

Long-distance transport of critically ill children on extracorporeal life support in Australia

Armando Perez, Warwick W Butt, Kenneth J Millar, Derek Best, Timothy Thiruchelvam, Andrew D Cochrane, Martin Bennett and Lara S Shekerdeman

Extracorporeal life support (ECLS) has been used at the Royal Children's Hospital, Melbourne, Australia, to treat patients with severe but potentially reversible cardiac and pulmonary disorders for the past 18 years. The Hospital currently has the only paediatric intensive care unit (PICU) in Australia that routinely offers non-postcardiotomy ECLS to infants and children; thus, a small number of patients from ICUs around Australia are referred annually to this ICU to receive ECLS for cardiac or pulmonary disease. The closest interstate PICU is 750 km from Melbourne. Fortunately, most children are in a sufficiently stable condition for conventional transport to the Royal Children's Hospital by a specialist retrieval team. However, on occasions, the likelihood of profound haemodynamic or pulmonary instability and death during a potentially lengthy transport may render transfer before ECLS unfeasible.

Since September 2003, we have offered "mobile ECLS" for children with severe cardiac or pulmonary disease who have been referred to the Hospital for ECLS from ICUs within Victoria or interstate, but whose condition is too unstable for conventional transport. We report our experience to date with mobile ECLS in infants and children.

Methods

The study was a retrospective review of all children who were transported on ECLS to the Royal Children's Hospital, Melbourne, from the inception of the mobile ECLS service in 2003 to 2007.

Results

Patients and criteria for ECLS

Eight children with intractable cardiac or respiratory failure underwent cannulation for ECLS at the referring hospital and were transported on ECLS to the Royal Children's Hospital between 2003 and 2007. They were aged from 1 day to 8 years (mean age, 27 months). All would have been considered suitable candidates for ECLS had they already been at the Royal Children's Hospital. They had potentially reversible, single-organ injury, and none had any known contraindication for ECLS, such as hypoxic brain injury or intracerebral haemorrhage. No patient had received cardi-

ABSTRACT

Background: The Royal Children's Hospital, Melbourne, Victoria, provides extracorporeal life support (ECLS) for infants and children from all around Australia. Since 2003, we have offered a mobile ECLS service to retrieve critically ill children whose condition is too unstable for conventional transport. The retrieval team comprises a paediatric intensive care unit specialist, an ECLS nurse specialist, a perfusionist and a cardiac surgeon.

Patients and methods: Retrospective review of eight children (aged between 1 day and 8 years) who were transported on ECLS to the intensive care unit at the Royal Children's Hospital, Melbourne, between 2003 and 2007.

Results: Seven patients underwent cannulation by our team in the referring ICU, and one underwent cannulation by the referring centre before our retrieval team arrived. Seven children were placed on ECMO (veno-venous in two, veno-arterial in five), and one was placed on a left ventricular assist device. Five children were retrieved from interstate ICUs by air, and three were transported from a metropolitan ICU by road. The median distance from the referral centre to Melbourne was 803 km, and the median duration of retrieval was 13 hours. Median duration of ECLS was 270 hours. Five patients survived to hospital discharge. There were no adverse outcomes related to transport.

Conclusions: This is the first report of ECLS transport in Australia. In our experience, children who would not otherwise be transportable can be safely transported long distances on ECLS, and should be offered this if appropriate resources exist. However, this approach should not replace the timely referral of patients who are likely to need ECLS.

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opulmonary resuscitation for more than 5 minutes before referral, and a clinical judgement was made as to whether the patient's condition was likely to remain sufficiently stable from the time of referral to the time of cannulation for ECLS. For example, the minimum interval between referral of an interstate patient and cannulation by the Royal Children's Hospital team is about 6 hours.

Table 1. Patient demographics, details of extracorporeal life support, diagnoses and outcomes

Patient (age)	Referral diagnosis	Premorbid condition	Pre-ECLS ventilation (h)	Other pre-ECLS treatment	ECLS mode for transport	Retrieval duration (h)	Retrieval distance (km)	Outcome	Cause of death	ECLS duration (h)	Final diagnosis
1 (2.1 years)	Myocarditis	None	33	CPR 2 min	V–A	14	732	Survived		186	Influenza A myocarditis
2 (0.3 years)	ARDS	None	528	HFOV, iNO	V–V	16	1671	Died	Failure to wean	1217	Not known
3 (8.4 years)	ARDS heart failure	Bone marrow transplant	149	HFOV, iNO, inotropes	V–A	12	874	Died	Intra-cerebral bleed	410	Probable graft versus host disease
4 (0.5 years)	Myocarditis	None	50	High-dose inotropes	LVAD	19	1671	Survived		468	Cytomegalovirus myocarditis
5 (6.3 years)	Pneumonitis	None	137	HFOV	V–V	14	874	Died	Septic shock	238	BOOP
6 (5 days)	PPHN (MAS)	None	115	HFOV, iNO, inotropes	V–A	6	35	Survived		86	PPHN
7 (2 days)	PPHN (MAS)	None	32	HFOV, iNO, inotropes	V–A	6	35	Survived		301	PPHN
8 (1 day)	Heart failure	Not known	22	High-dose inotropes	V–A	7	35	Survived		211	Cardiomyopathy

CPR = cardiopulmonary resuscitation. V–A = veno–arterial. ARDS = acute respiratory distress syndrome. HFOV = high frequency oscillatory ventilation. iNO = inhaled nitric oxide. V–V = veno–venous. LVAD = left ventricular assist device. CMV = cytomegalovirus. BOOP = bronchiolitis obliterans organising pneumonitis. PPHN = persistent pulmonary hypertension. MAS = meconium aspiration syndrome.

Indications for ECLS

Diagnoses at the time of referral are shown in Table 1. Five children were supported for severe respiratory failure, and three for severe cardiac failure and shock. At the time of referral, the underlying diagnoses were hypoxic respiratory failure, pulmonary hypertension and right heart failure secondary to severe meconium aspiration syndrome (2); severe acute respiratory distress syndrome (ARDS) of uncertain aetiology (2); severe ARDS and myocardial dysfunction after bone marrow transplantation (1); acute heart failure due to fulminant myocarditis (2), and uncertain aetiology (1). The initial modes of support were veno–venous extracorporeal membrane oxygenation (ECMO) in two, veno–arterial ECMO in five, and a left ventricular assist device (LVAD) in one.

Patient locations at the time of referral

At the time of referral for ECLS, all patients were being cared for in tertiary paediatric (5) or neonatal ICUs (3), in metropolitan Melbourne (3), Sydney (2), Brisbane (2), and Adelaide (1). Distances from these interstate PICUs to Melbourne are shown in Table 1.

The mobile ECLS team

The Royal Children's Hospital ECLS team comprises a senior PICU physician, an ECLS nurse specialist, a perfusionist and a cardiac surgeon. Cannulation for ECLS was performed by

our team at the referral hospital in all but one patient. In Patient 5, vascular cannulation for ECMO was performed by local cardiac surgeons, and the patient was maintained at the referral hospital for 24 hours until the appropriate personnel were available for the retrieval.

Transport details

Three children were transferred on ECLS by road ambulance from a tertiary neonatal ICU located approximately 35 km from the Royal Children's Hospital. Interstate transfers required road transport from the referral hospital to an aeromedical base, and air transport between states. The ECLS team flew from Melbourne to the interstate ICUs by fixed wing air ambulance (3) or commercial flights (2), and returned to Melbourne by air ambulance in all cases. The weight of additional equipment required specifically for ECLS retrieval was 45–60 kg, which included cases suitable for commercial airliners. The weight (and size) limitation for the air ambulance vehicles meant that all personnel could not accompany the retrieval team on all return journeys (see Cover). Thus, on two occasions, a team member returned separately to Melbourne on a commercial flight.

The median distance for retrievals was 803 km (interquartile range [IQR], 35–1273 km). The furthest interstate retrieval was from a hospital in Brisbane, 1671 km from Melbourne. The median duration of the retrievals was 13 hours (range, 6.5–15 hours). In one instance, a refuelling

stop was necessary during a return flight from Brisbane, which imposed an additional 2-hour delay. For individuals who could not accompany the ECLS team because of weight restrictions, the return to Melbourne was delayed by a further 6–8 hours.

Technical aspects of ECLS

Vascular access: All children had an indwelling arterial line and central venous line for invasive monitoring and blood sampling.

Cannulation for ECLS: The initial cannulation for ECMO patients was peripheral in all patients (neck, or neck-groin cannulation). Cannulation for LVAD support involved a midline sternotomy. Adequate veno–arterial ECMO support for cardiac failure was initially achieved without the need for left atrial decompression.

Circuit: The Jostra Rotoflow centrifugal pump was used for all patients for ECMO and LVAD support, with 1/4-inch or 3/8-inch tubing as appropriate. A blood-prime was used for all patients. For six of the ECMO patients, Jostra Quadrox D hollow-fibre oxygenators (Maquet, Hirrlingen, Germany) were used. For Patient 8, a Dideco Lilliput 2 infant ECMO oxygenator was used (Sorin Group, Mirandola, Italy).

Monitoring: All children had a chest x-ray following cannulation, to check the position of cannulas. A complete set of blood tests (full blood count, electrolyte and lactate concentrations, coagulation screen, and, if available, activated clotting time) were performed, and any significant abnormalities were corrected before the child left the referring hospital.

The circuit inlet and outlet pressures were measured after cannulation to confirm adequacy of the circuit. During transport, arterial blood pressure, heart rate, oxygen saturations and temperature were continuously monitored, and hourly blood gas analysis was performed (i-Stat, Abbott, Australia).

Medications

Vasoactive drugs: Patients placed on veno–arterial ECMO were all receiving high doses of inotropic agents before cannulation. In general, these were weaned before the patient left the referring hospital, and a low-dose dobutamine infusion (up to 5 µg/kg/min) was continued for transport. Systemic hypertension was treated with an intravenous infusion of sodium nitroprusside.

Anaesthetic drugs: Incremental doses of fentanyl (10–50 µg/kg) were given before cannulation, and sedation was maintained with intravenous morphine and midazolam infusion. Muscle relaxation was maintained (bolus pancuronium, 0.1 mg/kg) until stabilisation in our PICU.

Anticoagulation: Heparin was given to all children just before cannula insertion (100 units/kg), and thereafter hourly as a bolus (15 units/kg) until arrival in the Royal Children's Hospital PICU.

Ventilation during transport

All children were ventilated for transport using a Newport transport ventilator (Newport, Flight Medical Ltd, Calif, USA). Those receiving ECMO were on standard rest settings (pressure 20/10 cmH₂O; rate, 10 breaths per minute; and FiO₂, 0.21). The child receiving LVAD support was continued on full positive pressure ventilation (pressures 24/6 cmH₂O; rate, 25 breaths per minute; and FiO₂, 0.5) for the duration of the transfer.

Complications

The potential for transport-related complications is likely to be highest during transfer of the ECLS patient from bed to trolley and vice versa. Air transport requires a child to be lifted and transferred between bed and trolley four times:

- From hospital bed (referring hospital) to ambulance trolley;
- From ambulance trolley to aircraft stretcher;
- From aircraft stretcher to ambulance trolley; and
- From ambulance trolley to hospital bed.

On one occasion, the pump console fell from the trolley during transfer to an ambulance stretcher. Hand-pumping was immediately initiated and continued for about 35 minutes while the console was checked and re-secured. There was no adverse outcome from this event. One transfer from the referring hospital to the air ambulance was delayed by 2 hours because of incompatibility of the power source voltages between our own transport equipment and those of the interstate ambulance. However, an alternative vehicle was dispatched, and the transfer was subsequently uncomplicated. This did not result in any patient-related morbidity. There were no other adverse events related to transfers.

Subsequent clinical course

All patients were clinically stable throughout transfer, and activated clotting times on arrival at the Royal Children's Hospital were within the desired range (140–180 s).

Early re-interventions

Patients 1 and 3 had echocardiographic evidence of significant left atrial and ventricular distension on arrival in Melbourne, and underwent left atrial decompression. In both, a myocardial biopsy was also performed during this procedure.

Patient 4 developed worsening right ventricular dysfunction during the first 48 hours after retrieval, and was therefore converted from LVAD support to veno–arterial ECMO.

Outcomes (Table 1)

The median duration of ECLS was 270 hours (IQR, 200–439 hours). Five children survived to discharge from the Royal Children's Hospital. When in a sufficiently stable condition following decannulation, these patients were transferred to their "parent" neonatal or paediatric ICUs. All five were subsequently discharged home.

Three children died, including the two who initially received veno-venous ECMO. Patient 2 was supported on ECMO for 50 days, and all diagnostic tests, including lung biopsy, were inconclusive as to the underlying cause of ARDS. Empirical therapy with broad-spectrum antimicrobials, corticosteroids, and latterly immunosuppression did not appear to alter the disease course. The infant was ultimately decannulated from ECMO with high frequency oscillation and inhaled nitric oxide, but developed progressive hypoxia, and died within a few hours of decannulation.

Patient 3, whose early progress was complicated by worsening myocardial function, showed gradual cardiorespiratory improvement from Day 12 of ECMO onwards. However, on Day 17 of support, this patient developed fixed and dilated pupils. Urgent computed tomography confirmed an extensive intracerebral haemorrhage, and treatment was withdrawn.

Patient 5, with histological bronchiolitis obliterans organising pneumonitis developed septic shock caused by a *Pseudomonas* sp, and was converted to veno-arterial ECMO on Day 8 of admission. Despite this, the patient developed multi-organ failure and died on Day 10 of ECMO.

Discussion

ECLS has been a recognised mode of providing cardiac and/or pulmonary support in infants and children for three decades. ECMO has an established role in the management of acute hypoxaemic respiratory failure in newborn infants, and in the treatment of respiratory and cardiac disease in all age groups.^{1,2} A successful ECLS program requires substantial resources and expertise, as well as institutional and government support. Ad hoc or occasional ECMO in children is provided in cardiac surgical centres around the world, mostly for patients who cannot be separated from cardiopulmonary bypass or require circulatory support early after surgery for congenital heart disease. However, an ECLS program requires a service which extends beyond occasional ECMO, to include the more proactive support of infants and children with acute heart failure and cardiogenic shock, severe respiratory failure, systemic sepsis and shock. Most paediatric ECLS centres therefore offer ECLS to a broad referral base, and in Melbourne this potentially includes all of Australia.

Many ECLS specialist teams are familiar with the occasional scenario when a child is referred for ECMO from a peripheral hospital — located a road or an air trip away — but is deemed "too unstable" for transport either for respiratory reasons (the need for high pressure oscillation, pneumothorax or worsening hypoxaemia) or for cardiovascular reasons (escalating inotropes or arrhythmias). Adding to the dilemma is the fact that had these children been in the Royal Children's Hospital, they would have been supported with ECLS. Historically, many of us have been unable to offer the medical assistance required to keep these patients alive. However, the introduction of a mobile ECLS service has enabled us to offer this therapy to a handful of infants and children who would otherwise have died.

We are not the first group to offer mobile ECLS to paediatric patients.^{3,4} However, this is the first cohort of children to be reported from Australia.

When introducing a mobile ECLS service, a number of factors must be considered that are beyond the scope of a conventional paediatric emergency transport service. These include the number of senior personnel required, including a cardiac surgeon and perfusionist, and the fact that ECLS retrievals are lengthy and generally exceed a standard "shift" or working day. For interstate retrievals, personnel are frequently required to be awake for more than 24 hours (given that most retrievals are undertaken, at short notice, during a clinical shift), and require additional rest time after returning. The retrieval team at our PICU is staffed from the existing internal resources. Thus ECLS retrievals deplete the number of senior staff in-house for a considerable period of time, and, given the emergency nature of these retrievals, arranging alternative cover is not usually possible.

We would not advocate delaying ECLS in patients whose cardiopulmonary function is deteriorating and who are thought likely to require ECLS. Early referral to a specialist centre may, in some cases, avoid the need for ECLS during transport, and could potentially increase the likelihood of a successful outcome. However, it is clear that the patients we report had all experienced rapid deterioration in cardiac or respiratory function, and many were located several hours from our centre by air. The judgement of senior clinicians at the time of referral was that safe transfer would not be feasible without ECLS.

It is clear, even from this small cohort of patients, that the criteria for ECLS are changing and becoming much broader. Not long ago, patients with haematological or oncological disease were considered unsuitable for ECMO. However, ECMO is a recognised therapy for ARDS or severe pneumonitis in carefully selected patients who are immunosuppressed.^{5,6} The children in our series were considered to have potentially reversible disease, either with a predictable natural history (eg, acute myocarditis and severe meconium

aspiration), or without an absolute contraindication (ARDS of uncertain aetiology and neonatal heart failure). Patient 2 had received high-pressure positive pressure ventilation for 3 weeks before transfer and had severe parenchymal lung disease, which would have been considered by some practitioners to be a contraindication for ECMO. However, it is widely accepted that the criteria for veno-venous ECMO are becoming broader, and we did not consider this factor in isolation to contraindicate ECMO. Indeed, we recently reported successful weaning from ECMO in an older child with interstitial lung disease, who had severe ventilator-induced lung injury after a similar period of positive pressure ventilation.⁷ Given that the infant in our current series had no known underlying chronic condition or a diagnosis that precluded recovery, we chose to offer ECMO — while acknowledging the guarded prognosis and likely need for a prolonged period of support — to allow lung rest and recovery in an infant with single-organ disease.

Patient 4 was placed on LVAD support in the referral hospital. This required an extensive surgical procedure with a midline sternotomy, with associated additional risks of bleeding. Although there were no complications associated with the procedure in this child, we would not advocate undertaking such extensive intervention in a referral unit in the future. We therefore emphasise the importance of balancing the risks and benefits of the ideal primary intervention in a distant and unfamiliar environment with a more conservative approach, initially achieving clinical stability, with further optimisation on arrival back in our usual environment. This principle certainly applied to Patient 1 and Patient 3, who underwent left heart decompression shortly after arrival in Melbourne.

In our experience, critically ill children who would not otherwise be transportable can be safely transported long distances on ECLS. If appropriate resources exist, this intervention should be offered to carefully selected patients. However, it should be considered a last-resort therapy, and should not be considered an alternative to the early referral of potential ECLS candidates.

Author details

Armando Perez, Fellow in Intensive Care¹

Warwick W Butt, Intensivist,¹ and Associate Professor²

Kenneth J Millar, Intensivist¹

Derek Best, ECLS Co-ordinator¹

Timothy Thiruchelvam, Fellow in Intensive Care¹

Andrew D Cochrane, Cardiac Surgeon³

Martin Bennett, Perfusionist⁴

Lara S Shekerdeman, Director of Paediatric Intensive Care^{1,5}

1 Department of Intensive Care, Royal Children's Hospital, Melbourne, VIC.

2 University of Melbourne, Melbourne, VIC.

3 Department of Cardiac Surgery, Royal Children's Hospital, Melbourne, VIC.

4 Department of Perfusion, Royal Children's Hospital, Melbourne, VIC.

5 Murdoch Children's Research Institute, Melbourne, VIC.

Correspondence: lara.shekerdeman@rch.org.au

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