PDA: whom, when and how to treat

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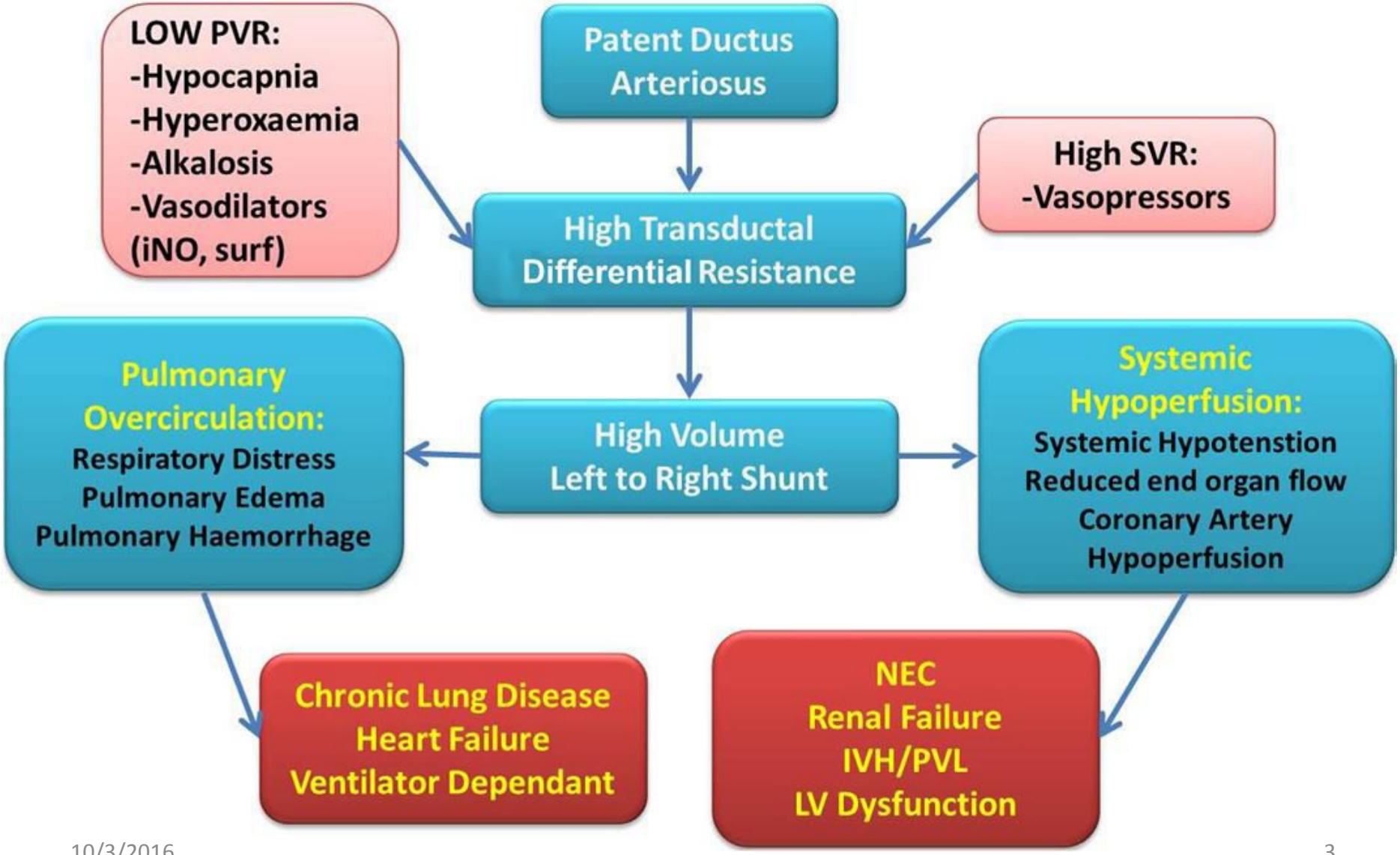
Learning Objectives

- Why
  - Why treat a PDA?
- What
  - Can we identify a PDA that should be treated?
- When
  - Can we identify the best time to treat?
- With what
  - Do we have a treatment that has an acceptable risk/benefit ratio?

Effects of PDA



PDA Morbidity

Risk	Reference
Systemic hypotension	Sarkar 2007
IVH/Low blood flow	Kluckow & Evans 2000
Pulmonary haemorrhage	Kluckow & Evans 2000
CLD	Marshall 1999
NEC	Dollberg 2005
ROP?	Gonzalez Viejo 2011
Mortality	Noori 2009

PDA Management
Potential benefits of treatment

- Avoid hypotension
- Reduced severe IVH (Prophylactic)
- Reduced pulmonary haemorrhage
- Reduced gut complications
- Reduced surgical ligation
- Possibly reduced CLD if closed earlier

What is a significant duct?

Significant for 'one' but NOT for 'other'

Significance or Uncertainty

- Clinical examination
- Echocardiography
- Biochemical markers

PDA Evaluation

- **In first 72 hrs PDA can ONLY be diagnosed with echocardiography as typical signs & symptoms of PDA shunting are absent**

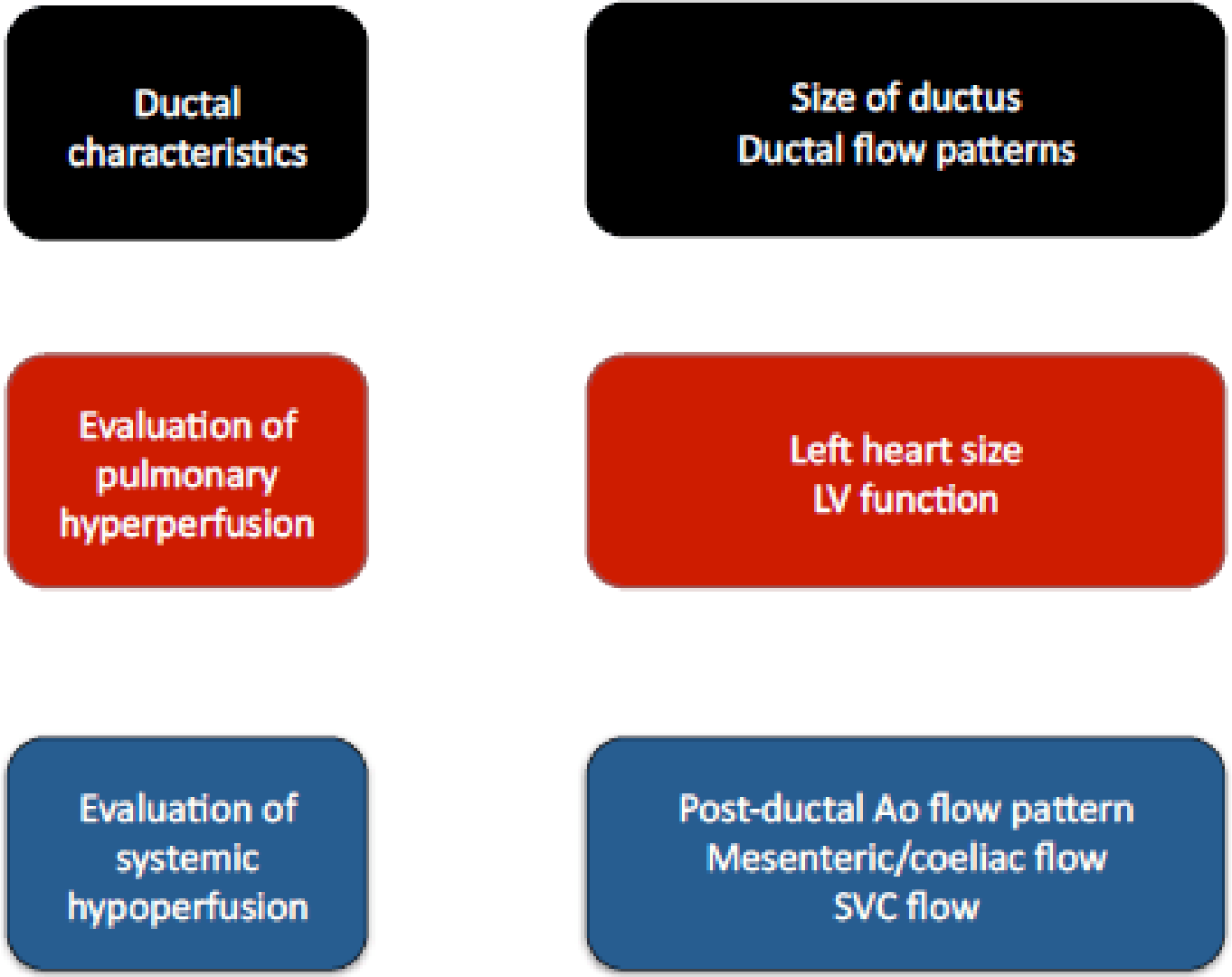
- **Haemodynamic significance precedes development of clinical signs by an average of 2 days (range 1–4 days)**

After 3 days

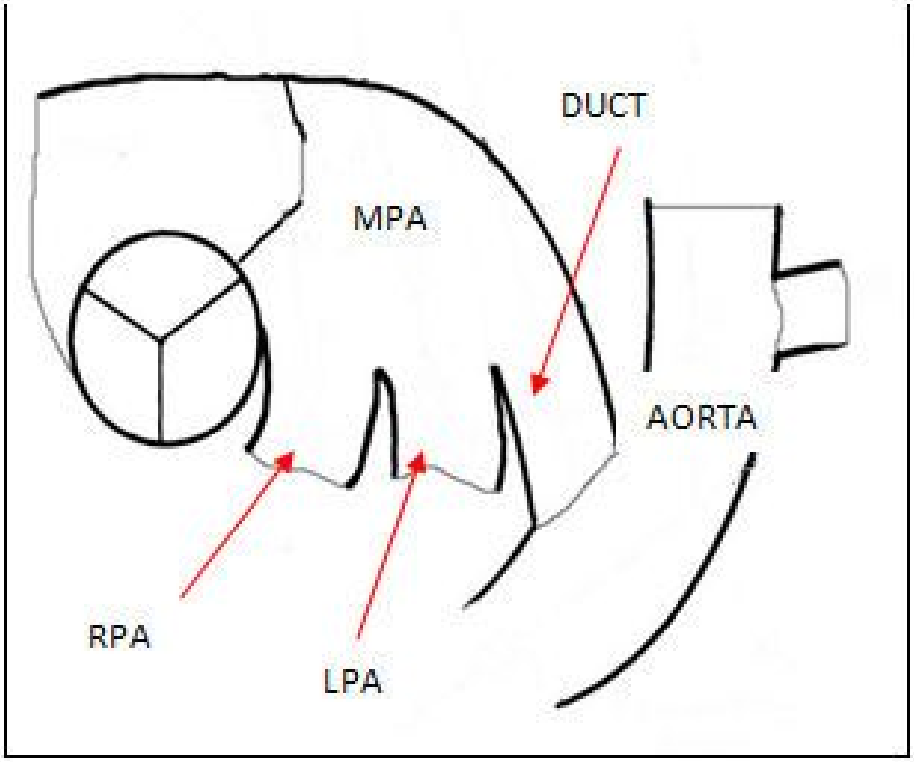
What is a clinically "significant" PDA?

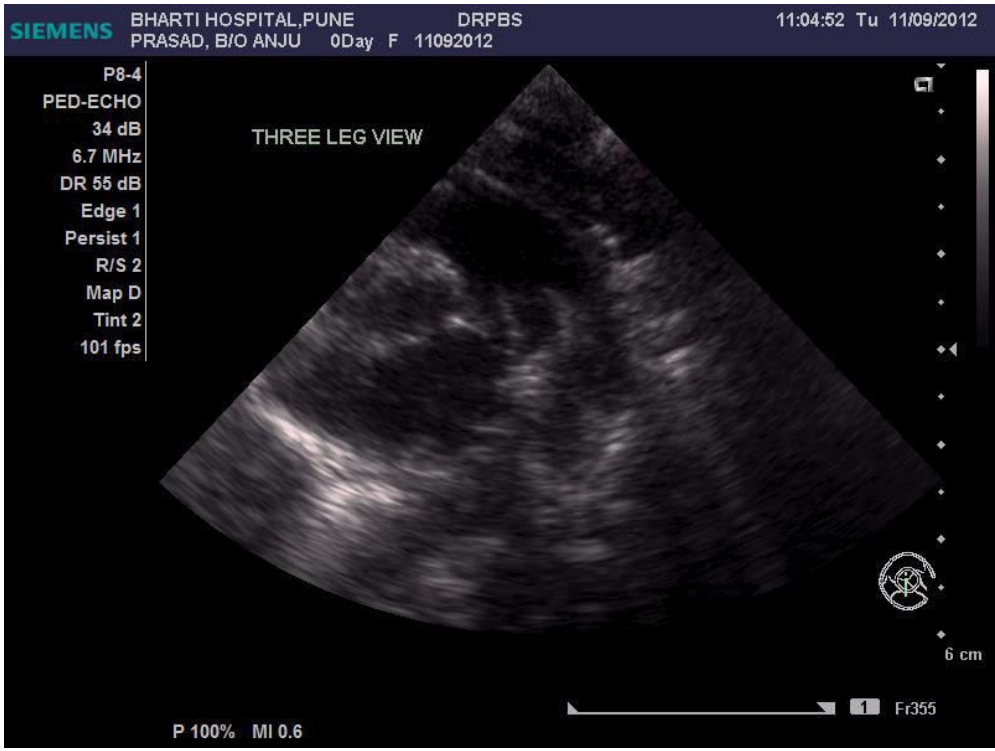
- Inability to wean on ventilator
  - Ventilated for at least 7 days continuously, and
  - Inability to wean oxygen
- Symptoms or signs of large PDA shunt
  - Persistent hypotension
  - Pulmonary haemorrhage
  - Signs of cardiac failure
- Hyperdynamic circulation
  - Wide pulse pressure
  - Bounding pulses

ECHO: What is a “significant” PDA?

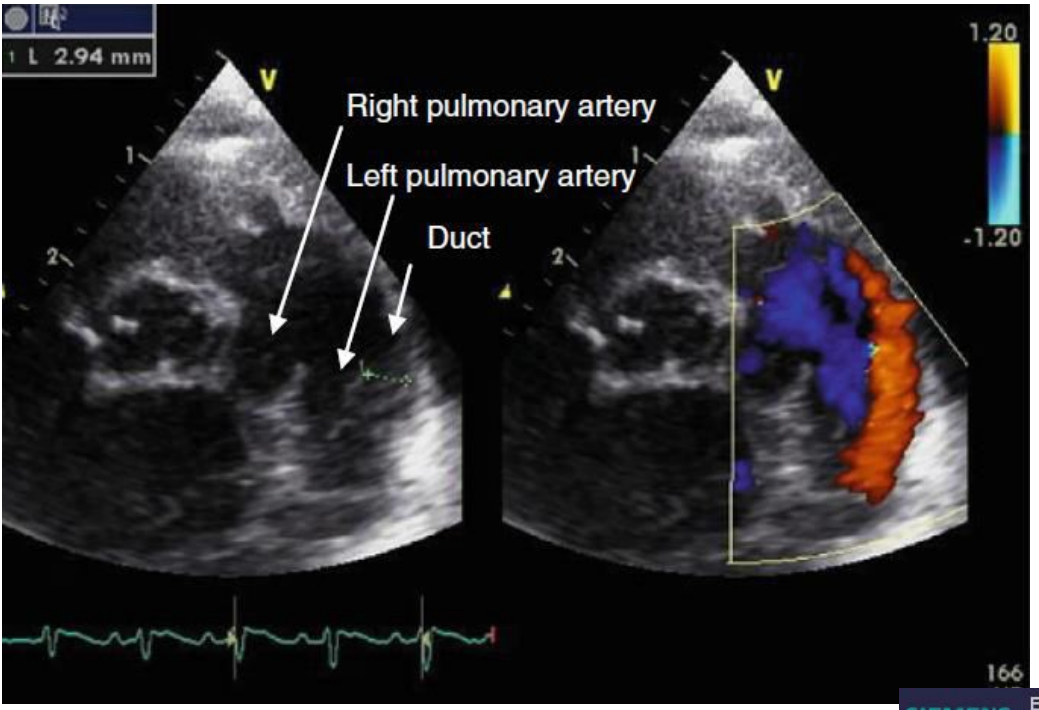


Is the ductus patent ?
Imaging the duct – 2 D





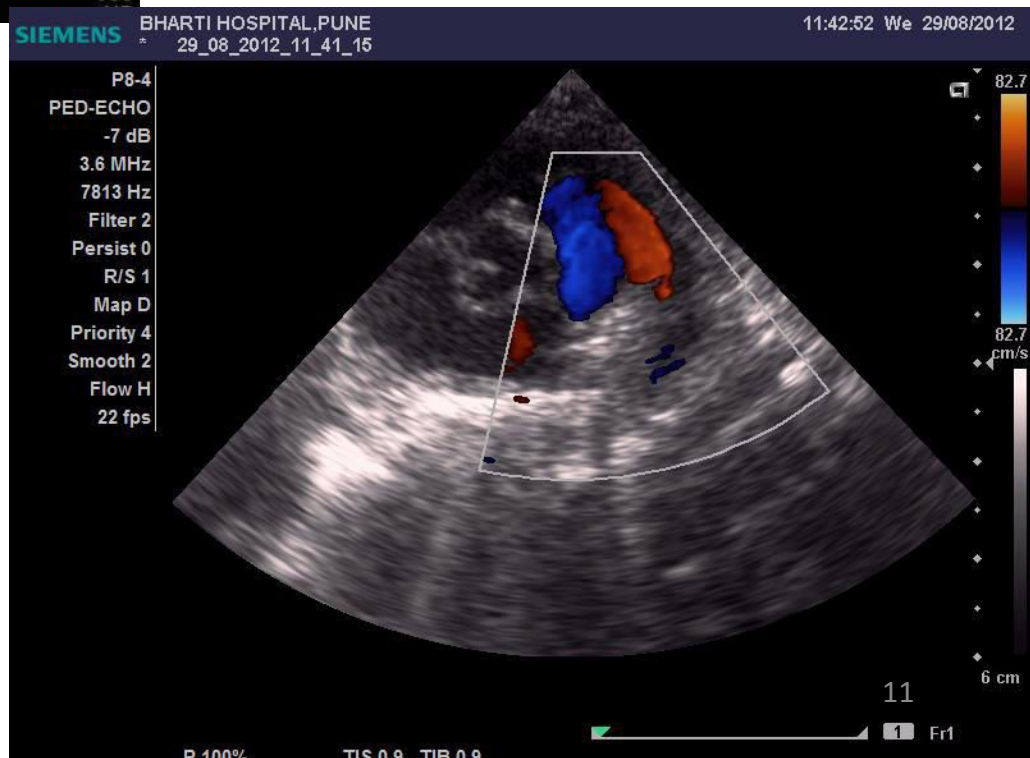
A ‘three - legged stool’ appearance -
Right pulmonary artery (RPA) and left pulmonary artery (LPA) forming the right and middle legs, and the duct forming the third leg



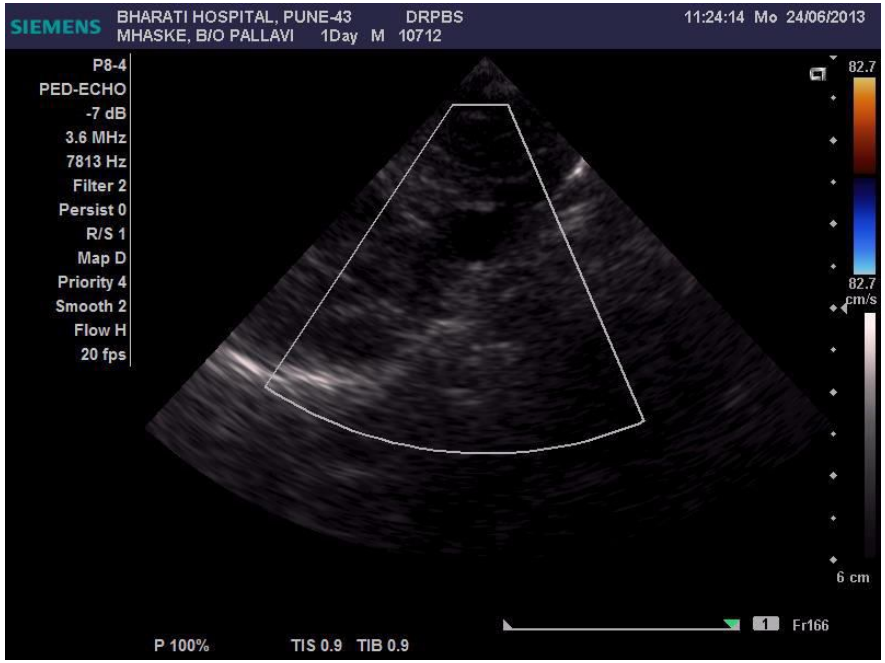
Is the ductus patent ? Imaging the duct – Colour

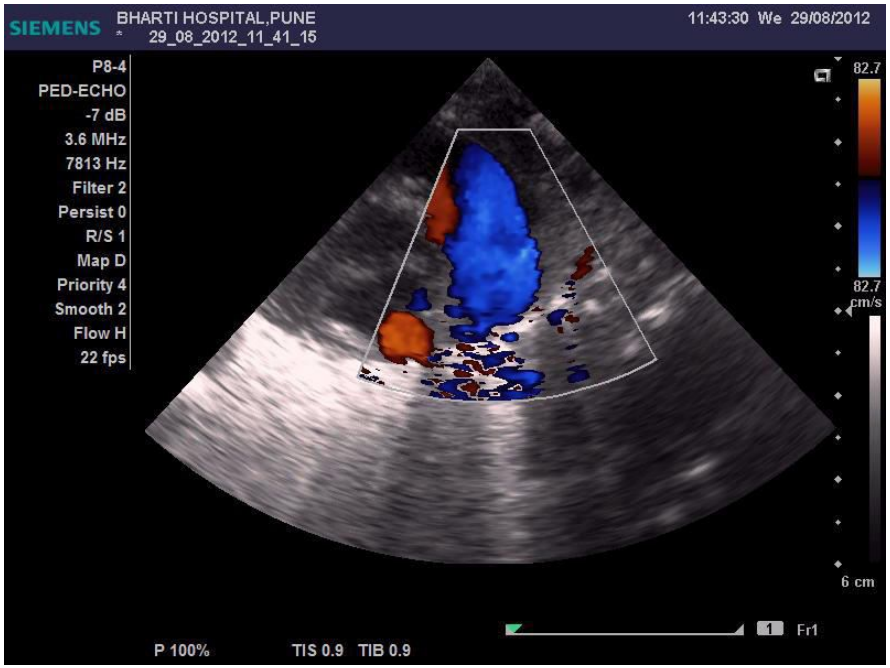
Colour Doppler ultrasound

- Bright flare of colour
- Detection of a patent duct easy



Color Doppler duct diameter

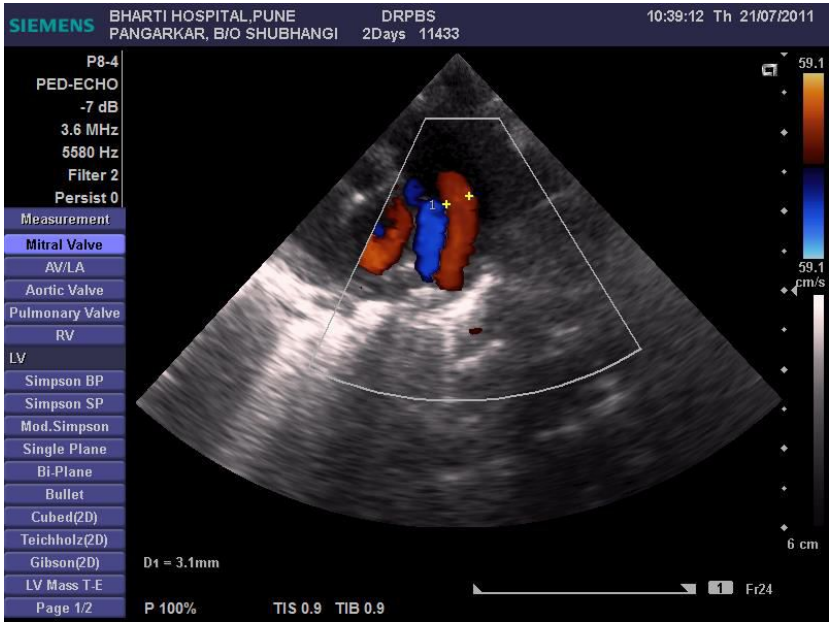


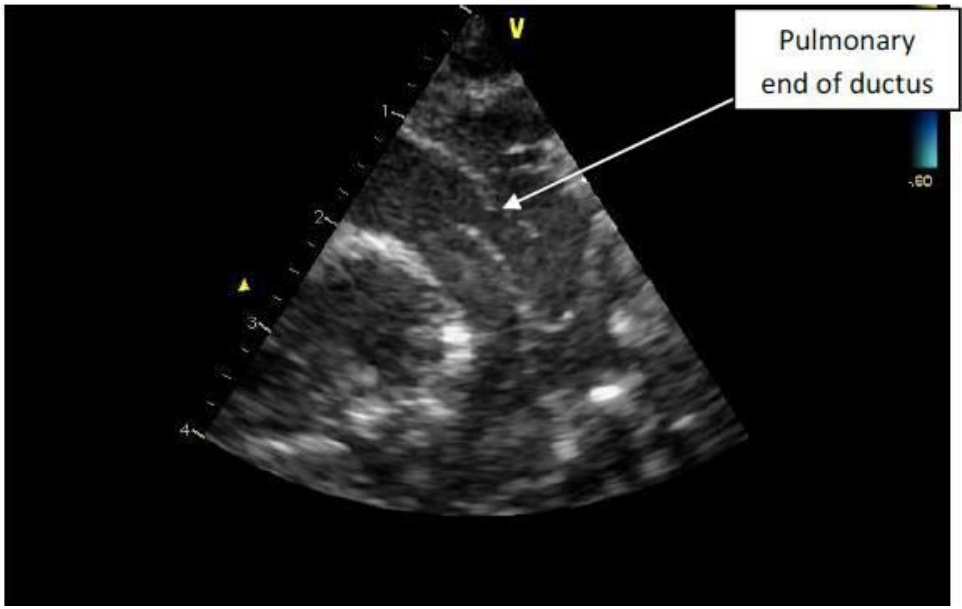


Small duct

Big duct

Size of Duct





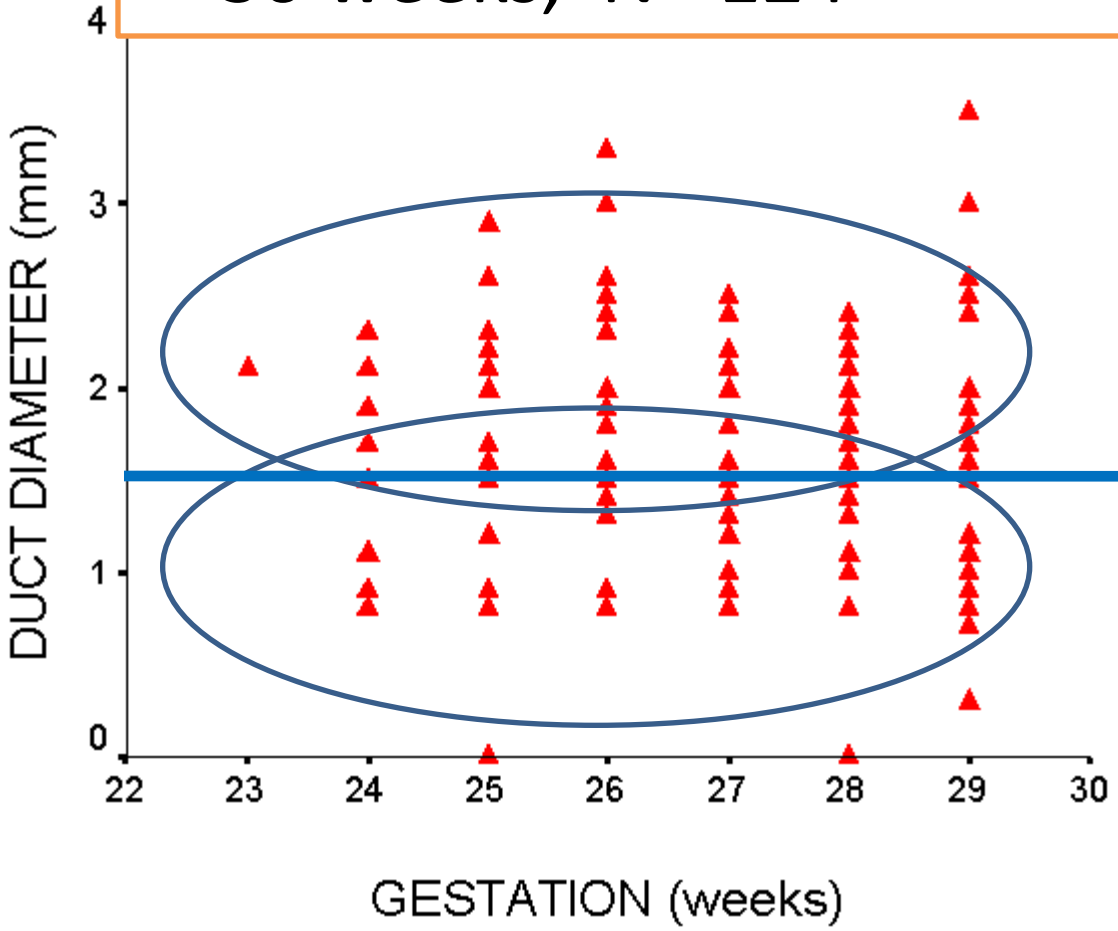
Message 4-

Duct Diameter < 1.5 mm – Usually insignificant

Duct Diameter 1.5 – 2 mm – Significant variable / Use with DA flow

Duct Diameter > 2.0 mm – Usually Significant

Range of ductal constriction at 5 hours
< 30 weeks, N= 124



Poor early constriction
Tend to stay patent

Good early constriction
Tend to close

Direction and Pattern of ductal shunt

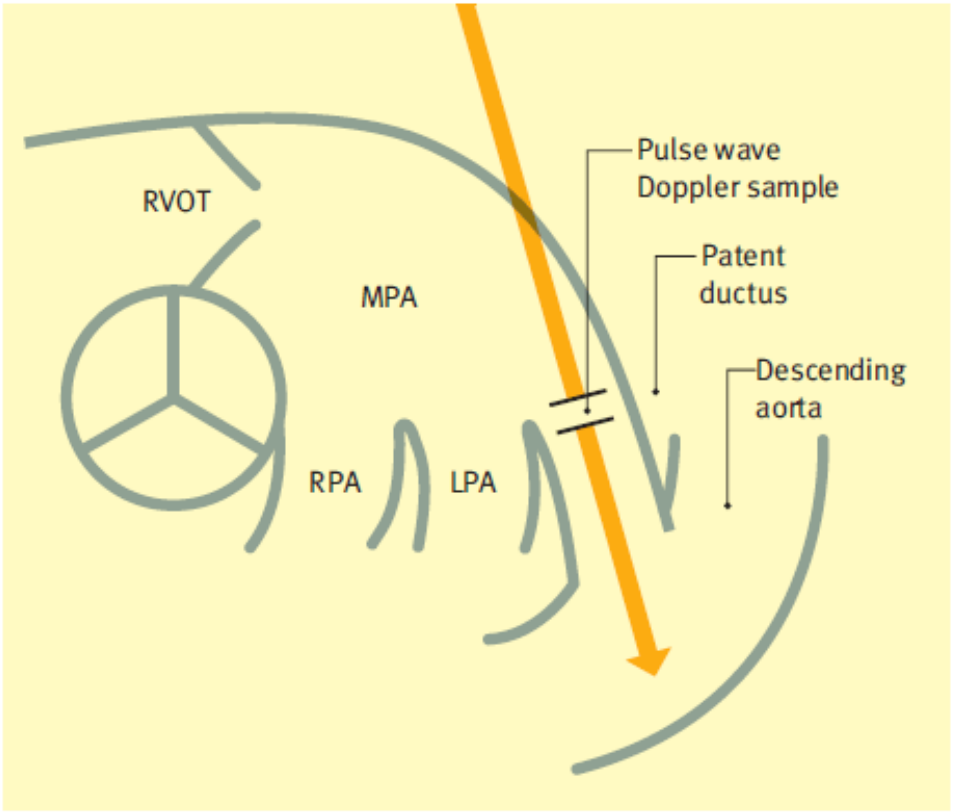
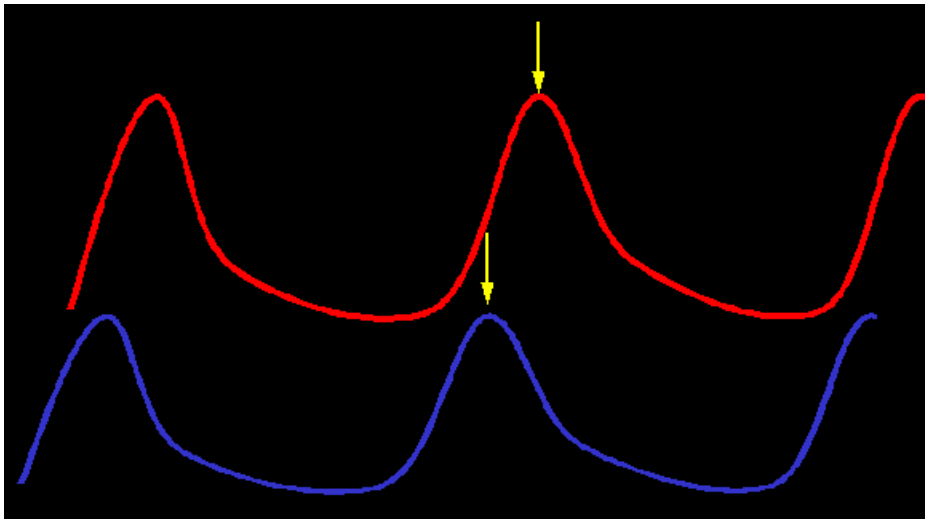


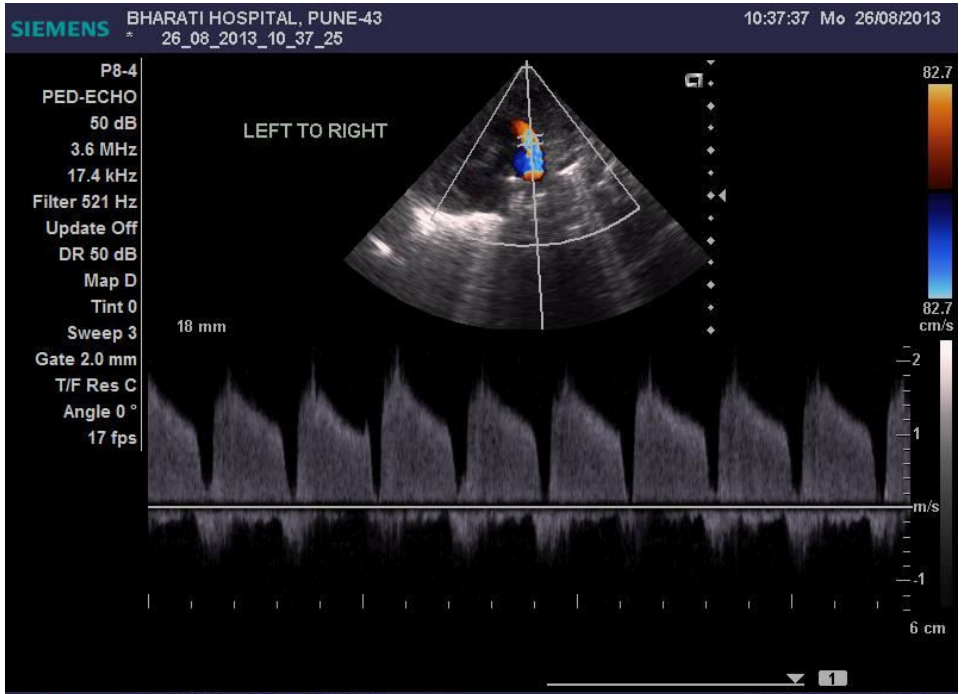
Figure 1 Schematic diagram of DA demonstrating position for Doppler of DA flow.

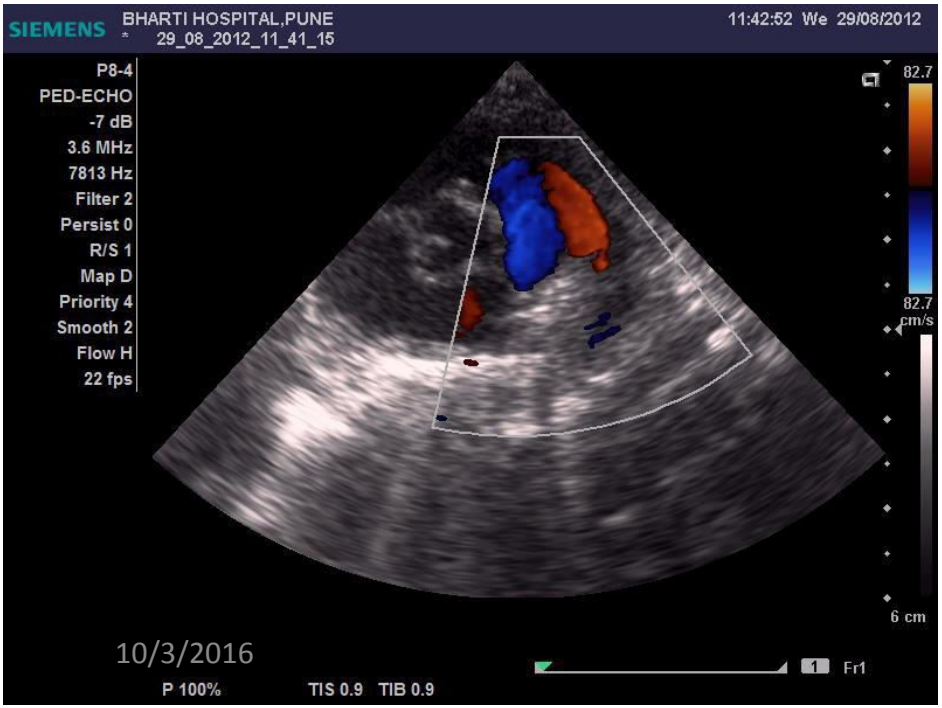
Analysis of the direction of ductal shunting requires PD/CW

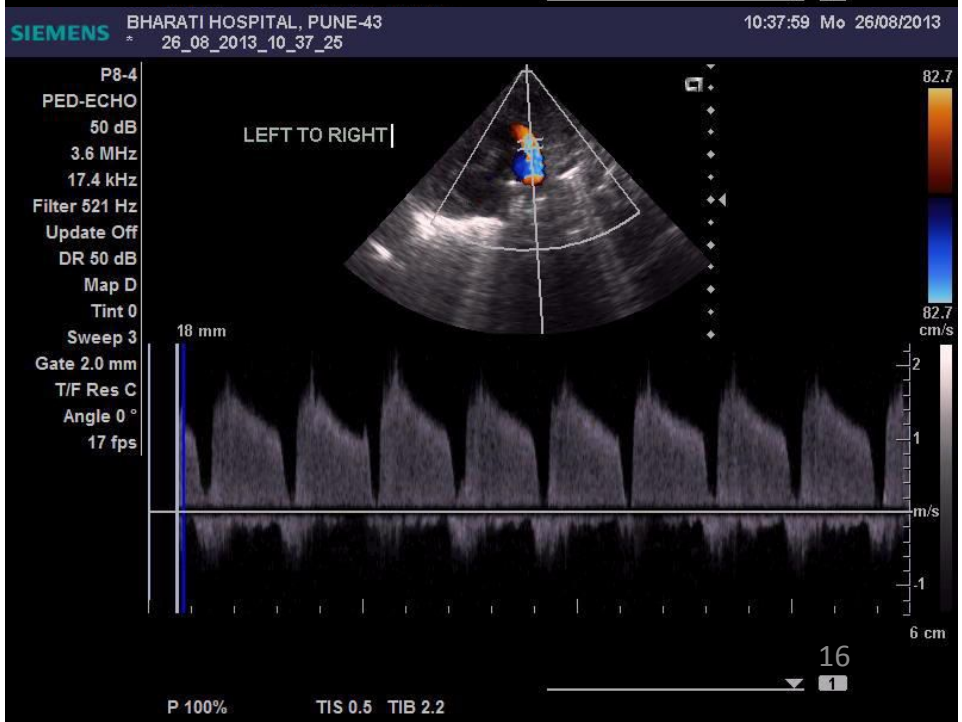
Sampling gate placed at pulmonary end of duct

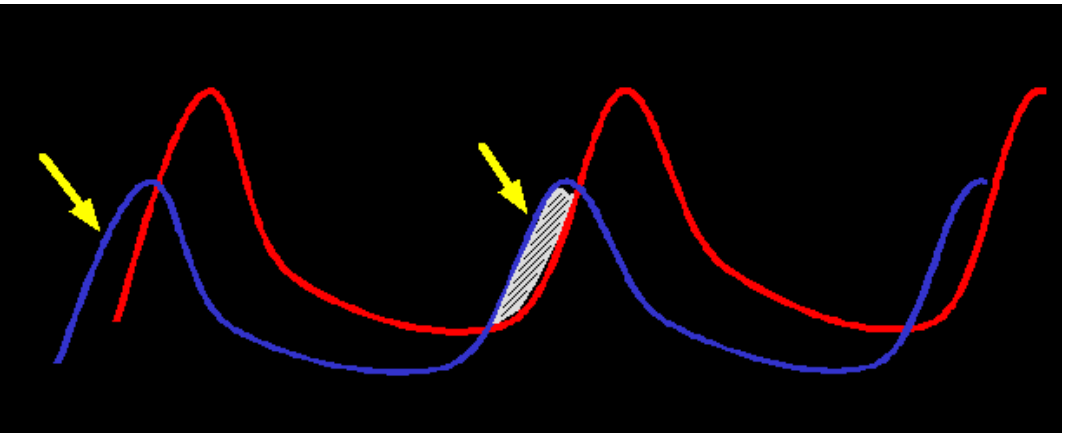
Pure Left to Right shunt

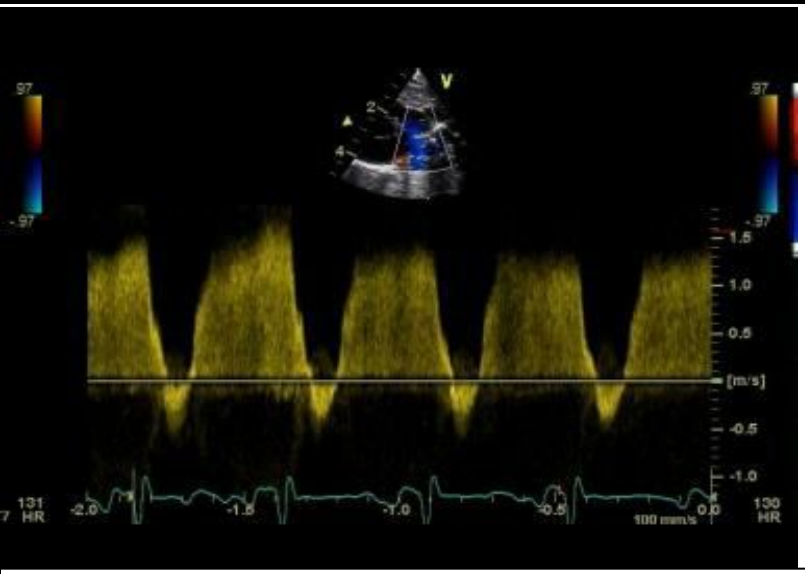


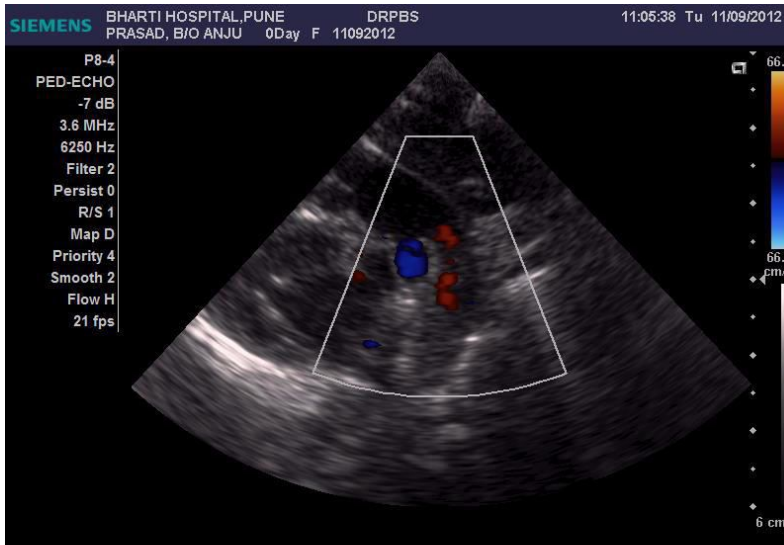


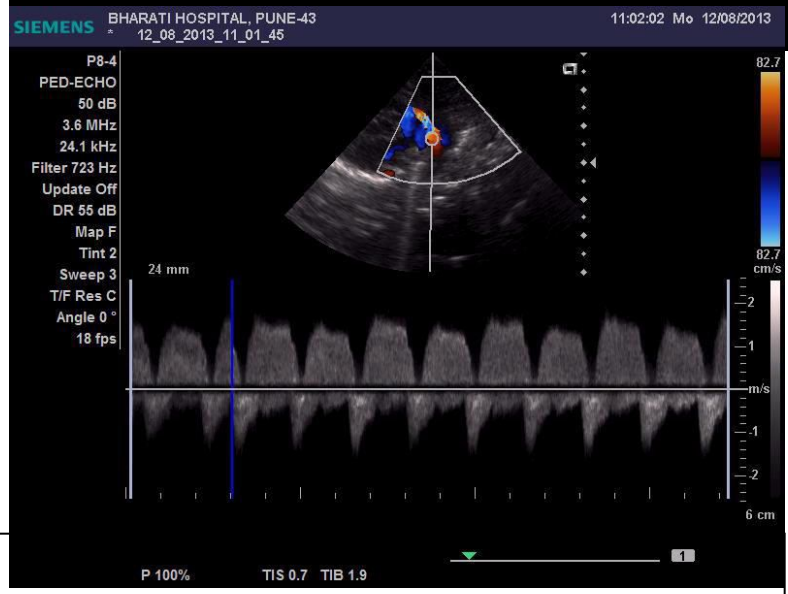












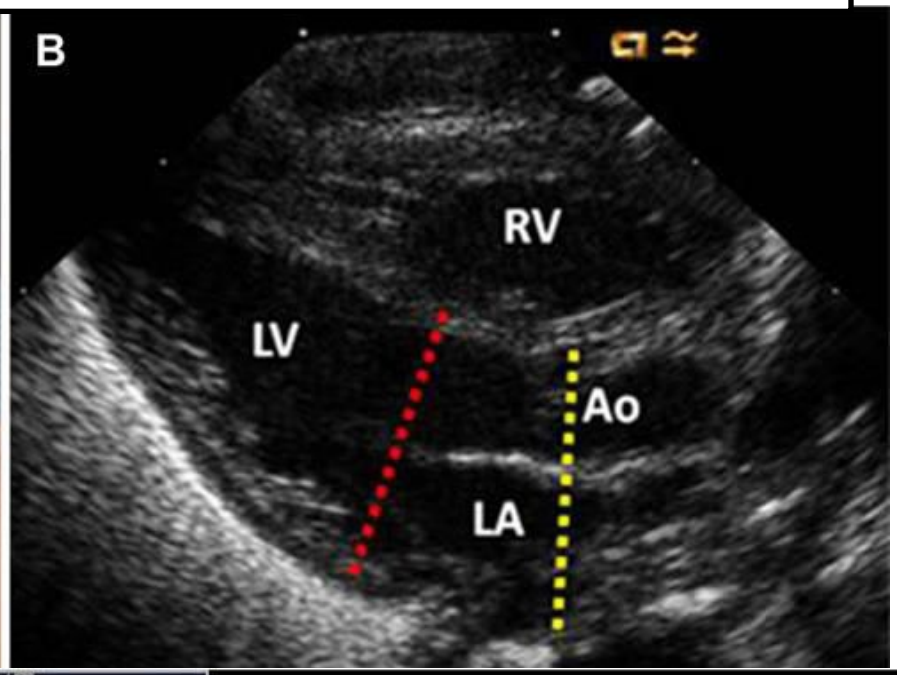
Bidirectional shunt

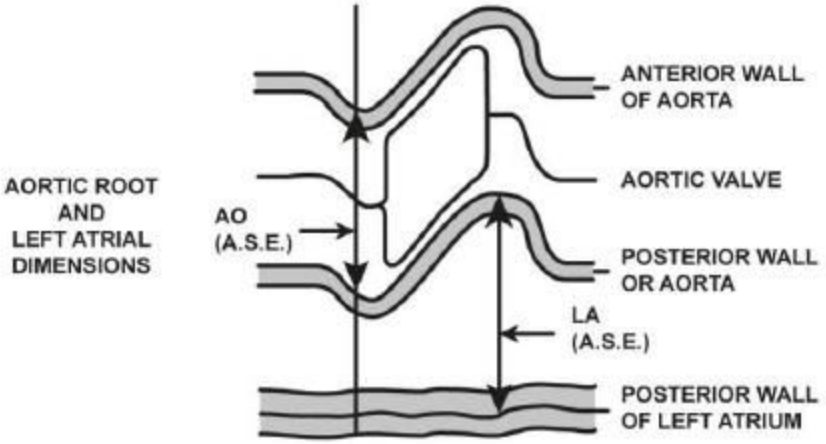
Pulmonary pressures are still below systemic pressures

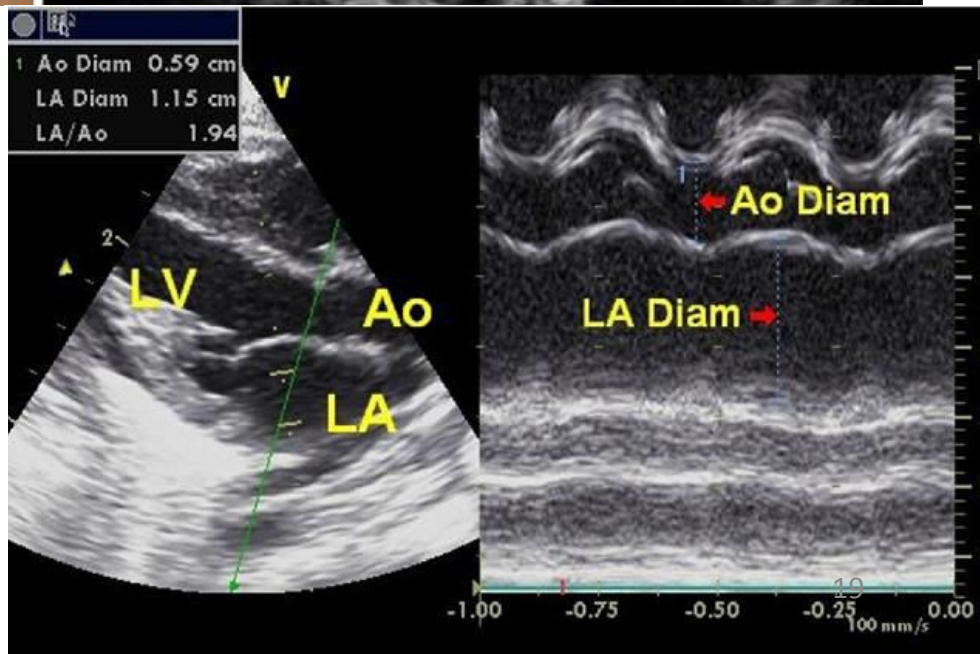
There is a period in early systole when pulmonary pressures > systemic pressures, there is an early period of a R to L shunt, followed by L to R shunt

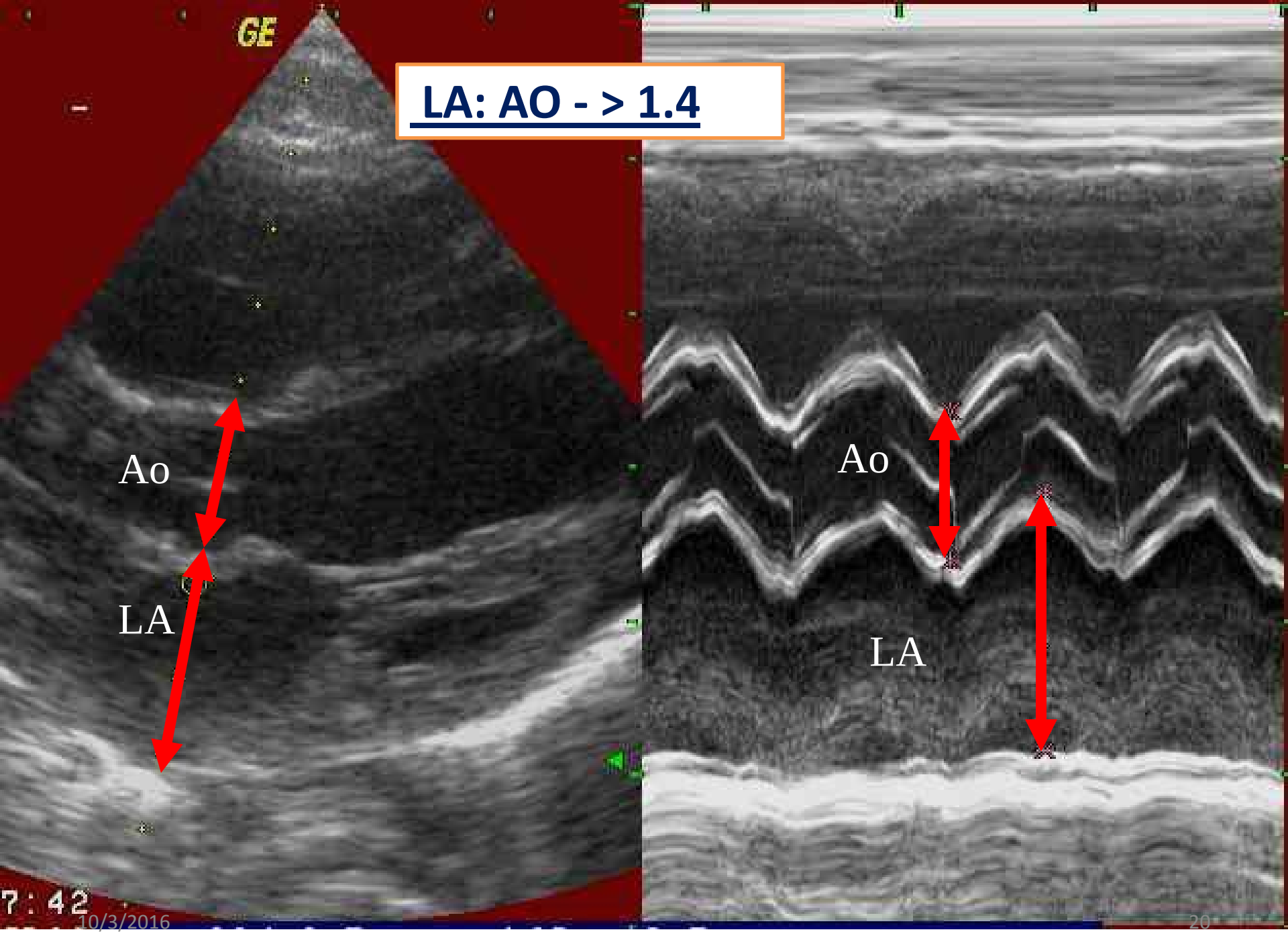
Ductal characteristics	Size of ductus Ductal flow patterns
Evaluation of pulmonary hyperperfusion	Left heart size LV function
Evaluation of systemic hypoperfusion	Post-ductal Ao flow pattern Mesenteric/coeliac flow SVC flow

Evaluation of chamber dilatation : LA: AO

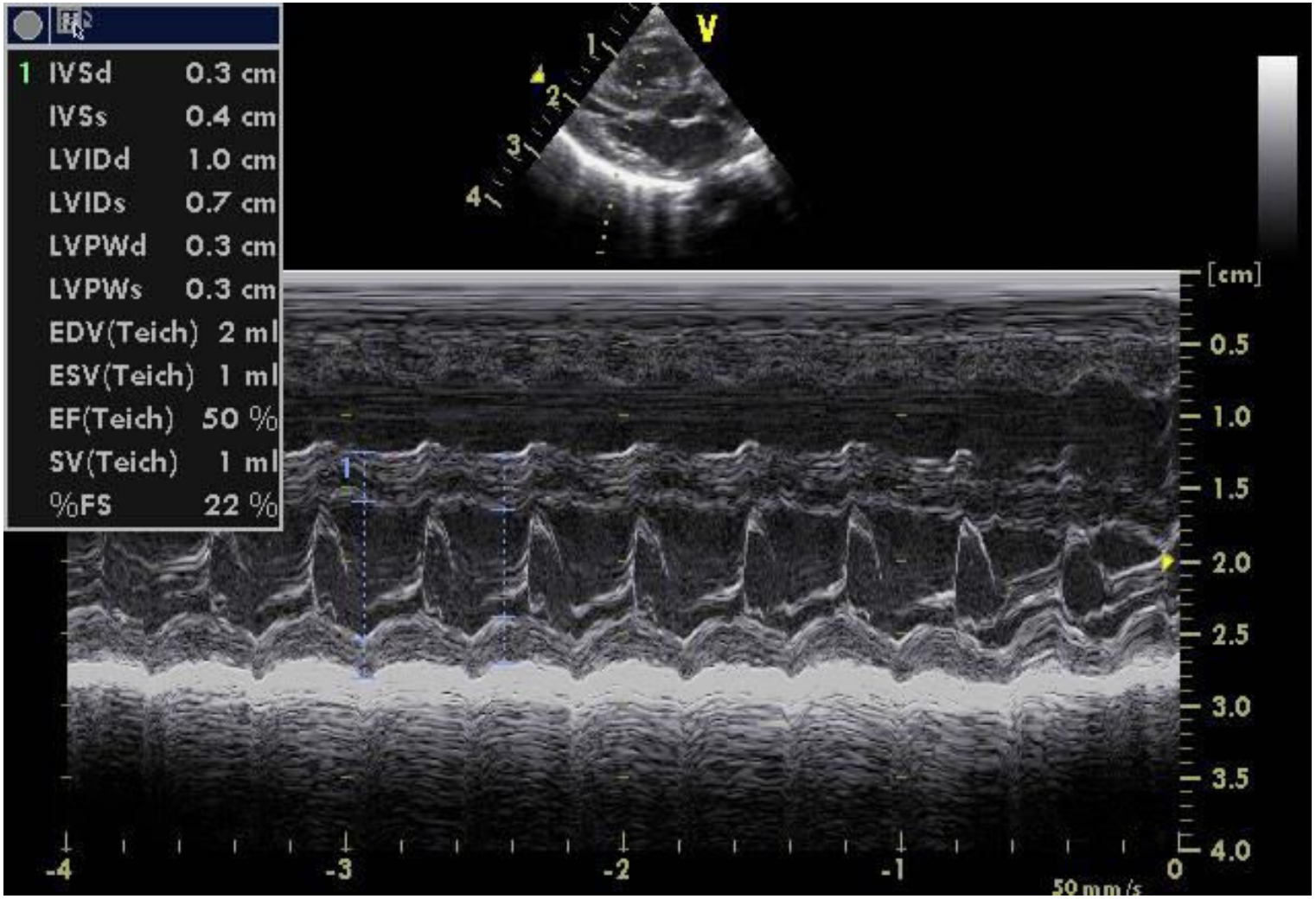


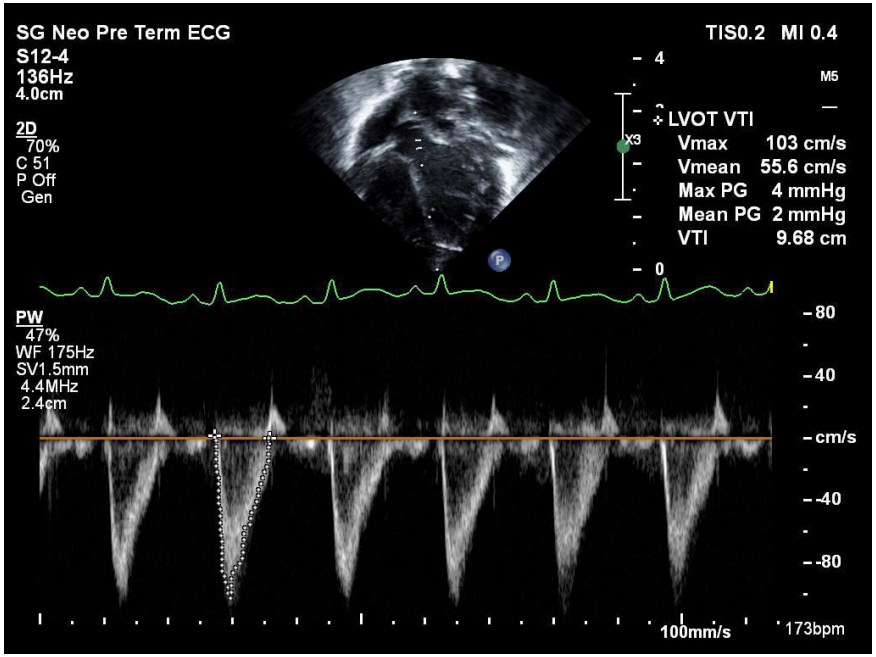


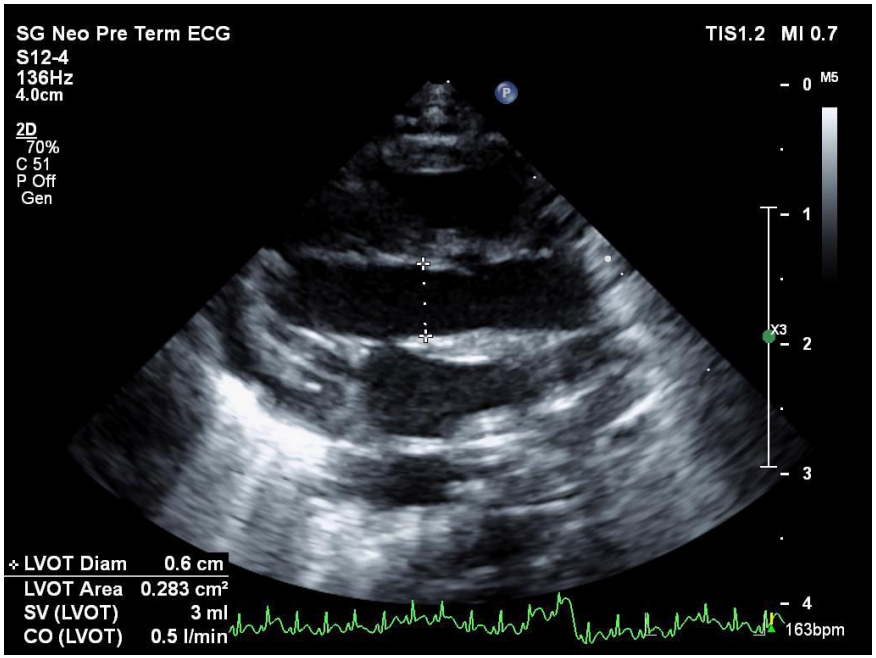



GE
LA: AO - > 1.4
Ao
LA
Ao
LA
7:42

LVEDD/Ao >2.1


1 IVSd 0.3 cm
IVSs 0.4 cm
LVIDd 1.0 cm
LVIDs 0.7 cm
LVPWd 0.3 cm
LVPWs 0.3 cm
EDV(Teich) 2 ml
ESV(Teich) 1 ml
EF(Teich) 50 %
SV(Teich) 1 ml
%FS 22 %
[cm]
0.5
1.0
1.5
2.0
2.5
3.0
3.5
4.0
-4
-3
-2
-1
0
50 mm/s





Ductal L to R flow

↓

Increased pulmonary blood flow

↓

Increased LV preload/LVO

↓

LV and LA dilatation

↓

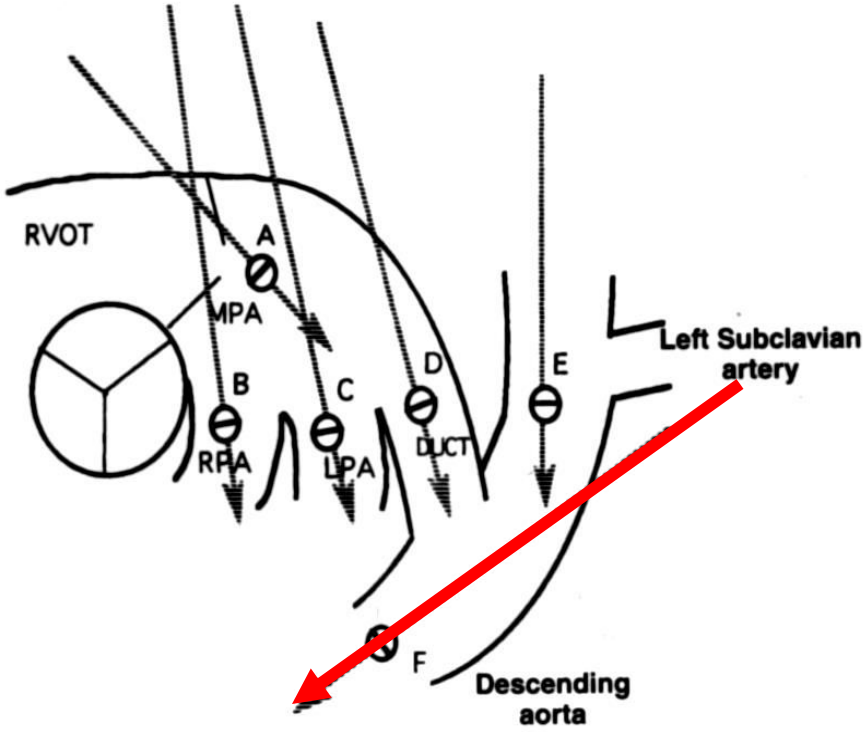
↑ Pulmonary venous pressure

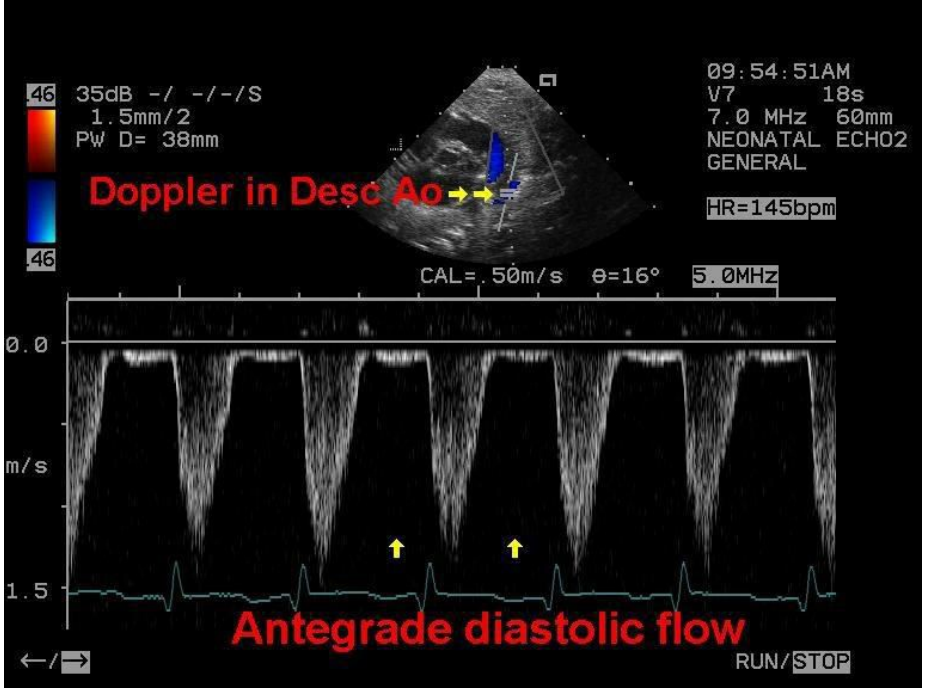
LVO > 400 ml/kg/min

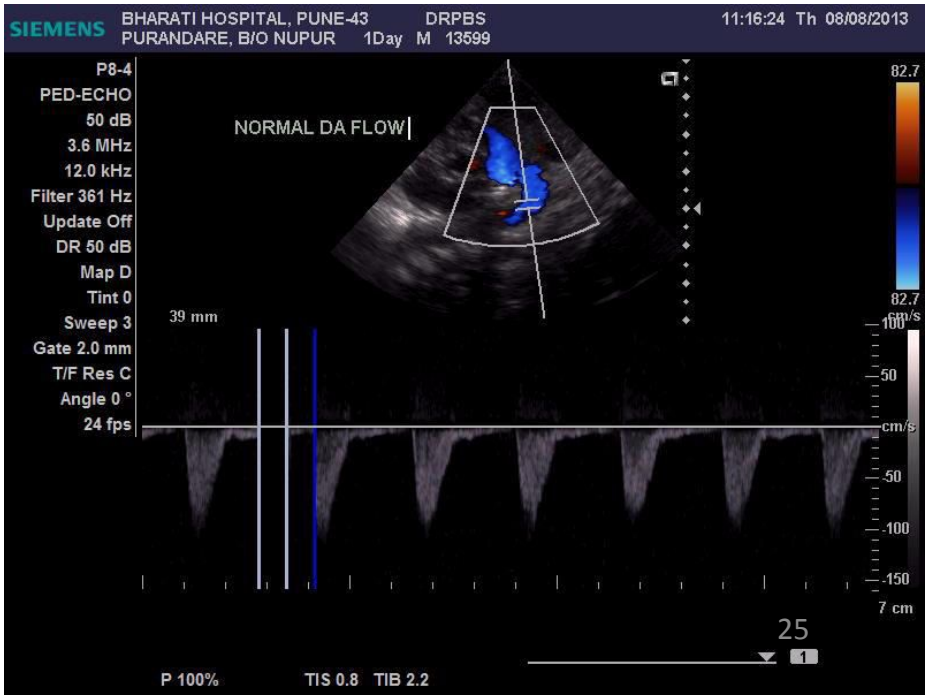
Ductal characteristics	Size of ductus Ductal flow patterns
Evaluation of pulmonary hyperperfusion	Left heart size LV function
Evaluation of systemic hypoperfusion	Post-ductal Ao flow pattern Mesenteric/coeliac flow SVC flow

PDA: ("Ductal steal")

- Diastolic aortic pressure is low with a large left to right ductal shunt - ductal steal
- Steal - Blood passing down the descending aorta during systole goes backwards up the arterial duct and into the pulmonary arteries during diastole
- Relative under perfusion of ALL systemic arteries
- Commonly "interrogated" arteries:
  - Descending aorta/Mesenteric/Renal/Anterior Cerebral

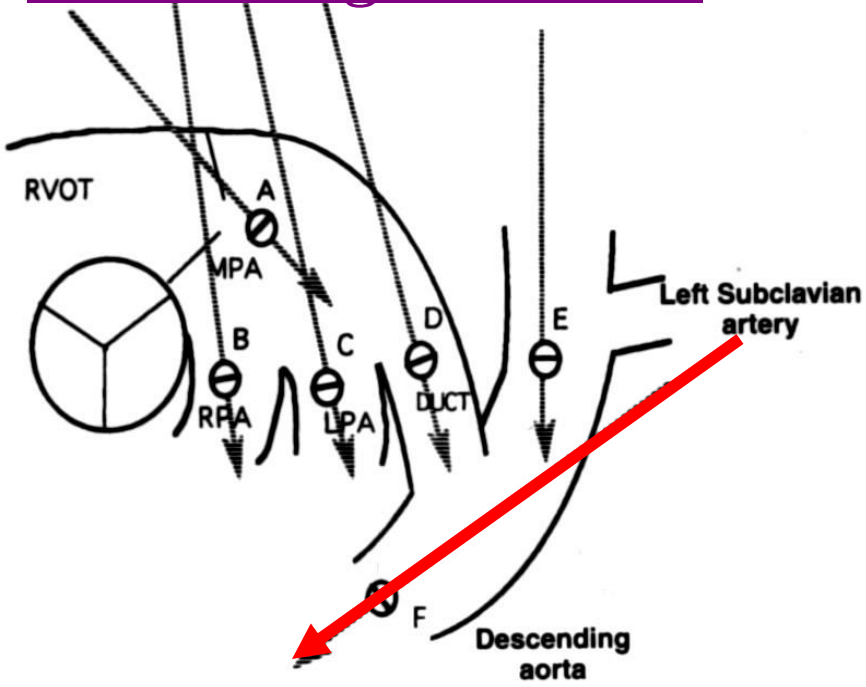


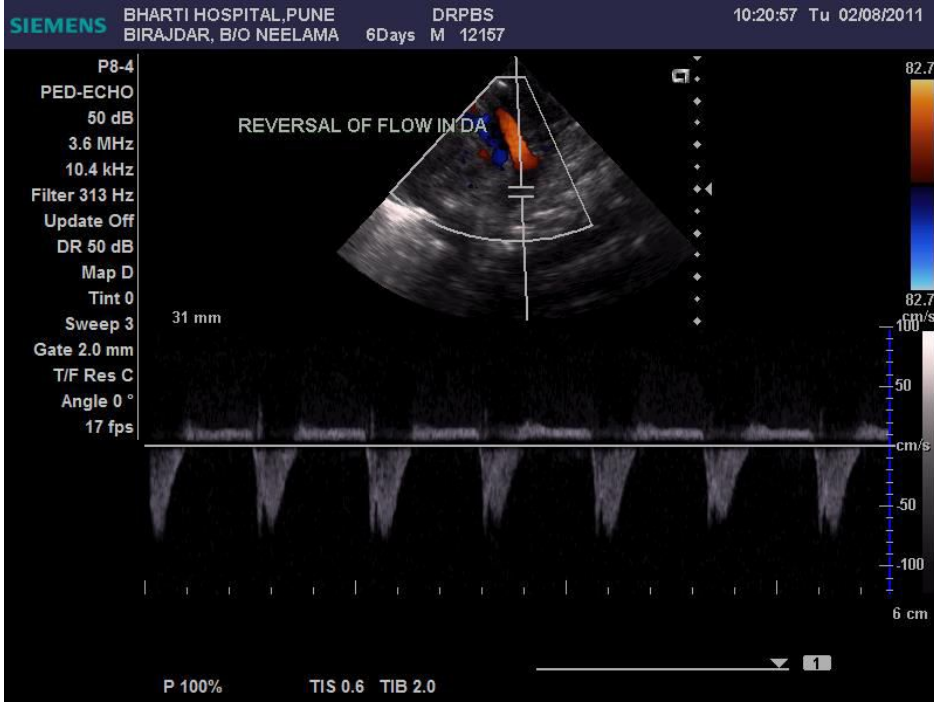


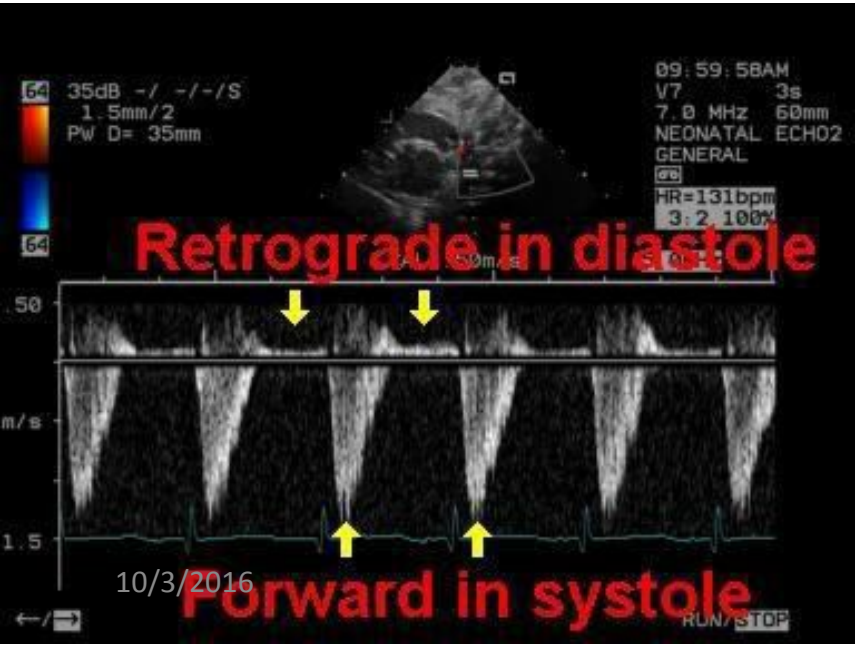


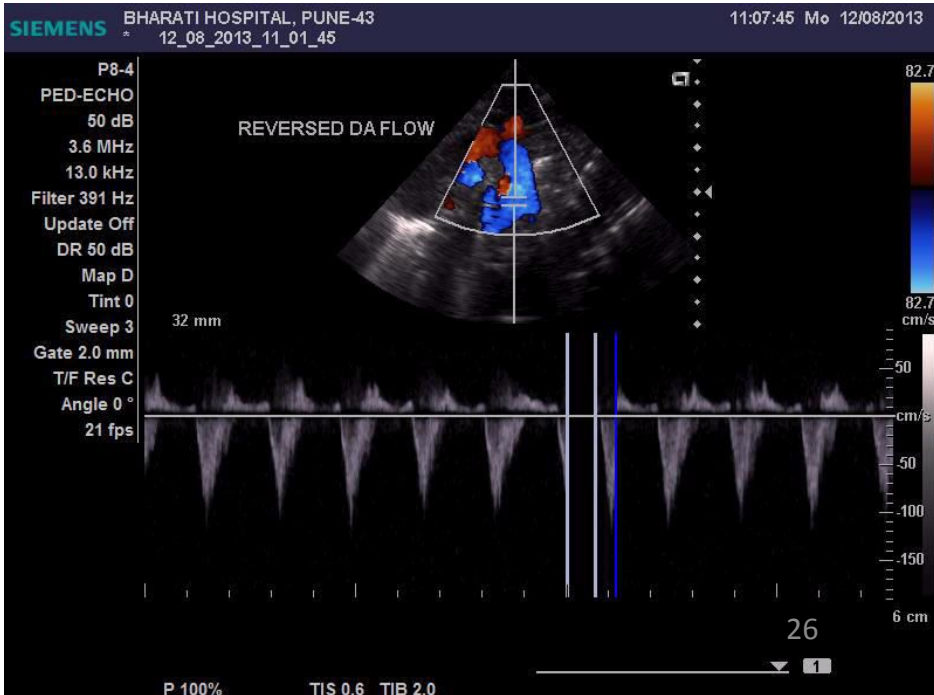
Descending aorta flow

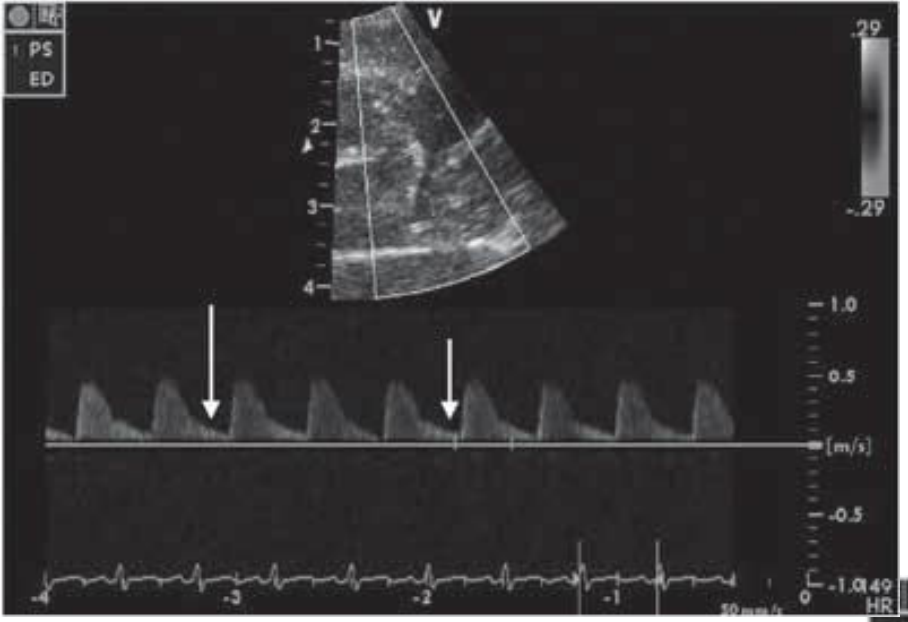
Descending aorta flow

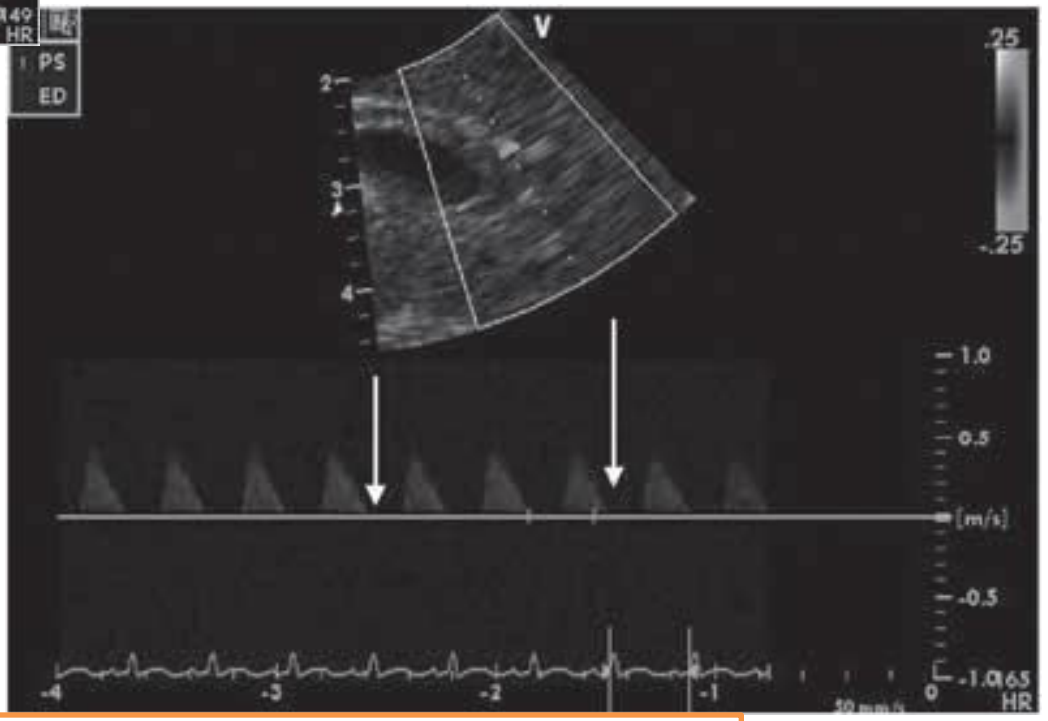




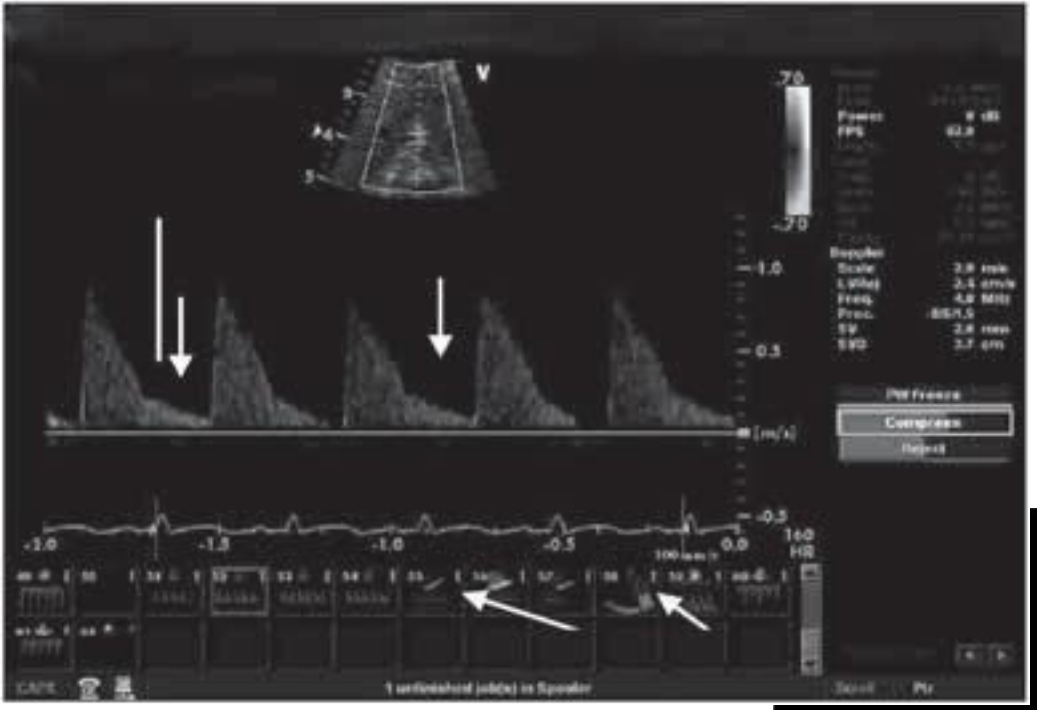


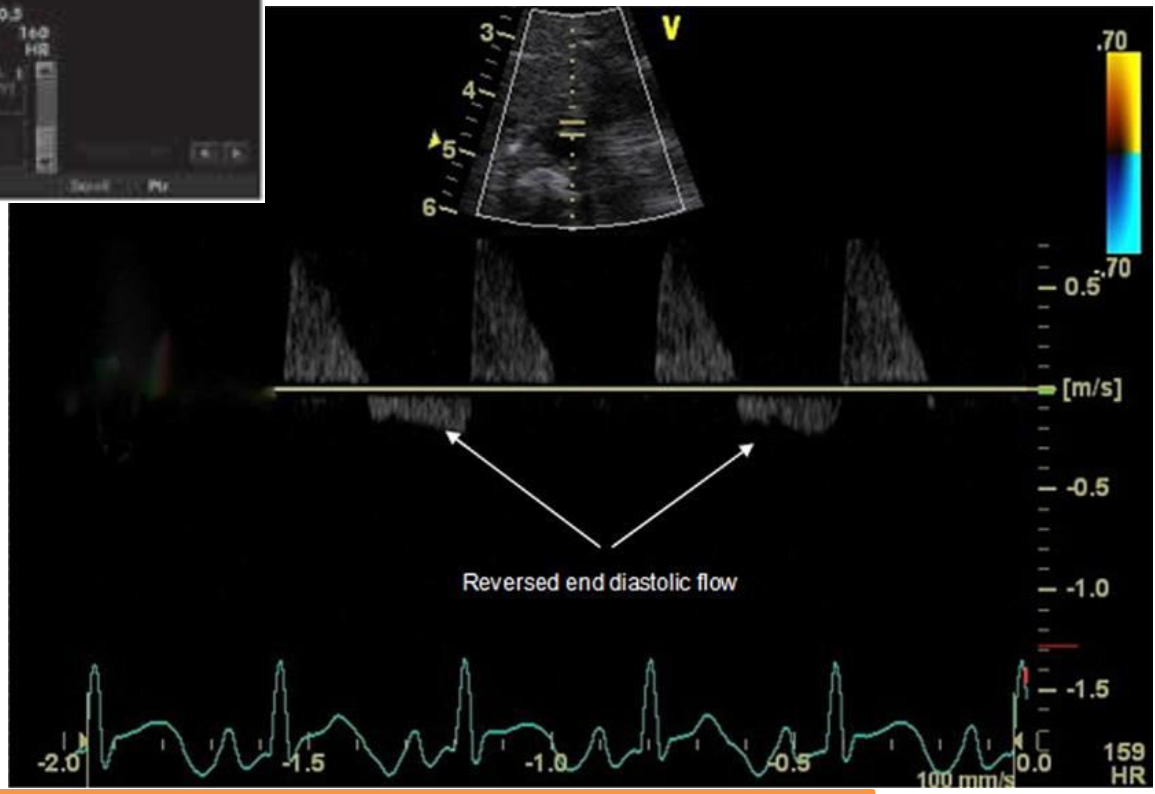




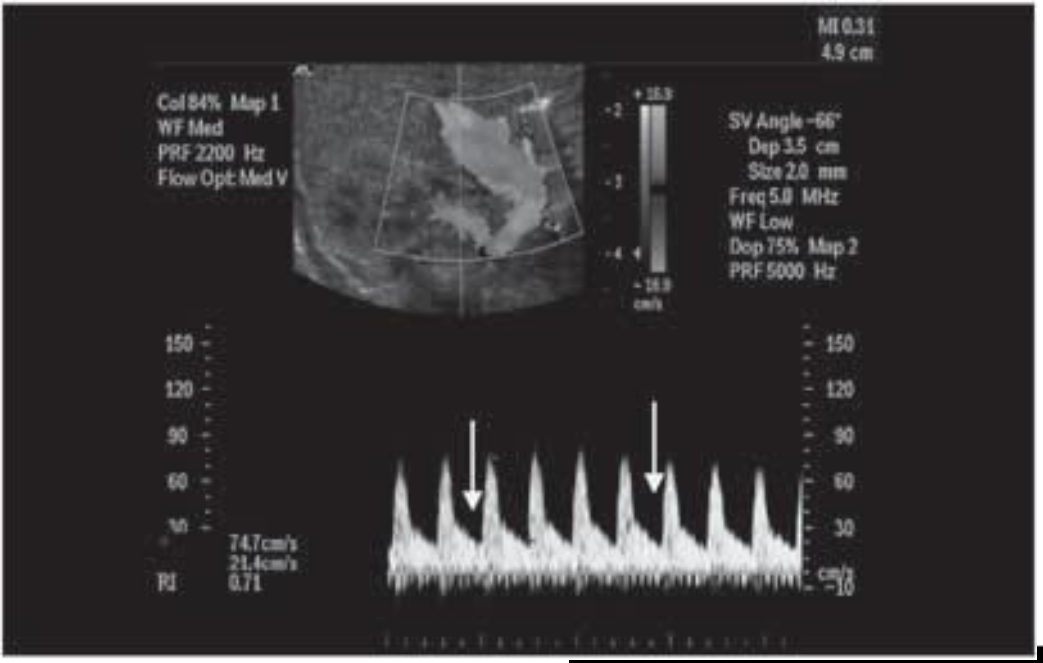


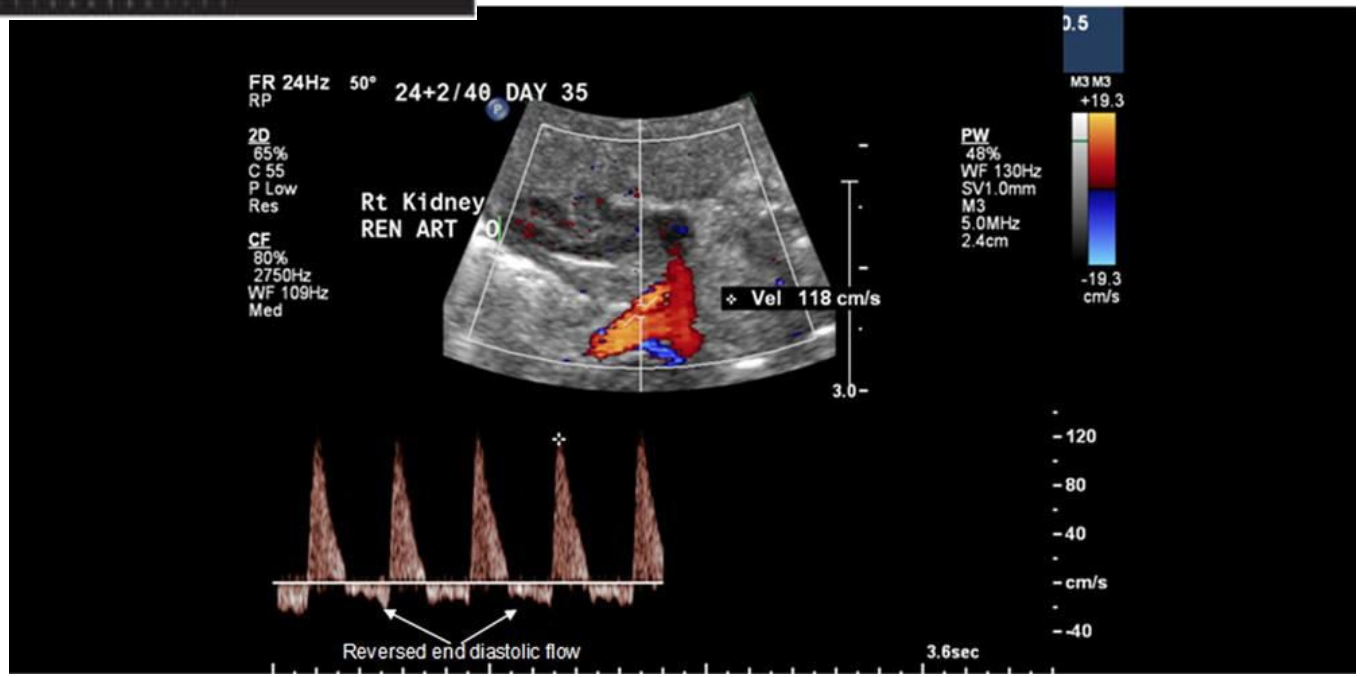
Abnormal flow pattern – Absent ACA





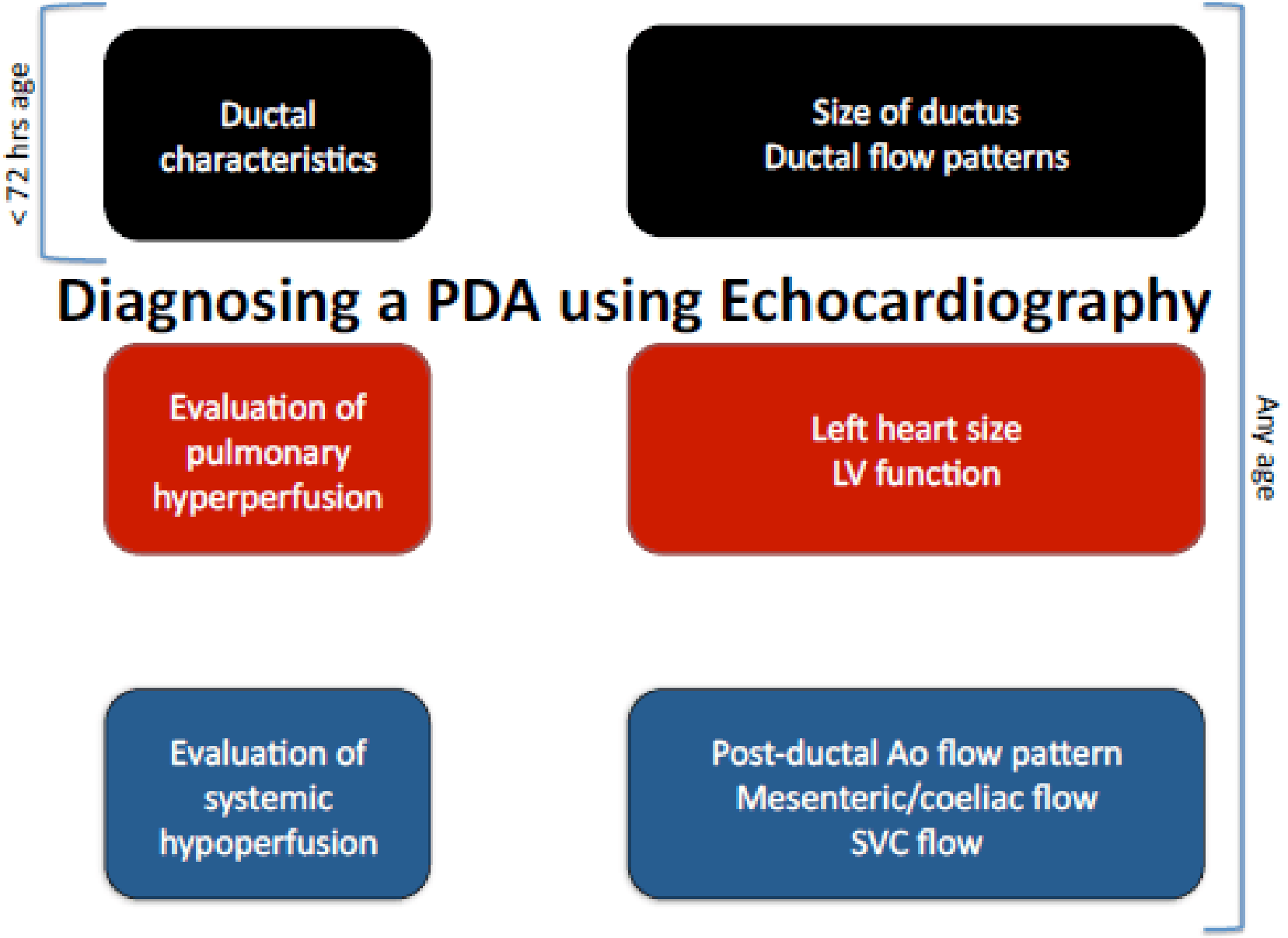
Abnormal flow pattern – REDF SMA





Abnormal flow pattern – REDF Renal Artery

Diagnosing a PDA using Echocardiography



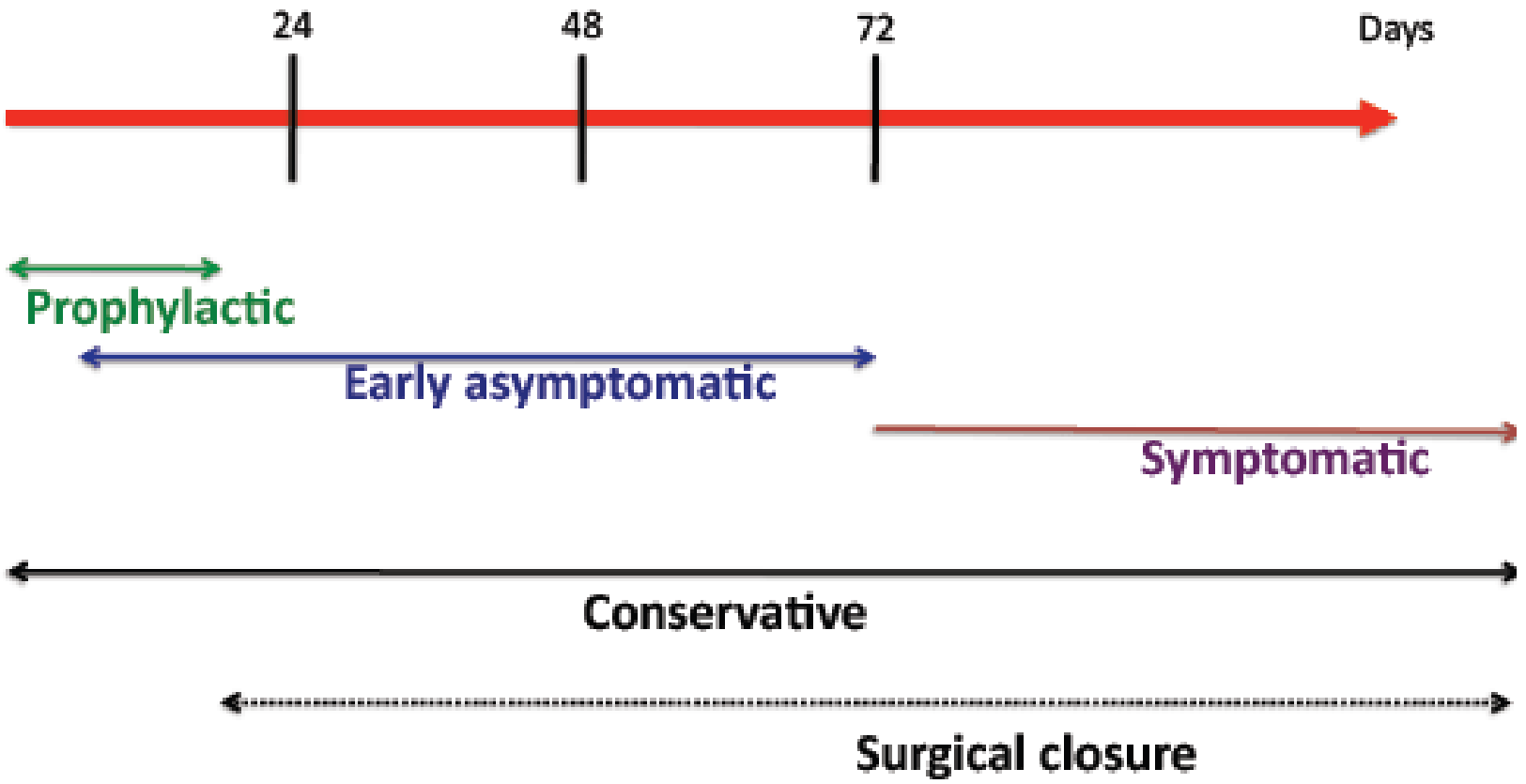
Take Home message

Surrogate markers of ductal significance

Measurement	Modality and sample gate	Moderate PDA	Large PDA
Ductus arteriosus			
Diameter (mm)	High parasternal ductal view	1.5–3.0	>3.0
Ductal velocity (m/s)	PWD at ductal view (PA)	1.5–2.0	<1.5
PA diastolic flow (m/s)	PWD at left PA	0.3–0.5	>0.5
Pulmonary overcirculation			
LA:Ao ratio	m-Mode: long axis view	1.5–1.7	>1.7
E wave:A wave ratio	Doppler: transmitral view	1.0–1.5	>1.5
IVRT (ms)	PWD between MV and AV	35–45	<35
Systemic hypoperfusion			
Left ventricular output (ml/kg/min)	PWD at LV outflow tract	200–300	>300
Diastolic descending Ao flow (%)	PWD at beyond PDA	30–50	>50
LVO/SVC ratio	PWD of flow at SVC	<2.4	>2.4
Celiac artery flow: LVO ratio	PWD at celiac artery	0.10–0.15	<0.10

Sehgal & McNamara Eur J Pediatrics. 2009

PDA Treatment Options



	Closure of PDA	↓ IVH & Pulm. Hem	↓ Ligation	Unnecessary Rx	Risk of NEC	Mortality
Prophylaxis (first 0-12 hours)	+++++	+++	+++	++++		
Pre-symptomatic (echo-based)	+++++	++	++	++		
Early symptomatic (hemodynamic symptoms)	++++		+	+		
Late symptomatic (early signs of organ failure)	+++				?	
Very late (heart failure)	++				++	?
No treatment	+				+++	+++

Shahab Noori 2014

Argument to treat early

- Effects of shunt
  - Short term – Hypotension, PH, IVH, Ductal steal
  - Medium term – CLD, PVL
- Effects of treatment
  - Acute – no increase shown in prophylaxis trials (NEC, SIP)
  - Long term – no difference in ND outcome (TIPP trial)
- Benefits to earlier treatment
  - Better timing
  - More efficacious
  - In right time frame for other benefits – reduced IVH, PH, hypotension

Morbidity and mortality in preterm neonates with patent ductus arteriosus on day 3

Anna Sellmer,[1,2,3] Jesper Vandborg Bjerre,[2] Michael Rahbek Schmidt,[4] Patrick J McNamara,[5] Vibeke Elisabeth Hjortdal,[6] Bente Høst,[2] Bodil Hammer Bech,[7] Tine Brink Henriksen[2,3]

What is already known on this topic

- The frequency of patent ductus arteriosus (PDA) is inversely related to gestational age.
- The clinical relevance of a PDA in preterm neonates is questionable.
- Outcome of a PDA is associated with the magnitude of the shunt across the PDA and the ability of the neonate to cope with it.

What this study adds

- Presence of a PDA on day 3 of life is associated with increased odds of mortality and severe morbidity in neonates born prior to 28 weeks gestation.
- In neonates born prior to 28 weeks gestation a PDA diameter ≥1.5 mm on day 3 is associated with greater odds of intraventricular haemorrhage, bronchopulmonary dysplasia and mortality or severe morbidity.

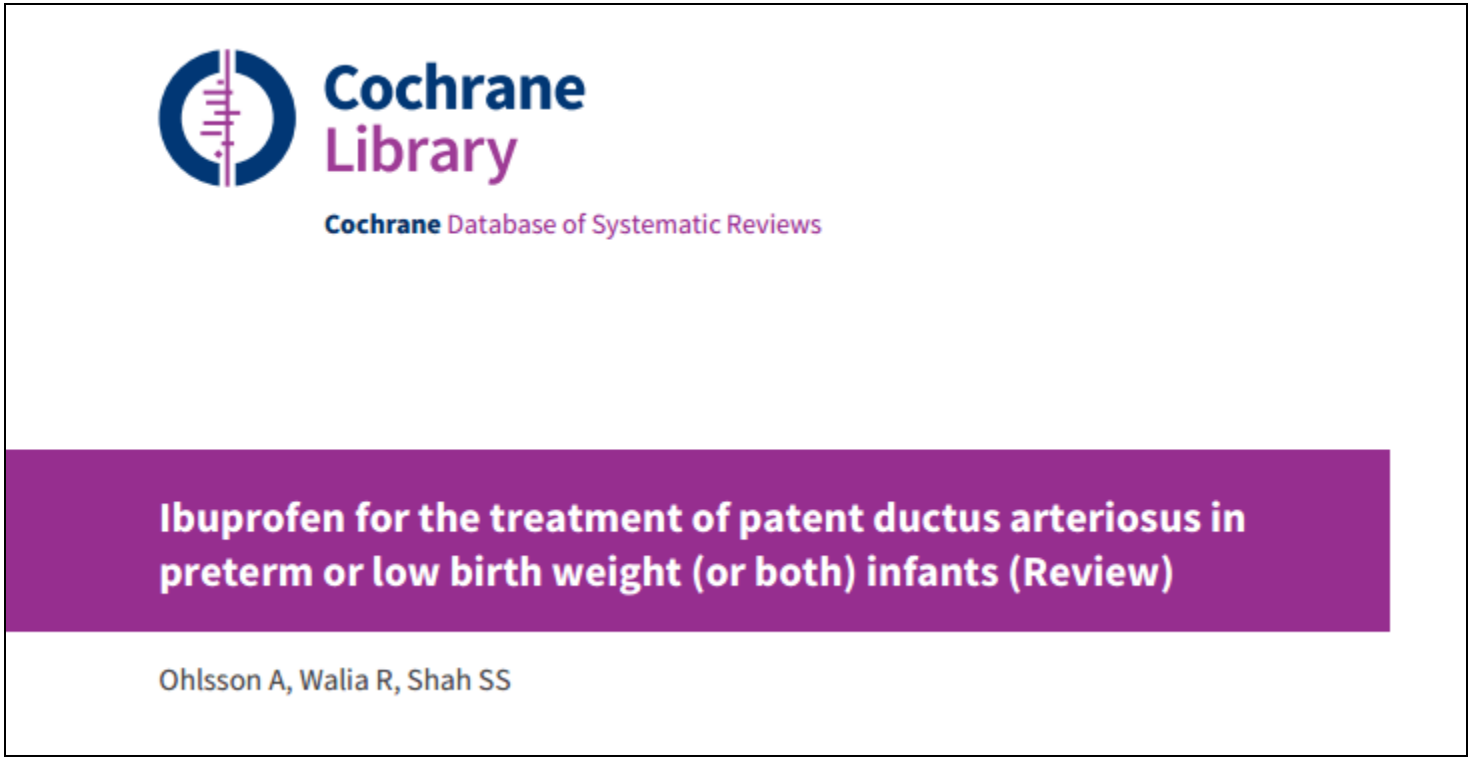
Sellmer et al. ADC F&N 2013

Trials of Early Asymptomatic Treatment

- **DETECT trial**, Australia (Indomethacin) – Trial prematurely closed due to drug non availability
- **TRIOCAPI trial,** France (Ibuprofen) – Recruiting
- **Baby-OSCAR trial,** UK (Ibuprofen) – Pilot phase

With what ? Treatment of PDA

- Conservative
  - positive pressure
  - fluid restriction/chemical banding(↑pCO2, ↓pO2)
  - Diuretics
  - increase hematocrit
- Medical
  - Indomethacin
  - Ibuprofen – Intravenous/Oral
  - Paracetamol
- Surgical ligation



Ibuprofen is as effective as indomethacin in closing a PDA and currently appears to be the drug of choice.

Ibuprofen reduces the risk of NEC and transient renal insufficiency.

Oro-gastric administration of ibuprofen appears as effective as iv administration.

Key Messages

- PDA is not benign and increases risk of death and complications of prematurity
- Clinical and echocardiography criteria differ for early targeted and late symptomatic treatment
- Late treatment of a symptomatic PDA does not improve clinical & long term outcomes
- If PDA unlikely to close spontaneously then treatment before it becomes symptomatic may be beneficial – trials are needed to assess this approach