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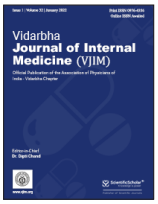

Review Article

Nutritional Practices in Critically Ill Patients – A Review

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ABSTRACT

Nutrition therapy during critical illness has been a focus of recent research, with a lot of publications accompanied by two updated international clinical guidelines. There have been many trials with conflicting results making the translation of this evidence into practice challenging. This review article aims to provide clinicians with a comprehensive summary of the latest nutritional practices in critically ill patients.

Keywords: Nutritional Practices, Criticall Ill Patients, Enteral Feeds

THE METABOLIC RESPONSE TO CRITICAL ILLNESS

There are complex metabolic, hormonal, and immunological changes that occur during a critical illness. In 1942, Cuthbertson described two distinct metabolic phases during acute illness—the 'ebb' or early shock phase, followed by the 'flow' or catabolic phase.[1] In brief, the 'ebb' phase is characterised by haemodynamic instability and hormonal changes (including insulin resistance) to prioritise the delivery of energy substrates to vital tissues.[1,2] The 'flow' phase involves the breakdown of tissue (including lean muscle tissue) to provide substrates to cover the immediate needs for the 'fight or flight' response and to reduce the risk of bleeding and infection.[3] More recently, a third, anabolic recovery phase has been described.[4] It is during this recovery phase when resynthesis of lost tissue can take place and the body may be more metabolically able to process delivered nutrients [Figure 1].[4]

2019 European Society of Parenteral and Enteral Nutrition (ESPEN) critical care guideline describes the following stages of critical illness [Figure 1]:

1. Acute early phase ICU day 1–2
2. Acute late phase ICU day 3–7
3. Recovery phase after ICU day 7.

Initially, it was thought that aggressive nutrition in the early phase of critical illness would improve outcome but evidence from recent RCTs does not support this finding.[5-8]

In fact, harm was observed in the early parenteral nutrition (PN) completing enteral nutrition in adult critically ill patients (EPaNIC) trial, the largest nutrition trial in critical illness.[7] In a study of 4640 mixed ICU patients (n = 2818 [61%] cardiac surgery patients) who were eligible to receive EN, late initiation of PN (started on day 8 of the ICU stay) led to an increase in the proportion of patients discharged alive and earlier from ICU and hospital (hazard ratio [HR] 1.06; 95% CI 1.00–1.13; P = 0.04 for both) when compared to PN commenced within 48 h of ICU admission.[7] There was a reduction in infectious complications (22.8% vs. 26.2%, P = 0.008), cholestasis, duration of mechanical ventilation, duration of renal replacement therapy, and healthcare costs in the group that had late initiation of PN.[7] Due to endogenous glucose production < 100% energy, expenditure should be targeted in these patients.

GUIDELINES FOR NUTRITIONAL THERAPY IN CRITICALLY ILL PATIENTS

At present, there are around four international clinical practice guidelines for nutritional therapy in critically ill patients [Tables 1 and 2].[9-12]

NUTRITIONAL REQUIREMENTS

Nutritional requirements for every individual should be estimated to select the appropriate formulation and rate of administration. Indirect calorimetry is by far the best method for resting energy expenditure (REE) measurement. As calorimeters are not widely available, predictive equations are used to estimate REE.

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DOSING WEIGHT

Appropriate body weight must be estimated to calculate caloric and protein intake before prescribing enteral or PN.

1. Underweight patients (BMI <18.5) use current weight as initial dosing weight. If ideal body weight is used then there could be a risk of excessive initial calorie intake and refeeding syndrome
2. Patients with normal body weight (BMI 18.5–24.9) and overweight patients (BMI 25–29.9) current weight should be used as dosing weight. An effort should be made to subtract the estimated weight of any peripheral oedema
3. For obese patients (BMI >30), guidelines recommend the use of current weight and the use of the Penn State University 2010 predictive equation. The purpose of adjusting the dosing weight of patients who are obese is to account for the absence of metabolic requirements by fat tissue.

- Dosing weight = IBW + 0.4 (ABW - IBW)
- IBW is Ideal body weight
- ABW is Actual body weight.
  - lBW (men) = 50+2.3 * (height over 60 inches)
  - lBW(women) = 45.5+2.3 * (height over 60 inches).

For patients who are volume overloaded (e.g., liver failure), an estimate of dry body weight should be used.

CALORIES

In the 1st week of critical illness, providing fewer calories than needed to meet energy needs may have some beneficial effects (less GI intolerance and fewer infections).

- In one randomised trial of 1000 mechanically ventilated patients with acute lung injury (EDEN), low calorie feeding (mean caloric intake 400 kcal/day) for the first 6 days, compared with full enteral feeding (mean caloric intake 1300 kcal/day), did not change ventilator-free days, 60-day mortality or infectious complications, but was associated with less gastrointestinal intolerance[13]
- In another randomised trial of 894 critically-ill patients (medical, surgical, and trauma) (PermiT), compared with standard enteral feeding (70–100% of calculated caloric requirements), 14 days of permissive underfeeding were not associated with a difference in mortality, gastrointestinal intolerance, infectious complications or length of hospital stay.[14] This effect was maintained inadequately nourished as well as malnourished critically ill patients.[15]

A safe starting point for most critically ill patients should be approximately 8–10 kcal/kg/day.[13] It should be gradually escalated to a goal of 25–30 kcal/kg/day after 1 week once the patient is stable.

PROTEIN

Guidelines indicate that protein requirements increase as the illness becomes more severe.

Mild – Moderate illness – 0.8–1.2 g/kg protein per day is given.

Critically ill patients – 1.2–1.5 g/kg protein per day is recommended.

Patients with severe burns may benefit from protein intake up to 2 g/kg/day.

PROTEIN DOSE/TIMING AND CLINICAL OUTCOMES

In RCTs comparing higher versus lower protein dose in critical illness, no benefit has been shown in higher protein dose, although most have been underpowered to demonstrate an effect on clinical outcomes.[8,16-18]

Timing of protein delivery may also influence clinical outcomes. In the largest study (n = 2253), early protein delivery (>0.7 g/kg/day vs. ≤0.7 g/kg/day) was associated with increased survival (adjusted HR 0.83, 95% CI 0.71–0.97, P = 0.017).[19] Contrary to these findings, in *post hoc* secondary analysis of the EPaNIC trial, during early ICU stay, a cumulative protein dose, rather than the cumulative glucose dose, was associated with delayed ICU discharge.[20] More RCTs are required to comment on the appropriate amount and timing of protein delivery in critically ill patients.

ENTERAL NUTRITION

The present international nutrition guidelines uniformly recommend the preferential use of EN in critically ill patients who are unable to maintain sufficient oral intake.[10] EN can be administered through a nasogastric or nasojejunal tube. If the need for EN will potentially exceed 4 weeks, placement of percutaneous endoscopic gastrostomy/jejunostomy is recommended.[21] Contraindications for EN according to the European Society Intensive Care Medicine (ESICM) Clinical Practice Guidelines particularly include haemodynamic instability (escalation of or high vasopressor medication and increased lactate) and GI intolerance from minor to major symptoms, for example, gastric residual volume (GRV) >500 mL/6 h or acute gastrointestinal injury grade >2. The early initiation of EEN within 24–48 h is uniformly recommended by the guidelines in the critically ill patient who is unable to maintain sufficient oral intake.[10,21]

COMBINATION OF EN WITH PN

The progression of EN up to calorie/protein target is often prevented by feeding intolerance or common interruptions of EN.[22] Thus, particularly in the patient's first ICU week,

EN alone may lead to macronutrient deficiency.[23-25] To avoid large cumulative energy and protein deficits, EN and PN may be combined, either early during the patient's ICU course (combined EN+PN) strictly on a case to case basis, or after several days once EN is proven to be insufficient or unfeasible (supplementary PN).[26] The ESPEN guideline recommends as good practice point: 'PN should not be started until all strategies to maximise EN tolerance have been attempted' and 'In patients who do not tolerate full dose EN during the 1st week in the ICU, the safety and benefits of initiating should be weighed on a case-by-case basis.'

FORMULA FEEDS

In most critically ill patients, standard polymeric formulas for EN should be used according to the guidelines.[9,21] For PN, all-in-one bags should be preferred.[9]

ENERGY-DENSE VERSUS STANDARD FORMULA

In a recent RCT, scintigraphic measurement of GRV at 120 min was greater in the group with the energy-dense formula, intestinal energy delivery and glucose absorption were not improved.[27] Energy dense formulas should be used in patients with fluid restrictions and malnourished patients.

PREDIGESTED FEEDS

Furthermore, previously known as chemically defined, semi elemental or elemental differs from standard enteral nutrition in that the protein is hydrolysed to short chain peptides and the carbohydrates are in a less complex form. There is currently insufficient evidence for the use of pre-digested enteral nutrition. It may be beneficial in patients with thoracic duct leak, chylothorax, chylous ascites, malabsorptive syndromes unresponsive to supplementation of pancreatic enzymes, and persistent diarrhoea due to intolerance to standard enteral nutrition.

SYNBIOTICS

It refers to the combination of both probiotics and prebiotics, containing *Lactobacillus* organisms alongside fibre. Synbiotics reveal trophic effects in the colon, focusing on the preservation of the microbiome, promoting mucosal regeneration in balance with the microenvironment. The A.S.P.E.N. guidelines suggest that a commercial mixed fibre formula should not be used routinely in the adult critically ill patient prophylactically to promote bowel regularity or prevent diarrhoea.[9] The German DGEM guidelines recommend probiotics for patients with severe trauma and those undergoing liver transplantation.[28]

SUPPLEMENTATION WITH SPECIFIC NUTRIENTS

To summarise

- The guidelines currently do not recommend pharmacotherapy with micronutrients in the general critically ill patient population
- Proven micronutrient deficits need to be treated
- Micronutrients must be supplemented whenever PN is administered to a patient
- While arginine and glutamine have no indication in the critically ill with special regard to those with organ failure, the enteral and parenteral supplementation of fish oil remains a matter of debate.

MONITORING - ADEQUACY AND TOLERANCE

Up to 500 ml of GRV should be used as cutoff as per recommendations by the ASPEN guidelines 2016.[2] Metoclopramide or erythromycin can be used in case of intolerance. In the Indian scenario, there is a marked difference of opinion regarding the cutoff value for GRV intolerance. To further clarity, a suggested approach would be to keep GRV cutoff between 300 and 500 ml in high-risk patients (who cannot be assessed and are unconscious or on a ventilator or are on bolus/intermittent feeds, in such patients continuous feeding is recommended. In patients who are on continuous feeding, frequent GRV monitoring may not be required [Table 1].

ENTERAL NUTRITION IN SPECIAL CONDITIONS

Haemodynamically unstable patients

Critically ill patients may be having reduced peristalsis, gastrointestinal hypoperfusion, mesenteric ischemia, poor neurological status, and decreased oral intake. In such patients, enteral nutrition may trigger intestinal ischemia. Hence, monitoring of gut function is important before initiating enteral nutrition. The guidelines are currently not clear when to start enteral nutrition in haemodynamically unstable patients. In haemodynamically unstable patients, enteral nutrition preferably trophic feeds (10–20 ml/h) should be started when the patient is on declining or stable doses of vasopressors and adequately volume resuscitated.

Undernourished patients

As per DGEM guidelines, the same energy and protein targets may be used, as in other patients, and should be started early. If enteral nutrition is not possible then an early hypocaloric PN should be administered (75% of caloric target, protein 1 g/kg/d).[28] A more aggressive approach is

not recommended to avoid GI and metabolic intolerance and potential complications such as acute hyperalimentation, refeeding syndrome, or increased rates of infection.[9] In contrast, A.S.P.E.N. suggests a rapid progression of preferably EN with the aim to reach the target within 24–48 h under careful monitoring. Within 48–72 h, >80% of energy and protein goals should be achieved.[9] However, these recommendations are debatable.

Obese patients

Hypocaloric high-protein nutrition may be achieved through enteral or parenteral protein supplements. In addition, patients who experienced weight loss in the past months or who underwent bariatric surgery should receive vitamin and trace element supplements with a special focus on thiamine.[9,28]

Elderly critically ill patients

ESPEN recommends a hypercaloric and high-protein supplementation (30 kcal/kg/d energy and ≥1 g/kg/d protein) in elderly critically ill patients.[29] Hydration should be well managed. The DGEM and A.S.P.E.N. do not provide special recommendations for elderly ICU patients due to lack of sufficient data.

Critically ill patients with central nervous diseases

Early enteral nutrition should be initiated in patients with head trauma, haemorrhagic or ischaemic stroke, and spinal trauma. Stroke patients are vulnerable to swallowing problems due to cognitive and perspective defects and thus should be screened often. If oral nutritional support is not possible due to impaired consciousness or dysphagia, enteral nutrition through a nasogastric tube should be initiated within 72 h. Higher protein supplementation of 1.5–2.5 g/kg/d should be considered in young patients with head trauma due to increased nutritional risk due to long ICU stays and profound muscle catabolism.[9,10] The A.S.P.E.N. suggests the administration of formulas including arginine and omega-3-fatty-acids.[9] If there is an additional risk of aspiration, EN boles should be avoided, a post-pyloric tube should be placed, the head should be elevated by 30° and prokinetics should be considered.[9,10] PN is another option for these patients, especially in cases with pre-existing malnutrition or if an EN is not sufficient to ensure adequate nutrition and hydration.[10]

Critically ill trauma and burn patients

For patients with burns, indirect calorimetry is preferred for estimating calorie needs. The ESPEN recommends — contrasting the DGEM — enteral glutamine to be supplemented (0.3–0.5 g/kg/d) for 10–15 days[10] and the A.S.P.E.N. a higher dosage of protein (1.5–2 g/kg/d).[9] According to the DGEM, protein losses through drains and dressings should be compensated. For trauma patients, the ESPEN recommends glutamine (0.2–0.3 g/kg/d) for the first 5 days (10–15 days if wound healing is complicated).[10] Immunomodulating solutions with fish oil and arginine may be considered for patients after severe trauma according to the A.S.P.E.N.[9]

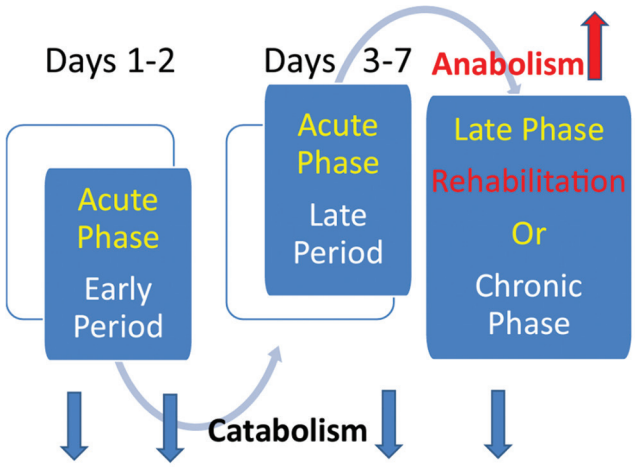

Figure 1: Description of the acute and late phases following infection/stress/injury.

Critically ill patients with respiratory diseases

EN should not be administered to patients with life threatening hypoxia, hypercapnia, and acidosis as a sign of respiratory decompensation. EN can be commenced in patients with stable and compensated respiratory failure.[10,11] Fluids should be restricted to avoid aggravating overhydration and oedema. Therefore, energy-dense formulae (1.5–2 kcal/mL) are recommended.[9] Hypophosphatemia is a common (and commonly unrecognised) problem and may lead to weakness of respiratory muscles and weaning-failure. Therefore, phosphate should be monitored and replaced. Hyperalimentation should be avoided because lipogenesis increases CO2 production.[9] Early enteral nutrition should be used in patients in the prone position.

Nutrition in critically ill COVID-19 patient

According to Ochoa *et al.*, COVID-19 patients present with three different phenotypes of nutrition risk: (1) The frail older patient, (2) the patient with severe ongoing chronic illness, and (3) the patient with severe and morbid obesity.[30]

So far, no RCTs exist regarding nutrition in COVID-19 patients. Instead, the ESPEN and A.S.P.E.N. have published expert statements as an adaptation of their

Table 1: Summarises all four of them.

Guideline	Energy requirements	Protein requirements	Commencement of EN	Commencement of PN
ASPEN/SCCM (2016)	Use IC (quality: Very low} In the absence or IC use 25–30 kcaL/kg/day (EC) Obesity: Hypocaloric nutrition, 65–70% measured requirements by IC. If no IC, BMI 30-50=11–14 kcal/kg ABW; BMI. 50=22–25 kcal/kg IBW/day (EC)	1.2–2 g/kg/day (quality: very low) Obesity. High protein BMI 30–40=2.0 g/kg IBW/day; BMI>40=up to 2.5 g/kg IBW/day (EC)	Early EN (24–48 h) (quality; very low) patients at low nutrition risk, well nourished and/or with low disease severity do not require specialised nutrition therapy over the 1st week in ICU (EC). Patients at high nutrition risk or severely malnourished, EN should advance to goal as quickly as tolerated for 24–48 h (monitor for refeeding)	Exclusive PN for patients at low nutrition risk, withhold for first 7 days (quality. very low). For patients at high nutrition risk or severely malnourished start PN as soon as possible (EC) Supplemental PN should be considered after 7–10 days if unable to meet>60% of energy and protein requirements by EN. (quality moderate)
European Society Intensive Care Medicine clinical practice guidelines (2017)	Nil	Nil	Early EN should be prescribed rather than delaying EN (low quality evidence)	Nil
ESPEN (2019)	Use IC (Grade B) In the absence of IC use VO2 for the VCo2 predictive equations (Grade 0) obesity; if no IC, 20–25 Kcal/kg ABW/day (Grade 0)	1.3 g/kg/day delivered progressively (Grade 0) obesity; 1.3 g/kg/day ABW/day (grade 0)	Early EN (<48 h) (Grade A) hypocalciuric nutrition (<70% of EE) in the early acute phase (ICU day 1–3) (Grade B) If using IC- isocaloric nutrition (80–100% EE) can be progressively implemented after day 3 (Grade 0) if using predictive equations hypocaloric nutrition (<70% of EE) for the 1st week (Grade B)	Exclusive PN within 3–7 days (Grade B) for severely malnourished patients, consider early and progressive PN (Grade 0) Supplemental PN should be considered on a case to case basis (Grade 0)

existing guidelines.[31,32] On admission to ICU, nutritional assessment is mandatory. While EN may be performed even in the prone position, Martindale *et al*. recommend a lower threshold for switching to PN in cases of intolerance, high risk of aspiration, or escalating vasopressor support.[32] In the case of ARDS, Thibault *et al*. have recommended the use of EN enriched with omega-3 fatty acids and for PN fish oil-enriched intravenous fat emulsions.[33] In case of respiratory decompensation, enteral nutrition should be avoided.

Nutrition in patients after GI surgery

Early enteral nutrition within 24–48 h should be started if the GI tract is functional.[9,10] After abdominal surgery with a complicated course, ESPEN recommends starting early supplemental PN.[10] Patients with open abdomen should receive an EEN (24–48 h post-injury) in the absence of bowel injury.[1,2] Protein losses through drains and dressings should be compensated in the form of enteral protein supplements or parenteral albumin (15–30 g protein/litre exudate).[1,9]

Nutrition in patients with liver failure

Indirect calorimetry should be used to assess REE. If not available, the patient's dry weight shall be used to estimate energy and protein targets and ×1.3 resting EE should be supplied.[34] A generalised protein restriction is not recommended to prevent muscle degradation, which contributes to the development of hepatic encephalopathy.[9] In patients with encephalopathy and high ammonia, the protein supplementation can be delayed for 24–48 h[34] because of insufficient evidence for the use of branched chain amino acids, normal EN formula should be used.[9,34]

Table 2: The present guideline recommendation regarding micronutrients, vitamins, and antioxidants.

Substrate	DGEM	ESPEN	A.S.P.E.N
Micronutrients (trace elements, vitamins)	A patient should receive vitamins and trace elements, if EN cannot meet daily needs and if supplemental PN is required to ensure the desired calorie and protein intake according to the disease phase and individual metabolic tolerance	To enable substrate metabolism, micronutrients should be provided daily with PN	N/A
Vitamin D	Patients may receive pharmacotherapy with Vitamin D when they have a severe Vitamin D deficiency	In critically ill patients with measured low plasma levels, a high dose of Vitamin D3 (500,000 UI) as a single dose can be administered within a week after admission	N/A
Antioxidants/ Selenium	Patients shall not receive pharmacotherapy with Selenium patients should not receive routinely pharmacotherapy with zinc, alpha-tocopherol, Vitamins A and C, or with a combination of those	Antioxidants as high dose monotherapy should not be administered without proven deficiency.	Critically ill patients requiring specialised nutrition therapy may be provided a combination of antioxidant vitamins and trace minerals in doses reported to be safe Selenium, zinc, and antioxidant supplementation in sepsis at this time due to conflicting studies cannot be recommended

DGEM: German Society for Nutritional Medicine, ESPEN: European Society of Enteral and Parenteral Nutrition, A.S.P.E.N: American Society of Enteral and Parenteral Nutrition

Nutrition in patients with acute pancreatitis

In moderate-to-severe cases, EEN should be started with a low infusion rate through the gastric or jejunal path. If the patient undergoes surgery for necrosectomy, placement of needle catheter jejunostomy should be considered.

Nutrition in patients with renal diseases

Patients with CKD have increased energy demands. Frequent electrolyte derangements are common. In case of electrolyte derangements and no indication for RRT, special renal formulae can be used.[9] These formulae contain less fluid and protein, are high in calories, have lower potassium and phosphate content, and can contain additional substances such as carnitine. As RRT increases losses of energy, water soluble molecules — such as amino acids, electrolytes, trace elements, and vitamins — and induce systemic inflammation and protein catabolism. The A.S.P.E.N guideline suggests administration of high protein dosages of 2.5 g/kg/d, to achieve nitrogen balance.[1,9] To cope with the increased need for vitamins and trace elements, and increased supply is recommended, with special regard to Vitamin C, folate, and thiamine [Table 2].

PN

In case, the nutrition requirement is not met adequately with EN even after 7 days of ICU admission, then usage of PN may be considered.[9] Only in patients with reasons to delay enteral nutrition and high nutritional risk, early PN should be considered.

CONCLUSION

The interaction of acute metabolic changes, inflammation, and nutrition in early critical illness is complex. Recent studies suggest that in the early phase of critical illness, progressive feeding for both protein and calories is essential to prevent overfeeding. After this phase, high protein intake and sufficient calories are essential to prevent further loss of muscle mass. After hospital discharge, patients should receive high protein targets either by tube feeding or by enhanced high protein oral nutrition supplements.

Scientific nutrition in the form of standard formula fields should be preferred in the majority of ICU patients over blenderised feed as they have better feed hygiene, certain nutrient delivery, and lesser osmolality and viscosity.

Further, more large multicentre trials are required to strengthen the nutrition practices.

Declaration of patient consent

Patient's consent not required as there are no patients in this study.

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Conflicts of interest

There are no conflicts of interest.

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