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Critical Care Perspectives

From Theory to Practice



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CHAPTER 6

Enteral Nutrition Therapy in Critically Ill Patients

Divya Arora, Bikram Kumar Gupta

CASE VIGNETTE

A 58-year-old male was admitted to the intensive care unit (ICU), following a road traffic accident. He had sustained fracture of right femur and traumatic brain injury (TBI) [Glasgow Coma Scale (GCS) = 8/15]. He was emergently intubated and burr-hole evacuation for subdural hematoma was performed and open reduction, internal fixation done for right femur fracture, following which he was continued on mechanical ventilator. When off-sedation, he withdraws to pain but does not open eyes. His height is 175 cm and weight of 60 kg [body mass index (BMI) = 19.6 kg/m^2]. He is a known hypertensive and diabetic, well-controlled on medications. Vitals recorded on postoperative day 0—heart rate = 88 beats/min, blood pressure (BP) = 108/64 mm Hg, oxygen saturation (SpO_2) = 98%, respiratory rate (RR) = 12 breaths/min. Cardiovascular (CVS) and respiratory examination show no abnormalities. Abdomen is soft to touch. Laboratory investigations showed hemoglobin (Hb) 9.5 g%, total leukocyte count (TLC) 9,300 cells/mm^3, differential leukocyte count—polymorphs 61% and lymphocytes 35%, and platelet count 1.32 lakhs/mm^3. The electrolytes, liver, and kidney function tests were within normal range, except albumin levels of 3.3 g/dL. The random blood sugars were 136, 144, and 141 mg/dL. Triglycerides recorded were high. His current medications included furosemide, mannitol, telmisartan, atorvastatin, esomeprazole, cefazolin antibiotic, and levetiracetam. Insulin was being used as per sliding scale to control sugar levels. Midazolam and fentanyl infusion was used to keep him sedated.

Q1 Should we start feeding in this patient? Is he likely to benefit from it?

Nutritional support is of utmost importance and should be a priority in this patient. Critically ill patients are expected to be in a *catabolic state* in response to stress, especially in their acute phase (early followed by late) that lasts 7–10 days.[1] This increased catabolism and energy expenditure (EE) leads to breakdown of protein reserves and increases the risk of malnutrition, that would worsen any existing malnutrition. Further, TBI often induces a state of malnutrition due to insufficient caloric and protein input.[2]

Malnutrition in ICU is associated with:

- Impaired immune function and increased susceptibility to infections
- Impaired wound healing
- Muscle wasting
- Impaired ventilatory drive
- Increased risk of infections
- Negative impact on cognitive functions
- Impaired gut function and dysbiosis, which propagates and accentuates inflammatory response leading to cellular dysfunction with end result being multiorgan failure
- Increased length of stay (LOS) in ICU and healthcare costs

Hence, optimal nutritional therapy is crucial for improving outcomes.[3] Further the European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend considering medical nutrition therapy for all patients staying in the ICU for >48 hours.[1]

Q2 When do you plan to initiate the feeding for this patient?

Adequate nutrition therapy must be initiated early in TBI patients to promote optimal recovery, decrease incidence of infections, and prevent secondary brain damage.[4] Both the ESPEN and American Society for Parenteral and Enteral Nutrition-Society of Critical Care Medicine

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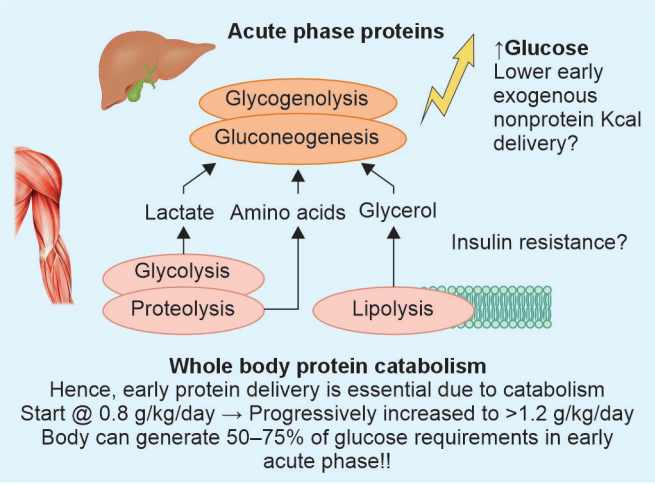

Fig. 1: Hypercatabolic response in acute phase of critical illness.[6] *Source:* Gillis C, Carli F. Promoting perioperative metabolic and nutritional care. Anesthesiology. 2015;123:1455-72. doi: 10.1097/ALN.0000000000000795.

(ASPEN-SCCM) guidelines also recommend initiating early enteral nutrition (EN) within 24–48 hours in critically ill patients if oral intake is not possible.[1,5]

Hypercatabolic state in such patients is characterized by negative nitrogen balance, increased resting energy expenditure (REE), and protein loss, leading to loss of lean body mass **(Fig. 1)**. Hence, early feeding is important. It provides adequate caloric requirements and substrates for healing, as also treat micronutrient deficiencies, resulting in increased survival.

Hypercatabolic state and preexisting malnutrition in critically ill patients leads to energy debt and loss of lean body mass, emphasizing the need for early medical nutrition therapy, preferably within 48 hours.

Q3 How would you assess and screen the nutritional risk for this patient?

Nutritional assessment is done to evaluate patient's nutritional status in detail and screen those at high nutritional risk.[7,8] This must be done at admission by dedicated staff and comprises:

- Complete nutrition history
- General clinical assessment (includes patient's account of their medical history, report of unintentional weight loss or decrease in physical performance before ICU admission, physical examination, general assessment of body composition, and muscle mass and strength)[7]

  To assess muscle mass: Ultrasound, computerized tomography scan, or bioelectric impedance analysis (BIA)[7]

  To assess muscle strength/function: Handgrip dynamometry[7]
- Anthropometric data (weight, BMI, skinfold thickness, and mid-arm circumference)
- Special cohorts such as trauma, burns, and malignancy have higher nutrition needs. Also at risk are patients staying in the ICU for >2 days, requiring mechanical ventilation, with infection, who are underfed for >5 days, and/or presenting with a severe chronic disease.[7]
- *Laboratory parameters and serum biomarkers*: Visceral proteins (serum albumin, prealbumin, and transferrin), serum zinc, urinary creatinine, cholesterol, trace elements, and vitamin levels.
- Use of *screening tools* and *assessment* are recommended in the daily practice.[7]

• Nutritional Risk Screening (NRS) 2002 • Malnutrition Universal Screening Tool (MUST) score • Nutritional Risk in Critically Ill (NUTRIC) score	• Subjective Global Assessment (SGA) • Mini Nutritional Assessment (MNA)

Thorough assessment of the critically ill helps in deciding the strategy of nutritional support and improves patient outcomes. Reevaluate the nutrition goals with changes in patients' conditions. Hence, energy targets are dynamic!

Q4 What variables are included in the NUTRIC score? How do you interpret it?

The NUTRIC score is a novel risk assessment tool proposed by Heyland et al. to stratify critically ill patients for their nutritional risk, based on disease severity.[9]

It includes age (in years), number of comorbidities, days from hospital to ICU admission, Acute Physiology and Chronic Health Evaluation II (APACHE II), Sequential Organ Failure Assessment (SOFA) score, and interleukin-6 (IL-6) levels **(Table 1)**. The sum of points is done to derive final score. If IL-6 is not included, it is referred to as modified NUTRIC (mNUTRIC) score.

0–5 points = Low NUTRIC		0–4 points = Low mNUTRIC
6–10 points = High NUTRIC	← Benefit most from nutrition	5–9 points = High mNUTRIC

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TABLE 1: NUTRIC score and the variables included.[9]

Variables included in NUTRIC score	*Scoring system (points)*			
	0	*1*	*2*	*3*
Age (years)	<50	50–74	≥75	
Comorbidities	0–1	≥2		
Days from hospital to ICU admission	0	≥1		
APACHE	<15	15–19	20–27	≥28
SOFA	<6	6–9	≥10	
IL-6 levels (pg/mL)	<400	≥400		

(APACHE: Acute Physiology and Chronic Health Evaluation; ICU: intensive care unit; IL-6: interleukin-6; NUTRIC: Nutritional Risk in Critically Ill; SOFA: Sequential Organ Failure Assessment)
Source: Heyland DK, Dhaliwal R, Jiang X, et al. Identifying critically ill patients who benefit the most from nutrition therapy: the development and initial validation of a novel risk assessment tool. Crit Care. 2011;15:R268. doi: 10.1186/cc10546.

Q5 What would be the preferred route of nutrition? What are its advantages and disadvantages?

It is recommended to initiate early EN in critically ill patients rather than early parenteral nutrition (PN).[7] EN uses the gastrointestinal tract (GIT) to supply nutrients.

Enteral nutrition is preferred over PN due to its beneficial effect on GI barrier and immune functions. Stick by the adage: *"If the gut is functional, use it or lose it!"*

Advantages of EN:[3]
- Physiological route
- Cheap and easy to administer
- No venous access required
- Safe and low risk of infection
- Prevent gut stasis and stress ulceration
- Improved gut mucosal integrity and prevent bacterial translocation (barrier function of the gut)
- Maintenance of intestinal microbiome diversity
- Promotion of adequate immunoglobulin A (IgA) secretion
- Enhanced immune responsiveness
- Decreased infectious complications and shorter LOS[1]

Disadvantages of EN:[3]
- Dependent on intact GI function
- Feeding intolerance
- Risk of aspiration pneumonia
- Frequent interruptions and suboptimal delivery rate

Indications of Early Enteral Nutrition
Early EN is indicated in:[7]
- Patients receiving extracorporeal membrane oxygenation (ECMO)
- Patients with TBI/stroke (ischemic or hemorrhagic)/spinal cord injury
- Patients with severe acute pancreatitis
- Patients after gastrointestinal surgery
- Patients after abdominal aortic surgery
- Patients with abdominal trauma when the continuity of the GIT is confirmed/restored
- Patients receiving neuromuscular blocking agents
- Patients managed in prone position
- Patients with open abdomen
- Regardless of the presence of bowel sounds unless bowel ischemia or obstruction is suspected
- Patients with diarrhea

Q6 When should enteral feeding be delayed? In what cases should it be started at low doses?

Enteral nutrition should be delayed in:[7]
- Uncontrolled shock (i.e., hemodynamic and tissue perfusion goals are not reached). EN, by increasing mesenteric blood flow, can elevate the oxygen demand on the intestine, thereby posing risks of bowel ischemia, necrosis, and perforation in hemodynamically unstable patients.[10]
- Uncontrolled life-threatening hypoxemia, hypercapnia, or acidosis
- Active upper GI bleed
- Overt bowel ischemia
- High-output intestinal fistula
- Abdominal compartment syndrome
- Gastric residual volume (GRV) >500 mL/6 hours

Hemodynamic stability must be ensured before initiating EN. In patients with high vasopressor supports, EN predisposes to the risk of bowel necrosis and mesenteric ischemia.

Low-dose EN is preferred in:[7]
- Patients receiving therapeutic hypothermia and increasing the dose after rewarming
- Patients with intra-abdominal hypertension without abdominal compartment syndrome
- Patients with acute liver failure when acute, immediately life-threatening metabolic derangements are controlled with or without liver support strategies, independent on grade of encephalopathy.

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Q7 How to achieve enteral access?

Gastric access [via nasogastric tube (NGT) or orogastric tube (OGT)] should be used as the standard approach to initiate EN.[7] This is easiest to insert.

Percutaneous endoscopic gastrostomy (PEG) tube is indicated in patients for long-term feeding (>30 days) with moderate to severe protein-calorie malnutrition.

Postpyloric, mainly jejunal feeding [nasojejunal tube (NJT) and feeding jejunostomy (FJ)] can be performed in patients deemed to be at high risk for aspiration and this cohort includes those unable to protect their airways, support with mechanical ventilation, old age (>70 years), reduced level of consciousness, poor oral care, inadequate nurse:patient ratio, supine positioning, neurologic deficits, gastroesophageal reflux, transport out of the ICU, and use of bolus intermittent EN.[7]

Nasojejunal tube is placed with the assistance of endoscopy or fluoroscopy. Confirmation of correct position is mandatory before feeds are administered.

Q8 What are the nutritional requirements of this patient?

To meet the nutritional requirements of the critically ill patients, the energy and protein targets must be identified using the following (in decreasing order of accuracy):[7]

- *Indirect calorimetry (IC):* Most accurate evaluation of patient's EE
- Using VO_2 (oxygen consumption) from pulmonary arterial catheter or VCO_2 (carbon dioxide production) derived from the ventilators

$$EE = 3.941 \times VO_2 + 1.11 \times VCO_2 \times 1{,}440 \rightarrow \text{"}\textit{Weir Formula}\text{"}$$

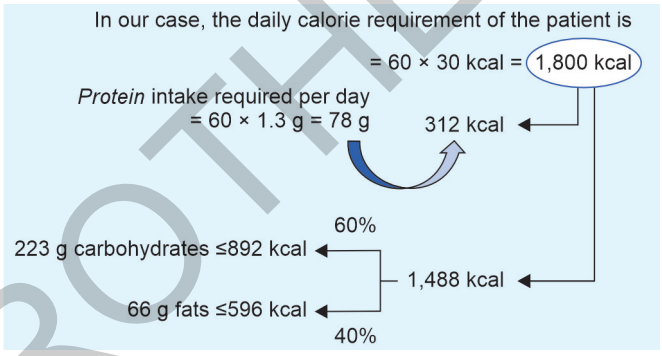
- Predictive equations such as the Harris–Benedict, Ireton–Jones, Penn State, Mifflin–St Jeor equations, or a basic weight-based equation *(25–30 kcal/kg/day)* to estimate energy requirements.[6,11]

  These could be inaccurate (up to 60%), leading to over- or underevaluation of the needs and inducing over- or underfeeding!

  Hypocaloric nutrition (Not more than 70% of EE) should be administered in the early phase of acute illness. After day 3, energy delivery can be increased up to 80–100% of measured EE. During critical illness, 1.3 g/kg protein equivalents per day can be delivered progressively.[7] Remaining calories are split between carbohydrates and fats as 60:40. Micronutrients and electrolytes are supplemented accordingly.

Other substrates:[7]

- Additional enteral glutamine (GLN) is indicated in burns patients who suffer excess exudative losses (0.3–0.5 g/kg/day for 10–15 days) and trauma patients (0.2–0.3 g/kg/day for 5 days).
- EN enriched with omega-3 fatty acids within nutritional doses can be administered, but was seen to yield no significant advantage.
- Status of micronutrients (trace elements and vitamins) needs to be established and replenished, if deficient.
- Benefit of antioxidants is not clear.



Q9 What regimen/protocol of feeding would you follow in this patient?

- Following hypocaloric nutrition (Not more than 70% of EE) in the early phase of acute illness, there is a *progressive implementation of isocaloric nutrition* (80–100% of EE) after day 3.

  Enteral feeding to deliver a moderate amount of nonprotein calories (40–60% of calculated caloric requirements) to critically ill adults was not associated with lower mortality than that associated with planned delivery of a full amount of nonprotein calories (80–100% of calculated requirement).[12]
- *Lower volume trophic feeds versus full feeds:* While trophic feeding may improve gastrointestinal tolerance, it does not significantly impact overall clinical outcomes in critically ill patients. EDEN randomized trial, where trophic enteral feeding (lower volume) was compared to full enteral feeding for the first 6 days reiterated the same. No significant difference was observed in ventilator-free days between the two groups.[13]
- *Bolus versus continuous feeds:* There are advantages and disadvantages of both the regimes **(Table 2)**, but continuous feeds are preferred. Bolus feeds significantly increase gastric volume and superior mesenteric artery blood volume in critically ill patients. Also, they provide a greater stimulus for protein synthesis.[7]

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TABLE 2: Advantages and disadvantages of continuous and bolus feeds.[14]

	Advantages	***Disadvantages***
Continuous feeds	• May improve gastric tolerance[14] • Decreased risk of aspiration • Increased time for nutrient absorption	• Feeding pump required • May restrict ambulation • More expensive
Bolus feeds	• More physiological • No feeding pumps required • Inexpensive, easy to administer • Limits feeding time • Patient free to ambulate	• Increase risk of aspiration • Hypertonic, high fat, or high fiber formulas may delay gastric emptying or result in osmotic diarrhea • Greater stimulus for protein synthesis

Source: Ichimaru S, Amagai T. Intermittent and Bolus Methods of Feeding in Critical Care. Germany: Springer; 2014. pp. 1-17.

Start @ 30 mL/h × 4 hours
Increase by 30 mL after 4 hours till goal is reached
1st to 4th hour = 30 mL/h
5th to 8th hour = 60 mL/h
9th to 12th hour = 90 mL/h
(Most enteral formulas contain 1–2 kcal/mL)

- *Gravitation bags versus feeding pumps:* Feeding pump provide accurate volumetric delivery, have audio and visual alarms for tube occlusion, air in tubing and also protects from overinfusion. The use of enteral feeding pump is now a standard-driven process.[15]
- At any sign of intolerance, utilize appropriate strategies to optimize EN delivery. These include:[7]
  - Using postpyloric feeding in patients with gastric feeding intolerance/high risk for aspiration
  - Vomiting/GRV monitoring
  - Using prokinetic drugs (erythromycin and metoclopramide)
  - Considering intra-abdominal pressure to initiate and maintain EN
  - Monitoring of gastrointestinal function with the use of scores such as the Gastrointestinal Dysfunction Score (GIDS)
- Physical activity (exercise) may improve the beneficial effects of nutritional therapy by preventing anabolic resistance, reducing morbidity and improving the level of activity.[7]

Avoid overfeeding in acute phase of critical illness, but focus on meeting protein needs early.

Q10 What are the different enteral feeds?

Based on Method of Preparation

- *Blenderized food:* Typically prepared in the kitchen by blending food/meals into a liquid feed. It may be completely prepared from home-made food or a combination of food and standard formula. This is more economical than scientific feeds, hence favored in developing countries.
- *Scientific food*

Limitations of blenderized feed:[8]

- High microbial contamination
- Inconsistency in amount and supply of nutrients
- High osmolality and viscosity
- Possibility of blockage of the feeding tube

Potential contraindications of blenderized feed:[8]

- Acute illness or immunosuppression (greater risk of infection from contaminated food)
- Fluid restrictions (may be difficult to meet nutrition needs)
- Continuous feedings (requires formula to be unrefrigerated for several hours)

Based on Composition of Diet

- *Polymeric:* Whole protein as the nitrogen source—need intact functioning bowel to break them down
- *Oligomeric:* Proteins are hydrolyzed to peptides (peptide based), amino acids (elemental), or combination (semi-elemental)—readily absorbed
- *Disease-specific:* Content varies in terms of caloric density, macronutrient distribution, amount/type of fiber, vitamin, mineral, and electrolyte composition
- *Immunomodulating:* Contains pharmacologically active substances (arginine, glutamine, ω-3 fatty acids, and antioxidants) to modulate immune function
- *Modular products:* Contain predominantly single nutrient.

Q11 What all do we need to monitor in ICU while feeding the patient via enteral route?

Medical nutrition therapy needs to be monitored so as to check:[7]

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Gastric intolerance, overfeeding, and underfeeding	***Re-feeding***
• Check glucose levels 4 hourly for first 2 days after initiation of nutrition. Reduce frequency thereafter, as a stable phase is reached • Insulin therapy if (glucose) >180 mg/dL • GRV measurement to identify intolerance to EN during initiation and progression of EN • Use of prokinetic agents (IV erythromycin or metoclopramide) in case of gastric feeding intolerance • EN delayed when GRV is >500 mL/6 h	• Electrolytes (Na^+, K^+, Cl^-, Mg^{2+}, PO^{4-}) measured at least once daily for the first week • If refeeding hypophosphatemia (<0.65 mmol/L or a drop of >0.16 mmol/L), measure electrolytes two to three times/day and supplement accordingly. Restrict feeds for 48 hours and gradually increased

Gastric intolerance (measured by GRV) and refeeding syndrome are the main complications of EN, hence we must monitor for these.

TABLE 3: Complications of enteral nutrition.[17]

Tube-related mechanical complications	• Tube malposition/obstruction • Accidental dislodgment of tube • Breakage of the feeding tube • Leakage of the feeding tube • Erosion and ulceration near the site of insertion • Intestinal obstruction • Bleeding
Infectious complications	• Infection at the site of tube insertion • Aspiration pneumonia • Ear and nasopharyngeal infection • Infective gastroenteritis with diarrhea • Peritonitis
Gastrointestinal complications	• Nausea and vomiting • Diarrhea • Constipation • Cramps and bloating • Regurgitation and aspiration
Metabolic complications	• Refeeding syndrome

Source: Adeyinka A, Rouster AS, Valentine M. Enteric Feedings. Treasure Island (FL): StatPearls Publishing; 2022.

Q12 Is there a role of supplemental PN along with EN?

In case the EN is unable to achieve the calorie/protein targets due to feeding intolerance or common interruptions (generally seen in first week of ICU stay), it may lead to macronutrient deficiency. PN can then be supplemented along with EN, preferably early (day 4–7). However, all the strategies to maximize EN tolerance must be exhausted prior to starting PN.[7,16]

Q13 What are the complications of enteral feeding?

Complications associated with EN are given in **Table 3**.[17]

Refeeding Syndrome

Refeeding syndrome is defined as the potentially fatal shifts in fluids and electrolytes that may occur in malnourished patients receiving artificial refeeding (more common with EN than PN). These shifts result from hormonal and metabolic changes. The hallmark biochemical feature of refeeding syndrome is hypophosphatemia. However, the syndrome is complex and may also feature abnormal sodium and fluid balance; changes in glucose, protein, and fat metabolism; thiamine deficiency; hypokalemia; and hypomagnesaemia.[18,19]

Laboratory investigations (electrolytes monitoring, glycemia, and liver function tests) are important to detect it.

Patients at risk for refeeding syndrome:

- Chronic alcoholism
- Anorexia nervosa
- Postoperative patients
- Elderly patients
- Prolonged fasting
- Morbid obesity associated with profound weight loss
- Malabsorption syndrome: Cystic fibrosis, inflammatory bowel disease, and short bowel syndrome.

We must be conservative while initiating calories in patients at risk for refeeding syndrome. Electrolytes must be monitored and replenished. Vitamin supplementation helps too.

Q14 What are the specific consideration with regards to nutritional therapy in special cohorts?[7]

There are certain special cases where the medical nutrition therapy needs special attention **(Table 4)**.

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TABLE 4: Enteral nutrition (EN) therapy in special cases.[7,20]

Special cohort	*Considerations for EN*
Nonintubated patients	• Oral nutrition is the preferred route • If unable to reach energy targets, consider oral nutritional supplements before switching to EN
Surgical patients	• In patients after abdominal or esophageal surgery, early EN preferred over delayed EN • If surgical complications after abdominal or esophageal surgery present and patient is unable to eat orally, EN [rather than parenteral nutrition (PN)] should be preferred unless discontinuity or obstruction of gastrointestinal tract, or abdominal compartment syndrome is present • In the case of an unrepaired anastomotic leak, internal or external fistula, a feeding access distal to the defect should be aimed for to administer EN if distal feeding access is not achieved, EN should be withheld and PN may be commenced
Burns patients	• Profound stress response • Early enteral nutrition with high-carbohydrate formulas • In patients with burns >20% body surface area, additional enteral doses of glutamine (GLN) (0.3–0.5 g/kg/d) should be administered for 10–15 days as soon as EN is commenced
Septic patients	• Early and progressive EN should be used in septic patients after hemodynamic stabilization • If contraindicated, EN should be replaced or supplemented by progressive PN
Malignancy patients[20]	• High risk of malnutrition • Regular evaluation of nutritional status to modify/guide medical nutrition therapy • Oral and EN should be the preferred routes • Postpyloric route of EN if risk of gastroparesis • Supplemental PN to avoid caloric and protein debt • Scrutinize closely for refeeding syndrome • Evaluate micronutrient deficiencies • Careful insertion of the NG tube in the presence of thrombocytopenia or coagulative disorders • Consider diets enriched with specific supplements (e.g., glutamine, ω-3 fatty acids, and immunonutrition formulas) in particular clinical scenarios (e.g., gut recovery after chemotherapy, long-term PN requirements, liver dysfunction, and chronic inflammatory state)
Obese patients	• Energy intake should be guided by indirect calorimetry (IC) [if IC unavailable, energy intake based on "adjusted body weight (ABW)"] • Protein delivery should be guided by urinary nitrogen losses or lean body mass determination (if unavailable, protein intake = 1.3 g/kg "adjusted body weight"/day)

Sources:
Singer P, Blaser AR, Berger MM, et al. ESPEN practical and partially revised guideline: Clinical nutrition in the intensive care unit. Clin Nutr. 2023;42:1671-89. doi: 10.1016/j.clnu.2023.07.011.
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CONCLUSION

Nutritional therapy in critically ill patients is of utmost importance as they are at risk of malnutrition due to hypercatabolism during the acute phase and appropriate nutrition helps to expedite their recovery. It must be initiated early preferably via the enteral route, with both macronutrients as well as micronutrients being supplemented. It is equally important to be vigilant of the complications like gastric intolerance and refeeding syndrome, which can be fatal if not monitored.

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