Translating the European Society for Clinical Nutrition and Metabolism 2019 guidelines into practice

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Purpose of review
To present a pragmatic approach to facilitate clinician's implementing the recent European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on clinical nutrition in the intensive care unit.

Recent findings
The ESPEN guidelines include 54 recommendations with a rationale for each recommendation. All data published since 1 January 2000 was reviewed and 31 meta-analyses were performed to inform these guidelines. An important aspect of the most recent ESPEN guidelines is an attempt to separate periods of critical illness into discrete – early acute, late acute and recovery – phases, with each exhibiting different metabolic profiles and requiring different strategies for nutritional and metabolic support.

Summary
A pragmatic approach to incorporate the recent ESPEN guidelines into everyday clinical practice is provided.

Keywords
critical illness, enteral nutrition, intensive care unit, nutrition guidelines, parenteral nutrition, route of nutrition, timing of nutrition

INTRODUCTION

The recently published European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines on clinical nutrition in the intensive care unit include 54 recommendations [1▪▪]. As an addendum, the monitoring of nutrition was addressed in a separate article [2▪▪]. The objective of this review is to assist clinicians implement these recommendations. A simplified explanation to grading of evidence used (Table 1) [3] and a summary approach to implementing these guidelines is provided (Table 2 and Fig. 1).

WHO SHOULD BE CONSIDERED FOR NUTRITIONAL THERAPY IN ICU?

The ESPEN guidelines include a recommendation that all patients admitted to an ICU, and particularly those staying for more than 48 h, should be considered for medical nutrition therapy [1▪▪]. Medical nutrition therapy includes administration of oral nutritional supplements, enteral nutrition and parenteral nutrition [4]. This 'good practice point' (GPP) (Table 1) is to identify the risk of prolonged underfeeding in all severely ill patients incapable of feeding themselves. It is important to realize that for many of these patients the period of inadequate nutrition, or even complete starvation, has started already several days before admission; thus, the nutritional aspects should be at attention from the beginning of ICU care. The time point of 48 h was chosen by the writing committee as it is a previously described threshold to define early enteral nutrition [5▪▪]. Early enteral nutrition, even with low dosages, may help to reduce cumulative negative energy and protein balances [6▪,7] that may be substantive of the entire hospitalization. Restricting the period of

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KEY POINTS

- New aspects in ESPEN guidelines are:
  - the concept of different phases of critical illness is introduced and emphasized,
  - only studies after year 2000 were included in meta-analyses,
  - monitoring of nutrition is addressed.
- Major differences when compared to previously published international guidelines are:
  - all ICU patients staying in the ICU for more than 48 h are at risk of malnutrition,
  - delivering full caloric target (via any route) based on total energy expenditure should not be aimed in the early acute phase of critical illness.

absolute starvation may attenuate the risk of subsequent refeeding syndrome.

NUTRITIONAL STATUS AND RISK OF MALNUTRITION

A general clinical assessment is recommended to assess nutritional status. Anamnesis, physical examination, general assessment of body composition, and muscle mass and strength are suggested to identify malnutrition at ICU admission. Although disagreeing with recent ASPEN guidelines [8], the ESPEN group recommends (as GPP) against using any specific methodology to identify or quantify malnutrition/nutritional risk; rather it is stated that every critically ill patient staying for more than 48 h in the ICU should be considered at risk for malnutrition. The latter statement identifies that the risk of 'acute' malnutrition during ICU and recovery phases may be independent from previous nutritional status. All severely ill patients will unavoidably have a negative energy balance at the beginning of their ICU admission [9]. Even though this is not desirable for previously (chronically) malnourished patients, feeding should be particularly cautious in such patients because of increased risk of refeeding syndrome [10]. Because the ESPEN approach is to gradually increase feeding during the acute phase in all patients, the recommended feeding rates do not differentiate between the chronically malnourished and previously well nourished in the acute early phase of critical illness. Acute malnutrition and tools to measure muscle mass and function warrant further evaluation.

ENERGY EXPENDITURE AND PRESCRIPTION

The guidelines recommend that for mechanically ventilated patients energy expenditure should be assessed by indirect calorimetry (Grade B). Indirect calorimetry is reliable only under stable resting conditions and with fraction of inspired oxygen below 60%. Measuring the actual energy expenditure

Table 1. Grading of recommendations

Grades of recommendation	
Grade	Explanation
A	Evidence from meta-analyses or RCTs directly applicable to the target population and demonstrating overall consistency of results
B	Evidence from well-conducted case control or cohort studies directly applicable to the target population or extrapolated evidence from RCTs or meta-analyses
0	Very low-quality (case series or cohort studies with high risk of bias) or extrapolated evidence
GPP	GPP recommended best practice based on the clinical experience of the guideline development group. No direct evidence available
Forms of recommendation	
Wording used in the recommendation	Explanation
'Shall'	Strong recommendation for = desirable consequences clearly outweigh undesirable consequences
'Shall not'	Strong recommendation against = undesirable consequences clearly outweigh desirable consequences
'Should' or 'Can'	Conditional recommendation for = desirable consequences probably outweigh undesirable consequences
'Should not'	Conditional recommendation against = undesirable consequences probably outweigh desirable consequences

GPP, good practice point; RCTs, randomized controlled trial.
Source: Simplified with permission from Refs. [1▪▪,3].

Table 2. Summary of recommendations

	General recommendation	Specific aspects/patient groups
Assessment of malnutrition	No specific tool, but general clinical assessment (anamnesis, physical examination, body composition, muscle mass and strength)	Abdominal CT scan for assessment of muscle mass
Assessment of energy expenditure	Indirect calorimetry if possible/ appropriate; CO_2 production derived from the ventilator (EE = $VCO_2 \times 8.19$); 3) 20–25 kcal/kg/day if EE not measured	Equations (e.g. Harris-Benedict) used to calculate EE may lead to over-estimation
body weight for nutritional calculations	Preadmission 'dry' weight (weight before fluid resuscitation)	Adjusted BW for obese (BMI > 30) = ideal BW + 0.25x (actual BW – ideal BW) Do not use ideal BW if underweight
Energy - Early acute phase (day 1–3) - Late acute phase (day 3–7) - Recovery phase (>day 7)	<70% of full target Full target (EE or 20–25 kcal/kg/day) Full target + consider exercise	Account for nonnutritional calories (propofol, dextrose, citrate) Obese patients – the same targets but calculated with adjusted BW
Protein	1.3 g/kg/day achieved progressively together with energy target	Obese patients – the same but calculated with adjusted BW
Other macronutrients	Glucose max. 5 mg/kg/min Lipids max. 1.5 g/kg/day	Some organs (e.g. brain) prefer glucose, ≈ 150 g/day probably needed
Early EN	Started within 24–48 h of ICU admission in patients who are not able to eat orally. Start always with slow rate under monitoring of GI symptoms, refeeding and IAP (if relevant)	Delay EN in: uncontrolled shock, uncontrolled hypoxemia, hypercapnia or acidosis, active upper GI bleeding, overt bowel ischaemia, abdominal compartment syndrome, high-output fistula without distal feeding access, GRV >500 ml/6 h
EN route	Gastric access and continuous administration as a standard initial approach	Post-pyloric if gastroparesis persists despite of prokinetics (erythromycin, metoclopramide)
Early PN	Early PN generally not recommended. Full early PN is considered harmful	Case-by-case in patients with previous mal/undernutrition if oral/EN not possible
Supplemental PN	In late acute phase (days 3–7) to avoid large energy deficits	
Glutamine	Not recommended in general	Recommended enterally in burns and can be considered in trauma
Specific fatty acids (ω-3)	High doses not recommended, nutritional doses can be used	
Micronutrients	Provided daily with PN	Single high dose is not recommended for any micronutrient
Antioxidants	High doses without proven deficiency not recommended	
Specific patient groups: - Dysphagia (non-intubated) - Bowel discontinuity - High output stoma/fistula	 - EN; post-pyloric EN and PN - distal access EN and PN - Consider chyme reinfusion	Early EN with slow progression and careful monitoring in controlled shock, therapeutic hypothermia, liver failure and intra-abdominal hypertension
Monitoring - During initiation of feeding - Later	Local standardized procedures: - GI symptoms, GRV, IAP, blood glucose 4–6x/d, electrolytes 2–3x/d; - GI symptoms, blood glucose 2x/d; electrolytes 1x/d; blood urea 3x/ week; liver tests and triglycerides 2x/ week	Monitoring of serum phosphate (together with potassium and magnesium) is important during initiation of feeding. If refeeding hypophosphatemia > restrict energy supply for 48 h and increase gradually thereafter

BW, body weight; CT, computed tomography; EE, energy expenditure; EN, enteral nutrition; GI, gastrointestinal; GRV, gastric residual volume; IAP, intra-abdominal pressure; PN, parenteral nutrition; VCO_2, carbon dioxide production; x/d, times/day.

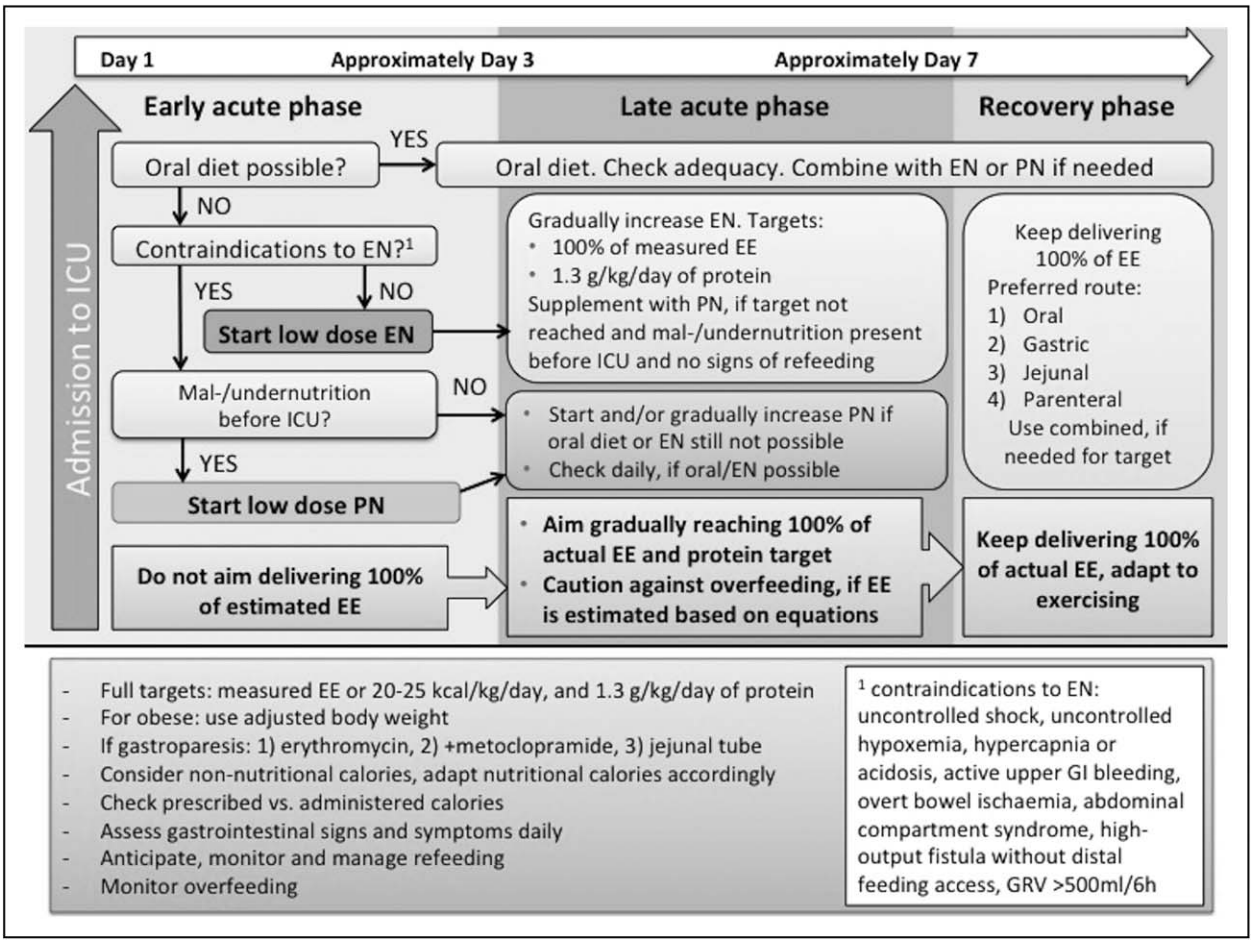

FIGURE 1. Flow chart for decision-making on nutrition. EE, energy expenditure; EN, enteral nutrition; GRV, gastric residual volume; PN, parenteral nutrition.

becomes useful after the early acute phase of critical illness (see definition below), when energy target can also be set according to results. If indirect calorimetry is not available, then using oxygen consumption from pulmonary arterial catheter or carbon dioxide production (VCO_2) derived from the ventilator are acceptable methods. The energy expenditure is calculated using VCO_2 values from ventilator and rewritten Weir formula (Energy expenditure = VCO_2 × 8.19; for respiratory quotient of 0.86) [11].

The guidelines recommend against using complex formulas for estimation of energy expenditure, because such predictive equations have shown poor correlation with measured energy expenditure [12]. A meta-analysis conducted as part of the guidelines revealed that the effect of so-called 'hypocaloric feeding' varies depending on whether the study groups are defined based on indirect calorimetry or with predictive equations. A likely explanation of the benefit of prolonged 'hypocaloric feeding' in studies using equations is that those assigned to 'full' or 'isocaloric' feeding received substantially greater calories than their true energy expenditure, that is they were overfed. Such overfeeding is aggravated in the early acute phase of critical illness when endogenous energy production is high (Fig. 2) [13]. This subtle distinction is important as the reader

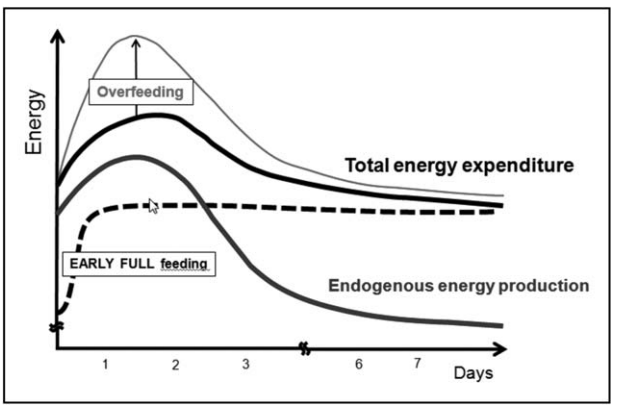

FIGURE 2. Overfeeding in the early phase of critical illness when full feeding covering 100% of energy expenditure is applied and/or when energy expenditure is overestimated with predictive equations. Source: Reproduced with permission from Ref. [13].

may falsely imply the terminology 'hypocaloric feeding' as recommending prolonged periods of calorie delivery much less than energy expenditure, which is not the intention.

In the absence of indirect calorimetry, straightforward weight-based predictive equations are recommended by the ESPEN group, with target of 20–25 kcal/kg/day.

When implementing measured or calculated energy expenditure into nutritional prescriptions, the ESPEN guidelines recommend consideration of the phase of body response to acute illness (Fig. 1). The phases of acute illness described differ considerably between patients and the presented number of days is only an approximate guide. The early period of the acute phase (usually 1–3 days after injury) is a period frequently associated with life threatening instability (e.g. hemodynamic and respiratory) that was the reason for initial ICU admission. It is hypothesized that full external energy supplementation at this stage may lead to detrimental overfeeding because endogenous glucose production cannot be completely suppressed with exogenous energy provision [14]. In the later period of the acute phase (usually days 3–7 but there is considerable inter-individual variation) stabilization of metabolic disturbances is thought to occur with continued substantial muscle wasting. In this phase, many patients gradually increase their capacity to utilize exogenous calories, and nutritional support is thought to become increasingly important. Energy target should be progressively reached during the late period of the acute phase. The post-acute phase (late/rehabilitation/recovery phase, usually after day 7) is commonly an anabolic phase with improvement and rehabilitation of organ functions and metabolism. Nutritional support at this stage, adjusted to energy expenditure and composed of balanced delivery of macro and micronutrients and vitamins, is thought to be crucial for optimal recovery [1▪▪]. It should, however, be recognized that there is considerable inter-patient variability: Some patients will have the maximum period of instability later than day 3 of ICU admission, some patients become stable before day 3. Some patients will suffer from persistent inflammatory and catabolic states, the so-called 'persistent critical illness' [15], or may suffer secondary insults. Therefore, this relatively simplistic linear model of acute illness and recovery is a guide only and may not apply to some patients.

Based on above-mentioned rationale, the following recommendations were made:

(1) If oral intake is not possible, early enteral nutrition (within 48 h) should be initiated rather than delayed enteral nutrition (Grade B) or early parenteral nutrition (Grade A);
(2) Continuous rather than bolus enteral nutrition should be used (Grade B), and gastric access should be used as the initial approach (GPP);
(3) To avoid overfeeding, early (within 48 h) full enteral nutrition and parenteral nutrition should not be used in critically ill patients (Grade A);
(4) Hypocaloric nutrition (not exceeding 70% of energy expenditure) should be administered in the early phase of acute illness (Grade B). After the early acute phase, usually day 3, caloric delivery can be increased up to 80–100% of measured energy expenditure (Grade 0);
(5) If indirect calorimetry is used, isocaloric nutrition rather than hypocaloric nutrition can be progressively implemented after the early phase of acute illness (Grade 0);
(6) If predictive equations are used to estimate the energy need, hypocaloric nutrition (below 70% of estimated needs) should be preferred over isocaloric nutrition for the first week of ICU stay (Grade B).

BODY WEIGHT FOR NUTRITIONAL CALCULATIONS

The body weight of immobile critically ill patient is challenging to precisely quantify. For nutritional calculations, it is recommended to use preadmission 'dry' weight (i.e. weight before fluid resuscitation, if known) [1▪▪]. If the precise body weight is unknown, it will need to be estimated. Calculation of ideal or normal body weight (weight related to the height) is useful but should probably not be used to calculate energy targets for critically ill patients who are clearly underweight. In the literature, many options to calculate ideal body weight based on patient pre-ICU height are available and it is easy to get confused. The most frequently used height-related calculation in the critical care nutrition literature is Devine formula [16,17], which has been used in trials of mechanical ventilation under the term 'predicted' body weight [18]. It is important to be aware that ideal body weight has been used as a surrogate for lean body weight and does not necessarily reflect 'normal' body weight for that patient [19]. To ensure consistency within each hospital, a single approach for all calculations could be advocated. In our opinion, using ideal body weight for underweight (BMI $< 18\,kg/m^2$) and malnourished patients increase the risk of both refeeding syndrome and overfeeding.

For obese patients (BMI $> 30\,kg/m^2$), adjusted body weight is recommended. It is calculated in two steps: ideal body weight related to height and a proportion of actual body weight (20–33% of

difference between actual and ideal body weight) is added. Different options to calculate ideal and adjusted body weights are available and some also presented in ESPEN guideline. The specific chapter suggests using the following:

(1) ideal body weight (Broca formula [20]): 0.9 × (height in cm – 100) for men; 0.9 × (height in cm – 106) for women;
(2) adjusted body weight = ideal body weight + 20–25% of difference between actual and ideal body weight (actual body weight – ideal body weight).

COMMENCING ENTERAL NUTRITION

In the guidelines, meta-analyses of studies published since year 2000 that compared enteral nutrition to no nutrition, or to parenteral nutrition within the first 48 h after ICU admission were provided [1▪▪]. Previous similar meta-analyses [5▪▪,21] included many older studies, justifying repeating analyses with only studies published since 2000. The time point for 2000 was arbitrary but based on relevant changes in practice and science regarding composition of feeds, determination of energy demands, clinical trials registration and higher quality standards for reporting of results of randomized controlled trials that occurred around the turn of the millennium.

The results of the meta-analyses were that early enteral nutrition is associated with reduction of infectious complications but no statistically significant effect on mortality. Unlike the previous meta-analyses [5▪▪] included studies were subdivided to 'clearly ICU' and 'unclear proportion of ICU' patients. The benefit observed with early enteral nutrition vs. delayed enteral nutrition remained statistically significant only if studies enrolling also patients from outside of the ICU were added to 'clearly' ICU studies.

Within the guidelines, the consensus was that early enteral nutrition in critically ill patients should always be started at a slow rate and advanced gradually while monitoring for enteral nutrition tolerance, biomarkers of refeeding syndrome (electrolytes) and, if appropriate, intra-abdominal pressure [5▪▪].

REASONS TO DELAY ENTERAL NUTRITION

Reasons to delay enteral nutrition were not specifically addressed during the evidence synthesis for the current ESPEN guidelines. Respective recommendations were adopted and then expanded from the European Society of Intensive Care Medicine (ESICM) clinical practice guidelines on early enteral nutrition [5▪▪]. In the original ESICM document, such recommendations were based on expert opinion and graded 2D (a weak recommendation with very low confidence in the estimated effect). Of note, different grading systems were used between these two guidelines. However, the Grade B (Table 1) recommendations in the ESPEN guideline should be interpreted with caution. An inherent limitation is the infrequent number of patients presenting with the conditions that were listed as a reason to delay enteral nutrition. Such infrequent presentations mean that an adequately powered randomized controlled trial (RCT) is not feasible. Accordingly, expert opinion with strong consensus may be the highest level of evidence achieved.

ESPEN guidelines evaluated some additional specific conditions that were not assessed in ESICM guidelines as potential reasons to delay enteral nutrition: dysphagia, frailty, sepsis, trauma, patients with complications after abdominal or oesophageal surgery and patients with high output stoma or fistula. Respective specific recommendations, including consideration of parenteral nutrition, were issued for patients with dysphagia, bowel discontinuity and high output stoma/fistula, and are summarized in Table 2.

HOW MUCH PROTEIN?

The optimal amount of protein to be administered to critically ill patients remains uncertain. The ESPEN guidelines recommend that eventually 1.3 g/kg/day of protein should be delivered but this should be achieved gradually (Grade 0 – no direct evidence). Recently, the concept of augmenting protein administration has gained favour amongst experts [22], and was included in the most recent ASPEN guidelines recommending 1.2–2.0 g/kg/day of protein [8]. This approach is based on promising results from observational studies and a physiological rationale supporting the hypothesis that increased protein intake is able to stimulate protein synthesis and possibly improve outcomes [23–27]. However, RCTs have not provided sufficient certainty that administration of protein more than 1.2 g/kg/day actually improves outcome and avoids muscle wasting [16,28]. Most importantly, a negative impact on outcomes, including mortality, has not been excluded [29,30]. Although awaiting future data [31], the current ESPEN recommendation regarding protein dosage is a compromise acknowledging potential beneficial effects but also possible negative effects of this approach. One small open-label single-centre RCT published since the ESPEN guidelines provides preliminary data

supporting the recommendation for augmenting protein delivery, with results suggesting that achieving 1.2 g/kg/day rather than 0.74 g/kg/day may attenuate muscle loss and reduce malnutrition [32]. Another small multicentre-blinded RCT reported no obvious harm when delivering protein dosage up to 1.5 g/kg/day [33]. Recommending one target dosage (1.3 g/kg/day), albeit one arbitrarily chosen, instead of a wide range, may facilitate implementation at bedside.

WHEN TO ADD PARENTERAL NUTRITION?

The dogma that parenteral nutrition *per se* is harmful has been challenged with recent trial results [34,35▪]. Early overfeeding because of endogenous energy production, refeeding and electrolyte disturbances and suppression of autophagy are the major underlying mechanisms whereby parenteral nutrition applied early and at 'full' dosages may be harmful [36,37]. Current ESPEN guideline recognizes parenteral nutrition as a reasonable option to provide energy and protein in patients in whom enteral nutrition is not successful or not possible. In patients who do not tolerate full dose enteral nutrition during the first week in the ICU, it is recommended that the safety and benefits of initiating parenteral nutrition should be weighed on a case-by-case basis (Grade 0). In some situations, it may be appropriate to commence parenteral nutrition early but this should be done cautiously. Even though the optimal timing, dosage and composition remains unclear, it is intuitive that parenteral nutrition should be commenced before very large iatrogenic nutritional deficits occur in those patients who are already malnourished and enteral nutrition cannot be commenced or is unlikely to be adequately delivered for some time. The guidelines state that early and progressive parenteral nutrition can be provided instead of no nutrition in case of contraindications for enteral nutrition in severely malnourished patients (Grade 0), whereas strongly recommending against delivery of full caloric target (via any route) within 48 h of admission (Grade A).

THE RISK OF OVERFEEDING

The ESPEN guidelines suggest considerable caution against overfeeding and its negative consequences. The aspect of nonsuppressible endogenous energy production [38] leading to hidden/unrecognized overfeeding in the early phase of critical illness is highlighted. Limited capacity of oxidation and using nutrients as energy is recognized and safety limits for the maximum dose for glucose and lipids based on physiological rationale and expert opinion (GPP) are provided. Suggestions for monitoring to detect/suspect overfeeding are provided in a separate article complementing ESPEN guidelines [2▪▪].

HOW TO MONITOR NUTRITIONAL THERAPY?

The main goals of monitoring of nutrition therapy in critical illness are [2▪▪]:

(1) to assure that appropriate nutritional support is chosen and provided as planned and prescribed;
(2) to assure that estimated energy and protein requirements are gradually met;
(3) to avoid or detect early any possible adverse effects related to feeding;
(4) to assess response to feeding;
(5) to detect specific deficiencies in patients at risk.

CONCLUSION

The ESPEN guidelines provide the most recent international consensus recommendations on nutrition therapy for critically ill adult patients. This current review provides a short summary of the ESPEN guidelines to facilitate the implementation of these guidelines into clinical practice.

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Conflicts of interest

There are no conflicts of interest.

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- ▪ of special interest
- ▪▪ of outstanding interest

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