

The Role of the Heart in Congenital Diaphragmatic Hernia

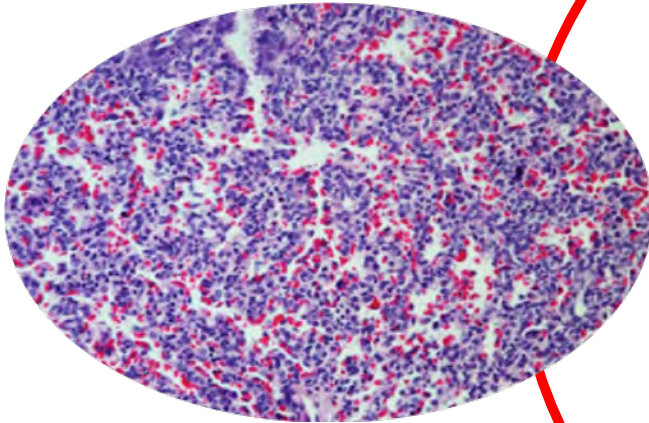
Neil Patel
Royal Hospital for Children
Glasgow, UK

**PEOPLE
MAKE
GLASGOW**



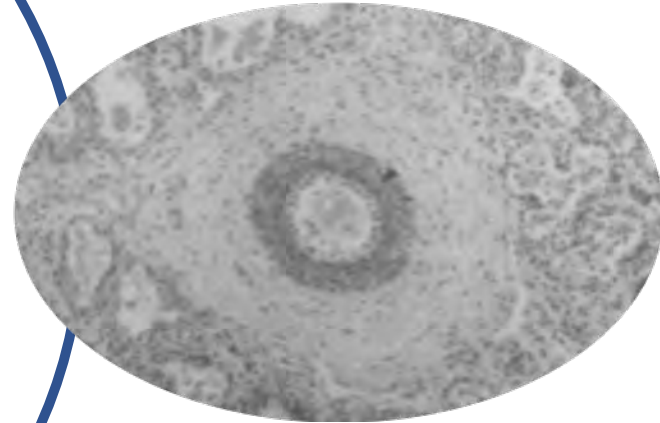


Pulmonary hypoplasia

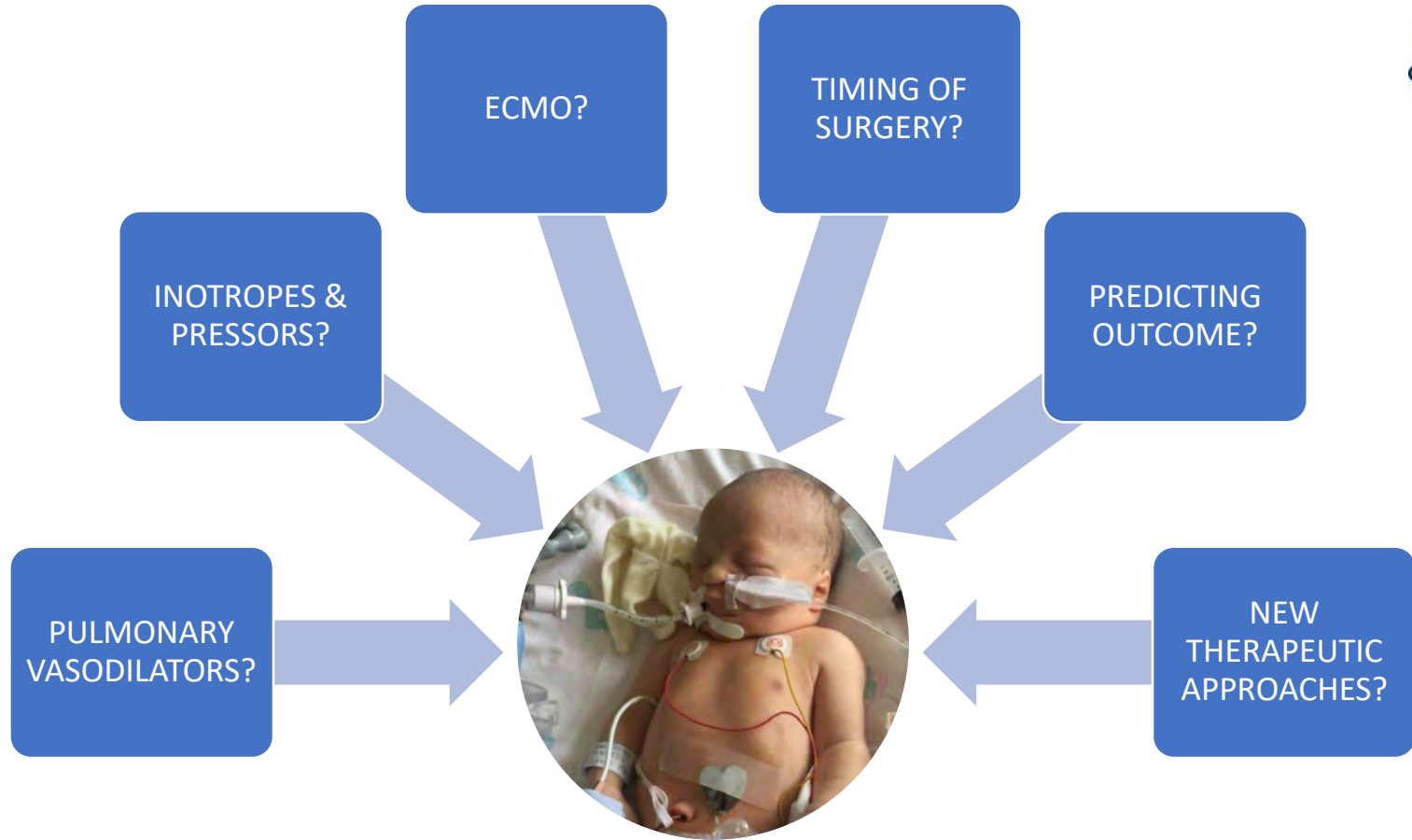


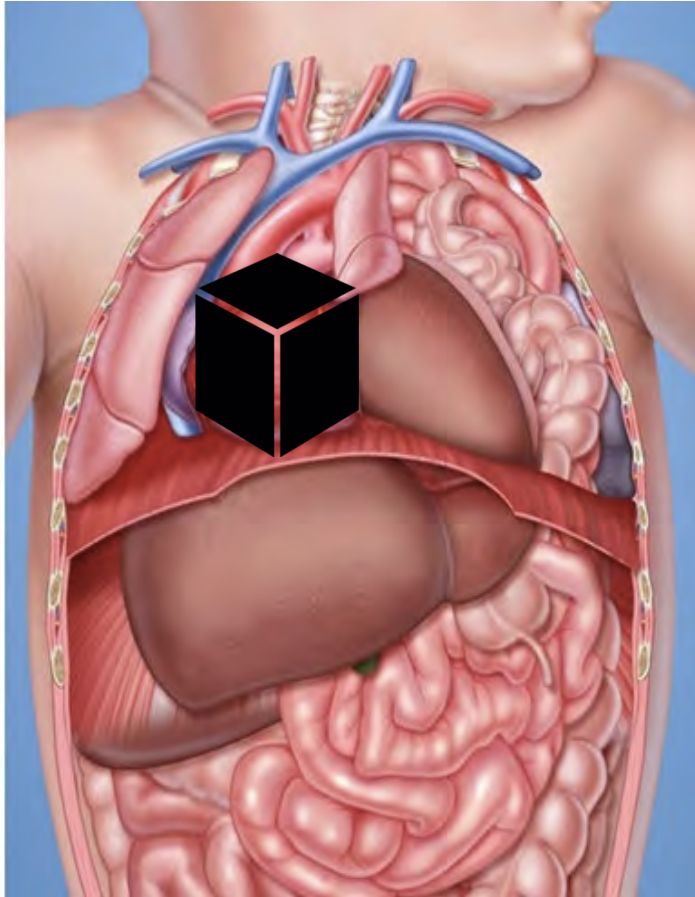
Schmidt et al, 2012

Pulmonary hypertension



Yamataka and Puri,
1997





Cardiac function in CDH

What?

Why?

When?

How often?

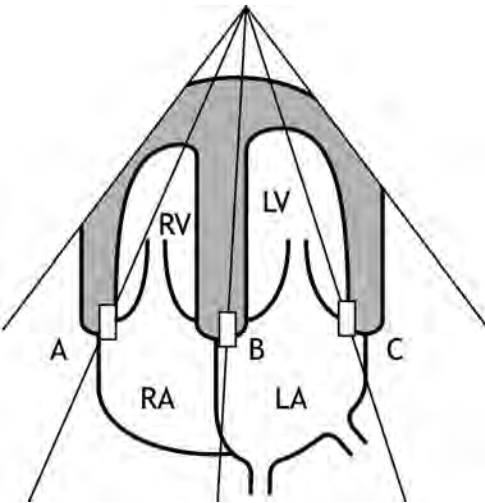
(Who cares?)



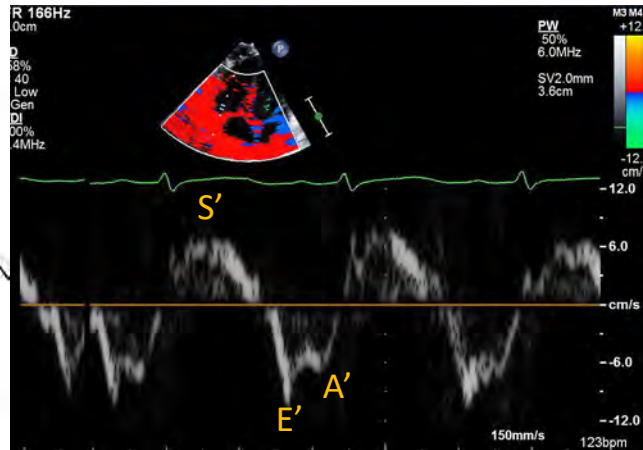
CDH 2020 Houston



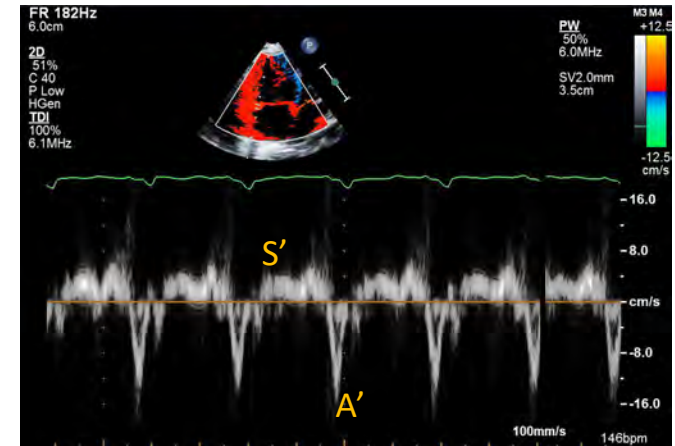
Tissue Doppler Imaging of RV in CDH



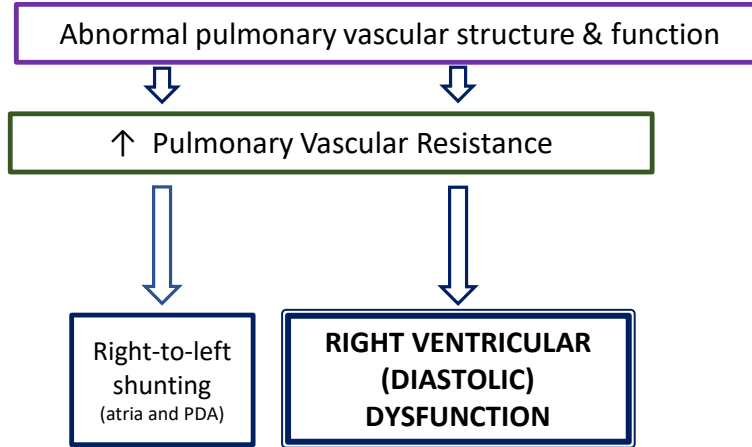
Control



CDH



- Reduced systolic velocities (S')
- Loss of diastolic (e') velocity

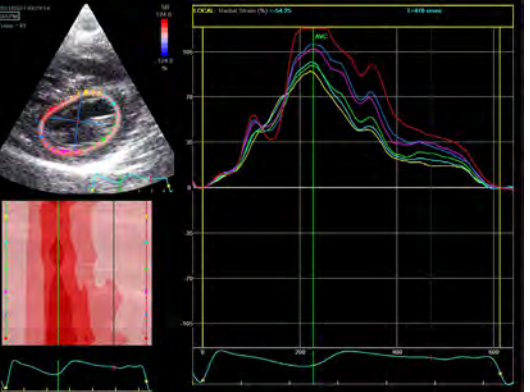
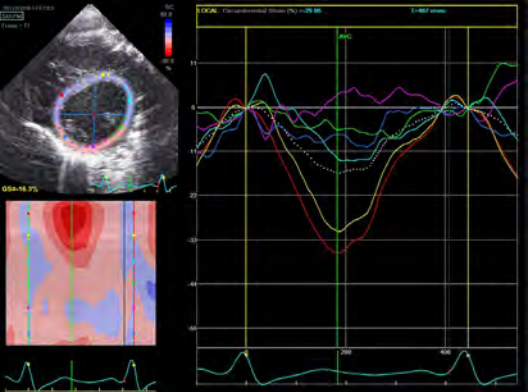
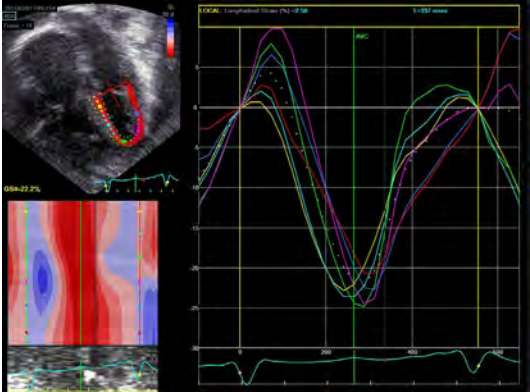


Speckle tracking echocardiography in CDH

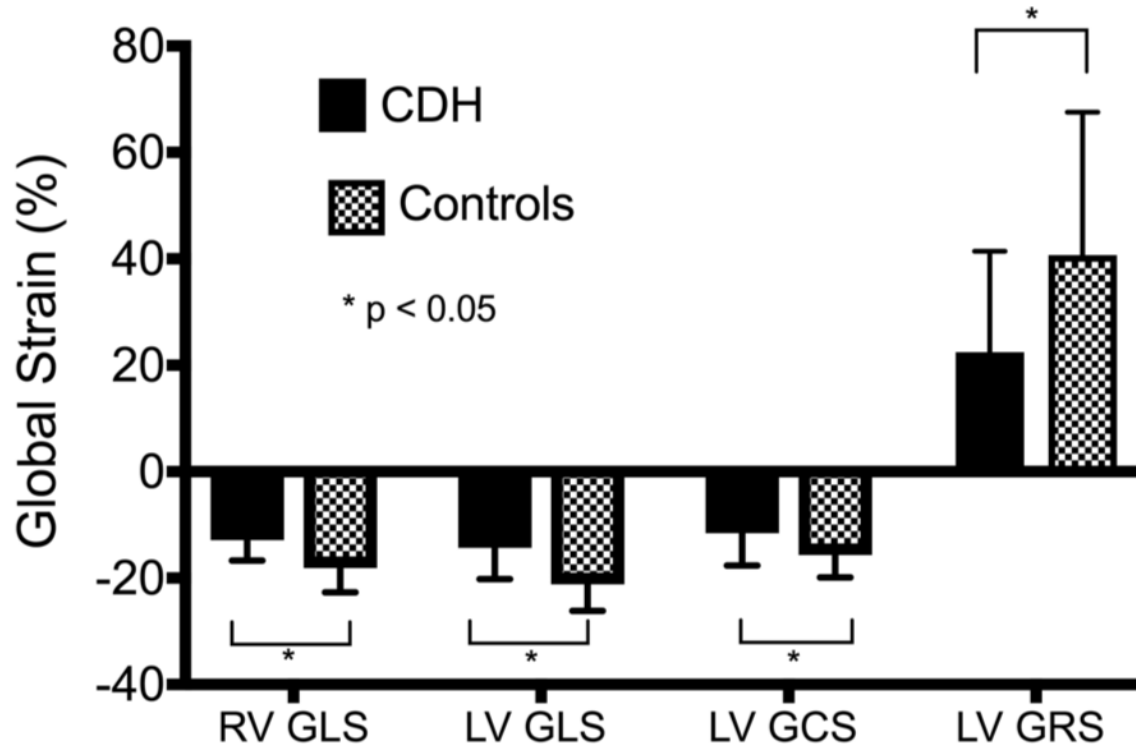
Longitudinal strain (LS)

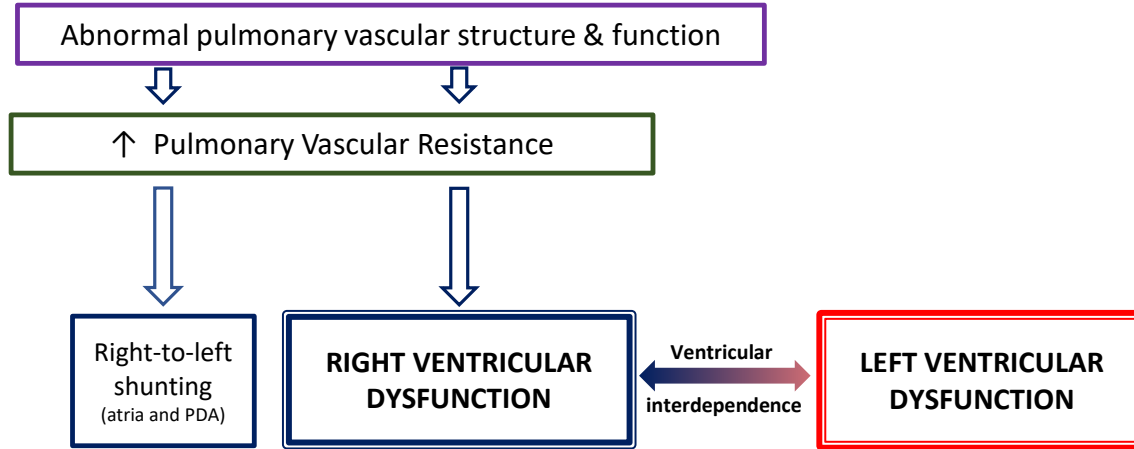
Circumferential strain (CS)

Radial strain (RS)



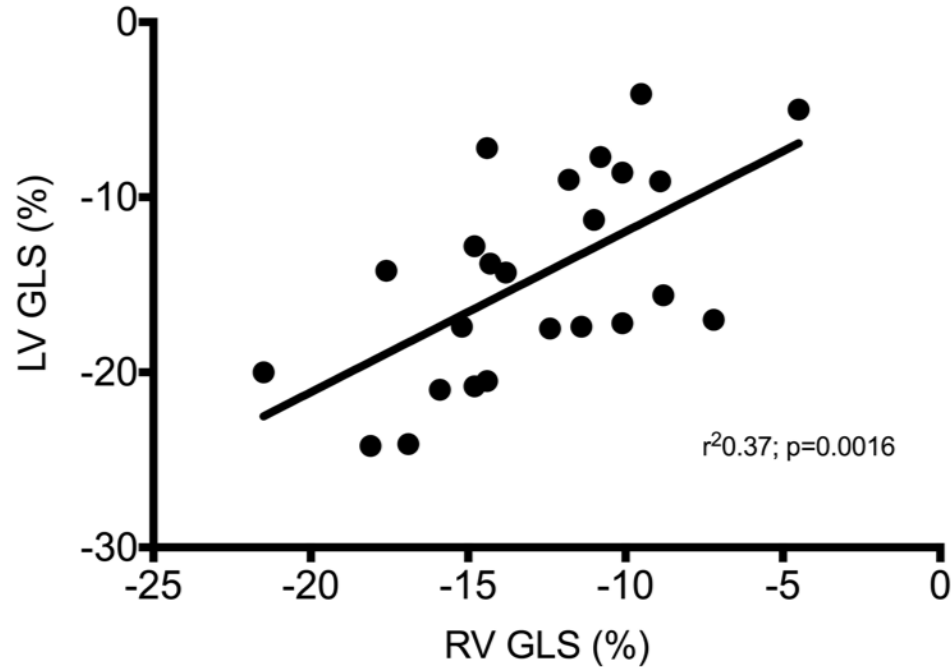
Ventricular strain in CDH (first 48h of life)





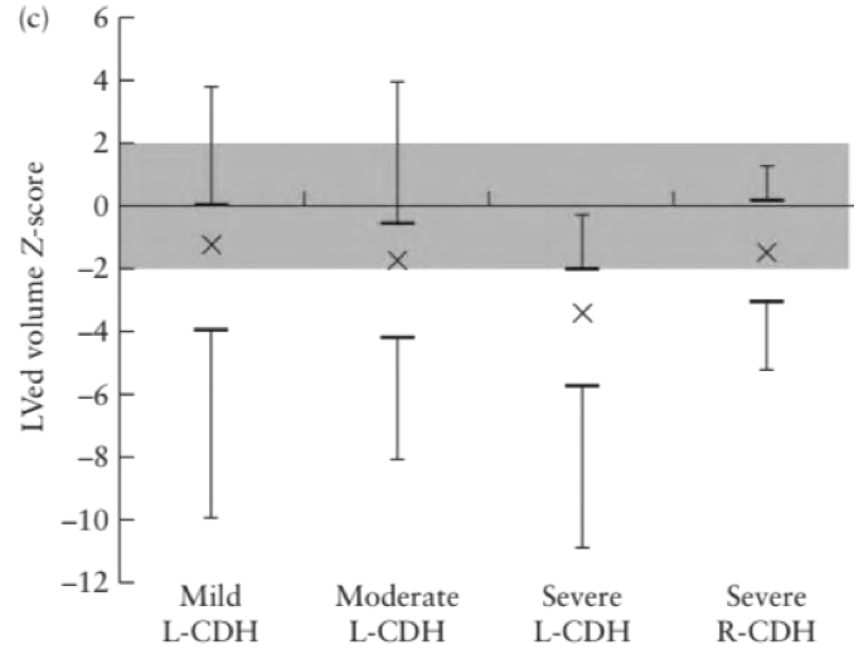
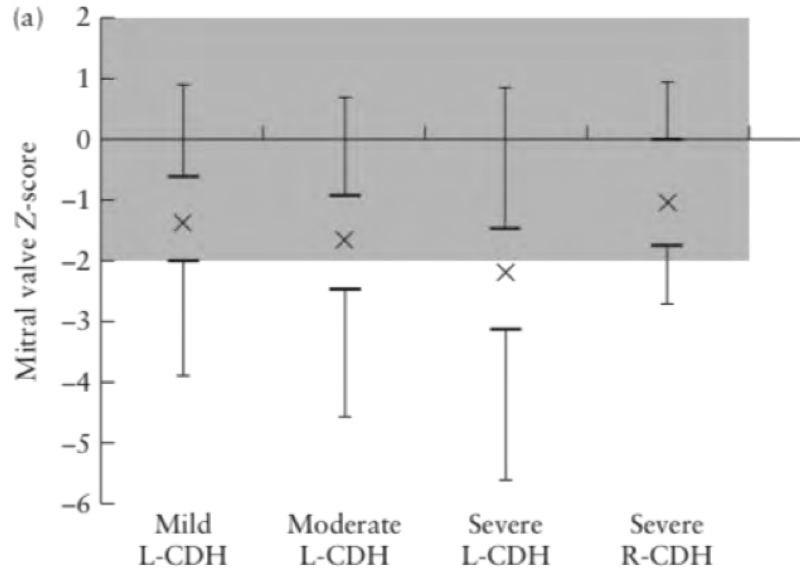
Ventricular inter-dependence in CDH

RV and LV global longitudinal strain in CDH



Severe left diaphragmatic hernia limits size of fetal left heart more than does right diaphragmatic hernia

F. A. BYRNE*, R. L. KELLER†, J. MEADOWS*, D. MINIATY‡§, M. M. BROOK*,
N. H. SILVERMAN* and A. I. MOON-GRADY*§



Possible mechanisms of fetal LV hypoplasia

- ★ Reduced pulmonary blood flow
- ★ Altered ductus venosus streaming
- ★ Mechanical compression

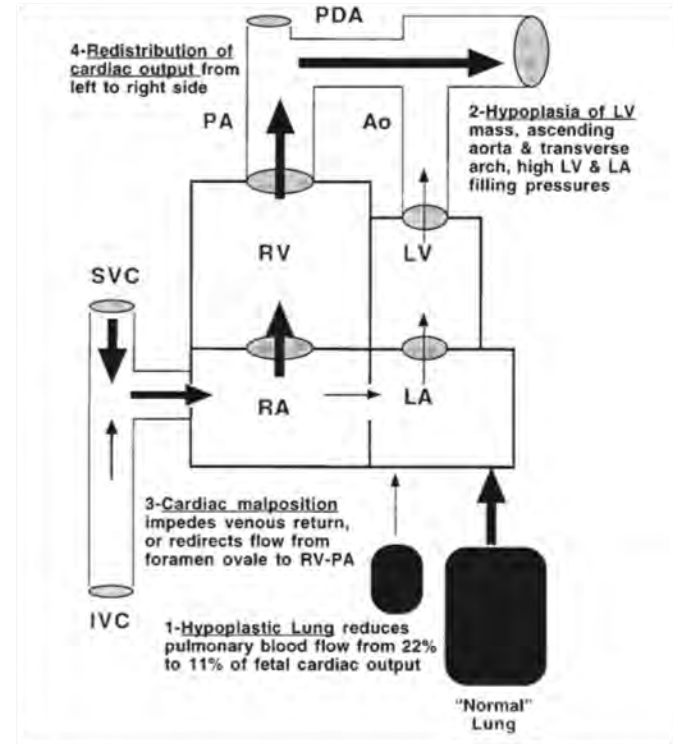
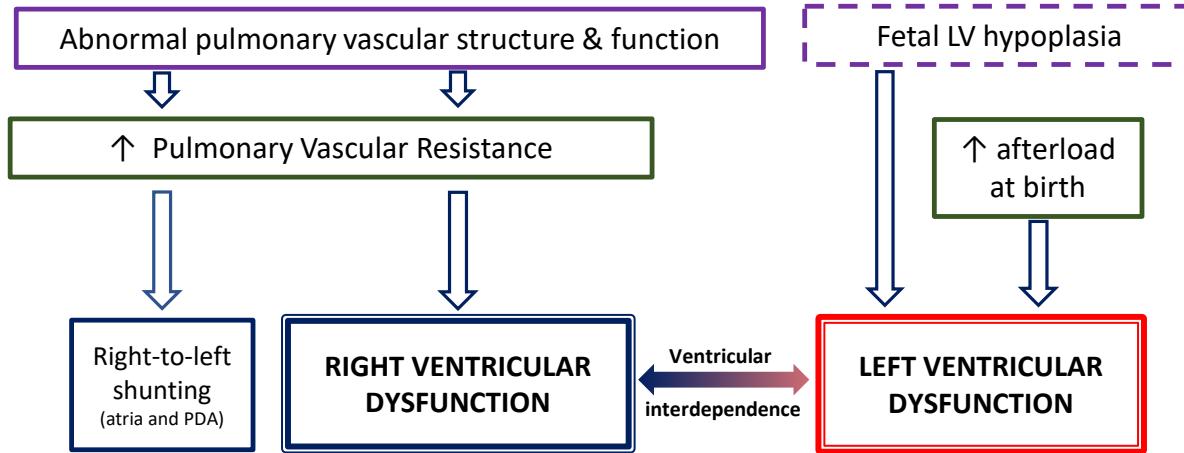
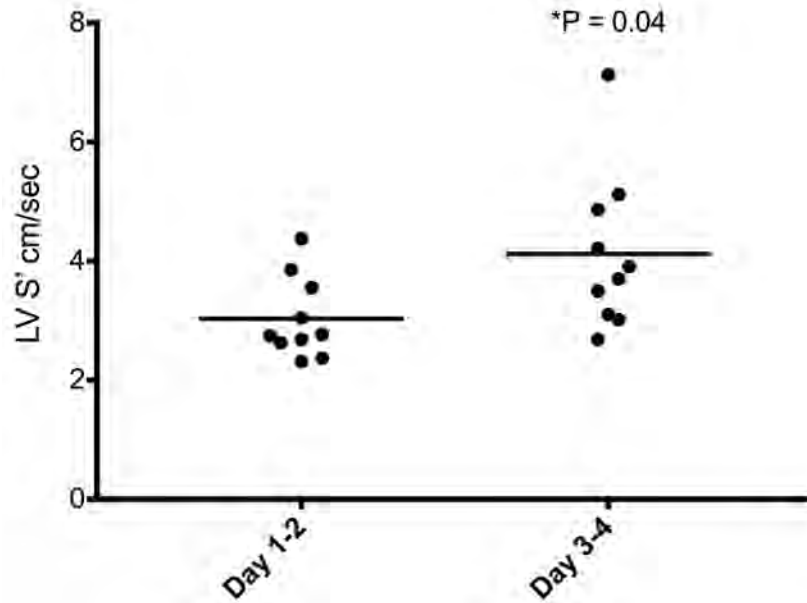


Fig. 2. Diagram summarizing four mechanisms for cardiovascular compromise during fetal life with severe CDH. (Adapted with permission from WB Saunders, Katz AL, Wiswell TE, Baumgart S. On Perinatal (1993).)

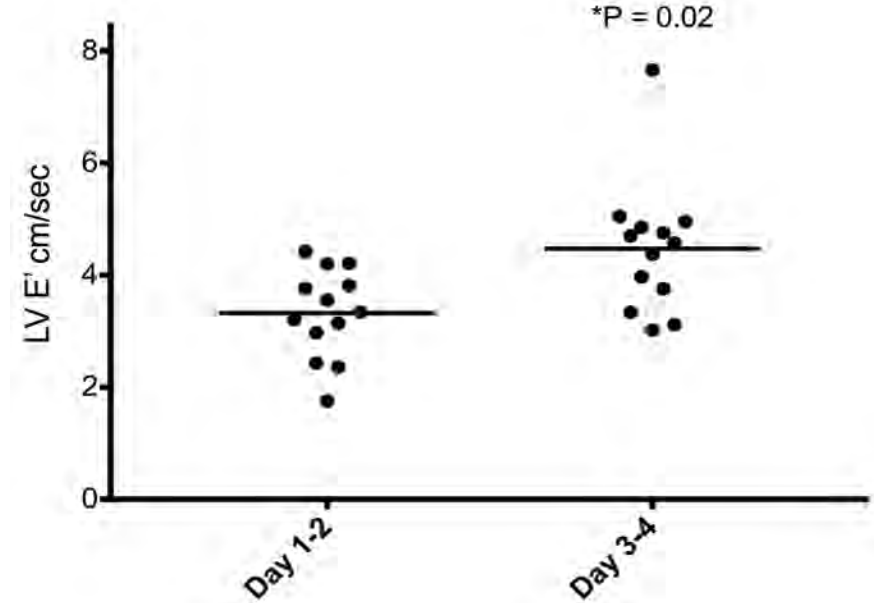


LV function improves in first days of life

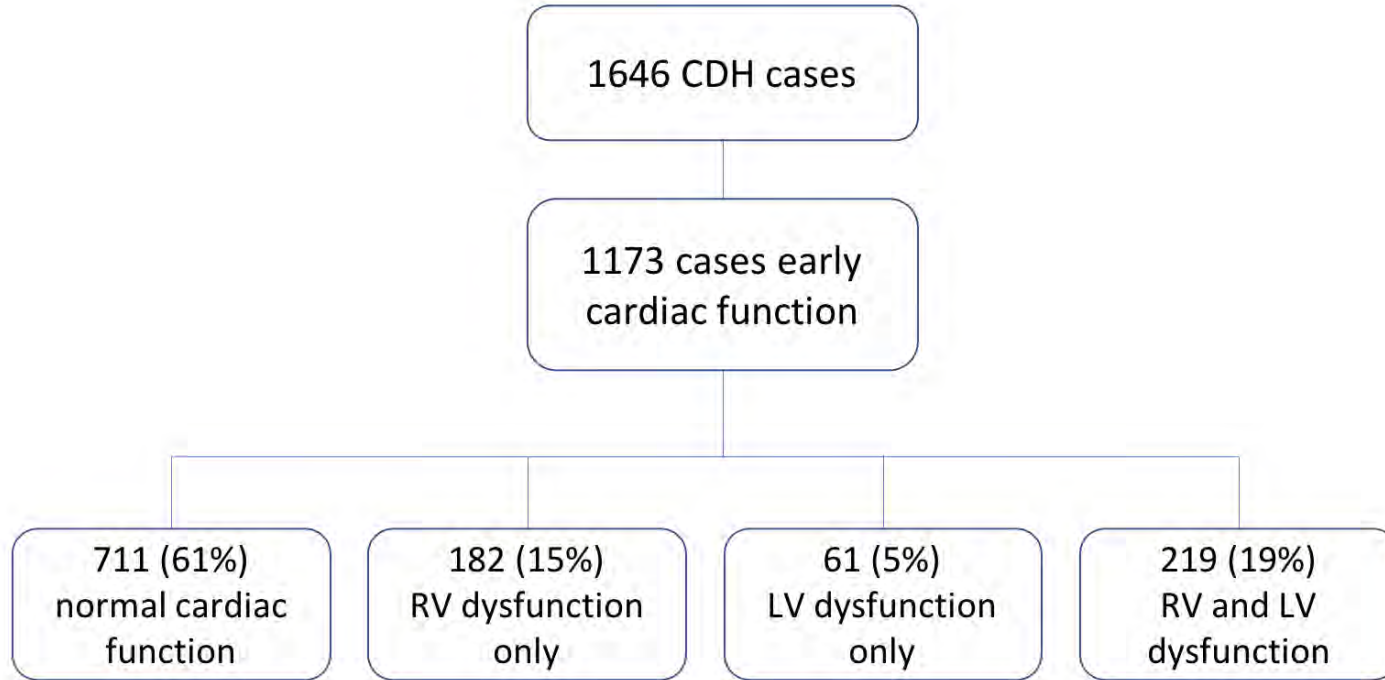
Systolic TDI velocities (LV S')



Diastolic TDI velocities (LV E')



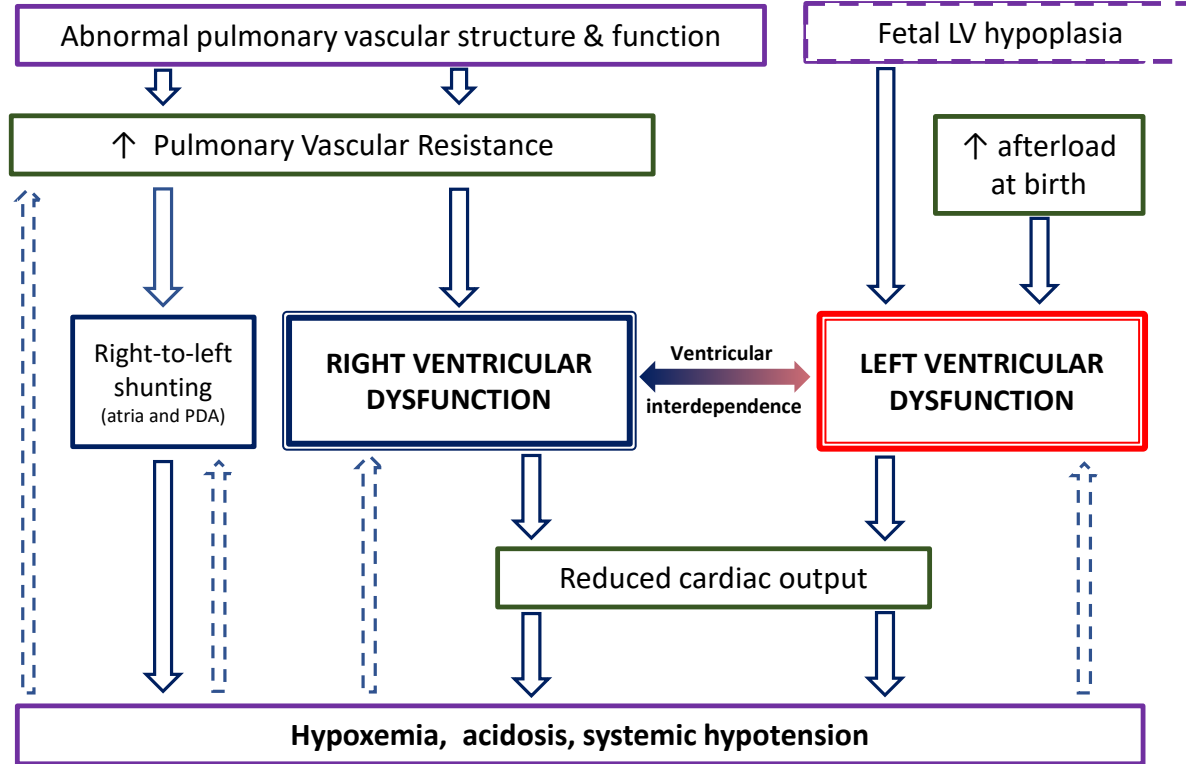
Early ventricular function: CDH Study Group Registry Analysis 2015-2018



| Variable | Cardiac Function Category | | | | P value |
|-------------------------------------|---------------------------|---------------------|---------------------|---------------------|------------------|
| | Normal function | RV dysfunction only | LV dysfunction only | RV & LV dysfunction | |
| N (%) | 711 (61) | 182 (15) | 61 (5) | 219 (19) | - |
| Birth weight, median (SD), kg | 2.93 (0.63) | 3.02 (0.61) | 3.00 (0.48) | 2.96 (0.56) | 0.489 |
| Gestational age, median (SD), weeks | 37.4 (2.33) | 37.5 (2.11) | 37.8 (1.80) | 37.6 (1.85) | 0.928 |
| Male n (%) | 410/709 (58) | 91/182 (50) | 36/61 (59) | 121/219 (55) | 0.275 |
| Inborn n (%) | 437/710 (62) | 122/181 (67) | 34/61 (56) | 159/219 (73) | 0.009 |
| Prenatal diagnosis n (%) | 534/708 (25) | 150/182 (82) | 44/61 (72) | 186/219 (85) | 0.007 |
| Left sided CDH n (%) | 599/710 (84) | 155/182 (85) | 50/59 (85) | 167/214 (78) | 0.145 |
| Major Cardiac anomaly n (%) | 49/711 (7) | 13 /180 (7) | 10/61 (16) | 20/219 (9) | 0.054 |
| Chromosomal anomaly n (%) | 57/710 (8) | 13/181 (7) | 4/61 (6) | 22/219 (10) | 0.685 |
| Other anomaly n (%) | 79/711 (11) | 20/180 (11) | 9 /61 (15) | 28/219 (13) | 0.778 |
| CDHSG Stage group | A/B n (%) | 335 (52) | 60 (37) | 19 (36) | <0.001 |
| | C/D n (%) | 307 (48) | 103 (63) | 33 (64) | |
| Liver in chest n (%) | 294/642 (46) | 92/163 (56) | 32/51 (63) | 105/161 (65) | <0.001 |
| Patch Repair n (%) | 345/645 (53) | 111/163 (68) | 35/51 (69) | 130/161 (81) | <0.001 |

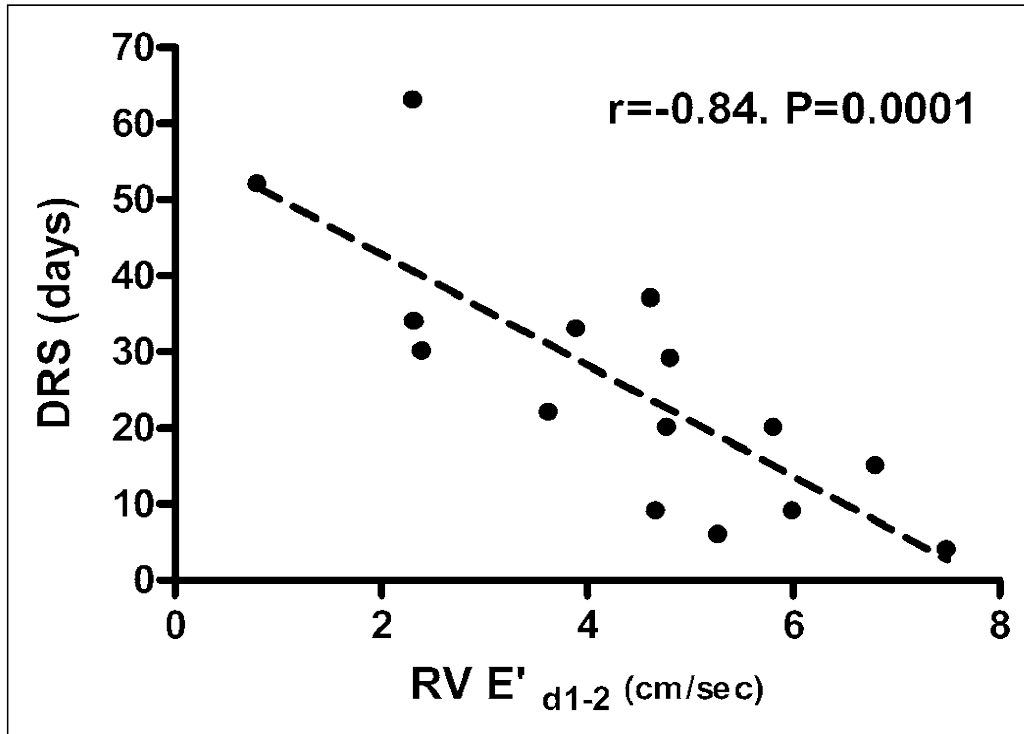
Mmmm, Tastes
like a combination
of Who Cares?
&
So What?





Right Ventricular Diastolic Function Measured by Tissue Doppler Imaging Predicts Early Outcome in Congenital Diaphragmatic Hernia

Florian Moenkemeyer, MD; Neil Patel, MD



CDH 2020 Houston

Ped Crit Care Med 2013

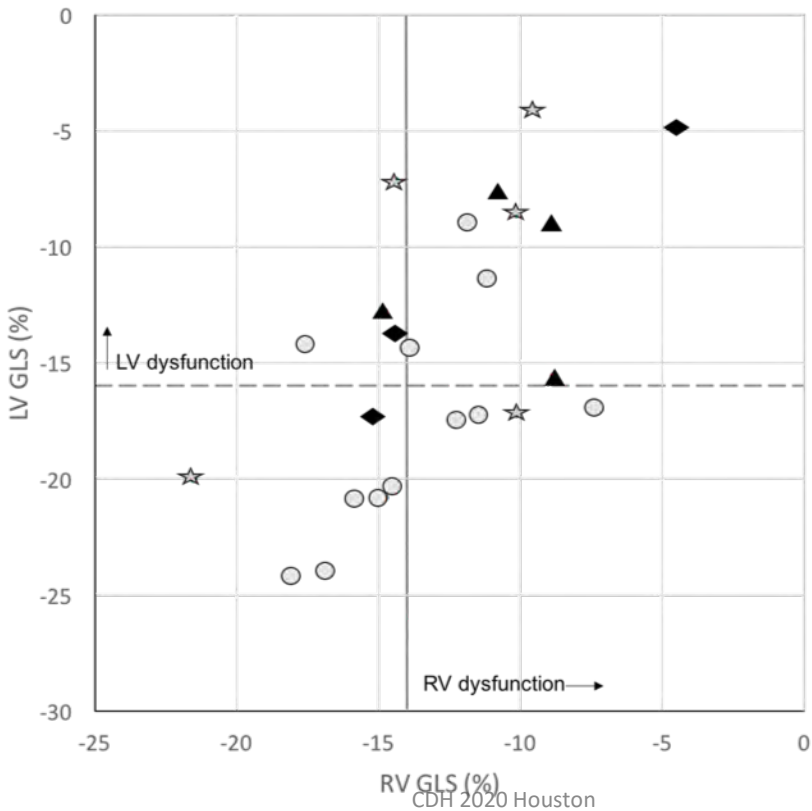
Ventricular Performance is Associated with Need for Extracorporeal Membrane Oxygenation in Newborns with Congenital Diaphragmatic Hernia

Gabriel Altit, MDCM, FRCPC, FAAP^{1,2,3}, Shazia Bhombal, MD, FAAP^{2,3}, Krisa Van Meurs, MD, FAAP^{2,3}, and Theresa A. Tacy, MD, FAAP^{1,3}

| | ECMO (n = 15) | Non-ECMO (n = 29) | <i>P</i> value |
|-------------|--------------------------|------------------------------|-----------------------|
| RV pGLS (%) | -5.2 (3.9) | -10.7 (5.0) | .001 |
| LV pGLS (%) | -9.1 (4.9) | -14.9 (5.3) | .002 |

Early Postnatal Ventricular Dysfunction Is Associated with Disease Severity in Patients with Congenital Diaphragmatic Hernia

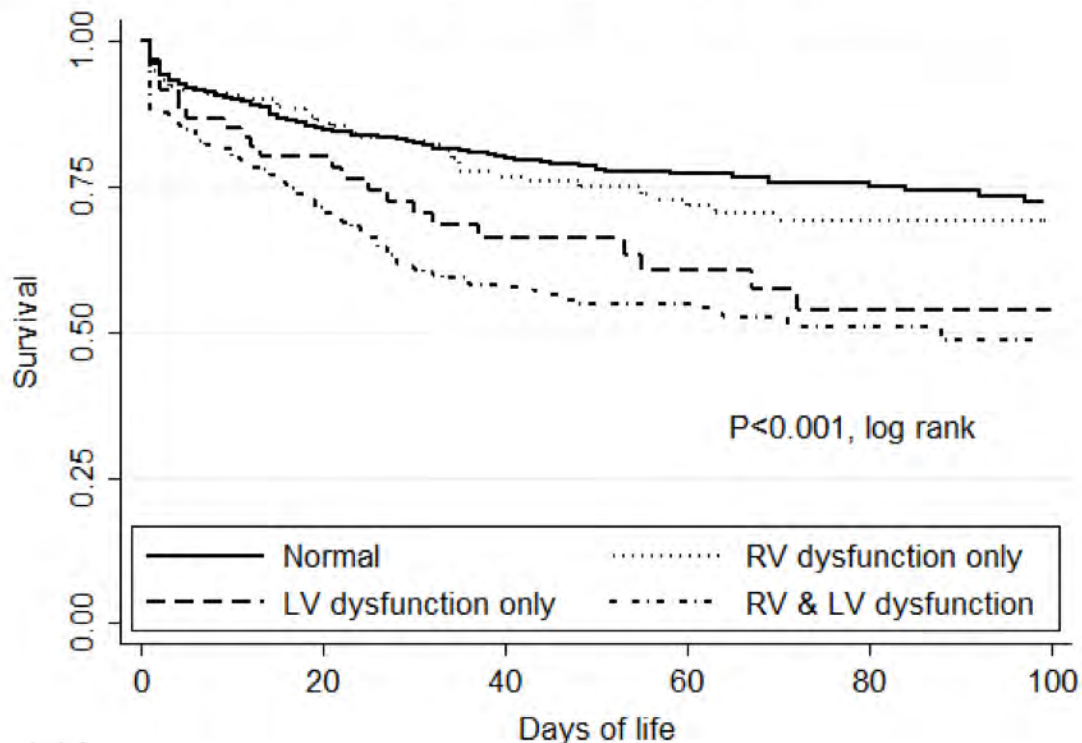
Neil Patel, MD¹, Anna Claudia Massolo, MD², Anshuman Paria, MBBS¹, Emily J. Stenhouse, MBChB³, Lindsey Hunter, MRCPCH⁴, Emma Finlay, BSE⁴, and Carl F. Davis, FRCS⁵



LV dysfunction significantly associated with ECMO and non-survival

Ventricular Dysfunction is a Critical Determinant of Mortality in Congenital Diaphragmatic Hernia

Neil Patel , Pamela A Lally , Florian Kipfmueller , Anna Claudia Massolo , Matias Luco , Krisa P Van Meurs , Kevin P Lally , Matthew T Harting , and , for the Congenital Diaphragmatic Hernia Study Group



Ventricular Dysfunction is a Critical Determinant of Mortality in Congenital Diaphragmatic Hernia

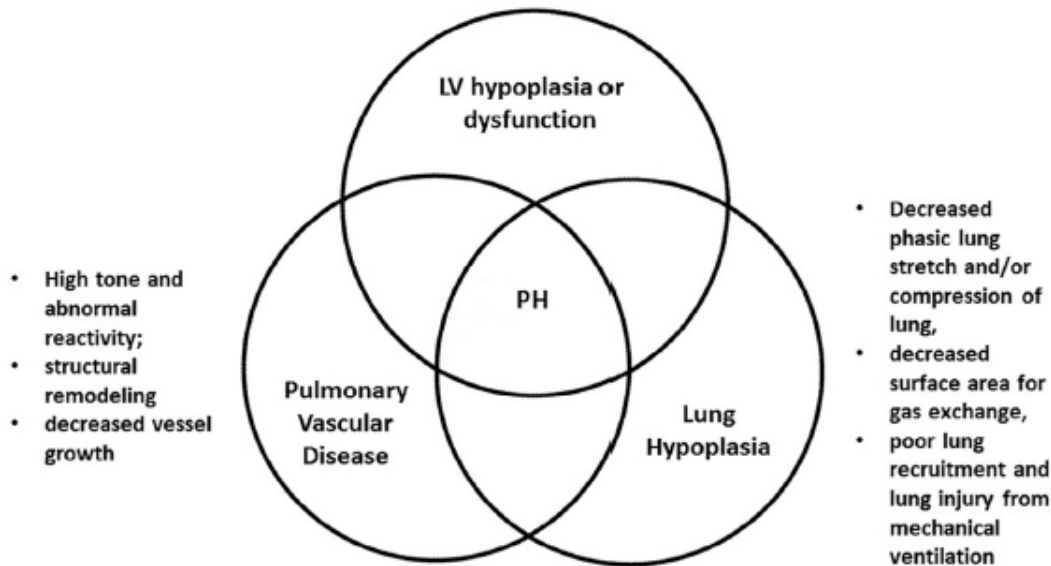
Neil Patel , Pamela A Lally , Florian Kipfmueller , Anna Claudia Massolo , Matias Luco , Krisa P Van Meurs , Kevin P Lally , Matthew T Harting , and , for the Congenital Diaphragmatic Hernia Study Group

| Variable | | Multivariate analysis | | | |
|---------------------|---------|-----------------------|------|--------|-------------|
| | | HR | SE | P | 95% CI |
| Birth weight <3kg | | 1.44 | 0.22 | 0.020 | 1.06 – 1.95 |
| Defect Stage C/D | | 3.37 | 0.92 | <0.001 | 1.97 – 5.77 |
| Liver in chest | | 1.63 | 0.34 | 0.018 | 1.09 – 2.46 |
| Cardiac Dysfunction | RV only | 1.02 | 0.23 | 0.92 | 0.66 – 1.58 |
| | LV only | 1.90 | 0.52 | 0.020 | 1.11 – 3.26 |
| | RV & LV | 1.59 | 0.29 | 0.011 | 1.11 – 2.27 |

The Left Ventricle in Congenital Diaphragmatic Hernia: Implications for the Management of Pulmonary Hypertension

John P. Kinsella, MD¹, Robin H. Steinhorn, MD², Mary P. Mullen, MD³, Rachel K. Hopper, MD⁴, Roberta L. Keller, MD⁵, D. Dunbar Ivy, MD⁶, Eric D. Austin, MD⁷, Usha S. Krishnan, MD⁸, Erika B. Rosenzweig, MD⁸, Jeffrey R. Fineman, MD⁹, Allen D. Everett, MD¹⁰, Brian D. Hanna, MD¹¹, Tilman Humpl, MD¹², J. Usha Raj, MD¹³, and Steven H. Abman, MD¹⁴, on behalf of the Pediatric Pulmonary Hypertension Network (PPHNet)

- Pulmonary Venous Hypertension
- Decreased cardiac output
- Pulmonary edema, worsened with PH drug therapy



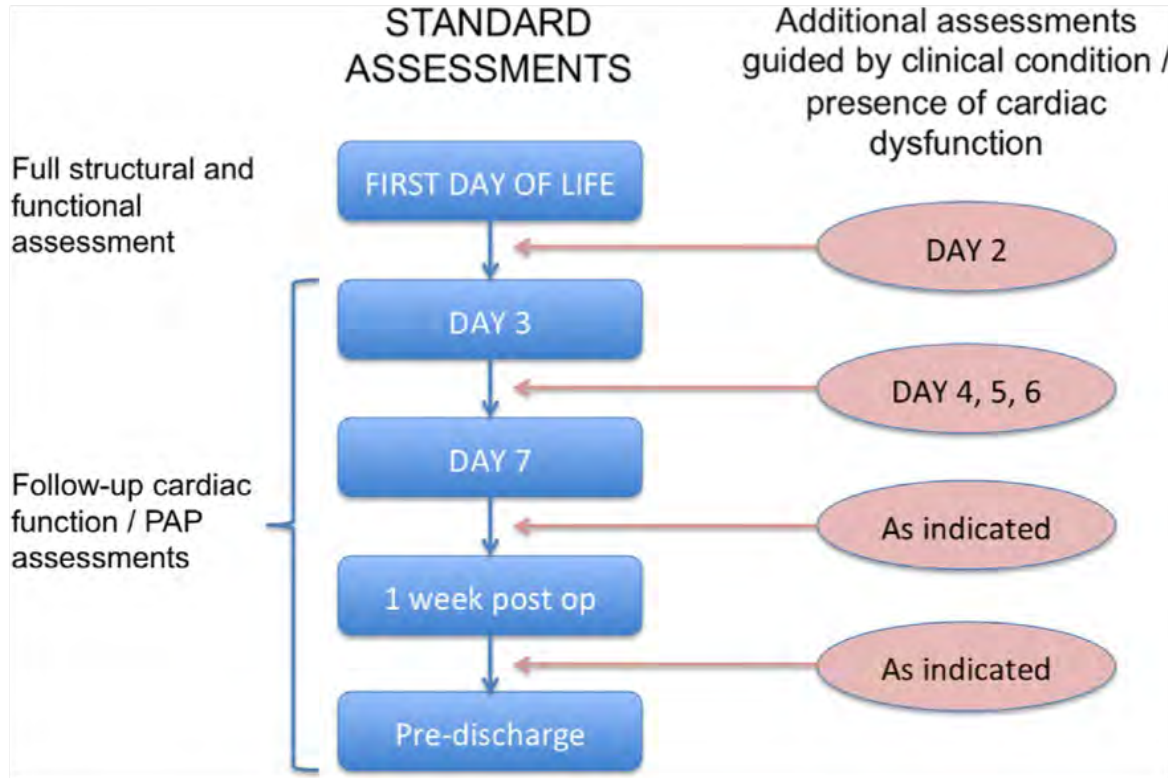


Fig. 3. Example protocol for timing of cardiac function assessment in CDH.

The Blind Men of Indostan and the Elephant in the Echo Lab

Lawrence G. Rudski, MDCM, FACC, FASE, and Jonathan Afilalo, MD, MSc, FRCPC, *Montreal, Quebec, Canada*

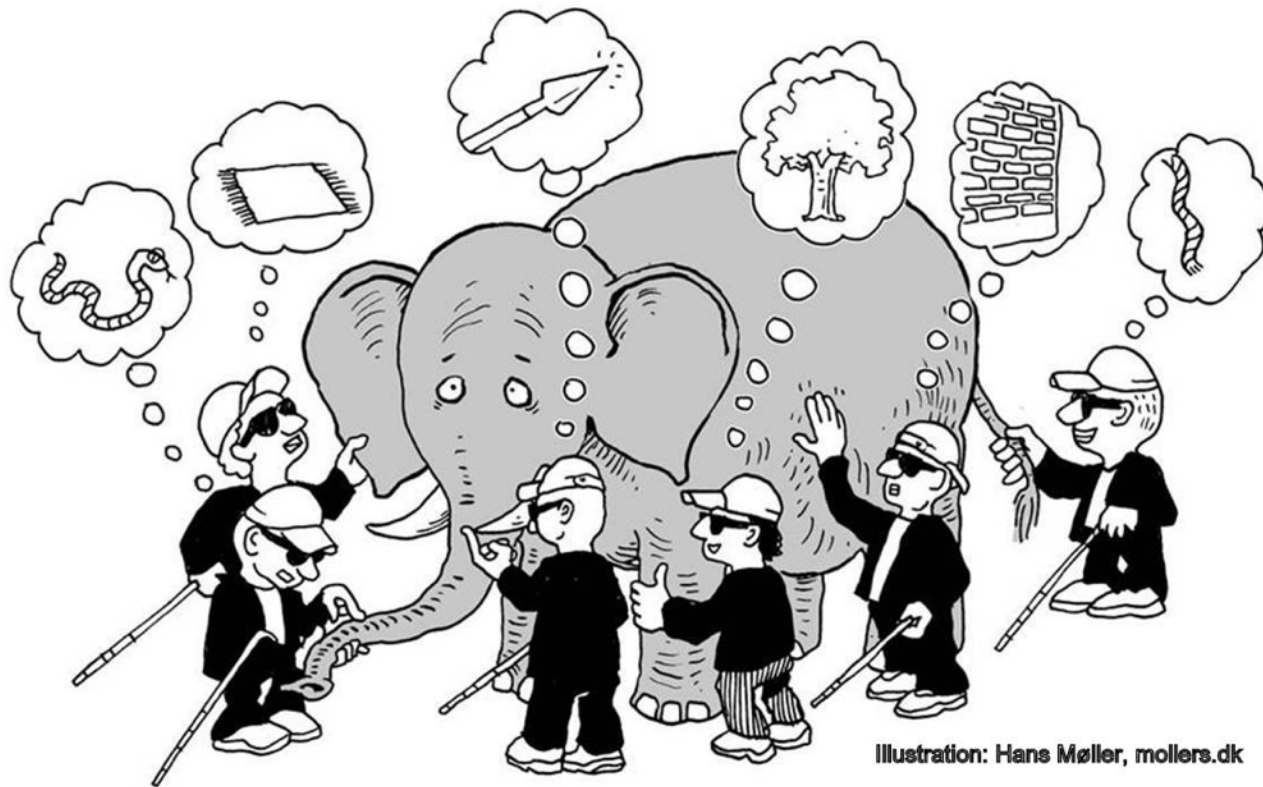
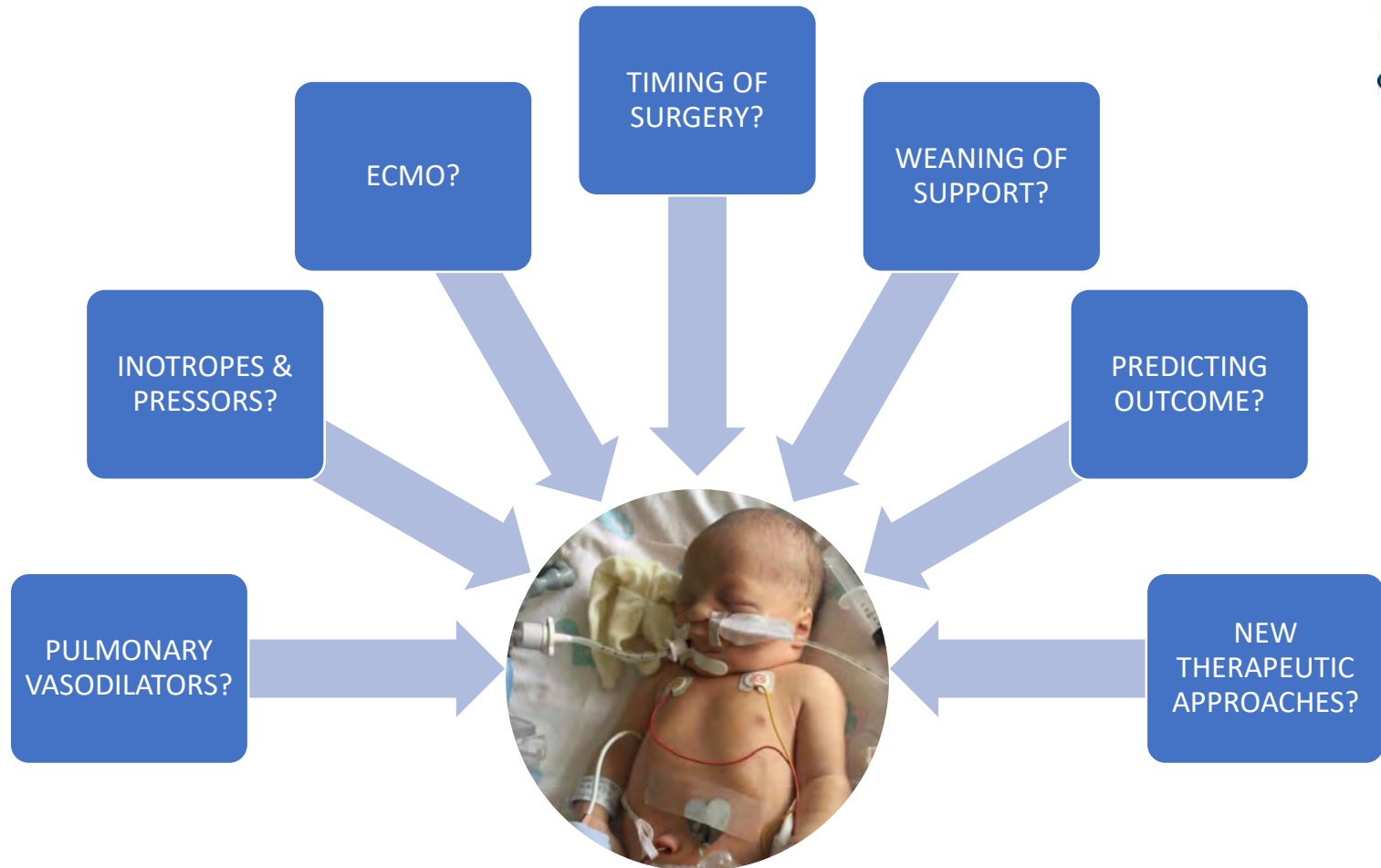
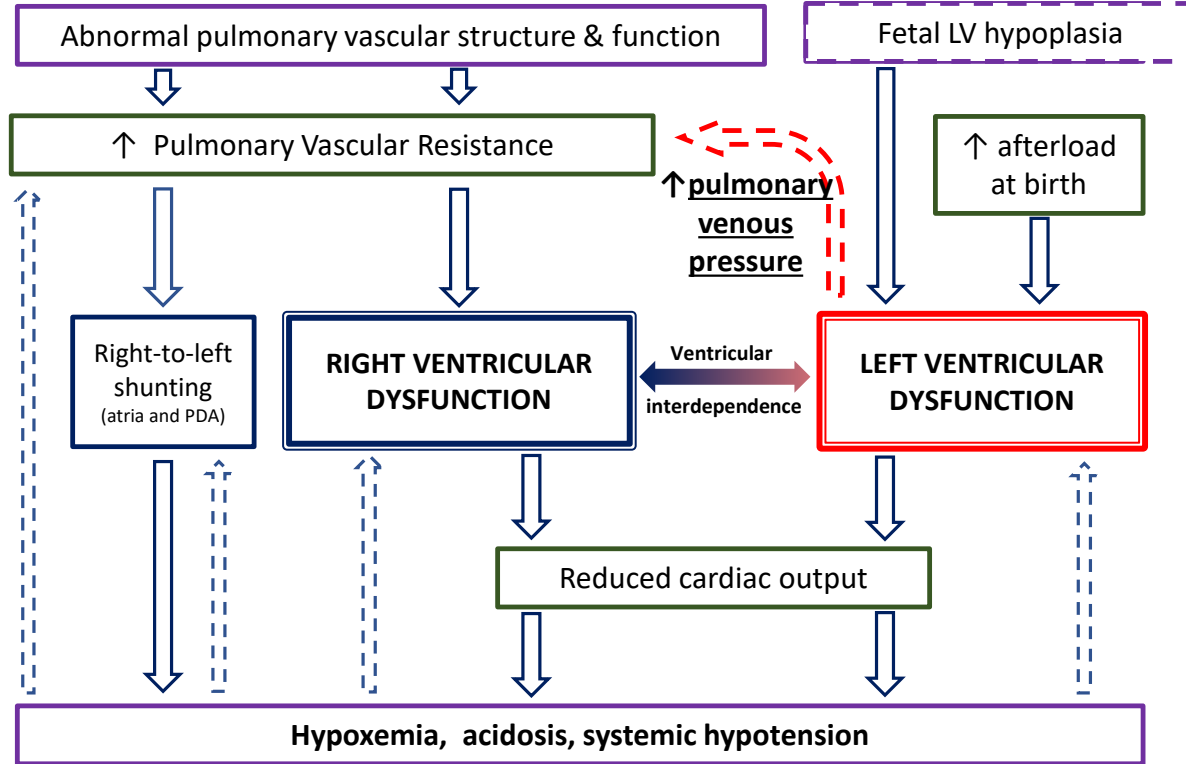


Illustration: Hans Møller, mollers.dk





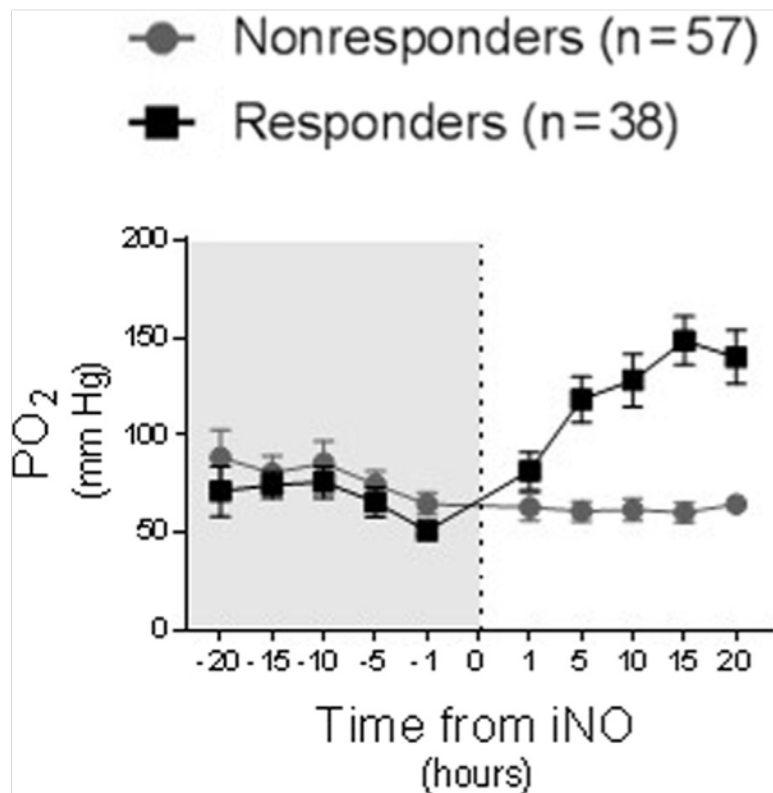
Implications of Atrial-Level Shunting by Echocardiography in Newborns with Congenital Diaphragmatic Hernia

Melissa Wehrmann, MD¹, Sonali S. Patel, MD, PhD¹, Caitlin Haxel, MD^{1,2}, Courtney Cassidy, RDCS¹, Lisa Howley, MD^{1,3}, Bettina Cuneo, MD¹, Jason Gien, MD⁴, and John P. Kinsella, MD⁴

Table II. Characteristics, outcomes, and echocardiographic measurements grouped by atrial-level shunt direction

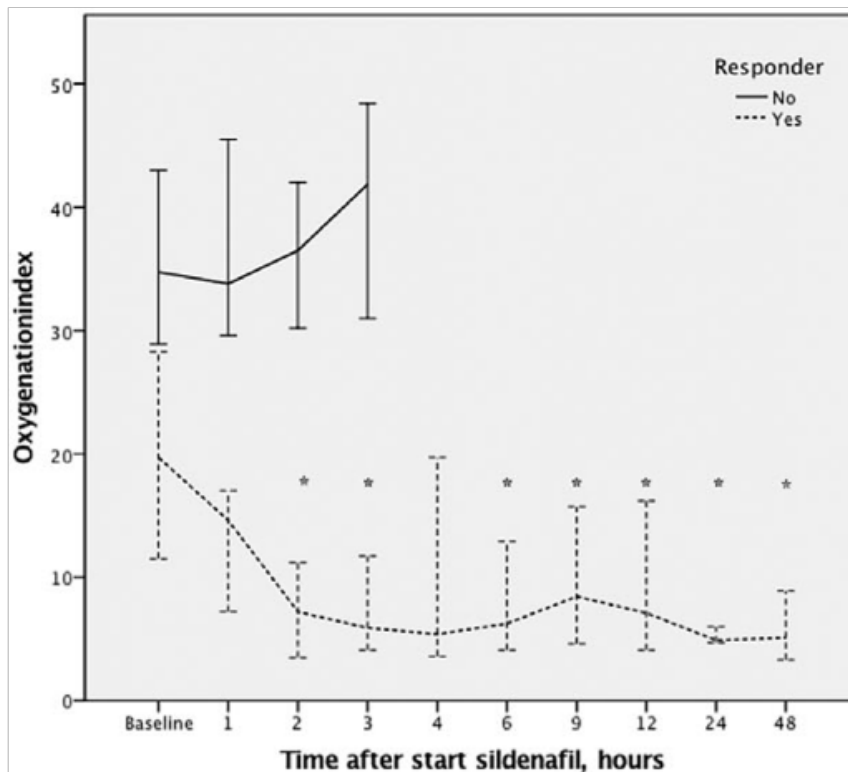
| Variables | Right-to-left | | Left-to-right | | P value |
|---|---------------|--------------|---------------|--------------|---------|
| | n | Value | n | Value | |
| Characteristics and outcomes | | | | | |
| Percent predicted lung volume, %, mean ± SD | 7 | 14.71 ± 8.30 | 24 | 24.63 ± 8.23 | .0091 |
| Liver up, n (%) | 9 | 9 (100) | 42 | 23 (54.8) | .0109 |
| ECMO during hospitalization, n (%) | 9 | 4 (44.4) | 42 | 9 (21.4) | .1505 |
| Survival to discharge, n (%) | 9 | 6 (66.7) | 42 | 38 (90.5) | .0596 |
| Echocardiographic measurements | | | | | |
| LV 2D area (diastole) z-score, mean ± SD | 9 | -1.89 ± 0.71 | 37 | -1.38 ± 0.90 | .1179 |
| LV 2D area (systole) z-score, mean ± SD | 9 | -1.42 ± 0.95 | 37 | -0.49 ± 1.24 | .0415 |
| LV myocardial performance index, mean ± SD | 5 | 0.18 ± 0.08 | 36 | 0.50 ± 0.66 | .0088 |
| RV myocardial performance index, mean ± SD | 4 | 0.49 ± 0.03 | 28 | 0.54 ± 0.24 | .3719 |
| Ductus arteriosus direction, n (%) [*] | 9 | | 39 | | .0002 |
| Right-to-left | | 6 (66.7) | | 3 (7.7) | |
| Left-to-right | | 0 | | 5 (12.8) | |
| Bidirectional | | 3 (33.3) | | 31 (79.5) | |

Inhaled Nitric Oxide Is Associated with Improved Oxygenation in a Subpopulation of Infants with Congenital Diaphragmatic Hernia and Pulmonary Hypertension



Continuous intravenous sildenafil as an early treatment in neonates with congenital diaphragmatic hernia

Florian Kipfmueller MD¹  | Lukas Schroeder MD¹ | Christoph Berg MD² |
Katrin Heindel MD¹ | Peter Bartmann MD, PhD¹ | Andreas Mueller MD¹



15 non-
responders
11 responders

Inhaled Nitric Oxide Is Associated with Improved Oxygenation in a Subpopulation of Infants with Congenital Diaphragmatic Hernia and Pulmonary Hypertension

Table I. Characteristics of initial responders and nonresponders to iNO therapy

| Patient characteristics | Nonresponder to iNO therapy (n = 57) | Responder to iNO therapy (n = 38) | P value |
|---|--------------------------------------|-----------------------------------|---------|
| Male sex (n, %) | 28 (49%) | 23 (61%) | .30 |
| Gestational age (wk) | 38.0 ± 0.2 | 38.4 ± 0.2 | .43 |
| Birthweight (kg) | 3.2 ± 0.1 | 3.2 ± 0.1 | .57 |
| LHR | 0.97 ± 0.05 | 1.01 ± 0.04 | .07 |
| LHR (observed to expected lung to head ratio) | 0.37 ± 0.02 | 0.34 ± 0.02 | .59 |
| Liver up position CDH (n, %) | 37 (65%) | 25 (66%) | >.99 |
| Right sided CDH (n, %) | 10 (18%) | 2 (7%) | .32 |
| PaO ₂ at initiation (mm Hg) | 65 ± 6 | 51 ± 3 | .27 |
| FiO ₂ at initiation (%) | 76 ± 4 | 78 ± 4 | .71 |
| P/F at initiation (mm Hg) | 121 ± 16 | 82 ± 10 | .45 |
| A-a gradient at initiation (mm Hg) | 397 ± 28 | 422 ± 30 | .77 |
| pH at initiation | 7.18 ± 0.02 | 7.20 ± 0.02 | .63 |
| All right to left shunting on echo (n, %) | 19 (37%) (n = 52) | 8 (22%) (n = 37) | .16 |
| Bowing ventricular septum (n, %) | 50 (56%) | 15 (43%) | .14 |
| LV dysfunction (n, %) | 14 (27%) (n = 52) | 3 (8%) | .03 |

Use of Milrinone to Treat Cardiac Dysfunction in Infants with Pulmonary Hypertension Secondary to Congenital Diaphragmatic Hernia:

| | | Duration of milrinone therapy | | |
|---|---------------|-------------------------------|--------------|----------------|
| | | pre | 12–24 h post | 48–72 h post |
| PDA flow velocity, m/s | left to right | 0.8 (1.1) | 0.8 (0.4) | 0.5 (0.13) |
| | right to left | 1.9 (0.6) | 1.3 (0.1) | 1.1 (0.3) |
| FiO ₂ | | 0.55 (0.19) | 0.47 (0.25) | 0.47 (0.43) |
| Mean airway pressure, cm H ₂ O | | 11.8 (4.1) | 10.3 (5.8) | 8.6 (1.7) |
| OI | | 10.6 (5.6) | 7.9 (6.2) * | 5.1 (2.6)*, ** |
| Mean BP, mm Hg | | 52.7 (4.3) | 53.7 (11.5) | 51 (7.3) |
| Systolic BP, mm Hg | | 72.6 (6.3) | 75 (20.7) | 67 (9.9) |
| Diastolic BP, mm Hg | | 42.8 (4.2) | 43 (6.9) | 43 (6.3) |

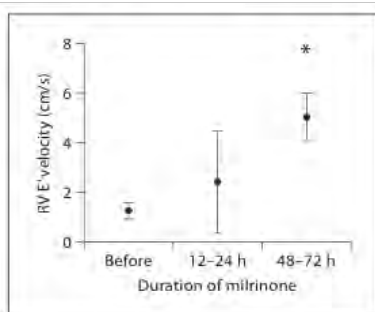


Fig. 1. Early diastolic velocities (E') in the RV before and during milrinone therapy. Circles represent means, bars represent 95% CI. * p < 0.05.

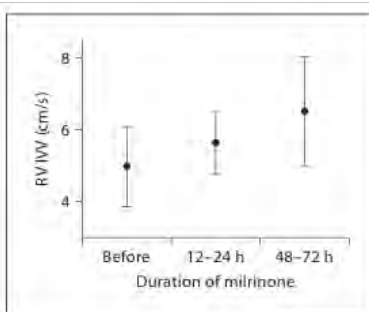


Fig. 2. Isovolumic contraction velocities (IVV) in the RV before and during milrinone therapy. Circles represent means, bars represent 95% CI.

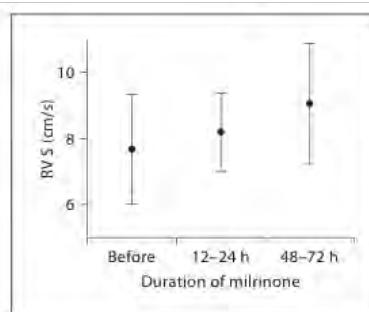
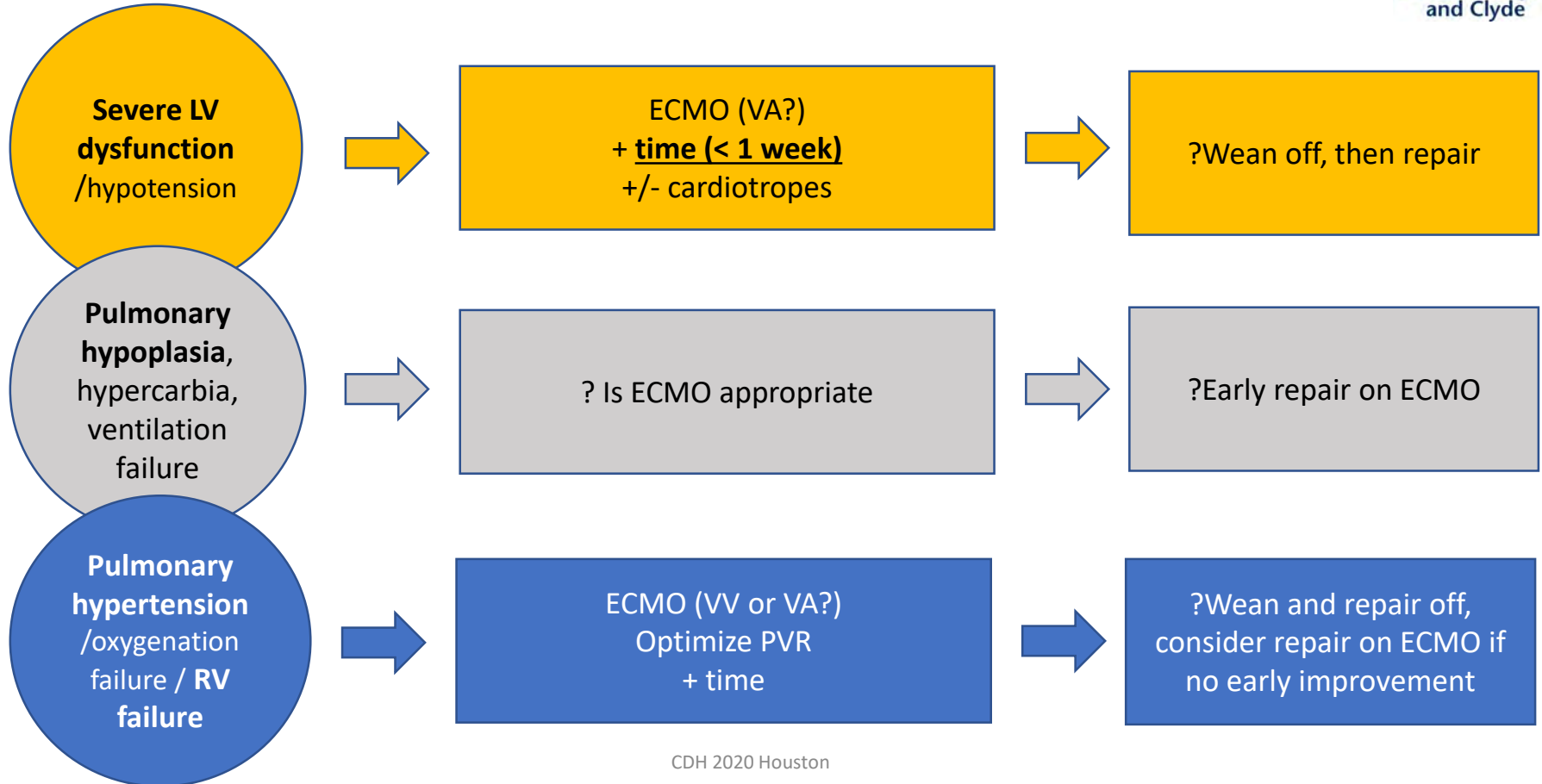
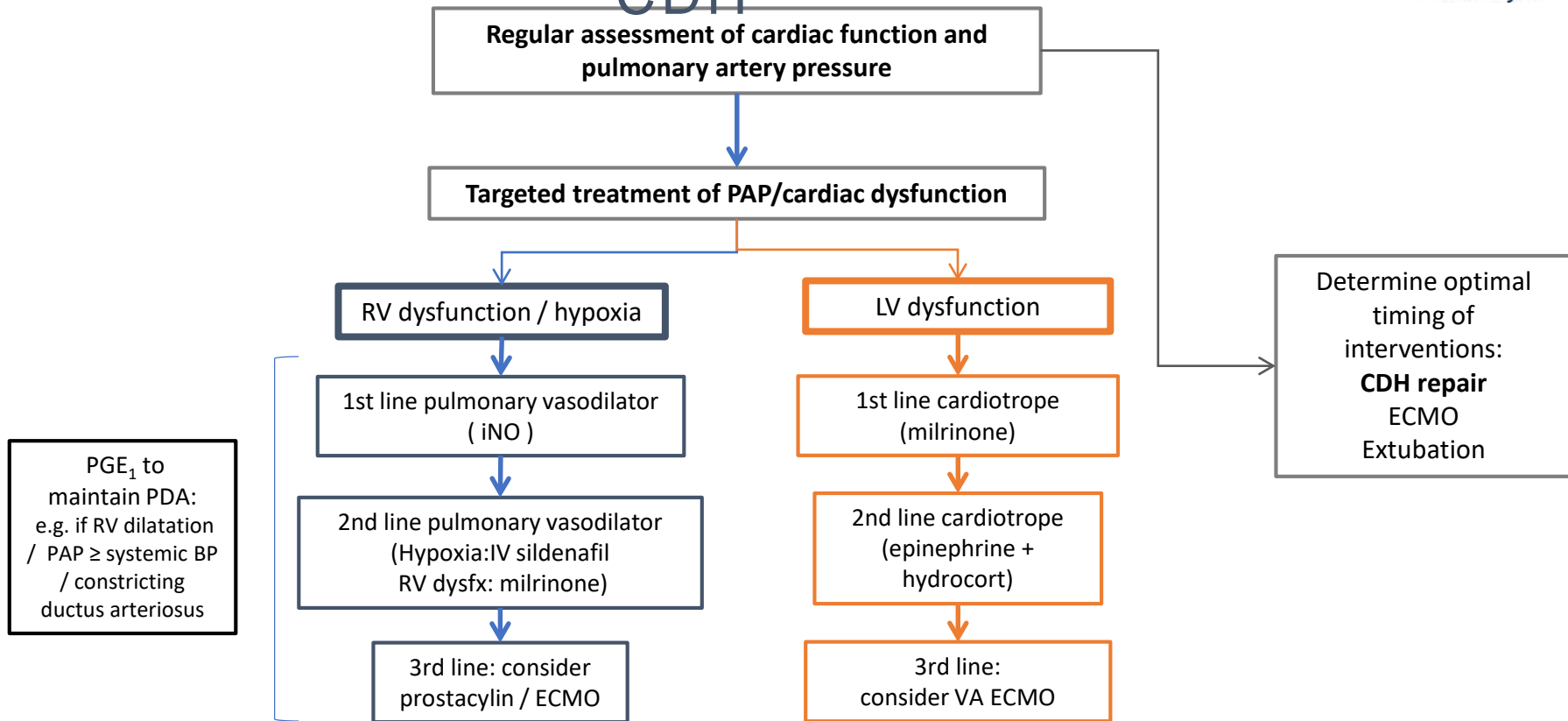


Fig. 3. Systolic ejection velocities (S) in the RV before and during milrinone therapy. Circles represent means, bars represent 95% CI.

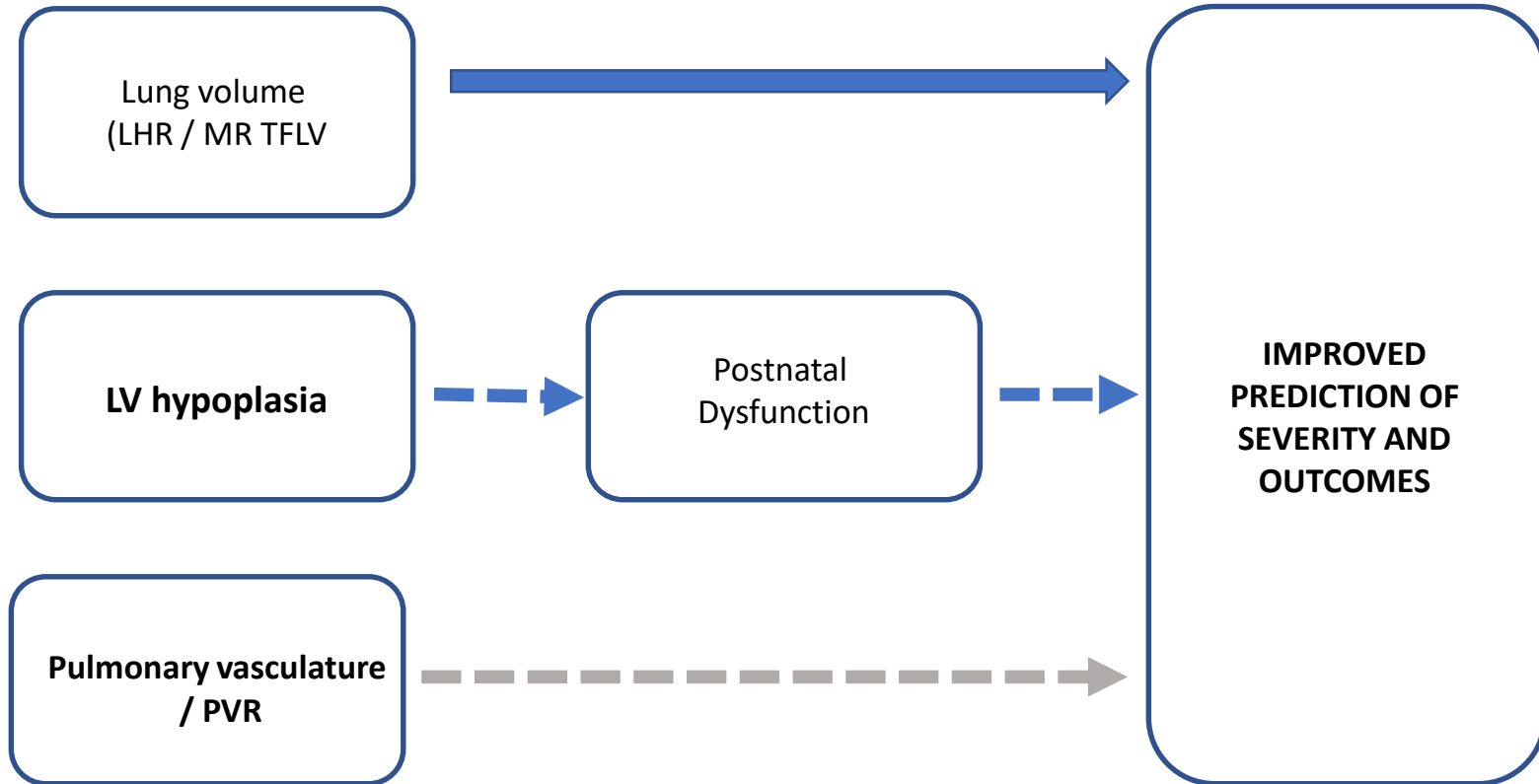
Informing ECMO strategy:



Targeted therapy of PH and cardiac function in CDH



? Improved pre-natal prognostication



Initiating resuscitation before umbilical cord clamping in infants with congenital diaphragmatic hernia: a pilot feasibility trial

Table 3 Physiological outcomes

| | Trial participants (n=19) | Historical controls (n=19) | P value |
|--|---------------------------|----------------------------|---------|
| Apgar score at 1 min, median (IQR) | 5 (3–7) | 7 (3–8) | 0.51 |
| Apgar score at 5 min, median (IQR) | 8 (5–8) | 8 (5–9) | 0.72 |
| First Haemoglobin, g/dL; mean (SD) | 17.6 (1.3) | 16.3 (1.9) | 0.02 |
| Mean blood pressure 1 hour after birth; mean (SD)* | 51.1 (8.5) | 44.3 (6.3) | 0.008 |
| First blood gas after birth* | | | |
| pH, mean (SD) | 7.02 (0.15) | 7.03 (0.13) | 0.74 |
| CO ₂ , mean (SD) | 90 (26) | 88 (25) | 0.82 |
| Base deficit, mean (SD) | 8.9 (3.3) | 9.8 (3.8) | 0.51 |
| Oxygenation index with first blood gas, median (IQR) | 17.5 (12.8–25.5) | 16.3 (12.2–22.8) | 0.74 |
| Vasopressors (first 48 hours), n (%) | 13 (68) | 16 (84) | 0.45 |
| iNO (first 48 hours), n (%) | 9 (47) | 11 (58) | 0.52 |
| ECMO (first 7 days), n (%) | 7 (37) | 4 (21) | 0.48 |
| Mortality (first 7 days), n (%) | 0 | 1 (5) | >0.99 |



Thanks to

Staff and patients of the:

Royal Hospital for Children, Glasgow
Royal Children's Hospital Melbourne

Claudia Massolo

Florian Moenkemeyer

Florian Kipfmueller

Lindsey Hunter

Carl Davis, Morag Liddell

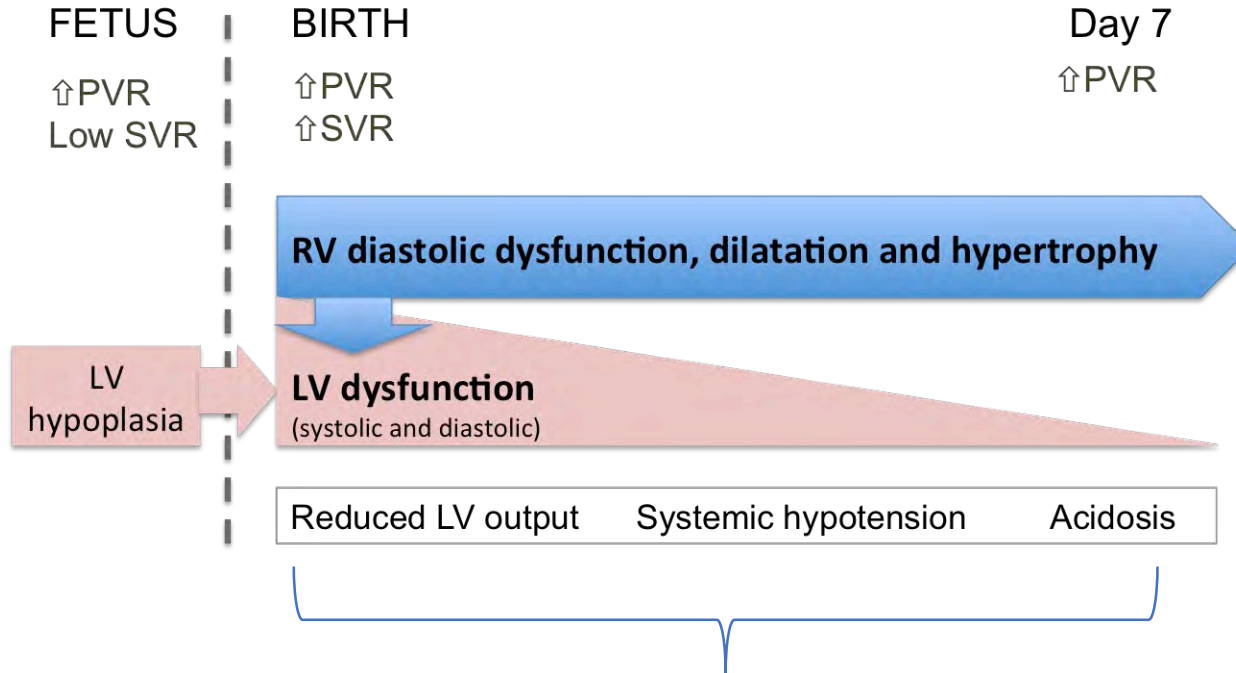
Kevin Lally, Pam Lally, Matt Harting

CDH Study Group and Registry

CDH Euroconsortium

CDH UK





Associated with outcomes:

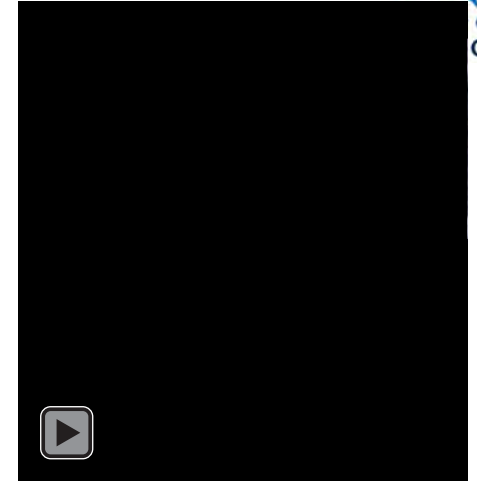
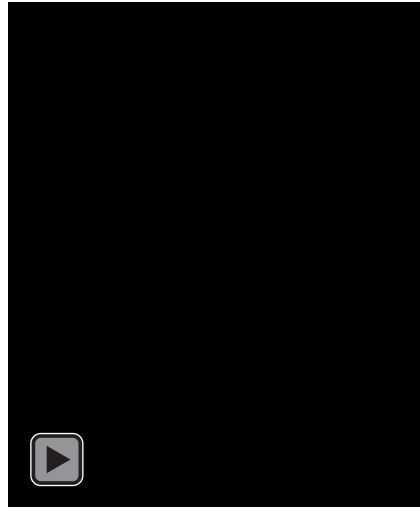
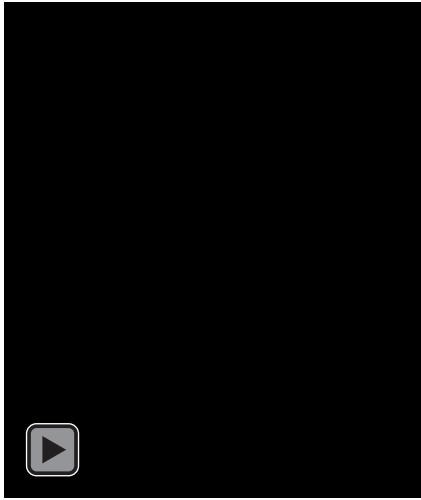
- Duration ventilation
- Length of stay
- Survival
- ECMO

Day 1

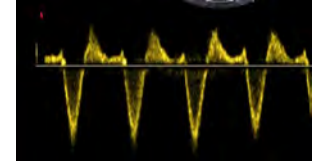
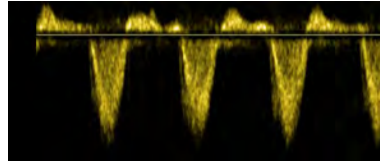
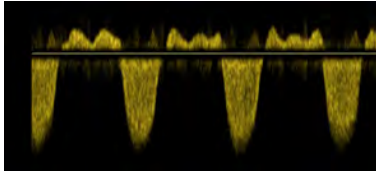
Day 3

Day 5

4
chamber
view



PDA flow



STE
Strain

RV GLS -
12%
LV GLS -
%

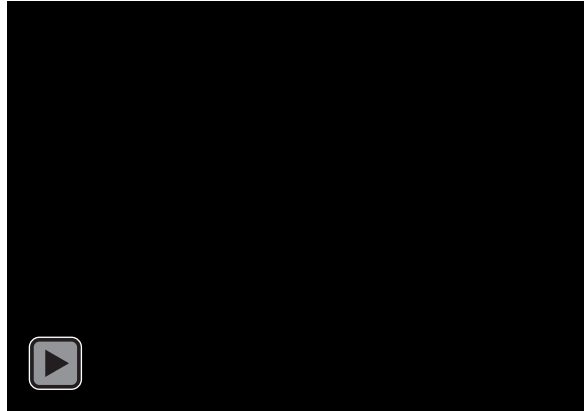
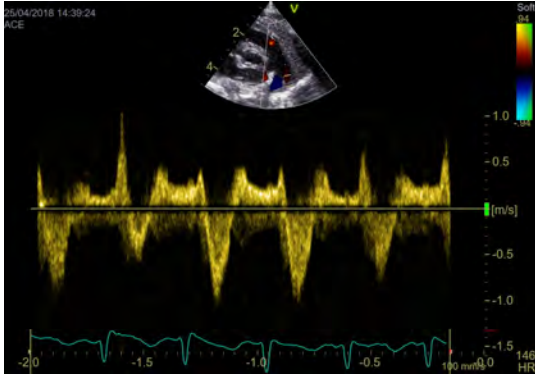
RV GLS -
12%
LV GLS -
%

RV GLS -
16%
LV GLS -20
%

Milrinone and epinephrine

IV sildenafil

Cardiac function and timing of repair?

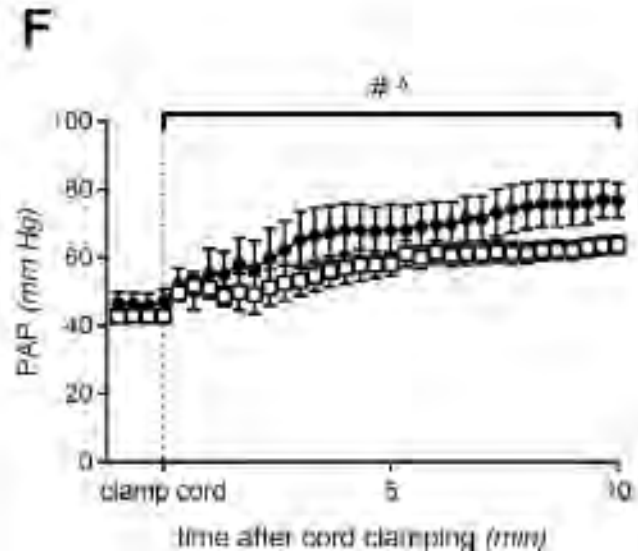
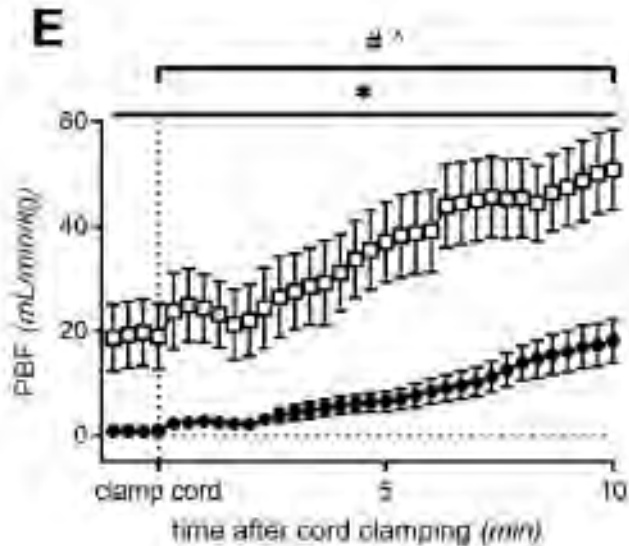


- 38/40. 3kg. L CDH. Day 1 of life
- Conventional ventilation: 22/5, FiO₂ 0.35. Sats 96/97%. BP 45/32 (36)
- Cardiac function improved spontaneously by day 3 of life
- Primary repair, day 3. Stage “A” defect

New therapies in CDH: Physiological based cord clamping?

Physiologically based cord clamping improves cardiopulmonary haemodynamics in lambs with a diaphragmatic hernia

Aidan J Kashyap,^{1,2} Ryan J Hodges,^{1,3} Marta Thio,^{4,5} Karyn A Rodgers,^{1,2}
Ben J Amberg,^{1,2} Erin V McGillick,^{1,2} Stuart B Hooper,^{2,6} Kelly J Crossley,^{1,2}
Philip L J DeKoninck^{6,7}



Segmental longitudinal strain in the RV and LV, in CDH and controls

