Enteral Nutrition Support in Critical Care

Miriam Theilla, RN, PhD[a], Michal Slevin Kish, MD[b], Pierre Singer, MD[c,*]

KEYWORDS

• Enteral nutrition • Intensive care • Timing • Energy-protein • Machine learning • Technologies

KEY POINTS

- Early enteral feeding is the preferred route for critically ill patients unable to eat.
- Progression to target should be guided by physiology and not chronology.
- Indirect calorimetry is the best guide for the energy target.
- Protein should be administered progressively.
- New technologies and artificial intelligence will improve the outcomes of intensive care unit patients even more.

INTRODUCTION

Critical illness triggers complex metabolic disturbances characterized by intense catabolism and inflammation, leading to insulin resistance, significant nutritional deficiencies, and poor clinical outcomes.[1,2] Enteral nutrition (EN) is crucial in intensive care and is strongly encouraged when oral nutrition is not possible or insufficient.[3] However, timing and dose play an increasing role in understanding physiological changes.[4] Early full dose has been clearly declared not recommended,[3] but the best way to progress remains unclear. In addition, a significant gap exists between international guidelines and bedside practice.[5,6] International nutrition organizations, such as the European Society for Clinical Nutrition and Metabolism (ESPEN)[3] and the American Society for Parenteral and Enteral Nutrition (ASPEN)[7,8], advocate for early EN implementation; however, its delivery is often hindered by clinical obstacles such as hemodynamic instability and gastrointestinal (GI) intolerance. These challenges frequently lead to feeding interruptions, resulting in substantial energy and

[a] School of Nursing Sciences, The Academic College of Tel Aviv–Yafo, Tel Aviv–Yafo, Israel; [b] Division of Perioperative, Department of Internal Medicine, Herzliyya Medical Center, Herzliyya, Israel; [c] Dina Recanati Medical School, Reichman University, Intensive Care Unit, Herzliya Medical Center, Herzliya, Israel
* Corresponding author.
E-mail address: pierre.singer@gmail.com

Crit Care Clin ■ (2026) ■–■
https://doi.org/10.1016/j.ccc.2026.09.007 **criticalcare.theclinics.com**
0749-0704/26/© 2026 Elsevier Inc. All rights are reserved, including those for text and data mining, AI training, and similar technologies.

Abbreviations	
AKI	acute kidney injury
ASPEN	American Society for Parenteral and Enteral Nutrition
EN	enteral nutrition
ESPEN	European Society for Clinical Nutrition and Metabolism
GI	gastrointestinal
GLIM	Global Leadership Initiative on Malnutrition
GRV	gastric residual volume
IC	indirect calorimetry
ICU	intensive care unit
PICS	post-intensive care syndrome
REE	resting energy expenditure
RS	refeeding syndrome
SPN	supplemental parenteral nutrition

protein deficits that impede tissue healing and muscle recovery. Issues like aspiration and diarrhea further complicate the delivery of optimal care.[9]

Current literature indicates that nutritional requirements vary throughout the acute, intermediate, and chronic phases of illness. Providing excessive nutrition during the initial acute phase (days 0–3).[10,11] can cause oxidative stress, whereas insufficient intake during the intermediate phase (days 4–14) exacerbates anabolic resistance.[12] An updated review is needed to synthesize the latest evidence on the timing, route, dosage, and composition of nutrition, factors ESPEN identifies as critical for improving intensive care unit (ICU) prognosis. This article offers essential guidance on monitoring and managing complications to ensure evidence-based guidelines are effectively implemented in clinical practice.

DEFINING MALNUTRITION AND NUTRITIONAL TARGET IN THE INTENSIVE CARE UNIT

Malnutrition affects 30% to 60% of ICU patients,[2] necessitating systematic screening upon admission using validated tools such as the Nutritional Risk Score 2002. Following the mandatory screening, the Global Leadership Initiative on Malnutrition (GLIM) criteria have been suggested to diagnose malnutrition and assess its severity.[13] They are used alongside objective assessments[14,15] such as ultrasound-measured muscle thickness, which provides independent prognostic value.[2] A recent study found that among 6065 Japanese ICU patients, 50% had moderate and 35% had severe malnutrition as defined by the GLIM criteria, which predicts increased mortality and prolonged hospitalization among ICU patients.[16] To refine nutritional delivery following initial stabilization (days 4–7), indirect calorimetry (IC) is recommended to establish personalized energy goals. Early IC measurements.[17,18] reveal that many patients are hypometabolic or normometabolic during the acute phase, contrary to historical assumptions of universal hypermetabolism.[19] Because resting energy expenditure (REE) increases progressively from the acute to the chronic phase and often deviates significantly from weight-based predictive equations, the use of IC is essential to prevent complications associated with underfeeding or overfeeding. Maintaining a delicate balance is vital: evidence indicates that providing approximately 70% of measured energy expenditure is associated with the lowest mortality rates, whereas significant deviations—either under or over this threshold—increase the risk of mortality and prolonged mechanical ventilation.[17] Energy deficit has been shown to be associated with increased mortality. A 3 day energy deficit of −3000 kcal is predictive of increased mortality in septic patients (Analysis of the

predictive value of 3 day cumulative energy deficit for 28 day mortality in patients with sepsis and nutritional risk: a retrospective study).[20] Cumulative energy deficit was associated with worse body composition and functional outcomes, including reductions in fat-free mass and physical function scores.[21] If the IC is unavailable, weight-based formulas ranging from 20 to 25 kcal/kg/day in the acute phase to 25 to 30 kcal/kg/day during convalescence offer viable estimates despite significant metabolic variability.[22]

Furthermore, computer-based monitoring systems featuring real-time intake tracking and predictive modeling show increasing promise for optimizing nutritional delivery.[23]

Complications Associated with Underfeeding and Over Nutrition

Complications of underfeeding

Malnutrition is the most prevalent nutritional issue in ICUs.[24,25] It is clinically defined as providing less than 70% of a patient's measured energy requirements.[24,25] The complications are described as follows.

Protein catabolism and muscle loss

Severe illness accelerates protein breakdown and the loss of lean body mass. Approximately 50% of severely injured patients develop malnutrition during hospitalization, which increases the risk of complications 3.4 fold.[26] This negative protein balance impairs skeletal muscle and respiratory function. Critical illness frequently initiates significant protein catabolism and rapid muscle wasting, particularly in the initial weeks of ICU admission. Research indicates a notable daily reduction in skeletal muscle thickness and cross-sectional area, resulting in an early peak loss in weeks 1 to 2 and an association with greater than 4%/day.[27–29] This rapid degeneration of muscle tissue is linked to prolonged hospitalization, the development of frailty, increased mortality, and enduring functional impairments postdischarge.[30–32]

Multiple factors contribute to this muscle breakdown, including systemic inflammation, malnutrition, diminished intramuscular energy, heightened protein degradation, and activation of proteolytic pathways such as the ubiquitin-proteasome system.[33–35] Simultaneously, anabolic resistance emerges, reducing muscle sensitivity to protein and amino acids. Increasing protein intake may prove ineffective and possibly harmful in specific scenarios.[36] The repercussions are not confined to skeletal muscles; the diaphragm also weakens, affecting approximately 60% to 80% of ventilated patients. This weakened condition prolongs mechanical ventilation and complicates weaning. Even after ICU discharge, muscle wasting may endure notwithstanding rehabilitation attempts, resulting in persistent weakness, reduced muscle regenerative capacity, and functional limitations for months following hospitalization.[37] In light of these challenges, the current paradigm underscores the significance of systematic monitoring of muscle mass, provision of personalized nutrition, early initiation of rehabilitation, and administration of targeted anabolic support as integral components of a comprehensive recovery approach.[38]

Respiratory failure and prolonged ventilation

Malnourished patients often struggle with ventilator weaning. Failure to meet protein goals by the fourth day of ICU admission is strongly associated with higher complication rates and longer periods of mechanical ventilation.[39] For optimal survival, reaching energy targets between days 4 and 6 is considered critical.[40]

Impaired healing and weakness

Energy and protein deficiencies hinder collagen synthesis and angiogenesis, leading to delayed surgical wound healing and higher rates of anastomotic leaks.[41] Malnutrition also significantly increases the risk of pressure ulcers, reaching 43.5% compared with 6% in well-nourished patients.[41,42] Furthermore, it is a primary risk factor for Intensive Care Unit Acquired Weakness.[43]

Long-term Outcomes: Early enteral feeding (EN) initiation within the first 3 days of ICU admission among critically ill patients has demonstrated associations with decreased in-hospital mortality rates, reduced lengths of hospital and ICU stays, fewer days requiring mechanical ventilation, and lower health care costs compared with delayed EN initiation.[5] Conversely, delays in the initiation of nutritional support have been linked to prolonged critical illness. Notably, in critically ill patients with abdominal infections, the early implementation of EN (within 48 hours) was correlated with lower 28 day mortality rates (19.0% vs 35.3%), shorter durations of ICU stays (10.8 $\pm$ 4.2 vs 13.6 $\pm$ 5.1 days), and expedited infection control measures in comparison to delayed initiation.[44] The implications of extended ICU stay extend beyond the duration of hospitalization. Patients remaining in the ICU for 14 days or more exhibited higher rates of ICU and hospital mortality (18.3% vs 15.7% and 31.2% vs 22.8%, respectively) and an escalated risk of mortality during a 2 year follow-up period (adjusted Cox proportional hazard ratio: 1.65, $P<.001$).[45] In the context of COVID-19 patients hospitalized in the ICU who received full EN, the median ICU stay was 28.0 days, the hospital stay averaged 31.0 days, and the 30 day mortality rate postdischarge reached 47%, highlighting the persistent mortality risk in the postdischarge phase.[46] Beyond immediate risks such as bloodstream infections, malnutrition contributes to "post-ICU syndrome," characterized by persistent cognitive and physical impairments that diminish long-term quality of life.[42,47] Post-intensive care syndrome (PICS) is a complex condition marked by a deterioration in the physical, cognitive, and psychological well-being of individuals following their discharge from the ICU. Common symptoms encompass enduring weakness, depressive symptoms, anxiety, and post-traumatic stress disorder, all of which exert a substantial impact on the overall quality of life for those affected.[48] This decline in health, recognized as PICS, carries personal and socioeconomic implications not only for patients themselves but also for their families, caregivers, and society at large.[49] A considerable portion of survivors of surgical intensive care may develop PICS within 6 months of their discharge, with prevalence rates of 55.4% at 3 months and 27.7% at 6 months. Studies have identified the duration of stay in the ICU as an independent risk factor for the onset of PICS.[50] Research suggests that a substantial percentage, ranging from 25% to 60% of ICU survivors experience PICS, presenting with symptoms such as muscle weakness, cognitive impairment, depressive symptoms, and post-traumatic stress disorder.[51]

Complications of Overnutrition (Overfeeding)

Overfeeding occurs when caloric delivery exceeds metabolic demand, triggering a cascade of physiological disorders.

Metabolic and glycemic distress

Hyperglycemia (>180 mg/dL) is a common complication when delivered calories exceed REE, often leading to increased mortality and longer ICU stays.[17] Furthermore, excess substrates in the presence of mitochondrial dysfunction generate free radicals (oxidative stress) rather than ATP, increasing the body's metabolic workload during recovery.[52]

Hepatic and gastrointestinal dysfunction

Prolonged overfeeding can lead to **hepatic steatosis (fatty liver)** and cholestasis in roughly 27.8% of patients, impairing the liver's ability to detoxify and produce essential proteins.[53]

Cellular and respiratory impact

A critical consequence of overfeeding, particularly of protein, is the suppression of autophagy.[54] This cellular "cleaning" process is essential for removing damaged organelles; its suppression impairs natural organ protection in the kidneys, lungs, and liver.[54] Additionally, overnutrition (over 110% of target) is an independent predictor of acquired infections, while excess carbohydrates increase CO_2 production, elevating ventilatory demand and complicating weaning.[52,55]

Refeeding syndrome (RS) is a life-threatening complication occurring during the transition from a starved state to rapid nutritional intake, characterized by dangerous shifts in electrolytes-specifically hypophosphatemia, hypokalemia, and hypomagnesemia-and fluid overload.[56] Hypophosphatemia is the hallmark of RS, impairing tissue oxygenation and weakening respiratory muscles.[57] High-risk patients require cautious, gradual feeding (5–10 kcal/kg/day) alongside rigorous monitoring.[58] The ESPEN GUIDELINE.[3] recommends avoiding full enteral feeding in the early period to prevent severe hypophosphatemia and RS.

CURRENT INTERNATIONAL GUIDELINES FOR ENTERAL NUTRITION IN THE INTENSIVE CARE UNIT

Timing of Enteral Nutrition Initiation

Current guidelines from the ESPEN and the ASPEN, updated through 2025, uniformly recommend initiating EN within 48 hours of ICU admission (**Table 1**).[3,59] This preferred route for critically ill patients is supported by evidence demonstrating that low-dose EN is both safe and effective, even for those receiving low to moderate vasopressor support.[18,60] However, enteral feeding should be started when the patient is hemodynamically and respiratory-stabilized and does not require increasing vasopressor doses (U). Such early initiation-typically within 24 to 48 hours-is consistently associated with improved clinical outcomes, including shorter durations of mechanical ventilation and decreased ICU stays,[61] as well as decreased mortality in some studies. Notably, a large observational study of mechanically ventilated patients identified a correlation between early EN and lower in-hospital mortality (OR 0.88), increased rates of discharge to home, and reduced health care costs.[5] Furthermore, meta-analytic data indicate that early EN significantly reduces mortality in septic patients (OR 0.59) across various severity levels.[62]

Despite these broad benefits, the advantages of early timing are contingent upon hemodynamic stability and disease severity. In scenarios involving profound hemodynamic instability, such as cyclic shock requiring high-dose vasopressors, standard-dose early EN has failed to improve outcomes and has been linked to increased GI complications in the NUTRIREA-2 and NUTRIREA-3 trials.[63]

This clinical paradox is most likely attributed to the intricate interplay among systemic hemodynamics, nutrient intake, and intestinal motility during periods of intense physiological stress.

ROUTE OF FEEDING: GASTRIC VERSUS POST-PYLORIC

For initiating EN in critically ill patients, gastric feeding via a nasogastric (NG) tube remains the preferred route due to its relative simplicity, speed of insertion, and

ARTICLE IN PRESS

Table 1
Decision-making in enteral feeding strategies

Technologies	GI Intolerance	Energy/Protein	Strategy	Route	Timing	Choice
Machine Learning	Prokinetics/monitor	Increase chronologically	continuous	Gastric	After 24–48 h	**First**
Feeding platforms	Supplemental parenteral nutrition	Increase according to physiology	Intermittent	Postpyloric	Not if hemodynamic instability	**Alternative**

Abbreviation: GI, gastrointestinal.

physiological advantages in stimulating antero-pyloric function and nutrient absorption.[3] While percutaneous endoscopic gastrostomy is generally reserved for patients requiring prolonged EN support exceeding 4 weeks to facilitate mobility and reduce the risk of sinusitis, post-pyloric feeding is indicated when gastric dysfunction or persistent feed intolerance—evidenced by high residual volumes despite prokinetic therapy—is documented.[59,64] Evidence from randomized trials suggests that post-pyloric access, such as nasojejunal or direct jejunal routes, effectively reduces the risks of vomiting, aspiration, and pneumonia compared with gastric feeding.[18] However, the clinical implementation of post-pyloric access is often constrained by its technical complexity, as it requires specialized expertise and equipment. These requirements may lead to delays in initiating nutrition or to higher rates of tube failure and reinsertion, depending on the availability of local clinical resources.[14,64]

Feeding Strategies: Continuous versus Intermittent

Although continuous feeding over 24 hours remains the standard ICU practice, emerging evidence suggests that cyclic feeding (10–16 hours daily) may offer metabolic advantages, such as enhanced autophagy and ketogenesis.[65] The ongoing DC-SCENIC trial is currently investigating whether these fasting-mimicking cycles can reduce organ failure in mechanically ventilated patients.[65] A recent meta-analysis compared intermittent to continuous enteral feeding.[66] Intermittent versus continuous EN in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. Intermittent feeding was associated with a significantly higher incidence of diarrhea (RR 1.56, 95% CI 1.23–1.98, I 2 = 19%) and abdominal distension (RR 1.68, 95% CI 1.10–2.57, I 2 = 18%), mainly in ventilated patients.[66]

Energy Prescription and Calorie Goals

Current evidence does not support providing full energy requirements during the early stages of critical illness. Studies such as EPANIC and NUTRIREA suggest that premature initiation of full nutritional support may increase the risk of infections, prolonged organ dysfunction, and worse clinical outcomes.[52] Therefore, guidelines from the ESPEN and the ASPEN recommend starting with a hypocaloric energy intake, around 60% to 70% of estimated needs (~15–20 kcal/kg/day). They advise against reaching full energy goals before the fourth to seventh day of critical illness.[18,22,59,67] IC is the preferred method for estimating energy needs. When unavailable, body weight-based equations can be used, but their accuracy may be limited due to metabolic differences among patients.[18,19,22] For obese patients, using adjusted body weight provides a more accurate estimate of energy expenditure.[68] The ideal timing to reach full energy goals may be between days 4 and 6 after admission to the ICU, as earlier or later achievement has been associated with adverse clinical outcomes and increased mortality rates[53] (**Fig. 1**A).

Regarding volume, initiating trophic feeding (10–20 mL/hour) during the early acute phase helps maintain GI mucosal integrity and immunologic function while minimizing metabolic stress.[52] Current evidence supports a gradual progression to nutritional targets over 5 to 7 days, rather than aggressive advancement within the first 48 hours, to ensure stage-appropriate support.[52] A recent retrospective study developed and preliminarily validated a physiology-based, trajectory-driven model to detect the metabolic transition window in 2350 critically ill patients. They compared patients who received full enteral feeding before or after the metabolic transition, based on improvements in insulin resistance, decreases in vasopressor requirements, lactate, and inflammation (White blood cell count, CRP, neutrophils), and stabilization of albumin.

Higher calorie delivery before transition was associated with an increase in 90 day mortality (OR 1.25, 95% CI 1.01–1.55), with a dose–response pattern. This increase in calorie delivery after the metabolic transition was associated with improved outcomes, supporting nutrition strategies aligned with physiological recovery rather than fixed calendar days (Fig. 1B).

Protein Dosage and Nitrogen Balance

Patients in critical condition often experience a significant negative nitrogen balance due to accelerated protein breakdown, reaching up to 900 g of muscle mass per day—3 times higher than in healthy individuals.[67] Despite muscle loss, ESPEN guidelines recommend a gradual approach to protein intake based on the disease stage and the patient's metabolism. Initially, protein intake can be modest, up to 0.8 g/kg/day, increasing to 1.3 g/kg/day during stable periods and rehabilitation to maintain muscle mass and support recovery.[67]

Given the anabolic resistance in critical illness, where amino acid utilization is limited, early high protein doses may not improve outcomes and could add metabolic stress.[59,68,69] New research supports restricted protein intake during the acute phase, with gradual increases as the patient stabilizes.[59] As recovery progresses, protein targets of 1.5 to 2.0 g/kg/day may be considered for some patients, but high-protein diets ($\geq$2.2 g/kg/day) have not shown mortality benefits and could be harmful, especially for patients with acute kidney injury (AKI) or critical illness due to catabolic byproducts accumulation and autophagy suppression.[1] Current evidence does not support the routine administration of high-dose protein to critically ill patients. The EFFORT trial, which involved over 1300 patients, found that providing 2.2 g protein/kg/day did not improve mortality or hospital discharge rates compared with 1.2 g/kg/day. In fact, it might even be harmful to patients with AKI and severe organ failure.[70] Subsequent analyses revealed that in AKI patients, high protein intake was associated with higher mortality and slower recovery, likely due to increased urea production and metabolic strain.[5,71] Elevated urea levels resulting from catabolism could be the underlying mechanism for adverse effects. These results were further supported by the PRECISe trial, which indicated a high risk of harm, with no improvement in quality of life or

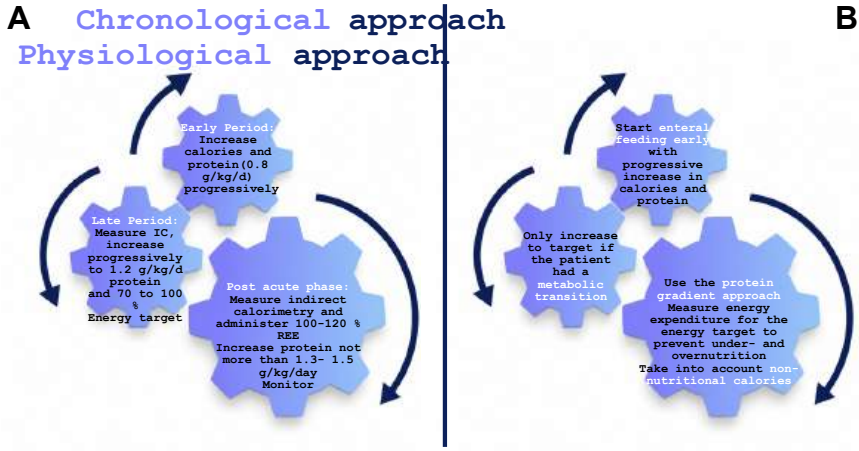


Fig. 1. (*A*) Chronological roadmap for optimizing EN during critical illness. (*B*) Precision clinical nutrition: physiologically guided enteral feeding strategies in critically ill patients. *Abbreviation:* EN, enteral nutrition.

survival observed with high protein intake.[72] Recent systematic reviews and meta-analyses do not recommend high protein administration to critically ill patients. A review of 19 RCTs and 1731 patients showed no advantage in terms of mortality or other clinical outcomes with higher protein intake compared with lower intake.[73] These conclusions were confirmed in an updated meta-analysis of 23 studies and 3303 patients, demonstrating that increasing protein intake does not improve clinical outcomes or survival. However, patients with AKI were found to face a higher mortality risk.[74] Similarly, another meta-analysis of 14 RCTs and 6553 patients found no impact of high protein on mortality in the general population but indicated a significant increase in mortality among AKI patients.[75] These findings suggest that high protein administration does not provide clear clinical benefits in critically ill patients and may even be harmful in specific subgroups, particularly those with AKI. Therefore, the current approach emphasizes tailoring protein intake to metabolic status and renal function, rather than universally implementing high-protein strategies. A balanced approach suggests that a moderate protein intake of 0.8 to 1.2 g/kg/day during the acute phase is preferable, as very low intake levels (<0.6 g/kg/day) are associated with muscle loss and weakness in ICU patients.[52] Patients with AKI who do not require continuous renal replacement therapy require careful adjustment of protein intake based on their clinical condition.[60]

Gastrointestinal Intolerance: Manifestations and Comprehensive Management of Enteral Feeding

EN is a cornerstone of intensive care management, yet GI intolerance frequently limits its successful delivery. In critically ill patients, feeding intolerance is characterized by an inability to meet nutritional targets—such as reaching 20 kcal/kg/day within 72 hours—due to adverse GI events. Clinical findings of GI intolerance span a broad spectrum of symptoms. The most common include increased gastric residual volumes (GRVs), vomiting, abdominal distension, diarrhea, and constipation.[76] GI intolerance is associated with increased morbidity and mortality.[9] Recently, Wang and colleagues[77] suggested that older patients suffering from a primary diagnosis of pulmonary disease, with a normal BMI and a SOFA less than 8, were more susceptible to adverse effects of GI intolerance. Enteral feeding intolerance is associated with increased morbidity and mortality.[9] Our team developed a machine learning approach to predict the occurrence of enteral feeding intolerance based on features such as large gastric residuals (greater than 250 mL) and inability to reach 70% of the energy target at day 3.[78,79]

In more severe clinical scenarios, GI dysmotility may progress to acute colonic pseudo-obstruction or bowel ischemia. Therefore, critically ill patients receiving EN require careful monitoring for feeding intolerance and early signs of gut ischemia, such as abdominal distention, increasing GRVs, and decreased stool passage.[18]

Supplemental Parenteral Nutrition in the Critically Ill

When EN fails to meet caloric targets, supplemental parenteral nutrition (SPN) serves as an effective strategy to bridge the nutritional deficit without abandoning the enteral route.[80] While both ASPEN and ESPEN guidelines endorse SPN as a valid therapeutic option for critically ill patients, its optimal timing remains a subject of ongoing debate.[3]

During the acute early phase of critical illness (days 1–2), endogenous glucose production cannot be suppressed by exogenous nutritional support, significantly elevating the risk of overfeeding. Consequently, SPN is generally not recommended during this window.[81] However, initiating SPN between days 3 and 7 is considered clinically appropriate for most patients experiencing inadequate EN delivery.[80]

Evidence favoring the earlier introduction of SPN primarily derives from surgical cohorts: in a multicenter randomized clinical trial involving high-nutritional-risk patients undergoing major abdominal surgery with poor EN tolerance, early SPN (initiated on postoperative day 3) resulted in significantly fewer nosocomial infections compared with late SPN (initiated on day 8) (8.7% vs 18.4%; risk difference 9.7%; 95% CI, 0.9%–18.5%; $P = .04$), alongside a reduction in therapeutic antibiotic days.[82]

These findings suggest that once the acute surgical stress response subsides, the early optimization of energy delivery via SPN is both safe and highly beneficial for nutritionally at-risk patients.

A recent meta-analysis further corroborates the clinical utility of targeted SPN, demonstrating reduced rates of nosocomial infections and ICU mortality, alongside improved nutritional intake and encouraging trends toward functional recovery.[83] Despite robust evidence, SPN remains markedly underutilized in clinical practice, accounting for only approximately 10% of nutrition days across European ICUs. This hesitation largely stems from concerns about overfeeding, limited access to IC, insufficient institutional protocols, and inadequate clinician training.[80] Therefore, utilizing IC for metabolic monitoring is strongly advocated when initiating SPN, as it mitigates the risk of overfeeding and provides necessary clinical reassurance.[60]

NEW TECHNOLOGIES TO IMPROVE THE EFFICACY OF ENTERAL FEEDING

In addition to the shift from chronological to physiological progression of enteral feeding administration,[84] recent approaches have been proposed to improve enteral feeding. In the field of artificial intelligence, our group has presented several machine-learning-based studies demonstrating the ability of algorithms to predict enteral feeding intolerance and prevent complications related to inadequate continuation of this route.[78,79]

The use of these algorithms must be validated across multiple centers. New technologies able to detect gastric reflux using esophageal sensors, stop the feeding if massive reflux occurs, drain the gastric content, but also compensate for the feeding deficit when the GI tract tolerates enteral feeding to reach a near to 100% feeding efficacy have been developed.[79,84,85] This approach evaluates not the gastric contents but the stomach's tolerance to continuous enteral feeding. The integration of a CO_2 consumption analyzer into the platform also enables a better definition of the energy target than using predictive equations.

COMPREHENSIVE MANAGEMENT AND TREATMENT STRATEGIES

Management of Enteral Nutrition Intolerance in Critically Ill Patients

The management of EN intolerance in critically ill patients requires a comprehensive approach that includes adjusting feeding doses, selecting appropriate formulas, using pharmacologic and non-pharmacological interventions, and preventing complications such as aspiration and RS.

Adjustment of Feeding Dose and Rate

Current literature indicates that the early initiation of EN at a reduced dose, with gradual increments based on the patient's metabolic status, is advantageous. Studies have shown that providing a lower caloric intake during the initial days of intensive care results in fewer GI complications and faster recovery compared with immediate full feeding, which may have detrimental effects.[76]

Consequently, enteral feeding can begin within 48 hours of admission to the ICU, even for patients receiving low-to moderate-dose vasopressors, without the need to

meet full energy requirements until the fourth to seventh day of hospitalization.[8] Early introduction of low-dose enteral feeding has been associated with reduced mortality rates in patients receiving low to moderate doses of norepinephrine, while high-calorie feeding has been correlated with an increased risk.

Complications such as emesis and intestinal ischemia may arise in patients undergoing EN.[86] For individuals at elevated risk of aspiration or gastric intolerance, continuous feeding is preferable to intermittent feeding, as it reduces the burden on the GI system and lowers the likelihood of diarrhea. The adoption of a volume-based feeding regimen not only accommodates temporary interruptions in feeding but also promotes adherence to nutritional goals.[87]

Adjusting Feeding Protocols and Formulas

In cases of persistent gastric intolerance or a notable risk of aspiration, transitioning to post-pyloric (duodenal or jejunal) feeding is recommended. Studies indicate that this shift can effectively mitigate complications associated with delayed gastric emptying[88]

Moreover, the use of high-energy, protein-peptide-based formulas may improve GI tolerance and facilitate the achievement of energy and protein targets in complex patients.[89] These specialized formulas are associated with enhanced nutrient absorption, maintenance of a positive nitrogen balance, reduced incidence of diarrhea, and preservation of intestinal mucosal integrity when compared with formulas based on whole protein or free amino acids.[90]

Management of Diarrhea and Gastrointestinal Intolerance

The occurrence of diarrhea should not immediately lead to the cessation of EN. It is essential to first explore potential causes such as infections, medications, or products containing sorbitol. Once other causes are ruled out, transitioning to continuous feeding or adjusting the feeding formula becomes a valid consideration.[91]

While immunomodulatory nutrition was valued, recent research underscores limited benefits and potential risks associated with specific formulations containing arginine and glutamine. Consequently, there is a shift toward personalized nutritional approaches rather than standardized recommendations for immunomodulatory supplements.[92] The 2024 Japanese Intensive Care Guidelines reflect this trend by cautiously endorsing the use of omega-3 and probiotics.[93]

Prokinetic Therapy

Prokinetic therapy plays a pivotal role in the management of impaired gastric emptying. A meta-analysis by Lewis and colleagues (2016)[94] has indicated that prokinetic drugs significantly reduce feed intolerance, decrease the incidence of high GRVs, and improve the success rate of post-pyloric feeding tube insertion.

Recent research suggests that proclopramide may be more effective than metoclopramide at reducing GRVs and improving the success of enteral feeding, with a favorable safety profile.[95] Additionally, erythromycin has been shown to promote gastric emptying and is sometimes combined with metoclopramide to achieve a synergistic effect.[96]

Reflux and Aspiration Prevention

One of the primary goals of medical nutritional therapy is to mitigate the risk of aspiration of gastric contents. Recommended strategies include elevating the head of the bed to 30° to 45°, transitioning to continuous feeding, and using prokinetic agents to improve GI motility.[91]

Endotracheal cuff pressure management

Maintaining appropriate cuff pressure is essential in ventilated patients to prevent aspiration and ventilator-associated pneumonia. Automated cuff pressure management, in conjunction with subglottic drainage, has been associated with a significant reduction in pneumonia rates compared with manual management.[97] The recommended range for cuff pressure is 25 to 30 cm H_2O.

Gastric Residual Volume Monitoring

The clinical utility of routine monitoring of GRV has been a subject of debate in recent years. A Cochrane review has indicated that the evidence does not strongly support improved clinical outcomes with this monitoring.[98] Moreover, following the cessation of routine GRV monitoring, there was an increase in the proportion of patients achieving feeding goals, a decrease in GI intolerance, and a reduced need for prokinetic therapy.[99] Consequently, it is now generally accepted that feeding should not be withheld for residual volumes less than 500 mL in the absence of other signs of intolerance.

Prevention of Refeeding Syndrome

When initiating enteral feeding, evaluating the risk of RS is crucial, particularly in patients with prolonged malnutrition. This syndrome is characterized by hypophosphatemia, hypokalemia, hypomagnesemia, and thiamine deficiency. Prevention strategies include commencing a low-calorie diet, gradual advancement, close monitoring of electrolytes, and administering thiamine prophylactically, in addition to potassium, magnesium, and phosphorus supplementation as needed.[100]

SUMMARY

The ESPEN and ASPEN guidelines are key to managing nutrition in critically ill patients, emphasizing core principles with a strong consensus. Both recommend early enteral feeding, personalized therapy, and monitoring of energy and protein intake.[3,8,14,18] While ESPEN provides detailed recommendations for energy and protein progression, ASPEN adopts a more cautious approach, acknowledging uncertainties in optimal doses and the significance of clinical judgment.[8,14] Given the complexity of critical illness, personalized strategies are essential, as a one-size-fits-all approach may not be suitable for all patients. Both organizations advocate for the use of IC to accurately assess energy needs while recognizing its limited availability in ICUs.[3,22] Despite the availability of evidence-based guidelines, a gap persists between recommendations and actual practice, primarily due to barriers such as hemodynamic instability, infrastructure constraints, and staff awareness.[101] Nonetheless, studies indicate that adherence to ESPEN and ASPEN protocols results in fewer complications, shorter ventilation periods, and reduced ICU stays.[102] In conclusion, although ESPEN and ASPEN may differ in certain respects, both emphasize the importance of transitioning to personalized nutrition based on disease stage, metabolic status, and clinical response. This shift underscores that timing and personalization are equally crucial in achieving nutritional goals.

CLINICS CARE POINTS

To optimize clinical outcomes, nutritional strategies must be tailored to the patient's evolving clinical state.

- Stage-Adapted Approach: Interventions should be adjusted based on the patient's current disease progression and risk factors,
- Utilization of IC: IC remains the gold standard for preventing the detrimental effects of both underfeeding and overfeeding
- Protein Titration: Experts recommend a "protein gradient" approach: starting with a conservative dose (up to 0.8 g/kg) and gradually increasing to above 1.2 g/kg only during the recovery phase
- Accounting for "Hidden" Calories: Total energy intake must include non-nutritional calories, such as those from propofol or dextrose infusions, to prevent unintentional overfeeding.

DISCLOSURES

M. Theilla and M.S. Kish have nothing to declare. P. Singer received speaker fees from Baxter, B Braun, Nestle, Fresenius Kabi, Nutricia, and institutional grants from Baxter, United States, Nestlé, Switzerland, Fresenius Kabi, Germany, and ART MEDICAL. PS is also a member of the advisory board of ART MEDICAL.

REFERENCES

1. Mottale R, Dupuis C, Szklarzewska S, et al. The metabolic response to stress in critical illness: updated review on the pathophysiological mechanisms, consequences, and therapeutic implications. Ann Intensive Care 2025;15:174.
2. Stoian M, Andone A, Bândilă SR, et al. Personalized nutrition strategies for patients in the intensive care unit: a narrative review on the future of critical care nutrition. Nutrients 2025;17(10):1659.
3.. Singer P, Blaser AR, Berger MM, et al. ESPEN practical and partially revised guideline: clinical nutrition in the intensive care unit. Clin Nutr 2023;42(9): 1671–89.
4. Berger MM, Blaser AR, Raphaeli O, et al. Early feeding in critical care: where are we now? Crit Care Clin 2025;41(2):213–31.
5. Haines K, Ohnuma T, Grisel B, et al. Early enteral nutrition is associated with improved outcomes in critically ill mechanically ventilated medical and surgical patients. Clin Nutr ESPEN 2023;57:311–7.
6. Thibault R, Bear DE, Fischer A, et al. Implementation of the ESPEN guideline on clinical nutrition in the intensive care unit: it is time to move forward. Clin Nutr ESPEN 2023;57:318–30.
7. Burnette A, Allen C. Nutrition considerations in the intensive care unit. AACN Adv Crit Care 2024;35(3):209–14.
8. Preiser JC, Arabi YM, Berger MM, et al. A guide to enteral nutrition in intensive care units: 10 expert tips for daily practice. Crit Care 2021;25(1):424.
9. Heyland DK, Ortiz L, Day AG. Prevalence, risk factors, and clinical consequence of enteral feeding intolerance in the mechanically ventilated critically ill: an analysis of a multicenter, multiyear database. Crit Care Med 2021;49(1): 49–59.
10. Moonen HPFX, van Zanten ARH. Mitochondrial dysfunction in critical illness during acute metabolic stress and convalescence: consequences for nutrition therapy. Curr Opin Crit Care 2020;26(4):346–54.
11. Wang Y, Li Y, Li N, et al. Protective nutrition strategy in the acute phase of critical illness: why, what and how to protect. Front Nutr 2025;12:1555311. https://doi.org/10.3389/fnut.2025.1555311.

12. Stoppe C, Lee ZY, Arabi YM. Nutritional therapy and a stepwise approach in critical illness: aligning provision with metabolic phases. Curr Opin Clin Nutr Metab Care 2026;29(2):184–92.
13. Fukushima N, Masuda T, Tsuboi K, et al. Impact of GLIM-defined malnutrition on short- and long-term outcomes after emergency gastrointestinal surgery. Nutrition 2026;149:113225.
14. Compher C, Bingham AL, McCall M, et al. Guidelines for the provision of nutrition support therapy in the adult critically ill patient: The American Society for Parenteral and Enteral Nutrition. JPEN J Parenter Enteral Nutr 2022;46(1):12–41.
15. Theilla M, Rattanachaiwong S, Kagan I, et al. Validation of GLIM malnutrition criteria for diagnosis of malnutrition in ICU patients: an observational study. Clin Nutr 2021;40(5):3578–84.
16. Ishida Y, Maeda K, Inoue T, et al. Malnutrition defined by the GLIM criteria predicts increased mortality and prolonged hospitalisation among intensive care unit patients: a nationwide database study. Clin Nutr 2026;61:106657.
17. Zusman O, Theilla M, Cohen J, et al. Resting energy expenditure, calorie and protein consumption in critically ill patients: a retrospective cohort study. Crit Care 2016;20(1):367.
18. Singer P, Blaser AR, Berger MM, et al. ESPEN guideline on clinical nutrition in the intensive care unit. Clin Nutr 2019;38(1):48–79.
19. Wasyluk W, Fiut R, Świetlicka I, et al. Time-course changes in energy expenditure in sepsis: a prospective observational study. Ann Intensive Care 2025;15(1):158.
20. Luan H, Liu Q, Fan H, et al. Analysis of the predictive value of 3-day cumulative energy deficit for 28-day mortality in patients with sepsis and nutritional risk: a retrospective study. Front Nutr 2026;13:1749483.
21. Fetterplace K, Beach LJ, MacIsaac C, et al. Associations between nutritional energy delivery, bioimpedance spectroscopy and functional outcomes in survivors of critical illness. J Hum Nutr Diet 2019;32(6):702–12.
22. Zusman O, Kagan I, Bendavid I, et al. Predictive equations versus measured energy expenditure by indirect calorimetry: A retrospective validation. Clin Nutr 2019;38(3):1206–10.
23. Lee I, Kim J, Ku M, et al. Effect of nutrition support team on 28-day mortality in Korean patients with acute respiratory failure. Acute Crit Care 2025;40(2):313–21.
24. Huang X, Wang Y, Geng S, et al. Nutritional practices and impact of feeding adequacy on clinical outcomes in Chinese respiratory intensive care units patients: a prospective observational study (ORIENT study). Front Nutr 2025;12:1719386.
25. Salciute-Simene E, Stasiunaitis R, Ambrasas E, et al. Impact of enteral nutrition interruptions on underfeeding in intensive care unit. Clin Nutr 2021;40(3):1310–7.
26. Verheul EAH, Dijkink S, Krijnen P, et al. Prevalence, incidence, and complications of malnutrition in severely injured patients. Eur J Trauma Emerg Surg 2025;51(1):72.
27. Osooli F, Abbas S, Farsaei S, et al. Identifying critically ill patients at risk of malnutrition and underfeeding: a prospective study at an academic hospital. Adv Pharm Bull 2019;9(2):314–20.
28. Fazzini B, Märkl T, Costas C, et al. The rate and assessment of muscle wasting during critical illness: a systematic review and meta-analysis. Crit Care 2023;27(1):2.

29. Kolck J, Hosse C, Fehrenbach U, et al. The extent of skeletal muscle wasting in prolonged critical illness and its association with survival: insights from a retrospective single-center study. BMC Anesthesiol 2025;25(1):266.
30. Kim S, Kang D, Kim D, et al. Early skeletal muscle loss and clinical outcomes in critically ill patients in the medical intensive care unit: a retrospective cohort study. PLoS One 2025;20(12):e0338315. https://doi.org/10.1371/journal.pone.0338315.
31. Schefold JC, Wollersheim T, Grunow JJ, et al. Muscular weakness and muscle wasting in the critically ill. J Cachexia Sarcopenia Muscle 2020;11(6):1399–412.
32. Batt J, Herridge MS, dos Santos CC. From skeletal muscle weakness to functional outcomes following critical illness: a translational biology perspective. Thorax 2019;74(11):1091–8.
33. van Gassel RV, Baggerman M, van de Poll MCG. Metabolic aspects of muscle wasting during critical illness. Curr Opin Clin Nutr Metab Care 2020;23(2):96–101.
34. Lees M, Prado CM, Wischmeyer PE, et al. Skeletal muscle: a critical organ for survival and recovery in critical illness. Crit Care Clin 2024;41(2):299–312.
35. Haberecht-Müller S, Krüger E, Fielitz J. Out of control: the role of the ubiquitin proteasome system in skeletal muscle during inflammation. Biomolecules 2021;11(9):1327.
36. Chapela SP, Simancas-Racines D, Montalvan M, et al. Signals for muscular protein turnover and insulin resistance in critically ill patients: a narrative review. Nutrients 2023;15(5):1071.
37. Santos CC, Hussain SNA, Mathur S, et al. Ultrasound-derived rates of muscle wasting in the intensive care unit and in the post-intensive care ward for patients with critical illness: post hoc analysis of an international multicentre randomised controlled trial of early rehabilitation. Aust Crit Care 2024;37(6):873–81.
38.. Deutz NEP, Ashurst I, Ballesteros-Pomar MD, et al. The underappreciated role of low muscle mass in the management of malnutrition. J Am Med Dir Assoc 2018. https://doi.org/10.1016/j.jamd.a.2018.11.021.
39.. Hartwell JL, Cotton A, Wenos CD, et al. Early achievement of enteral nutrition protein goals by intensive care unit day 4 is associated with fewer complications in critically injured adults. Ann Surg 2021;274(6):e988–94.
40. Yue X, Zhu X, Li Y, et al. Relationship between timing of achieving energy sufficiency and clinical outcomes in critically ill patients. Front Nutr 2025;12:1565394.
41.. Pašić F, Elezovic H. Impact of preoperative enteral nutrition on clinical outcomes in malnourished colorectal surgery patients. Med Arch 2025;79(3):227–32.
42. Ben Othman R, Cherni A, Dergaa I, et al. High prevalence of malnutrition and sarcopenia with inadequate nutritional support in intensive care unit patients: a prospective observational study of clinical outcomes. Nutrients 2026;18(6):883.
43. Weimann A, Edel A, Lücke L, et al. Lean mass loss in the intensive care unit and its restoration: a narrative review. Nutr Clin Pract 2026;41(2):350–68.
44. Fan X, Chen L, Zhang Y, et al. The impact of timing of enteral nutrition initiation on the prognosis of abdominal infection in critically ill patients. Medicine (Baltim) 2025;104(37):e44343. https://doi.org/10.1097/MD.0000000000044343.
45. Rodrigues A, Oliveira A, Vieira T, et al. A prolonged intensive care unit stay defines a worse long-term prognosis: insights from the critically ill mortality by age (CIMBA) study. Aust Crit Care 2024;37(5):734–9.

46. López-Gómez JJ, Lastra-González P, Gómez-Hoyos E, et al. Evolution of the COVID-19 patient with complete enteral nutrition in intensive care unit at hospital discharge. Clin Nutr ESPEN 2021;46:S649.
47. Al-Dorzi HM, Albarrak A, Ferwana M, et al. Lower versus higher dose of enteral caloric intake in adult critically ill patients: a systematic review and meta-analysis. Crit Care 2016;20(1):358.
48. Tilburgs B, Simons KS, Corsten S, et al. Associations between physical, cognitive, and mental health domains of post-intensive care syndrome and quality of life: a longitudinal multicenter cohort study. Crit Care Med 2025;53(1):e74–86.
49. Morgan A. Long-term outcomes from critical care. Surgery 2020;39(1):53–7.
50. Lui K, Luo G, Li S, et al. Incidence and risk factors of post-intensive care syndrome (PICS) in surgical ICU survivors: a prospective Chinese cohort study. BMC Public Health 2024;24(1):3277.
51. Leemans O, Rosseel Z, Pichard C, et al. Individualizing post-ICU nutrition: from guideline intent to bedside practice. Curr Opin Crit Care 2026;5:528–35.
52. Chen S, Chang Z. Haste makes waste: early nutrition prescription for critically ill patients. Aging Med (Milton) 2024;7(3):279–82.
53. Cehan V, Cehan AR, Pui MC, et al. A new perspective on overfeeding in the intensive care unit (ICU): challenges, dangers and prevention methods. Life 2025;15(5):828.
54. Vanhorebeek I, Casaer M, Gunst J. Nutrition and autophagy deficiency in critical illness. Curr Opin Crit Care 2023;29(4):306–14.
55. Mehta NM, Compher C, A.S.P.E.N. Board of Directors. A.S.P.E.N. Clinical Guidelines: nutrition support of the critically ill child. J Parenter Enteral Nutr 2009; 33(3):260–76.
56. Borriello R, Esposto G, Ainora ME, et al. Understanding refeeding syndrome in critically ill patients: a narrative review. Nutrients 2025;17(11):1866.
57. Sinatra N, Cuttone G, Geraci G, et al. Correlation between hypophosphatemia and hyperventilation in critically ill patients. Biomedicines 2025;13(10):2382.
58. Martinez-Esteban A, Peña-Solórzano S, Sanchez-Saavedra EP, et al. Assessment of electrolyte imbalances as an early manifestation of refeeding syndrome in critically ill patients receiving total parenteral nutrition at a tertiary hospital in Mexico City. Cureus 2026;18(1):e101608.
59. Patel JJ, Martindale R, McClave SA. Contemporary rationale for delivering enteral nutrition in critically ill adults. Crit Care Med 2025;53(7):e1481–90.
60. Wischmeyer PE, Bear DE, Berger MM, et al. Personalized nutrition therapy in critical care: 10 expert recommendations. Crit Care 2023;27(1):261.
61. Hadi V, Khosroshahi RA, Imani H, et al. Impact of early versus delayed enteral nutrition on ICU outcomes: a comparative study on mortality, ventilator dependence, and length of stay. Eur J Med Res 2025;30(1):315.
62. Xu J, Zhang J, Yang L, et al. Influence of early enteral nutrition on mortality of adult patients with sepsis: a meta-analysis of randomized controlled trials. Eur J Med Res 2025;30(1):1112.
63. Reignier J, Rice TW, Arabi YM, et al. Nutritional support in the ICU. BMJ 2025; 388:e077979.
64. Kano KI, Yamamoto R, Yoshida M, et al. Strategies to maximize the benefits of evidence-based enteral nutrition: a narrative review. Nutrients 2025;17(5):845.
65. Callahan JC, Parot-Schinkel E, Asfar P, et al. Impact of daily cyclic enteral nutrition versus standard continuous enteral nutrition in critically ill patients: a study protocol for a randomised controlled trial in three intensive care units in France

(DC-SCENIC). BMJ Open 2024;14(1):e080003. https://doi.org/10.1136/bmjopen-2023-080003.
66. Zhang S, Yu S, Zhang K, et al. Intermittent versus continuous enteral nutrition in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials. Front Nutr 2026;13:1786580.
67. Preiser JC, Arabi YM, Berger MM, et al. A guide to enteral nutrition in intensive care units: 10 expert tips for the daily practice. Crit Care 2021;25(1):424. A guide to enteral nutrition in intensive care units: 10 expert tips for the daily practice.
68. de Heer G, Burdelski C, Ammon C, et al. Energy expenditure in critically ill obese patients: a prospective observational study. Nutrients 2025;17(13):2060.
69. Deutz NEP, Engelen MPKJ. Compartmental analysis: a new approach to estimate protein breakdown and meal response in health and critical illness. Front Nutr 2024;11:1388969. https://doi.org/10.3389/fnut.2024.1388969.
70. Heyland DK, Patel J, Compher C, et al. The effect of higher protein dosing in critically ill patients with high nutritional risk (EFFORT protein): an international, multicentre, pragmatic, registry-based randomised trial. Lancet 2023;401-(10376):568–76.
71. Stoppe C, Patel JJ, Zarbock A, et al. The impact of higher protein dosing on outcomes in critically ill patients with acute kidney injury: a post hoc analysis of the EFFORT protein trial. Crit Care 2023;27(1):399.
72. Schouteden E, Heuts S, Bels J, et al. The impact of high versus standard enteral protein provision on functional recovery following intensive care admission: a pre-planned Bayesian analysis of the PRECISe trial. Clin Nutr 2025;48:153–60.
73. Lee ZY, Yap CSL, Hasan MS, et al. The effect of higher versus lower protein delivery in critically ill patients: a systematic review and meta-analysis of randomized controlled trials. Crit Care 2021;25(1):260.
74. Lee ZY, Dresen E, Chin C, et al. The effects of higher versus lower protein delivery in critically ill patients: an updated systematic review and meta-analysis of randomized controlled trials with trial sequential analysis. Crit Care 2024;28(1):15.
75. Summers M, Bels J, Karahalios A, et al. Optimal delivery of enteral protein in the critically ill: a systematic review and meta-analysis of randomised controlled trials. Clin Nutr 2026;61:106665. https://doi.org/10.1016/j.clnu.2026.106665.
76. Blaser AR, Rooyackers O, Bear DE. How to avoid harm with feeding critically ill patients: a synthesis of viewpoints of a basic scientist, dietitian and intensivist. Crit Care 2023;27(1):258.
77. Wang Y, Reintam Blaser A, Li Y, et al. Which critically ill patients are more susceptible to the adverse effects associated with feeding intolerance? A secondary analysis of a cluster-randomized controlled trial. Front Nutr 2026;13:1729192.
78. Singer P, Kish MS, Raphaeli O. Artificial intelligence in nutritional assessment and decision making. Curr Opin Clin Nutr Metab Care 2026;29(5):434–40.
79. Singer P, Raphaeli O. Smart feeding: the role of artificial intelligence and integrated nutrition platforms in the ICU. Curr Opin Crit Care 2026;32(4):359–65.
80. Berger MM, Burgos R, Casaer MP, et al. Clinical nutrition issues in 2022: what is missing to trust supplemental parenteral nutrition in ICU patients? Crit Care 2022;26(1):271.
81. Ridley EJ. Parenteral nutrition in critical illness: total, supplemental or never? Curr Opin Clin Nutr Metab Care 2021;24(2):176–82.

82. Gao X, Liu Y, Zhang L, et al. Effect of early vs late supplemental parenteral nutrition in patients undergoing abdominal surgery: a randomized clinical trial. JAMA Surg 2022;157(5):384–93.
83. Alsharif DJ, Alsharif FJ, Aljuraiban GS, et al. Effect of supplemental parenteral nutrition versus enteral nutrition alone on clinical outcomes in critically ill adult patients: a systematic review and meta-analysis of randomized controlled trials. Nutrients 2020;12(10):2968.
84. Gargi Yonatan, Levran N, Vine J, et al. Detecting the metabolic transition to personalize nutritional timing: model development and preliminary validation in a large ICU cohort. Critical Care [London] 2026;3(1):132.
85. Kagan I, Hellerman-Itzhaki M, Bendavid I, et al. Controlled enteral nutrition in critical care patients: a randomized clinical trial of a novel management system. Clin Nutr 2023;42(9):1602–9.
86. Ohbe H, Jo T, Matsui H, et al. Differences in effect of early enteral nutrition on mortality among ventilated adults with shock requiring low-medium-and high-dose noradrenaline: a propensity-matched analysis. Clin Nutr 2020;39(2):460–7.
87. Zhou Z, Zhou J. Intermittent vs. continuous: a comparative narrative review of enteral and parenteral nutrition support strategies in the perioperative setting. Eur J Clin Nutr 2026;80(2):140–5.
88. Li Z, Cao L, Zhong X, et al. A meta-analysis of the efficacy of ultrasound-guided nasojejunal tube placement. Nurs Crit Care 2026;31(2):e70382. https://doi.org/10.1111/nicc.70382.
89. Green B, Phillips M, Morgan L, et al. Critically ill patients with and without SARS-CoV-2 better achieve energy and protein targets with a high-energy, high-protein peptide-based enteral tube feed: insights from a multicentre clinical audit performed during the COVID-19 pandemic. Clin Nutr ESPEN 2022;48:506–7.
90. Selimoğlu M, Kansu A, Aydoğdu S, et al. Nutritional support in malnourished children with compromised gastrointestinal function: utility of peptide-based enteral therapy. Front Pediatr 2021;9:610275. https://doi.org/10.3389/fped.2021.610275.
91. Tatsumi H. Enteral tolerance in critically ill patients. J Intensive Care 2019;7:30.
92. Rehani C, Pelekhaty SL, Kozar R. Enteral nutrition: what happened to immune-enhancing diets? Surg Clin North Am 2026;106(2):261–71.
93. Nakamura K, Yamamoto R, Higashibeppu N, et al. The Japanese critical care nutrition guideline 2024. J Intensive Care 2025;13(1):18.
94. Lewis K, Alqahtani Z, McIntyre L, et al. The efficacy and safety of prokinetic agents in critically ill patients receiving enteral nutrition: a systematic review and meta-analysis of randomized trials. Crit Care 2016;20(1):259.
95. Elmokadem E, Fadl DKAE, Eissa N, et al. Comparison of enteral prucalopride versus intravenous metoclopramide for feeding intolerance in patients with critical illness: a randomized double-blinded study. Front Pharmacol 2024;15:1413246. https://doi.org/10.3389/fphar.2024.1413246.
96. Szczupak M, Jankowska M, Jankowski B, et al. Prokinetic effect of erythromycin in the management of gastroparesis in critically ill patients—our experience and literature review. Front Med 2024;11:1440992. https://doi.org/10.3389/fmed.2024.1440992.
97. De Pascale G, Cutuli SL, Vargas M, et al. Personalized automatic management of tracheal cuff pressure and subglottic secretions drainage to prevent pneumonia in critically ill intubated patients: the MICROINHALO multicenter randomized controlled trial. Intensive Care Med 2026;52(6):1235–47.

98.. Yasuda H, Kondo N, Yamamoto R, et al. Monitoring of gastric residual volume during enteral nutrition. Cochrane Database Syst Rev 2021;9(9):CD013335.
99. Wiese AN, Rogers M, Way M, et al. The impact of removing gastric residual volume monitoring and enteral nutrition rate titration in adults receiving mechanical ventilation. Aust Crit Care 2020;33(2):155–61.
100. Corsello A, Trovato CM, Dipasquale V, et al. Refeeding syndrome in pediatric age, an unknown disease: a narrative review. J Pediatr Gastroenterol Nutr 2023;77(6):e75–83.
101. Rupert A, Seres D, Li J, et al. Factors associated with delayed enteral nutrition in the intensive care unit: a propensity score-matched retrospective cohort study. Am J Clin Nutr 2021;114(1):295–302.
102.. Hegazy SE, Mostafa MF, Kandeel NA. Enteral nutrition guidelines improve critically ill patients' outcomes: a quasiexperimental study. Dimens Crit Care Nurs 2026;45(1):31–40.