Eur J Trauma Emerg Surg (2013) 39:203–213
DOI 10.1007/s00068-013-0272-8

REVIEW ARTICLE

Nutrition therapy for critically ill and injured patients

I. Afifi · S. Elazzazy · Y. Abdulrahman · R. Latifi

Received: 24 October 2012 / Accepted: 19 February 2013 / Published online: 8 March 2013

Abstract
Background Nutrition support has undergone significant advances in recent decades, revolutionizing the care of critically ill and injured patients. However, providing adequate and optimal nutrition therapy for such patients is very challenging: it requires careful attention and an understanding of the biology of the individual patient's disease or injury process, including insight into the consequent changes in nutrients needed.
Objective The objective of this article is to review the current principles and practices of providing nutrition therapy for critically ill and injured patients.
Methods Review of the literature and evidence-based guidelines.
Results The evidence demonstrates the need to understand the biology of nutrition therapy for critically ill and injured patients, tailored to their individual disease or injury, age, and comorbidities.
Conclusion Nutrition therapy for critically ill and injured patients has become an important part of their overall care. No longer should we consider nutrition for critically ill and injured patients just as "support" but, rather, as "therapy", because it is, indeed, a key therapeutic modality.

I. Afifi · Y. Abdulrahman · R. Latifi
Trauma Section, Hamad General Hospital,
Doha, Qatar

S. Elazzazy
National Center of Cancer Care and Research,
Doha, Qatar

R. Latifi (✉)
Department of Surgery, University of Arizona,
Tucson, AZ, USA
e-mail: rlatifi@email.arizona.edu

Keywords Nutrition therapy · Critically ill patients · Intensive care unit · Immune nutrition · Immune-enhancing diet · Immune-modulating diet

Introduction

Nutrition support for critically ill and injured patients has undergone significant advances in recent decades—the direct result of scientific progress and our increased knowledge of the biology and biochemistry of key nutrient changes induced by injury, sepsis, and other critical illnesses, both in adults and in children. The science of nutrition support (or, more accurately, of nutrition *therapy*) has become more disease-based. Also called "specialized" or "artificial" nutrition support, nutrition therapy refers to the provision of either enteral nutrition (EN) via tube feeding or total parenteral nutrition (TPN). In contrast, "standard therapy" refers to a patient's own volitional intake, without the provision of nutrition therapy [1].

Depending on the individual patient's metabolic needs, nutrition therapy helps ensure that key nutrient substrates are replenished, or added in larger amounts, to supplement specific deficiencies or to simply prevent further deterioration and clinical consequences [2]. The benefit of early institution of either EN or TPN in the overall care of critically ill and injured patients has now been well established. After a critical illness or injury, the patient's energy and overall metabolic requirements greatly increase, in order to sustain increased metabolism and the process of wound repair. Given current evidence derived from randomized controlled trials (RCTs), early provision of nutrition for critically ill and injured patients is now a level I recommendation [2].

The mainstay of nutrition delivery in intensive care units (ICUs), EN has benefits for the patient's gastrointestinal (GI) tract and associated immune system. The methods of delivering nutrition therapy, however, continue to be debated. Some clinicians mistakenly hoped that EN could be used in all patients and at all times. No doubt, the GI tract should be used when possible, but TPN continues to be a great modality for many critically ill and injured patients. However, the risks and pitfalls of interruptions in EN, as well as mechanical problems associated with its delivery, are now better appreciated. Improvements in TPN formulations have also undercut the notion that EN can be given to every patient. Thus, TPN remains an important technique in patients with GI feed intolerance or EN failure [3].

Pathophysiology of nutrition imbalance

No patient is more difficult to feed than one with multiple injuries and/or multiple organ failure. As levels of catecholamines, cytokines, and insulin rise in response to such traumatic insults, energy expenditure and protein turnover increase. It is difficult to develop guidelines applicable to all critically and injured patients, given the heterogeneity of this patient population. There is a profound need for clinical judgment [4]. Critical illness and tissue injury initiate a complex series of rapid homeostatic events in an attempt to prevent ongoing tissue damage and to activate the repair process. Classically, inflammation has been recognized as the hallmark of the homeostatic response. But, more recently, attention has focused on defining the response at the metabolic, cellular, and molecular levels [5].

Three response phases

The response to stress and injury has been described as involving three phases: the ebb phase, the catabolic flow phase, and the anabolic flow phase [6, 7]. Each of these phases has distinct changes that require specific interventions in order to eliminate or minimize the consequences of illness and/or injury. First, the *ebb phase* is dominated by circulatory changes that require resuscitation (with fluid, blood, and blood products) over a period of 8–24 h. Second, the *catabolic flow phase*, dominated by catabolism, typically lasts 3–10 days, but may last longer; this phase is driven by cytokine mediators released from lymphocytes and macrophages in the cellular immune reaction, dominated by interleukin-6 (IL-6) [7]. The release of these mediators is proportional to the intensity of the injury, but the release of cytokines themselves is upregulated by hormonal and humoral events [7]. Third, the *anabolic flow phase* emerges as the patient's metabolism shifts to synthetic activities and reparative processes [7].

Protein and nitrogen metabolism

The metabolic response to injury is associated with a striking increase in protein catabolism, a negative nitrogen balance, and a marked increase in urinary loss of nitrogen, phosphorus, sulfur, potassium, magnesium, and creatinine. This process peaks several days after injury and gradually returns to normal over several weeks [5, 8]. Measurement of the excretion of 3-methylhistidine serves as an index of muscle protein catabolism [9]. Amino acid requirements increase by 2–3 times as a result of hypercatabolism and the inefficient reuse of endogenous nitrogen [10]. Furthermore, amino acids are redistributed from peripheral tissues to splanchnic organs in order to maintain protein synthesis in the gut mucosa and immune system [11].

Acute phase response and proteins

The acute phase response (APR) is an early and nonspecific response to systemic tissue injury. Responsible for the reprioritization (depending on the magnitude and severity of the injury) of protein synthesis in the liver, the APR is characterized by an exponential increase in positive acute phase proteins and by a decrease in negative acute phase proteins [12–14]. A variety of cytokines, released at the site of injury or infection, have been implicated in the production of acute phase proteins from the liver, including IL-1 and IL-6, as well as tumor necrosis factor-alpha (TNF-alpha) [15].

The acute phase proteins reach a maximum concentration within a few days after the onset of tissue damage and return to their normal concentrations within a week [15]. First, the serum concentration decreases for most of these proteins, both for positive reactants and for negative reactants. Later, the hepatic synthesis of negative acute phase proteins decreases, and the concentration of serum albumin remains depressed for days to weeks after the injury. Albumin reaches a nadir by the fifth post-injury day [16]. Whether or not nutrition therapy in the immediate post-injury period can alter or blunt the APR has not been adequately investigated. In one study, nutrition therapy increased the concentration of prealbumin within the first week after the injury, although the concentration lagged behind the increased protein–calorie intake and nitrogen balance; serum albumin levels slowly declined within the first week and still decreased 18 days after the injury [13]. C-reactive protein (CRP) is the earliest acute phase reactant to respond; its serum concentration peaks at 48 h

[15]. The serum protein concentration of positive acute phase proteins after *minor* injuries returns to normal by the end of the first week.

Continued and prolonged production of acute phase proteins in critically ill patients may be an indicator of ongoing sepsis and tissue damage, however, and is associated with higher mortality rates [17]. Perhaps some of the changes at this stage are responsible for what is defined as compensatory anti-inflammatory response syndrome (CARS). CARS, which follows systemic inflammatory response syndrome (SIRS), is characterized by cutaneous anergy, a reduction in the number of lymphocytes because of apoptosis, a decrease in the cytokine response of monocytes to stimulation, downregulation of human leukocyte antigen (HLA) receptors, and the production of transforming growth factor-beta and prostaglandin-E_2 [18].

Positive acute phase proteins seem to be a protective response to tissue injury. They have diverse functions as antioxidants, proteolytic inhibitors, and mediators of coagulation. Negative acute phase proteins are albumin, prealbumin, retinol-binding protein, and transferrin. Their serum concentrations fall immediately after an injury, in proportion to its severity. They are used to monitor the nutritional status of acutely ill patients [5].

Preadmission nutritional status

The preadmission nutritional status of patients is a critical factor. If patients are malnourished or have a limited nutritional reserve, their outcome is poorer [19]. Having a low body mass index (BMI) is an independent predictor of increased mortality and of multiple organ failure [20].

Thermal injuries, severe central nervous system (CNS) insult, sepsis, and certain comorbidities, such as cancer, chronic obstructive pulmonary disease (COPD), alcoholism, and heart disease, produce added metabolic challenges and complications. Such conditions exacerbate energy expenditure and protein catabolism brought on by severe injury and critical illness, thereby, evoking variation even among patients with the same disease process [21]. It is imperative to evaluate the nutritional status of patients upon admission.

The safety and practicality of nutritional support

In most critically ill patients, EN is practical and safe. The beneficial effects of EN over TPN have been well documented in numerous RCTs involving a variety of critically ill patient populations (including those with trauma, burns, head injuries, and acute pancreatitis, as well as those who have undergone major surgery) [22–24]. Nonetheless, a number of patients cannot be fed either orally or enterally, and will require TPN. About 10–20 % of ICU patients have either a contraindication to EN (such as bowel obstruction, short bowel syndrome, abdominal compartment syndrome, or mesenteric ischemia) or a very limited tolerance to EN. Problems with tolerance to EN are frequently limited to about 3–5 days, so are a relative indication for TPN. But in some patients, intolerance to EN lasts much longer and, thus, is an absolute indication for TPN [25]. TPN is efficacious in patients who are malnourished and unable to receive adequate oral or enteral nutrients (in particular, those with short gut syndrome, severe gut dysfunction, mesenteric vascular insufficiency, prolonged bowel obstruction, high-volume fistulas, and sepsis with hemodynamic instability) [26].

To prevent undernutrition and related adverse effects, all ICU patients who are not expected to be on a full oral diet within 3 days should receive EN. Accordingly, EN is recommended as the first choice for nutrition therapy in ICU patients; however, in critically ill patients on nutrition therapy, there is a large discrepancy in the frequency of EN [27–32]. The American Society for Parenteral and Enteral Nutrition (ASPEN) Board of Directors and the American College of Critical Care Medicine Guidelines Committee expressed concern that continuing to provide standard therapy (that is, no nutrition therapy) beyond 7 days would lead to deterioration of the patient's nutritional status and would have an adverse effect on clinical outcome [1].

If EN cannot be provided and if the patient has evidence of protein–calorie malnutrition (usually defined by recent weight loss of >10–15 % or by an actual body weight <90 % of the ideal body weight), then the use of TPN is mandatory [33]. The use of TPN (vs. standard therapy) in malnourished ICU patients was associated with a significantly lower rate of overall complications [34].

The best timing for the initiation of TPN in ICU patients has not been demonstrated. On the other hand, the European Society of Parenteral and Enteral Nutrition (ESPEN) [35] and the Canadian Society for Nutritional Sciences (CSCN) [36] both recommend early EN initiation after ICU admission (within 24 h, per ESPEN; within 24–48 h, per CSCN). It seems reasonable to assume that all patients who are not expected to be on normal nutrition within 2–3 days after ICU admission should receive TPN, if EN is contraindicated or not tolerated. No significant differences in clinical outcome have been shown between EN versus TPN in ICU patients [37].

Nutritional assessment

The best assessment of a patient's prior nutritional state comes from a detailed history of prior illness, but obtaining such a history is not possible in some critically ill and

injured patients. Calculating a patient's nutritional intake, combined with a clinical examination of fat and muscle distribution, would also be ideal, but again, not necessarily doable. The BMI (weight in kg/height in m^2) is useful, but obtaining an accurate weight can be difficult as well; moreover, it may be distorted by resuscitative fluid administration [3]. The challenges of alcohol intoxication, coma, ventilator support, and frequent use of anesthetics can also add to the inherent difficulty. If a patient's history is obtainable, it should note any alcoholic tendencies (which are associated with malnutrition) and history of diabetes, chronic pulmonary disease, renal failure, weight gain, and weight loss (all of which are associated with increased morbidity) [38]. One of the most common methods for estimating caloric needs or basal energy expenditure (BEE) is the Harris–Benedict equation (HBE), calculated as follows:

$$\text{Males: BEE} = 66.5 + 13.8\,(\text{weight in kg}) + 5\,(\text{height in cm}) - 6.8\,(\text{age})$$

$$\text{Females: BEE} = 65.5 + 9.6\,(\text{weight in kg}) + 1.7\,(\text{height in cm}) - 4.7\,(\text{age})$$

The HBE yields a calculation of basic energy requirements that are frequently multiplied by various activity factors and/or stress factors, thereby, generating an individual patient's estimated resting energy expenditure (REE). For example, for stress factors, minor surgery is assigned a multiplier of 1.2; trauma, 1.35; sepsis, 1.6; and major burns, 2.1. Thus, REE = BEE × stress factors. The patient's current actual body weight may change after a period of aggressive volume resuscitation, which could result in the overestimation of caloric requirements. Ideally, an admission weight before initial resuscitation should be obtained [39–41]. An accurate measurement of body weight is an arduous task in critically ill and injured patients, who often have bulky dressings, catheters, monitoring wires, tubes, and drains. Under such circumstances, the ideal body weight (IBW) may prove useful, calculated as follows:

$$\text{Males: IBW} = 50 + (2.3 \times \text{height [in inches]} - 60)$$

$$\text{Females: IBW} = 45.5 + (2.3 \times \text{height [in inches]} - 60)$$

Obesity poses another scenario where overfeeding may result if the patient's actual body weight is used. It is defined as an actual body weight more than 120 % above the patient's IBW or as a BMI >30. For all of the above reasons, the adjusted body weight (ABW) is commonly used for calculating energy requirements:

$$\text{ABW} = 0.25 \times (\text{actual weight} - \text{IBW}) + \text{IBW}$$

A more specific method that may be used to determine caloric needs in patients who are on mechanical ventilators is indirect calorimetry (IC), which is considered to be the gold standard for caloric assessment. A computerized "metabolic cart" is used to collect the patient's expired gases to determine CO_2 production and O_2 consumption, which are then used to calculate the REE using the Weir equation [39–41]:

$$\text{REE} = [3.9\,(\text{VO2}) + 1.1\,(\text{VCO2})]\,1.44$$

Energy requirements

Current recommendations for most surgical patients and for patients during the acute and initial phase of critical illness are to provide about 20–25 kcal/kg/day through the administration of carbohydrates (70 %) and lipids (<30 %). During the anabolic recovery phase and in patients with severe undernutrition, the aim should be to provide 25–30 total kcal/kg/day (ESPEN guidelines, level III). Protein should not be included in these energy calculations: the intent is for the protein to be incorporated into new muscle, rather than metabolized into energy.

Assessment of immune competence

Immunity is suppressed by malnutrition. Cell-mediated immunity is affected more than humoral immunity [42]. The two most frequently used tests are the total lymphocyte count (TLC) and the delayed hypersensitivity skin test (DHST). A TLC under 3,000/mm^3 reflects immunodeficiency, but it is not a useful test in critically ill patients, in whom sepsis, trauma, and disseminated intravascular coagulopathy also depress immune function. DHST results and morbidity have been strongly associated; in addition, mortality rates are higher in patients with negative (vs. normal) DHST results [43].

Choice of nutritional formulations and key nutrients

In critically ill and injured patients, immune-modulating or immune-enhancing enteral formulations that are supplemented with agents such as arginine, glutamine, nucleic acid, omega-three fatty acids, and antioxidants should be used, depending on their clinical condition. Patients with acute lung injury (ALI) or acute respiratory distress syndrome (ARDS) should be on an enteral formulation characterized by an anti-inflammatory lipid profile (that is, omega-3 fish oil, borage oil) and antioxidants [44]. Furthermore, nutritional therapy must be tailored to the individual patient's disease or disorder and unique metabolic changes. The seemingly logical strategy would be to replace deficiencies of key nutrients (such as amino acids, proteins, vitamins, minerals, and trace elements) in the doses required, within the appropriate time, and in the

manner (early oral feeding, enteral, and/or parenteral) most conducive to helping prevent cellular injury and clinical consequences. But, given so many complicating factors, many immune-enhancing and immune-modulating formulas have been developed for use in critically ill and injured patients [5].

Although it is difficult to demonstrate the precise impact of nutrition therapy, and in particular the individual effects of certain nutrients, enteral formulas fortified with immune-enhancing substrates have been associated with a significant reduction in the risk of infectious complications and a reduction in overall hospital stay [38–41, 45–49]. Certain nutrients can modulate inflammatory, metabolic, and immune processes. Amino acids such as arginine and glutamine improve body defenses and tumor cell metabolism, increase wound healing, and reduce nitrogen loss. RNA and omega-3 fatty acids also modulate immune function [50–58]. We will review a few key nutrients as part of immune-enhancing or immune-modulating formulation (Table 1).

Glutamine

A nonessential amino acid, glutamine serves as the primary fuel for enterocytes and for other rapidly proliferating cells, such as cells in wounds [59]. It is involved in many immune functions, including the production of heat shock proteins [60].

Immune-enhancing enteral diet containing glutamine reduced septic complications in patients with severe trauma [51] and significantly reduced the morbidity of, and shortened the time on, mechanical ventilation [54]. Another study found that the use of glutamine was associated with a significant reduction in the incidence of bacteremia, of septic episodes, and of pneumonia [55].

Glutamine seems to protect against Gram-negative bacteria in the most critically ill patients, but the mechanism is not entirely clear [5]. Supplementation with glutamine may lead to a decrease in nosocomial infections in patients with systemic inflammatory response [61], a decrease in blood infections in burn patients [62], and a decrease in pneumonia, sepsis, and bacteremia in trauma patients [54]. Parenterally administered glutamine has been associated with a decrease in Gram-negative bacteremia [52]. Thus, the addition of glutamine to enteral nutrition has been recommended for burn, trauma, and other ICU patients in the 2009 Society of Critical Care Medicine (SCCM)/ASPEN nutritional guidelines [33]. Glutamine should be added to the standard enteral formula in burn patients and trauma patients (ESPEN guidelines, level I).

Table 1 Immune-enhancing nutrients

Nutrients	Benefits
Glutamine	Beneficial in PN for general ICU and burn patients.
	Possibly beneficial in elective surgical patients.
Arginine	Beneficial in elective surgical patients.
Omega-3 fatty acids	Beneficial in patients with acute lung injury.
Antioxidants	Possibly beneficial in general ICU patients.

Adapted from Edmondson [78]

ICU intensive care unit, *PN* parenteral nutrition

Arginine

A nonessential or conditionally essential amino acid, arginine seems to be necessary for normal T-lymphocyte function; the levels of arginine are closely regulated by some specialized immune cells called myeloid suppressor cells [33]. Arginine may also stimulate the release of hormones such as growth hormone, prolactin, and insulin [63]. Arginine appears to have trophic effects on the immune system in humans, resulting in weight gain, increased nitrogen retention, and improved wound healing [64, 65]. A systematic review of 22 RCTs showed that, in a priori subgroup analysis, patients fed commercial formulations with high arginine levels experienced a significant reduction in infectious complications. The current recommendations are that immune-modulating formulations containing arginine are safe to use in patients with mild to moderate sepsis, but that caution should be employed in patients with more severe sepsis [33].

Nucleotides

Nucleotides have a role in the synthesis of deoxyribonucleic acid (DNA) and ribonucleic acid (RNA) and in adenosine triphosphate (ATP) metabolism; they are a part of many coenzymes involved in carbohydrate, protein, and lipid synthesis [66].

In the clinical setting, immune-modulating formulas containing nucleotides have been shown to significantly reduce infections, ventilator days, and length of hospital stay, in both critically ill and postsurgical patients [67, 68].

Antioxidants and trace minerals

Vitamins with antioxidant properties include vitamins E and C (ascorbic acid); trace minerals include selenium, zinc, and copper. A meta-analysis of 11 clinical trials showed that the overall use of antioxidants was associated with a significant reduction in mortality, but had no effect on infectious complications [69]. Among the antioxidants, selenium may be the most effective [70, 71]. The current recommendation is to

provide a combination of antioxidant vitamins (especially selenium) and trace minerals to all critically ill patients receiving specialized nutrition therapy [33].

Omega-3 fatty acids

Omega-3 fatty acids can be given through the administration of fish oil. Omega-3 fatty acids from an individual's diet are rapidly incorporated into the cell membranes, influencing membrane stability, membrane fluidity, cell mobility, and cell signaling pathways. They are able to mitigate the potency of the inflammatory response and have, thus, been implicated in a reduction in cardiovascular disease. Their role in modulating the immune system in conditions such as ARDS is well described [72].

Branched-chain amino acids

After injury and sepsis, an energy deficit may develop in skeletal muscle, but it is met by increased oxidation of branched-chain amino acids (BCAAs) [35]. A study by García-de-Lorenzo et al. [73] demonstrated that critically ill patients who were unable to be fed enterally—but who were on TPN fortified with BCAAs at a high concentration (at either 23 or 45 %)—had significantly lower morbidity and mortality rates as compared with patients on standard TPN (1.5 g/kg/day of protein). Their decreased mortality rate correlated with higher doses of BCAAs (0.5 g/kg/day or higher) [73].

Initiation for enteral nutrition

Enteral feeding should be started early, within the first 24–48 h after admission if possible. Then, over the next 48–72 h, the feedings should be advanced toward the nutrition goal for the individual patient. In the ICU patient population, the initiation of enteral feeding does not require either the presence or the absence of bowel sounds, nor does it require any evidence of passage of flatus and stool [1]. In the setting of hemodynamic compromise (that is, when significant hemodynamic support is required to maintain cellular perfusion, including high-dose catecholamine agents, alone or in combination with large-volume fluid or blood product resuscitation), EN should be withheld until the patient is fully resuscitated and/or stable [1]. Other contraindications to EN are listed on Table 2. Either gastric or small-bowel feedings are acceptable in ICU patients. If critically ill patients are at high risk for aspiration or if they are intolerant to gastric feeding, they should be fed via an enteral access tube placed in the small bowel. The need to withhold enteral feedings because of repeated high gastric residual volumes may be a sufficient reason to switch to small-bowel feedings [1].

Table 2 Contraindications to enteral nutrition

Mechanical bowel obstruction
Bowel ischemia
Hemodynamic instability
Use of large doses of vasopressor
Severe small bowel ileus
Recent bowel anastomosis
Necrotizing hemorrhagic pancreatitis or other forms of severe pancreatitis
Short gut syndrome
High-output fistula (>500 mL)
Failed enteral access attempts
Severe malnutrition on admission

Energy requirements

Energy requirements may be calculated by predictive equations or measured by indirect calorimetry. During the first week of hospitalization, every effort should be made to provide >50–65 % of the individual EN patient's target goal calories. After 7–10 days of EN, if the patient's full energy requirements (that is, 100 % of the target goal calories) are not met via the enteral route alone, then supplemental TPN should be considered. The use of additional modular protein supplements is common, because standard enteral formulations tend to have a high nonprotein calorie to nitrogen ratio. In trauma patients with a BMI <30, protein requirements should be ≥2.0 g/kg of actual body weight per day [1]. In all obese patients with a BMI ≥30, the goal of EN should not exceed 60–70 % of the target energy requirements or 11–14 kcal/kg of actual body weight/day (or 22–25 kcal/kg of ideal body weight/day). Protein requirements should be ≥2.0 g/kg of ideal body weight/day for class I and class II patients (BMI 30–40), but ≥2.5 g/kg of ideal body weight/day for class III patients (BMI ≥40) [1].

Monitoring

To initiate EN in the ICU, evidence of bowel motility (resolution of clinical ileus) is not required, but patients should be monitored for EN intolerance (determined by any complaints of abdominal pain and/or distention, physical examination, passage of flatus and stool, and/or abdominal radiographs). In the absence of other signs of intolerance, EN should not be withheld in patients with gastric residual volumes <500 mL.

Prescribing nil per os (NPO, nothing by mouth) while the patient is undergoing diagnostic tests or procedures should be minimized, in order to prevent inadequate delivery of nutrients and prolonged periods of ileus, which

may be propagated by the NPO status [1]. In addition, measures to reduce aspiration risk—such as elevation of the bed and use of prokinetic drugs (metoclopramide and erythromycin) or narcotic antagonists (naloxone and alvimopan)—should be initiated where clinically feasible [1]. Diarrhea in critically ill patients on EN can be complex and should be carefully monitored.

Initiation for TPN

Early nutrition therapy via TPN has the potential to reduce disease severity, diminish complications, and decrease the ICU length of stay, when EN is not possible, by providing ongoing requirements for calories, protein, electrolytes, vitamins, minerals, trace elements, and fluids [26]. The major indication for TPN is failure of the GI tract. In general, TPN should be started when the GI tract cannot be used for more than 5 days in patients in a catabolic state (with or without evidence of malnutrition), or when patients cannot be fed for 3 days after major surgery. The underlying clinical conditions include short gut syndrome, severe gut dysfunction, mesenteric vascular insufficiency, bowel obstruction, GI bleeding, severe diarrhea, large-volume fistulas, sepsis, severe burns, and trauma associated with continuous hemodynamic instability and with severe fulminant acute and chronic pancreatitis. In many of these patient subgroups, TPN is life-saving [26].

TPN has numerous specific advantages over EN. Providing adequate intravenous (IV) nutrition, for as long as necessary, when use of the GI tract is impractical, inadequate, ill-advised, or impossible, and reduction of the urgency for surgical intervention in patients who might eventually require such intervention, but in whom prolonged, progressive malnutrition will greatly increase the operative risk and the risk of postoperative complications, are two main benefits of TPN.

Furthermore, nutrient bioavailability is better, and many nutrient effects can be obtained in shorter times [74, 75]. The major advantage is that TPN does not require a functioning GI tract or gut access. In patients with complications associated with EN (such as aspiration, gut ischemia, or diarrhea), TPN is the technique of choice. Nutrients can be easily administered, and the quantity given or delivered is not affected by abdominal distention, fistula drainage, ischemia, or nausea/vomiting [26]. Some relative contraindications to TPN include evidence that it is unlikely to be required for more than 5–7 days, intolerance of the IV fluid load required, severe hyperglycemia, severe electrolyte abnormalities, and adequate GI tract function with access for EN [76].

Table 3 Complications of parenteral nutrition therapy

I. Catheter-related complications
1. Pneumothorax
2. Subclavian artery injury
3. Venous air embolism
4. Atrial injury
5. Catheter embolization
6. Catheter dislocation
7. Venous thrombosis
8. Catheter occlusion
9. Phlebitis
10. Catheter sepsis
II. Hepatic steatosis
III. Gastrointestinal atrophy
IV. Macronutrient-related complications
1. Calories
2. Glucose
a. Hyperglycemia
b. Hypoglycemia
3. Refeeding syndrome
4. Protein
5. Lipids
V. Fluid- and electrolyte-related complications
1. Fluid overload
2. Sodium
a. Hyponatremia
b. Hypernatremia
3. Potassium
a. Hypokalemia
b. Hyperkalemia
4. Chloride
a. Hypochloremia
b. Hyperchloremia
5. Calcium
a. Hypocalcemia
b. Hypercalcemia
6. Phosphorus
a. Hypophosphatemia
b. Hyperphosphatemia
7. Magnesium
a. Hypomagnesemia
b. Hypermagnesemia
VI. Acid–base disorders
1. Metabolic acidosis
2. Metabolic alkalosis
VII. Trace element abnormalities
VIII. Long-term complications
1. Metabolic bone disease

Adapted from Piazza-Barnett R et al. [79]

Table 4 Recommendations for nutrition therapy, per current evidence

a. All critically ill patients, as soon as they are fully resuscitated, should be fed via EN if at all possible.

b. Patients with blunt or penetrating abdominal injuries should be fed via EN, when feasible (EAST, level I).

c. Patients with severe head injuries should preferentially receive early EN: outcomes are similar, and costs and complications are lower as compared with TPN. If early EN is not feasible or not tolerated, TPN should be instituted Eastern Association for Trauma Surgery (EAST), Level I [77].

d. Severely injured patients with blunt or penetrating trauma should not begin EN within 24 h after admission, because doing so appears to confer no outcome advantage, as compared with 72 h after admission (EAST, level I).

e. All patients who are not expected to be on normal nutrition within 3 days should receive TPN within 24–48 h if EN is contraindicated or not tolerated (ESPEN, level III).

f. A central venous access device should be used, when needed, to administer the high-osmolarity TPN mixture designed to fully cover nutritional needs.

g. Peripheral venous access devices should be considered for low-osmolarity (<850 mOsmol/L) TPN mixtures designed to cover a proportion of nutritional needs and to mitigate negative energy balance. If peripherally administered TPN does not allow full provision of nutritional needs, then TPN should be centrally administered European Society for Parenteral and Enteral Nutrition (ESPEN), level III [27].

h. All EN patients not receiving their target goal calories after 2 days should be considered for supplementary TPN (ESPEN, level III)[a].

i. EN formulations enhanced with "adequate" doses of arginine and glutamine should be used in severely injured trauma patients, in order to reduce length of stay and septic morbidity (Injury Severity Score >20, Abdominal Trauma Index >25)[b].

j. Patients with ARDS and severe acute lung injury should be placed on an EN formulation characterized by an anti-inflammatory lipid profile (that is, omega-3 fish oil, borage oil) and antioxidants American Society of Parenteral and Enteral Nutrition (ASPEN), level I [1, 33].

k. TPN should be initiated only if its duration is anticipated to be ≥7 days (ASPEN, level II). A shorter duration has no beneficial impact on outcome and may even increase risk.

l. In burn patients, intragastric feedings should be started as soon after admission as possible, because delayed EN (>18 h) results in a high rate of gastroparesis and the need for IV nutrition (EAST, level II).

m. Patients with severe head injuries who do not tolerate gastric feedings within 48 h after their injuries should be switched to post-pyloric feedings, ideally beyond the ligament of Treitz, if feasible and safe (EAST, level II).

n. Patients who are incompletely resuscitated should not have direct small-bowel feedings instituted because of the risk of GI intolerance and possible intestinal necrosis (EAST, level III).

o. In severely injured patients undergoing a laparotomy for blunt and penetrating abdominal injuries, direct small-bowel access should be obtained (via a nasojejunal feeding tube, a gastrojejunal feeding tube, or a feeding jejunostomy); EN should begin as soon as feasible after resuscitation from shock (EAST, level III).

p. Moderately to severely injured patients (Injury Severity Score 25–30) should be provided 25–30 total kcal/kg/d or 120–140 % of the predicted BEE, as measured by the Harris–Benedict equation (EAST, level II).

q. Patients with severe head injuries (Glasgow Coma Scale score <8) who are not pharmacologically paralyzed should be provided about 30 total kcal/kg/d (about 140 % of the measured resting energy expenditure [MREE]); those who are pharmacologically paralyzed, about 25 total kcal/kg/d (about 100 % of MREE) (EAST, level II).

r. Within the first 2 weeks after a spinal cord injury, quadriplegic patients should be provided 20–22 total kcal/kg/d (55–90 % of the predicted BEE per the Harris–Benedict equation); paraplegic patients, 22–24 total kcal/kg/d (80–90 % of the predicted BEE per the Harris–Benedict equation) (EAST, level II).

s. Patients with burns exceeding 50 % of their total body surface area should not receive TPN supplementation of EN to achieve Curreri-predicted caloric requirements; in such patients, TPN supplementation is associated with a higher mortality rate and aberrations in T cell function (EAST, level II).

t. In patients with severe burns, energy expenditure via calorimetry should be determined once or twice a week; doing so may be of benefit in avoiding over- or underfeeding (EAST, level II).

u. Burn patients who require frequent burn wound debridement should continue EN intraoperatively; this practice is safe and leads to more successful attainment of calorie and protein goals (EAST, level II).

v. Most injured patients should be provided about 1.25 g of protein per kilogram of body weight per day; however, severely burned patients should be provided up to 2 g of protein per kilogram of body weight per day (EAST, level II).

w. Carbohydrate administration should not exceed 5 mg/kg/mi (25 kcal/kg/d) in burn patients, and even less in non-burn trauma patients, in order to avoid predisposing patients to the metabolic complications associated with overfeeding (EAST, level II).

x. IV lipid or fat intake should be carefully monitored and maintained at less than 30 % of the total calories. Zero, or minimal, fat should be administered to burned or traumatically injured patients during the acute phase of injury, in order to help minimize their susceptibility to infection and to decrease length of stay (EAST, level II).

y. In head-injured patients, and in trauma patients with multiple injuries, serum pre-albumin levels should be monitored in order to determine the adequacy of nutrition therapy (EAST, level II).

[a] ASPEN and EAST recommendations (level III) extend this time to 7 days

[b] The precise doses of, and length of treatment with, arginine and glutamine required to obtain this effect have not yet been determined. Whether an additional benefit is gained from further supplementation with omega-3 fatty acids, nucleotides, and trace elements is unclear (EAST, level III; ASPEN, level II)

Monitoring

Although life-saving, TPN has its own inherent complications. The complications of TPN fall into two main categories: catheter-related and metabolic (Table 3). Most of these complications can be prevented or are easily treatable with proper and detailed attention. Glycemic control is the most crucial of all metabolic components: even moderate degrees of hyperglycemia can result in an increased incidence of infection and adverse outcomes [36, 76]. Inadequate

glycemic control should be seen as a marker of overfeeding and of excessive carbohydrate administration. Lipid monitoring and the lipid response to TPN are also vital. Evidence suggests that critically ill and injured patients should not be given lipid emulsions. The latest ASPEN guidelines call for no fat during the first week in the ICU [77]. Levels of urea, creatinine, and electrolytes must be determined at least daily. In addition, attention should be paid to any abnormalities of calcium, magnesium, and, in particular, phosphate. Perhaps the most decisive parameter to watch is the clinical well-being of the patient. Appreciation that a patient is subtly deteriorating may be the first clue of a TPN-related complication, rather than an abnormal value of a specific metabolic test [35]. The general rule is that nothing should be added to TPN solutions. They should never be co-administered via the same port with any other medication; a dedicated line is imperative. Unfortunately, precipitation in TPN solutions may be obscured by their lipid component; precipitation of calcium and phosphate has been reported, even when nothing was added to TPN solutions [74].

Conclusion

A multidisciplinary approach to nutrition therapy for all injured and critically ill patients is required and should be based on the anatomy and biology of disease, and should be individualized for each patient and based on current published evidence and guidelines (Table 4). A close partnership and good communication among physicians, clinical dietitians, nurses, pharmacists, and other critical care practitioners is invaluable to the overall care of critically ill and injured patients, and the ultimate success of nutrition therapy.

Conflict of interest None.

References

1. Martindale RG, McClave SA, Vanek VW, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine and American Society for Parenteral and Enteral Nutrition: Executive Summary. Crit Care Med. 2009;37(5):1757–61.
2. Latifi R. Editorial: Nutritional support of critically ill or injured patients: do it early and do it right. Eur Surg. 2011;43(1):5–6.
3. Griffiths RD, Bongers T. Nutrition support for patients in the intensive care unit. Postgrad Med J. 2005;81:629–36.
4. Slone DS. Nutritional support of the critically ill and injured patient. Crit Care Clin. 2004;20:135–57.
5. Dogjani A, Zatriqi S, Uranues S, Latifi R. Biology-based nutritional support of critically ill and injured patients. Eur Surg. 2011;43(1):7–12.
6. Hill AG, Hill GL. Metabolic response to severe injury. Br J Surg. 1998;85:884–90.
7. Ingenbleek Y, Bernstein L. The stressful condition as a nutritionally dependent adaptive dichotomy. Nutrition. 1999;15(4):305–20.
8. Latifi R, Caushaj PE. Nutrition support in critically ill patients: current status and practice. J Clin Ligand Assay. 1999;22:279–84.
9. Young VR, Munro HN. N′-Methylhistidine (3-methylhistidine) and muscle protein turnover: an overview. Fed Proc. 1978;37:2291–300.
10. Latifi R, Dudrick SJ, editors. Surgical nutrition: strategies in critically ill patients. Austin: Springer-Verlag/R.G. Landes; 1995.
11. Souba WW, Wilmore DW. Postoperative alteration of arteriovenous exchange of amino acids across the gastrointestinal tract. Surgery. 1983;94:342–50.
12. Kudlácková M, Anděl M, Hájková H, et al. Acute phase proteins and prognostic inflammatory and nutritional index (PINI) in moderately burned children aged up to 3 years. Burns. 1990;16:53–6.
13. Boosalis MG, Ott L, Levine AS, et al. Relationship of visceral proteins to nutritional status in chronic and acute stress. Crit Care Med. 1989;17:741–7.
14. Church JM, Hill GL. Assessing the efficacy of intravenous nutrition in general surgical patients: dynamic nutritional assessment with plasma proteins. JPEN J Parenter Enteral Nutr. 1987;11:135–9.
15. Isshiki H, Akira S, Sugita T, et al. Reciprocal expression of NF-IL6 and C/EBP in hepatocytes: possible involvement of NF-IL6 in acute phase protein gene expression. New Biol. 1991;3:63–70.
16. Bankey PE, Mazuski JE, Ortiz M, et al. Hepatic acute phase protein synthesis is indirectly regulated by tumor necrosis factor. J Trauma. 1990;30:1181–7.
17. Fleck A, Colley CM, Myers MA. Liver export proteins and trauma. Br Med Bull. 1985;41:265–73.
18. Ward NS, Casserly B, Ayala A. The compensatory anti-inflammatory response syndrome (CARS) in critically ill patients. Clin Chest Med. 2008;29:617–25.
19. Giner M, Laviano A, Meguid MM, et al. In 1995 a correlation between malnutrition and poor outcome in critically ill patients still exists. Nutrition. 1996;12:23–9.
20. Galanos AN, Pieper CF, Kussin PS, et al. Relationship of body mass index to subsequent mortality among seriously ill hospitalized patients. SUPPORT Investigators. The Study to Understand Prognoses and Preferences for Outcome and Risks of Treatments. Crit Care Med. 1997;25:1962–8.
21. McClave SA, Snider HL. Understanding the metabolic response to critical illness: factors that cause patients to deviate from the expected pattern of hypermetabolism. New Horiz. 1994;2:139–46.
22. Windsor AC, Kanwar S, Li AG, et al. Compared with parenteral nutrition, enteral feeding attenuates the acute phase response and improves disease severity in acute pancreatitis. Gut. 1998;42:431–5.
23. Kudsk KA, Croce MA, Fabian TC, et al. Enteral versus parenteral feeding. Effects on septic morbidity after blunt and penetrating abdominal trauma. Ann Surg. 1992;215:503–13.
24. Kalfarentzos F, Kehagias J, Mead N, et al. Enteral nutrition is superior to parenteral nutrition in severe acute pancreatitis: results of a randomized prospective trial. Br J Surg. 1997;84:1665–9.
25. Heyland DK, Schroter-Noppe D, Drover JW, et al. Nutrition support in the critical care setting: current practice in Canadian ICUs—opportunities for improvement? JPEN J Parenter Enteral Nutr. 2003;27:74–83.
26. Joseph B, Kulvatunyou N, Tang A, et al. Total parenteral nutrition in critically ill and injured patients. Europ Surg. 2011;43(1):19–23.

27. Kreymann KG, Berger MM, Deutz NE, et al. ESPEN guidelines on enteral nutrition: intensive care. Clin Nutr. 2006;25:210–23.
28. Payne-James JJ, de Gara CJ, Grimble GK, et al. Artificial nutrition support in hospitals in the United Kingdom—1991: second national survey. Clin Nutr. 1992;11:187–92.
29. Hill SA, Nielsen MS, Lennard-Jones JE. Nutritional support in intensive care units in England and Wales: a survey. Eur J Clin Nutr. 1995;49:371–8.
30. De Jonghe B, Appere-De-Vecchi C, Fournier M, et al. A prospective survey of nutritional support practices in intensive care unit patients: what is prescribed? What is delivered? Crit Care Med. 2001;29:8–12.
31. Preiser JC, Berré J, Carpentier Y, et al. Management of nutrition in European intensive care units: results of a questionnaire. Working Group on Metabolism and Nutrition of the European Society of Intensive Care Medicine. Intensive Care Med. 1999;25:95–101.
32. Lipman TO. Grains or veins: is enteral nutrition really better than parenteral nutrition? A look at the evidence. JPEN J Parenter Enteral Nutr. 1998;22:167–82.
33. McClave SA, Martindale RG, Vanek VW, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). JPEN J Parenter Enter Nutr. 2009;33(3): 277–316. http://www.nutritioncare.org.
34. Braunschweig CL, Levy P, Sheean PM, et al. Enteral compared with parenteral nutrition: a meta-analysis. Am J Clin Nutr. 2001;74:534–42.
35. Blackburn GL, Moldawer LL, Usui S, et al. Branched chain amino acid administration and metabolism during starvation, injury, and infection. Surgery. 1979;86:307–15.
36. Heyland DK, Dhaliwal R, Drover JW, et al. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. JPEN J Parenter Enteral Nutr. 2003;27(5):355–73.
37. Heyland DK, MacDonald S, Keefe L, et al. Total parenteral nutrition in the critically ill patient: a meta-analysis. JAMA. 1998;280:213–9.
38. Studley HO. Percentage of weight loss: a basic indicator of surgical risk in patients with chronic peptic ulcer. 1936. Nutr Hosp. 2001;16:141–3.
39. Boullata J, Williams J, Cottrell F, et al. Accurate determination of energy needs in hospitalized patients. J Am Diet Assoc. 2007;107:393–401.
40. Campbell CG, Zander E, Thorland W. Predicted vs measured energy expenditure in critically ill, underweight patients. Nutr Clin Pract. 2005;20:276–80.
41. Ahmad A, Duerksen DR, Munroe S, et al. An evaluation of resting energy expenditure in hospitalized, severely underweight patients. Nutrition. 1999;15:384–8.
42. Smith LC, Mullen JL. Nutritional assessment and indications for nutritional support. Surg Clin North Am. 1991;71:449–57.
43. Twomey P, Ziegler D, Rombeau J. Utility of skin testing in nutritional assessment: a critical review. JPEN J Parenter Enteral Nutr. 1982;6:50–8.
44. Gadek JE, DeMichele SJ, Karlstad MD, et al. Effect of enteral feeding with eicosapentaenoic acid, gamma-linolenic acid, and antioxidants in patients with acute respiratory distress syndrome. Enteral Nutrition in ARDS Study Group. Crit Care Med. 1999;27(8):1409–20.
45. Davis KA, Kinn T, Esposito TJ, et al. Nutritional gain versus financial gain: the role of metabolic carts in the surgical ICU. J Trauma. 2006;61:1436–40.
46. Alexander E, Susla GM, Burstein AH, et al. Retrospective evaluation of commonly used equations to predict energy expenditure in mechanically ventilated, critically ill patients. Pharmacotherapy. 2004;24:1659–67.
47. Faisy C, Guerot E, Diehl JL, et al. Assessment of resting energy expenditure in mechanically ventilated patients. Am J Clin Nutr. 2003;78:241–9.
48. Cheatham ML, Safcsak K, Brzezinski SJ, et al. Nitrogen balance, protein loss, and the open abdomen. Crit Care Med. 2007;35:127–31.
49. Gibbs J, Cull W, Henderson W, et al. Preoperative serum albumin level as a predictor of operative mortality and morbidity: results from the National VA Surgical Risk Study. Arch Surg. 1999;134:36–42.
50. Kudsk KA, Minard G, Croce MA, et al. A randomized trial of isonitrogenous enteral diets after severe trauma. An immune-enhancing diet reduces septic complications. Ann Surg. 1996;224:531–43.
51. Bower RH, Cerra FB, Bershadsky B, et al. Early enteral administration of a formula (Impact) supplemented with arginine, nucleotides, and fish oil in intensive care unit patients: results of a multicenter, prospective, randomized, clinical trial. Crit Care Med. 1995;23:436–49.
52. Wischmeyer PE, Lynch J, Liedel J, et al. Glutamine administration reduces Gram-negative bacteremia in severely burned patients: a prospective, randomized, double-blind trial versus isonitrogenous control. Crit Care Med. 2001;29:2075–80.
53. Atkinson S, Sieffert E, Bihari D. A prospective, randomized, double-blind, controlled clinical trial of enteral immunonutrition in the critically ill. Guy's Hospital Intensive Care Group. Crit Care Med. 1998;26:1164–72.
54. Houdijk AP, Rijnsburger ER, Jansen J, et al. Randomised trial of glutamine-enriched enteral nutrition on infectious morbidity in patients with multiple trauma. Lancet. 1998;352(9130):772–6.
55. Martindale R, Miles J. Is immunonutrition ready for prime time? Two points of view. Nutr Clin Pract. 2003;18:489–96.
56. Braga M, Gianotti L, Nespoli L, et al. Nutritional approach in malnourished surgical patients: a prospective randomized study. Arch Surg. 2002;137:174–80.
57. Seto Y, Fukuda T, Yamada K, et al. Celiac lymph nodes: distant or regional for thoracic esophageal carcinoma? Dis Esophagus. 2008;21:704–7.
58. Fukuda T, Seto Y, Yamada K, et al. Can immune-enhancing nutrients reduce postoperative complications in patients undergoing esophageal surgery? Dis Esophagus. 2008;21:708–11.
59. Souba WW, Klimberg VS, Plumley DA, et al. The role of glutamine in maintaining a healthy gut and supporting the metabolic response to injury and infection. J Surg Res. 1990;48:383–91.
60. Ziegler TR, Ogden LG, Singleton KD, et al. Parenteral glutamine increases serum heat shock protein 70 in critically ill patients. Intensive Care Med. 2005;31:1079–86.
61. Conejero R, Bonet A, Grau T, et al. Effect of a glutamine-enriched enteral diet on intestinal permeability and infectious morbidity at 28 days in critically ill patients with systemic inflammatory response syndrome: a randomized, single-blind, prospective, multicenter study. Nutrition. 2002;18:716–21.
62. Garrel D, Patenaude J, Nedelec B, et al. Decreased mortality and infectious morbidity in adult burn patients given enteral glutamine supplements: a prospective, controlled, randomized clinical trial. Crit Care Med. 2003;31:2444–9.
63. Davis SL. Plasma levels of prolactin, growth hormone and insulin in sheep following the infusion of arginine, leucine and phenylalanine. Endocrinology. 1972;91:549–55.
64. Saito H, Trocki O, Wang SL, et al. Metabolic and immune effects of dietary arginine supplementation after burn. Arch Surg. 1987;122:784–9.
65. Daly JM, Reynolds J, Thom A, et al. Immune and metabolic effects of arginine in the surgical patient. Ann Surg. 1988;208:512–23.

66. Kulkarni AD, Rudolph FB, van Buren CT. The role of dietary sources of nucleotides in immune function: a review. J Nutr. 1994;124(8 Suppl):1442S–6S.
67. Beale RJ, Bryg DJ, Bihari DJ. Immunonutrition in the critically ill: a systematic review of clinical outcome. Crit Care Med. 1999;27:2799–805.
68. Braga M, Gianotti L, Radaelli G, et al. Perioperative immunonutrition in patients undergoing cancer surgery: results of a randomized double-blind phase 3 trial. Arch Surg. 1999;134:428–33.
69. Heyland DK, Dhaliwal R, Suchner U, et al. Antioxidant nutrients: a systematic review of trace elements and vitamins in the critically ill patient. Intensive Care Med. 2005;31:327–37.
70. Crimi E, Liguori A, Condorelli M, et al. The beneficial effects of antioxidant supplementation in enteral feeding in critically ill patients: a prospective, randomized, double-blind, placebo-controlled trial. Anesth Analg. 2004;99:857–63.
71. Angstwurm MW, Engelmann L, Zimmermann T, et al. Selenium in Intensive Care (SIC): results of a prospective randomized, placebo-controlled, multiple-center study in patients with severe systemic inflammatory response syndrome, sepsis, and septic shock. Crit Care Med. 2007;35:118–26.
72. Con J, Joseph B, Kulvatunyou N, et al. Evidence-based immune-modulating nutritional therapy in critically ill and injured patients. Eur Surg. 2011;43(1):13–8.
73. García-de-Lorenzo A, Ortíz-Leyba C, Planas M, et al. Parenteral administration of different amounts of branch-chain amino acids in septic patients: clinical and metabolic aspects. Crit Care Med. 1997;25:418–24.
74. Battistella FD, Widergren JT, Anderson JT, et al. A prospective, randomized trial of intravenous fat emulsion administration in trauma victims requiring total parenteral nutrition. J Trauma. 1997;43:52–8.
75. Christman JW, McCain RW. A sensible approach to the nutritional support of mechanically ventilated critically ill patients. Intensive Care Med. 1993;19:129–36.
76. Ziegler TR. Parenteral nutrition in the critically ill patient. N Engl J Med. 2009;361:1088–97.
77. EAST Practice Management Guidelines Work Group. Nutritional Support in Trauma Patients. J Trauma. 2004;57(3):660–679.
78. Edmondson WC. Continuing education in anaesthesia. Contin Educ Anaesth Crit Care Pain. 2007;7:199–202.
79. Piazza-Barnett R, Matarese LE, Seidner DL, Steiger E. Techniques and monitoring of total parenteral nutrition. In: Latifi R, Dudrick SJ, editors. The biology and practice of current nutritional support. 2nd ed. Georgetown: Landes Bioscience; 2003.