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Role of early enteral nutrition in critical care outcomes: Current evidence and challenges - A review

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Abstract
Early enteral nutrition (EEN) has emerged as a critical component of modern intensive care, supported by robust evidence demonstrating its ability to preserve gut integrity, modulate immune responses, and improve metabolic stability during critical illness. Initiating enteral feeding within the first 24-48 hours of ICU admission has been shown to reduce mortality, decrease infectious complications, shorten ICU and hospital stays, and limit organ dysfunction compared with delayed enteral or parenteral nutrition strategies. Despite its well-documented benefits, the implementation of EEN is often hindered by concerns regarding hemodynamic instability, gastrointestinal intolerance, procedural interruptions, and resource constraints, particularly in high-acuity or low-resource settings. This review synthesizes current evidence on the physiological mechanisms, clinical outcomes, and practical challenges associated with EEN in critically ill adults, emphasizing the need for standardized protocols, improved multidisciplinary coordination, and targeted research in high-risk populations to optimize nutritional support and enhance critical care outcomes.

Keywords: Early enteral nutrition, gastrointestinal intolerance, critical nutrition, human health, infectious complications

Introduction
Critical illness induces profound metabolic and inflammatory disturbances, including hypermetabolism, enhanced protein catabolism, oxidative stress, and immune dysfunction (Preiser *et al*., 2014) [15]. Nutritional therapy is an essential component of supportive care aimed at mitigating these disturbances, reducing complications, and improving survival (Awuchi *et al*., 2020) [4]. Early enteral nutrition (EEN)—defined as enteral feeding initiated within 24-48 hours of ICU admission—has been increasingly endorsed by clinical guidelines due to its physiological benefits, cost-effectiveness, and association with improved outcomes compared to delayed enteral or exclusive parenteral nutrition (Reintam Blaser *et al*., 2017) [18, 19].

Physiological Rationale for Early Enteral Nutrition
1. Maintenance of Gut Integrity
Early enteral nutrition (EEN) plays a vital role in maintaining gut integrity during critical illness, a condition often marked by intestinal hypoperfusion, mucosal atrophy, and compromised barrier function (Schörghuber and Fruhwald, 2018) [20]. When the gastrointestinal tract is deprived of nutrients, the mucosal villi quickly begin to atrophy, weakening the epithelial layer and increasing the risk of bacterial translocation. Initiating EEN within the first 24-48 hours help preserve villous architecture, maintain tight junction integrity, and prevent the passage of bacteria and endotoxins into systemic circulation (Clissold *et al*., 2010) [8]. Moreover, EEN stimulates gut-associated lymphoid tissue (GALT), which is essential for local immune defenses and the production of secretory IgA. By preserving both structural and immunological components of the gut, EEN reduces infection risk and supports overall clinical stability in critically ill patients.

2. Modulation of Immune Response
Feeding the gut early stimulates immune mediators, enhances IgA secretion, and decreases systemic inflammation. It prevents the "leaky gut" phenomenon often associated with sepsis and multi-organ dysfunction (Clissold *et al*., 2010) [8].

3. Improved Metabolic Regulation
Early enteral nutrition (EEN) contributes significantly to improved metabolic regulation in critically ill patients by ensuring a continuous and physiologically balanced supply of nutrients (Reintam Blaser *et al*., 2017) [18, 19]. This steady substrate availability helps maintain better glucose homeostasis, reducing fluctuations that commonly occur during stress-induced hyperglycemia. As a result, patients often require lower doses of insulin to achieve target glucose levels (Mechanick, 2006) [14]. EEN also plays a crucial role in preventing excessive protein catabolism—a hallmark of critical illness—by providing amino acids that support muscle preservation and reduce nitrogen losses. Additionally, early nutrient delivery facilitates the prompt restoration of hepatic acute-phase responses, enabling the liver to synthesize essential proteins involved in immune modulation, coagulation, and tissue repair. Through these mechanisms, EEN supports metabolic stability and improves overall clinical outcomes in the critical care setting.

4. Hemodynamic Stability
Low-volume feeds can be administered safely even in patients on vasopressors when monitored properly (Mechanick, 2006) [14].

Clinical Evidence Supporting Early Enteral Nutrition
1. Mortality Outcomes
Multiple randomized controlled trials (RCTs) and meta-analyses consistently demonstrate that early enteral nutrition (EEN) is associated with significant reductions in mortality among critically ill patients. Initiating enteral feeding within the first 24-48 hours has been shown to lower overall mortality compared with delayed enteral nutrition or parenteral nutrition-dominant strategies, largely due to improved gut integrity, reduced infection risk, and better metabolic stability (McClave *et al*., 2016; Taylor *et al*., 2016) [13, 24, 25]. Studies specifically highlight that patients requiring mechanical ventilation or presenting with sepsis experience notable survival benefits when started on EEN, as early feeding mitigates systemic inflammation and supports immune function (Alhazzani *et al*., 2017; Yang *et al*., 2020) [2, 4, 31]. Compared to delayed feeding, EEN also reduces complications such as bloodstream infections and multiple organ dysfunction, contributing to a measurable survival advantage across heterogeneous critical care populations (Casaer & Van den Berghe, 2014; Singer *et al*., 2019) [7, 21, 22].

2. Reduced Infectious Complications
Early enteral nutrition (EEN) significantly decreases the incidence of infectious complications in critically ill patients by preserving gut integrity and modulating immune function. Studies consistently show that EEN lowers the rates of ventilator-associated pneumonia, central-line-associated bloodstream infections, and surgical site infections, largely because early feeding maintains tight junction integrity, reduces bacterial translocation, and minimizes the reliance on parenteral nutrition, which carries infection risks associated with central venous catheters (McClave *et al*., 2016; Reintam Blaser *et al*., 2017) [13, 18, 19]. By stabilizing the gut barrier and preventing immune dysregulation, EEN plays a central role in interrupting the cycle of systemic inflammation and infection commonly observed in critical illness (Casaer & Van den Berghe, 2014; Singer *et al*., 2019) [7, 21, 22].

3. Shorter ICU and Hospital Length of Stay
Meta-analyses indicate that EEN is associated with a significant reduction in both ICU and overall hospital length of stay. This benefit is attributed to its ability to reduce complications, enhance metabolic stability, and support immune function, which collectively promote faster clinical recovery. By preventing infectious events, stabilizing organ function, and improving nutritional adequacy, EEN accelerates the trajectory toward recovery and reduces the time patients require intensive monitoring and supportive therapies (McClave *et al*., 2016; Singer *et al*., 2019) [13, 21, 22].

4. Reduced Organ Dysfunction
EEN has been shown to reduce the incidence and severity of organ dysfunction in critically ill patients by providing timely metabolic support and mitigating systemic inflammation. Early feeding is linked to lower rates of acute kidney injury, improved hepatic function, and decreased levels of inflammatory markers such as C-reactive protein (CRP) and interleukin-6 (IL-6). Additionally, patients receiving EEN typically require fewer days on mechanical ventilation, owing to better preservation of respiratory muscle mass and reduced inflammatory lung injury. These effects collectively translate into more stable multisystem organ function and improved overall outcomes (Reintam Blaser *et al*., 2020) [17].

5. Impact on Nutritional Adequacy
EEN plays a vital role in achieving nutritional adequacy during critical illness by improving total caloric intake, protein delivery, and nitrogen balance. Early feeding ensures that metabolic demands are met promptly, preventing progressive muscle catabolism and preserving lean body mass. Enhanced protein provision through EEN supports tissue repair, immune function, and overall metabolic resilience. As a result, patients who receive EEN maintain better nutritional status throughout their ICU stay, which is strongly associated with improved survival and recovery (Bear *et al*., 2017) [5].

Sepsis and Septic Shock
In sepsis and septic shock, low-dose EEN has been shown to improve hemodynamic stability, reduce systemic inflammation, and enhance lactate clearance by supporting gut perfusion and preventing barrier dysfunction. Because full enteral feeding may not be well tolerated in the very early stages of septic shock, guidelines recommend trophic or minimal-dose feeding to maintain gut function without overwhelming a compromised circulatory system. This cautious approach allows metabolic and immune benefits of EEN to be achieved while minimizing the risk of intolerance or ischemic complications (Wischmeyer, 2020) [28].

1. Trauma and Traumatic Brain Injury (TBI)
In trauma and TBI patients, EEN is associated with stabilization of intracranial pressure, reduced infection rates, and improved neurological outcomes. Early feeding helps counteract the hypermetabolic and catabolic state induced by trauma while supplying essential substrates for neuronal repair and mitochondrial function. By mitigating oxidative stress and inflammation, EEN supports better cognitive and functional recovery. Evidence shows that trauma patients receiving early enteral feeding experience fewer complications and improved overall outcomes compared with delayed feeding strategies (Taylor *et al*., 1999) [26].

2. Acute Respiratory Distress Syndrome (ARDS)
In ARDS, EEN contributes to improved clinical outcomes by supporting lung repair and reducing the severity of systemic and pulmonary inflammation. Early feeding helps lower oxidative stress, preserve respiratory muscle mass, and reduce the duration of mechanical ventilation. By maintaining metabolic and immunological stability, EEN enhances oxygenation status, reduces ventilator dependence, and supports recovery of damaged alveolar structures, ultimately improving survival and reducing ICU stay (Alrjoob *et al*.., 2023) [3].

3. Post-Surgical and Abdominal Conditions
Enhanced recovery after surgery (ERAS) protocols strongly advocate early enteral feeding for patients undergoing

gastrointestinal, oncological, and transplant surgeries, as long as no contraindications such as bowel ischemia are present (Gustafsson *et al*., 2013) [10]. Early feeding in these settings improves wound healing, reduces infectious complications, and restores gut motility more rapidly. Evidence demonstrates that enteral feeding is both safe and effective in post-surgical patients and contributes to shorter recovery time, improved immune function, and reduced postoperative morbidity (Abela, 2017) [1].

Timing and Dosage: What Constitutes "Early"?

Guidelines from major nutrition societies—including ASPEN, SCCM, and ESPEN—recommend initiating enteral nutrition within 24-48 hours of ICU admission to maximize clinical benefits. Early feeding typically begins with trophic or low-dose nutrition at approximately 10-20 kcal per hour, which is gradually advanced based on gastrointestinal tolerance. Protein intake is targeted at 1.2-2.0 g/kg/day to support tissue repair and metabolic needs, while hypercaloric feeding is avoided during the initial phase to prevent metabolic complications. These evidence-based recommendations underscore the importance of timely feeding to optimize outcomes in critically ill patients (Taylor et a., 2016) [24, 25].

Challenges in Implementing Early Enteral Nutrition

1. Hemodynamic Instability

Hemodynamic instability remains a major concern that often delays the initiation of early enteral nutrition (EEN) in critically ill patients, especially when high-dose vasopressors are required or there is fear of precipitating mesenteric ischemia. Clinicians frequently hesitate to feed patients during shock states due to potential reductions in splanchnic perfusion and the possibility of exacerbating gut hypoxia (Yang *et al*., 2014) [29, 30]. However, emerging evidence indicates that cautious, low-dose trophic feeding can be safely initiated once patients show signs of stabilization, such as decreasing vasopressor requirements and improving perfusion markers. This approach helps maintain gut integrity while mitigating the risk of ischemic complications, highlighting the importance of individualized assessment rather than routine withholding of nutrition.

2. Gastrointestinal Intolerance

Gastrointestinal intolerance is one of the most common barriers to successful EEN delivery, presenting as high gastric residual volumes (GRVs), vomiting or regurgitation, abdominal distention, or diarrhea (Reintam Blaser *et al*., 2021) [16]. These symptoms often trigger feeding interruptions or delays, resulting in inadequate caloric and protein intake. To improve tolerance, strategies such as administering prokinetic agents, using post-pyloric feeding tubes, and adopting more liberal GRV thresholds have been widely recommended (Tatsumi, 2019) [23]. These interventions help enhance gastric motility, reduce aspiration risk, and ensure more consistent nutrient delivery, thus supporting the overall goals of EEN even in patients with compromised gastrointestinal function (Feng *et al*., 2025) [9].

3. Feeding Interruptions

Frequent interruptions are a persistent challenge that limits the effectiveness of EEN, even when feeding is initiated early (Hasenstab and Jadcherla, 2022) [11]. Medical and surgical procedures, airway interventions, imaging studies, and patient positioning requirements often necessitate temporary cessation of enteral feeding. Over time, these cumulative interruptions lead to significant nutritional deficits, preventing patients from meeting their daily caloric and protein needs. Addressing this issue requires coordinated interdisciplinary communication, standardized feeding protocols, and proactive strategies such as catch-up calories or volume-based feeding to minimize the nutritional impact of interruptions (Varghese *et al*., 2022) [21].

4. Resource and Staffing Limitations

Resource and staffing limitations further hinder optimal implementation of EEN, particularly in low-resource or high-acuity settings. A lack of trained dietitians, inconsistent nutrition protocols, insufficient ICU nurse availability for ongoing feeding monitoring (Berger *et al*., 2019) [6], and shortages of essential equipment such as infusion pumps and feeding tubes can all compromise timely and consistent enteral nutrition delivery. These challenges highlight the need for institutional investment in training, standardized clinical pathways, and adequate supply chains to ensure that evidence-based nutritional care can be reliably implemented for all critically ill patients (Losonczy *et al*., 2021) [12].

5. Uncertainty in Special Populations

Despite strong evidence supporting EEN in general critical care populations, uncertainties remain regarding its safety and efficacy in certain high-risk groups. Patients with severe refractory shock requiring high-dose vasopressors, those with severe pancreatitis, or individuals with unstable intra-abdominal pathology may not tolerate early feeding in the same way as other ICU patients. More high-quality clinical trials are needed to establish clear guidelines for these populations, as current recommendations often rely on cautious, individualized decision-making rather than robust evidence. Developing stronger data in these areas would help clinicians balance the benefits of EEN with the potential risks in vulnerable subgroups (Yang *et al*., 2014) [29, 30].

Conclusion

Early enteral nutrition has compelling physiological and clinical benefits, including reduced mortality, fewer complications, improved immune function, and shorter hospital stay. Despite its advantages, barriers such as GI intolerance, hemodynamic instability, and logistical limitations often impede its optimal use. Strengthening clinical protocols, improving staff training, and adopting tailored feeding strategies are essential to enhance nutrition therapy in critical care. Continued research is crucial to refine guidelines and ensure safe implementation across diverse patient populations.

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