Nutrition therapy in adult patients receiving extracorporeal membrane oxygenation: a prospective, multicentre, observational study

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ABSTRACT

Objectives: To describe current nutrition delivery practices and to identify barriers to nutrition in patients receiving venovenous or venoarterial extracorporeal membrane oxygenation (ECMO) in multiple centres in Australia and New Zealand.

Design, setting and participants: A prospective, multicentre, observational study, set in eight intensive care units in Australia and New Zealand, of adults treated with ECMO who were expected to receive enteral nutrition (EN) or parenteral nutrition (PN) therapy for > 72 hours. Data were collected from the start of ECMO until 7 days after ECMO cessation.

Results: There were 107 patients enrolled, with a median age of 42 years (interquartile range [IQR], 31–56 years), and 54 patients (50%) were men. EN was the most commonly delivered mode of nutrition (on 84% of days) although it was interrupted on 53% of days. The median interruption duration was 8 hours (IQR, 4–5 hours] per episode. The two most common barriers to EN delivery were fasting for a therapeutic or diagnostic procedure and high gastric residual volumes. Median daily calorie and protein deliveries from EN and/or PN were 1680 kcal (IQR, 960–2100 kcal) and 72 g (IQR, 42–98 g) of protein. For patients who received EN and/or PN, median calorie and protein deficits during the study period were – 7118 kcal (IQR, – 11 614 to – 4510 kcal) and – 325 g (IQR, – 525 to – 188 g) of protein.

Conclusions: EN was the most commonly used nutrition-delivery mode during ECMO treatment but was frequently interrupted. Compared with estimated calorie and protein requirements, lesser but reasonably acceptable amounts were delivered, although calorie and protein deficits still existed.

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Extracorporeal membrane oxygenation (ECMO) is a mode of life support used for adult patients with refractory cardiac or respiratory failure.[1,2] ECMO provides short-term, scalable support for reversible forms of cardiac and respiratory failure, or can act as a bridge to heart or lung transplantation or ventricular assist device placement when recovery does not occur. ECMO appears to be more increasingly used over the past decade.[3-6]

Nutrition therapy is an essential element of critical care, and although the exact benefits and optimal administration remain unclear, it is used in almost all mechanically ventilated patients.[7-15] Because patients who receive ECMO are some of the most severely unwell patients in any intensive care unit, and often have long ICU and hospital stays, it could be postulated that nutrition may be more important to these patients than to less severely ill ICU patients, yet little research has been done in this area. Patients receiving ECMO are often treated with large doses of vasoactive and sedative medicines, both of which are known to impair gastric emptying and interrupt the delivery of enteral nutrition (EN).[16] This may decrease the energy and protein delivered to the patient, leading to deficits in expected requirements.[16] It has been commonly observed that patients not receiving ECMO are delivered little more than half the EN they are predicted to require, mostly due to gastrointestinal (GI) intolerance and fasting.[17-19] In addition, it has been hypothesised that use of the ECMO equipment may increase protein catabolism and inflammation, with significant metabolic consequences, and perhaps increasing nutrition requirements.[16]

Until recently there were only small, descriptive, single-centre case series reporting on nutrition delivery in ECMO patients. One retrospective study observed the inadequate provision of nutrition therapy, including slow commencement and difficulties with progression towards the target amount.[20] A more recent, single-centre prospective study reported that patients undergoing ECMO received about 80% of the nutrition identified in their nutritional goals.[21]

Our primary aims were to perform a multicentre study in Australia and New Zealand to describe current nutrition-delivery practices and to identify barriers to nutrition therapy in patients receiving venovenous (VV) or venoarterial (VA) ECMO. We specifically aimed to observe how calorie and protein requirements were estimated, the proportions of these requirements that were actually delivered, and the deficits that accumulated during ECMO therapy and for 7 days after ECMO discontinuation.

Methods

Patients were screened at eight specialist ECMO ICUs in Australia and New Zealand from 10 June 2012 until 10 June 2013. Consecutive adult patients treated with ECMO, for any indication, who were expected to receive EN or parenteral nutrition (PN) therapy for more than 72 hours were included. Patients were excluded if death was deemed imminent by the treating intensivist at the time of screening.

Data were collected daily for the duration of ECMO therapy and for 7 days after ECMO discontinuation. Variables collected were those relevant to the study aims and included patient demographic details, nutrition assessment information, daily nutrition delivery data, clinical data (including adverse events) and routinely available biochemical markers. Nutrition management (including choice of delivery route, time of commencement, formula type and composition, advancement of delivery rate and management of GI intolerance) followed usual practice at each site. In particular, the estimation method used to determine calorie and protein requirements followed the site's usual practice and was recorded. The calorie estimation methods used were classified as:

- predictive equation (eg, Schofield)
- weight-based estimation method, or
- other method.

Any changes in calorie and protein requirements were recorded daily. The volume of EN was recorded after discarded gastric residual volumes (GRVs) were subtracted from the total volume received. Barriers to the delivery of EN (such as fasting for a therapeutic procedure or diagnostic intervention, GI intolerance and occurrences of abdominal distension and vomiting) were noted daily. If PN was delivered, the reasons for its use and the volume administered were recorded. Reasons for PN use were determined using the evidence-based data collection tools from an international nutrition survey.[22] For those who received EN, PN or both, caloric and protein deficits were calculated on a daily basis and over the whole study period. The sums of calories and protein received from EN, PN and propofol were subtracted from the daily calorie and protein requirements estimated for each patient by the site. The daily deficits were summed to determine the overall deficit during the study period. Data on oral nutrition were collected, but only whether the patient received oral nutrition on a particular day, not the calorie and protein contribution. Outcome data such as durations of ECMO therapy, mechanical ventilation, and ICU and hospital stays were also collected and censored at Day 60.

Approval was provided by each site's human research ethics committee, and informed consent was waived at all sites because of the low-risk nature of this research. Based on previous information, it was anticipated that over a 12-month period, about 100 patients would be treated with ECMO in these centres. This sample size would allow us to report proportions with a 95% confidence interval of about 10%. Proportions are reported as numbers and percentages, or as percentages and 95% CIs, and continuous data are reported as medians and interquartile ranges (IQRs). All analyses were performed using SAS, version 9.3 (SAS Institute).

Results

There were 107 patients enrolled in the study. The median age of the population was 42 years (IQR, 31–56 years), and 54 patients (50%) were men. The median estimated calorie and protein requirements were 2040 kcal/day (IQR, 1851–2391 kcal/day) and 95 g of protein/day (IQR, 72–106 g/day). The Schofield equation with use of an added stress factor (55 patients [51%]) was the most commonly used method to estimate calorie requirements.[23,24] The median time from ICU admission to first delivery of nutrition was 13 hours (IQR, 7–30 hours). Further demographic data and aspects of ECMO delivery are shown in Table 1, and nutrition assessment data are shown in Table 2.

On the 1602 total study days, EN was provided on 1342 days (84%), PN on 111 days (7%), oral nutrition (ON) on 155 days (10%) and no nutrition on 83 days (5%). The most common EN delivery route was through a gastric tube on 1207 EN delivery days (90%), and EN was delivered through a postpyloric tube on 135 days (10%). The most commonly provided calorie concentration of the EN formulae was 1.25 kcal/mL (given on 451 EN delivery days [34%]), followed by 2.0 kcal/mL (given on 382 EN delivery days [28%]), 1.5 kcal/mL (given on 290 EN delivery days [22%]) and 1.0 kcal/mL (given on 272 EN delivery days [20%]). Patients could receive more than one EN formula on any study day. Combined nutrition was provided as EN in combination with PN on 52 study days (3%) or EN in combination with ON on 39 study days (2%). There were no important differences in energy and protein prescription or nutrition delivery when patients receiving VV ECMO or VA ECMO were compared.

When we considered the barriers to the provision of nutrition, we found that EN was interrupted on 629 of the days it was delivered (53%). The median EN interruption duration per episode was 8 hours (IQR, 4–15 hours). Fasting for a therapeutic procedure or diagnostic intervention, and high GRV, were the most frequently reported barriers to EN delivery (Table 3). The median total daily GRV measured during routine practice was 80 mL (IQR, 5–345 mL). The reasons for PN provision are shown in Table 4. "Not tolerating EN" was the most commonly chosen reason for PN provision, followed by "GI bleeding".

Table 1. Baseline and outcome characteristics of study population ($n = 107$)

Characteristic	Study result
Age, years*	42 (31–56)
Sex (male)†	54 (50%)
APACHE II score at ICU admission*	20 (12–28)
BMI, kg/m^2*	25.8 (23–31)
Weight, kg*	79 (65–93)
Initial ECMO configuration†	
Venovenous	42 (39%)
Venoarterial	65 (61%)
Initial ECMO access site†	
Jugular	29 (27%)
Femoral	79 (74%)
Mediastinal	6 (6%)
Lactate level on Day 1, U/L*	4 (2–8)
Never mechanically ventilated†	1 (1%)
Time from ICU to ECMO, hours*	3 (0–26)
Time from hospital admission to nutrition, hours*	25 (11–57)
Time from ICU admission to nutrition, hours*	13 (7–30)
Hospital LOS, days*	32 (21–50)
ICU LOS, days*	16 (9–25)
Duration of ventilation, days*	14 (7–22)
Overall study days patients received RRT†	615 (38%)
Last reported day of EN or PN in study period*	14 (9–17)
Death, ICU†	39 (36%)
Ventricular assist device during study period†	11 (10%)
Heart transplant during study period†	4 (4%)
Lung transplant during study period†	13 (12%)

APACHE = Acute Physiology and Chronic Health Evaluation. BMI = body mass index. ECMO = extracorporeal membrane oxygenation. ICU = intensive care unit. LOS = length of stay. RRT = renal replacement therapy. EN = enteral nutrition. PN = parenteral nutrition. * Median (interquartile range). † *n* (%).

The median number of calories delivered to patients per day from EN, PN or both was 1680 kcal (IQR, 960–2100), and the median amount of protein was 72 g (IQR, 42–98 g). Calorie and protein delivery over the first 10 study days from EN and/or PN are shown in Figures 1 and 2. Based on the median estimated body weight reported, this is equivalent to a median daily delivery of 20.0 kcal/kg and 0.9 g/kg protein. For patients who received EN and/or PN (and adding calories from propofol if received) there was a daily median deficit of –416 calories (IQR, –1200 to –6 calories) and –18 g protein (IQR, –53 to 0 g protein). During the study period, this accumulated to –5924 calories (IQR, –10 581 to –3619 calories) and –325 g protein (IQR, –525 to –188 g protein). When propofol was not counted as a calorie source the median deficit during the study period increased to –7118 calories (IQR, –11 614 to –4510 calories).

Propofol was administered on 495 of the study days (31%) and contributed a median of 266 kcal (IQR, 132–421 kcal), which equates to about 13% of the median daily caloric requirement (95% CI, 10–16%). Prokinetic medica-

Table 2. Baseline nutrition assessment*

Characteristic	Study population
Median overall energy prescription estimated by treating team, calories (IQR)	2040 (1851–2391)
Estimation method for energy requirements, *n* (%)	
Schofield equation with stress factor	55 (51%)
Fixed prescription estimation method†	35 (33%)
Other method‡	17 (16%)
Median stress factor for Schofield equation (IQR)	1.5 (1.0–1.5)
Median estimated protein requirement/day, g (IQR)	95 (72–106)

* Information collected to understand which energy estimation method was used to estimate daily energy requirements and what daily energy and protein amount was prescribed to the study population. † Options were: ⩽ 20 kcal/kg, 20–24.9 kcal/kg, 25–29.9 kcal/kg, 30–34.9 kcal/kg or ⩾ 35 kcal/kg; the choice to use this method was for the individual clinician and site management. ‡ Other methods reported were an "average" or combination of estimation method; the choice to estimate was for the individual clinician and site management.

Table 3. Reasons for interruptions to EN on days EN was provided*

Reason	No. EN interruptions during study period (% of all EN interruptions)
Fasting, procedure or examination in ICU or theatre	198 (31%)
High gastric residual volume	136 (22%)
No EN access or tube-related issue	88 (14%)
No reason known	78 (12%)
EN delivery process issue†	75 (12%)
Medical team request	59 (9%)
Other EN tolerance concern‡	50 (8%)
Fasting for extubation	38 (6%)
Other	16 (2.5%)
Death/palliation/poor prognosis	11 (2%)
Transition to oral nutrition	6 (1%)
Medical emergency	4 (1%)

EN = enteral nutrition. * More than one reason could be selected. † Comments included "not at target rate", "gradual increase", "commenced late", "changing enteral feed bags", "late admission" and "awaiting dietitian review". ‡ Comments included "increased abdominal girth", "vomiting" and "documented 'GI dysfunction'".

Table 4. Reasons for provision of PN on days it was given*

Reason	No. PN interruptions during study period (% of all PN interruptions)
Not tolerating EN	41 (37%)
Gastrointestinal bleeding	27 (24%)
Other	14 (13%)
Small bowel ileus	11 (10%)
Bowel ischaemia	5 (4.5%)

PN = parenteral nutrition. EN = enteral nutrition. * More than one reason could be selected.

tions (metoclopramide and erythromycin) were administered to 71 patients (66%) on 554 study days (34%). The median daily dose of metoclopramide was 30 mg (IQR, 20–30 mg), and of erythromycin was 500 mg (IQR, 250–1000 mg).

The median morning blood glucose level during the study was 7.5 mmol/L (IQR, 6.4–8.7 mmol/L), and insulin was provided on 677 study days (58%). The median amount of insulin provided was 55 U/day (IQR, 26.0–92.5 U/day). Supplementary micronutrients were administered on 516 study days (32%) and continuous renal replacement therapy was provided to 60 patients (56%) on 615 study days (38%). Bowel actions were reported to have occurred on 913 study days (57%) and aperients were administered on 1009 study days (63%).

Of the 68 survivors, 36 patients (34%) had resumed ON by ICU discharge, and 55 patients (51%) had resumed ON by hospital discharge (Table 5). The median duration of ECMO therapy was 9 days (IQR, 5–12 days), and 39 patients (36%) died in the ICU. There were 16 patients (15%) in hospital at Day 60. Of the 52 patients who were discharged before Day 60, 33 (63%) returned home, nine (17%) went to a rehabilitation centre, eight (15%) went to another hospital and two (4%) went to an unknown location. None of the patients who were discharged before Day 60 went to a high-level care facility. There were no important differences in clinical outcomes when patients receiving VV ECMO and VA ECMO were compared. Other important clinical outcomes can be seen in Table 1.

Figure 1. Median total daily energy contribution in first 10 study days, from enteral nutrition (EN) and parenteral nutrition (PN), and from propofol

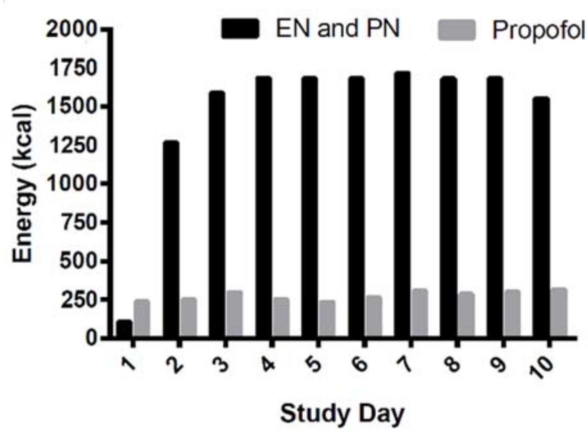

Figure 2. Median total daily protein contribution in first 10 study days, from enteral and/or parenteral nutrition

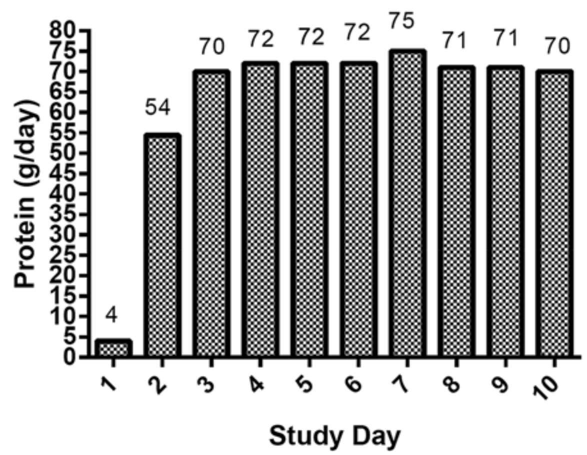

Table 5. Nutrition therapy at intensive care unit discharge and hospital discharge, *n* (%)

Nutrition therapy at time of discharge	Discharge site: ICU	Hospital
Combination oral and EN	14 (13%)	0
EN only	18 (17%)	13 (12%)
EN tube location		
Nasogastric	29 (27%)	9 (8%)
Percutaneous endoscopic gastrostomy	1 (1%)	1 (1%)
Nasojejunal	4 (4%)	3 (3%)
Oral intake only	36 (34%)	55 (51%)

EN = enteral nutrition.

Discussion

In this relatively young cohort of adult patients who received ECMO therapy, we observed that nutrition was most commonly provided via the enteral route and it was interrupted on about half of the days it was delivered. The most common barriers to nutrition delivery were fasting for a therapeutic procedure or diagnostic intervention and elevated GRVs. EN formulae containing 1 kcal/mL were uncommonly prescribed, and over 80% of patients received EN formulae containing 1.25–2 kcal/mL. The use of PN was relatively low, and elevated GRV was the main reason reported for PN usage. We observed that, compared with estimated calorie and protein requirements, lesser but reasonably acceptable amounts were delivered, although calorie and protein deficits still accrued on a daily basis and during the study period. About two-thirds of patients received a prokinetic medication. On days when propofol was administered, it contributed 13% of daily calorie intake. Over one-third of the patients died in the ICU. Patients frequently resumed oral intake before hospital discharge, with very few requiring EN or PN at hospital discharge.

To our knowledge, this is the first prospective, multicentre study observing the nutrition prescription and delivery practices of clinicians to adult patients receiving ECMO therapy. Although we did not specifically compare populations, it appears that the provision of nutrition to patients on ECMO is generally better now than 5 years ago, which possibly indicates an improved understanding of the importance of nutrition and a change in management and/or populations who receive ECMO therapy.[20,25] Compared with other studies in general ICU patient populations where cumulative calorie deficits were calculated, we observed lower calorie deficits.[14,26-28] The finding of such a calorie deficit is important to note, as three of the previous studies of general ICU patients reported negative outcomes associated with increased caloric deficits, and one reported no difference in a post hoc analysis of patients requiring renal replacement therapy. Importantly, the threshold for harm in relation to calorie deficit has not yet been determined in the general ICU population or specific subpopulations.

As with the general ICU population, there remain several important unanswered questions about the provision of nutrition therapy to adult ECMO patients. Unfortunately, indirect calorimetry, the gold standard for measurement of calorie use, is not accurate for use in patients receiving ECMO, thus making the determination of energy expenditure limited to estimation methods only.[29] Thus, clinicians have insufficient knowledge of the true requirements to target with nutrition therapy to achieve optimal patient outcomes in this population. It is also unknown if the metabolic and inflammatory effects of ECMO therapy have any significant effects on nutritional requirements. Somewhat surprisingly, we also found that calorie and protein delivery amounts in our study were at least as high as in other recent studies of the critically ill that did not focus specifically on the ECMO subpopulation.[9,26] Patients who receive ECMO therapy often require significant doses of sedative and vasoactive drugs, which are known to affect GI motility, so it could be hypothesised that a general ICU population (not including patients receiving ECMO therapy) may be easier to deliver nutrition to than those unwell enough to receive ECMO. In our study, EN was the most commonly used form of nutrition therapy. We found lower PN usage compared with other studies and, when delivered, it was nearly always delivered in combination with EN.[20,21,25]

EN was commonly interrupted due to fasting. This is a consistently reported barrier to the delivery of EN and ultimately contributes to increased caloric and protein deficit.[19] The second most common barrier to delivery of EN was elevated GRV. We did not collect information on individual GRV threshold policies at each site, but we collected the total daily (cumulative) GRV. The median total daily cumulative GRV appeared to be low, at 80 mL (IQR, 5–345 mL), although this included patients who were not intolerant of EN. Recent evidence has shown that tolerance of a higher GRV target or even not measuring GRV at all has minimal adverse consequences in the general critically ill population.[30,31] In our study, the most common reason for PN usage was "not tolerating EN". The only way we attempted to define this was via measurement of GRV (as is common in clinical practice). Therefore, it seems that the interpretation of EN tolerance and supplementation with PN was determined via subjective means, and that there were varying criteria between sites. Review of local procedures or policies on GRV management and ensuring consistency of practice may help prevent unnecessary interruptions to EN, reduce the caloric and protein deficits and reduce unnecessary use of PN.

The second most common reason for the provision of PN was GI bleeding (recorded for 24.3% of days PN was provided). GI bleeding is not unexpected in this population (who are mostly receiving therapeutic anticoagulation agents), but it is unclear if episodes of bleeding should be a contraindication to EN.

Our study showed lower use of 1 kcal/mL formulae and higher use of more protein-dense, concentrated formulae (1.25–2 kcal/mL) compared with previous studies in Australia and New Zealand.[32]

The use of propofol as a sedative was common in our study and it contributed significant calories intravenously. This may have two potential patient consequences; first, clinicians may reduce calories delivered to patients by nutrition therapy to account for the lipids delivered by propofol, and second, patients may receive large doses of lipids.[33] The impact this may have on patients is unknown.

Strengths and limitations

Our study was multicentre, prospective and the largest reported to date, but it has the limitations of an observational study design. To improve accuracy, we provided a structured data dictionary and predefined data collection forms to ensure systematic data collection methods. Data were collected by research coordinators and dietitians with research and clinical experience in the ICU. We did not expect patients receiving ECMO therapy to have received oral nutrition, alone or in combination with EN, so we cannot report the nutrition contribution once EN or PN was ceased and oral diet started. Also, no premorbid nutritional status information or outcome assessments were performed.

Conclusions

We observed that EN was the most commonly delivered mode of nutrition, and it was frequently interrupted because the patient was fasting for a therapeutic procedure or diagnostic intervention, or because of reported raised GRVs. Compared with estimated calorie and protein requirements, lesser but reasonably acceptable amounts were delivered to patients during ECMO treatment but a calorie and protein deficit still accrued daily over the study period. The effect of this on outcomes should be investigated further.

Competing interests

None declared.

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Appendix 1. The Australian and New Zealand nutrition therapy in adult patients receiving extracorporeal membrane oxygenation study principal investigators (PIs) and investigators

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