



## RECOMMENDATIONS FOR SPECIALIZED NUTRITIONAL-METABOLIC MANAGEMENT OF THE CRITICAL PATIENT

### Recommendations for specialized nutritional-metabolic management of the critical patient: Monitoring and safety. Metabolism and Nutrition Working Group of the Spanish Society of Intensive and Critical Care Medicine and Coronary Units (SEMICYUC)<sup>☆</sup>



### Recomendaciones para el tratamiento nutrometabólico especializado del paciente crítico: monitorización y seguridad. Grupo de Trabajo de Metabolismo y Nutrición de la Sociedad Española de Medicina Intensiva, Crítica y Unidades Coronarias (SEMICYUC)

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## Introduction

There is sufficient evidence to confirm that malnutrition is an independent morbidity-mortality risk factor in the critically ill, being associated to an increased incidence of infections, longer stay in the Intensive Care Unit and in hospital, more days of mechanical ventilation (MV), and greater wound healing problems.

In routine clinical practice it is difficult to reach the nutritional targets, particularly in the case of enteral nutri-

tion, due both to interruptions caused by gastrointestinal intolerance and other reasons (radiological examinations, endoscopic techniques, surgeries). On the other hand, the existence of complications inherent to the administration of EN and parenteral nutrition (PN) makes it necessary to establish monitoring and safety protocols with the aim of ensuring administration of the calculated requirements, with the fewest complications possible.

## Questions

### 1. What parameters should we monitor during specialized nutritional management of the critical patient?

The monitoring of nutritional management of the critical patient should help up to reach the caloric and protein supply targets, identifying the presence of obstructing factors, and allowing early identification of the possible complications that may arise.

In PN it is relatively easy to cover the scheduled requirements, though not so in EN. In both feeding modalities, the start should be gradual (50–60% of the measured or calculated supply), with the aim of meeting the requirements by day three or four. In EN, we must control the real amount of diet administered in 24h (effective volume), avoiding unnecessary interruptions as far as possible. In those patients requiring the interruption of EN in order to perform diagnostic or therapeutic procedures, interruption should be as brief as possible in order to avoid inadequate nutrient supply. Enteral nutrition administration and monitoring protocols improve compliance with the nutritional targets or objectives, and therefore should be applied,<sup>1</sup> including water, caloric and protein balances, the control of possible signs of dehydration or hyperhydration, and checking of positioning of the EN tube after insertion and before the start of feeding (Table 1).

The gastrointestinal complications of EN, such as an increase in gastric residual content, constipation, diar-

rhea associated to EN, vomiting, regurgitation, abdominal bloating or pain and bronchoaspiration are a cause of hyponutrition and therefore should be identified, with the application of adequate management protocols.<sup>1,2</sup>

Dysglycemia (hyperglycemia, hypoglycemia and glycemic variability) is a common metabolic complication in the critical patient (whether diabetic or otherwise) and can be exacerbated with both parenteral and enteral nutritional support; protocols for controlling this condition are therefore needed.

Biochemical controls both upon admission and on a daily and weekly basis should form part of the monitoring protocol, mainly to detect possible ion disorders and prevent refeeding syndrome, particularly in patients with chronically altered kidney, liver or cardiac function<sup>1,3</sup> (Table 1). Such controls have not been shown to be useful for assessing the efficacy of nutritional support.

### 2. Are there criteria for defining intolerance to enteral nutrition? How can we optimize the caloric/protein target in patients with intolerance to enteral nutrition?

In routine practice it is often difficult to cover the calculated requirements in EN due to a certain degree of intolerance, which may have an impact upon the outcome of the critically ill. A number of criteria have been established for assessing intolerance – the most important being increased gastric residual content (IGR), abdominal bloating and diarrhea<sup>4</sup> (Table 2).

Increased gastric residual content is a frequent complication of EN in the critically ill, though the volumes accepted as representing IGR vary considerably, with contradictory results referred to the incidence of aspiration pneumonia in patients with IGR. The REGANE study<sup>5</sup> recorded no differences in the incidence of pneumonia on comparing a residue of 200 ml (control) versus 500 ml (study). The patients in the study group received a greater EN supply, and the measurement of residue made it possible to detect slowed gastric emptying and to adopt measures to reduce the consequences. Other studies have found no benefits of monitoring residue<sup>6</sup> and even point to inconveniences associated to monitoring of this parameter. The appearance of vomiting and regurgitation of the diet is related to IGR, favored by factors such as incorrect positioning of the feeding tube or of the patient – this in turn representing a high risk of bronchoaspiration.<sup>4</sup>

Abdominal bloating is an alarm sign indicating incapacity of the digestive tract to process the administered nutrients. The increase in intraabdominal pressure (IAP) can lead to compartmental syndrome, since blood flow in the intestinal mucosa is reduced, the intragastric mucosal pH decreases and ischemia may result – this in turn being responsible for the onset and persistence of an inflammatory response and multiorgan dysfunction syndrome.<sup>7</sup>

The IAP value has been related to intolerance to EN both at the start of nutrition and over time. Hill et al.<sup>8</sup> found high IAP values to be predictive of intolerance to EN and associated them to longer hospital stay and greater patient mortality. A study of the Metabolism and Nutrition Working Group of the SEMICYUC assessed the association between

**Table 1** Principal parameters to be monitored in nutritional support.

Parameters	Frequency of monitoring
Effective volume administered (proteins and calories)	Every 24 h
Mechanical complications (in relation to insertion or maintenance of tubes and catheters)	Every 24 h
Metabolic complications (dysglycemia, water balance, water-electrolyte imbalances)	Monitoring according to protocols
Ions: sodium, potassium, chloride, phosphorus and magnesium	At least every 24 h
Albumin and/or short half-life proteins, cholesterol, triglycerides and lymphocytes	Once a week

**Table 2** Gastrointestinal complications in enteral nutrition.

Complications	Definition	Measures to be considered
Increased gastric residual content	Presence of a residual volume of over 500 ml at each assessment of gastric content	Torso of the patient raised 30–45° Use of prokinetic drugs Transpyloric access route
Regurgitation	Presence of diet in the oral or nasal spaces of the patient, with or without exteriorization	Torso of the patient raised 30–45°
Abdominal bloating	Change in abdominal exploration findings with respect to what the patient presented before the start of enteral nutrition, with tympanism and/or absence of peristaltic sounds	Measurement of intraabdominal pressure Suspend diet infusion
Diarrhea associated to enteral nutrition	Presence of daily stools $\geq 5$ or at least two daily bowel movements with an estimated volume of 1000 ml	Do not suspend enteral nutrition as first measure Check administered medication Discard infectious origin ( <i>Clostridium difficile</i> ) Change diet and lower infusion rate
Constipation	Absence of bowel movements for 7 days from admission of the patient or absence of stools every 3 days after the start of enteral nutrition	Change type of diet

IAP levels and intolerance to EN in critically ill patients subjected to MV, and investigated whether the absolute IAP value could predict intolerance to EN.<sup>9</sup> An IAP value of 14 mmHg was established as cut-off point for predicting intolerance, though the sensitivity and specificity were low.

Diarrhea is common in the critical patient, though in only 10–18% of all cases is it secondary to EN (diarrhea associated to EN); in most instances the disorder is multifactorial. Considering the enteral diet as the cause of diarrhea should constitute a diagnosis of exclusion. Protocolized management in the event of diarrhea associated to EN, such as modifying the formula, adding fiber or lowering the infusion rate, often makes it possible to maintain EN and avoid interruption. The exact underlying cause therefore needs to be identified. Checking the administered medication and investigating possible infectious causes often allows us to identify the origin.<sup>10</sup>

Once the possibility of intolerance has been detected, measures must be adopted in an attempt to optimize nutrient supply, such as assessing patient positioning, the use of prokinetic agents, complementary PN or the placement of a postpyloric feeding tube.

Although raising the torso of the patient 30–45° is an accepted standard in the critically ill receiving EN, the measure is not adequately applied in the clinical setting. Positioning the patient in the semi-raised position lessens the incidence of ventilator-associated pneumonia.<sup>11</sup>

The addition of prokinetic agents such as erythromycin or metoclopramide improves gastric emptying, gastroesophageal reflux, pulmonary aspiration and tolerance to EN. A systematic review and meta-analysis of 13 randomized clinical trials has shown prokinetic agents to reduce intolerance to EN compared with placebo or no intervention – with no clear impact upon pneumonia, mortality or ICU stay.<sup>12</sup>

It has been seen that using the jejunal route instead of the gastric route results in fewer gastrointestinal complications, thanks to a decrease in IGR episodes.<sup>13</sup> However, there are no differences in terms of the incidence of

nosocomial pneumonia, the duration of nutrition, the length of ICU stay or mortality; the jejunal route is therefore only recommended in cases with a high probability of gastric intolerance.

### 3. How should the transition from enteral nutrition to oral nutrition be made safely? How should dysphagia be dealt with in the critical patient?

Oral nutrition (ON) should supply the energy, nutrients and fluids which the patient needs, adapted to the clinical situation. Before starting ON, due evaluation of the clinical and nutritional stability of the patient is required, together with assessment of the respiratory pattern, swallowing and cognitive function. Transition to ON must be done carefully, with adequate control and constant monitoring of the efficacy and safety of swallowing – increasing ON gradually to reach 75% of the calculated requirements, with a descending EN regimen until suspension is reached.<sup>14</sup>

The incidence of pharyngeal and laryngeal incompetency in patients requiring artificial airway use has not been clearly established, though it is estimated to affect over 40% of all recently extubated patients and between 50% and 84% of all patients requiring tracheostomy.<sup>15</sup> Dysphagia is accompanied by dehydration, malnutrition and an increased risk of secretion and food aspiration, causing serious respiratory complications.<sup>16</sup>

The artificial airway increases the risk of upper airway damage and laryngeal problems, which in turn affects the airway mechanics, aerodynamics and protective reflexes – though no relationship has been established to date between intubation time and the presence of dysphagia.<sup>16</sup>

No studies are available in extubated patients demonstrating the best timing for the reintroduction of ON. In patients subjected to MV for over 96 h, and due to the increased probability of some degree of dysphagia,<sup>16</sup> ON should be started 24 h after extubation. In the rest of

patients a margin of 12–24 h of absolute diet should be observed in order to avoid possible complications associated to bronchoaspiration in the event of reintubation due to failure of extubation.<sup>15</sup>

The test most widely used to assess dysphagia in the critically ill is the Clinical Bedside Assessment, which comprises a patient interview, physical examination, and the assessment of potential signs of aspiration during swallowing (cough, wet voice).<sup>17</sup> The volume-viscosity clinical exploration method<sup>18</sup> can detect swallowing disorders and allows us to establish the most adequate viscosity and volume. The limitation of this exploration is referred to the detection of silent aspirations, making it necessary to resort to instrumental exploration in order to establish a definitive diagnosis of dysphagia, based on videofluoroscopy or fiberoendoscopy.

In tracheostomized patients the existence of dysphagia can be checked through correct physical examination, observing chewing efficacy and – in the event of persistent doubts – ON can be started after a negative methylene blue test (Evans test). If the test proves positive, an oral absolute diet is indicated.<sup>15</sup>

In patients with dysphagia, modifying the volume and texture of food facilitates oropharyngeal transit and minimizes the risk of tracheobronchial aspiration. When the nutrition and hydration needs are not covered with the adopted feeding protocol, complementing with oral supplements or EN is indicated.<sup>14,17</sup>

#### 4. What glycemia level should be maintained in the critical patient? Is the glycemic target in diabetic patients different from that in non-diabetic individuals?

Stress hyperglycemia is independently correlated to mortality in the critical patient.<sup>19</sup> However, the NICE-SUGAR study,<sup>20</sup> with 6104 patients and representing the largest multicenter study to date in comparing strict glycemia control (80–108 mg/dl) versus conventional control ( $\leq 180$  mg/dl), found strict blood glucose control to be associated to greater mortality at 90 days (27.5% versus 24.9%, 95% confidence interval [95% CI] 1.02–1.28;  $p = 0.02$ ) and a greater incidence of severe hypoglycemia (6.8% versus 0.5%;  $p < 0.001$ ).

Subsequent meta-analyses have confirmed that intensive treatment with insulin increases the risk of severe hypoglycemia and does not afford benefits in terms of lesser mortality in the critically ill,<sup>21</sup> except in elective surgery patients (including heart surgery).

Diabetes influences glycemic control in the critical patient, though as has been evidenced by a meta-analysis,<sup>22</sup> diabetes mellitus in itself is not associated to increased mortality in the ICU – with the exception of heart surgery patients.

Krinsley et al.<sup>23</sup> carried out an international multicenter study involving 44,964 patients, analyzing the role of diabetes and the association between hyperglycemia, hypoglycemia and glycemic variability and mortality in a heterogeneous group of critically ill patients. The multivariate analysis found the glycemia ranges independently correlated to decreased mortality in diabetic patients to be 110–180 mg/dl when compared with a glycemia range of

>180 mg/dl. In the non-diabetic patients, mortality was seen to be lower in the range of 110–140 mg/dl than in glycemia >180 mg/dl.

In a retrospective observational study involving 10,320 critically ill patients,<sup>24</sup> strict glycemia control was seen to result in greater mortality among diabetic patients with poor blood glucose control (high glycosylated hemoglobin concentration).

Other later studies,<sup>22–24</sup> in the same way as the NICE-SUGAR trial<sup>20</sup> and subsequent meta-analyses,<sup>21</sup> found hypoglycemia to be independently correlated to increased mortality in both diabetic patients and in non-diabetic individuals. This was moreover seen to be applicable not only to severe hypoglycemia (<40 mg/dl), but also to moderate hypoglycemia (<70 mg/dl).

Krinsley et al.<sup>23</sup> also found that in relation to their entire cohort of 44,964 patients, diabetes was independently associated to decreased mortality risk, though without being able to determine the causes.

#### 5. Should we monitor glycemic variability in the critical patient? Can enteral diets specific for hyperglycemia reduce glycemic variability and improve glycemic control?

Hyperglycemia, hypoglycemia and glycemic variability are the parameters used to address glycemic control in the critical patient.<sup>23</sup> The indices most commonly used to monitor glycemic variability are: (1) the standard deviation (SD) of blood glucose, defined as the mean square root of the deviation of values with respect to the mean; (2) the percentage coefficient of variation (CV), which is the ratio between the SD of a sample and its mean; and (3) the glycemic lability index, which is based on the changes in glucose over time to obtain a measure of its lability – the most adequate value for the critical patient not having been established to date.<sup>23,25,26</sup>

Glycemic variability is independently associated to increased mortality in the critical patient.<sup>26,27</sup> It has been seen that the presence or not of diabetes determines changes in this respect. Specifically, an increase in glycemic variability ( $CV \geq 20\%$ ) is associated to increased mortality in non-diabetic patients.<sup>23,24</sup> Consequently, glycemic variability should be considered for improved glycemic control.

Specific enteral diets for hyperglycemia are generally characterized by a lesser amount and different nature of carbohydrates (lesser glycemic index), a greater richness in monounsaturated fats, and the use of fiber (mainly soluble fiber) together with soya proteins and antioxidants.

Although very few studies have evaluated specific diets in the critical patient, improved glycemic control, with a significant decrease in the plasma and capillary blood glucose levels, as well as in the insulin requirements, has been observed when compared with standard diets.<sup>28,29</sup> Mesejo et al. published a randomized, prospective multicenter clinical trial involving 157 patients subjected to MV in which two diabetes-specific diets (including a new generation diet) were compared with a standard diet – all diets being hyperproteic.<sup>25</sup> The diabetes-specific diets achieved better glycemic control, with a decrease in capillary and plasmatic glucose and in the insulin requirements, as well

as a reduction in nosocomial infection risk. A strong association was moreover seen in the first week of stay between the glycemic variability indices and the appearance of tracheo-bronchitis/1000 days of MV (glycemic lability index  $r=0.962$ ,  $p=0.05$ ; SD  $r=0.969$ ,  $p=0.06$ ; CV  $r=0.961$ ,  $p=0.04$ ).

With regard to the relationship between specific diets and glycemic variability, the published data are even more limited, and only one study has addressed this issue in the critical patient.<sup>25</sup> The mentioned study found that critical patients receiving diabetes-specific diets also exhibited a decrease in glycemic variability measured on the basis of the SD, the CV and the modified glycemic lability index, during the first week of stay in the ICU.

## 6. Does the type of parenteral nutrition, with triple-chamber bag or prepared in Pharmacy, influence the development of catheter-related infection?

The advantages attributed to the use of premixed PN formulas versus those prepared in the Pharmacy are referred to greater safety and lower costs.<sup>30</sup> This includes a lower risk of contamination thanks to lesser manipulation of the product, improved preservation conditions, a smaller risk of error in preparation, immediate availability, and a reduction in global costs. A number of limitations have been described, however: (a) scant variability in macronutrient and electrolyte contents; (b) a high glucose content, which implies a greater risk of hyperglycemia; (c) the possibility of contamination during manipulation to add vitamins and oligoelements; and (d) possibly similar safety with a reduction of staff costs when automated preparation processes are used in the Pharmacy.

The existing information regarding the use of premixed PN formulas in the critically ill is limited, and most of the available data have been drawn from retrospective and observational studies. Accordingly, some expert recommendations indicate that the use of premixed PN formulas offers no advantages in terms of the patient clinical outcomes versus PN prepared in the Pharmacy under laminar flow.

One of the potential clinical benefits of premixed formulas would be a reduction of bacteremia and catheter-related infections, due to the lesser risk of contamination of the mixture during preparation – though the existing evidence is weak. A number of retrospective observational studies have reported a significantly lesser incidence of bacteremia in patients receiving premixed PN versus PN prepared in the Pharmacy,<sup>31,32</sup> without the presence of lipids in the premixed formula having been significantly associated to an increase in the incidence of infections. In a randomized, prospective, open-label multicenter international study (the EPICOS trial) including 406 critically ill patients,<sup>33</sup> the group receiving PN prepared in the Pharmacy experienced a significant increase in the incidence of bacteremia compared with the group administered premixed PN (46 events [22.5%] versus 34 events [16.8%];  $p=0.03$ ). The incidence of catheter-related infection (bacteremias/1000 catheters-day) was greater in the group receiving PN prepared in the Pharmacy versus the group with premixed PN (13.2/1000 versus 10.3/1000;  $p<0.0001$ ). There were no significant differences in the incidence of severe sepsis, organ dysfunction, hyper-

hypoglycemia episodes, mortality after 28 days, or ICU or hospital stay between the two groups. The lack of information on the preparation processes and sterility of the PN formulas prepared in the Pharmacy of the different participating hospital centers limits the validity of the mentioned study. A randomized, prospective multicenter trial comparing a triple-chamber bag commercial formulation versus a PN formula prepared in the Pharmacy, involving 240 postsurgical patients, recorded no significant differences in relation to complications, mortality or duration of stay.<sup>34</sup>

## 7. How can we safely administer drugs through the feeding tube in patients receiving enteral nutrition?

It is important to consider the compatibility of the prescribed drugs with the supplied nutrition when both are administered through the same enteral access, since alterations may result in their physicochemical or pharmacokinetic characteristics, with a decrease in efficacy or an increase in toxicity.<sup>35,36</sup>

The absorption and activity properties may vary depending on the site of administration in the digestive tract and on the pharmaceutical form used.<sup>37</sup> In general, liquid forms are to be preferred over solid forms, since more homogeneous mixtures result, with better dissolution of the drug substance. The solid forms are to be crushed to a fine powder and should be reconstituted with 10–15 ml of water to facilitate absorption and avoid obstruction of the tube. Sustained release formulations should not be administered through the tube, in the same way as pills, soft gelatin capsules or sublingual tablets. Likewise, liquid formulas with a pH of under 3.5 should not be administered, because the pH of the jejunum is neutral or alkaline, and there may be incompatibilities due to differences in pH.<sup>37</sup>

In the case of highly viscous liquid formulations, it is advisable to dilute the medication in order to avoid obstruction of the tube, reaching an osmolarity of about 300 mOsm/kg, particularly when using a postpyloric tube. The adequate dilution volume can be calculated from the following formula: final volume (ml) = solution volume (ml) × (osmolarity of the preparation/desired osmolarity).<sup>37</sup> Likewise, in order to avoid incompatibilities and prevent obstruction of the tube, the latter should be washed before and after the administration of each drug, using 10 ml of water.<sup>35</sup>

Different drugs are to be administered separately. In the case of liquid forms, it is advisable to first administer the less viscous medications, followed by those of greater viscosity.<sup>35</sup> Furthermore, they should not be administered together with EN and should not be added to the EN formula, since the available stability data are insufficient. When the patient receives intermittent EN, we can take advantage of the intervals without nutrition to administer the medication, washing the tube before and after administration. If EN is provided as a continuous infusion, the tube should be washed after administration of the drug, using 20 ml of water.<sup>35,36</sup>

## 8. Should local protocols for the prescription and administration of specialized nutritional treatment be developed for increasing the safety and efficiency of use?

The use of protocols in routine practice in the ICU results in a decrease in care variability and improves the quality and safety of patient care. Inadequate nutrition is associated to a poorer prognosis in critical patients, with longer hospital stay, a greater incidence of infections, delayed wound healing, increased costs and higher mortality.<sup>38</sup>

Specialized nutritional management protocols should be able to improve nutrient provision and identify the appearance of related complications. Such protocols moreover are to be adapted to the particularities of each ICU, with a training process targeted to the implicated professionals before they are applied.

It has been seen that the programmed requirements in EN are often not covered. Among other factors, this is attributable to under-prescription, the start of feeding at a low rhythm and with slow progression of the infusion rate, the maintenance of a constant rate without compensation due to temporary interruptions, or the presence and management of gastrointestinal complications.<sup>38</sup> Some of these factors could be corrected or avoided with the use of EN protocols.

The application of EN protocols in the critically ill is associated to an increase in nutrient provision, an earlier start of feeding, and a greater probability of covering the requirements – though no decrease in mortality or significant clinical results have been evidenced.<sup>39</sup> A randomized, prospective multicenter trial involving 1118 critically ill patients found the use of an EN protocol according to the evidence-based nutritional guides to reach the caloric targets more often, with an earlier start of EN, than in those cases where no such protocol was used.<sup>40</sup> However, clinical outcomes such as mortality, organ dysfunction and duration of stay in the ICU and in hospital were similar in both groups. Another randomized, prospective multicenter trial involving 1059 critically ill patients evaluated a novel EN protocol compared with the traditional protocols – the objective being based on the daily administered volume.<sup>41</sup> Significantly increased efficacy in administering the caloric and protein supply was evidenced, with no differences in the clinical outcomes between the two groups. A systematic review has confirmed the data obtained in these studies.<sup>42</sup>

In relation to specialized PN management, it has been seen that the use of protocols and the availability of nutritional support improve the efficacy and safety, with a decrease in the associated complications.<sup>40</sup>

### Recommendations

- It is advisable to monitor the appearance of gastrointestinal complications in the critical patient receiving EN, in particular increased gastric residual content, abdominal bloating and diarrhea. (Level of evidence: moderate. Grade of recommendation: high).
- During the administration of EN it is advisable to raise the patient torso 30–45°. (Level of evidence: high. Grade of recommendation: high).
- 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).
- 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).
- In patients subjected to prolonged MV 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).
- 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).
- 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).
- 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).
- 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).
- The administration of drugs through the feeding tube in patients with EN should consider 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).
- It is advisable to apply protocols for the administration and maintenance of PN and EN 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).

### Conflicts of interest

Dr. Mar Juan-Diaz has received payment from Nestle Healthcare Nutrition, Abbott Nutrition, Fresenius Kabi and Vegemat Nutrition for participation in educational studies and for attending scientific events. Dr. Mateu-Campos has received payment from Fresenius Kabi, Gambro and Pfizer for participation in scientific congresses. Dr. Sanchez-Miralles and Dr. Martinez-Quintana declare that they have no conflicts of interest. Dr. Mesejo-Arizmendi has received payment for participation in activities sponsored by Vegemat Nutrition, Nestle Healthcare Nutrition, Abbott Nutrition and Baxter Nutritional Care, comprising clinical studies, participation in scientific congresses, courses and symposia, and working group meetings.

## Note to supplement

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