Original Article

How to Feed the Critically Ill—A Review

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Abstract

Introduction: Number of recently published studies on nutritional support in the intensive care unit (ICU) have resulted in a paradigm shift of clinical practices. This review summarises the latest evidence in four main topics in the ICU, namely: (1) function of validated nutrition screening/assessment tools, (2) types and validity of body composition measurements, (3) optimal energy and protein goals, and (4) delivery methods. Methods: Recent studies that investigated the above aims were outlined and discussed. In addition, recent guidelines were also compared to highlight the similarities and differences in their approach to the nutrition support of critically ill patients. Results: Regardless of nutritional status and body composition, all patients with >48 hours of ICU stay are at nutrition risk and should receive individualised nutrition support. Although a recent trial did not demonstrate an advantage of indirect calorimetry over predictive equations, it was recommended that indirect calorimetry be used to set energy targets with better accuracy. Initiation of enteral nutrition (EN) within 24–48 hours was shown to be associated with improved clinical outcomes. The energy and protein goals should be achieved gradually over the first week of ICU stay. This practice should be protocolised and regularly audited as critically ill patients receive only part of their energy and protein goals. Conclusions: Metabolic demands of critically ill patients can be variable and nutrition support should be tailored to each patient. Given that many nutrition studies are on-going, we anticipate improvements in the individualisation of nutrition support in the near future.

Ann Acad Med Singapore 2020;49:573–81

Key words: Critical care, Critical illness, Intensive care, Nutrition, Nutritional intake, Nutrition support

Introduction

Critically ill patients require non-volitional nutrition support. Therefore, clinicians ought to prescribe regimens that provide nutrients in amounts that minimise the risk of morbidity and mortality. This, however, can be challenging because patients in the intensive care unit (ICU) are heterogeneous and their metabolic demands depend on a complex interplay between age, body composition, surgical status, comorbidities as well as the types and severity of disease.

Given the complex nature of nutrition support, clinicians often refer to the literature for guidance. Evidence in the arena of critical illness nutrition has evolved tremendously over the last decade, owing to the growing number of large and well-conducted randomised controlled trials (RCTs), and basic science studies offering new insights into metabolism during critical illness. As a result of the new knowledge,

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there is a paradigm shift in nutritional practice within the ICU.

This review summarises the latest evidence on the nutrition support practices in the ICU. We will first discuss the performance of validated nutrition screening/assessment tools in the ICU, and how they could be combined with objective body composition measurements to comprehensively assess nutrition risk. Thereafter, we discuss the current evidence for the optimal dosage of energy and protein, as well as how they should be delivered in critically ill patients.

Nutrition Screening and Assessment

Malnutrition is associated with increased risk of mortality and morbidity.[1] Therefore, it is generally suggested that clinicians should assess the nutritional status of critically ill patients, and provide higher energy and protein to the malnourished in the hopes of reducing the risk of adverse outcomes associated with malnutrition. There are 2 assumptions to this practice. The first is that existing nutritional screening and assessment tools are able to accurately identify the malnourished who are at risk of poor outcomes. The second is that higher energy and protein intake can reduce the risk of poor outcomes in patients at-risk or diagnosed with malnutrition. However, there appear to be limitations to these assumptions.

A recent systematic review identified ten screening and two nutrition assessment tools used in the ICU.[1] Amongst them, the Nutrition Risk Score-2002 (NRS-2002) and Subjective Global Assessment (SGA) (Table 1) have the most consistent prognostic ability and are recommended to be used in the ICU.[2–3] Another popular tool is the modified Nutrition Risk in Critically ill (mNUTRIC) which has been proposed to identify patients who may benefit from higher nutritional intake.[4] This score is arguably not a nutrition screening/ assessment tool because it does not contain any nutritional parameters (Table 1). This is exemplified by Lew et al. and Coruja et al. in which the mNUTRIC was demonstrated to have very poor agreement with established nutrition screening and assessment tools.[5–6] Subsequent studies also have cast doubts on the utility of the mNUTRIC score in identifying patients who may benefit from higher nutritional intake.[7–10] One of the best validation studies is a post-hoc analysis of a RCT specifically designed to determine the effects of standard feeding versus permissive underfeeding.[8] In this post-hoc analysis, patients with high mNUTRIC score who received higher energy had similar mortality risk as compared to those who received lower energy.[8] The cumulative evidence from the literature suggests that the mNUTRIC score is at best a mortality prognostic score. Hence it is not recommended to be used for routine nutrition assessment.

Will malnourished patients benefit from aggressive nutritional intake in the first week of ICU admission? Thus far, this question has not been directly answered because the malnourished population are understudied. However, there are 5 studies (2 RCTs and 3 observational studies) that may shed some light. In the post-hoc analysis of the RCTs, patients at risk of malnutrition who received higher energy and protein had similar mortality risk as compared to their counterparts who received lower intakes.[11,12] Similarly, in the observational studies, the association between energy intake and mortality

Table 1. Parameters of Nutrition Screening and Assessment Tools Used in Critically Ill Patients

	Nutritional parameters		Other parameters	
	Anthropometry and/or Physical Assessment	**Diet-Related and/or Gastrointestinal Symptoms**	**Severity of Illness**	**Others**
Subjective Global Assessment	Percentage of weight loss, subcutaneous fat loss, muscle wasting, and oedema at the ankle and sacral regions	Diet history, and gastrointestinal symptoms that lasted more than two weeks	Metabolic demands of diagnoses	Functional capacity
Nutritional Risk Screening-2002	Percentage of weight loss, body mass index	Diet history	Metabolic demands of diagnoses	Age
Modified Nutrition Risk in the Critically Ill			APACHE II, SOFA, number of comorbidities	Age, duration of hospitalisation before admission to the intensive care unit

APACHE II: Acute Physiology and Chronic Health Evaluation II; SOFA: Sequential Organ Failure Assessment.

was not modified by the nutritional status of critically ill patients.[13–15] The rationale for the above observations is unclear but could be related to misclassification of nutritional status and not including other important variables like degree of muscularity, which may be the most important nutritional parameter associated with survival.[16–17]

Given the lack of a nutrition screening and assessment tool that can identify patients who would benefit from higher nutritional intake, clinicians should consider that all critically ill patients with >48 hours of ICU stay are at nutritional risk, and should receive individualised nutrition support, as suggested by the latest clinical practice guideline.[18]

Body Composition Assessment

Traditional nutrition screening and assessment tools have incorporated weight and the Body Mass Index (BMI) as a determinant of nutritional status, with a higher and lower BMI indicating better and worse nutritional statuses, respectively.[2,3] A clear limitation of the BMI is its inability to differentiate between the various body components of fat mass and fat-free mass.[19] Low muscle mass has been reported in 60–70% of critically ill adults, and as high as 71% of ICU adults with high BMI have been shown to have low musculature on admission.[17,20]

Body composition is emerging as an important component of nutritional assessment in critical illness. This stems from observations of acute skeletal muscle wasting that occurs during critical illness, likely attributable to a combination of factors including immobility, inflammation and malnutrition.[21] Muscle wasting is associated with persistent weakness, functional impairment and reduced health-related quality of life.[22] Several studies have demonstrated associations between lower baseline musculature and greater risk of mortality, ventilator dependence and longer ICU stay.[17,20] Aside from muscle size, lower muscle quality or density has also been associated with greater mortality risk and worse function.[23,24] Compared to BMI, body composition measurements are also better predictors of worse outcomes in critically ill adults.[17,20]

Three most commonly used tools for assessment of body composition and musculature are summarised in Table 2. Computed tomography scans taken for diagnostic purposes have been used to assess skeletal muscle and various adipose tissue types in critically ill patients. Low muscle area on a single computed tomography slice at the L3 level has been associated with fewer ventilator and ICU-free days and higher risk for hospital mortality.[17,20] Lower muscle density has also been associated with greater mortality risk, although a specific cut-off is yet to be established.[25] Computed tomography scans are precise but not routinely done for this purpose, and seldom repeated due to high cost, manpower requirements and associated radiation. If available, such scans may aid baseline musculature assessment, but are unlikely to be repeated to allow monitoring of muscle changes.

Bioelectrical impedance analysis and ultrasonography may be able to overcome these limitations. Bioelectrical impedance analysis utilises the principles of varying resistance through the different body components of water, muscle and fat, and can provide an estimate of lean body mass.[26] However, lean body mass estimations are often inaccurate in critically ill patients due to fluctuating fluid status. Other bioelectrical impedance analysis properties such as phase angle and impedance ratio have thus been used instead. Lower phase angle and higher impedance ratio were shown to predict a longer ICU stay and greater mortality risk.[27,28]

Ultrasound machines are now ubiquitous in the ICU, and portable or handheld ultrasound devices have made bedside assessment of muscle size fast and easy, facilitating routine monitoring. Ultrasound reveals quadriceps muscle wasting rates of 2–4% per day during ICU stay, as well as an increase in echogenicity indicating myonecrosis.[21,24] Both of these observations are associated with reduced muscle function.[23] However, cut-offs for identifying low muscle mass and quality at baseline in relation to outcomes are yet to be established.

The ideal tool for monitoring body composition in critically ill patients is currently unknown. Body composition techniques for the ICU should be able to identify those with low body stores, and support monitoring of body composition changes throughout critical illness and recovery. Repeatability, inter-operator reliability and ability to detect changes in response to nutritional and physical rehabilitation interventions also need to be considered. Methods to incorporate body composition measurements into nutritional screening and assessment in critically ill patients is an important area of future research.

Table 2. Body Composition Assessment Methods Studied in Critically Ill Patients

Method	Properties studied	Predictive ability	Advantages	Disadvantages	References
Computed tomography	**Muscle size**	• L3 muscle size: <110 cm^2 in females or <170cm^2 in males associated with higher mortality risk • L3 muscle index: <38.9 cm^2/m^2 in females and <55.4 cm^2/m^2 in males (aged ≥65 years) associated with fewer VFD and IFD	Precise Able to differentiate between different types of adipose tissue	High cost Cannot be repeated too frequently due to associated radiation Difficult to conduct in ICU patients	17, 20, 25, 58
	Muscle density	• Lower muscle density at baseline associated with higher 6-month mortality risk			
	Adipose tissue	• Higher intramuscular adipose tissue at baseline not significantly associated with higher 6-month mortality risk • Loss in visceral adipose tissue during ICU stay associated with mortality			
Bioelectrical impedance analysis	**Phase angle**	• PA of <4.8° associated with higher mortality risk • PA of <6.75° in men and <5.85° in women associated with less likelihood of live discharge from ICU	Relatively inexpensive Allows repeated bedside measurement	Lean body mass measurements inaccurate with fluid shifts	27, 28, 59
	Impedance ratio	• IR of >0.78 in men and >0.81 in women associated with less likelihood of live discharge from ICU			
Ultrasound	**Muscle size**	• Rectus femoris cross-sectional area moderately associated with muscle function at ICU discharge • Vastus intermedius thickness strongly associated with muscle function at ICU awakening and discharge	Relatively inexpensive Allows for repeated bedside measurement	No cut-offs available to determine low muscle mass or quality Accuracy is operator-dependent	23, 60
	Muscle echogenicity	• Vastus intermedius echogenicity strongly associated with muscle function at ICU discharge			

ICU: Intensive care unit; IFD: Intensive care unit free days; L3: Level of the third lumbar vertebrae; VFD: Ventilator-free day

Optimal Energy and Protein Doses, and When They Should be Achieved

Nutritional status deteriorates rapidly in critically ill patients even in the previously well-nourished. This is likely related to the pro-inflammatory state, catabolism due to the increase in stress-related cytokines/hormones and high sympathetic drive. Many patients also have a pre-ICU phase during which nutritional intake is low, predisposing them to the risk of developing refeeding syndrome. Pro-inflammatory conditions, immobility and poor nutritional intake contribute to muscle loss, which starts early in the ICU.[21]

Optimal Energy Dose in Critically Ill

Observational studies have suggested that achieving higher energy adequacies were associated with better outcomes.[4,29,30] However, several RCTs have demonstrated that permissive underfeeding (achieving 40–60% adequacy)[31] and trophic feeding (up to 500 kcal/day)[32] resulted in similar clinical outcomes as compared to full feeding (100% adequacy). In addition, a recent RCT demonstrated that full feeding (103% adequacy) compared to lesser calorie delivery (69% adequacy) during the acute phase of critical illness resulted in similar quality of life, functional outcomes, disability and mortality 6 months after randomisation.[33] These studies suggest that a one-size-fits-all approach to setting the optimal energy dose may lead to oversimplification and individualised nutrition therapy may be preferable.

When individualising energy targets, clinicians should first assess the risk of refeeding syndrome and in at-risk patients, prescribe 100 mg thiamine for 5–7 days or longer in patients with severe starvation, and provide 10–20 kcal/kg for day-1 and advance by 33% of energy goal every 1–2 days.[34] In patients not at risk of refeeding syndrome, predictive equations are commonly used to estimate energy expenditure. They remain inaccurate since the critical and dynamic state of the patient is not considered.[18] Caloric requirements in early phases of critical illness are lower than the late phase, partly due to endogenous energy production. Therefore, the risk of overfeeding leading to fatty liver, higher CO_2 production and prolonged ventilation time is greater in the early phase. To set energy targets with better accuracy, indirect calorimetry has been used. This measurement is more accurate than predictive equations (especially in obese patients) and provides real-time energy expenditure.[35] However, its accuracy is limited by common treatment modalities used in the ICU (e.g. renal replacement therapy, high FiO_2, chest tube).[36] Maximum benefit is likely when 70% of measured or estimated energy expenditure (20–25 kcal/kg/day)[18] is met during the first three days of ICU admission since feeding at 100% may lead to overfeeding for reasons mentioned above.[18] A recent RCT (EAT-ICU)[37] showed that individualised energy targets based on indirect calorimetry did not result in improved outcomes. This may be attributed to overfeeding because 100% of the energy targets were achieved on the first day of ICU admission.

Optimal Protein Dose in Critically Ill

Following absorption in a fed state, amino acids are delivered to the muscle resulting in muscle protein synthesis. In the fasted state, obligatory oxidation of muscle amino acids occurs to maintain essential physiological functions. Anabolic resistance where increased supply of amino acids has a limited impact of muscle protein synthesis is common in critically ill patients.[38] Consequently, protein breakdown exceeds synthesis leading to a negative nitrogen balance.

Similar to energy, the optimal protein dose remains unclear and several trials are ongoing to provide evidence on the optimal dose, timing, and the interaction with caloric intake.[39] While incorporating exercise with adequate protein intake may prevent anabolic resistance, results are mixed and more studies are needed.[18] Current recommendations differ among different clinical practice guidelines. While the ASPEN/SCCM guidelines[40] recommend a daily protein intake of 1.2–2.0 g/kg actual body weight in patients not exposed to continuous renal replacement therapy, the ESPEN guidelines[18] recommend 1.3 g/kg delivered progressively to this patient group. The lower protein recommendation stems from some signals of harm associated with higher protein provision at the early phase of critical illness.[39] Nevertheless, most commercially available enteral formulas are energy-based and do not provide protein at the above recommended amount. Therefore, a protein modular may be required to achieve the 1.3 g/kg recommendation.

Feeding Route and Timing

Enteral nutrition (EN) is easier, more physiological and maintains gut mucosal integrity. However, EN should be withheld or delayed in the presence of uncontrolled shock, upper gastrointestinal bleeding, bowel ischaemia or obstruction, abdominal compartment syndrome and high-output fistulas.[41] Current clinical practice guidelines recommend starting EN within 24–48 hours

of ICU admission, but the rate of increment to achieve energy target remains controversial.[18,40] Based on expert consensus, the ASPEN/SCCM guidelines recommend increasing to 70–80% adequacy by 48–72 hours (for both energy and protein) whereas based on Grade-A evidence, the ESPEN guidelines recommend hypocaloric feeding [70% of measured or estimated energy expenditure (20–25 kcal/kg/day)] in the first 3 days of ICU admission, and progressive increment to 100% adequacy within 3 to 7 days. [18, 40]

Parenteral nutrition (PN) may be associated with complications and timing of initiation remains controversial. In the EPaNIC study late PN was associated with shorter ICU stay, duration of mechanical ventilation and lower ICU infections whereas the CALORIES trial showed that EN and PN delivered to achieve similar targets were associated with similar outcomes.[11,42] A Swedish study showed that early supplemental PN is beneficial if EN achieved less than 60% of energy adequacy.[43] PN is currently suggested in patients with (1) low-nutrition risk but unable to tolerate EN over a week, (2) high-nutrition risk or severely malnourished, when EN is not feasible and (3) not able to achieve at least 60% of energy and protein requirements via EN after 7–10 days.[40] Details on the type of lipid emulsions and additives are beyond the scope of this review, but can be found elsewhere.[44]

How Energy and Protein Goals Should Be Achieved in Critically Ill Patients

While the dose of protein and calories necessary to minimise iatrogenic complications and promote recovery remains debated, unintentional underfeeding of critically ill patients is common.[45] Strategies to identify and remediate barriers to improve the delivery of prescribed nutrients to critically ill patients should be implemented. These barriers may occur at the patient, health provider or organisational level and require systematic evaluation to improve practice.[46] At the patient level, strategies to help promote nutrition delivery include, but are not limited to, post-pyloric feeding, the use of prokinetic agents to promote gastric emptying and tolerance of higher gastric residual volumes (>500 mL). Detailed discussion on these strategies is published elsewhere.[18,40] Attention should also be given to interruptions to EN, particularly procedural-related and potentially avoidable causes which are associated with almost ¾ of all EN interruptions.[47,48]

Clinical practice variation can also substantially contribute to the under-delivery of nutrition to critically ill patients.[49] One approach to help make practice more consistent is the use of nutrition protocols and guidelines. The use of protocols has been shown to improve nutrition care practices such as timing and delivery of both protein and calories.[50] For example, practice changes that incorporate starting EN at goal rate can help eliminate under-delivery of prescribed nutrition.[51] Similarly, more complex protocols such as the PEP-up protocol incorporate components such as volume-based feeding (or low volume of a concentrated feeding solution for patient unable to tolerate higher volumes), use of a semi-elemental feeding solution to enhance tolerance, supplemental protein, early prokinetics, and tolerating a higher gastric residual volume.[52] These strategies have been shown to improve protein and calorie intake, albeit modestly. Standing instructions or automated computer orders are helpful and allow initiation of nutrition to precede, rather than follow, dietitian consultation.[53]

Although in the research context, the use of guidelines and protocols can help reduce practice variability and increase nutrition delivery, sustainability of these practices can be challenging in everyday clinical context. Auditing practices is a common approach to monitor changes and sustainability. One such method was adopted internationally through The Nutrition Day ICU survey and previously through the International Nutrition Survey, which was conducted five times between 2008 and 2014.[45] Such strategies allow ICUs worldwide to compare their clinical practice against evidence-based recommendations and benchmark against other ICUs. However, these audit data provide a unit-level appraisal of clinical practice and particular subgroups of patients for whom nutrition care is suboptimal may not be easily identified. Additionally, the focus is on nutrition practices in the ICU where it is usually much easier for clinicians to ensure delivery of adequate amounts of protein and energy. Once the patient is extubated and resumes volitional intake, intake can significantly decrease and this places the patient at increased nutrition risk during recovery from critical illness.[54]

Nutrition is important not just in the ICU but also as patients continue to recover in the hospital, during rehabilitation and once they return home.[54] Engaging patients and their families as partners in optimising nutrition intakes is a strategy which holds promise for use throughout the critical illness recovery trajectory.[55] Whether family partnerships in nutrition care result in an increase in protein or energy intake throughout hospitalisation is the focus of a current clinical trial.[56]

Conclusion

Clinicians should individualise their approach to nutrition support because critically ill patients are heterogeneous, and their metabolic demands can be vastly different (Table 3). Although the assessment of nutritional status and body composition can be used to prognosticate clinical outcomes, their utility in identifying patients who require aggressive nutrition support require further research. The pragmatic approach at this juncture is to provide nutrition support to all critically ill patients with more than 48 hours of ICU stay. The dose of energy and protein should be individualised to their severity of shock and degree of inotrope support, phases of critical illness, comorbidities, type and degree of organ failure, exposure to treatment modalities (surgery, dialysis, medications etc), and tolerance to EN. Given these technicalities, a team approach is required to maximise the efficacy and efficiency of nutrition support. Guidelines and protocols should be developed with inputs from the intensivist, ICU nurse, dietitian and pharmacist. In addition, regular audits will help identify challenges and help in the refinement of the protocols. Currently, nutrition and metabolic care in the ICU is an evolving area and a list of prioritised research are recently published.[57] We anticipate improvements in the individualisation of nutrition support in the near future.

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Table 3. Key Recommendations

Domains	Key recommendations
Nutrition screening and assessment	• All critically ill patients with >48 hours of ICU stay are at nutritional risk, and should receive individualised nutrition support
Body composition assessment	• Objective assessment of body composition should be part of nutrition screening and/or assessment. Common assessment tools include: computed tomography, bioelectrical impedance analysis, and ultrasound
Optimal energy and protein doses, and when they should be achieved	**Energy** • Clinicians should always assess the risk of refeeding syndrome and in at-risk patients, prescribe 100 mg thiamine for 5–7 days, and provide 10–20 kcal/kg for day-1 and advance by 33% of energy goal every 1-2 days. • In patients not at risk of refeeding syndrome, provide 70% of measured or estimated energy expenditure (20–25 kcal/kg/day) during the first 3 days of ICU admission and progressive increment to 100% of energy goal within 3–7 days **Protein** • 1.3 g of protein/kg should be delivered progressively during the first week of ICU admission
How energy and protein goals should be achieved in critically ill patients	• Feeding guidelines and protocols should be developed with inputs from the intensivist, ICU nurse, dietitian and pharmacist to maximise the efficacy and efficiency of nutrition support • Regular audits will help identify challenges and help in the refinement of the feeding guidelines and protocols

ICU: Intensive care unit

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