Enteral Nutrition in Critical Care

Carlos Seron-Arbeloa\textsuperscript{a,b}, Monica Zamora-Elson\textsuperscript{a},
Lorenzo Labarta-Monzon\textsuperscript{a}, Tomas Mallor-Bonet\textsuperscript{a}

Abstract

There is a consensus that nutritional support, which must be provided to patients in intensive care, influences their clinical outcome. Malnutrition is associated in critically ill patients with impaired immune function and impaired ventilator drive, leading to prolonged ventilator dependence and increased infectious morbidity and mortality. Enteral nutrition is an active therapy that attenuates the metabolic response of the organism to stress and favorably modulates the immune system. It is less expensive than parenteral nutrition and is preferred in most cases because of less severe complications and better patient outcomes, including infections, and hospital cost and length of stay. The aim of this work was to perform a review of the use of enteral nutrition in critically ill patients.

Keywords: Enteral nutrition; Critical care; Nutritional support; Intensive care; Enteral feeding; Critical ill

Introduction

Several ancient physicians, such as Hippocrates, Celsius, and Avicenna, among others, already prescribed certain foods for the treatment of diseases and for the patient’s convalescence. However, the concept of nutrition did not appear in the literature until the second half of the 19th century, under the term ‘Dietetics’.

It was not until the first half of the 20th century that physicians began to show interest in feeding patients incapable of eating enough, either because they should not or could not, in order to address their increased metabolic needs during severe and prolonged diseases.

The first attempts were carried out at the end of the 19th century. In 1872, Clouston described a method for intragastric feeding, infusing milk, eggs, jelly, alcohol and sugar, and in 1882, Bliss attempted providing food through the rectum. At the beginning of the 20th century, the techniques for gastrointestinal tract access began to improve, and around the 1950s, more refined mixtures started to be used, resulting in major advances, such as the development of foods for astronauts, and that of elementary diets.

In 1937, Elman carried out the first successful intravenous infusion of hydrolyzed casein to a patient. From that moment on, two schools of thought appeared: one in Sweden, which succeeded in intravenously administering lipids, together with glucose and a source of nitrogen, first as hydrolyzed casein, and then as crystalline amino acids; and another one in Philadelphia, which administered hypertonic glucose and nitrogen through a central venous catheter, using the insertion technique described by Aubaniac in 1952. In 1967, Wilmore and Dudrick reported the case of an infant that was successfully nourished intravenously for more than six weeks. From then on, this feeding method began to spread. With the booming of parenteral nutrition, enteral nutrition remained relegated until 25 years ago [1].

Over the last 30 years, enteral nutrition has developed continuously, especially because malnutrition has been established as an independent risk factor for morbidity, leading to an increasing in the rate of infections, in the length of stay in the hospital and intensive care unit, and in the number of days of mechanical ventilation, as well as a more difficult healing of wounds, and ultimately, an increase in mortality. Throughout the years, the indications have increased, the most appropriate administration routes have been established, and increasingly specific infusion systems and nutrients have been developed. Thanks to calorimetric studies, hyperalimentation could be avoided, and the supply in substrates could be better adapted to the needs specific to each situation of malnutrition and stress, thus reducing the incidence of complications and improving the outcomes.

The 1980s saw great advances in the development of chemically defined and organ-specific diets, and in the development of more advanced techniques for access. Feeding tubes have been improved so that they are thinner, more...
comfortable and safer. In addition, gastrointestinal tract accesses through radiological, surgical and endoscopic techniques for nasoenteric intubation and gastrojejunostomy tube placement have been improved [1].

In the last decades, multiorgan failure became the main cause of death among critically ill patients and in 1988, Wilmore [2] hypothesized that bacterial translocation could be the main source and trigger for sepsis. Therefore, research focused on studying the gastrointestinal tract, which went from being considered a mere nutrient digestion and absorption organ to the spotlight as a barrier against bacteria and intraluminal toxins and an organ with significant hormonal, metabolic and immune functions.

**Justification for the Nutritional Support of the Critically Ill Patients**

Critically ill patients are at particular risk of malnutrition, which occurs in up to 40% of the cases. The metabolic changes that occur in response to stress lead to an increase in protein catabolism, resulting in a significant loss of lean body mass, which in turn results in a higher incidence of complications, especially infectious ones, in an increase in wound dehiscence and in unfavorable outcomes. The main purpose of nutritional support is to prevent malnutrition and its associated complications, by modulating the stress response of the patients [3]. This objective will be achieved by: (1) providing the appropriate doses of macro- and micronutrients to meet the calculated or measured needs; (2) avoiding complications associated with nutritional support; (3) reducing nitrogen deficits; and (4) modulating the inflammatory response through the use of different substrates.

**Indications, Contraindications and Complications of Enteral Nutrition in Critically Ill Patients**

In general, intensive care unit patients who present with malnutrition or a high probability of developing malnutrition during their hospital stay and those who are not expected to be on a full oral diet within three days should receive specialized enteral and/or parenteral nutritional support. In case of enteral nutrition, feeding should be started early within the first 24 - 48 hours following admission to facilitate diet tolerance, reduce the risk of intestinal barrier dysfunction and infections, and reduce the length of hospital stay and mechanical ventilation [4].

The most widely used guidelines of different scientific societies on the use of enteral nutrition in critically ill patients [5-8] and their level of evidence according to the GRADE Working Group [9] are summarized in Table 1. Moreover, the most common contraindications and complications associated with enteral nutrition are reported in Tables 2, 3, respectively [10-14].

**Considerations About the Provision of Nutritional Support toCritically Ill Patients**

Usually, the caloric intake of critically ill patients receiving artificial nutrition is much lower than desired, recommended or measured, especially with the enteral route [15-19]. Some studies have found a relationship between hypocaloric intake and mortality, infection and nosocomial bacteremia [11]. Dvir et al [20] revealed in a study on patients undergoing mechanical ventilation that the cumulative caloric deficit strongly correlated with the occurrence of complications, but not with mortality, the length of hospital stay or the length of mechanical ventilation. Rubinson et al [21] found an association between a caloric intake below 25% of the recommended and the incidence of bacteremia, and Krishnan [11] found that moderate caloric intake (between 33 and 66% of the recommended) was associated with better clinical outcomes. These data suggest that the optimal amount of calories required by critically ill patients continues to be controversial [21, 22].

The most reliable method for calculating energy consumption is indirect calorimetry. If not available, an amount of approximately 25 kcal/kg of current weight/day is recommended in patients with a body mass index below 30. In mechanically ventilated patients, the caloric needs should be estimated with the Penn State equation [23]. Carbohydrate intake should not exceed 4 g/kg/day and blood glucose levels should remain below 180 mg/dL. The recommended lipid supply is 0.7 - 1.5 g/kg/day, and the use of lipid emulsions with a high omega-6 fatty acid content should be avoided in critically ill patients. The supply in amino acids must be adjusted to 1 - 1.8 g/kg/day, depending on the level of metabolic stress. The supply of micronutrients, such as vitamins and trace elements, is also recommended, although the amounts required cannot be determined [24].

Regarding some specific amino acids, there is scientific evidence that supports a supply of parenterally administered glutamine of 0.5 g/kg/day. However, there are not enough studies to support its enteral administration, which does not seem to be associated with an increase in the corresponding plasma levels [25]. Another amino acid considered to be conditionally essential in critically ill patients is arginine. Its administration is recommended to critical trauma and surgical patients; however, it is currently under discussion for patients with severe sepsis [7].

A hypocaloric intake during the first phases of stress could have beneficial effects, such as a better glycemic control, that would reduce the occurrence of infectious complications, although this mechanism remains to be proven [26]. Some authors recommend the supply of 80% of the nutri-
Table 1. Summary of Recommendations for Enteral Nutrition in Critically Ill Patients

| Summary of recommendations for enteral nutrition in critically ill patients | Level of evidence |
|---------------------------------------------------------------------------|-------------------|
| 1. Enteral nutrition is associated with an improvement of nutritional variables, a lower incidence of infections and a reduced length of hospital stay. | A                 |
| 2. Critically ill patients who cannot be fed orally for a period of more than three days must receive specialized nutritional support. | C                 |
| 3. Enteral nutrition is preferable to parenteral nutrition.                | B                 |
| 4. Enteral nutrition should be started within the first 24-48 hours of admission. | A                 |
| 5. Enteral nutrition should provide 25 to 30 kcal/kg/day.                  | C                 |
| 6. The feedings should be advanced toward goal over the next 48-72 hours. | C                 |
| 7. The enteral nutrition must be deferred until the patient is hemodynamically stable. | C                 |
| 8. In intensive care unit patients, neither the presence nor absence of bowel sounds and evidence of passage of flatus and stool is required for initiation of enteral nutrition. | B                 |
tional needs during the first seven to ten days, and their in-
crease during convalescence [27, 28].
Among the reasons for this low initial caloric supply by
enteral nutrition, the increase in gastric residual volume, as
well as the different nursing, diagnostic and surgical pro-
cedures carried out on critically ill patients, are particular-
ly noteworthy [29]. Some authors, such as Montejo [30],
showed that an upper limit of tolerability for gastric residual
volume, as an indicator for enteral nutrition intolerance, im-
proves the volume provided through enteral nutrition. The
use of postpyloric access routes, the use of procedural pro-
tocols and an early start of nutritional support have been
shown to improve the enteral nutrient supply [6, 29].

Another important consideration to take into account for
the nutritional support of critically ill patients is the delay in
the onset of nutritional support. The clinical practice guide-
lines recommend that nutritional support be started early in
critically ill patients [5, 6, 8] which is in practice achieved
for approximately 50% of the patients, because the initial
hemodynamic alterations which characterize critically ill pa-
ients, impede early feeding in many cases [10, 13, 31, 32].
Early, as opposed to late, enteral nutrition has been shown
to have beneficial effects on patient outcome, in terms of
length of mechanical ventilation, incidence of infections
and/or mortality [33]. Moreover, nutrition seems to be ben-
eficial regardless of the access route [8]. In our experience,
early nutritional support is associated with lower mortality,
although we did not observe a reduction in the incidence of
infectious complications [34].

Benefits of Enteral Nutrition

In addition to its digestive, absorptive, endocrine and met-
abolic functions, the intestine is also an effective barrier
against bacteria and intraluminal toxins, thanks to the high
turnover rates of the enterocytes of the intestinal epithelium,
the mucus secreted by goblet cells, and the large amount of
lymphoid tissue that forms an immune barrier. Eighty per-
cent of immunoglobulins synthesized in the organism, es-
pecially IgA, are secreted through the gastrointestinal tract,
and 50% of the immune mass is found in this organ [2].

Intestinal dysfunction is common in critically ill pa-
ients, but there is no objective definition for it. Enteral nutri-
tion intolerance is the most simple and useful sign to evalu-
ate it. Its causes are multifactorial and have been identified
through different experimental studies, which showed that
intestinal bacteria are the cause of infectious complications
in hospitalized patients, and that the increase in intestinal
permeability could favor bacterial translocation. Intestinal
ischemia resulting from shock and sepsis states can produce
hypoxia and reperfusion injuries that affect the intestinal
wall permeability, through oxygen-free radicals, cytokines,
acidosis, ATP depletion and neutrophil activation. More-
over, fasting also causes the disruption of intestinal integrity,
through atrophy and a decrease in the size of microvilli, of
the depth of the crypts, of the intestinal weight and cellular
mass, resulting in a decrease in the number of cellular mito-
ses [35].

Enteral nutritional support has been shown to stimulate
intestinal growth and function, both directly intraluminally,
because it supplies substrates for enterocyte oxidation, and
indirectly, because it promotes hormone secretion through
the intestinal trophic effect, which would reduce bacterial
translocation and the problems associated with it. Enteral
nutrition seems to present benefits in comparison with par-
ental nutrition, such as a lower number of infectious com-
lications, non-infectious complications and associated costs
[5, 36-41].

Gramlich et al performed a systematic review of the lit-
erature and found that enteral nutrition was associated with
a lower number of infections, although there was no differ-
ce in terms of mortality, length of hospital stay or length
of mechanical ventilation [38]. Elke et al showed that paren-
teral nutrition was independently associated with mortality
in septic patients [39]. However, other authors reported dif-
f erent results. Simpson et al performed a meta-analysis, and
showed that enteral nutrition was associated with a lower
mortality than parenteral nutrition, but with a higher num-
ber of infectious complications [3]. Peter et al also found,
through another meta-analysis, that there was no difference
in mortality between early enteral and early parenteral nu-
trition, although the incidence of complications, both infec-
tious and non-infectious, was higher in patients under paren-
teral nutrition [40].

This lack of uniformity regarding the benefits of enteral
over parenteral nutrition suggests that once the need of nutri-
tional support has been established, enteral nutrition should
be preferably used. However, if enteral nutrition cannot be
used, parenteral nutrition should be immediately started.

Enteral Nutrition in Special Disease States

Renal failure

Acute renal failure is increasingly common in critically ill
patients. Nutritional support is aimed at preserving the lean
mass and energy reserves, avoiding malnutrition, attenuating
the inflammatory response and oxidative stress, and improv-
ing endothelial function [42, 43].

Normal diets are inadequate for non-hypercatabolic pa-
tients with renal failure conservatively treated or in intermit-
tent hemodialysis because of oligoanuria, because of their
low density and excessive sodium, potassium and phosphate
content. In these patients, hypoprotein or normoproteinic di-
ets are recommended, with high biological value proteins, high
energy density and low potassium, sodium and phosphate
Table 2. Contraindications to Enteral Nutrition

**Absolute contraindications to enteral nutrition:**

1. Diseases associated with ileus: multiple trauma with significant retroperitoneal hematoma and peritonitis
2. Intestinal obstruction
3. Active gastrointestinal hemorrhage
4. Hemodynamic instability: enteral nutrition in an ischemic small bowel can worsen the ischemia and lead to necrosis and bacterial overgrowth

**Relative contraindications, use of a mixed nutritional support:**

1. Diverticular abscess
2. Early stages of Short bowel syndrome
3. Severe malabsorption
4. Small bowel fistulas, depending on the flow rate and localization
5. Need for early nutritional support and full enteral feeding impossible:
   - Severely malnourished patients with severe hypercatabolism
   - Patients in whom an appropriate intestinal approach cannot be carried out or who do not tolerate the full requirements
### Table 3. Complications of Enteral Nutrition

#### Mechanic

1. Erosion and/or necrosis and/or infection at the contact zones
2. Pharyngeal, esophageal and/or tracheobronchial perforation and stenosis
3. Tracheoesophageal fistula
4. Malpositioning and removal of the probe
5. Obstruction and tethering of the probe
6. Intraperitoneal leakage through osteotomy site
7. Leakage of the formulation
8. Pulmonary aspiration
9. Hemorrhage

#### Metabolic

1. Hypertonic dehydration
2. Hyperosmolarity
3. Nonketotic hyperosmolar coma
4. Hyper/hypoglycemia
5. Dyselectrolytemia
6. Hyperhydration
7. Dumping syndrome
8. Refeeding syndrome
9. Hypercapnia

#### Infectious

1. Sinusitis and otitis
2. Aspiration pneumonia
3. Necrotizing peritonitis and enteritis
4. Dietary contamination

#### Gastrointestinal

1. Increased gastric residual volume
2. Constipation
3. Abdominal fullness and distention
4. Vomiting and regurgitation
5. Diarrhea
6. Hypertransaminasemia, hepatomegaly
Enteral Nutrition

content [44, 45].

However, hyperproteic diets (2 - 2.5 g/kg/day) must be provided to hypercatabolic patients on daily dialysis or continuous renal replacement procedures, adjusted to the underlying pathology and supplemented with glutamine. In some cases, the content in tyrosine, taurine, histidine and branched-chain amino acids should be increased [46].

Monitoring of serum electrolytes (phosphorus, potassium, magnesium) and the micronutrient levels (zinc, selenium, thiamin, folic acid and vitamins A, C, and D) is recommended, to individualize the supply.

Liver failure and transplantation

Malnutrition is a frequent finding in patients with liver failure and significantly impacts on mortality, especially in patients with alcoholic cirrhosis, as opposed to viral cirrhosis [47]. Thus, in patients who are candidates for liver transplant, malnutrition negatively affects the outcome of the procedure [48].

Enteral nutrition should be considered first, if nutritional support is required. Esophageal or gastric varices and coagulopathy are typical contraindications in clinical practice for nasogastric tube insertion, although this contraindication is not based on clinical studies and has been discussed by some authors. Parenteral nutrition should be provided if the gastrointestinal tract is not functioning properly because of a digestive hemorrhage, if enteral nutrition is not well tolerated, if enteral nutrition is not enough to meet the nutritional needs, or if there is a high risk of aspiration, as a result of alterations in the level of consciousness associated with advanced stages of encephalopathy [8].

In these patients, a caloric intake of 25 to 40 kcal/kg/day is recommended, with a mixed energetic supply (carbohydrates and fats). In patients with liver failure, the regular use of diets enriched in branched-chain amino acids is not recommended. These should be restricting to patients with encephalopathy arising during enteral nutrition. However, the supply of vitamins and trace elements should be increased, especially that of zinc, magnesium and potassium.

In patients with liver transplantation, nutritional support should be started early after the transplantation procedure, preferably via the enteral route and through transpyloric access [49].

Acute severe pancreatitis

Severe acute pancreatitis provokes a systemic inflammatory response that leads to a highly catabolic, hypermetabolic and hyperdynamic stress states [50].

The classical treatment of this syndrome consists of bowel rest and parenteral nutrition, but in the last decade, numerous studies have shown that this approach is associated with a high mortality and morbidity [51].

Intestinal barrier dysfunction occurs during the early phase of acute pancreatitis, and is associated with infectious pancreatic necrosis, multiorgan failure and mortality [52]. For these reasons, the preferred route of the nutritional support is enteral feeding into the jejunum, which should be started early, within the first 48 h. Even in patients who do not tolerate enteral nutrition well, it is recommended to maintain a minimum enteral nutrient supply [51].

Respiratory failure

Respiratory failure requiring mechanical ventilation is one of the most common reasons for intensive care unit admission, in addition to flare-ups chronic obstructive lung disease and acute respiratory distress. These patients are at high risk of malnutrition because of their underlying disease, their catabolic situation and the mechanical ventilation itself.

In patients with acute exacerbation of chronic respiratory failure, the recommended level of protein supply ranges from 1.0 to 1.8 g/kg/day and the use of specific high-fat, low-carbohydrate formulas is not indicated. Special attention should be paid to the supply of potassium, phosphorus, magnesium and antioxidants. In patients with acute lung injury and acute respiratory distress syndrome, an enteral diet enriched in omega-3 fatty acids and antioxidants is recommended [53].

Abdominal surgery

The nutritional needs of patients undergoing abdominal surgery are similar to that of other critically ill patients, although it should be taken into account that the surgery itself can trigger both inflammatory and metabolic changes. Malnutrition is associated with changes in body composition, as well as a delay in wound healing, a decrease in functional ability and a deterioration of the immune function; therefore, these patients have a higher risk of infectious and cardiorespiratory complications, which can result in an increase in hospital length of stay and in a higher mortality [54].

Early postoperative enteral feeding is effective and well tolerated, even in the presence of ileus and if the integrity of the newly constructed anastomosis is compromised, and it is associated with a reduction in the incidence of postoperative infectious complications and improved tissue healing [55]. In patients undergoing gastrointestinal tract surgery with proximal anastomosis, enteral nutrition using a feeding catheter placed distally to the anastomosis is recommended [54]. In case of enteral nutrition intolerance, the administration of prokinetic drugs should be considered. A complementary parenteral nutrition should be started when less than 60% of the nutritional needs are met on the third day after admission or during the hospital stay for at last two consecutive days [56].

In case of parenteral nutritional support, the supply of
omega-3 fatty acids [57] and supplementation in glutamine has been recommended, although there are not enough data to justify their use in surgical patients receiving enteral nutrition [54].

**Multiple trauma**

Multiple trauma patients are previously healthy patients who suddenly suffer a severe aggression; therefore, nutritional support should be started early, preferably enterally and with a protein supply adapted to the catabolism of the patient and supplemented in glutamine. In non-obese patients, a total daily caloric supply of 25 to 30 kcal/kg/day is recommended, and in patients with a spinal cord injury, a supply of 20 to 24 kcal/kg/day is recommended [58]. The latter show a specific evolution; it is thought that after a period of metabolic lethargy, a phase of intense proteolysis begins, which is difficult through nutritional support, since its pathophysiological base is more related to denervation than to the neuroendocrine storm of acute critically ill patients. During the first four weeks following spinal cord injury, weight loss occurs, which can be estimated at 10-20% of body weight, and about 85% of it corresponds to lean mass.

The supply of glutamine and other pharmacological nutrition agents, such as omega-3 fatty acids, arginine and antioxidants, is also recommended in multiple trauma patients [58-60].

**Sepsis**

Specialized nutritional support should be delayed in patients in septic shock and hemodynamic instability, until correct resuscitation and hemodynamic stability has been achieved.

Enteral feeding is the first choice of nutritional support in a septic patient, and it can be supplemented with different substrate mixtures, such as arginine, since it does not affect the evolution of the patient [61], although only the benefits of omega-3 supplementation have been demonstrated [62].

**Will it be Possible to Eliminate Parenteral Nutrition Support in Critically Ill Patients?**

Considering the historical evolution of nutritional support, its development has been fundamentally based on three elements [31]: 1) The development of practical, effective and safe access systems for the administration of nutrients through both routes, there have been great advances in enteral access to the gastrointestinal tract: in addition to the classical nasogastric tube, nasojejunal access and gastrosomy and jejunostomy tubes inserted through surgical, endoscopic and radiological techniques have been developed; 2) The increase in nutritional support indications and the scientific development of our knowledge. The proof that patients with diseases such as renal and hepatic failure, who were typically treated with parenteral nutrition, could also be treated with enteral nutrition in a safe manner, the favorable effect of enteral nutrition on the flare-ups of intestinal inflammatory disease, the possibility to use an enteral access in different types of fistulas, the proof of enteral nutrition tolerance in the immediate postoperative period, and the change in mentalities on the mere supply of substrates to treat or recover a state of malnutrition, which is currently referred to as nutritional support, with the aim of modulating the inflammatory response to the aggression; and 3) The development of increasingly sophisticated nutrient solutions, both for parenteral and enteral nutrition, that can administrate a number of nutrients with specific properties, such as glutamine, arginine, monounsaturated fatty acids, fish oils, taurine, nucleosides and nucleotides, as well as a wide selection of fats, micronutrients and antioxidants.

In the future, the research in this field will be focused on, among others: 1) Establishing the real benefits of the different nutrients in different types of diseases and in the different types of stress that affect critically ill patients; 2) Establishing the real benefits of the different elements of immunomodulating foods; 3) Establishing which is the caloric and nitrogen supply needed during the various stages of the stress response (early vs. late), now that the benefits of early enteral nutrition seem to be clearly established; 4) Determining if the initial hyperalimentation of critically ill patients provides real benefits; and 5) Determining if in case of difficulty meeting the nutritional needs with enteral feeding during the first phases, a complementary parenteral nutrition should (or not) be started.

Recent years have seen a steady growth and development of systems to use the best option in terms of route of access, supply and type of nutrients for nutritional support. Currently, enteral feeding is the method of choice for the nutritional support of critically ill patients, and it can be supplemented with parenteral nutrition if the nutritional needs cannot be completely met, leaving parenteral nutrition for very specific cases or for cases where an effective access is impossible. Therefore, only the scientific and technological limitations on the previously mentioned elements will determine the achievement of the objective of solving the current limitations and complications of nutritional support.

**Conflict of Interest**

The authors declare no conflict of interest.

**References**

1. Dudrick SJ, Palesty JA. Historical highlights of the development of enteral nutrition. Surg Clin North Am.
2. Wilmore DW, Smith RJ, O’Dwyer ST, Jacobs DO, Ziegler TR, Wang XD. The gut: a central organ after surgical stress. Surgery. 1988;104(5):917-923.

3. Simpson F, Doig GS. Parenteral vs. enteral nutrition in the critically ill patient: a meta-analysis of trials using the intention to treat principle. Intensive Care Med. 2005;31(1):12-23.

4. Fernandez-Ortega JF, Herrero Meseguer JL, Martinez Garcia P. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE): indications, timing and routes of nutrient delivery]. Med Intensiva. 2011;35(Suppl 1):7-11.

5. Heyland DK, Dhaliwal R, Drover JW, Gramlich L, Dodek P. Canadian clinical practice guidelines for nutrition support in mechanically ventilated, critically ill adult patients. JPEN J Parenter Enteral Nutr. 2003;27(5):355-373.

6. Fernandez Ortega EJ, Ordonez Gonzalez FJ, Blesa Malpica AL. [Nutritional support in the critically ill patient: to whom, how, and when?]. Nutr Hosp. 2005;20(Suppl 2):9-12.

7. Kreymann KG, Berger MM, Deutz NE, Hiesmayr M, Jolliet P, Kazandjiev G, Nitenberg G, et al. ESPEN Guidelines on Enteral Nutrition: Intensive care. Clin Nutr. 2006;25(2):210-223.

8. Singer P, Berger MM, Van den Berghe G, Biolo G, Calder P, Forbes A, Griffiths R, et al. ESPEN Guidelines on Parenteral Nutrition: intensive care. Clin Nutr. 2009;28(4):387-400.

9. Atkins D, Best D, Briss PA, Eccles M, Falck-Ytter Y, Flottorp S, Guyatt GH, et al. Grading quality of evidence and strength of recommendations. BMJ. 2004;328(7454):1490.

10. Rice TW, Swope T, Bozeman S, Wheeler AP. Variation in enteral nutrition delivery in mechanically ventilated patients. Nutrition. 2005;21(7-8):786-792.

11. Krishnan JA, Parce PB, Martinez A, Diette GB, Brower RG. Caloric intake in medical ICU patients: consistency of care with guidelines and relationship to clinical outcomes. Chest. 2003;124(1):297-305.

12. Montejo JC. Enteral nutrition-related gastrointestinal complications in critically ill patients: a multicenter study. The Nutritional and Metabolic Working Group of the Spanish Society of Intensive Care Medicine and Coronary Units. Crit Care Med. 1999;27(8):1447-1453.

13. Villet S, Chiolero RL, Bollmann MD, Revelly JP, Cayeux RNM, Delarue J, Berger MM. Negative impact of hypocaloric feeding and energy balance on clinical outcome in ICU patients. Clin Nutr. 2005;24(4):502-509.

14. Grau T, Bonet A. [Multicenter study on incidence of total parenteral nutrition complications in the critically-ill patient. ICOMEPE study. Part II]. Nutr Hosp. 2005;20(4):278-285.

15. O’Meara D, Mireles-Cabodevilla E, Frame F, Hummell AC, Hammel J, Dweik RA, Arroliga AC. Evaluation of delivery of enteral nutrition in critically ill patients receiving mechanical ventilation. Am J Crit Care. 2008;17(1):53-61.

16. Engel JM, Muhling J, Junger A, Menges T, Karcher B, Hempelmann G. Enteral nutrition practice in a surgical intensive care unit: what proportion of energy expenditure is delivered enterally? Clin Nutr. 2003;22(2):187-192.

17. Petros S, Engelmann L. Enteral nutrition delivery and energy expenditure in medical intensive care patients. Clin Nutr. 2006;25(1):51-59.

18. De B, Chapman M, Fraser R, Finnis M, De Keulenaer B, Liberalli D, Satanek M. Enteral nutrition in the critically ill: a prospective survey in an Australian intensive care unit. Anaesth Intensive Care. 2001;29(6):619-622.

19. Berger MM, Chiolero RL. Hypocaloric feeding: pros and cons. Curr Opin Crit Care. 2007;13(2):180-186.

20. Dvir D, Cohen J, Singer P. Computerized energy balance and complications in critically ill patients: an observational study. Clin Nutr. 2006;25(1):37-44.

21. Rubinson L, Diette GB, Song X, Brower RG, Krishnan JA. Low caloric intake is associated with nosocomial bloodstream infections in patients in the medical intensive care unit. Crit Care Med. 2004;32(2):350-357.

22. De Jonghe B, Appere-De-Vechi C, Fournier M, Tran B, Merrer J, Melchior JC, Outin H. A prospective survey of nutritional support practices in intensive care unit patients: what is prescribed? What is delivered? Crit Care Med. 2001;29(1):8-12.

23. Frankenfield D, Smith JS, Cooney RN. Validation of 2 approaches to predicting resting metabolic rate in critically ill patients. JPEN J Parenter Enteral Nutr. 2004;28(4):259-264.

24. Bonet Saris A, Marquez Vacaro JA, Seron Arbeloa C. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE): macro-and micronutrient requirements]. Med Intensiva. 2011;35(Suppl 1):17-21.

25. Wernerman J. Glutamine supplementation. Ann Intensive Care. 2011;1(1):25.

26. McClave SA, Kleber MJ, Lowen CC. Indirect calorimetry: can this technology impact patient outcome? Curr Opin Clin Nutr Metab Care. 1999;2(1):61-67.

27. Ortiz Leyba C, Gomez-Tello V, Seron Arbeloa C. [Requirements of macronutrients and micronutrients]. Nutr Hosp. 2005;20(Suppl 2):13-17.
28. Jeejeebhoy KN. Permissive underfeeding of the critically ill patient. Nutr Clin Pract. 2004;19(5):477-480.
29. McClave SA, Sexton LK, Spain DA, Adams JL, Owens NA, Sullins MB, Blandford BS, et al. Enteral tube feeding in the intensive care unit: factors impeding adequate delivery. Crit Care Med. 1999;27(7):1252-1256.
30. Montejo JC, Minambres B, Bordeje L, Mesejo A, Acosta T, Heras A, Ferre M, et al. Gastric residual volume during enteral nutrition in ICU patients: the REGANE study. Intensive Care Med. 2010;36(8):1386-1393.
31. Heyland DK, Schrotter-Noppe D, Drover JW, Jain M, Keefe L, Dhalliwal R, Day A. Nutrition support in the critical care setting: current practice in canadian ICUs opportunities for improvement? JPNEN J Parenter Enteral Nutr. 2003;27(1):74-83.
32. Seron Arbeloa C, Zamora Elson M, Labarta Monzon L, Garrido Ramirez de Arellano I, Lander Azcona A, Marquina Lacueva MI, Lopez Claver JC, et al. Nutritional support outcomes in critical care. Nutr Hosp. 2011;26(6):1469-1477.
33. Marik PE, Zaloga GP. Early enteral nutrition in acutely ill patients: a systematic review. Crit Care Med. 2001;29(12):2264-2270.
34. Seron Arbeloa C, Puzo Foncillas J, Garces Gimenez T, Escos Orta J, Labarta Monzon L, Lander Azcona A. A retrospective study about the influence of early nutritional support on mortality and nosocomial infection in the critical care setting. Clin Nutr. 2011;30(3):346-350.
35. Alpers DH. Enteral feeding and gut atrophy. Curr Opin Clin Nutr Metab Care. 2002;5(6):679-683.
36. Woodcock NP, Zeigler D, Palmer MD, Buckley P, Mitchell CJ, MacFie J. Enteral versus parenteral nutrition: a pragmatic study. Nutrition. 2001;17(1):1-12.
37. Braunschweig CL, Levy P, Sheean PM, Wang X. Enteral compared with parenteral nutrition: a meta-analysis. Am J Clin Nutr. 2001;74(4):534-542.
38. Gramlich L, Kichian K, Pinilla J, Rodych NJ, Dhaliwal R, Heyland DK. Does enteral nutrition compared to parenteral nutrition result in better outcomes in critically ill adult patients? A systematic review of the literature. Nutrition. 2004;20(10):843-848.
39. Elke G, Schadler D, Engel C, Bogatsch H, Frerichs I, Ragaller M, Scholz J, et al. Current practice in nutritional support and its association with mortality in septic patients-results from a national, prospective, multicenter study. Crit Care Med. 2008;36(6):1762-1767.
40. Peter JV, Moran JL, Phillips-Hughes J. A metaanalysis of treatment outcomes of early enteral versus early parenteral nutrition in hospitalized patients. Crit Care Med. 2005;33(1):213-220; discussion 260-211.
41. Cao Y, Xu Y, Lu T, Gao F, Mo Z. Meta-analysis of enteral nutrition versus total parenteral nutrition in patients with severe acute pancreatitis. Ann Nutr Metab. 2008;53(3-4):268-275.
42. Cano N, Fiaccadori E, Tesinsky P, Toigo G, Druml W, Kuhlmann M, Mann H, et al. ESPEN Guidelines on Enteral Nutrition: Adult renal failure. Clin Nutr. 2006;25(2):295-310.
43. Cano NJ, Aparicio M, Brunori G, Carrero JJ, Cianciaruso B, Fiaccadori E, Lindholm B, et al. ESPEN Guidelines on Parenteral Nutrition: adult renal failure. Clin Nutr. 2009;28(4):401-414.
44. Lopez Martinez J, Sanchez Izquierdo Riera JA, Jimenez Jimenez FJ. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMCYUC-SENPE): acute renal failure]. Med Intensiva. 2011;35(Suppl 1):22-27.
45. Fiaccadori E, Cresmaschi E. Nutritional assessment and support in acute kidney injury. Curr Opin Crit Care. 2009;15(6):474-480.
46. Shahid M, Johnson J, Nightingale P, Neuberger J. Nutritional markers in liver allograft recipients. Transplantation. 2005;79(3):359-362.
47. Caly WR, Strauss E, Carrilho FJ, Laudanna AA. Different degrees of malnutrition and immunological alterations according to the aetiology of cirrhosis: a prospective and sequential study. Nutr J. 2003;2:10.
48. Shahid M, Johnson J, Nightingale P, Neuberger J. Nutritional markers in liver allograft recipients. Transplantation. 2005;79(3):359-362.
49. Montejo Gonzalez JC, Mesejo A, Bonet Saris A. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMCYUC-SENPE): liver failure and transplantation]. Med Intensiva. 2011;35(Suppl 1):28-32.
50. Fossard JL, Steer ML, Pastor CM. Acute pancreatitis. Lancet. 2008;371(9607):143-152.
51. Bordeje Laguna L, Lorencio Cardenas C, Acosta Escribano J. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMCYUC-SENPE): severe acute pancreatitis]. Med Intensiva. 2011;35 (Suppl 1):33-37.
52. Besselink MG, van Santvoort HC, Renooij W, de Smet MB, Boermeester MA, Fischer K, Timmerman HM, et al. Intestinal barrier dysfunction in a randomized trial of a specific probiotic composition in acute pancreatitis. Ann Surg. 2009;250(5):712-719.
53. Grau Carmona T, Lopez Martinez J, Vila Garcia B. Guidelines for specialized nutritional and metabolic support in the critically-ill patient: update. Consensus
SEMICYUC-SENPE: respiratory failure. Nutr Hosp. 2011;26(Suppl 2):37-40.

54. Sanchez Alvarez C, Zabarte Martinez de Aguirre M, Bordeje Laguna L. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE): gastrointestinal surgery]. Med Intensiva. 2011;35(Suppl 1):42-47.

55. Windsor JA, Hill GL. Risk factors for postoperative pneumonia. The importance of protein depletion. Ann Surg. 1988;208(2):209-214.

56. Heidegger CP, Darmon P, Pichard C. Enteral vs. parenteral nutrition for the critically ill patient: a combined support should be preferred. Curr Opin Crit Care. 2008;14(4):408-414.

57. Heller AR, Rossler S, Litz RJ, Stehr SN, Heller SC, Koch R, Koch T. Omega-3 fatty acids improve the diagnosis-related clinical outcome. Crit Care Med. 2006;34(4):972-979.

58. Blesa Malpica AL, Garcia de Lorenzo y Mateos A, Robles Gonzalez A. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE): patient with polytrauma]. Med Intensiva. 2011;35(Suppl 1):68-71.

59. Wernerman J. Glutamine and acute illness. Curr Opin Crit Care. 2003;9(4):279-285.

60. Marik PE, Zaloga GP. Immunonutrition in critically ill patients: a systematic review and analysis of the literature. Intensive Care Med. 2008;34(11):1980-1990.

61. Ortiz Leyba C, Montejo Gonzalez JC, Vaquerizo Alonso C. [Guidelines for specialized nutritional and metabolic support in the critically-ill patient. Update. Consensus of the Spanish Society of Intensive Care Medicine and Coronary Units-Spanish Society of Parenteral and Enteral Nutrition (SEMICYUC-SENPE): patient with sepsis]. Med Intensiva. 2011;35(Suppl 1):72-76.

62. Peterik A, Milbrandt EB, Darby JM. Immunonutrition in critical illness: still fishing for the truth. Crit Care. 2009;13(3):305.