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Nutrition support during extracorporeal membrane oxygenation (ECMO) in adults: a retrospective audit of 86 patients

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Abstract *Purpose:* Extracorporeal membrane oxygenation (ECMO) is increasingly being used to support critically ill patients with severe cardiac and/or respiratory failure. It has been claimed that the resulting haemodynamic alterations, particularly in venoarterial ECMO, mean that enteral feeding is unsafe and/or poorly tolerated. This study aims to investigate this question and to identify any barriers to optimal nutrition. *Methods:* Data were retrospectively collected for 86 patients who received ECMO between January 2007 and July 2012 in a tertiary critical care unit/ECMO referral centre. All were fed using existing protocols that emphasise early enteral feeding in preference over parenteral or delayed enteral nutrition. *Results:* Thirty-one patients required ECMO for cardiac failure, and all of these received venoarterial ECMO; the remainder received venovenous ECMO. Enteral feeds started for all patients at average 13.1 h [standard deviation (SD) 16.7 h] after ICU admission, reaching goal rate on day 2.6 (SD 1.4). Thirty-three patients experienced significant feeding intolerance during the first 5 days, but of these 20 were managed effectively with prokinetic medications; 18 required parenteral nutrition to supplement inadequately tolerated tube feeds. Intolerance did not differ between ECMO modes. Overall patients tolerated 79.7 % of goal nutrition each day in the first 2 weeks. *Conclusions:* Enteral feeding can be well tolerated by patients who are receiving ECMO, whether in venovenous or venoarterial mode. ECMO should not exclude patients from receiving the well-documented benefits of early enteral feeding in critical illness.

Keywords Nutritional support ·
Extracorporeal membrane
oxygenation · Quality improvement

Introduction

Extracorporeal membrane oxygenation (ECMO) based on a modified heart–lung machine is increasingly being used to support critically ill patients with severe cardiac and/or respiratory failure. It has been claimed that the resulting haemodynamic alterations, particularly in venoarterial (VA) ECMO, which decreases pulsatile flow to the microcirculation and therefore reduces gut perfusion [1], may mean that enteral feeding is unsafe and/or poorly tolerated [2]. While pulsatile flow is better preserved in venovenous (VV) ECMO, gut dysfunction may also be exacerbated by ECMO generally, as it activates systemic inflammation, which could cause gut barrier dysfunction and allow bacterial translocation [3]. If this were the case, reduced feeding tolerance would be expected in all patients receiving ECMO, but more so in VA ECMO. However, there are limited published data on nutrition support in ECMO and no studies on the relative effects of VV and VA ECMO on gut function. Large ECMO studies

generally do not mention nutritional management [4–6], and it may not be correct to assume that patients were fully fed in these studies [7]. Scott et al. [2] reported on 27 patients in a Louisiana hospital who received veno-venous (VV) ECMO; 9 of these required sole or supplemental parenteral nutrition, and patients received 68 % of goal nutrition while on ECMO. Lukas et al. [8] reported on 48 patients in an Australian hospital (35 on VA ECMO, 13 on VV ECMO); 14 of the 48 patients required sole or supplemental parenteral nutrition, and overall patients received only 55 % of goal nutrition while they were on ECMO.

During the 2009 Southern Hemisphere winter, the influenza A (H1N1) epidemic led to an increase in the use of ECMO [9] (including patients retrieved on ECMO from other hospitals [10]). Existing nutrition protocols emphasise early enteral nutrition in preference over parenteral nutrition, but it was unclear to what extent this was being successfully implemented in these cases. This audit was conducted to assess the frequency of enteral nutrition intolerance amongst ECMO patients, to identify any barriers to successful nutrition delivery, and to investigate whether there is a difference between patients on VA ECMO and VV ECMO with regard to feeding tolerance.

Materials and methods

Data were collected retrospectively for all patients requiring VA or VV ECMO in a large Australian tertiary referral hospital/ECMO referral centre from January 2007 to July 2012. The local ethics committee advised that a formal ethics review would not be required. All patients in the study received nutrition support according to the unit's usual protocols, aiming to start nutrition support via nasogastric tube within 24 h of admission to the intensive care unit (ICU) and favouring enteral over parenteral nutrition whenever possible. Patients received aperients according to the unit's bowel management protocol [11]. Nutritional goals were set by the ICU dietitian as for the other patients in the ICU [12], estimating daily energy requirements using the Schofield equation [13] with stress factor adjustment (usually 1.1–1.2) according to the condition of the patient, and estimating daily protein requirements to be at least 1.2 g/kg body weight based on European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines [14].

The total nutritional intake for each day (including propofol calories) was recorded for the first 2 weeks of ICU admission or until oral nutrition was commenced, and totals were compared with nutritional goals. (Daily totals exceeding 100 % of goal were recorded as 100 %.) Where nasogastric enteral nutrition was not tolerated (defined as occurrence of two or more consecutive gastric aspirates of >200 mL in association with abdominal distension or discomfort), prokinetic agents were added per protocol, and post-pyloric feeding was considered. Supplemental parenteral nutrition was considered on day 3 of feeding intolerance after other measures had failed. When patients were tolerating nutrition at the goal rate and also receiving significant amounts of propofol, overfeeding was avoided by reducing the feed rate if propofol lipid was providing more than 250 calories/day or 15 % of the patient's total energy requirement (whichever was lower).

Descriptive measures were used to analyse data, expressed as mean (standard deviation) for normally distributed data and median [interquartile range (IQR)] for non-parametric data. Student's t test was used to compare groups with respect to continuous variables, and chi square was used to compare proportions. p-Value <0.05 was considered statistically significant. Analyses were performed using SPSS version 18.

Results

During the study period, 86 patients received ECMO: 31 who required ECMO for cardiac indications and received VA ECMO, and 55 who received VV ECMO for respiratory indications. Of the latter, 19 were existing inpatients of the hospital and 36 were retrieved from other hospitals on VV ECMO after median 5 (IQR 3–9) days' admission at the previous hospital. There were also 3 patients retrieved on VA ECMO (see Table 1 for demographic details for all patients). There were 53 patients with a two-cannula configuration, 21 with three cannulae, and 12 with a bi-caval dual-lumen cannula. Thirteen of the 55 (24 %) patients on VV ECMO died in ICU, compared with 20 of the 31 (65 %) patients on VA ECMO ($p < 0.001$).

All patients were started on enteral feeds initially, and only two did not reach goal feed rate. Time from ICU admission to starting nasogastric feeds was average 13.1 h (SD 16.7 h), reaching goal rate on day 2.6 (SD 1.4) (see Table 2 for details of nutrition and clinical management of the patients). Bowel management systems (such as rectal tubes) were used for 34 (40 %) patients, and overall 69 patients received laxatives. In 33 patients (38 %), significant feeding intolerance occurred during the first 5 days; in 20 patients this was managed effectively with prokinetic medications according to the existing ICU enteral feeding protocol. No patients received post-pyloric feeding. Eighteen patients received parenteral nutrition to replace or supplement poorly tolerated enteral feeding, but 10 of these were able to be re-established on sole enteral nutrition within 4 days. There was no significant difference between ECMO modes in incidence of feeding intolerance ($p = 0.40$) or use of

Table 1 Patient demographics

Age, years [mean (SD)]	44.4 (15.9)
Gender (number, male:female)	50:36
Nutritional status, SGA (number A:B:C)	78:4:4
APACHE II score [mean (SD)]	26.0 (7.2)
Mode of ECMO (number, VV:VA)	55:31
Indication for ECMO (*n*):	
Influenza A (H1N1)	18
Other infectious respiratory failure	24
Other respiratory failure	13
Cardiac failure: surgical	22
Cardiac failure: medical	6
Chest trauma	3
ECMO days [median (IQR)]	7 (4–13)
Dialysis days [median (IQR)]	0 (0–8)
Ventilator days [median (IQR)]	13 (8–27)
ICU days [median (IQR)]	17 (10–39)
ICU mortality (*n*, %)	27 (32 %)
Hospital days [median (IQR)]	25 (13–39)

SGA subjective global assessment of nutritional status (*A* well nourished, *B* mild or moderately malnourished, *C* severely malnourished), *APACHE* Acute Physiology and Chronic Health Evaluation

parenteral nutrition ($p = 0.96$). Patients who received continuous renal replacement therapy (CRRT) during their first 14 days on ECMO started feeds significantly later [19.2 (21.4) h after ICU admission compared with 9.0 (11.2) h, $p = 0.02$], had longer time to first bowel motion [23.3 (37.7) days compared with 4.2 (2.5) days, $p = 0.002$], and experienced more feeding intolerance ($p = 0.03$). Overall patients tolerated an average of 79.7 % of daily energy goal and 73.0 % of daily protein goal each day in the first 2 weeks on ECMO.

There were several significant associations between outcomes and successful nutrition delivery (Table 3).

Improved nutrition delivery was associated with longer hospital stay and longer time on ventilation and ECMO, with a non-significant trend towards longer length of stay in ICU. All of these differences became insignificant when only survivors were included in the analysis, but the direction of the trend remained the same. The same relationships were observed when energy and protein intakes were analysed separately.

Figure 1 shows daily energy and protein intakes for VA and VV ECMO patients during the first 2 weeks of ICU admission. Protein input lagged significantly behind energy input in VV ECMO patients, and this was mainly associated with the use of low-volume feed formula (which is relatively low in protein) and with high-rate propofol infusions (which provide energy but not protein). Propofol contributed significantly to energy input, requiring a reduction in feed rate, for 72 patients (81.6 %) and provided more than 1,670 kJ (400 Cal) in a single day in the case of 32 patients. Patients on more than 100 mL per day of propofol (daily average for the first 14 days on ECMO) received an average of 65 % of goal protein, compared with the other patients who received 76 % ($p = 0.03$). Fluid restrictions were imposed on the feeding regimen for 68 patients (77.6 %). When patients with two cannulae versus three cannulae were compared, there was no significant difference in incidence of fluid restrictions being placed on nutrition regimens ($p = 0.224$). VV ECMO patients with the bi-caval dual-lumen cannula were less likely to be fluid-restricted than those with two or three conventional cannulae ($p = 0.028$). There was no difference in total average fluid balance between the different cannula configurations, over the first 14 days on ECMO. Patients with high positive fluid balances had significantly higher mortality

Table 2 Nutritional and clinical management during the first 14 days on ECMO

	All patients, $n = 86$	VA ECMO, $n = 31$	VV ECMO, $n = 55$	
Time to start nutrition, h	13.1 (16.7)	32.2 (21.8)***	6.3 (6.1)	
Time to reach goal nutrition rate, days	2.6 (1.4)	4.0 (1.4)***	2.2 (1.0)	
Time to reach 24 uninterrupted hours at goal rate, days	4.3 (1.8)	5.3 (1.5)*	4.0 (1.7)	
Patients experiencing intolerance, *n* (%)	33 (38 %)	14 (45 %)	19 (35 %)	
Time to first bowel motion, days	4.6 (2.5)	6.7 (2.5)***	4.0 (2.2)	
Mean daily total energy intake, Cal	1,594 (628)	1,058 (713)***	1,608 (584)	
Mean daily energy from propofol, Cal	130 (124)	70 (103)***	135 (129)	
Mean daily protein intake, g	58 (29)	54 (33)***	59 (26)	
Mean daily fluid balance in first 7 days, mL	+850 (1,475)	+1,134 (1,771)	2 cannulae	+903 (832)
			3 cannulae	+319 (1,462)
			Bi-caval cannula	+600 (1,053)
Paralysis, days in first 14 days	3.8 (3.7)	2.2 (2.0)*	3.8 (4.0)	
Sedation, days in first 14 days	9.0 (4.5)	3.9 (8.6)*	10.0 (4.2)	
Dialysis, days in first 14 days	3.7 (5.4)	4.9 (5.4)	3.3 (5.4)	
Serum albumin, g/L	29 (7)	25 (5)***	31 (7)	

All values expressed as mean (SD) for all values over the first 14 days unless otherwise indicated

* Significant difference between VA and VV groups, $p < 0.05$

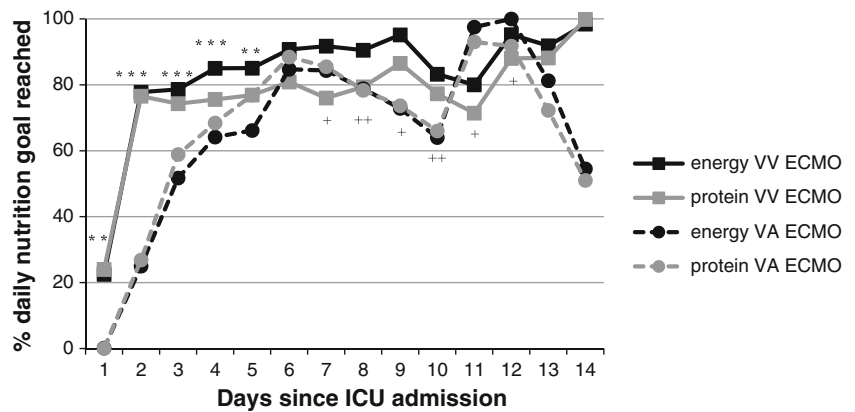** Significant difference between VA and VV groups, $p < 0.01$

*** Significant difference between VA and VV groups, $p < 0.001$

Table 3 Association between outcomes and successful nutrition delivery during the first 14 days on ECMO

	Mean daily nutrition delivery		p
	≥80 % of goal	<80 % of goal	
Number of patients	52	34	
APACHE II score [mean (SD)]	25.7 (7.7)	26.5 (6.3)	0.674
Time to start nutrition, h [mean (SD)]	5.4 (3.8)	22.0 (21.5)	<0.001
Time to reach goal nutrition rate, days [mean (SD)]	2.1 (1.0)	6.7 (20.4)	0.069
Time to reach 24 uninterrupted hours at goal rate, days [mean (SD)]	3.9 (1.6)	14.6 (33.0)	0.008
Patients experiencing enteral feeding intolerance* [n (%)]	14 (27 %)	19 (56 %)	0.046
Time to first bowel motion, days [mean (SD)]	3.8 (2.2)	20.3 (37.9)	<0.001
Patients receiving parenteral nutrition [n (%)]	10 (19 %)	11 (32 %)	0.083
ECMO days [median (IQR)]	9 (6–15)	5 (4–7)	<0.001
Ventilator days [median (IQR)]	25 (11–28)	9 (5–13)	0.010
ICU days [median (IQR)]	27 (16–36)	11 (7–28)	0.103
Hospital days [median (IQR)]	34 (22–47)	23 (9–36)	0.043
Mortality [n (%)]	8 (15 %)	19 (56 %)	0.017

* Intolerance defined as any vomiting, abdominal distension or large gastric aspirates resulting in an actual decrease in enteral feed rate

Fig. 1 Energy (note energy totals include calories from propofol) and protein intakes during ECMO

* Significant difference between VA and VV groups, p<0.05

** Significant difference between VA and VV groups, p<0.01

*** Significant difference between VA and VV groups, p<0.001

+ Significant difference between energy and protein within VV group, p<0.05

++ Significant difference between energy and protein within VV group, p<0.01

($p = 0.002$), but there were no other significant differences in outcome. Patients with higher positive fluid balance received 69 % of their nutritional goals, compared with 83 % in patients with low or negative average fluid balance ($p = 0.007$), mostly due to fluid restrictions being imposed on the feeding regimen rather than intolerance—there was no significant difference in the incidence of intolerance ($p = 0.35$). Use of paralysis and sedation did not appear to affect feeding tolerance significantly in terms of time to reach goal rate ($p = 0.40$), incidence of intolerance in the first 5 days ($p = 0.91$) or time until first bowel motion ($p = 0.35$).

Discussion

There appears to have been uncertainty about the feasibility of providing adequate nutrition during ECMO. This study shows that adequate nutrition can be provided during ECMO, with about 80 % of nutritional goals being met each day in the first 2 weeks on ECMO. Early commencement of enteral nutrition appears to be associated with greater success in meeting these nutritional goals. The surprising trend towards longer time on ventilator and ECMO amongst these patients may simply reflect the increased nutrition delivery seen after the first

few unstable days, resulting in higher average tolerance the longer the patient remains ventilated.

Uncertainty about nutrition in ECMO may be because the use of VA neonatal ECMO traditionally involved paralysis and/or heavy sedation, which may have affected gut function, in addition to the effect of VA ECMO itself, which might be expected to reduce perfusion of the gut. Additionally, the function of the earlier style of microporous membrane oxygenators was impaired by the use of IV lipid infusion [15] [this does not appear to be a problem with the new generation of diffusional (polymethylpentene) membrane oxygenators used during the data collection period of this study]. For an ECMO retrieval service, the concern may be that patients could have prolonged hypoxia or a low cardiac output state in the peripheral hospital for several days before retrieval, which could impair gut function and promote intolerance to enteral feeding. During VV ECMO, the use of very large volumes of intravenous fluid to maintain high flow rates can cause generalised oedema that may involve the gut and reduce absorption and motility. (As airway pressure is reduced, the venous congestion of the bowel would be expected to resolve, and feeding tolerance to improve.)

In this study, none of these concerns were confirmed, with nutritional goals being met in similar time-frames to the ICU as a whole, but other obstacles to adequate nutrition were identified. Paralysis and sedation did not appear to affect tolerance of enteral feeding, and large positive daily fluid balances were not associated with decreased feeding tolerance even early in the ECMO period, although patients with high positive fluid balance did receive significantly less nutrition during their first 2 weeks on ECMO. The real nutritional effect of the extra fluid volume was that it led to restriction of other fluids (including nutrition). With this restriction, the choice of enteral feed formula is limited to the available low-volume products that are relatively low in protein and micronutrients, sometimes being delivered deliberately at a rate below target. To meet patients' needs in this situation, new products are required that provide higher amounts of protein and micronutrients in a low-volume formula.

An additional barrier to adequate nutrition is the use of propofol for sedation. This was particularly noted in the H1N1 cohort. In these relatively young and often obese patients with single-system organ failure, propofol clearance rates were increased [16–18] and very high infusion rates were required to achieve adequate sedation. The lipid content of the propofol in some cases exceeded the patient's total daily lipid requirement, solely as soybean oil, which would not normally be a first-line choice for the fat source in critical illness [19]. Over 80 % of patients had their nutrition regimen changed to avoid overfeeding due to the additional energy provided by propofol. As propofol contains neither protein nor micronutrients, this strategy necessarily reduced the nutritional value of their feeding regimen. High-protein nutrient-dense feed formulae (1 Cal/mL with 63 g protein per 1,000 Cal, providing complete micronutrients in 930 Cal) allow patients' protein and micronutrient needs to be met despite a reduction in feed rate, but when these patients are also fluid-restricted they are typically receiving a low-volume feed formula, which is relatively low in protein (2 Cal/mL with 42 g protein per 1,000 Cal, providing complete micronutrients in 1,680 Cal). The lower-protein formula cannot fully meet their nutritional needs, and the situation is exacerbated when the rate is further reduced because of the high-rate propofol. Patients receiving parenteral nutrition could be changed to a fat-free solution, but there is no comparable strategy for fluid-restricted patients who are enterally fed. To avoid this problem, the use of alternative calorie-free sedatives would be recommended. It has recently been appreciated that fentanyl, otherwise very commonly used in ICU, cannot be used during ECMO due to drug loss by adsorption in the polyvinyl chloride (PVC) tubing of the ECMO circuit [20]. Morphine and midazolam, which do not appear to experience adsorption to the same extent [20], are an alternative that should be considered.

Comparisons between VV ECMO and VA ECMO highlight the effects of these barriers to feeding. A clear difference is seen between the two groups, with VV ECMO patients reaching nutritional goals earlier. This may have been due to the high number of ECMO retrievals in this group, who were stabilised on ECMO at the source hospital prior to transfer, and were therefore ready to start feeds on arrival. In contrast, feeding was not commenced early in the VA ECMO patients as the majority of these (22 out of 31 patients) were post-surgical and often unstable initially on arrival to ICU, and were anticipated to require a relatively brief duration of ECMO support as a bridge to recovery in all cases. Nutrition support may therefore have been commenced only in those patients who failed to progress as expected.

Once enteral feeds were established, however, there was a clear difference in protein intakes between the VA and VV groups, with VV ECMO patients receiving significantly less protein. This may have been due to the greater use of propofol and fluid restriction in the VV ECMO cases. VV ECMO patients are more likely to be very heavily sedated in order to optimise ventilation and minimise oxygen consumption as well as to protect the integrity of the circuit; they are also more likely to be fluid-restricted.

The main finding is that it was possible to start enteral feeds early and achieve reasonable tolerance using standard feeding protocols, in both VA and VV ECMO patients. The patients in this study achieved a higher proportion of nutritional goals than in previously published series. However, some of this difference might be

due to the energy contribution from propofol, which was accounted for in this study but not stated in other published studies [2, 8].

Conclusions

Enteral feeding can be well tolerated by patients who are receiving ECMO. Feeding success was not significantly affected by the mode of ECMO support, although this finding should be interpreted with caution, given the relatively small number of VA cases in this study. ECMO should not exclude patients from receiving the well-documented benefits of early enteral feeding in critical illness. There is room for improvement in managing feeding intolerance, and in meeting patients' protein and micronutrient requirements when there are constraints such as fluid restriction and significant energy contribution from high-rate propofol infusion.

Conflicts of interest None of the authors had any conflict of interest to declare.

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