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RECOMMENDATIONS FOR SPECIALIZED NUTRITIONAL-METABOLIC TREATMENT OF THE CRITICAL PATIENT

Recommendations for specialized nutritional-metabolic management of the critical patient: Introduction, methodology and list of recommendations. Metabolism and Nutrition Working Group of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)☆

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Scientific evidence

Abstract The Metabolism and Nutrition Working Group of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC) has reviewed and updated the recommendations for specialized nutritional and metabolic support in critically ill patients published by the Group in 2011, with the primary aim of helping decision making in daily clinical practice.

The recommendations have been formulated by an expert panel with broad experience in nutritional and metabolic support in critically ill patients, and were drafted between March 2016 and February 2019.

A level of evidence has been provided for each of the recommendations, based on the GRADE methodology (Grading of Recommendations Assessment, Development and Evaluation Working Group). A grade of recommendation has also been produced, taking into account the clinical impact of the recommendation, regardless of the level of evidence established by the GRADE scale.

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◊ The names of the members of the expert panel are listed in Appendix A.

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PALABRAS CLAVE
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Recomendaciones para el tratamiento nutrometabólico especializado del paciente crítico: introducción, metodología y listado de recomendaciones. Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)

Resumen El Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC) ha revisado y actualizado las recomendaciones del tratamiento nutrometabólico en el paciente crítico (previamente publicadas por el grupo en el año 2011) con la finalidad de ayudar a la toma de decisiones en la práctica clínica diaria.

Para su elaboración, llevada a cabo entre marzo de 2016 y febrero de 2019, se ha contado con un panel de expertos dedicados a la Medicina Intensiva con amplia experiencia en el tratamiento nutricional de los pacientes críticos. Para cada una de las recomendaciones se ha establecido un nivel de evidencia basado en la metodología del grupo GRADE *(Grading of Recommendations Assessment, Development and Evaluation Working Group)* y un grado de recomendación que ha tenido en cuenta el impacto clínico de la recomendación, independientemente del nivel de evidencia establecido por la escala GRADE.

Introduction

Specialized nutritional-metabolic management (SNMM) of the critical patient remains one of the most discussed therapeutic interventions, and although other treatments continue to be considered more important, nutritional-metabolic management makes a fundamental contribution to improved clinical outcomes in these patients.

There is currently sufficient evidence that malnutrition is an independent risk factor for morbidity, with an increased rate of infections, longer Intensive Care Unit (ICU) and hospital stay, more days of mechanical ventilation, difficulty for wound healing, and increased mortality.[1] Over the last two decades we have gathered enough evidence to accept the effectiveness and influence of SNMM in securing improved clinical outcomes in these patients.[2] Furthermore, we are increasingly aware of the importance of SNMM in the global evolution of the critically ill, with a view to restoring patient function and quality of life as they were before the disease.[3]

The difficulty of defining the critically ill and the heterogeneity of the studies that include patients from different categories (medical, surgical, trauma, etc.), with their concrete disease processes, different degrees of severity and different evolutive moments, makes it difficult to adequately interpret the results obtained in the medical literature. This means that the results of nutritional support – both beneficial and harmful – are often transferred from patients that are not necessarily in critical condition to the critically ill population, with the errors that this can entail. Furthermore, in the last 15 years there have been important changes in the general management of the critically ill, and this implies that older studies are more difficult to interpret and compare with the data published in more recent times.

At present, SNMM of the critical patient continues to generate points of controversy, such as for example the type of nutritional treatment (enteral or parenteral), or the timing of introduction of nutritional support. The different nutrients, their amount and quality, as well as the administration route, remain aspects requiring clarification, due to the methodological difficulties involved in validating the indications. We find ourselves in a situation where on one hand it is argued that the association between malnutrition and increased morbidity-mortality has been clearly established, while on the other there is not enough evidence to establish a clear indication of SNMM. The term ''critically-ill patient'' refers to a group of patients with diverse diseases, and with sometimes very different or even opposing metabolic responses. As a result, no global recommendations can be established for all patients admitted to a Department of Intensive Care Medicine or to other critical care units, regardless of the underlying cause.

Adequate nutritional-metabolic support adapted to the evolutive phase of the patient forms part of the integral management of the critically ill, and seeks not only to supply micro- and macronutrients, but also to modulate the inflammatory, metabolic and immune responses in concrete clinical scenarios, with the purpose of modifying the overall outcome.[4] Knowledge of the function of the digestive tube as an organ, and of the microbiome as part of health and disease, is also contributing to change SNMM in a rapid and still uncertain way. As a result of the above, different scientific societies consider it necessary to revise and adapt their previously published recommendations.

In recent years there have been many documents that have questioned some of our previous recommendations. Consequently, the Metabolism and Nutrition Working Group (MNWG) of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (*Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias* [SEMICYUC]) considered the need to review and update the SNMM recommendations previously published by the group,[5] with the aim of evaluating the currently available evidence, in order to assist decision making in daily clinical practice.

The structure of the recommendations is more novel than in the year 2011, since transversal chapters are included (addressing basic aspects such as calorie/protein supply, the timing of introduction of nutritional support, controversies, monitoring, follow-up, safety, etc.), along with 8 chapters referred to specific disease conditions and which highlight the differential aspects of these disorders. The unique feature of these guidelines remains that of providing specific recommendations for the different populations of critically ill patients, in the most practical way possible.

Methodology

The primary aim for establishing the recommendations was to evaluate the best available scientific evidence for the indications of SNMM, with special attention to the assessment of the nutritional status, the nutrients that should be provided, the administration route and the time of initiation of nutritional support, as well as the existing evidence on the provision of pharmaconutrients. These recommendations were developed in the period between March 2016 and February 2019.

The recommendations have been formulated by an expert panel, all of whose members belonged to the MNWG of the SEMICYUC, with extensive experience in nutritional and metabolic support in critically ill patients. Presentation of the project developed by the supervising editorial committee took place at the 80th ordinary meeting of the Group held on 3 and 4 March 2016. Following discussion of the topics and the securing of consensus among the Group members, a working plan was designed and timelines were established. After establishing the methodology, the table of contents of the chapters was circulated among all members of the MNWG, with selection of the authors who would be responsible for writing each chapter, based on their own experience and the criterion of the editorial committee (Table 1).

On the part of the editorial committee, and after discussion in the ordinary meeting of the MNWG, the most relevant and controversial questions related to each chapter were defined (Table 1). The authors were required to reach consensus for final drafting.

Each chapter was reviewed by at least three members of the editorial committee, who advised the authors on changes to be made in each subject before final approval. The final approval of each chapter and of the recommendations included in it was based on discussion in meetings of the MNWG – one of which was a physical presence and extraordinary meeting held on 5 October 2017 – until final consensus was reached regarding the contents of each topic and the recommendations of the experts in those fields where scientific evidence was scarce. Any discrepancies or points on which any member of the group expressed his/her disagreement were discussed and agreed upon by consensus on occasion of this physical presence meeting, placing special emphasis on review of the established levels of evidence and grades of recommendation.

The editorial committee then proceeded to make the final adjustments to each chapter, including the literature review, for submission and final approval by the MNWG, before sending for publication in the journal *Medicina Intensiva*.

The recommendations were based on analysis of the existing literature on each topic, using the key words: nutritional support, specialized nutritional management, enteral nutrition, parenteral nutrition, monitoring, safety, critical patient, recommendations and scientific evidence, as well as those terms referred to specific subjects such as sepsis, pharmaconutrition, etc. Evaluations were made of meta-analyses, randomized clinical trials and observational studies, and of systematic reviews referred to adult critical patients. The MEDLINE and EMBASE databases and Cochrane Database of Systematic Reviews were consulted, with a final inclusion date of 30 March 2017. Discussion was made of the methodology to be to used for establishing the corresponding evidences; the criteria selected were those of the GRADE (Grading of Recommendations Assessment, Development and Evaluation Working Group),[6–9] which take into account the methodological design, quality and consistency of the study for establishing the level of evidence. The level of evidence was adapted from the same methodology, as specified in Table 2.

Although the strength of a recommendation is fundamented upon the quality of its supporting evidence, in some cases this may not be enough, since the magnitude of the effect upon a given outcome of interest could be irrelevant from the clinical perspective. In addition to the level of evidence, the MNWG therefore decided to add the grade of recommendation (high, moderate, low), establishing a high grade of recommendation if the measure in question had a relevant clinical impact even if the supporting level of evidence was low. The factors applied to raise or lower the quality of the evidence are described in Table 3.

The final step of the process was presentation of the final document to the scientific committee of the SEMICYUC for subsequent publication.

Terminology and definitions used

In the process of preparation of the recommendations, specific terms were used (employed by the MNWG in all its works), some of which are described below:

- Increased gastric residual volume. Volume of diet aspirated through the nasogastric tube, and considered indicative of gastric ileus. The volume used in this respect by the MNWG is 500 ml, with checking every 6–24 h.
- Nitrogen balance. Measure of body nitrogen balance. It is considered neutral when intake equals excretion, positive when intake exceeds losses, and negative when excretion is greater than intake.
- Bronchoaspiration. Passage of nutritional content into the airway. Regurgitations of small volume (silent) are common, but the incidence of major regurgitation causing acute respiratory failure is 1–4%. The underlying cause is related to disturbances in swallowing in neurological patients, and in patients with gastric nutrition to an increased gastric residual volume secondary to a decrease in gastric emptying.
- Glycemic control. Administration of insulin as a continuous infusion to normalize the blood glucose values in

Table 1 Index of chapters on the recommendations for the specialized nutritional-metabolic management of the critical patient.

1. Introduction, methodology and list of recommendations

2. Metabolic response to stress

What are the metabolic and hormonal changes in the critically ill? Do these changes vary according to the evolutive phase of the patient?

What are the clinical consequences of the neuroendocrine changes in the critically ill?

What is and what are the consequences of persistent inflammation, immune depression and catabolism syndrome in the critically ill?

To what extent do the critical condition of the patient and the loss of muscle mass condition the metabolic-nutritional requirements?

3. Assessment of the nutritional status and consequences of malnutrition in the critical patient

Does nutritional status of the critical patient condition the clinical outcome?

Should nutritional screening be performed upon admission to the ICU?

Are the nutritional prognostic scores and indexes useful?

How should nutritional status of the critical patient be evaluated? Are the anthropometric and biochemical variables and structured questionnaires useful?

Can other estimations be used to assess nutritional status of the critical patient?

How do we define and prevent refeeding syndrome in the critical patient?

4. Requirements referred to macronutrients and micronutrients

What are the caloric needs of the critical patient and what method should we use to calculate them?

What are the requirements and what type of proteins should be administered to the critical patient?

What are the type and amounts of carbohydrates that should be administered to the critical patient?

What are the type and amounts of lipids that should be administered to the critical patient?

What are the needs in terms of micronutrients (vitamins and oligoelements) and fiber in critical patients?

Is permissive underfeeding indicated in the critical patient? When is trophic enteral nutrition indicated?

How should the caloric/protein supply of micronutrients and fiber be adjusted in the hemodynamically unstable patient?

How should the caloric/protein supply of micronutrients and fiber be adjusted in the obese critical patient?

How should the caloric/protein supply and provision of micronutrients and fiber be adjusted in the patient acute renal failure?

How should the caloric/protein supply and provision of micronutrients and fiber be adjusted in the sarcopenic elderly patient?

How should the caloric/protein supply and provision of micronutrients and fiber be adjusted in the diabetic patient and in individuals with stress hyperglycemia?

5. Indications, timing and access routes

Is specialized nutritional support indicated in the critical patient?

When should enteral nutrition be started?

When should enteral nutrition be started in hemodynamically unstable patients?

When should parenteral nutrition be started?

What routes can be used to administer specialized nutritional support in the critical patient?

Does the specialized nutritional support administration route influence the patient outcome?

What are the indications of complementary parenteral nutrition?

When should the caloric objective and the protein objective be reached?

6. Pharmaconutrients, specific nutrients, fiber, synbiotics

Does the supply of pharmaconutrients and other specific nutrients improve the inflammatory response to injury in the critically ill?

What critical patients benefit from diets with a mixture of pharmaconutrients?

Do critical patients benefit from the administration of glutamine?

Is there evidence supporting the use of pharmaconutrients dissociated from the administration of specialized nutritional therapy?

Should all critical patients with enteral nutrition receive fiber? What type of fiber is indicated?

Do the critically ill benefit from the administration of probiotics or a mixture of prebiotics and probiotics (synbiotics)?

Table 1 (*Continued*)

7. Monitoring and safety
What parameters should we monitor during specialized nutritional management of the critical patient?
Are there criteria for defining intolerance to enteral nutrition? How can we optimize the caloric/protein target in patients with intolerance to enteral nutrition?
How should the transition from enteral nutrition to oral nutrition be made safely?
How should dysphagia be dealt with in the critical patient?
What glycemia level should be maintained in the critical patient? Is the glycemic target in diabetic patients different from that in non-diabetic individuals?
Should we monitor glycemic variability in the critical patient? Can enteral diets specific for hyperglycemia reduce glycemic variability and improve glycemic control?
Does the type of parenteral nutrition, with triple-chamber bag or prepared in Pharmacy, influence the development of catheter-related infection?
How can we safely administer drugs through the feeding tube in patients receiving enteral nutrition?
Should local protocols for the prescription and administration of specialized nutritional treatment be developed for increasing the safety and efficiency of use?

8. Patients with acute lung disease
What is the best formula for the critically ill with acute lung disease? Are high calorie density diets indicated for restricting volume supply?
Do low carbohydrate and high fat content diets play a role?
Are diets enriched with ω-3 fatty acids, γ-linolenic acid and antioxidants indicated?
Is it necessary to monitor the levels of phosphorus and other micronutrients?
How does mechanical ventilation in prone decubitus condition the administration of nutritional support?
How do noninvasive mechanical ventilation and high-flow oxygen therapy condition the administration of nutritional support?

9. Patients with sepsis and septic shock
Do the energy and protein requirements of patients with sepsis and septic shock differ from those of the rest of critical patients?
Is it safe to administer early enteral nutrition in septic shock patients?
What is the best administration route? When is parenteral nutrition indicated?
What is the best formula for the specialized nutritional management of these patients?
Do diets enriched with arginine and other pharmaconutrients play a role
Is supplementation with selenium and other micronutrients indicated?

10. Patients with nonsurgical abdominal disease
Can patients with severe acute pancreatitis be fed via the gastric enteral route?
When is postpyloric enteral feeding indicated?
When is parenteral nutrition indicated in patients with severe acute pancreatitis?
What is the best enteral nutrition formula for patients with severe acute pancreatitis?
Should patients with acute liver failure receive a diet modified in nutrient quantity or quality?
Should special enteral nutrition formulas be used in patients with short bowel syndrome?

11. Patients subjected to digestive tract surgery
What patients can benefit from early postsurgery enteral nutrition?
What is the most recommended feeding route in these patients? When is postpyloric nutrition indicated?
When is nutritional management with parenteral nutrition indicated?
Is glutamine indicated in these patients?
What is the most adequate formula for specialized nutritional management? Do diets enriched with arginine, pharmaconutrients and other substrates such as fiber play a role?
Should patients with intestinal fistula and those with an open abdominal wall receive specific nutritional management in terms of quantity and quality? What is the most appropriate administration route?
What is the most adequate nutritional management strategy in liver transplant patients?

12. Neurocritical patients
Do the energy and protein requirements of these patients differ from those of the rest of critical patients?
What is the best feeding route for neurocritical patients? Is routine postpyloric feeding indicated?
What is the best formula for the specialized nutritional management of neurocritical patients? Do diets enriched with glutamine and other pharmaconutrients play a role?
What is the recommended glycemia range in neurocritical patients?
What are the calorie/protein requirements in patients with acute spinal cord injury?

Table 1 (*Continued*)

13. Polytraumatized patients and critical burn patients
Do the caloric and protein requirements of these patients differ from those of the rest of critical patients?
What is the most advisable administration route in these patients?
Do diets enriched with glutamine and other pharmaconutrients play a role?
14. Patients with heart disease
Do the energy and protein requirements of these patients differ from those of the rest of critical patients?
What is the most widely recommended administration route in these patients?
Is early nutritional management with enteral nutrition indicated in patients with low cardiac output and in patients subjected to extracorporeal oxygenation and ventricular assist measures?
What is the best formula for the nutritional management of cardiological critical patients? Do diets enriched with ω-3 fatty acids and other pharmaconutrients play a role?
Should cardiac transplant patients receive specific nutrition in terms of quantity and quality or as regards the administration route used?
15. The chronic critical patient
How is the chronic critical patient defined?
Do the energy and protein requirements of these patients differ from those of the rest of critical patients?
What is the most adequate feeding route?
What is the most adequate nutritional formula in the chronic critical patient?
What specific nutrients and micronutrients are required?
What other nutritional-metabolic interventions are useful in chronic critical patients?

Table 2 Grade of recommendation according to the level of evidence.

Level of evidence	Requirements
High	Meta-analyses of randomized controlled trials with low heterogeneity
	Well designed randomized controlled trials
Moderate	Meta-analyses of cohort studies (well designed)
	Systematic reviews (without meta-analysis) of cohort and case-control studies (well designed)
	Well designed prospective cohort studies
	Well designed case-control studies
	Well designed controlled trials without randomization
Low	Poorly designed controlled studies
	Poorly designed observational studies, with biases
	Case series, comparison studies
Expert opinion	Opinions of experts and/or clinical experience of reputed experts

critically ill patients with hyperglycemia. An adequate and safe value would range between 110 and 150 mg/dl.

- Diarrhea. Increased number and volume of daily bowel movements, with the evacuation of liquid or semi-liquid stools. The MNWG defines diarrhea as 5 or more daily bowel movements or an estimated total volume in 24 h of over 1000 ml.
- Multiorgan dysfunction. Body response to aggression, with altered function of two or more organs, and which requires clinical intervention to maintain body homeostasis.
- Pharmaconutrient. A substrate which in addition to its intrinsic nutritional effect stimulates mediators that favor immunity, inhibits proinflammatory factors, and attenuates response to aggression, and reduces infection rate. Within this group are found glutamine and arginine, ω-3 fatty acids, and some oligoelements (trace elements), vitamins and fiber.
- Hypernutrition. A state in which the calorie supply exceeds the recommended value, possibly resulting in metabolic complications with a harmful effect upon the body.
- Hyponutrition. A deficient calorie/protein supply. At present, the different clinical studies define hyponutrition as the administration of $\leq$20 kcal/kg/day in the stable phase of the disease.
- Permissive hyponutrition. Defined as the administration of <70% of the energy supply needed to cover the estimated basal energy expenditure, maintaining a protein supply of at least 1.3 g/kg/day.
- Severe hypoglycemia. Blood glucose values of <40 mg/dl. It is the most common complication of insulin therapy in critical patients receiving such therapy in order to maintain normoglycemia (110–150 mg/dl). If not detected and treated, severe hypoglycemia results in seizures, coma and even death.
- Hemodynamic instability. The patient presents a mean blood pressure of $\leq$60 mmHg, increasing lactate concentration and/or a need for increasing vasoactive drug doses. In these cases splanchnic perfusion can be

Table 3 Factors that modify quality of the evidence.

Factors lowering quality of evidence	
Limitations in study design or conduction	↓ 1 or 2 grades
Inconsistency between the results of different studies	↓ 1 or 2 grades
Availability of indirect evidence	↓ 1 or 2 grades
Imprecision of the effect estimators	↓ 1 or 2 grades
Publication bias	↓ 1 grade
Factors increasing quality of evidence	
Important effect size	↑ 1 or 2 grades
Relevant dose-response gradient	↑ 1 grade
Plausible impact of the confounder variables	↑ 1 grade

impaired by inadequate perfusion pressure, making it necessary to postpone the start of nutritional support.

- Insulin resistance. Inability of insulin to exert its usual biological effects at concentrations that are effective in normal subjects. It usually manifests in the hypermetabolic state typical of the critically ill patient, associated or not to obesity, type 2 diabetes mellitus, dyslipidemia and arterial hypertension.
- Malnutrition. A nutritional state in which a deficiency, excess, or imbalance of energy, protein and other nutrients causes adverse effects in body tissues (structure, size and composition), as well as in their function and clinical outcomes. It may be due to unbalanced or insufficient nutrition or to inadequate absorption or use.
- Macronutrients. Elements in the diet that supply most of the metabolic energy of the body. The main macronutrients are carbohydrates, proteins and lipids.
- Micronutrients. Elements in the diet used not for the production of energy but for metabolic or structural purposes, and which are found in minor amounts in the body. They include trace elements and vitamins.
- Enteral nutrition. All forms of nutritional support involving the use of ''dietary foods for special medical purposes'', as defined by European Union regulations, irrespective of the administration route involved. It includes oral nutritional supplements, and feeding via nasogastric or nasoenteral or percutaneous tubes.
- Early enteral nutrition. All forms of nutritional support that involve the use of ''dietary foods for special medical purposes'', and which are administered to the patient in the first 24–48 h after hemodynamic stabilization. Its use has been associated with a reduction in infectious complications and mortality in critically ill patients.
- Parenteral nutrition. Nutrients administered via the intravenous route to supply the basic elements needed by the body in a harmless way for body metabolism.
- Complementary parenteral nutrition. The administration of parenteral nutrition supplemental to enteral nutrition, when the calculated nutritional requirements of the patient are not covered by the enteral supply. Complementary parenteral nutrition should be started when 60% of the nutritional requirements are not met by day four of admission, or for at least two consecutive days during the length of stay.
- Peripheral parenteral nutrition. Parenteral nutrition that allows the supply of nutrients directly into the bloodstream via a peripheral line, because its osmolarity is <600–900 mOsm/l. Consequently, in most cases the calorie/protein requirements of the patient are not met and, therefore, this type of nutrition is only indicated for short periods or until a central venous access becomes available for starting total parenteral nutrition (TPN).
- Trophic nutrition. The supply of small amounts of enteral nutrition (10–20 ml/h), generally corresponding to $\leq$10 kcal/kg/day, with the purpose of facilitating early enteral stimulation and avoiding atrophy of the intestinal villi due to fasting.
- Sarcopenic elderly patient. A patient over 60 years of age presenting age-related, progressive loss of skeletal muscle mass and strength, resulting in increased morbidity-mortality in the ICU when intensive care is needed.
- Chronic critical patient. A critical patient with an ICU stay of at least 8 days and with one or more of the following conditions: prolonged mechanical ventilation (>96 h), tracheostomy, sepsis or severe infection, major burns and multiorgan dysfunction. These patients are characterized by a need for prolonged intensive care, with important resource utilization.
- Nutritional supplement. Nutritional products administered via the oral route and which contain some food ingredient or a mixture of such ingredients, and are used to supplement the diet. They are not intended to substitute a conventional food or the diet.
- Persistent inflammation, immune depression and catabolism syndrome. This syndrome defines a group of chronic critical patients with depressed adaptive immunity, with a low but persistent level of inflammation, diffuse apoptosis, loss of lean mass and poor healing, together with pressure ulcers. These are weakened patients with scant functional and respiratory capacity for returning to normal life.
- Refeeding syndrome. Hormonal and metabolic changes that occur during nutritional repletion via the oral, enteral or parenteral route in patients with severe malnutrition or prolonged fasting. Refeeding syndrome can cause neurological, cardiological, hematological, neuromuscular and pulmonary complications, with increased patient morbidity-mortality. The main biochemical characteristics of the clinical condition are hypophosphatemia with or without hypopotassemia, hypomagnesemia and thiamine deficiency.

- Specialized nutritional management. The administration of nutrients in adequate amounts according to the type of patient and the clinical situation, with a view to supplying energy and proteins to avoid malnutrition, improve the clinical outcomes, and minimize the loss of lean body mass.
- Specialized nutritional-metabolic management. The administration of nutrients as drugs, adapting the dose and combinations to the clinical situation of the patient and to the affected organ or organs, seeking to modify the clinical course.

List of recommendations for specialized nutritional-metabolic management of the critical patient

Assessment of the nutritional status and consequences of malnutrition in the critical patient

- The use of isolated anthropometric or biochemical variables is recommended for initial nutritional assessment, but not for nutritional follow-up of the critically ill (Level of evidence: moderate. Grade of recommendation: moderate).
- Follow-up of the evolution of shorter half-life proteins such as prealbumin or retinol binding protein, and the determination of 3-methylhistidine, may be useful for the nutritional follow-up of critical patients (Level of evidence: low. Grade of recommendation: low).
- The NUTRIC Score upon admission should be used to assess the patient prognosis, but not as a nutritional assessment tool (Level of evidence: moderate. Grade of recommendation: moderate).
- It is advisable to evaluate the patient muscle compartment over the course of ICU stay using imaging tools such as magnetic resonance imaging, computed tomography and ultrasound (Level of evidence: moderate. Grade of recommendation: moderate).
- It is advisable to identify refeeding syndrome in critical patients with malnutrition or who have received a low energy supply for a prolonged period of time, and to prevent the syndrome by administering thiamine, with water-electrolyte correction and the slow and progressive start (72–96 h) of estimated or measured calorie/protein supply (Level of evidence: low. Grade of recommendation: high).

Recommendations regarding the macronutrient and micronutrient requirements of the critical patient

- When available, indirect calorimetry is suggested as the method of choice for calculating the caloric requirements in patients subjected to mechanical ventilation (Level of evidence: moderate. Grade of recommendation: high).
- In the absence of indirect calorimetry, predictive formulas are advised, particularly the Penn State equation, in patients subjected to mechanical ventilation, or simplistic formulas based on body weight (Level of evidence: expert opinion. Grade of recommendation: moderate).
- During the first days of the critical disease (acute phase), it is advisable to supply about 70% of the energy expenditure as measured by indirect calorimetry or 20–25 kcal/kg usual body weight/day. Following this period (patient in stable phase), the recommended supply is 25–30 kcal/usual body weight/day (Level of evidence: expert opinion. Grade of recommendation: moderate).
- An early hyperproteic supply is advised of between 1.2 and 1.5 g/usual body weight/day of proteins in the early phase, and between 1.5 and 2 g/usual body weight/day in the stable phase, particularly in patients at high nutritional risk (Level of evidence: low. Grade of recommendation: moderate).
- In patients receiving parenteral nutrition, it is advisable not to exceed 3.5 g/usual body weight/day of glucose (use adjusted weight in obese individuals with BMI $\geq$ 30 kg/m^2) (Level of evidence: expert opinion. Grade of recommendation: moderate.
- In critical patients in general, the suggested daily lipid supply is 0.7–1.3 g/kg usual body weight/day (use adjusted weight in obese individuals with BMI $\geq$ 30 kg/m^2), with a reduction in supply if the plasma triglyceride levels exceed 400 mg/dl (Level of evidence: expert opinion. Grade of recommendation: moderate).
- No generalized recommendations can be made in critical patients regarding the type of lipids to be supplied, though the use of mixed formulas that reduce the ω-6/ω-3 ration could be useful as a pharmacological strategy associated to artificial nutrition (Level of evidence: expert opinion. Grade of recommendation: moderate).
- It is advisable for nutrition of the obese critical patient to be hypocaloric, covering approximately 50–70% of the estimated energy requirements, and hyperproteic, with between 2 and 2.5 g proteins/kg of ideal body weight/day, adjusting the supply to secure an acceptable nitrogen balance (Level of evidence: expert opinion. Grade of recommendation: moderate).
- The caloric and protein supply in patients with acute kidney injury requires frequent re-evaluation according to the degree of catabolism and the need for renal replacement techniques (Level of evidence: expert opinion. Grade of recommendation: moderate).
- In patients with continuous renal replacement therapy, the advised protein supply is at least 2 g/kg usual body weight/day, without exceeding 2.5 g/kg usual body weight/day (use ideal weight in obese patients with BMI $\geq$ 30 kg/m^2) (Level of evidence: low. Grade of recommendation: moderate).
- Supplementing with vitamins and trace elements is advised inpatients with high output gastrointestinal fistulas, cases of prolonged stay and the prolonged use of continuous renal replacement therapy (Level of evidence: expert opinion. Grade of recommendation: moderate).
- In diabetic patients it is advisable to administer a fiber-enriched diet (with at least 50% of the fiber in soluble form) (Level of evidence: expert opinion. Grade of recommendation: moderate).
- In sarcopenic elderly patients with vitamin D deficiency, supplementing is advised (Level of evidence: low. Grade of recommendation: moderate).

Recommendations regarding the indications, timing and access routes of nutritional-metabolic management in the critical patient

- o It is advisable to start specialized nutritional support in the acute phase in malnourished patients, individuals at high nutritional risk, and in critical patients in which complete oral feeding over the next 5 days is unlikely (Level of evidence: moderate. Grade of recommendation: high).
- o When specialized nutritional support is indicated and there are no contraindications, it is advisable to start early enteral nutrition (in the first 24–48 h), after adequate patient resuscitation (Level of evidence: high. Grade of recommendation: high).
- o In patients presenting hemodynamic alterations, with correct resuscitation even in the presence of a low cardiac output, and the administration of one or more vasoactive drugs, enteral nutrition may be started with the adoption of correct monitoring measures (Level of evidence: low. Grade of recommendation: moderate).
- o The enteral route using a nasogastric tube is the option of choice in the critical patient (Level of evidence: low. Grade of recommendation: high).
- o In critical patients at nutritional risk and in which enteral nutrition is not possible, parenteral nutrition should be started early (in the first 48 h) at adequate doses, avoiding hypernutrition (Level of evidence: moderate. Grade of recommendation: moderate).
- o Complementary parenteral nutrition is suggested in patients in which the caloric-protein objective is not reached by day four of the start of nutritional support via the enteral route (Level of evidence: moderate. Grade of recommendation: moderate).
- o It is advisable to establish protocols to improve nutritional efficacy, with involvement of the entire care team, and to define the indications of postpyloric feeding via gastrostomy and jejunostomy (Level of evidence: low. Grade of recommendation: high).

Recommendations regarding pharmaconutrients, specific nutrients, fiber and synbiotics in the critical patient

- o The use of pharmaconutrients could be considered as a therapeutic strategy seeking to modulate the inflammatory/immune response in the critically ill (Level of evidence: low. Degree of recommendation: low).
- o The use of enteral diets enriched with mixtures of pharmaconutrients (arginine, ω-3 fatty acids, antioxidants) is suggested in postsurgery critically ill patients and in cases of severe trauma (Level of evidence: moderate. Degree of recommendation: moderate).
- o The use of enteral diets enriched with ω-3 fatty acids, docosahexaenoic acid (DHA) and antioxidants could be considered in patients with sepsis (Level of evidence: low. Degree of recommendation: low).
- o Glutamine dipeptide at adequate doses (0.25–0.35 g of glutamine/kg b.w./day), in the absence of contraindications, is suggested as part of nutritional therapy in the critically ill receiving parenteral nutrition (Level of evidence: moderate. Degree of recommendation: moderate).
- o Glutamine supplementing via the enteral route is suggested in burn patients (Level of evidence: moderate. Degree of recommendation: moderate).
- o The supply of pharmaconutrients dissociated from the nutritional regimen is not routine practice and is not suggested in the critically ill (Level of evidence: moderate. Degree of recommendation: moderate).
- o The use of diets containing 100% insoluble fiber in the critically ill is not recommended (Level of evidence: low. Degree of recommendation: high).
- o The routine use of diets containing fiber mixtures (insoluble/fermentable) for the prevention of diarrhea associated to enteral nutrition is not advised (Level of evidence: expert opinion. Degree of recommendation: low).
- o Diets with a high soluble fiber content are advised among the measures for controlling diarrhea associated to enteral nutrition (Level of evidence: expert opinion. Degree of recommendation: moderate).
- o The routine use of probiotics in critically ill patients receiving enteral nutrition is not advised (Level of evidence: low. Degree of recommendation: moderate).

Recommendations regarding monitoring and safety of nutritional-metabolic management in the critical patient

- o It is advisable to monitor the appearance of gastrointestinal complications in the critical patient receiving enteral nutrition, in particular increased gastric residual content, abdominal bloating and diarrhea (Level of evidence: moderate. Grade of recommendation: high).
- o During the administration of enteral nutrition it is advisable to raise the patient torso 30–45° (Level of evidence: high. Grade of recommendation: high).
- o In patients with gastric intolerance or a risk of aspiration, it is advisable to administer prokinetic agents for 3–5 consecutive days and/or to place a postpyloric tube (Level of evidence: moderate. Grade of recommendation: moderate).
- o If oral feeding is not possible, it is advisable to maintain tube feeding until the patient is able to ingest at least 75% of his or her requirements via the oral route (Level of evidence: low. Grade of recommendation: moderate).
- o In patients subjected to prolonged mechanical ventilation and/or with tracheostomy, clinical exploration is recommended to assess the presence of dysphagia before starting oral feeding, and to administer adapted food products (Level of evidence: low. Grade of recommendation: moderate).
- o It is advisable to keep glycemia below 180 mg/dl and, if possible, close to 150 mg/dl, starting insulin treatment when glycemia exceeds 150 mg/dl (Level of evidence: high. Grade of recommendation: high).
- o Avoid strict glycemia control (80–110 mg/dl), particularly in diabetic patients (Level of evidence: moderate. Grade of recommendation: moderate), and avoid hypoglycemia in all the critically ill, whether diabetic or otherwise (Level of evidence: high. Grade of recommendation: high).

- o It is advisable to measure and control glycemic variability, due to its strong impact upon critical patient morbidity-mortality (Level of evidence: moderate. Grade of recommendation: moderate).
- o It is advisable to administer enteral diets specifically designed for diabetes in the control of stress hyperglycemia (Level of evidence: moderate. Grade of recommendation: moderate).
- o The administration of drugs through the feeding tube in patients with enteral nutrition should take into account the administration site, the preference of liquid over solid forms, spacing intervals between drugs, and whether they can be administered together with the enteral nutrition (Level of evidence: low. Grade of recommendation: moderate).
- o It is advisable to apply protocols for the administration and maintenance of PN and enteral nutrition including: administered volume, nutritional balances, the prevention and treatment of gastrointestinal complications and dysglycemia, and control laboratory tests (Level of evidence: moderate. Grade of recommendation: high).

Recommendations regarding nutritional-metabolic management in the critical patient with acute lung disease

- ○ In patients with acute lung disease, low carbohydrate and high fat diets have not been found to be effective; their use is therefore not recommended (Level of evidence: moderate. Grade of recommendation: high).
- ○ Based on the existing evidence, the routine use of lipid diets or emulsions enriched with ω-3 fatty acids in patients with acute respiratory distress syndrome (ARDS) is not recommended (Level of evidence: moderate. Grade of recommendation: moderate).
- ○ In patients with ARDS, it is not advisable to administer ω-3 fatty acids dissociated from enteral nutrition. (Level of evidence: moderate. Grade of recommendation: moderate).
- ○ In patients with ARDS, it is advisable to monitor the phosphorus levels, particularly during weaning from ventilation (Level of evidence: low. Grade of recommendation: high).
- ○ Enteral nutrition is recommended during ventilation in prone decubitus, provided adequate monitoring is used (Level of evidence: moderate. Grade of recommendation: high).
- ○ In patients subjected to noninvasive mechanical ventilation, the use of enteral nutrition may be considered, even though at trophic doses, with close monitoring of signs of intolerance (Level of evidence: low. Grade of recommendation: moderate).

Recommendations regarding nutritional-metabolic management in patients with sepsis and septic shock

- o It is advisable for calorie supply in the acute phase of the septic process to be no greater than 20 kcal/kg/day (Level of evidence: low).
- o The early administration of enteral nutrition (both trophic and complete) is safe in septic shock patients, provided close monitoring is ensured (Level of evidence: moderate).
- o It is advisable for septic patients to receive a protein supply of at least 1.2 g/kg/day (Level of evidence: low).
- o The administration of parenteral nutrition is safe in the septic patient (Level of evidence: moderate).
- o It is advisable to consider administering enteral diets enriched with mixtures of pharmaconutrients, together with the administration of omega-3 fatty acids, in septic patients (Level of evidence: low).
- o It is advisable to consider administering arginine in septic patients (Level of evidence: low).
- o Selenium supplementing in septic patients is not recommended (Level of evidence: high).

Recommendations regarding nutritional-metabolic management of the critical patient with nonsurgical abdominal disease

- o In patients with severe acute pancreatitis, the enteral route is the option of choice – the parenteral route being limited to patients in which enteral nutrition is contraindicated, proves insufficient or is poorly tolerated (Level of evidence: moderate. Grade of recommendation: moderate).
- o In severe acute pancreatitis, enteral nutrition should be provided via the jejunal route whenever possible (Level of evidence: moderate. Grade of recommendation: moderate), though the gastric route may be a valid and safe alternative in cases of less severe pancreatitis (Level of evidence: moderate. Grade of recommendation: low).
- o In patients with severe acute pancreatitis receiving parenteral nutrition, it is advisable to evaluate the administration of a minimum amount of nutrients via the enteral route (trophic enteral nutrition)(Level of evidence: low. Grade of recommendation: moderate).
- o In patients with severe acute pancreatitis requiring parenteral nutrition, it is advisable to supplement parenteral nutrition with ω-3 fatty acids. (Level of evidence: low. Grade of recommendation: moderate), with the administration of 0.5 g/kg/day of glutamine dipeptide, in the absence of contraindications (Level of evidence: moderate. Grade of recommendation: moderate).
- o Nutrition via the enteral route is the option of choice in patients with liver failure, and protein restriction is not recommended (Level of evidence: low. Grade of recommendation: moderate).
- o In patients with hepatic encephalopathy, branched amino acids can be considered (Level of evidence: low. Grade of recommendation: low).
- o In severe acute pancreatitis, short bowel syndrome and acute liver failure, both polymeric and peptidic diets can be used (Level of evidence: moderate. Grade of recommendation: moderate).
- o As first strategy in short bowel syndrome, it is advisable to administer nutrition via the parenteral route (Level of evidence: low. Grade of recommendation: moderate).
- o In short bowel syndrome it is advisable to administer subcutaneous teduglutide at a dose of 0.05 mg/kg/day

to reduce the use of total parenteral nutrition and fluid therapy (Level of evidence: moderate. Grade of recommendation: moderate).

Recommendations regarding nutritional-metabolic management of the critical patient subjected to gastrointestinal surgery

- Nutritional risk should be evaluated in all digestive tract surgery patients admitted to intensive care (Level of evidence: low. Grade of recommendation: moderate).
- Early enteral nutrition is advised in the presence of enteral access distal to the anastomosis (Level of evidence: moderate. Grade of recommendation: moderate).
- In post-abdominal surgery critical patients with enteral access proximal to the anastomosis, early enteral nutrition is advised even if at trophic doses, provided there are no manifestations of intolerance or intestinal alarming signs (Level of evidence: low. Grade of recommendation: moderate).
- Glutamine dipeptide at a dose of 0.5 g/kg/day is advised, in the absence of contraindications, as part of the nutritional management of post-abdominal surgery critical patients receiving parenteral nutrition (Level of evidence: moderate. Grade of recommendation: moderate).
- Enteral nutrition is recommended in patients with open abdominal surgery, with close monitoring (Level of evidence: low. Grade of recommendation: moderate).
- In patients with gastric and/or duodenal fistulas, enteral nutrition should be administered in the jejunum through a nasojejunal tube (Level of evidence: low. Grade of recommendation: moderate).
- Parenteral nutrition is recommended in patients with jejunal fistulas (Level of evidence: low. Grade of recommendation: moderate).
- In patients with a high output intestinal fistula and/or open abdomen, it is advisable to increase the protein supply to 2–2.5 g/kg/day (Level of evidence: low. Grade of recommendation: moderate).
- Vitamin and trace element supplementing is recommended in patients with high output gastrointestinal fistulas (Level of evidence: low. Grade of recommendation: moderate).
- The administration of early enteral nutrition is safe in liver transplant patients if oral feeding (the first choice option) is not possible (Level of evidence: low. Grade of recommendation: moderate).

Recommendations regarding nutritional-metabolic management of the neurocritical patient

- The suggested calorie supply target in neurocritical patients is 60–100% of the calories calculated on the basis of indirect calorimetry or using predictive formulas (Level of evidence: low. Grade of recommendation: moderate).
- It is advisable to increase protein supply to 1.4–1.6 g/kg/day in patients with severe traumatic brain injury (Level of evidence: low. Grade of recommendation: moderate).
- In neurocritical patients with repeated increased gastric residual volume episodes, it is advisable to administer enteral nutrition via the postpyloric route (Level of evidence: moderate. Grade of recommendation: high).
- The administration of enteral diets enriched with mixtures of pharmaconutrients (arginine, ω-3 fatty acids, antioxidants) is recommended in patients with severe traumatic brain injury (Level of evidence: low. Grade of recommendation: low).
- Strict glycemia control (80–110 mg/dl) is not indicated in neurocritical patients (Level of evidence: moderate. Grade of recommendation: moderate).
- In patients with isolated acute spinal cord injury it is advisable to reduce the calorie supply to 19–22 kcal/kg/day once the acute phase has been left behind, due to the decrease in metabolic demand – this decrease being proportional to the level and depth of the spinal cord injury (Level of evidence: expert opinion. Grade of recommendation: low).

Recommendations regarding nutritional-metabolic management of the critical polytraumatized and burn patient

- It is recommended that patients with burns affecting more than 20% of their body surface should receive early nutrition via the oral route, and if this is not possible, via the gastric or postpyloric route (Level of evidence: moderate. Grade of recommendation: moderate).
- In critical polytraumatized and burn patients, a supply of 1.5–2 g/kg/day of protein is recommended, with over 70% of the non-protein calories in the form of carbohydrates, and limiting lipids to the remaining 30% (Level of evidence: low. Grade of recommendation: moderate).
- The use of enteral diets enriched with mixtures of pharmaconutrients (arginine, ω-3 fatty acids, antioxidants) is suggested in severe trauma patients (Level of evidence: low. Grade of recommendation: moderate).
- The administration of glutamine via the enteral route is recommended in burn patients (Level of evidence: moderate. Grade of recommendation: moderate).
- In critical polytraumatized and burn patients, supplementing with selenium and zinc is suggested, probably at doses higher than those used in critical patients in general (Level of evidence: moderate. Grade of recommendation: moderate).
- In critical burn victims it is advisable to administer oxandrolone at a dose of 0.1 mg/kg/12 h via the oral route (Level of evidence: moderate. Grade of recommendation: moderate), as well as beta-blockers (Level of evidence: low. Grade of recommendation: low).

Recommendations regarding nutritional-metabolic management of the critical patient with heart disease

- The administration of 20–30 kcal/kg current body weight/day and of 1.2–1.5 g/kg/day of proteins is recommended in the cardiological critical patient, in a way similar to any other critical patient, though with volume restriction (1.5–2 l/day), high caloric density and low

sodium content (Level of evidence: expert opinion. Grade of recommendation: low).
- o In patients subjected to extracorporeal membrane oxygenation (ECMO) or ventricular assist measures, early and safe enteral nutrition is advised after hemodynamic stabilization, with close monitoring of signs of intolerance (Level of evidence: low. Grade of recommendation: moderate).
- o The administration of glutamine and arginine is recommended in patients with myocardial ischemia (Level of evidence: expert opinion. Grade of recommendation: low).
- o The routine provision of ω-3 fatty acids in the cardiological critical patient is not advised (Level of evidence: low. Grade of recommendation: low).
- o Supplementing with vitamin E and selenium may be considered in the cardiological critical patient, due to their possible contribution to improved cardiac function (Level of evidence: low. Grade of recommendation: low).
- o It is not advisable to administer pharmaconutrients (arginine, ω-3 fatty acids) to post-cardiac transplant patients receiving nutritional support (Level of evidence: low. Grade of recommendation: low).

Recommendations regarding nutritional-metabolic management of the chronic critical patient

- o In the nutritional strategy of chronic critical patients, a hyperproteic polymeric diet is advised (1.5–2 g/kg/day), with a calorie supply of 25–30 kcal/kg/day, avoiding caloric overload (Level of evidence: expert opinion. Grade of recommendation: moderate).
- o Systematic pharmaconutrition is not advised. The use of pharmaconutrients with anabolizing effects (L-leucine, beta-hydroxy-beta-methylbutyrate and L-carnitine) is an option currently subjected to study (Level of evidence: expert opinion. Grade of recommendation: low).
- o Enteral nutrition via the nasogastric route is recommended (Level of evidence: low. Grade of recommendation: high). Feeding through a percutaneous gastrostomy should be evaluated in chronic critical patients if prolonged enteral nutrition (>30 days) is expected (>30 days) (Level of evidence: low: Grade of recommendation: moderate).
- o Periodic supplementing with vitamins and oligoelements may be decided in the chronic critical patient, particularly in patients subjected to continuous or frequent intermittent renal replacement therapy (Level of evidence: expert opinion. Grade of recommendation: moderate).
- o Vitamin D supplements are suggested in chronic critical patients with confirmed deficits of this vitamin (Level of evidence; low. Grade of recommendation: moderate).
- o Early mobilization is indicated in the chronic critical patient, with resistance exercises and neurostimulation guided by objectives whenever possible (Level of evidence: low. Grade of recommendation: moderate).

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