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LETTER

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Long-term survival after extracorporeal life support in children with neutropenic sepsis

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Dear Editor,

Extracorporeal life support (ECLS) is an established intervention for paediatric patients with cardiorespiratory failure failing conventional therapy. Malignancy was historically regarded as a contraindication to ECLS, but analyses of the Extracorporeal Life Support Organization registry demonstrated that ECLS could be appropriate in carefully selected patients [1, 2]. Neutropenic sepsis that complicates chemotherapy has also been regarded as a contraindication to ECLS because of the uncertain long-term prognosis and vulnerability of these children to nosocomial infection. However, there are minimal data on the use of ECLS for this indication. We reviewed our institutional experience of children with febrile neutropenia receiving ECLS.

The study was approved by the institutional review board and waiver of informed consent was granted. A retrospective chart review was conducted on all paediatric patients with known malignancy commenced on ECLS at the Royal Children's Hospital, Melbourne, Australia, from 1993 to 2014. Our approach to ECLS has been described elsewhere [3]. In brief, ECLS is instituted in patients with both potentially curable malignancy and reversible shock deemed refractory to all other forms of pharmacological and ventilator management.

Fourteen paediatric patients with malignancy underwent ECLS over this time period, nine of whom were neutropenic at the time of ECLS cannulation. Eight (88 %) of the nine neutropenic patients were cannulated onto venoarterial ECLS and 4 (44 %) survived to hospital discharge (Table 1). The mean duration of ECLS was 117.6 h (SD 66.8 h). Major complications were as follows: 2 (22 %) patients developed new infection on ECLS, 5 (55 %) patients had significant bleeding at the cannulation site, 1 (11 %) developed intracranial infarction, and 6 (67 %) required continuous renal replacement therapy.

Of the four children who survived to hospital discharge, only 2 (22 %) were alive at a mean follow-up time of 4.2 years (range 0.7–10). One suffers from left foot drop but both have otherwise completely recovered and attend school. One of the initial survivors later died of sepsis and one died of recurrent malignancy. The survivors were all from the most recent decade, 2005–2014. Over this same period, another 113 children with neutropenic sepsis and malignancy were admitted to our ICU. Fifty per cent of those treated with mechanical ventilation, inotropes and haemofiltration survived to hospital discharge, compared to 71 % treated with ventilation and inotropes, and 96 % who did not require any of these therapies.

This report suffers from a number of obvious limitations, including small sample size, retrospective design, and only providing data from a single centre. Nonetheless, it highlights that although the standard outcome measure in ECLS—survival to hospital discharge—can seem encouraging in children with malignancy [1], longer-term outcomes may be bleaker. However, our results also support the view that neutropenic sepsis is not an absolute contraindication to ECLS and that, as mortality and morbidity in critically ill children with malignancy improve overall [4, 5], it is possible to restore a minority of children with these conditions back to full health. Further research into this area should focus on the quality of life in survivors.

Table 1 Characteristics of febrile neutropenic patients on ECLS

Diagnosis	$N = 9$	Demographics	Median	IQR
ALL	4	Age (years)	9	5–11
AML	1	Weight (kg)	28	15–38
B cell lymphoma	2			
Rhabdomyosarcoma	2	Pre-ECLS variables		
Auto-HSCT	1	Duration of mechanical ventilation (h)	6.0	3.1–24
Chemotherapy pre-ECLS	9	pH	7.28	7.18–7.29
Indication for ECLS		PaO_2 [kPa (mmHg)]	9.4 (71)	7.4–13.6 (56–102)
Respiratory failure	1	$PaCO_2$ [kPa (mmHg)]	6.8 (51)	5.2–9.3 (39–70)
Shock	7	Oxygenation index	19	9.5–44.5
Cardiac arrest	1	Mean airway pressure (cmH_2O)	17.6	12.6–19
Source of sepsis		Vasoactive inotrope score	75	32.5–190
Gram-negative bacteria	4	PIM 3 score	0.24	0.18–0.43
Viral	2	Neutrophil count at cannulation ($\times 10^9$/L)	0.11	0–0.26
Fungal	1	Duration of neutropenia pre-ECLS (days)	3.0	1.8–5.3
No organism identified	2	Platelet count at cannulation ($\times 10^9$/L)	65	25–125
Cause of death	7			
On ECLS		Duration (h)		
Worsening shock	2	ECLS	120	93–161
Multiorgan failure	1	ICU	277	120–335
Extracranial haemorrhage	1	Hospital	441	121–964
Failure of myocardial recovery	1			
After hospital discharge				
Recurrent malignancy	1			
Sepsis	1			

Vasoactive inotrope score = dose of dopamine (μg/kg/min) + dose of dobutamine (μg/kg/min) + 100 × dose of adrenaline (μg/kg/min) + 100 × dose of noradrenaline (μg/kg/min) + 10 × milrinone dose (μg/kg/min) + 10,000 × dose of vasopressin (U/kg/min)

ECLS extracorporeal life support, *IQR* interquartile range, *ALL* acute lymphoblastic leukaemia, *AML* acute myeloid leukaemia, *HSCT* haemopoietic stem cell transplant, *ICU* intensive care unit, *PIM* paediatric index of mortality

Compliance with ethical standards

Conflicts of interest On behalf of all authors, the corresponding author states that there is no conflict of interest.

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