A Guide to the Nutritional Assessment and Treatment of the Critically Ill Patient

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Supported by an education grant from GE imagination at work
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Foreword

As a key component to the interdisciplinary health care team, respiratory therapists must be cognizant of all of the variables that impact the care of the critically ill patient in the intensive care unit. This team includes nurses, pharmacists, physicians, dietitians, nutritionists, physical therapists, and respiratory therapists.

Proper nutritional assessment and treatment is a key component in the management of these patients. Malnutrition of the critically ill patient (and especially those on mechanical ventilation) is not a rare event; it happens fairly often. Malnutrition can lengthen time spent in the ICU, extend hospital length of stay, and for the mechanically ventilated patient, it can delay or impede the weaning process, which brings with it other associated risks. Therefore, it is the obligation of all bedside clinicians to be sure that critically ill patients be assessed for nutritional adequacy and that appropriate intervention is taken. In short, this intervention should be a multidisciplinary effort. All disciplines play an important role in managing the nutritional needs of the critically ill patient as there are several factors that must be considered beyond the patient’s caloric intake. This guide provides these considerations in a thoughtful and comprehensive manner.

This guide not only covers nutritional assessment and management of the adult critically ill patient, but also discusses specific patient populations where malnutrition is more prevalent. Obese patients, pediatric patients, and the elderly population are such classifications that are presented in this guide. Proper nutrition is key to everyone but carries greater importance in the critically ill or mechanically ventilated patient.

The American Association for Respiratory Care is grateful for the unrestricted grant from GE Healthcare that allowed us to write and publish this document. It provides a balanced review of the literature for the diagnosis, treatment, and management of the nutritional needs of the critically ill patient. This document should be in the hands of all respiratory therapists at the bedside who are managing patients in the ICU and on mechanical ventilation.

Thomas Kallstrom, MBA, RRT, FAARC
Executive Director/Chief Executive Officer
American Association for Respiratory Care
Executive Summary

Introduction

The purpose of this guide is to provide an overview of the important considerations regarding nutritional assessment and treatment that the health care team must address to ensure patients are provided with appropriate nutritional support. The goal of this work is to review a broad list of topics that covers the nutritional support and care process to provide the health care team with a broad understanding of the nutrition assessment and treatment process for the hospitalized critically ill patient.

Overview

Appropriate nutrition is essential for improving outcomes in the health care environment. Hospitalized patients have high rates of malnutrition. Unmet nutritional needs and malnutrition lead to increased morbidity and mortality, decreased quality of life, prolonged duration of mechanical ventilation, and increased length of hospital stay, all of which contribute to the higher cost of health care. Critically ill patients and those patients with respiratory failure require special attention to prevent muscle wasting and to avoid overfeeding and complications associated with nutritional care. A functional nutrition support system should include an interdisciplinary team approach for assessment and treatment, which incorporates an evaluation of nutritional risk, standards for nutritional support, an appropriate assessment and reassessment process, proper implementation, route of support based on patient condition, and a means of measuring nutrient requirements to determine if target goals are being met.

Interdisciplinary Approach

The Society of Critical Care Medicine recognizes the value and importance of a multidisciplinary team approach to nutritional care as a means to improve clinical outcomes. Each discipline in an intensivist-led interdisciplinary team, which includes dietitians, nurses, pharmacists, respiratory therapists, speech pathologists, and physical therapists, can contribute to improved outcomes and reduced health care costs.

Nutritional Risk and Assessment

Assessment of nutritional status is performed to identify patients at higher risk for malnutrition-related complications. Patients with moderate or severe malnutrition are likely to have longer ICU and hospital length of stay and higher risk of death. After the initial assessment, the primary goals of nutritional support are to maintain lean body mass in at-risk patients and to provide continuous evaluation of the nutrition care plan. Minimized risk of malnutrition can be achieved by prompt initiation of nutritional support, proper targeting of appropriate nutrient quantities, and promotion of motility through the gastrointestinal tract.

A registered dietitian or other trained clinician gathers information to examine the patient’s nutrition-related history and physical findings, anthropometric physical measurements, biochemical data, and medical tests and procedures, and then screens the patient for other nutrition-associated conditions such as malnutrition, obesity, and the risk of refeeding syndrome.

Route of Nutritional Support

Enteral nutrition (EN) is the preferred route of nutritional support. EN should be started within the first 24–48 hours after admission in patients who are incapable of volitional intake. Gastric or small bowel feeding is acceptable in the ICU setting. Enteral feeding tube placement in the small bowel should be done in patients at high risk for aspiration or whose intolerance to gastric feeding is demonstrated. Holding enteral feeding for high gastric residual volumes (GRV) in the absence of clear signs of intolerance and demonstrated risk of aspiration may result in an inappropriate cessation of EN and cause a calorie deficit over time. The definition for high GRV should be determined by individual institutional protocol; but use of GRV up to 500 mL has not been shown to increase the risks of regurgitation, aspiration, or pneumonia.

The decision to initiate parenteral nutrition (PN) is influenced by the patient’s nutritional risk, clinical di-
agnosis and condition, gastrointestinal tract function, and duration of anticipated need. PN in a previously healthy patient should be considered when EN is not feasible for the first 7–14 days after hospital admission. Patients with evidence of moderate-to-severe malnutrition where EN is not an option should receive PN within the first few days following admission.

**Nutritional Considerations During Critical Illness**

The general goals of nutritional care in all patients, including those with respiratory disorders and critical illness, are to provide adequate calories to support metabolic demands, to preserve lean body mass, and to prevent muscle wasting.

Nutritional support during critical illness attenuates the metabolic response to stress, prevents oxidative cellular injury, and modulates the immune system. The stress response to critical illness causes wide fluctuation in metabolic rate. The hyper-catabolic phase can last for 7–10 days and is manifested by an increase in oxygen demands, cardiac output, and carbon dioxide production. Caloric needs may be increased by up to 100% during this phase. The goal is to provide ongoing monitoring and support with high-protein feedings while avoiding overfeeding and underfeeding. Nutritional modulation of the stress response includes early EN, appropriate macro- and micronutrient delivery, and glycemic control.

**Determination of Nutritional Requirements**

Nutrient requirements can be calculated by over 200 different equations. Predictive equations use traditional factors for age, sex, height, weight, and additional factors for temperature, body surface area, diagnosis, and ventilation parameters. Additional data such as injury-stress, activity, medications received, and obesity have been added to improve accuracy. Several predictive equations were developed with a focus on specific patient populations and medical conditions.

Predictive equations have varying degrees of accuracy. Error rates can be significant and result in under- and overestimation of caloric needs that impact outcomes. Some equations are unsuitable for use in critically ill patients, while others have been validated with improved accuracy. Due to the extreme metabolic changes that can occur during critical illness, energy needs should be measured using indirect calorimetry (IC) in patients not responding to nutritional support, have complex medical conditions, and are ventilator dependent.

Indirect calorimetry relies on accurate determination of oxygen consumption (VO₂) and carbon dioxide production (VCO₂) using precise measurements of inspired and expired fractions of oxygen and carbon dioxide. The abbreviated Weir equation uses the measured VO₂ and VCO₂ to determine resting energy expenditure (REE). The respiratory quotient (RQ), the ratio of VCO₂ to VO₂, can then be calculated. The RQ was once thought to be a means to determine nutritional substrate use, but this assumption has never been substantiated and use of the RQ measurement is of limited clinical value. Measured values of RQ between the physiologic ranges of 0.67–1.3 should be used as a way to validate test quality. Values of RQ outside of this range invalidate the results due to technical measurement errors and should be repeated.

**Clinical Practice Recommendations**

Several clinical practice guidelines are available to guide nutritional support. The Society of Critical Care Medicine and the American Society of Parenteral and Enteral Nutrition (SCCM/ASPEN), the European Society for Clinical Nutrition and Metabolism (ESPEN), the Academy of Nutrition and Dietetics (AND), and the Canadian Clinical Practice Guidelines for Nutritional Support (CCPG) have developed best practice recommendations based on the interpretation of available evidence, consensus agreement, and expert opinion.

The following present summaries of some of the best-practice recommendations from the various organizations:

- Nutritional support should be initiated early within the first 24–48 hours in critically ill patients.
- Primary goals of nutritional support and care are to: preserve and maintain lean muscle mass; provide continuous assessment, reassessment, and modification to optimize outcome; monitor the patient for tolerance and complications such as refeeding syndrome; prevent protein energy malnutrition by giving higher protein content while providing adequate total calories; monitor nutrition goals and target achievement rate of > 50% within the first week; and prevent accumulation of a caloric deficit.
• Indirect calorimetry should be used when available or when predictive equations are known to be inaccurate.

• Current EN practice recommendations are to: preferentially feed via the enteral route; initiate EN within 24–48 hours; reduce interruptions of EN for nursing care and bedside procedures to prevent underfeeding; maintain head of bed (HOB) elevation to reduce aspiration risk; accept GRV up to 500 mL before reducing or stopping EN in the absence of clear signs of intolerance; use motility agents to improve tolerance and reduce GRV; and promote post-pyloric feeding tube placement when feasible.

• Current PN practice recommendations are to: only use PN when enteral route is not feasible; use PN based on the patient’s nutritional risk classification for malnutrition; delay PN up to seven days if the patient is in Nutritional Risk Class I or II; initiate PN early if the patient is in Nutritional Risk Class III or IV; convert to EN as soon as tolerated to reduce the risks associated with PN.

• Use of trophic or “trickle feeding” and permissive underfeeding may be beneficial.

• Use of pharmaconutrients and immunonutrition: omega-3 fatty acids (fish oils) may be beneficial in acute respiratory distress syndrome (ARDS) patients; utilize high omega-3 fatty acid to omega-6 fatty acid ratios. The use of arginine, glutamine, nucleotides, antioxidants, and probiotics may be beneficial in specific patients. The use of arginine should be avoided in patients with severe sepsis.

Appropriate nutritional support in hospitalized patients and the prevention of malnutrition can improve outcomes and reduce health care costs. The nutritional care plan should utilize the team approach and be supported by organizational standards with policies and procedures that are based on the best available evidence. The health care team’s proper implementation, continuous assessment, and monitoring of the nutrition care plan are key elements for success.
The Importance of Appropriate Nutrition

Appropriate nutrition is essential for health and healing. In hospitalized patients, malnutrition is a common problem affecting both adult and pediatric populations. Rates of malnutrition have been observed in 15–60% of hospitalized patients. Critically ill patients are at high risk for malnutrition-related complications. The resulting detrimental effects of malnutrition include increased morbidity and mortality, decreased functional quality of life, prolonged duration of mechanical ventilation, and increased length of hospital stay, all of which contribute to higher health care costs.

Critical illness associated with respiratory failure requires special attention to prevent catabolic or destructive metabolism. Nutritional therapy in this setting requires maintenance of adequate calorie and protein intake to prevent muscle wasting and avoid overfeeding and complications associated with nutritional care.

Malnutrition is a risk factor for the onset of respiratory failure and can worsen further after respiratory failure is established. Nutritional support can affect respiratory muscle strength, endurance and function, carbon dioxide production, and immune system response. To ensure successful support and recovery from respiratory failure, the nutritional care plan must also consider other important aspects, such as fluid and electrolyte balance, micronutrient requirements, and acid-base status. Recovery from respiratory failure requires a regimented nutritional support process that includes a comprehensive assessment of risk, proper implementation, ongoing reassessment of caloric requirements, tolerance of treatment monitoring, and avoiding the development of complications.

Importance of Interdisciplinary Collaboration

The role of health care team members in providing expertise regarding nutritional support has evolved around interdisciplinary collaboration. Registered dietitians and physicians complete specialized training programs to attain the Certified Nutrition Support Clinician (CNSC) credential and are increasingly involved in nutrition support organizations such as the American Society of Parenteral and Enteral Nutrition (ASPEN).

Respiratory therapists have traditionally maintained the responsibility and technical expertise in performing metabolic measurements by indirect calorimetry assessments, especially in the mechanically ventilated critically ill patient. Clinical practice guidelines developed by the American Association for Respiratory Care (AARC) maintain an evidence-based framework for nutritional assessments using indirect calorimetry for patients receiving mechanical ventilation.

Speech pathologists aid in the assessment of post-extubation dysphagia. Detection of swallowing dysfunction that is common after prolonged mechanical ventilation can help prevent the detrimental impact and risks associated with aspiration and poor nutrition among patients with or without neurologic dysfunction. Post-extubation dysphagia is associated with longer hospitalization in survivors of critical illness with neurologic impairment.

Critical care organizations such as the Society of Critical Care Medicine (SCCM) recognize the importance of an intensivist-led multidisciplinary team consisting of nurses, dietitians, pharmacists, respiratory therapists, and physical therapists. Each discipline provides expertise pertinent to nutritional support and care, contributes to improved outcomes, and reduces costs.

The future and ongoing challenge to the evolution of health care is to facilitate the team approach toward best practices and therapeutic efficacy. Appropriate nutritional assessment and treatment protocols require devoted resources toward diagnosis, intervention, and monitoring. The integrated health care delivery team trained in nutritional assessment and treatment will be better equipped to optimize and ensure health care resources are maximized.

Importance of Adequate Nutritional Assessment and Treatment

Nutritional deficits related to chronic disease and acute illnesses are frequently found in patients admitted to the ICU. Many patients who cannot resume oral food ingestion within the first few days of admission are prone to losing body mass due to poor nutrient intake and are at risk for developing an acute and pro-
longed inflammatory process. Patients in the ICU for more than 48 hours need nutritional assessment and support maintained constantly throughout their period of critical illness and hospitalization. Many critically ill patients experience severe gastrointestinal motility disorders and can experience dysphagia following extubation, which may increase the risks for aspiration. Complications associated with critical illness can have serious consequences that can be diminished with early recognition and intervention. The promotion of effective nutrition can only be achieved with a standardized nutritional support protocol that incorporates regular assessments of gastrointestinal function and tolerance of parenteral and enteral feeding.¹²

In critically ill patients unable to take nutrition by mouth, EN through the gastrointestinal tract is the preferred route. PN by intravenous access is another alternative. Use of an evidence-based nutritional management protocol increases the likelihood that patients receive nutrition via the enteral route (see Figure 1).

A standardized approach targeting gastric or post-pyloric feeding tube placement when indicated, gastric decompression and monitoring for high residual volumes, and use of bowel motility agents can shorten the duration of mechanical ventilation and reduce the risk of death. Clinical outcome benefits from improving the rate of EN can be significant when adjusted for nutritional risk of moderate-to-severe malnutrition at baseline.¹³

Development and maintenance of a best-practice nutritional support program reduces costs and improves outcomes. Maintenance of nutritional support requires continuous monitoring of the appropriate route of administration and the adequacy of usage in order to minimize costs and reduce waste.¹⁴ Insufficient calorie intake is associated with an increase in mortality risk. The reasons for failure to achieve recommendations for best clinical practice include lack of sufficient nutritional support services to monitor adherence, inadequate training in nutritional support, and restricted use of nutrient formulations that show improved outcomes secondary to their higher cost or disagreement about the supporting evidence.¹⁵

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**Figure 1. Example of a Nutrition Management Protocol**

Used with permission. See reference 13.
Nutritional Assessment

**Nutritional Risk Assessment**

Assessment of nutritional status is performed to identify patients at higher risk for malnutrition-related complications. Obesity is a risk factor for increased morbidity in the ICU with complications such as prolonged ventilation, infections, poor wound healing, and pressure ulcers. There is an increased understanding that acute and chronic inflammation are key risk factors in the pathophysiology of disease or injury associated with malnutrition. Patients determined to have a nutritional status of Class III (moderate malnutrition) or Class IV (severe malnutrition) (see Table 1) are more likely to have longer ICU and hospital length of stay and higher risk of death.

<table>
<thead>
<tr>
<th>Class</th>
<th>Nutritional Status</th>
</tr>
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<tbody>
<tr>
<td>I</td>
<td>Normal, no nutrition compromise, nutritionally stable.</td>
</tr>
<tr>
<td>II</td>
<td>Mild malnutrition, mildly compromised, somewhat nutritionally unstable with a few nutrition-related problems or indicators that affect health status.</td>
</tr>
<tr>
<td>III</td>
<td>Moderate malnutrition, moderately compromised, several nutrition-related problems or indicators that directly affect health status, and the patient may be medically unstable.</td>
</tr>
<tr>
<td>IV</td>
<td>Severe malnutrition, severely compromised, overt nutritional deficiencies or malnutrition, many nutrition-related problems or indicators that have profound effect on health status, the patient is considered medically and nutritionally unstable.</td>
</tr>
</tbody>
</table>

Table 1. Nutritional Risk Classification for Malnutrition

Nutrition risk assessment should encompass two necessary elements. The initial assessment should establish the presence or estimate of lean body mass loss prior to ICU or hospital admission. The goal of preventing further loss of lean body mass can be achieved when acute illness is promptly controlled and with the formation of an adequate nutritional support process. Additionally, the safe provision of nutritional support requires a continuous evaluation of the risks of nutritional care. Minimized risk can be achieved by prompt initiation of nutrition, targeting the appropriate nutrient quantities, promoting motility through the gastrointestinal tract, and averting serious life-threatening complications such as refeeding syndrome. Patients found to be at higher risk for nutrition-related problems should receive specialized nutritional support. Development of nutritional assessment and care protocols designed for the specific needs of critically ill patients are required to minimize the reduction of lean body mass until discharge. Nutritional care from admission to hospital discharge is essential to reducing risk of nutrition-related complications and promoting recovery (see Figure 2).

**Standards for Nutritional Support**

Nutritional support standards for adult acute care have been developed to guide the nutrition support process. These standards are designed to optimize the development and performance of a competent nutritional care plan (see Figure 3). Components of a nutritional support program should include the following:

**Organization**

A nutritional support service or interdisciplinary team approach with established policies, procedures, and a performance improvement process should be initiated for each admitted patient.

**Nutritional Care Process**

The process for nutritional care should identify at-risk patients using a screening process that is formalized and documented. Regulatory agencies such as The Joint Commission (PC.01.02.01 – EP 4) require that a nu-
Nutritional screening be completed when the patient’s condition warrants within the first 24 hours after admission. Identified nutritionally at-risk patients should undergo a formal nutritional assessment that includes subjective and objective criteria, classification of nutritional risk, requirements for treatment, and an assessment of appropriate route of nutrition intake.

**Development of a Nutritional Care Plan**

The nutritional care plan should include clear objectives, use a multidisciplinary approach, have defined goals, select the most appropriate route, select the least costly substrate formulation for the patient’s disease process, and include a process for reassessment of adequacy and appropriateness.

**Implementation Process**

The ordering process for the nutritional care plan should be documented before administration occurs. The appropriate nutritional access device should be inserted by a qualified health care professional using standardized procedures with appropriate placement confirmed and placement and/or adverse events documented. Enteral and parenteral formulations should be prepared accurately and safely using established policies and procedures. Parenteral formulation should be prepared in a sterile environment using aseptic techniques. Additives to formulations should be checked for incompatibilities and prepared under direct supervision of a pharmacist. All nutritional formulations should be labeled appropriately and administered as prescribed while monitoring patient tolerance. Protocols and procedures should be used to reduce and prevent the risks of regurgitation, aspiration and infection, and a process for Sentinel Event review should be established.

**Monitoring and Re-evaluating the Nutritional Care Plan**

Establish the frequency and parameters for monitoring the nutritional care plan based on the patient’s degree of nutritional risk. Standard procedures for monitoring and re-evaluation should be established to determine whether progress toward short- and long-term goals are met, or if realignment of goals are necessary.

**Transition of Therapy Process**

Assess achievement of targeted nutrient intake to ensure that at least 60% of estimated requirements are
being met before nutritional support is transitioned between parenteral, enteral, and oral intake. Maintain continuity of care when transitioning between levels of care or changes in the care environment. Termination of nutritional support should follow protocols that take into account ethical and legal standards and the patient’s advance directives.18

**Nutritional Assessment**

The nutritional assessment process includes the collection of data to determine the nutritional status of an individual. A registered dietitian or physician trained in clinical nutrition gathers data to compare various social, pharmaceutical, environmental, physical, and medical factors to evaluate nutrient needs. The purpose of nutrition assessment is to obtain, verify, and interpret data needed to identify nutrition-related problems, their causes, and significance. This data is then used to ensure adequate nutrition is provided for the recovery of health and well-being.19

**Food/Nutrition-related History**

Past dietary behaviors can be identified in the nutritional assessment to determine the individual’s pattern of food consumption. Assessment of dietary history should include:

- Appetite
- Weight history (loss, gain)
- Taste changes
- Nausea/vomiting
- Bowel pattern (constipation, diarrhea)
- Chewing, swallowing ability
- Substance abuse
- Usual meal pattern
- Diet restrictions
- Food allergies or intolerances
- Medications, herbal supplements
- Meal preparation, ability to buy/obtain food
- Activity level
- Knowledge/beliefs/attitudes
- Nutrient intake

The registered dietitian may use a 24-hour recall or a usual daily intake recall, a food diary or food record, or a food frequency questionnaire. The 24-hour recall or food frequency questionnaire employ retrospective data that can be easily used in a clinical setting. The 24-hour recall is a commonly used technique incorporated into the patient interview in which the individual states the foods and the amount of each food consumed in the previous 24 hours. Accuracy of the recall is dependent on the patient’s memory, the perception of serving size, and the skill of the interviewer to elicit complete information. The 24-hour recall may underestimate usual energy intake. Food frequency questionnaires (FFQ) collect information on both the frequency and amount consumed of specific foods.20 The FFQ can help to identify eating patterns; however, intake of nutrients may be overestimated. In food diaries or food records, dietary intake is assessed by prospective information and contains dietary intake for three to seven days. These methods provide the most accurate data of actual intake but are very labor intensive and time consuming to analyze. Therefore, they are typically used in the research or outpatient setting.

**Anthropometric Measurements**

Anthropometrics refers to the physical measurements of the body. The measurements are used to assess the body habitus of an individual and include specific dimensions such as height, weight, and body composition (i.e., skin-fold thickness, body circumference including points at the waist, hips, chest, and arms).16

**Height and weight**

Height and weight can be assessed by asking the patient or caregiver, or by taking a direct measurement. When recording data, note the date and whether the height and weight were stated or measured. Once these two measurements are obtained, a more useful number (the body mass index [BMI]), can be calculated. BMI is defined by weight and height measurements where:

Using pounds and inches:

\[
\text{BMI} = \frac{\text{Weight in pounds}}{\text{Height in inches}^2} \times 703
\]

Using kilograms and meters:

\[
\text{BMI} = \frac{\text{Weight in kilograms}}{\text{Height in meters}^2}
\]

BMI can have a strong correlation between body fat and risk of disease. This number is a useful tool for determining the BMI category: underweight, healthy weight, overweight, obese, or morbidly obese.

**BMI categories**

A healthy weight may be confirmed by a BMI of between 18.5 and 24.9 for adults or a BMI-for-age between the 10th and 85th percentiles for children. A BMI of 25.0
to 29.9 indicates excessive weight in the adult. BMI-for-age in children suggestive of excessive weight is between the 85th and 95th percentiles. Obesity is defined as a BMI greater than 30 in the adult and greater than the 95th percentile in boys and girls aged 2 to 20 years. Adults who are categorized as underweight have a BMI of less than 18.5, while underweight children score in the bottom 10th percentile for BMI-for-age. See Table 2.

Body composition

Body composition measures body fat, muscle mass, and bone density. Body weight variations in individuals of similar height differ in the proportion of lean body mass, fat mass, and skeletal size. Several common measurements, which include skin-fold thickness, circumference measurements, and more high-tech measurements like bioelectrical impedance analysis (BIA) or dual-energy X-ray absorptiometry (DXA) scans, can be used to determine body fat to body mass, intracellular water to extracellular water ratios, and bone density.

Skinfolds

Skinfold thickness measures subcutaneous fat with the assumption that it comprises 50% of total body fat. Usually, the triceps and subscapular skinfolds are the most useful for evaluation. Skinfold thickness measurements are limited by reliability due to proper equipment and technique of the examiner and have limited practical application in the acute care setting.

Arm muscle area

The triceps skinfold (TSF) measurement, along with mid-upper arm circumference (MAC), is used to calculate the arm muscle area (AMA). The MAC is measured halfway between the acromion process of the scapula and the tip of the elbow. The results indicate muscle stores available for protein synthesis or energy needs. Changes over time in AMA will show whether the patient has been deprived of protein or calories. AMA is one of the markers of nutritional status and can be a predictor of mortality.

Waist circumference

An alternative to BMI, waist circumference can be a more accurate predictor of excess body fat and risks associated with obesity. The measurement of waist circumference has been correlated with visceral fat; and the distribution of body fat, specifically as visceral fat, which is deposited in the abdominal region, is correlated with obesity-related health risks. (See Figure 4.)

According to the U.S. Department of Health and Human Services (HHS), the following individuals are at increased risk for developing chronic diseases:

- Women with a waist circumference of more than 35 inches
- Men with a waist circumference of more than 40 inches.

However, the World Health Organization, due to recent research findings, has recommended lower thresholds for waist circumference for Asian populations. Therefore, those at increased risk for developing chronic disease include:

- Asian women with a waist circumference of more than 31 inches
- Asian men with a waist circumference of more than 35 inches.

### Table 2. BMI Classifications for Adults

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Classification</th>
<th>Risk of Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;16.0</td>
<td>Severe underweight</td>
<td>Severe</td>
</tr>
<tr>
<td>16.0–16.9</td>
<td>Moderate underweight</td>
<td>Moderate</td>
</tr>
<tr>
<td>17.0–18.5</td>
<td>Mild underweight</td>
<td>Average</td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>Underweight</td>
<td>Low, but risk of other clinical problems increases</td>
</tr>
<tr>
<td>18.5–24.9</td>
<td>Normal weight</td>
<td>Average</td>
</tr>
<tr>
<td>25.0–29.9</td>
<td>Overweight (pre-obese)</td>
<td>Increased</td>
</tr>
<tr>
<td>30.0–34.9</td>
<td>Obese Class I</td>
<td>Moderate</td>
</tr>
<tr>
<td>35–39.9</td>
<td>Obese Class II</td>
<td>Severe</td>
</tr>
<tr>
<td>≥40.0</td>
<td>Obese Class III</td>
<td>Very Severe</td>
</tr>
</tbody>
</table>

Used with permission. See reference 21.
Nutritional Assessment

Other body assessment tools

More accurate measurements of body composition include the more advanced techniques of bioelectrical impedance analysis (BIA), low-density X-rays (DXA), computed tomography (CT) scan, and magnetic resonance imaging (MRI). These methods are very accurate and noninvasive; however, they are not necessarily ideal in the clinical setting, are expensive, and time consuming.

Biochemical Data

Laboratory values of particular significance used in assessing nutritional status include serum proteins and lymphocytes. An individual’s protein stores may indicate the degree of nutritional risk. Protein-energy malnutrition (PEM) may be reflected in low values for albumin, transferrin, transthyretin (prealbumin), retinol-binding protein, and total lymphocyte count. Blood levels of these markers indicate the level of protein synthesis and thus yield information on overall nutritional status. However, inadequate intake may not be the cause of low protein values. Certain disease states, hydration level, liver and renal function, pregnancy, infection, and medical therapies may alter laboratory values of circulating proteins. It is important to note that a nutritional disorder diagnosis cannot be made from one single laboratory value but should be utilized with other assessment data to determine the nutritional status of the patient. The majority of laboratory values used in nutritional assessments lack sensitivity and specificity for malnutrition. See Table 3.

Albumin

Comprising the majority of protein in plasma, albumin is commonly measured. The half-life of albumin is 14–20 days, which reduces its usefulness for monitoring the effectiveness of nutrition in the acute care setting. However, the general availability and stability of albumin levels from day to day make it one of the most common tests for assessing long-term trends and provides the clinician with a general idea of baseline nutritional status prior to a procedure, insult, or acute illness. Albumin levels often reflect the metabolic response and severity of disease, injury, or infection and can be a useful prognostic indicator. Albumin synthesis is affected by nutrition and also by inflammation. During an inflammatory state, the production of albumin diminishes. The effect of inflammation and hypoalbuminemia has been linked with increased morbidity, mortality, and longer hospitalization.

Transferrin

The transport protein for iron (transferrin) has a half-life of 8–10 days and, therefore, can be a better indicator of improved nutritional status than albumin. However, lack of iron influences its values along with a number of other factors, including hepatic and renal disease, inflammation, and congestive heart failure.

Table 3. Common Biomarkers of Nutritional Status and Inflammation

<table>
<thead>
<tr>
<th>Biomarker</th>
<th>Normal Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>3.5–5 g/dL</td>
</tr>
<tr>
<td>Transferrin</td>
<td>200–400 mg/dL</td>
</tr>
<tr>
<td>Prealbumin (Transthyretin)</td>
<td>18–50 mg/dL</td>
</tr>
<tr>
<td>Retinol-binding protein</td>
<td>3.0–8.0 mg/dL</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0–1.0 mg/dL</td>
</tr>
</tbody>
</table>

Used with permission. See reference 28.
Transthyretin and retinol-binding protein

Transthyretin, also called prealbumin, and retinol-binding protein have a half-life of just two to three days and 12 hours, respectively. Each responds to nutritional changes much quicker than either albumin or transferrin. However, a number of metabolic conditions, diseases, therapies, and infectious states influence their values. Levels of transthyretin and retinol-binding protein are influenced by many factors other than nutritional status. Similar to albumin, their use is limited in the setting of stress and inflammation. Because these conditions are so common among the critically ill, visceral protein markers are of limited usefulness for assessing nutritional deficiency but are of greater importance in assessing the severity of illness and the risk for future malnutrition.

Total lymphocyte count

The immune system may be compromised by a lack of protein. Two laboratory values, white blood cells and percentage of lymphocytes, have been used as measures of a compromised immune system. However, many non-nutritional variables influence lymphocyte count; therefore, their usefulness in assessing nutritional status is limited.

Biomarkers of inflammation

Biomarkers of inflammation are important values to measure along with serum proteins. The presence of inflammation affects the nutritional status of the patient. The inflammatory response increases the catabolic rate and causes albumin to leak out of the vascular compartment. Inflammation triggers a chemical cascade that causes a loss of appetite or anorexia, therefore decreasing dietary protein intake and further catabolism.

One of the most common biomarkers of inflammation used in clinical practice is C-reactive protein (CRP). The production of CRP increases with infection and inflammation along with pro-inflammatory cytokines (i.e., IL-1a, IL-1b, IL-6, TNF) while the production of albumin and prealbumin decreases. Other biomarkers of inflammation include prolactin, cholesterol, hyperglycemia, and ferritin.

Other Tests and Procedures

Creatinine-height index

Because the rate of creatinine formation in skeletal muscle is constant, the amount of creatinine excreted in the urine every 24 hours reflects skeletal muscle mass and can indicate muscle depletion. However, it requires an accurate urine collection and normal renal function. Other factors that influence creatinine excretion that can complicate interpretation of this index include age, diet, exercise, stress, trauma, fever, and sepsis.

Nitrogen balance (protein catabolism)

Nitrogen balance reflects skeletal muscle, visceral or organ, blood cell, and serum protein stores. Because nitrogen is a major byproduct of protein catabolism, its rate of urinary excretion can be used to assess protein adequacy. The amount of nitrogen excreted in the urine is typically measured as the 24-hour urinary urea nitrogen (UUN). If there is a positive urinary nitrogen balance, protein metabolizing is sufficient, and nitrogen is excreted in the urine. A UUN value less than zero indicates a negative nitrogen balance, which indicates that the patient needs a higher protein intake. Theoretically, by increasing exogenous protein, loss of endogenous protein is reduced. However, because of invalid 24-hour urine collections, alterations in renal or liver function, large immeasurable insensible losses of protein from burns, high-output fistulas, wounds, ostomies, and inflammatory conditions, nitrogen balance calculations are generally negative and do not accurately reflect nutrition status.

Pulmonary function

Pulmonary function test results may change with malnutrition. Weakness of the diaphragm and other muscles of inspiration can lead to a reduced vital capacity and peak inspiratory pressures. The strength and endurance of respiratory muscles are affected, particularly the diaphragm. Respiratory muscle weakness can affect the ability to cough and clear secretions, which may impact rates of pulmonary complications. Dietary antioxidants are thought to protect tissue from oxidant injury or stress, due to their ability to stabilize reactive molecules. Oxidative stress contributes to airflow limitation; therefore, antioxidant vitamins provide pulmonary antioxidant defense.

Nutrition-focused physical findings

The nutritional-focused physical assessment is the evaluation of body systems, oral health, suck/swallow/breathing ability, and appetite, conducted by the Registered Dietitian or another member of the health care team as part of the nutritional assessment. Physical examination can reveal observable signs of nutrition deficiencies where high cell turnover occurs, like the hair, skin, mouth, and tongue. Signs of weight loss,
including loss of lean body mass and subcutaneous fat, should be investigated. Special attention should be given to fluid retention as this can mask weight loss. Other physical findings such as skeletal muscle depletion can be clinical indicators of inflammation or signs of systemic inflammatory response.

**Patient History**

Interviewing the patient or the caregiver to determine past and current eating practices can be helpful. The patient’s medical record can also reveal additional information regarding social, pharmaceutical, environmental, and medical issues. Much of this data can give insight into a patient’s nutritional status. The patient’s social history indicates marital status, employment, education, and economic status. Drug-nutrient interactions may be identified from the prescribed medications that lead to potential nutrient deficiencies. Environmental issues could point out the difficulties the patient has in procuring, storing, and/or preparing food. The education acquired by the health care provider could determine the potential for understanding and applying nutrition counseling. The economic status of the patient may drive certain food choices. Much of the information can be helpful to raise suspicion and guide the investigation further into revealing the nutritional status of the patient.
Malnutrition

Once a nutritional assessment is completed, the degree and severity of malnutrition (if present) can be determined. Malnutrition is characterized by deficient, excess, or unbalanced nutrient intake. Malnutrition syndromes can be associated with acute or chronic inflammation. Etiology-based diagnosis of malnutrition falls into three categories: “starvation-related malnutrition,” when there is chronic starvation without inflammation (e.g., secondary to anorexia nervosa), “chronic disease-related malnutrition,” when inflammation is chronic and of mild-to-moderate degree (e.g., organ failure, pancreatic cancer, rheumatoid arthritis, or sarcopenic obesity), and “acute disease or injury-related malnutrition,” when inflammation is acute and severe (e.g., major infection, burns, trauma, or closed head injury).37 See Figure 5.11

Identification of two or more of the following is recommended for a diagnosis of malnutrition:

• Insufficient nutrient intake < 50–75% of estimated energy requirements over time
• Loss of weight
• Loss of muscle mass
• Loss of subcutaneous fat
• Localized or generalized fluid accumulation that may mask weight loss or loss of lean body mass

Malnutrition is a major contributor to increased morbidity and mortality, decreased functional quality of life, prolonged duration of mechanical ventilation, increased length of hospital stay, and higher health care costs.3,11

Undernutrition and Protein Energy Malnutrition

Undernutrition is a nutritional deficiency resulting from the lack of nutrient intake. Undernutrition suppresses immune function and is often a precursor of disease progression and/or worsening infection.38 During critical illness, proteolysis (muscle protein breakdown) increases, which can cause dietary protein needs to more than double. Failure to meet this increased protein requirement can lead to a state of protein energy malnutrition, which can be characterized by weight loss and muscle wasting.39

Overnutrition, Obesity, and Metabolic Syndrome

Overnutrition in the obese patient can lead to fluid overload, hyperglycemia, fatty liver deposits and liver dysfunction, and the need for prolonged ventilator support.40 Obese individuals have a higher incidence of inflammation-associated chronic diseases, greater susceptibility to infection,41,42 and have an increased risk of mortality.43,44 Obesity-induced inflammation is an important contributor to the development of insulin resistance and hyperglycemia.45 Obesity increases the risk and prevalence of asthma in both adults and children.46 Sarcopenic obesity is obesity associated with a decline in muscle strength and mass in elderly patients, which may further reduce physical activity and result in additional weight gain.47 The additional weight loading of the chest wall increases the work of breathing, reduces lung volume, decreases functional residual capacity, and can result in atelectasis, hypoxemia, and hypercapnia. Obese patients have a high
prevalence of obstructive sleep apnea and are prone to developing obesity hypoventilation syndrome.48,49

The metabolic syndrome consists of a grouping of risk factors that have shown to be strongly associated with an increased risk for cardiovascular disease and the development of type-2 diabetes mellitus. Metabolic risk factors for metabolic syndrome consist of: hyperlipidemia, hypertension, hyperglycemia, a proinflammatory state, and a prothrombotic state. The predominant underlying risk factors include abdominal obesity and insulin resistance.50 Obesity hypoventilation syndrome, obstructive sleep apnea, and congestive heart failure are associated with the development of metabolic syndrome.51-56

**Refeeding Syndrome**

Refeeding Syndrome is a term used to describe the complex metabolic and clinical disturbances that occur after the reinstitution of nutrition to patients who are severely malnourished or starved.57 Clinical manifestations of refeeding syndrome are related to the resulting electrolyte and vitamin deficiencies cause by starvation and malnutrition, and the
subsequent abnormalities that develop once nutritional support is initiated. Refeeding after a period of malnutrition and starvation increases the basal metabolic rate, which results in major alterations in macronutrient metabolism. This leads to hypophosphatemia, hypomagnesemia, hypokalemia, and thiamine deficiency and can cause hyperglycemia during refeeding, decreased excretion of sodium and water, and an expansion of fluid compartments. The development of refeeding syndrome can result in severe cardiovascular and pulmonary complications. Cardiac arrhythmias and death have been seen in chronically malnourished patients receiving aggressive parenteral nutrition and early carbohydrate administration. Other significant complications include confusion, coma, and seizures. Congestive heart failure, pulmonary edema, diaphragm and intercostal muscle weakness, decreased tissue oxygen delivery, and increased carbon dioxide production can cause respiratory failure and can make weaning from mechanical ventilation more difficult.58,59 See Table 4.58

Factors that aid in the identification of patients at risk for refeeding syndrome include.57,60

• BMI < 16–18.5 kg/m²
• Unintentional weight loss >10–15% within last 3–6 months
• Little or no nutritional intake for >5–10 days
• A history of alcohol abuse or drugs, including insulin, chemotherapy, antacids, or diuretics
• Low levels of phosphorous, potassium, or magnesium prior to feeding
• Uncontrolled diabetes mellitus (diabetic ketoacidosis)
• Abused/neglected/depressed elderly adults
• Bariatric surgery
• Dysphagia
• Malabsorption (short bowel syndrome [SBS], inflammatory bowel disease [IBD], cystic fibrosis [CF], persistent nausea/vomiting/diarrhea, chronic pancreatitis)
• Chronic disease conditions (tuberculosis, HIV, cancer)
• Prolonged hypocaloric feeding or fasting
• Unconventional/eccentric diets.
The two routes of nutritional support are enteral and parenteral. Enteral nutrition (EN) is provided via the gastrointestinal tract, either by mouth or through a feeding tube. Parenteral nutrition (PN) is an intravenous solution composed of nutrients infused through an IV line that bypasses the gastrointestinal tract. Determination of the most appropriate route is influenced by the patient’s nutritional risk, clinical diagnosis and condition, gastrointestinal tract function, and duration of anticipated need. See Figure 6.4

### Parenteral Nutrition

PN provides nutrition to patients who are unable to digest or absorb sufficient nutrition via the gastrointestinal tract. These patients may include those with an obstruction, severe malabsorption, bowel hypomotility (ileus), or bowel ischemia (see Table 5). EN is the preferred modality over PN as it has been shown to have cost, safety, and physiologic benefits. EN may reduce disease severity, complications, and length of stay, and improve patient outcome.10

Administration of PN requires insertion of a central venous catheter or peripherally inserted central catheter (PICC). Due to the risks of catheter-related complications and infection, current recommendations suggest that PN should only be used if early EN is not feasible for the first 7–14 days following ICU admission, especially in patients who were previously

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**Figure 6. Algorithm for Determining Route of Nutrition Administration**

Nutritional Support

A Guide to the Nutritional Assessment and Treatment of the Critically Ill Patient © 2013

10 Healthy prior to hospitalization. In a recent multicenter, randomized controlled trial, later initiation of PN was associated with shorter length of ICU stay, fewer infections and other complications, and fewer days on mechanical ventilation when compared with early initiation.61 Patients with evidence of moderate-to-severe malnutrition where EN is not an option should receive PN within the first few days following admission.10

Parenteral nutrition formulations

PN is customized to individual patient needs for nutrients, electrolytes, vitamins, and trace elements by specially certified pharmacists through a process called compounding.62 Manual and automated compounding devices are available, but numerous cases of parenteral compounding errors in ordering, transcribing, compounding, and infectious complication have been reported.63,64 To address these problems, preparation of PN can be outsourced to specialized compounding pharmacies. Standardized, premixed, and commercial products are available. To improve the safe administration of parenteral nutrition, standardized procedures for ordering, labeling, nutrient dosing, screening orders, administering, and monitoring are recommended.65

Enteral Nutrition

Short-term EN is typically administered via a nasally or orally inserted small bore weighted tip feeding tube called a “Dobhoff” tube. The weighted tip helps the tube travel past the stomach and through the pyloric valve into the duodenum and jejunum. Initial placement is performed with a guide wire inserted into the tube. Complications during insertion can include soft-tissue trauma and hemorrhage, esophageal perforation, and placement into the lungs. Definitive verification of tube placement is determined by chest radiograph.

Percutaneous endoscopic gastrostomy (PEG) or jejunostomy tubes placed surgically through the abdominal wall should be considered for long-term enteral feeding when nutritional support is expected for at least four weeks.66

Enteral nutrition formulations

Numerous EN formulations are available with various products designed for specific disease states such as renal failure, gastrointestinal disease, diabetes and hyperglycemia, hepatic failure, acute and chronic pulmonary disease, and immunocompromised states. See Table 6.

Unfortunately, most of these specialty products lack strong scientific evidence to promote routine use because of inconsistent, inconclusive, or unavailable clinical trial results.67,68 Until clinical evidence becomes available, standard formulas should be used for the majority of patients requiring enteral feeding. In the critically ill, at-risk patient, evaluation of the nutritional needs, physical assessment, metabolic abnormalities, gastrointestinal (GI) function, and overall medical condition should be used to identify the enteral formula that will meet the individual patient requirements and determine product selection.66,69

Feeding Tube Placement — Gastric versus Post-Pyloric

There is an ongoing controversy in clinical practice regarding post-pyloric versus gastric feeding tube placement. Generally, in the intensive care unit it is preferred to place the feeding tube in the post-pyloric position due to the assumption that delayed gastric emptying results in a predisposition to bleeding, regurgitation, reflux, and aspiration.70-72 The clinical condi-

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Table 5. Contraindications to Enteral Nutrition Support

<table>
<thead>
<tr>
<th>Contraindications to Enteral Nutrition Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Nonoperative mechanical GI obstruction</td>
</tr>
<tr>
<td>• Intractable vomiting/diarrhea refractory to</td>
</tr>
<tr>
<td>medical management</td>
</tr>
<tr>
<td>• Severe short-bowel syndrome (&lt; 100 cm</td>
</tr>
<tr>
<td>small bowel remaining)</td>
</tr>
<tr>
<td>• Paralytic ileus</td>
</tr>
<tr>
<td>• Distal high-output fistulas (too distal to</td>
</tr>
<tr>
<td>bypass with feeding tube)</td>
</tr>
<tr>
<td>• Severe GI bleed</td>
</tr>
<tr>
<td>• Severe GI malabsorption (eg, enteral</td>
</tr>
<tr>
<td>nutrition failed as evidenced by progressive</td>
</tr>
<tr>
<td>deterioration in nutritional status)</td>
</tr>
<tr>
<td>• Inability to gain access to GI tract</td>
</tr>
<tr>
<td>• Need is expected for &lt; 5–7 days for malnourished</td>
</tr>
<tr>
<td>adult patients or 7–9 days if adequately</td>
</tr>
<tr>
<td>nourished</td>
</tr>
<tr>
<td>• Aggressive intervention not warranted or</td>
</tr>
<tr>
<td>not desired</td>
</tr>
</tbody>
</table>

GI, gastrointestinal.

tion of the patient generally dictates the placement of the feeding tube. Patients who are at high risk for aspiration and delayed gut motility should be considered for post-pyloric small bowel access. Per ASPEN guidelines, these patients include those who have sustained severe blunt and penetrating torso and abdominal injuries, severe head injuries, major burns, undergone major intra-abdominal surgery, had a previous episode of aspiration or emesis, had persistent high gastric residuals, are unable to protect the airway, require pro-

longed supine or prone positioning, or are anticipated to have multiple surgical procedures.4

Post-pyloric feeding access can be difficult and may delay the introduction of EN. The repeated attempts of placement and using more advanced modalities such as fluoroscopy to determine placement can increase costs of providing care.73

Multiple studies have not shown a significant difference in improved clinical outcomes with post-pyloric feeding tube placement. Meta-analysis of clinical out-

<table>
<thead>
<tr>
<th>Enteral Formula Type</th>
<th>Description</th>
<th>Products</th>
</tr>
</thead>
</table>
| Standard Formulas    | • Meant to match nutrient requirements for healthy individuals  
                       • Concentrations vary from 1.0–2.0 kcals/mL  
                       • May or may not include soluble/insoluble fiber | Osmolite1  
                       Jevity1  
                       Promote1  
                       TwoCal HN1  
                       Nutren2  
                       Isosource2  
                       Fibersource2  
                       Replete2 |
| Diabetic             | • Lower carbohydrate with increased fat  
                       • Contain more complex carbohydrates  
                       • Concentrations vary from 1.0–1.5 kcal/mL | Glucerna1  
                       Glytrol2  
                       Diabetisource AC2 |
| Renal                | • Generally lower in protein, calorically dense, and lower in potassium, magnesium and phosphorus  
                       • May vary in protein, electrolytes, vitamins, and minerals depending on renal replacement therapy | Nepro1  
                       Suplena1  
                       Novasource Renal2  
                       Renalcal2 |
| Liver                | • Increased amounts of branched chain amino acids (BCAA) with decreased aromatic amino acids (AAA)  
                       • Calorically dense, low in total protein, sodium, and fat-soluble vitamins and minerals | Nutrihep2 |
| Pulmonary            | • Calorically dense, low in carbohydrates, and high in fat (COPD)  
                       • Calorically dense, high omega-3 to omega-6 fatty acid ratio, antioxidants, (ARDS) | Pulmocare (COPD)1  
                       Nutren Pulmonary (COPD)2  
                       Oxepa (ARDS)1 |
| Immune Modulating    | • Key ingredients include arginine, glutamine, nucleotides, and omega-3 fatty acids | Pivot 1.51  
                       Impact2 |
| Bariatric            | • Designed for critically ill morbidly obese patients  
                       • Very high in protein  
                       • Contains omega-3 fatty acids | Peptamen Bariatric2 |
| Pediatric            | • Formulated for pediatric nutrient needs and conditions | Pediasure1  
                       Elecare1  
                       Nutren Junior2  
                       Peptamen Junior2 |

**LEGEND:** Abbott Nutrition1, Nestle Health Science2
comes of several small sample size studies have evaluated mortality, incidence of pneumonia, and reducing aspiration risk. The only clinical outcome that has been shown to have an improvement with post-pyloric feeding is an increase in the volume of targeted nutrient delivery.

Current recommended practice is to target post-pyloric feeding tube placement but not to delay gastric feeding unless clear signs of intolerance, aspiration risk, and high gastric residual volume are evident.

**Gastric Residual Volume**

The practice of measuring GRV is a standard nursing practice used to determine tolerance of gastric tube feedings. It is assumed that high GRV is correlated with an increased risk of reflux, aspiration, and pneumonia. However, little evidence exists in the literature correlating GRV with these risks. GRV has not been shown to be a marker of aspiration. Aspiration occurs in critically ill patients whether GRV is low or high, but aspiration risk may increase with high GRV. It has also been shown that GRV does not correlate with gastric emptying.

The practice of checking GRV is time intensive, and small-bore feeding tubes often occlude during the process. In fact, the practice of checking GRV may result in inappropriate cessation of EN and cause a decrease in nutrient delivery and accumulation of calorie deficit over time. Caloric deficit in already at-risk mechanically ventilated patients may increase complications and morbidity.

In the absence of other signs of intolerance (such as emesis and abdominal distension), the most recent ASPEN/SCCM clinical practice guidelines for holding or reducing enteral nutrition is a GRV of 500 mL. This highly controversial recommendation is supported by several studies that show that a higher tolerable GRV was not associated with an increase in adverse events such as regurgitation, emesis, and aspiration. Higher GRV in combination with prokinetic agents to promote bowel motility have been shown to improve nutrient volume administered and reduce the time to reach target goals without increasing complications. Two prospective studies compared routine GRV monitoring to not checking GRV and also found no difference in adverse events. Therefore, the controversial practice of tolerating a higher GRV of 500 mL is supported by current evidence.

Regardless of the acceptable GRV used by an institution, the following practices have been proven to reduce the risk of aspiration:

- Use of bowel motility agents such as metoclopramide
- Post-pyloric or small-bowel feeding tube placement when indicated.

**Trophic Feedings**

Low-dose, “trickle,” or trophic feeding is the practice of feeding minimal amounts (10–30 mL/hr) of EN with the primary goal to maintain gut function and integrity despite not meeting daily caloric needs. It is most often used in preterm infants on PN or in adult patients with impaired enteral feeding tolerance or gut function. EN stimulates organs of digestion to function in their normal capacity and to assist in the digestion and absorption of nutrients. It also prevents passage of bacteria across the GI tract into the systemic circulation, reducing infection rates, enhancing immune function, and preserving GI mucosal structure and function. Trophic feeding may also reduce the development of a postoperative ileus. Studies in mechanically ventilated patients with respiratory failure or ARDS show that trophic feedings resulted in fewer episodes of gastrointestinal intolerance but resulted in similar clinical outcomes compared to early advancement to full enteral feeding.

**Stress Prophylaxis**

Critically ill patients are at risk of GI bleeding from gastric or duodenal ulcers due to increased gastric acidity and decreases in the gastric mucosal barrier. EN can improve mucosal blood flow and reverse the production of inflammatory mediators that cause gastropathy. EN may provide stress prophylaxis and help to reduce the use of acid-suppressive therapy in the ICU. Additional randomized controlled trials and protocols are needed to investigate this further.

**Nutrient Requirements and Distribution**

The purpose of a nutritional assessment is to determine a nutrition care plan with the primary goal of meeting the nutritional requirements of the patient. This includes determination of total energy, protein, carbohydrate, fat, and micronutrient needs.

**Carbohydrate requirements**

Carbohydrates are the primary fuel source for the body. It is recommended that approximately 45–65% of total calories come from carbohydrates. A minimum daily amount of 100–150g/day is necessary to provide adequate glucose to the brain. If consumed in insufficient amounts, an accumulation of ketone bodies develops...
as a result of excessive fat and protein catabolism, and acidosis occurs.96

**Protein requirement**
Amino acids or proteins are essential to maintaining or restoring lean body mass. Because illness usually increases protein catabolism and protein requirements, the recommended dietary allowance (RDA) of 0.8 g/kg per day is generally insufficient for critically ill patients. Based on the assessment of the protein catabolism rate, protein intake may need to be doubled or even tripled above the RDA (1.5 to 2.5 g/kg/day). Ideally, approximately 20% of a patient’s estimated calorie needs should be provided by protein. Higher percentages of protein may be needed in patients with “wasting syndrome” or cachexia, elderly persons, and persons with severe infections. However, whenever high protein intakes are given, the patient should be monitored for progressive uremia or azotemia (rising BUN > 100 mg/dl).96 Too much protein is harmful, especially for patients with limited pulmonary reserves. Excess protein can increase O2 consumption, REE, minute ventilation, and central ventilatory drive.97 In addition, overzealous protein feeding may lead to symptoms such as dyspnea in patients with chronic pulmonary disease.

**Fat requirements**
The remaining calories (20–30%) should be provided from fat. A minimum of 2–4% is needed to prevent essential fatty acid deficiency. Fat intakes in excess of 50% of energy needs have been associated with fever, impaired immune function, liver dysfunction, and hypotension.96

**Vitamins, minerals, and electrolytes**
The dietary reference intakes (DRI) provide the recommended optimal level of intake for vitamins, minerals, and electrolytes. The primary goal is to prevent nutrient deficiencies as well as help reduce the risk of chronic diseases. Some nutrients may need to be supplemented above the DRI for certain disease states, therapies, or conditions.96

**Fluid requirements**
Fifty to sixty percent of body weight consists of water. Fluid requirements are estimated at 1 ml/kcal/day or 20–40 ml/kg/day. Depending on a patient’s medical condition, fluid restriction may be warranted. Additional fluid may be required for excessive fluid losses (urinary, fecal, blood, wound, emesis) and with excessive insensible losses (fever).96

**Nutrition Support and Respiratory Function**
Patients with acute and chronic respiratory failure may present with or have the potential to develop nutrition-related complications. Nutrition support plays a significant role in treatment as further deterioration can have a direct effect on respiratory function, further decline, and poor outcomes.96 Specific nutrition recommendations exist for intervention and treatment of acute and chronic respiratory failure.

**Respiratory consequences of malnutrition** may include the following:99

- Loss of diaphragmatic and accessory muscle mass and contractility
- Ineffective cough
- Decreased maximum expiratory pressure and maximum inspiratory pressure
- Decreased FVC or FEV1
- Reduced production of surfactant
- Fluid imbalance
- Congestive heart failure
- Decreased lung compliance, atelectasis, and hypoxemia
- Decreased hypoxic and hypercapnic response
- Increased CO2 production
- Increased incidence of hospital-acquired infections
- Decreased lung clearance mechanisms
- Increased bacterial colonization
- Emphysematous changes to lung parenchyma

**Chronic Obstructive Pulmonary Disease**
Disease-related malnutrition is common in patients with chronic obstructive pulmonary disease (COPD). Between 30–60% of inpatients and 10–45% of outpatients with COPD are at risk for malnutrition.107,108 Malnourished COPD patients exhibit a higher degree of gas trapping, reduced diffusing capacity, and a diminished exercise tolerance when compared to patients with normal body weight, adequate nutrition, and comparable disease severity.109 The underlying mechanism between malnutrition and COPD is thought to be from a variety of contributing factors (see Figure 7).

Malnutrition may be responsible for the respiratory muscle wasting, which intensifies the progression of COPD or may simply be a consequence of disease severity. Similarly, long-term caloric malnutrition is associated with the loss of body weight that includes an extensive loss of lung tissue and reduction in diffusion
capacity. Emphysematous-like changes are found to occur in persons with chronic anorexia nervosa and those who die of starvation.\textsuperscript{105,106}

In COPD patients with acute respiratory failure, malnutrition may have detrimental effects, especially in weaning from ventilatory support.\textsuperscript{110} Malnutrition is associated with a decrease in diaphragmatic muscle strength,\textsuperscript{111} a decrease in ventilatory drive,\textsuperscript{102} reduced surfactant production,\textsuperscript{112} and an increased risk of nosocomial pneumonia.\textsuperscript{104,107} Protein energy malnutrition is common in COPD patients.\textsuperscript{113} Early and aggressive nutritional support in COPD patients can produce significant improvements in several functional outcomes including respiratory and limb muscle strength.

Increased protein intake may improve ventilatory response to CO\textsubscript{2}.\textsuperscript{102} Several meta-analyses of nutritional support studies have demonstrated improved nutrition related to anthropometric improvements,\textsuperscript{114} inspiratory and expiratory muscle strength, exercise tolerance, and quality of life.\textsuperscript{107} The most recent Cochrane systematic review found evidence of significant improvements in weight gain, indices of respiratory muscle strength, walking distance, and quality of life in malnourished COPD patients who received nutritional supplementation.\textsuperscript{115}

CO\textsubscript{2} is produced with the metabolism of all macronutrients, with the largest amount coming from carbohydrates. It is well known that overfeeding with an excess carbohydrate load increases CO\textsubscript{2} production. However, overfeeding with non-carbohydrate calories can be as detrimental in regards to CO\textsubscript{2} production and the increased work of breathing.\textsuperscript{116} A high-fat, reduced carbohydrate nutrition formulation has been marketed in an effort to encourage the benefits of nutrition repletion and weight gain while reducing CO\textsubscript{2} production;\textsuperscript{117} however, several studies have refuted this theoretical benefit, and the practice is not recommended.\textsuperscript{118–123}

**Underlying causes of malnutrition**

Underlying causes of malnutrition in COPD patients include increased energy expenditure due to increased caloric cost of breathing, increased systemic inflammation, and the thermogenic effect of medications such as bronchodilators. Also, COPD patients have an inadequate caloric intake caused by dyspnea while eat-
Nutritional Support During Critical Illness

The general goals of nutritional support in the critically ill patient are to provide the energy and protein necessary to meet metabolic demands and to preserve lean body mass. Nutritional support is also an important therapy in critical illness as it attenuates the metabolic response to stress, prevents oxidative cellular injury, and modulates the immune response. Nutritional modulation of the stress response includes early enteral nutrition, appropriate macro and micronutrient delivery, and meticulous glycemic control.127

Stress Response in Critical Illness

Metabolic needs vary during critical illness. The metabolic response to critical illness occurs in three phases: the stress phase, the catabolic phase, and the anabolic phase. The stress phase typically lasts for 24–48 hours and is characterized by hypovolemic shock, hypometabolism and insulin resistance is also seen. The primary goal during this time period is resuscitation and metabolic support. Metabolic support may consist of permissive underfeeding. Permissive underfeeding is where patients are fed below their REE, and the primary goal is to support cellular metabolic pathways without compromising organ structure and function.136 The catabolic phase occurs after resuscitation. In hypercatabolism, increased oxygen demands, cardiac output, and carbon dioxide production are seen. This phase usually lasts 7–10 days, and the goal is to provide ongoing metabolic support with high-protein feedings while avoiding overfeeding. Caloric needs may be increased.
by up to 100% during the catabolic phase in patients with severe burns. As the catabolic phase resolves, the anabolic phase begins and can last for months. Caloric needs may remain elevated during the anabolic phase for repletion of lean body mass and fat stores.

**Under- and Overfeeding During Critical Illness**

Providing inadequate provision of nutrients can have negative effects on the critically ill patient (see Table 7). Underfeeding can result in a loss of lean body mass, immunosuppression, poor wound healing, and an increased risk of infection. This can also result in an inability to respond to hypoxemia and hypercapnia, and a diminished weaning capacity. Continual underfeeding in the ICU results in a cumulative caloric deficit, which increases length of stay, days of mechanical ventilation, and mortality.

Overfeeding patients can be equally detrimental as well. Excess amounts of nutrients can exacerbate respiratory failure by increasing carbon dioxide production and, therefore, increase the work of breathing. If under- or overfeeding is suspected, indirect calorimetry is an important tool to help determine accurate energy requirements.

**Systemic Inflammatory Response Syndrome**

The systemic inflammatory response syndrome (SIRS) underlies many critical illnesses, including sepsis and ARDS. Metabolism in SIRS is characterized by increased total caloric requirements, hyperglycemia, triglyceride intolerance, increased net protein catabolism, and increased macronutrient and micronutrient requirements. Requirements for micronutrients are also increased in SIRS. Because of the potential high losses of potassium, zinc, magnesium, calcium, and phosphorus, serum levels of these minerals need to be closely monitored and maintained within the normal range.

**Glycemic Control in Critical Illness**

Control of serum glucose levels in non-diabetic patients during critical illness is important due to the adverse effect of hyperglycemia in patient outcomes. Control of hyperglycemia has been shown to reduce morbidity and mortality in hospitalized patients. Hyperglycemia is a normal response to physiologic stress and the inflammatory response related to critical illness. Since hyperglycemia can be caused by enteral and parenteral nutrition, control of hyperglycemia during nutritional support is of critical importance. The stress response to critical illness causes wide swings in nutrient requirements. Therefore, the nutritional support process needs to balance the potential detrimental effects of both under- and overfeeding with glycemic control. Current recommendations are to maintain a target blood glucose goal range of 140–180 mg/dL and to consider a blood glucose value of <70 mg/dL during nutritional support as a treatable hypoglycemia.

**Permissive Underfeeding**

Permissive underfeeding is recommended for the critically ill obese patient. Guidelines suggest the goal of EN should not exceed 60–70% of target energy requirements with a high protein goal of 2.0–2.5 g/kg of ideal body weight. It is essential to provide adequate protein in these patients to maintain nitrogen balance and lean body mass while encouraging the use of adipose...
tissue for fuel. Morbidly obese patients receiving high protein through permissive underfeeding have reduced insulin resistance, lower insulin requirements, better glycemic control, decreased ICU stay, and reduced duration of mechanical ventilation.\textsuperscript{147-149}

The practice of permissive underfeeding should avoid global starvation of protein and nutrients and the development of protein energy malnutrition. The role of permissive underfeeding where total calories are reduced while compensating with increased protein intake may have generalized benefits in critically ill patients.\textsuperscript{150}

Permissive underfeeding has been shown to reduce infection,\textsuperscript{151} decrease hospital and ventilator days,\textsuperscript{151} decrease the incidence of hyperglycemia,\textsuperscript{152} and also trends toward decreased mortality.\textsuperscript{152-154}

**Pediatric Critical Illness**

Optimizing nutritional therapy in pediatric patients can improve clinical outcomes. As in the adult, the goals of pediatric nutrition support encompass preservation of tissue stores and resolution of disease progress. A recent multicenter international study demonstrated that pediatric intensive care units that used protocols for starting and advancing EN support had a higher percent of target calorie goals administered, reduced 60-day mortality, and lower rates of acquired infections. Also, use of PN was associated with higher mortality.\textsuperscript{155} However, the goals of pediatric nutrition are more complicated than those for adult patients. In addition, needs that address the support for appropriate growth and development, and the need for preservation of oral motor skills should be considered.\textsuperscript{156} Components of energy requirements in pediatrics consist of basal or resting energy expenditure, activity, growth, gender, maintenance of normal body temperature, and stress factors. Requirements for vitamins and minerals vary based on age, medical status, and size of the child.\textsuperscript{157}

**Immunonutrition**

**Trauma, surgery, burns, and large wounds**

Critical illness is often complicated by systemic inflammation and generalized immunosuppression. Both of these conditions can be responsive to immunonutrition therapy. Immunonutrition using immune modulating nutrition formulations containing omega-3 fatty acids, arginine, glutamine, nucleotides, and antioxidants are used with the goal to modulate the immune system, promote wound healing, attenuate the inflammatory response, and improve organ function.\textsuperscript{4} The use of these formulas in surgical patients has been shown to decrease risk for infections, reduce length of stay, and reduce mortality.\textsuperscript{158} However, caution is advised within the use of arginine in critically ill severe septic patients.\textsuperscript{158}
Calculating, estimating, or measuring the number of calories required by an individual determines nutrient requirements. A calorie is a unit of energy equivalent to the amount of potential heat produced or contained in food when released during the metabolic oxidation processes of the body. A calorie is defined as the amount of heat needed to raise the temperature of 1 gram of water by 1 C° (also called a small calorie, abbreviated as cal). A calorie (also called a large calorie, abbreviated as Cal) is defined as the amount of heat needed to raise the temperature of 1 kilogram of water by 1 C°, is equivalent to 1,000 calories and is also referred to as a kilocalorie. Kilocalories (kcal) are used to quantify the energy value of foods.

Calorie or energy needs are fundamental to the recommendations of the nutritional care plan. Macronutrients supply the body’s energy requirements. The calorie contribution of the three major macronutrients are: protein = 4 kcal/g; carbohydrate = 4 kcal/g; and fat = 9 kcal/g. Alcohol is the only other calorie source with approximately 7 kcal/g.

Energy needs vary according to activity level and state of health. Energy needs of critically ill patients can be significantly different than normal values. Additional factors such as energy expended in catabolic states may be needed to adjust the estimate in patients with medical conditions such as injury, major wounds, and infection.160 Energy needs for obese individuals are less because adipose tissue uses less energy than muscle uses.

The estimated energy requirement is the average dietary energy intake needed to maintain energy balance in an individual.161 Estimating energy requirements for people according to their age, sex, weight, height, and level of physical activity is accomplished by the use of predictive equations.

**Predictive Equations**

Numerous equations have been developed to predict caloric requirements. The Harris Benedict Equation (HBE), the most well known predictive equation, was developed in 1919 by comparing measured calories and their correlation to height, weight, age, and gender in normal subjects to estimate the basal metabolic rate (BMR). BMR is defined as the amount of heat produced in a state at rest with complete muscle inactivity during a post-absorptive period 12–14 hours after the last meal. Since BMR as defined by Harris and Benedict is not necessarily reflective of the way nutritional requirements are determined in hospitalized patients, the more relevant terms — resting metabolic rate (RMR) or resting energy expenditure (REE) — are used in clinical practice to predict or measure caloric needs.

Predictive equations use factors validated by the original work by Harris and Benedict and incorporate additional factors such as temperature, body surface area, diagnosis, and ventilation parameters, as shown in Table 8.162

Predictive equations have been modified as additional data (such as injury-stress, activity, medications received, and obesity) and have been added to the regression correlation equations. Several predictive equations were developed with a focus on specific patient populations and medical conditions.

Predictive equations have varying degrees of agreement compared to measured calorie requirements. Error rates are not insignificant and, therefore, can have high degrees of under- and overestimation of caloric needs. This variability can result in errors large enough to impact outcomes.163 Error rates with some equations make them unsuitable as assessment methods of energy expenditure in critically ill patients. A recent systematic review comparing measured calorie requirements show that the Penn State 2003, Ireton-Jones 1992, and Swinamer equations may be useful in critically ill non-obese patients. The Mifflin-St Jeor, Penn State 1998, and Ireton-Jones 1992 equations might also be useful in obese patients.163 Many of the studies were compared for accuracy and currently, per the Academy of Nutrition and Dietetics (AND), The Mifflin-St Jeor equation was found to be the most reliable, predicting REE within 10% of measured in more non-obese and obese individuals than any other equation, and it also had the narrowest error range. However, error rates can still be significant regardless of the prediction method used. For example, in obese patients, there are no clinical fea-
There are more than 200 predictive equations in existence. Many were developed as long as 50–80 years ago and may not reflect body composition, nutritional risks, age, or ethnicity of the populations they are applied to. There is often no consensus on how a predictive equation is selected, and results can vary significantly between clinicians. Furthermore, there are large segments of populations in whom predictive equations have no validation studies performed. These groups include the elderly and many non-white racial groups. The limitations and variability of predictive equations when applied to an individual patient accentuates the need to use a regimented nutritional risk assessment process and sensible clinical judgment when deciding whether to use a predictive equation. Figure 9 provides an example algorithm for using predictive equations.

**Kilocalories/kilogram calculation.** The American College of Chest Physicians’ 1997 equation is a simple and prompt method to estimate daily energy needs of the average adult using a factor of 25–35 kcals/kg. This
method is not necessarily as accurate as predictive equations, as it does not take into account gender, age, stature, and severity of illness. To rapidly estimate the energy needs of the average adult in kcal/day, identify the target goal for weight change and multiply the individual's actual body weight in kilograms times the factor listed as follows:167

<table>
<thead>
<tr>
<th>Goal</th>
<th>Energy Needs (kcal/kg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight mainten</td>
<td>25 to 30</td>
</tr>
<tr>
<td>Weight gain</td>
<td>30 to 35</td>
</tr>
<tr>
<td>Weight loss</td>
<td>20 to 25</td>
</tr>
</tbody>
</table>

To overcome the limitations of predictive equations and estimating formulas, energy needs can be measured at the bedside using calorimetry to measure RMR or REE by calorimetry.

**Calorimetry**

Calorimeters measure heat released from chemical reactions or physical changes. Calorimetry has been used since the late 19th and early 20th centuries and was adopted as the major method of determining energy needs in individuals. Calculations of calorie requirements by mathematical equation were developed from the use of direct and indirect calorimetry.

**Direct calorimetry**

Direct calorimeters measure heat. A bomb calorimeter measures the energy value of food by measuring the precise amount of heat liberated as the food is burned in a closed chamber. Another type of direct calorimeter requires that the subject be enclosed in a sealed chamber for extended periods and a precise measurement of heat transfer conducted. The early experimentation
conducted by nutrition scientists led to the development of the respiration chamber and IC.

**Respiration chamber**

The development of the respiration chamber combined the process of direct calorimetry with measurements of oxygen consumption (VO2) and carbon dioxide production (VCO2). See Figure 10.

Around the turn of the century, the correlation of heat production in calories, the rate of VO2 and VCO2, the quantity of nutrients consumed, and the mass of carbon and nitrogen excreted was used to derive the caloric value of oxygen and carbon dioxide.168–172 By simultaneous measurement of the ratio VCO2 to VO2, the respiratory quotient (see Table 9) and caloric equivalent of each gas (see Table 10) in relation to the oxidation of specific food substrates could be determined.

It was observed that during short observational periods, the errors in computation of heat production and calories using indirect measurements of VO2 and VCO2 were less than the errors in computation when using direct calorimetry measurements.170 Direct calorimetry and respiration chambers in relation to metabolic testing to this day primarily remain as a research tool in animals.

**Indirect calorimetry**

Indirect calorimetry is the most accurate method for determining RMR and REE in various states of health and disease and is considered to be the gold standard for measuring energy expenditure in critically ill patients179,180. Indirect calorimetry relies on the determination of VO2 and VCO2 using precise measurements from a metabolic analyzer of the inspired and expired fractions of oxygen and carbon dioxide where:

\[ \text{VO}_2 \text{ (mL/min)} = (\text{Vi x FiO}_2) - (\text{Ve x FeO}_2) \quad (1) \]

\[ \text{VCO}_2 \text{ (mL/min)} = (\text{Ve x FeCO}_2) - (\text{Vi x FiCO}_2) \quad (2) \]

The abbreviated Weir equation uses the measured VO2 and VCO2 to determine REE where:

\[ \text{REE} = (3.9 \times \text{VO}_2) + (1.1 \times \text{VCO}_2) \times 1.44 \quad (3) \]

The respiratory quotient, the ratio of VCO2 to VO2, can then be calculated where:

\[ \text{RQ} = \frac{\text{VCO}_2}{\text{VO}_2} \quad (4) \]

Since the normal RQ = 0.85, the volume of CO2 produced is lower than the volume of O2 consumed. Therefore, small differences in the inhaled versus exhaled volumes occur. In order to accurately calculate VO2 and VCO2, the gas concentration measurements of a metabolic analyzer need to be within ± 0.01%. In regards to VO2 measurements, elevated FiO2 introduces error as the oxygen concentration approaches 1.0. As a result, the accuracy of IC diminishes as FiO2 increases. Additionally, any error in gas concentration analysis or delivery is amplified at a higher FiO2. Due to this technical

---

**Table 9. RQ Substrate Interpretation: Interpretation of Substrate Utilization Derived from the Respiratory Quotient**

<table>
<thead>
<tr>
<th>Substrate Utilized</th>
<th>Respiratory Quotient</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>0.67</td>
</tr>
<tr>
<td>Ketones</td>
<td>0.67</td>
</tr>
<tr>
<td>Fat oxidation</td>
<td>0.71</td>
</tr>
<tr>
<td>Protein oxidation</td>
<td>0.80–0.82</td>
</tr>
<tr>
<td>Mixed substrate oxidation</td>
<td>0.85–0.90</td>
</tr>
<tr>
<td>Carbohydrate oxidation</td>
<td>1.0</td>
</tr>
<tr>
<td>Lipogenesis</td>
<td>1.0–1.3</td>
</tr>
</tbody>
</table>

*Used with permission. See references 173-175.*

**Table 10. Caloric Equivalence**

<table>
<thead>
<tr>
<th>Substrate</th>
<th>Respiratory Quotient</th>
<th>Oxygen Caloric Equivalent (kcal/L)</th>
<th>Carbon Dioxide Caloric Equivalent (kcal/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Carbohydrate</td>
<td>1.0</td>
<td>5.05</td>
<td>5.05</td>
</tr>
<tr>
<td>Mixed</td>
<td>0.90</td>
<td>4.83</td>
<td>5.52</td>
</tr>
<tr>
<td>Protein</td>
<td>0.80</td>
<td>4.46</td>
<td>5.57</td>
</tr>
<tr>
<td>Fat</td>
<td>0.71</td>
<td>4.74</td>
<td>6.67</td>
</tr>
</tbody>
</table>

*Used with permission. See references 176-178.*
limitation, IC is not recommended or considered to be accurate at FiO₂ > 0.60.²,¹⁷³,¹⁸¹

Respiratory quotient was once thought to be useful as a means to determine nutritional substrate utilization. However, the accuracy of this assumption has never been substantiated. The large stores of CO₂ in the body can be mobilized with ventilation and, thus, would reflect an increase in CO₂ excretion but not necessarily production. An increase in VCO₂ measured as a result of this mechanism would have an erroneous effect on the measured RQ. See Figure 11.¹⁷³

Therefore, the use of the RQ measurement is of limited clinical value. Measured values of RQ between the physiologic ranges of 0.67–1.3 should be used as a means of quality control and a way to verify test validity. Values of RQ outside of this range obtained during IC testing invalidate the results due to technical measurement errors and should be repeated.¹⁷³

Indirect calorimetry is performed using a standalone metabolic cart by hood, face mask, and mouthpiece, or by connection to a ventilator. See Figure 12.

Open circuit systems sample inspired gas concentrations, measured expired gas concentrations, and expired minute volume collected back into the analyzer to determine VCO₂, VO₂, and RQ. Indirect calorimetry has also been integrated into several ventilators.¹⁸²,¹⁸³ See Table 11. Handheld calorimeters are also available.¹⁸⁴–¹⁸⁶ See Figure 13.

Newer open-circuit breath-by-breath designs use a system where inspired and expired gases and volumes are measured at the airway, which simplify the measurement procedure. See Figure 14.

Accuracy of indirect calorimetry measurements are dependent on the technical aspects of test performance and patient care related variables.

Technical considerations when performing IC measurements during mechanical ventilation include:⁹⁹,¹⁸⁷
• Warm-up time of 30 minutes for the indirect calorimeter
• Errors in calibration of flow, oxygen, and carbon dioxide sensors
• Presence of leaks (ventilator circuit, artificial airway, broncho-pleural fistulas)
• FiO₂ > 60%
• Fluctuation of FiO₂ > ± 0.01%
• Changes in the ventilator setting within 1 to 2 hours of testing
• Acute hyperventilation or hypoventilation (changes body CO₂ stores)
• Moisture in the sampling system
• Bias flow through the ventilator may affect accuracy of indirect calorimeter

Figure 11. Effect of Acute Hyperventilation on VCO₂, RQ, and EtCO₂ in a Patient with Head Injury

Used with permission. See reference 173.
Attachment of indirect calorimeter may affect ventilator function
• Use of inhaled nitric oxide
• Presence of anesthetic gases

Recommendations for improving accuracy of IC include:

1. Patient should be hemodynamically stable.
2. Patient should be in a comfortable resting position for 30 minutes before the study.
3. Avoid instability caused by disconnection from high levels of positive end-expiratory pressure (PEEP).
4. Avoid voluntary activity for 30 minutes.
5. Avoid intermittent feedings or meals taken four hours before study.
6. Nutrient infusion should remain stable for at least 12 hours before and during the study.
7. Measurements are made in a quiet, neutral-thermal environment.
8. Limited voluntary skeletal muscle activity during the study.
9. Use of steady state data (coefficient of variation ≤ 10%).
10. No general anesthesia within six to eight hours before the study.
11. Analgesics or sedatives for pain or agitation given at least 30 minutes prior to study.
12. Delay study for three to four hours after hemodialysis.
13. Delay study for one hour after painful procedures.
15. Routine care or activities avoided during the study.
Indications for Indirect Calorimetry

Indirect calorimetry measurements are indicated when the use of predictive equations are inaccurate because of the patient’s clinical condition, when patients fail to respond to nutrition support based on predictive equations, and when serial adjustments to the nutritional support plan are necessary as caloric requirements change during the stress response phases of critical illness. Use of this methodology and use of IC improves nutritional care and reduces complications associated with over- or underfeeding.187

The conditions where caloric requirements estimated by predictive equations may be inadequate include:175,182,187,189,193

- Acute respiratory distress syndrome
- Chronic respiratory disease
- Large or multiple open wounds, burns
- Multiple trauma or neurologic trauma
- Multisystem organ failure
- Systemic inflammatory response syndrome, sepsis
- Postoperative organ transplantation
- Use of sedation and paralytic agents
- Altered body composition:
  - Limb amputation
  - Peripheral edema
  - BMI <18
  - BMI >30
  - Ascites

Use and Interpretation of Indirect Calorimetry Measurements

Resting energy expenditure from indirect calorimetry is recognized as an accurate, objective, patient-specific reference standard for determining energy expenditure. Current recommendations are to decrease the reliance on predictive equations in critically ill patients.
Several studies have shown that a cumulative negative energy balance >10,000 kcal determined by IC measurements resulted in worse clinical outcomes. In a small multi-center study comparing nutritional support guided by predictive equations (control group) to measured energy requirements by IC (study group), the proportion of patients with a positive energy balance was higher in the study group and there was a significant difference in ventilator and ICU days when patients had a positive versus a negative energy balance. See Table 12.192,196

Another study using IC reported a lower incidence of organ failure and mortality of 26% when the calorie deficit was < 10,000 kcal versus a mortality of 75% when the calorie deficit was > 10,000 kcal.197

In a third study, there was a correlation with calorie deficit determined by IC and the development of pressure ulcers in nursing home patients. This correlation was stronger in patients where the negative energy balance exceeded 10,000 kcal.188,198

This data suggests that nutritional support guided by sequential monitoring and use of IC to maintain a positive energy balance may provide important clinical benefits.

Indirect Calorimetry Calculated Using Other Methods

Modifications to the Weir equation can be used to calculate REE. By substituting a calculated factor for either VO₂ or VCO₂ adjusted for a normal RQ, the REE based on VO₂ (REE-O₂) or VCO₂ (REE-CO₂) can be calculated where:

\[
\text{REE-O}_2 = 3.9 \times \text{VO}_2 + (1.1 \times [\text{VO}_2 \times .85]) \times 1.44 \quad (5)
\]

or

\[
\text{REE-C}_2 = 3.9 \times \text{VCO}_2/.85) + (1.1 \times \text{VCO}_2) \times 1.44 \quad (6)
\]

When the actual RQ is equal to 0.85, both the REE-O₂ and REE-CO₂ equations will return a REE value equivalent to the value calculated by the standard Weir method. The CCM Express® metabolic analyzer (Medical Graphics Corporation, St. Paul, MN) uses Equation 2 to calculate REE-CO₂ with an accuracy of approximately +/- 10% compared to the REE.189,199

The REE measured by the CCM Express using the standard Weir equation was retrospectively compared to the calculated REE-CO₂ in 67 adult medical and surgical ICU patients.190,200 The correlation coefficient \( r = 0.99 \) and the coefficient of determination \( r^2 = 0.98 \), with bias and precision between measurements of -15 ± 126 kcal/day. When comparing the differences between REE to REE-CO₂ to the measured RQ, there was a distinct pattern of agreement, whereby as RQ approached 0.70 the percent error (mean bias / mean REE for the range of RQ) became more positive, and as RQ approached 1.0 the percent error became more negative. More importantly, when RQ was within the normal range of 0.80 to 0.90, the average error was approximately ± 5%. See Figure 16.200

The ability to perform IC measurements using just a determination of VCO₂ has several important implications. VCO₂ determinations are technically easier to perform compared to VO₂ and VCO₂, and measurement capabilities are increasingly more available on standalone monitors and ventilators. This makes IC estimates of REE more accessible where metabolic analyzers are not available. Additionally, FiO₂ does not affect the accuracy of the REE-CO₂ calculation. Therefore, settings of FiO₂ > 0.60 may no longer be a limitation of measuring REE within a known range of acceptable error of ± 5–10%. This means that even the most severe critically ill patients on mechanical ventilation receiving 100% oxygen can have REE estimates performed to manage their complex nutritional needs using the REE-CO₂.

Both the REE-O₂ and REE-CO₂ equations can be further simplified. By solving either equation with any

<table>
<thead>
<tr>
<th>Table 12. Impact of Energy Balance on Clinical Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Impact of energy balance on clinical outcome</strong></td>
</tr>
<tr>
<td>( ^* p &lt; 0.005 \quad ^t p &lt; 0.05 )</td>
</tr>
<tr>
<td>Positive Energy Balance (PEB)</td>
</tr>
<tr>
<td>Negative Energy Balance (NEB)</td>
</tr>
</tbody>
</table>

Note: Negative energy balance was defined by > 10,000 kcal deficit.
Control patients received nutrition support per standard estimations of energy and protein (blinded to MREE and UUN). Study patients received nutrition support per daily MREE and UUN.

Used with permission. See references 192 and 196.
combination of VCO\(_2\) and VO\(_2\) that equals an RQ of 0.85, and dividing the calculated REE by the measured VCO\(_2\) or VO\(_2\), a single factor can be derived for calculating REE-CO\(_2\) and REE-O\(_2\), whereby:

\[
\text{REE-CO}_2 = 8.19 \times \text{VCO}_2 \quad (7)
\]

\[
\text{REE-O}_2 = 6.96 \times \text{VO}_2 \quad (8)
\]

For example, when VCO\(_2\) = 221 mL/min and VO\(_2\) = 260 mL/min, RQ = 221/260 = 0.85, the Weir equation returns a calculated REE of 1810 kcal/day whereby:

\[
\text{REE} = (3.9 \times 260) + (1.1 \times 221) \times 1.44 = 1810 \text{ kcal/day}
\]

REE-CO\(_2\) can be calculated as follows:

\[
\text{REE-CO}_2 = (3.9 \times (221/0.85)) + (1.1 \times 221) \times 1.44 = 1810 \text{ kcal/day},
\]

REE-CO\(_2\) Factor = 1810/221 = 8.19, and

\[
\text{REE-CO}_2 = 8.19 \times 221 = 1810 \text{ kcal/day}.
\]

Similarly, REE-O\(_2\) becomes:

\[
\text{REE-O}_2 = (3.9 \times 260) + (1.1 \times [260 \times .85]) \times 1.44 = 1810 \text{ kcal/day},
\]

REE-O\(_2\) Factor = 1810/260 = 6.96, and

\[
\text{REE-O}_2 = 6.96 \times 260 = 1810 \text{ kcal/day}.
\]

The MedGem\textsuperscript{®} (Microlife USA Inc., Clearwater, FL) handheld calorimeter uses measurements of VO\(_2\) and a calculation similar to Equation 8 above. The accuracy of this handheld device shares the same technical limitations and inaccuracies as traditional metabolic testing using IC and can only be performed on spontaneously breathing patients using a mouth piece and nose clips.

The caloric equivalence of oxygen and carbon dioxide can also be used to indirectly calculate REE. (See Table 10.) When the RQ = 0.90, the CO\(_2\) or O\(_2\) caloric equivalent factors equal 5.52 and 4.83 kcal/L respectively, where:

\[
\text{REE-CO}_2 \text{ Equivalent} = 5.52 \times \text{VCO}_2 \times 1.44 \quad (9)
\]

\[
\text{REE-O}_2 \text{ Equivalent} = 4.83 \times \text{VO}_2 \times 1.44 \quad (10)
\]

See Table 10, Caloric Equivalence.\textsuperscript{176-178} This technique has been compared to the Harris Benedict calculation and the Weir equation. The HBE significantly underestimated REE, but there was no significant difference between the Weir and REE-O\(_2\) or CO\(_2\) equivalent calculations.\textsuperscript{176} Due to the technical complexity of measuring VO\(_2\), the REE-CO\(_2\) equivalent equation is simpler and should be the preferred method, especially when the FiO\(_2\) is >0.60 or when small air leaks that would otherwise invalidate the VO\(_2\) calculation are present.\textsuperscript{177}

The Weir equation is a superior method for IC measurements, especially when RQ is at or close to the physiologic extremes of 0.67 and 1.3. However, due to the cost and availability of metabolic analyzers or ventilators with an integrated function, and the technical
problems associated with measuring VO$_2$, REE measurement based on VCO$_2$ is an attractive alternative. The accuracy of equations 6, 7, and 9 above compared to the Weir equation are within clinically acceptable limits needed for monitoring nutritional interventions. Since VCO$_2$ monitoring is becoming more readily available, can be performed on any FiO$_2$, and is less costly than traditional metabolic testing, its use should be considered for incorporation into a standard nutrition assessment and treatment process. Additional validation studies and outcome measurements are needed to determine the true impact of these alternative methods of indirect calorimetry.
Clinical Practice Recommendations for Nutritional Support

Several clinical practice guidelines from different organizations for the various aspects of nutritional assessment and treatment have been developed. The Society of Critical Care Medicine and the American Society of Parenteral and Enteral Nutrition (SCCM/ASPEN), the European Society for Clinical Nutrition and Metabolism (ESPEN), the Academy of Nutrition and Dietetics (AND), and the Canadian Clinical Practice Guideline for Nutritional Support (CCPG) have developed best practice recommendations based on the interpretation of available evidence, consensus agreement, and expert opinion. The present concentration on evidence-based practice dictates that guidelines be supported by the available literature. The problem with multiple guidelines from different professional societies is that they often contradict one another. See Table 13.201–206

Varying degrees of agreement, disagreement, and controversy over the strength of the evidence can be confusing to the clinician. The review and interpretation of practice recommendations, knowledge of the current available literature, clinical judgment, the specific patient population, and the needs of the individual patient should drive the translation of recommendations into clinical practice.

The following is a summary of some of the “best practice” recommendations from the various organizations:

Nutritional support should be initiated early within the first 24–48 hours in critically ill patients.

Primary goals of nutritional support and care are to:

- Preserve and maintain lean muscle mass
- Provide continuous assessment, reassessment, and modification to optimize outcome
- Monitor the patient for tolerance and complications, such as refeeding syndrome
- Prevent protein energy malnutrition by giving higher protein content while providing adequate total calories
- Monitor nutrition goals and target achievement rate of > 50% within the first week
- Prevent accumulation of a caloric deficit.

Indirect calorimetry should be used when available or when predictive equations are known to be inaccurate.

Current EN practice recommendations are to:

- Preferentially feed via the enteral route
- Initiate EN within 24–48 hours
- Reduce interruptions of EN for nursing care and procedures to prevent underfeeding
- HOB elevation to reduce aspiration risk
- Accept GRV up to 500 mL before reducing or stopping EN in the absence of clear signs of intolerance
- Use of motility agents to improve tolerance and reduce GRV
- Promote post-pyloric feeding tube placement when feasible.

Current PN practice recommendations are to:

- Only use PN when enteral route not feasible
- Use PN based on the patient’s nutritional risk classification for malnutrition
- Initiate PN early if Nutritional Risk Class III or IV
- Delay PN up to seven days if the patient is in Nutritional Risk Class I or II
- Convert to EN as soon as tolerated to reduce the risks associated with PN.

The following is a summary of some of the “best practice” recommendations from the various organizations:

Use of trophic or “trickle feeding” and permissive underfeeding may be beneficial.

Use of pharmaconutrients and immunonutrition:

- Omega-3 fatty acids (fish oils) may be beneficial in ARDS patients
- Increase omega-3 fatty acids to omega-6 fatty acid ratios
- Use of arginine, glutamine, nucleotides, antioxidants, and probiotics may be beneficial
- Avoid using arginine in patients with severe sepsis.
## Table 13. Summary of Clinical Practice Guidelines for Nutrition Therapy in Critically Ill Patients

<table>
<thead>
<tr>
<th>Topics</th>
<th>ASPEN/SCCM</th>
<th>AND</th>
<th>Canadian</th>
<th>ESPEN</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Route of Nutrition</strong></td>
<td>EN</td>
<td>EN</td>
<td>EN</td>
<td>EN</td>
</tr>
<tr>
<td>Use and Timing of EN</td>
<td>24-48 hours following admission to ICU</td>
<td>24-48 hours following admission to ICU</td>
<td>24-48 hours following admission to ICU</td>
<td>&lt;24 hours</td>
</tr>
<tr>
<td>Use of Indirect Calorimetry</td>
<td>IC or predictive equations</td>
<td>IC is the standard for determining RMR</td>
<td>Insufficient data</td>
<td>Use predictive equations if IC is not available</td>
</tr>
<tr>
<td>Dose of Nutrition and Achieving Target</td>
<td>Provide &gt;50-65% of goal calories over the first week of hospitalization; BMI &gt;30 22-25 kcals/kg ideal body weight</td>
<td>At least 60-70% of total estimated energy requirements</td>
<td>No specific recommendation</td>
<td>No specific recommendation</td>
</tr>
<tr>
<td><strong>Protein Target Per Day</strong></td>
<td>BMI ≤ 30 1.2 - 2.0 g/kg actual body weight; BMI 30-40 ≥ 2.0 g/kg ideal body weight/day; BMI ≥ 40 ≥ 2.5 gm/kg ideal body weight/day</td>
<td>No specific recommendation</td>
<td>Insufficient data, No specific recommendation</td>
<td>EN/PN 1.2 - 2.0 g/kg Ideal or actual body weight depending patient condition</td>
</tr>
<tr>
<td><strong>EN: Arginine</strong></td>
<td>Recommended for use with surgical ICU patients, but caution with medical ICU patients and those with severe sepsis</td>
<td>Not recommended for routine use</td>
<td>Should not be used</td>
<td>Use in elective upper GI surgical patients; trauma, mild sepsis; avoid with severe sepsis</td>
</tr>
<tr>
<td><strong>EN: Fish Oil (omega-3 fatty acids)</strong></td>
<td>Recommended for ARDS</td>
<td>No specific recommendation</td>
<td>Should be considered for ARDS</td>
<td>Recommended for ARDS</td>
</tr>
<tr>
<td><strong>EN: Glutamine</strong></td>
<td>Consider in burn, trauma and mixed ICU patients</td>
<td>No specific recommendation</td>
<td>Consider in burn/trauma, caution with shock and MOF</td>
<td>Consider in burn and trauma patients</td>
</tr>
<tr>
<td><strong>EN: High Fat, Low CHO</strong></td>
<td>Not recommended</td>
<td>No specific recommendation</td>
<td>Insufficient data</td>
<td>No specific recommendation</td>
</tr>
<tr>
<td><strong>EN: Gastric Residual Volume (GRV)</strong></td>
<td>Holding EN for GRVs &lt;500 mL in the absence of other signs of intolerance should be avoided.</td>
<td>Hold EN if GRV &gt;250 mL on two more occasions</td>
<td>GRVs &gt;250 mL consider post pyloric feeding tube</td>
<td>No specific recommendation</td>
</tr>
<tr>
<td><strong>EN: Motility Agents</strong></td>
<td>Use when clinically feasible</td>
<td>If history of gastroparesis or high GRVs</td>
<td>Recommended with EN intolerance</td>
<td>Recommended with EN intolerance</td>
</tr>
<tr>
<td><strong>EN: Small Bowel Feeding</strong></td>
<td>Gastric or small bowel feeding is acceptable</td>
<td>Gastric is acceptable; consider small bowel for supine position or heavy sedation</td>
<td>Routine use of small bowel feeding tubes</td>
<td>No significant difference in jejunal versus gastric</td>
</tr>
<tr>
<td>EN: Body Position</td>
<td>HOB should be elevated</td>
<td>HOB &gt;45 degrees</td>
<td>HOB &gt;45 degrees</td>
<td>No specific recommendation</td>
</tr>
<tr>
<td>---</td>
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</tr>
<tr>
<td>EN: Prebiotics/Probiotics/Synbiotics</td>
<td>No specific recommendation; may consider in transplant, major abdominal surgery, and severe trauma</td>
<td>No specific recommendation</td>
<td>Consider probiotics</td>
<td>No specific recommendation</td>
</tr>
<tr>
<td>EN: Continuous vs Bolus</td>
<td>For high-risk patients or those shown to be intolerant</td>
<td>No specific recommendation</td>
<td>Insufficient data</td>
<td>No specific recommendation</td>
</tr>
<tr>
<td>EN with PN</td>
<td>If unable to meet energy needs after 7-10 days via EN</td>
<td>No specific recommendation</td>
<td>Not recommended</td>
<td>Not recommended; consider if unable to be fed sufficiently</td>
</tr>
<tr>
<td>Parenteral Nutrition</td>
<td>After 7-10 days in nourished patient, as soon as possible in malnourished patient</td>
<td>No specific recommendation</td>
<td>Not recommended</td>
<td>Consider if unable to feed by EN; do not exceed nutrition requirements</td>
</tr>
<tr>
<td>PN: Lipids</td>
<td>Avoid omega-6 soy-based lipid in the first week</td>
<td>No specific recommendation</td>
<td>Reduce omega-6 load; insufficient data on type</td>
<td>Integral part of PN for energy; varying lipid emulsions available in Europe</td>
</tr>
<tr>
<td>PN: Glutamine</td>
<td>Consider</td>
<td>No specific recommendation</td>
<td>Strongly recommended; avoid in shock and MOF</td>
<td>Strongly recommended</td>
</tr>
<tr>
<td>PN: Intensive Insulin Therapy</td>
<td>Protocol should be in place; 110-150 mg/dL</td>
<td>80-110 mg/dL; &lt;140 mg/dL</td>
<td>120-160 mg/dL</td>
<td>80-110 mg/dL</td>
</tr>
</tbody>
</table>

Used with permission. See references 10 and 201-206.
Summary

Nutritional support is important in the care of patients with acute and chronic illness. The prevention of malnutrition and the maintenance of appropriate nutritional care brings with it the potential for reducing morbidity and mortality, shortening the duration of mechanical ventilation and the length of hospital stay, and lowering health care costs while improving functional quality of life. Appropriate nutritional management is best achieved by using a comprehensively designed nutritional care process supported by the best available evidence. This process should include an interdisciplinary team approach and organizational standards of care with policies and procedures that ensure implementation, continuous assessment, and monitoring of the nutrition care plan.

Varying degrees of agreement, disagreement, and controversy from various organizations regarding nutritional support include the role and timing of enteral versus parenteral route, positioning of feeding tubes, thresholds for GRV, and use of predictive equations and indirect calorimetry. The use of immunonutrition and dietary supplements continue to evolve as practice changes develop when new evidence becomes available. All members of the integrated health care team should maintain awareness of the importance and continued evolution of best practices for nutritional assessment and treatment. Optimizing nutritional support and care of the critically ill and patients with acute and chronic respiratory disorders will contribute to improved outcomes and reduced health care costs.
References


52. Lin WY, Yao CA, Wang HC, Huang KC. Impaired lung function is associated with obesity and metabolic syndrome in adults. Obesity (Silver Spring) 2006; 14(9):1654-1661.
References

References


## Acronyms

<table>
<thead>
<tr>
<th>Acronym</th>
<th>Description</th>
<th>Acronym</th>
<th>Description</th>
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<tbody>
<tr>
<td>AARC</td>
<td>American Association for Respiratory Care</td>
<td>GI</td>
<td>gastrointestinal</td>
</tr>
<tr>
<td>AMA</td>
<td>arm muscle area</td>
<td>GRV</td>
<td>gastric residual volumes</td>
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<tr>
<td>AND</td>
<td>Academy of Nutrition and Dietetics</td>
<td>HBE</td>
<td>Harris Benedict Equation</td>
</tr>
<tr>
<td>ARDS</td>
<td>acute respiratory distress syndrome</td>
<td>HHS</td>
<td>Health and Human Services</td>
</tr>
<tr>
<td>ASPEN</td>
<td>American Society of Parenteral and Enteral Nutrition</td>
<td>IC</td>
<td>indirect calorimetry</td>
</tr>
<tr>
<td>BIA</td>
<td>bioelectrical impedance analysis</td>
<td>kcal</td>
<td>kilocalories</td>
</tr>
<tr>
<td>BMI</td>
<td>body mass index</td>
<td>MAC</td>
<td>mid-upper arm circumference</td>
</tr>
<tr>
<td>BMR</td>
<td>basal metabolic rate</td>
<td>MRI</td>
<td>magnetic resonance imaging</td>
</tr>
<tr>
<td>CCGP</td>
<td>Canadian Clinical Practice Guidelines for Nutritional Support</td>
<td>PEM</td>
<td>protein-energy malnutrition</td>
</tr>
<tr>
<td>CF</td>
<td>cystic fibrosis</td>
<td>PICC</td>
<td>peripherally inserted central catheter</td>
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<tr>
<td>CNSC</td>
<td>Certified Nutrition Support Clinician</td>
<td>PN</td>
<td>parenteral nutrition</td>
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<tr>
<td>CO2</td>
<td>carbon dioxide</td>
<td>RDA</td>
<td>recommended dietary allowance</td>
</tr>
<tr>
<td>COPD</td>
<td>chronic obstructive pulmonary disease</td>
<td>REE</td>
<td>resting energy expenditure</td>
</tr>
<tr>
<td>CRP</td>
<td>C-reactive protein</td>
<td>RMR</td>
<td>resting metabolic rate</td>
</tr>
<tr>
<td>CT</td>
<td>computed tomography</td>
<td>RQ</td>
<td>respiratory quotient</td>
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<tr>
<td>DRI</td>
<td>dietary reference intakes</td>
<td>SBS</td>
<td>short bowel syndrome</td>
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<tr>
<td>DXA</td>
<td>dual-energy X-ray absorptiometry</td>
<td>SCCM</td>
<td>Society of Critical Care Medicine</td>
</tr>
<tr>
<td>EN</td>
<td>enteral nutrition</td>
<td>SIRS</td>
<td>systemic inflammatory response syndrome</td>
</tr>
<tr>
<td>ESPEN</td>
<td>European Society for Clinical Nutrition and Metabolism</td>
<td>TSF</td>
<td>triceps skinfold</td>
</tr>
<tr>
<td>FFQ</td>
<td>food frequency questionnaires</td>
<td>UUN</td>
<td>urinary urea nitrogen</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VCO2</td>
<td>carbon dioxide production</td>
</tr>
<tr>
<td></td>
<td></td>
<td>VO2</td>
<td>oxygen consumption</td>
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