Nutritional support in adult patients receiving extracorporeal membrane oxygenation

George Lukas, Andrew R Davies, Andrew K Hilton, Vincent A Pellegrino, Carlos D Scheinkestel and Emma Ridley

ABSTRACT

Background: Patients receiving extracorporeal membrane oxygenation (ECMO) are some of the most critically ill in the intensive care unit. In such patients, malnutrition is associated with increased morbidity and mortality.

Objectives: To describe the use, methods and adequacy of nutritional support in a consecutive group of patients receiving ECMO; to determine differences between the periods during and after ECMO support; and to determine differences in nutritional adequacy between ECMO survivors and ECMO non-survivors.

Design, setting and participants: We conducted a retrospective study of patients who received ECMO at the Alfred Hospital between January 2005 and December 2007. Patients who received venoarterial (VA) or venovenous (VV) ECMO had their case notes reviewed for clinical and nutritional outcomes. Nutritional adequacy was defined as the ratio of delivered nutrition to target nutrition, expressed as a percentage.

Results: Of 48 patients included in our analysis, 35 had VA ECMO and 13 had VV ECMO. Overall, the mean nutritional adequacy achieved for all patients over the periods during and after ECMO support was 62% (SD, 19%). Nutritional adequacy was lower during ECMO support (55%) than after ECMO removal (71%) ($P = 0.003$). Survivors did not achieve better nutritional adequacy than non-survivors (52% v 61%; $P = 0.345$).

Conclusions: Patients receiving ECMO received inadequate nutritional support, with only 55% of their nutritional targets being achieved while receiving ECMO. Optimal nutritional support should be a major goal in the care of these patients, and measures to improve nutritional delivery require careful consideration.

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Extracorporeal membrane oxygenation (ECMO) is becoming an accepted modality of short-term support for severe cardio-respiratory dysfunction in the adult population. ECMO can be instituted for the management of life-threatening respiratory or cardiac failure (or both) when other forms of treatments have failed. It is most commonly instituted in an emergency or urgent situation. ECMO is used as temporary support when recovery of the lungs or heart is anticipated, or can be used as a bridge to a ventricular assist device or cardiac transplantation.

Venovenous (VV) ECMO involves removing venous blood from the large central veins, passing it through an oxygenator and returning it to the venous system near the right atrium. It provides support for patients with severe respiratory failure where no major cardiac dysfunction exists. Venoarterial (VA) ECMO involves removing venous blood from the large central veins, passing it through an oxygenator and returning it to the arterial system. It provides support for patients with severe cardiac failure (usually with associated respiratory failure).

In critically ill patients, malnutrition is associated with increased morbidity and mortality,[1] and the benefits of enteral nutrition (EN) in these patients are becoming increasingly understood and recognised.[2-5] However, many patients can not tolerate EN, especially when illness is severe.[6] While parenteral nutrition (PN) is an alternative, its value for critically ill patients is debated.[7]

Patients receiving ECMO are some of the most critically ill. They have prolonged stays in the intensive care unit, usually require high doses of vasopressor drugs prior to ECMO, and would be expected to benefit from nutritional support. The adequacy and benefit of nutritional support for adult patients receiving ECMO has not been well documented in the literature. There are theoretical concerns with regard to the timing of initiation and the dose of EN in patients with circulatory failure requiring vasoactive drugs, particularly the risk of non-occlusive bowel necrosis.[8]

Abbreviations

APACHE	Acute Physiology and Chronic Health Evaluation
ECMO	Extracorporeal membrane oxygenation
EN	Enteral nutrition
GRV	Gastric residual volume
MPM-0	Mortality Prediction Model at time zero
PN	Parenteral nutrition
SAPS	Simplified Acute Physiology Score
VA	Venoarterial
VV	Venovenous

Although recent data have been published supporting the safety and tolerability of EN in adult VV ECMO patients,[9] there are sparse data regarding adult VA ECMO patients, who often have major circulatory dysfunction and are often receiving large doses of vasopressor drugs at the time ECMO is commenced.

The aims of our study were to describe the use, methods and adequacy of nutritional support in a consecutive group of patients receiving ECMO; to determine differences between the periods during and after ECMO support; and to determine differences in nutritional adequacy between ECMO survivors and ECMO non-survivors.

Methods

We performed a retrospective case review of patients receiving ECMO in the ICU of the Alfred Hospital, a quaternary level hospital, over a 3-year period (January 2005 to December 2007). The ICU is a mixed medical/surgical/trauma ICU and a heart and lung transplant centre, as well as a regional referral centre for patients requiring ECMO. We included all patients receiving any form of ECMO. Patients on ventricular assist devices (cardiac support devices that do not provide extracorporeal oxygenation) were excluded from our study.

Local ethical review guidelines allowed us to conduct this retrospective study without the need for individual patient consent or a formal application to the hospital ethics committee. Nutritional support was provided during the study period in a protocolised fashion. Daily energy requirements were calculated by a dietitian using the Schofield equation[10] with application of a stress factor (1.2–1.5). The Schofield equation is the method used in clinical practice to determine energy requirements in all patients admitted to our ICU. Protein targets were in the range of 1.2–1.5 g/kg/day unless the patient received continuous renal replacement therapy, when the range was increased to 1.5–2.0 g/kg/day to compensate for amino acid losses in the dialysate.[11,12] Indirect calorimetry was not used for this study. EN products administered were feeds already used in the ICU and were usually a standard isocaloric polymeric formula, with choice of product determined by the dietitian based on clinical need and delivered through a nasogastric tube. Enteral immunonutrition products were not used.

EN was administered continuously over the 24-hour period. Clinical staff were recommended to assess gastric residual volumes (GRVs) every 4 hours and to return the fluid back to the patient as a bolus if the volume was less than 200 mL. Amounts greater than 200 mL were considered to indicate intolerance and were discarded.

When EN was not tolerated, decisions about initiation of prokinetic agents, nasojejunal tubes and PN were at the discretion of the treating multidisciplinary intensive care team (including a dietitian). However, an ICU nutrition guideline in place during the study recommended the use of a prokinetic drug (metoclopramide at the first occurrence of a GRV > 150 mL followed by erythromycin at the second). Recommendations for ongoing intolerance were to place a nasojejunal tube (unless contraindicated), followed by commencement of PN. EN was to be considered on a daily basis when total PN was being administered.

Data were collected on each patient's nutritional intake on every day they received ECMO as well as the 5 days following ECMO removal. Day 1 was defined as the day ECMO was commenced, and the day on which ECMO was removed was treated as a day on ECMO for analysis purposes. A prokinetic agent was considered to have been administered for a particular day if metoclopramide or erythromycin were administered more than once.

The amounts of EN and PN delivered each day were compared with target requirements. Nutritional adequacy was defined as the ratio of delivered nutrition to target nutrition, expressed as a percentage. The amount of GRV discarded was considered as being the equivalent volume of nutrition product discarded. If the combined EN and PN intake amounted to more than 100% of daily requirements, the daily intake for that day was considered 100%.

A narcotic infusion was considered administered for a particular day if it was running for at least 1 hour at a dose of $\geqslant$ 1 mg/h of morphine or $\geqslant$ 10 μg/h of fentanyl. Other data collected included patient age and sex, reasons why ECMO was initiated, type of ECMO, duration of ECMO support, and the use of nasojejunal feeding tubes. Patients were followed to assess survival at 28 days after ECMO removal, at ICU discharge, and at hospital discharge.

Data analysis

Data analysis was descriptive, using mean and standard deviation for normally distributed data and median and interquartile range (IQR) for skewed data. Comparisons of proportions were made using χ^2 tests for equal proportion. Continuous variables were compared using *t*-tests. All reported *P* values are two-sided and were not adjusted for multiple comparisons. $P < 0.05$ was considered statistically significant. Analyses were performed using Microsoft Excel 2003.

Results

Fifty-seven patients received ECMO during the 3-year period. Of these, nine were excluded from our analysis: one died in the operating room during ECMO placement, two had data missing from their medical records, and six had ECMO support withdrawn within 48 hours (these six patients were excluded because they were not supported for long enough to obtain meaningful information about nutritional support).

The remaining 48 patients (11 women; 37 men; median age, 44 years [range, 16–75 years]) were included in our analysis. Of these, 35 received VA ECMO (17 had cannulae inserted peripherally and 18 centrally) and 13 received VV ECMO. The median duration of ECMO support was 8 days (IQR, 7–10 days). There were 34 survivors (28 VA ECMO, 6 VV ECMO) and 14 non-survivors (7 VA ECMO, 7 VV ECMO). The indications for ECMO support are shown in Table 1.

EN was provided to 45/48 patients (94%), and PN was provided to 14 (29%). Twelve patients (25%) received combined EN and PN; 33 (69%) received EN as the sole nutritional source; and two (4%) received PN as the sole nutritional source. One patient who died on Day 3 received no nutrition at all.

A narcotic infusion was administered to 46 patients (96%) and prokinetic drugs to 34 patients (71%). Three patients (6%) had a frictional nasojejunal tube (Cook Medical, Bloomington, Ind, USA) inserted while receiving ECMO. Serious bleeding that commenced during insertion of one of these required removal of the device. This was the only identified complication linked directly to nutritional support. There were no documented episodes of line sepsis related to PN.

The mean nutritional adequacy achieved of all patients, combining the periods during and after ECMO support, was 62% (SD, 19%). The mean nutritional adequacy while receiving ECMO support was 55% (SD, 23%) compared with 71% (SD, 25%) in the 5 days following ECMO support (P= 0.003). The mean total nutritional adequacy was 18% for the first 2 days while receiving ECMO and 30% for the first 3 days while receiving ECMO. It took until Day 6 for the mean cumulative nutritional adequacy to reach 50% and until Day 9 to reach over 60% (Figure 1). The number of patients receiving ECMO was 40 at Day 6 and 18 at Day 9.

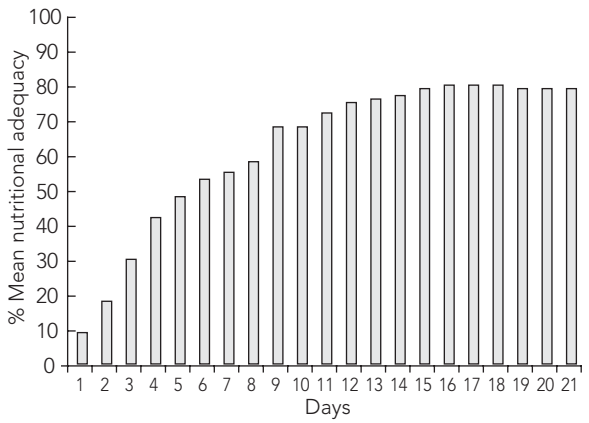
Table 1. Indications for ECMO support

Indication	Venoarterial ECMO	Venovenous ECMO
Unweanable after heart transplant	14	—
Idiopathic dilated cardiomyopathy	4	—
Unweanable after cardiac surgery	3	—
Heart transplant rejection	3	—
Acute myocardial infarction	1	—
Aspiration	1	—
Drug cardiomyopathy	1	—
Fat emboli due to trauma	1	—
Out-of-hospital cardiac arrest	1	—
Pulmonary emboli	1	—
Viral myocarditis	1	—
Other	4	2
Infections	—	4
Lung transplants	—	4
Caused by/related to trauma	—	3

ECMO = extracorporeal membrane oxygenation.

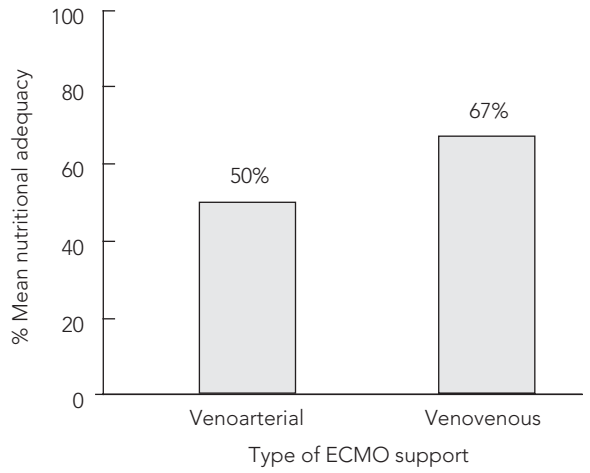
During ECMO support, the mean nutritional adequacy achieved was 50% (SD, 21%) in VA ECMO patients versus 67% (SD, 26%) in VV ECMO patients (P=0.052) (Figure 2); and 52% (SD, 20%) in survivors versus 61% (SD, 30%) in non-survivors (P=0.345). Over the first 2 and first 3 days of ECMO support, there were no significant differences in mean total nutritional adequacy between survivors (16% and 30%

Figure 1. Cumulative mean nutritional adequacy in patients receiving ECMO



ECMO = extracorporeal membrane oxygenation.

Figure 2. Mean nutritional adequacy, by type of ECMO received



ECMO = extracorporeal membrane oxygenation.

over 2 and 3 days, respectively) and non-survivors (24% and 30% over 2 and 3 days, respectively).

Discussion

We found that patients receiving ECMO were provided with nutritional support, mostly in the form of EN, but with a moderate number of patients requiring PN. Nutritional adequacy was 62% overall and 55% during ECMO support. Nutritional therapy was generally delayed, with patients receiving a mean of only 30% of estimated requirements by Day 3. These amounts seem generally inadequate for a cohort of severely unwell patients, but are consistent with reports of other observational studies of critically ill patients.[13]

Given that we could not identify any serious adverse effects related to nutritional support, we believe that improved efforts to maximise delivery of nutritional support should be made. The use of protocols, prokinetic drugs, small bowel feeding tubes and supplemental PN have all been recommended in recent publications of evidence-based guidelines (Canadian,[14] European,[15] Australian and New Zealand[16]) for critically ill patients. We believe that dissemination and implementation of such guidelines are extremely important.

In our patient cohort, total nutritional adequacy was particularly unsatisfactory for the first 2 and 3 days, with only 18% and 30%, respectively, of total nutritional requirements achieved. This improved over the next 3–6 days as increasing efforts were made to optimise nutritional therapy, but it took until Day 6 for the cumulative mean nutritional adequacy to be over 50%. This highlights the energy "debt" that patients can develop and which may be difficult to overcome. Such a debt may theoretically have a significant negative effect on the most severely unwell patients such as those requiring ECMO. This is important and relevant, as both the Canadian[14] and European[15] guidelines recommend early EN for critically ill patients because it has been associated with improved survival.[17] It is also worth noting that a large retrospective study has shown a significant reduction in ICU and hospital mortality in an early feeding group of patients with an Acute Physiology and Chronic Health Evaluation (APACHE) II score of >25, Simplified Acute Physiology Score (SAPS) II >56 or an MPM–0 (Mortality Prediction Model at time zero) probability of survival of <0.54.[18] Patients receiving ECMO are at this level of illness severity.

Although the mean nutritional adequacy of all patients during combined periods on and after ECMO support was 62%, the average total nutritional adequacy during ECMO support was only 55%, improving to 71% after ECMO removal. The improvement of nutritional adequacy after cessation of ECMO may be a result of gradual recovery from critical illness and improved gastrointestinal function. However, delays in commencing feeding, instituting prokinetic drugs, starting nasojejunal feeding and supplementing with PN may also play a major role in the initial inadequacy of nutrition.

The reason for the greater mean nutritional adequacy achieved for VV compared with VA ECMO patients, which almost reaches statistical significance, is unclear. It is not explained by differences in PN or prokinetic drug administration. Differences in type and amount of vasopressor support may be a contributing factor, but these differences were not recorded.

As a basis for comparison we used data from our institution that were collected for the International Nutrition Survey coordinated by Critical Care Nutrition. In 2007, 22 mechanically ventilated patients (median APACHE II score 24.5) had their nutritional adequacy documented from the time of ICU admission for 12 days or until discharge from ICU, whichever occurred first. These patients were ventilated for a median of 9 days. The mean nutritional adequacy achieved was 78% (SD, 35%), with a median of 88%. This level of nutritional intake is substantially higher than that achieved for ECMO patients in our study.

Other reasons for our patients not meeting their target nutritional requirements may have included the interruption of feeds due to procedures (eg, return to the operating room or requirement for transoesophageal echocardiography), and lack of clear guidelines on how to manage GRVs and when to initiate prokinetic drug treatment, small bowel feeding with a nasojejunal tube and PN. Prokinetic drugs were frequently required (71% of patients) because of gastrointestinal dysmotility associated with critical illness, and the requirement for a narcotic infusion was almost universal (96% of patients), usually as a combined sedative agent with a benzodiazepine such as midazolam. There are no clear guidelines relating to narcotic dose minimisation in the setting of large GRVs and constipation. Only three patients had a nasojejunal tube, as it seemed that there was reluctance to use this option because of concerns about bleeding if manipulations were subsequently required to guide the tube into the jejunum. Patients receiving ECMO are predisposed to bleeding because of heparinisation and associated qualitative platelet dysfunction from the circuit. It must also be remembered that ECMO patients are usually nursed flat rather than with the head of the bed elevated. This would contribute to larger GRVs and reduced enteral absorption. The low rates of nutritional adequacy and slow rate of improvement highlight the need to establish clear protocols to address all the above points in ECMO patients.

Nutritional support is considered to be an integral part of ICU management, and all measures to increase energy delivered should be implemented. Promotility drugs and nasojejunal tubes should be used initially, although the risk of bleeding for anticoagulated patients needs to be considered. Supplemental PN (particularly if given early or when signifi-

cant intolerance of EN continues) is another important strategy. The requirement of central access for PN, which in turn may predispose to line sepsis, must be borne in mind in relation to these patients, who are often severely immunosuppressed. Another important issue in managing these often highly stressed patients is that of glucose control associated with PN.

Of the seven deaths in VA ECMO patients, three occurred while receiving ECMO and four after ECMO removal. Of the seven deaths in VV ECMO patients, all occurred while on ECMO. Active treatment withdrawal was the mode of death in all VA and VV ECMO patients. Intestinal ischaemia was not thought to be a contributing factor to any of these deaths, but needs to be remembered as a possible contributor to a deteriorating clinical state.[8]

To our knowledge, our study is the largest to be published on nutritional support in adult ECMO patients. Its limitations include its retrospective and single-centre nature as well as its small sample size. Nonetheless, we believe that the information it provides can be used to improve nutritional support in adults receiving ECMO. We also recognise that survivors and non-survivors may not be homogeneous when making comparisons. Importantly, we could not identify any general hindrance to delivery of nutritional support for ECMO patients as opposed to non-ECMO patients.

In conclusion, our results show that, in the early period of ECMO support, low amounts of nutrition were delivered, with 18% of total nutritional requirements being delivered over the first 2 days, 30% over the first 3 days, and 55% over the entire period of ECMO support. While the optimal approach to delivering nutrition to this population is unknown, we believe it is important to differentiate between physiological barriers and inadequate clinical focus on nutritional aspects of care, as this will have implications for improving the guidelines for nutritional support. Lack of clinical focus and diligence in recognising inadequate nutritional support appears to be the major factor here. Our group of patients receiving ECMO support were most commonly given EN. PN supplementation was quite commonly required, but despite this, we did not achieve nutritional goals. To improve nutritional delivery, we suggest implementation of clear and comprehensive guidelines for initiation and maintenance of nutritional support and dissemination among medical and nursing staff.

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Author details

George Lukas, Senior Registrar
Andrew R Davies, Deputy Director of Intensive Care
Andrew K Hilton, Intensivist
Vincent A Pellegrino, Intensivist
Carlos D Scheinkestel, Director of Intensive Care
Emma Ridley, Dietitian
Department of Intensive Care, Alfred Hospital, Melbourne, VIC.
Correspondence: glukas@bigpond.com

References

1 Giner M, Laviano A, Meguid MM, et al. In 1995 a correlation between malnutrition and poor outcomes in critically ill patients still exists. *Nutrition* 1996; 12: 23-9.
2 Hadfield RJ, Sinclair DG, Houldsworth PE, et al. Effects of enteral and parenteral nutrition on gut mucosal permeability in the critically ill. *Am J Respir Crit Care Med* 1995; 152: 1545-8.
3 Kudsk KA. Early enteral nutrition in surgical patients. *Nutrition* 1998; 14: 541-4.
4 Vincent JL, Preiser JC. Management of the critically ill patient with severe sepsis. *J Chemother* 1999; 11: 524-9.
5 Heyland DK. Nutritional support in the critically ill patients. A critical review of the evidence. *Crit Care Clin* 1998; 14: 423-40.
6 Mentec H, Dupont H, Bocchetti M, et al. Upper digestive intolerance during enteral nutrition in critically ill patients: frequency, risk factors, and complications. *Crit Care Med* 2001; 29: 1955-61.
7 Marik PE, Pinsky M. Death by parenteral nutrition. *Intensive Care Med* 2003; 29: 867-9.
8 Rokyta R, Matejovic M, Krouzecky A, et al. Enteral nutrition and hepatosplanchnic region in critically ill patients — friends or foes? *Physiol Res* 2003; 52: 31-7.
9 Scott LK, Boudreaux K, Thaljeh F, et al. Early enteral feedings in adults receiving venovenous extracorporeal membrane oxygenation. *JPEN J Parenter Enteral Nutr* 2004; 28: 295-300.
10 Schofield WN. Predicting basal metabolic rate, new standards and review of previous work. *Hum Nutr Clin Nutr* 1985; 39 Suppl 1: 5-41.
11 Scheinkestel CD, Adams F, Mahoney L, et al. The impact of increasing parenteral protein loads on amino acid levels and balance in critically ill anuric patients on continuous renal replacement therapy. *Nutrition* 2003; 19: 733-41.
12 Scheinkestel CD, Kar L, Marshall K, et al. Prospective randomized trial to assess caloric and protein needs of critically ill anuric patients on continuous renal replacement therapy. *Nutrition* 2003; 19: 909-16.
13 De Beaux, Chapman M, Fraser R, et al. Enteral nutrition in the critically ill: a prospective survey in an Australian intensive care unit. *Anaesth Intensive Care* 2001; 29: 619-22.
14 Heyland DK, Dhaliwal R, Drover JW, et al. Canadian clinical practice guidelines for nutritional support in mechanically ventilated, critically ill adult patients. *JPEN J Parenter Enteral Nutr* 2003; 27: 355-73.
15 Kreymann KG, Berger MM, Deutz NE, et al. ESPEN guidelines on enteral nutrition: intensive care. *Clin Nutr* 2006; 25: 210-23.
16 Doig GS, Simpson F, chairs; Australian and New Zealand Intensive Care Society Clinical Trials Group. Evidence-based guidelines for nutritional support of the critically ill: results of a bi-national guideline development conference; 2003 Oct 27-28; Sydney, Australia. Sydney: EvidenceBased.net, 2005. http://www.evidencebased.net/files/EBG-forNutSupportofICUpts.pdf (accessed Sep 2010).
17 Doig GS, Heighes PT, Simpson F, et al. Early enteral nutrition, provided within 24 h of injury or intensive care unit admission, significantly reduces mortality in critically ill patients: a meta-analysis of randomised controlled trials. *Intensive Care Med* 2009; 35: 2018-27.
18 Artinian V, Krayem H, DiGiovine B. Effects of early enteral feeding on the outcome of critically ill mechanically ventilated medical patients. *Chest* 2006; 129: 960-7. ❑