An Overview of Malnutrition in Critically Ill Patients

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Abstract

Malnutrition is defined as any variation in degree of nutrition (either over nutrition or under nutrition) with or without inflammation that has led to variations in body. Also it is linked to increased incidence of morbidity and mortality in intensive care units. Therefore, early identification of patients at risk of malnutrition is of paramount importance. Fortunately many screening tools have been developed to identify those at risk of malnutrition. Hyper catabolic state induced by inflammation and stress response that associated with critical illness highly increases negative nitrogen balance. Optimal nutrients supply may improve patients' outcome during critical illness. However, the adequate needs of energy and protein vary considerably between patients and should be tailored for each individual. The aim of this review is to discuss nutritional screening, assessment, and consequences of malnutrition in critically ill patients.

Keywords: malnutrition, NRS-2002 score, critically ill patient

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Introduction

In critically ill patients, the prevalence of malnutrition ranges between 38% and 78%. At admission to hospital, at least one-third of patients have some degree of malnutrition and two-thirds of them progress to further decline without adequate nutritional provision. Additionally, two-thirds of patients who were without malnutrition will become malnourished during hospitalization. Early identification and appropriate nutritional intervention in malnourished patients have consistently shown to decrease hospital stay, infectious complications, and overall cost [1]. Malnutrition is defined as any variation in the degree of nutrition (either overnutrition or undernutrition) with or without inflammation that has led to variations in body composition [2]. According to a consensus statement by the Academy of Nutrition and Dietetics (AND) and the American Society for Parenteral and Enteral Nutrition (ASPEN), malnutrition is defined as the presence of any two or more of these entities: Insufficient energy intake, weight loss, loss of muscle mass, loss of subcutaneous fat, localized or generalized fluid accumulation, or decreased functional status [1].

Screening for Malnutrition

Nutritional screening is utilized for critically ill patients to detect individuals who are at risk of malnutrition. The American Society for Parenteral and Enteral Nutrition characterizes nutritional screening as a procedure aimed at identifying individuals who are either malnourished or at risk of malnutrition, thereby determining the necessity for a comprehensive nutritional assessment. It is recommended that screening be conducted within 24 to 48 hours following hospital admission by the attending medical staff. Additionally, screening can offer insights into the patient's nutritional status over the duration of their hospital stay [1].

An optimal screening instrument must demonstrate sufficient validity, reliability, sensitivity, specificity, and positive predictive value to effectively identify high-risk patients. Nevertheless, to this point, no screening tool has successfully met all these requirements. Numerous nutritional screening assessment tools have been examined, with many integrating biomarkers of the inflammatory system and severity scores, as these factors are intricately linked to the pathophysiological mechanisms of malnutrition in critically ill individuals [4].

The screening tools must assess dietary, physical, anthropometric, psychological, social, and clinical factors. Each variable assessed must be justified with an evidence-based risk factor or outcome. The tools must also be simple to use at the bedside and cost-effective [3].

Among all the screening tools, only the Nutritional risk screening (NRS 2002) and theNutrition Risk in the Critically ill (NUTRIC) have been extensively studied [5].

The NRS-2002, created by Kondrup and colleagues, serves as a versatile instrument within hospital environments, effectively identifying a majority of patients who may gain from nutritional intervention. Recent findings from a substantial multicenter randomized controlled trial involving a medical inpatient cohort have corroborated this utility, revealing a significant decrease in critical clinical outcomes, such as mortality, among patients identified as at risk of malnutrition through the NRS-2002 assessment **(table1)** [6].

Table 1. Nutritional Risk Screening 2002. APACHE: acute physiology and chronic health evaluation; BMI: body mass index; COPD: chronic obstructive pulmonary disease; ONS: oral nutritional supplement [6].

Pre-Screening	
Is the BMI of the patient < 20.5 kg/m^2	Yes
Did the patient lose weight in the past 3 months?	Yes
Was the patient's food intake reduced in the past week?	Yes
Is the patient critically ill?	Yes
If yes to one of those questions, proceed to screening.	
If no for all answers, the patient should be re-screened weekly.	
Screening	

Nutritional status	score	Stress metabolism (severity of the disease)	score
None	0	None	0
Mild Weight loss >5% in 3 months **OR** 50–75% of the normal food intake in the last week	1	Mild stress metabolism Patient is mobile Increased protein requirement can be covered with oral nutrition Hip fracture, chronic disease especially with complications e.g., liver cirrhosis, COPD, diabetes, cancer, chronic hemodialysis	1
Moderate Weight loss >5% in 2 months **OR** BMI 18.5–20.5 kg/m^2 AND reduced general condition **OR** 25–50% of the normal food intake in the last week	2	Moderate stress metabolism Patient is bedridden due to illness Highly increased protein requirement, may be covered with ONS Stroke, hematologic cancer, severe pneumonia, extended abdominal surgery	2
Severe Weight loss >5% in 1 month **OR** BMI <18.5 kg/m^2 AND reduced general condition **OR** 0–25% of the normal food intake in the last week	3	Severe stress metabolism Patient is critically ill (intensive care unit) Very strongly increased protein requirement can only be achieved with (par)enteral nutrition APACHE-II >10, bone marrow transplantation, head traumas	3
Total (A)		Total (B)	
Age			
<70 years: 0 pt			
≥70 years: 1 pt			
TOTAL = (A) + (B) + Age			
≥3 points: patient is at nutritional risk. Nutritional care plan should be set up			
<3 points: repeat screening weekly			

Nutrition Risk in the Critically Ill

Heyland et al. [7] developed a screening tool for critically ill patients. Previous screening tools implicated all critically ill patients in high-risk category and no screening tool was studied exclusively in critically ill population. The NUTRIC score was able to discriminate critically ill patients who will benefit from aggressive protein energy provision. This was the first screening tool that was validated and developed in critically ill patients. The score can be easily calculated with parameters measured in daily care of critically ill patient **(table 2)**. Addition of IL-6 marker was called as modified NUTRIC score by the authors **(table 3)**. However, the addition of IL-6 did not improve the discriminative ability of the score; hence, the authors suggest using the score also when IL-6 values are not available **(table 4)** [7].

The A.S.P.E.N./society of critical care medicine guidelines suggest using either NRS 2002 or NUTRIC/m NUTRIC for nutritional screening in critically ill patients [8]. The NUTRIC score is more useful in critically ill patients as it was developed in critically ill patients and recent food intake and weight change which is difficult to obtain in ICU patients were not included. The limitations of the NUTRIC score were that it did not include nutritional parameters and also micronutrient deficiencies were not included. The NUTRIC score is still not prospectively tested in a randomized control trial. The NUTRIC score performed better as compared to the MUST score in critically ill patients [9]. Comparative studies between NUTRIC and NRS 2002 scores showed inconsistent results. In one retrospective study, NRS 2002 showed higher sensitivity and specificity for the diagnosis of malnutrition when compared to NUTRIC score, [10] while another retrospective study by Canales et al. [11] found that NUTRIC score was superior to NRS 2002 for assessing malnutrition risk. An observational study by Coltman et al. [12] found that NUTRIC score was no different to routine screening. In a recent observational study, NUTRIC score was also able identify high-risk critically ill COVID-19 patients [13].

Table 2: NUTRIC score variables [7].

Variable	*Range*	*Points*
Age	<50	0
	50 to <75	1
	>75	2
APACHE II	<15	0
	15 to <20	1
	20–28	2
	>28	3
SOFA	<6	0
	6 to <10	1
	>10	2
Number of comorbidities	0–1	0
	>2	1
Days from hospital to ICU admission	0 to <1	0

	>1	1
IL-6	0 to <400	0
	>400	1

Table 3: NUTRIC scoring system: if IL-6 available

Sum of points	*Category*	*Explanation*
6–10	High score	Associated with worse clinical outcomes (mortality, ventilation).
		These patients are the most likely to benefit from aggressive nutrition therapy.
0–5	Low score	These patients have a low malnutrition risk.

Table 4: NUTRIC scoring system: If no IL-6 available

Sum of points	*Category*	*Explanation*
5–9	High score	Associated with worse clinical outcomes (mortality, ventilation). These patients are the most
0–4	Low score	Likely to benefit from aggressive nutrition therapy. These patients have a low

Nutritional Assessment

Nutritional assessment is a formal assessment of the nutritional status of a patient by a trained healthcare professional usually a dietician, and results in nutrition-related diagnosis [17]. Once a patient is identified as at risk from the screening tools detailed, nutritional assessment should be performed. Indian Society of Critical Care Medicine practice guidelines for nutrition in critically ill patients recommend the nutritional assessment by Subjective Global Assessment (SGA) [14]. Assessments by anthropometry like body mass index (BMI) is difficult to measure in critical care setting. Measurement of serum albumin, transferrin, and prealbumin is not reliable in critically ill patients **(Tables 3 and 4)**.

Subjective Global Assessment

It is a subjective nutritional assessment tool initially developed for post-gastrointestinal surgery patients [15]. The tool was later studied in critically ill patients. The SGA scale includes parameters to assess subcutaneous fat, muscle wasting, fluid retention, weight change, recent food intake, gastrointestinal symptoms, and functional capacity. Subjective Global Assessment class C includes severe malnutrition, SGA class B includes moderate malnutrition, and SGA class A includes no malnutrition. In a meta-analysis of studies of use of SGA in critically ill patients, SGA was more favorable than other assessment tools and SGA grade B and C had poor outcomes [18]. Subjective

Global Assessment is simple and easy to assess at the bedside and is cost-effective also. The main limitations of SGA were that severity of illness were not included, assessment of weight and food history in critically ill patients was difficult, changes in SGA grade takes a long time usually many days.

Besides the subjective assessment, it is also important to assess the gastrointestinal tract with gastric residual volumes to assess the nutritional status in critically ill patients [17].

Other methods studied were use of computed tomography (CT) scan to assess the muscle mass, as CT scan is cumbersome use of ultrasonography assessment of quadriceps muscle thickness has been studied. Ultrasonography is a simple, noninvasive, bedside tool to assess muscle mass. It can be performed serially and detect short-term changes. A prospective study by Rodrigues et al. [16] assessed quadriceps and rectus femoris muscle thickness using ultrasonography and the reduction in muscle mass was correlated with severe malnutrition. Ultrasonographic assessment of muscle mass needs further validation and is a useful future tool. Bioelectrical impedance is another tool used to measure fat free mass; however, the fluid electrolyte imbalance in critically ill patients affects the measurements taken.

Practical Implications Of Nutritional Assessment In Critically Ill Patients

Nutrition assessment and prescription in critically ill patients is often ignored world over. International guidelines recommend that every patient should be screened for malnutrition within 24–48 hours of ICU admission, as many of these patients are at a risk or may have malnutrition at admission to ICU due to the underlying severity of the illness.

Malnutrition and muscle wasting set in early during the ICU stay because of the imbalance between energy and protein requirements and intake. A trained nutrition expert or a dietician is not necessary to identify patients who are, or at risk of malnutrition. Nutrition assessment starts with a good patient history and physical examination for emaciation and loss of muscle mass. But loss of muscle function may occur much before loss of muscle mass, which may go unnoticed in an obese or fluid retained critically ill patient, unless actively screened. Anthropometric measurements like patient's weight in ICU are technically difficult and may fluctuate widely due to fluid shifts during the ICU stay.

The NUTRIC score is an easy screening tool which can be used at the bedside. The patient should be assessed in detail by a nutritionist/dietician or by the treating clinician if nutritionist is not available. Nutritional assessment should be performed using the SGA tool. The SGA although validated in critically ill patients has its limitations; to obtain the necessary anthropometric measurements and muscle function assessment in a sedated patient may be near impossible.

Body composition assessment using ultrasound, computed tomography, and bioimpedance are relatively new tools and technically limited in critically ill patients, currently being used only for research.

Nutrition screening and assessment should be a continuous process for all hospitalized patients so as to intervene early with necessary protein and energy supplementation.

Laboratory Assessment for Malnutrition

1. **Serum Proteins**

Serum protein levels are commonly utilized as indicators of nutritional status in ICU. The proteins that are most often assessed include albumin, prealbumin (also referred to as transthyretin or thyroxin-binding prealbumin), retinol-binding protein, and transferrin [19].

1.1. Albumin

Albumin, present in both the intravascular and extravascular compartments, is the most extensively researched serum protein. It is unique among the monitored proteins in that a reduced concentration upon admission (below 2.5 g/dl) has been associated with a higher risk of mortality. While serum albumin serves as an effective prognostic indicator, it is not a reliable marker for nutritional recovery due to its prolonged half-life of 18 days and substantial body reservoir. The normal concentration range of albumin is 3.5 g/dl to 5 g/dl [20, 21].

1.2. Prealbumin

Prealbumin, which has a normal concentration range of 17 mg/dl to 40 mg/dl, serves as a transport protein for thyroxine and vitamin A. It exists in circulation as a complex with retinol-binding protein. Due to its half-life of 2–3 days, prealbumin is a valuable marker for short-term nutritional assessment. Concentrations falling below 11 mg/dl, or a lack of increase in prealbumin levels despite nutritional intervention, can be attributed to several factors. These include the liver's reprioritization of protein synthesis during stress responses, the presence of concurrent illnesses such as hepatic failure, or insufficient caloric and protein intake. Additionally, certain medications, including corticosteroids, and conditions like renal failure may elevate prealbumin levels without indicating true nutritional recovery. In patients with renal impairment, increased prealbumin levels may result from partial catabolism and reduced degradation. However, these elevations do not entirely diminish the utility of prealbumin monitoring; rather, they suggest that tracking trends in concentration is more informative than relying on isolated measurements. Given its advantageous properties, ease of collection, and understanding of its limitations, prealbumin is currently regarded as the preferred serum protein marker for evaluating short-term nutritional changes in intensive care settings [21].

1.3. Retinol-binding Protein

Retinol-binding protein has a small body pool size and a short biologic half-life (12 hours), which makes it a good short-term marker of nutrition. Retinol-binding protein circulates in plasma with plasma transthyretin, and has a binding site for one molecule of retinol. However, renal dysfunction affects the clearance of retinol-binding protein, thereby decreasing its usefulness in critically ill patients [22].

1.4. Transferrin

Transferrin binds and transports the ferric ion, is synthesized in the liver, and has a half-life of 8–9 days. Transferrin concentrations have been used as a predictor of morbidity and mortality, with concentrations less than 100 mg/dl indicative of severe serum protein depletion, 100–150 mg/dl suggestive of moderate depletion, and values of 150–200 mg/dl, indicating mild nutritional depletion. In periods of physiological stress, this marker may not be reflective of nutritional

repletion because of reprioritization of hepatic protein synthesis. It is also important to note that transferrin is elevated in states of iron deficiency secondary to increased hepatic synthesis [22].

Overall, these serum protein markers can be used independently or in combination with nitrogen balance to assess the aggressiveness of protein repletion necessary. The usefulness of these serum protein markers in assessing nutritional status is limited by a lack of research correlating protein concentrations with clinically important outcomes, by decreased protein synthesis that may occur in patients with hepatic dysfunction, and by decreased protein clearance that may occur in patients with renal dysfunction [22].

1.5. **Somatomedin C or Insulin-like Growth Factor**

Somatomedin C or IGF-1 represents a biochemical marker of malnutrition and a sensitive index of nutritional repletion in patients with eating disorders and is a good parameter for nutritional follow-up. Cost and complexity for its determination restrict its use [23].

The application of this plasma protein, similar to other plasma proteins, is restricted due to the reduction in its levels during the early phases of inflammatory diseases.

1.6. **Creatinine-height index**

In situations characterized by malnutrition and hypercatabolism, the substantial degradation of skeletal muscle can be assessed through the analysis of urinary creatinine, a byproduct formed from the breakdown of creatine, which is produced at a relatively constant rate. This assessment acts as a marker for muscle catabolism and indicates any nutritional deficiencies present upon admission; however, it lacks prognostic or follow-up value when utilized in isolation. The interpretation of results may be influenced by various factors, including age, stress levels, dietary protein intake, and renal function. Additionally, it necessitates a 24-hour urine collection, and any failure in this collection or instances of oliguria may result in inaccurate interpretations and misdiagnosis of malnutrition [23].

1.7. **3-methylhistidine**

This substance is a metabolite produced during the breakdown of muscle proteins. It is observed to increase in conditions of hypercatabolism and decrease in individuals who are aged or undernourished. This metabolite serves as an important indicator for monitoring nutritional status, assessing nutritional recovery, and evaluating muscle catabolism [23].

1.8. **Urea excretion**

It is a measurement of protein catabolism. Values vary in relation to intravascular volume, nitrogen increase, and renal function [23].

2. **Biomarkers of Inflammation**

Biomarkers of inflammation are crucial values to assess in conjunction with serum proteins. The existence of inflammation has a significant impact on the nutritional condition of the patient. The inflammatory response elevates the catabolic rate and leads to the leakage of albumin from the vascular compartment. Additionally, inflammation initiates a biochemical cascade that results in reduced appetite or anorexia, consequently diminishing dietary protein consumption and exacerbating catabolism [24].

C-reactive protein (CRP) is among the most frequently utilized biomarkers of inflammation in clinical settings. Its synthesis escalates in response to infection and inflammation, accompanied by an increase in pro-inflammatory cytokines such as IL-1a, IL-1b, IL-6, and TNF, while the levels of albumin and prealbumin decline. Additional inflammation biomarkers comprise prolactin, cholesterol, and ferritin [25, 26, 27].

Consequences of Malnutrition in the Critically Ill Patient

Respiratory Consequences of Malnutrition

- **Decreased respiratory muscle mass:**

  In patients who are at ~70% of their ideal body mass, the diaphragmatic muscular mass was reduced by 43%. Half of this reduction is due to thinning of the diaphragm, and half is due to loss of its length. Also, intercostal and accessory muscles are wasted [28].

- **Decreased capacity to compensate for respiratory disease:**

  There is a diminished ability to compensate for an acute increase in demand: there is decreased respiratory muscle bulk, and respiratory muscle fatigue occurs with less effort. Thus, these patients are more susceptible to respiratory failure. This is illustrated in the increased propensity of malnourished COPD patients to undergo mechanical ventilation, as compared to their well-nourished counterparts [29].

  Respiratory muscle loss results in a greater propensity towards hypercapneic respiratory failure, and also in a decreased capacity to compensate for a metabolic acidosis [29].

- **Decreased ventilatory drive:**

  Nutritional depletion affects the CNS respiratory drive center. As nutrient-restricted volunteers (on 550kcal/day) had a 58% reduced ventilatory response to hypoxia [30].

- **Poor spirometry:**

  The vital capacity was reduced by 37% from expected normal values in malnourished individuals who did not have respiratory disease, and their maximum inspiratory and expiratory pressures were also reduced by 63% when compared to healthy age-matched controls [31].

- **Structural changes of lung tissue:**

  Lungs of rats starved to lose 40% of their total body weight demonstrated emphysema-like changes and a decrease in the surfactant properties [32].

- **Prolonged ventilator weaning:**

  Decreased muscle mass and easier fatigue give rises to poorer responses in spontaneous breathing trials; these people tire faster and require either shorter trials, or a slower decremental wean of pressure support, so the duration of ventilation correlates with the severity of nutritional depletion [33].

- **Blunted respiratory immune defenses:**

  Impaired regeneration of respiratory epithelium and decreased alveolar macrophage activity and number as well as decreased levels of IgA in the respiratory secretions. Thus, increased incidence and severity of respiratory tract infections [34].

Airway-related Consequences of Malnutrition

- **Tracheostomy complications:**

  Malnutrition leads to the development of premature age-related changes in the trachea. In other words, you may be thirty with an eighty-year-old trachea. Protein malnutrition may delay wound healing in the case of tracheostomy and increase the risk for complications (e.g., puncture of the posterior wall and tracheal cartilage damage as a result of decreased elasticity) [35].

Circulatory Consequences of Malnutrition [36]

- **Cardiac muscle atrophy and reduced left ventricular function:**

  Cardiac mass is lost in proportion to body mass. This is mainly due to LV wall thinning but the intrinsic properties of the myocardium are usually maintained.

- **Bradycardia, hypotension, and decreased cardiac output:**

  Decreased whole-body metabolic rate tends to result in decreased demand on the myocardium. The energy-conserving adaptations to prolonged starvation include the following cardiac changes: Bradycardia, hypotension, and decreased cardiac contractility. So there is a decreased capacity to compensate for increased demand, e.g., septic shock state.

- **Consequences of micronutrient depletion:**

  Key micronutrients involved in cardiac metabolism are coenzyme Q10, L-carnitine, thiamine, and amino acids, including taurine. The depletion of thiamine may give rise to a high output cardiac failure state (wet Beri Beri).

Endocrine and Electrolyte Consequences of Malnutrition

- **Depression of hypothalamic and pituitary function:**

  Nonessential metabolic activities are suppressed, e.g., gonadotropins and other reproductive hormone secretion is impaired. Thyroid and adrenal functions are depressed, and though not clinically hypoadrenal, the patient has diminished adrenal reserve and may more easily develop the relative adrenal insufficiency of critical illness. Also in starvation, menstruation is suspended and amenorrhea develops [37].

- **Electrolyte derangement in response to refeeding:**

  In brief, one can expect the following characteristic abnormalities:

  Hypokalemia, hypophosphatemia, hyponatremia, and hypomagnesaemia [38].

Effects of Malnutrition on the Function of Other Organ Systems

- **Increased mortality in malnourished renal failure patients [39]**

  Malnourished patients have increased mortality when they develop acute renal failure, particularly when it is in association with septic or cardiogenic shock. Hemodialysis patients are at risk of malnutrition because they suffer a constant amino acid loss via the circuit, and CRRT leads to removal of water-soluble vitamins.

- **Gastrointestinal consequences of malnutrition:**

Increased propensity to gastric ulceration (and decreased rate of gastric ulcer healing) and poor healing of anastomotic points in cases of resection and anastomosis, also poor barrier function of the gut, thus increased rate of bacterial translocation and increased rate of sepsis [40].

- **Hematological consequences of malnutrition [41]**
- Decreased hematopoiesis: Iron deficiency or Hematinic vitamin deficiency
- Structurally abnormal cells (e.g., the macrocytosis of B12 depletion)
- Diminished synthesis of clotting factors
- **Immunological consequences of malnutrition**

Malnutrition leads to a decrease in immune cell number and function, decreased wound healing, decreased phagocytosis, and decreased synthesis of complement proteins and immunoglobulins [34].

Conclusion:

Malnutrition is characterized by inadequate or excessive nutrient consumption, an imbalance of vital nutrients, or dysfunction in nutrient absorption with prevalence rates ranging from 38% to 78% in ICU. The effects of malnutrition on the body's physiological functions are numerous. It correlates with increased rates of illness and death among hospitalized patients and considerably raises healthcare costs. The use of a straight forward screening tool can help identify at-risk patients, enabling the initiation of early and suitable care, which can greatly enhance clinical outcomes and minimize healthcare expenses. Recommendations advise using NRS 2002 or NUTRIC score for nutritional assessment in critically ill individuals. The NUTRIC score is particularly applicable for critically ill patients due to its exclusion of recent food intake and weight change, which are difficult to obtain in ICU patients. The NUTRIC score was limited in that it omitted nutritional parameters and did not consider micronutrient deficiencies. Studies comparing NUTRIC and NRS 2002 scores had mixed findings. One study found that NRS 2002 had better sensitivity and specificity for diagnosing malnutrition than NUTRIC score, while another study found that NUTRIC score was better for assessing malnutrition risk than NRS 2002, but another study observed that there was no difference between the NUTRIC score and routine screening. Following the evidence-based nutritional protocol is the cornerstone to maximize benefit and lessen side effects of nutritional interventions.

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