The Heart in CDH pathophysiology
A brief history

Neil Patel

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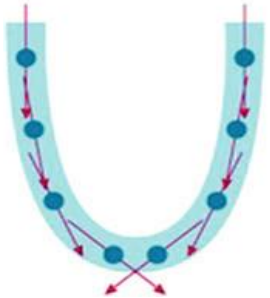
Clinical Innovation Director

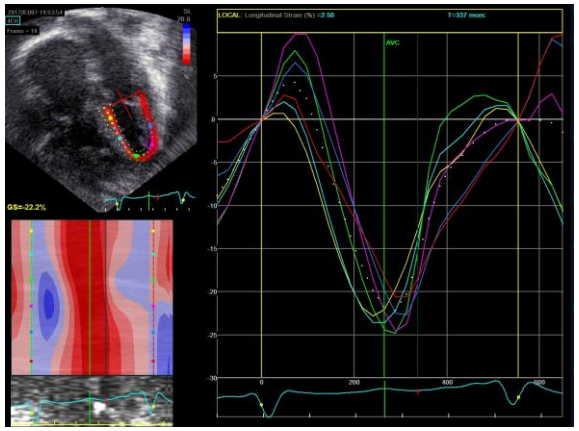
Children's Healthcare Innovation. From Glasgow to the world.

CDH 2024 Congenital Diaphragmatic Hernia International Symposium
Lille, France

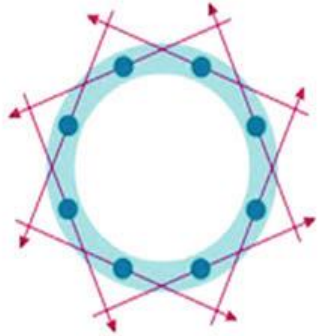
Speckle-tracking echo: deformation analysis

Longitudinal strain (LS)

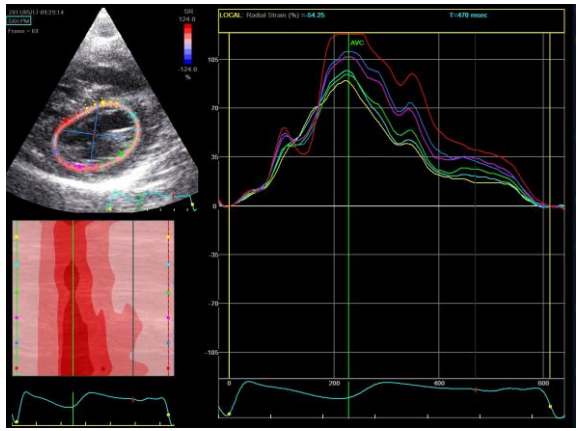




Circumferential strain (CS)



Radial strain(RS)



Early LV dysfunction demonstrated by speckle tracking echocardiography

Diminished Cardiac Performance and Left Ventricular Dimensions in Neonates with Congenital Diaphragmatic Hernia

Gabriel Altit[1] · Shazia Bhombal[2] · Krisa Van Meurs[2,3] · Theresa A. Tacy[4]

Table 3 Comparison of deformation measures of ventricular function in study and control patients

Deformation measurements			
	CDH ($n=44$)	Controls ($n=18$)	p value
RV-GLS (%)	−9.0 (5.3)	−19.5 (1.4)	0.0001*
RV GLSR (1/s)	−0.98 (0.41)	−1.53 (0.17)	0.0001*
RV EDSR (1/s)	1.12 (0.58)	1.93 (0.63)	0.0001*
Time to RV EDSR (ms)	332.6 (72.0)	328.9 (46.1)	0.87
LV GLS (%)	−13.2 (5.8)	−20.8 (3.5)	0.0001*
LV GLSR (1/s)	−1.35 (0.57)	−1.80 (0.38)	0.004*
LV EDSR (1/s)	1.3 (0.7)	2.1 (1.0)	0.001*
Time to LV EDSR (ms)	291.7 (111.8)	302.8 (59.8)	0.71

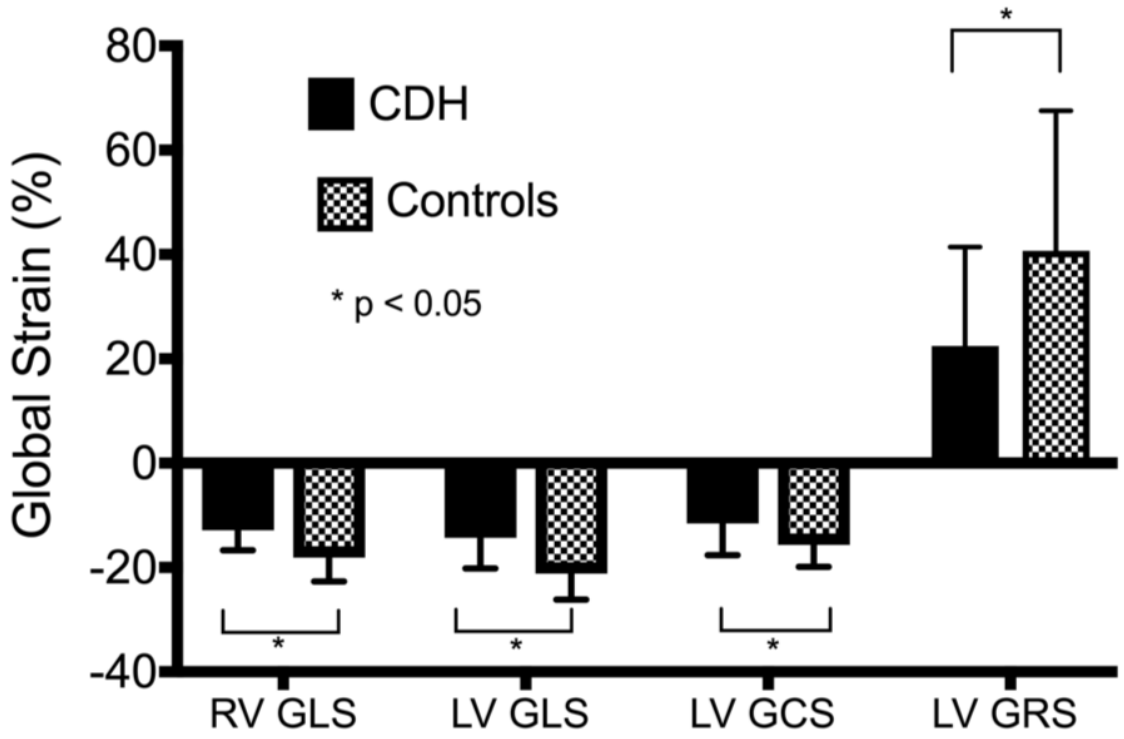
EDSR early diastolic strain rate, *GLS* global longitudinal strain, *GLSR* global longitudinal strain rate, *LV* left ventricle, *RV* right ventricle

All values are expressed as mean (standard deviation), *p value < 0.05

Ped Card 2018

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

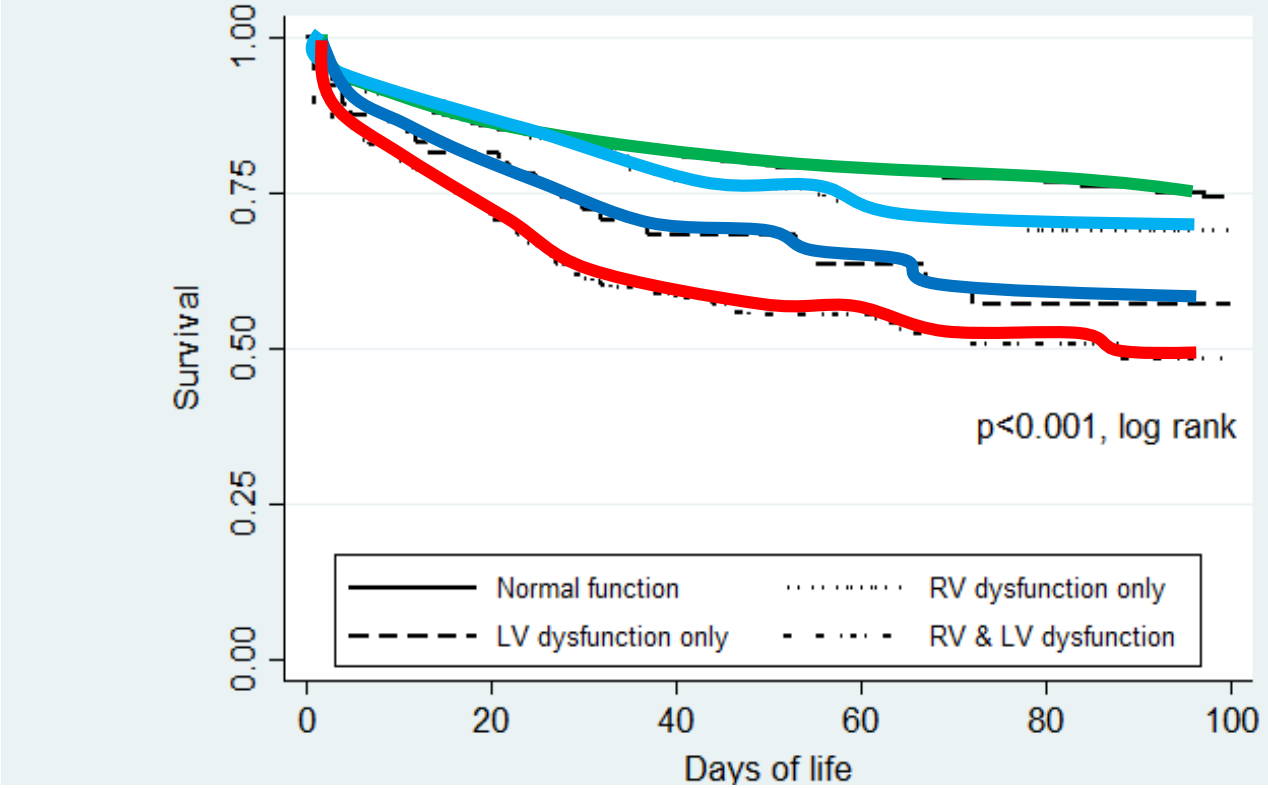
Neil Patel, MD[1], Anna Claudia Massolo, MD[2], Anshuman Paria, MBBS[1], Emily J. Stenhouse, MBChB[3], Lindsey Hunter, MRCPCH[4], Emma Finlay, BSE[4], and Carl F. Davis, FRCS[5]



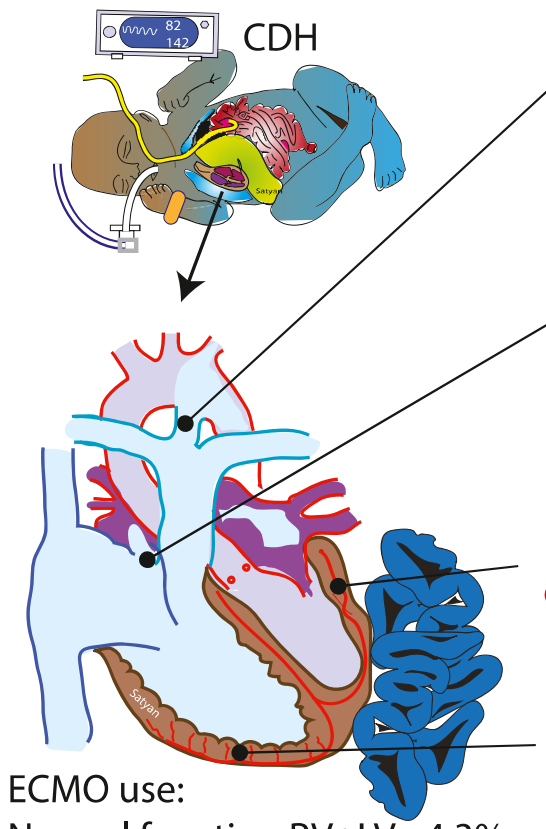
J Peds 2018

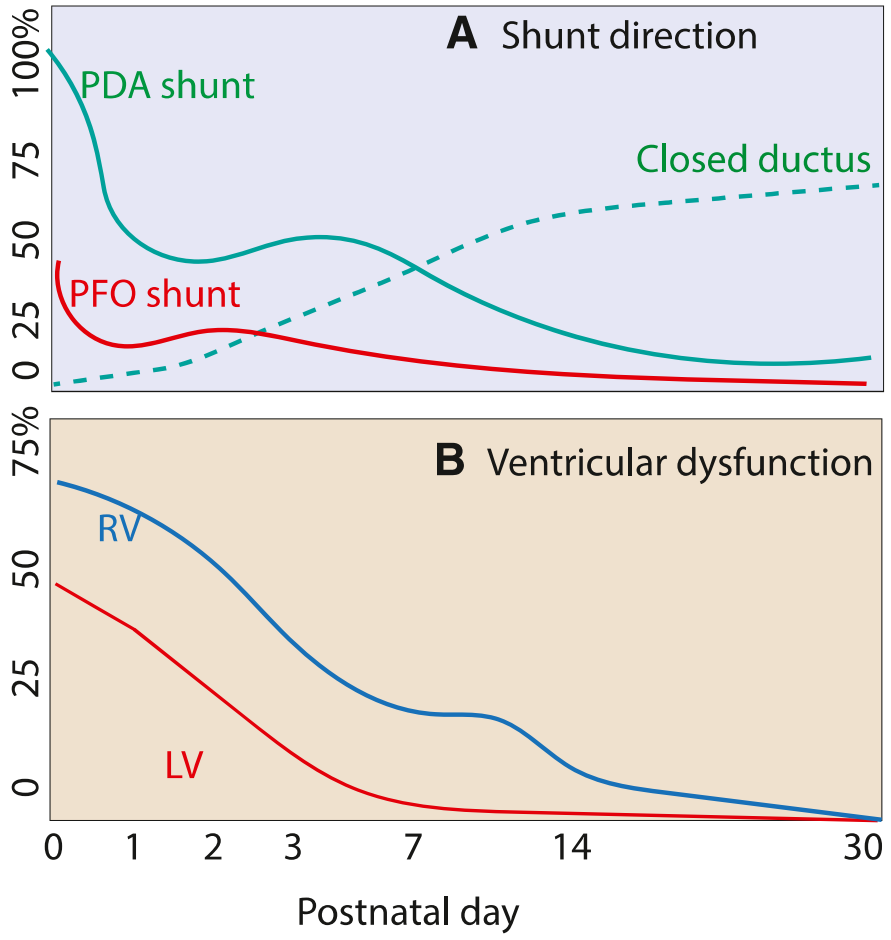
Ventricular Dysfunction Is a Critical Determinant of Mortality in Congenital Diaphragmatic Hernia

Neil Patel[1], Pamela A. Lally[2], Florian Kipfmueller[3], Anna Claudia Massolo[4], Matias Luco[5], Krisa P. Van Meurs[6], Kevin P. Lally[2], and Matthew T. Harting[2]; for the Congenital Diaphragmatic Hernia Study Group



Am J Resp Crit Care Med 2019

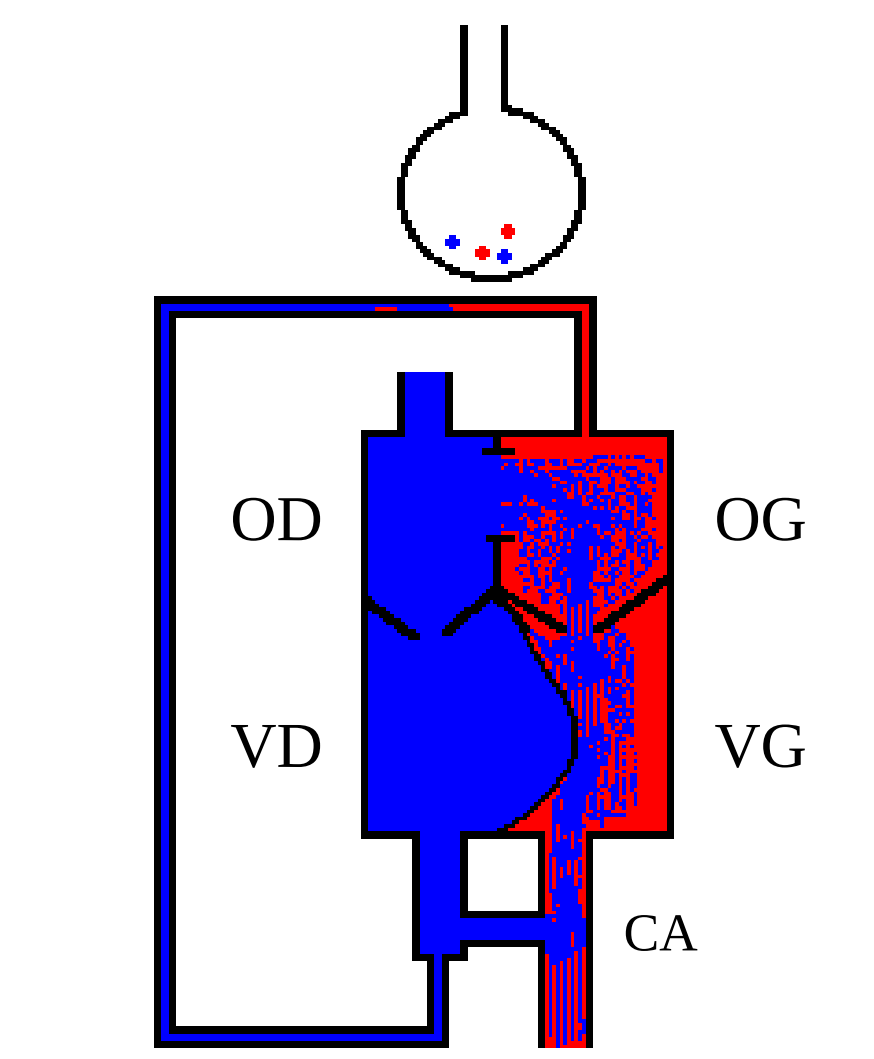




ECMO use:
Normal function RV+LV - 4.3%
One dysfunctional ventricle - 23.5%
Biventricular dysfunction - 90.9%

Data from from Le et al J Pediatr 2023
Lakshminrusimha & Fraga, J Pediatr 2023

Obstructive shock

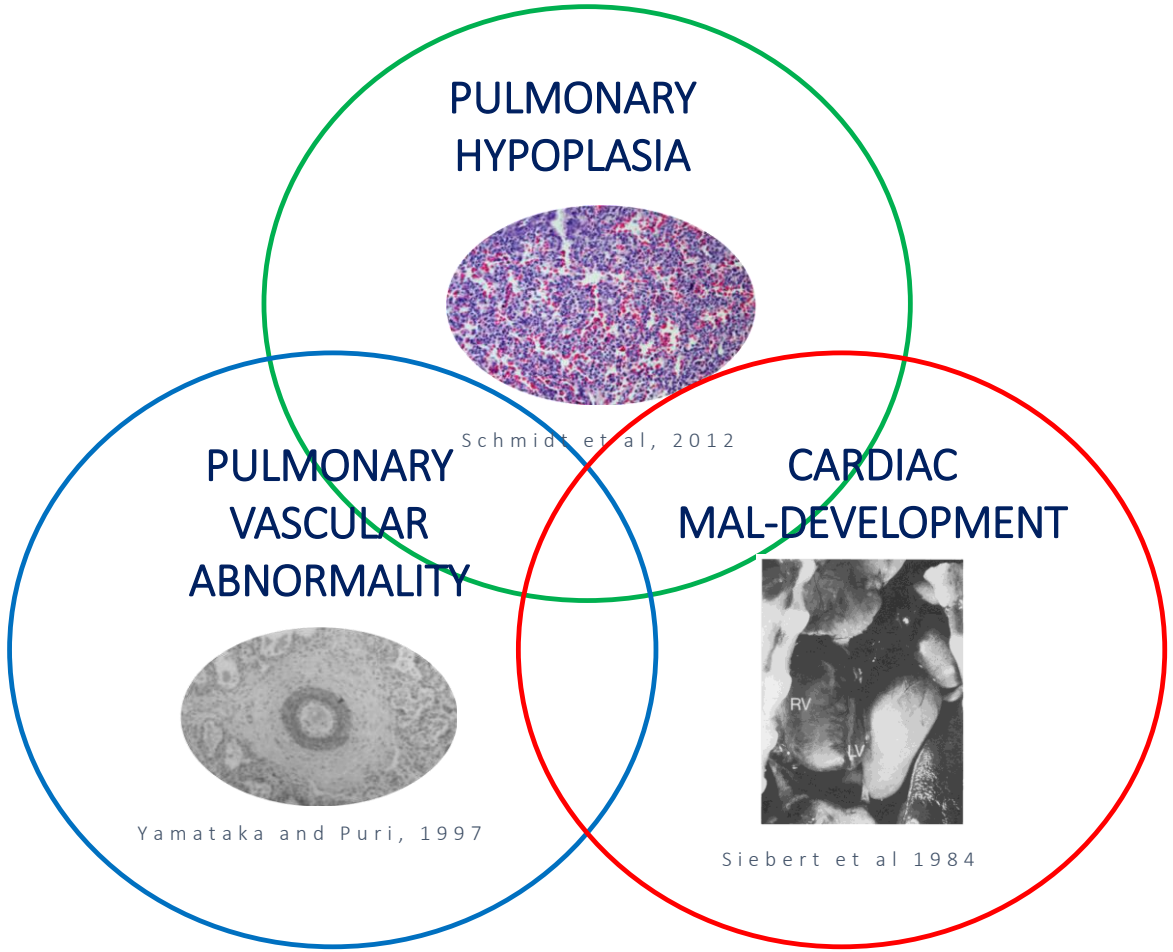


- ⇓ In preductal SpO2
- + Symptoms of shock
- + Symptoms of hypoxia

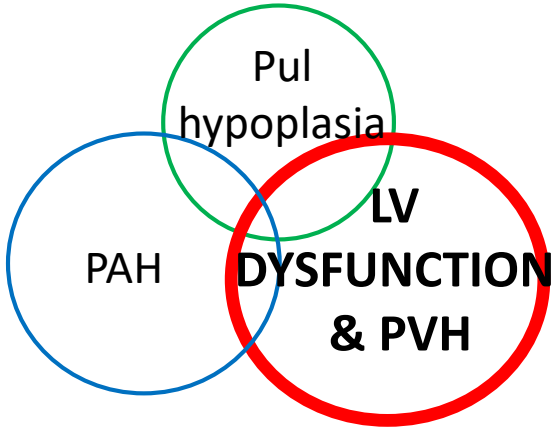
2 mechanisms :

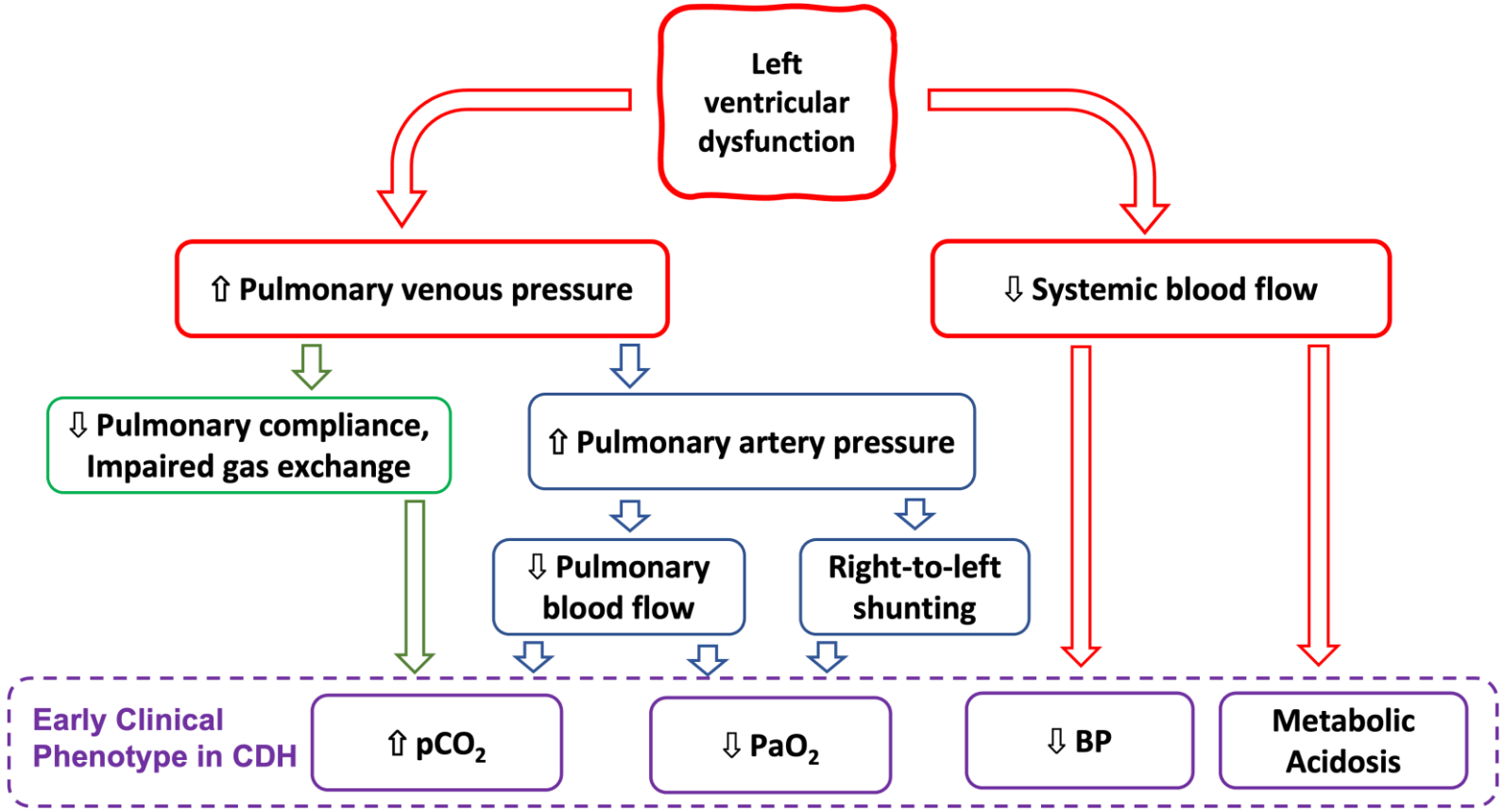
1. ⇓ LAP : ⇓ Q pulm
2. ⇑ RAP : RV failure

"*Cardiac era*": an updated model of CDH pathophysiology



Early LV dysfunction as a key disease mediator





A paradigm shift: from "one-size-fits-all" to pathophysiology-based therapy

Define PH phenotype

Pre-capillary PAH
RV dysfunction / hypoxia

⇩ PVR

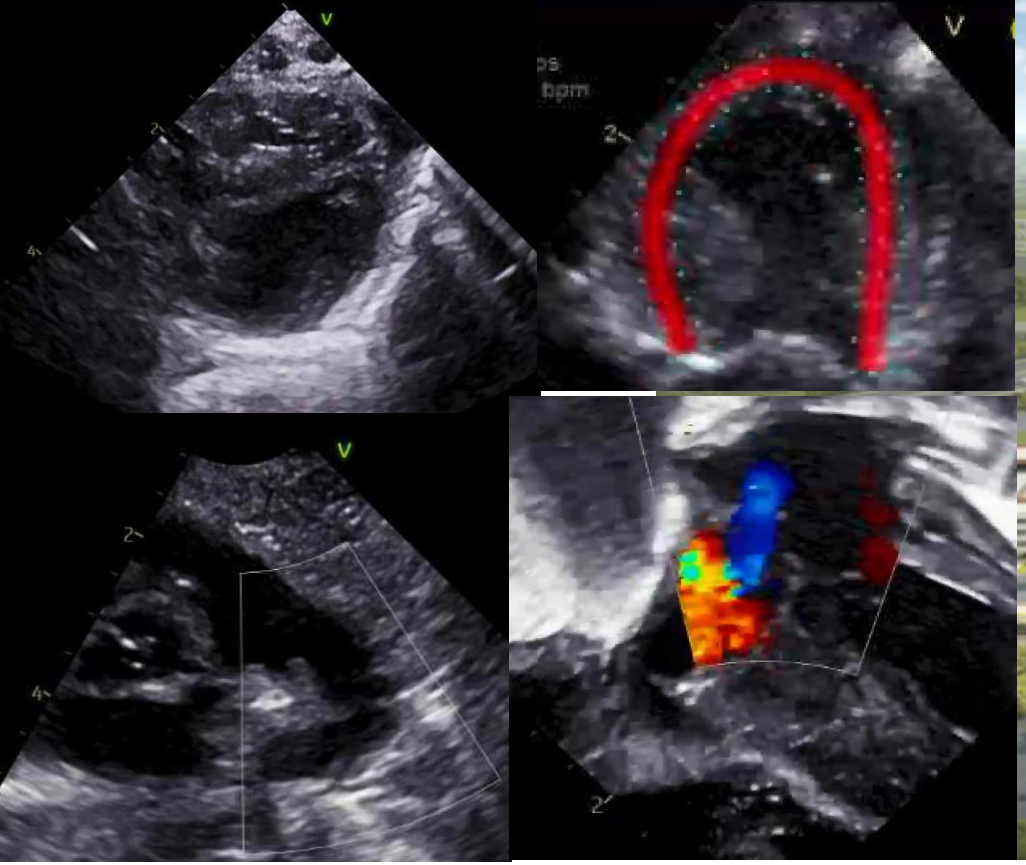
Pulmonary vasodilator therapies
Support RV function and SVR

Post-capillary PH
LV dysfunction, hypotension

⇧ **LV function**

Inotropes
+/-ECMO
Avoid⇧ SVR or HR

Avoid pulmonary vasodilators



Clinical assessment of the neonatal heart in CDH - when, who and how?

Shazia Bhombal, MD
Associate Professor of Pediatrics
Medical Director of Neonatal Services at Children's Healthcare of Atlanta- Egleston

CDH 2024 Congenital Diaphragmatic Hernia International Symposium
Lille, France

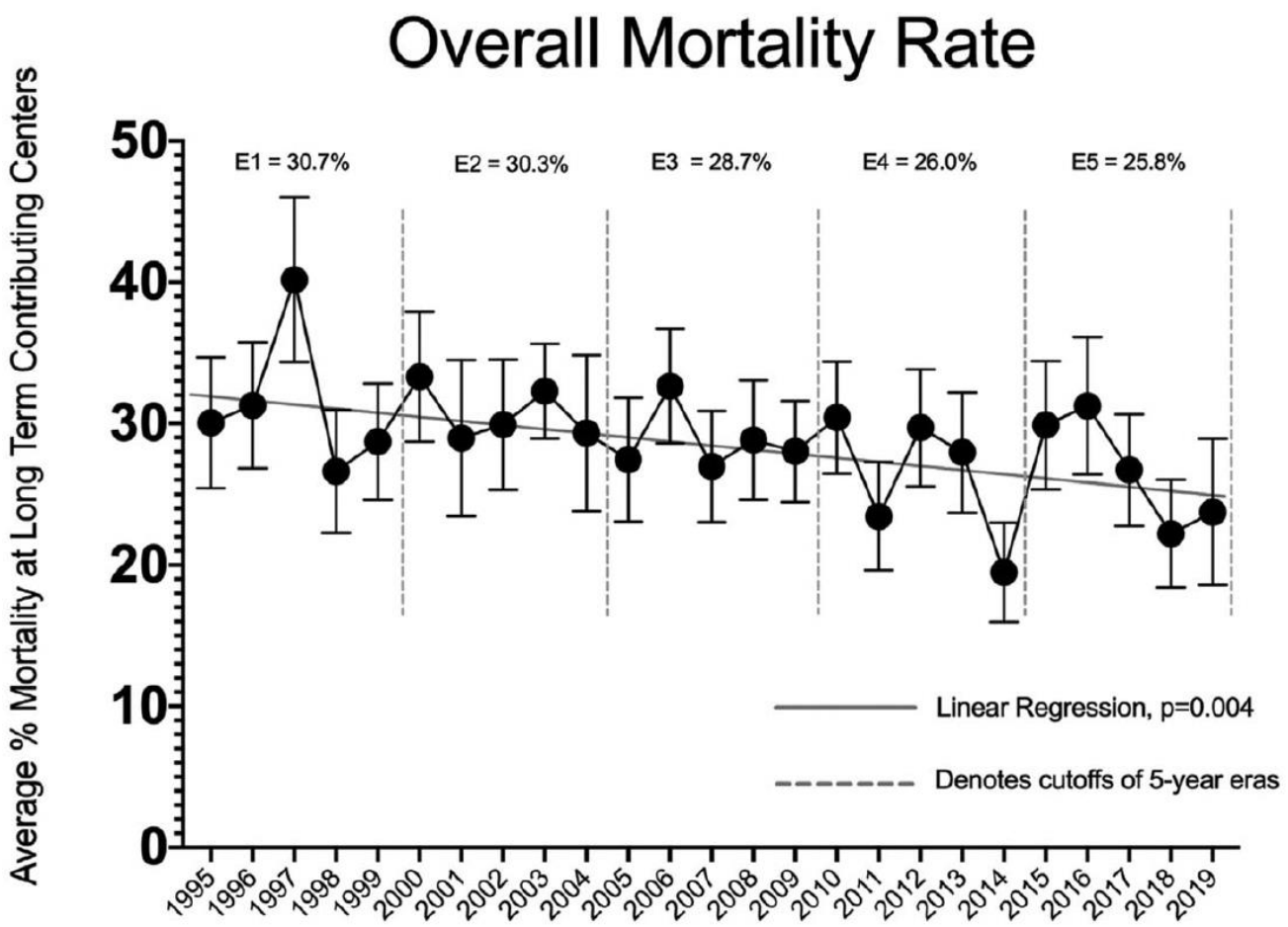
Children's℠ Healthcare of Atlanta | EMORY UNIVERSITY

Mortality in Congenital Diaphragmatic Hernia

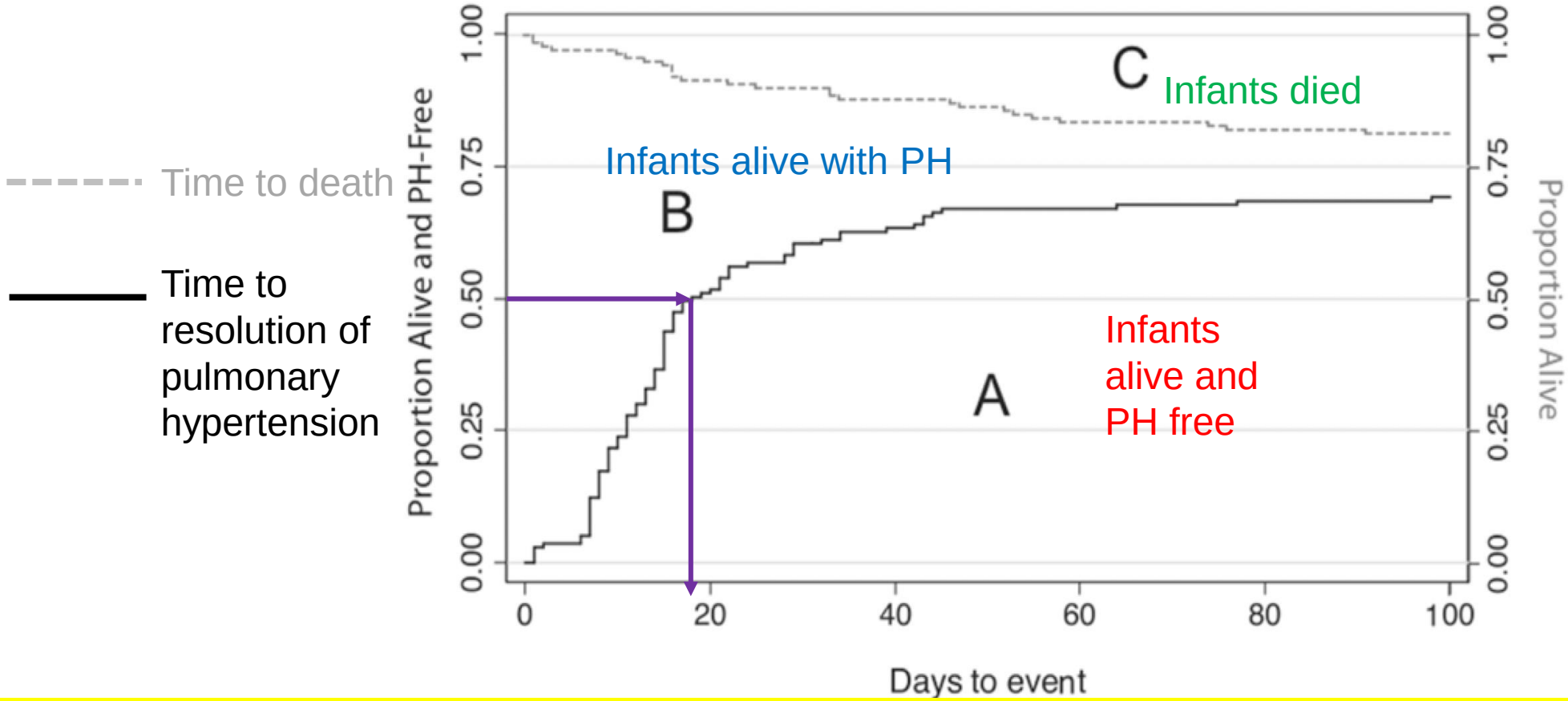
A Multicenter Registry Study of Over 5000 Patients Over 25 Years

Vikas S. Gupta, MD, Matthew T. Harting, MD, MS,* Pamela A. Lally, MD,* Charles C. Miller, MD,† Ronald B. Hirschl,‡ Carl F. Davis, MD,§ MelvinIII S. Dassinger, MD,‖ Terry L. Buchmiller, MD,¶ Krisa P. Van Meurs,# Bradley A. Yoder, MD,** Michael J. Stewart, MD,†† and Kevin P. Lally, MD, MS, FACS,*✉, for the Congenital Diaphragmatic Hernia Study Group*

CDH Survival has improved over years, however still with mortality in the CDH registry ~25%



Pulmonary hypertension plays a role in outcomes



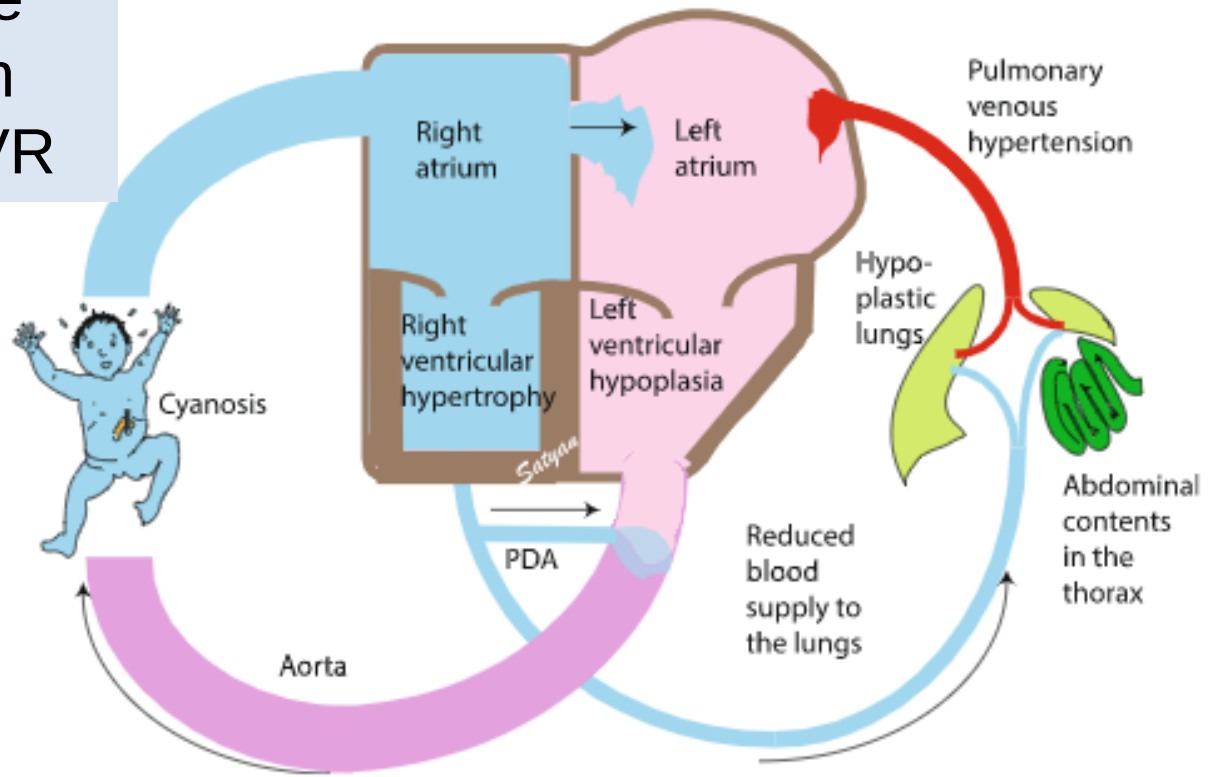
Lusk et al, J Peds 2015

Term healthy infants achieve PAp < 2/3 systemic by 24 hours; ½ CDH patients achieved this by 2-3 weeks, with persistence associated with increased morbidity and respiratory complications

Heart Lung Interactions with CDH

Maldevelopment of pulmonary vasculature resulting in elevated PVR

Left ventricular hypoplasia



1. Reduced pulmonary blood flow due to structural pulmonary vascular changes

2. Ductus venosus flow directed towards right heart -> less flow to left heart

3. Lateral compression on developing heart

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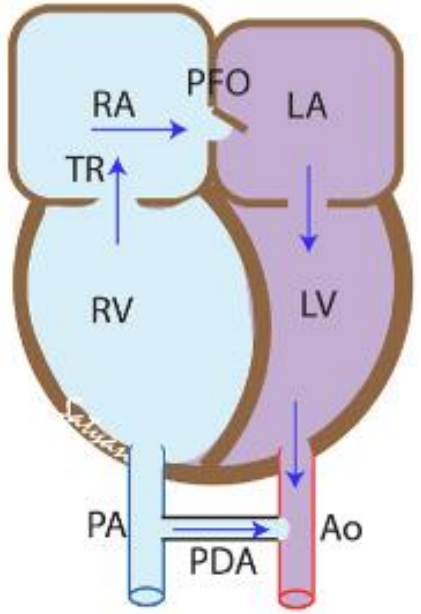
Patel et al, Frontiers 2022

3 CDH Cardiac Phenotypes related to pulmonary hypertension and LV compliance

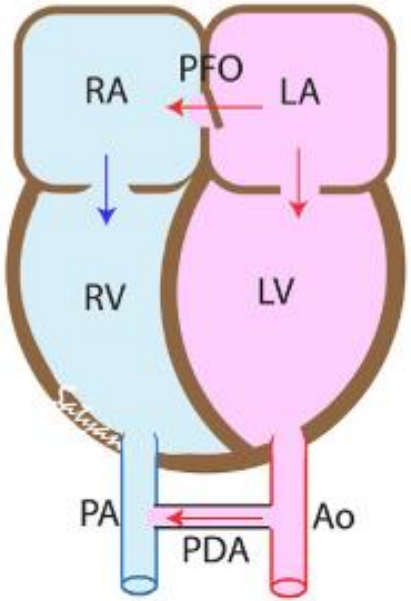


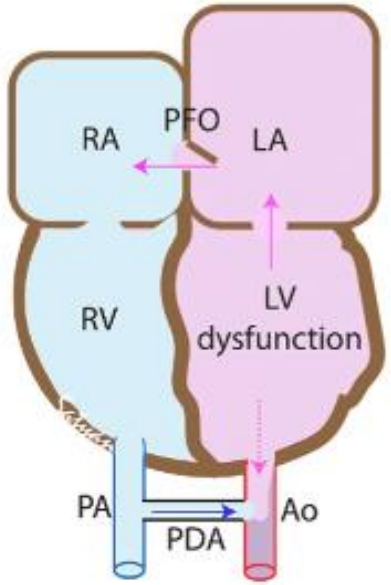
#2

Worsening LV compliance

Increasing pulmonary hypertension

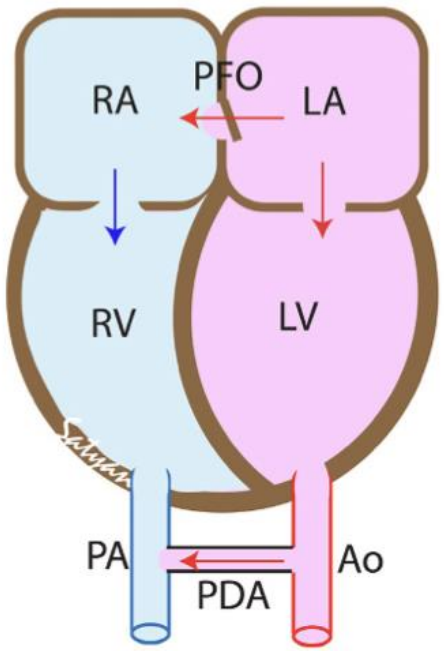
#1



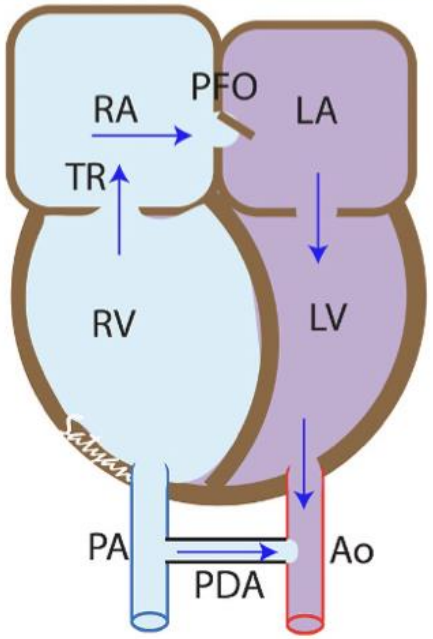


#3

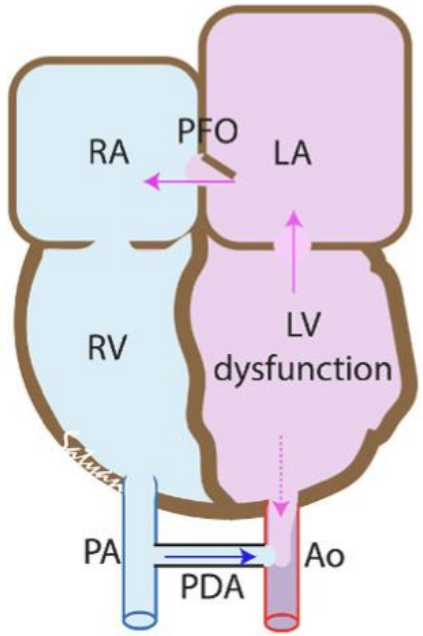
Phenotype #1	Phenotype #2	Phenotype #3
No/mild PH No cardiac dysfunction	PH No cardiac dysfunction/ Primary RV dysfunction	PH Primary LV dysfunction
	Precapillary PH Phenotype	Postcapillary PH Phenotype



Left to Right atrial shunt
Left to Right PDA



Right to left atrial shunt
Right to left PDA



Left to right atrial shunt
Right to left PDA

Bhombal and Patel, Sem Fetal and Neo Med 2022

LA strain

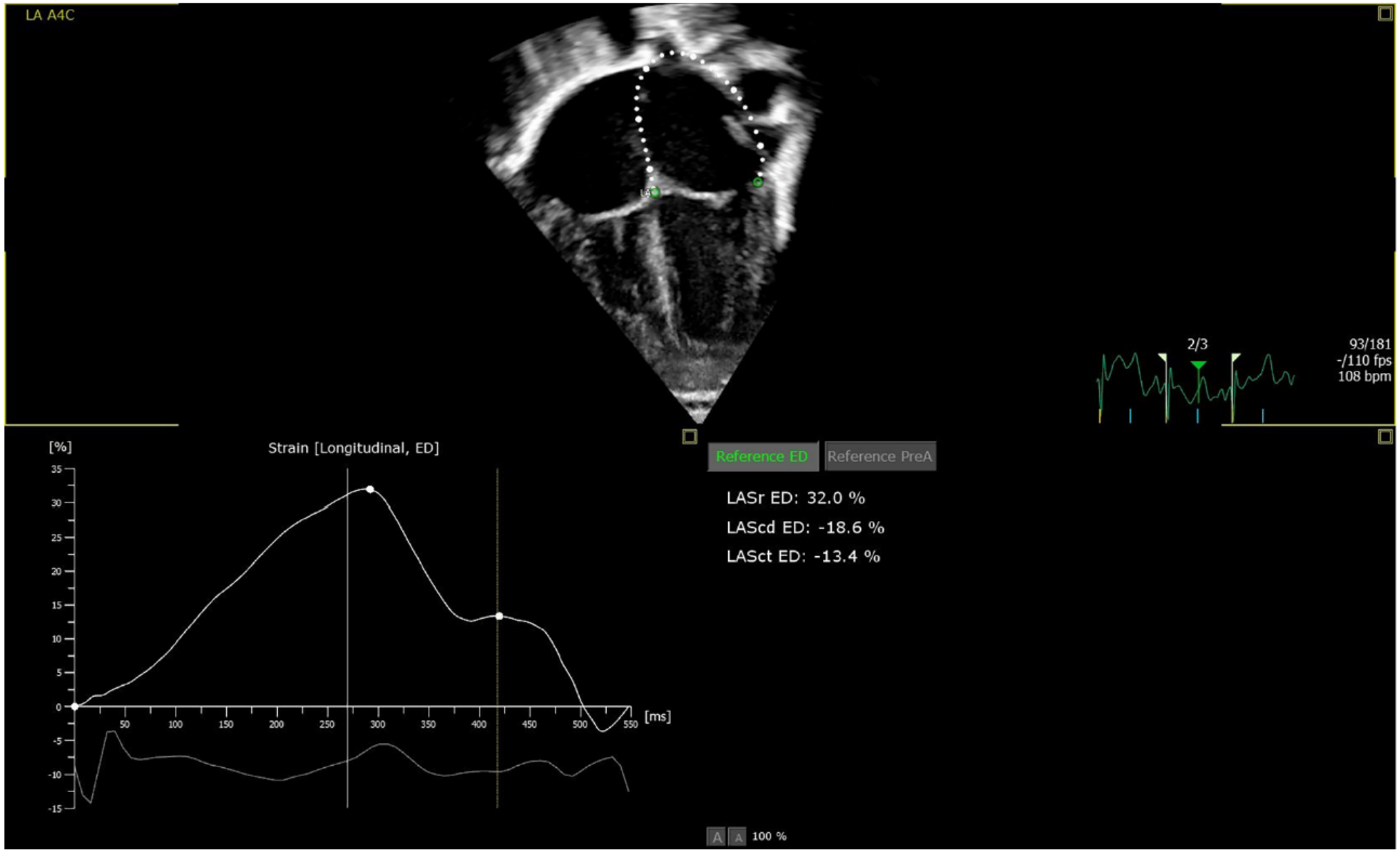
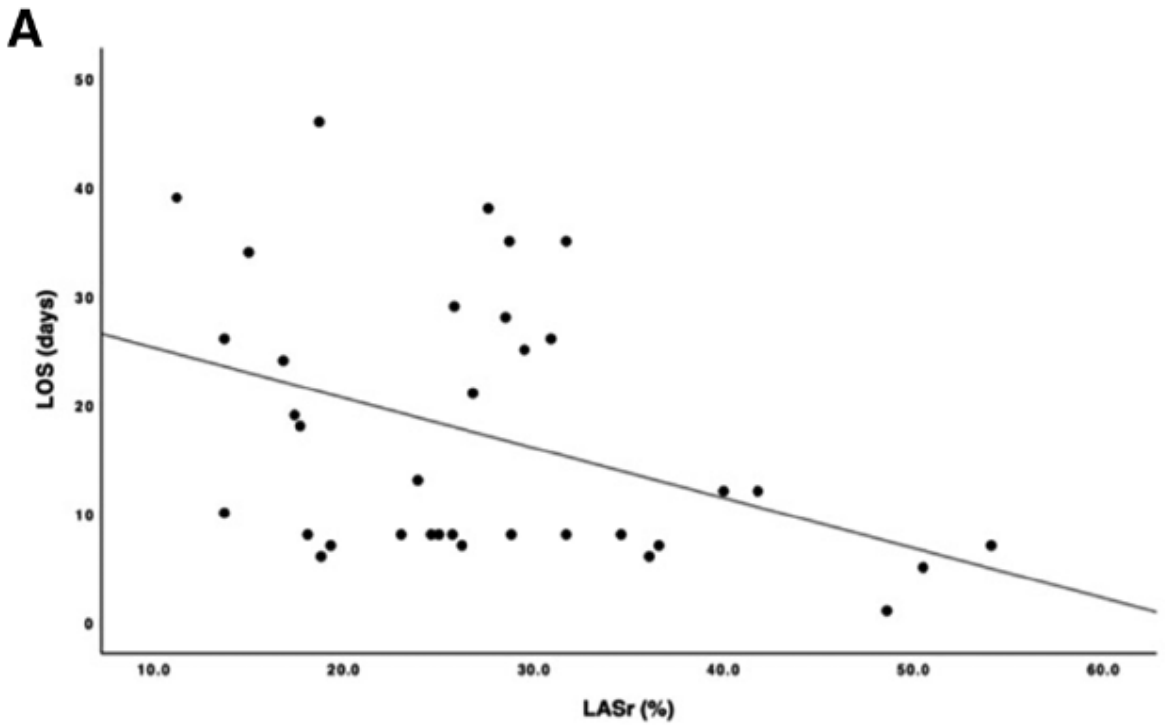


FIGURE 1
Picture of apical four chamber view: software automatically measuring LASr, defining the endocardial border as region of interest, excluding the pulmonary veins and/or LA appendage orifice.

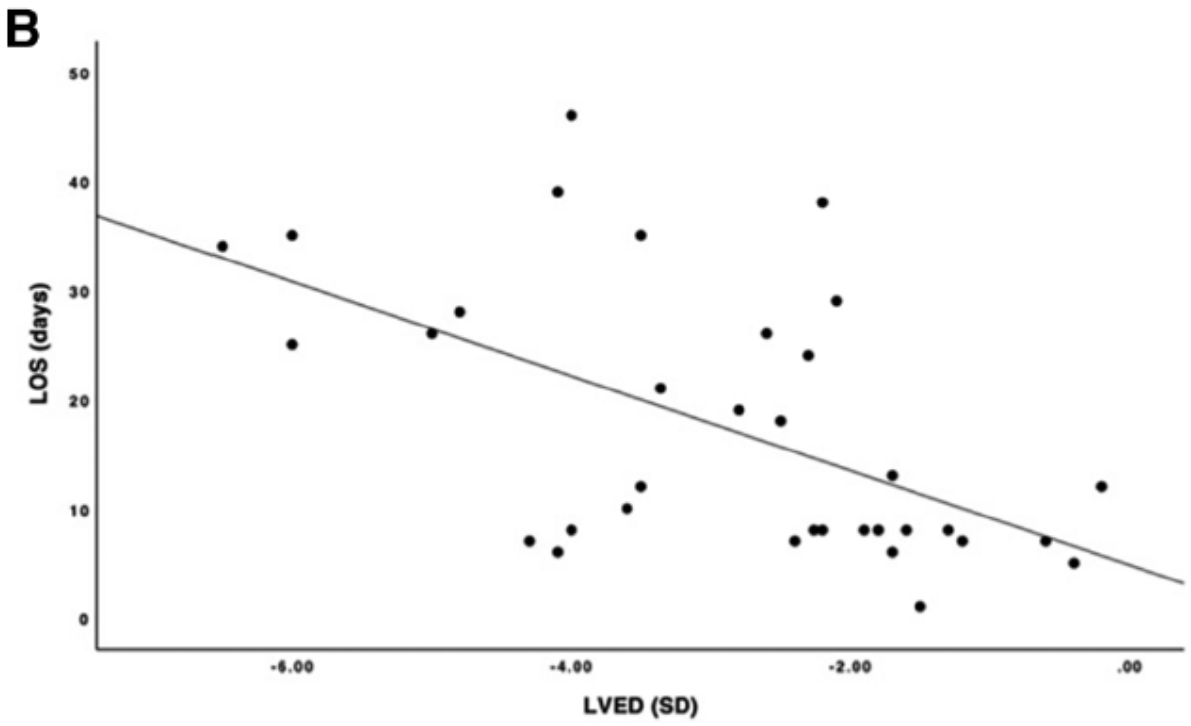
Burgos, Front Pediatr 2024

Durée d'hospitalisation



Left atrial reservoir strain

Durée d'hospitalisation

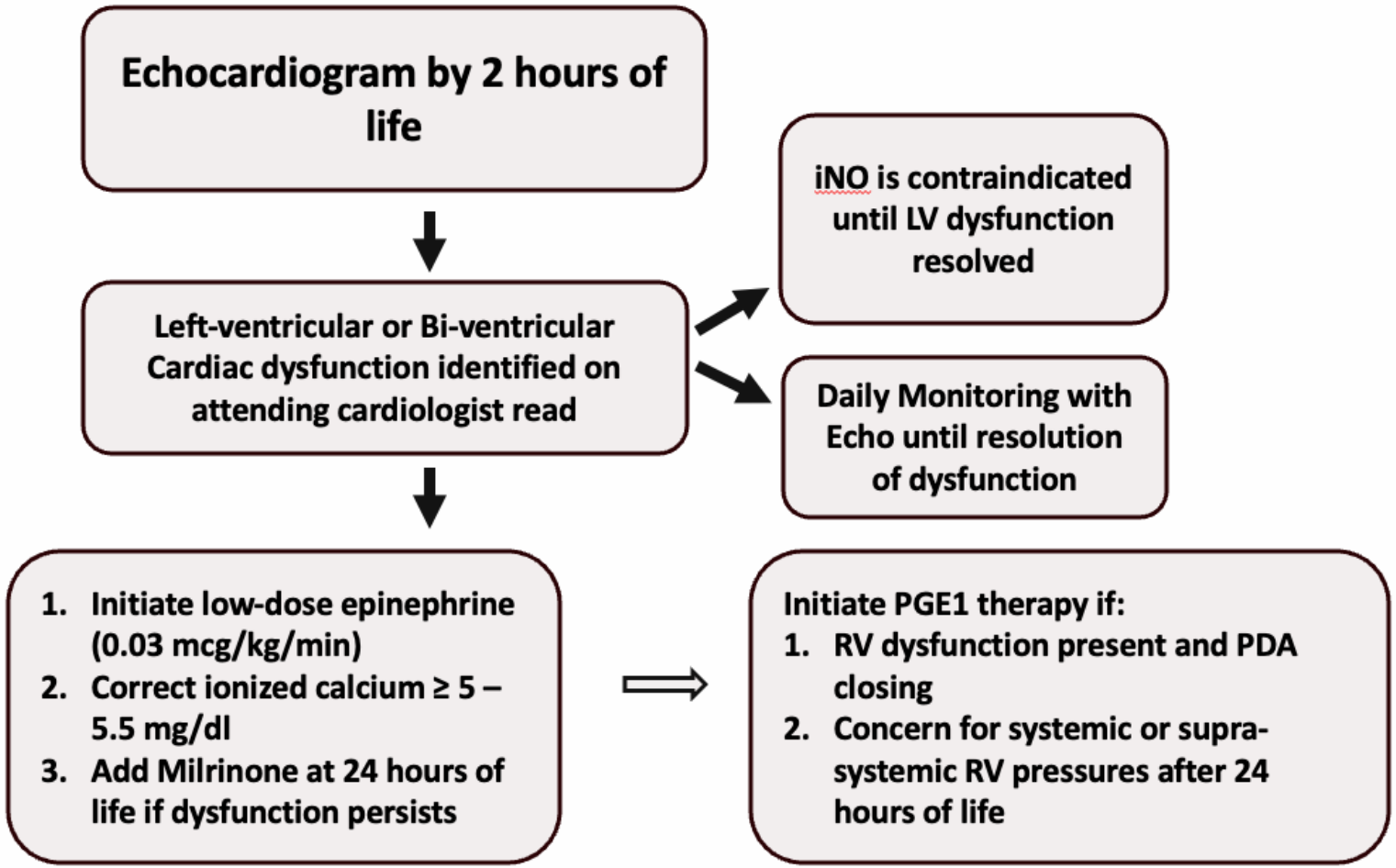


Left ventricular end-diastolic dimension

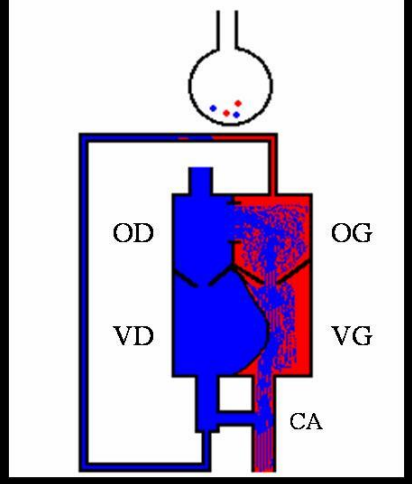
Burgos, Front Pediatr 2024

Early postnatal echocardiogram guides our hemodynamic approach

Slide courtesy of Dr. Patrick Sloan



Persistent Pulmonary Hypertension



Ductus arteriosus

⇑ PVR

PA

Right heart

Left heart

Aorta

⇓ pulmonary flow

Systemic blood flow

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Neonatologie und Pädiatrische Intensivmedizin

UNIVERSITÄT BONN

(Patho)physiology-based cardiorespiratory therapy in CDH – State of the art?

Florian Kipfmueller

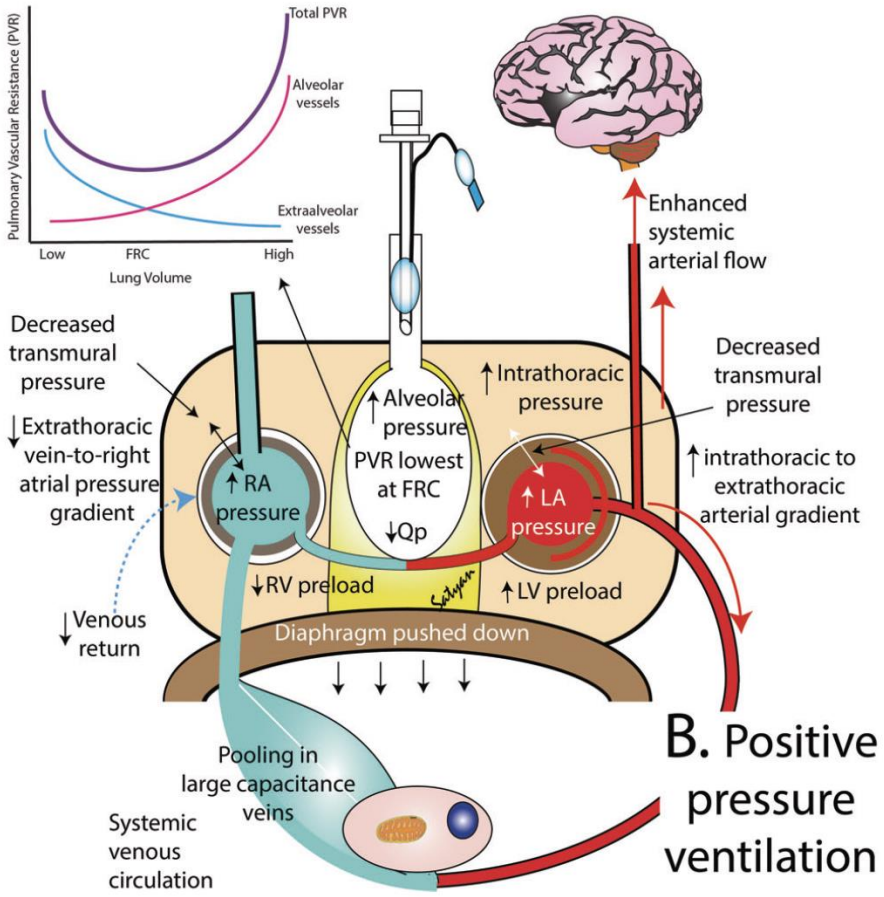
Department of Neonatology and Pediatric Intensive Care Medicine

Children's Hospital| University of Bonn

REVIEW ARTICLE OPEN
Check for updates

Hemodynamic consequences of respiratory interventions in preterm infants

Arvind Sehgal[1,2]✉, J. Lauren Ruoss[3], Amy H. Stanford[4], Satyan Lakshminrusimha[5] and Patrick J. McNamara[4]



A) Impact on alveolus

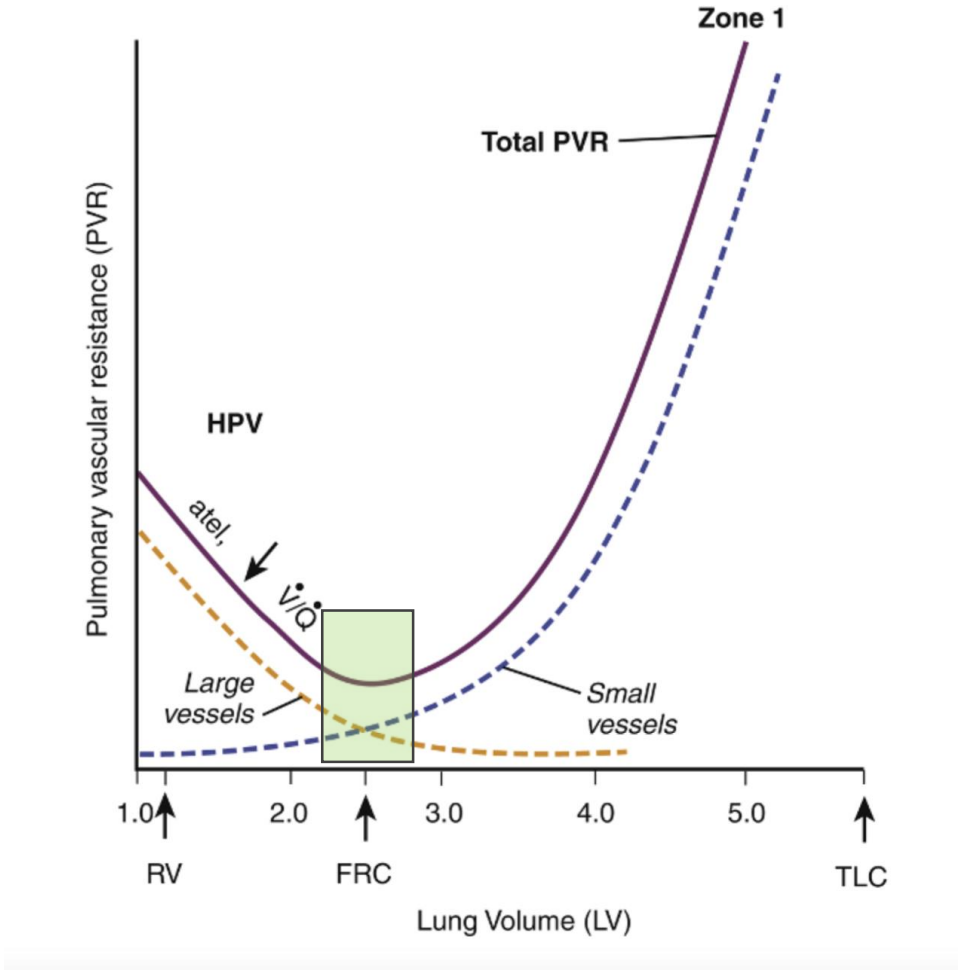
B) Right ventricle:

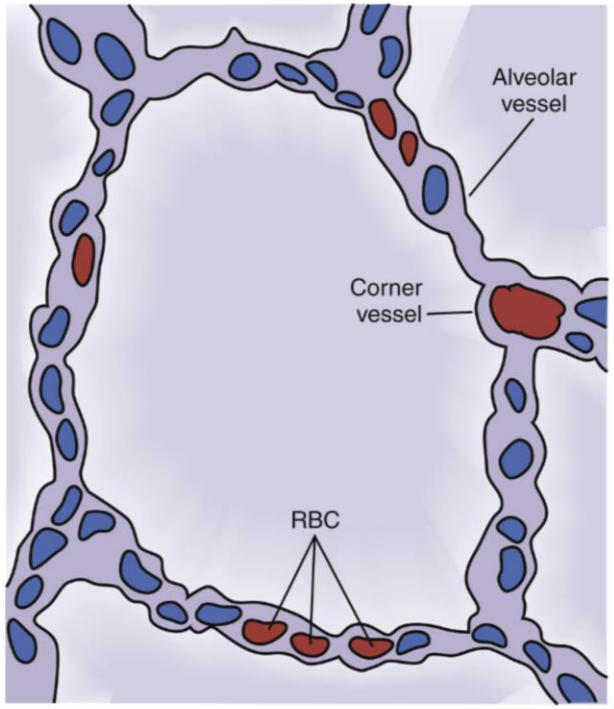
- Incr. RA pressure
- Decr. Venous return
- Decr. RV preload and PBF

C) Left ventricle:

- Incr. LA pressure
- Reduction of transmural pressure may improve LV function and output

Cardiopulmonary Interaction





Fuhrman & Zimmerman‘s, Ped Critical Care

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Neonatologie und Pädiatrische Intensivmedizin

Evaluation of Regional Ventilation Distributions in Newborns with Congenital Diaphragmatic Hernia

Lukas Schroeder[1], Florian Kipfmueller[1], Benjamin Hentze[2,3], Christian Putensen[2], Soyhan Bagci[1], Till Dresbach[1], Hemmen Sabir[1], Andreas Mueller[1], and Thomas Muders[2]

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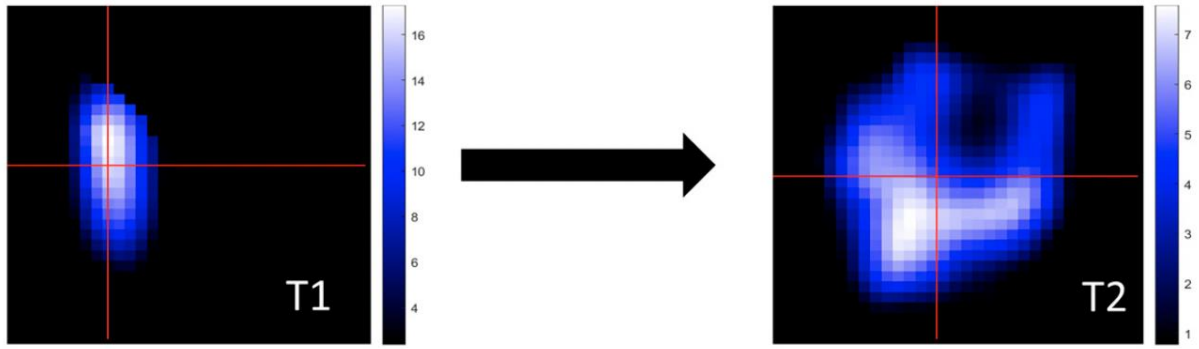
A



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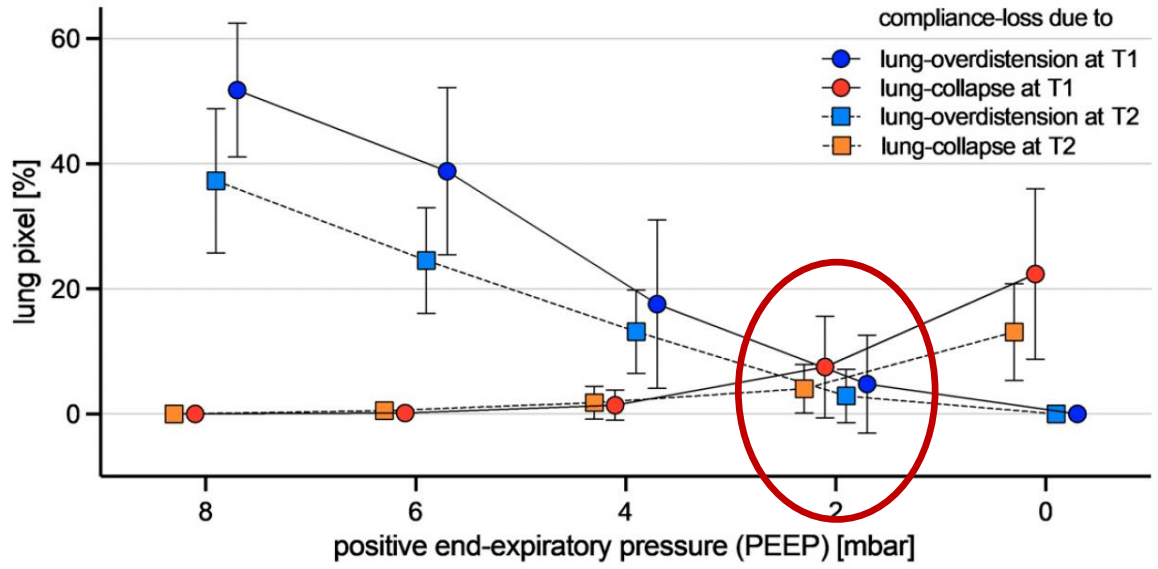


Sp_{O_2} at T1	$PEEP_{meas}$ at T1
96 (93.5–99)	4.3 (4.1–4.6)
95.5 (92–99)	8.2 (8.1–8.6)
97.5 (92.3–99.3)	6.2 (6.0–6.8)
96.5 (94.3–99.3)	4.3 (4.1–4.6)
94 (90.5–98.3)	2.4 (2.1–2.8)
90 (87.5–92.8)	0.8 (0.7–1.0)

VT_{exp} at T1 (*ml/kg BW*)
4.4 (1, 8.1)
3.6 (0.9, 5.4)
4.4 (1, 6.4)
5.4 (1.1, 9.5)
5.9 (1.1, 9.8)
5.4 (0.8, 8.5)

AJRCCM, 2023

Lower Distending Pressure Improves Respiratory Mechanics in Congenital Diaphragmatic Hernia Complicated by Persistent Pulmonary Hypertension

David Guevorkian, MD[1,2], Sebastien Mur, MD[2,3], Eric Cavatorta, MD[1], Laurence Pognon, MD[2,3], Thameur Rakza, MD[2,3,4], and Laurent Storme, MD[2,3,4]

Post repair: PEEP 2 cm H_2O versus 5 cm H_2O

Table I. Fetal and neonatal characteristics of the studied population

Characteristics	Studied population (n = 17)
Prenatal diagnosis, n	13
Left CDH, n	14
LHR o/e by echography, 24-28 wk gestational age, %	35 ± 13
Gestational age, weeks	39 ± 1
Intrathoracic position of the liver	15
Birth weight, g	3300 ± 550
Sex, male/female	9/8
Age at surgery, d, median [range]	1 [1-3]

LHR, Lung-to-head ratio; *o/e*, observed/expected.
Expressed as mean ± SD unless otherwise specified.

Table II. Comparison of respiratory variables measured at 2 cmH_2O and 5 cmH_2O of PEEP in newborn infants with CDH and PPHN (n = 17)

Variables	PEEP 2 cmH_2O	PEEP 5 cmH_2O	*P* value*
FiO_2, %	0.25 [0.21-0.6]	0.35 [0.21-0.7]	.0005
Preductal SpO_2, %	95 [83-100]	92 [84-99]	.08
Postductal SpO_2, %	91 [71-100]	81 [65-100]	.04
pH	7.31 [7.14-7.36]	7.20 [7.13-7.30]	.0134
$PaCO_2$, mm Hg	47 [37-69]	67 [51-96]	<.0001
Respiratory rate, bpm	60 [35-81]	65 [31-85]	.013
PIP, cmH_2O	21 [11-24]	24 [14-25]	<.0001
Expiratory tidal volume, mL/kg	4.9 [3.2-7]	4.0 [2.5-6.4]	<.0001
Expiratory minute volume, L/min	1.1 [0.4-2.1]	0.8 [0.3-1.2]	.0002
Compliance, mL/cmH_2O/kg	0.34 [0.16-0.67]	0.24 [0.13-0.60]	.0001
Resistances, cmH_2O/L/s	98 [64-222]	111 [65-234]	.86
Ventilation index	52 [16-787]	74 [17-146]	<.0001

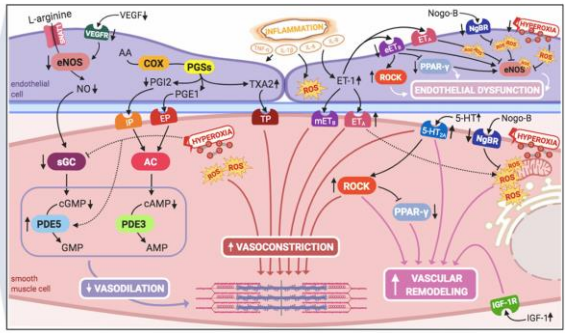
Compliance, compliance of the respiratory system; *Resistances*, resistances of the respiratory system.
Expressed as median [range].
*Wilcoxon distribution-free signed rank test.

Smart approach to pulmonary vasodilator use:

Define PH phenotype

Pre-capillary PAH
RV dysfunction / hypoxia

Systematic use of pulmonary vasodilator therapies



LV dysfunction
Post-capillary PH

Avoid pulmonary vasodilators
Treat LV dysfunction.

Pathophysiology-based approach to cardiorespiratory therapy/interactions