Severity of Illness in the Early Pre-Surgical Management of Congenital Diaphragmatic Hernia

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Scope of the Problem:

- Congenital diaphragmatic hernia (CDH) carries significant morbidity and mortality despite critical and surgical intervention.
  - Maintains an estimated 60% - 70% survive Rate
    - High-volume centers.
- Approximate: 1:3000 live births[1]
  - Highly unpredictable outcomes
  - Significant resource allocation:
    - iNO/ECMO
    - "Long course of course of care"
    - "Follow-up care"

Side of Hernia	Incidence
Left Side	~85%
Ride Side	~13%
Bilateral	~2%

[1] Losty PD, et al. Congenital diaphragmatic hernia: Where and what is the evidence?. Seminars in Pediatric Surgery. 2014; 23: 278-282
[2] Congenital Diaphragmatic Hernia: Updates and Outcomes. Jennifer R. Benjamin, MD, Matthew J. Bizzarro, MD and C. Michael Cotten, MD, MHS. NeoReviews Vol. 12 No. 8 August 1, 2011. pp. e439 -e452

Objectives:

- Frame the ongoing controversies regarding Pre-surgical management of infant with CDH
- Introduce Potential Pre- and Post-neonatal mortality risk factors
- Discuss the Pre-surgical Clinical Measures and mortality risk
- Review use of ECMO and its relationship to
  - Outcomes
  - Risk Scoring

Background:

- Early pre-surgical management is often complicated by physiologic derangement 2° to:
  - Degree of lung hypoplasia
  - Pulmonary hypertension
  - Need for inter-facility transport
    - Not without risk
- Infants who ***fail*** to achieve adequate oxygenation and/or perfusion with maximum medical support are regularly supported by extracorporeal membrane oxygenation (ECMO)

Background

- Questions remain regarding the best practice approaches to stabilization intervention and patient selection for advance therapies.
  - Validated postnatal inter-institutionally applicable adjusted measure of CDH outcomes remains elusive
- Currently, no one risk matrix has the ability to discern:
  - Level of Pulmonary compromise/hypoplasia
  - Resource needs
  - Survival

Prenatal Diagnosis:

- Beneficial in improving postnatal management
- Suggested Measures:
  - Observed to Expected - Head: Lung Ratios
  - MRI Lung Volumetry
  - Side of Herniation (right worse prognosis)
  - Herniation Size (liver/stomach in chest)
  - Associated congenital abnormalities
  - Delivery site
  - Physiologic Derangement/Clinical Status

[1] Solevag AL & Cheung P. Predicting the Outcome of Congenital Diaphragmatic Hernia in a SNAP (Score for Neonatal Acute Physiology). Pediat Critical Care Med. 2016; 17(6): 570 - 571

O/E Lung:Head Ratio

- Retrospective Review:
  - Prenatally Diagnosed
  - 18 to 38 weeks
  - Excluded:
    - Major congenital abnormalities
    - Bilateral CDH
    - Delivery < 30 Weeks
    - Terminated pregnancies
  - N=41
    - <45% Severe Risk
    - >45% Low Risk

Conclusion:

- O/E LHR does not correlate with long term outcome.

Table 2
Demographics for surviving neonates, classified according to O/E LHR.

O/E LHR	Moderate to severe risk <45% (n = 28)	Low risk >45% (n = 13)
Gender (M:F)	19:9	5:8
Gestational age at diagnosis (weeks)	24, 18–36	23, 18–37
Laterality (L:R)	26:2	13:0
LHR (mean)	1.30, 0.64–1.99	1.65, 0.87–2.70
Liver up on antenatal US	13 (46%)[a]	1 (8%)
Gestational age at birth (weeks)	38, 33–40	38, 33–40
Birth weight (kg)	3.20, 1.65–4.18	3.23, 2.00–3.88
Apgar (1 min)	7, 1–9	5, 0–8
Apgar (5 min)	8, 3–9	8, 1–9
Umbilical arterial pH	7.3, 7.05–7.40	7.27, 7.04–7.35
Neonatal pH	7.19, 6.86–7.40	7.18, 6.35–7.31
Surfactant use	1	0
Nitric oxide use	11 (39%)	3 (23%)
Ventilation (days)	11, 3–48	12, 5–25
Oxygen requirement (days)	19, 1–67	17, 8–85
ECMO required	1	0
Age at repair (days)	3, 1–21	3, 2–12
Open repair (laparotomy)	19 (68%)	9 (69%)
Thoracoscopic repair	4 (14%)	4 (31%)
Intrathoracic liver	10 (36%)	5 (38%)
Patch/flap required	17 (61%)	5 (38%)
ICU admission (days)	16, 5–71	16, 7–54
Hospital admission (days)	40, 9–111	41, 13–117
CDH recurrence	8 (29%)	5 (38%)[b]
Bayley scale (abnormal)	7/19 (37%)	2/8 (25%)
AIMS (abnormal)	8/23 (35%)	7/13 (54%)
REEL-3 (abnormal)	8/19 (42%)	2/10 (20%)
Neurodevelopment concerns	9 (32%)	3 (23%)
Echocardiogram abnormal	5 (18%)	0
V/Q differential	38, 10–70	32, 16–42
Height (<50th centile)	18/28 (64%)	7/13 (53%)
Weight (<50th centile)	20/28 (71%)	10/13 (77%)
Age at last review (years)	6.8, 1–11	6, 4–10

Results shown are mean values with ranges.
AIMS – Alberta Infant Motor Score; REEL – receptive-expressive emergent language.
[a] $p = 0.03$.
[b] Two patients had multiple hernia recurrences.

King SK, et al. Journal of Pediatric Surgery 2016; 51: 699-702

MRI Lung Volumes

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Table 3—Summary of study characteristics

	Study site	Study period	Study population				MRI settings			Study quality			Author	
Reference	City	Start-End	LCDH	RCDH	n	Survival (%)	GA at MRI (wk)	Slice thickness (mm)	Gap size (mm)	Prospective study	MRI setting	Population	replied	Raw data
Barnewolt *et al.*, 2007	Boston	12/00 - 01/05	11	3	14	78.6	-	-	-	1	1.5	3	no	-
Bonfils *et al.*, 2006	Grenoble	01/96 - 08/04	18	4	22	45.5	26-36	-	-	0	1	3	yes	-
Gaillot *et al.*, 2007	Rennes	11/03 - 03/06	5	2	7	85.7	32-40	-	-	0	0.5	2	yes	yes
Gorincour *et al.*, 2005	multicentre[a]	01/99 - 04/03	66	11	77	40.3	24-37	3-5	-	1	2.5	2	no	-
Hayakawa *et al.*, 2007	Nagoya	07/97 - 06/06	21	0	21	61.9	27.9-35.9	7-10	1.4-2	1	2.5	2	no	-
Hedrick *et al.*, 2007	Philadelphia	01/96 - 01/06	89	0	89	66.3	29.1-36.1	-	-	0	0.5	2	no	-
Jani *et al.*, 2008	Barcelona, Leuven, Lille, Paris	from 95	127	21	148	64.2	22-38	-	-	0	1	3	no	-
Kitano *et al.*, 2005	Tokyo (National Center for Child Health and Development)	04/02 - 10/04	15	2	17	76.5	21-39	-	-	0	1	3	yes	-
Leuven Group	Leuven	01/02 - 07/07	22	1	23	82.6	22.3-34.4	4	0	-	-	-	yes	yes[b]
Liu *et al.*, 2001	New York	05/99 - 12/00	2	0	2	0	30-33	4	0	0	3	3	no	yes[b]
Mahieu-Caputo *et al.*, 2001	Paris	98 - 99	11	2	13	61.5	28-37	3	-	1	1	2	yes	yes[b]
Mannheim Group	Mannheim	09/01- 08/06	76	10	87[c]	81.6	22.9-38.7	3-4	0	-	-	-	yes	yes[b]
Matsuoka *et al.*, 2003	Kobe	03/97 - 09/01	2	0	2	0	30	5-7	0-1	1	2.5	2	no	yes

Prenat Diagn 2011; 31: 1086–1096. DOI: 10.1002/pd

Mayer S, Klaritsch P, Petersen S, et al. Prenat Diagn 2011; 31: 1086-1096

Meta-analysis: Prospective Studies

- Nineteen studies (n = 602 fetuses) were included
- Survival associated
  - Left sided defects (OR 2.52;p = 0.01)
  - Liver down (OR 0.18; p<0.0001)
  - Higher TFLV (MD 9.63; p<0.0001)
  - O/E TFLV (SMD 0.98; p<0.0001)
  - Higher birth weight (MD 146.60; p = 0.04).
- Not correlated with Survival
  - GA at MRI (MD 0.70)
  - GA at birth (MD 0.33)

Mayer S, Klaritsch P, Petersen S, et al. Prenat Diagn 2011; 31: 1086-1096

MRI FLV - Survival

- Association between **survival** and FLV measurement
  - 25±9.7 vs. 7.6±4.4 ml ($p<0.0001$)
- All infants with FLV <8.1 ml died whereas all with FLV >15.6 ml survived to discharge
  - Death even if ECMO therapy was initiated
  - FLV of 8.1-39.9 ml survived and may benefit from ECMO
- All infants with FLV >36.9 ml (50.9% rFLV) survived without ECMO support
  - Average FLV of healthy controls 77.7±25.5 ml

Fetal MR lung volumetry in congenital diaphragmatic hernia (CDH): prediction of clinical outcome and the need for ECMO. *Kilian AK et al. Klin Padiatr. 2009 Sep; 221 (5):295-301. Mannheim, Germany*

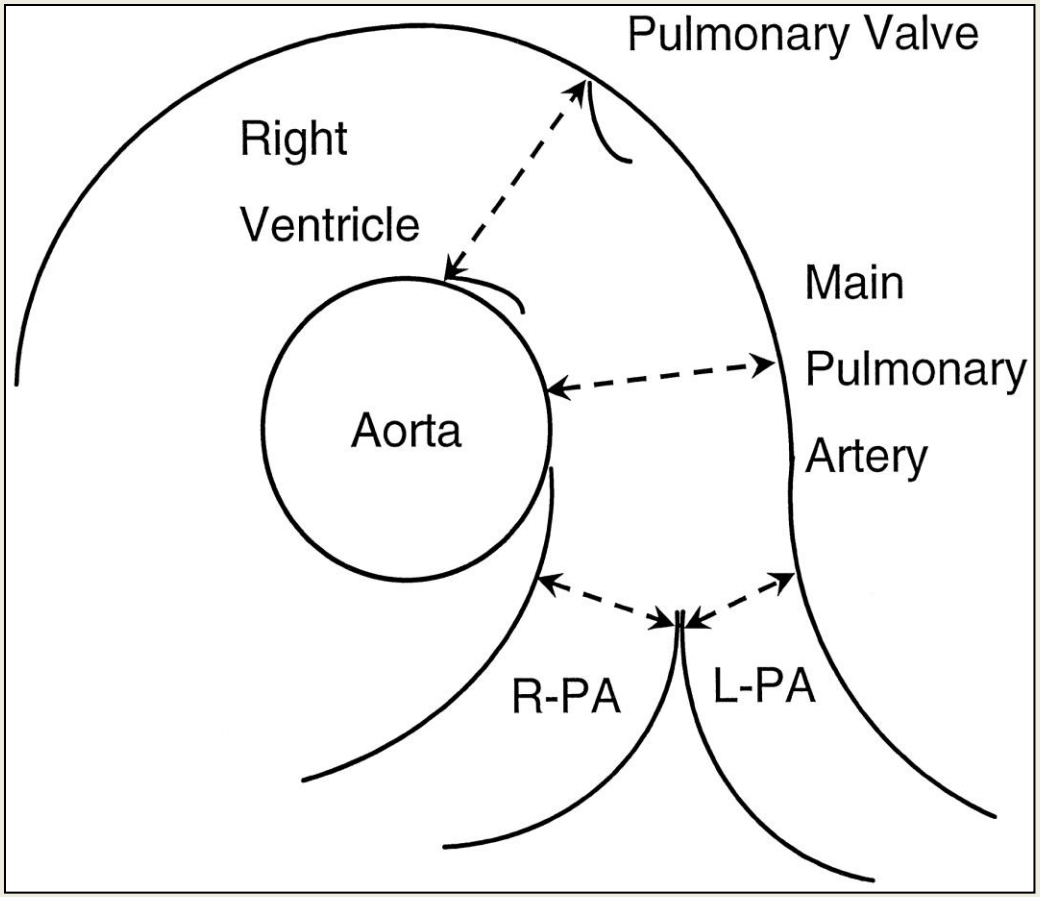
MRI-FLV – ECMO Support

- FLV Associated with ECMO Support
  - 18.2±10.1 vs. 27.2±10.2 ml (p=0.003)
- Associated ECMO Survival
  - 22.3±8.6 vs. 8.3±5.9 ml (p=0.005)
- Side of defect did not influence ECMO (p=0.838)

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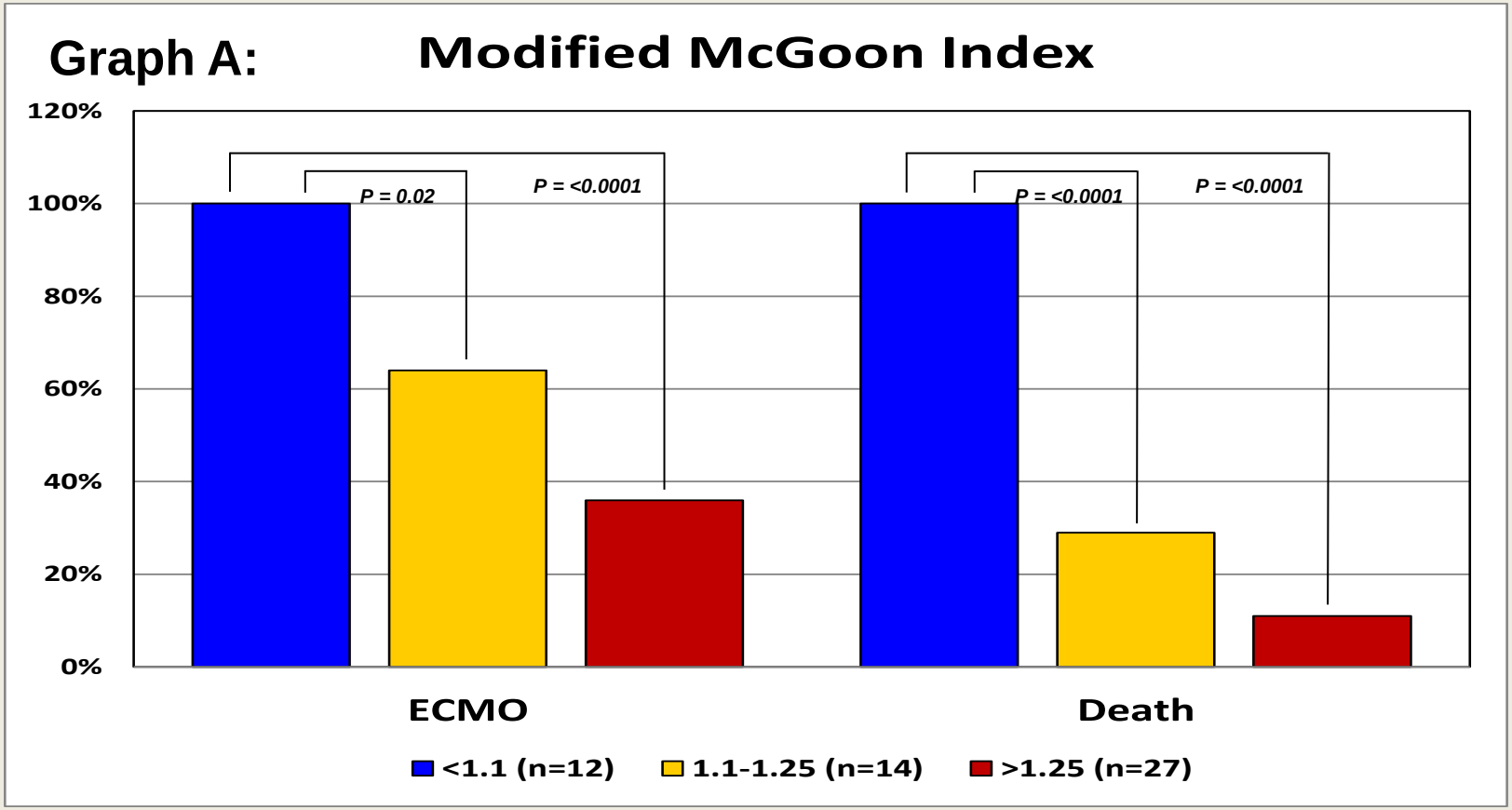
Modified McGoon Index

$$MGI = (RPA_d + LPA_d) / Aortic_d$$



Suda K et al Pediatrics. 2000 May;105(5):1106-9.Echocardiographic predictors of outcome in newborns with congenital diaphragmatic hernia.

MGI Appears to Predict ECMO and Outcome



Leif, L., Kuch, B.A. , Potoka, D. , Debrunner, M. , Brozanski, B. , Mahmood, B. Presented at ELSO, 2013

Demographic Distribution: (<34 Vs. ≥34 weeks)

Table 1 Demographic variables associated with CDH patients referred to CHND NICUs

Variable	All	GA/BW stratification		*p* Value
		< 34 wks or < 2 kg	≥ 34 wks and > 2 kg	
Number of CDH patients	572	64 (11)	508 (89)	
Median GA in weeks (IQR)	38 (36, 39)	32 (31, 33)	38 (37, 39)	< 0.001
Median BW in grams (IQR)	3,000 (2,580, 3,345)	1,777 (1,438, 1,970)	3,068 (2,745, 3,400)	< 0.001
SGA (< 10%ile)	68 (12)	14 (22)	54 (11)	0.014
Multiple gestations	23 (4)	8 (13)	15 (3)	0.002
Cesarean delivery	256 (45)	42 (66)	214 (42)	0.001
Antenatal steroids	65 (11)	26 (41)	39 (8)	< 0.001
APGAR @1 minute ≤ 5	333 (58)	47 (73)	286 (56)	0.004
APGAR @5 minute ≤ 5	142 (25)	26 (41)	116 (23)	0.007
APGAR @10 minute ≤ 5	55 (10)	11 (17)	44 (9)	0.005
Surfactant before referral	90 (16)	33 (52)	57 (11)	< 0.001

Abbreviations: BW, birth weight; CDH, congenital diaphragmatic hernia; GA, gestational age; IQR, interquartile range; SGA, small for gestational age.
Note: Using published gender-specific and gestational age-specific normative values.[8] Data presented are *N* (%) or median (IQR).

Grover TR, Murthy K, Brozanski B, et al. Short-term Outcomes and Medical and Surgical Intervention in Infants with Congenital Diaphragmatic Hernia. Am J Perinatol 2015; 32:1038-1044

Resource Utilization (<34 Vs. ≥34 weeks)

Table 2 Respiratory support during CDH hospitalization, stratified by gestational age and birth weight

VARIABLE	ALL, ($N = 572$)	< 34 wks or < 2 kg ($n = 64$)	≥34 wks and > 2 kg ($n = 508$)	*p* Value
Advanced respiratory support				
Median days on respiratory support (median, IQR)	18 (10, 38)	46 (13, 74)	18 (10, 36)	0.039
Median days on mechanical ventilation	15 (6, 29)	17 (5, 38)	15 (6, 28)	0.735
High-frequency oscillatory ventilation, *N* (%)	225 (39)	23 (36)	202 (40)	0.590
Median duration in days	5 (2, 13)	7 (2, 19)	5 (2, 13)	0.214
Conventional ventilation	510 (89)	50 (78)	460 (91)	0.005
Median duration in days	12 (5, 23)	14 (3, 47)	12 (5, 22)	0.366
Vasopressors				
Dopamine	419 (73)	50 (78)	369 (73)	0.454
Epinephrine	192 (34)	23 (36)	169 (33)	0.675
Milrinone	172 (30)	17 (27)	155 (31)	0.565
Dobutamine	76 (13)	12 (19)	64 (13)	0.173
Vasopressin	30 (5)	4 (6)	26 (5)	0.764
Norepinephrine	15 (3)	1 (1.5)	14 (3)	1.000
Vasodilators				
Inhaled nitric oxide	353 (62)	39 (61)	314 (62)	0.892
Sildenafil	126 (22)	12 (19)	114 (22)	0.631
Prostaglandin E1	37 (6)	4 (6)	33 (7)	1.000
Prostacyclin	19 (3)	1 (1.5)	18 (4)	0.711
Bosentan	12 (2)	0 (0)	12 (2)	0.378
ECMO	186 (33)	6 (9)	180 (35)	< 0.001
Total days on ECMO	11 (7, 18)	19 (15, 37)	11 (7, 17)	0.037

Abbreviations: CDH, congenital diaphragmatic hernia; ECMO, extracorporeal membrane oxygenation.
Note: Data presented are *n* (%) or median, (interquartile range).

Grover TR, Murthy K, Brozanski B, et al. Short-term Outcomes and Medical and Surgical Intervention in Infants with Congenital Diaphragmatic Hernia. Am J Perinatol 2015; 32:1038-1044

Critical Care Intervention Distribution:
Survivors vs. Non-Survivors

Table 4 Therapies utilized by CDH patients during initial hospitalization

Variable	All ($N = 572$)	Survivors ($n = 405$)	Nonsurvivors ($n = 167$)	p Value
Advanced respiratory support				
Median days on mechanical ventilation (median, IQR)	15 (6, 29)	15 (7, 29)	15.5 (2, 27)	0.013
High frequency oscillatory ventilation, *N* (%)	347 (61)	199 (49)	148 (89)	< 0.001
Median duration in days	5 (2, 13)	6 (2, 13)	3.5 (1, 14)	0.039
High-frequency jet ventilation	11 (2)	6 (1.5)	5 (3)	0.31
Median duration in days	4 (1, 9)	2 (1, 4)	9 (6, 15)	0.016
Conventional ventilation	510 (89)	385 (95)	125 (75)	< 0.001
Median duration in days	12 (5, 23)	12 (6, 23)	10 (3, 22)	0.009
Vasopressors				
Dopamine	419 (73)	271 (67)	148 (89)	< 0.001
Epinephrine	192 (34)	103 (25)	89 (53)	< 0.001
Milrinone	172 (30)	91 (22)	81 (49)	< 0.001
Dobutamine	76 (13)	36 (9)	40 (24)	< 0.001
Vasopressin	30 (5)	18 (4)	12 (7)	0.215
Norepinephrine	15 (3)	11 (3)	4 (2)	1.000
Vasodilators				
Sildenafil	126 (22)	81 (20)	45 (27)	0.076
Prostaglandin E1	37 (6)	19 (5)	18 (11)	0.014
Inhaled Prostacyclin	19 (3)	9 (2)	10 (6)	0.036
IV Prostacyclin	19 (3)	7 (2)	12 (7)	0.003
Bosentan	12 (2)	7 (2)	5 (3)	0.346
ECMO	186 (33)	95 (23)	91 (54)	< 0.001
Total days on ECMO	11 (7, 18)	9 (6, 14)	14 (9, 21)	< 0.001
VV	42 (7)	22 (5)	20 (12)	0.012
VA	140 (24)	72 (18)	68 (41)	< 0.001
VV-VA	7 (1.2)	2 (0.5)	5 (3.0)	0.025

Abbreviations: CDH, congenital diaphragmatic hernia; ECMO, extracorporeal membrane oxygenation; VA, venoarterial; VV, venovenous; VV-VA, venovenous converted to venoarterial.
Note: Data presented are *n* (%) or median (interquartile range).

Grover TR, Murthy K, Brozanski B, et al. Short-term Outcomes and Medical and Surgical Intervention in Infants with Congenital Diaphragmatic Hernia. Am J Perinatol 2015; 32:1038-1044

SNAPP-II

(*Score for Neonatal Acute Physiology Version II*)

- Aggregate score derived from a standardized index which records illness severity by the magnitude of derangement physiologic parameters
- Six variables
- Designed for comparing:
  - Acuity across neonatal ICU's
  - Bench Making of outcomes
  - Research adjustment
- Not meant for ethical decision making

Variable	β	Odds ratio	95% CI†	SNAP-II points
MBP 20-29 mm Hg	.88	2.40	1.86-3.10	9
MBP <20 mm Hg	1.94	6.99	4.04-12.08	19
Lowest temperature 95°-96°F	.81	2.23	1.61- 3.10	8
Lowest temperature <95°F	1.55	4.69	2.99-7.24	15
Po_2/Fio_2 ratio 1.0-2.49	.49	1.63	1.20-2.21	5
Po_2/Fio_2 ratio 0.3-0.99	1.57	4.79	3.57-6.41	16
Po_2/Fio_2 ratio <0.3	2.80	16.51	10.00-27.28	28
Lowest serum pH 7.10-7.19	.71	2.02	1.42-2.87	7
Lowest serum pH <7.10	1.57	4.81	3.27-7.07	16
Multiple seizures	1.87	6.50	4.01-10.53	19
Urine output 0.1-0.9 mL/kg/h	.46	1.59	1.22-2.06	5
Urine output <0.1 mL/kg/h	1.82	6.15	4.31- 8.77	18
Constant	–4.69			

MBP, Mean blood pressure; Fio_2, fraction of inspired oxygen.
*Model χ^2 1008.659 with *df* 16, $P < .0000$.
†All variables significant to $P < .001$ or less.

Skarsgard ED, et al. J Perinatol. 2005; 25, 315-319

SNAP-II Predicts Mortality Among Infants with CDH

- Mortality increases consistently as admission Snap-II increases among infants with CDH
- Snap-II yielded a predictive model with comparable discrimination and superior calibration

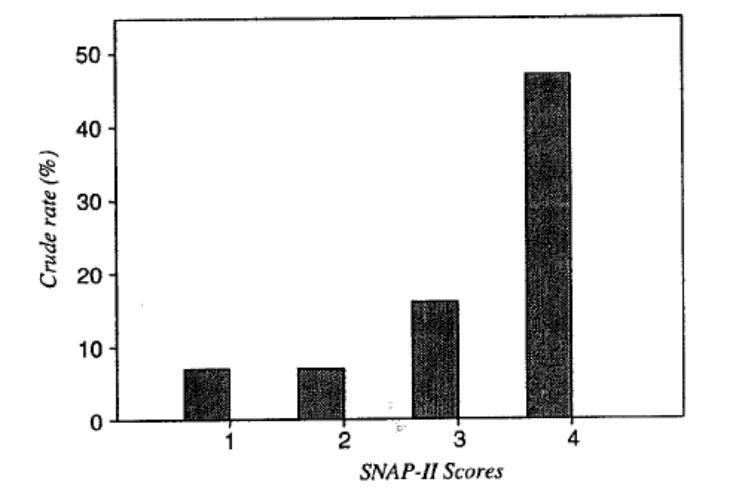


Table 3 Predictive Performance and Goodness-Of-Fit of Logistic Regression Models for Predicting Mortality among Infants with CDH

Variables in model	Gestational age	SNAP-II score	Combined model (gestational age+SNAP-II)	CDHSG model (birth weight+Apgar at 5 minutes)
Mortality				
AUC	0.68	0.76	0.81	0.83
χ^2	2.7	3.8	3.7	19.9

Skarsgard ED, et al. J Perinatol. 2005; 25, 315-319

Distribution of Demographic: ECMO Vs. No ECMO

Table 1 Distribution of demographic and first 24-h of admission physiologic characteristics: ECMO vs. no ECMO.

Variables	ECMO (n = 24)	No ECMO (n = 23)	p Value
Gestational age (weeks)	38.50 [37.0–39.0]	38.0 [36.0–39.0]	0.25
Weight (kg)	3.04 [2.62–3.31]	2.90 [2.45–3.22]	0.36
Male gender	13 (54.2%)	16 (69.6%)	0.22
Median APGAR (5 min)	7.00 [4.0–8.0]	8.0 [6.0–8.0]	0.33
Right-sided defect	3 (12.5%)	5 (21.7%)	0.32
Physiologic characteristics			
Pulmonary hypertension	24 (100%)	16 (69.6%)	0.004*
24-h SNAP-II score	32.0 [25.5–44.0]	20.0 [6.75–24.0]	0.002*
Vasoactive agents	12 (50%)	8 (34.8%)	0.22
Inhaled nitric oxide	21 (87.5%); OR 16.0 [3.57–71.76]	7 (30.4%)	<0.001*
Cardiac arrest	5 (20.8%); 1.23 [1.03–1.55]	0.0 (0.0%)	0.03*
Lowest pH	7.11 [7.00–7.22]	7.21 [7.13–7.31]	0.019*
Lowest PaO_2	29.5 [20.5–46.5]	53.0 [43.3–92.3]	0.015*
Highest $PaCO_2$	79.0 [56.3–99.3]	57.5 [48.0–64.0]	0.006*
Lowest HCO_3	20.0 [18.0–22.0]	21 [19.0–21.8]	0.958
Lowest base excess	−8.0 [−9.0 to −6.0]	−5.0 [−8.5 to −4.8]	0.229
In-hospital mortality	18 (75.0%); OR 31.5 [5.6–175.9]	2 (8.7%)	<0.001*

Categorical data are presented as odds ratio (OR) and 95% confidence interval for statistically significant variables. Continuous data are presented as median [interquartile range].

* Denotes statistical significance defined as a p value < 0.05.

Coleman A, et al. First 24-h SNAP-II score and highest $PaCO_2$ predict the need for ECMO in Congenital Diaphragmatic Hernia. J Ped Surgery. 2013; 48: 2214-2218

Mortality Distribution (SNAP-II & $PaCO_2$)

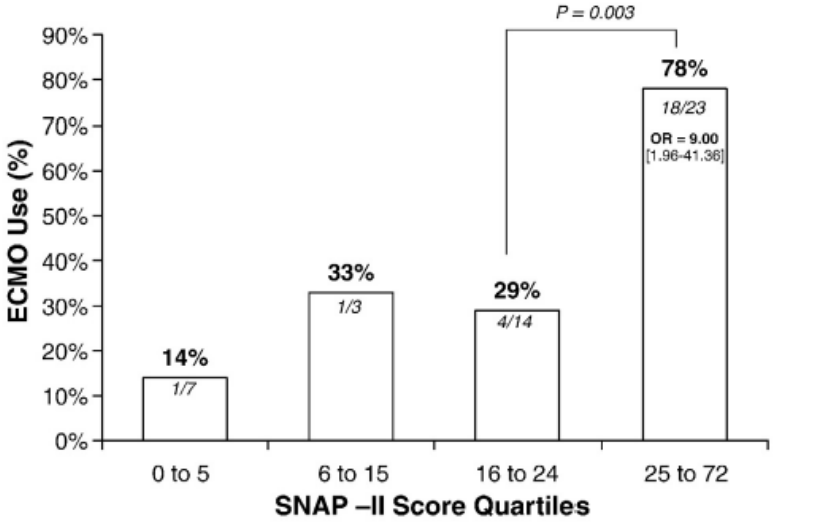


Fig. 2 The rate of ECMO use was found to increase in a stepwise fashion with the highest first 24-h SNAP-II score. *x*-Axis is the highest SNAP-II score in the first 24 h of hospital admission; *y*-axis is the rate of ECMO support.

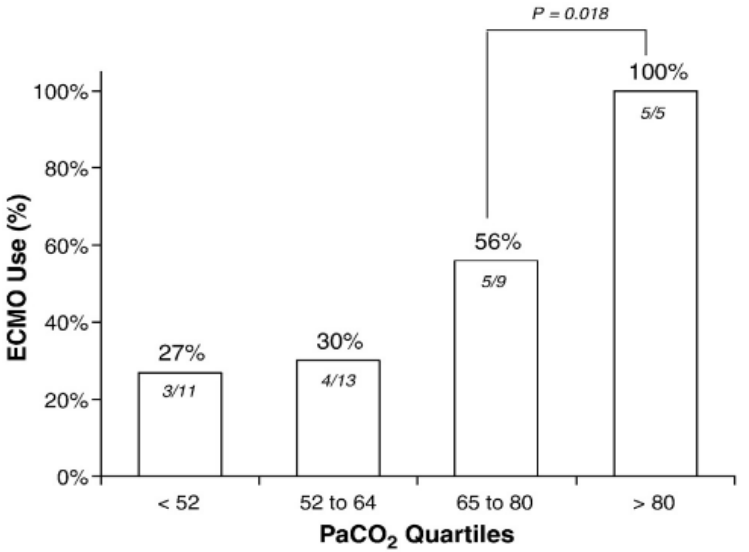
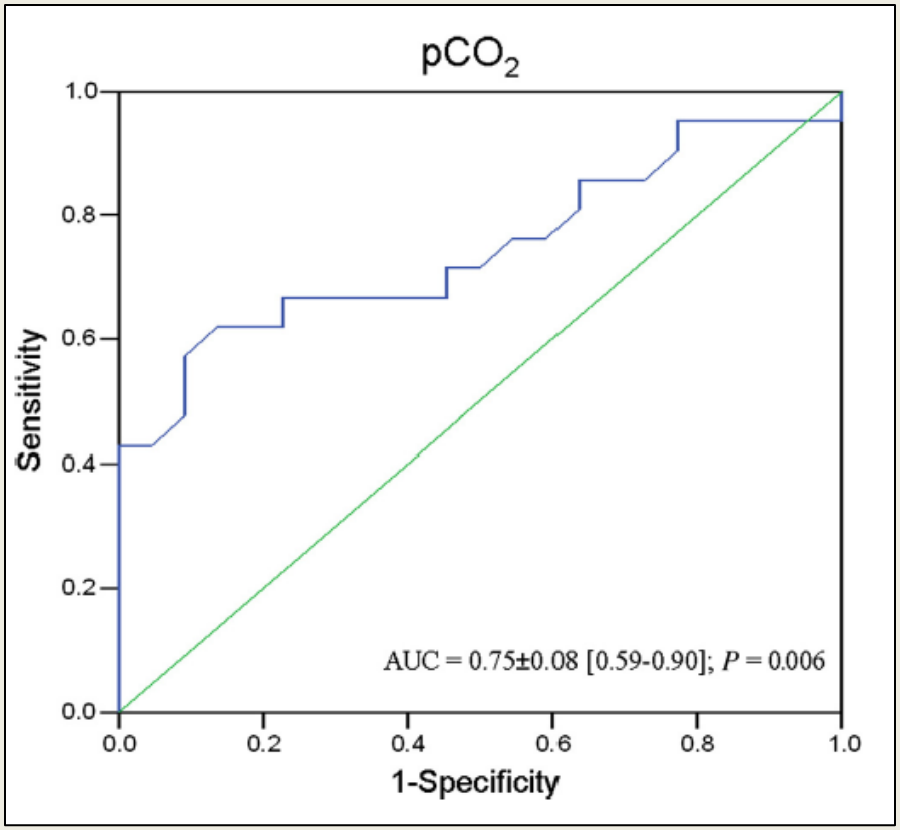
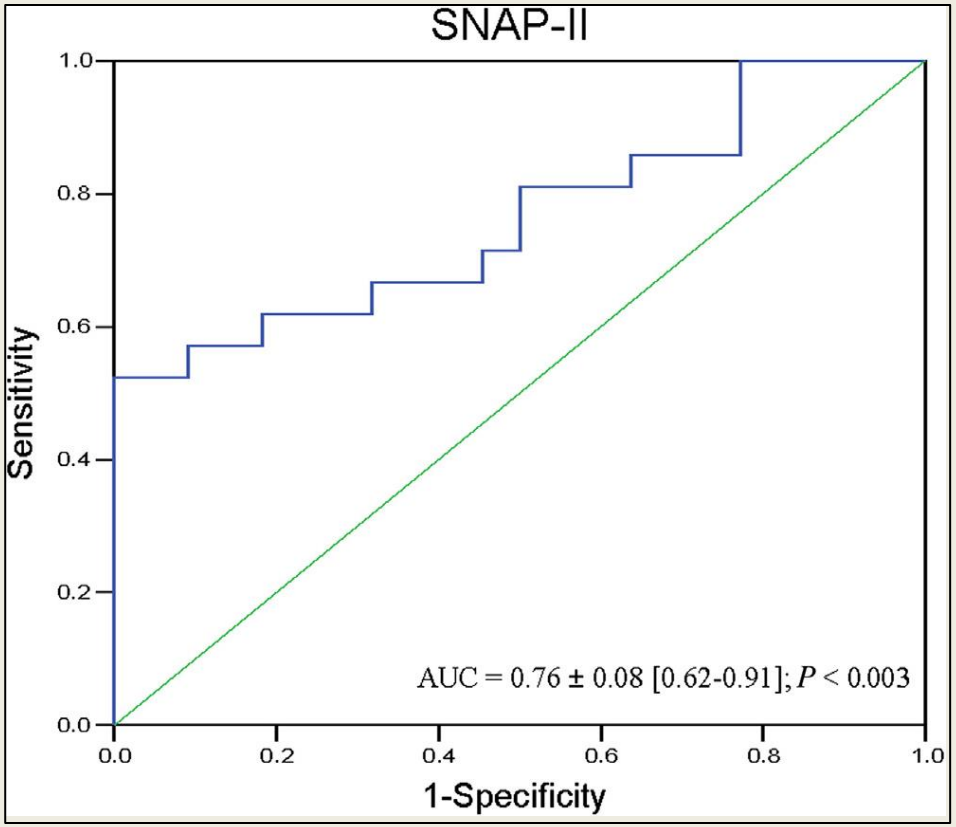


Fig. 4 There was a stepwise increase in the use of ECMO with increasing first 24-h $PaCO_2$. *x*-Axis is the highest P_aCO_2 in the first 24 h of admission to the receiving; *y*-axis is the percent receiving ECMO support.

Coleman A, et al. First 24-h SNAP-II score and highest $PaCO_2$ predict the need for ECMO in Congenital Diaphragmatic Hernia. J Ped Surgery. 2013; 48: 2214-2218

SNAP-II Vs. $PaCO_2$ Predicting ECMO





Coleman A, et al. First 24-h SNAP-II score and highest $PaCO_2$ predict the need for ECMO in Congenital Diaphragmatic Hernia. J Ped Surgery. 2013; 48: 2214-2218

Logistic Regression: *ECMO*

Confounding Variables	Adjusted Odd Ratio	95% Confidence Intervals	P Value
24 Hour SNAP-II Score	1.03	0.97 – 1.09	0.32
Highest $PaCO_2$	1.05	0.99 – 1.09	0.051 *
Gestational Age (weeks)	1.36	0.89 – 2.09	0.16

* Trend towards increase risk of ECMO

Coleman A, et al. First 24-h SNAP-II score and highest $PaCO_2$ predict the need for ECMO in Congenital Diaphragmatic Hernia. J Ped Surgery. 2013; 48: 2214-2218

Logistic Regression: *Mortality*

Confounding Variables	Adjusted Odd Ratio	95% Confidence Intervals	P Value
24 Hour SNAP-II Score	1.09	1.01 – 1.67	0.03 ¥
Highest $PaCO_2$	1.00	0.97 – 1.04	0.82
Gestational Age (weeks)	1.14	0.76 – 1.71	0.53

¥ Remains associated with mortality following adjustment for Highest $PaCO_2$ and gestational age.

CBG – Predictions of Outcome

- Retrospective Review
  - Out-born CDH (2000-2014)
  - Pre-ductal CBG 1st 24 hours
    - CBG and Pulse-oximetry
    - pH and $PaCO_2$
  - CDHSG Probability of Survival
    - Low POS = 0-33%
    - Moderate POS = 34-66%
    - High POS = 67-100%
- N = 44 (*high risk*)
  - Survivors: n=25 (56%)
  - Non-survivors: n=19 (43%)

Table 1 Demographic data, disease characteristics, and therapeutic interventions for neonates with congenital diaphragmatic hernia (CDH)[a]

Characteristic	Hospitalization outcome		*P* value
	Survival (*n* = 25)	Death (*n* = 19)	
Prenatal diagnosis of CDH	9 (36)	9 (47)	0.54
Male sex	16 (64)	11 (58)	0.76
Gestational age, wk	38.6 ± 2.2	37.8 ± 3.4	0.30
Birth weight, kg	3.15 ± 0.67	2.92 ± 0.73	0.29
Small for gestational age	2 (8)	1 (5)	
Apgar score 1 min	6.1 ± 2.6	4.3 ± 2.5	0.02
Apgar score 5 min	6.4 ± 2.5	4.7 ± 1.9	0.02
CDH type			
Left	23 (92)	13 (68)	0.07
Right	2 (8)	5 (26)	
Bilateral	0 (0)	1 (5)	
Liver-up	8 (32)	16 (84)	<0.001
Probability of survival score, %	64 ± 27	45 ± 19	0.01
High (67 %-100 %)	13 (52)	3 (16)	
Moderate (34 %-66 %)	9 (36)	11 (58)	
Low (0 %-33 %)	3 (12)	5 (26)	
Pulmonary hypertension[b]	13 (52)	18 (95)	0.003
Diaphragmatic agenesis	0 (0)	4 (21)	0.03
Peritoneal sac present	4 (16)	0 (0)	0.12
Inhaled nitric oxide	11 (44)	19 (100)	<0.001
Surfactant administration	4 (16)	12 (63)	0.002
Vasoactive support	24 (96)	19 (100)	>0.99
Surgical repair[c]			
Primary closure	23 (92)	3 (43)	0.01
Patch repair	2 (8)	3 (43)	
Muscle flap repair	0 (0)	1 (14)	

[a]Continuous data are presented as mean ± SD; categorical data as number of patients (percentage of sample); [b]Diagnosed with Doppler echocardiography; [c]Twelve patients died before surgery; 7 died after surgical repair

Grizelj et al. Survival prediction of high-risk out-born neonates with congenital diaphragmatic hernia from capillary blood gases. BMC Pediatrics. 2016; 16:114

Distribution of CBG Parameters:
Survivors Vs. Non-survivors

Table 2 Preductal capillary blood gas data at admission and during the first 24 h after admission[a]

Characteristic	Hospitalization outcome				*P* value[b]
	Survival ($n = 25$)[d]		Death ($n = 19$)		
	N	Mean ± SD	N	Mean ± SD	
Admission blood gas					
PcO_2, mm Hg	25	54.9 ± 20.9	19	45.5 ± 18.6	0.13
PcO_2/FIO_2, mm Hg	25	72.2 ± 37.3	19	50.3 ± 30.2	0.04
$PcCO_2$, mm Hg	25	70.1 ± 25.2	19	91.3 ± 31.1	0.02
pH	24	7.15 ± 0.19	17	7.01 ± 0.19	0.03
Base deficit, mEq/L	24	−5.20 ± 6.92	17	−9.92 ± 8.57	0.058
Postadmission blood gas (≤24 h)[c]					
Highest PcO_2, mm Hg					
Alive at 24 h	24	87.0 ± 36.7	12	70.6 ± 21.1	0.16
Death at ≤24 h	—	—	7	65.7 ± 19.6	—
Highest PcO_2/FIO_2, mm Hg					
Alive at 24 h	24	140.5 ± 65.2	12	75.2 ± 23.8	0.002
Death at ≤24 h	—	—	7	67.8 ± 19.7	—
Highest $PcCO_2$, mm Hg					
Alive at 24 h	24	73.3 ± 25.0	12	100.1 ± 34.6	0.01
Death at ≤24 h	—	—	6	117.7 ± 26.7	—
Lowest pH					
Alive at 24 h	23	7.14 ± 0.19	10	7.01 ± 0.20	0.09
Death at ≤24 h	—	—	6	6.88 ± 0.09	—
Highest base deficit, mEq/L					0.131
Alive at 24 h	23	−6.35 ± 6.71	10	−10.42 ± 7.43	—
Death at ≤ 24 h	—	—	5	−17.92 ± 3.66	—

Grizelj et al. Survival prediction of high-risk outborn neonates with congenital diaphragmatic hernia from capillary blood gases. BMC Pediatrics. 2016; 16:114

ROC Curves

Risk Measure vs. Outcomes

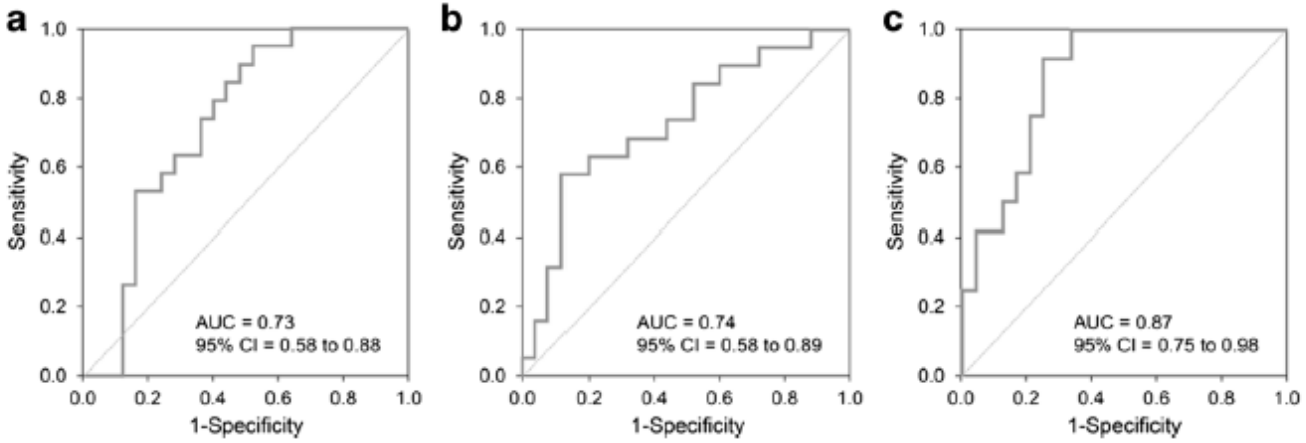


Fig. 1 Receiver Operating Characteristic Curve and Area Under the Curve (AUC) for: **a** Probability of survival score (POS) for all neonates. **b** Partial pressure of carbon dioxide in the preductal capillary blood ($PcCO_2$) for all neonates on admission. **c** Highest ratio of partial pressure of oxygen in the preductal capillary blood to fraction of inspired oxygen (PcO_2/FIO_2) during the first 24 h after admission for neonates who survived more than 24 h after admission

- PcO_2/FiO_2 highest of the 3 risk measure AUC=0.87 (0.75 to 0.98)
- Limitations:
  - CBG is effected by Cardiovascular status (i.e. Shock, ↓ pH, etc.)
    - Large % Vasopressors [96% vs. 100%]

Grizelj et al. Survival prediction of high-risk outborn neonates with congenital diaphragmatic hernia from capillary blood gases. BMC Pediatrics. 2016; 16:114

Risk Assessment: CDH & ECMO

- Mortality Risk Stratification Neonatal ECMO
- ELSO Database (2000-2010)
  - 5,455 neonates (<30 days old)
- Longer ECMO Runs
- Decrease survival

Table 2. Calculation of the PIPER Score

Mean arterial pressure < 49 mm Hg	6 pts
pO_2 < 34 mm Hg (4.5 kPa)	7 pts
Patient not on iNO	8 pts
pH < 7.25	8 pts
Apgar at 5 minutes < 7	8 pts
Birth weight < 3 kg	10 pts
Age >10 days	15 pts
CDH	15 pts
Total	77 pts

CDH, congenital diaphragmatic hernia; ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide; PIPER, Pittsburgh Index for Pre-ECMO Risk.

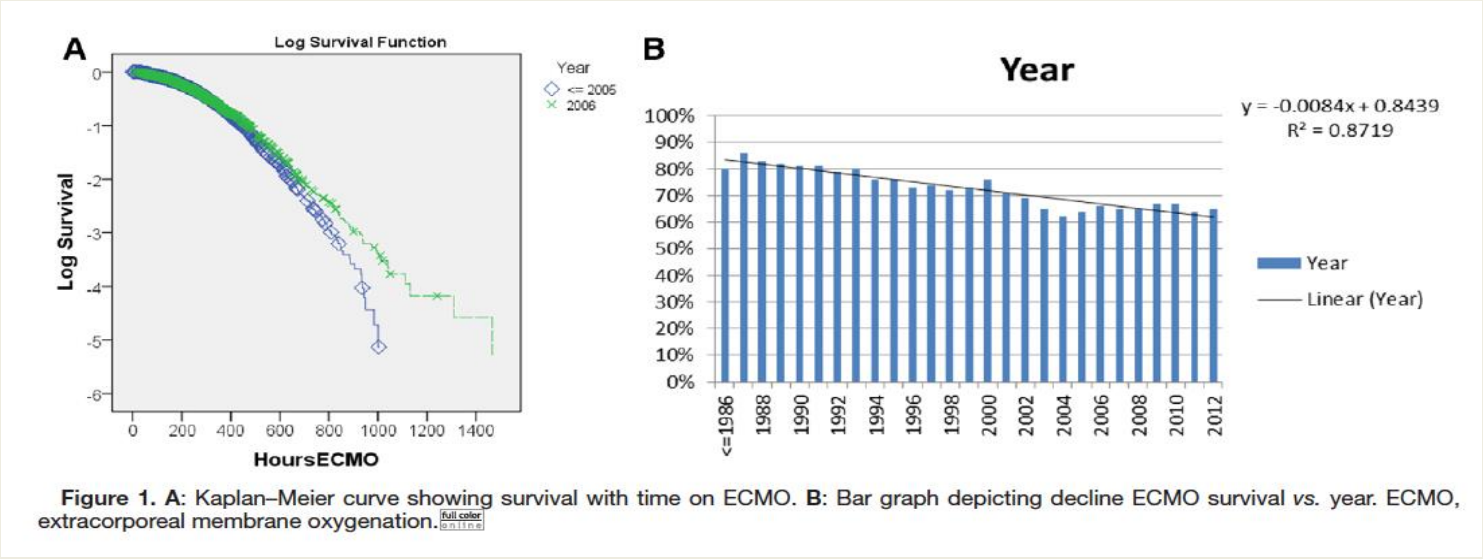
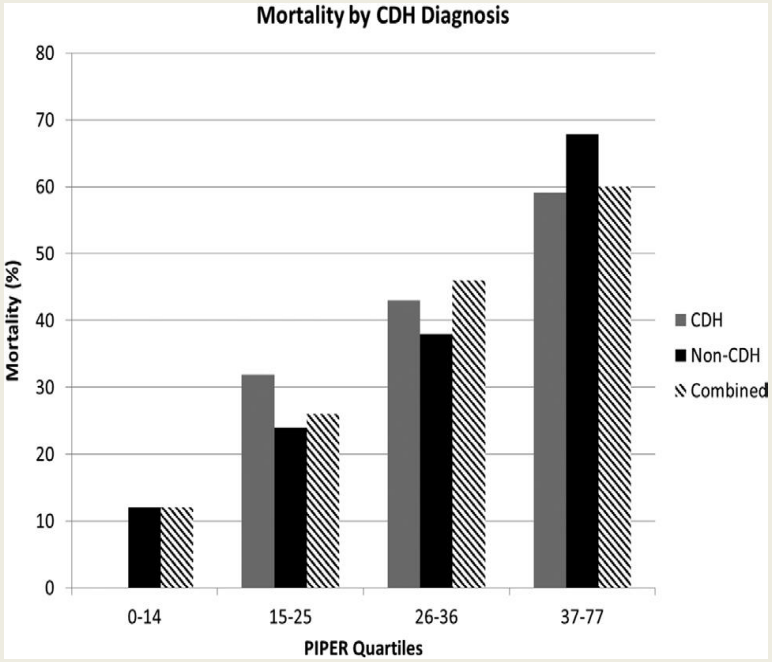


Figure 1. A: Kaplan–Meier curve showing survival with time on ECMO. **B**: Bar graph depicting decline ECMO survival *vs.* year. ECMO, extracorporeal membrane oxygenation.

Mual TM, Kuch BA, Wearden PD. Development of Risk Indices fro Neonatal Respiratory Extracorporeal Membrane Oxygenation. ASAIO 2016; 584-590

CDH & ECMO Mortality Risk



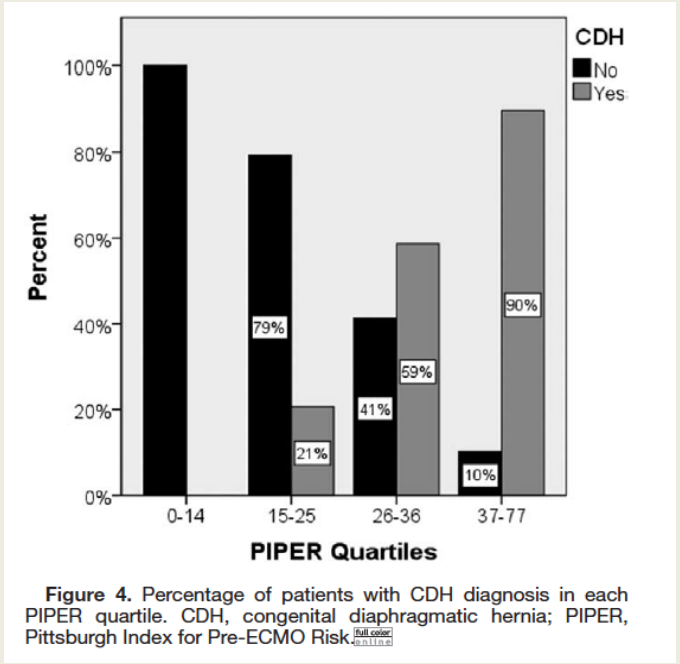


Figure 4. Percentage of patients with CDH diagnosis in each PIPER quartile. CDH, congenital diaphragmatic hernia; PIPER, Pittsburgh Index for Pre-ECMO Risk.

- Mortality for CDH, non-CDH, and the combined cohort for each PIPER quartile were similar
- Score may offer risk stratification over simple CDH classification
  - Evidence that not all CDH patients should be expected to have such a high mortality

Mual TM, Kuch BA, Wearden PD. Development of Risk Indices fro Neonatal Respiratory Extracorporeal Membrane Oxygenation. ASAIO 2016; 584-590

Considerations:

- SNAPP-II is valuable tool for:
  - CDH Outcome Research
  - QI Bench Marking
- Serial Scoring is superior to a “snapshot” SNAPP-II score in the first 24 hours?
- SNAP-II is not validated nor intended for clinical or ethical decision making.[1]
- May be useful in combination with Prenatal Risk Measure.

[1] Solevag AL & Cheung P. Predicting the Outcome of Congenital Diaphragmatic Hernia in a SNAP (Score for Neonatal Acute Physiology). Pediat Critical Care Med. 2016; 17(6): 570 - 571

Thank You!