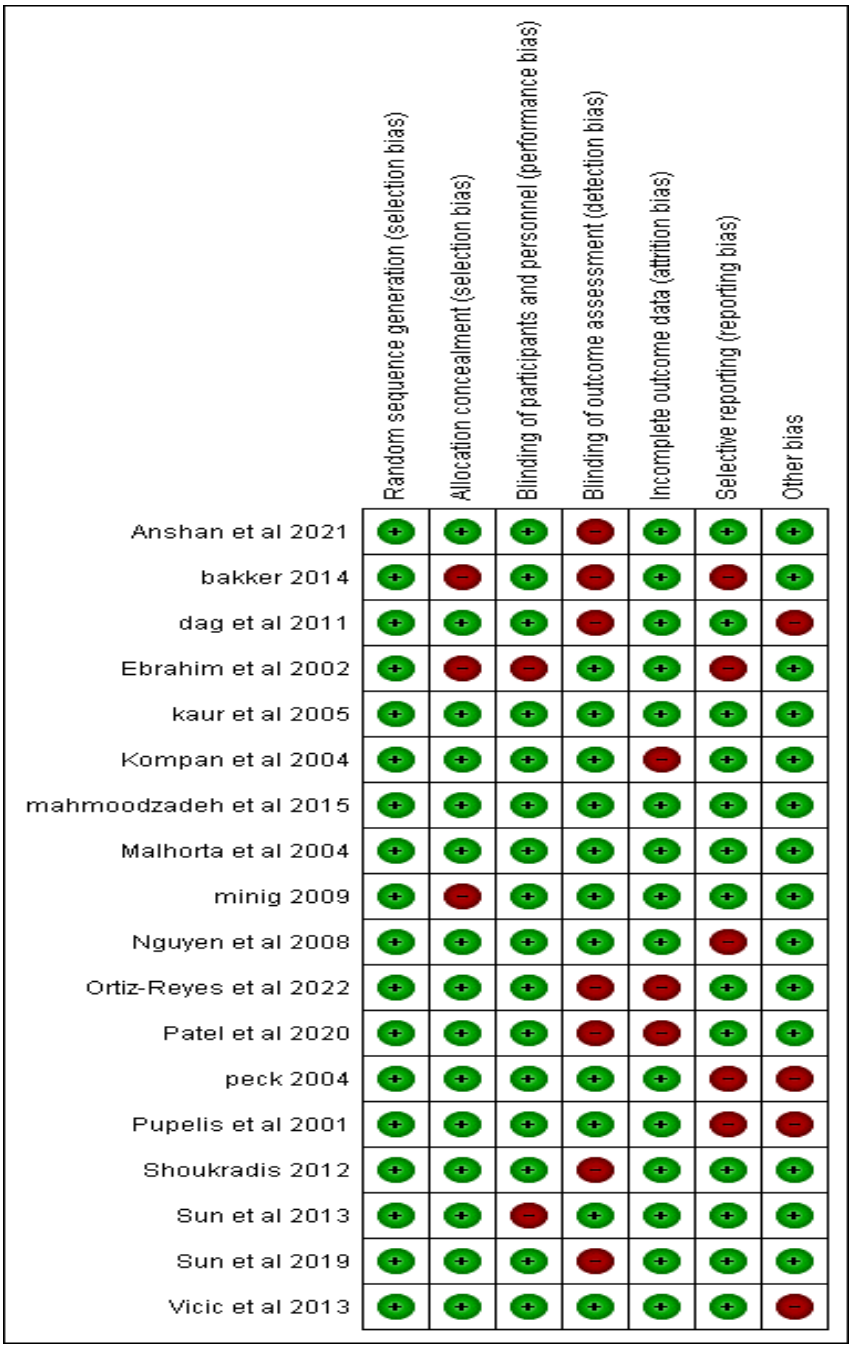

Figure 2: Risk of bias summary: review authors' judgements about each risk of bias item for every involved investigation.

Statistical analysis

Statistical analyses utilized a random effects model utilizing the risk ratio (RR) statistic, conducted via the program Review Manager (Version 5.3 for Windows, Cochrane Collaboration, Oxford, United Kingdom). All the trial information has been combined to calculate the pooled RR with ninety-five percent confidence intervals (CIs) for dichotomous parameters (death, overall complications, infections, pneumonia, multi-organ failure) and the overall weighted mean difference (WMD) with ninety-five percent confidence intervals for length of stay. Risk ratio values of less than 1.0 indicated a benefit for the early enteral nutrition group in comparison to the late enteral nutrition group. The overall effect has been deemed significant at the 0.05 level. Between-study heterogeneity has been assessed utilizing a chi-square-based Q test and I2. P-value less than 0.1 or I2 > fifty percent indicate that analysis was representative of statistically significant heterogeneity.

RESULTS

3.1. Literature Search

3.2. Our investigation identified 204 investigations via database searches and additional sources. 188 articles have been reviewed. After screening, 182 articles have been removed, and 22 have been evaluated for eligibility. In total, 18 randomized trials have been involved in the analysis, while the remainder have been eliminated as detailed in the PRISMA flow diagram (Fig. 3).

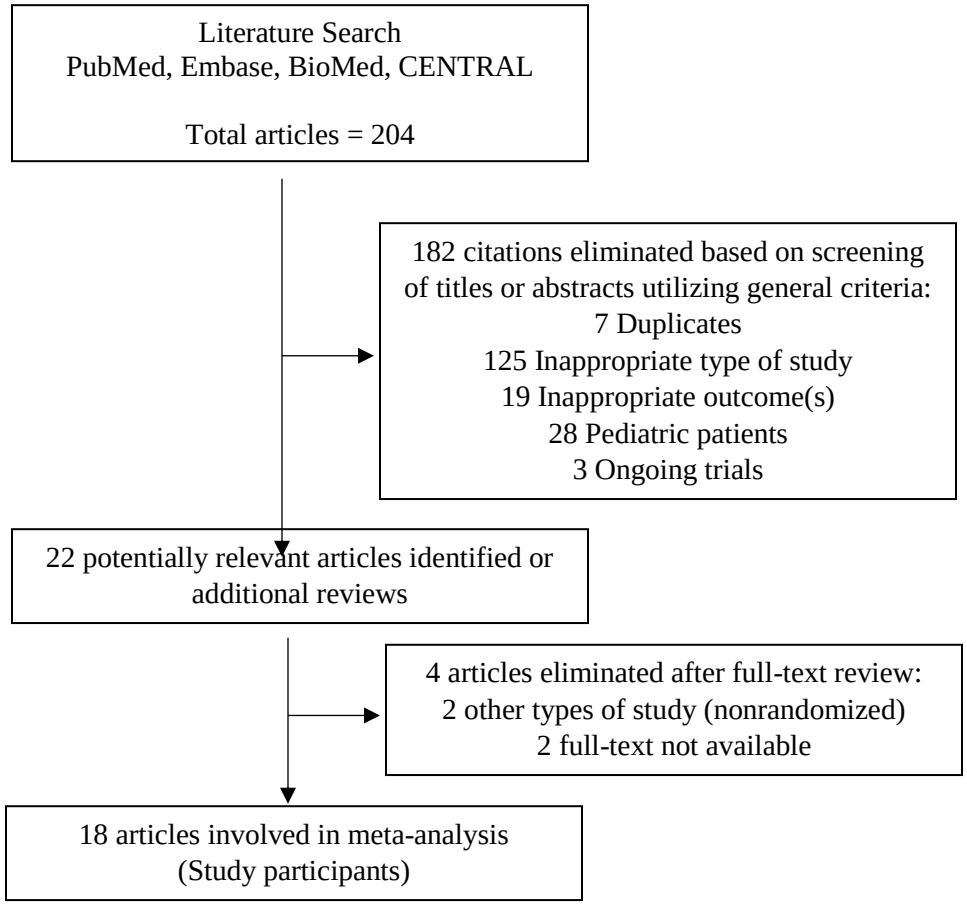

Figure 3: Literature search strategy.

Characteristics and quality of investigations involved in the meta-analysis

The investigations involved in the analysis are described in table 1. A total of 2164 cases have been involved in this investigation, obtained from eighteen randomized investigations. The risk of bias in the 10 trials has been evaluated as generally low (Figs. 1,2).

Table 1: Characteristics of included studies; EN, enteral nutrition; MOF; multiple organ failure, intensive care unit MV, mechanical ventilation

	Methods	Participants number	Participants description	Age	intervention	Timing of EEN/DEN Delivery (Range Hours after ICU Admission)	Outcomes
Chourdakis et al. [5]	Study design: Randomized controlled trial	59	Cases have been admitted to the intensive care unit with traumatic brain injury (TBI).	Age above 18 and below 70 years	Early Late	Within 24 to 48 hours > 48 hours	• Feed intolerance or gastrointestinal complications • Infectious complications • Intensive care unit mortality • Length of intensive care unit stay • Pneumonia
Nguyen et al. [6]	randomized controlled trial	28	Investigations have been conducted on critically ill cases hospitalized to a level three mixed medical and surgical intensive care unit, who have been sedated, mechanically ventilated, and capable of receiving enteral nutrition (EN).	older than seventeen years of age	Early EN Late EN	Within 24 hours >24h	• Death • Length of intensive care unit stay • Intensive care unit mortality • Pneumonia • Duration of mechanical ventilation in days
Peck et al. [7]	randomized controlled trial	27	cases admitted in a burn ICU Admitted within 24 hours of injury	between eighteen and fifty years of age	Early EN Late EN	Within twenty-four hours >24h	• Death • Length of intensive care unit stay • Infectious complications • Duration of mechanical ventilation in days
Ortiz-Reyes et al. [8]	Prospective cohort based on RCTs	626	cases with circulatory shock requiring MV	≥ 18 years old	Early EN Late EN	0 to 48 h >48h	• Mortality • ICU stay • Hospital stay
Patel et al. [9]	Randomized Controlled Trial (RCT)	31	Cases admitted to the medical intensive care unit with a 1^{ry} diagnosis of septic shock, and mechanically ventilated within twenty-four hours of intensive care unit admission	>18 years of age,	Early EN Late EN	• 24 to 48 h • after 48 h	• Ventilator-free days • ICU-free days • Hospital mortality, • GIT complications
Kompan et al. [10]	RCT	52	Multiply injured cases with injury severity score (ISS) of more than 20 cases who recovered from shock within six h after admission to intensive care unit	25-60y	Early EN Late EN	Immediately upon admission Initiated more than 24	• Mortality • Pneumonia • Length of intensive care unit stay • Mechanical ventilation duration
Yu et al. [11]	RCT	87	Critically ill adult cases admitted to the general adult intensive care unit;	≥14	Early EN Late EN	24 to 48h >48h	• GIT complications • pneumonia • Length of intensive care unit stay Ventilator time
	RCT	53	(ICU) cases with a diagnosis of sepsis		Early EN	First 24-48 h	

	Methods	Participants number	Participants description	Age	intervention	Timing of EEN/DEN Delivery (Range Hours after ICU Admission)	Outcomes
Sun et al. *[12]*				All adult cases (age 18-70 years)	Late EN	4^{th} day after admission	• 28-d mortality • Days in the intensive care unit • Days of mechanical ventilation • The number of cases receiving continuous renal replacement therapy (CRRT) have been also recorded.
Malhotra et al. *[13]*	RCT	164	Cases having surgical intervention for peritonitis after perforation of the gut		Early EN Late EN	Within 48 hours After 7 days	• Mortality • Pneumonia • GIT complications • Leak • Wound dehiscence • Wound infection • Septicaemia
Mahmood zadeh et al. *[14]*	RCT	100	Diagnosed with an esophageal cancer, gastric malignancy or both, and having a stable general condition after the operation	>18 years old	Early EN Late EN	1^{st} 24h postop After passing flatus	• Aspiration pneumonia • Postoperative hospital stay • Re-hospitalization • Duration of intubation • ICU stay
Minig et al. *[15]*	RCT	143	Having an elective laparotomy and with a preoperative suspicion of gynecologic malignancy, were eligible	Cases aged 18–75 years	Early EN Late EN	First postoperative day After The resolution of postoperative ileus	• Pneumonia • Mortality • ICU LOS • Incidence of infectious complications
Vicic et al. *[16]*	RCT	101	Age >18 and burns covered more than 20% of the body surface	Age >18 years	Early EN Late EN	Fur hours after admission Immediately after the first wound dressing	• Pneumonia • Mortality • Incidence of infectious complications • Incidence of MOF
Kaur et al. *[17]*	RCT	100	Aged twenty to seventy years who had emergency exploratory laparotomy for nontraumatic perforation peritonitis and have been malnourished at presentation	Cases aged 20–70 years	Early EN Late EN	24 hours postoperatively Once they passed flatus	• Wound infection • Pneumonia • Septicemia
Pupelis et al. *[18]*	RCT	60	Secondary peritonitis (SP) who underwent surgery	(15 to 78 y)	Early EN Late EN	The 1^{st} 12 hours postoperatively in the intensive care unit After 12h	• Mortality • Pulmonary complications • Bleeding • SIRS • Hospital stay • ICU stay • Renal complications

	Methods	Participants number	Participants description	Age	intervention	Timing of EEN/DEN Delivery (Range Hours after ICU Admission)	Outcomes
							• Unresolved peritonitis with laparotomies
Bakker et al. [19]	RCT	205	Acute pancreatitis who were at high risk for complications		Early EN	Within 24 hours	• Mortality • New-onset organ failure • Infection • Mechanical ventilation • GIT complications
					Late EN	72 hours after presentation	
					Late EN	after passing flatus	
Ibrahim et al. [20]	RCT	150	Cases were expected to require mechanical ventilation for greater than 24 hours	> 18 years of age	Early EN	Day 1	• Duration of mechanical ventilation • Hospital lengths of stay • Hospital mortality • Diarrhoea related to Clostridium difficile infection • Necessity for a gastrostomy tube • Total number of antibiotic days in the intensive care unit
					Late EN	Day 5	
Sun et al. [21]	RCTs	60	cases with severe acute pancreatitis (SAP)	18-70	Early EN	Within 48 h	• Hospital mortality • ICU stay • MODS • Pancreatic infection
					Late EN	From the 8th day	

The forest plot diagram (Fig. 4) demonstrates that the early initiation of enteral nutrition led to an insignificant change in pneumonia, with a RR of 0.96 and low heterogeneity (ninety-five percent CI, RR = 0.89 [0.71, 1.12]; $I^2 = 47\%$; P = 0.32). M-H, Mantel and Haenszel.

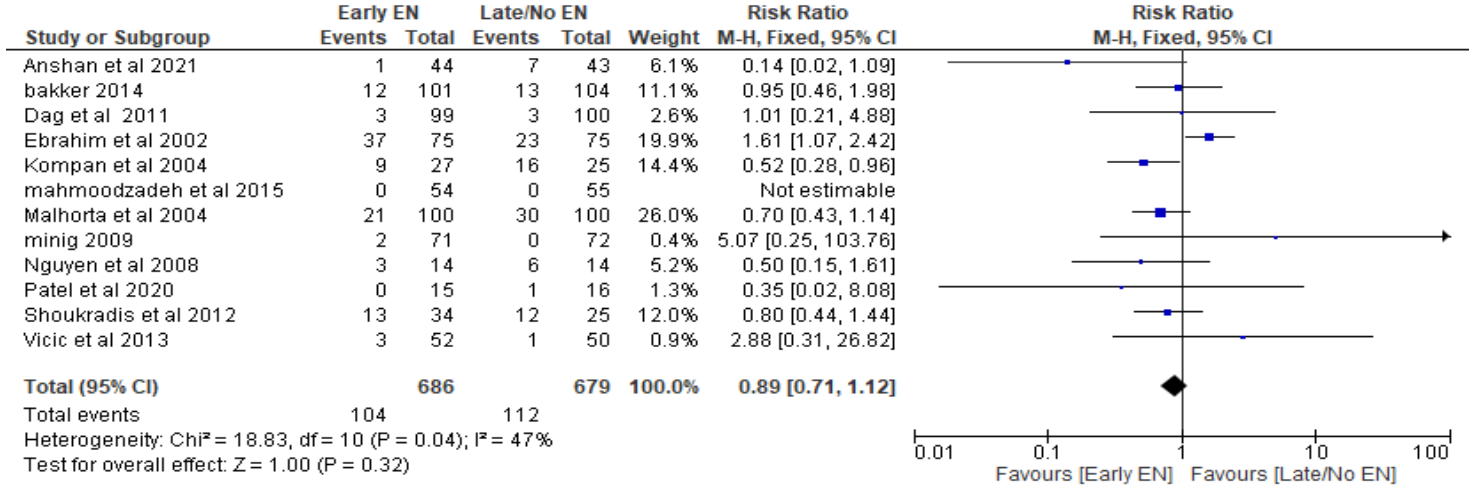

Figure 4: Incidence of pneumonia.

The forest plot diagram (Fig. 5) demonstrates that the early initiation of enteral nutrition led to an insignificant change in mortality, with a RR of 0.80 and low heterogeneity (95% CI, RR = 0.86 [0.70, 1.05]; $I^2 = 0\%$; P = 0.14).

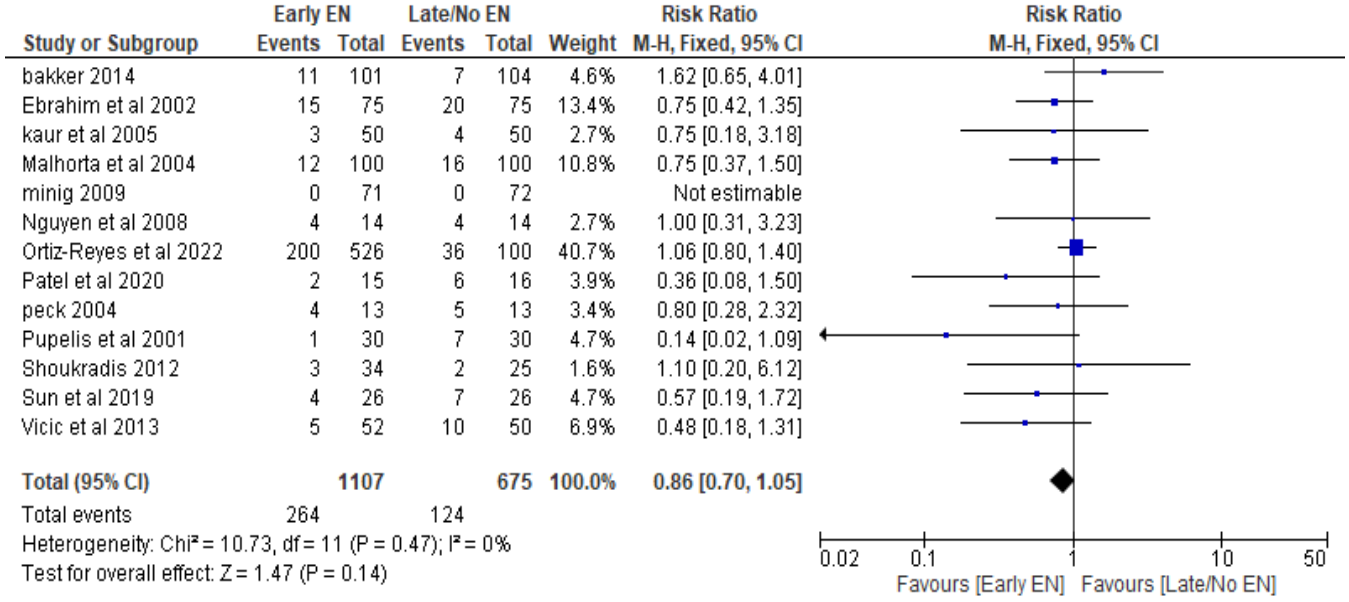

Figure 5: Incidence of Mortality.

The forest plot diagram (Fig. 6) demonstrates that the early initiation led to a significant reduction in intensive care unit length of stay, with a MD of 0.48 and high heterogeneity (Ninety-five percent CI, MD = 0.48 [-0.78, 1.18]; $I^2 = 92\%$; P = 0.002). V, inverse variance; MD, mean difference.

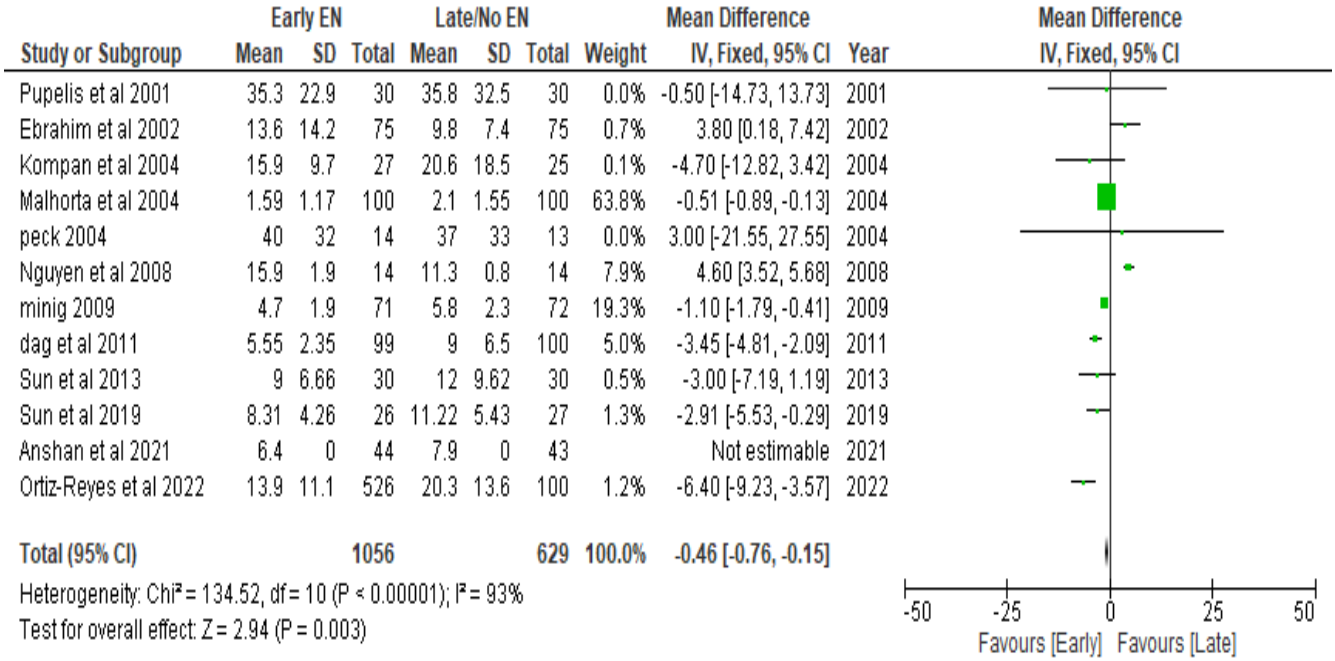

Figure 6: ICU LOS.

The forest plot diagram (Fig. 7) demonstrates that the early initiation led to a significant decrease in ventilator free days, with a MD of -3.72 and high heterogeneity (Ninety-five percent CI, MD = -3.72 [-4.63, -2.81]; $I^2 = 92\%$; P = 0.00001).

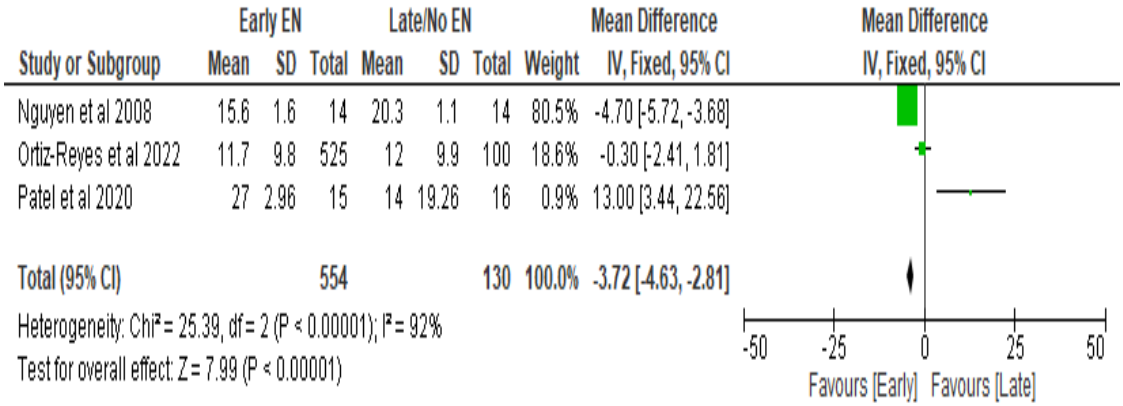

Figure 7: Ventilator free days

The forest plot diagram (Fig. 8) demonstrates that the early initiation of enteral nutrition resulted in an insignificant change in GIT complications, with a RR of 1.16 and high heterogeneity (Ninety-five percent CI, RR = 1.16 [0.88, 1.54]; $I^2 = 62\%$; P = 0.29).

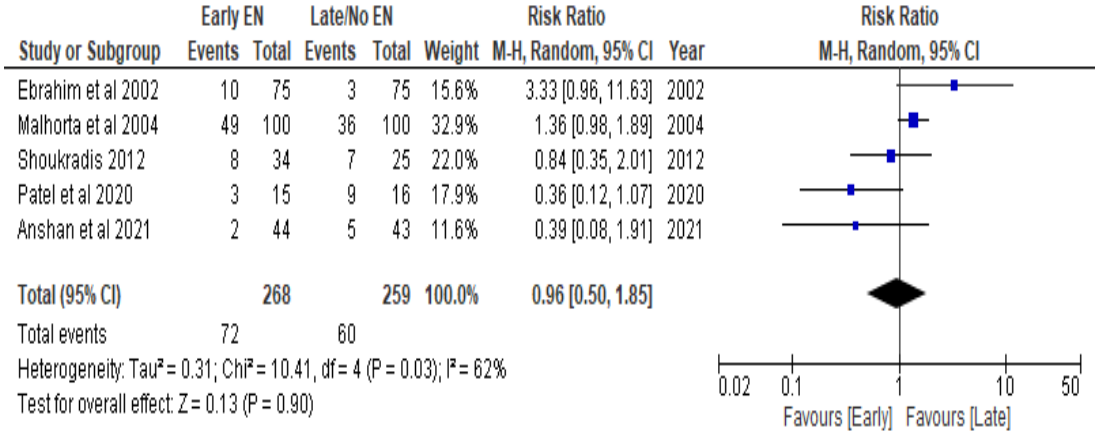

Figure 8: Incidence of GIT complications

The forest plot diagram (Fig. 9) demonstrates that the early initiation led to a significant reduction in MV days, with a mean difference of 1.25 and high heterogeneity (Ninety-five percent CI, MD = 1.25 [0.47, 2.02]; $I^2 = 93\%$; P = 0.002).

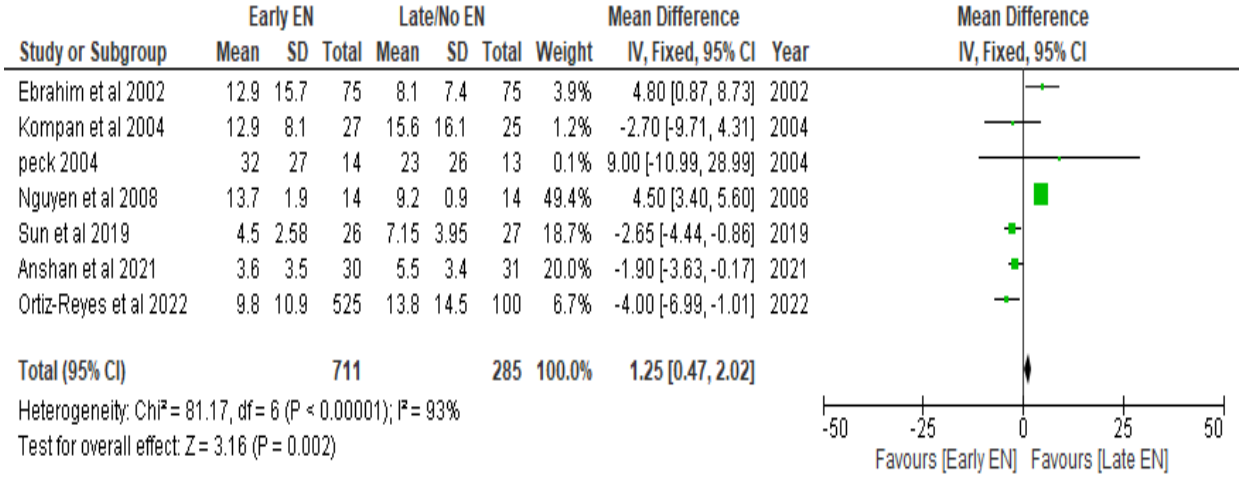

Figure 9: Mechanical ventilation days

The forest plot diagram (Fig. 10) demonstrates that the early initiation of enteral nutrition led to a significant reduction in infectious complications, with a RR of 0.65 and low heterogeneity (95% CI, RR = 0.65 [0.50, 1.76]; $I^2 = 32\%$; P = 0.32).

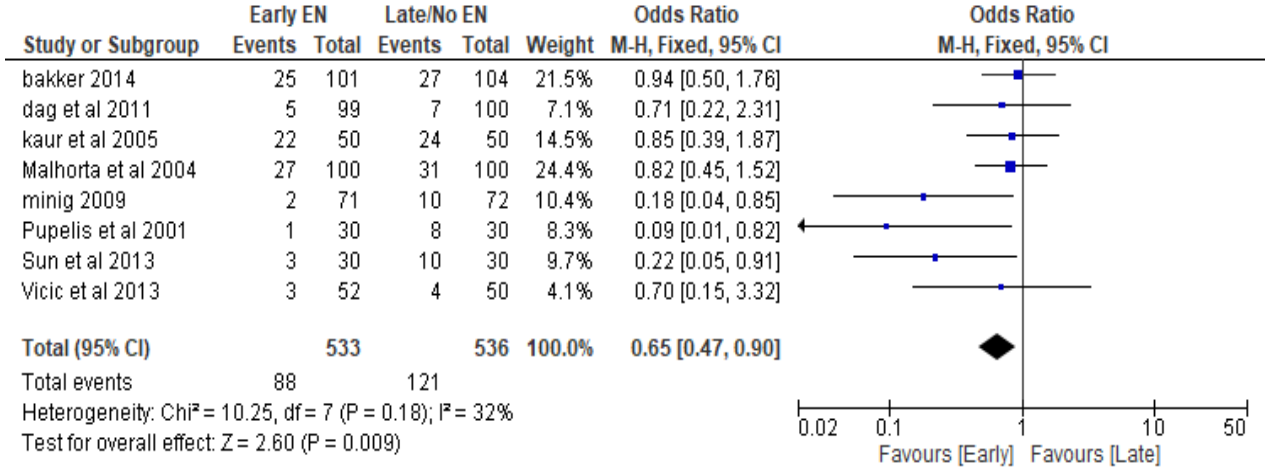

Figure 10: Incidence of infectious complications

The forest plot diagram (Fig. 11) demonstrates that the early initiation of enteral nutrition led to an insignificant change in MOF, with a RR of 0.88 and low heterogeneity (Ninety-five percent CI, RR = 0.88 [0.44, 1.79]; $I^2 = 0\%$; P = 0.73).

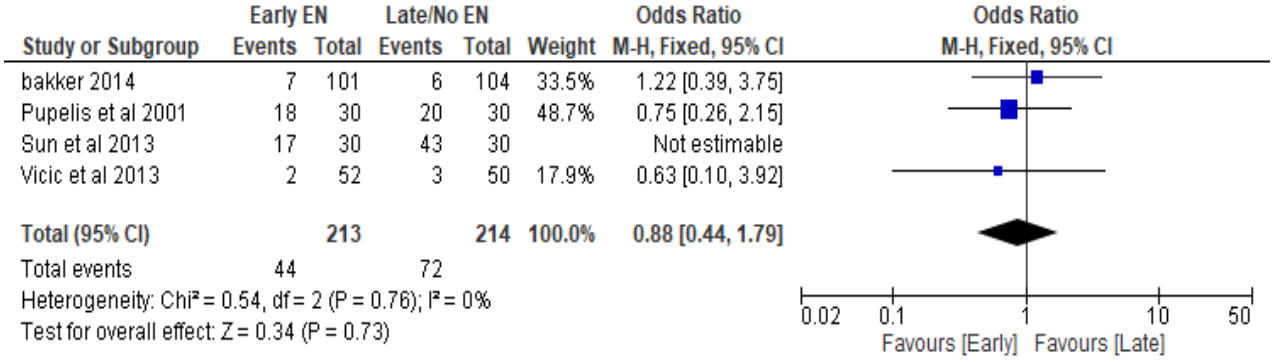

Figure 11: Incidence of MOF

The forest plot diagram (Fig. 12) shows that the early initiation led to a significant decrease in SOFA Score, with a MD of 1.07 and high heterogeneity (ninety-five percent CI, MD = 0.48 [-0.78, 1.18]; $I^2 = 98\%$; P = 0.0001).

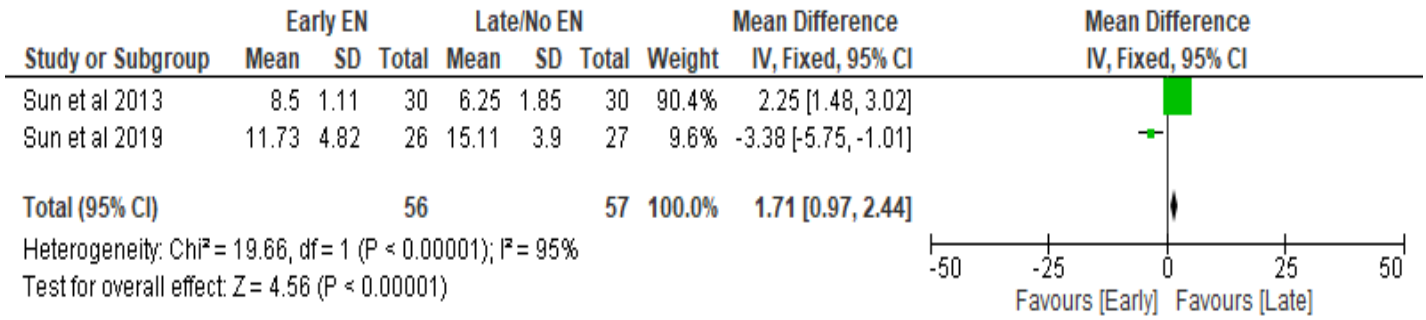

Figure 12: SOFA Score

The forest plot diagram (Fig. 13) shows that the early initiation resulted in a significant decrease in APACHE 2 Score at day 7, with a MD of 1.71 and high heterogeneity (Ninety-five percent CI, MD = 1.71 [0.97, 2.44]; $I^2 = 95\%$; P = 0.00001).

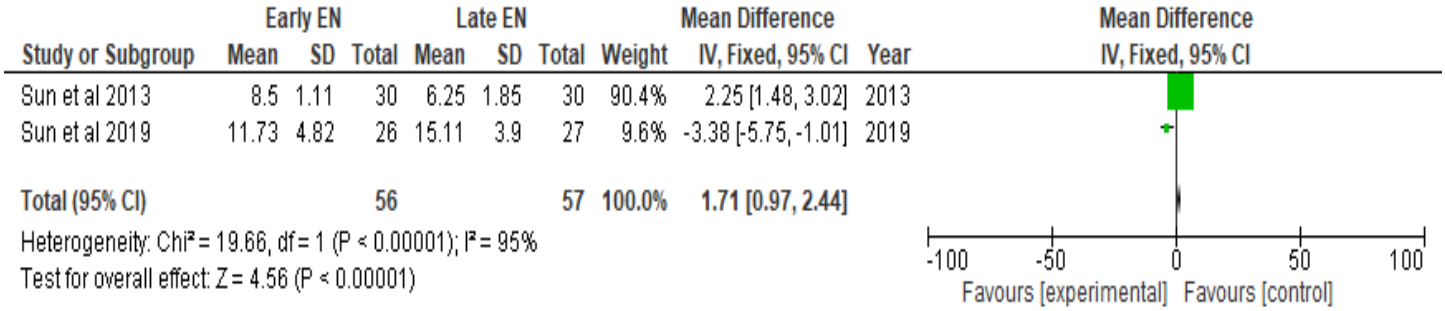

Figure 13: APACHE 2 Score at day 7

The forest plot diagram (Fig. 14) shows that the early initiation led to a significant decrease in antibiotic days, with a MD of 4.81 and high heterogeneity (Ninety-five percent CI, MD = 4.81 [2.21, 7.42]; $I^2 = 95\%$; P = 0.0003).

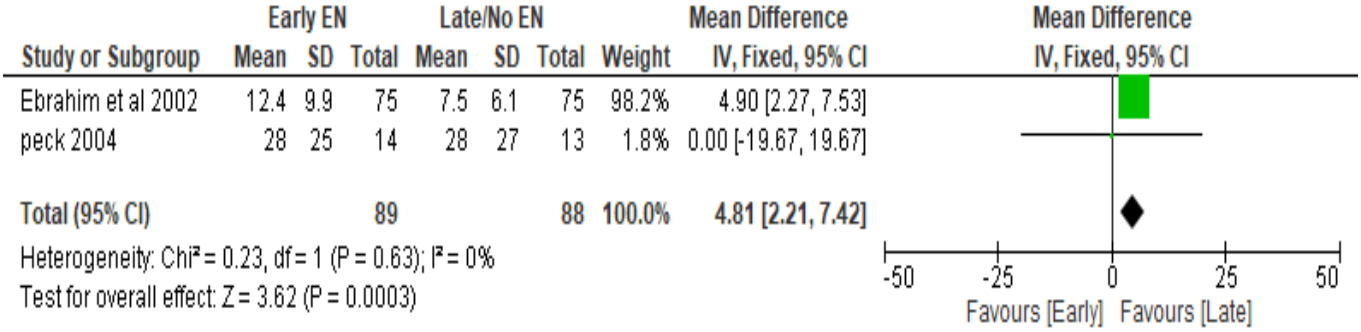

Figure 14: Administration of antibiotic days.

DISCUSSION

This updated meta-analysis examining the impact of early enteral nutrition versus delayed enteral nutrition on clinical outcomes encompassed eighteen randomized controlled trials involving 2,146 critically ill adult cases. It demonstrated that early enteral nutrition administered within forty-eight hours of admission or post-operation significantly decreased the possibility of infectious complications, as well as decreased APACHE II scores, SOFA scores, days on mechanical ventilation, ventilator-free days, and days of antibiotic administration, in comparison to DEN. Nonetheless, there was no benefit in decreasing death, pneumonia, GIT complications, and MOF between the two groups.

Nutritional support is cornerstone in the treatment of critically ill cases, seeking to enhance clinical outcomes by alleviating metabolic disturbances, decreasing infection risks, and promoting recovery. Major guidelines advocate for the commencement of nutritional therapy within twenty-four to forty-eight hours of ICU admission for cases with stable hemodynamic state [22]. Enteral nutrition is frequently regarded as the primary intervention owing to its physiological advantages, such as sustaining gut integrity, protecting immunological function, and decreasing the possibility of infection problems.

When enteral nutrition is not feasible because of gastrointestinal impairment or contraindications, parenteral nutrition serves as an alternative method for nutritional support. Nonetheless, the ideal timing and symptoms for parenteral nutrition continue to be subjects of debate. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines highlight the rapid start of enteral nutrition, accentuating its clinical benefits [23]. Conversely, the 2022 guideline from the American Society for Parenteral and Enteral Nutrition (ASPEN) recognizes that early enteral nutrition or parenteral nutrition might be suitable based on case characteristics, indicating a more adaptable method [24].

The early initiation of EN led to an insignificant change in death, with a RR of 0.80 and low heterogeneity (ninety-five percent confidence interval, RR = 0.86 [0.70, 1.05]; $I^2 = 0\%$; P = 0.14) consistent with meta-analyses **Tian *et al.*** [25], **Padilla *et al.*** [26], **Grillo-Ardila *et al.*** [27], **Xu *et al.*** [28]. Finally, the fifth meta-analysis conducted in accordance with the ESICM clinical practice guidelines revealed that early enteral nutrition didn't significantly decrease death in comparison to delayed nutritional intake

(RR 0.76; ninety-five percent confidence interval 0.52-1.11; P=0.149; I2=0%).

In contrast to **Doig *et al.*** [29], which encompassed six randomized controlled trials involving 234 participants, it has been demonstrated that early enteral nutrition, administered within twenty-four hours of injury or intensive care unit admission, could significantly reduce death rates (odds ratio = 0.34, ninety-five percent confidence interval 0.14-0.85), aligning with the clinical practice guidelines of the European Society of Intensive Care Medicine (ESICM).

The early initiation of EN led to a significant decrease in ventilator free days, with a MD of -3.72 and high heterogeneity (Ninety-five percent confidence interval, MD = -3.72 [-4.63, -2.81]; I 2 = 92%; P = 0.00001) consistent with **Grillo-Ardila *et al.*** [27], which included three RCTs [10,30,31] and eight NRSs [8,12,32,33], which analyzed these results. Low-confidence evidence from the randomized controlled trails and NRSs suggests that cases who receive early enteral support might need fewer days of MV compared to late support (mean difference −2.65; 95% CL, −4.44–0.86; and mean difference−2.94; ninety-five percent confidence interval, −3.64–−2.23, correspondingly).

Early initiation of EN resulted in a non-significant change in MOF, with a risk ratio of 0.88 and low heterogeneity (95% CI, RR = 0.88 [0.44, 1.79]; I 2 = 0%; P = 0.73), but led to a significant decrease in SOFA Score, with a mean difference of 1.07 and high heterogeneity (ninety-five percent confidence interval, MD = 0.48 [-0.78, 1.18]; I 2 = 98%; P = 0.0001), which is consistent with **Grillo-Ardila *et al.*** [27] that showed lower SOFA scores throughout monitoring compared to late support (mean difference−1.64 points; ninety-five percent confidence interval, −2.60–−0.68; and mean difference−1.08 points; ninety-five percent confidence interval, −1.90–−0.26, correspondingly)

The early initiation of EN led to an insignificant change in pneumonia with a RR of 0.96 and low heterogeneity (ninety-five percent confidence interval, RR = 0.89 [0.71, 1.12]; I 2 = 47%; P = 0.32), in contrast to the study of **Doig *et al.*** [29] meta-analysis, which revealed that early enteral nutrition, provided within twenty-four hours of injury or ICU admission, could significantly reduce pneumonia (OR = 0.31, ninety-five percent confidence interval 0.12–0.78), **Zheng *et al.*** [34] showing significantly reduction of pneumonia (risk ratio=0.76, ninety-five percent confidence interval: 0.60-0.97, P=0.03; heterogeneity I2=0% , and **Tian *et al.*** [25] meta-analysis showing significantly reduction of pneumonia (p = 0.052); nevertheless, heterogeneity was present (p = 0.049; I2 = 50%).

The early initiation of EN led to a significant reduction in infectious complications, with a RR of 0.65 and low heterogeneity (Ninety-five percent confidence interval, risk ratio = 0.65 [0.50, 1.76]; I 2 = 32%; P = 0.32), which is consistent with **Zheng *et al.*** [34] showing a significant decrease in the frequency of infectious complications (risk ratio=0.68, ninety-five percent confidence interval: 0.51-0.91, P=0.009; heterogeneity I2=22%)

The early initiation of EN led to a significant reduction in ICU LOS, with a mean difference of 0.48 and high heterogeneity (ninety-five percent confidence interval, MD = 0.48 [-0.78, 1.18]; I 2 = 92%; P = 0.002), which is consistent with **Marik and Zaloga** [35] who included 15 RCTs. The length of stay was significantly shorter in the early nutrition group (p .0012; mean reduction of 2.2 days; ninety-five percent confidence interval, 0.81–3.63 days).

The early initiation of EN led to an insignificant change in GIT complications, with a risk ratio of 1.16 and high heterogeneity (ninety-five percent confidence interval, RR = 1.16 [0.88, 1.54]; I 2 = 62%; P = 0.29).

The early initiation of EN led to a significant decrease in mechanical ventilation days, with a mean difference of 1.25 and high heterogeneity (ninety-five percent confidence interval, MD = 1.25 [0.47, 2.02]; I 2 = 93%; P = 0.002.

The early initiation of EN led to a significant decrease in APACHE 2 Score at day 7, with a MD of 1.71 and high heterogeneity (ninety-five percent confidence interval, MD = 1.71 [0.97, 2.44]; I 2 = 95%; P = 0.00001).

The early initiation of EN led to a significant decrease in antibiotic days, with a mean difference of 4.81 and high heterogeneity (ninety-five percent confidence interval, MD = 4.81 [2.21, 7.42]; I 2 = 95%; P = 0.0003).

While there have been a limited number of investigations on this topic, the patient criteria in our investigation are more inclusive. The present ICU treats a wide range of conditions, such as trauma, transplant cases, burn victims, post-surgical cases, those with acute pancreatitis, traumatic brain injuries, individuals on mechanical ventilation, and those with severe infections, among others. To reduce selection bias, all of these conditions have been involved in our analysis. Additional strengths of our meta-analysis include the large number of enrolled cases and the absence of significant publication bias.

There are numerous limitations in our investigations.

There is clinical heterogeneity among the patient groups included in the trials. Variations exist in the enteral nutrition formula utilized, the initial rate of nutrition, the nutritional targets, and the delayed enteral nutrition groups across the trials. Additionally, we didn't perform a subgroup analysis based on different illnesses.

CONCLUSION

Enteral nutrition therapy must be initiated as early as possible.

Early enteral nutrition within forty-eight hours of admission or post-operation decreased the statistically significant risk of infectious complications, APACHE 2, SOFA score, mechanical ventilation days, ventilator free days, antibiotic days, compared to delayed enteral nutrition. However, there was no benefit in decreasing death, pneumonia, GIT complications, and MOF among both groups.

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