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Nutritional implications for the patient undergoing extracorporeal membrane oxygenation

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Abstract

Extracorporeal membrane oxygenation (ECMO) for cardiovascular collapse or catastrophic respiratory failure in the critically ill patient imposes a multidisciplinary approach. Nutritional support is one of the issues that must be faced, as this population presents a state of increased metabolic activity, elevated catabolism of protein and rapid accumulating energy deficiency. Provision of adequate nutritional therapy is hard to achieve due to different factors. This article provides a brief overview of the current literature regarding nutritional support during ECMO in adult patients, as no current guidelines address this issue.

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Key words: *Extracorporeal membrane life support. ECMO. Nutrition therapy. Nutritional support.*

ASPECTOS NUTRICIONALES DEL PACIENTE SOMETIDO A ECMO (EXTRACORPOREAL MEMBRANE OXYGENATION)

Resumen

La oxigenación por membrana extracorpórea (OMEC) en casos de colapso cardiovascular o falla respiratoria catastrófica en pacientes críticos impone un planteamiento multidisciplinar. El soporte nutricional es uno de los problemas a afrontar, ya que esta población presenta un estado de actividad metabólica aumentada, un elevado catabolismo proteico, y una deficiencia de energía de rápida acumulación. Es difícil conseguir una provisión de terapia nutricional adecuada debido a distintos factores. Este artículo ofrece una breve presentación de la bibliografía actual relativa al soporte nutricional durante la OMEC en pacientes adultos, ya que actualmente no contamos con directrices que aborden este tema.

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Palabras clave: *Soporte vital con membrana extracorpórea. OMEC. Terapia nutricional. Soporte nutricional.*

Abbreviations

ECMO: Extracorporeal membrane oxygenation.
VV: Venovenous ECMO.
VA: Venoarterial ECMO.
ICU: Intensive care unit.
EN: Enteral nutrition.
PN: Parenteral nutrition.
CRP: C-reactive protein.

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Introduction

Extracorporeal membrane oxygenation (ECMO) is a mechanical system that provides respiratory and/or hemodynamic support to patients who are in imminent risk of death due to respiratory or cardiac failure[1]. Venovenous (VV) ECMO is usually used in catastrophic respiratory failure while venoarterial (VA) ECMO is used in cardiovascular collapse. Usually the predicted survival for these patients is less than 20%.

Critically ill patients requiring vital organ support in the ICU are usually unable to meet nutrient needs orally for a long period. They generally develop a state of increased metabolic activity accompanied by elevated catabolism of protein, insulin resistance, and negative nitrogen balance in the body. If such patients are not provided with macronutrients in the form of enteral nutrition (EN) or parenteral nutrition (PN), they accumulate an energy deficiency that rapidly contributes to lean-tissue wasting, which is associated with adverse outcomes[2].

Provision of adequate nutritional support on these patients can be hard to achieve due to hemodynamic alterations and the need for high doses of vasoactive drugs, deep sedation, and occasionally, high doses of steroids. As a result, gastric emptying is impaired, beginning with enteral nutrition that is delayed, and the calorie/protein target is poorly reached[3].

Clinical guidelines are developed for the nutrition therapy of neonates supported with ECMO[4], but no guidelines have been established for adults. The enteral route is preferred in critical patients and should be considered in this specific population. Few personal experiences have been published in literature (as retrospective analysis from case series)[5-10], showing that EN is possible in ECMO patients, always under certain considerations and specific medical supervision. Supplemental PN, particularly if given early or/and when significant intolerance to EN is maintained, is another strategy to be considered[11].

To achieve better long-term outcomes in ECMO patients, an interdisciplinary approach that includes a nutrition support team may be desirable. This team work should develop a local protocol and a nutrition strategy customized for each ECMO patient. Regular meetings to discuss nutrition status and goal achievement should also be performed in the ICU setting.

Clinical Studies on Adults

There is limited published data on nutritional support in ECMO and the exact effect of this device on human gut function is unknown, as it has only been studied on porcine models showing increased risk for gut barrier dysfunction and bacterial translocation[12].

Anderson et al[13] first presented a series of 24 adult trauma patients with respiratory failure supported on either VV or VA ECMO in which EN was attempted but not tolerated. Kolla et al published their experience with 100 adult ECMO patients with respiratory failure. Nutrition management with enteral delivery was included in their protocol as the first choice for nutritional support, but the authors did not describe their tolerance, caloric target or complications on their study[14].

More recent small retrospective series indicate that EN in patients receiving ECMO is not only possible, but safe. A case series of 27 patients with respiratory failure supported by VV ECMO was reported by Scott et al[6]. Ninety-six (96%) of the patients received EN, or in combination with PN, started within 24 to 36 hours. Eighteen patients received EN as their only source of nutrition, and 8 patients combined EN with PN to meet nutritional requirements according to their protocol for non-ECMO critical patients. A commercial oligomeric non-enhanced formula was used in the first 16 patients, and for the other 11 patients an arginine- and glutamine-enhanced immune-modifying formula was used. Target caloric goals were 25 kcal/kg/day with protein targeted at 1.2 to 1.5 gr/kg/day. They did not compare outcomes between both groups. Most of the patients received prokinetic agents within 48 hrs (erythromycin). No patient developed intestinal ischemia, gastrointestinal bleeding, or other complications related to early feeding. Ferrie et al reported their retrospective experience on 86 patients using ECMO, 55 patients with respiratory failure requiring VV ECMO and 31 for cardiac indication with VA ECMO[8]. EN began on all patients at a mean time of 13.1 hours after UCI admission reaching goal rate on day 2.6. Only two patients failed to reach goal feed rate, requiring exclusive PN. Of the patients presenting intolerance, 20 of 33 were managed with prokinetic medications, while 18 required combination with PN to reach target nutritional requirements. All were fed using an existing local protocol emphasizing early nasogastric enteral feeding with caloric targets estimated with the Schofield equation[15], (with stress factor 1.1 to 1.2) and protein at least 1.2 gr/kg/day. There was no difference between ECMO models in incidence of feeding intolerance (p=0.40).

In another retrospective study with 48 patients receiving ECMO (35 VA and 13 VV ECMO), Lukas et al[9] demonstrated a mean nutritional goal achievement of only 55% of their nutritional targets, 50% for VA ECMO patients, and 67% for VV ECMO patients, (which almost reached statistical significance), estimated with the Schofield equation with a stress factor of 1.2-1.5. Protein targets were in the range of 1.2–1.5 g/kg/day except the patient that received continuous renal replacement therapy, when the range was increased to 1.5–2.0 g/kg/day. This study was performed in a single mixed ICU of medical/surgical/trauma critical patients and heart/lung transplant patients. There were no differences in achieving better nutritional adequacy between survivors and non-survivors (52% v 61%; P= 0.345). Nutritional support was provided mostly in the form of EN, with a moderate number of patients requiring PN.

A prospective observational study performed in a cardiac surgical ICU investigated whether early EN in adults receiving VA ECMO was tolerated. Nutritional support was provided using their ICU nutrition protocol. Energy goals were calculated with 25 kcal/kg/day to be reached over 4 days. Nutrition tolerance was defined as the ratio of effective delivered nutrition to caloric goal. More than 70% of nutrition tolerance was achieved within the first week. All patients were maintained on EN only and no adverse events were noticed[10].

Factors Associated With Safety Outcomes

Hemodynamic Stability

The hemodynamically unstable patient represents a therapeutic challenge in terms of nutritional management[16]. Hemodynamic failure usually leads to a hypotensive state, where blood is generally shunted from the gut and other peripheral organs to the central circulation of the heart and brain. This situation can critically compromise the splachnic perfusion. According to this scenario, adequate blood irrigation and motility of the gastrointestinal tract are prerequisite to initiate any enteral delivery[17].

ECMO initiation usually accomplishes an oxygenation and hemodynamic unloading which has a direct effect on VA ECMO improving blood gases and lowering intrathoracic pressures in VV support. All this provides a better circulatory status by lowering the risk of gastrointestinal hypo perfusion and other complications such as mesenteric ischemia, depressed peristalsis, abdominal distention, and diarrhea[18].

Initial Nutritional Assessment

Nutritional assessment should always be included in the patient evaluation. The first step is to define the degree of malnutrition and estimate the severity of illness, the metabolic state, the catabolism and the inflammatory stress. No single method is universally accepted. For nutritional assessment, we used the *Subjective Global Assessment* (SGA)[19] which assesses nutritional status based on features of the history and physical examination. Ratings are most affected by loss of subcutaneous tissue, muscle wasting, and weight loss. Five features of the history were elicited: weight loss in the previous six months expressed as both kilograms and proportionate loss, the history of dietary intake in relation to a patients usual pattern, the presence of significant gastrointestinal symptoms (anorexia, nausea, vomiting, diarrhea), the patients functional capacity or energy level (bedridden to full capacity), and the disease and its relation to nutritional requirements. Physical examination includes loss of subcutaneous fat, muscle wasting (quadriceps, deltoids), ankle edema, sacral edema and ascites. According to the SGA criteria, the patient is categorized into three groups: class A (well nourished); class B, (moderately malnourished); and class C (severely malnourished). When the patient is severely malnourished and very ill, lean-tissue wasting is a contributing factor to adverse outcomes and it is recommended to start nutrition support[20].

In terms of anthropometric parameters such as body weight and body mass index (BMI), a retrospective analysis of the international Extracorporeal Life Support Organization (ELSO) registry (n=1,334 adults) did not show increased risk of death for patients in the higher quartile of body weight in respiratory failure. They did not consider BMI or nutrition status as risk factors to be analyzed[21]. Another study from 140 ECMO treated acute respiratory distress syndrome patients admitted in three French ICUs showed that a higher BMI is independently associated with better survival by 6 months post ICU discharge[22]. Therefore, high body weight or BMI should not be regarded as a contraindication to initiation of ECMO in patients with respiratory distress. This differed, however, from the patients requiring ECMO for cardiogenic shock, where higher weight is described as a worsening factor by the Survival After Veno-arterial ECMO (SAVE) score, from a multivariate analysis of VA cases[23]. BMI was not available for their set of data.

Adequate energy administration is essential to maintain metabolic needs, minimize catabolism, promote cardiac cachexia recovery and wound healing. In general, calculation of energy requirements can be estimated by indirect calorimetry (gold standard) or by a predictive equation[24]. The technique of indirect calorimetry is based on measurement of oxygen (O2) consumption and carbon dioxide (CO2) production. This is not possible on patients supported by ECMO because the CO2 is removed across the extracorporeal membrane and cannot be identified by the calorimeter. Estimation of energy needs can be based on weight in kilograms for critically ill patients. ICU patients should receive 25 kcal/kg/day increasing to target over the next 2–3 days[25,26]. For weight determination, dry body weight (edema free) should be used[27]. Estimated energy for the obese patient (BMI >30) can be estimated as 22-25 kcal/kg/day of ideal body weight[26].

Protein catabolism and increased protein turnover are major elements of the metabolic response to illness and injury. In general, the recommended daily protein administration to achieve increased protein synthesis and minimize muscle wasting in ill patients can be from 1.3 to 1.5 g/kg/day, and adjusted for each patient´s individual condition, impacted by severity of illness, inflammatory response, surgery, and infection. Higher amounts are needed for patients with renal replacement therapy. When PN is indicated in ICU patients, supplementation with glutamine continues to be associated to a significant reduction on hospital mortality and ICU length of stay[28]. Because this amino acid is conditionally essential in catabolic and stress state, supplementation with doses from 0.2 to 0.4 g/kg/day of L-glutamine can be used, but there is no study in ECMO. The minimal amount of carbohydrate required is 2 gr/kg of glucose per day. Hyperglycemia (glucose >10 mmol/L) contributes to death in the critically ill patient and should also be avoided to prevent infectious complications[25,26].

Fluid and sodium administration should be discussed with the ECMO team. Sodium restriction may be necessary to improve fluid balance, minimize fluid weight gain, and optimize diuretic therapy on some patients[27].

Nutritional management on ECMO patients should be similar to other critically ill patients with respect to timing of initiation and route of EN. Use of early EN within the first 24-48 hours of ICU admission it is recommended when possible and continued to achieve goals over the next 48-72 hrs. Patients receiving less than their targeted enteral feeding after 2 days should be considered for supplementary PN[25,26]. The most appropriate route of EN is a controversial area. Even though small-bowel feeding may decrease the risk of gastro esophageal reflux, recent meta-analyses comparing gastric versus small-bowel feeding have not found significantly different incidences of pneumonia, ICU length of stay, or mortality[29,30]. Some benefits from using gastric feeding in this group of patients include easy tube placement at the moment of connecting to ECMO and early feeding initiation.

Monitoring Nutritional Parameters

Careful monitoring of nutritional support is essential and involves many parameters. Tables I and II provide a checklist that can be used when starting and following nutritional management. The response to nutrition therapy is related to many factors, especially the severity of the inflammatory status. C-reactive protein (CRP) is an index of the inflammatory response, and therefore, the metabolic and catabolic response decreases as the CRP declines. Transthyretin (Pre-albumin) is a negative acute-phase reactant and, with an adequate nutritional support, should rise as CRP falls[31].

Blood Volume and Fluid Status

Fluid management is very challenging during the resuscitation phase with fluid overload[32,33]. Once the patient is supported by ECMO, VV and VA ECMO are very different in its impact on the patients physiology and fluid status. In VV ECMO, blood is drained from and returned into the venous system in-series with the natural circulation. Because the same amount of blood is continuously drawn and replaced into circulation, no changes on preload status occur. In VA ECMO, the extracorporeal circuit is parallel to native circulation, dramatically decreasing the right heart preload and increasing left ventricle afterload[34].

There is no data regarding the exact additional fluid in adult ECMO patients. In pediatric population, Swaniker et al reported worse survival in patients who did not decrease their fluid overload over dry weight. Survivors decreased by 4-9% body weight while non-survivors increased by 25-35% (p=0.001)[35]. This can be related to the exposure of blood to a non biologic surface circuit. As a consequence, a complex inflammatory response is initiated leading to capillary leakage similar to a systemic inflammatory response syndrome[36]. All this data indicates that fluid overload is, at least, a common associated problem.

Reaching nutritional goals may also be related to fluid status. In fact, patients with higher positive fluid balances have shown less achievement of nutritional target compared to patients with low or negative fluid balance[8]. Therefore, management of diuresis or hemofiltration to achieve dry weight, and maintenance of intravascular volume are contributing factors for better results[37]. On the other hand, the effect of the extra fluid volume leads to a restriction of other fluid inputs, including nutrition. With this restriction for the nutritional management, the choice of enteral formula can be restricted to the available concentrated products, not always being the better choice in terms of toleration. Sometimes the enteral formula has to be delivered at a rate below the target. The data on using an immune-enhancing formula on critically ill patients are conflicting and open to considerable debate. Fiber enriched formulae can be well tolerated[16].

A special situation is when the patients hematocrit is too low, requiring frequent blood transfusions. The secondary increased likelihood of antibody sensitization can be a potential barrier for patients waiting for a heart and/or lung transplant because the time being bridged to transplant may be a long period under immunomodulatory agents. The resulting accumulation of these drugs dramatically increases protein catabolism negatively affecting the patient´s nutritional status[38].

Table I
Initial laboratory evaluation: Chemistry studies.

- **Comprehensive metabolic profile:**
  Albumin; Pre-albumin; total proteins; CRP, Electrolytes
  Na; K; Cl;
  BUN; Cr
  AST; ALT
  Ionized Calcium; Mg; Phosphate
  Triglycerides.
- **Hematology:**
  Hgb; Hct; WBC; lymphocyte count, Platelets.
- **Other Nutritional Studies:**
  Vitamin B12; 25 OH-Calciferol; Folic Acid, Twenty-four hour urinary nitrogen excretion.

Abbreviations: CRP: C-Reacive Protein, Na: Sodium, K: Potassium, Cl: Chloride, BUN: Blood Urea Nitrogen, Cr:Creatinine, AST: Aspartate aminotransferase, ALT:Alanine Aminotransferasa, Mg: Magnesium, Hgb: Hemoglobin, Hct: Hematocrit, WBC:White Blood Cells, 25 OH-Calciferol: 25-hydroxycholecalciferol

Table II
Follow-up Studies during Nutrition Support

- **Daily until stable (or when PN is required), then PRN:**
  BUN, Cr, Na, K, Cl, Ionized Ca, Mg, Phosphate.
- **Weekly during nutrition support:**
  Triglycerides, Pre-albumin, CRP.
- **PRN based on nutritional assessment:**
  Vitamin levels, TSH, Iron study.

Abbreviations: BUN: Blood Urea Nitrogen, Cr: Cretinine, Na: Sodium, K: Potassium, Cl: Chloride, Mg: Magnesium, CRP: C-Reacive Protein, TSH: Thyroid Stimulating Hormone

Use of Prokinetics

EN is often discontinued in patients who present large gastric residual volumes. Using prokinetic medications such as metoclopramide or eritromycin has been advocated to improve gastric emptying on patients in ECMO patients. Eritromycin seems to be more effective than metoclopramide on critical illness[39], but the efficiency and comparison of both prokinetric agents on patients undergoing ECMO have not been performed.

Use of vasoactive agents

Hypotension and sepsis in critically ill patients may warrant the use of vasopressors (eg. dobutamine, epinephrine, norepinephrine, milrinon, vasopresin) to maintain adequate hemodynamic parameters. The use of inotropic agents (eg. dobutamine, milrinone) should not discourage the clinician from initiating EN in patients with no other contraindication, because this drug increases cardiac output and consequently perfusion to the gut is improved[40]. All vasopressors produce vasoconstriction, and therefore each agent has a potential to affect gastrointestinal motility and perfusion. There are deeper decreases on splachnic blood flow and oxygen uptake after epinephrine use in shock patients when compared with dobutamine and norepinephrine, suggesting undesirable effects on splachnic perfusion[41]. Theoretically, dopamine should have moderate to no negative effects on gut perfusion at a low dose, (<5 μg/kg/min) wich primarily increases mesenteric perfusion, whereas at a higher dose its vasoconstricting properties are enhanced by α-adrenergic activity, and a conservative approach should be taken[42]. Risk for undesirable events and intolerance to EN require close monitoring in patients receiving vasoactive drugs, especially in certain doses. We have to consider that there are intra- and inter-individual variability in drug pharmacokinetics, making dosing based on body weight not predictable for blood concentrations[43].

Anticoagulation Management

Patients on ECMO need anticoagulation as part of the patient and circuit management. In fact, bleeding and thrombosis are frequent complications with severe impact on prognosis. Infusion of unfractionated heparin is the most commonly used drug[44]. Active bleeding and bleeding risk can be contraindications for using or replacing the enteral feeding tube, requiring PN support[25].

Conclusion

Nutritional support is currently considered an integral part of ICU management, and all sources to increase energy delivered and nutritional status should be implemented for patients during extracorporeal life support[45]. Nutritional therapy for adults receiving ECMO has not been well documented in literature. The enteral route is proposed as the preferred source of nutritional delivery. However there are concerns in patients with circulatory failure on VA ECMO or those who require vasoactive drugs, especially due to the risk for developing bowel ischemia.

In this article we reviewed key considerations for nutritional management during ECMO and presented our local protocol. Until specific guidelines are available for this population, it seems that the guidelines for the assessment of nutritional therapy in the critically ill adult, and the collective multicenter experience on ECMO patients, are the best resource of information for the clinician who is caring for the nutritional management of a patient requiring this device.

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Relevant Authors' information

Dr. Rodrigo Diaz is past president of the international Extracorporeal Life Support Organization (ELSO), Latin American Chapter

Declaration

Authors disclose any financial or non-financial competing interests.

Authors Contributions:

Farias MM: 1, 2, 3, 4
Olivos C: 1, 2, 3, 4
Diaz R: 1, 2, 3, 4

1) have made substantial contributions to conception and design, or acquisition of data, or analysis and interpretation of data; 2) have been involved in drafting the manuscript or revising it critically for important intellectual content; 3) have given final approval of the version to be published; and 4) agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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