Nutritional Considerations for ICU Patients. Part 2: Complications, Special Populations, and Post-ICU Nutrition

Dr Gothyang Makuya[1,3†], Dr Zainub Jooma[2,3]

[1]Anaesthetic Registrar, Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa
[2]Consultant Anaesthetist and Intensivist, Chris Hani Baragwanath Academic Hospital, Johannesburg, South Africa
[3]University of the Witwatersrand, Faculty of Health Sciences, School of Clinical Medicine, Department of Anaesthesia

Edited by: Dr Subramani Kandasamy, Senior Professor of Critical Care Medicine, Christian Medical College, Vellore, India

[†]Corresponding author email: gothyang.makuya@wits.ac.za

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KEY POINTS

- Enteral nutrition (in this article, enteral nutrition refers to assisted enteral nutrition) and parenteral nutrition are associated with complications like overfeeding, underfeeding, hyperglycaemia, and refeeding syndrome.
- Refeeding syndrome is potentially lethal, requiring careful monitoring and gradual nutritional reintroduction.
- Parenteral nutrition can lead to mechanical, electrolyte, metabolic, and liver-related complications and infection, necessitating careful management.
- Challenges of enteral nutrition include aspiration, gastrointestinal intolerance, and diarrhoea, requiring dietary modifications and monitoring.
- Patients on renal replacement therapy and those with obesity require tailored nutritional strategies to meet their unique needs.
- Post-intensive care unit nutritional support is crucial for recovery, with increased caloric and protein intake being key.

COMPLICATIONS ASSOCIATED WITH NUTRITIONAL SUPPORT

Both enteral (EN) and parenteral nutrition (PN) can lead to a range of complications. While some of these complications are common to both routes, others are method specific. Below are key complications associated with nutritional support.

Common Complications of EN and PN

Over- and Underfeeding

In critical care patients, over- and underfeeding are common due to differing metabolic effects of nutritional substrates administered intravenously or enterally. Overfeeding is more prevalent in those receiving PN. It is recommended to gradually increase protein intake to 1.3 g/kg/d to avoid overfeeding. Underfeeding, defined as providing less than 70% of the intended amount, commonly occurs during EN due to factors such as feeding intolerance, airway management difficulties, or interruptions in feeding caused by investigations, procedures, and elective operations.[1,2]

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Hyperglycaemia

It is commonly observed in patients in the intensive care unit (ICU), particularly among those receiving PN. When managing critically ill patients with complex nutritional needs, excessive glucose intake may place patients at risk for complications such as infection and delayed wound healing. The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines recommend initiating insulin therapy when blood glucose exceeds 10 mmol/L.[1,2]

Refeeding Syndrome

Refeeding syndrome is a severe and potentially fatal metabolic complication that can occur in patients in the ICU when nutrition is reintroduced after a period of malnutrition or fasting.[2] The pathophysiology of refeeding syndrome involves a rapid shift from a catabolic state to an anabolic state, leading to a surge in insulin secretion in response to carbohydrate intake. This increase in insulin levels drives the uptake of glucose, potassium, and phosphate into cells, potentially causing electrolyte imbalances, for example, hypophosphataemia (<0.65 mmol/L or a drop of > 0.16 mmol/L from baseline), which is considered a hallmark feature, hypokalaemia, and hypomagnesaemia.[2,3] These disturbances usually occur within the first 72 hours of medical nutritional therapy (MNT) initiation and may result in various complications, such as cardiac arrhythmias, respiratory failure, muscle weakness, and neurological symptoms. Risk factors for refeeding syndrome are outlined in Table 1.[4-6]

Close monitoring and gradual reintroduction of nutrition are crucial for preventing and managing refeeding syndrome in these patients. The guidelines recommend starting feeds at a rate of 10 kcal/kg/d or lower and gradually increasing it over at least 4 days to meet nutritional needs. Electrolytes (potassium, phosphate, and magnesium) should be measured at least 2 to 3 times daily. Sufficient daily micronutrient intake should be ensured. Additionally, thiamine supplementation of 200 to 300 mg per day is recommended for the first 10 days.[2,7]

Complications Specific to PN

Complications Related to Catheter Insertion

Mechanical complications associated with PN are primarily related to catheter insertion and include issues such as pneumothorax, arterial puncture, and catheter dislodgement or malposition. Thrombosis and catheter-related infection, although common, are distinct from mechanical issues. Thrombosis may impede nutrient delivery and increase the risk of embolism, while infections may predispose patients to bacterial or fungal bloodstream infections and require cessation of nutrition. These complications highlight the importance of using strict aseptic techniques and close monitoring of catheter usage and complications.

Metabolic Complications

PN is associated with several metabolic complications, including hyperglycaemia, hypertriglyceridaemia, electrolyte imbalances, Wernicke's encephalopathy, liver dysfunction, and refeeding syndrome. Long-term PN use can result in osteoporosis, osteomalacia, and intestinal failure-associated liver disease, which encompasses a clinical spectrum that may include cholestasis, cholelithiasis, hepatic steatosis, and fibrosis.[2]

Literature advises close monitoring of metabolic status and suggests considering a reduction in energy doses if the patient experiences any of the following: a decrease in serum phosphate of >0.16 mmol/L from baseline, serum glucose levels of >10 mmol/L despite adequate insulin therapy, or acute severe hypertriglyceridemia of >4.5 mmol/L.[8]

- Body mass index of <16 to 18.5 kg/m^2
- Unintentional weight loss of >10 to 15% within the last 3 to 6 months
- Little or no nutritional intake for >5 to 10 days
- A history of alcohol abuse or drugs, including insulin, chemotherapy, antacids, and diuretics
- Uncontrolled diabetes mellitus (diabetic ketoacidosis)
- Abused/neglected/depressed older adults
- Bariatric surgery
- Dysphagia
- Malabsorption (short bowel syndrome, inflammatory bowel disease, cystic fibrosis, persistent nausea/vomiting/diarrhoea, and chronic pancreatitis)
- Chronic disease conditions (tuberculosis, human immunodeficiency virus, and cancer)
- Prolonged hypocaloric feeding or fasting
- Unconventional/eccentric diets

Table 1. Risk Factors for Refeeding Syndrome

PN-Associated Cholestasis

PN-associated cholestasis (PNAC) is a prevalent condition affecting approximately 55% of individuals undergoing long-term PN therapy. Several risk factors, including a small bowel remnant shorter than 50 cm and a history of recurrent bacterial or fungal infections contribute to its development. To mitigate the risk of PNAC, various nutritional strategies are commonly used.[9] Notably, lipid emulsions containing soybeans and proinflammatory phytosterols have been linked to cholestasis and can be avoided. In cases where bile flow is compromised due to PN, the administration of ursodeoxycholic acid can aid in promoting flow and reducing the risk of cholestasis. Additionally, cycling PN over 12- to 18-hour intervals, rather than continuous PN, has been shown to prevent elevated levels of conjugated bilirubin. It is also crucial to monitor copper and manganese levels in PNAC cases, as the risk of toxicity escalates when bilirubin levels surpass 5 mg/dL.[9]

Complications Specific to EN

EN is generally preferred over PN due to its ability to maintain gastrointestinal integrity and function. However, it is not without complications. Table 2 provides an overview of the specific complications associated with EN. Among these, enteral feeding intolerance (EFI) and diarrhoea are most frequently encountered. The following sections elaborate on these complications, their underlying mechanisms, and appropriate management strategies.

Enteral Feeding Intolerance

EFI may present as gastric residual volumes (GRV) of >500 mL/6 h, vomiting, abdominal pain, distention, and/or elevated intra-abdominal pressure. Early full initiation of EN is associated with a higher incidence of EFI.[10] If the small bowel is the source of intolerance, the patient may present with an absence of bowel motion and worsening distention. There is currently no consensus as to the definition of EFI and there are no validated scores for assessment. However, it is widely recognised that upper GIT EFI is easier to recognise than lower GIT EFI, and a high index of suspicion for lower GIT EFI should be maintained in patients presenting with lower GIT symptoms, with diarrhoea being the most common presentation.[3,10,11]

Strategies for managing EFI[12] include the following:

- Exclude a pathological cause (sepsis, intra-abdominal collection, or obstruction)
- Temporarily reducing EN (if the GRV is 200 to 500 mL/6 h) or pausing EN (GRV of >500 mL/6 h)
- Administering prokinetics (intravenous erythromycin first line and/or metoclopramide)
- Considering postpyloric feeding if no bowel distension

For suspected bowel paralysis, intra-abdominal pressure can be monitored.

Diarrhoea

Diarrhoea remains a common complication of EN, influenced by the content and composition of feeds, including carbohydrates, lipid types, nitrogen sources, lactose, milk protein, dietary fibre, and osmotic load.[11,13]

Additional contributing factors include the use of hyperosmotic drugs, broad-spectrum antibiotics, *Clostridioides difficile* infection, intestinal infections (e.g., methicillin-resistant *Staphylococcus aureus* and cytomegalovirus enteritis), inflammatory bowel disease,

Mechanical complications	• Perforation of the intestinal tract • Ulceration and necrosis of nostril skin and mucosa • Primary malposition, for example, into the lungs or proximal oesophagus, increasing the risk of aspiration pneumonia • Obstruction • Dislodgement
Infections	• Otitis media • Sinusitis • Aspiration pneumonia • Necrotising peritonitis • Enteritis and infective diarrhoea
Metabolic complications	• Electrolyte disturbances • Hyper- and hypoglycaemia • Vitamin and trace element deficiency • Refeeding syndrome (can occur with enteral nutrition or parenteral nutrition)

Table 2. Complications from Enteral Nutrition

intestinal graft-versus-host disease, post-stem cell transplantation, and anticancer drugs. Intermittent feeding shows a higher incidence of diarrhoea than continuous feeding.[13] Treatment for EN-associated diarrhoea typically involves the following[13]:

- Identifying and addressing the underlying cause
- Modifying the enteral feeding formula
- Considering opioids or antidiarrhoeal agents in cases without identifiable pathology
- Administering anticholinergic drugs to promote gut peristalsis
- Optimising fluid replacement

If diarrhoea is not directly related to EN and the underlying condition is being treated, EN should be continued at a low rate.

SPECIAL POPULATIONS

Extracorporeal Membrane Oxygenation (ECMO)

Patients with mechanical assist devices such as ECMO or ventricular assist devices should adhere to the same guidelines as other critically ill patients. Guidelines recommend prioritising EN for patients with stable haemodynamics and a functioning gastrointestinal system. Gastrointestinal bleeding should be closely monitored in patients undergoing therapeutic anticoagulation. Frequent interruptions of EN are common due to due to diagnostic procedures. Although evidence is limited, PN is considered safe in ECMO patients and should be administered via a central venous catheter rather than through the ECMO circuit. IC is not a valid method for determining energy objectives in this patient group due to extracorporeal CO_2 elimination, and weight-based methods are recommended.[1]

Renal Replacement Therapy (RRT)

Critically ill patients with acute or chronic kidney injury undergoing RRT have comparable energy requirements to those of other critically ill individuals. Monitoring electrolyte levels is crucial, and renal nutrition formulations can address imbalances while limiting fluid intake in patients with renal failure.[14]

RRT exacerbates losses of water-soluble substance losses—including micronutrients, trace elements, and vitamins—and triggers systemic inflammation and protein breakdown, which complicate the determination of calorie needs. IC is the gold standard recommended for energy prescription in these patients. Additionally, lactate and citrate may be added to the dialysis or hemofiltration solution, contributing to caloric intake and should be considered when estimating total caloric requirements. Protein requirements are influenced by baseline illness and RRT duration, and protein catabolic rate may provide a more accurate estimate than body weight-based predictors.[14] The American Society for Parenteral and Enteral Nutrition (ASPEN) guidelines recommend administering high protein doses of 2.0 to 2.5 g/kg/d to achieve nitrogen balance in patients on RRT, whereas ESPEN recommends lower doses between 1.5 and 1.7 g/kg/d. To address the heightened requirements for vitamins and trace elements, it is advisable to increase their intake, particularly for vitamin C, folate, and thiamine.[1,2]

Obesity

The primary goal of MNT for obese patients is multifaceted, aiming to preserve muscle mass, enhance body composition, mitigate insulin resistance and hyperglycaemia, and decrease infection susceptibility. Identifying malnutrition in this demographic is challenging. Nevertheless, potential malnutrition should be considered based on clinical judgment, indications of macronutrient/micronutrient deficiencies, and signs of poor muscle quality despite adequate muscle mass. Vigilant monitoring for refeeding syndrome is crucial in the care of these patients. The optimal management of obese individuals remains a subject of ongoing discussion due to limited empirical data. IC and urinary nitrogen excretion are recommended for determining energy needs and protein requirements.[3,15] Individuals who have recently lost weight or undergone bariatric surgery require vitamin and trace element supplementation, with a particular emphasis on thiamine. Divergence exists between ESPEN and ASPEN guidelines regarding calorie and protein requirements in this population.[1]

In situations where IC is not available, the ASPEN guidelines propose using predictive equations or weight-based formulas to estimate energy needs. For patients with a body mass index (BMI) between 30 and 50 kg/m^2, a daily intake of 11 to 14 kcal/kg adjusted body weight (ABW) is advised, whereas a range of 22 to 25 kcal/kg ideal body weight (IBW) is recommended for patients with a BMI exceeding 50 kg/m^2. When determining protein requirements, consideration should be given to the possibility of sarcopenic obesity. Accordingly, ASPEN recommends increasing protein intake to 2 to 2.5 g/kg IBW per day—based on nitrogen balance studies—to help preserve lean body mass.

ESPEN recommends that caloric intake be determined using IC; alternatively, ABW can be used to calculate daily energy requirements. Protein delivery can be guided using methods such as urinary nitrogen losses or by determining lean body mass

through techniques such as computed tomography scans.[16] In the absence of these tools, ESPEN recommends a protein intake of 1.3 g/kg IBW/day, with the possibility of increasing this amount in severely ill obese patients.[16]

POST-INTENSIVE CARE NUTRITION

In 2012, Needham et al coined the term "post-intensive care syndrome" to describe the emergence or worsening of physical, cognitive, or mental health that persist beyond the acute hospital stay. To enhance functional outcomes and quality of life, it is essential to implement a cost-effective strategy by providing appropriate nutrition throughout the ICU stay and subsequent recovery phase.[7]

Studies have demonstrated that an increase in calorie and protein energy requirements is necessary to support functional muscle mass recovery and prevent further loss during the late phase of critical illness.[7] However, these studies also found that most patients received barely more than 50% of their prescribed calorie and protein needs, with even lower intakes observed in patients whose enteral tubes had been removed at ICU discharge.

IC studies indicate that total expenditure during the recovery phase may increasing by approximately 1.7 times the resting energy expenditure.[7]

A stepwise increase in calories and protein is therefore recommended[7]:

Post-ICU discharge

Calories increase to 125% of predicted equations or IC or 30 kcal/kg/d

Protein intake increases to 1.5 to 2.0 g/kg/d

Post-hospital discharge

Calories increase to 150% of predictive equations or IC or 35 kcal/kg/d

Protein intake increases to 2.0 to 2.5 g/kg/d

Prolonged EN, along with protein and oral nutritional supplements, has been shown to reduce mortality, hospital complications, and healthcare costs. One study reported nearly a 50% reduction in 90-day mortality among elderly malnourished patients using high-protein oral nutritional supplements.[7] However, few randomised controlled trials have evaluated feeding strategies in the late phase of critical illness and the postdischarge period, resulting in a lack of specific guideline recommendation.[17]

SUMMARY

Nutritional support is considered a standard of care for critically ill patients; however, it is not without complications. Both EN and PN are associated with shared risks—such as overfeeding, underfeeding, hyperglycaemia, and potentially life-threatening conditions like refeeding syndrome—as well as route-specific adverse events. Special populations, including those receiving extracorporeal life support, renal replacement therapy, individuals with obesity, and patients recovering from critical illness, present unique nutritional challenges that necessitate tailored approaches. Individualised nutritional strategies and close monitoring are crucial to mitigate complications, support recovery, and improve long-term outcomes in these vulnerable patient groups. Despite advancements in clinical practice, gaps remain in the literature regarding specific guideline recommendations for the post-intensive care period, highlighting the need for further research to optimise nutritional practices across the continuum of recovery after critical illness.

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