Chapter 15
Severe Undernutrition

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Abstract Undernutrition in critically ill patients appears to be common, being encountered both at the time of admission and developing during the ICU stay. While many definition criteria for this state are available, loss of muscle mass and strength seem to be the most relevant signs. During the ICU stay, the main reason for undernutrition is underfeeding, a frequent occurrence in ICU practice, together with bed rest. Negative energy and nitrogen balance may result in an increase in morbidity and a prolonged rehabilitation period. While nutritional support is essential for these patients, it is important not to induce the refeeding syndrome. Enteral feeding is the preferred route for providing nutritional support but is not always achievable, usually the result of prolonged feeding interruptions. The calorie target should be reached progressively using the gastrointestinal route or the parenteral route if necessary. Indirect calorimetry remains the best guide for appropriately prescribing nutritional support. Protein administration should follow current guidelines. Careful monitoring of electrolytes (mainly phosphorus, magnesium, and potassium) is mandatory. Nutritional support is of extreme importance not only to provide enough nutrients in a deficiency condition but also to prevent prolonged rehabilitation periods for survivors.

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15.1 Introduction

Malnutrition among hospitalized patients has been recognized as a major health problem, reaching 30–54 % of all patients [1]. The recent ESPEN definition of malnutrition focused on weight loss and a decrease in lean body mass assessed by measurement of the free fat mass index [2]. However, of more concern than the body mass index, which might be normal in malnutrition, is the loss of lean body mass. The definition describes various categories of undernutrition, including starvation-related underweight, cachexia/disease-related malnutrition, frailty, and sarcopenia [2]. In addition, obesity sarcopenia may also be described as malnutrition, and the larger the loss of weight and the decrease in muscle mass, the more severe the undernutrition. In the intensive care unit (ICU), most patients are recognized during screening as suffering from or at risk of malnutrition, according to the screening tool Nutrition Risk Score 2002 (NRS 2002) [3]. In addition, the concept of frailty in the intensive care has been suggested [4]. Whereas frailty has been strongly correlated with age and disability status as well as the burden of comorbid disease [5], among critically ill patients, decrease in muscle mass, strength and endurance, as well as mobility makes these patients very analogous to the typically frail, geriatric patient. The purpose of this chapter is to define undernutrition and its nutritional profile, evaluate its prevalence in the ICU setting, and suggest a nutritional plan, which also takes into account the problem of refeeding, in this very high-risk population.

15.2 Definitions

Most of the tools described below have been validated in the intensive care setting (Table 15.1). The *Subjective Global Assessment* (SGA) is a well-known tool that includes patient history and physical examination [6]. In an attempt to validate SGA, others have shown a correlation with percentage of weight loss, BMI, ICU stay, and APACHE II score [7]. Sheean et al. compared SGA to the mini-nutritional assessment (*MNA*), NRS 2002, as well as MNA short form (MNA-SF) [8]. SGA and MNA-SF had the highest specificity, while NRS 2002 had the highest sensitivity. According to *the new ESPEN definition*, patients suffering from

Table 15.1 Diagnosis of undernutrition based on nutritional parameters

	SGA	MNA-SF	ESPEN diagnosis	Sarcopenia	Frailty
Weight loss <10 %	+	+	+		
Muscle loss	+		+	+	
Edema	+				
Calf circumference	+	+			
BMI <18.5		+	+		
Muscle function		+		+	+
Clinical frailty score					+

malnutrition include those with a BMI <18.5 kg/m^2 or suffering from an unintentional weight loss >10 % irrespective of time or >5 % over the last 3 months combined with either a BMI <20 if <70 years of age or <22 if >70 years of age or an FFMI <15 and 17 kg/m^2 in women and men, respectively [2]. Validation of this score in the ICU is pending. An additional score, the *Clinical Frailty Score* [9], ranging from 1 (very fit) to 7 (very frail), has been validated in the ICU and is useful mainly in elderly patients [10]. *Sarcopenia* has been defined as a decrease in muscle loss and/or function and is frequent in undernourished patients admitted to the ICU [11]. Muscle mass may also be assessed by various tools such as *handgrip dynamometer* [12] if the patient is conscious, being an especially good prognostic factor in conscious ARDS patients [13]. *Bioelectrical impedance* can be used to assess body composition and mainly lean body mass in a stabile patient not suffering from fluid compartment shifts [14]. However, its use is limited. Finally, recently *CT scan* has been used in the ICU to assess lean body mass and may be a promising tool for patients undergoing abdominal CT [15].

Length of stay and immobility increase catabolism in critically ill patients [16]. In addition, patients are frequently underfed. Thus the nutrition day survey in the ICU revealed that >40 % of patients had not received nutrition on the first hospital day and >20 % remained without nutrition on day 2 [17]. Enteral feeding was prescribed to only 10 % of the patients on the first day but this number increased to more than 40 % after 5 days. Parenteral nutrition was prescribed to around 10 % of the patients and supplemental parenteral nutrition was ordered after 3–5 days in only 15 % of the population studied. Total energy intake appeared to be randomly assigned and ranged from no intake up to 4000 kcals/day. Interestingly, the longer the patients stayed in the ICU, the more calories they received. The mean caloric intake was 1409 kcal/day and many patients failed to reach their caloric target, mainly as assessed by predictive required energy equations.

15.3 Prevalence

Exclusively chronic starvation-related malnutrition is extremely rare. Most patients with undernutrition have an acute disease associated with a small or a large subset of comorbidities. According to Bector et al., the prevalence of malnutrition on the intensive care assessed by SGA was 35 % [6]. Mortality was increased in the moderate (45.5 %) and severely malnourished (55.6 %) groups when compared to the well-nourished (10.8 %) group ($p = 0.04$). Another study found a prevalence rate of 40 % in 161 trauma patients according to SGA, and length of stay was found to be related to SGA [18]. Albumin and prealbumin levels are not useful for the diagnosis of undernutrition. Nutrition day data [17] from 9137 patients revealed that the mean BMI was 26.6 ± 6.4 kg/m^2. Heyland et al., in a study of the prevalence of iatrogenic underfeeding in nutritionally at-risk critically ill patients, found that enteral feeding was commenced 39 h in mean after admission and 74 % failed to meet the target of at least 80 % of the energy requirements [19].

15.4 Nutritional Profile

Patients suffering from severely malnutrition are characterized by significant decrease in weight before admission, loss of lean body mass as well as fat mass, and impaired immune function. These alterations in body composition and function are often associated with numerous comorbidities such as renal failure, history of cancer, past surgical history, as well as pulmonary, liver, and cardiac diseases which may further complicate the metabolic profile. Elderly patients are the most vulnerable but the definition of frailty is not limited to admission demographics. This nutritional profile may also be acquired during the ICU stay as a consequence of immobilization, inadequate nutritional supplementation, and the use of neuromuscular blockade and steroids [20].

Stress combined with undernutrition is associated with a negative energy balance and loss of lean body mass. This condition leads to worsening of clinical outcomes, increased complications such as infections and new organ failures, as well as prolonged mechanical ventilation and ICU stay. Positive nitrogen balance, adequacy of caloric administration, upper extremity strength assessed by handgrip dynamometer, and self-reported assessment may be good prognostic factors for this category of patient. On the other hand, albumin and prealbumin are not very useful in the nutritional assessment, since they are the reflect of capillary leakage.

Indirect calorimetry is extremely useful in the evaluation of energy requirements of these complex patients who may also be at risk for overfeeding. De Waele et al. [21] screened 266 ICU patients and found that 86.5 % were at risk of malnutrition. Indirect calorimetry which was assessed in 118 revealed that the measured energy expenditure was 1649 ± 544 kcal/day, which poorly correlated with predictive equations. In 210 malnourished hospitalized patients aged ≥75 years suffering from weight loss of >4 kg in the preceding month, measured resting energy expenditure (REE) was found to be as low as 1473 ± 311 kcal/day, with a fat-free mass of 47.6 ± 8 kg. The study also found that predictive equations were found to have only 40 % accuracy compared to REE [22]. Since predictive equations have such a poor accuracy, there is a risk of both over- and underfeeding which may increase complication rates [23]. Patients with both high-calorie intake and deficient in protein were found less likely to be discharged in 213 surgical ICU patients, confirming that inadequate macronutrient delivery is associated with worse clinical outcomes after critical illness [24].

15.5 Nutritional Needs and Therapy: Risk of Refeeding

After repeated stress and inadequate oral intake, the undernourished patient requires nutritional support which should be provided as early as possible via the digestive tract. The absence of enteral stimulation may negatively affect the gut microbiota, the enteric nervous system, as well as the gut epithelium and gut-associated lymphoid tissue [25]. These systems often interact with each other although the

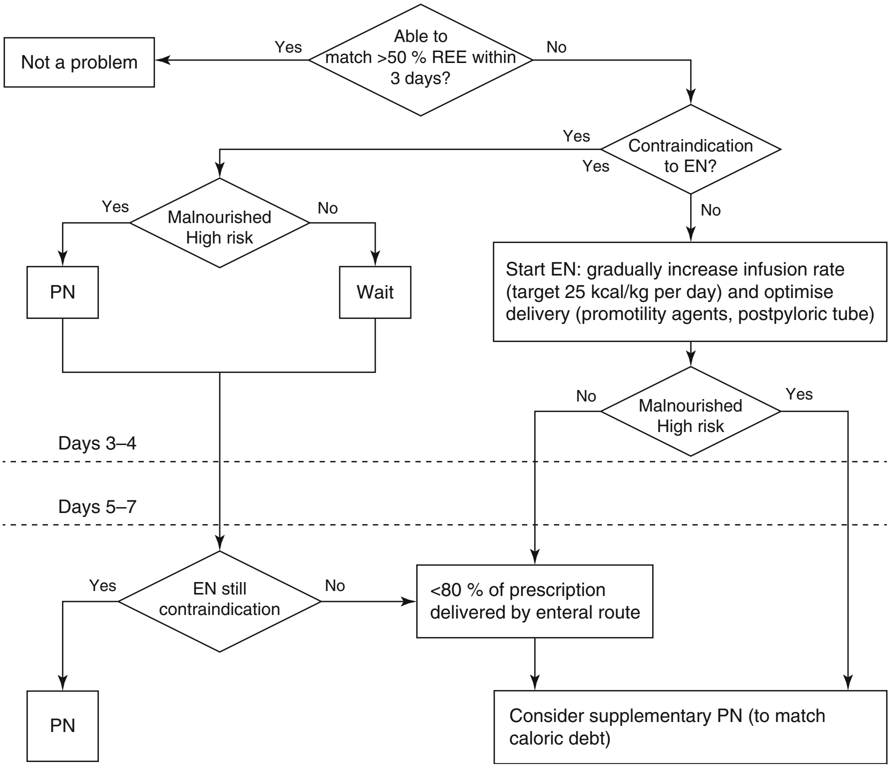

Fig. 15.1 Diagram proposed to optimize nutritional support in malnourished patients. From Weimann and Singer [30]. Proposed framework for starting parenteral nutrition in severely ill patients. *REE* resting energy expenditure, *EN* enteral nutrition, *PN* parenteral nutrition

mechanisms involved are still not fully understood. Early enteral feeding has been demonstrated to decrease infectious complications and may also improve survival [26]. However, early feeding may result in the refeeding syndrome, which is important to avoid [27]. When nutritional therapy is started, intracellular demands for phosphate and potassium are increased due to enhanced glycolysis and Na/K-ATPase pump stimulation. In practice, phosphate and potassium delivery should increase from 15–30 to 30–60 mmol PO_4/day and from 80–120 to 120–200 mmol KCL/day. In many cases, intolerance to enteral feeding is encountered which may be manifested by large gastric residual volumes, intestinal ileus, diarrhea, and abdominal pain [28]. Because of the large energy deficit existing in many patients, some guidelines recommend starting parenteral nutrition early in order to reach nutritional targets as soon as possible [29], while others advise commencing on days 7–10 [26]. An approach (see Fig. 15.1) to determine when to start parenteral nutrition has recently been proposed [30]. In malnourished patients, targeting calorie needs according to indirect calorimetry is preferred if available. If necessary, supplemental or total parenteral nutrition should be prescribed at an early stage if the target is not met by enteral nutrition. Recent studies on early parenteral nutrition have given disparate messages. The EPaNIC study [31] suggested that supplemental parenteral nutrition (SPN) might increase morbidity (infection rate and length of ventilation) in a large population of ICU patients. However, most were cardiothoracic surgical patients and the study excluded undernourished patients. The SPN study [32] did not exclude patients with severe malnutrition, but the mean BMI of the included population was 26 kg/m^2. All patients had an energy deficit at inclusion to the study. This study demonstrated that where the calorie target was not reached by enteral nutrition alone SPN was beneficial in terms of reduction of infection. A further study [33] in a similar patient population received SPN without any significant side effects.

Protein and muscle depletion endanger critically ill patients, and the highest priority should therefore be given to protein administration even if the patient is at a stage of progressive refeeding requiring a lower amount of calories. The recommended dose of protein is 1.2–1.5 g/kg/day [29].

Undernourished patients undergoing cardiothoracic surgery are more prone to delirium in the postoperative period [34]. In a multivariate logistic regression analysis, NRS 2002 defined risk of malnutrition as an independent preoperative and intraoperative risk factor for the development of postoperative delirium (OR 6.316, 95 % CI 1.384–28.819). In a further study, low preoperative fat-free body mass was found in 8.3 % of 325 adult patients undergoing cardiac surgery and was independently associated with the occurrence of infections (18.5 % vs. 4.7 %, OR 6.9, 95 % CI 1.8–27.7, $p = 0.01$) as well as a tendency for a prolonged ICU stay [35].

Refeeding hypophosphatemia is well described in malnourished patients [27]. Thus patients with a high NRS score before commencing nutrition support are more at risk of refeeding hypophosphatemia [27]. In particular, patients receiving a continuous parenteral nutrition regimen providing >70 % of the required calorie requirements containing <12 mmol phosphate are at an increased risk of hypophosphatemia [36]. In addition, we found [37] that severe hypophosphatemia was present in 34.3 % of 566 consecutive patients after major cardiac surgery and was associated with prolonged ventilation, increased requirements for cardioactive drugs, and a prolonged hospital stay.

Protein wasting and loss of body weight are associated with immobility and acute illness [16]. Early mobilization should therefore be encouraged. Maintenance of correct posture and passive mobilization of the legs are important. Muscle strength and endurance performance can be improved using cycle ergometry [38]. In addition, a mobilization algorithm comprising waking of the patient, positioning on the bed, sitting on the edge of the bed, transfer to the chair, the use of orthostatic and walking techniques, and finally the implementation of assisted exercises and exercises with resistance and use of the ergometer bicycle on the bed has been described [39]. An elegant demonstration of the importance of muscle mass was shown in a study including a population of 338 mainly cachexic liver transplantation candidates who underwent pre-transplant computed tomography to identify muscle and fat mass [40]. Muscle mass but not fat mass predicted ICU and hospital length of stay, as well as length of ventilation. Muscle mass also predicted survival and disposition to home versus another facility, demonstrating the fundamental importance of this component.

Patients suffering from acute kidney injury represent another patient population where protein-energy wasting is common and is a major negative prognostic factor. Insulin resistance and the release of pro-inflammatory mediators lead to lean body mass wasting and fat mass depletion. In this condition too, targeted calorie intake together with a protein intake of 1.7–2.0 g/kg BW/day in the case of severe catabolism or continuous renal replacement therapy is recommended [41]. Aging has a positive influence on nitrogen accretion in renal failure showing that with each increase in nitrogen intake, there was an increase in nitrogen balance [42].

The paradigm of correcting nutritional deficit using enteral or mainly parenteral nutrition has been recently challenged by Puthacheary et al. who reported that increased protein delivery during the first week in the ICU was associated with more pronounced muscle wasting [43]. Early parenteral nutrition increased the incidence of weakness and decreased recovery potential [44]. However, the 600 patients included in the study were from a study which excluded malnourished patients [31].

15.6 Conclusions

Undernutrition in critically ill patients appears to be common, being encountered both at the time of admission and mainly developing during the ICU stay. Weight loss related to muscle deficiency and decrease in strength are associated with increased morbidity. Numerous tools are available to assess muscle loss and may also be used to assess the response to nutritional therapy. Indirect calorimetry should ideally be used to plan appropriate energy administration. Adequate protein intake is an important goal and should reach 1.2–1.5 g/kg/day. Promising research is being performed to explore the use of physiotherapy together with a high-protein regimen to counteract the anabolic resistance often encountered in the undernourished bedridden patient.

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