

## Extracorporeal membrane oxygenation support in neonates: a single center experience in Turkey

Emel OKULU<sup>1\*</sup>, F. Begüm ATASAY<sup>1</sup>, Gaffari TUNÇ<sup>1</sup>, Hasan AKDUMAN<sup>2</sup>, Ömer ERDEVE<sup>1</sup>,  
Saadet ARSAN<sup>1</sup>, Zeynep EYİLETEN<sup>3</sup>, Tayfun UÇAR<sup>4</sup>, H. Ercan TUTAR<sup>4</sup>

<sup>1</sup>Division of Neonatology, Department of Pediatrics, Faculty of Medicine, Ankara University, Ankara, Turkey

<sup>2</sup>Department of Neonatology, Sami Ulus Maternity and Children Research and Training Hospital, Ankara, Turkey

<sup>3</sup>Department of Cardiovascular Surgery, Faculty of Medicine, Ankara University, Ankara, Turkey

<sup>4</sup>Division of Pediatric Cardiology, Department of Pediatrics, Faculty of Medicine, Ankara University, Ankara, Turkey

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**Background/aim:** Extracorporeal membrane oxygenation (ECMO) is a form of life support for patients with respiratory failure, cardiac failure, or both. The aim of this study was to evaluate neonates supported with ECMO and report our experience as a Turkish neonatal intensive care unit.

**Materials and methods:** We retrospectively reviewed 11 newborn infants treated with ECMO at Ankara University for respiratory and cardiac failure. We reported the demographic, diagnostic, laboratory, and clinical data of the patients.

**Results:** Eleven patients (9 male, 2 female) received ECMO support with a mean gestational age of  $39.1 \pm 1.6$  weeks and mean birth weight of  $3513 \pm 506$  g. Six patients received venoarterial (VA) ECMO and five patients received venovenous (VV) ECMO. Mean age at initiation and duration of ECMO was  $7.2 \pm 7.4$  days (2–24 days) and  $10.4 \pm 4.9$  days (5–21 days), respectively. Mean oxygenation index (OI) before ECMO was  $48.5 \pm 5.7$ . ECMO was withdrawn from one patient due to severe brain injury. The survival rate for ECMO was 73% and the survival rate to discharge was 64%, whereas the survival rate in congenital diaphragmatic hernia (CDH) cases was 40%.

**Conclusion:** Our early results from ECMO for neonates are encouraging. Identification of patients for ECMO support and timely referral will offer a survival opportunity to complex neonatal cases.

**Key words:** Extracorporeal membrane oxygenation, neonate, neonatal intensive care unit

### 1. Introduction

Extracorporeal membrane oxygenation (ECMO) is a temporary form of life support for patients with respiratory failure, cardiac failure, or both, via a modified form of cardiopulmonary bypass. ECMO was first used successfully in 1975 by Bartlett et al. in a newborn with respiratory failure. In the following years, two randomized trials reported improved survival for neonates treated with ECMO for respiratory failure in congenital diaphragmatic hernia (CDH), meconium aspiration syndrome (MAS), sepsis, and persistent pulmonary hypertension of the newborn (PPHN) (1–3).

After the successful use of ECMO in neonates in the 1980s, the number of ECMO centers throughout the world increased and ECMO therapy became a mainstay in many pediatric hospitals in the United States. Over the past 15 years, advanced respiratory therapies for neonates with acute hypoxic respiratory failure, such as

high-frequency ventilation (HFV), inhaled nitric oxide (iNO), and surfactant, have evolved (4–7). Parallel to this progress, there has been worldwide reduction in the use of ECMO for neonatal acute hypoxic respiratory failure, as reported by the Extracorporeal Life Support Organization (ELSO) registry. In the past decade, ECMO use gradually increased in neonatal cardiac support (8–12). To the present, more than 85,000 neonates treated with ECMO have been reported to ELSO, which was founded in 1989. ELSO provides ECMO guidelines to all practicing facilities, and has an online registry system to share their outcomes globally and provide ECMO guidelines (13).

In Turkey, the use of extracorporeal life support has been practiced for a while. However, most patients are adults and postcardiotomy cases. Pediatric ECMO applications have increased and been reported in recent years; however, there are no data of neonates treated with ECMO (14–16). Our center is the first and only center to

\* Correspondence: emelokulu@gmail.com

perform ECMO in a neonatal intensive care unit (NICU) for neonates with respiratory or cardiac failure in Turkey. As the only NICU with ECMO service, we reviewed our ECMO records to evaluate demographic, clinical, laboratory, and outcome data. In this paper we report our experience using ECMO for neonates.

## 2. Materials and methods

### 2.1. Study population

The NICU of the Children's Hospital, Faculty of Medicine, Ankara University, is a tertiary center with a 30-bed capacity that cares for high-risk infants among 5000 annual inborn deliveries and high-risk referrals from all over Turkey. Approximately 1000 patients per year are admitted to the NICU. The newborn ECMO program started in mid-2015, and the first ECMO application was in September 2015.

In this study, data from neonatal ECMO cases have been retrospectively collected between September 2015 and June 2017. The study is approved by the local ethics committee.

### 2.2. ECMO criteria

The infants were referred to ECMO according to the criteria reported by ELSO (17). Neonates with severe hypoxic respiratory failure, refractory to maximal medical management, and a potentially reversible etiology with the following criteria were supported with ECMO:

1. Gestational age (GA)  $\geq$  34 weeks and body weight  $\geq$  2000 g
2. Oxygenation index (OI)  $>$  40 for 4 h [oxygenation index: (mean airway pressure  $\text{FiO}_2$  / postductal  $\text{PaO}_2$ )  $\times$  100]
3. OI  $>$  20 with lack of improvement, despite prolonged ( $>$ 24 h) maximal medical therapy or persistent episodes of decompensation
4. Severe hypoxic respiratory failure with acute decompensation ( $\text{PaO}_2 <$  40 mmHg)
5. Progressive respiratory failure and/or pulmonary hypertension with evidence of right ventricular dysfunction or continued high inotropic requirement.

We excluded neonates with life-threatening congenital anomalies, uncontrolled bleeding, and irreversible brain damage.

### 2.3. ECMO application and care

In our institution, neonates were cannulated for ECMO by pediatric cardiovascular surgeons and underwent cannulation through the right internal jugular vein and common carotid artery. Typically, 8–10 Fr cannulas were used for arterial cannulation and 10–13 Fr for venous access.

We applied ECMO with centrifugal pumps (Maquet Rotaflow, Maquet Cardiopulmonary AG, Hirrlingen, Germany) and hollow-fiber membrane oxygenators

(Maquet Quadrox-iD, Maquet Cardiopulmonary AG, Hirrlingen, Germany). The usual practice is to start with a pump flow of 100–150 mL/kg/min. Body temperature was maintained at around 36–37 °C by the heater cooler in the ECMO circuit. The ventilator was adjusted to 'rest settings', i.e. tidal volume 4–6 mL/kg, peak inspiratory pressure 15–25 cm  $\text{H}_2\text{O}$ , positive end expiratory pressure 5–8 cm  $\text{H}_2\text{O}$ , rate 20–30/min, and oxygen fraction 21%–40%. A continuous heparin infusion ranging 20–50 units/kg/min was administered with the ECMO initiation. It aimed to keep activated clotting time (ACT) level at around 160–220 s. ACT level was monitored every 6 h, and platelet count, hematocrit (HCT), and fibrinogen levels were monitored every day, unless otherwise indicated. The blood components were transfused if HCT  $<$  35%, platelet count  $<$  100,000  $\text{mm}^3$ , and fibrinogen  $<$  1.5 g/L.

With the improvement of the underlying disease and clinical condition, we tried to wean the patient from ECMO by reducing the pump flow. During the weaning process, ventilator support was increased and inotrope support was initiated if necessary. If the patient's hemodynamic status was stable at a 50 mL/kg/min pump flow, decannulation was anticipated by pediatric cardiovascular surgeons.

### 2.4. Data collection

The demographic characteristics of the patients, pre-ECMO diagnosis, indication of ECMO, ECMO support course, rate of survival and survival to discharge, length of hospitalization, and complications were recorded.

### 2.5. Data analysis

Statistical analysis was performed using SPSS 21 for Windows (SPSS Inc., Chicago, IL, USA). The demographic and clinical findings of the patients were described with rates and percentages, mean  $\pm$  SD, and median values. Independent t-test and chi-square test were used to compare baseline characteristics.

## 3. Results

In our center, 11 patients (9 male, 2 female) were supported with ECMO. Mean GA was  $39.1 \pm 1.6$  (range: 36.4–41 weeks) and mean birth weight (BW) was  $3513 \pm 506$  g (range, 2700–4245 g). The demographic and clinical data of the patients are shown in Table 1. Mean age at initiation of ECMO was  $7.2 \pm 7.4$  days (range: 2–24 days). The underlying diseases were CDH ( $n = 5$ ), MAS ( $n = 4$ ), PPHN ( $n = 1$ ), and congenital heart disease (CHD) ( $n = 1$ ).

Six patients received venoarterial (VA) ECMO, whereas five patients received venovenous (VV) ECMO. Mean OI was  $48.5 \pm 5.7$ , and mean ventilator day was  $3.7 \pm 2.8$  days before ECMO for all patients. Ventilation modes and parameters with arterial pH,  $\text{HCO}_3$ , and lactate levels before and after ECMO within 24 h are listed in Table 2.

**Table 1.** Demographic and clinical data of patients.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Mean ± SD	Median (range)
Gestational age (weeks)	39.4	37.1	40.2	37.4	40.5	39	40	36.4	41	38	41.2	39.1 ± 1.6	39.4 (36.4–41.2)
Birth weight (g)	3185	3820	3400	2700	4245	3550	3650	2780	3310	3800	4200	3513 ± 506	3550 (2700–4245)
Sex	F	M	M	M	M	M	M	F	M	F	M	NA	NA
APGAR 5'	8	7	7	2	3	9	8	8	5	8	9	NA	7 (5–9)
Mode of delivery	CS	CS	CS	CS	NVD	NVD	NVD	CS	NVD	CS	CS	NA	NA
Birth place	Inborn	Inborn	Inborn	Inborn	Outborn	Outborn	Outborn	Inborn	Outborn	Outborn	Outborn	NA	NA
Age at admission (days)	1	1	1	1	2	2	1	1	1	24	12	4.2 ± 7.3	1 (1–24)
ECMO indication	CDH	MAS	MAS	MAS	MAS	CHD	CDH	CDH	CDH	PPHN	CDH	NA	NA
Age at ECMO placement (days)	3	3	3	3	2	17	2	7	3	24	12	7.2 ± 7.3	3 (2–24)
OI before ECMO	43	50	45	56	42	45	58	44	44	54	52	48.4 ± 5.7	45 (42–58)
A-a gradient before ECMO	592	620	700	632	640	740	450	720	520	760	700	643.1 ± 95.5	640 (450–760)
ECMO type	VV	VV	VV	VA	VV	VA	VA	VA	VA	VV	VV	NA	NA
Duration of ECMO (days)	6	8	8	5	8	8	8	16	13	21	14	10.4 ± 4.9	8 (5–21)
Length of hospitalization (days)	12	34	42	6	30	57	20	38	14	46	28	29.7 ± 15.7	30 (6–57)
Survival to discharge	Exitus	Discharged	Discharged	Exitus	Exitus	Discharged	Exitus	Discharged	Exitus	Discharged	Discharged	NA	NA

F: female, M: male, CS: cesarean section, NVD: normal vaginal delivery, CDH: congenital diaphragmatic hernia, MAS: meconium aspiration syndrome, CHD: congenital heart disease, PPHN: persistent pulmonary hypertension of the newborn, OI: oxygenation index, VV: venovenous, VA: venoarterial, NA: not applicable

**Table 2.** Ventilation and blood gas analysis before and after ECMO.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Patient 10	Patient 11	Mean ± SD	Median	
Ventilation day prior to ECMO	3	3	3	3	2	2	2	7	3	2	11	3.7 ± 2.8	3 (2-11)	
Ventilation mode before ECMO	HFV Fr: 10 Delta P: 45 MAP: 20 FiO <sub>2</sub> : 1.0	HFV Fr: 7 Delta P: 40 MAP: 19 FiO <sub>2</sub> : 1.0	HFV Fr: 7 Delta P: 35 MAP: 20 FiO <sub>2</sub> : 1.0	HFV Fr: 8 Delta P: 30 MAP: 18 FiO <sub>2</sub> : 1.0	HFV Fr: 6 Delta P: 40 MAP: 19 FiO <sub>2</sub> : 1.0	Ass/C Rate: 40 TV: 5* PEEP: 5 FiO <sub>2</sub> : 1.0	HFV Fr: 8 Delta P: 30 MAP: 18 FiO <sub>2</sub> : 1.0	HFV Fr: 10 Delta P: 35 MAP: 20 FiO <sub>2</sub> : 1.0	HFV Fr: 6 Delta P: 35 MAP: 19 FiO <sub>2</sub> : 1.0	HFV Fr: 8 Delta P: 35 MAP: 22 FiO <sub>2</sub> : 1.0	HFV Fr: 8 Delta P: 40 MAP: 21 FiO <sub>2</sub> : 1.0			
Ventilation mode during ECMO	Ass/C Rate: 20 TV: 4 PEEP: 6 FiO <sub>2</sub> : 0.6	SIMV Rate: 25 PIP: 25 PEEP: 5 FiO <sub>2</sub> : 0.5	SIMV + VG Rate: 25 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.3	SIMV + VG Rate: 30 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.4	SIMV + VG Rate: 20 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.21	SIMV + VG Rate: 25 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.3	SIMV + VG Rate: 25 TV: 4* PEEP: 5 FiO <sub>2</sub> : 0.21	SIMV + VG Rate: 25 TV: 5* PEEP: 6 FiO <sub>2</sub> : 0.21	SIMV + VG Rate: 25 TV: 3* PEEP: 7 FiO <sub>2</sub> : 0.21	SIMV + VG Rate: 25 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.4	SIMV + VG Rate: 30 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.4	SIMV + VG Rate: 40 TV: 5* PEEP: 5 FiO <sub>2</sub> : 0.4		
Blood flow**	200	150	120	150	140	150	130	150	140	130	100	NA	NA	
pH <sup>a</sup>	7.17	7.21	7.01	6.99	7.13	7.22	6.99	7.05	7.05	7.19	7.06	7.1 ± 0.9 (6.99-7.22)	7.06 (6.99-7.22)	
pH <sup>b</sup>	7.41	7.34	7.31	7.21	7.34	7.38	7.23	7.41	7.32	7.52	7.47	7.35 ± .09 (7.21-7.52)	7.34 (7.21-7.52)	
pCO <sub>2</sub> <sup>a</sup>	50.2	60.6	48.6	56.7	56.5	58	72.3	58.9	63.7	59	68.6	59.4 ± 7 (48.6-72.3)	58.9 (48.6-72.3)	
pCO <sub>2</sub> <sup>b</sup>	25	33.9	36.5	48.9	24.1	32.1	21.1	32.9	38.5	30.1	23.2	31.5 ± 8.1 (21.1-48.9)	32.1 (21.1-48.9)	
pO <sub>2</sub> <sup>a</sup>	32.5	55.9	52.6	43.8	37.6	51.2	39.3	27.2	43.6	29.3	27.5	40 ± 10.3 (27.2-55.9)	39.3 (27.2-55.9)	
pO <sub>2</sub> <sup>b</sup>	45.5	70.7	52.4	48.3	67.7	72.4	190.0	48.9	181.0	61.1	69.8	82.5 ± 51.9 (45.5-190.9)	67.7 (45.5-190.9)	
HCO <sub>3</sub> <sup>a</sup>	18.9	20.4	17.8	15.2	15.2	17.1	22.1	21.9	16.8	21.6	18.9	18.7 ± 2.5 (15.2-22.1)	18.9 (15.2-22.1)	
HCO <sub>3</sub> <sup>b</sup>	21.5	19.7	19.8	16.8	16.7	18.9	17.9	18.5	21.6	24.6	17.0	19.3 ± 2.4 (16.7-24.6)	18.9 (16.7-24.6)	
Lactate <sup>a</sup>	8.1	6.7	6.8	14.2	11	12.5	5.1	12.4	10.4	8.3	10.3	9.6 ± 2.8 (5.1-14.2)	10.3 (5.1-14.2)	
Lactate <sup>b</sup>	1.7	2.0	4.1	15.3	3.1	2.4	4.1	1.1	2.7	3.6	3.5	3.9 ± 3.8 (1.1-15.3)	3.1 (1.1-15.3)	

HFV: high frequency ventilation, Ass/C: assist control, Fr: frequency, MAP: mean airway pressure, FiO<sub>2</sub>: fractional inspired oxygen, SIMV + VG: synchronized intermittent mandatory ventilation with volume guarantee, PEEP: positive end expiratory pressure, pH<sup>a</sup>, pCO<sub>2</sub><sup>a</sup>, pO<sub>2</sub><sup>a</sup>, HCO<sub>3</sub><sup>a</sup>, and lactate<sup>a</sup>: pH, pCO<sub>2</sub>, pO<sub>2</sub>, HCO<sub>3</sub>, and lactate before ECMO, pH<sup>b</sup>, pCO<sub>2</sub><sup>b</sup>, pO<sub>2</sub><sup>b</sup>, HCO<sub>3</sub><sup>b</sup>, and lactate<sup>b</sup>: pH, pCO<sub>2</sub>, pO<sub>2</sub>, HCO<sub>3</sub>, and lactate within 24 h after ECMO, \*: TV in mL/kg, \*\*: maximum blood flow in mL/kg/min, NA: not applicable

Mean pH increased from  $7.09 \pm 0.9$  to  $7.36 \pm 0.09$  ( $P < 0.05$ ), mean  $p\text{CO}_2$  levels decreased from  $59.3 \pm 7$  mmHg to  $31.5 \pm 8.1$  mmHg ( $P < 0.05$ ), mean  $p\text{O}_2$  levels increased from  $40 \pm 10.3$  mmHg to  $82.5 \pm 51.8$  mmHg ( $P < 0.05$ ), mean  $\text{HCO}_3$  levels increased from  $18.7 \pm 2.5$  to  $19.4 \pm 2.4$  ( $P < 0.05$ ), and mean lactate levels decreased from  $9.6 \pm 2.8$  to  $3.9 \pm 3.8$  mmol/L ( $P < 0.05$ ) with ECMO support. The mean duration of ECMO was  $10.4 \pm 4.9$  days (range: 5–21 days). Nine (81.8%) patients were weaned from ECMO. Their mean ventilation day after ECMO was  $6.9 \pm 3.7$  days (range: 3–12), although 7 (64%) of them were discharged. The remaining two patients could not be decannulated.

The type of all CDHs ( $n = 5$ ) was left-sided Bochdalek hernia. Four of them were antenatally diagnosed, but the lung-to-head circumference ratio (LHR) was measured only in two. LHR was 1.6 in Patient 1, who did not survive, and 1.2 in Patient 8, who survived. CDH repair was performed in two patients (Patients 1 and 7) under ECMO, both of which were transabdominal repairs. One received VV (Patient 1) and the other received VA ECMO (Patient 7). They were both decannulated postoperatively, but died due to pulmonary hypertension

that was unresponsive to iNO or other therapies. One patient (Patient 9) had VA ECMO preoperatively but withdrawn ECMO run on the 13th day due to severe brain injury. Two surviving patients received ECMO support postoperatively (Patient 8, VA ECMO, and Patient 11, VV ECMO). The duration of ECMO in these patients was 16 and 14 days, respectively.

There was no difference among the CDH and non-CDH patients in GA, BW, birth place, ventilation day prior to ECMO, age at ECMO placement, pH,  $p\text{CO}_2$ ,  $p\text{O}_2$ ,  $\text{HCO}_3$ , lactate, MAP, OI, A-a gradient prior to ECMO, type, and duration of ECMO and survival rate ( $P > 0.05$ ) (Table 3).

Bleeding was the most frequent complication (45%). It was mostly observed as transient hematuria in Patients 2, 7, 9, 10, and 11. We had to withdraw ECMO support from one patient (Patient 9) due to severe brain injury caused by bleeding. In Patient 2, we had to change the circuit due to clots. We did not observe any complication of infection. Among the survivors, three patients diagnosed with MAS (Patient 4), CHD (Patient 6), and CDH (Patient 9) required continuous renal replacement therapy during the ECMO run.

**Table 3.** Comparison of CDH and non-CDH cases.

	CDH (n = 5)	Non-CDH (n = 6)	P
Gestational age (weeks)	$39.6 \pm 1.9$	$38.7 \pm 1.4$	0.417
Birth weight (g)	$3425 \pm 533$	$3586 \pm 521$	0.627
Outborn (n, %)	3 (60)	3 (50)	0.752
Ventilation day prior to ECMO (days)	$5.2 \pm 3.8$	$2.5 \pm 0.5$	0.114
Age at ECMO placement (days)	$5.4 \pm 4.1$	$8.7 \pm 9.4$	0.494
pH prior to ECMO	$7.1 \pm 0.1$	$7.12 \pm 0.1$	0.263
$p\text{CO}_2$ prior to ECMO	$62.7 \pm 8.6$	$56.6 \pm 4.2$	0.154
$p\text{O}_2$ prior to ECMO	$34 \pm 7.3$	$45.1 \pm 10.2$	0.073
$\text{HCO}_3$ prior to ECMO	$19.7 \pm 2.2$	$17.9 \pm 2.6$	0.246
Lactate prior to ECMO	$9.3 \pm 2.8$	$9.9 \pm 3.1$	0.721
MAP prior to ECMO	$19.6 \pm 0.5$	$19.6 \pm 1.4$	0.901
OI prior to ECMO	$48.2 \pm 6.6$	$48.7 \pm 5.6$	0.903
A-a gradient prior to ECMO (mmHg)	$596.4 \pm 115.4$	$682 \pm 59.8$	0.187
Type of ECMO (VV/VA) (n, %)	2/3 (40/60)	2/4 (33/67)	0.399
Duration of ECMO (days)	$11.4 \pm 4.2$	$9.7 \pm 5.7$	0.576
Survival (Discharged) (n, %)	2 (40)	5 (83)	0.156

CDH: congenital diaphragmatic hernia, MAP: mean airway pressure, OI: oxygenation index, VV: venovenous, VA: venoarterial.

\*Data reported as mean  $\pm$  SD or n (%).

The survival rate for ECMO was 73%, and the overall survival rate to discharge was 64%. All patients with PPHN and CHD survived (100%). The survival rate of MAS was 75%; however, survival in CDH cases was 40% (2 of 5 patients). Patients treated with VV ECMO had a survival rate of 80% compared with 50% in the VA ECMO patients.

#### 4. Discussion

ECMO is a lifesaving therapy for neonates with severe respiratory and/or cardiac failure. Its efficiency has been shown for neonates in randomized controlled studies (18,19). However, its use has been reduced in respiratory failure, and gradually increased in cardiac failure (8–12). Until July 2016, there were a total of 86,287 patients registered on the ELSO who received ECMO treatment worldwide, and neonatal cases constituted 44.8% (38,643/86,287) of all cases (20). This report includes 11 neonates that received ECMO support. ECMO was applied to neonates for hypoxic respiratory failure ( $n = 10$ , 91%), except one, who received ECMO after surgery for CHD.

ECMO requires the diversion of blood from a major systemic vessel through a gas exchange device (membrane oxygenator) and back to a major blood vessel. VA ECMO, with ligation of the right carotid artery and internal jugular vein, served as the primary mode of support for both cardiac and respiratory failure in neonates. For VV ECMO, a double-lumen VV catheter placed in the right internal jugular vein provides support for severe respiratory failure for neonates that do not require cardiac support. The preference of ECMO for the neonatal population differs worldwide (21–23). In our center, VA ECMO is essentially reserved for infants who cannot be cannulated for VV ECMO due to cannula vs. vessel size incompatibility, or who have cardiovascular instability. One patient (Patient 4) with MAS received VA ECMO as well as having cardiac failure. Three patients with CDH were supported with VA ECMO. One patient (Patient 8) was supported due to absence of appropriate cannula size, and the others due to concomitant cardiac failure.

There are widely practiced variations in the use of lung rest ventilator settings during neonatal ECMO. In a recent cohort study, it was shown that the use of HFV compared with conventional mechanical ventilation (MV) for lung rest during ECMO support is associated with longer duration of ECMO and MV (24). We used conventional MV modes for lung rest strategies during ECMO run for all our patients, regardless of their illness type and severity.

CDH is a birth defect that is associated with high mortality and morbidity due to pulmonary hypoplasia and hypertension. Prenatal diagnosis has led to improved outcomes by offering prenatal intervention (25). LHR is one of the indicators utilized to recruit candidates for fetal surgery. Although LHR is used as a favorite prognostic tool

for fetal CDH, this is not supported by current evidence (26). In our series, four of five CDH cases were antenatally diagnosed, and LHR was measured in only two, where both  $> 1$ . The postnatal approach of CDH includes supportive management as iNO, HFV, and ECMO, followed by surgical intervention. There are no universally accepted criteria for the initiation of ECMO in neonates with CDH or timing of repair once commenced on ECMO (27).

Higher OI, older age at ECMO initiation, and longer ventilation day prior to ECMO proved to be strongly associated with poor outcome in non-CDH neonates. The length of ECMO run has been reported to be associated with the outcome in both CDH and non-CDH patients (28–30). Our patients had an average OI of  $48.5 \pm 5.7$  before ECMO support. OI, age at ECMO placement, ventilation day before ECMO, and duration of ECMO were similar in CDH and non-CDH cases ( $P > 0.05$ ). Although the survivors had similar OI with nonsurvivors prior to ECMO ( $47.4 \pm 4.5$  and  $50.2 \pm 7.8$ ,  $P > 0.05$ ), survivors had higher A-a gradient than nonsurvivors ( $697.1 \pm 50.9$  vs.  $548.5 \pm 80.3$ ,  $P = 0.025$ ). We suggest that this is associated not only with patient's illness severity, but also with type of illness, other organ support, and potential complications related to ECMO.

Bleeding and thrombosis have been reported to be the most common complications in patients undergoing ECMO. The most common bleeding events included surgical site or cannulation site bleeding and intracranial hemorrhage (31). The only severe bleeding complication was reported in a patient with CDH, who was put on VA ECMO and whose ECMO support was withdrawn due to intracranial hemorrhage and severe brain injury. We reported transient hematuria in our patients. Thrombotic events included clots in the circuit, clots in the oxygenator, hemolysis, intracranial infarction, and disseminated intravascular coagulation (31). In our series, only one patient's circuit was changed due to clots.

According to the ELSO registry, survival rates to discharge were 73% and 40% in neonates with respiratory and cardiac failure, respectively (20). Though ECMO is an incipient treatment in our unit, the overall survival rate of our center is similar (73% vs. 70%), yet survival rate-to-discharge is better (64% vs. 56%) than that reported in the ELSO registry. In our report, the combined survival rate for patients excluding CDH has been consistently over 85%. The overall survival rate of CDH patients that received ECMO in our center is 40%, which is lower than the rate reported in the ELSO registry (50%) (20).

Less invasive VV ECMO with no injury to the carotid artery has certain theoretical advantages over VA such as higher survival rate and lower neurological morbidity (84% vs. 71%) (32). However, a comparison of patients matched for GA, BW, and severity of illness shows that VV ECMO

has a similar outcome to VA (33). The improved survival rate for VV ECMO may be due to a bias in selection of less sick neonates for VV ECMO compared to VA mode (21,34,35). In our center, six patients received VA ECMO and five received VV ECMO. Mortality rate is higher in VA ECMO than VV ECMO in our patients (50% vs. 20%).

To the best of our knowledge, our NICU serves as the single pre- and postnatal ECMO referral center in Turkey. Our experiences with ECMO have guided us to learn more and develop our knowledge about the procedure. Our center started the neonatal ECMO program in

mid-2015 and our early results are encouraging. We think that improved survival rates are possible with increased experience, proper organization of transport, and advancement in ECMO circuit technology. Owing to advanced respiratory therapies, including HFV, iNO, and all the surgical facilities in our unit, identification of ECMO support candidates and timely referral for ECMO will offer a survival opportunity for these complex neonatal cases. Long-term follow-up is warranted to evaluate the neurodevelopmental and pulmonary functions of neonatal ECMO survivors.

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