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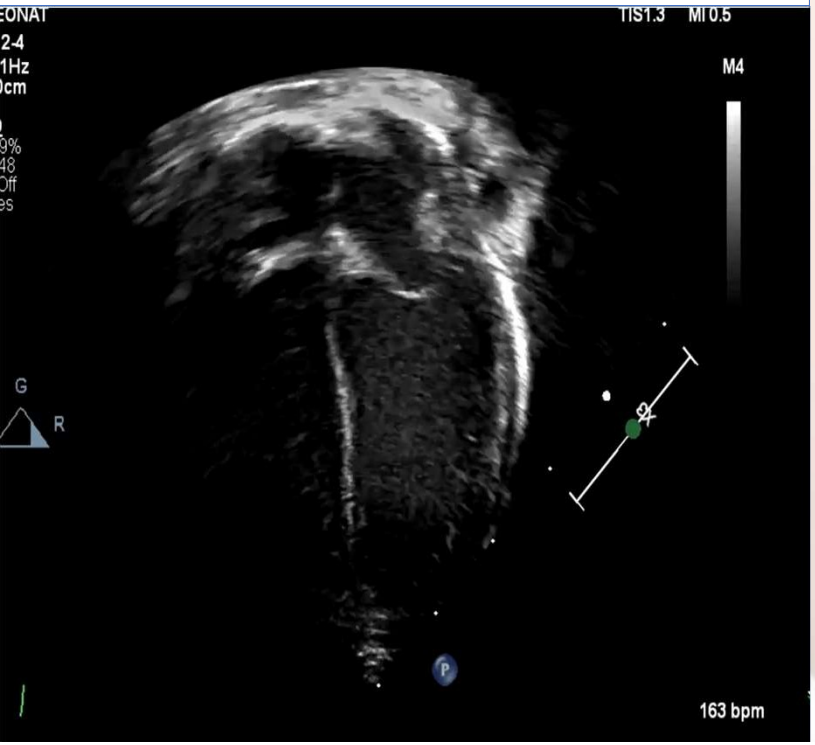

Management of pulmonary hypertension in newborns with prematurity and lung disease

November 30, 2022

By: Gabriel Altit (Neonatologist)

I CONGRESSO INTERNACIONAL DE NEONATOLOGIA DO DF

Hôpital de Montréal pour enfants
Centre universitaire de santé McGill

Montreal Children's Hospital
McGill University Health Centre

www.paulomargotto.com.br Brasília, 30 de novembro de 2022

Disclosure / Acknowledgements

- No Disclosures relative to the content of this presentation

- This presentation will involve comments or discussion of unapproved or off-label, experimental or investigational use of iNO, inotropic, or pulmonary vasodilators in prematurity. No RCT.

- *Agradeço à comissão organizadora por me convidar para esta magnífica conferência e para o seu extraordinário país, para a sua magnífica capital. É uma grande honra.*

Plan of the presentation

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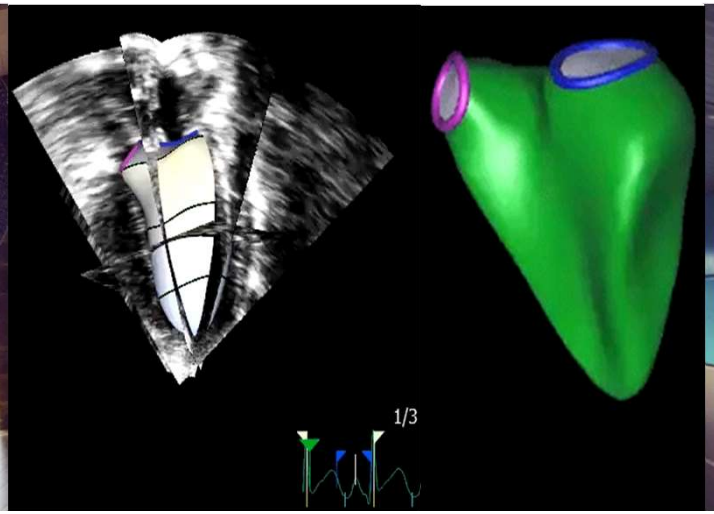
- Definition of pulmonary hypertension (PH)
- PH – Brief summary of evaluation by echocardiography
- Why is my “BPD” patient at risk of PH?
- Importance of assessing cardiac performance in BPD-PH
- My approach to these patients at discharge





CASE - Kevin

- Kevin born at 23+3
- Mother pre-eclampsia, placental insufficiency (reversed end-diastolic flow in umbilical vessels)
- Growth restricted – 430 grams
- C-Section, required intubation + surfactant, high oxygen requirements, remained on prolonged mechanical ventilation.
- NEC, perforation requiring surgery, followed by failure to thrive.
- Steroids, now 36 weeks corrected on CPAP of 12 with FiO2 of 45%
- Frequent desaturations;
- CO2 is 78 with pH of 7.30
  - ECHO is requested

CASE - Kevin

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- Why an ECHO?

AHA/ATS Guideline

Pediatric Pulmonary Hypertension

Guidelines From the American Heart Association and American Thoracic Society

Bronchopulmonary Dysplasia

1. **Screening for PH by echocardiogram is recommended in infants with established BPD (*Class I; Level of Evidence B*).**

THE JOURNAL OF PEDIATRICS • www.jpeds.com MEDICAL PROGRESS

Evaluation and Management of Pulmonary Hypertension in Children with Bronchopulmonary Dysplasia

Usha Krishnan, MD[1,*], Jeffrey A. Feinstein, MD[2,*], Ian Adatia, MBChB[3], Eric D. Austin, MD[4], Mary P. Mullen, MD, PhD[5], Rachel K. Hopper, MD[6], Brian Hanna, MD, PhD[6], Lew Romer, MD[7], Roberta L. Keller, MD[8], Jeffrey Fineman, MD[9], Robin Steinhorn, MD[10], John P. Kinsella, MD[11], D. Dunbar Ivy, MD[12], Erika Berman Rosenzweig, MD[1], Usha Raj, MD[13], Tilman Humpl, MD[14], and Steven H. Abman, MD[15], for the Pediatric Pulmonary Hypertension Network (PPHNet)[†]

Evaluation and Diagnosis

Recommendation # 2: Premature infants should have an echocardiogram performed to screen for PH in the following scenarios:

(1) *severe hypoxemic respiratory failure shortly after birth attributed primarily to persistent pulmonary hypertension of the newborn (PPHN) physiology despite optimal management of underlying lung disease. (class 1, LOE B)*
(2) *continued need for ventilator support at postnatal day 7, as echocardiogram evidence of PH at day 7 suggests high risk for BPD and may alter therapy. (class1, LOE C)*
(3) *with sustained need for significant respiratory support at any age, especially with recurrent episodes of hypoxemia. (class 1, LOE B)*
(4) *at the time of formal BPD diagnosis per current practice (36 weeks postmenstrual age [PMA]). (class 1, LOE B)*

CASE

- Inter-atrial communication (PFO) bidirectional
- PDA closed
- Flat septum at the end of systole
  - RV assumed to have same pressure as PA, LV same pressure as Aorta – because valves are open
- Tricuspid Regurgitant Jet: RV-RA of 65 mmHg. Systolic Blood pressure of 70 mmHg.
- RV dilation. RV systolic function decreased by TAPSE & FAC (RV function markers)
- LV function is normal
- 4 pulmonary veins seen with normal triphasic profile

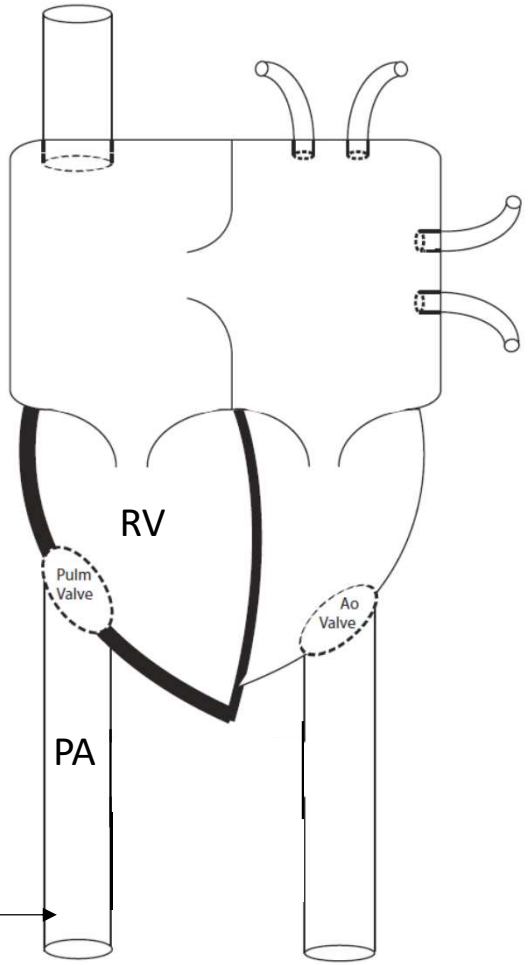
- Conclusions: Pulmonary hypertension iso-systemic with signs of RV dysfunction

What is “pulmonary hypertension”?

Pulmonary Hypertension (PH) - Definition

- Similar to systemic hypertension = abnormal high BP in systemic compartment
  - Etiologies: idiopathic, renal, cancer, steroids, etc.
  - Identify cause to tailor treatment

- **PH = abnormally high pressure in pulmonary artery (PA)**
  - PH is a symptom of underlying process:
    - Congenital heart, BPD, HIV, Pulmonary Embolus, Mitral Regurgitation, PPHN…
  - Identify cause to tailor treatment



”Abnormally” High pressure in PA = PH

AHA/ATS Guideline

Pediatric Pulmonary Hypertension

Guidelines From the American Heart Association and American Thoracic Society

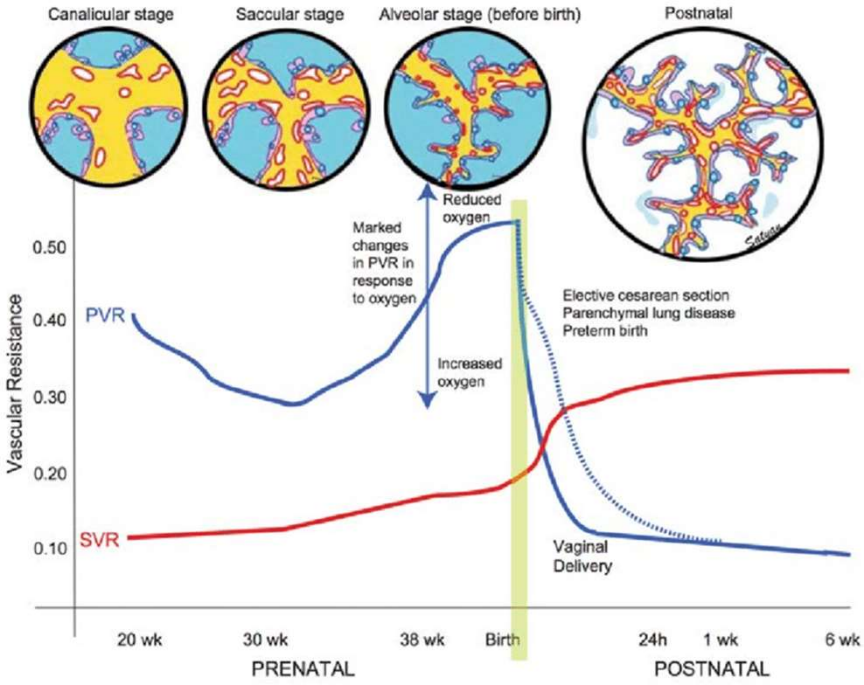
Abnormal PA pressure defined (> 3 months of age):

- Mean PAP ≥ 20 mmHg (measured by cath but can be estimated by echo),
- Suspect if systolic PAP ≥ 40 mmHg, estimated by Echo
- First 3 months: PVR dropping and should be < systemic.

Normal PA pressure usually= 15/5 (mean of 10) after 3 months of age
First 3 months: PVR dropping and should be < systemic.

CONSENSUS STATEMENT

2019 updated consensus statement on the diagnosis and treatment of pediatric pulmonary hypertension: The European Pediatric Pulmonary Vascular Disease Network (EPPVDN), endorsed by AEPC, ESPR and ISHLT



Changes in systemic vascular resistance (SVR) and pulmonary vascular resistance (PVR) during gestation. (Lakshminrusimha and Saugstad, 2016).

Pulmonary hypertension
Suspicion using ECHO

By ECHO – PH suspected:

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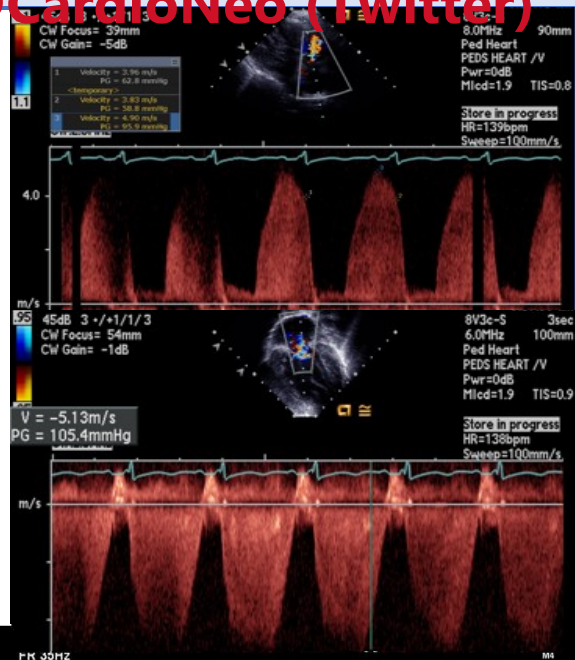
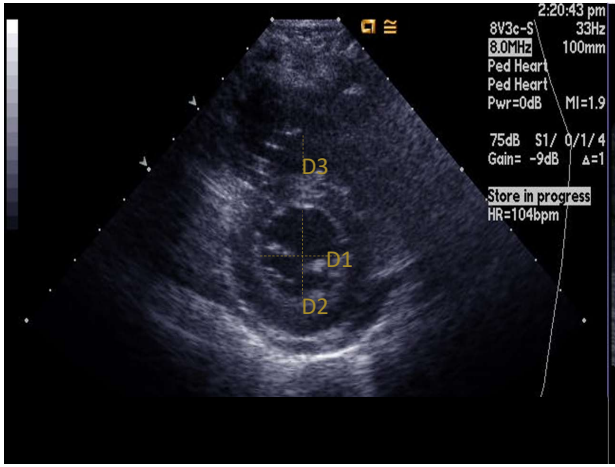
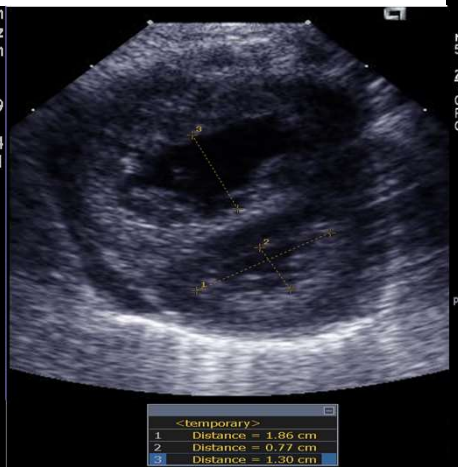
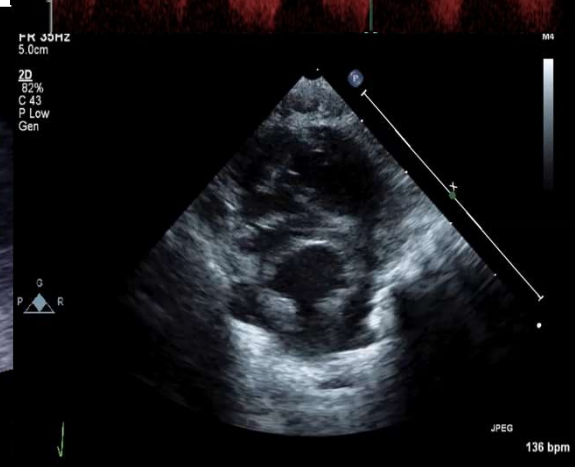
- mPAP ≥ 20 mmHg (pulmonary insufficiency jet)
  - P.I. in diastole
- sPAP ≥ 40 mmHg by ECHO, using:
  - TRJ ≥ 35 mmHg, or
  - A restrictive PDA, or VSD velocity gradient (sBP – gradient)
  - Otherwise: flattening of interventricular septum (IVS) at end of systole used as surrogate of increased PAP
    - Eccentricity index ≥ 1.3



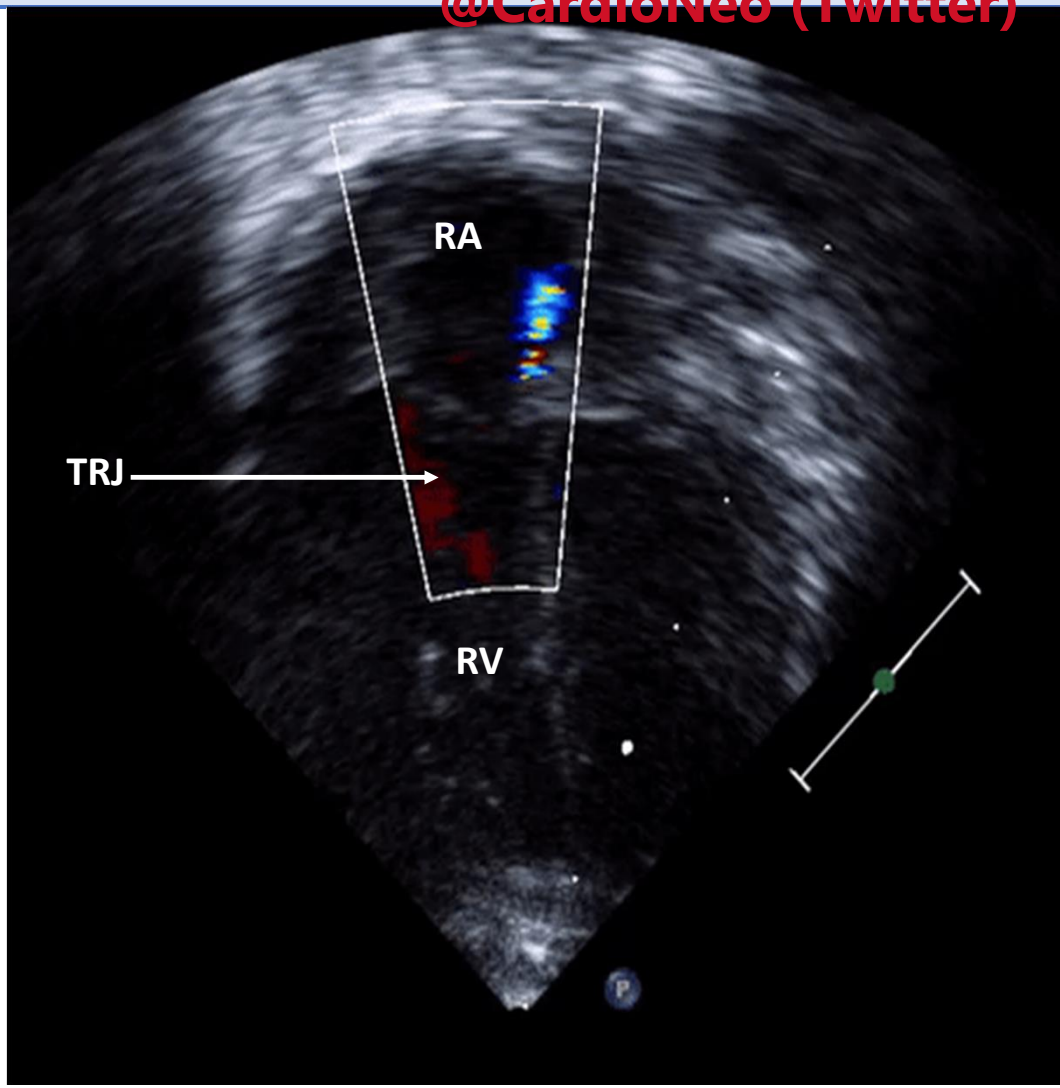






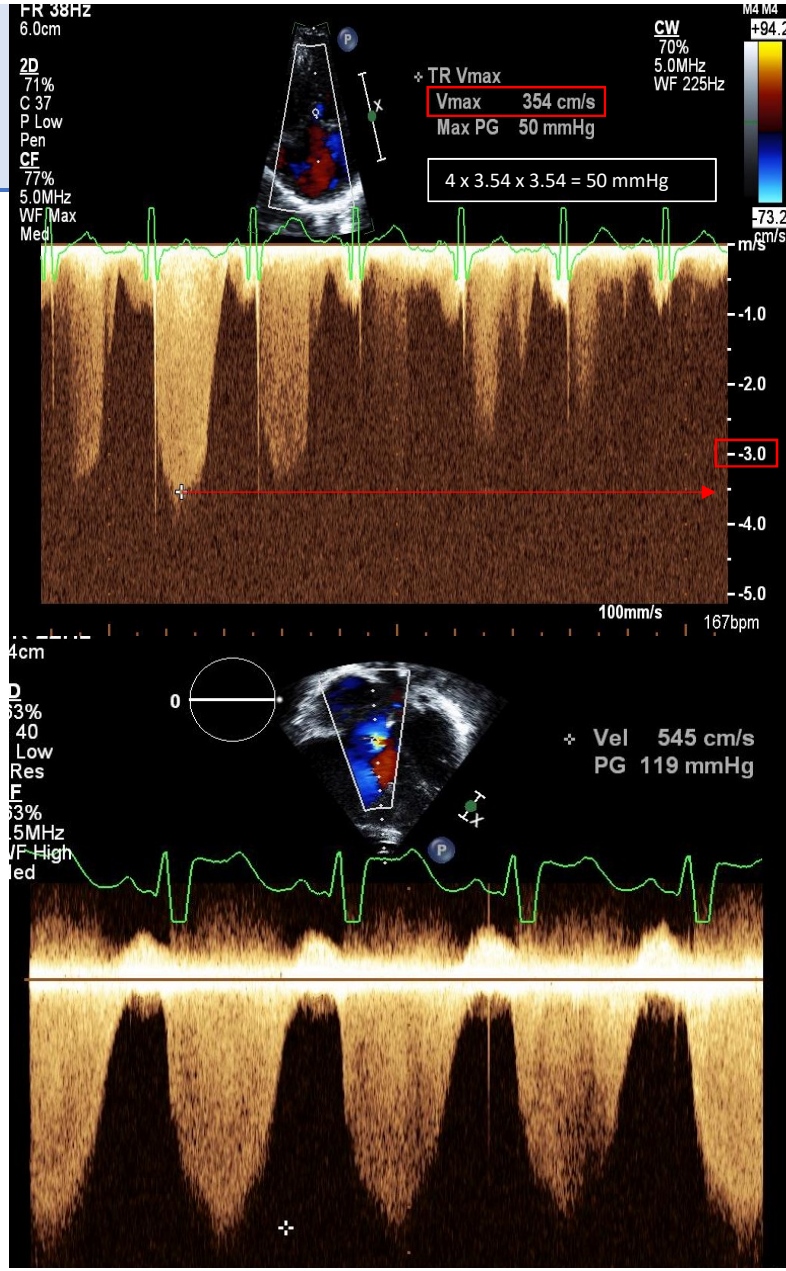
Tricuspid Regurgitant Jet (TRJ) Velocity

- During systole, tricuspid valve closed (prevents backflow in RA)
- With PH: RV dilates, TR appears



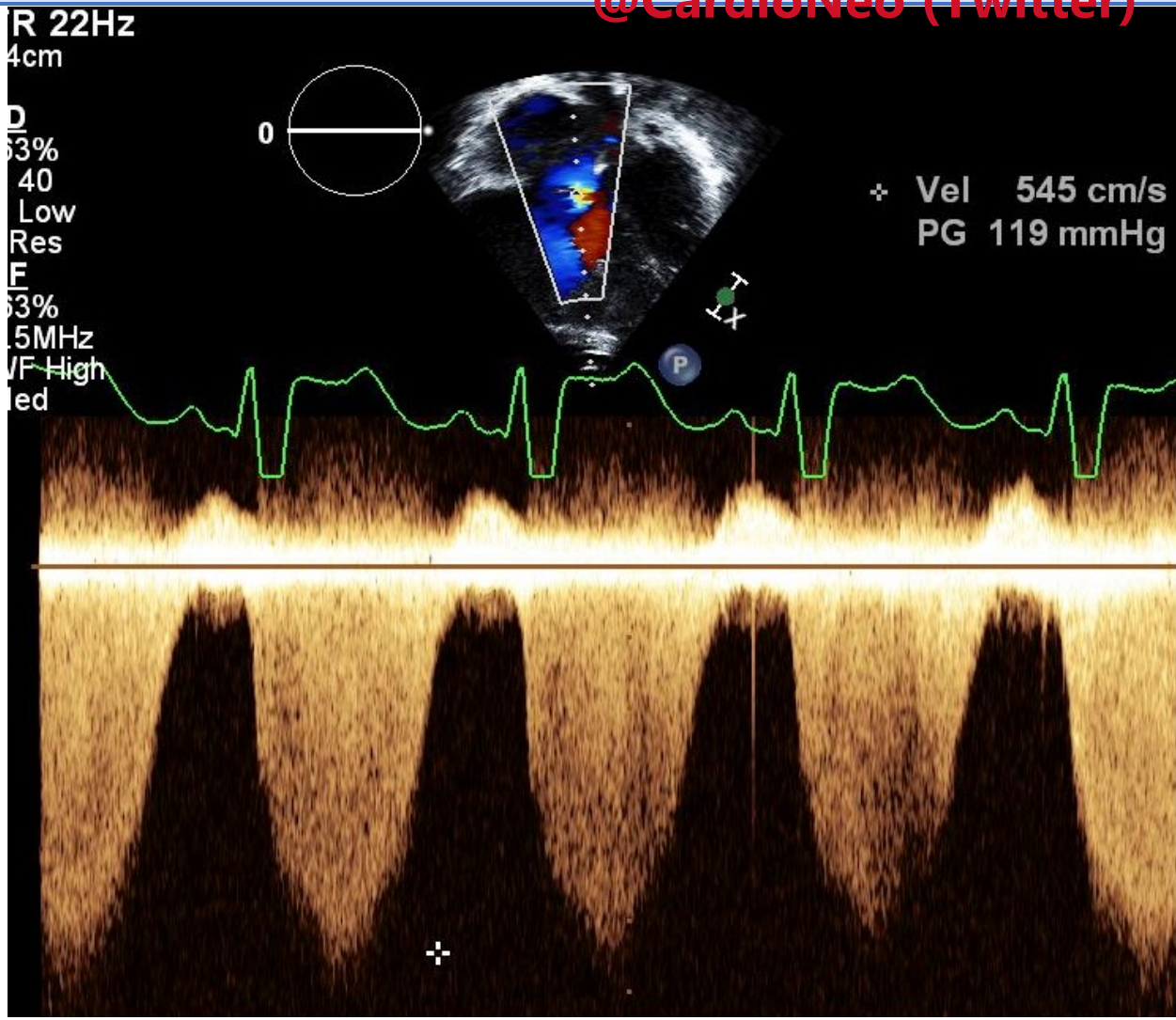
Tricuspid Regurgitant Jet (TRJ) Velocity

- Doppler – estimates "gradient" (difference) between RV and RA at peak of <u>systole</u>
- Simplified Bernouilli equation:
  - Pressure difference between the 2 cavities = 4 x velocity^2
- Assuming RA pressure – 0-5mmHg (will increase with diastolic RV dysfunction)



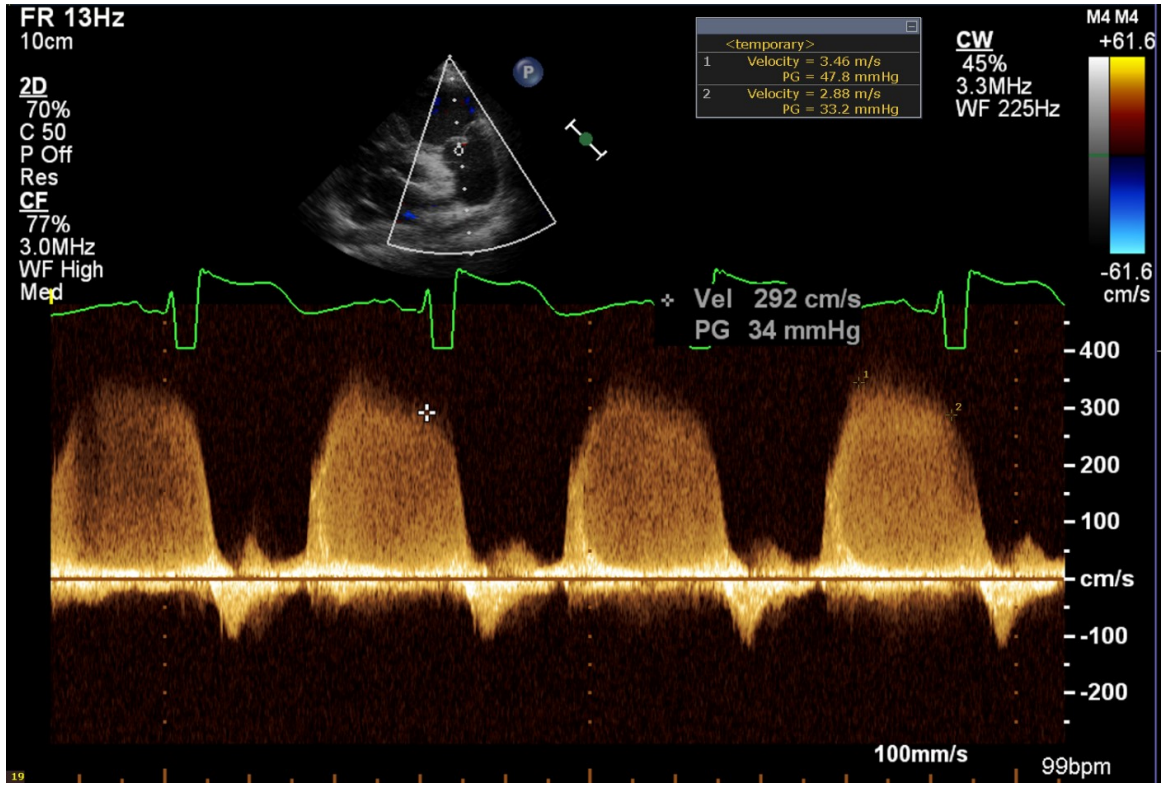
Tricuspid Regurgitant Jet (TRJ) Velocity

- TR = 5.45 m/s → $4v^2$ = 119 mmHg at peak of systole → RV-RA gradient of 119 mmHg
- Assuming RA pressure about 5 mmHg: estimate of <u>systolic</u> PAP = 119+5 = 124 mmHg
- If systolic systemic BP 65 at ECHO: 124/65 = 2x systemic



Pulmonary Insufficiency Jet Velocity

- Same concept as TR
- Pulmonary valve is closed during diastole
- If RV/PA dilation → PV annulus dilate → Pulm Ins.
- Early Insufficiency jet speed gives you estimate of mean PA pressure; end diastolic of diastolic PA pressure



Diastolic pulm pressure (DPAP) estimated from pulm regurgitation jet from velocity of end-diastolic PI velocity

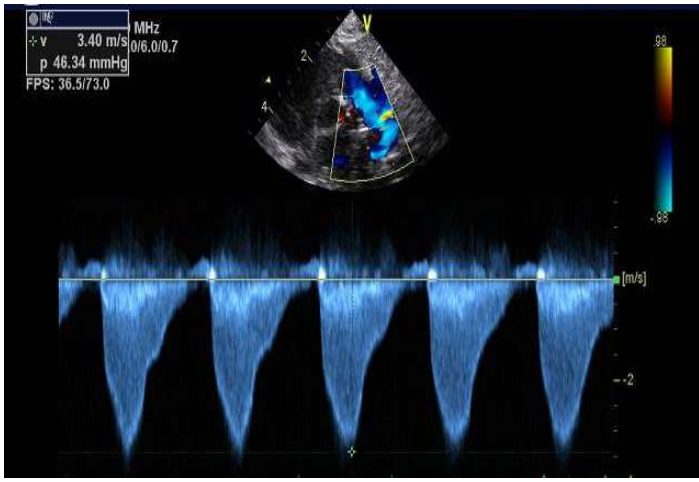
DPAP = 4 (end-diastolic PI velocity)^2 + estimated RA pressure*
mPAP = 4 (early diastolic PI velocity)^2 + estimated RA pressure*

*estimated RA pressure = RV end-diastolic pressure

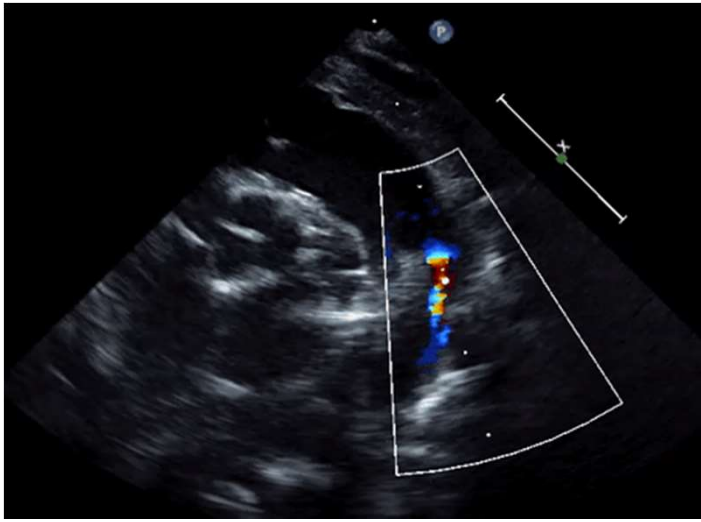
Jone and Ivy, Echocardiography in pediatric pulmonary hypertension, Frontiers in Pediatric, Nov 2014, Volume 2, Article 124

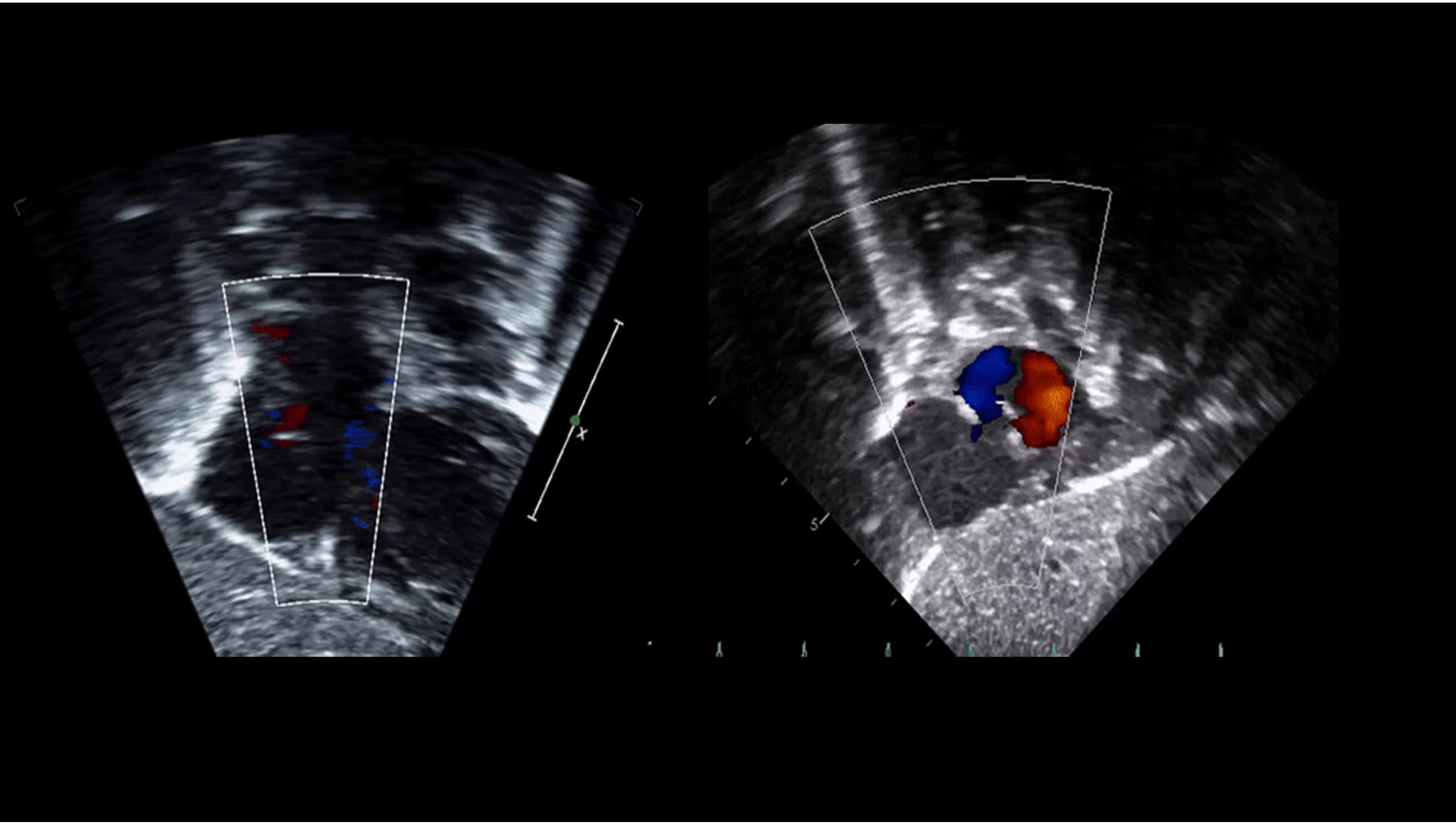
By ECHO – PH suspected:

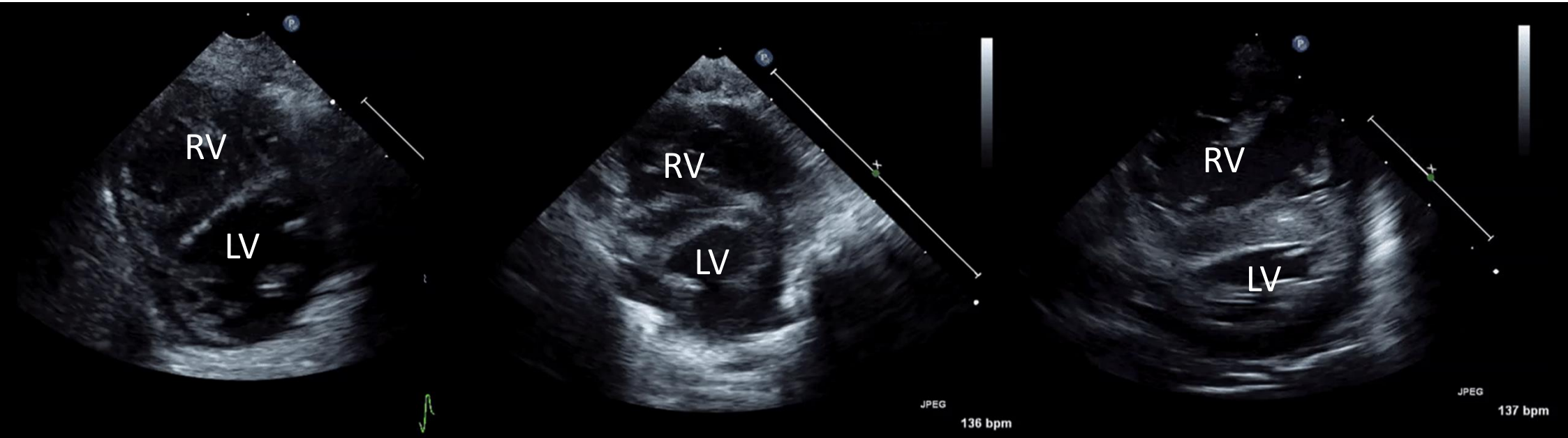
- Inter-atrial shunt bidirectional or right to left:
  - Brings de-O2 blood in systemic circulation
  - Informs that the RA pressure is ≥ LA pressure
    - LA pressure low (low venous return because of decreased pulm circulation)
    - RA pressure high (RV diastolic compromise)



- Post-tricuspid bidirectional or right to left shunt (VSD / PDA):
  - Informs that RV pressure ≥ LV pressure; or PA pressure ≥ Aortic pressure







Increasing RV afterload

As pressure rises on RV side (or pressure decreases on LV side), it can become iso-systemic (same as pressure on the LV compartment) or supra-systemic (higher pressure than on RV side).

Because there is a shared wall:

Isosystemic = Flat Interventricular septum at peak of contraction - D-Shape LV

Supra-systemic = Bowing septum into the LV cavity (Type 3)

With persistent increased afterload, RV hypertrophies and dilate, fails – LV fails because pancaking

- Many times not straightforward, some examples:
  - Large ASD (left to right): RV volume overload
  - Large PDA/VSD
    - Pressure equalization between Ao and PA (flow/pressure transmission) vs high PVR?
  - Difficult to image…
  - Left-heart disease?

Why is my “BPD” patient at risk of PH?

Table 5. Classification of Pediatric PHVDs (Panama): General Categories

Prenatal or developmental PH vascular disease
Perinatal pulmonary vascular maladaptation
Pediatric cardiovascular disease
Bronchopulmonary dysplasia
Isolated pediatric pulmonary hypertensive vascular disease (isolated pediatric PAH)
Multifactorial pulmonary hypertensive vascular disease in congenital malformation syndromes
Pediatric lung disease
Pediatric thromboembolic disease
Pediatric hypobaric hypoxic exposure
Pediatric pulmonary vascular diseases associated with other system disorders

PAH indicates pulmonary arterial hypertension; and PHVD, pulmonary hypertensive vascular disease.

Modified from Cerro et al.[7]

Prematurity and BPD

- Immature lungs
  - Reactive oxygen species, volu-, baro-, atelecta-trauma
  - Immature and abnormal repair / fibrosis
  - Inflammation (NEC, infections, ventilation)
  - Disturbed growth / sub-optimal nutrition
  - Post-natal steroids (alters vascular growth but helps inflammation)
  - Genetic predisposition / Fetal environment / Chorio, etc.
- Pulmonary vascular disease in BPD:
  - Abnormal vascular pruning and remodelling, muscularisation of vasculature (arteries and veins)
  - Abnormal response to substances regulating vascular tone
  - V/Q mismatch, chronic lung injury, aspiration, airway disease, CO2 retention
  - Increased PVR, Heterogenous vascular tone, decreased vascular territory, Abnormal venous drainage
- Lung getting better = Vessels getting better

Berkelhamer SK, et al. Seminars in perinatology. 2013;37(2):124-31.
Subhedar N, et al . Archives of Disease in Childhood-Fetal and Neonatal Edition. 2000;82(3):F243-F7.
Walsh MC, et al. Pediatrics. 2006;117(3 Pt 2):S52-6.
Farrow KN, et al. American journal of respiratory and critical care medicine. 2015;191(1):12-4.

Prematurity and BPD

- Risk factors:
  - Extreme prematurity, growth restriction (pre-eclampsia, gestational HTN), oligo, duration of ventilation, NEC and prolonged O2
- PH and RV failure in up to 25 % of BPD in some reports
- **Increased mortality** with some reports death rate up to 35% in 6 months after PH diagnosis

Berkelhamer SK, Mestan KK, Steinhorn RH. Pulmonary hypertension in bronchopulmonary dysplasia. Seminars in perinatology. 2013;37(2):124-31.
Subhedar N, Shaw N. Changes in pulmonary arterial pressure in preterm infants with chronic lung disease. Archives of Disease in Childhood-Fetal and Neonatal Edition. 2000;82(3):F243-F7.

Journal of Perinatology (2019) 39:415–425
https://doi.org/10.1038/s41372-018-0303-8

ARTICLE

Death or resolution: the "natural history" of pulmonary hypertension in bronchopulmonary dysplasia

Gabriel Altit[1] · Shazia Bhombal[2] · Rachel K. Hopper[3] · Theresa A. Tacy[3] · Jeffrey Feinstein[3]

- N=61 BPD-PH (before era of screening).
  - 26.5 ± 1.5 weeks
- Follow-up (average 5 years), 28% mortality.
  - Age at diagnosis and severity of lung disease = increasing risk of death
- In survivors, 34% persistent PH and remaining on PH medications.
  - **16 developed Pulm Vein Stenosis (median 56 weeks) = LATE FINDING**

	All PH ($n = 61$)	Death ($n = 17$)	Alive ($n = 44$)	p value
Maternal/perinatal factors				
Gestational age (weeks)	26.4 (2.3)	26.6 (2.2)	26.4 (2.4)	0.70
Male (%)	32 (52)	13 (76)	19 (43)	0.02*
Admitted to LPCH NICU (%)	41 (67)	12 (71)	29 (66)	1.00
Birth weight (grams)	709 (322)	698 (319)	714 (327)	0.87
SGA (%)	23 (39)	7 (41)	16 (36)	0.77
Neonatal clinical characteristics				
NEC Grade 2 and more (%)	17 (28)	5 (29)	12 (27)	1.00
Use of post-natal steroids (%)	32 (63)	15 (88)	17 (39)	0.0005*
Mild BPD (%)	3 (4.9)	0 (0)	3 (7)	0.55
Moderate BPD (%)	4 (6.6)	0 (0)	4 (9)	0.57
Severe BPD (%)	54 (88.5)	17 (100)	37 (84)	0.17
*Invasive ventilation—36 weeks PMA (%)	19 (35)	7 (41)	12 (27)	0.55
*Non-invasive ventilation—36 weeks PMA (%)	35 (65)	10 (59)	25 (57)	0.55
Days of positive ventilation—invasive and non-invasive	120 (88)	157 (133)	114 (81)	0.37
Moderate to long-term outcomes				
ROP requiring treatment (%)	21 (34)	3 (18)	18 (41)	0.13
Home oxygen/ventilation after 1st hospitalization (%)	40/46 (87)	4 (100)	36/42 (86)	1.00
Hospitalization after discharge (%)	36/48 (75)	4/4 (100)	32/44 (73)	0.56
PICU at least once at re-hospitalization (%)	24/34 (71)	4/4 (100)	20/30 (67)	0.30
Pulmonary hypertension characteristics				
Pulmonary vein stenosis (%)	16 (26)	5 (29)	11 (25)	0.75
PMA at diagnosis of PH (weeks)	42 (38–52)	39 (38–42)	43 (39–56)	0.20
PMA at ECHO with worst PH (weeks)	50 (42–66)	48 (43–63)	49 (42–58)	0.81
sPAP at worst ECHO (mmHg)	76 (21)	86 (19)	71 (21)	0.01*
Worst sPAP/sBP ratio on ECHO during follow-up in %	92 (26)	109 (27)	83 (20)	0.0002*
Suprasystemic PH at worst ECHO (%)	11 (18)	8 (47)	3 (7)	0.001*
iNO use after 32 weeks PMA (%)	37 (61)	16 (94)	21 (48)	0.0009*
PH vasodilators (other than iNO) during NICU stay (%)	28 (46)	13 (76)	15 (34)	0.004*

All values are expressed as mean (SD) or median (IQR)

*p value < 0.05

Cardiac performance in the context of BPD-PH

Diminished right ventricular function at diagnosis of pulmonary hypertension is associated with mortality in bronchopulmonary dysplasia

Gabriel Altit[1,2], Shazia Bhombal[3], Jeffrey Feinstein[4], Rachel K. Hopper[4] and Theresa A. Tacy[4]

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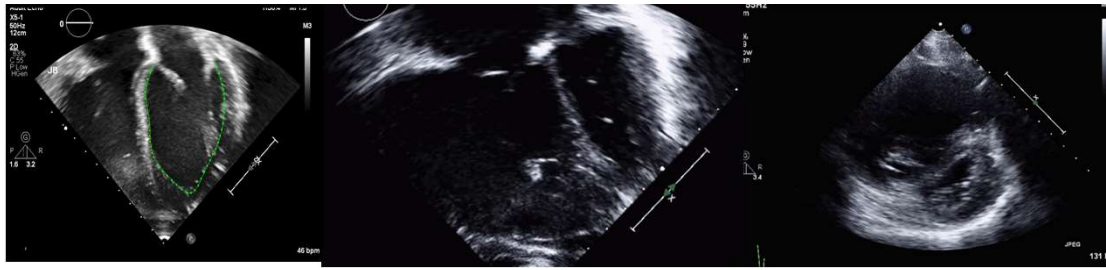


- Associated with mortality at diagnosis of PH:
  - RV function - TAPSE, FAC, Strain
  - PH severity (sPAP/sBP)
- These patients die from cardiac and/or respiratory failure

Table 3. Cox proportional hazards model – univariate analysis.

	HR	CI 5%	CI 95%	*p* value
GA at birth	0.96	0.9	1.02	0.16
Male status	0.24	0.07	0.85	0.03
Birth weight	1.00	0.998	1.001	0.76
SGA status	1.19	0.44	3.19	0.34
NEC	0.92	0.29	2.88	0.88
PMA at PH diagnosis	1.07	0.88	1.31	0.48
sPAP	1.03	1.002	1.05	0.04
sPAP/sBP	1.02	1.01	1.04	0.003
Eccentricity index	2.02	1.14	3.59	0.02
LV/RV ratio	0.16	0.03	0.9	0.04
TAPSE Z-score	0.65	0.50	0.85	0.002
FAC of RV	0.88	0.83	0.94	0.0001
RV pLS	1.22	1.06	1.41	0.007
RV pLSR	3.82	0.95	15.41	0.06
RV LSRe	0.29	0.10	0.83	0.02

Severity

- Abnormal performance may lead to decreased RV/LV output, end-organ damage
- Early recognition may allow targeted approach to management

Table III. Echocardiogram findings of pulmonary hypertension and its severity

None: RVSP <1/3 systemic pressure by TR gradient; septal position rounded and committed to LV; no RVH; normal RV size and function; If present, large VSD or PDA gradients suggesting <1/3 systemic RV pressures (Ao pressure – gradient = PA pressure)
Mild: RVSP 1/3-1/2 systemic pressure; septal flattening in systole, mild RVH and RV dilatation, RV function may be normal.*
Moderate: RVSP ½-2/3 systemic pressure; septum flat or with late systolic posterior bowing, moderate RVH or dilatation, RV may have reduced function*.
Severe: RVSP >2/3 systemic pressure; If present, shunt with predominant R-L gradient, pansystolic posterior septal bowing, Severe RVH, RV dysfunction, RV dilatation, "low-velocity" shunting across PDA or VSD.*

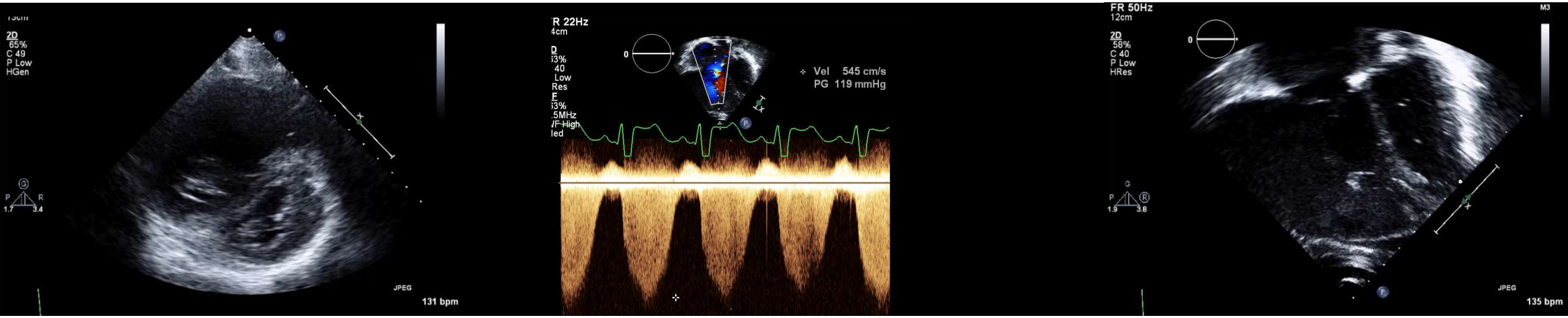


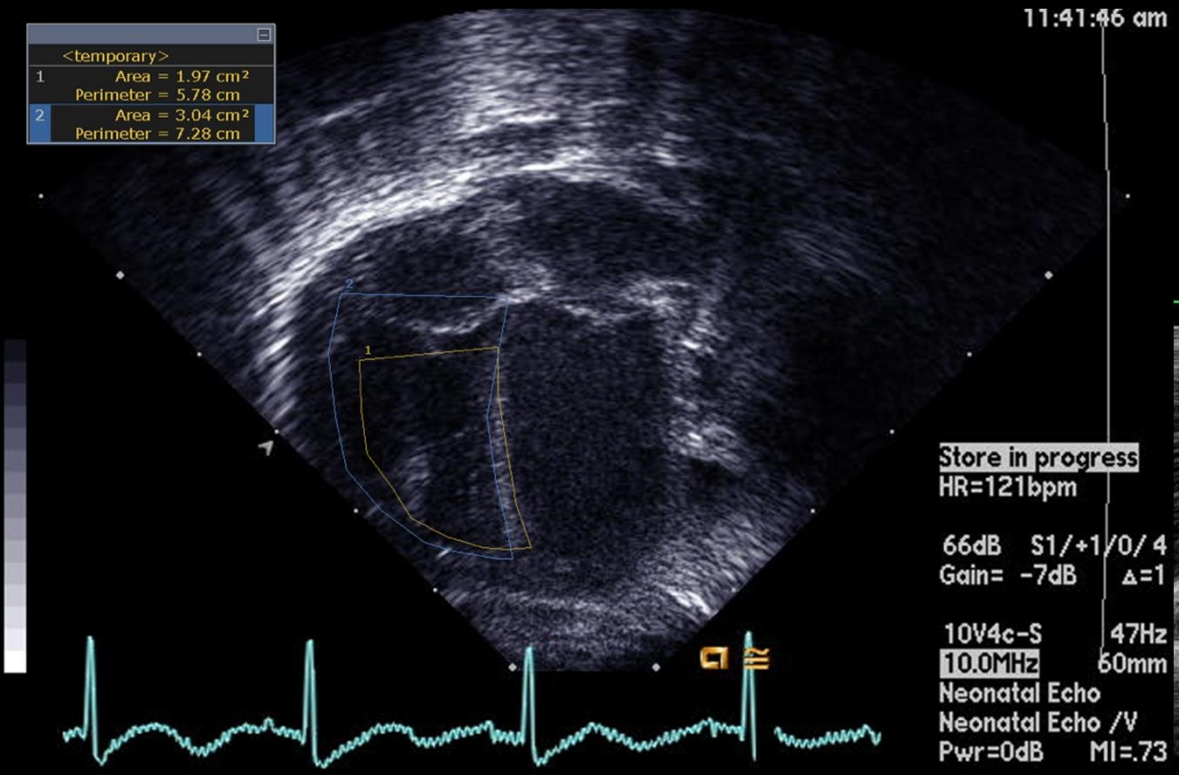
Table II. Echocardiographic assessment of pulmonary hypertension in preterm infants with BPD

Recommended measurements for each study

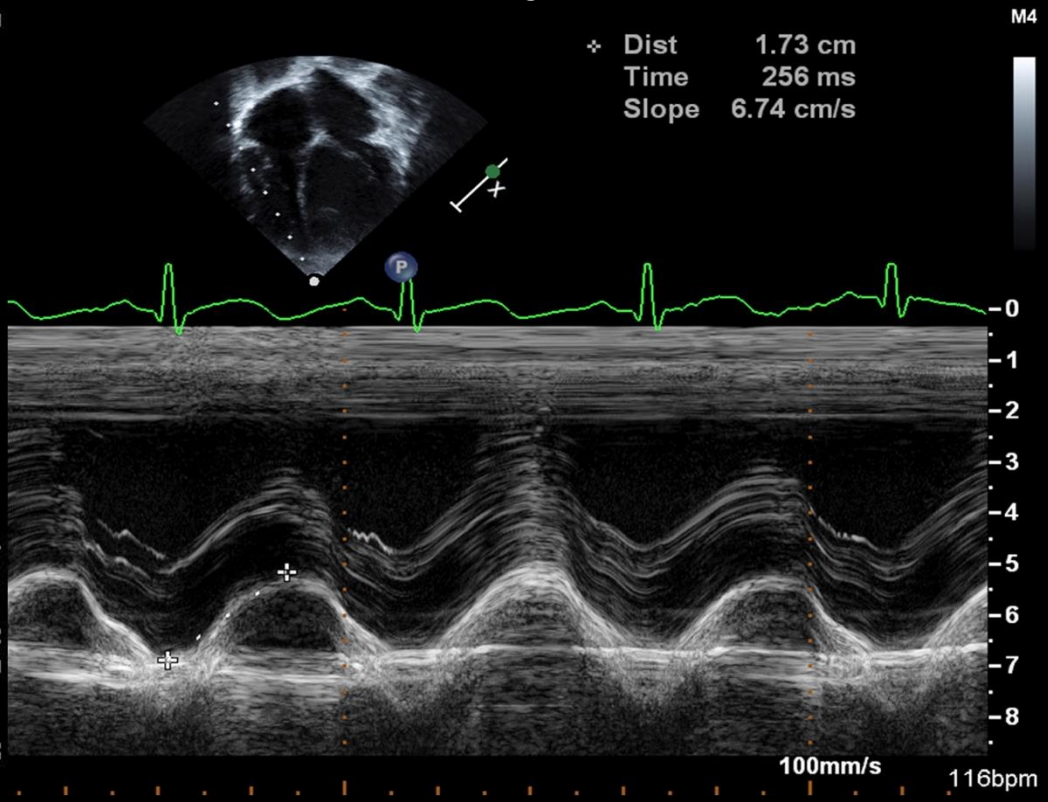
Echo measurements	Views	Information	Comments
Standard measures:			
RV size and RVH	PSAX, Apical 4 chamber	Multiple views	Qualitative measure
IVS position	PSAX; subcostal and apical 4 chamber views	Indirect estimation of RVSP	Flat, ~ 1/2 systemic RVSP; Flat-Posterior systolic bowing – systemic RVSP; severe posterior systolic bowing-LV pancaking- suprasystemic RVSP
RV function	PSAX, subcostal	RV systolic function	Qualitative measure (not very accurate)
TRJV	Ap4CH, PSAX, PLAX	Estimate RV systolic pressures using the Bernoulli equation. $RVSP = 4TRJV^2$	TR may not be always present even with PH and TRJV may be inconsistent for reliable quantification
PR gradient	RV outflow Doppler PSAX	Estimate mean and end diastolic PA pressures	Useful adjunct to TR gradient
Shunt gradient (VSD or PDA)	All views obtained with adequate Doppler alignment	Estimate RV and PA systolic pressures and physiologic role	Useful to assess RV pressures and potential contribution of shunt to PH
LV size and LVH, systolic and diastolic function	M-Mode, PSAX, Ap4CH, Doppler, tissue Doppler	Assess LV measurement	Important in severe PH with septal flattening or systemic hypertension
Pericardial effusion	Subcostal, PSAX, Ap4CH	Document presence and size	Associated with severe PH
Additional measurements of PH			
TAPSE	Ap 4CH- M-Mode or 2D Echo	Useful RV measurement for PH and longitudinal contractility	correlates with S' on tissue Doppler (mention utility of metric here)
RVFAC	Ap 4CH	Derived from planimetric areas of the RV in systole and diastole	Quantitative measure- requires good visualization of the RV walls
RV/LV ratios during systole and diastole	Ap 4CH and PSAX	RV/LV ratio and LV eccentricity index, a marker of dysfunction	LV eccentricity index is LV end systolic dimension parallel and perpendicular to the septum.
RVOT Doppler profile	PSAX, Ap4CH	Midsystolic notch correlates with PVR	Absent notch in established PH suggests pulmonary venous hypertension (79,80)
Tissue Doppler indices for RV and LV function	Ap 4 CH at mitral, septal and tricuspid valve annulus	LV and RV Diastolic function- E/E'; S'; E'/A'	Measure of LV and RV diastolic function
Tei index (by inflow Doppler)	Ap 4Ch- Tricuspid and mitral inflow Doppler	Systolic and diastolic Function	
RV MPI (tissue Doppler)	Ap 4CH	RV systolic and diastolic function	RV MPI is estimated from tricuspid valve inflow Tissue Doppler images. The time from cessation to the beginning of tricuspid inflow (a) and RV ejection time (b) are measured. RV MPI = (isovolumic contraction time + isovolumic relaxation time) / ejection time = (a - b) / b

Ap 4CH, apical 4-chamber; *IVS*, interventricular septum; *MPI*, myocardial performance index; *PA*, pulmonary artery; *PLAX*, parasternal long axis; *PR*, pulmonary regurgitation; *PSAX*, parasternal short axis; *PV*, pulmonary vein; *RA*, right atrium; *RVH*, right ventricular hypertrophy; *RVSP*, RV systolic pressure; *TAPSE*, tricuspid annular plane systolic excursion; *VSD*, ventricular septal defect.

FAC = (EDA – ESA) / (EDA) in 4 or 3 Chamber view



TAPSE



- **Normative values by GA for TAPSE and FAC**
- Usually FAC > 35% normal

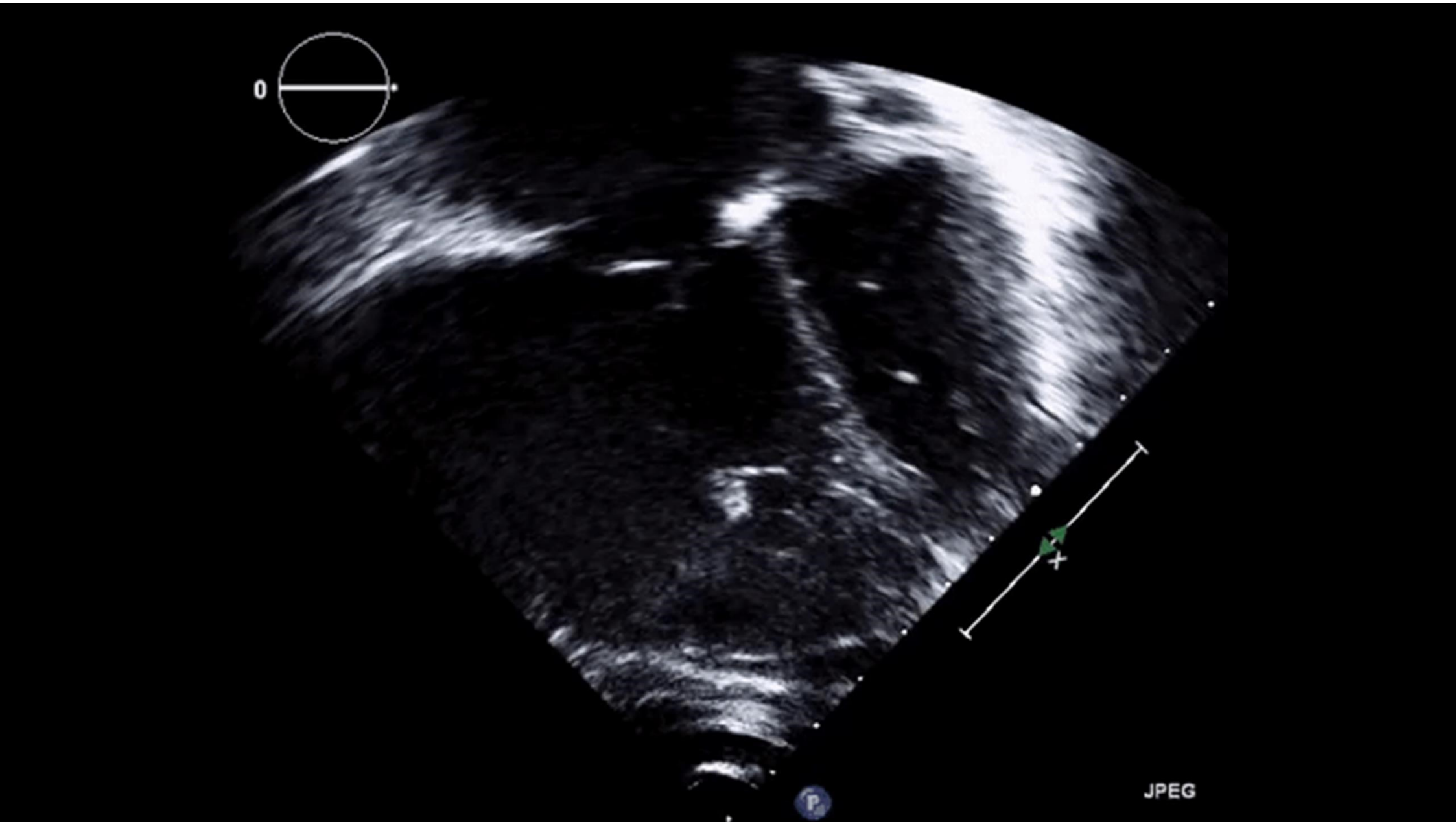
Lang, R et al. J Am Soc Echocardiogr 2005.18; 12:443-7

Systolic Right Ventricular Function in Preterm and Term Neonates: Reference Values of the Tricuspid Annular Plane Systolic Excursion (TAPSE) in 258 Patients and Calculation of Z-Score Values

Table 1. Classification table for TAPSE values[1]

Week of gestation	TAPSE, cm							Birth weight, kg observed		
	observed				predicted			mean	min.	max.
	n	mean	−2 SD	+2 SD	mean	−2 SD	+2 SD			
26	14	0.44	0.30	0.59	0.45	0.32	0.58	0.66	0.53	0.80
27	12	0.48	0.36	0.61	0.48	0.35	0.61	0.88	0.68	1.00
28	15	0.52	0.37	0.68	0.52	0.39	0.65	0.97	0.73	1.20
29	14	0.57	0.41	0.73	0.56	0.43	0.69	1.10	0.85	1.45
30	14	0.60	0.48	0.71	0.59	0.46	0.72	1.14	0.86	1.50
31	20	0.63	0.53	0.74	0.63	0.50	0.76	1.38	0.98	1.70
32	14	0.68	0.51	0.85	0.66	0.53	0.80	1.54	1.15	1.95
33	15	0.70	0.58	0.83	0.70	0.57	0.83	1.69	1.25	2.09
34	24	0.73	0.60	0.87	0.74	0.61	0.87	1.81	1.41	2.70
35	14	0.74	0.61	0.88	0.77	0.64	0.90	1.95	1.55	2.30
36	18	0.78	0.65	0.92	0.81	0.68	0.94	2.13	1.62	3.04
37	14	0.82	0.68	0.96	0.84	0.71	0.98	2.31	1.78	3.20
38	13	0.86	0.75	0.97	0.88	0.75	1.01	2.50	1.96	3.25
39	19	0.90	0.77	1.02	0.92	0.79	1.05	2.73	2.12	3.14
40	20	0.95	0.81	1.10	0.95	0.82	1.08	3.32	2.66	3.83
41	18	1.03	0.85	1.21	0.99	0.86	1.12	3.64	2.85	4.20

Mean, minimum and maximum birth weight were calculated for several weeks of gestation.
[1] The observed and predicted means and the 95% confidence intervals are presented for each gestational week.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ARTICLE

The biventricular contribution to chronic pulmonary hypertension of the extremely premature infant

Gabriela de Carvalho Nunes[1,2], Punnanee Wutthigate[1,2,3], Jessica Simoneau[1,2], Adrian Dancea[1,4], Marc Beltempo[1,2], Claudia Renaud[1,4] and Gabriel Altit[1,2]✉

- Once screening established – retrospective study (MCH)
  - 222 <29 weeks
  - 144 free of PH (65%)
  - 78 with “HP” (35%) - n=6 mortality post-diagnosis (less than literature; 8%)
  - n=24 > 2/3 systémique (11%) – Minority with significant / severe PH
  - Small for gestational age, duration of ventilation and BPD severity associated

Table 2. Echocardiographic measurements of patients by pulmonary hypertension status.

	Available data (*N* = 222)	**Free of PH (*N* = 144)**	**Any PH (*N* = 78)**	***p*-value**	**No significant* PH (*N* = 198)**	**Significant* PH (*N* = 24)**	***p*-value**
PMA at echo	222	37.1 (2.1)	37.4 (2.8)	0.38	37.3 (2.4)	37.0 (2.0)	0.62
Weight at echo (kg)	218	2.5 (0.5)	2.4 (0.7)	0.27	2.5 (0.6)	2.2 (0.5)	**0.008**
Systolic BP at echo (mmHg)	215	78 (11)	78 (11)	0.67	78 (11)	75 (10)	0.12
Diastolic BP at echo (mmHg)	215	43 (11)	45 (13)	0.18	44 (12)	42 (12)	0.57
Heart rate at echo (bpm)	191	153 (13)	159 (18)	**0.01**	156 (15)	153 (18)	0.605
On room air or low flow O2 at Echo	201	93 (64%)	40 (51%)	**0.03**	125 (63%)	8 (33%)	**0.009**
PDA	211	23 (16%)	37 (47%)	**<0.001**	43 (21%)	17 (70%)	**<0.001**
PDA size (mm)	211	0.2 (0.1)	0.2 (0.1)	0.28	1.7 (0.6)	2.5 (0.9)	**0.001**
Markers of pulmonary pressure							
sPAP estimated by TR	169	27.6 (6.0)	41.4 (15.9)	**<0.001**	30.2 (9.0)	55.7 (17.2)	**<0.001**
sPAP/sBP ratio	164	0.4 (0.1)	0.5 (0.2)	**<0.001**	0.4 (0.1)	0.8 (0.2)	**<0.001**
Eccentricity index	211	1.1 (0.1)	1.3 (0.2)	**<0.001**	1.2 (0.2)	1.3 (0.2)	**0.002**
LV and RV systolic function							
LV shortening fraction in % by M-Mode	211	36.0 (6.3)	37.0 (7.0)	0.32	36.2 (6.4)	38.0 (7.7)	0.19
EF by 5/6	192	63.9 (8.6)	64.9 (7.6)	0.42	64.0 (8.3)	66.3 (7.5)	0.24
TAPSE	206	0.9 (0.3)	0.9 (0.2)	0.78	0.9 (0.3)	0.8 (0.2)	**0.05**
FAC of RV	199	47.4 (7.5)	45.9 (8.1)	0.18	47.3 (7.4)	43.1 (9.3)	**0.02**
LV and RV measurements							
LV EDV by 5/6 (mL)	193	5.5 (1.6)	5.6 (2.0)	0.74	5.5 (1.7)	5.5 (2.0)	0.94
LV ESV by 5/6 (mL)	193	2.3 (0.9)	2.2 (0.9)	0.4	2.2 (0.9)	2.2 (1.1)	0.82
RV End diastolic area	192	4.3 (1.0)	4.4 (1.0)	0.46	3.1 (0.8)	3.3 (1.0)	0.42
RV End systolic area	193	2.5 (0.8)	2.4 (0.7)	0.27	2.5 (0.8)	2.4 (0.8)	**0.04**

		LV-pLS	LV-pLSR	RV-pLS	RV-pLSR	RV-FAC
Unadjusted	Any PH	β: 1.1 $p = 0.10$	β: 0.07 $p = 0.11$	β: 0.74 $p = 0.37$	β: 0.04 $p = 0.42$	β: −1.89 $p = 0.13$
Adjusted		β: 0.94 $p = 0.03$	β: 0.08 $p = 0.009$	β: 0.35 $p = 0.53$	β: 0.03 $p = 0.66$	β: −1.03 $p = 0.08$
Unadjusted	sPAP > 2/3 systemic	β: 2.31 $p = 0.02$	β: 0.06 $p = 0.36$	β: 3.54 $p = 0.004$	β: 0.13 $p = 0.10$	β: −6.8 $p < 0.001$
Adjusted*		β: 3.05 $p = 0.006$	β: 0.12 $p = 0.01$	β: 3.83 $p = 0.009$	β: 0.18 $p = 0.33$	β: −6.8 $p = 0.003$

*Adjusted for: Diastolic blood pressure at echocardiography, PMA at echocardiography, PDA presence at ECHO and exposure to systemic steroids.
FAC fractional area change, *LV* left ventricle, *pLS* peak longitudinal strain, *pLSR* peak longitudinal strain rate, *RV* right ventricle, *sPAP* systolic pulmonary arterial pressure.

- At screening ECHO, alteration of RV and LV function
- Complex phenotype with bi-ventricular involvement
  - Consequence or source of the disease?
  - Why: prematurity, inflammation, shunt physiology, nutrition, extra-uterine growth, mechanical ventilation, oxygen, steroid, prenatal factors?

Early Cardiac Function and Pulmonary Hypertension are Associated with Adverse Cardio-Respiratory Outcomes in Extremely Preterm Infants

Short title: Early Echocardiography in Extremely Preterm Infants.

Authors:
Shiran Sara Moore, MD[1,3], Gabriela De Carvalho Nunes, MD[1], Adrian Dancea, MD[2], Punnanee Wutthigate, MD[4], Jessica Simoneau, DIT[2], Marc Beltempo, MD[1], Guilherme Sant'Anna[1], MD Gabriel Altit, MD[1]

- Retrospective
- Echo early (21 days)
- 176 <29 weeks
  - ECHO < 21 days
  - 59 (death or PH)
  - Early signs of PH associated with later death or PH, possibly an early process in the disease.

Manuscript is submission

	No for parameter	Death or BPD-related PH (n=59)	Alive without BPD-related PH (n=117)	p-value
Age in days at analyzed ECHO	176	7 [4-13]	11 [6-14]	0.01
Weight at ECHO in grams	176	840 (248)	893 (212)	0.14
Markers of PDA significance				
LA/Ao	166	1.55 (0.36)	1.51 (0.34)	0.47
Ductus patent	171	52/56 (92.9)	102/115 (88.7)	0.59
Ductal size in cm	151	0.23 (0.08)	0.21 (0.06)	0.22
LV output in mL/kg/min	96	299 (131)	327 (164)	0.40
Markers of RV pressure and dilation				
Estimated sPAP at ECHO in mmHg	105	41.6 (13.7)	33.7 (12.2)	0.003
LV-EI	137	1.35 (0.2)	1.26 (0.19)	0.02
EI ≥ 1.3	137	26/47 (55.3)	31/90 (34.4)	0.03
Flat or bowing septum at peak systole	163	19/54 (35)	20/109 (18)	0.02
Ratio of RV/LV diameters in PSAX	115	0.67 (0.5)	0.47 (0.15)	0.002

Role of left atrial hypertension in pulmonary hypertension associated with bronchopulmonary dysplasia

Rachel T. Sullivan[1]*, Megha D. Tandel[2], Shazia Bhombal[3], Gregory T. Adamson[4], Derek B. Boothroyd[2], Michael Tracy[5], Amanda Moy[3] and Rachel K. Hopper[4]

- 34 with BPD-PH
- Cath < 2 years
- 11 (33%) with LAH
- Post-capillary component

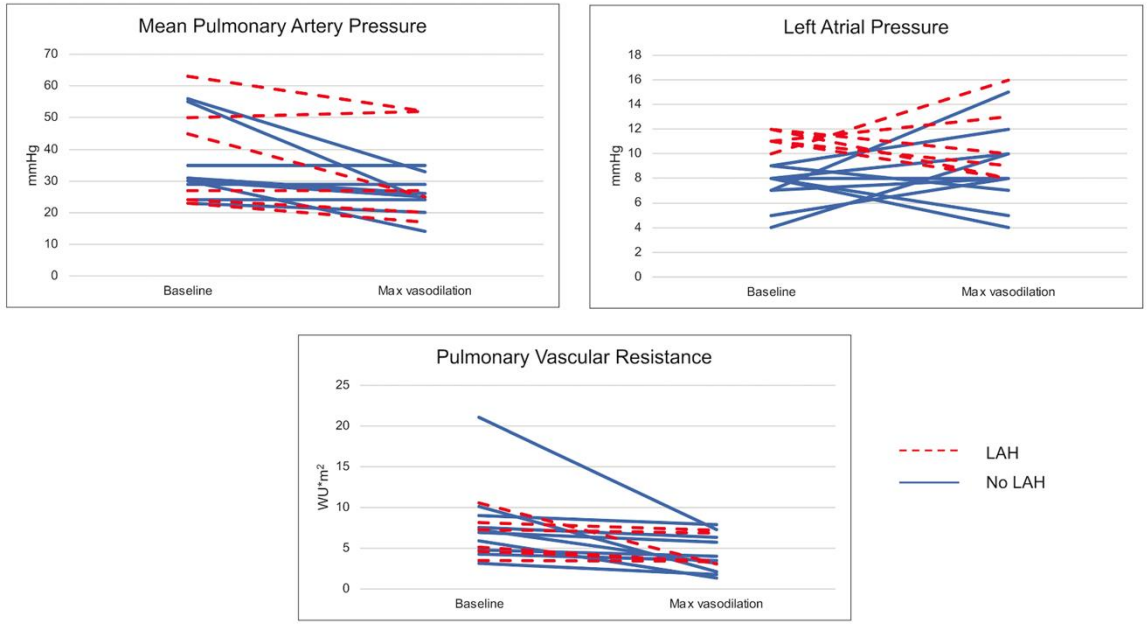

FIGURE 2
Hemodynamic changes with acute vasodilator testing. Changes in mean pulmonary artery pressure, left atrial pressure, and pulmonary vascular resistance are demonstrated at baseline and with maximal vasodilation (100% FiO2 ± inhaled nitric oxide) utilized in acute vasodilator testing, which was performed in 16 patients.

Assessment of LV side

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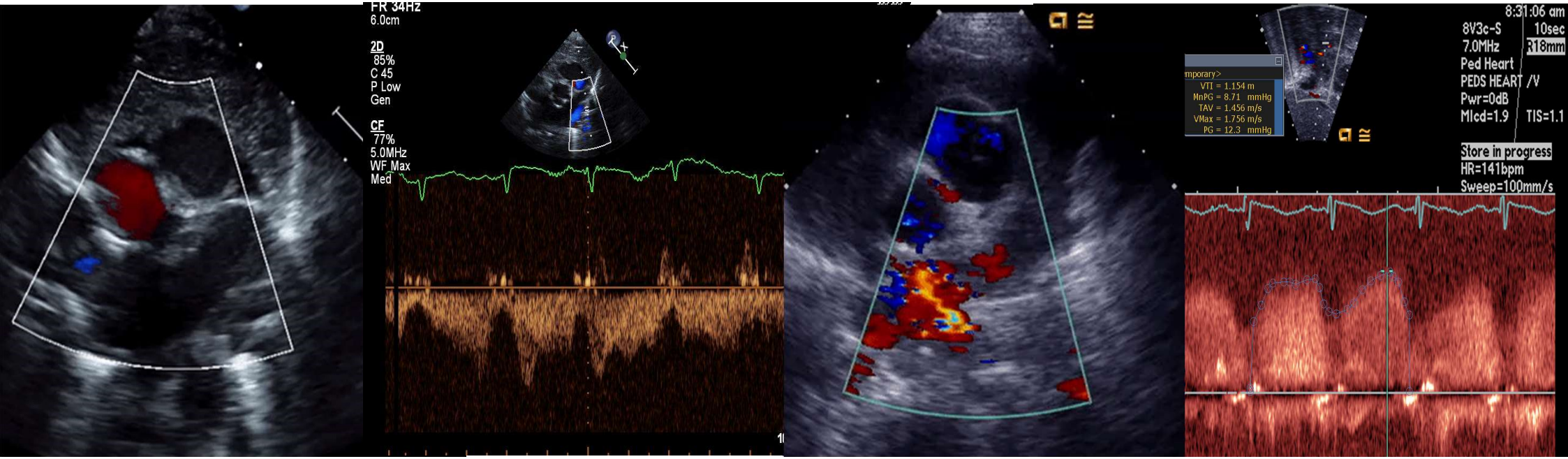
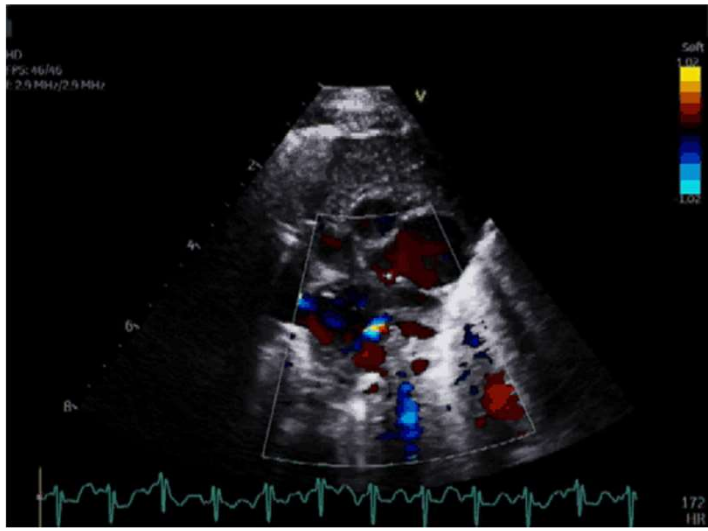
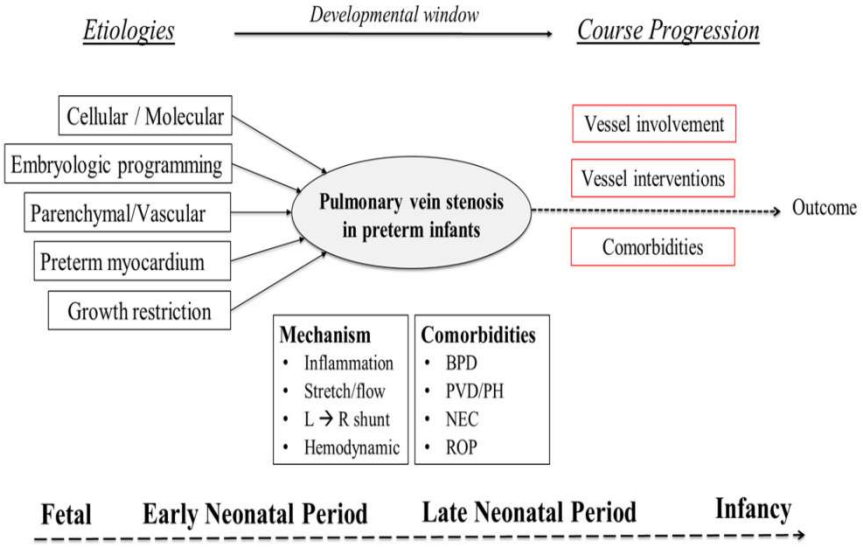
- In the context of PH, must assess LV sided structures
- LV dimensions and function, pulmonary venous flow, mitral regurgitation / stenosis



Pulmonary Vein Stenosis

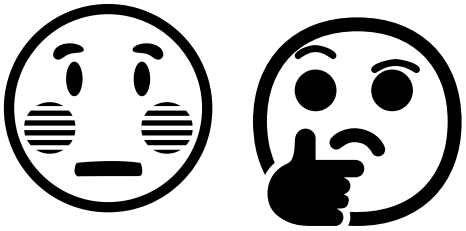
- Increasingly recognized entity in context of BPD: inflammatory, genetic, fibrosis, metabolic?
- Usually appear later (often at 3-6 months corrected age)
- Diagnosis difficulty – suspicion needs to be on high level:
  - Pulmonary edema
  - Worsening with pulmonary vasodilation
  - Often underlying pulmonary arterial disease too
- Can be suspeted by CT or ECHO (but if atresia may not see it on ECHO).
  - Always Doppler All Osteum if possible at each ECHO (36 weeks and follow-up).
- Difficult management – not a lot of data
  - Cath? Surgery? Inflammatory (Sirolimus / steroids?)
- Worst prognosis





Vyas-Read S, Varghese NP, Suthar D, Backes C, Lakshminrusimha S, Petit CJ, Levy PT. Prematurity and Pulmonary Vein Stenosis: The Role of Parenchymal Lung Disease and Pulmonary Vascular Disease. Children (Basel). 2022 May 12;9(5):713.

My baby with BPD has PH, what do I do?



Journal of Perinatology
https://doi.org/10.1038/s41372-020-00791-z

CORRESPONDENCE

Management of chronic pulmonary hypertension in neonates with bronchopulmonary dysplasia: perspectives of neonatologists with hemodynamic expertise and pediatric cardiologists

Audrey Hébert[1] · Christine Drolet[1] · Gabriel Altit[2] · Andréanne Villeneuve[3] · Anie Lapointe[3] · Brahim Bensouda[4] · Regan E. Giesinger[5] · Patrick J. McNamara[5]

Journal of Perinatology (2018) 38:361–367
https://doi.org/10.1038/s41372-017-0025-3

ARTICLE

Practices surrounding pulmonary hypertension and bronchopulmonary dysplasia amongst neonatologists caring for premature infants

Gabriel Altit[1,2] · Henry C. Lee[3] · Susan Hintz[4] · Theresa A. Tacy[5] · Jeffrey A. Feinstein[6] · Shazia Bhombal[3]

- Despite guidelines - many variations in the evaluation and management of these patients.

- My “educated” approach to these patients + guidelines

Prevention

- BPD prevention is key – usually: no BPD = no PH
- PH usually reflects lung disease
  - Airway and respiratory care is key in prevention
  - Protocolized approach to prematurity, avoid lung injury
  - Bubble CPAP associated with drop in BPD in many centers adopting it, non-invasive support
  - Consider dexamethasone in infants still mechanically ventilated > 7 days of life to extubate or decrease pulmonary inflammation
  - Track growth (not excessive, not too much)
    - Judicious use of fluids

Management

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- PH will not get better if lungs do not get better
- PAH medications are not the initial focus, treat the baby and the lungs
  - Avoid hypoxemia: aim 92-95%
  - Airway evaluation
  - Avoid reflux / aspiration
  - Maximize calories but do not "flood" with fluids. Track the growth and make sure weight-to-height ratio appropriate (avoid obesity and failure to thrive)

Recommendation #5: Further evaluation and treatment of comorbidities that impact the severity of lung disease should be undertaken with the diagnosis of BPD-PH infants before the initiation of pulmonary arterial hypertension (PAH)-targeted therapy. Studies should include evaluation for intermittent or sustained hypoxemia, aspiration, gastroesophageal reflux disease, structural airways disease, pulmonary artery and vein stenosis, left ventricular diastolic dysfunction, and aortopulmonary collaterals. (class 1, LOE B)

Recommendation # 7: Supplemental oxygen therapy should be used to avoid episodic or sustained hypoxemia and with the goal of maintaining oxygen (O_2) saturations between 92%-95% in patients with established BPD and PH. (class 1, LOE B)

CASE – Kevin – BPD-PH initial management

- Prolonged gavage time in naso-gastric to avoid aspiration
  - Consider saliva aspiration – may need Botox
- Aimed saturations ≥ 92% for > than 95% of time
- Rule out pulmonary venous anomaly, consider CT scan
- Evaluated for upper airway obstruction with ENT (scope)
- Vaccination for avoidance of pulmonary infections
- Optimize nutrition (less volume more concentrate, aim normal weight/length ratio)
- Although evidence is weak – we consider initiation of HCTZ/Spironolactone = heart failure management - edema
  - ?LV diastolic dysfunction
  - We have seen patients dramatically deteriorate upon abrupt stop of diuretics.

CASE – Kevin – Acute PH crisis

- Acute PH: Hypoxic resp failure if ASD Right to Left, poor cardiac output and heart failure if no (or insufficient) pop-off. Hypotensive, cyanotic and/or poorly perfused
- Stress (viral, surgery, infection) – can trigger acute PH exacerbation (crisis)
  - Again: ventilation / airway care priority
  - May need re-intubation → some eventually tracheostomy
- During acute PH crisis: sedation, aggressive chest physio and airway toilette + recruitment to minimize V/Q mismatch
  - Optimize ventilation
  - Optimize hemoglobin > 100
  - iNO 20 ppm – will reach vessels of lung areas that are ventilated (VQ mismatch)
  - Consider Milrinone – Lusitropic medication to promote RV function and filling
  - Consider stress dose hydrocortisone 30 mg/m2/day
  - Rule out concomitant infection +/- Abx (urine, viral, bacterial, pneumonia, etc.)
  - Adjust nutrition, possibly induce diuresis with furosemide (evidence = poor)

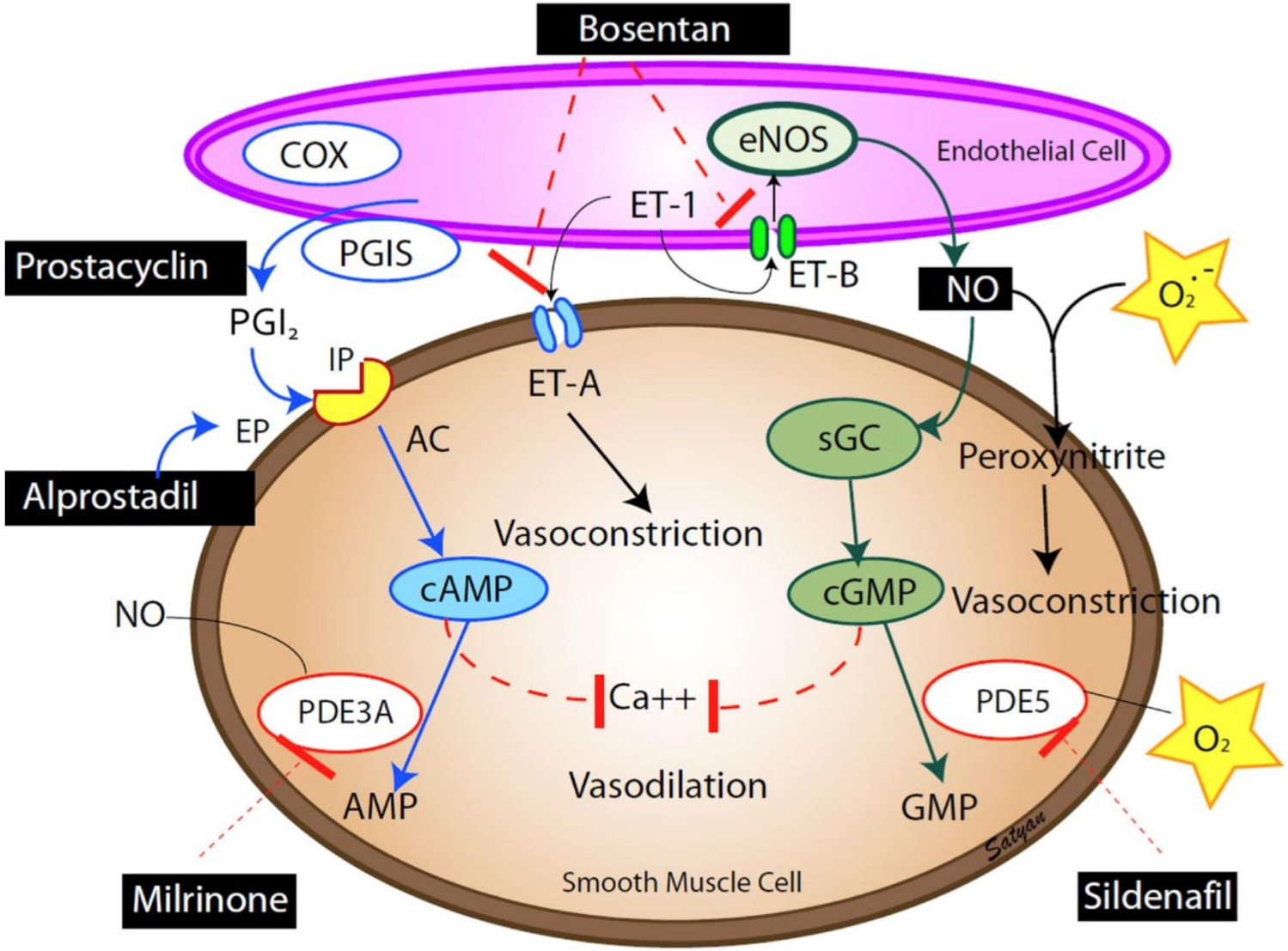
Evaluation and Management of Pulmonary Hypertension in Children with Bronchopulmonary Dysplasia

Recommendation # 8: iNO should be used for acute PH crises and weaned after stabilization. (class I, LOE B) The addition of sildenafil therapy may be helpful in weaning from nitric oxide. (class IIa, LOE B)

Recommendation # 9: PH-targeted therapy should be considered for infants with BPD and sustained PH after optimal treatment of underlying respiratory and cardiac disease. (class I, LOE B) Pharmacologic therapy should be initiated in patients with evidence of significantly elevated pulmonary vascular resistance and right ventricular impairment (moderate hypertrophy or dysfunction) not related to left heart disease or pulmonary vein stenosis. (class I, LOE B) (**Table IV**)

In most current settings:

- If RV failure and respiratory optimized, consider pulmonary vasodilation by expert team and close follow-up (ensure no pulmonary edema if LV disease)
  - Sildenafil often first-line. Usually, if significant PH (>2/3 systemic) and/or RV dysfunction
  - Before adding another agent (Bosentan-ERA / Prostacyclin-Treprostinil), consider catheterization study
  - Cath with cardiac anesthesia! High-risk.



Satyan Lakshminrusimha and Martin Keszler NeoReviews December 2015, 16 (12) e680-e692; DOI: https://doi.org/10.1542/neo.16-12-e680

Names	Dose/titration	Side effects	Comments
Sildenafil phiosphodiesterase-5 inhibitor	PO: 1 mg/kg 6-8 h; start with low dose (0.3-0.5 mg/kg/dose) and increase gradually to 1 mg/kg/dose as tolerated; slower as outpatient. Maximal dose of 10 mg q 8 h per EMA guidelines for infants. Intravenous:0.25-0.5 mg/kg/dose q 6-8 h (titrate slowly and administer over 60 min.	Hypotension, GER, irritability (headache), bronchospasm, nasal stuffiness, fever, rarely priapism	Monitor for adverse effects, lower the dose or switch to alternate therapy if not tolerated
Bosentan (Endothelin receptor antagonist)	1 mg/kg PO q 12 h as starting dose; may increase to 2 mg/kg BID in 2-4 wk, if tolerated and liver enzymes stable.	Liver dysfunction especially during viral infections, VQ mismatch, hypotension, anemia (edema and airway issues rare in infants)	Monitor LFTs monthly (earlier with respiratory infections); monitor CBC quarterly. Teratogenicity precautions for caregivers
Inhaled Iloprost	2.5-5 mcg every 2-4 h. Can be given as continuous inhalation during mechanical ventilation. Can titrate dose from 1-5 mcg and frequency from every 4 h to continuous.	Bronchospasm, hypotension, ventilator tube crystallization and clogging, pulmonary hemorrhage, prostanoid side effects (GI disturbances), may be teratogenic to caregivers	Need close monitoring for clogged tubing, may need further dilution. May need bronchodilators or inhaled steroid pretreatment with bronchospasm.
Intravenous Epoprostenol (Flolan)	Start at 1-2 ng/kg/min, titrate up slowly every 4-6 h to 20 ng/kg/min; need to increase dose at regular intervals because of tachyphylaxis. Further increases as guided by clinical targets and avoiding adverse effects.	Hypotension, VQ mismatch, GI disturbances. Needs dedicated line, very short half-life with high risk for rebound PH with brief interruption of therapy; line related complications include infection, clogging, breaks in line, thrombosis, arrhythmia)	Monitor closely if added to other vasodilator therapies, such as milrinone; careful attention to line care is essential.
Treprostinil (Remodulin) IV or Subcutaneous	Start at 2 ng/kg/min and titrate every 4-6 h up to 20 ng/kg/min, then slow increase dose as tolerated (dose often 1.5-2 times greater than equivalent epoprostenol dose, if switching medications)	SQ: local site pain; IV: similar risks as with epoprostenol, but treprostinil has a longer half- life, which reduces risk for severe PH with interruption of infusion	Site pain managed with local and systemic measures
Milrinone (IV) (phosphodiesterase-3 inhibitor)	0.15-0.5 mcg/kg/min –lower dosage range when used with other vasodilators	Arrhythmogenic; systemic hypotension and high risk for decreased myocardial perfusion; caution with renal dysfunction	May need to add a pressor, such as vasopressin, to mitigate effects of decrease in systemic pressures.

My approach regarding chronicity

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- Multi-disciplinary care and follow-up: occupational therapy, ENT (airway evaluation), GERD/aspiration evaluation and management, respiratory medicine, cardiology, development.
- Prevent severe flare-up with viral / respiratory infections:
  - Rigorous vaccination child/family (pneumococcal, influenza, RSV, COVID)
  - Avoidance of crowded areas (shopping center, kindergarten, parties).
- Ensure saturation $\geq$ 92 % for > 95% of the time (avoid vasculature vaso-spasm).
  - Often require Home Oxygen support.
- Parental education:
  - Recognize sign of PH, resp distress or RV failure: diaphoresis, retraction, work of breathing, cyanosis, abnormal neurological status, failure to thrive, decreased energy, decreased perfusion
  - Teach basic CPR to families of infants known with established PH
- Follow-up q1-2 months until stable cardiac function, and then can space out.

My approach

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- Travelling by plane can be complicated by PH crises
  - Assessment for fit to travelling with hypoxic challenge once PH infra-systemic and stable in room air
- Sildenafil can accentuate GERD, ensure to manage reflux and follow growth: avoid abnormal Weight-Length Ratio.
  - Energy needs can be up to 140 kcal/kg/d (Small volumes but high caloric fortification)
- Evidence regarding diuretics is controversial: we locally use it (absence of evidence).
- Follow Hgb (ensure no anemia), regular blood gaz and electrolytes (especially if on diuretics),
  - Some centers follow BNP (NT-proBNP) for RV overload (baseline and at follow-ups).
- No elective surgery until normal PA pressure. Cardiac Anesthesia if needs OR.
- Consider: Genetic (BMPR?), TSH, Sweat test, occasional chest X-ray to rule out aspiration (especially if oral challenges) and CT scan of chest if progressive worsening of clinical status.

Many resources on PH

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CardioNeo

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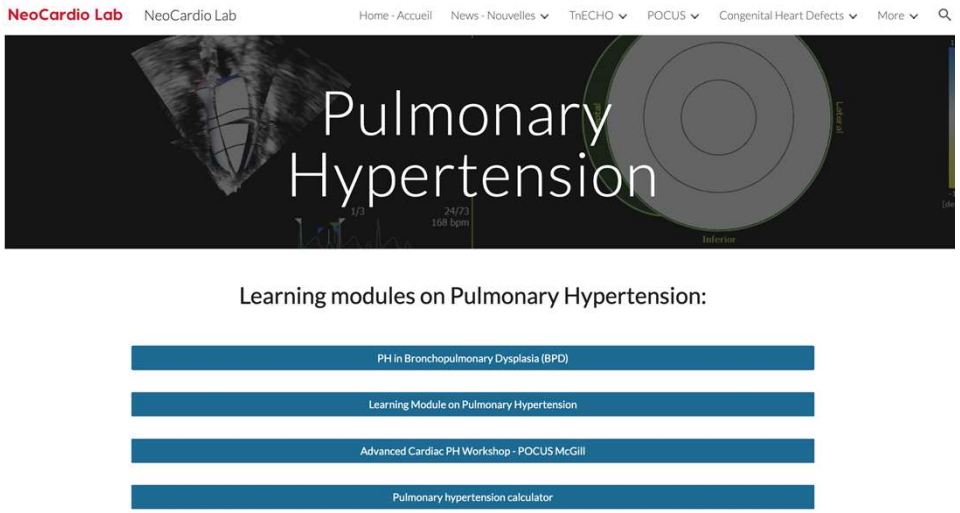
ANDROID APP ON Google play

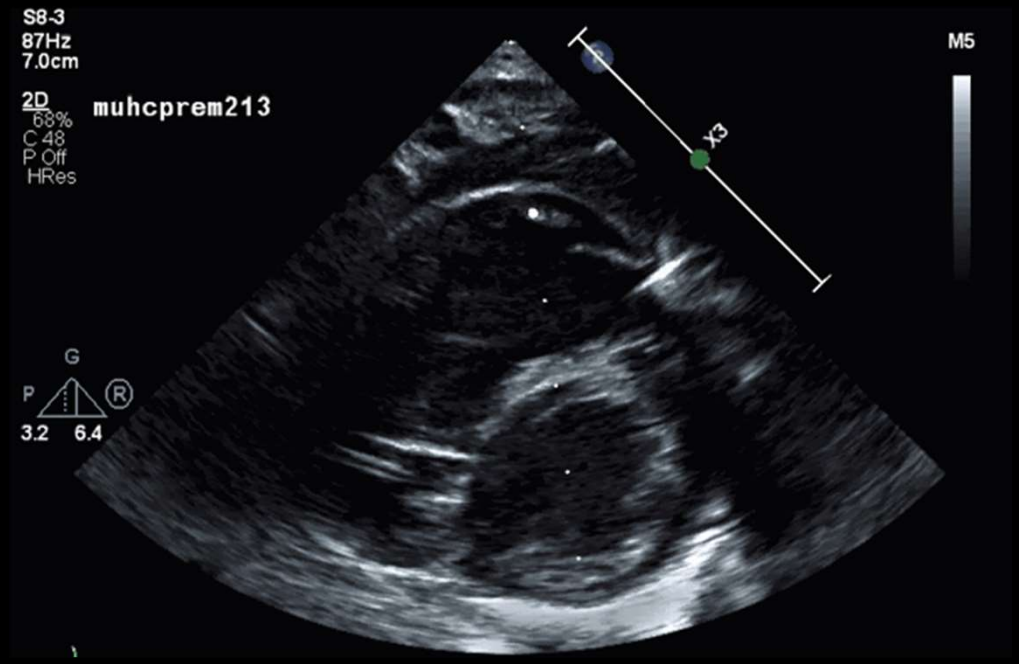


Many knowledge gaps…

Key advices:
- Keep high level of suspicion
- Do not loose these patients to follow-up

Story of Massimo, Priyanka and Anthony

- Born at 24 weeks
- ”Severe” BPD (CPAP at 36 weeks – 23%)
- Went home in room air
- Participated to a prospective natural history research project with ECHO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muhcprem213
M5
x3
G
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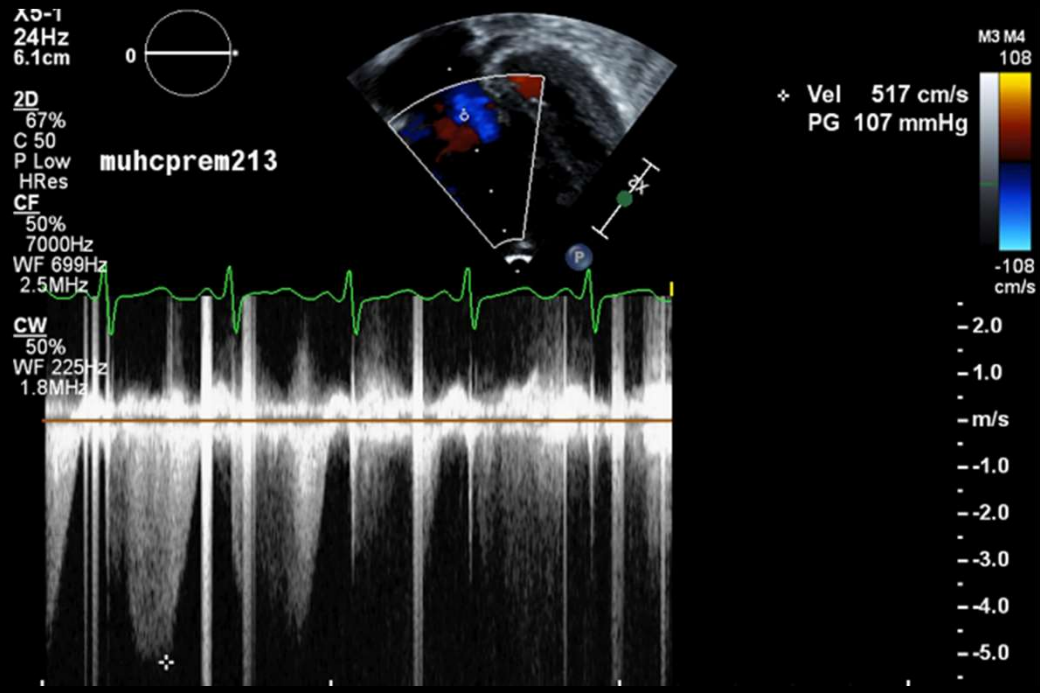
6.4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2D
67%
C 50
P Low
HRes
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CF
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2.5MHz
CW
50%
WF 225Hz
1.8MHz
x4
P
Vel 517 cm/s
PG 107 mmHg
M3 M4
108
-108
cm/s
2.0
1.0
m/s
-1.0
-2.0
-3.0
-4.0
-5.0

Story of Massimo

- PH – Sneaky disease
  - “looks asymptomatic”
  - Diagnosis at 9 months
  - Supra-systemic PH
  - Almost arrested in cath
- 1 year on Treprostinil post cath + Sildenafil
- Today:
  - Off Treprostinil and Sildenafil
  - Normal follow-up ECHO 1 year post-treatment
  - Followed 1/year
- Thanks to family to share their story

Cardiac contributor in adult ex-premature newborn

Association of Bronchopulmonary Dysplasia and Right Ventricular Systolic Function in Young Adults Born Preterm

Daniela Ravizzoni Dartora, PhD; Adrien Flahault, MD, PhD; Thuy Mai Luu, MD; Anik Cloutier, MSc; Jessica Simoneau, MSc; Michel White, MD; Anie Lapointe, MD; Andréanne Villeneuve, MD; Jean-Luc Bigras, MD; Gabriel Altit, MD; and Anne Monique Nuyt, MD

- Prospective study
  - HAPI cohort
- 86 adults premature <30 week (23 yr) vs terme (23 yr).
- RV function and dimension alterations
  - TAPSE
  - S' by Tissue Doppler
- Do not loose track of these infants, they may have life-long involvement

TABLE 2] RV Measurements According to Term or Preterm Status

Variable	Term		Preterm		*P* Value
	ND	Mean ± SD	ND	Mean ± SD	
M-mode dimensions					
RV internal diameter, mm	1 (1%)	23.3 ± 3.7	1 (1%)	21.5 ± 3.4	.0010[a]
RV internal diameter (indexed), mm/m^2	1 (1%)	13.1 ± 2.1	1 (1%)	12.9 ± 2	.68
Functional 2D assessment					
RV end-diastolic area, mm^2	27 (32%)	21.1 ± 5.4	19 (22%)	18.7 ± 4.3	.0097[a]
RV end-diastolic area (indexed), mm^2/m^2	27 (32%)	11.8 ± 2.5	19 (22%)	11.2 ± 2.2	.20
RV end-systolic area, mm^2	27 (32%)	12.9 ± 3.7	20 (23%)	11.5 ± 3	.019
RV end-systolic area (indexed), mm^2/m^2	27 (32%)	7.2 ± 1.71	20 (23%)	6.83 ± 1.4	.19
RV longitudinal RV length in diastole, mm^2	20 (24%)	79 ± 8.8	15 (17%)	76 ± 10.3	.067
RV longitudinal RV length in diastole (indexed), mm^2/m^2	20 (24%)	44.8 ± 5.1	15 (17%)	45.6 ± 5.8	.39
Systolic function					
RV TAPSE, mm	14 (16%)	20.7 ± 3.9	14 (16%)	19.1 ± 3.5	.012[a]
RV TAPSE < 16 mm	14 (16%)	6 (8%)	14 (16%)	15 (21)	.057
RV systolic/diastolic duration ratio, %	20 (24%)	70.3 ± 18.8	18 (21%)	79.2 ± 23.7	.0091[a]
RVOT VTI, cm	2 (2%)	18.2 ± 2.5	3 (3%)	17.6 ± 3.1	.13
RV fractional area change, %	27 (32%)	38.4 ± 8.3	20 (23%)	38.2 ± 8.3	.89
RV s', cm/s	5 (6%)	13.5 ± 1.8	2 (2%)	12.5 ± 1.6	.0007[a]
Diastolic function					
RV TV E/A	8 (9%)	1.75 ± 0.44	6 (7%)	1.74 ± 0.36	.89
RV TV deceleration time, ms	8 (9%)	208 ± 50	6 (7%)	193 ± 51	.057
RV TV E/e'	11 (13%)	3.66 ± 0.75	6 (7%)	3.71 ± 0.68	.67
Myocardial performance index by tissue Doppler imaging					
RV myocardial performance index	14 (16%)	0.453 ± 0.123	12 (14%)	0.466 ± 0.122	.53

TABLE 4] RV Systolic Function According to BPD Status in Preterm Participants

Variable	Term		Preterm: No BPD		Preterm: BPD		*P* Value[a]
	ND	Mean ± SD	ND	Mean ± SD	ND	Mean ± SD	
Systolic function							
RV TAPSE	14 (16%)	20.7 ± 3.9	11 (19%)	19.3 ± 3.3	3 (11%)	18.9 ± 3.9	.016[b]
RV systolic/diastolic duration ratio, %	22 (26%)	68.4 ± 15.6	16 (28%)	75 ± 14.3	5 (18%)	76.9 ± 17.8	.011[b]
RVOT VTI, cm	2 (2%)	18.2 ± 2.5	3 (5%)	18 ± 3.4	0	16.7 ± 2.4	.024[b]
RV fractional area change	27 (32%)	38.4 ± 8.3	16 (28%)	37.1 ± 7.6	4 (14%)	40.1 ± 9.2	.60
RV s′, cm/s	5 (6%)	13.5 ± 1.8	2 (3%)	12.7 ± 1.4	0	12.3 ± 2.0	.0006[b]
Diastolic function							
RV TV E/A	8 (9%)	1.75 ± 0.44	5 (9%)	1.71 ± 0.34	1 (4%)	1.82 ± 0.41	.69
RV TV deceleration time, ms	8 (9%)	208 ± 50	5 (9%)	191 ± 48	1 (4%)	197 ± 57	.14
RV TV E/E′	11 (13%)	3.66 ± 0.75	5 (9%)	3.71 ± 0.66	1 (4%)	3.71 ± 0.74	.69
Pulmonary artery measurements							
PAAT, ms	2 (2%)	130 ± 23	3 (5%)	130 ± 22	0	122 ± 18	.19
PAAT/RV ET	2 (2%)	0.421 ± 0.065	3 (5%)	0.429 ± 0.067	0	0.401 ± 0.054	.36

P values were calculated by using a linear regression model. E/A = mitral inflow peak E-to-A wave velocities ratio; ET = ejection time; ND = not determined; PAAT = pulmonary artery acceleration time; RV = right ventricular; TAPSE = tricuspid annular plane systolic excursion.
[a]*P* value for the effect of the three-level ordinal independent variable (1 = full term; 2 = preterm/no BPD; 3 = preterm/BPD) on RV systolic function.
[b]$P < .05$ following adjustment for multiple comparisons according to the false discovery rate method.

- Even more if BPD

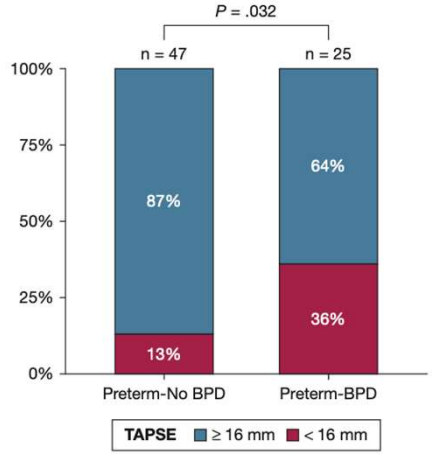

Figure 1 – *Proportion of preterm individuals with abnormal TAPSE values according to history of BPD. BPD = bronchopulmonary dysplasia. TAPSE = tricuspid annular plane systolic excursion. P value calculated by using Fisher exact test.*

Article

Left Ventricle Structure and Function in Young Adults Born Very Preterm and Association with Neonatal Characteristics

Adrien Flahault [1,†], Gabriel Altit [2,†], Aurélie Sonea [1], Anne-Sophie Gervais [1], Muhammad Oneeb Rehman Mian [1], Rong Wu [1], Eva Desbrousses [1], Ly Mai [1], Anik Cloutier [1], Jessica Simoneau [2], Anie Lapointe [3], Andréanne Villeneuve [3], Patrick Garceau [4], Michel White [4], Jean-Luc Bigras [1,3], Thuy Mai Luu [1,3] and Anne Monique Nuyt [1,3,*]

	Term $n = 85$		Preterm $n = 86$		
	Missing n (%)	**Mean ± SD**	**Missing n (%)**	**Mean ± SD**	***p*-Value**
Heart rate, bpm	0 (0)	69.3 ± 12.7	0 (0)	75.4 ± 12.2	0.003
Left Ventricular Outflow Tract Doppler (Pulsed-Wave)					
Stroke volume, mL	4 (5)	66.8 ± 9.5	2 (2)	59.9 ± 9.3	<0.001
Stroke volume indexed, mL/m^2	4 (5)	37.6 ± 5.9	2 (2)	36 ± 5.3	0.16
Cardiac output, L/min	4 (5)	4.43 ± 0.6	2 (2)	4.15 ± 0.51	0.003
Cardiac output indexed, L/min/m^2	4 (5)	2.5 ± 0.4	2 (2)	2.51 ± 0.35	0.89
Doppler–Mitral Valve					
MV E/A ratio	1 (1)	1.8 ± 0.42	1 (1)	1.73 ± 0.38	0.26
E/e' ratio	3 (4)	4.44 ± 0.8	1 (1)	4.59 ± 0.79	0.20
Tissue Doppler Imaging (Lateral)					
LV S' wave (cm/s)	3 (4)	11.5 ± 2.3	1 (1)	10.7 ± 2.3	0.036
LV e' wave (cm/s)	3 (4)	19.2 ± 2.6	1 (1)	17.7 ± 2.8	0.001

L'histoire de Florence, Elise et Antoine

The Story of Florence, Elise and Antoine (French)

The story of Massimo, Priyanka and Anthony

L'histoire de Massimo, Priyanka et Anthony

The story of Teo, Ode and Marko

L'histoire de Téo, Ode et Marko

The story of Noah, Alina and Armen

L'histoire de Noah, Alina et Armen

Conclusion

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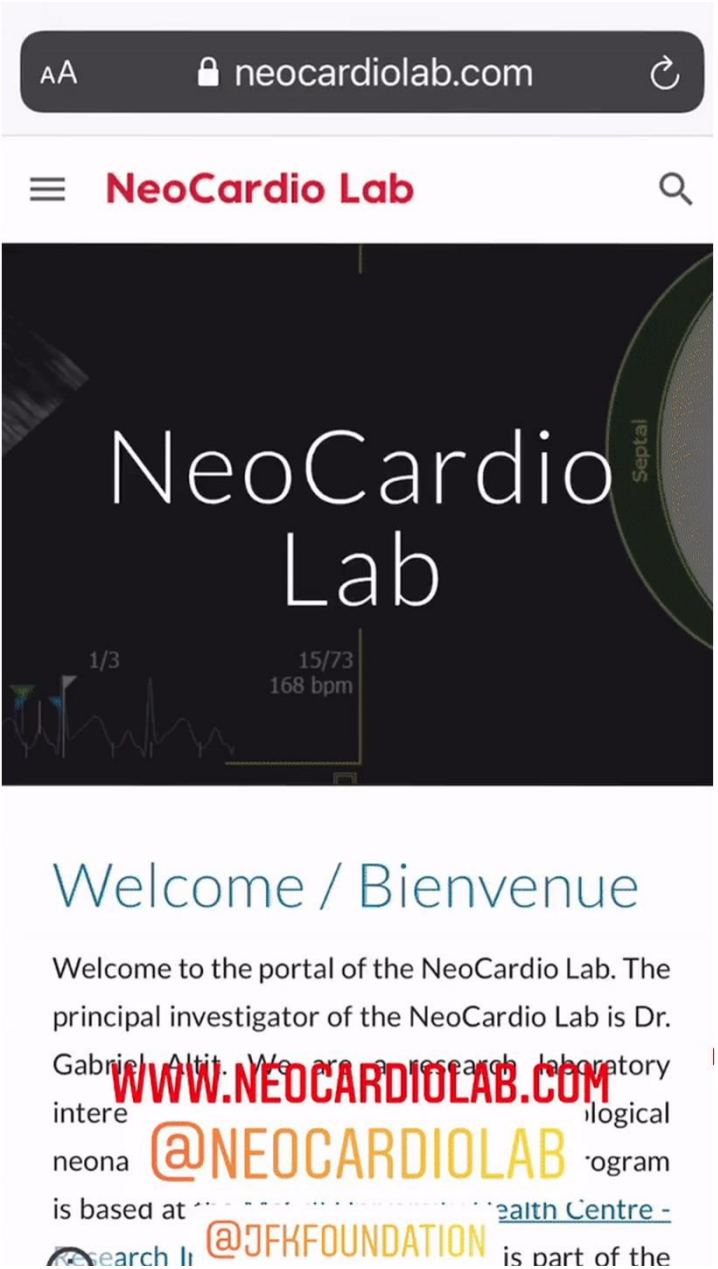
@CardioNeo (Twitter)

- Extreme premature newborns with BPD should have a screening echo at 36 weeks for PH
- Multiple etiologies unique to BPD (Heterogeneous, PVR, Venous drainage, LV/RV disease).
- PH increases mortality: management still under evaluation but should initially aim to **optimize respiratory status**, avoid profound desaturations and respiratory infections, provide appropriate nutrition with avoidance of GERD/aspiration, ensure no airway contributor to CO2 retention.
  - These patients should be followed by a multi-disciplinary team with expertise in PH
  - Some may need pulmonary vasodilators (but not all).
- Outcomes are highly influenced by the underlying cardiac performance (LV and/or RV)
- Lifelong disease
- Future research: prevention, natural history, targeted management and refining diagnosis/management pathways.



Questions? Comments?
Merci – Thank you - Obrigado

- **<u>A special thanks to the organizing committee and to my mentor (Pr G. Sant'Anna)</u>**
- Gabriel Altit – gabriel.altit@neocardiolab.com

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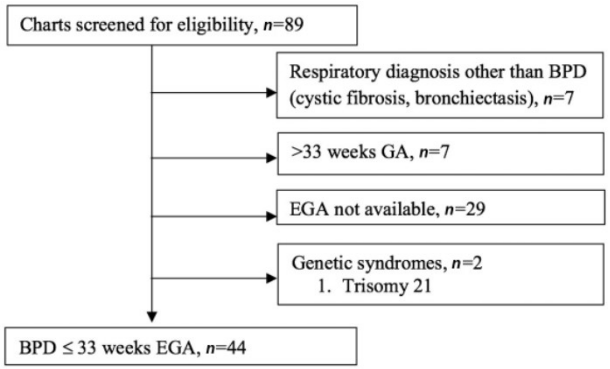
Cardiopulmonary Function Abnormalities in Cohort of Adults following Bronchopulmonary Dysplasia as Preterm Infants

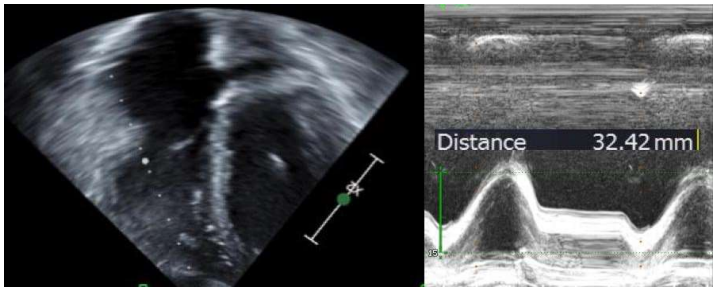
Ariane Lasry, BSc[1] Patrick Kavabushi, MD[1] Anne-Marie Canakis, MD[2] Thuy M. Luu, MD[3]
Anne-Monique Nuyt, MD[4] Thérèse Perreault, MD[5] Jessica Simoneau[5] Jennifer Landry, MD[6]
Gabriel Altit, MDCM[5]

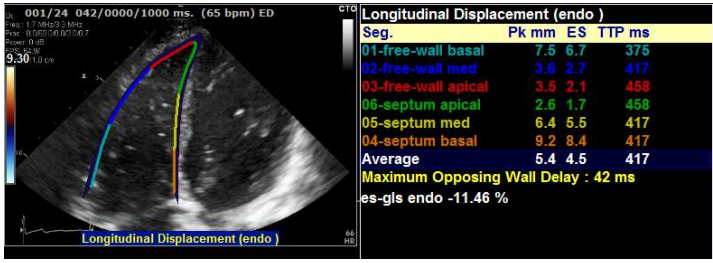


n = 44	n (%)	Mean (SD)	Median (range)
Gestational age (wk)		26.4 (2.7)	26 (22–32)
Age at follow-up (y)		19 (4.7)	
Male	31 (70.5)		

Table 3 Echocardiography results

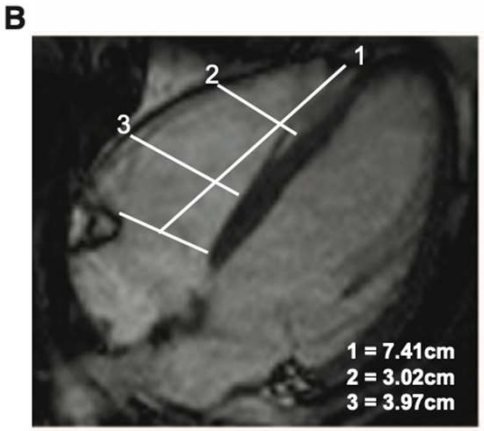
	All (n = 12)	Obstructive PFT (n = 5)	Nonobstructive PFT (n = 7)	p-Value
Weight (kg)	50.83 (7.45)	45.78 (3.80)	55.04 (7.25)	0.03
Body surface area (cm)	1.52 (0.17)	1.40 (0.08)	1.61 (0.16)	0.04
Systolic BP at ECHO	114.60 (4.28)	116.67 (3.79)	111.50 (3.54)	0.22
Diastolic BP at ECHO	75.20 (6.30)	75.0 (8.89)	75.5 (0.71)	0.94
Markers of pulmonary pressures				
sPAP by TRJ	24.93 (4.13)	25.1 (1.83)	24.79 (5.62)	0.92
LV parameters of size and performance				
LV-GLS (%)	−17.86 (3.45)	−17.07 (3.02)	−18.11 (3.81)	0.74
LV ejection fraction in (%)	64.33 (6.91)	59.67 (3.94)	66.33 (7.14)	0.18
E/A of mitral valve	2.16 (0.44)	2.21 (0.26)	2.14 (0.54)	0.85
RV parameters of performance				
RV-GLS (%)	−21.90 (6.73)	−14.91 (4.59)	−24.89 (5.11)	0.02
RV free wall basal displacement (mm)	13.30 (4.19)	9.41 (1.89)	15.53 (3.40)	0.01
TAPSE (mm)	20.81 (4.94)	16.61 (4.60)	23.21 (3.40)	0.02





Right Ventricular Systolic Dysfunction in Young Adults Born Preterm

Adam J. Lewandowski, BSc (Hons), DPhil; William M. Bradlow, MD, MRCP; Daniel Augustine, MRCP; Esther F. Davis, MBBS; Jane Francis, DCR(R), DNM; Atul Singhal, FRCP; Alan Lucas, FMedSci; Stefan Neubauer, MD, FRCP, FMedSci; Kenny McCormick, FRCPCH; Paul Leeson, PhD, FRCP



Preterm Heart in Adult Life

Cardiovascular Magnetic Resonance Reveals Distinct Differences in Left Ventricular Mass, Geometry, and Function

Adam J. Lewandowski, BSc (Hons); Daniel Augustine, MRCP; Pablo Lamata, PhD; Esther F. Davis, MBBS; Merzaka Lazdam, MRCP; Jane Francis, DCR(R), DNM; Kenny McCormick, FRCPCH; Andrew R. Wilkinson, FRCPCH; Atul Singhal, FRCP; Alan Lucas, FMedSci; Nic P. Smith, PhD; Stefan Neubauer, MD, FRCP, FACC, FMedSci; Paul Leeson, PhD, FRCP

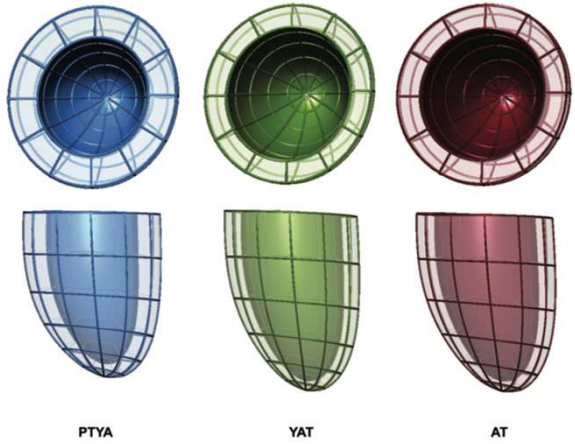
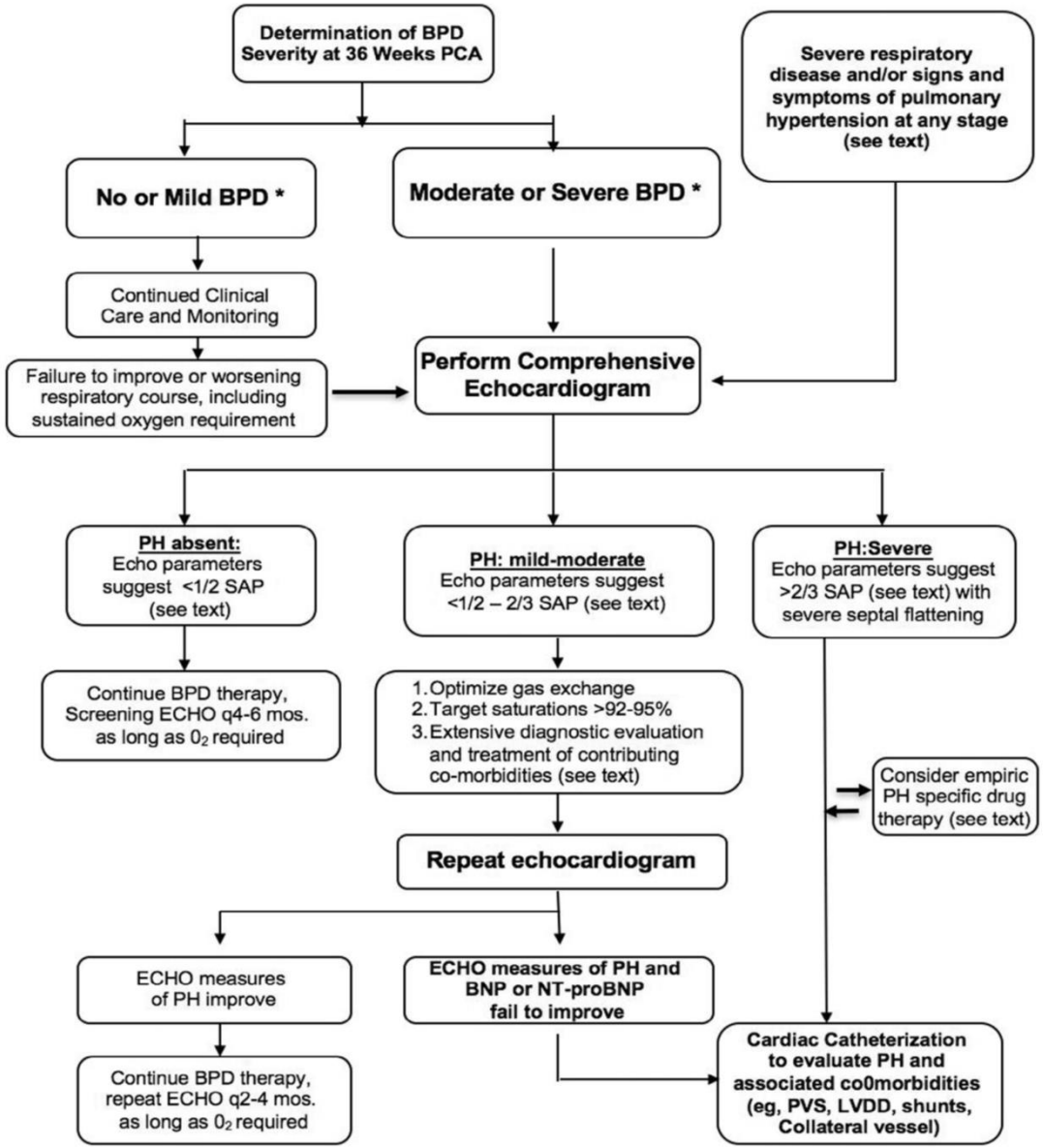


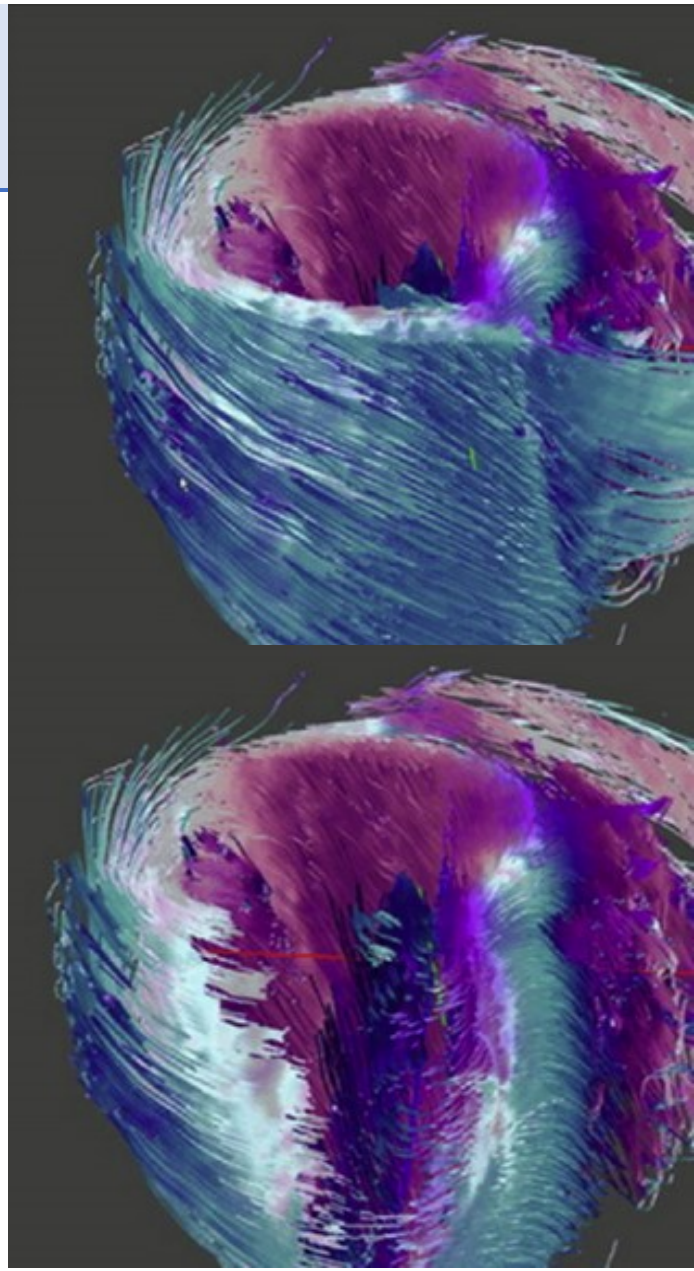
Figure 3. Statistical average shape for each group. AT indicates older term-born adults (red); PTYA, preterm-born young adults (blue); and YAT, term-born young adults (green).


Determination of BPD Severity at 36 Weeks PCA
Severe respiratory disease and/or signs and symptoms of pulmonary hypertension at any stage (see text)
No or Mild BPD *
Moderate or Severe BPD *
Continued Clinical Care and Monitoring
Failure to improve or worsening respiratory course, including sustained oxygen requirement
Perform Comprehensive Echocardiogram
PH absent: Echo parameters suggest <1/2 SAP (see text)
PH: mild-moderate Echo parameters suggest <1/2 – 2/3 SAP (see text)
PH:Severe Echo parameters suggest >2/3 SAP (see text) with severe septal flattening
Continue BPD therapy, Screening ECHO q4-6 mos. as long as 0_2 required
1. Optimize gas exchange
2. Target saturations >92-95%
3. Extensive diagnostic evaluation and treatment of contributing co-morbidities (see text)
Consider empiric PH specific drug therapy (see text)
Repeat echocardiogram
ECHO measures of PH improve
ECHO measures of PH and BNP or NT-proBNP fail to improve
Continue BPD therapy, repeat ECHO q2-4 mos. as long as 0_2 required
Cardiac Catheterization to evaluate PH and associated co0morbidities (eg, PVS, LVDD, shunts, Collateral vessel)

Cardiac function: how?

Continuous process from filling of ventricles to ejection in outflow tracts

- **Dependent on architecture of each ventricles**
- **Dependent on afterload of outflow tract (s)**
- Cross-talk between RV-LV (Septum)
- Precise activation by conducting system
  - Results in “2 phases” of cardiac cycle



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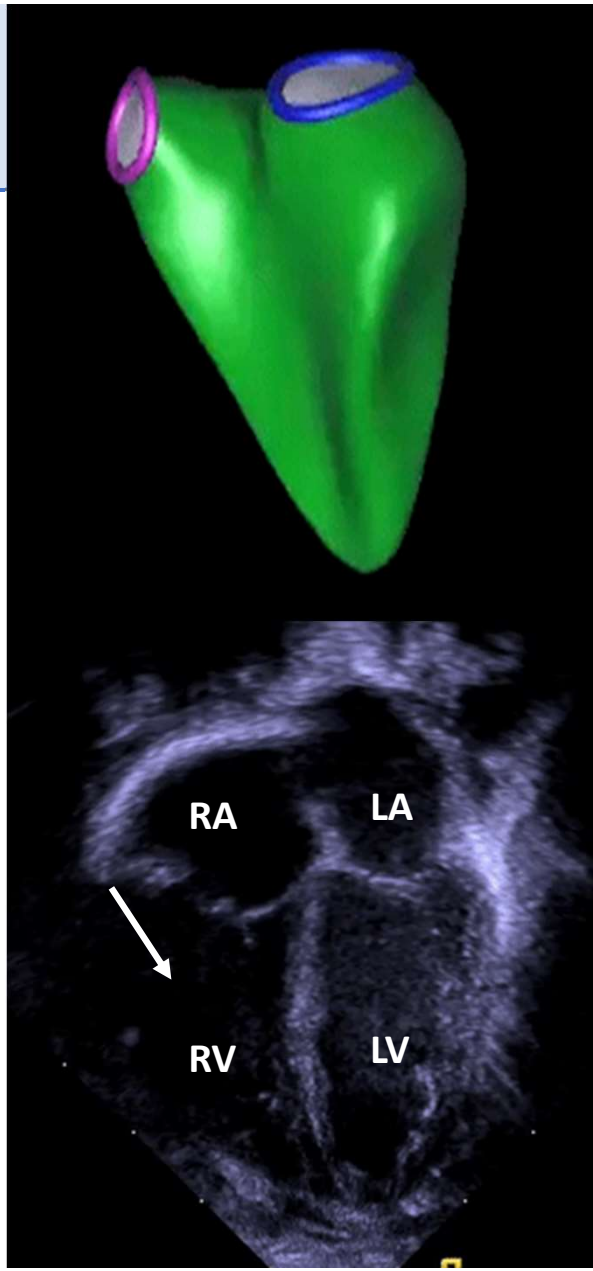
Right Ventricle

RV contracts **<u>longitudinally</u>**

- Peristaltic motion from inflow (tricuspid valve) to RVOT (pulmonary valve)
- IV septum bulging in RV cavity
- Free wall going towards IVS

RV function by ECHO

- TAPSE: Tricuspid Annular Plane Systole Excursion
    - Longitudinal movement as it plunges in RV cavity
- FAC: Fractional area change
    - FAC = (EDA – ESA) / (EDA) in Apical 4 or 3 Chamber view
- Normative values by GA for TAPSE and FAC



Cardiac function

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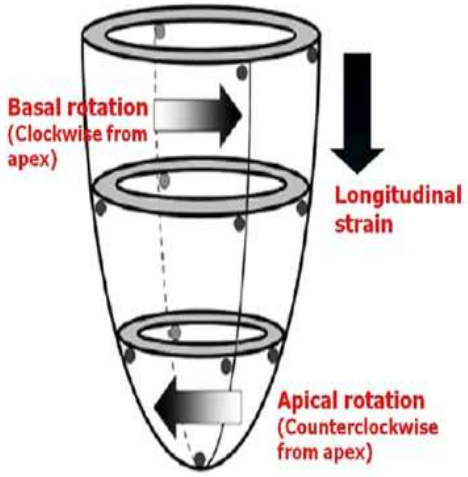
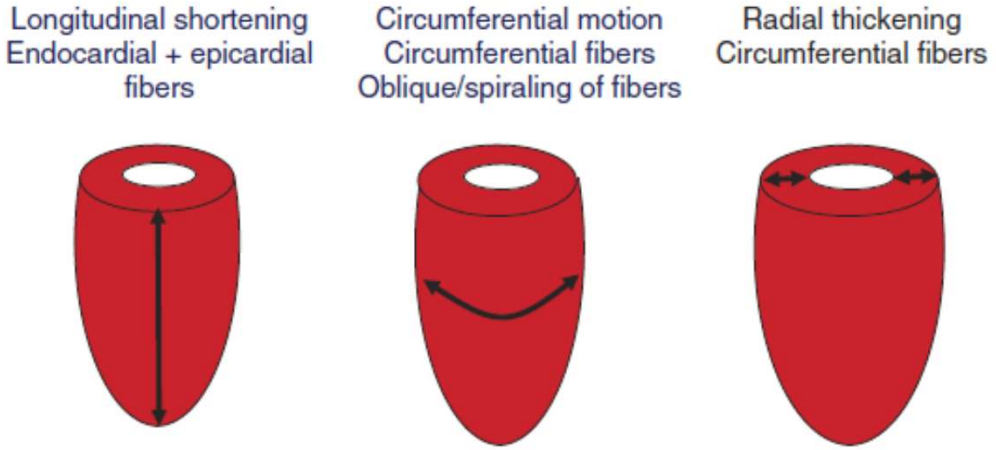
- LV contracts mostly circumferentially and with torsion (wringing movement)
- Minor longitudinal contribution
- Wringing motion. Relaxation with base counterclockwise and apical clockwise rotation. Rate at which untwisting happens gives insight on diastolic function.





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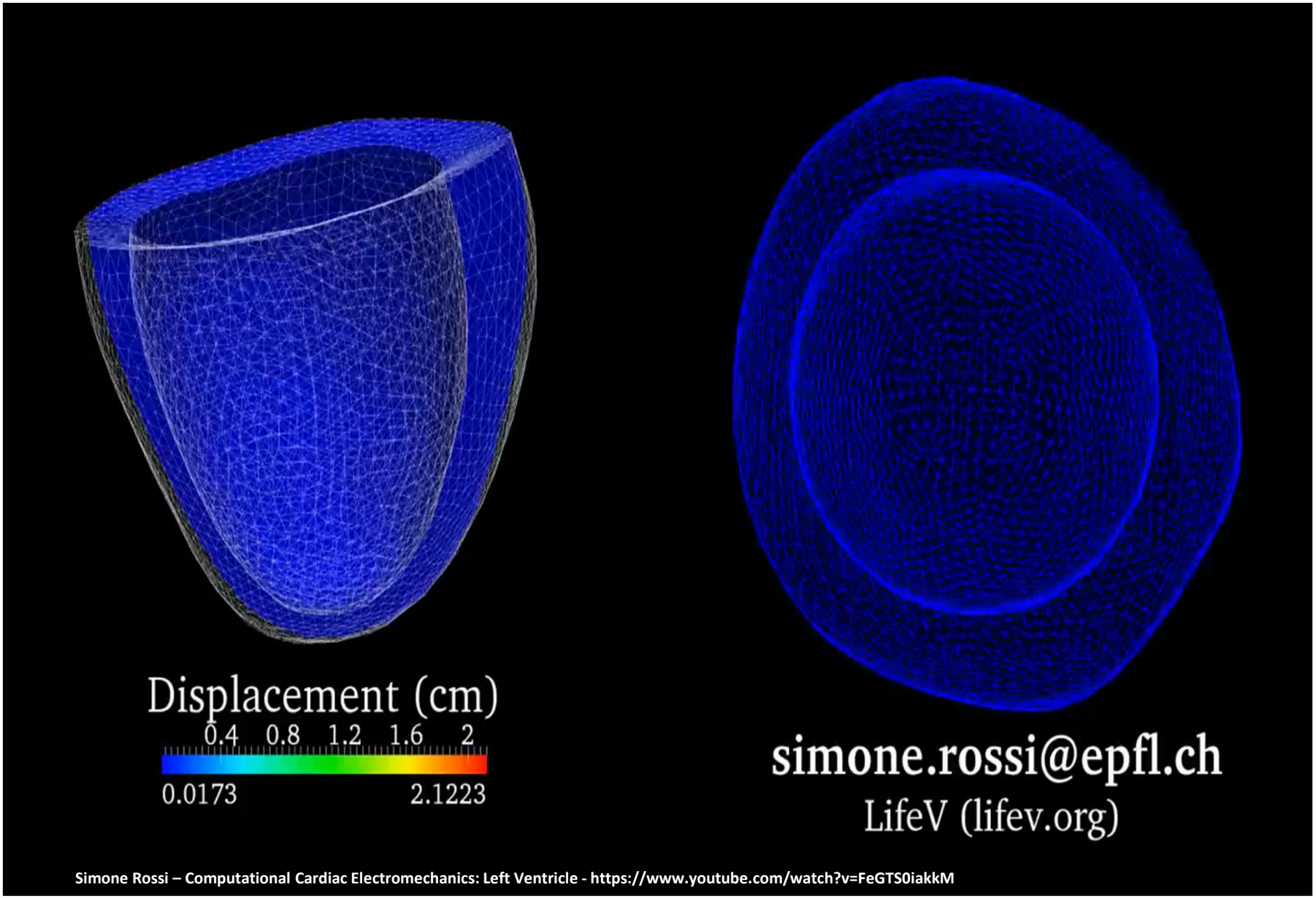
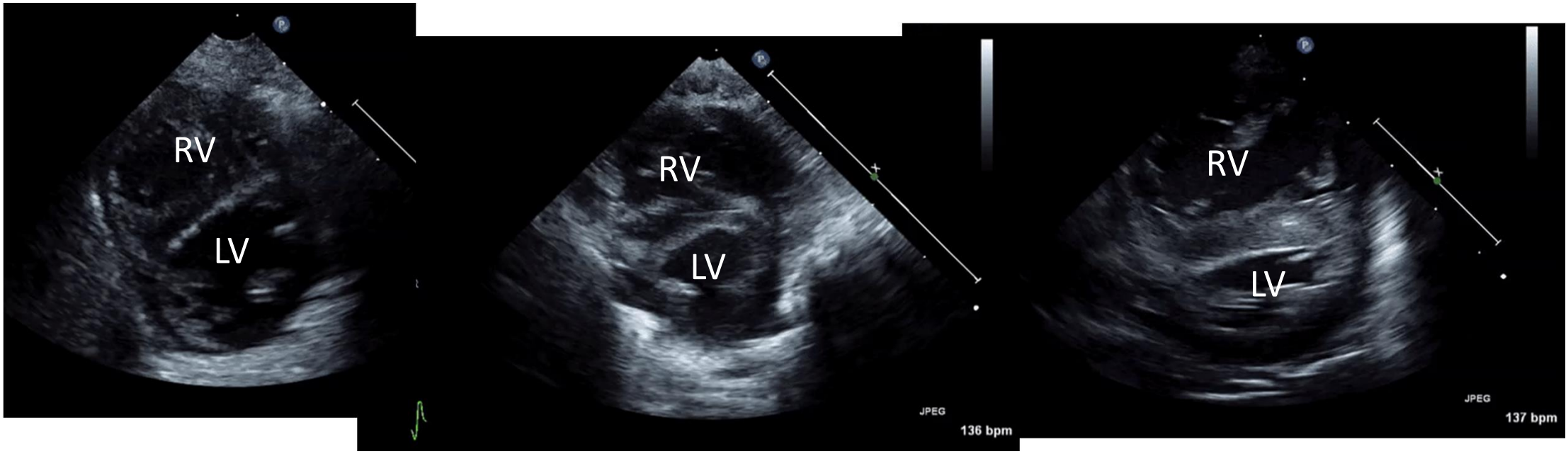


Simone Rossi – Computational Cardiac Electromechanics: Left Ventricle - https://www.youtube.com/watch?v=FeGTS0iakkM

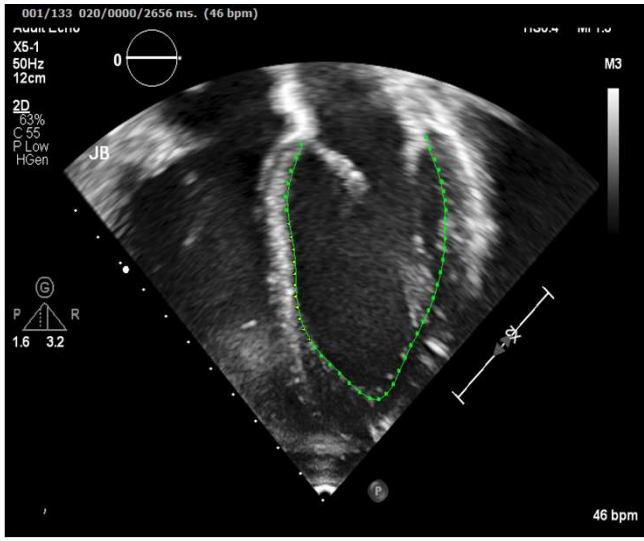

RV
LV
RV
LV
JPEG
136 bpm
RV
LV
JPEG
137 bpm

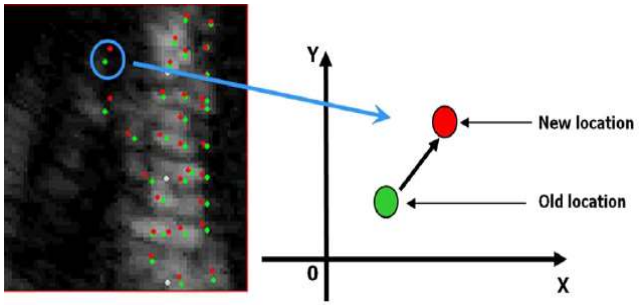
Strain by STE

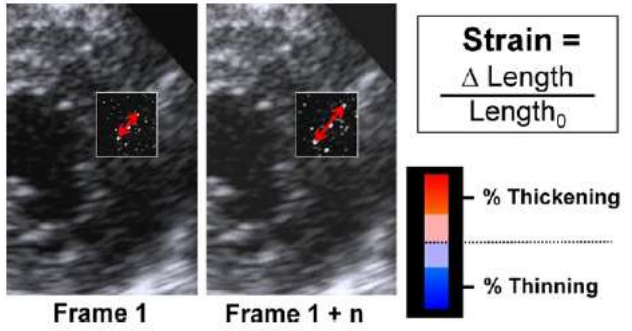
- Speckles (echodensities) form the ECHO images
  - Tracked on a frame by frame to measure magnitude (or percentage) of deformation
  - Speckle Tracking Echocardiography (STE)

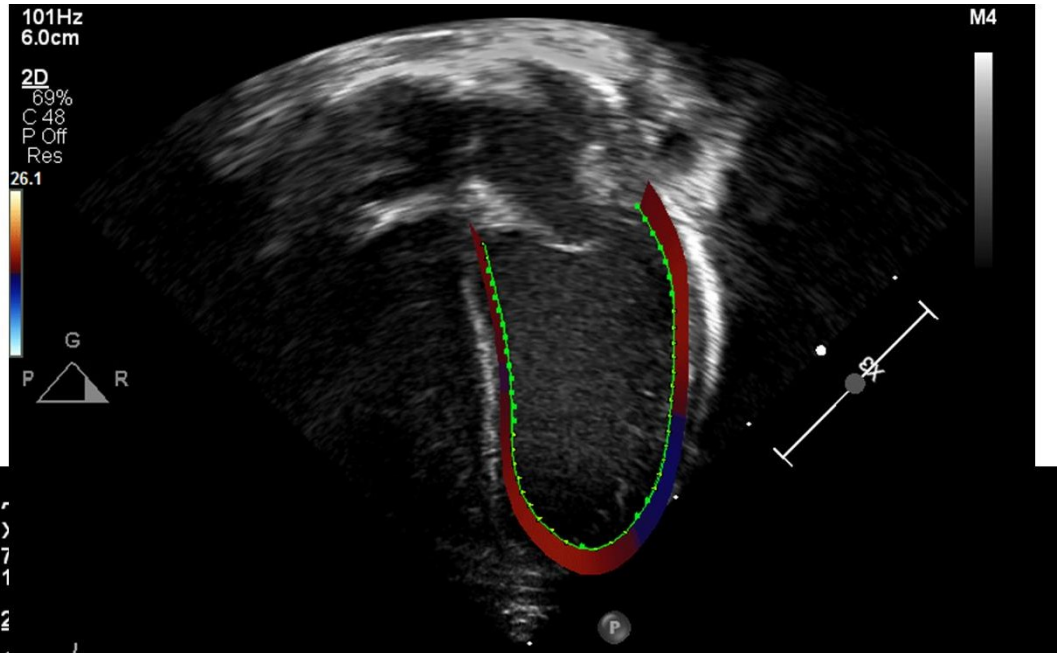
- Strain is absolute percentage of deformation of each segment and overall ventricle

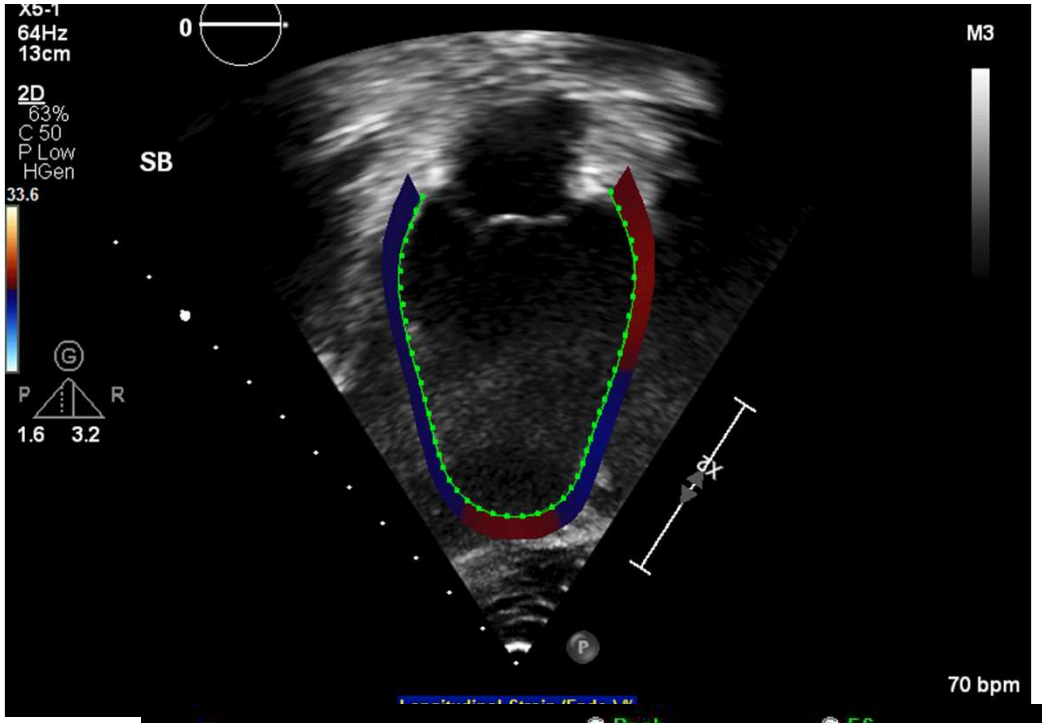
- STE allows for:
  - Segmental analysis
  - Rate of myocardial expansion (diastole)
  - Circumferential, radial and rotational assessment of LV

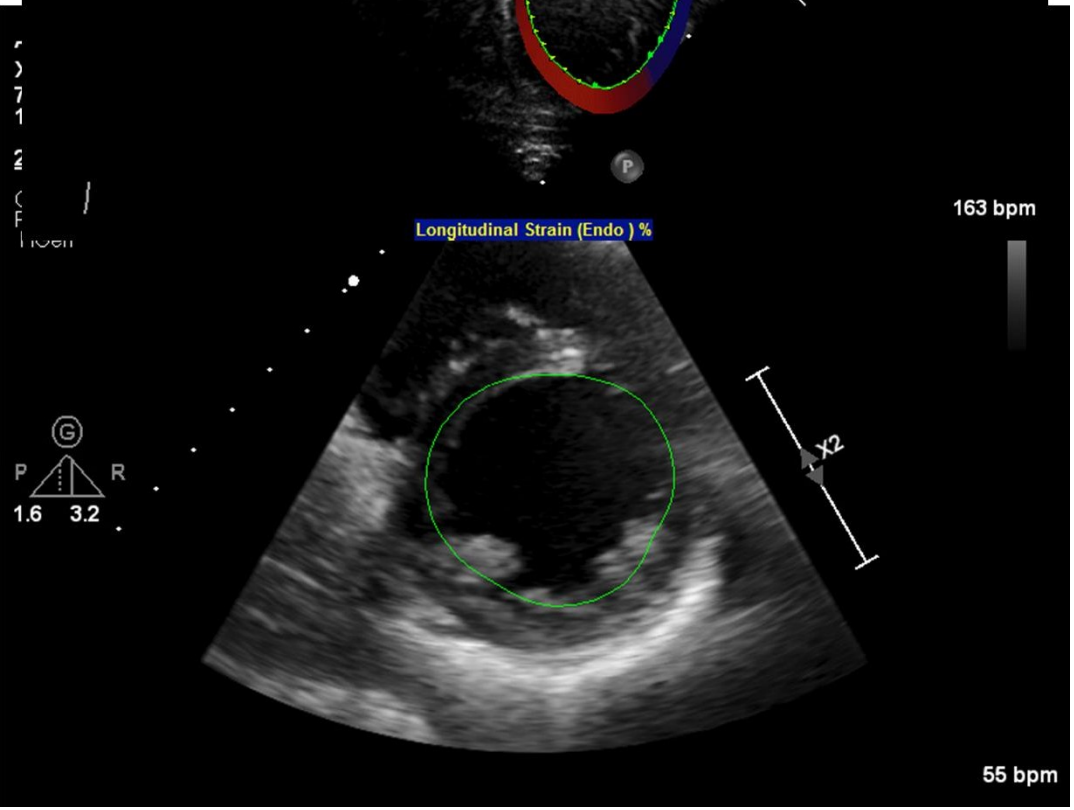




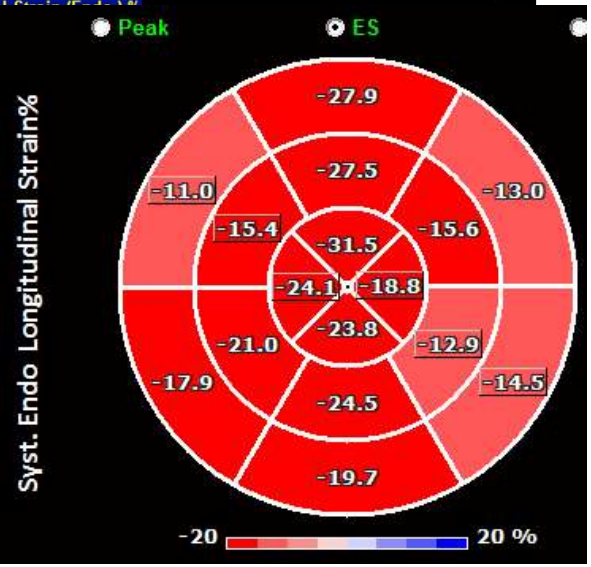








Average		
EndoGLS	-20.13	%
EF	49.40	%
EDV	8.32	ml
ESV	4.21	ml
ESL	2.60	cm
ESDbas	1.41	cm
EDL	3.22	cm
EDDbas	1.67	cm
SD-LS-Syst.	6.1	%



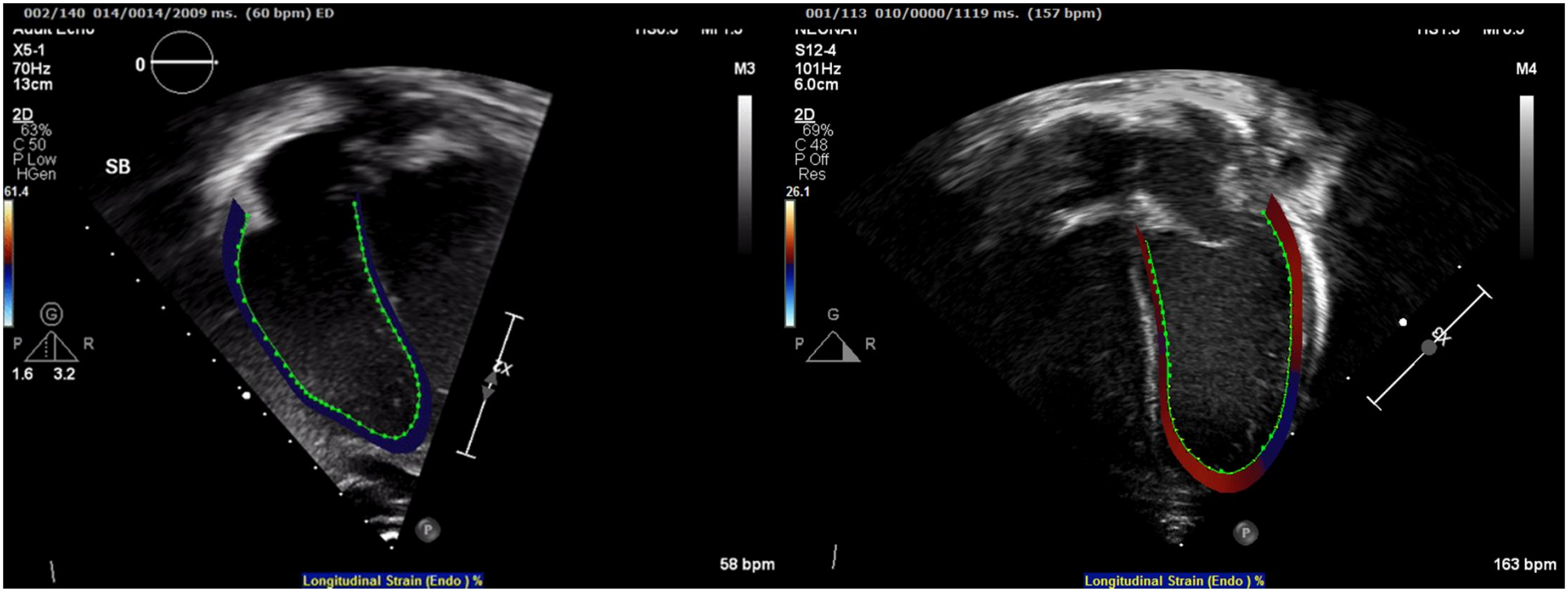


Table 4. Deformation analysis.

	All ($n = 52$)	Alive ($n = 36$)	Death ($n = 16$)	p value
RV pLS	−15.6 (4.5)	−16.9 (4.1)	−13.1 (4.5)	0.006
RV pLSR	−1.37 (0.48)	−1.47 (0.50)	−1.18 (0.38)	0.04
RV LSRe	1.73 (0.66)	1.90 (0.64)	1.39 (0.59)	0.01
LV pLS	−17.0 (4.4)	−17.6 (4.1)	−15.8 (4.8)	0.21
LV pLSR	−1.57 (0.64)	−1.57 (0.71)	−1.57 (0.51)	0.51
LV LSRe	2.00 (0.64)	2.00 (0.49)	1.99 (0.90)	0.40
LV circumferential strain	−18.8 (6.0)	−18.9 (6.0)	−18.5 (6.1)	0.83
LV circumferential SR	−1.7 (−2.2 to −1.5)	−1.69 (1.17)	−1.71 (0.44)	0.40

LSRe: early diastolic longitudinal strain rate; LV: left ventricle; pLS: peak systolic longitudinal strain; pLSR: peak longitudinal systolic strain rate; RV: right ventricle; SR: strain rate.