

Nutritional Considerations for ICU Patients. Part 1: When, What, and How to Feed

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KEY POINTS

- Critical illness progresses through 3 metabolic phases: early acute, late acute, and recovery.
- Indirect calorimetry is the gold standard for assessing energy needs in critically ill patients. Other methods include predictive equations and weight-based methods.
- Assessment of malnutrition may be guided by clinical assessment and nutritional scoring systems.
- Oral nutrition should be prioritized over assisted enteral or parenteral nutrition whenever possible.
- Nutritional therapy should be initiated at a low dose of calories and protein and progressively increased to achieve full nutrition within 3 to 7 days.

INTRODUCTION

Nutrition plays a crucial role in the care of patients in the intensive care unit (ICU), where adequate nutrition support is essential for optimising outcomes and promoting recovery.¹ Nutrition is no longer a support but a therapy in critically ill patients.

The European Society for Clinical Nutrition and Metabolism (ESPEN) categorises the stages of critical illness into 3 distinct phases: the early acute phase (1 to 2 days ICU), the acute late phase (3 to 7 days ICU), and the recovery phase (>7 days to months).² During the early acute phase, there is an initial response to stress characterised by increased metabolic rate, hyperglycaemia, and insulin resistance; however, energy expenditure in this stage is decreased.³ The hypercatabolic phase follows in the late acute phase, marked by a sustained increase in metabolic rate, muscle protein breakdown, and ongoing inflammatory response, all causing a rise in energy expenditure. Finally, the recovery phase focuses on anabolic processes, tissue repair, and restoration of normal metabolic functions.

Understanding the pathophysiology of the stages is crucial for tailoring nutrition interventions to meet critically ill patients' changing metabolic and nutritional needs throughout their ICU stay, thus reducing morbidity and mortality related to inappropriate nutritional therapy.⁴ The time periods for the phases of critical illness are arbitrary, with no current biomarker or metabolic monitor to indicate the change from one phase to the next.⁵

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Early identification of nutritional risk, appropriate assessment of energy expenditure, and timely initiation of nutrition interventions are key components of a comprehensive approach to nutrition care in the ICU.¹ Medical nutritional therapy (MNT) is not only aimed at preventing malnutrition and micronutrient deficiencies but also aimed at achieving metabolic optimisation, preserving gut integrity, and attenuating the stress-induced immune response.⁶

NUTRITIONAL RISK ASSESSMENT

Conducting a nutritional risk screening for patients in the ICU is a crucial aspect of their care. A systematic review found that the prevalence of malnutrition ranged between 38% and 78% of ICU patients.⁷ Malnutrition is a substantial predictive risk factor for critically ill patients, impacting important outcomes such as duration of hospitalisation, length of time on mechanical ventilation, rates of infection, and mortality.⁸ Most nutritional scoring systems identify patients with cachexia, low body mass index (≤ 18.5 to 20.5 kg/m^2), $>5\%$ weight loss in the last month, and reduced general condition as severely malnourished and at high risk for malnutrition and recommended early MNT.⁹

Nutritional assessment in clinical practice lacks standardisation. Various tools, such as the Nutritional Risk Screening 2002, Nutrition Risk in Critically Ill score, modified Nutrition Risk in Critically Ill, Subjective Global Assessment, and Malnutrition Screening Tool, are available and can be used.^{1,6}

However, the Nutritional Risk Screening 2002 and modified Nutrition Risk in Critically Ill scores were designed for critically ill patients and proved superior in predicting clinical outcomes in critically ill patients. Both scoring systems pay special attention to nutrition status and disease severity. The ESPEN guidelines recommend a thorough clinical assessment, including a detailed medical history, evaluation of muscle mass and strength, unintentional weight loss, and body composition. ESPEN also suggests using a practical approach, considering patients at risk for malnutrition if they are expected to stay in the ICU for more than 48 hours, on ventilator support, have severe infections or chronic diseases, or were undernourished for more than 5 days before ICU admission.^{1,3}

DETERMINING ENERGY REQUIREMENTS

To determine energy requirements, both ESPEN and American Society of Parenteral and Enteral Nutrition (ASPEN) recommend using indirect calorimetry (IC) as the gold standard.³ This noninvasive method measures the volume of consumed oxygen (VO_2) and exhaled carbon dioxide (VCO_2) through a ventilatory circuit and thus estimates the patient's resting metabolic rate and total energy expenditure. The Fick method is another way to calculate energy expenditure, but it relies on the placement of a pulmonary artery catheter, which limits its applicability in clinical practice.³ The resting energy expenditure (REE) can be calculated using Weir's equation with or without urinary nitrogen (UN) measurements. Nitrogen is assumed to be biologically inactive, eliminating the need for urine measurements. The REE formula is as follows¹⁰:

$$\text{REE(kcal/d)} = 1.44 \times ([\text{VO}_2(\text{mL/min})] \times 3.94] + [\text{VCO}_2(\text{mL/min}) \times 1.11]) - 2.17(\text{UN})$$

In the absence of IC, ESPEN recommends using exhaled CO_2 from the ventilator (Figure 1). Assuming that the respiratory quotient (RQ) is normal, energy expenditure can be calculated by substituting VO_2 with the RQ value of 0.86. RQ is calculated

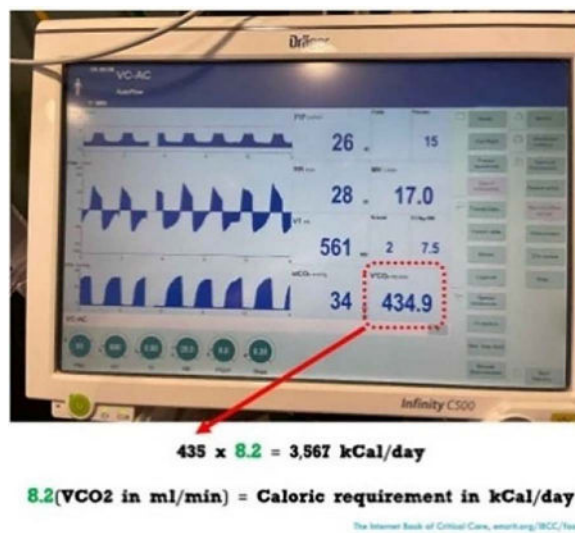


Figure 1. Ventilator-assisted energy expenditure estimation using VCO_2 .²⁵

as VCO_2/VO_2 , depending on the proportion of carbohydrates, fat, and protein consumed. An RQ of 0.86 is characteristic of most nutritional products. This adjustment allows for the use of a modified Weir's equation⁹:

$$\text{Energy expenditure (kcal/d)} = VCO_2 \text{ (mL/min)} \times 8.19$$

IC has some limitations that may lead to unreliable results, for example, patients with high oxygen requirements, nitrous oxide usage, hemodynamic instability, or ventilator adjustments.¹⁰

In the absence of IC or VCO_2 , ESPEN recommends using a calorie intake formula based on weight. This entails limiting calorie consumption to 20 to 25 kcal/kg/d progressively during the acute phase and increasing intake to 25 to 30 kcal/kg/d during recovery. Weight-based formulas may not be adequate for all patients, particularly those who are underweight or overweight.³

An alternative approach to estimating energy requirements involves the use of predictive equations. Several such equations exist, including the Penn State, Mifflin-St. Jeor, and Ireton-Jones. Although these equations are commonly used, there is currently no conclusive evidence to suggest that they are more accurate than the revised Harris-Benedict (H-B) equation. However, it should be noted that the H-B equation is based on data from average individuals and may not accurately reflect the energy needs of all individuals, particularly those with atypical stress levels (Table 1).¹¹

To accurately estimate total daily calorie requirements, the H-B equation must incorporate both activity-level and stress factors. The equation becomes:

$$\text{Daily Calorie Requirement} = \text{REE} \times \text{Activity Level} \times \text{Stress Factor}$$

Activity-level factors consider the patient's mobility (bed bound or ambulatory), whereas stress factors account for the impact of illness or injury on metabolic rate.¹²

Predictive equations, with a potential error margin of up to 60%, may overestimate or underestimate energy requirements.¹¹ In response, Pavlidou et al have developed a revised H-B equation tailored to various populations, including individuals with specific diseases, ethnicities, life stages, and body compositions.¹³

Following the initial Tight Calorie Control Study (TICACOS), 3 subsequent studies have been published comparing an MNT guided by IC to a regimen based on predictive equations. The ESPEN guidelines incorporated a meta-analysis of 4 publications, which revealed a favourable trend regarding short-term mortality in patients receiving MNT guided by IC (RR 1.28, 95% CI 0.98 – 1.67, $P = .07$). However, they did not find any significant differences in long-term mortality, infection rates, or length of stay.^{3,14} While the benefits of IC guided MNT throughout critical illness are evident, recent research suggests that IC may be particularly valuable after the acute phase when considerable metabolic changes occur.⁵

WHAT TO FEED

Tailoring nutritional intake to the specific needs of critically ill patients is paramount. Key considerations that require regular assessment include the stage of critical illness (acute versus postacute), the ability of the gastrointestinal system and metabolism to tolerate substrates, the primary disease being treated, other health conditions, pre-existing nutrient deficiencies, and the trajectory of the patient's illness.

Macronutrients

Water: 30 mL/kg/d. Fluids provided by medications and enteral nutrition (EN) or parenteral nutrition (PN) contribute to this and should also be factored in the total fluid requirements.¹¹

Electrolytes: Sodium (Na^+), chloride (Cl^-) = 1 to 2 mmol/kg/d

Potassium (K^+) = 0.8 to 1.2 mmol/kg/d

Calcium (Ca^{2+}), magnesium (Mg^{2+}) = 0.1 mmol/kg/d

Phosphate = 0.2 to 0.5 mmol/kg/d¹¹

Carbohydrates: carbohydrates account for 45 to 60% of calorie requirements.^{3,15} The maximum recommended intake is 5 mg/kg/min.

Men	$REE \text{ (kcal/d)} = (13.397 \times \text{weight in kg}) + (4.799 \times \text{height in cm}) - (5.677 \times \text{age in years}) + 88.362$
Women	$REE \text{ (kcal/d)} = (9.247 \times \text{weight in kg}) + (3.098 \times \text{height in cm}) - (4.330 \times \text{age in years}) + 447.593$

Table 1. Harris-Benedict Equation. REE, resting energy expenditure

Protein: the suggested dose range is 0.8g/kg/d in the acute early phase and progressively increases to 1.3 g/kg/d by day 4 of ICU. Frail and sarcopenic patients exhibit enhanced survival rates when consuming a protein intake of 1.3 g/kg/d, as opposed to 0.8 g/kg/d.^{3,16,17} Conversely, septic patients demonstrate a lack of responsiveness to increased protein consumption. Increases up to 2 g/kg/d later in critical illness may be necessary in patients with obesity, burns or trauma patients.¹⁵ The EFFORT trial suggests that using high doses of protein (≥ 2.2 g/kg/d) has not significantly improved mortality outcomes, with worse outcomes in cohorts of patients with acute kidney injury and high multiorgan failure scores (SOFA score ≥ 9). These findings may be linked to the presence of anabolic resistance during the initial phases of critical illness.¹⁶⁻¹⁸

Lipids: for intravenous lipids, the recommendation is 1 g/kg/d with a tolerance of up to 1.5 g/kg/d. Lipids accounts for the remaining 30 to 40% of the calorie requirement. Excess administration may lead to waste, storage, and toxicity. Propofol is a source of fatty acids that contains 1.1 kcal/mL and can provide a significant energy load.³

Micronutrients and immunonutrition (INT): measurement of micronutrient plasma levels in critical illness is unreliable as inflammation causes redistribution.⁵ Provision of maintenance doses of micronutrients is necessary.⁵ Most EN formulations are enriched with micronutrients, meeting the daily requirements of patients who consume ≥ 1500 kcal/d.¹⁹ However, additional supplementation may be necessary for special cases like trauma, major burns, and those requiring PN. Commercially available PN formulations lack micronutrients, including vitamins and trace elements, necessitating a separate prescription.^{3,19}

INT aims to provide specific nutrients that enhance immune function, reduce inflammatory responses, and support healing. INT components include glutamine, omega-3 fatty acids, arginine, antioxidants, and nucleotides.

Glutamine depletion is a common occurrence in critical illness, often linked to compromised immune function and intestinal barrier integrity. Glutamine supplementation may mitigate gut bacterial translocation, enhance immune cell activity, reduce proinflammatory cytokine production, and increase antioxidant levels. Enteral glutamine (0.2 to 0.3 g/kg/d) can be considered for burn and trauma patients in the ICU for up to 5 days, potentially extending to 10 to 15 days in cases of complicated wound healing. However, its use in other ICU patients remains unestablished.^{3,16}

Fatty acids, including medium-chain triglycerides, omega-9, monounsaturated fatty acids, and omega-3 polyunsaturated fatty acids, play a role in critical illness. Omega-3 fatty acids, found in fish oils, particularly eicosapentaenoic acid and docosahexaenoic acid, have documented anti-inflammatory properties and can modulate the production of inflammatory mediators, including eicosanoids and cytokines. Patients with conditions like adult respiratory distress syndrome, acute lung injury, and sepsis have shown improved outcomes in length of stay, ventilator days, and mortality with the use of enteral formulas enriched with borage oil and/or omega-3 fatty acids.²⁰ The ESPEN practical guideline recommends considering omega-3 fatty acid supplementation for patients

ESPEN micronutrient recommendations suggest giving vitamin C at 100 mg/1500 kcal/d with EN and 100 to 200 mg/d PN. In addition, individuals with chronic oxidative stress (such as diabetes, heart failure or dialysis) may require larger dosages of 200 to 500 mg daily.^{19, 20}

ESPEN recommends that a high dose of vitamin D3 (500,000 IU) be administered to critically ill patients with low plasma levels (25-hydroxy-vitamin D < 12.5 ng/mL or 50 nmol/L) within 1 week after admission. Low plasma concentrations of vitamin D are associated with poor outcomes in critically ill patients, such as increased mortality, extended hospital stays, higher rates of sepsis, and prolonged mechanical ventilation.¹⁹

The diagnosis of vitamin E deficiency should be based on the presence of clinical manifestations, and a high index of suspicion for deficiency should be maintained in patients with conditions such as cystic fibrosis, abetalipoproteinaemia, or thrombotic thrombocytopenic purpura. Where there are no indications, assessing vitamin E levels during PN is unnecessary. To test for vitamin E deficiency, one needs to measure the level of plasma α -tocopherol. EN should supply a minimum of 15 mg/d/1500 kcal, whereas PN should provide 9 to 10 mg/d. Supplementation is also advised if α -tocopherol levels fall below 12 μ mol/L, starting with 100 mg/d.¹⁹

The recommended daily intake of selenium is 50 to 150 μ g/1500 kcal for those receiving EN and 60 to 100 μ g/d for individuals receiving PN. If plasma selenium levels fall below 0.4 μ mol/L, supplementation of 100 μ g/d is advised until normalisation. As selenium is primarily excreted renally, excessive intake above the dietary reference intake should be avoided in patients with renal failure.^{2,19}

Critically ill patients often experience low zinc levels due to pre-existing deficiencies, inflammation, or increased losses, leading to poor clinical outcomes. Current guidelines recommend a daily zinc intake of 10-15 mg/1500 kcal for EN and 3-5 mg for PN. For individuals experiencing higher levels of gastrointestinal tract losses, the dose of intravenous zinc can be escalated to a maximum of 12 mg/d. Although there are guidelines for administering intravenous zinc to burn patients (30 to 35 mg/d intravenously over 2 to 3 weeks), there are no specific zinc dosing guidelines for other critically ill subgroups of patients beyond general recommendations.^{2,19}

Table 2. Micronutrient Administration in Critical Illness. EN, enteral nutrition; ESPEN, European Society for Clinical Nutrition and Metabolism; ICU, intensive care unit; PN, parenteral nutrition

receiving EN (in nutritional doses) or patients requiring PN. However, high-dose omega-3 enriched enteral formulations should not be administered routinely or as bolus doses.³

Arginine has shown potential benefits in critically ill patients. However, caution is advised for patients with severe sepsis and septic shock due to its potential to increase nitric oxide production that can exacerbate hypotension.⁸

Antioxidant vitamins and trace elements, including vitamins C, D, and E as well as zinc, copper, and selenium, are important in combating oxidative stress (Table 2).²¹

The guidelines currently do not recommend the routine use of INT in critically ill patient populations. Regular monitoring of nutritional status and immune function is crucial for optimising INT in ICU patients, and supplementation requires careful consideration on a case-by-case basis.²²

MODES OF NUTRITIONAL SUPPORT

Routes of nutritional support are enteral and parenteral. EN is further divided to oral and assisted enteral (tube feeding).

- (1) Oral. This is the most preferred method when gastrointestinal tract (GIT) function is intact, and the patient can safely swallow and digest food and liquids without complications.
- (2) Assisted enteral. Nutrients delivered via a feeding tube directly into the GIT is a preferred method for patients unable to consume food orally or with difficulty swallowing but with intact gut function. Tubes can be inserted nasally, orally, or via the abdominal wall. ESPEN recommends establishing a gastrostomy or jejunostomy for patients anticipated to require enteral feeding for more than 3 to 4 weeks.²³ (In this article, EN refers to assisted EN.)

Feeding Mode	Indications	Advantage	Disadvantage
Oral	<ul style="list-style-type: none"> • Patient is fully conscious and alert and has an intact swallowing reflex • If all nutritional requirements can be met 	<ul style="list-style-type: none"> • Maintains normalcy and routine for the patient • Potentially reduces infections compared with invasive methods • Cost-effective 	<ul style="list-style-type: none"> • Not feasible if the patient is unconscious or unable to swallow • Risk of aspiration, especially in patients with compromised swallow reflex or altered level of consciousness • May not meet the full nutritional requirements of critically ill patients
Assisted Enteral	<ul style="list-style-type: none"> • Patient has a functioning gastrointestinal tract • Enteral access can be safely established and maintained • Patient is haemodynamically stable/improvement of shocked state • Need for long-term nutritional support 	<ul style="list-style-type: none"> • Cost-effective and easier to administer • Maintains gut integrity and function • Reduces risk of infections compared with parenteral feeding • Can be easily continued as the patient transitions to oral intake 	<ul style="list-style-type: none"> • Risk of aspiration in critically ill patients • Not suitable for patients with severe gastrointestinal disease • Slower rate of nutrient absorption than parenteral feeding • Tube displacement, clogging, or other complications, such as gastrointestinal necrosis, may occur
Parenteral	<ul style="list-style-type: none"> • Nonfunctional gut • Patient unable to tolerate enteral feeding due to severe gastrointestinal tract issues • Severe haemodynamic instability • Significant malabsorption issues or short bowel syndrome • High risk of aspiration or complications with enteral feed • Requirement for precise control of nutrient intake or specific nutrient formulations 	<ul style="list-style-type: none"> • Provides essential nutrients directly into the blood • Useful for patients with severe gastrointestinal tract disease • Can meet precise nutritional needs when enteral feeding is not feasible or sufficient 	<ul style="list-style-type: none"> • Expensive and complex to administer • Higher risk of infections, sepsis, and metabolic complications • May lead to hepatic dysfunction and electrolyte disturbances with long-term use • Limited or no contribution to maintain gut integrity

Table 3. Indications, Advantages, and Disadvantages of Medical Nutritional Therapy

(3) Parenteral. Parenteral nutrition involves the direct infusion of artificial nutrients into the bloodstream via a vein. It is indicated when oral or enteral feeding is not feasible or contraindicated. PN encompasses 2 modalities: peripheral PN (PPN) and central PN (CPN). PPN is delivered through a peripheral intravenous catheter inserted into the arm or leg, whereas CPN requires a central venous catheter or peripherally inserted central catheter.^{23,24}

PPN can serve as a temporary nutritional supplement until EN becomes feasible or as a rapid intervention when central venous access is unavailable. PPN offers several advantages over CPN, including reduced risks associated with central venous lines, minimised delays in nutritional support, and lower costs. However, PPN also carries certain drawbacks, such as a higher risk of thrombophlebitis, limitations in delivering a full complement of nutrients, unsuitability for prolonged feeding beyond 4-7 days, and the need for solutions with lower osmolality than CPN.²⁴

Central venous access devices for PN vary based on duration. Short-term catheters are non-tunneled and intended for hospitalised patients requiring temporary nutrition. Medium-term catheters, such as peripherally inserted central catheters and Hohn catheters, offer intermittent use and can support long-term PN for up to 3 months, both in and out of the hospital. Peripherally inserted central catheters are commonly used for home PN but may pose challenges for self-care due to catheter placement. Long-term or home PN exceeding 3 months typically requires long-term venous access devices like cuffed tunneled central catheters or implanted ports.^{23,24}

While PN is continuous, EN can be delivered as boluses or continuous infusion with feed pumps. Continuous infusion is delivered over 18 to 24 hours. If a patient is on insulin, a 24-hour continuous infusion would be ideal for glycaemic control.

Table 3 summarises the indications, advantages, and disadvantages of modes of MNT.^{3,25}

WHEN AND HOW DO YOU DECIDE FEED TYPE

A comprehensive clinical assessment is essential for evaluating critically ill patients' nutritional risk and severity of malnutrition. This assessment includes medical and weight loss history, physical examination, body composition analysis, and nutritional scoring. Patients staying in the ICU for more than 48 hours are at high risk of malnutrition and require priority attention to nutritional

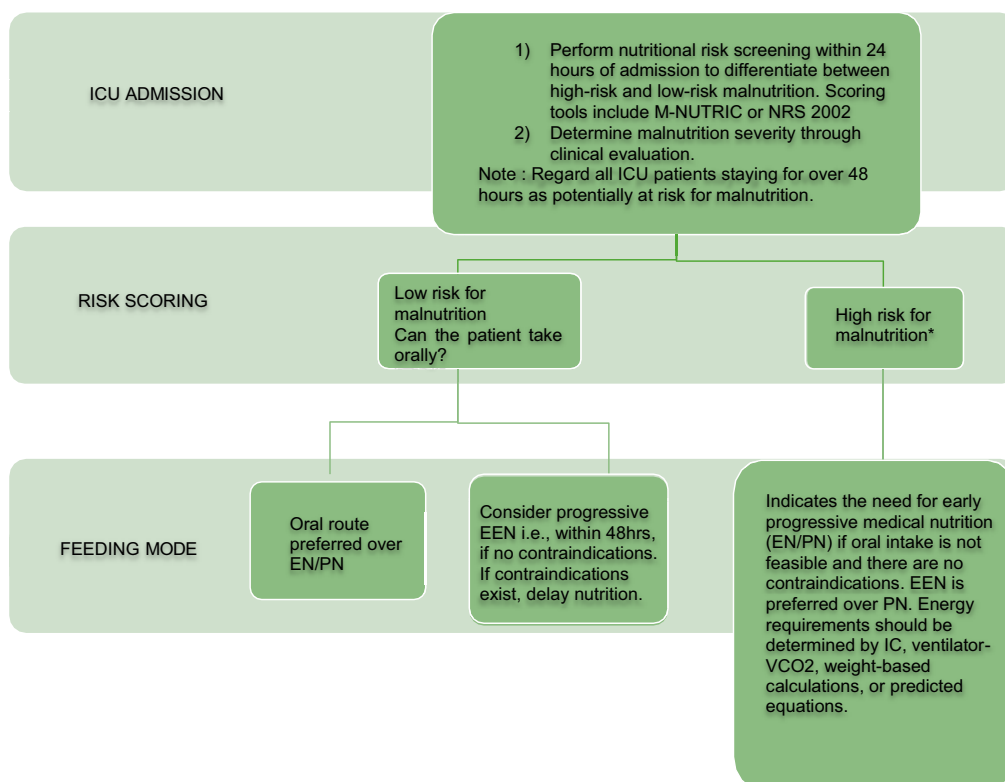


Figure 2. Recommendations for nutritional management based on nutritional status.³ Disclaimer: the algorithms mentioned above are based primarily on European Society for Clinical Nutrition and Metabolism recommendations and are meant to be used as a guide for initiating medical nutrition in the intensive care unit. It is important to assess each patient on a case-by-case basis, as some special populations may require different management. Abbreviations: EEN, early enteral nutrition; EN, enteral nutrition; IC, indirect calorimetry; ICU, intensive care unit; M-NUTRIC, modified Nutrition Risk in Critically Ill score; NRS 2002, Nutritional Risk Screening (NRS) 2002; PN, parenteral nutrition.

status. Oral intake should be prioritised over EN or PN for patients who can tolerate it. If oral feeding is not feasible, ESPEN recommends early initiation of low-dose EN within 48 hours, aiming to achieve the full energy target during the acute last phase of critical illness.⁵ PN may be considered as a last resort for severely malnourished patients when EN is contraindicated.³ However, PN should only be initiated during the acute late phase of critical illness (days 3 to 7) and after exhausting all reasonable strategies to improve enteral tolerance.³

Strategies include the following:

- Temporarily stop EN or introduce EN at a low rate (trophic feeds) while monitoring for worsening symptoms of enteral feeding intolerance.

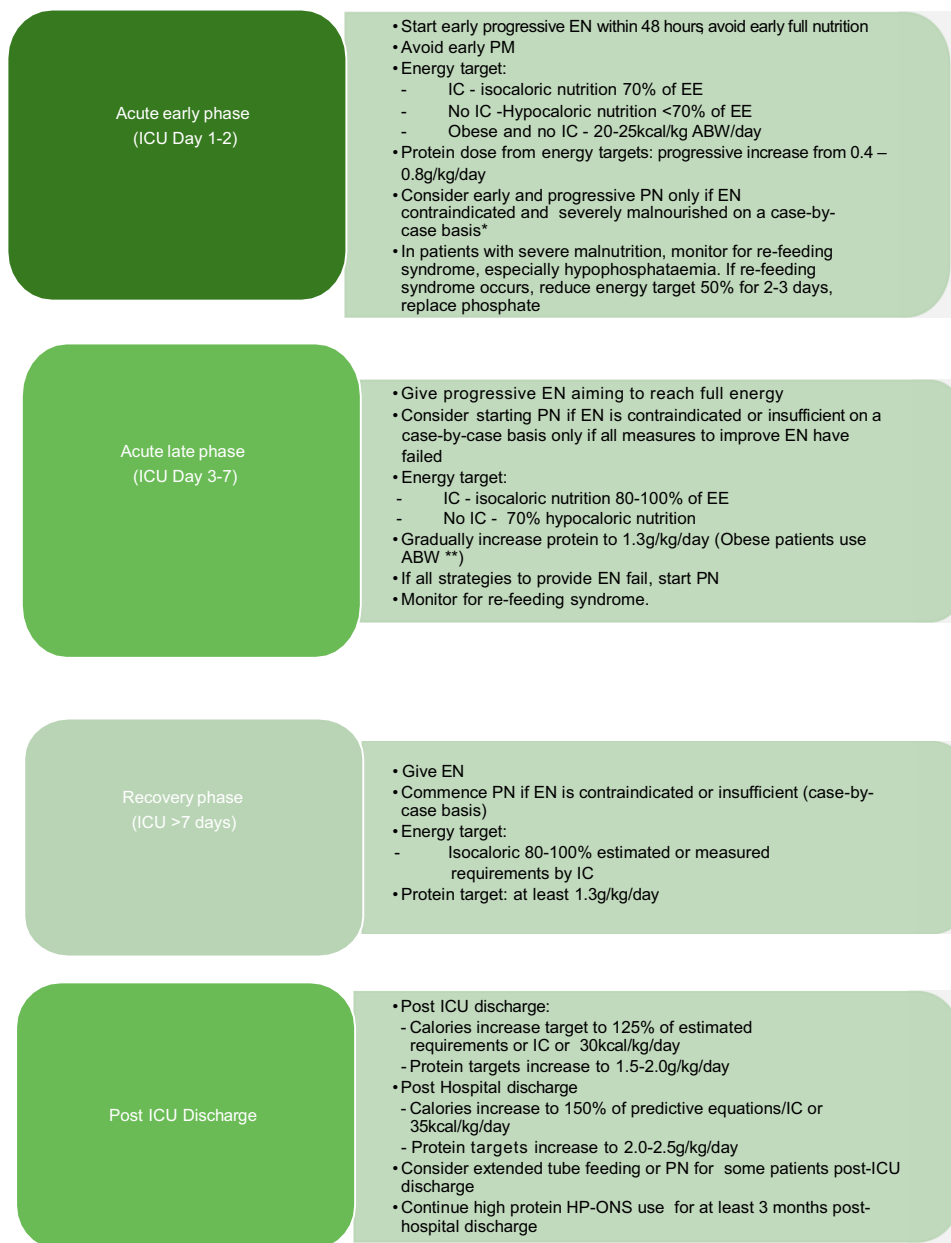


Figure 3. Recommendations for nutritional management based on the phase of critical illness.³ **Adjusted body weight (ABW) = (current BW – ideal BW) × 0.33 + ideal BW. This equation should be used when body mass index (BMI) is >25 kg/m². The ideal BW is calculated as 2.2 × BMI + 3.5 × BMI × (height – 1.50 m). Disclaimer: the algorithms mentioned above are based primarily on European Society for Clinical Nutrition and Metabolism recommendations and are meant to be used as a guide for initiating medical nutrition in the intensive care unit. It is important to assess each patient on a case-by-case basis, as some special populations may require different management. Abbreviations: EE, energy expenditure; EN, enteral nutrition; HP-ONS, high-protein oral nutritional supplements; IC, indirect calorimetry; ICU, intensive care unit; PN, parenteral nutrition.

- Patients at high risk for aspiration should be fed in a 35° to 40° head-up position.
- Use of prokinetics. ESPEN recommends using intravenous erythromycin as the first line of therapy, intravenous metoclopramide as a second line, or a combination of both.
- Use of a jejunal tube, that is, postpyloric feeding. Postpyloric tube placement demands specialised expertise; it may be less physiologically optimal than gastric EN and could pose risks in individuals with GIT motility issues beyond the stomach. Postpyloric feeding is advocated in patients with poor neurological status to reduce the risk of regurgitation.

Consider supplementing with PN on a case-by-case basis in patients not tolerating full-dose EN during their initial ICU week, weighing safety and potential benefits.^{2,3}

Early initiation of full nutrition poses harm in a dose-dependent manner, regardless of the route of administration, and should be avoided.^{4,5} This is due to the suppression of recovery pathways, including autophagy and ketogenesis, during the early catabolic phase.^{4,5} Future research in initiating nutritional therapy needs to focus on identifying readiness for medical nutrition and monitoring response to nutritional therapy. Currently, the use of biomarkers for this purpose has not been validated.⁵

Figures 2 and 3 summarise recommendations for deciding on nutritional therapy based on the ESPEN guidelines.³

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