Thursday 28th April 14.00 – 15.00
Live Abstract Presentations (live streamed with recording) in Main Auditorium

25 Early Use of Inhaled Nitric Oxide in Neonates with Congenital Diaphragmatic Hernia: Which Echocardiographic Subgroups Benefit?

Caroline Yeon-Kyeong Noh[1], Valerie Chock[1], Shazia Bhombal[1], Enrico Danzer[2], Neil Patel[3], Alex Dahlen[1], Matthew Harting[4], Kevin Lally[4], Ashley Ebanks[4], Krisa Van Meurs[1]
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29 Free hemoglobin, hemolysis, and mortality in CDH neonates receiving venovenous ECMO: a prospective observational study.

Lotte Lemloh, Bartolomeo Bo, Ramona Dolscheid-Pommerich, Andreas Mueller, Dr. Florian Kipfmueller[1], Ms. Lotte Lemloh
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48 CDH pathophysiological phenotypes and ECMO

Dr Abhijit Bhattacharya[1], Dr AC Massolo[2], Dr Sandy Kirolos[1], Dr F Kipfmueller[3], Dr C Davis[1], Dr Abhijit Bhattacharya, Dr Neil Patel[1]
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69 Dynamics of pulmonary hypertension severity in the first 48 hours in neonates with prenatally diagnosed CDH

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85 Impact of repeat extracorporeal life support on mortality and short-term in-hospital morbidities in neonates with congenital diaphragmatic hernia

Dr. Enrico Danzer[1], Dr. Matthew T. Harting[2], Alex Dahlen[1], Dr. Carmen Mesas Burgos[3], Dr. Björn Frenckner[3], Pamela A. Lally[2], Dr. Kevin P. Lally[2], Ashley H. Ebanks[2], Dr. Krisa P. van Meurs[1]
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100 Effect of PDA ligation on Morbidity and Mortality in CDH neonates: A propensity score matched retrospective analysis

Dr. Hamzah Mansoura[1], Dr. Dan Robie[2], Dr. Vikas Gupta[3], Chelsea Drennan[2], Dr. Shobhan Vachhrajani[2], Dr. Kevin Lally[3], Dr. Neal Patel[3], Ashley Ebanks[3], Dr. Matthew Harting[3], Dr. Daniel Robie
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25

Early Use of Inhaled Nitric Oxide in Neonates with Congenital Diaphragmatic Hernia: Which Echocardiographic Subgroups Benefit?

Caroline Yeon-Kyeong Noh[1], Valerie Chock[1], Shazia Bhombal[1], Enrico Danzer[2], Neil Patel[3], Alex Dahlen[1], Matthew Harting[4], Kevin Lally[4], Ashley Ebanks[4], Krisa Van Meurs[1]
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[Background] Inhaled nitric oxide (iNO) has been widely used for the management of pulmonary hypertension (PH) in infants with CDH; however, there is limited evidence of its benefit.
[Methods] This is a retrospective study of CDH Study Group Registry data collected in 2015-2020 to evaluate the impact of early iNO use in the first 3 days of life on outcomes and to identify subgroups who may or may not benefit from iNO. Echocardiographic characteristics from the first study prior to extracorporeal life support (ECLS) or repair were analyzed to determine the impact of early iNO treatment on mortality or use of ECLS. A series of multivariate logistic regression models to test robustness and subgroup analyses wherein patients were stratified by echocardiographic characteristics and defect size were performed.
[Results] Out of 1777 infants, 863 (48.6%) infants received early iNO treatment. Infants treated with iNO had lower birth weight, larger defect size, more severe PH, and abnormal ventricular size and function. After controlling for these factors (in Model C), early iNO use was associated with increased mortality (OR 2.08, 95%CI 1.06-4.06) and increased ECLS use (OR 3.36, 95%CI 2.07-5.45) (Figure 1). Subgroup analyses after stratification by echocardiographic characteristics and defect size failed to identify a subgroup of infants for which early iNO treatment was associated with decreased ECLS use or improved survival, including those with severe PH without LV dysfunction. In addition, early iNO use when used in milder forms of disease with smaller defects and less severe echocardiographic parameters was also associated with significantly higher mortality.
[Conclusions] Use of iNO in the first 3 days of life prior to ECLS or repair was not associated with a reduction in mortality or ECLS use in any of the echocardiographic subgroups identified. Further study of iNO use is warranted in the CDH population.

Images

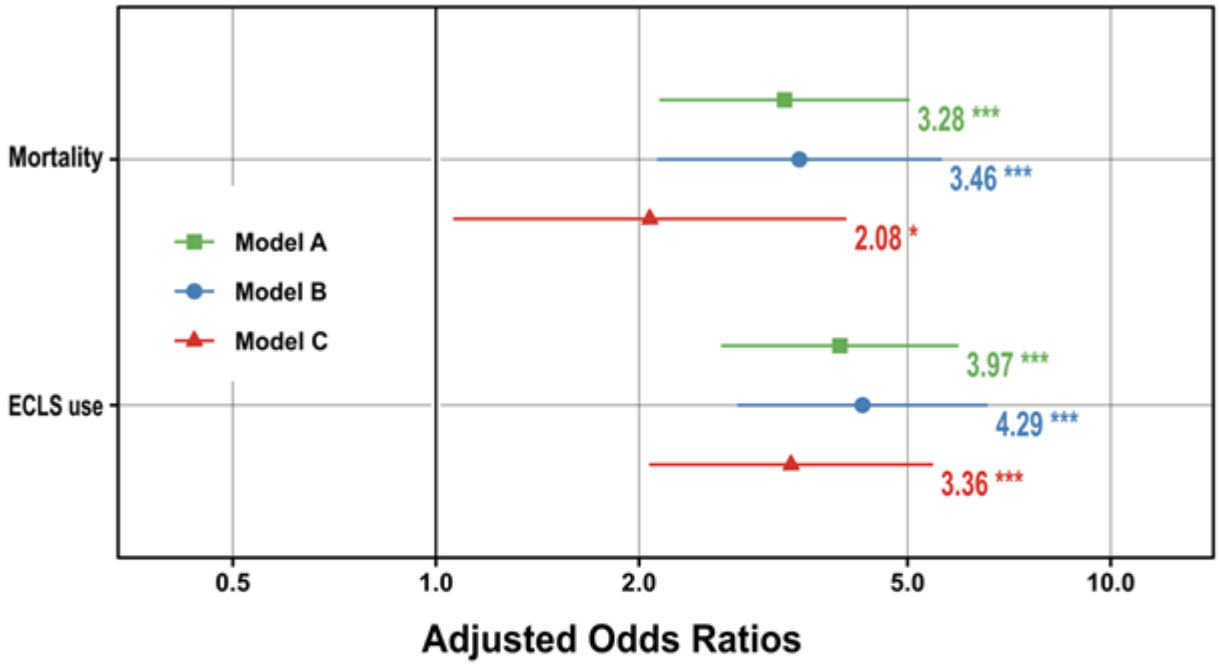

Figure 1. The impact of early iNO therapy on death and ECLS use based on a series of multivariate regression models. Values are presented as 'adjusted OR [95% CI]'. (***, $p < .001$; **, $p < .01$; *, $p < .05$)

Model A: Early iNO use adjusted for echocardiographic characteristics (severity of PH, ductal and atrial shunt patterns, and ventricular size and function)

Model B: Model A adjusted for neonatal characteristics (birth weight, delivery method, 5-minute Apgar score, and inborn status) and defect side

Model C: Model B adjusted for anatomic characteristics (defect size and repair type)

29

Free hemoglobin, hemolysis, and mortality in CDH neonates receiving venovenous ECMO: a prospective observational study.

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Objective: Hemolysis, defined as a plasma free hemoglobin (PFH) >50 mg/dl, has been associated with mortality and poor outcome in neonates receiving extracorporeal life support (ECLS). Among neonates receiving ECLS for respiratory failure, those with congenital diaphragmatic hernia have a high mortality of approximately 50%. Aim of this study was to investigate the kinetics of PFH and its association with outcome in CDH neonates during venovenous ECLS.

Methods: Sixty-two patients were prospectively enrolled. Venovenous ECLS was performed using a Medos DP3 pump with a Hilite 800LT oxygenator (Xenios AG). PFH was determined once daily during ECLS using spectrophotometric testing. Hemolysis was defined as a PFH >50mg/dl. Group allocation according to presence or absence of hemolysis.

Results: Hemolysis occurred in 50% during ECLS and in 33.9% within the first 7 days. Characteristics of patients with and without hemolysis are demonstrated in table 1. Mortality for neonates with hemolysis was 64.5% compared to 29% (p=0.005). The ECLS duration was < 7d in 41.9%, 7-14 days in 25.8%, and > 14d 32.3%, with a mortality of 23.1%, 37.5%, and 85%, respectively. 19.2%, 50% and 90% of patients developed hemolysis within one, two, and > 2 weeks of ECLS, respectively. On univariate analysis hemolysis, ECLS duration >10 days, and prematurity <35weeks were significantly associated with mortality. On multivariate analysis, only hemolysis remained significantly associated with death (HR: 2.72; 95%CI: 1.04-7.09, p=0.041), but neither prematurity <35 weeks (HR: 1.32; 95%CI: 0.56-3.13, p=0.523) nor ECLS duration >10 days (HR: 1.86; 95%CI: 0.80-4.31, p=0.150).

Conclusion: In our cohort, we observed a high rate of hemolysis during venovenous ECLS in CDH neonates which remained independently associated with mortality after correcting for confounders. For routine use it must be considered that preanalytical handling impacts PFH testing.

Images

	Group allocation		
Variables	**No Hemolysis**	**Hemolysis**	**p-value**
Sex, male	59.0%	51.8%	0.617
Gestational age, weeks	**38.0 [IQR 36.9-38.7]**	**36.6 [IQR 34.1-38.4]**	**0.028**
Prematurity <35 weeks	**6.5%**	**38.7%**	**0.002**
Left-Sided CDH	80.7%	77.4%	0.760
Liver-up CDH	71.0%	83.9%	0.231
13 French canula	**90.3%**	**64.5%**	**0.015**
ECLS duration, days	**7.5 [IQR 3.6-9.0]**	**16.8 [IQR 8.2-21.6]**	**<0.001**
Dialysis	6.5%	22.6%	0.073
Mortality	**29.0%**	**64.5%**	**0.005**
Weaning failure	**0.0%**	**38.7%**	**<0.001**

48

CDH pathophysiological phenotypes and ECMO

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Background
ECMO is an established therapy in severe CDH. However, controversies persist in relation to patient selection, ECMO mode, and timing of repair. Improved understanding of underlying patient pathophysiology may guide individualized ECMO strategies and improved outcomes.

This study aimed to describe pre-ECMO pathophysiological phenotypes and their relationship to ECMO course and outcomes.

Method
Retrospective single-centre cohort analysis of eligible CDH cases between 2017-2021. Pre-ECMO phenotypes were based on physiological and echocardiographic parameters in the first 24 hours of life using previously described cut-off values:

- Pulmonary hypoplasia (PHypo): lowest pCO2 60 mmHg (8 kPa) 1
- Pulmonary hypertension (PH): PDA shunt bidirectional or right-to-left AND either pre-ductal SpO2 85% OR RV dysfunction (tissue Doppler RV E' 4.6 cm/sec or RV Global Longitudinal Strain (GLS) -14% 2,3
- LV dysfunction (LV Dysfx): LV global longitudinal strain (GLS) -16% 2

Outcomes were compared between phenotypic subgroups.

Results
13 eligible CDH cases were identified. All received VA ECMO and had CDH stage C or D defects. Two pre-ECMO phenotypes were identified: PH+LV Dysfx in 5 (38%) cases, and PH+PHypo+LV dysfx in 8 (62%) cases, Table 1.

The PH+PHypo+LV dysfx phenotype was associated with significantly longer duration of ECMO [16 (4-28) vs. 6 (2-10) days, p 0.047]. All cases with PH+LV dysfx phenotype were repaired after ECMO decannulation, whereas the majority of PH+PHypo+LVDsyfx cases were repaired on ECMO 5 (71%), p 0.03.

Conclusion
Pre-ECMO pathophysiology may influence ECMO course, including duration of ECMO and timing of repair. Recognition of different CDH phenotypes may improve prognostication and guide personalized management strategies in patients receiving ECMO.

Images

Table 1: Pre-ECMO phenotypes and ECMO characteristics in CDH

	Pre-ECMO Phenotype		P value
	PH+LVdysx	PH+PHypo+LVdysfx	
N (%)	5 (38)	8 (62)	-
Left sided CDH, n (%)	5 (100)	6 (75)	0.49
ECMO duration (days)	6 (2-10)	16 (4-28)	**0.047**
Repair on ECMO, n (%)	0 (0)	5 (71)	**0.03**
Survival, n (%)	4 (80)	5(63)	0.99

PH, pulmonary hypertension; PHypo, pulmonary hypoplasia; LVdsyfx, left ventricular dysfunction.

69

Dynamics of pulmonary hypertension severity in the first 48 hours in neonates with prenatally diagnosed CDH

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Background

Pulmonary hypertension (PH) is one of the major contributing factors for the high morbidity and mortality in congenital diaphragmatic hernia (CDH), however early postnatal course of PH is poorly investigated. This study aims to describe the early course of CDH-PH and identify contributing factors in developing and sustaining severe PH.

Methods
Newborns with prenatally diagnosed CDH received three standardized echocardiographic examinations at 2-6 hours, 24 and 48 hours of life. The degree of PH was graded in one of three categories: mild/no, moderate, and severe PH. The three groups and their course of PH over 48 hours were compared in their characteristics using univariate and correlational analysis.

Results
Initially, approximately one third of patients had mild/no, moderate or severe PH, respectively (Figure 1). The course of PH varied markedly based on the initial staging. No patient with initial mild/no PH developed severe PH, required extracorporal membrane oxygenation (ECMO)-therapy or died. Most patients with initial severe PH had persistent PH at 48 hours (63%), required ECMO (69%), and died (54%). Major risk factors included younger gestational age, intrathoracic liver herniation, prenatal fetoscopic endoluminal tracheal occlusion (FETO)-intervention, lower lung to head ratio (LHR) and total fetal lung volume (TFLV). Patients with moderate and severe PH showed no difference in these characteristics, but in their mortality (p=0.001) and ECMO-rate (p=0.001 – 0.035). Regardless of PH-severity, infants with left-sided CDH and LHR >45 % had a 100% survival.

Conclusions
To our knowledge, this is the first study assessing the course of CDH-PH in the first postnatal 48 hours at three defined time points. The prognosis for patients with initial mild/no PH is excellent. Patients with severe PH at any point have a significantly higher risk for ECMO and mortality. Assessing PH early should be a primary goal in the care for CDH neonates.

Images

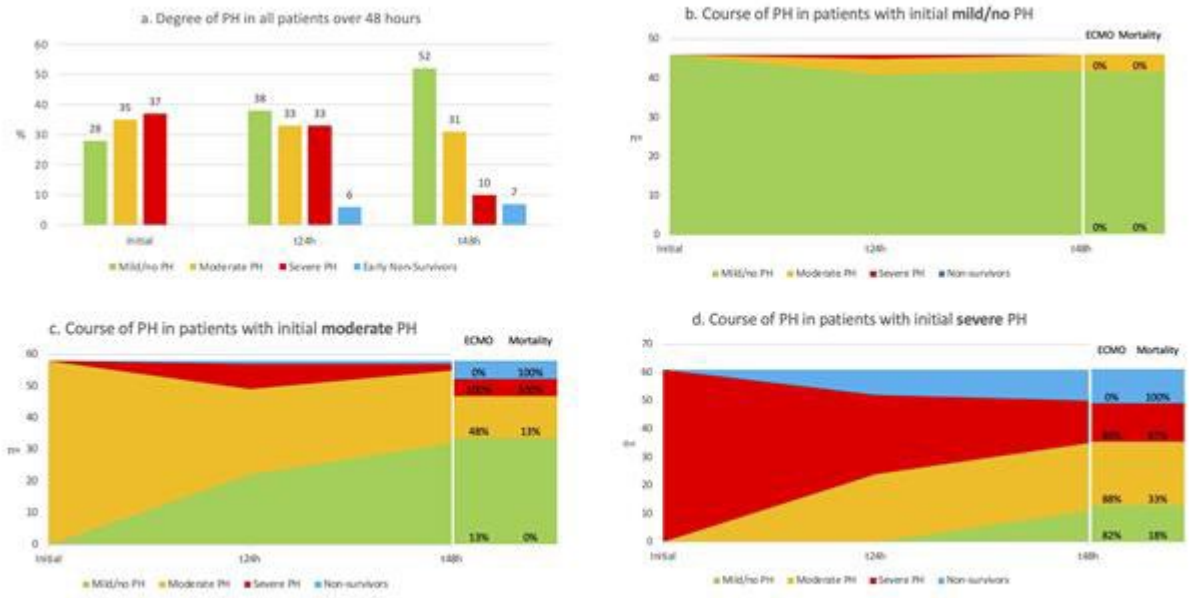

Figure 1: a) Overall distribution of patients showing mild/no, moderate or severe PH at initial, 24- and 48-hour evaluation. b-d) Course of PH in patients with initial mild/no (b), moderate (c), and severe (d) PH. ECMO-rate and mortality are given in relation to the degree of PH at 48 hours.

85

Impact of repeat extracorporeal life support on mortality and short-term in-hospital morbidities in neonates with congenital diaphragmatic hernia

Dr. Enrico Danzer[1], Dr. Matthew T. Harting[2], Alex Dahlen[1], Dr. Carmen Mesas Burgos[3], Dr. Björn Frenckner[3], Pamela A. Lally[2], Dr. Kevin P. Lally[2], Ashley H. Ebanks[2], Dr. Krisa P. van Meurs[1]
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Objective
To evaluate the impact of repeat extracorporeal life support (ECLS) on survival and short-term in-hospital outcomes in neonates with congenital diaphragmatic hernia (CDH).
Methods
This is a retrospective cohort study of all ECLS-eligible CDH neonates enrolled in the CDH Study Group registry between January 1995 to December 2019. The primary outcomes were survival and short-term in-hospital morbidities.
Results
Of 10,089 ECLS-eligible CDH infants, 3025 (30%) received one ECLS course, and 160 (1.6%) required multiple courses. Of those, 155 received two courses, and 5 required three ECLS courses. CDH neonates who received more ECLS courses had more severe disease, as well as lower overall survival rates. The overall survival rate for patients who underwent no ECLS courses, one ECLS course, and two or more ECLS courses were 86.9% ± 0.8%, 53.8% ± 1.8%, and 43.1% ± 7.7%, respectively. Despite this, the ECLS survival rate is increased by 4.6%±4.7% (p=0.05), when adjusted for institutional experience and case severity, for CDH neonates treated at centers that conduct repeat ECLS support compared to those that do rarely offer repeat ECLS. This suggests that there would be an overall survival benefit from increased use of multiple ECLS (Figure 1). Infants who did not require ECLS support had the lowest morbidity risk while survivors of multiple ECLS courses had the highest rates of short-term in-hospital cardiopulmonary and neurological morbidities ($p<0.05$ for all).
Conclusions
Although survival is lower for a repeat ECLS course, the use of multiple ECLS courses has the potential to increase overall survival for CDH neonates. Higher annual volume of multi-course ECLS is associated with improved survival. This potential survival advantage of repeat ECLS support must be balanced against the increased risk of short-term in-hospital morbidities.

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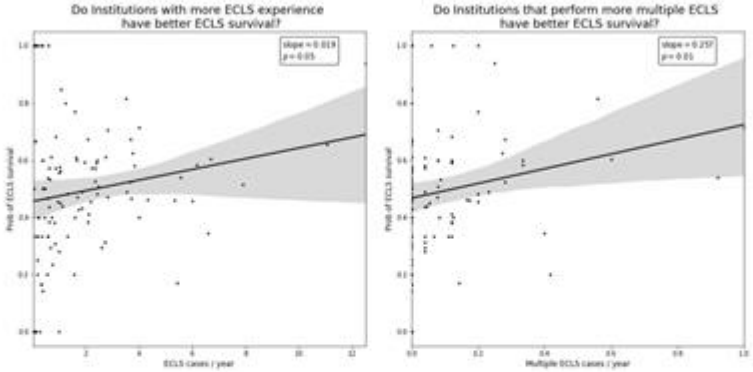

Figure 1. Relationship between institutional experience and the survival rates for the CDH patients requiring ECLS. The black line shows a linear fit; confidence intervals, and p-values, are based on heteroskedasticity-robust confidence intervals. (**Left**) Institutions that perform ECLS cases more frequently have better ECLS survival rates (p=0.05). (**Right**) institutions that regularly perform multiple ECLS also have better ECLS survival rates (p=0.01). We performed an ad hoc estimate of the survival benefit associated with institutions that regularly perform multiple ECLS compared to institutions that rarely perform multiple ECLS: adjusting for other measures of institutions experience and patient severity, we found a survival benefit of 4.6 ± 4.7 percentage points (p=0.05).

100

Effect of PDA ligation on Morbidity and Mortality in CDH neonates: A propensity score matched retrospective analysis

Dr. Hamzah Mansoura[1], Dr. Dan Robie[2], Dr. Vikas Gupta[3], Chelsea Drennan[2], Dr. Shobhan Vachhrajani[2], Dr. Kevin Lally[3], Dr. Neal Patel[3], Ashley Ebanks[3], Dr. Matthew Harting[3], Dr. Daniel Robie

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Background:
Neonates with congenital diaphragmatic hernia (CDH) frequently require aggressive treatment of CDH-associated pulmonary hypertension (CDH-PH). In select patients, the patent ductus arteriosus (PDA) persists and is occasionally ligated, with incompletely understood consequences. This study aims to compare outcomes between ligated and non-ligated infants. We hypothesize that PDA ligation is associated with increased risk of morbidity and mortality.
Methods:
All repaired patients with CDH who lived >30 days and were diagnosed within 28 days of life (DOL) between 2007-2020 in the CDH study group were included. Patients with PDA ligation at <14 DOL were excluded. Using propensity scores, patients were matched on 7 covariates: birth- weight, EGA, 5min APGAR, cardiac abnormalities, chromosomal abnormalities, defect size, and liver position. We performed conditional logistic regression for matched-pair analysis. Primary outcome was mortality, and morbidities were secondary outcomes.
Results:
3950 patients with CDH were identified in the database. 392 were excluded for missing data for at least one covariate and 5 excluded because PDA ligation was performed <14DOL. Of the remaining 3558 patients, 50 (1.3%) underwent PDA ligation; of these, 25 (50%) were female, 12 (24%) had major cardiac abnormalities, 8 (16%) had chromosomal abnormalities, 36 (72%) had liver position in chest, and 39 (78%) had C/D size defects. Prior to matching, the PDA ligation group had significantly higher mortality (OR 2.9, 95% CI 1.32-5.84, p=0.004). PS- matching (4:1) identified two well-balanced groups (-PDA=176, +PDA=44) for analysis. Mortality was not significantly different after matching (OR 1.0, 95%CI 0.442-2.26 p=1.0). The odds of mechanical ventilation at discharge (OR 7.69, 95%CI 2.71-21.8 p=0.00013), and of CDH-PH medication at discharge (OR 4.69, 95%CI 2.28-9.63, p<0.0001) were significantly higher in the ligated group.
Conclusions:
PDA ligation was not associated with increased mortality, but was associated with an increased risk of mechanical ventilation and CDH-PH pharmacotherapy at discharge.

Graph

		Propensity Score 4:1 Matched Pairs				
		No PDA Ligation	PDA Ligation	p value	SMD	
		n=176	n=44			
BirthWt (mean (SD))		2.69 (0.59)	2.72 (0.57)	0.703	0.065	
APGAR5 (median [IQR])		6.00 [5.00, 8.00]	7.00 [5.00, 8.00]	0.731	0.046	
Preterm (<37wks) (%)	No	127 (72.2)	31 (70.5)	0.852	0.038	
	Yes	49 (27.8)	13 (29.5)			
CardAbn (%)	None	112 (63.6)	27 (61.4)	0.941	0.062	
	Minor	36 (20.5)	9 (20.5)			
	Major	28 (15.9)	8 (18.2)			
ChromAbn (%)	No	162 (92.0)	39 (88.6)	0.547	0.116	
	Yes	14 (8.0)	5 (11.4)			
Defect Size (%)	A	0 (0.0)	0 (0.0)	0.845	0.09	
	B	32 (18.2)	9 (20.5)			
	C	102 (58.0)	26 (59.1)			
	D	42 (23.9)	9 (20.5)			
Liver (%)	Abdomen	49 (27.8)	12 (27.3)	1	0.013	
	Chest	127 (72.2)	32 (72.7)			
	Unadj. OR	95%CI	p value	Adj. OR	95%CI	p value
Mortality	2.9	1.3-5.8	0.0042	1.0	0.4-2.3	1
Mechancial Ventilation at discharge	12.6	6.2-25.1	<0.0001	4.0	1.7-9.4	0.0014
Any ECMO	2.0	1.1-3.7	0.0154	1.2	0.6-2.4	0.619
PHTN medication at discharge	5.8	3.2-10.7	<0.0001	6.0	2.8-13.0	<0.0001
Length of Stay >100D	31.0	12.7-91.2	<0.0001	25.6	6.0-110.0	<0.0001