Journal of Cardiothoracic Surgery

RESEARCH Open Access

Extracorporeal membrane oxygenation for Chinese neonates with severe respiratory and cardiac failure

Xiao-Juan Zhang[1], Ying-Yue Liu[2], Hui Wang[2] and Xiao-Yang Hong[2,3*]

Abstract

Objective We aimed to outline the experience with extracorporeal membrane oxygenation (ECMO) for respiratory and cardiac failure in neonates in our institution and compare our results with those from other countries.

Method The clinical data of 28 neonates who required ECMO assistance were studied retrospectively.

Results A total of 28 neonates underwent support with veno-arterial ECMO, including 14 cardiac support and 14 respiratory support. The neonates with a median age of 5 days (1–28 days) and a median weight of 3.3 kg (2.4–4.2 kg). Of these neonates, 4 were female, and 24 were male. Among the neonates. For neonates requiring ECMO support for cardiac conditions, 9 survived, resulting in a 64% survival rate. In contrast, for those requiring ECMO support for respiratory conditions, 6 survived, indicating a 42% survival rate. The survivors exhibited a significant reduction in lactic acid levels within the first 24 h. In the 15 successful weaning neonates, four neonates died at the end of the study; one was for the cardiac function failure; two were for the respiratory failure; one was given up for Bipedal necrosis; the other 11 neonates were successful discharge. Notably, two neonates underwent ECMO ventilation in the prone position without experiencing any complications.

Conclusion The utilization of ECMO support in neonates experiencing severe respiratory and cardiac failure efficiently improves cardiopulmonary function and significantly reduces mortality rates among critically ill neonates. The neonates with a respiratory indication in our study have a lower survival rate than other reported in the literature. Monitoring the trend in lactate levels following ECMO support proves valuable in estimating the prognosis of affected children.

Keywords Extracorporeal membrane oxygenation (ECMO), Heart failure, Neonate, Respiratory failure

*Correspondence:
Xiao-Yang Hong
hongxiaoyangxy@126.com
[1]Department of Cardiopulmonary Bypass, Beijing Anzhen Hospital, Capital Medical University, Beijing 100029, China
[2]Department of PICU of Pediatric Medicine, Seventh Medical Center, PLA General Hospital, Beijing 100000, China
[3]Department of PICU of Pediatric Medicine, Seventh Medical Center, PLA General Hospital, No.5 Dongforty South Gate Warehouse, Dongcheng, Beijing 100000, China

Introduction

Extracorporeal membrane oxygenation (ECMO) is a lifesaving procedure for critically ill neonates with severe cardiac and/or respiratory failure and refractory to maximal conventional management. The primary function of ECMO is to act as a surrogate for the cardiopulmonary system of a patient, facilitating the circulation of oxygenated blood throughout the body. Now ECMO remains an important support treatment tool for neonates with reversible congenital cardiopulmonary diseases [1, 2]. The use of ECMO to support neonates with cardiorespiratory failure in China has a relatively recent change in care strategy. The overall survival rate in cardiac ECMO is lower, with congenital heart defect representing the main indication. This review provides an overview of the available evidence in the field of neonatal ECMO. ECMO is a life support with a potential impact on long-term patients' outcomes. In the past years, clinical technology, and expertise have push neonatal ECMO towards more premature, but also complex, all doctors want to reduce the burden of ECMO-related complications and improve the outcomes [3]. The ECMO centers doctors should keep on learning, to know as much as possible of the experience. Therefore, we reviewed our institutional experience with Neonatal ECMO support, showed our experiences and our problems, shared our work to explore potential areas for improvement.

Method and material

Study participants

From 2012 to 2016, 28 neonates diagnosed with severe respiratory and cardiac failure at the BaYi Children's Hospital of PLA Army General Hospital, were provided with ECMO support. Among them, there were 6 females and 22 males with a median age was 5 days (ranging from 1 to 28 days) and a median weight was 3.3 kg (ranging from 2.4 to 4.2 kg). All neonates experienced severe respiratory or cardiac failure post CHD operation, whose clinical symptoms were unresponsive to conventional treatments and had no contraindications for ECMO. Among them, 14 neonates required ECMO support for cardiac conditions, while another 14 required it for respiratory issues. The decision for ECMO support was made after obtaining consent from the families of the neonates.

Indications for ECMO support in this study were as follows:

Indications for respiratory failure: Oxygenation index>40 for >4 h; Oxygenation index>20 without improvement after prolonged duration (>24 h), severe hypoxic respiratory failure with abrupt decompensation (PaO2<40) resistant to intervention, and progressive respiratory failure and/or pulmonary hypertension with signs of right ventricular dysfunction or sustained high inotropic demand.

Indications for heart failure: Inability to be weaned from extracorporeal circulation following surgery for congenital heart disease, severe low cardiac output syndrome persisting after surgery for congenital heart disease, and unsuccessful cardiopulmonary resuscitation (CPR) after a cardiac arrest.

Contraindications

Gestational age<34 weeks, weight<2 kg, irreparable cardio-pulmonary injury, irreversible nerve injury, multiple organ failure, fatal chromosomal anomalies, and refusal of ECMO support by the families.

Methods

The ECMO setup utilized a Medtronic ECMO bio-console 560 and a water tank, along with a Medtronic Minimax Plus Oxygenator (CB2503R1). The cannulation sites for respiratory support were right jugular vein for venous outflow and the jugular arterial for arterial inflow. For cardiac support, the right atrium served as the venous outflow, and the aorta was used for arterial inflow. Cardiac support was initiated through the chest, following a V-A model configuration. The flow rate range was 100–150 ml/kg/min. Anticoagulation was maintained through a heparin infusion at a rate of 5–10 u/kg.h, aiming to keep activated clotting times within the range of 150–200 s. Blood routine and blood gas samples were monitored, ensuring PLT levels were above 75×10^9/L, HCT ranged between 30 and 40%, and SvO2 levels remained above 50%. During ECMO support, active vascular drug dosage was decreased, with the end-expiratory volume between 5 and 8 ml/kg, high peep pressure between 5 and 8 mmHg, and end-expiratory pressure between 18 and 25 mmHg, in an effort to maintain lung inflation. Hemodynamic stability, blood gas samples, chest X-rays, urine output, and mixed venous oxygen saturation were continuously monitored to assess cardio-pulmonary function. If these indicators improved, the ECMO flow rate was gradually reduced. Once the flow rate fell below 10–30 ml/kg/h and both circulation and oxygenation remained stable, the ECMO support was discontinued. The lactide levels in different group were compared by ANOVA using the SPSS version 16 software.

Results

In this study, 28 infants underwent ECMO support, comprising 6 females and 22 males, with ages ranging from 1 day to 28 days, The duration of support varied, ranging from 11 h to a maximum of 173 h. .Out of the 14 cases supported for cardiac-related issues, 9 neonates survived, resulting in a 65% survival rate. For the 14 cases supported for respiratory conditions, 6 neonates survived, leading to a survival rate of 42%. Among the cases, 3 neonates had meconium aspiration syndrome, 2 had

Table 1 The neonates requiring ECMO support and survival rate

		Died	Survived	Survival rate
Cardiac		5	9	64%
Respiratory	RDS/SEPSIS	4	2	42%
	MAS	1	3	
	PH	2	0	
	PPHN	1	0	
	CDH	0	1	
Sex (f/m)		3/10	1/14	
Weight (kg)		3.40 ± 0.75	3.54 ± 0.84	

ECMO: Extracorporeal Membrane Oxygenation; CDH: Diaphragmatic hernia; MAS: Meconium aspiration syndrome; PPHN: Neonatal persistent pulmonary hypertension; RDS: Respiratory distress syndrome; PH: Pulmonary hypoplasia

Table 2 Lactate levels (mmol/L) during the initial 24 h of ECMO support

	0 h	6 h	12 h	24 h
Survival group	12.83 ± 2.77	8.31 ± 3.73[1]	6.06 ± 3.83[1,2]	3.01 ± 0.97[1, 3, 4]
Death group	10.33 ± 4.80	9.97 ± 4.83[5]	10.47 ± 5.32[5,6]	10 ± 1.97[5,6,7]

Note Survival group: 1 was 24 h compared with 0 h, $p < 0.05$

2 was 12 h compared with 6 h, $p > 0.05$

3 was 24 h compared with 6 h, $p < 0.05$

4 was 24 h compared with 12 h, $p > 0.05$

Death group : 5 was compared with 0 h, $p > 0.05$

6 was compared with 6 h, $p > 0.05$

7 was compared with 12 h, $p > 0.05$

respiratory distress syndrome (RDS) due to sepsis, and 1 had diaphragmatic hernia (CDH), as outlined in Table 1. In the 15 successful weaning neonates, four neonates died at the end of the study. One was given up for the cardiac function failure; two were given up for the respiratory failure; one was given up for Bipedal necrosis; the other 11 neonates were successful discharge.

The neonates whose lactate levels declined significantly in the first 24 h had a better prognosis, while those whose lactate levels decreased slowly or did not change had a worse prognosis (see Table 2).

Among the ECMO cases, 5 experienced complications: 2 cases developed diffuse intravascular coagulation, 1 suffered a pipeline accident, and 2 faced venous cannula obstruction, leading to lower limb ischemia necrosis in those instances. Notably, no instances of bleeding or other complications were observed, resulting in a complication rate of 17%.

Discussion

ECMO plays a pivotal role in rapidly and effectively improving severe cardiopulmonary function loss, providing a critical window for recovery. Its widespread application in severe respiratory and heart failure treatment is well-established, encompassing neonates, children, and adults. Specifically in neonatal settings, ECMO serves as a valuable tool for heart support, ventilator assistance, and in vitro cardiopulmonary resuscitation (CPR). The neonatal ECMO requiring specific expertise and technical skill, especially for the special pathophysiological characteristics of neonates. it becomes nearly impossible to separate the role of pediatric surgeons from the continuous involvement with and management of neonatal ECMO patients. This technology, well-established overseas, has recently gained traction in China's clinical landscape. Data from the External Life Support Organization (ELSO, 2016) [4] indicates that 36,946 neonates have undergone ECMO support, comprising 29,153 cases for cardiac support with a 42% survival rate, 6,475 cases for respiratory support with a 72% survival rate, and 1,336 cases for external cardiopulmonary resuscitation (ECPR) with a 41% survival rate [1, 3–10], ESLO(In January 2016) data revealed that there were only 9 neonates who received ECMO, 3 for respiratory support with a 0% survival rate and 6 for cardiac assistance with a 50% survival rate; hence, ECMO for neonates in China lags Western countries. Since 2012, our hospital has developed ECMO for neonates; we have performed ECMO on 28 infants, 14 for cardiac support with a 64% survival rate and 14 for respiratory conditions with a 42% survival rate. So many years passed, the data of 2023 from ESLO shows 167 neonates who received ECMO, 70 for respiratory support with a 68.6% survival rate, 78 for cardiac assistance with a 42.3% survival rate and 19 for ECPR assistance with a 11.4% survival rate. In our center, the survival rate for cardiac support (41%) was marginally higher than that for respiratory support, not consistent with ESLO data., maybe due to the limited number of cases in our center, the comparability is weak, and it is essential to collect more cases for a comprehensive analysis.

The survival rate for respiratory assistance was significantly lower than what is published internationally; potential factors include the following:

1) In our study, the initiation of ECMO procedures was delayed, resulting in fewer than 15 cases annually. This indicates a need to enhance our management and operational proficiency. Freeman et al. demonstrated a correlation between patient survival rate and the volume of cases managed by a center [11]. Notably, centers handling approximately 22 cases annually exhibited a significant decrease in mortality rates.

2) The initiation of ECMO support for neonates in our center was considerably delayed, predominantly due to the limited knowledge and experience with ECMO among neonatal physicians. While surfactant therapy, high-frequency ventilation, and inhaled nitric oxide are commonly employed in clinical settings, by the time neonates were considered for ECMO intervention, their physiological status had often deteriorated significantly. The majority of these neonates presented with profound internal environmental imbalances, marked hypoxemia

(arterial oxygen tension less than 20 mmHg), and cardiac insufficiency. Out of the total cohort, 20 out of 28 neonates exhibited lactate levels exceeding 15 mmol/L prior to ECMO intervention. Consequently, a significant proportion of these neonates experienced severe fluid leakage following ECMO initiation, leading to circulatory instability. This rendered resuscitative measures ineffective, resulting in an inability to rescue these neonates. Within the first 24 h of ECMO intervention, neonates whose lactate levels normalized exhibited a favorable prognosis. Conversely, those who maintained elevated lactate levels or experienced a further rise demonstrated a poor prognosis.

3) In our center, the veno-arterial (V-A) ECMO model was exclusively employed for neonatal patients. While it is widely recognized that the venous-venous (V-V) model is optimal for patients with primary respiratory ailments, the absence of a V-V circuit in our institution necessitated our reliance on the V-A configuration for neonatal interventions [12]. The intricacies associated with the administration of the V-A model, coupled with its potential impacts on circulatory dynamics, may be contributory factors to the observed diminished survival rates.

During the ECMO support phase, lung management plays a pivotal role in patient prognosis, with particular emphasis on modifications in patient positioning, such as adopting the prone position. Kredel conducted a retrospective case analysis in 2014 and scrutinized 9 patients diagnosed with ARDS who were positioned prone during their ECMO support [13]. Based on the comparison of the oxygenation index and lung compliance, there were notable improvements post-proning. Specifically, the oxygenation index improved from a median value of 47 (ranging from 41 to 47) before proning, to 12 (ranging from 11 to 14) after. Similarly, lung compliance revealed enhancement from 20 (ranging from 17 to 28) before proning, to 42 (ranging from 27 to 43) after the intervention, now there also some opinion shows the prone positioning did not facilitate earlier weaning from ECMO [14]. In our center, beginning from June 2016, two patients were placed in the prone position during ECMO support, the lung of two babies occurred hypostatic pneumonia, so we tried the prone intervention. Remarkably, these patients did not encounter complications such as facial edema, pipeline issues, or pump failure. This indicates that positioning patients supported by ECMO in the prone orientation is both safe and practicable. However, we did not find the benefit from the prone position, so we acknowledge the necessity for additional data collection to definitively assess the effects of this positioning on parameters such as the oxygenation index and lung compliance.

Neonates requiring ECMO mechanical intervention present with a diverse array of clinical conditions including congenital diaphragmatic hernia (CDH), meconium aspiration syndrome (MAS), neonatal persistent pulmonary hypertension (PPHN), respiratory distress syndrome (RDS), sepsis, neonatal pneumonia, and air leakage, among others [15, 16]. A review of existing literature indicates that MAS has the highest association with ECMO use, followed by CDH, followed by PPHN, sepsis, RDS, pneumonia, and air leakage. Survival rates were most favorable for MAS, estimated around 94%, followed by RDS (84%), PPHN (77%), and sepsis (73%), with CDH registering the lowest at approximately 51%. The reduced survival rate in CDH may be attributed to concurrent pulmonary hypoplasia (PP). In our center, 14 neonates had ECMO support primarily for respiratory issues, 6 had SEPSIS/RDS, 4 had MAS, 2 displayed PP, and 1 was diagnosed with CDH. The distribution of conditions diverges from commonly cited literature, potentially due to unique admission patterns and national circumstances. Our center has proficiency in neonatal transport, but the presented state of the neonate with CDH was critically compromised, and the capabilities of primary healthcare facilities are restricted. Consequently, many neonates were deprived of opportunities for escalated care in tertiary healthcare centers. While the patient volume is insufficient to facilitate a comparison with the ELSO data, it is evident from our observations that neonates with sepsis/MAS generally have a favorable prognosis.

Since the 1970s, technology, management, and clinical applications of neonatal ECMO have improved. Pulmonary diseases still represent the principal neonatal diagnosis, with an overall 74% survival rate, and up to one-third of cases are due to congenital diaphragmatic hernia. The overall survival rate in cardiac ECMO is lower, with congenital heart defect representing the main indication [3]. However, in our center the survival was lower with the pulmonary diseases, the reason may be the seriously ill, or maybe the example was small. Yu et al. [17] reported 23 neonates who received ECMO support for cardiac failure in their center from January 2017 to June 2019, The successful weaning rate was 78.26% and discharge rate was 52.17% in their center, the survival rate was similar with ours, So ECMO is a safe and efficacious therapeutic modality, emblematic of the critical emergency technological capabilities of a hospital, region, or even a country. It was Bartlett, who, in 1976, pioneered the successful application of ECMO for neonates with ARDS [18]. Subsequent to this achievement, the clinical utilization of ECMO expanded, leading to significant improvements in survival rates for patients who are critically ill. In China, while ECMO has been extensively adopted for adult patients, its implementation in pediatric settings has been comparatively gradual [19, 20].

Conclusion

As ECMO becomes increasingly integrated into neonatal critical care, the technology will undergo continuous refinement, paving the way for a new era in neonatal critical care in China.

Abbreviations

ECMO	Extracorporeal Membrane Oxygenation
CPB	Extracorporeal circulation
CPR	Cardiopulmonary resuscitation
CDH	Diaphragmatic hernia
MAS	Meconium aspiration syndrome
PPHN	Neonatal persistent pulmonary hypertension
RDS	Respiratory distress syndrome
PH	Pulmonary hypoplasia

Acknowledgements
We are particularly grateful to all the people who have given us help on our article.

Author contributions
Conception and design of the research: Xiao-juan Zhang，Xiao-yang Hong. Acquisition of data: Hui Wang, Ying-yue Liu. Analysis and interpretation of the data: Hui Wang, Ying-yue Liu. Statistical analysis: Xiao-juan Zhang. Obtaining financing: Xiao-yang Hong. Writing of the manuscript: Xiao-juan Zhang. Critical revision of the manuscript for intellectual content: Ying-yue Liu. All authors read and approved the final draft.

Funding
This study was supported by a grant from Capital's funds for health improvement and research(2020-2-5093).

Data availability
The datasets used and analysed during the current study available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the declaration of Helsinki. This study was conducted with approval from the Ethics Committee of BaYi Children's Hospital of PLA Army General Hospital.

Consent for publication
Written informed consent was obtained from the minor(s)' legal guardian for the publication of any potentially identifiable images or data included in this article.

Competing interests
The authors declare no competing interests.

Received: 30 July 2024 / Accepted: 24 December 2024
Published online: 06 January 2025

References

1. Lior Sasson I, Cohen AT. Extracorporeal Membrane Oxygenation in Pediatric Patients: Our Experience in the Last Ten Years. Orginial article, 2013, January, 15:13–16.
2. Artur Chernoguz 1. Julie Monteagudo [2], neonatal venoarterial and venovenous ECMO. Semin Pediatr Surg. 2023;32(4):151326. https://doi.org/10.1016/j.sempedsurg.2023.151326.
3. Ilaria Amodeo1. Matteo Di Nardo[2], Genny Raffaeli[1,3], neonatal respiratory and cardiac ECMO in Europe. Eur J Pediatrics. 2021;180:1675–92.
4. Thiagarajan RR, Barbaro RP, Rycus PT, et al. Extracorporeal life support Organization Registry International Report 2016. ASAIO J. 2017;63(1):60–7. https://doi.org/10.1097/MAT.0000000000000475.
5. Maslach-Hubbard A, Bratton SL. Extracorporeal membrane oxygenation for pediatric respiratory failure: history, development and curr ent status. World J Crit Care Med. 2013;2(4):29–39.
6. Bartlett RH, Gattinoni L. Current status of extracorporeal life support (ECMO) for cardiopulmonary failure. Minerva Anestesiol. 2010;76(7):534–40.
7. Amodeo I, Nardo MD. Genny Raffaeli1, etc neonatal respiratory and cardiac ECMO in Europe. Eur J Pediatrics. 2021;180:1675–92.
8. Bennett CC, Johnson A, Field DJ. Lancet. 2001;357(9262):1094–6. UK collaborative randomised trial of neonatal extracorporeal membrane oxygenation: follow-up to age 4 years.
9. McNally H, Bennett CC, Elbourne D. United Kingdom collaborative randomized trial of neonatal extracorporeal membrane oxygenation: follow-up to age 7 years. Pediatrics. 2006;117(5):e845–54.
10. Fliman PJ, deRegnier RA, Kinsella JP. Neonatal extracorporeal life support: impact of new therapies on survival. Pediatr. 2006;148:595–9.
11. Freeman CL, Bennett TD, Casper TC. Pediatric and neonatal extracorporeal membrane oxygenation: does center volume impact mortality? Crit Care Med. 2014;42(3):512–9.
12. Guner YS, Khemani RG, Qureshi FG. Outcome analysis of neonates with congenital diaphragmatic hernia treated with venovenous vs venoarterial extracorporeal membrane oxygenation. J Pediatr Surg. 2009;44:1691–701.
13. Kredel M, Bischof L, Wurmb TE. Combination of positioning therapy and venovenous extracorporeal membrane oxygenation in ARDS patients.Perfusion. Mar. 2014;29(2):171–7.
14. Wiener C. Albert. ECMO and prone position in patients with severe ARDS. JAMA. 2024;331(14):1232. https://doi.org/10.1001/jama.2024.1870.
15. Schaible T, Hermle D, Loersch F. A 20-year experience on neonatal extracorporeal membrane oxygenation in a referral center. Intensive Care Med. 2010;36:1229–34.
16. Nasr VG, Faraoni D, DiNardo JA, Thiagarajan RR. Association of Hospital Structure and complications with Mortality after Pediatric extracorporeal membrane oxygenation. Pediatr Crit Care Med. 2016;17(7):684–91. https://doi.org/10.1097/PCC.
17. Xindi Yu Y, Yang W, Zhang, et al. Postcardiotomy extracorporeal membrane oxygenation in neonates, Pediatric and congenital cardiology. Thorac Cardiovasc Surg. 2021;69:e41–7.
18. Bartlett RH, Gazzaniga AB, Jefferies MR. Extracorporeal membrane oxygenation (ECMO) cardiopulmonary support in infancy. Trans Am Soc Artif Intern Organs. 1976;22:80–93.
19. Wang CW, Zhou XY. Application of extracorporeal membrane oxygenation in critical neonates. Chin J Practical Pediatr. 2016;31(2):104–6.
20. Xy H, Gx ZU, Yh L. Application of extracorporeal membrane oxygenation in pediatric cardiopulmonary failure.Clin Pediatr, 2015, 33(1):5–8.

Publisher's note