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© Malaysian Journal of Anaesthesiology 2024; 3:42-54
Review article
https://doi.org/10.35119/myja.v3i1.71

Optimal nutritional therapy in critically ill patients: a narrative review

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Abstract

Inadequate nutrition delivery remains a pervasive issue in critically ill patients, with significant challenges in accurately measuring nutritional requirements and personalising nutrition. Current medical nutrition therapy is constrained by difficulty in objectively measuring nutritional requirements and patient responses. Both enteral (EN) and parenteral nutrition (PN) are effective, but achieving and assessing nutritional targets pose substantial challenges. The adoption of computerised nutrition monitoring is on the rise, with future strategies potentially incorporating advanced muscle monitoring tools such as ultrasound and bioelectrical impedance analysis (BIA). Early enteral nutrition has been shown to reduce complications and shorten ICU stays; however, it should be delayed in specific conditions such as gastrointestinal bleeding. When EN is not feasible, PN serves as a safe alternative. Indirect calorimetry (IC) offers a method to measure energy expenditure and guide nutritional interventions, though larger trials are necessary to validate its benefits in personalised nutrition strategies. Significant muscle mass loss is prevalent in ICU patients, necessitating optimal amino acid delivery. Protein intake should be tailored to lean mass rather than total body weight, and bedside techniques like BIA and muscle ultrasound can aid in personalising protein delivery. While high protein intake may help mitigate muscle loss, its effect on clinical outcomes remains debated. Further trials are essential to enhance personalised ICU nutrition and improve patient outcomes throughout their ICU and post-ICU care journey.

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Keywords: critically ill patients, malnutrition, nutrition assessment, optimal nutrition delivery, personalised nutrition therapy

Introduction

Traditionally, nutrition support for critically ill patients was regarded as adjuvant care aimed at providing an exogenous energy source to preserve lean body mass (LBM) and support patients during stress response. Recently, this strategy has evolved into medical nutrition therapy (MNT), where feeding is believed to mitigate the metabolic response to stress, prevent oxidative cellular injury, and favourably modulate immune response. Optimal MNT is an essential component of care for critically ill patients, impacting recovery, morbidity, and mortality. Successful nutritional management requires a comprehensive strategy involving thorough assessment, precise energy requirement estimation, continuous monitoring, and personalised interventions. Nutritional strategies should be adapted to the patient's characteristics, diagnosis, ongoing treatments, and state of metabolism during intensive care unit (ICU) stay and convalescence. A personalised nutrition plan may prevent detrimental over- or underfeeding and attenuate muscle wasting. These patients frequently experience hypermetabolism, catabolism, and inflammation, which can worsen malnutrition and have adverse effects on clinical outcomes.[1]

In the ICU, critically ill patients are highly susceptible to developing malnutrition due to the rapid deterioration of their nutritional status following admission. In a recent meta-analysis encompassing 20 studies and 1,168 patients, the prevalence of malnutrition among ICU patients ranged from 38% to 78%.[2] Inflammation, undernutrition-driven catabolism, and inadequate dietary intake are key drivers of malnutrition. If left untreated, disease-related malnutrition is linked to unfavourable outcomes, including increased mortality rates and prolonged ICU and hospital stays. Critical illness often leads to immediate and significant muscle mass (MM) loss, ranging from 17.7% to 21.8% within 10 days.[3] This substantial muscle loss is associated with an increased incidence of complications and, ultimately, mortality. Early initiation of MNT is recommended for all patients who are admitted to the ICU for over 48 hours. The FASTHUG mnemonic is widely recognised and encompasses key aspects of the general care of critically ill patients in the ICU. It starts with the letter "F" for feeding, emphasising the importance of commencing nutrition early upon ICU admission and regularly reviewing the nutritional plan.[4]

This narrative review aims to provide an overview of nutritional therapy for critically ill patients, covering various aspects such as nutritional assessment, malnutrition risk, estimation of energy needs, monitoring, and personalised approaches in general adult ICU patient. The complex interplay of various factors affecting the nutritional needs of critically ill patients, coupled with variations in outcomes and research methodologies, poses significant challenges in formulating effective guidelines.

Nutritional assessment

Critically ill patients are at increased risk of developing malnutrition, which is linked to unfavourable clinical outcomes. The nutritional status of critically ill patients deteriorates rapidly after admission, irrespective of their initial nourishment status. Nutritional status is crucial in determining several patient outcomes, including the duration and expenses of hospitalisation, as well as morbidity and mortality rates. Nutritional assessment serves as a tool to evaluate a patient's nutritional status and needs, identify existing nutritional risks, and detect signs of malnutrition.[5] The World Health Organization defines malnutrition as encompassing both insufficient and excessive or imbalanced nutritional intake. In hospital settings, malnutrition is commonly referred to as undernutrition (inadequate intake or absorption of nutrients), a deficiency that affects bodily functions.[6] The European Society of Clinical Nutrition and Metabolism (ESPEN) defines malnutrition as "a state resulting from lack of intake or uptake of nutrition that leads to altered body composition (decreased fat free mass) and body cell mass leading to diminished physical and mental function and impaired clinical outcome from disease".[7] Critically ill patients are at high risk of malnutrition due to factors such as increased metabolic demands, inflammation, gastrointestinal dysfunction, and prolonged periods of fasting or inadequate nutrient intake. Malnutrition risk in critically ill patients refers to the likelihood that a patient will develop malnutrition during their stay in the ICU or while recovering from a critical illness. Recent recommendations suggest that any critically ill patient staying more than 48 hours in the ICU should be considered at risk for malnutrition. To establish an adequate and personalised nutritional regimen, conducting an individualised nutritional assessment in the initial hours of ICU admission is crucial. This approach enables the early identification of malnutrition risk and promptly initiating appropriate nutritional therapy.[8]

Nutritional assessment in critically ill patients is a multifaceted process that requires a thorough evaluation of various parameters. Traditional methods include clinical judgment, anthropometric measurements (*e.g.*, weight, height, body mass index [BMI]), and biochemical markers (*e.g.*, serum albumin, prealbumin,

transferrin). However, these markers can be influenced by acute phase responses and may not accurately reflect nutritional status in critically ill patients. Advanced tools such as bioelectrical impedance analysis (BIA) and dual-energy X-ray absorptiometry can provide more precise body composition measurements.[3,5]

ESPEN's updated guidelines of clinical nutrition for ICU patients recommend conducting a general clinical assessment to evaluate malnutrition in ICU settings until a specific tool is validated. This clinical evaluation may include gathering patient history, noting unintentional weight loss or reduced physical function before ICU admission, performing a physical examination, and conducting a general assessment of body composition, MM, and strength, if feasible. While no specific nutritional scoring system has been validated for use in the ICU, existing tools such as the Nutrition Risk Screening (NRS) 2002 and the Malnutrition Universal Screening Tool (MUST)5 score have not been developed specifically for critically ill patients. The NUTRIC (Nutritional Risk In Critically) tool is a novel risk assessment tool primarily based on disease severity. The Global Leadership Initiative on Malnutrition (GLIM) consensus statement outlines a set of risk factors that characterise malnutrition in a clinical context. According to the GLIM criteria, diagnosing malnutrition in critically ill patients necessitates the presence of at least 1 phenotypic criterion and 1 aetiologic criterion. After screening, the diagnostic assessment links a phenotype (weight loss percentage, BMI, decrease in appetite, and/or low MM) with an aetiology, *e.g.*, critical illness.[9]

A systematic review examining the significance of nutritional assessment tools in critically ill patients analysed 14 scientific articles that met selection criteria from 7 countries.[10] The reviewed instruments included mNUTRIC, NUTRIC, SGA, MUST, and the ESPEN and American Society for Parenteral and Enteral Nutrition (ASPEN) criteria. All studies highlighted beneficial effects following a nutritional risk assessment, with mNUTRIC being the most utilised tool, showing superior predictive validity for mortality and adverse outcomes. The review emphasised that employing nutritional assessment tools enables a comprehensive understanding of patient's nutritional status and facilitates tailored interventions to enhance their nutritional well-being. Notably, tools such as mNUTRIC, NRS 2002, and SGA have demonstrated the most effective outcomes.

Several techniques are now available to assess MM, LBM, or fat-free mass in ICU patients. MM can be assessed by ultrasound, computerised tomography (CT) scan, or BIA.[11] Sarcopenia is commonly observed in undernourished patients admitted to the ICU. Muscle function can be measured using handgrip dynamometry. BIA effectively evaluates body composition and is valuable for prognostic assessment in critically ill patients.[12] Studies indicate that patients demonstrating low MM upon admission, as determined by a CT scan, tend to experience longer hospital stays and

higher mortality rates.[13] Identifying patients at malnutrition risk and detecting MM loss are simple ways to contribute to better patient outcomes.

Evaluating the nutritional status of critically ill patients is challenging as there is no universally accepted gold standard assessment tool. Nonetheless, utilising the most effective tools for assessing these patients and implementing the best possible nutrition strategies is crucial.[14] Further research is needed to develop a better-validated screening tool for assessing nutrition in critically ill patients.

Malnutrition risk and outcome

In a systematic review, the prevalence of malnutrition in critically ill patients varied from 38% to 78%.[2] This review established an independent association between malnutrition and poorer clinical outcomes. Upon hospital admission, around one-third of patients already exhibit signs of malnutrition, and without adequate nutrition therapy, two-thirds of them will experience a worsening of their condition. Furthermore, during their hospital stay, two-thirds of initially non-malnourished patients will develop malnutrition. Malnutrition in critically ill patients is associated with a range of adverse outcomes, including increased infection rates, delayed wound healing, muscle wasting, prolonged mechanical ventilation, and higher mortality rates.[14] The pathophysiology of malnutrition in this population is complex, involving factors such as poor dietary intake, increased nutrient losses, and altered nutrient metabolism.[1] Early identification and management of malnutrition are critical to mitigate these risks. Studies have shown timely nutritional intervention can significantly improve clinical outcomes, highlighting the importance of proactive nutritional support in critically ill patients. According to the GLIM criteria, 2 steps are needed to diagnose malnutrition. The first step requires a validated screening tool to identify patients at risk, and the second step involves diagnosing and grading the severity of malnutrition.[9]

Malnutrition is more common in critically ill patients, mainly due to several contributing factors. Factors such as immobility, prolonged mechanical ventilation, and high levels of inflammation exacerbate the problem, putting patients at risk of skeletal muscle loss and weakness. Energy deficit in critically ill patients is closely linked to longer stays in the ICU, higher likelihood of infections, and increased mortality rates. The relationship between malnutrition and adverse outcomes is complex, influenced by factors such as age, the severity of the disease process, and other underlying medical illnesses.[15]

Malnutrition can be explained through 2 main factors: stress-induced breakdown

of the body and insufficient food intake. In cases of severe illness, the body releases catabolic hormones and proinflammatory agents to increase the breakdown of nutrients. Hormones such as glucagon, cortisol, and catecholamines are produced, releasing stored nutrients such as glucose, amino acids, and fatty acids to support essential organ functions. Inflammatory agents such as interleukin (IL)-1, IL-6, and tumour necrosis factor-alpha, triggered by infection or injury, further contribute to this breakdown process. The primary focus during such conditions is to provide adequate nutrition to sustain organ function and bolster the immune response. Moreover, critically ill patients often have limited nutrient reserves, exacerbated by challenges such as reduced food intake in the ICU, extended periods without eating, and interruptions in feeding schedules, which can inadvertently worsen malnutrition. Detecting and starting feeding protocols early can speed up recovery from severe illness.[16]

Most critically ill patients are in hypercatabolic condition, characterised by increased glycogenolysis, reduced protein synthesis, increased protein breakdown, increased insulin resistance, and lipolysis. These processes result in protein breakdown, hyperglycaemia, sarcopenia, weight loss, and undernutrition. The hypercatabolic condition progresses through different phases, starting with an early acute phase within the initial 48 hours, then a late acute phase spanning the subsequent 3–7 days, and then a chronic phase after 8 days.

In critically ill patients, significant physical stress triggers a catabolic response, resulting in muscle wasting and weakness. The longer the stay in the ICU, the higher the risk of weakness and the poorer the outcome. As stated in GLIM guidelines, MM is a new and innovative marker of malnutrition. Therefore, employing a rapid, non-invasive technique to assess both the quantity and quality of skeletal muscle in critically ill patients could have significant prognostic implications for the diagnosis of malnutrition.

A prospective, observational, multicentre study (EPNIC) conducted by Servia-Goixart *et al.* aimed to evaluate the influence of nutritional therapy on mortality rates among 639 critically ill patients. The study found that old age, higher organ failure scores, and elevated nutritional risk appear to be associated with higher mortality. Additionally, patients who required parenteral nutrition (PN) after initially starting enteral nutrition (EN) were identified as a high-risk subgroup for mortality, likely due to the severity of illness and challenges in receiving adequate nutritional therapy.[17] The average intake of calories and protein also seemed to affect outcomes. Moreover, the prognosis of ICU patients suffering from pre-existing malnutrition and sarcopenia is further complicated by the acute catabolic response typical of critical illness, which leads to rapid loss of LBM, resulting in muscle wasting, weakness, and functional decline.

Assessment of energy expenditure requirements

Accurate estimation of daily resting energy expenditure (REE) is crucial for determining the caloric requirements of critically ill patients to prevent harmful under- or overfeeding. As ICU patients typically engage in minimal physical activity, REE will be close to the total energy expenditure (EE). EE may vary during different phases of critical illness. Indirect calorimetry (IC) is considered the gold standard for measuring REE, as it directly assesses oxygen consumption and carbon dioxide production. However, its use may be limited by availability and practicality in ICU. Predictive equations (PEs) such as the Harris-Benedict, Mifflin-St Jeor, and Penn State equations are commonly used as alternatives. It is widely recognised that PEs are not reliable in predicting EE in the ICU, showing correlations ranging from 0.24 to 0.73 across 12 different equations.[18] Recent data indicates that the metabolic rate measured by IC in COVID-19 patients significantly differed from the values predicted by all commonly used PEs.[19]

Nevertheless, the precision of PEs can exhibit considerable variability depending on the patient population and clinical state. EE estimations derived from PEs can markedly diverge from measurements obtained through IC, potentially resulting in discrepancies of up to 1000 kcal/day from the actual EE. Research conducted by Duan *et al.* demonstrated that the implementation of IC-guided energy provision reduced short-term mortality rates by 23%, likely by averting detrimental effects of under- or overfeeding. Recent meta-analyses published in 2021 reported that patients receiving isocaloric nutrition guided by IC exhibited significantly decreased short-term mortality rates.[20] However, the outcomes of the recent TICACOS-II trial failed to replicate this observed reduction in mortality.[21]

Factors such as fever, sepsis, and mechanical ventilation can significantly alter energy expenditure, necessitating frequent reassessment and adjustment of caloric goals. In a local study recently published by Tah *et al.*, PEs tended to either over- or underestimate REE at different phases of critical illness. PEs with dynamic variables and respiratory data had better agreement with REE measured by IC compared with PEs developed for healthy adults or PE based on static variables.[22] Limited evidence suggests that certain equations are more specific for certain ICU populations. For example, the Penn State equations are considered by some experts as the most appropriate for ICU patients on mechanical ventilation.[15] Tah *et al.* found that even though none of the REEs calculated from PEs had excellent agreement, Swinamer (1990) appears to provide relatively good agreement across 3 phases and could be used to predict REE when IC is unavailable.[22]

Due to the shortcomings of current PEs, there is a continuous discussion

regarding the need for new models to better account for the specific metabolic demands of critically ill patients. The current formulas frequently underestimate energy requirements, increasing the risk of over- or underfeeding. Tah *et al.* developed and validated a new PE from acute phase data and found that it could provide optimal estimates of REE for patients in acute and late phases.[23] However, the equation has not been tested in multicentre trials. Emerging research suggests that artificial intelligence (AI) and machine learning may provide more advanced and individualised predictive tools. AI-driven models can potentially increase the accuracy of EE predictions by analysing large datasets and identifying complex patterns. AI-driven models would ultimately improve the effectiveness of nutritional therapy for patients in critical condition.

According to guidelines outlined by ESPEN and ASPEN on mechanically ventilated critically ill patients, EE assessment should be conducted through IC following stabilisation post- ICU admission.[24] Multiple meta-analyses have underscored the limited utility of PEs, variability exacerbated by challenges in assessing body weight. If IC is used, isocaloric nutrition rather than hypocaloric nutrition can be progressively introduced after the early phase of acute illness. When IC is unavailable, deriving EE evaluations from oxygen consumption (VO2) measurements via a pulmonary arterial catheter or carbon dioxide production (kcal/24 h = VCO_2 x 8.19) from the ventilator is recommended over reliance on PEs.[25] Applying basic weight-based formulas, such as 20-25 kcal/kg/day, may be preferred in cases where both methods are not feasible. If PEs are employed, a preference for hypocaloric nutrition (below 70% of estimated needs) over isocaloric nutrition is recommended during the initial week of ICU admission.[8]

Optimal nutritional delivery

Poor nutrition delivery in ICUs remains a global issue. One potential solution is the objective diagnosis of nutritional needs and personalisation of nutrition delivery for patients. Current ICU nutrition therapy has remained at the “beginning of knowledge”. Accurately measuring ICU patients’ nutritional requirements and their metabolic and clinical responses to nutritional interventions remains challenging. Although EN is preferred, PN is also adequate and produces comparable outcomes. The 3 main challenges in ICU nutrition delivery include:

1. Determining the nutritional target.
2. Achieving this target.
3. Assessing the impact on patient outcomes.

Healthcare providers must know the energy and protein delivered and how this compares to the targets. The availability of computerised nutrition monitoring systems is increasing. Future strategies may involve using muscle monitoring such as ultrasound, CT scans, and BIA to evaluate nutritional risk and monitor responses. In the post-ICU phase, continued use of IC and other muscle assessments should be considered to guide nutrition. Ideally, nutrition should be personalised, incorporating "ready-to-feed" indicators and markers showing when energy delivery is optimised, and protein is used to build lean mass. It is also important to determine the adequacy of energy intake while avoiding overfeeding or underfeeding. Therefore, current and future devices for measuring energy needs and body composition must be developed to achieve these goals.[26]

Current guidelines advocate early EN due to the observation that changes in the gut barrier can occur within 24 hours, manifesting as signs of gut ischaemia, increased permeability, bacterial translocation, and gut microbial imbalance (dysbiosis). Recent meta-analyses reveal that early EN, as opposed to delaying, is associated with reduced complications, lower rates of infectious morbidity, and shorter stays in ICU/hospital. It is advisable to postpone or slow down the advancement of EN in cases of gastrointestinal bleeding, mesenteric ischaemia, gastrointestinal intolerance, risk of aspiration, bowel obstruction, abdominal compartment syndrome, risk of refeeding syndrome (or phosphate levels < 0.65 mmol/L), or when there is unresuscitated haemodynamic instability while on vasopressors. However, no delay is recommended for patients on vasopressors (with norepinephrine infusion < 0.3 mcg/kg/min) who have been adequately resuscitated (evidenced by normal levels of lactate), those with an open abdomen, undergoing neuromuscular blockade, therapeutic hypothermia, extracorporeal membrane oxygenation, or in a prone position. In situations where EN is not viable, ASPEN guidelines emphasise that providing PN for a short period is safe, effective, and yields outcomes comparable to EN. Feeding intolerance is a frequent issue that can usually be effectively managed with prokinetic medications and by providing postpyloric feeding for patients who do not respond to prokinetics. There is no evidence of the superiority of intermittent feeding over continuous EN to support the practice change.[8]

Routine objective measurement EE in the ICU is now feasible due to IC technology advancements. The respiratory quotient (RQ) can reveal underfeeding (RQ < 0.7) or overfeeding (RQ > 1.0).[27] Utilising IC to guide nutritional targets and measure EE may be crucial for future personalised nutrition in the ICU, but should be applied carefully. Measurements are recommended after adequately resuscitating patients, typically after the third day in the ICU. The global availability and advancement of IC technology have made these measurements more accurate and easier to obtain, making it practical for many centres to consider incorporating IC into their practices.

Proper use of IC in suitable patients can help prevent the common issues of underfeeding or overfeeding in the ICU. This approach could enhance the focus on the importance of nutrition therapy in both the ICU and post-ICU settings. Larger trials are needed to confirm the potential benefits of using IC for personalised nutrition and to determine energy requirements across different patient populations accurately.

Significant MM loss is commonly observed during ICU stays. The optimal delivery of amino acids is crucial for maintaining protein homeostasis and counteracting catabolism in healthy individuals. International guidelines suggest increasing protein intake to 1.3–2.0 g/kg/day. However, these recommendations are based on retrospective and prospective cohort studies and lack data on how protein provision affects functional and metabolic outcomes. Despite normal gut protein absorption, it is important to note that increased amino acid provision may not enhance muscle protein synthesis during the acute phase.[28] The anabolic response in the ICU may be diminished due to factors such as anabolic resistance, immobilisation, insulin resistance, inflammation, and low muscle ATP levels. Even though protein can help preserve MM, this does not necessarily lead to improved muscle function. Early resistance training might help maintain MM and reduce muscle loss during critical illness. Recent studies suggest that the timing of protein intake is also important. Protein intake is typically calculated based on total body weight, but it should ideally be based on LM.[29]

In cases of sarcopenic obesity, using total body weight can result in protein overdosing, while it can lead to underdosing in non-sarcopenic obesity. Therefore, it makes sense to base protein provision on absolute LBM, and body composition measurements should be considered. BIA and muscle ultrasound are reliable, affordable, and accessible methods for assessing body composition at the bedside to estimate LBM. Tailoring protein provision to individual ICU protein requirements is challenging and still in the early stages. Bedside techniques such as BIA, muscle ultrasound, and new biomarkers for muscle breakdown, autophagy, inflammation, and insulin resistance may further help personalise protein delivery. Ongoing debate exists about whether high protein intake improves clinical outcomes; however, it may mitigate MM loss. Although protein absorption is normal in critically ill patients, severe skeletal muscle anabolic resistance may limit the benefits of high protein intake.[28] There is an urgent need for trials to evaluate the devices and technologies to determine the best ways to personalise ICU nutrition and improve outcomes throughout the entire ICU patient journey. Developing new markers and technologies to identify when patients can tolerate increased protein/calorie delivery and to measure substrate utilisation is essential.[26]

Conclusion

Malnutrition is a significant and prevalent issue in the ICU, affecting a substantial proportion of critically ill patients. The objective delivery of EE is crucial for managing the nutritional needs of these patients effectively. Ensuring optimal nutrition, particularly concerning adequate caloric and protein intake, is fundamental for ICU patients' recovery and overall health. Implementing personalised nutritional strategies tailored to the specific needs of each critically ill patient can play a vital role in preventing the adverse effects associated with both underfeeding and overfeeding. These strategies should consider each patient's unique metabolic and physiological demands to provide the most appropriate nutritional support. Additionally, comprehensive assessment tools are essential in determining the best approaches to optimise nutritional interventions. These tools can help healthcare providers identify patients at risk of malnutrition, monitor nutritional status, and adjust nutritional plans accordingly. By leveraging these assessment tools, clinicians can improve the efficacy of nutritional support and ultimately enhance clinical outcomes for critically ill patients.

Declarations

Ethics approval and consent to participate
Not required as this is a review.

Competing interests
None to declare.

Funding
None to declare.

Acknowledgements
None to declare.

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