Congenital diaphragmatic hernia

Long term follow-up

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CDH

- ✓ Prenatal diagnosis & treatment
- ✓ Mechanical ventilation
- ✓ Drugs
- ✓ Surgery
- ✓ +/- ECMO
- ✓ DISCHARGE

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CDH: long term sequelae

"Now this is not the end. It is not even the beginning of the end.

But it is, perhaps, the end of the beginning."

Sir Winston Churchill, El Alamein, November 1942

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CDH: long term sequelae

Auxological	Up to 70%
Cardio-pulmonary	Up to 60%
Gastrointestinal	Up to 70%
NDO	Up to 40%
Orthopedic	Up to 30%
Surgical	Up to 50%

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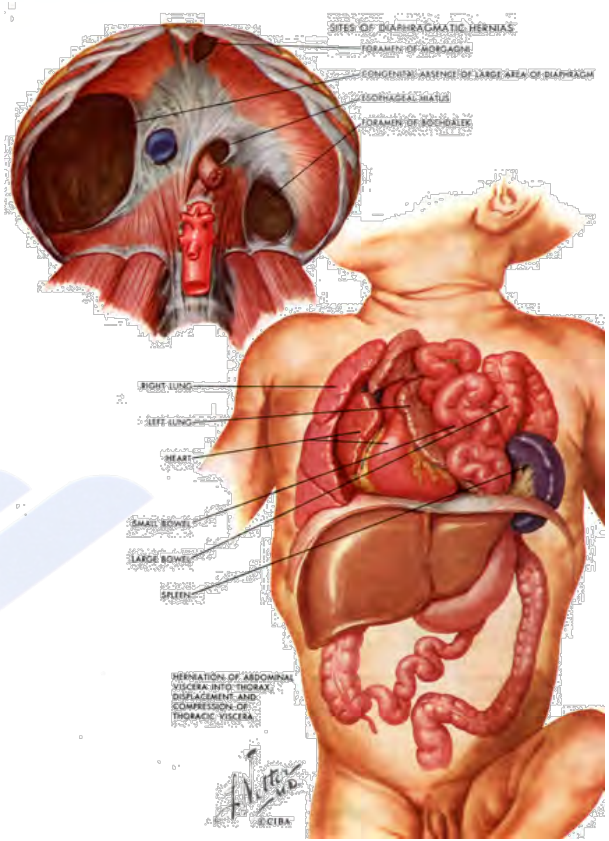
CDH

- ✓ Diaphragmatic defect
- ✓ Pulmonary hypoplasia
- ✓ Pulmonary hypertension



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CDH

GENETIC COUNSELING, Vol. 26, No 3, 2015, pp 281-298

ASSOCIATED NON DIAPHRAGMATIC ANOMALIES AMONG CASES WITH CONGENITAL DIAPHRAGMATIC HERNIA

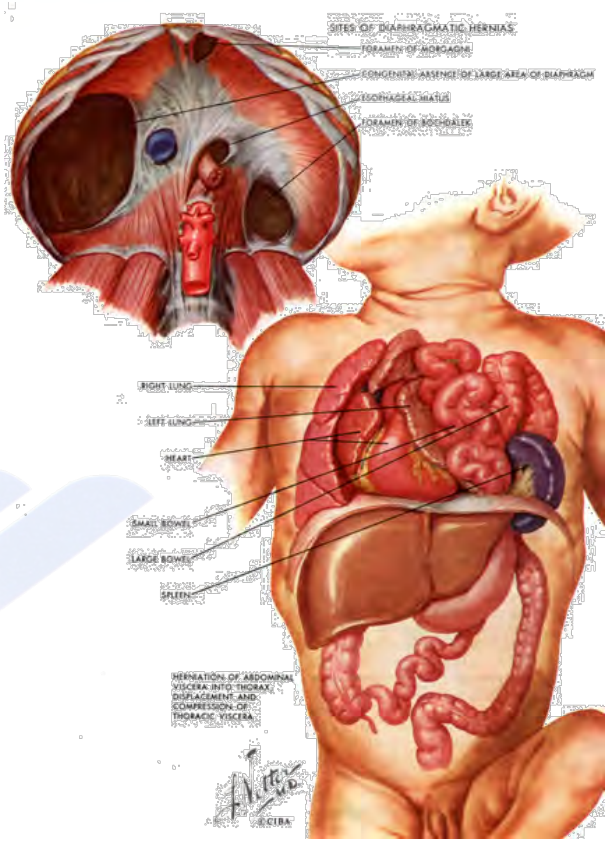
BY C. STOLL, Y. ALEMBIK, B. DOTT AND M.-P. ROTH

Table I: Isolated and associated anomalies in 139 cases with congenital diaphragmatic hernia (CDH) ascertained from 1979 to 2007 in 386,088 consecutive pregnancies in Northeastern France

	Number	%	P[c]
CDH with associated anomalies			
Nonchromosomal			
Recognized conditions[a]	24	17.3	
MCA[b]	36	25.9	
Chromosomal	25	18.0	
Total Associated	85	61.2	2.20
Isolated CDH	54	38.8	1.39
Total	139		3.60

[a]Included syndromes, associations, sequences, and complexes
[b]MCA: multiple congenital anomalies
[c]Prevalence per 10,000 pregnancies.

Stoll C et al., Genet Couns, 2015



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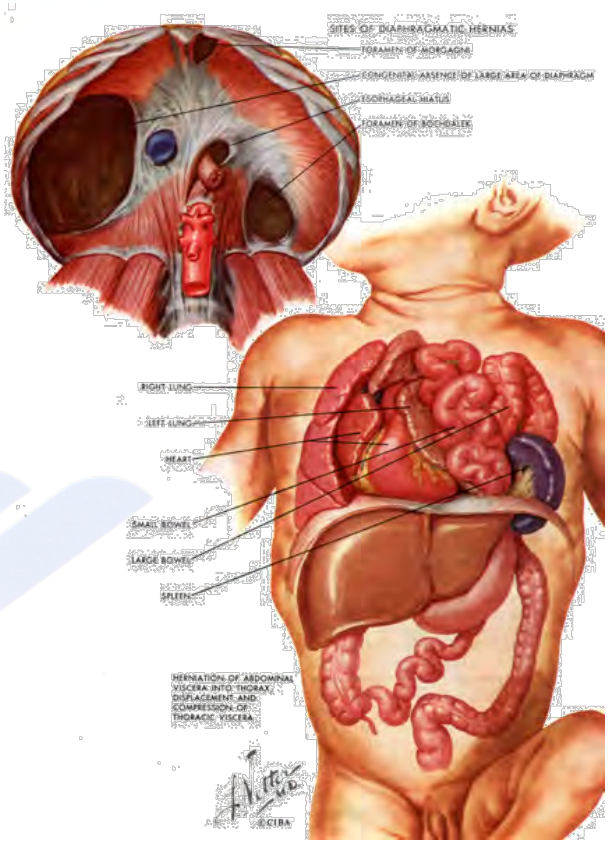
CDH

- ✓ Prenatal treatment
- ✓ Mechanical ventilation
  - ✓ FiO2
  - ✓ Pressure
- ✓ Drugs
- ✓ ECMO
- ✓ Minimal access surgery
- ✓ Patch repair



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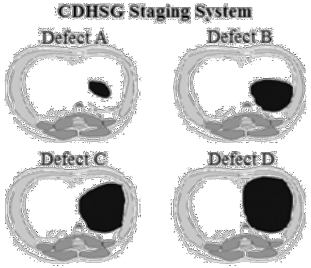
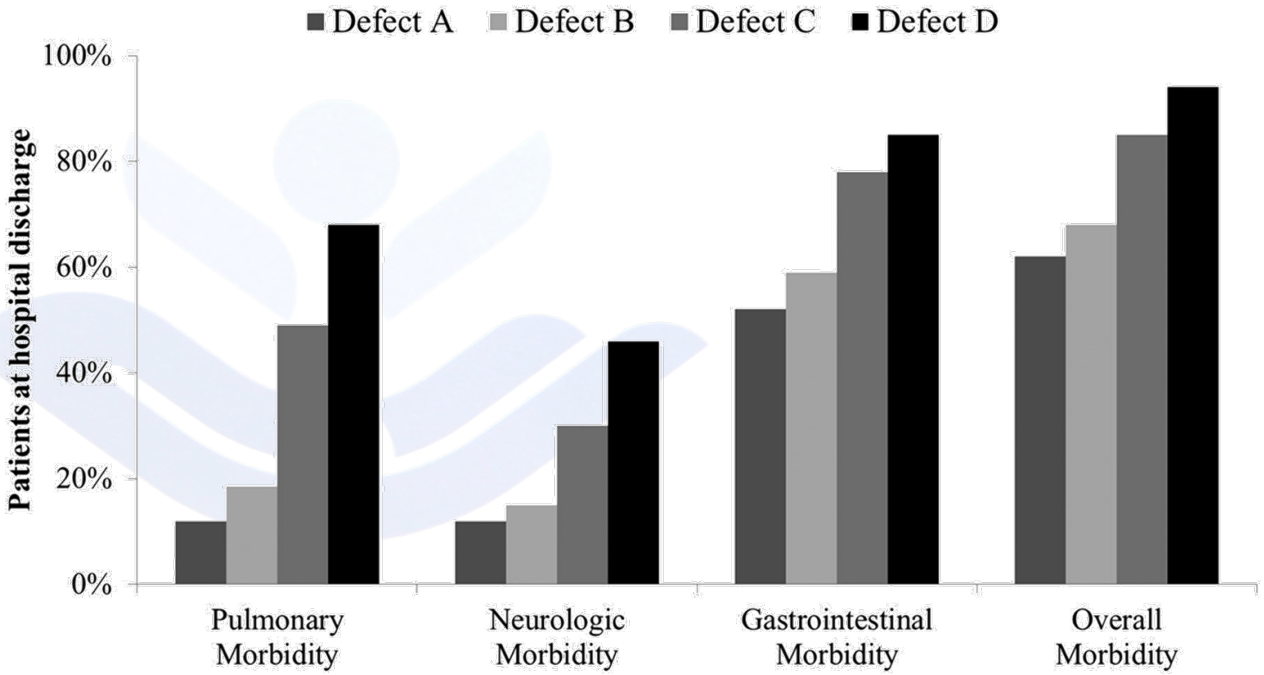
CDH sequelae

Congenital Diaphragmatic Hernia Defect Size and Infant Morbidity at Discharge

Luke R. Putnam, MD, MS,[a] Matthew T. Harting, MD, MS,[a] Kuojen Tsao, MD,[a] Francesco Morini, MD,[b] Bradley A. Yoder, MD,[c] Matias Luco, MD,[d] Pamela A. Lally, MD,[a] Kevin P. Lally, MD, MS,[a] on behalf of the Congenital Diaphragmatic Hernia Study Group





Putnam LR et al., Pediatrics, 2016

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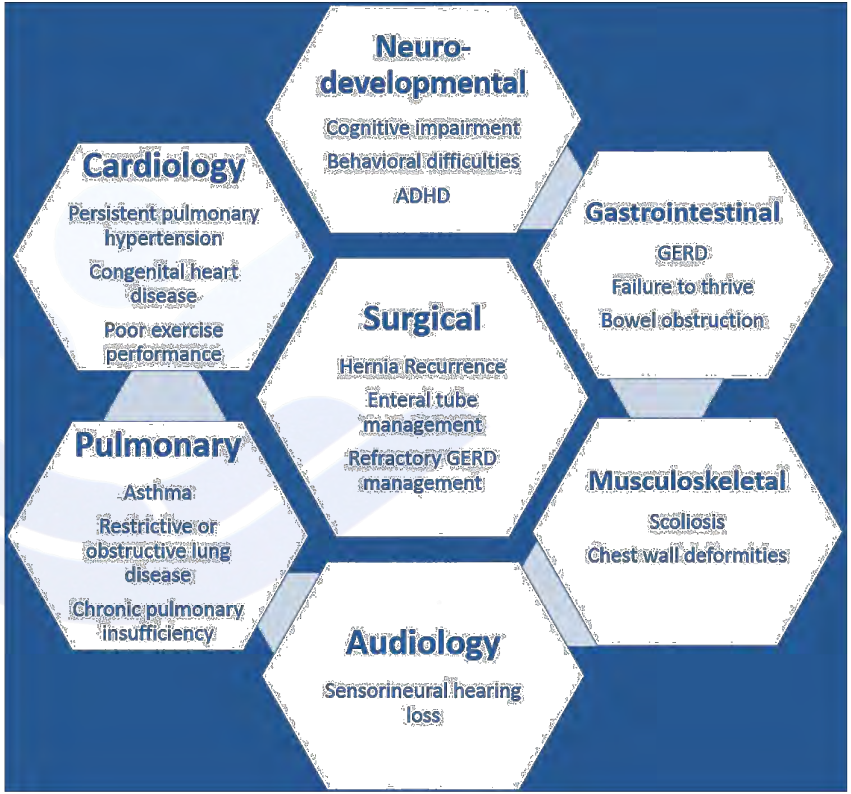
CDH: long term sequelae

Long term follow-up in congenital diaphragmatic hernia

Laura E. Hollinger[a,*], *and Terry L. Buchmiller*[b]

[a]*Department of Surgery, Medical University of South Carolina, 96 Jonathan Lucas Street, MSC 613/CSB 417, Charleston SC 29425, USA*
[b]*Department of Surgery, Boston Children's Hospital, Boston MA, USA*



Hollinger LE & Buchmiller TL, Semin Perinatol, 2019

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Giorgia

Lung Transplantation for Late-Onset Pulmonary Hypertension in a Patient with Congenital Diaphragmatic Hernia

Chiara Iacusso[1] Francesco Morini[1] Irma Capolupo[1] Andrea Dotta[1] Stefania Sgrò[2] Francesco Parisi[3] Adriano Carotti[4] Pietro Bagolan[1]

- GA 33 wks; BW 1.6 kg
- STABILZATION: 72 h
- LEFT CDH (Type D defect, Liver up, Stomach up)
- REPAIR: Patch
- PO COURSE: Uneventful (O2 dependent at 30 days)
- DISCHARGE: 60 days after birth
- No O2-support

Iacusso C et al., Eur J Pediatr Surg Rep, 2018

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Giorgia

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Francesco Parisi[3] Adriano Carotti[4] Pietro Bagolan[1]

4 years-old…climbing!

- Regular follow up check-visits
- Unremarkable first 9 years of life…

JANUARY 21st, 2007
Abdominal pain, vomiting… Emergency admission…

Iacusso C et al., Eur J Pediatr Surg Rep, 2018

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Giorgia

Lung Transplantation for Late-Onset Pulmonary Hypertension in a Patient with Congenital Diaphragmatic Hernia

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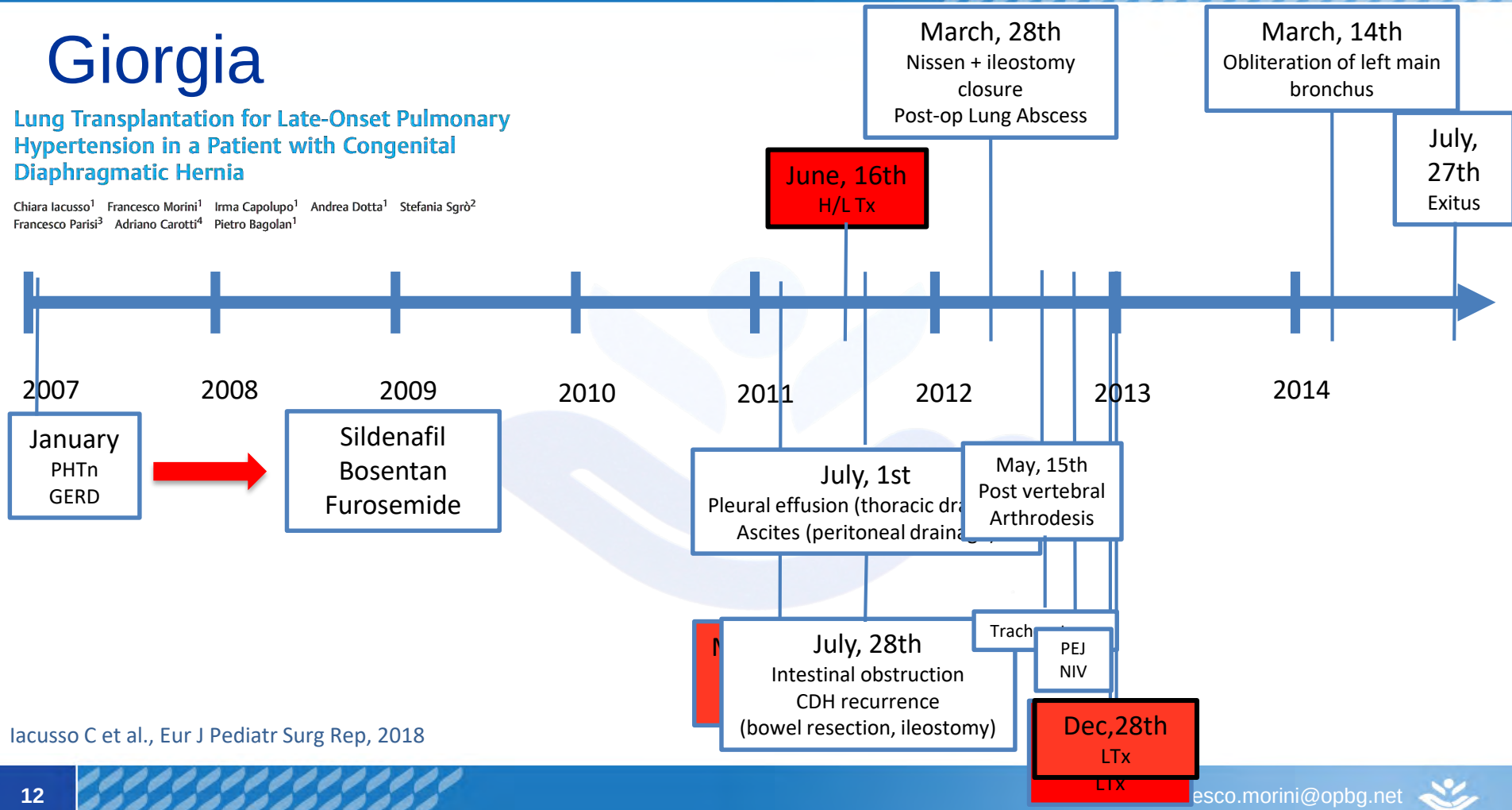

Iacusso C et al., Eur J Pediatr Surg Rep, 2018

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CDH & Persistent/recurrent PHTn

Addressing the causes of late mortality in infants with congenital diaphragmatic hernia

Carmen Mesas Burgos *, Agnes Modée, Elin Öst, Björn Frenckner

Department of Pediatric Surgery, Karolinska Institutet, Stockholm, Sweden

sidered. One of the patients dying from persistent pulmonary hypertension was treated during the newborn period, but had been free from medication and symptoms during several years until a new onset of pulmonary hypertension occurred, which at this time not responded to treatment. One patient died because of respiratory insuf-

Patient	4
Age at death	9 yr. 4 mo
Cause of death	PPH
Gender	Female
Intubated <6 h	Yes
Patch repair	Yes
Liver up	Yes
ECMO	Yes
Other GI surgery	Yes (GT)
Recurrence	No
Side	Left
Failure to thrive	Yes

Mesas Burgos C et al., J Pediatr Surg, 2017

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CDH & lung transplantation

Lung Transplantation for Late-Onset Pulmonary Hypertension in a Patient with Congenital Diaphragmatic Hernia

Chiara Iacusso[1] Francesco Morini[1] Irma Capolupo[1] Andrea Dotta[1] Stefania Sgrò[2]
Francesco Parisi[3] Adriano Carotti[4] Pietro Bagolan[1]

Author	Year	No. of patients	Prenatal diagnosis	ECMO	CDH side	Type of Tx	Age at Tx	Outcome	Follow-up
Van Meurs et al	1994	1	No	Yes	R	Lung	17 d	Alive	4 y
Lee et al	2002	1	18 wk	Yes	L	Lung	36 d	Died 51 d post-Tx	–
Lee et al	2002	2	27 wk	Yes	L	Lung	105 d	Alive	3 y
Lee et al	2002	3	18 wk	Yes	L	Heart–lung	19 d	Died 84 d post-Tx	–
Rama et al	2010	1	ns	ns	ns	Lung	ns	ns	ns
Rama et al	2010	2	ns	ns	ns	Lung	ns	ns	ns
Schmidt et al	2013	1	ns	Yes	L	Lung	10 y	Died 109 d post-Tx	–
Iacusso et al (this study)	2017	1	31 wk	No	L	Heart–lung Lung	12 y 17 y	Died 4 y after first Tx	–

Iacusso C et al., Eur J Pediatr Surg Rep, 2018

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CDH & PHTn

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CDH & gastroesophageal reflux

Long-term follow up of infants with congenital diaphragmatic hernia

Pietro Bagolan, MD, Francesco Morini, MD

From the Department of Medical and Surgical Neonatology, "Bambino Gesù" Children's Hospital, Rome, Italy.

Author	Pts	Follow-up (mos)	GER (%)	Surgery for GER (%)
Stolar et al, 1990[67]	17	32	17	0
Koot et al, 1993[72]	31	6	52	16
Van Meurs et al, 1993[30]	18	8–72	17	0
Nagaya et al, 1994[74]	86	6–120	12	8
Lund et al, 1994[11]	33	5–72	—	18
D'Agostino et al, 1995[15]	16	0.6–12	81	12
Kieffer et al, 1995[73]	74	36	62	32
Rais-Bahrami et al, 1995[70]	33	24	76	—
Stolar et al, 1995[50]	25	31	—	—
Wischermann et al, 1995[34]	45	7–360	13	—
Vanamo et al, 1996[16]	60	355	63	18
Naik et al, 1996[77]	15	6–36	13	13
McGahren et al, 1997[47]	37	3–120	—	22
Schoeman et al, 1999[71]	8	2–32	67	62
Huddy et al, 1999[92]	13	24–84	23	15
Muratore et al, 2001[18]	121	12–120	60	21
Bétrémieux et al, 2002[78]	12	12–72	50	—
Jaillard et al, 2003[19]	51	24	27	6
Davis et al, 2004[25]	27	>12	52	15
Hedrick et al, 2004[27]	19	0.7–88	47	11
Cortes et al, 2005[23]	16	24	62	60
Colvin et al, 2005[84]	37	24–156	27	5
Crankson et al, 2006[28]	31	6–108	26	6
Chiu et al, 2006[10]	38	36	45	32
TOTAL	863		39	19

Bagolan P & Morini F, Semin Pediatr Surg, 2007

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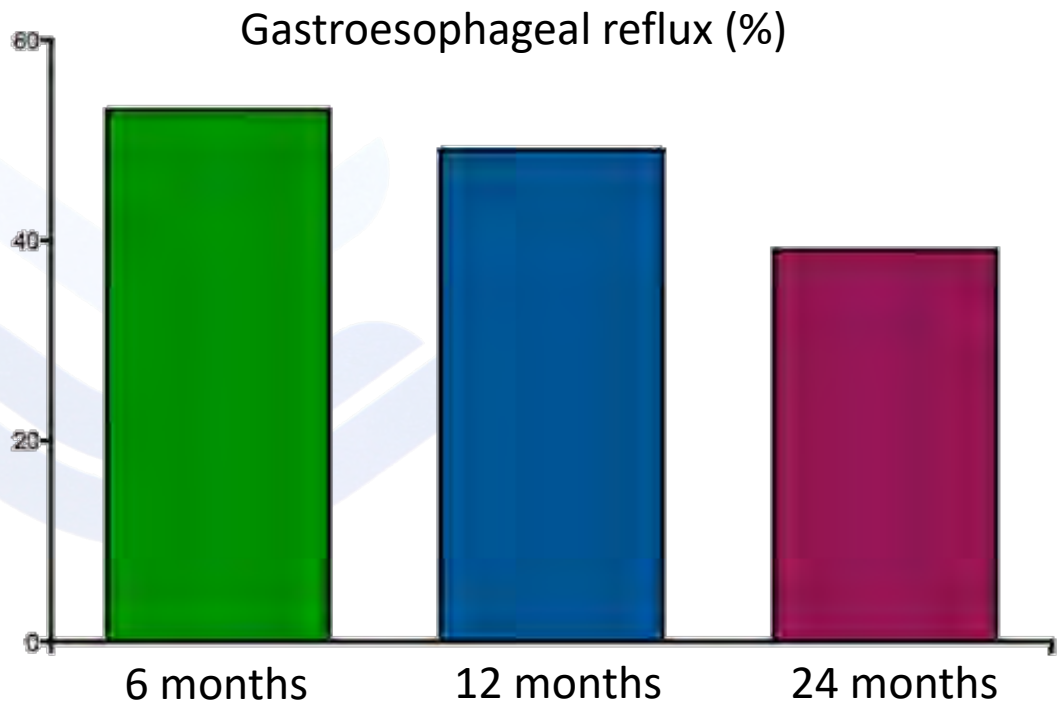
CDH & gastroesophageal reflux

Long term follow-up in high-risk congenital diaphragmatic hernia survivors: patching the diaphragm affects the outcome

Laura Valfrè*, Annabella Braguglia, Andrea Conforti, Francesco Morini, Alessandro Trucchi, Barbara Daniela Iacobelli, Antonella Nahom, Natalia Chukhlantseva, Andrea Dotta, Carlo Corchia, Pietro Bagolan

Neonatal Surgery Unit, Department of Medical and Surgical Neonatology, Bambino Gesù Children's Research Hospital, 00165 Rome, Italy

- ✓ 61 CDH survivors
  - ✓ 61 @ 6 mos
  - ✓ 49 @ 12 mos
  - ✓ 43 @ 24 mos



Valfrè L et al., J Pediatr Surg, 2011

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CDH & gastroesophageal reflux

Endoscopic Surveillance for Congenital Diaphragmatic Hernia: Unexpected Prevalence of Silent Esophagitis

Anna Morandi[1] Francesco Macchini[1] Andrea Zanini[1] Noemi Pasqua[1] Giorgio Farris[1]
Lorena Canazza[1] Valerio Gentilino[1] Antonio Di Cesare[1] Ernesto Leva[1]

[1]Department of Pediatric Surgery, Fondazione IRCCS Ca' Granda, Ospedale Maggiore Policlinico, Milano, Italy

Eur J Pediatr Surg 2016;26:291–295.

Address for correspondence Anna Morandi, MD, Department of Pediatric Surgery, Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Via Commenda 10 Milano 20122, Italy (e-mail: anna_morandi@hotmail.it).

Grade 0	No mucosal abnormalities
Grade I	No macroscopic erosions but erythema, hyperemia, or mucosal friability
Grade II	Superficial erosions, involving < 10% of the mucosal surface of the last 5 cm of esophageal squamous mucosa
Grade III	Superficial erosions or ulceration involving 10 to 50% of the mucosal surface of the last 5 cm of esophageal squamous mucosa
Grade IV	Deep peptic ulceration anywhere in the esophagus or confluent erosion of > 50% of the mucosal surface of the last 5 cm of esophageal squamous mucosa

Materials and Methods Patients operated on for posterolateral CDH and undergoing general anesthesia for concomitant pathologies between January and October 2013 were included in the study. GERD was investigated both clinically (Manterola questionnaire) and endoscopically. The severity of esophagitis was evaluated according to the Hetzel–Dent classification and multiple biopsies were performed. The correlation between clinical score and severity of esophagitis was evaluated.

Results Twelve patients were included in the study (mean age: 14.5 years; range, 9–18 years). Only three children (25%) had a pathological questionnaire. At endoscopy, three children (25%) were affected by grade 1 esophagitis, six (50%) by grade 2, two (17%) by grade 3, and one (8%) by grade 4. One of the children presented Barrett esophagus. A moderate negative correlation was found between clinical data and endoscopic findings (r: −0.54 and *p*: 0.067).

- ✓ 12 CDH survivors
- ✓ Mean age 14.5 yrs
- ✓ 75% asymptomatic

Morando A et al., Eur J Pediatr Surg, 2016

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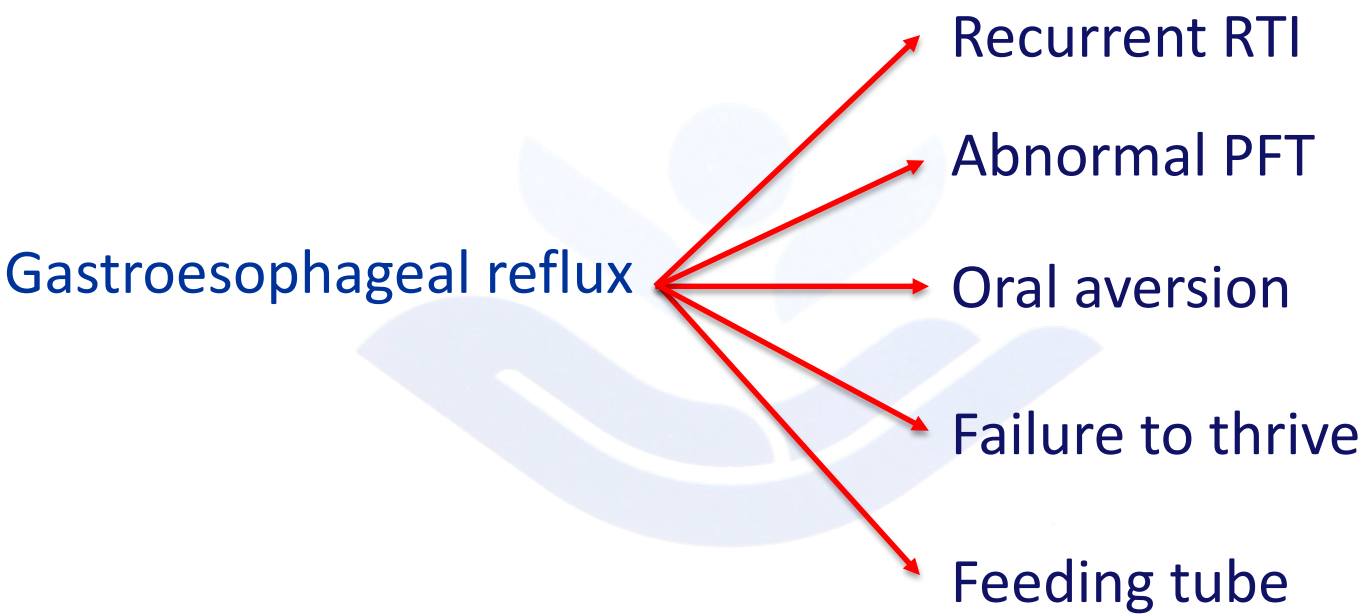
CDH & gastroesophageal reflux



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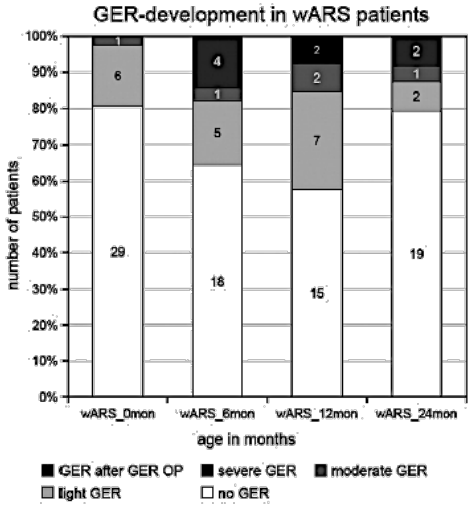
CDH & gastroesophageal reflux

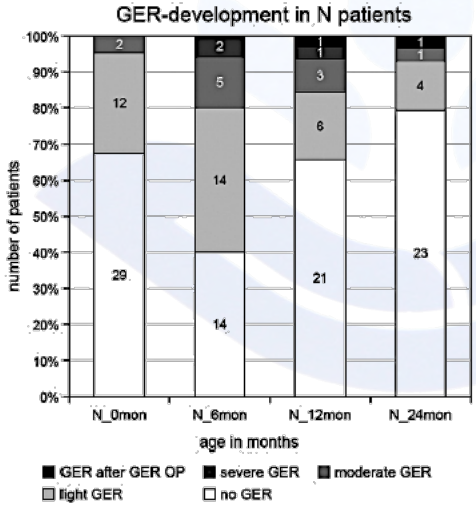
Preventive antireflux surgery in neonates with congenital diaphragmatic hernia: a single-blinded prospective study☆

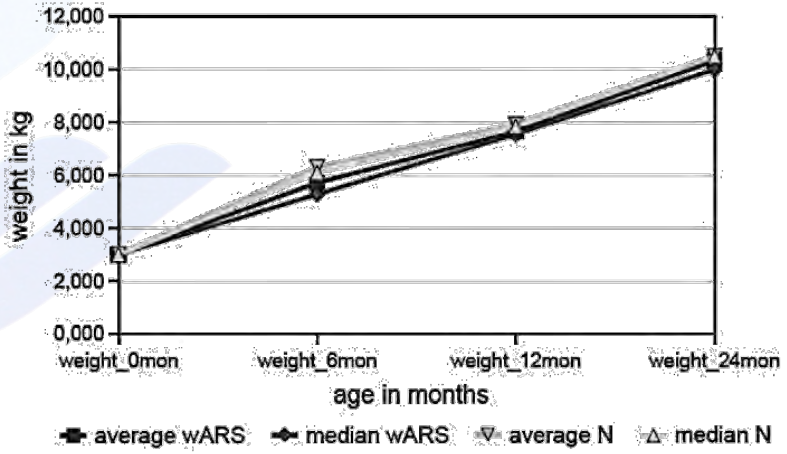
Susanne Maier[a,*,1], Katrin Zahn[a,1], Lucas M. Wessel[a], Thomas Schaible[b], Joachim Brade[c], Konrad Reinshagen[a]

[a]Department of Pediatric Surgery, Universitätsklinikum Mannheim, University of Heidelberg, Mannheim 68167, Germany
[b]Department of Neonatology, Universitätsklinikum Mannheim, University of Heidelberg, Mannheim 68167, Germany
[c]Department of Statistics, Universitätsklinikum Mannheim, University of Heidelberg, Mannheim 68167, Germany

- ✓ 79 L-CDH survivors
- ✓ 36 wARS
- ✓ 43 controls







Maier S et al., J Pediatr Surg, 2011

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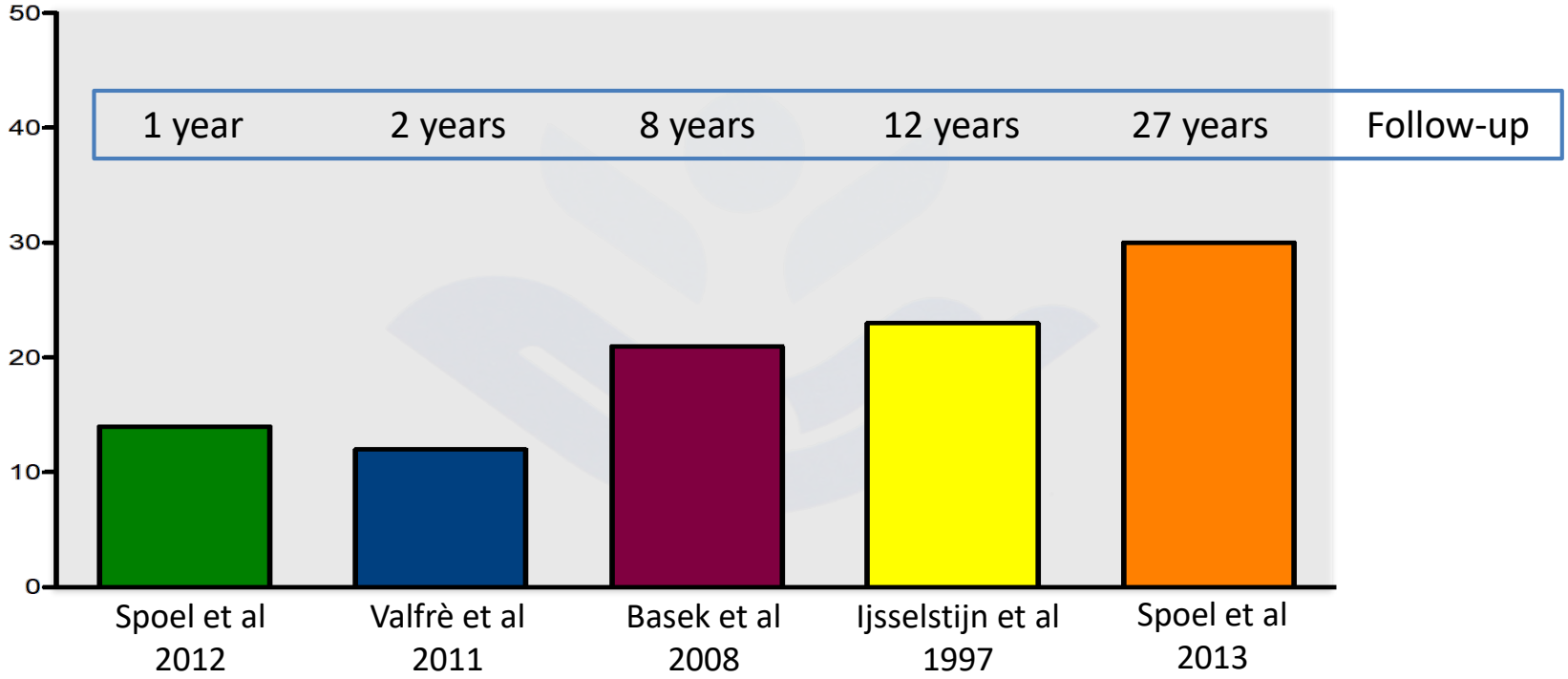
CDH & obstructive manifestations



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CDH & obstructive manifestations

Pulmonary function and exercise capacity in survivors of congenital diaphragmatic hernia

M.G. Peetsold*, H.A. Heij#, A.F. Nagelkerke*, H. IJsselstijn*, D. Tibboel*, P.H. Quanjer* and R.J.B.J. Gemke*

- ✓ 53 CDH survivors
- ✓ Mean age 12 yrs
- ✓ Asthma 28%

	CDH		Controls		p-value	95% CI of the difference
	Mean±SD	Range	Mean±SD	Range		
Before bronchodilation						
Spirometry						
Subjects n	48		48			
FEV_1	-1.63±1.78	-7.14–1.45	0.08±0.90	-1.53–2.38	<0.001	-2.28– -1.14
FVC	-1.28±1.62	-6.33–1.93	0.05±0.87	-1.57–2.76	<0.001	-1.85– -0.80
FEV_1/FVC	-0.84±1.27	-4.03–1.07	0.05±0.90	-2.04–1.90	<0.001	-1.33– -0.44
MMEF	-1.57±1.70	-6.18–1.08	0.16±1.03	-2.31–2.27	<0.001	-2.30– -1.16
PEF $L \cdot s^{-1}$	4.89±1.79	1.42–8.23	6.45±2.10	3.16–10.34	<0.001	-2.34– -0.78
After bronchodilation						
Spirometry						
Subjects n	38					
FEV_1	-1.45±1.51	-6.22–1.43				
FVC	-1.45±1.46	-5.67–2.05				
FEV_1/FVC	-0.22±1.30	-2.83–1.77				
MMEF	-0.22±1.30	-5.54–2.19				
PEF $L \cdot s^{-1}$	5.38±1.80	2.36–9.02				
Lung volumes						
Subjects n	48		29			
TLC	0.16±1.91	-4.16–1.55	0.03±1.04	-1.86–1.93	0.70	-0.54–0.80
RV	0.98±2.06	-5.37–2.44	-0.24±0.84	-2.17–0.98	0.001	0.55–1.89
RV/TLC %	26.7±9.0	6–47	20.4±3.0	14–25	<0.001	3.50–9.13

Data are expressed as z-scores calculated from a reference population [20], unless otherwise stated. CI: confidence interval; FEV_1: forced expiratory volume in 1 s; FVC: forced vital capacity; MMEF: maximum mid-expiratory flow; PEF: peak expiratory flow; TLC: total lung capacity; RV: residual volume.

Peetsold MG et al., Eur Respir J, 2009

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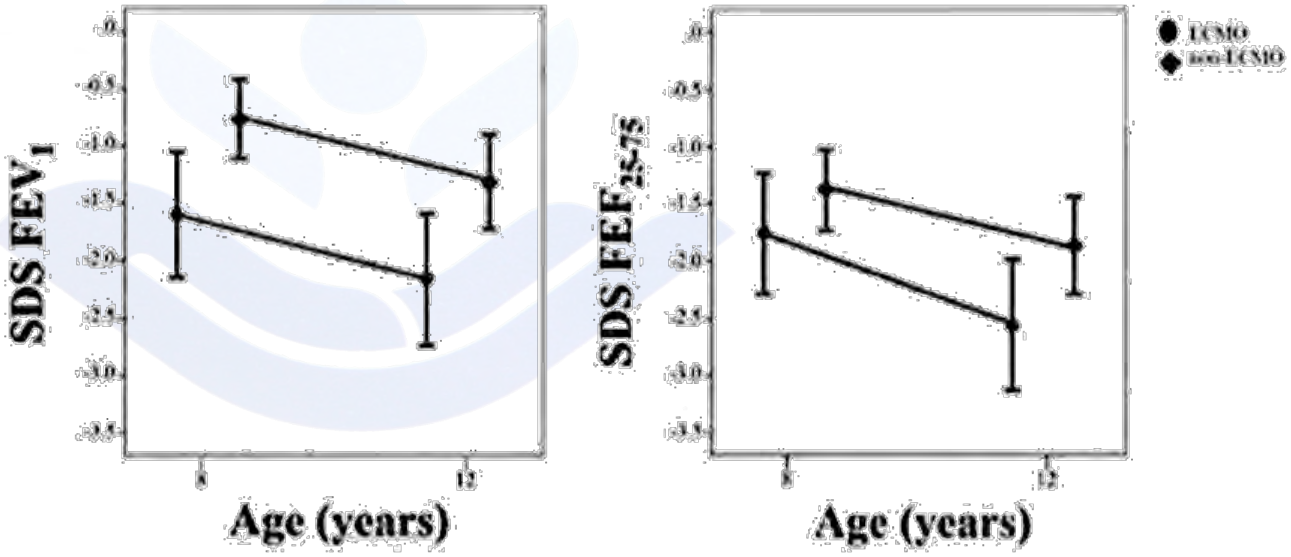
CDH & obstructive manifestations

Congenital diaphragmatic hernia and exercise capacity, a longitudinal evaluation

Leontien C.C. Toussaint-Duyster MPPT[1,2] | Monique H.M. van der Cammen-van Zijp PhD[1,2] | Johan C. de Jongste MD, PhD[3] | Dick Tibboel MD, PhD[1] | Rene M.H. Wijnen MD, PhD[1] | Saskia J. Gischler MD, PhD[1] | Joost van Rosmalen PhD[4] | Hanneke IJsselstijn MD, PhD[1]



Toussaint-Duyster LCC et al., Pediatr Pulmonol, 2019

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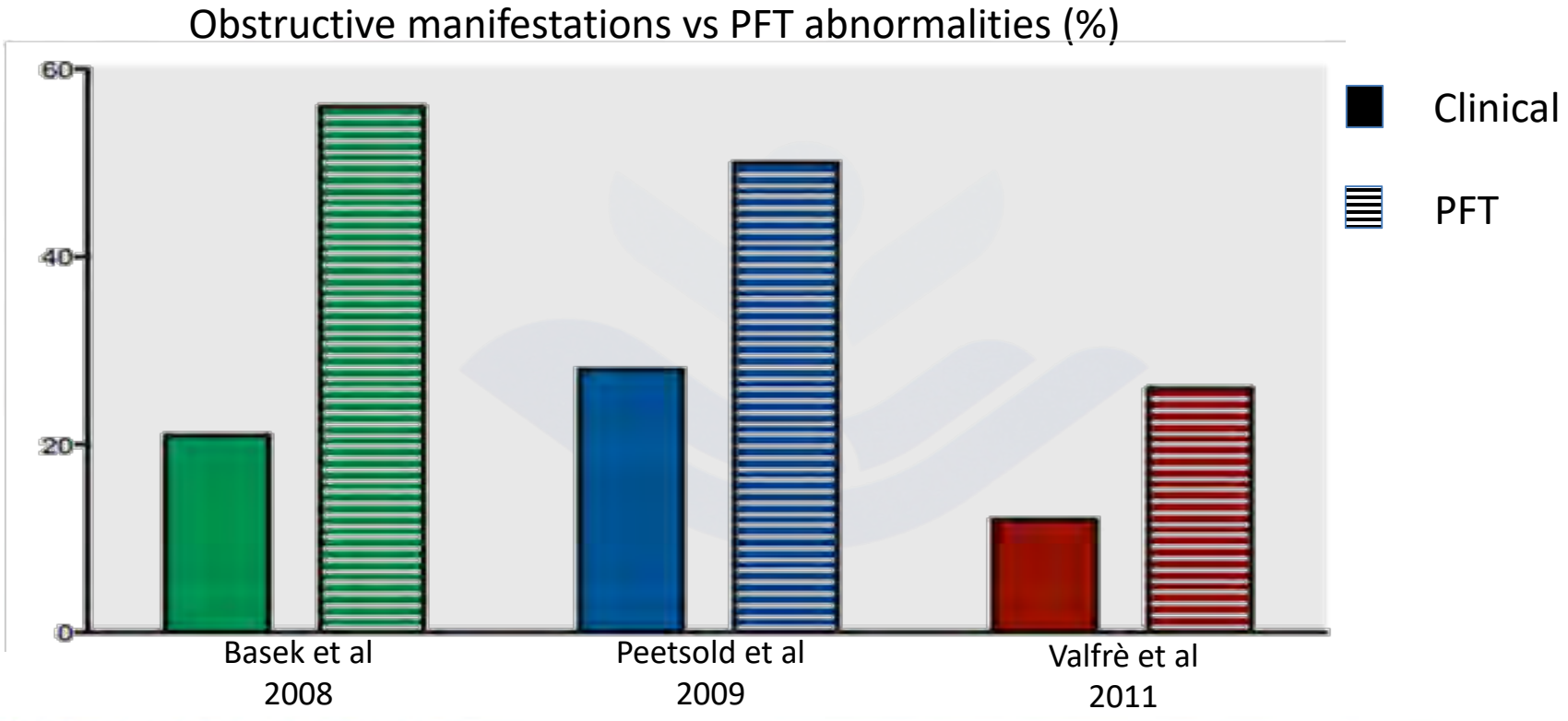
CDH & obstructive manifestations



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CDH & Fitness

Resting and Exercise Cardiorespiratory Function in Survivors of Congenital Diaphragmatic Hernia

Daniel Trachsel, MD,[1] Hiran Selvadurai, MD, PhD,[1]* Ian Adatia, MD,[2] Desmond Bohn, MD,[3] Jane Schneiderman-Walker, MSc,[1] Donna Wilkes, MSc,[1] and Allan L. Coates, MD[1]

1.2 ± 1.6, $P < 0.01$). Exercise capacity was mildly reduced in CDH compared to controls and predictive data (maximum workload, 77% ± 12% vs. 91% ± 16% of predicted, $P < 0.01$). Cardiorespiratory response to exertion was not significantly different between groups. In conclusion, most adolescent CDH survivors have nearly normal exercise capacity and cardiorespiratory response to exertion. This study may prove useful in comparisons with future cohorts comprising more severely affected individuals now surviving due to improved neonatal care.

		CDH	Controls	*P*-value
Wmax (percent predicted for height)		77 ± 12	91 ± 16	<0.01
Wmax (watts)		116 ± 37	149 ± 53	<0.02
Wmax/weight (watts/kg)		2.5 ± 0.6	2.8 ± 0.6	NS (0.08)
Wmax/LBM (watts/kg)		3.2 ± 0.6	3.7 ± 0.6	<0.01
Heart rate maximum (min^{-1})		189 ± 11	191 ± 9	NS
Respiratory rate maximum (min^{-1})		50 ± 7	54 ± 7	0.02
$V_E$max (l/min)		68 ± 21	84 ± 22	0.01
$V_E$max/MVV*100 (%)		81 ± 19	83 ± 16	NS
V_{O2}max (percent predicted for height)		88 ± 17	99 ± 17	0.03
V_{O2}max (l/min)		1.8 ± 0.6	2.2 ± 0.8	NS (0.06)
V_{O2}max/Wmax (ml/min/watts)		0.016 ± 0.002	0.015 ± 0.002	NS
V_{CO2}max (l/min)		2.0 ± 0.7	2.5 ± 0.9	NS (0.07)
V_{CO2}max/Wmax (l/min/watts)		0.017 ± 0.002	0.017 ± 0.002	NS
V_E/V_{O2} at Wmax		38 ± 6	39 ± 5	NS
V_E/V_{CO2} at Wmax		34 ± 5	35 ± 5	NS
$V_T$max (l)		1.4 ± 0.45	1.6 ± 0.49	NS
$V_T$max/weight (ml/kg)		29 ± 5	30 ± 5	NS
	Watts	CDH	Controls	*P*-value
Cardiac output (l/min)	75	10.5 ± 3.1	10.9 ± 1.8	NS
	110	13.0 ± 2.7	12.5 ± 2.5	NS
	135	14.5 ± 3.3	13.2 ± 1.8	NS
Cardiac index (l/min/m^2)	75	7.3 ± 1.3	7.3 ± 1.1	NS
	110	8.2 ± 1.4	8.2 ± 1.5	NS
	135	8.7 ± 1.4	8.5 ± 0.9	NS
Stroke-volume index (ml/m^2)	75	45 ± 11	48 ± 9	NS
	110	47 ± 10	48 ± 10	NS
	135	47 ± 9	48 ± 7	NS

Trachsel D et al., Pediatr Pulmonol, 2006

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CDH & Fitness

Physical Activity, Fitness, and Dyspnea Perception in Children With Congenital Diaphragmatic Hernia

Attilio Turchetta,[1]* Danilo Fintini,[1] Giulia Cafiero,[1] Armando Calzolari,[1] Ugo Giordano,[1] Renato Cutrera,[2] Francesco Morini,[3] Annabella Braguglia,[3] and Pietro Bagolan[3]

difference in CDH severity between the two groups. Group A had a statistically significant lower duration of exercise ($P < 0.01$), maximal oxygen consumption (VO_2 max $P < 0.0001$), VO_2 ml/kg/min ($P < 0.001$), higher throat closing feeling ($P < 0.004$), chest dyspnea ($P < 0.001$), and effort perception ($P < 0.04$) compared to group B. No differences were found in lung function tests. In conclusion, our data may suggest that children with a history of CDH who are active maintain a higher level of performance with less perception of dyspnea and effort. **Pediatr**

Turchetta A et al., Pediatr Pulmonol, 2011

	Total (n = 18) (M/F = 11/7)	No sport, Group A (n = 11; M/F = 7/4)	Sport, Group B (n = 7; M/F = 4/3)	*P*
Age	6.6 ± 2.6	6.5 ± 3.5	6.6 ± 1.1	NS
Weight (kg)	22.7 ± 12.2	25.6 ± 15.1	18.8 ± 6.2	NS
Height (cm)	120.9 ± 19.5	121 ± 26.1	120.8 ± 6.7	NS
BMI	14.6 ± 3.5	16.1 ± 2.3	12.8 ± 4.0	NS
GA (weeks)	38.1 ± 2	38.2 ± 2.2	38.0 ± 1.9	NS
Surgery (days)	7.0 ± 7.3	9 ± 9.4	4.4 ± 0.8	NS
Vent (days)	18.6 ± 12.3	14.3 ± 9.9	24 ± 13.5	NS
Patch (yes/no)	6/12	3/8	3/4	NS
TE%	68.4 ± 12.9	62.3 ± 10.4	78.1 ± 10.5	<0.01
HR%	96.4 ± 10.8	97.8 ± 12.0	94.7 ± 9.7	NS
BP%	97.4 ± 6.8	96.9 ± 7.7	98.0 ± 5.9	NS
VO_2 max %	68.6 ± 14.4	59.9 ± 4.8	83.7 ± 10.5	≤0.0001
VO_2/kg/min	28.2 ± 7.4	23.3 ± 2.9	35.7 ± 5.8	≤0.001
SaO2 max	95.8 ± 1.1	95.8 ± 1.0	95.7 ± 1.3	NS
FEV_1%	78.7 ± 19.3	75.5 ± 18.9	82.7 ± 20.5	NS
FVC%	75.5 ± 15	74.7 ± 18	76.2 ± 13	NS
PEF%	74.9 ± 22	73.6 ± 21	76.1 ± 22	NS
MVV	35.5 ± 14.7	34.3 ± 8.9	36.7 ± 20.5	NS
VE	25.9 ± 9.8	25.2 ± 4.9	24.7 ± 14.7	NS
VE/MVV	0.71 ± 0.1	0.75 ± 0.1	0.67 ± 0.1	NS
Throat	5.2 ± 1	5.7 ± 0.8	4.4 ± 0.8	≤0.004
Chest	4.5 ± 1.0	5.3 ± 0.6	3.6 ± 0.5	≤0.001
Effort	5.3 ± 0.8	5.8 ± 0.9	4.9 ± 0.7	≤0.04

Physical, respiratory, and treadmill parameters and Dalhousie Scale results are shown. All data were divided between sedentary children (Group A) and active children (Group B). Data are expressed as mean ± SD (M, males; F, females; BMI, body mass index; GA, gestational Age; Surgery, day of surgery after birth; Vent, ventilation days; TE%, time of exercise during treadmill test expressed as percentage of normal value for age and sex; HR%, maximal heart rate during treadmill test expressed as percentage of normal value for age and sex; BP%, maximal BP during treadmill test expressed as percentage of normal value for age and sex; VO_2, maximal oxygen consumption; MVV, maximal voluntary ventilation; VE, ventilation (L/m); Throat, Chest, Effort, parameters of Dalhousie Dyspnea Scale collected from children at the end of treadmill test).

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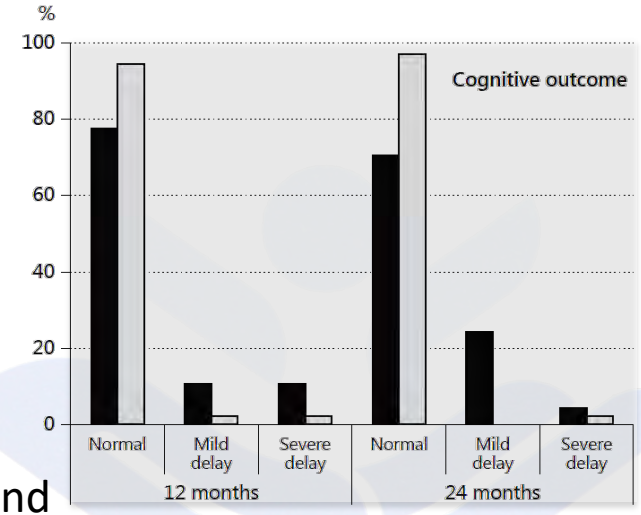
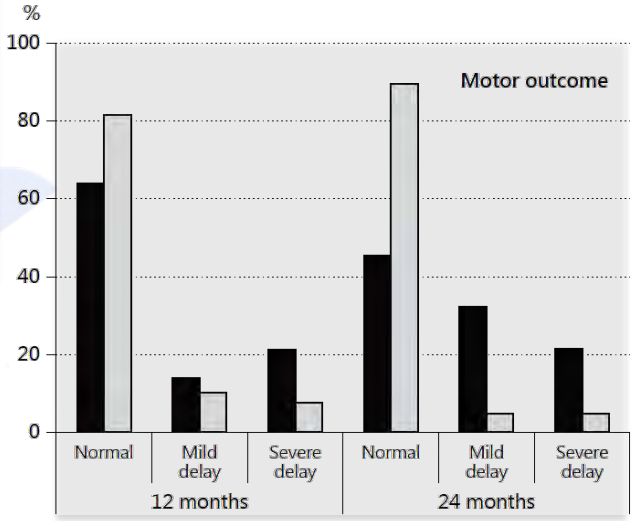
CDH & Neurodevelopmental outcome

Neurodevelopmental Outcome in High-Risk Congenital Diaphragmatic Hernia Patients: An Appeal for International Standardization

Kitty G. Snoek[a] Irma Capolupo[c] Annabella Braguglia[c] Lucia Aite[c]
Joost van Rosmalen[b] Laura Valfrè[c] René M. Wijnen[a] Pietro Bagolan[c]
Dick Tibboel[a] Hanneke IJsselstijn[a]

[a]Intensive Care and Department of Pediatric Surgery, Erasmus MC-Sophia Children's Hospital, and [b]Department of Biostatistics, Erasmus MC, Rotterdam, The Netherlands; [c]Department of Medical and Surgical Neonatology, Bambino Gesu Children's Hospital, Rome, Italy





Different diagnostic tool (Bayley II vs III)
Different professional background (physical therapist vs developmental psychologist)
Different patients' population

Snoek KG et al., Neonatology, 2016

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CDH & Neurodevelopmental outcome

Does Ventilatory Time Retain Its Validity in Predicting Neurodevelopmental Outcome at Two Years of Age in High-Risk Congenital Diaphragmatic Hernia Survivors?

Francesca Bevilacqua, PsD[1] Francesco Morini, MD[2] Antonio Zaccara, PhD[3] Laura Valfrè, MD[2]
Lelia Rotondi Aufiero, MD[4] Simonetta Gentile, PsD[1] Pietro Bagolan, MD[2] Lucia Aite, PsD[1]

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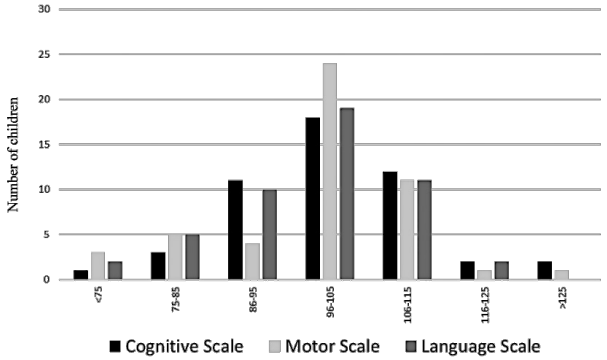
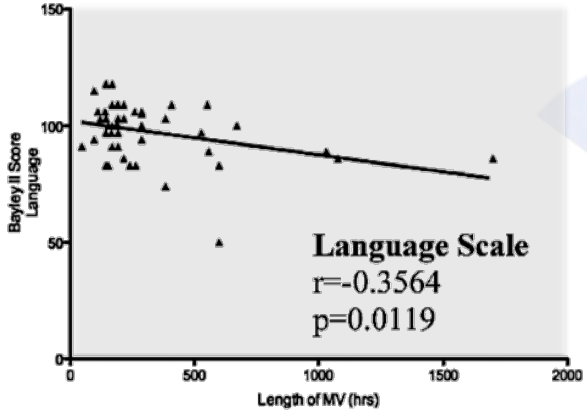
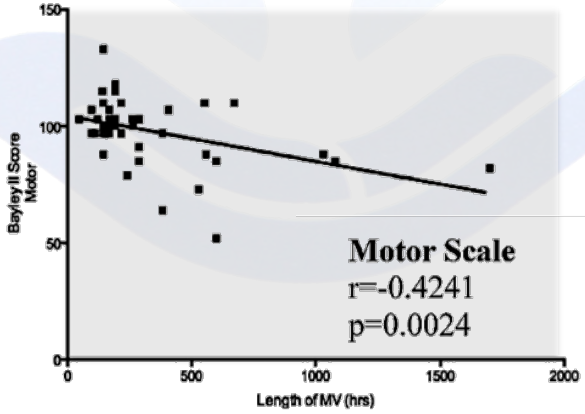
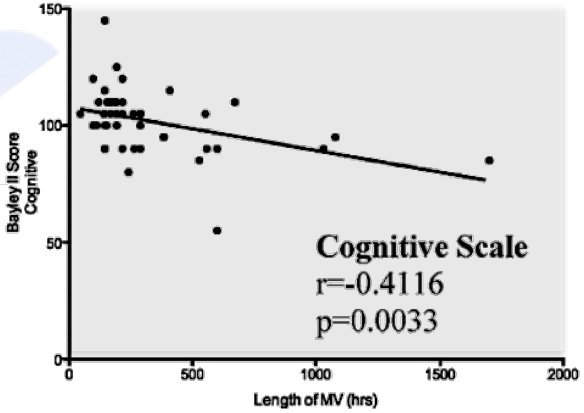
22% delay









Bevilacqua F et al., Am J Perinatol, 2017

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CDH & Neurodevelopmental outcome

Neurodevelopmental outcomes at 5 years of age in congenital diaphragmatic hernia

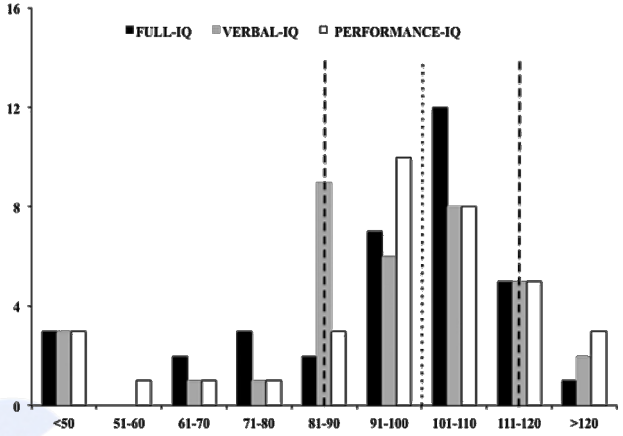
Enrico Danzer *, Casey Hoffman, Jo Ann D'Agostino, Marsha Gerdes, Judy Bernbaum, Ryan M. Antiel, Natalie E. Rintoul, Lisa M. Herkert, Alan W. Flake, N. Scott Adzick, Holly L. Hedrick

The Center for Fetal Diagnosis and Treatment, The Children's Hospital of Philadelphia, Philadelphia, PA, USA

Table 5
OLS regression modeling of the relationship between adverse developmental and functional outcomes and clinical important predictors.

	WPPSI-III Full IQ		WPPSI-III Verbal IQ		WPPSI-III Visual–spatial IQ		VMI	
	b (95% CI)	*P* value	b (95% CI)	*P* value	B (95% CI)	*P* value	b (95% CI)	*P* value
Low LHR	−13.4 (−25.1 to −1.8)	**<0.03**	−12.6 (−24.2 to −0.9)	**<0.04**	−6.9 (−19.3 to 5.5)	0.26	−6.4 (−18.6 to 5.9)	0.26
Prolonged ventilatory support	−0.2 (−0.4 to −0.02)	**0.02**	−0.2 (−0.4 to −0.02)	**0.03**	−0.2 (−0.4 to −0.04)	**0.02**	−0.1 (−0.2 to 0.1)	0.36
HFOV	−13.2 (−26.3 to −0.3)	**0.05**	−10.2 (−22.9 to 2.4)	0.11	−14.2 (−28.1 to −0.3)	**<0.05**	−3.4 (−16.3 to 9.5)	0.60
Tracheostomy	−20.4 (−38.3 to −2.4)	**<0.03**	−14.6 (−32.2 to 2.9)	0.10	−26.3 (−44.6 to −7.9)	**0.006**	−18.1 (−36.6 to 0.4	0.06
Need for supplemental O2 at DOL 30	−13.7 (−16.1 to −1.2)	**0.03**	−11.8 (−23.7 to 0.2)	0.053	−14.6 (−27.8 to −1.3)	**0.03**	−5.5 (−17.9 to 6.9)	0.37
pHTN	−15.4 (−30.5 to −0.2)	**0.05**	−18.5 (32.3 to −4.7)	**0.01**	−20.1 (−35.6 to −4.5)	**0.01**	−7.3 (−21.9 to 7.4)	0.32
Need for fundoplication	−13.5 (−27.2 to 0.2)	**0.05**	12.6 (−25.6 to 0.4)	0.06	−15.2 (−29.7 to −0.9)	**<0.04**	−13.1 (−26.5 to 0.4)	0.06
Prolonged LOS	−0.1 (−0.1 to −0.4)	**<0.0001**	−0.1 (−0.1 to −0.03)	**<0.0001**	−0.1 (−0.1 to −0.04)	**<0.0001**	−0.1 (−0.1 to −0.01)	**<0.02**
Below average BSID-III scores during infancy	−14.9 (−21.3 to −8.7)	**<0.0001**	−12.3 (−19.0 to −5.6)	**0.001**	−13.8 (−20.8 to −6.7)	**<0.0001**	−11.9 (−18.5 to −5.3)	**0.001**
Abnormal BAERs	−35.0 (−49.9 to −20.0)	**<0.0001**	−28.3 (−43.7 to −12.9)	**0.001**	−37.4 (−53.2 to −21.6)	**<0.0001**	−25.7 (−40.9 to −10.9)	**0.002**
Below average length percentile at follow-up	0.3 (0.1 to 0.6)	**0.006**	0.2 (−0.04 to 0.5)	0.105	0.4 (0.1 to 0.6)	**0.007**	0.3 (0.01 to 0.5)	**<0.05**
Autism	−30.0 (−48.5 to −11.5)	**0.002**	−25.5 (−43.5 to −7.4)	**0.007**	−28.7 (−48.8 to −8.5)	**0.007**	−22.9 (−40.7 to −5.1)	**0.01**
Need for g-tube or j-tube or nutritional support	−16.1 (−33.1 to 0.9)	0.06	−22.7 (−37.7 to −7.6)	**0.004**	−18.1 (−35.9 to −0.2)	**<0.05**	−17.3 (−32.6 to −1.9)	**<0.03**
Microcephaly	−15.3 (−43.9 to 13.4)	0.29	−13.1 (−40.4 to 14.1)	0.34	−19.8 (−49.9 to 10.3)	0.19	−25.9 (−51.1 to −0.8)	**0.04**

LHR, lung-to-head ratio; LOS, length of stay; HFOV, high frequency oscillatory ventilation; pHTN, pulmonary hypertension; DOL, day of life; BSID-III, Bayley Scales of Infant Development 3rd Edition; BAERs, brainstem auditory evoked responses; g-tube, gastrostomy tube; j-tube; jejunostomy tube; f/u, follow-up.



Danzer E et al., J Pediatr Surg, 2017

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CDH & Psychiatric problems

Neurodevelopmental outcomes at 5 years of age in congenital diaphragmatic hernia

Enrico Danzer *, Casey Hoffman, Jo Ann D'Agostino, Marsha Gerdes, Judy Bernbaum, Ryan M. Antiel, Natalie E. Rintoul, Lisa M. Herkert, Alan W. Flake, N. Scott Adzick, Holly L. Hedrick

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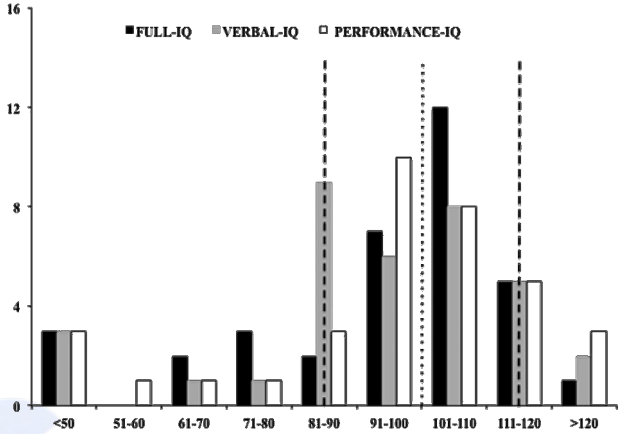
Table 4
CDH CBCL scores in comparison to normative data.

	Prevalence of at risk or clinical significant CBCL/1.5–5 normative data [23]	Prevalence of at risk or clinical significant CBCL results of CDH patients	*P*-value*
Total problems	18%	23%	0.48
Externalizing problems	17%	12%	0.42
Internalizing problems	21%	31%	0.15
Emotionally reactive	10%	23%	**0.02**
Anxious/depressed	8%	15%	0.18
Somatic problems	9%	12%	0.65
Withdrawn	7%	8%	1.00
Sleep problems	5%	0%	0.06
Attention problems	7%	12%	0.34
Aggressive behavior	7%	12%	0.34
DSM-affective	7%	12%	0.34
DSM-anxiety	8%	15%	0.18
DSM-pervasive	7%	27%	**0.0003**
DSM-ADHD	9%	4%	0.25
DSM-oppositional defiant	7%	8%	1.00

* The *P*-values were calculated using chi-square statistics.



Autism was diagnosed in 11% of female and 11% of male patients, which is significantly higher than the general population (0.5% and 2.4% respectively, $P < 0.01$) [25].

Danzer E et al., J Pediatr Surg, 2017

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CDH: long term sequelae

- ✓ May be severe
- ✓ May be smoldering
- ✓ Tend to worsen over time

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CDH: long term sequelae

Long term follow-up in congenital diaphragmatic hernia

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[b]*Department of Surgery, Boston Children's Hospital, Boston MA, USA*

Hollinger LE & Buchmiller TL, Semin Perinatol, 2019

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CDH: long term follow-up

Long-term morbidity of congenital diaphragmatic hernia: A plea for standardization

Francesco Morini, Laura Valfrè, Pietro Bagolan*

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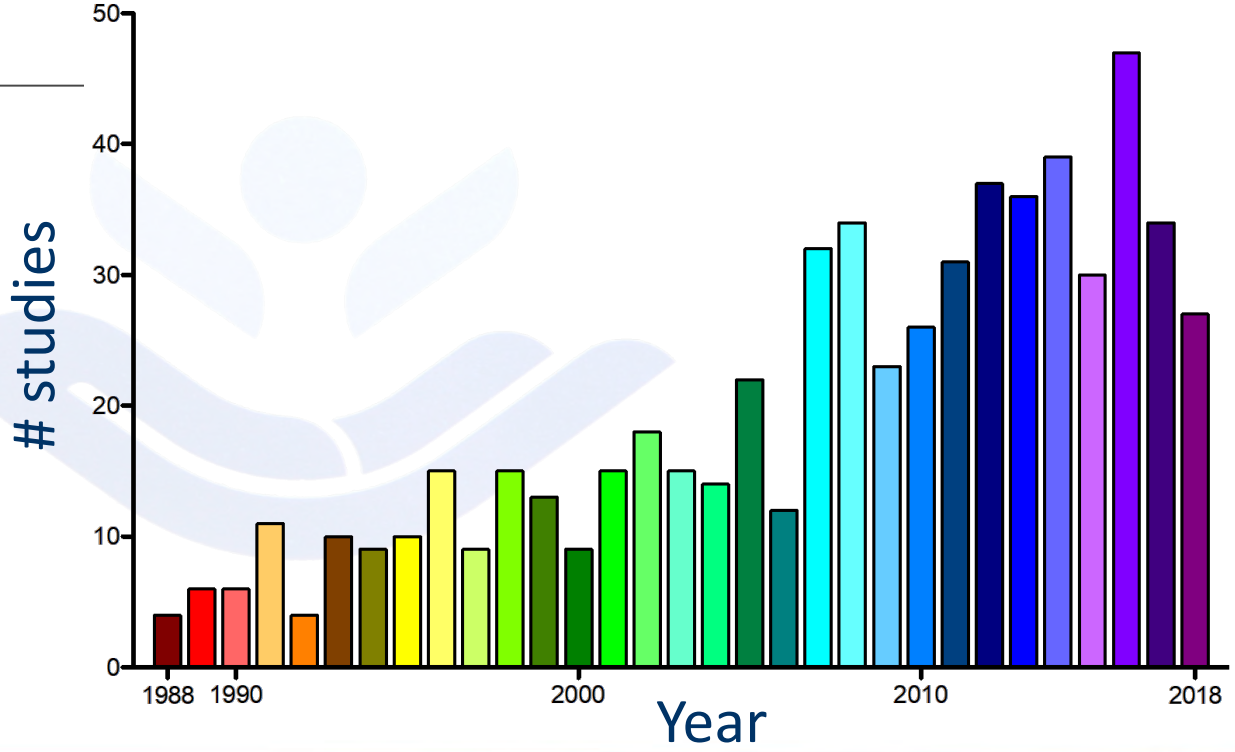

Morini F et al., Semin Pediatr Surg, 2017

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CDH follow-up

CLINICAL REPORT

Postdischarge Follow-up of Infants With Congenital Diaphragmatic Hernia

Section on Surgery and the Committee on Fetus and Newborn

TABLE 1 Recommended Schedule of Follow-up for Infants With CDH

	Before Discharge	1–3 mo After Birth	4–6 mo After Birth	9–12 mo After Birth	15–18 mo After Birth	Annual Through 16 y
Weight, length, occipital-frontal circumference	X	X	X	X	X	X
Chest radiograph	X	If patched	If patched	If patched	If patched	If patched
Pulmonary function testing			If indicated		If indicated	If indicated
Childhood immunizations	As indicated throughout childhood	X	X	X	X	X
RSV prophylaxis	RSV season during first 2 years after birth (if evidence of chronic lung disease)	X	X	X	X	X
Echocardiogram and cardiology follow-up	X	If previously abnormal or if on supplemental oxygen	If previously abnormal or if on supplemental oxygen	If previously abnormal or if on supplemental oxygen	If previously abnormal or if on supplemental oxygen	If previously abnormal or if on supplemental oxygen
Head computed tomography or MRI	If (1) abnormal finding on head ultrasound; (2) seizures/abnormal neurologic findings*; or (3) ECMO or patch repair	As indicated	As indicated	As indicated	As indicated	As indicated
Hearing evaluation[44]	Auditory brainstem evoked response or otoacoustic emissions screen	X	X	X	X	Every 6 mo to age 3 y, then annually to age 5 y
Developmental screening evaluation	X	X	X	X		Annually to age 5 y
Neurodevelopmental evaluation	X			X		Annually to age 5 y
Assessment for oral feeding problems	X	X	If oral feeding problems	If oral feeding problems	If oral feeding problems	If oral feeding problems
Upper gastrointestinal study, pH probe, and/or gastric scintiscan	Consider for all patients	If symptoms	If symptoms	Consider for all patients	If symptoms	If symptoms
Esophagoscopy		If symptoms	If symptoms	If symptoms or if abnormal gastrointestinal evaluations	If symptoms	If symptoms
Scoliosis and chest wall deformity screening (physical examination, chest radiograph, and/or computed tomography of the chest)				X		X

AAP Section on Surgery and Committee on Fetus and Newborn, Pediatrics, 2007

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CDH sequelae: our long term follow-up

Multidisciplinary follow-up clinic:

Pediatrician

Pediatric surgeon

Psychologist

Nurse

& physiotherapist, neurologist, radiologist, ENT, …

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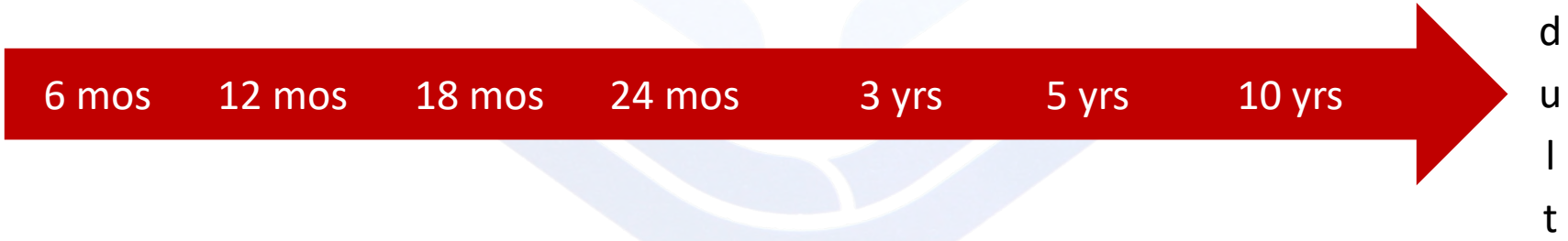
CDH sequelae: our long term follow-up

Multidisciplinary follow-up clinic:



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CDH follow-up: the tale of three cities

Long-term morbidity of congenital diaphragmatic hernia: A plea for standardization

Francesco Morini, Laura Valfrè, Pietro Bagolan*

Neonatal Surgery Unit, Department of Medical and Surgical Neonatology, Bambino Gesù Children's Hospital, IRCCS, Rome, Italy

	Hospital for sick children Toronto	Sophia children's hospital Rotterdam	Bambino Gesù Chiuldren's Hospital Rome
4 wks	General surgical clinic + CXR	Pediatric surgeon	Pediatric surgeon
3–4 mos	CXR, neonatal FU (AIMS, PFMA-I), hearing test	–	Neonatologist, pediatric surgeon, developmental psychologist (parental emotional assesment)
6 mos	–	Pediatric surgeon, pediatrician, clinical geneticist, cardiologist (ECHO, ECG), PFT (LCI), pH-metry	Neonatologist, pediatric surgeon, clinical geneticist, developmental psychologist (Bayley III + parental emotional assesment), PFT (LCI), hearing test
8 mos	CXR, neonatal FU (AIMS, PFMA-I, CSBS if concerns), cardiologist if PTHN/PDA/PFO	–	–
12 mos	CXR, neonatal FU (AIMS, PFMA-I, CSBS), hearing test	Pediatric surgeon, pediatrician, cardiologist (ECHO, ECG), PFT (LCI), developmental psychologist (Bayley II)	Neonatologist, pediatric surgeon, developmental psychologist (Bayley III+ parental emotional assesment), PFT (LCI), cardiologist (ECHO), upper GI contrast study, pH-metry, hearing test
18 mos	CXR, neonatal FU (Bayley III, M.CHAT, REEL III)	–	Neonatologist, pediatric surgeon, developmental psychologist (parental emotional assessment), PFT (LCI), hearing test, orthopedic surgeon
2 yrs	CXR, cardiologist if no PTHN/PDA/PFO at first assessment	Pediatric surgeon, pediatrician, developmental psychologist (Bayley II-Dutch version, mental scale), physiotherapist (Bayley II, motor scale)	Neonatologist/pediatrician, pediatric surgeon, developmental psychologist (Bayley III + parental emotional assessment), CXR, PFT (LCI), orthopedic, hearing test
3 yrs	Neonatal FU (Bayley III, BRIEF-P, CBCL, Vineland II)	–	Neonatologist/pediatrician, pediatric surgeon, developmental psychologist, orthopedic surgeon, cardiologist, hearing test
5 yrs	CXR, PFT (spirometry), neonatal FU clinic	Pediatric surgeon, pediatrician, psychologist (QoL and social emotional assessment), physiotherapist (movement ABC, Bruce treadmill protocol), PFT (LCI)	Neonatologist/pediatrician, pediatric surgeon, developmental psychologist (Leiter-R), PFT (spirometry and CPET), cardiologist (ECHO), orthopedic surgeon, hearing test
7 yrs	CXR, PFT (spirometry + lung volumes), neonatal FU clinic (if not assessed at 5 years)		–
8 yrs	–	Pediatric surgeon, pediatrician, psychologist (intelligence, neuropsychological assessment, QoL, social emotional assessment), physiotherapist (movement ABC, Bruce treadmill protocol), PFT (spirometry, body pletismography, diffusion capacity, LCI), pH-metry	Neonatologist/pediatrician, pediatric surgeon, developmental psychologist, orthopedic surgeon, hearing test
10 yrs	CXR, PFT (complete with MIPS/MEPS), cardiologist (ECHO, ECG, CT scan, VO_2 exercise test)	–	–
12 yrs	–	Pediatric surgeon, pediatrician, cardiologist (ECHO, ECG), pulmonologist (MRI diaphragm, lungs and vessels), psychologist [neuropsychological assessment, QoL, social-emotional assessment), physiotherapist (movement ABC, Bruce treadmill protocol), PFT (spirometry, body pletismography, diffusion capacity, LCI)	Neonatologist/pediatrician, pediatric surgeon, developmental psychologist, PFT (spirometry and CPET), cardiologist (ECHO), orthopedic, hearing test
15 yrs			Neonatologist/pediatrician, pediatric surgeon, developmental psychologist, PFT (spirometry and CPET), cardiologist, orthopedic, hearing test
17 yrs	Cardiology (ECHO, ECG)	Pediatric surgeon, pediatrician, clinical geneticist, psychologist [neuropsychological assessment, QoL, social-emotional assessment), physiotherapist (movement ABC, maximal exercise test), PFT (spirometry, body pletismography, diffusion capacity, LCI)	Neonatologist/pediatrician, pediatric surgeon, developmental psychologist, PFT (spirometry and CPET), cardiologist, orthopedic, hearing test

Morini F et al., Semin Pediatr Surg, 2017

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CDH follow-up

Multi-institutional follow-up of patients with congenital diaphragmatic hernia reveals severe disability and variations in practice ☆

Arash Safavi[a], Anne R. Synnes[b], Karel O'Brien[c], Monping Chiang[d], Erik D. Skarsgard[a], Priscilla P.L. Chiu[d,*]
Canadian Pediatric Surgery Network

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[d]*Division of Pediatric General and Thoracic Surgery, The Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada*

Table 1 Characteristics of surveyed CAPSNet centers

Center		Where			Who					When	What							
		Community based	Center-based multiple clinics	Center-based multidisciplinary CDH clinic	Pediatric surgeon	General pediatrician	Subspecialty pediatrician	Other health care providers[a]	Audiologist	Duration (y)	Neurodevelopmental	Hearing	Nutritional	Chest x-ray	PFT	Echo	GER	Neuroimaging
A	▲		✓		✓		✓ ✪	✓		2-4	✓	✓	✓	✓		✓		
B	▲			✓	✓ ✪		✓	✓		>10	✓	✓	✓	✓	✓	✓		HR
C	▲				✓ ✪	✓	✓			2-4	HR			✓				HR
D	▲	✓			✓	✓ ✪	✓			6-10	HR	✓		✓		✓		HR
E		✓			✓	✓ ✪	✓			2-4	HR	✓		✓				HR
F		✓			✓	✓ ✪	✓	✓	✓	VAR	HR	✓		✓				
G		✓			✓	✓ ✪	✓	✓	✓	2-4	✓	✓	✓	✓		✓	✓	HR
H	▲				✓	✓	✓ ✪			1-2	HR	✓		✓				HR
I					✓ ✪					2-4	HR	✓		✓				HR
J					✓ ✪	✓	✓	✓		2-4	HR	✓	✓	✓		✓		HR
K	▲	✓				✓ ✪	✓	✓	✓	2-4	✓	✓	✓	✓			✓	HR
L		VAR					✓	✓	✓	<1	HR	HR	✓	✓		✓		HR

Safavi A et al., J Pediatr Surg, 2012

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CDH follow-up

Pediatric RESEARCH

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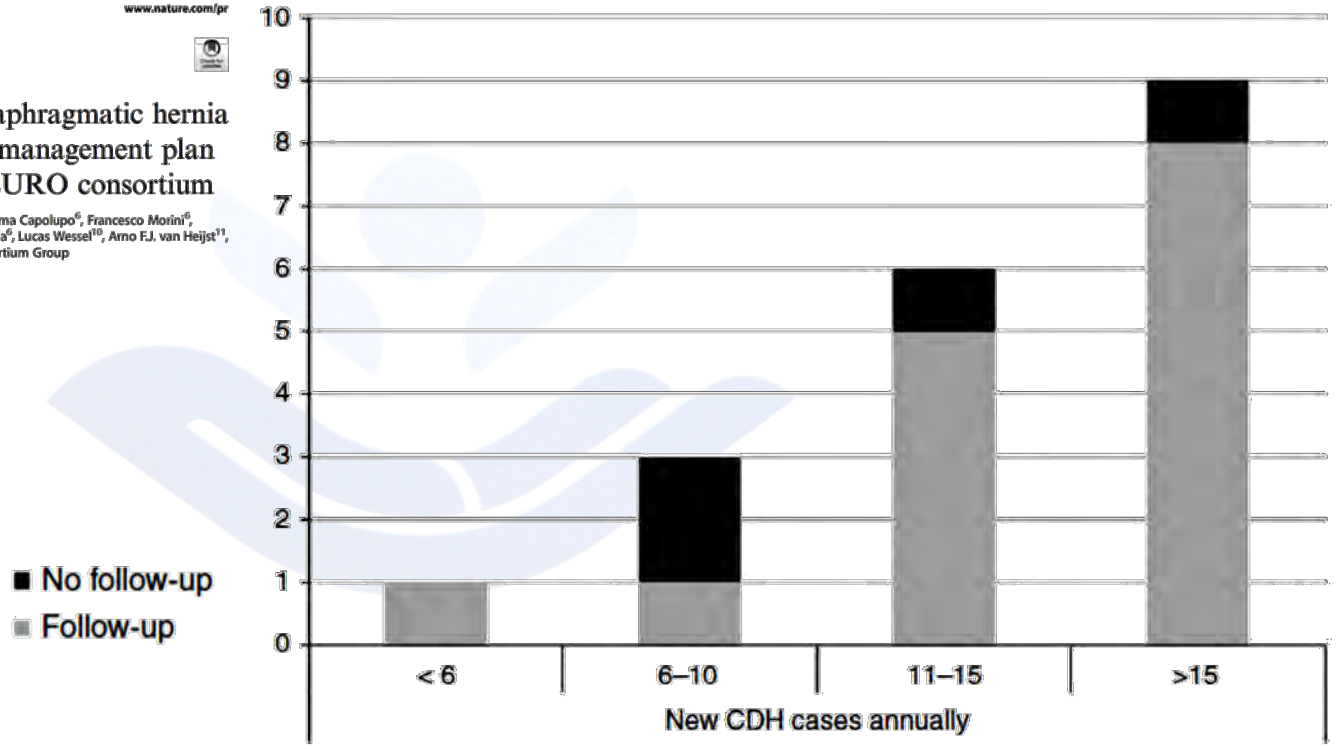
REVIEW ARTICLE

Defining outcomes following congenital diaphragmatic hernia using standardised clinical assessment and management plan (SCAMP) methodology within the CDH EURO consortium

Hanneke IJsselstijn[1], Cormac Breatnach[2], Aparna Hoskote[3], Anne Greenough[4], Neil Patel[5], Irma Capolupo[6], Francesco Morini[6], Horst Scharbatke[7], Florian Kipfmueller[8], Kjetil Ertresvag[9], Ulrike Kraemer[1], Annabella Braguglia[6], Lucas Wessel[10], Arno F.J. van Heijst[11], Inger Moinichen[9], Raghnild Emblem[9] and Dick Tibboel[1] on behalf of the CDH EURO Consortium Group



IJsselstijn A et al., Pediatr Res, 2018

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Table 2. Follow-up programs provided within the CDH EURO consortium centers

Age of follow-up	Infancy	15 (100%)	Assessments performed	Anthropometry (height, weight)	15 (100%)
	Toddler	13 (87%)		Chest radiograph	11 (73%)
	(Pre)school	13 (87%)		Gastroesophageal reflux	11 (73%)
	Adolescence (>12 yrs)	8 (53%)		Pulmonary function	10 (67%)
	Up till 20 yrs	1 (7%)		Mental development	8 (53%)
Disciplines involved	Pediatric surgeon	14 (93%)		Motor-function development	8 (53%)
	Pediatrician	11 (73%)		Audiometry	8 (53%)
	Pulmonologist	11 (73%)		Echocardiography	6 (40%)
	Pediatric physical therapist	6 (40%)		Maximal exercise test	5 (33%)
	Dietician	5 (33%)		Social–emotional well-being	4 (27%)
	Pediatric cardiologist	5 (33%)		Extensive neuropsychological testing	3 (20%)
	Speech-language pathologist	4 (27%)		Electrocardiogram	3 (20%)
	Psychologist	3 (20%)		Quality-of-life assessment	3 (20%)
	Neonatologist	2 (13%)		Intracranial imaging ultrasound	3 (20%)
	Orthopedic surgeon	1 (7%)		Orthopedic assessment	2 (13%)
	Clinical geneticist	1 (7%)		CT chest	1 (7%)
				Ventilation/perfusion scan	1 (7%)
				Intracranial imaging MRI	1 (7%)
				Thoracic MRI	1 (7%)
				Genetic assessment	1 (7%)
				Cardiac catheterization	0

Ijsselstijn A et al., Pediatr Res, 2018

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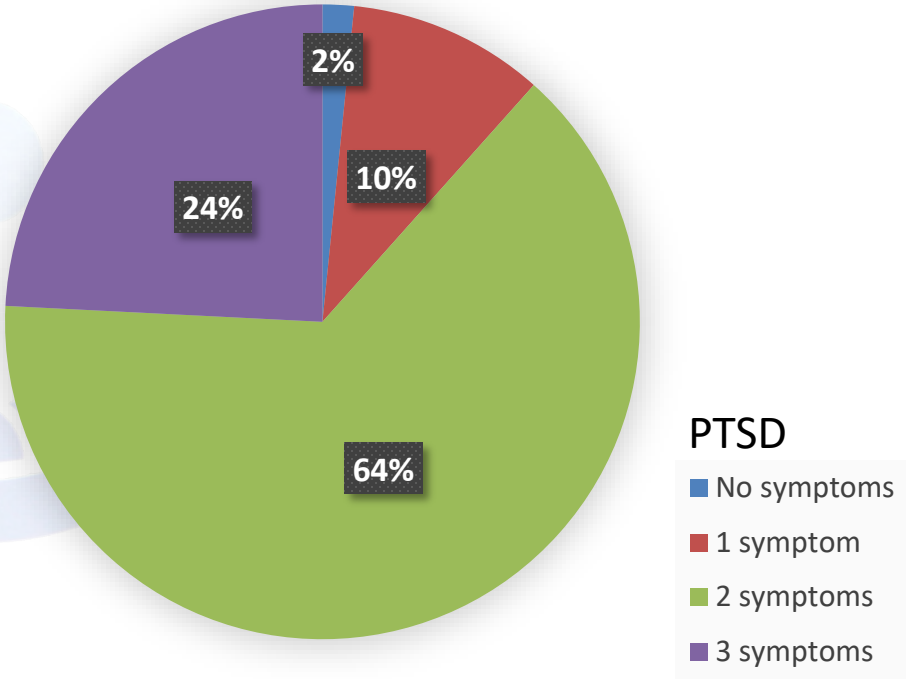
CDH parents: who cares?

Seeing Their Children in Pain: Symptoms of Posttraumatic Stress Disorder in Mothers of Children with an Anomaly Requiring Surgery at Birth

Lucia Aite, PsD[1] Francesca Bevilacqua, PsD[1] Antonio Zaccara, MD[2] Edoardo La Sala, MS[3]
Simonetta Gentile, PsD[1] Pietro Bagolan, PhD[4]

- ✓Failed project
- ✓Uncertainty for the future
- ✓Fear for loss
- ✓Change of familial routine



Aite L et al., Am J Perinatol, 2016

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CDH parents: who cares?

Couples Facing the Birth of a Newborn with a Congenital Anomaly: PTSD Symptoms in the First Year

Francesca Bevilacqua, PsD[1] Francesco Morini, MD[2] Antonio Zaccara, MD[3] Chiara De Marchis, MD[2]
Annabella Braguglia, MD[2] Simonetta Gentile, PsD[1] Pietro Bagolan, MD[2] Lucia Aite, PsD[1]

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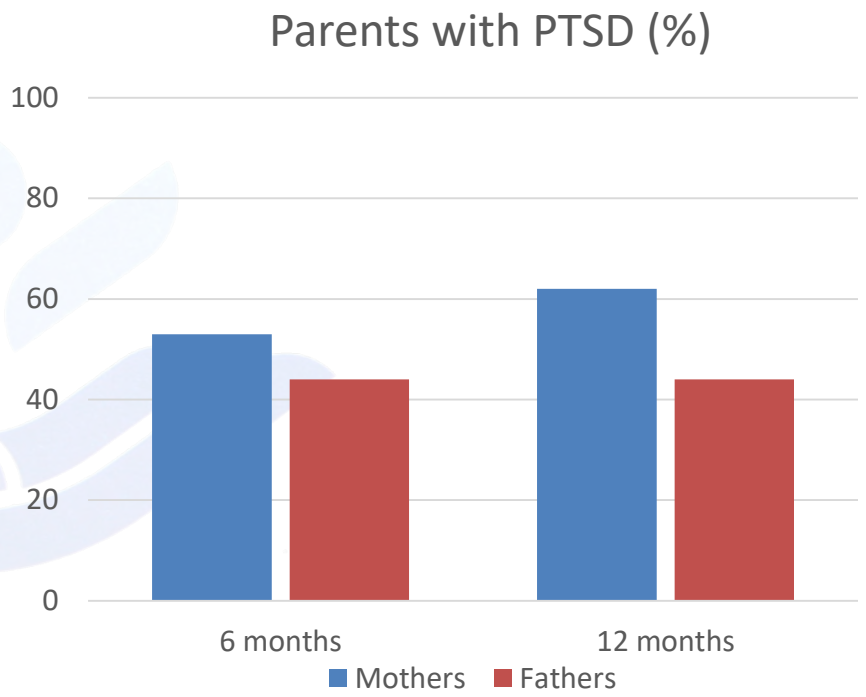

Bevilacqua F et al., Am J Perinatol, 2018

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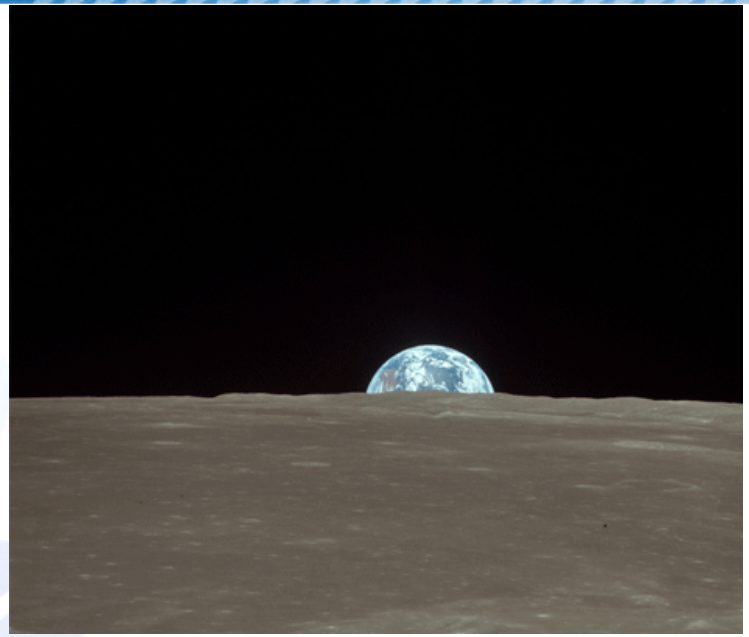
Take home messages



- ✓ CDH patients may have serious long term sequelae
- ✓ In CDH patients long term sequelae may be smoldering
- ✓ Long term, family-centered follow-up programs are needed
- ✓ Standardization of follow-up programs is desirable
- ✓ Future: TRANSITION

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Thank you