The Role of Pre- and Postnatal Echocardiography in Congenital Heart Disease: State of My Art.

MD 1 World
Connecting the Global Medical World
www.MD1World.com

COLLAGE CONGRESSI
E.C.M.
Educazione Continua in Medicina

Norman H Silverman MD. D Sc (Med), FACC, FASE, FAHA.

Professor of Pediatrics (Cardiology) U.C. San Francisco,

Professor Emeritus, Stanford University,

Honorary Professor University of Cape Town

Questions to ask.

- How has echocardiography helped recognize cardiac disease after delivery
- What is the contribution of prenatal echocardiography
- What lesions does echocardiography help plan delivery and postnatal course.

Lesions to be discussed

- Transposition of the great arteries
- Totally anomalous pulmonary venous return
- Ebstein's malformation
- Spongy myocardium
- Cardiac manifestations of TTTS

Transposition of the great arteries

The Hypothetical Question:-

- Can fetal echocardiography identify the neonate with transposition at risk from a restrictive atrial communication?
- Will an urgent balloon atrial septostomy prevent hypoxemic encephalopathy?

Rationale

- After birth in complete transposition of the great vessels (D-TGA) without a ventricular communication, a restrictive patent foramen (PFO) leads to inadequate circulatory mixing and severe cyanosis.
- Urgent balloon atrial septostomy (uBAS) improves mixing and bridges neonates to surgery.
- Several studies have determined risk factors *in utero* for poor outcomes postnatally in D-TGA, particularly the restrictive PFO and ductus arteriosus (PDA).
- In addition to these risk factors, we studied two new features: the hyper-mobile septum (HMS) and reverse diastolic PDA shunting (RPDA) to determine which patients will need an uBAS.

Fetal Transposition

Issues:-

- In the fetus with transposition, why is:-
- The ductus arteriosus often narrowed?
- The foramen ovale often restrictive?
- Why does persistent pulmonary hypertension of the newborn (PPHN) occur in neonates with transposition?
- Can anything be done about it?

Prenatal Features of Ductus Arteriosus Constriction and Restrictive Foramen Ovale in d-Transposition of the Great Arteries

Yasuki V. Maeno, MD; Steven A. Kamenir, MD; Brian Sinclair, MD; Mary E. van der Velde, MD; Jeffrey F. Smallhorn, MD; Lisa K. Hornberger, MD

Background—Although most neonates with d-transposition of the great arteries (TGA) have an uncomplicated preoperative course, some with a restrictive foramen ovale (FO), ductus arteriosus (DA) constriction, or pulmonary hypertension may be severely hypoxemic and even die shortly after birth. Our goal was to determine whether prenatal echocardiography can identify these high-risk fetuses with TGA.

Methods and Results—We reviewed the prenatal and postnatal echocardiograms and outcomes of 16 fetuses with TGA/intact ventricular septum or small ventricular septal defect. Of the 16 fetuses, 6 prenatally had an abnormal FO (fixed position, flat, and/or redundant septum primum). Five of the 6 had restrictive FO at birth. Five fetuses had DA narrowing at the pulmonary artery end in utero, and 6 had a small DA (diameter z score of <-2.0). Of 4 fetuses with the most diminutive DA, 2 also had an abnormal appearance of the FO, and both died immediately after birth. One other fetus had persistent pulmonary hypertension. Eight fetuses had abnormal Doppler flow pattern in the DA (continuous high-velocity flow, n=1; retrograde diastolic flow, n=7).

Conclusions—Abnormal features of the FO, DA, or both are present in fetuses with TGA at high risk for postnatal hypoxemia. These features may result from the abnormal intrauterine hemodynamics in TGA. A combination of restrictive FO and DA constriction in TGA may be associated with early neonatal death. (*Circulation*. 1999;99:1209-1214.)

Jouannic et al. Circulation 110:1743, 2004

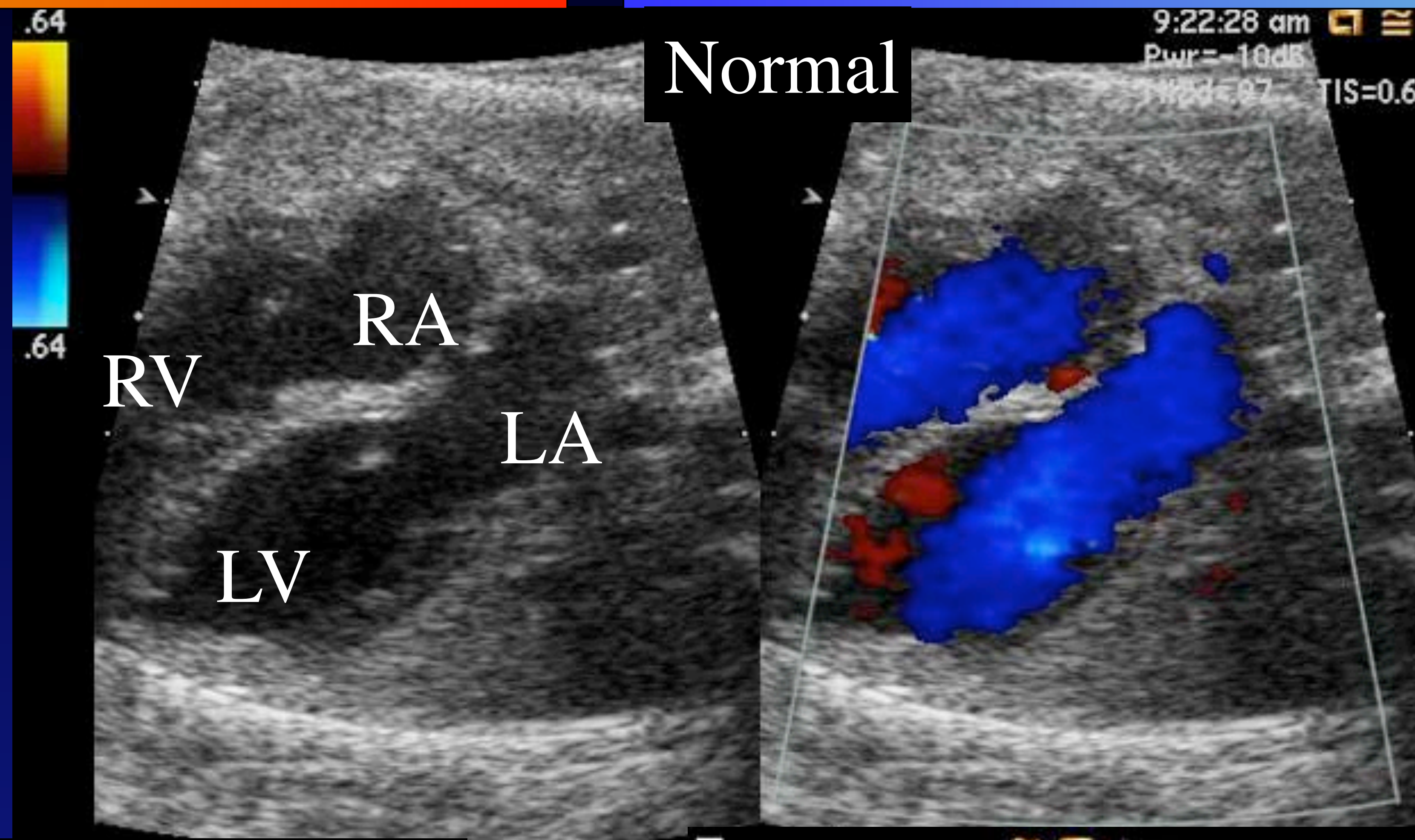
130 fetuses with aortopulmonary transposition;
FO and DA examined in 119 at 36+/-2.7 wk.

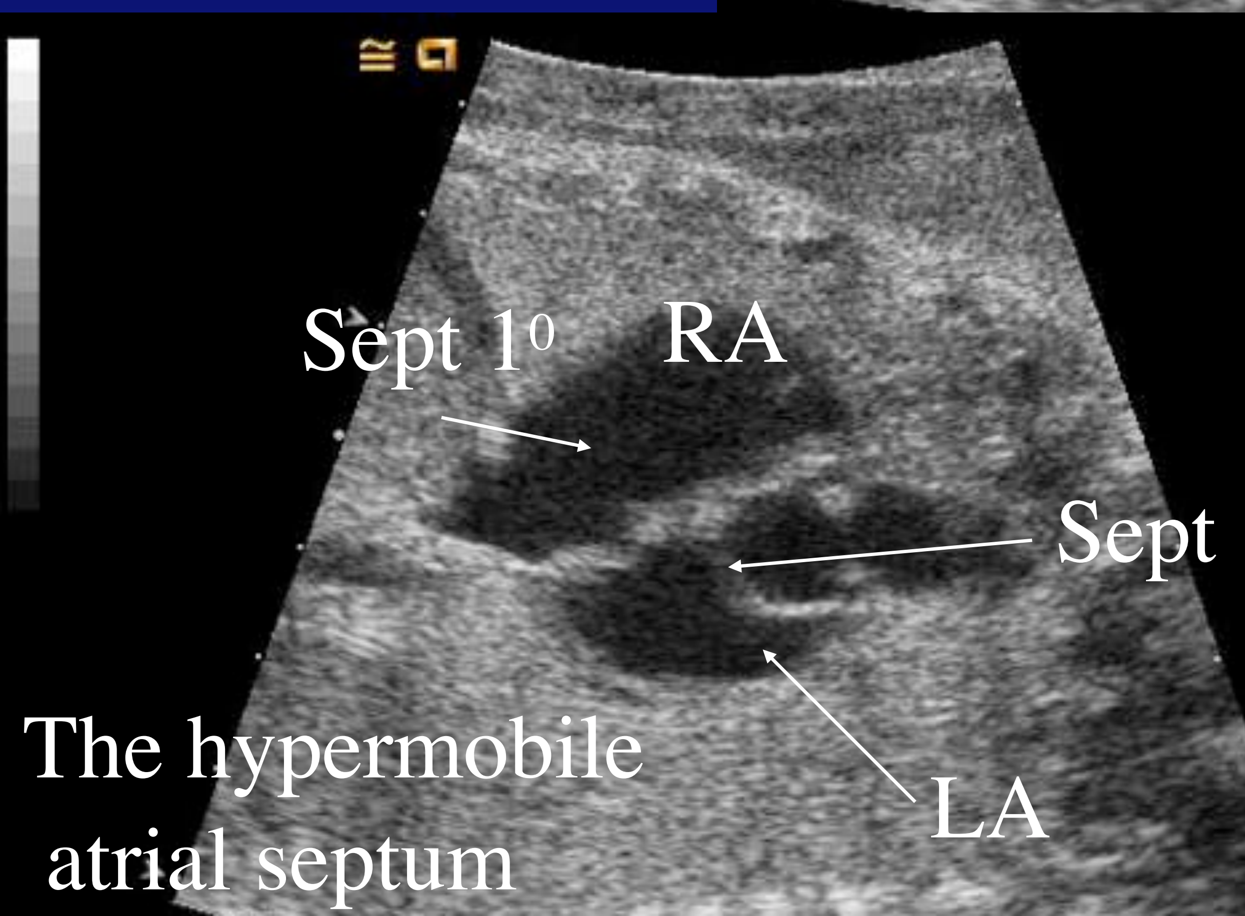
24 had abnormal shunts,
23 had a constricted FO,
5 had a narrowed DA,
4 had abnormal FO and DA.

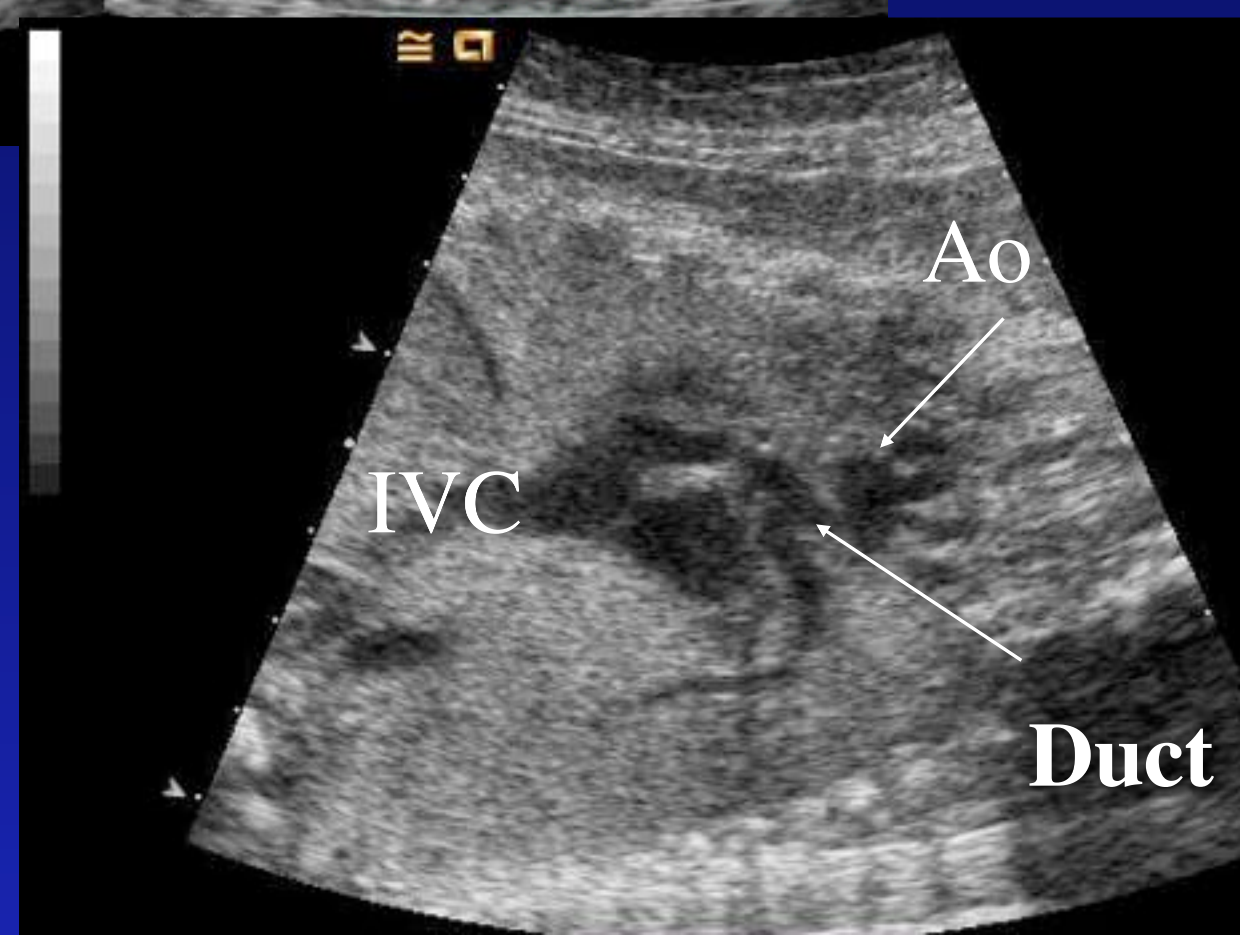
13 had severe hypoxia immediately after birth.

2 with narrow FO and DA died despite resuscitation attempts.

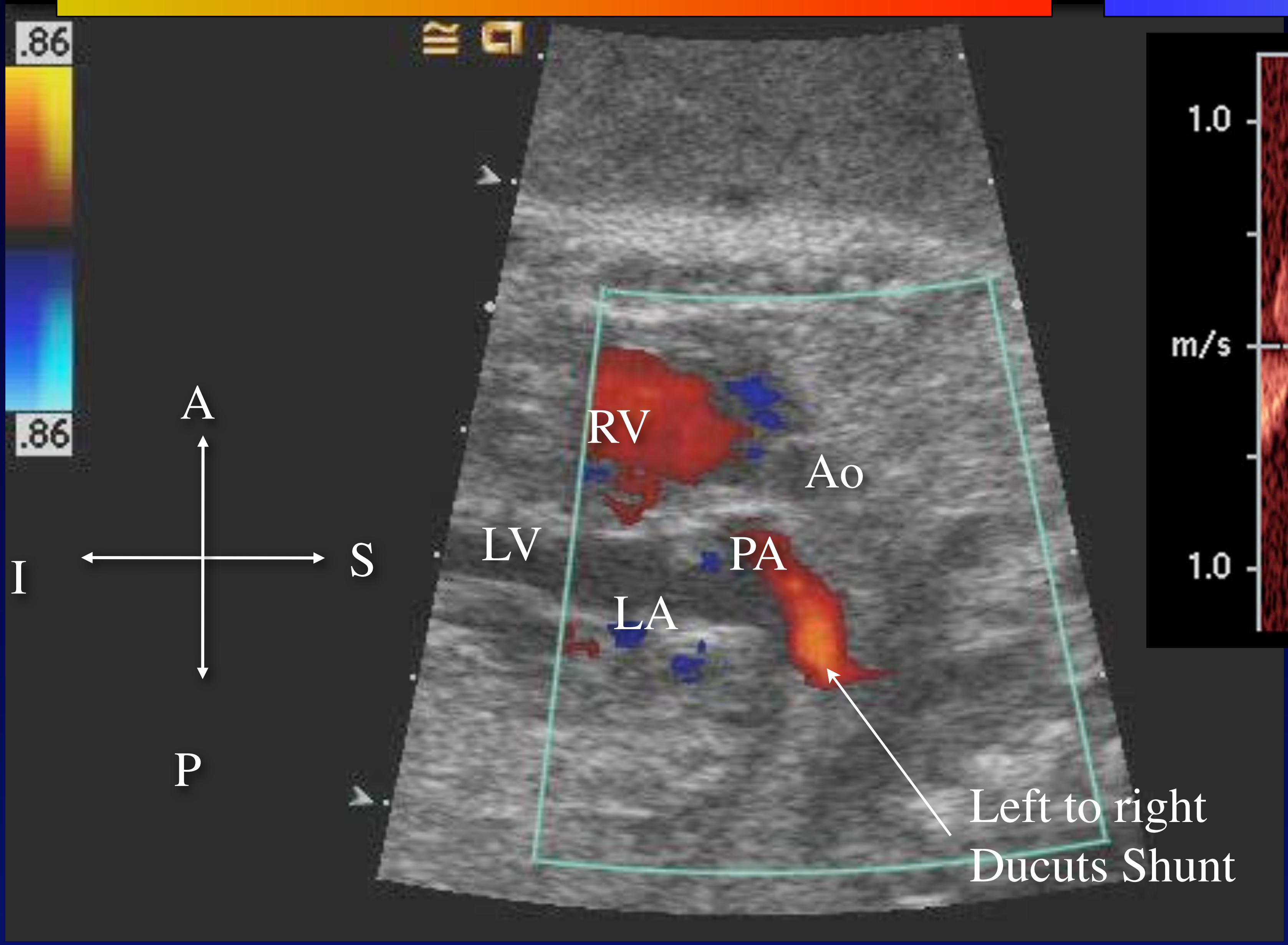
Stanford Study: Transposition, the Patent Foramen Ovale

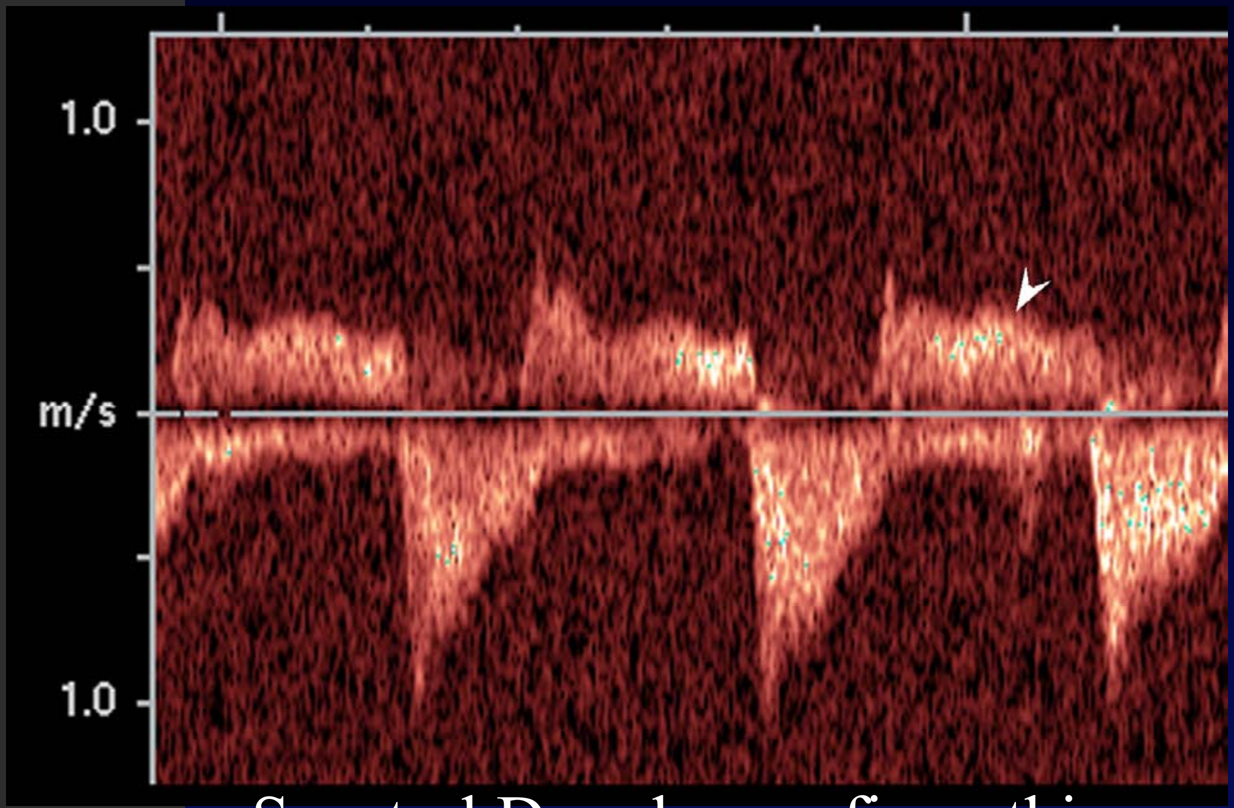






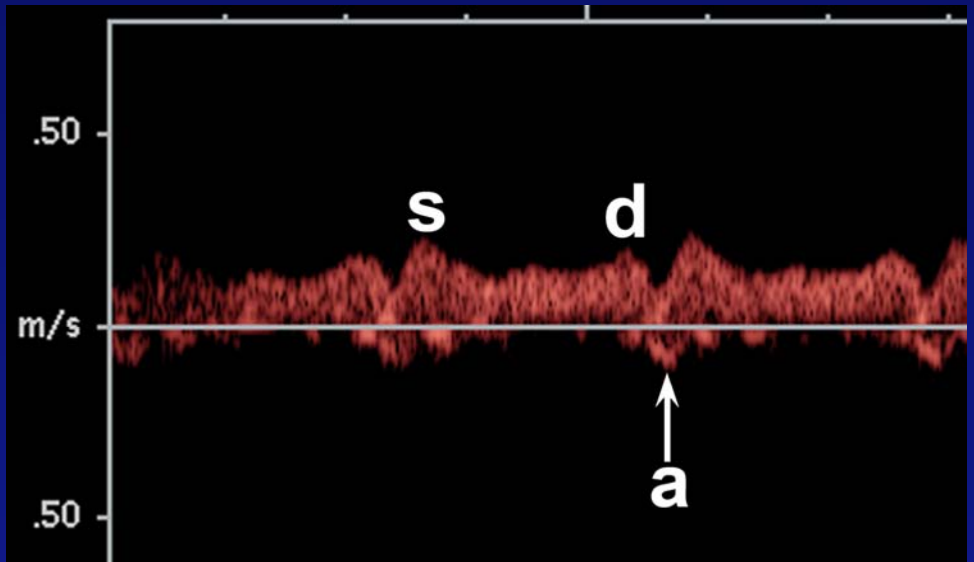
Transposition, the Duct





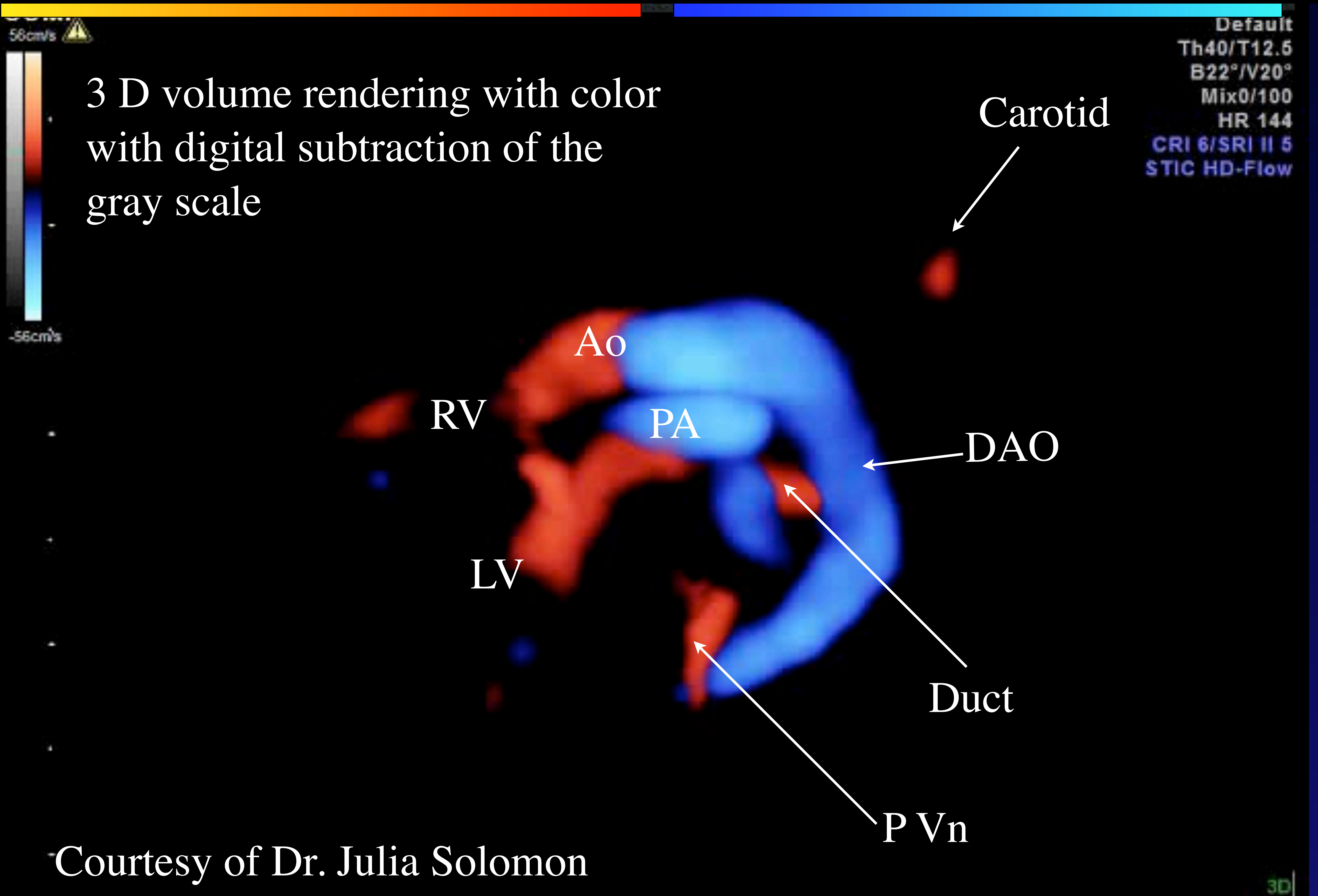
Spectral Doppler confirms this finding with flow above the baseline representing reverse ductal flow (arrowhead) and below the baseline normal antegrade ductal flow

Typical fetal pulmonary venous Doppler noted in our series. Note the normal systolic (s) and diastolic flows (d) with minimal (a) atrial flow reversal



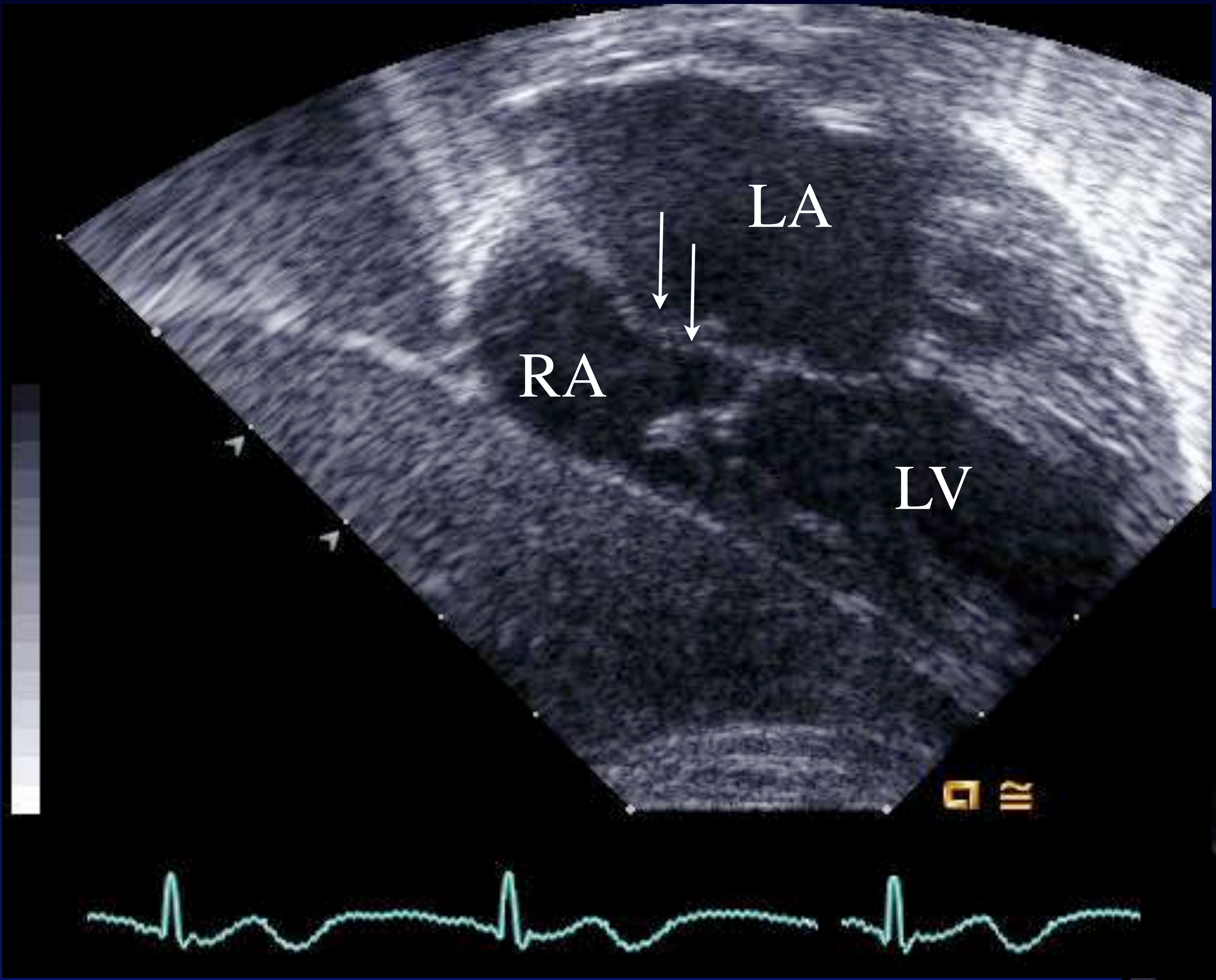
NHS.

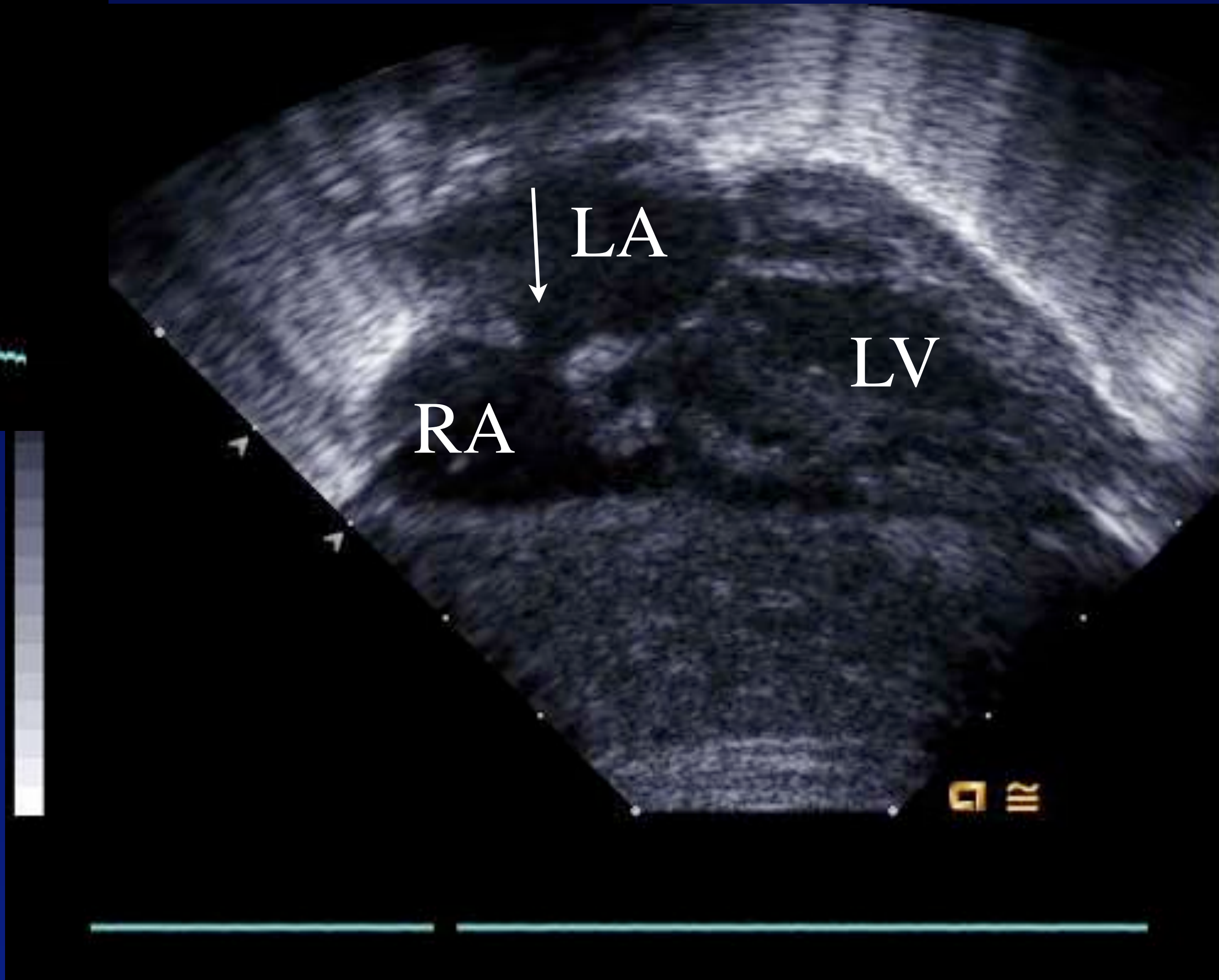
3 D volume rendering with color with digital subtraction of the gray scale



Courtesy of Dr. Julia Solomon

Immediate Postnatal ECHO For Cyanosis++





Before (top left) &
After Balloon Atrial
Septostomy (Bottom Right)
Immediately Neonatal
Subcostal Imaging

Reversed Shunting Across the Ductus Arteriosus or Atrial Septum In Utero Heralds Severe Congenital Heart Disease

RICHARD A. BERNING, MD, NORMAN H. SILVERMAN, MD, FACC, MARIA VILLEGAS, DAVID J. SAHN, MD, FACC,* GERARD R. MARTIN, MD, FACC,† MARY JO RICE, MD, FACC*

San Francisco, California; Portland, Oregon; and Washington, D.C.

(J Am Coll Cardiol 1996;27:481–6)

Conclusions. The finding of reversed flow by Doppler color flow mapping during fetal life provides a key to subsequent accurate diagnosis and denotes a spectrum of diseases with a very poor prognosis.

NHS.

Methods

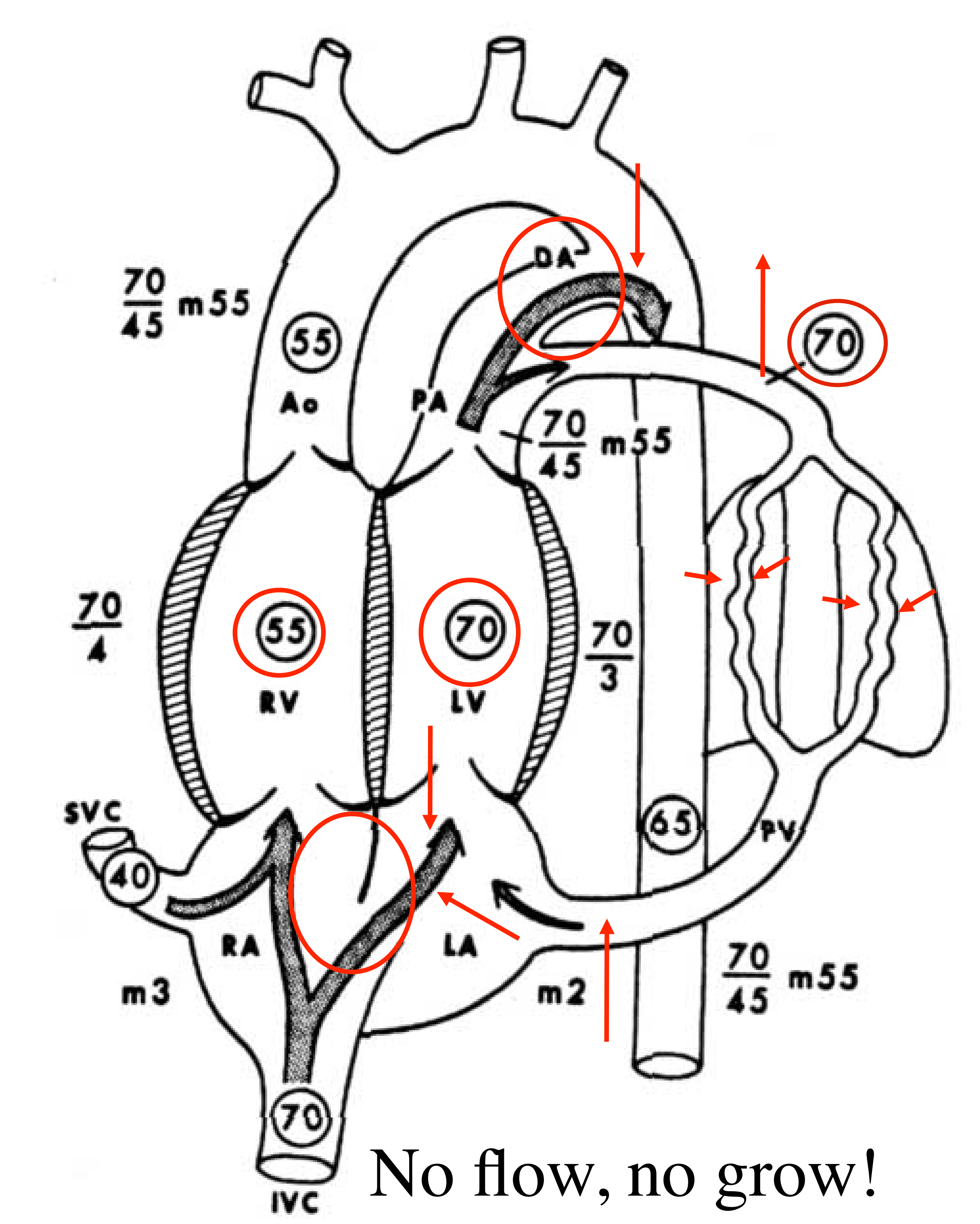
- We reviewed all fetuses from 2001-2009 for D-TGA and closely examined the PFO and septum primum for hypermobility, restriction, flat appearance, or redundancy.

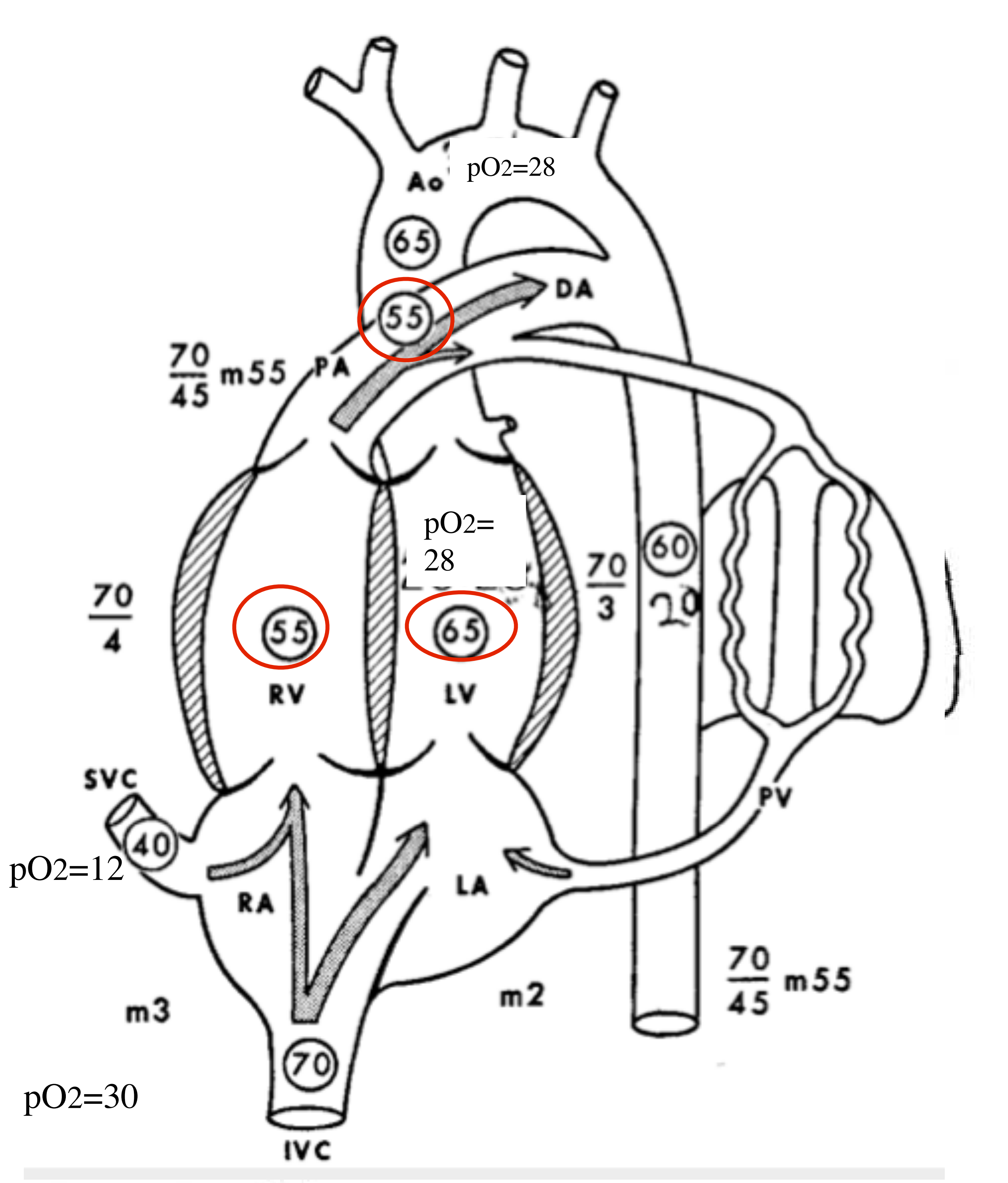
- We defined hypermobility as a septum primum flap that oscillates between the both atria.

- We also examined the PDA size and shunting pattern to evaluate whether these features contributed to uBAS.

- <u>Exclusion criteria</u>: Patients with moderate to large ventricular septal defects or double outlet right ventricle were excluded from the study

Transposition & Oxygen Saturations



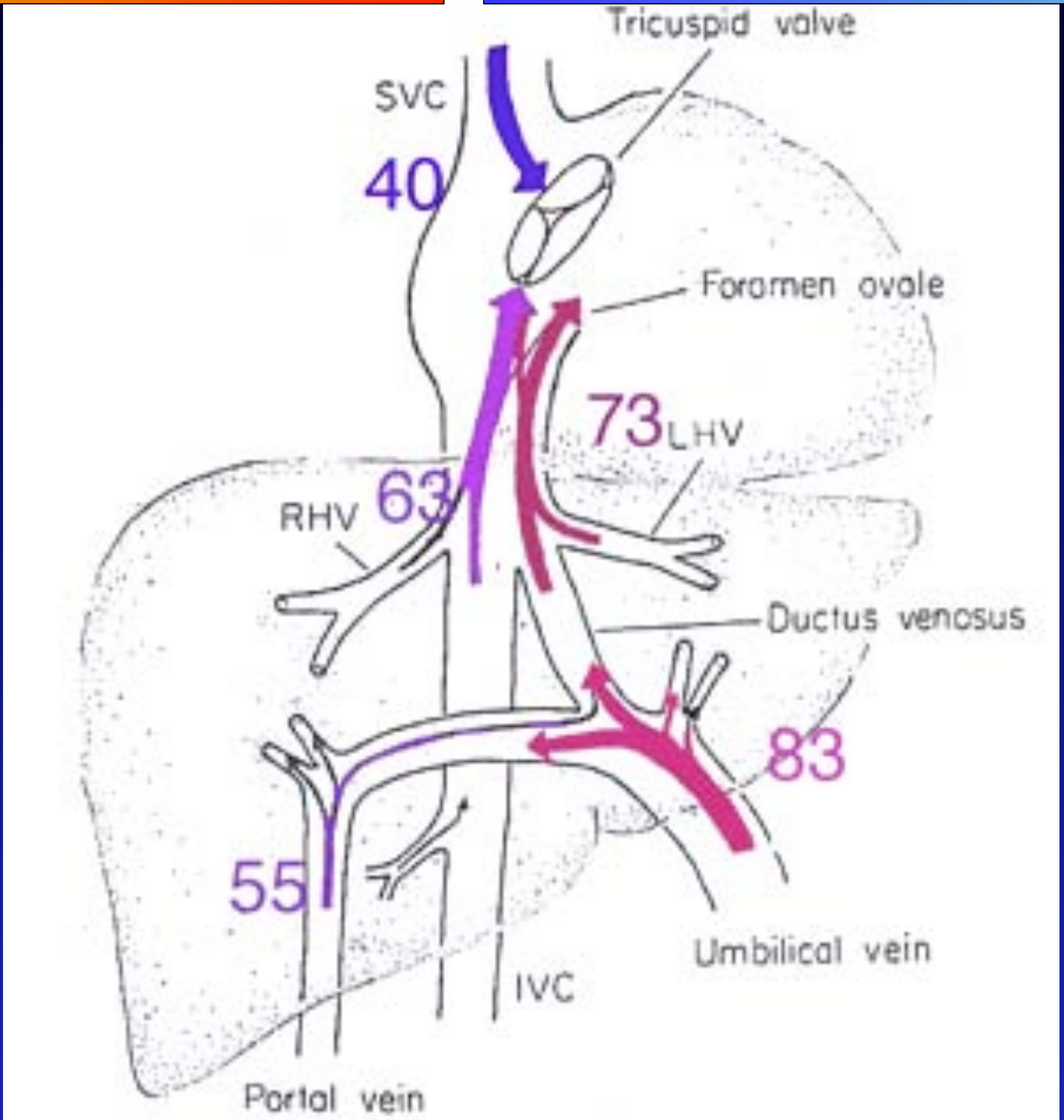


Intact ventricular septum

Normal Fetus

NHS.

Ductus Venosus Contribution to O_2 Saturation



NHS.

Results: n=26

Fetal Predictors of Urgent Balloon Atrial Septostomy in Neonates with Complete Transposition (J Am Soc Echocardiogr 2011;24:425-30.)

Rajesh Punn, MD, and Norman H. Silverman, MD

Fetal predictors of postnatal urgent balloon atrial septostomy

Risk factor	Urgent BAS	No urgent BAS	*P* value	Sensitivity	Specificity	PPV	NPV
Hypermobile septum	9	0	.0007	0.64	1.00	1.00	0.71
Normal mobility	5	12					
Diastolic reverse ductal flow	8	1	.0145	0.57	0.92	0.89	0.65
Normal ductal flow	6	11					
Redundant septum	4	7	.4283	0.31	0.46	0.36	0.40
Septum without redundancy	9	6					
Both reverse and hypermobile	5	0	.0425	0.36	1.00	1.00	0.57
Patients without both features	9	12					

BAS, Balloon atrial septostomy; *PPV*, positive predictive value; *NPV*, negative predictive value.

	u-bas	no u-bas	Total
both hms/rpda	12	1	13
neither hms/rpda	2	11	13
Total	14	12	26

Sensitivity = 86% Specificity = 92% PPV = 92% NPV = 85%

Outcomes: Urgent Balloon Atrial Septostomy

- 12/18 patients required an uBAS; all of which improved the oxygen saturation to acceptable levels.

- One patient developed complete heart block after the procedure, requiring a pacemaker at the time of the arterial switch procedure

Caution

As pulmonary blood flow increases in the last trimester of pregnancy the events described here are more likely to present themselves toward the latter half of pregnancy, a normal finding in mid-gestation does not assure that later evaluation may not show a restrictive atrial septum in late gestation or at birth.

I recommend, therefore, that these patients be studied for a second time between 28-36 weeks of gestation to evaluate this finding.

How has all this changed our practice?

If there are signs of a restrictive atrial septum the following procedure is followed:-

1. The mother is delivered into a sterile setup room as a precaution

2. The interventional cardiology team is in the delivery room with the mother and fully prepared to perform urgent balloon atrial septostomy of saturators indicate its necessity.

Conclusions

- Selection of fetal patients in need of urgent balloon atrial septostomy is necessary to provide optimal care for neonates with complete transposition.
- The hyper-mobile primum septum in fetal patients with complete transposition is a risk factor for urgent balloon atrial septostomy postnatally.
- Diastolic reverse ductal flow is also a risk factor for inadequate mixing postnatally.
- Taken together with other reported findings, these factors may improve postnatal outcome for neonates with transposition and inadequate circulatory mixing.

- **Re-examine in the last trimester!!!!**

Totally Anomalous Pulmonary Venous Return in the Fetus: New Insights

Diagnosis	+ve #	-ve #	% pre-natal diagnosis (post-natal survey)	Fetuses TOP # † (n)	% prenatal diagnosis (post-natal survey+ TOP / total)
Tetralogy of Fallot	7	31	18%	7	7+7/45 (31%)
Left Heart obstructive lesions (excluding HLHS*)	6	30	17%	3	6+3/39 (23%)
d-& l-Transposition	6	25	17%	0	6/31 (19%)
HLHS *	9	7	56%	2	9+2/18 (61%)
Heterotaxy Syndrome	5	3	63%	9	5+9/17 (82%)
Atrio-ventricular Canal	6	8	43%	2	6+2/16 (50%)
Double Outlet R Ventricle	2	9	18%	1	2+1/12 (25%)
Single ventricle	5	4	56%	2	5+2/11 (64%)
Pulmonary Stenosis/Atresia (IVS)	3	4	43%	1	3+1/8 (50%)
TAPVR (Anom Venous Return)	0	6	0%	0	0/6 (0%)
Tricuspid valve anomalies	1	3	25%	0	1/4 (25%)
Truncus Arteriosus	2	2	50%	0	2/4 (50%)

† TOP = Termination of pregnancy

* HLHS = Hypoplastic Left Heart Syndrome

Overall Detection Rate 28 %

Mark Friedberg,, Norman Silverman, MD, , Anita J. Moon-Grady, , Elizabeth Tong, RN, Jennifer Nourse,Beatrice Sorenson, Jaimie Lee, and Lisa K. Hornberger, J Pediatr 2009;155;26-31).

Significance of TAPVR.

- Total anomalous pulmonary venous return ***with obstruction*** remains a ***cardiac surgical emergency*** even in these times and carries a fatal prognosis without surgery. Without obstruction the prognosis and risk are much lower.
- Doppler and Doppler Color flow signals are helpful in making the diagnosis.
- Signs of obstruction are critical in terms of management.
- Once these are identified, direct referral prenatally is recommended.

Direct Operating Room Triage of Neonates With Total Anomalous Pulmonary Venous Connection

Jason Aguirre · Constantine Mavroudis · Marshall Jacobs · Robert Stewart

Pediatr Cardiol (2013) 34:1874–1876

Abstract Total anomalous pulmonary venous connection with obstruction constitutes a surgical emergency. Medical therapy is palliative and unlikely to result in significant or sustained physiologic improvement. Two cases demon-

The duration of circulatory and respiratory embarrassment and poor oxygen delivery to vital end organs was minimized.

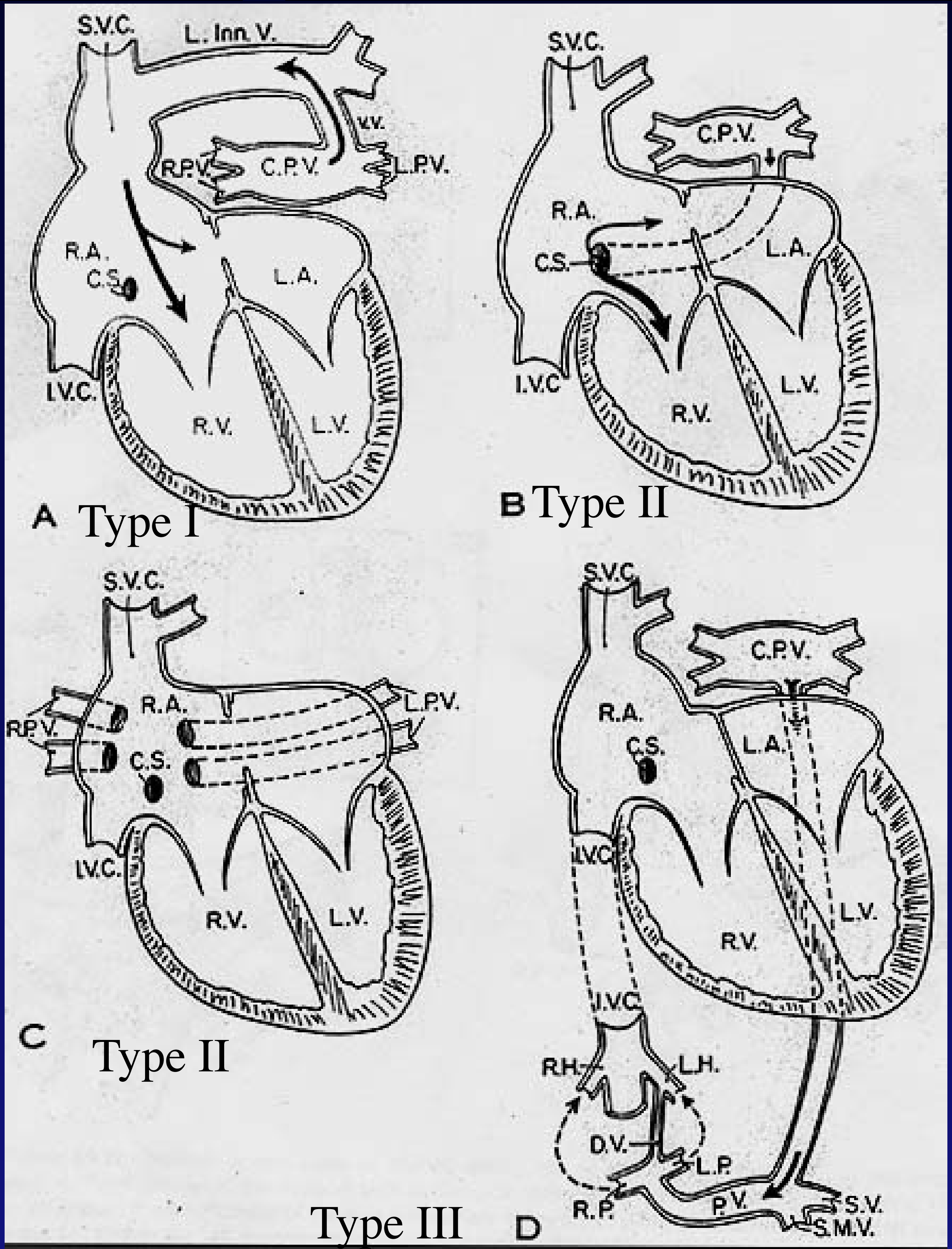
Totally Anomalous Pulmonary Venous Connections.

TYPE I: Above the Heart

Text

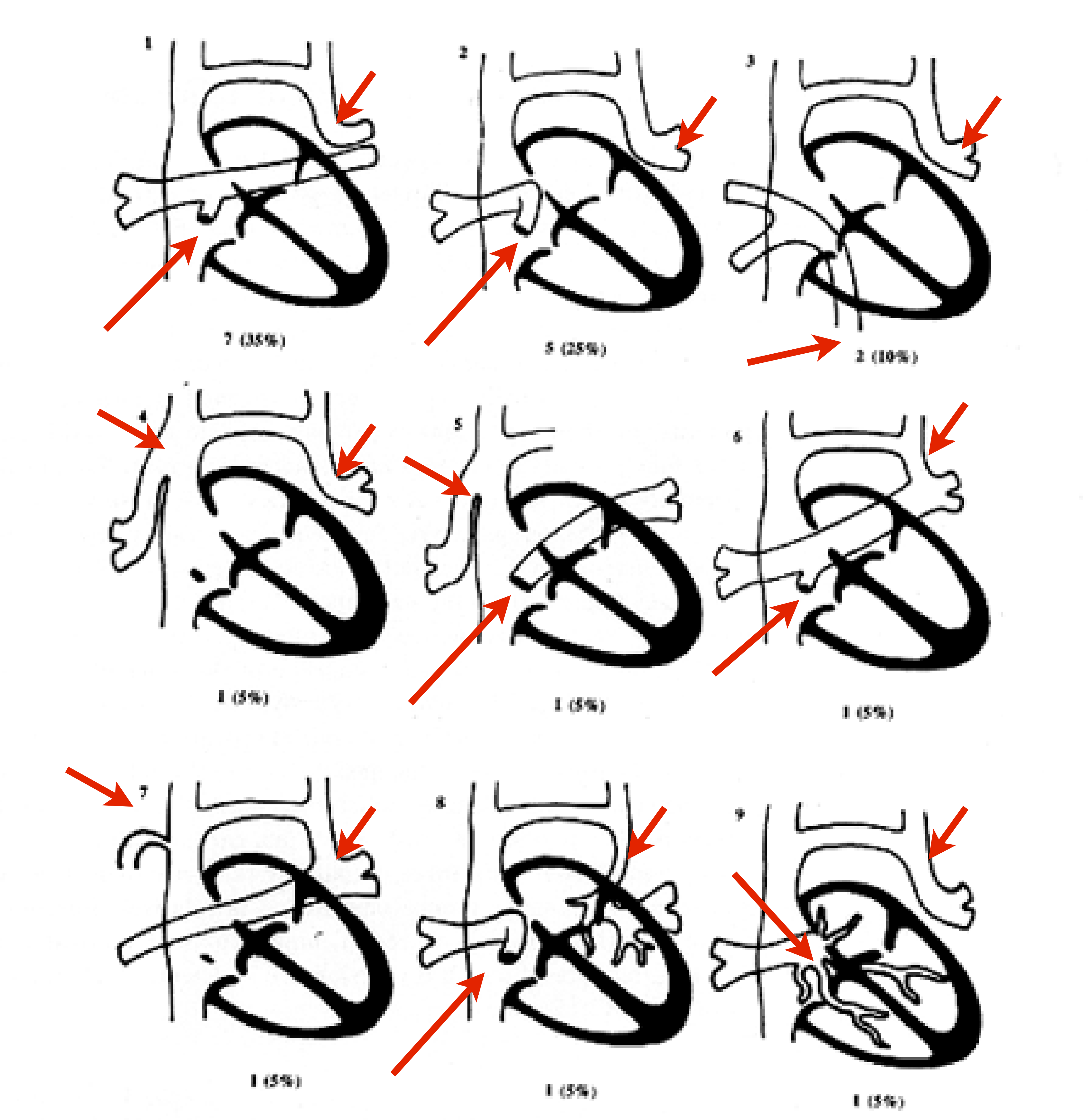
TYPE II: To the Heart

TYPE III: Below the Heart

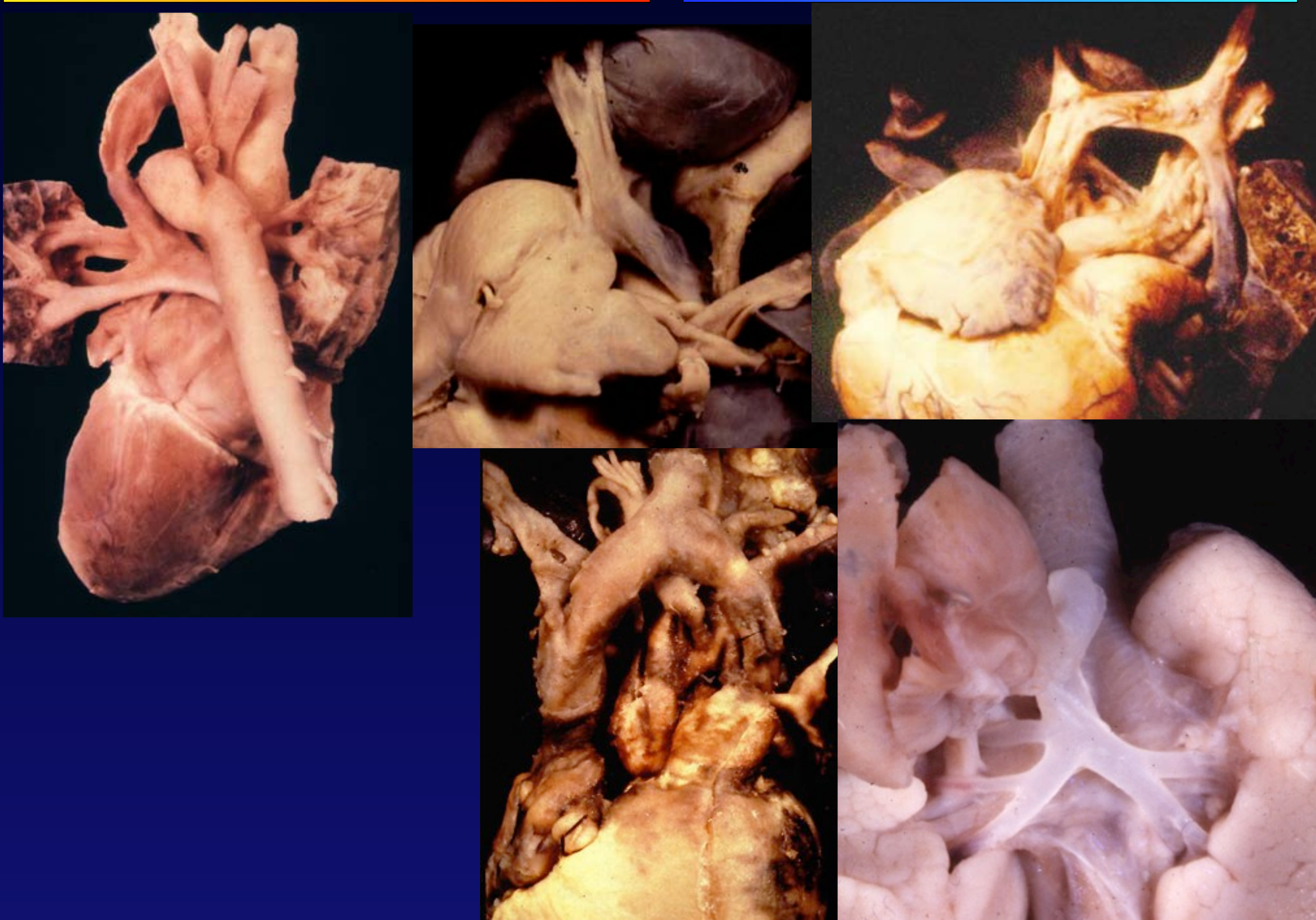


NHS.

Anomalous Pulmonary Venous Return : Mixed Types



Pathology: Type 1 TAPVR

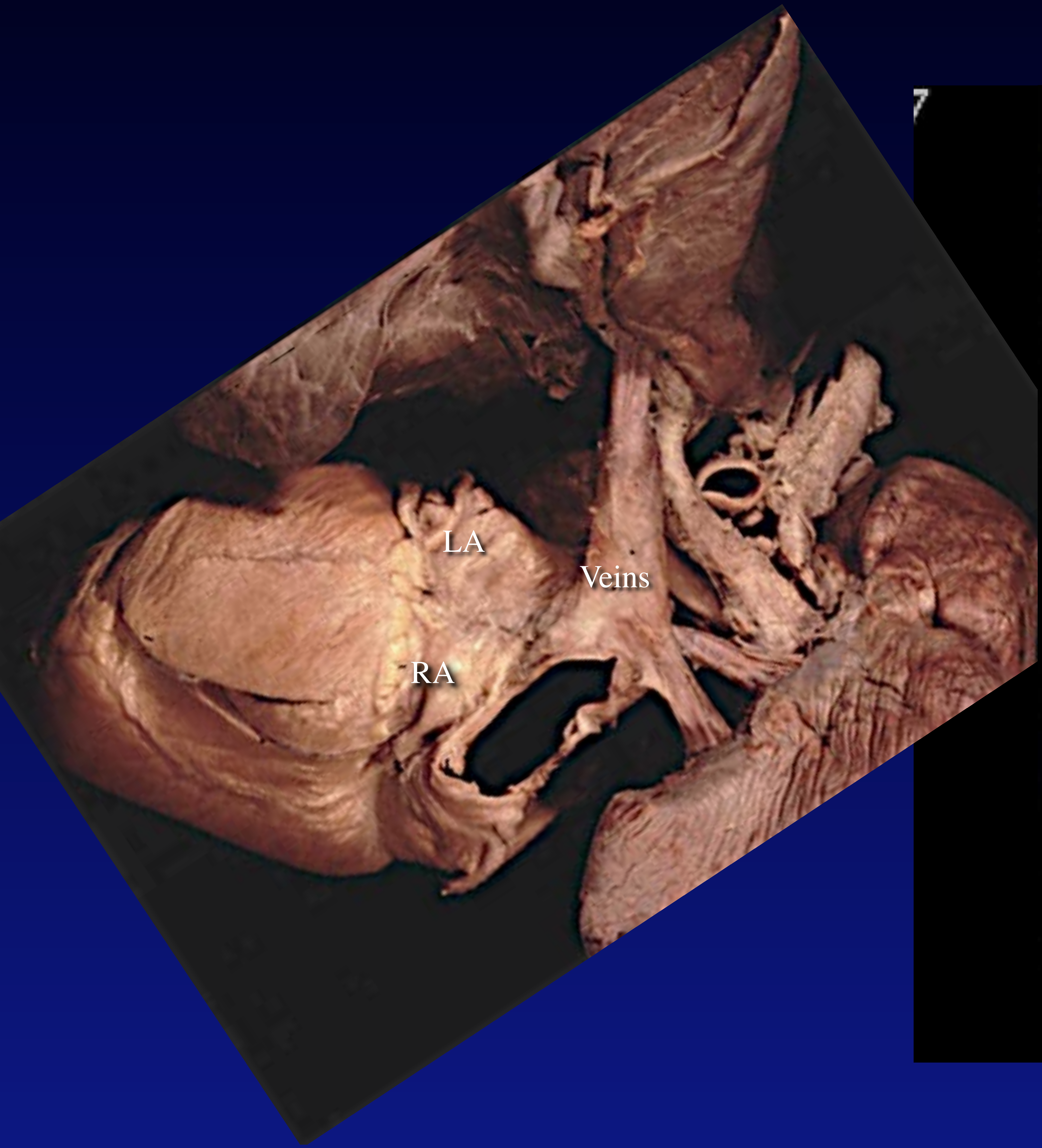


Pathology: Total Veins to the Coronary Sinus (II)

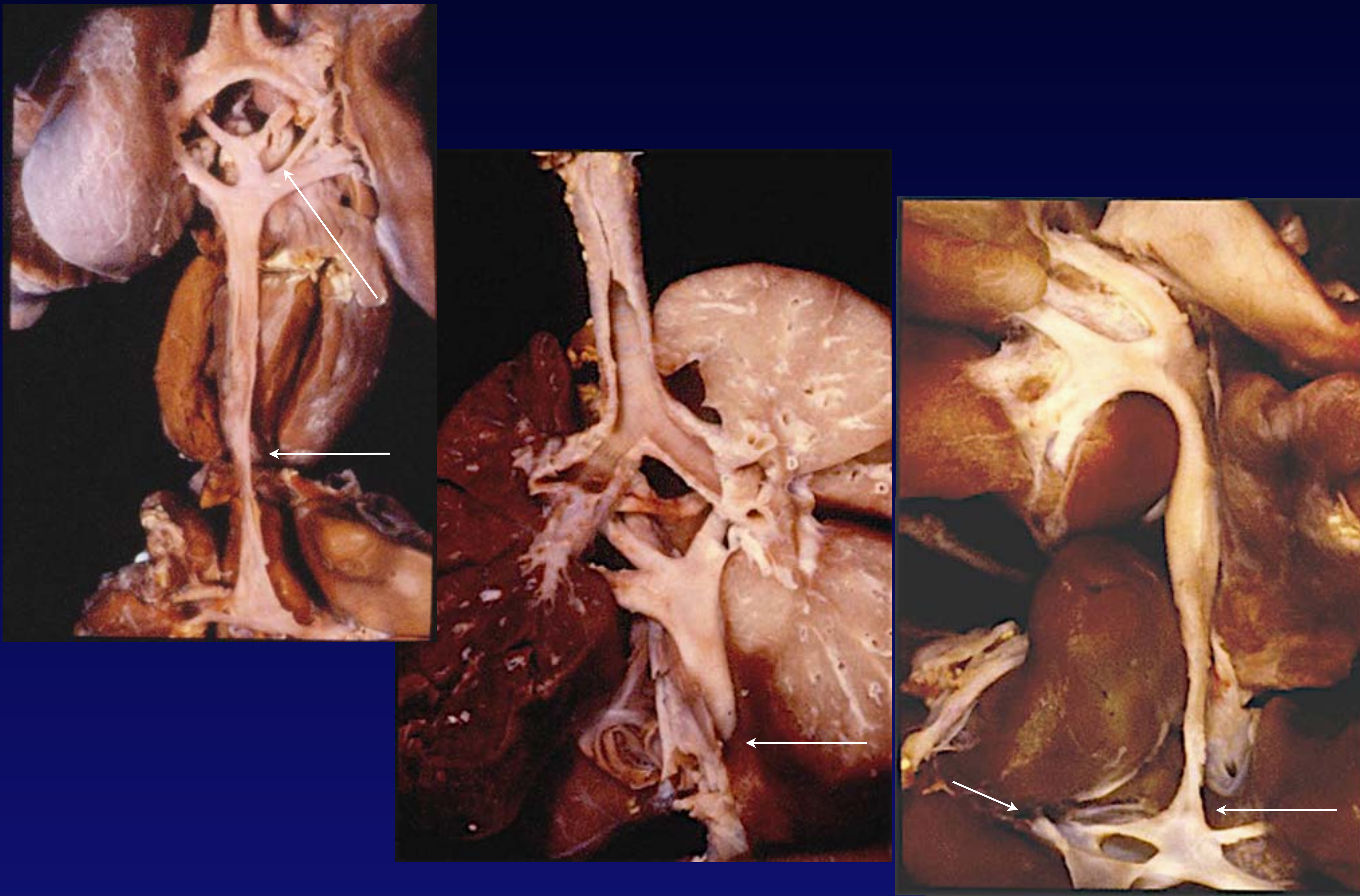
Echo cut from the front

Dissection from the back

Totally Anomalous Pulmonary veinous return to the Right Atrium (Type II)



Pathology: Type III

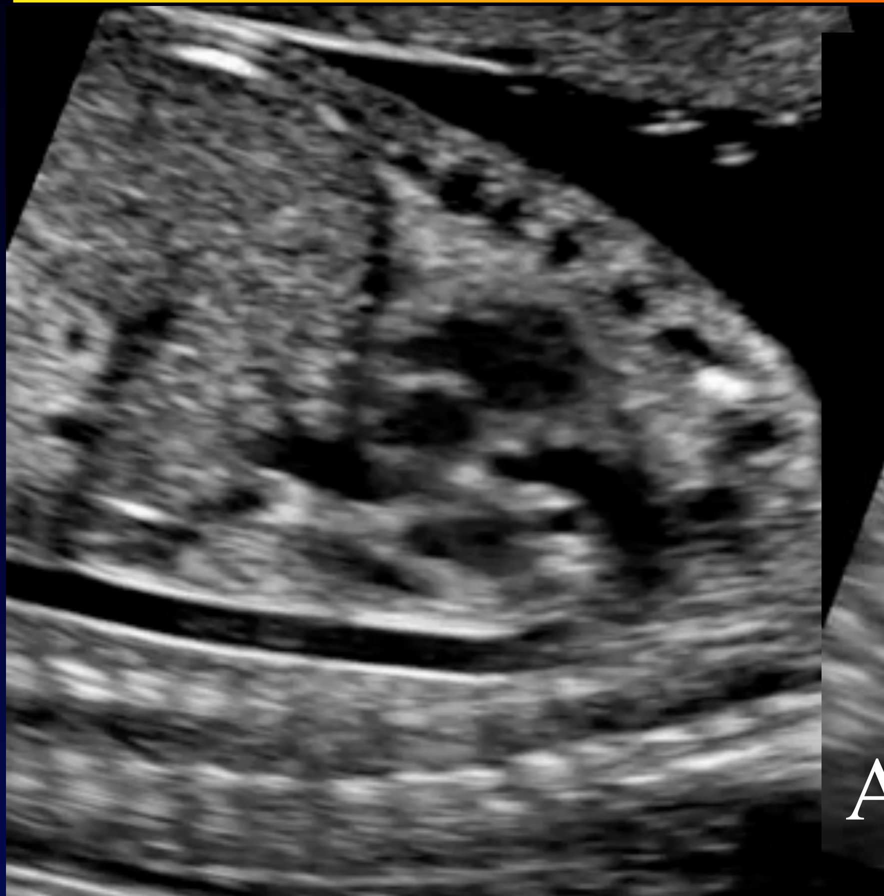


The Normal 4 Chamber Sweep

Cardiac

Obstetric

Views for seeking TAPVR

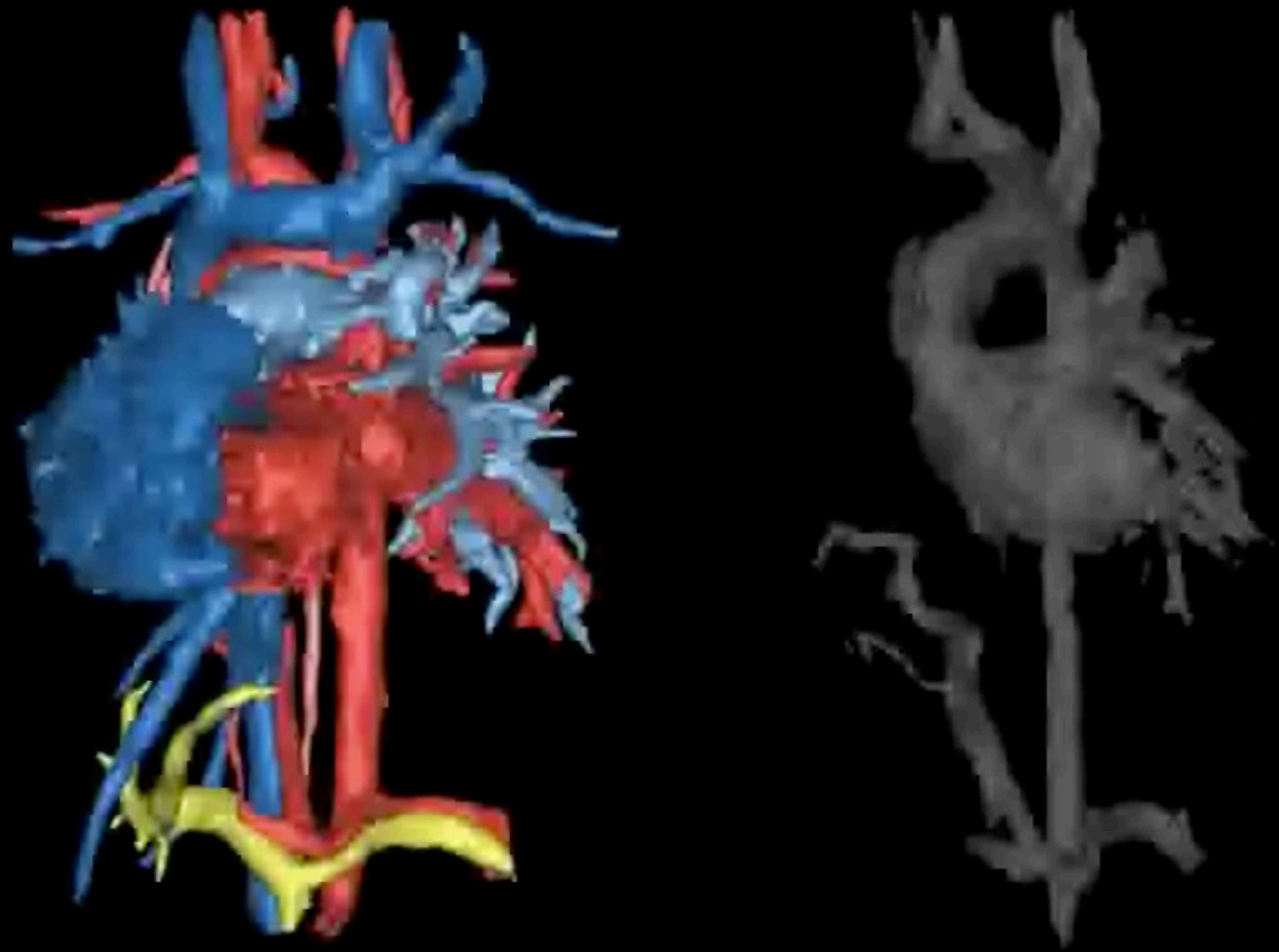


Arterial axis

3 Vessel views

Systemic venous long axis

Scimitar Syndrome: Anomlaously Draining Right Pulmonary Veins to IVC.



The Study.

- Antenatal diagnosis has however long been a challenge. We aimed to identify consistent prenatal ultrasound features in this condition in a large cohort in whom the diagnosis was made antenatally and confirmed postnatally.

- Abnormal pulmonary venous drainage can be isolated, or seen in conjunction with other complex cardiac malformations, mainly heterotaxy syndromes

- Four of the prenatally diagnosed fetuses represented isolated cases of TAPVR, 22 had heterotaxy syndrome and/or additional cardiac abnormalities. Prenatally diagnosed abnormal pulmonary venous connections were supra-cardiac (Type I) in 18 cases, cardiac (Type II) in 1 and infradiaphragmatic (Type III) in 7.

PRENATAL FINDINGS IN TOTAL ANOMALOUS PULMONARY VENOUS RETURN – A DIAGNOSTIC ROAD MAP STARTS WITH STANDARD SCREENING VIEWS

Suguna GANESAN, Michael BROOK, Norman SILVERMAN, Anita MOON-GRADY

JUM 2014

Methods: retrospective, review of (2D) and Doppler features that had helped make the diagnosis of TAPVR at our institution from 2001-2012.

Results: 26 prenatal diagnosis of TAPVR (mean gestational age: 24.1 weeks)

only one patient diagnosed postnatally after having had a prenatal echocardiogram.

4 isolated cases of TAPVR

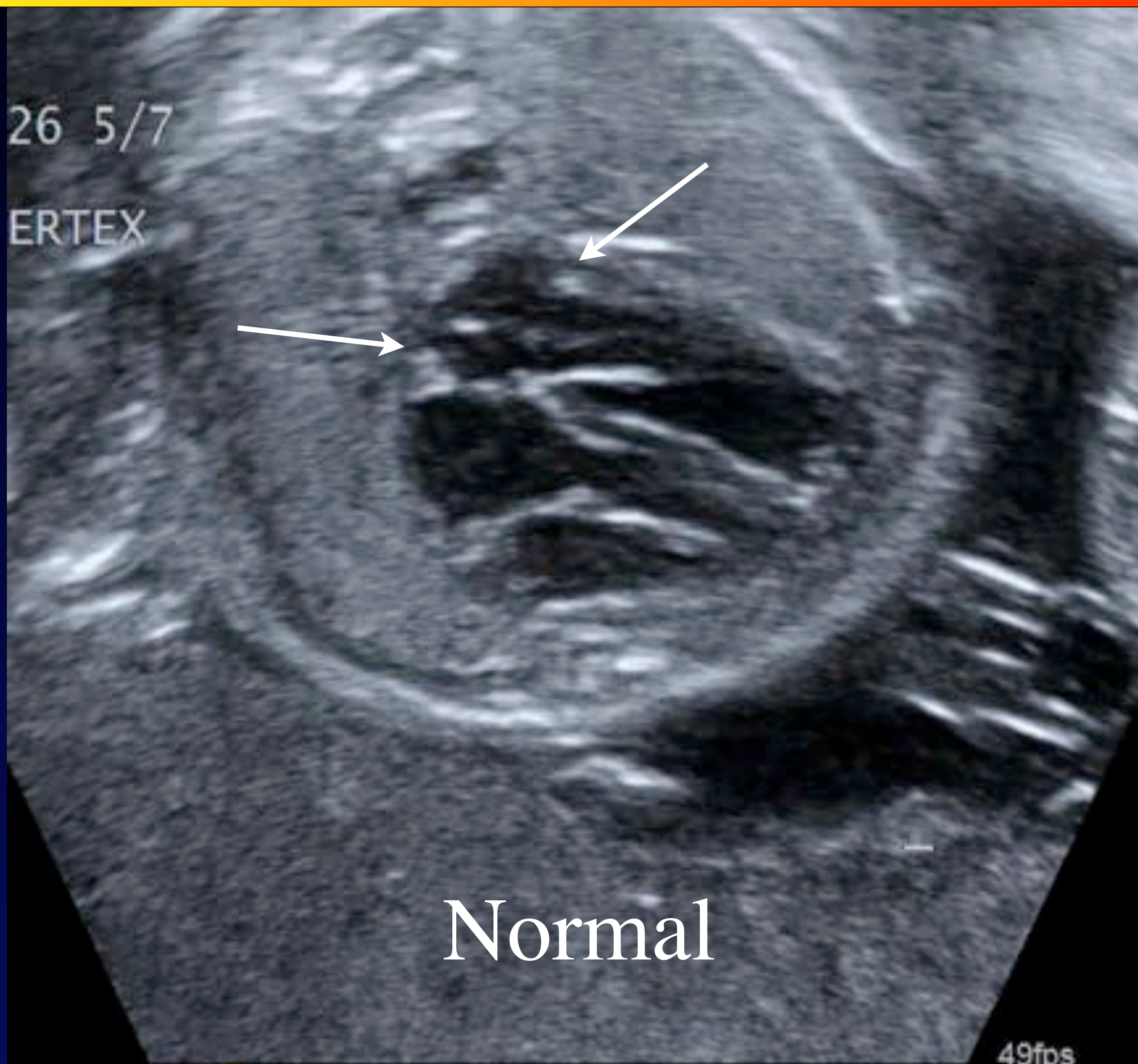
22 heterotaxy syndrome and/or additional cardiac abnormalities.

Supra-cardiac (Type I) in 18 cases, cardiac (Type II) in 1 and infra-diaphragmatic (Type III) in 7. Cardiac asymmetry was not consistently noted.

A venous structure posterior to the left atrium on standard axial images and additional vertical venous channels on 3-vessel or axial abdominal views were useful 2D markers.

Abnormal pulmonary venous spectral Doppler was present in 25/26 of the prenatally diagnosed patients.

Normal & Abnormal Four Chamber view and Doppler

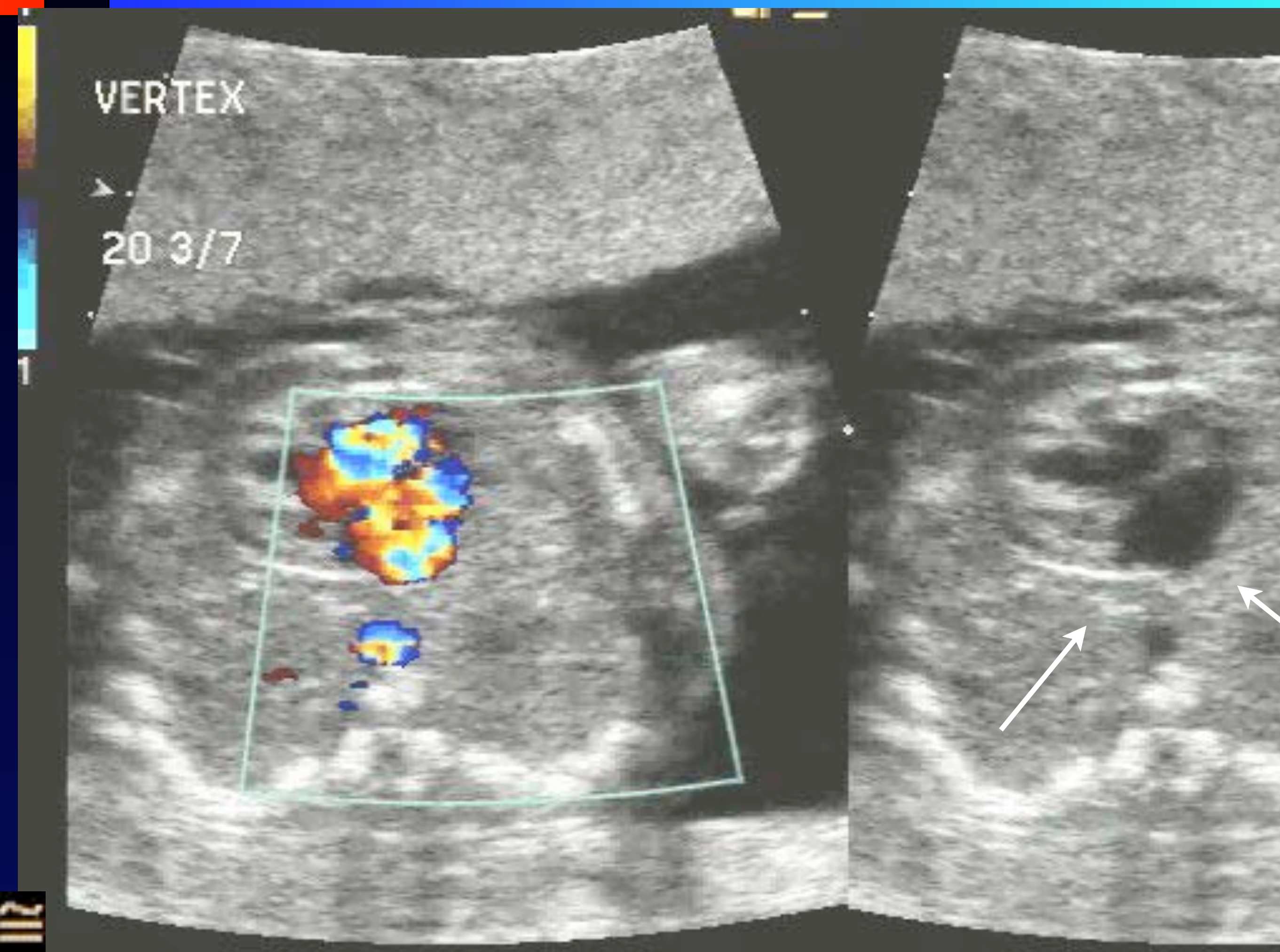


- Normal intracardiac anatomy
- (?slight R>L asymmetry)

Abnormal

- Normal 4-chamber view
- Position, axis, symmetry

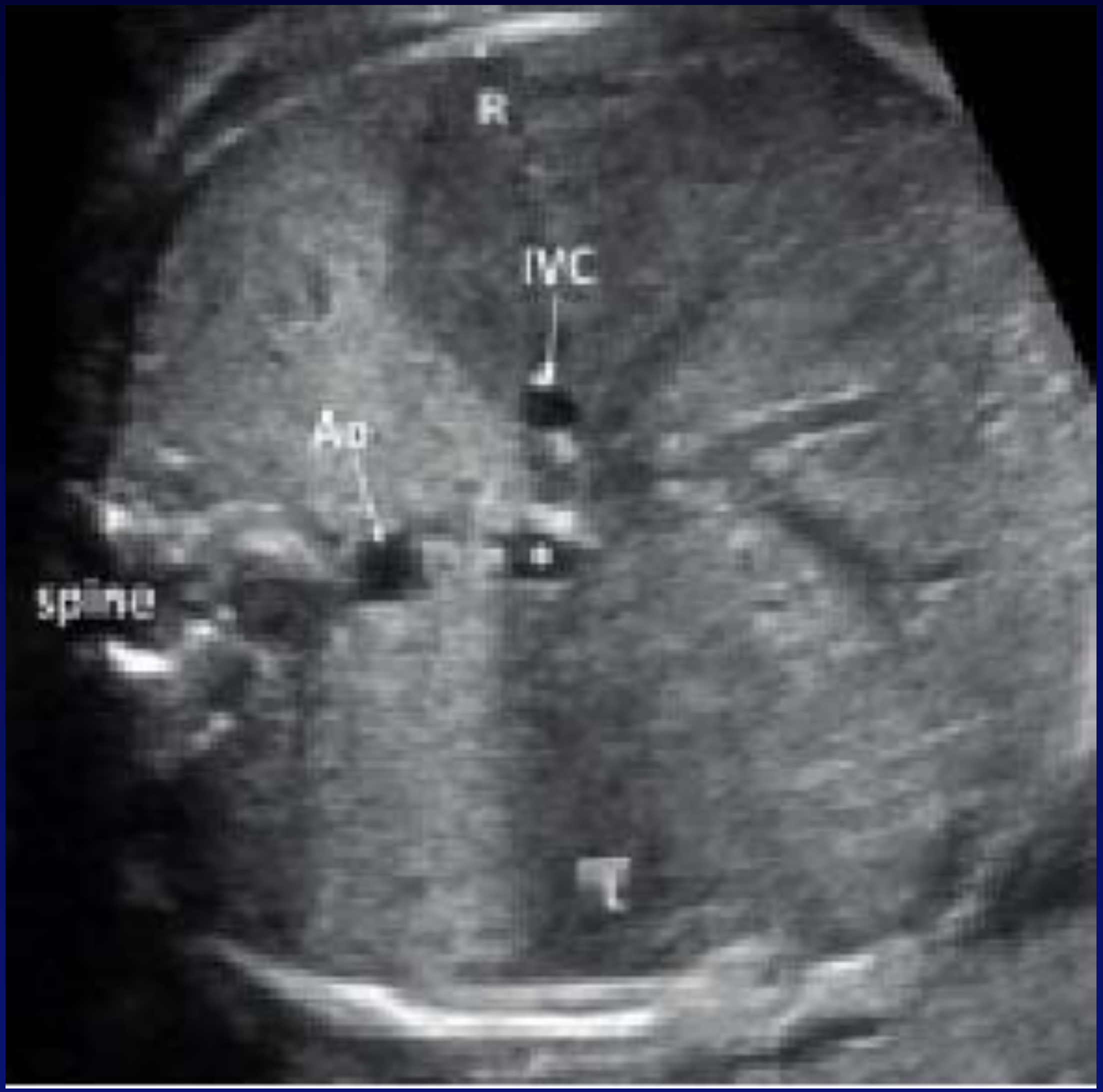
Bald Left Atrium and Pulmonary Veins.



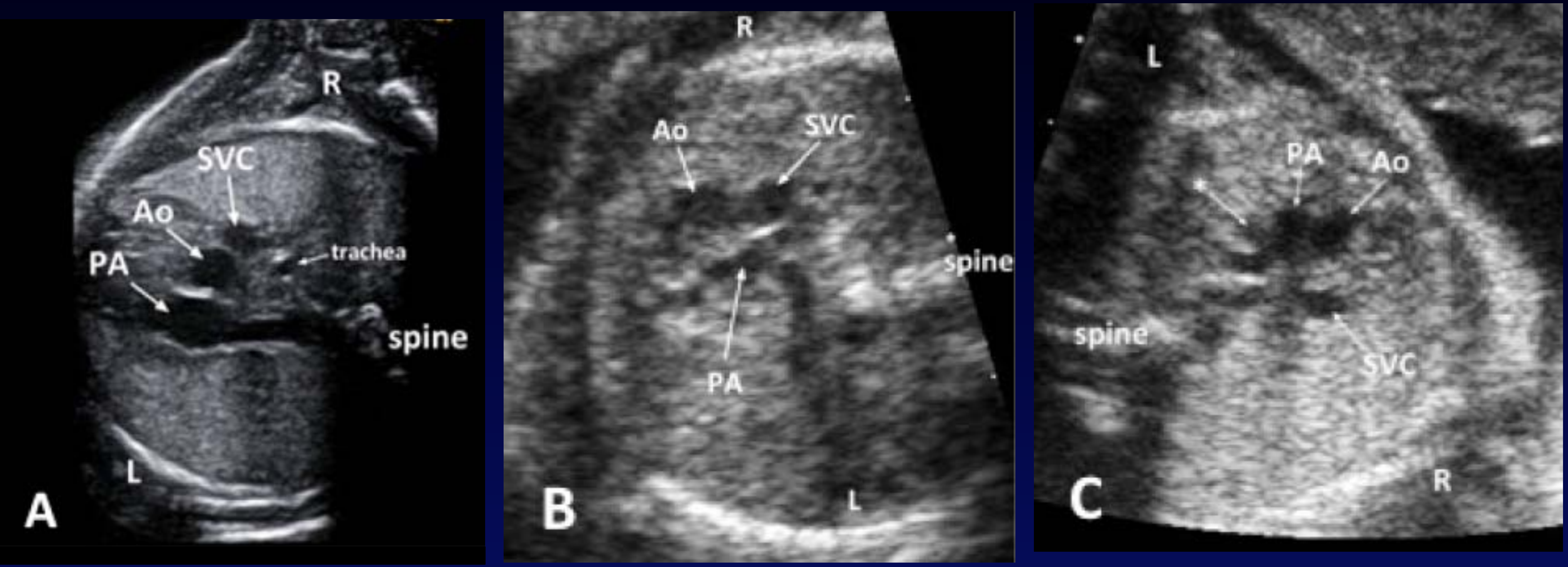

22fps


7 WKS

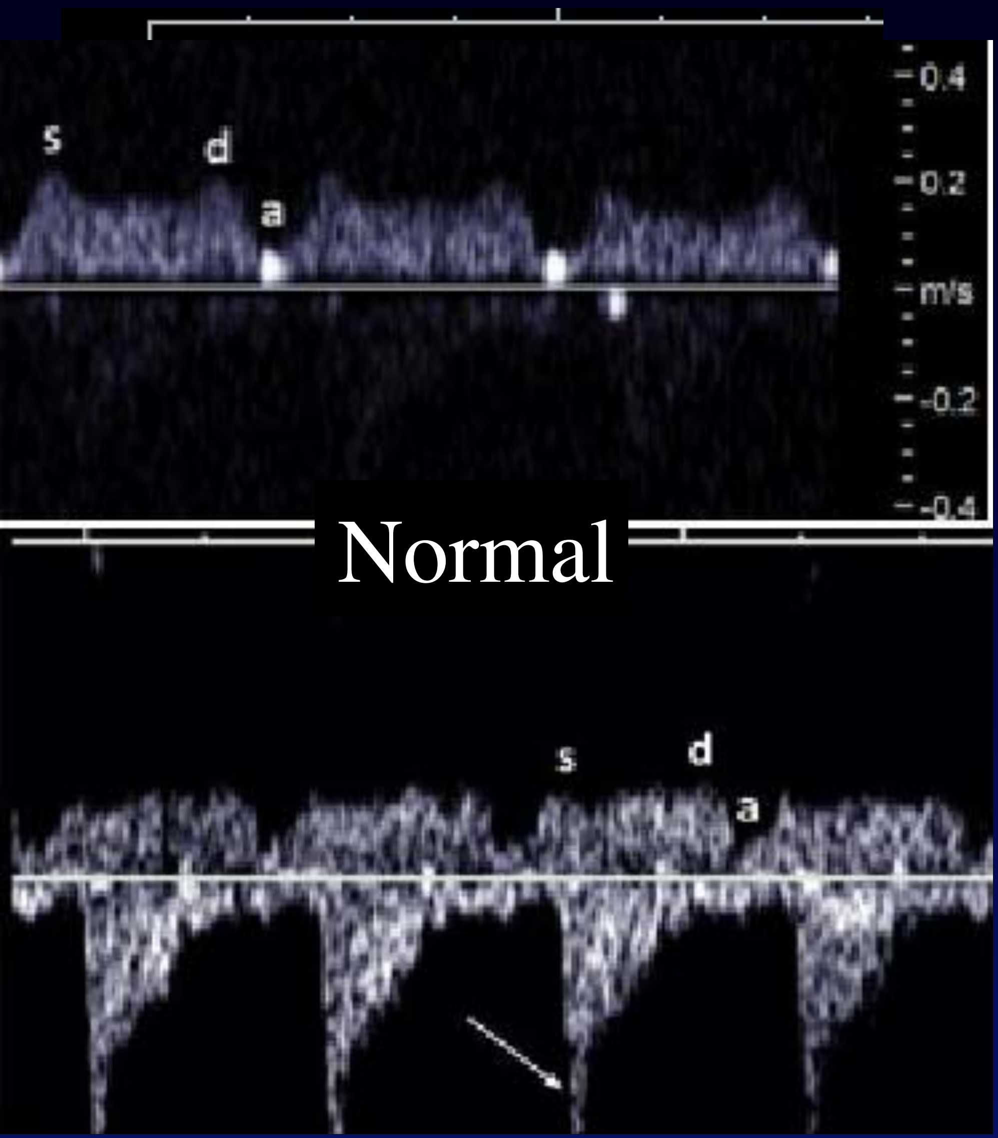
Transverse Abdominal View. (For Type III Veins)



3 VesselViews to make Diagnosis of TAPVR: The SVC



Pulmonary Vein Doppler: Normal and Abnormal.

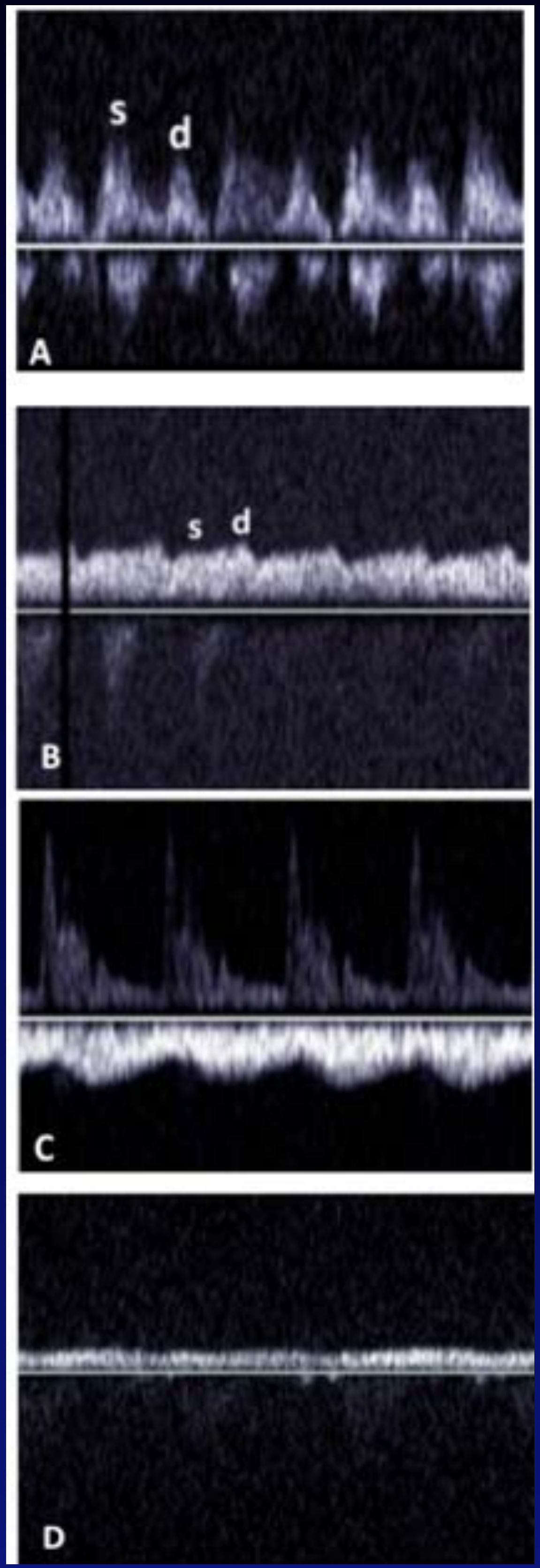


abnormal “s” and “d” appearance
but bi-phasic with normal pulsatility
(“pseudonormal”),

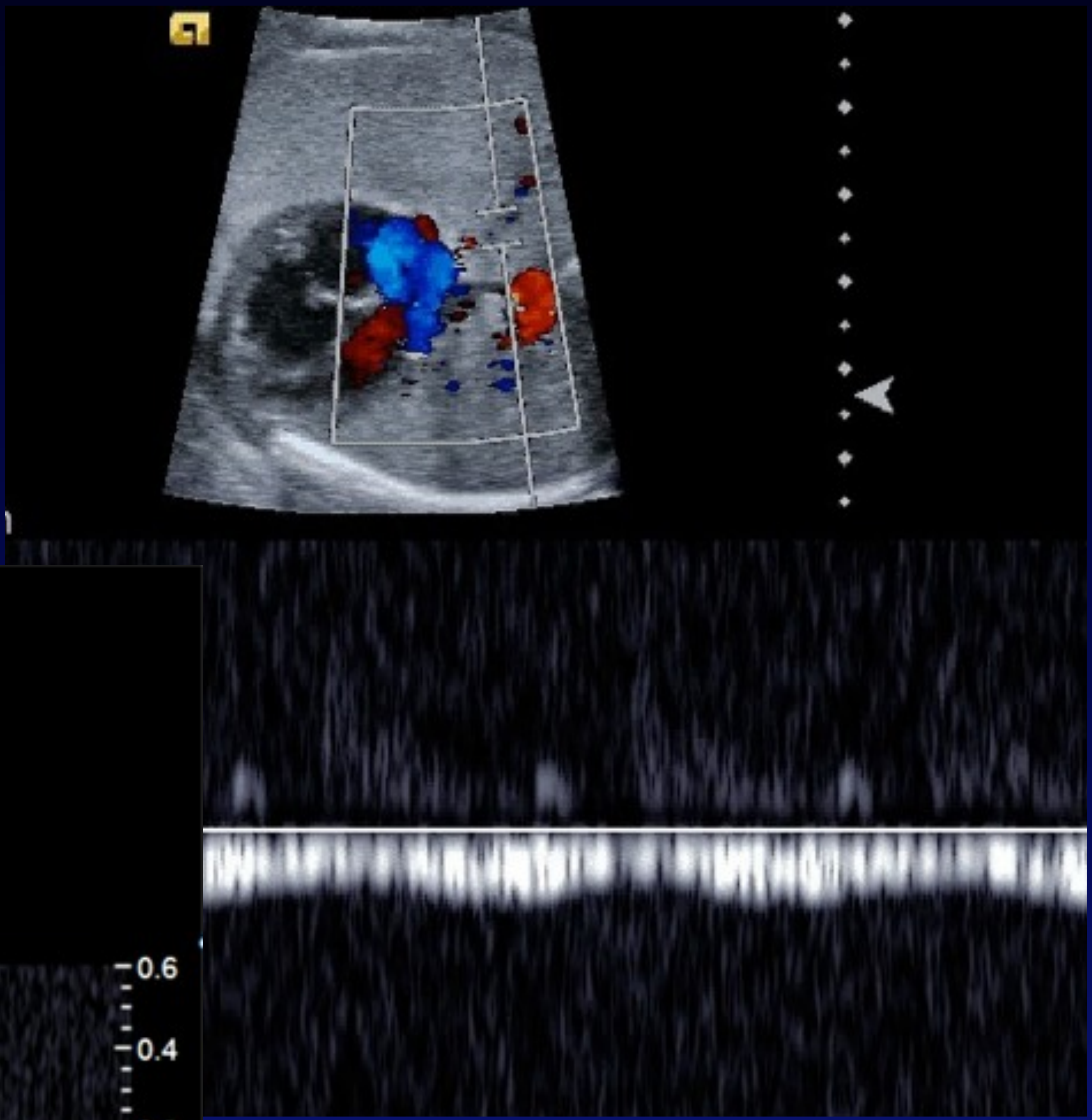
abnormal with bi-phasic waveform
but decreased pulsatility

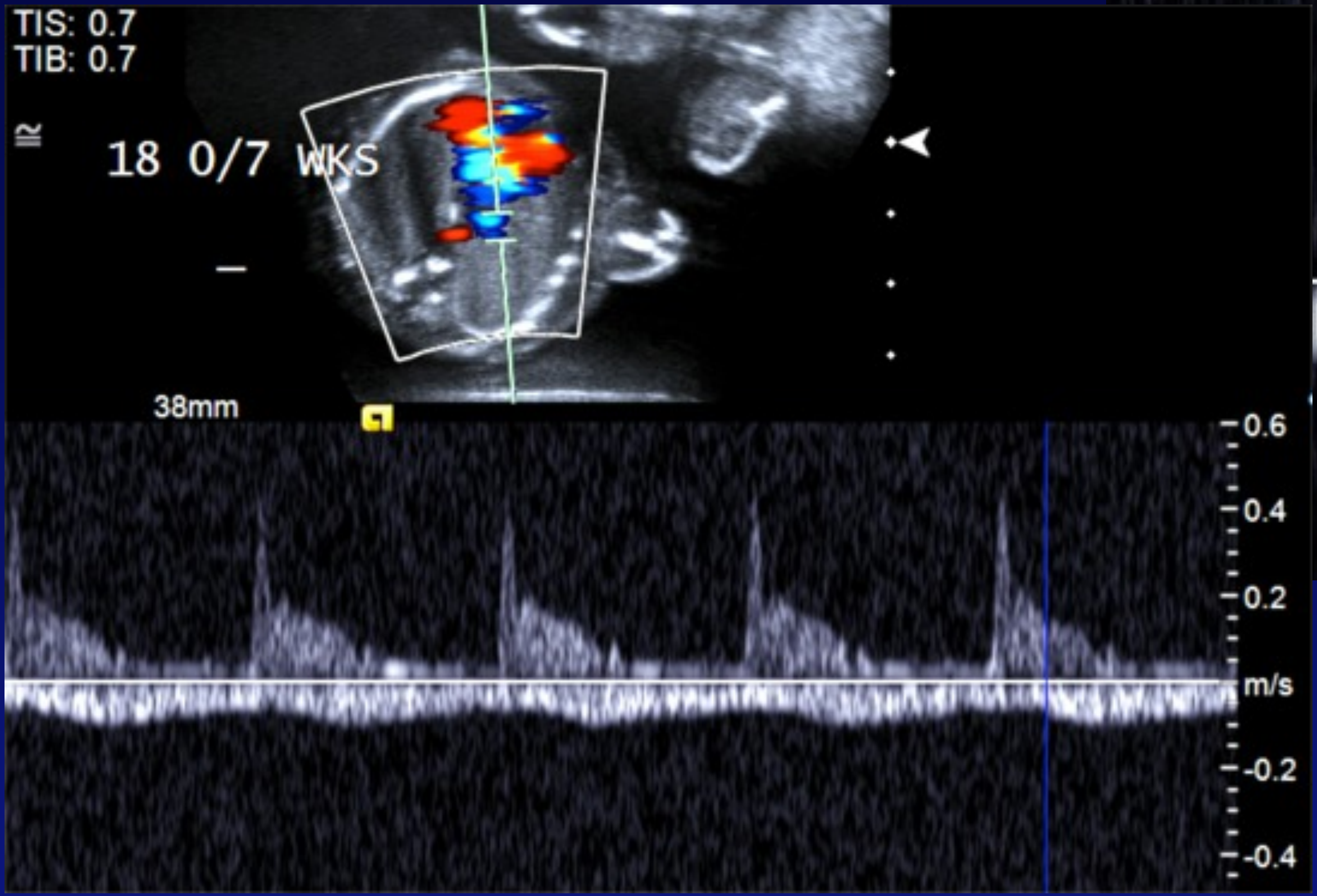
abnormal with monophasic pulsatile pattern

low-velocity monophasic and continuous.

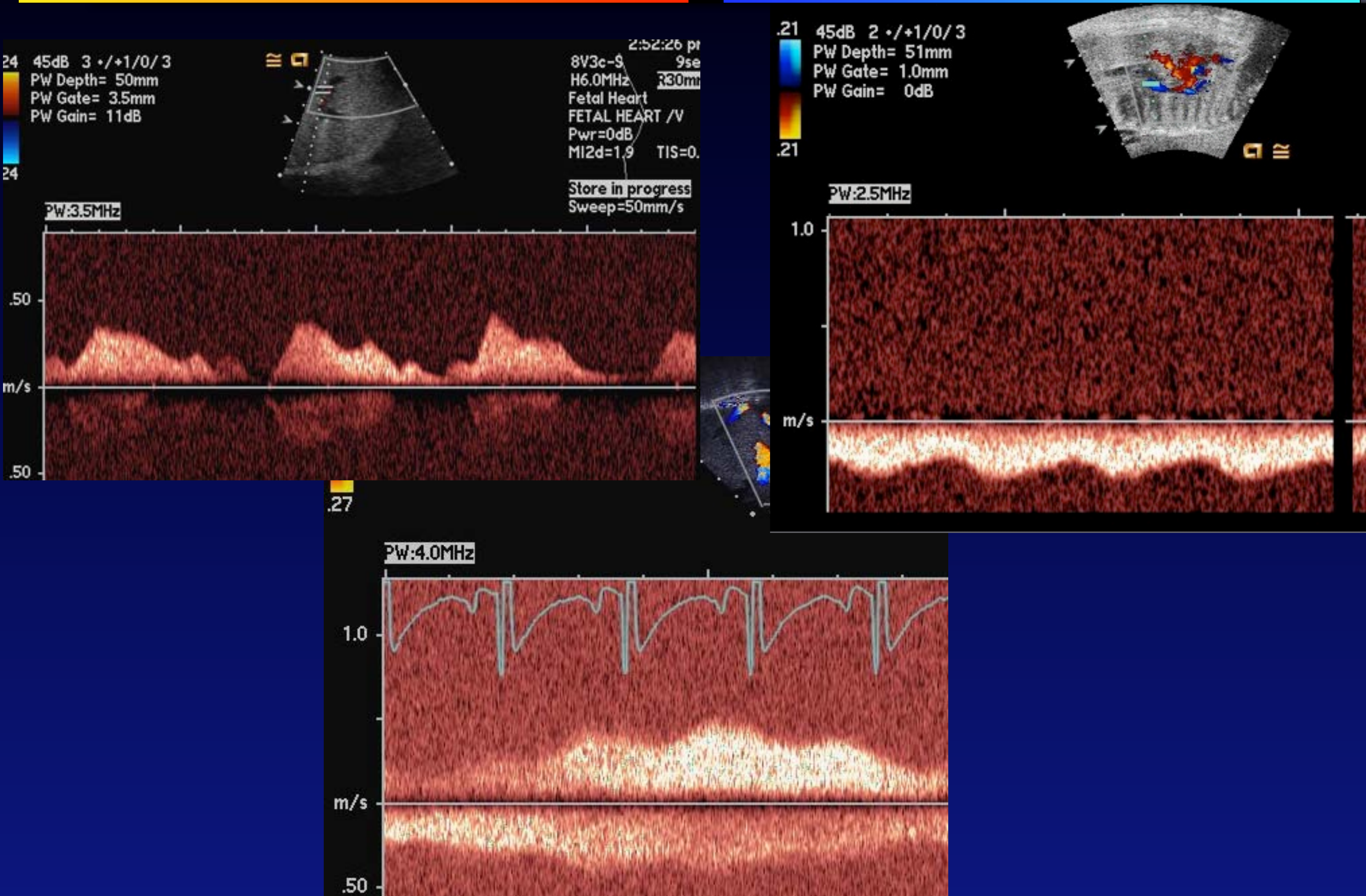


TAPVR With Heterotaxy



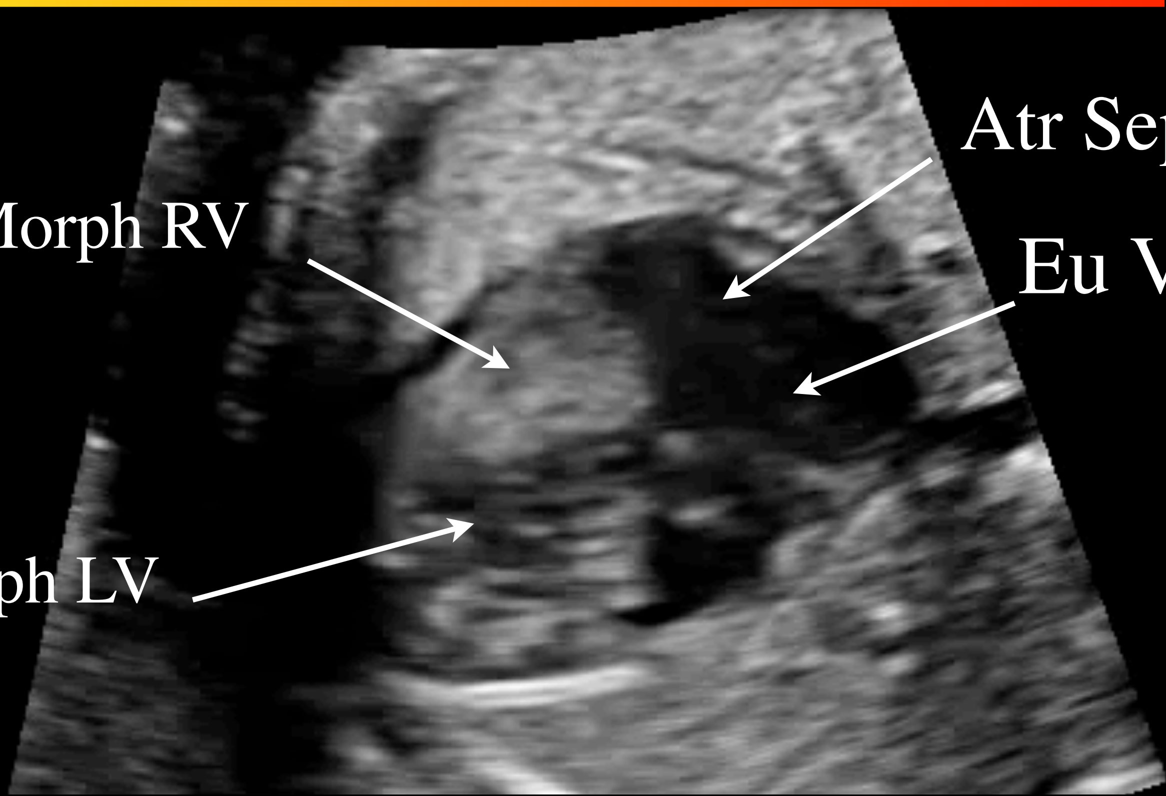


Total Anomalous Vein Doppler

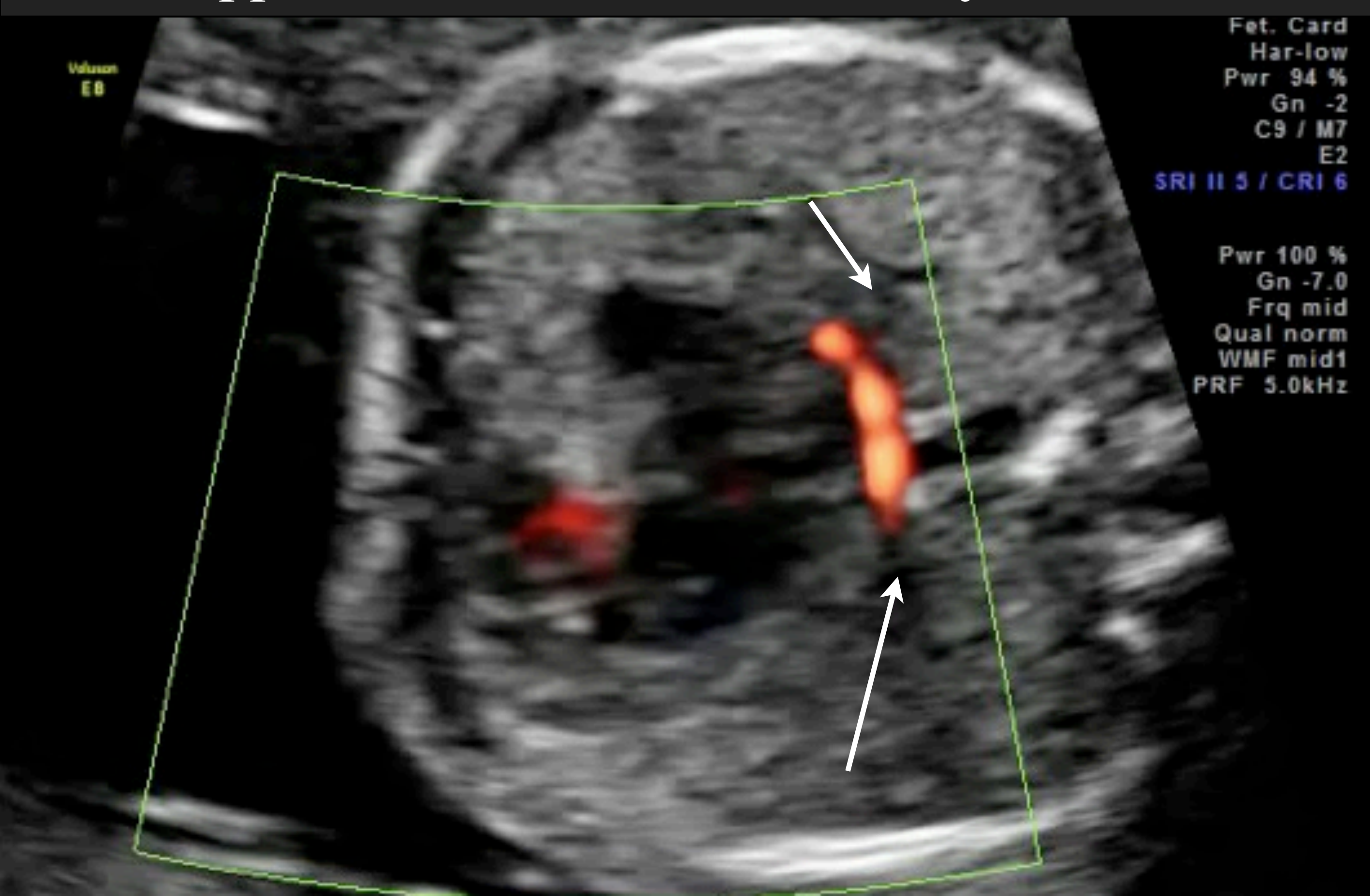


Right Isomerism, Tricuspid Atresia (TAPVR Type II)

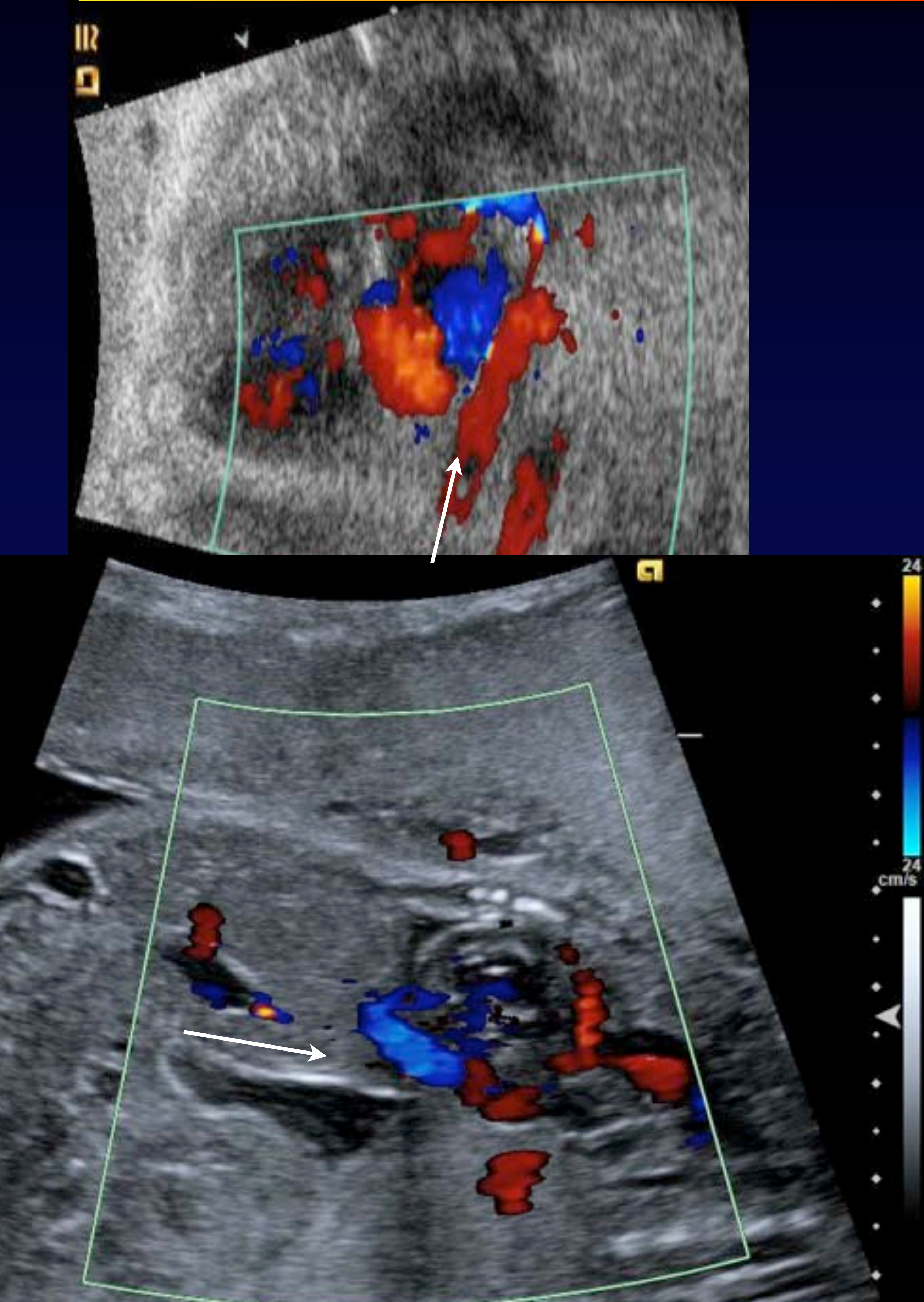
Julia Solomon, John Stock Randy Richardson, Norman Silverman. Fetal Heterotaxy with Tricuspid Atresia, Pulmonary Atresia and Isomerism of the Right atrial appendages at 22 weeks. Am J Perinatol Reports 2013; 3: 97-101

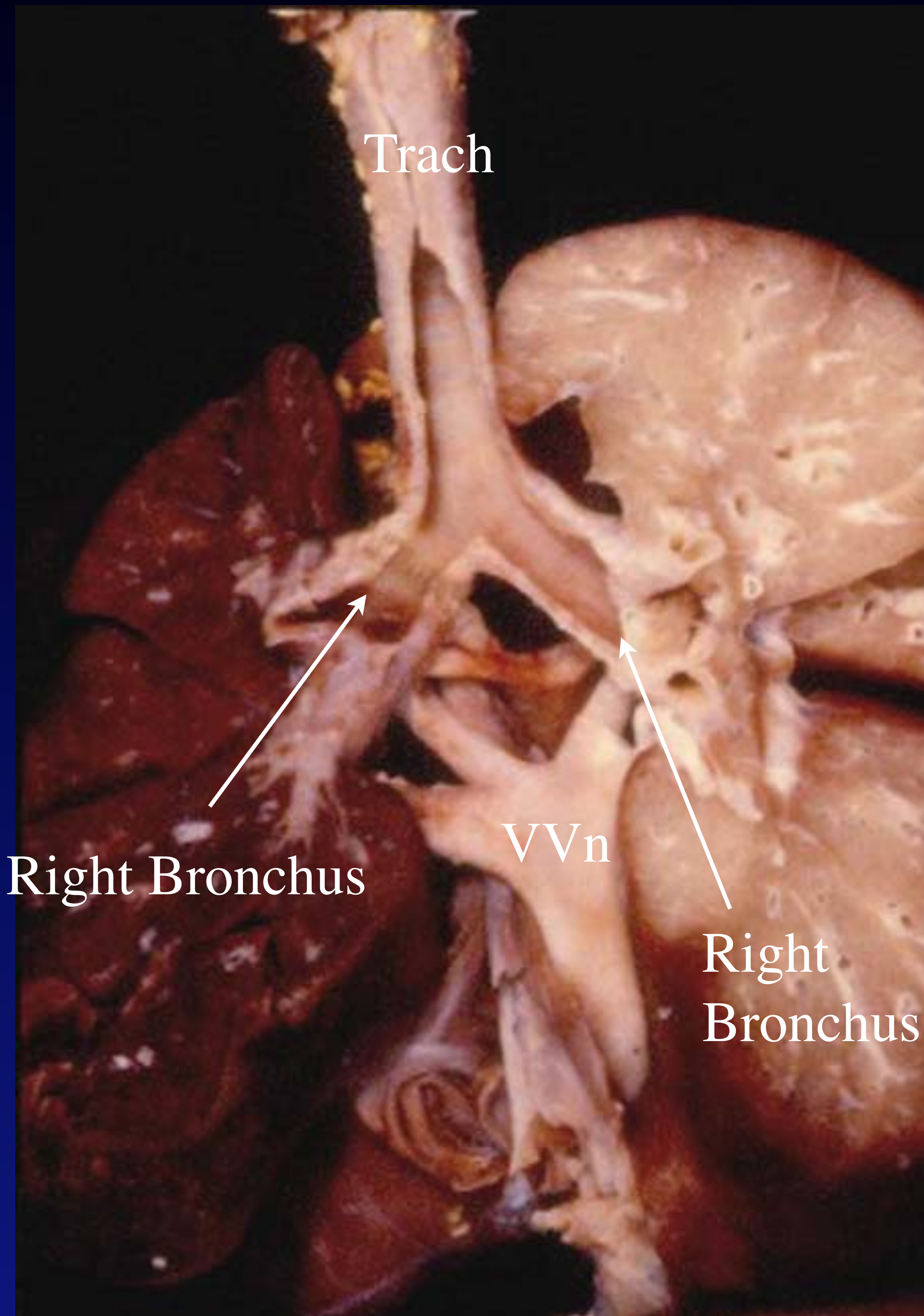


Doppler Color Flow is Mandatory



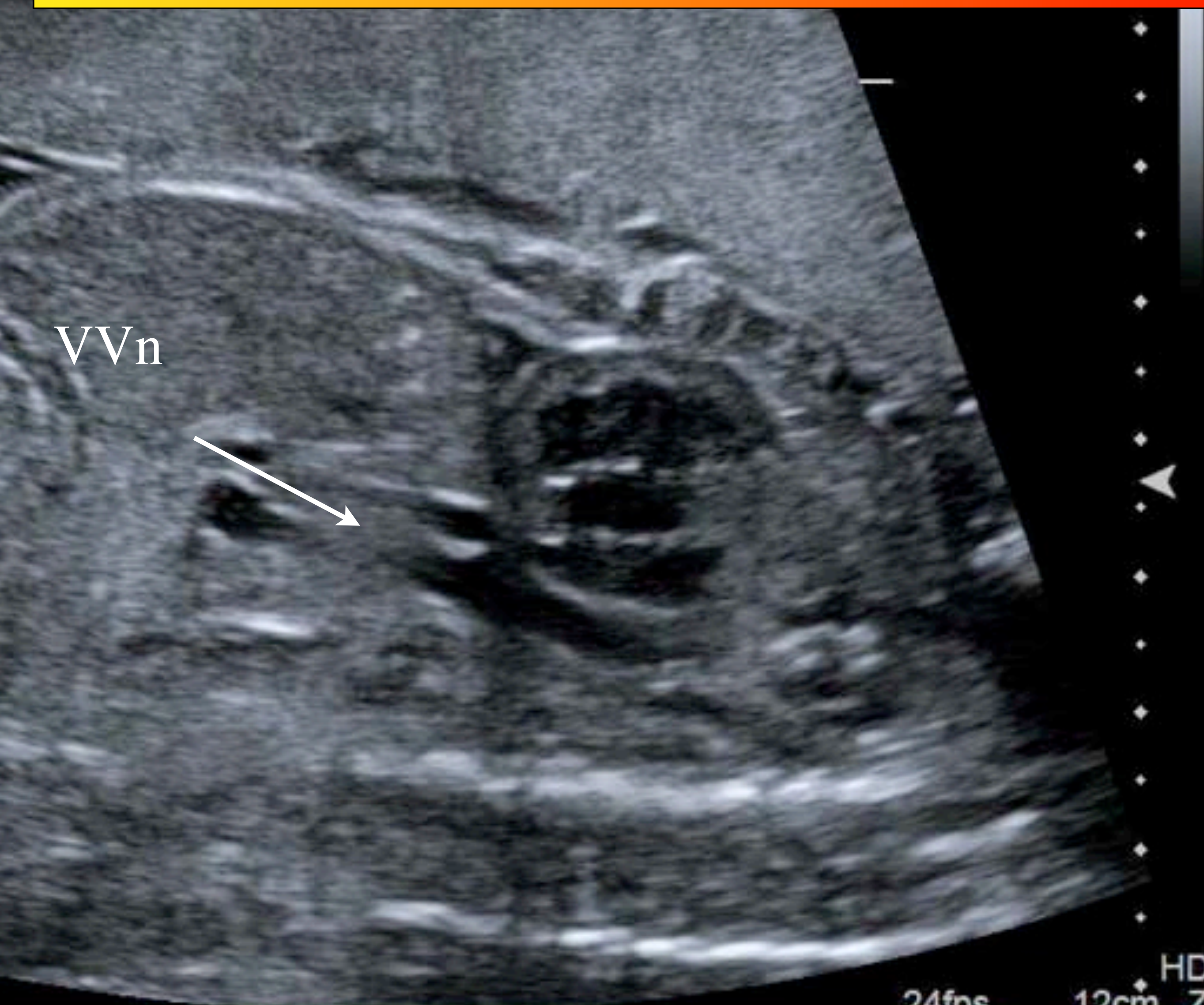
Right Isomerism

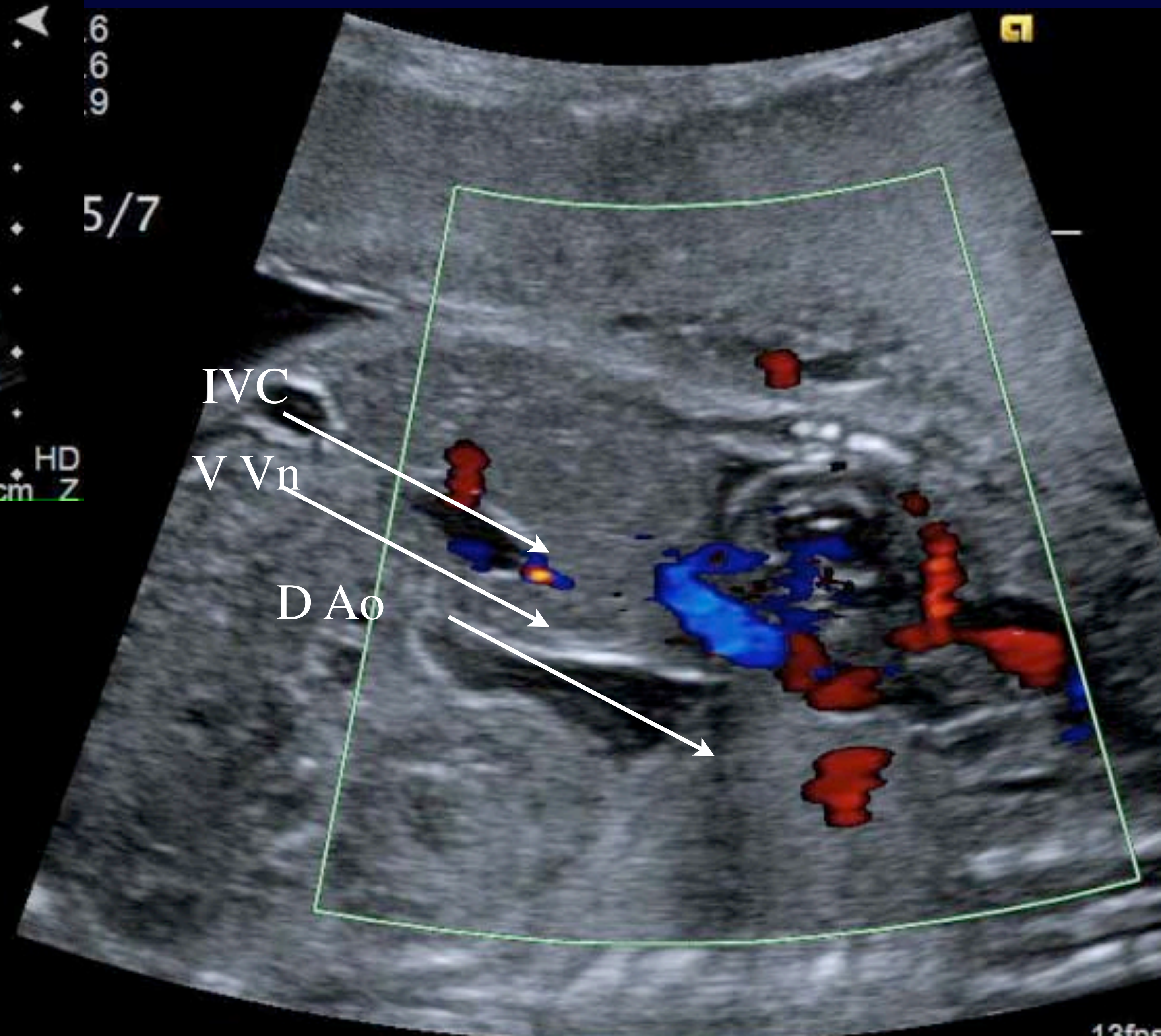




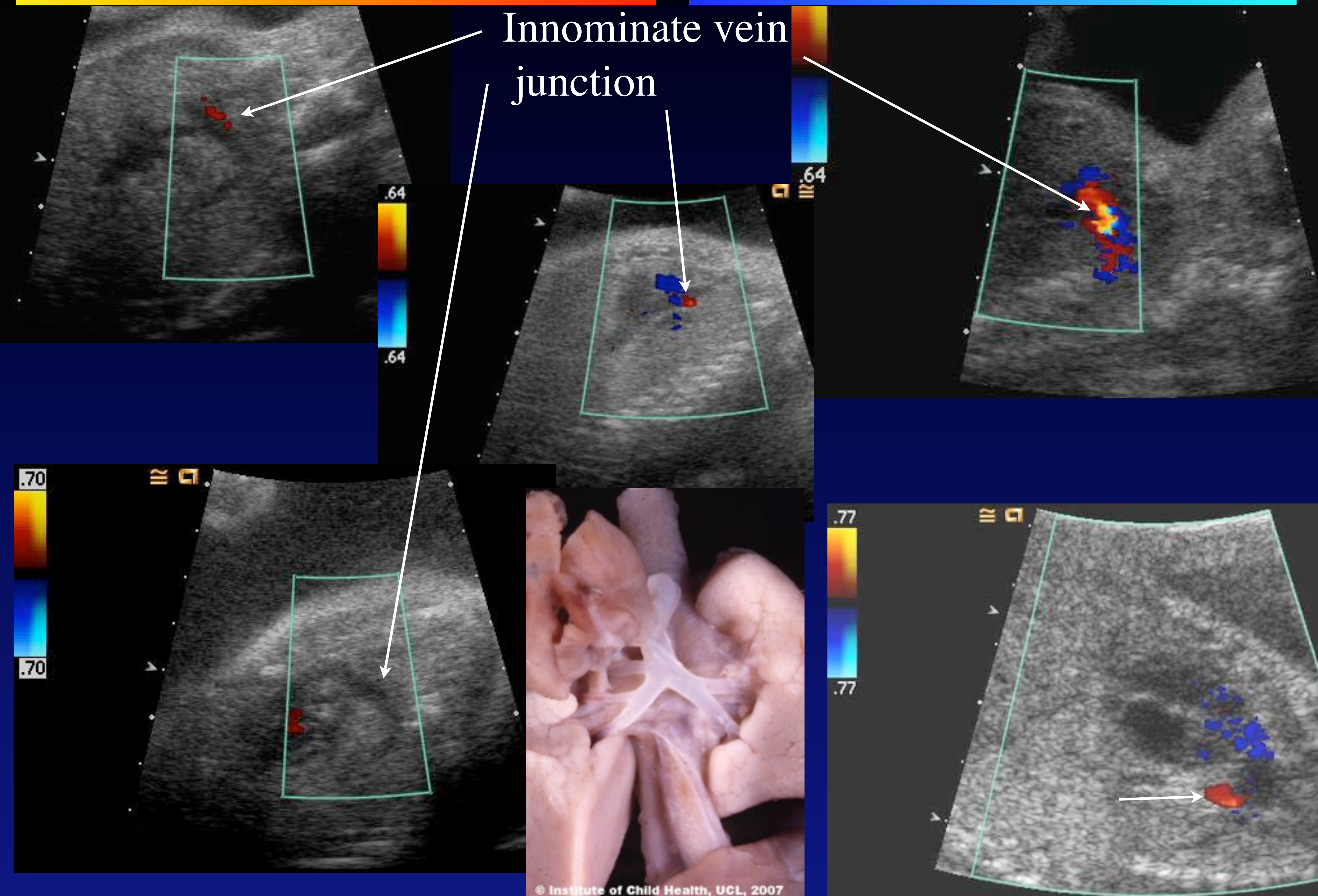
TAPVR Type III

All infradiaphragmatic TAPVRs are or will become obstructive postnatally

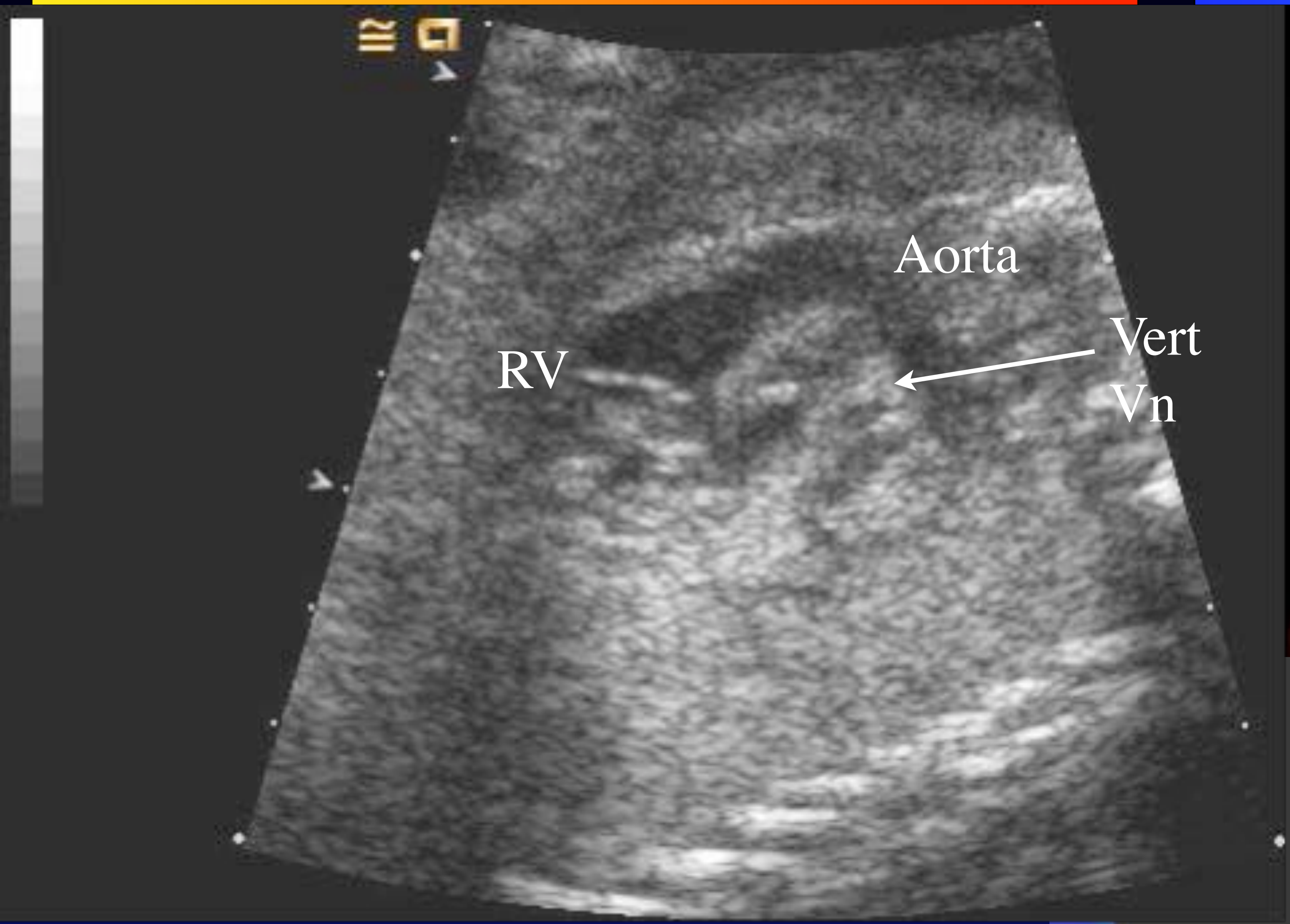


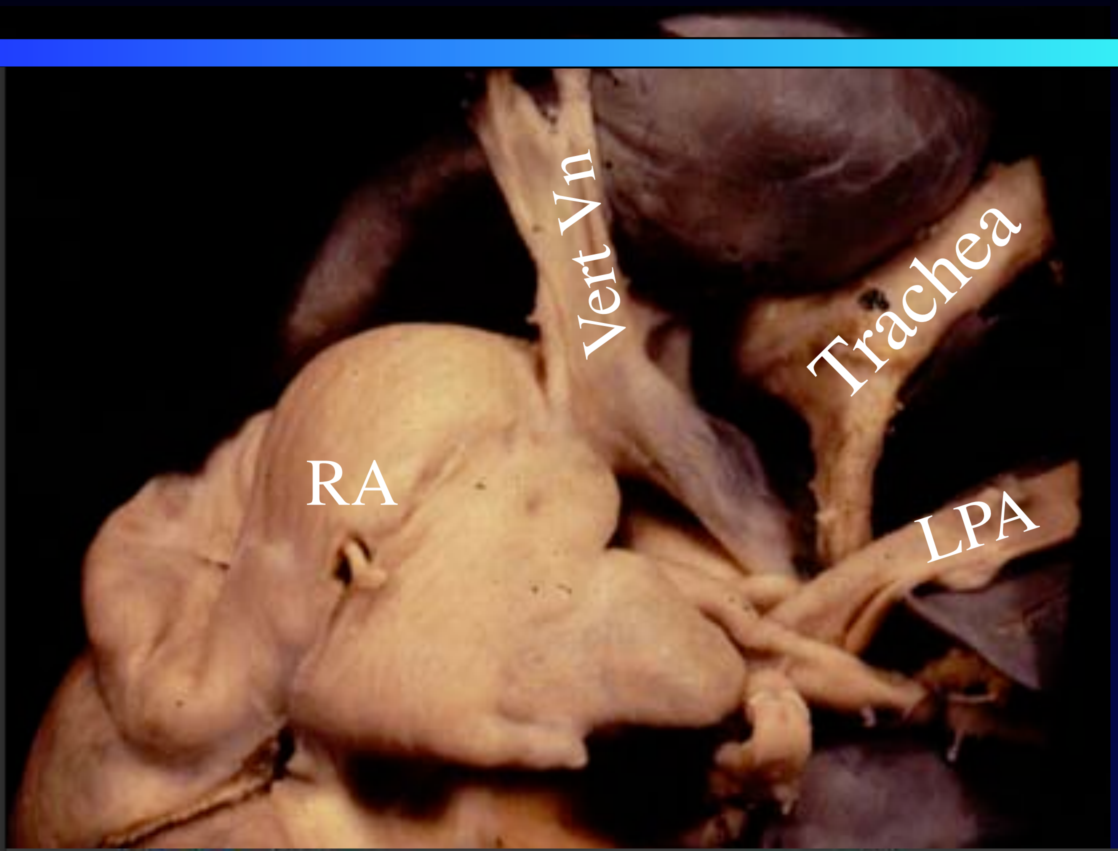


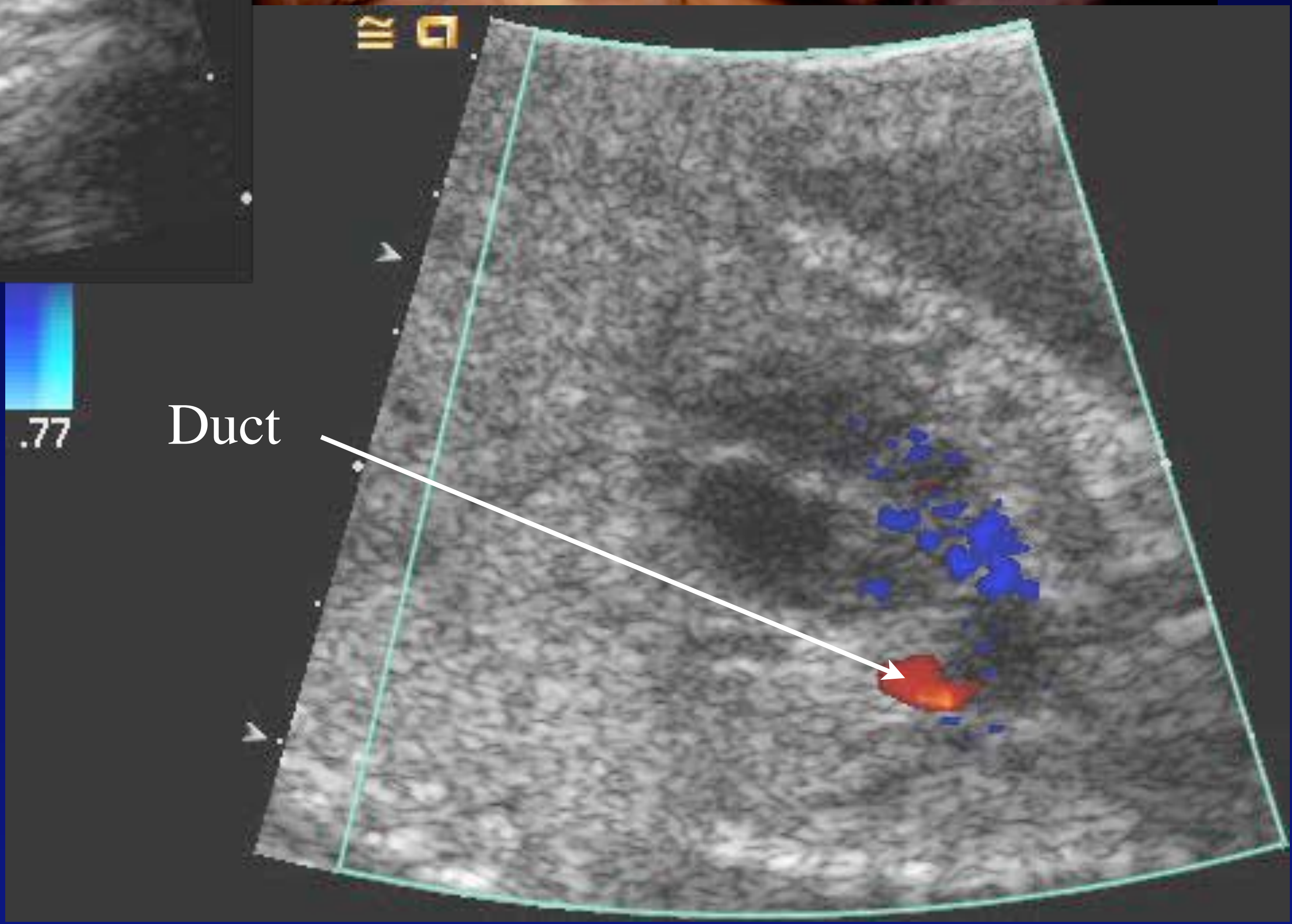
TAPVR (Type I) to Vertical Vein with Obstruction.



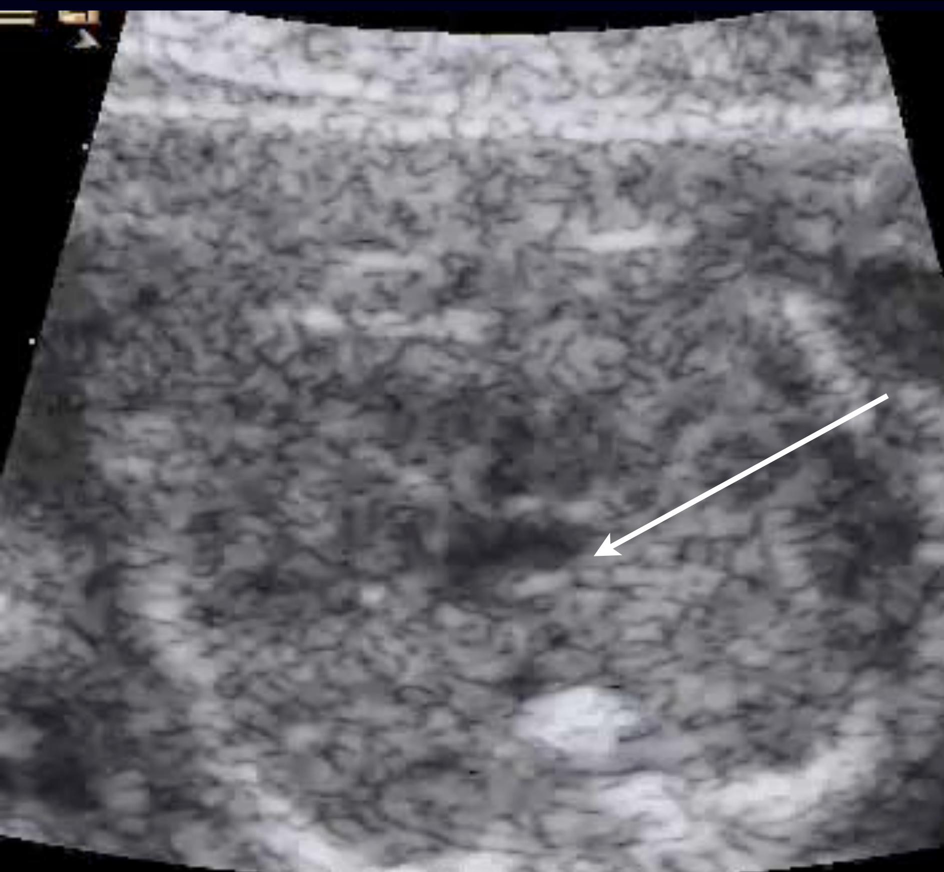
Type 1 TAPVR: Vertical Vein with Obstruction

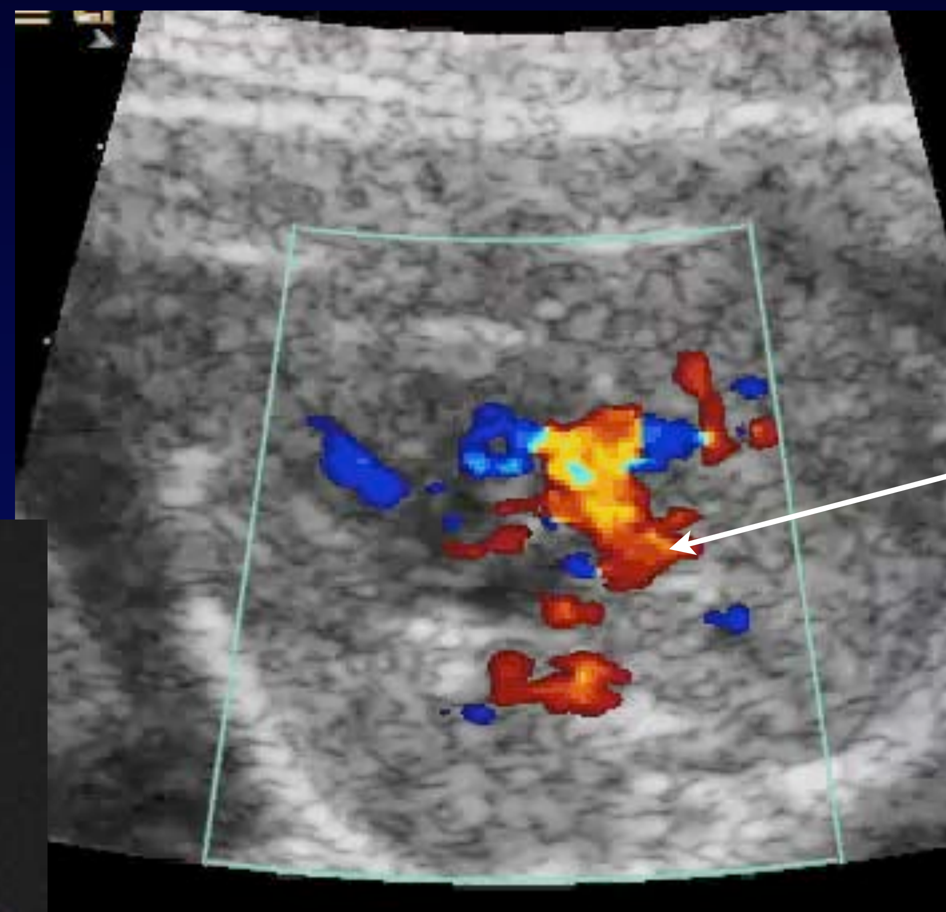


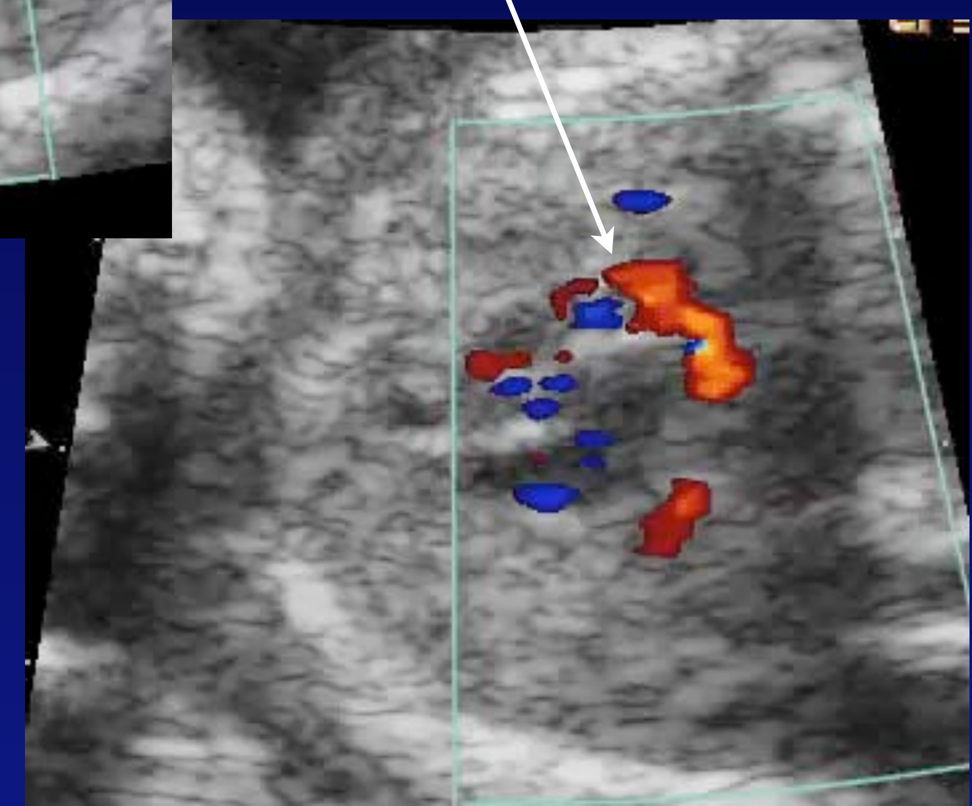




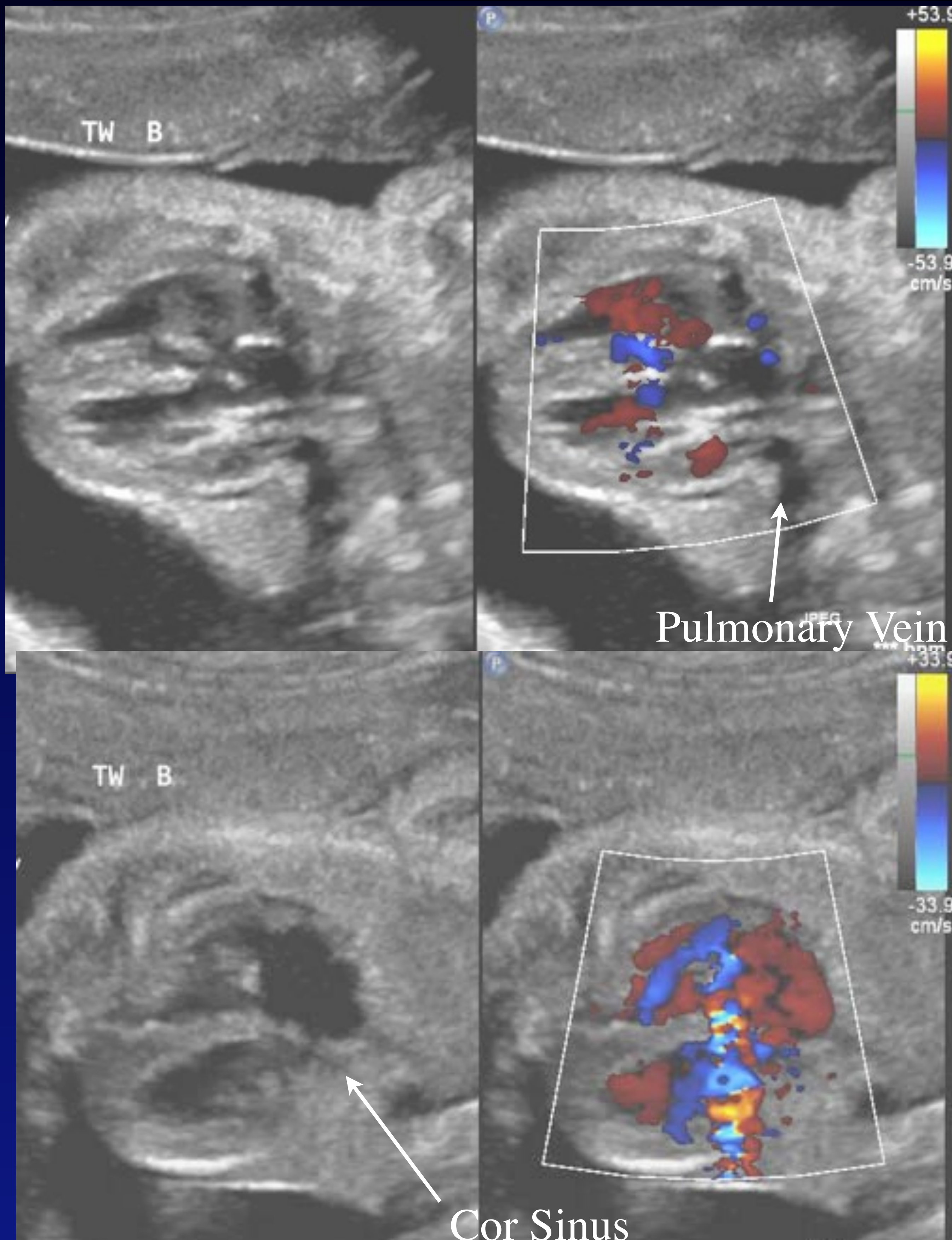
TAPVR to SVC without obstruction: Type I

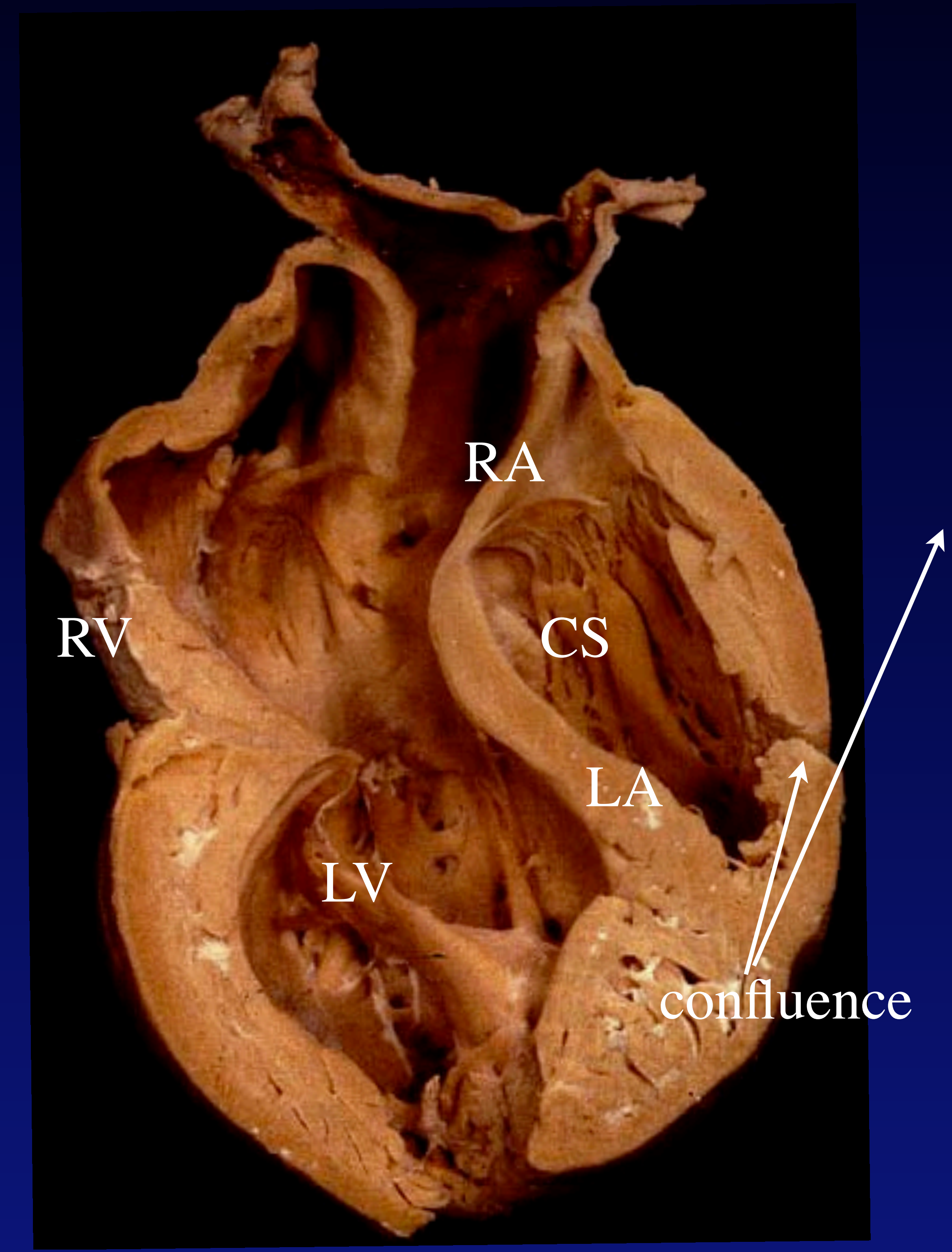






TAPVR (Type II) to Coronary Sinus (With Tetralogy & Hypoplastic Left Lung)



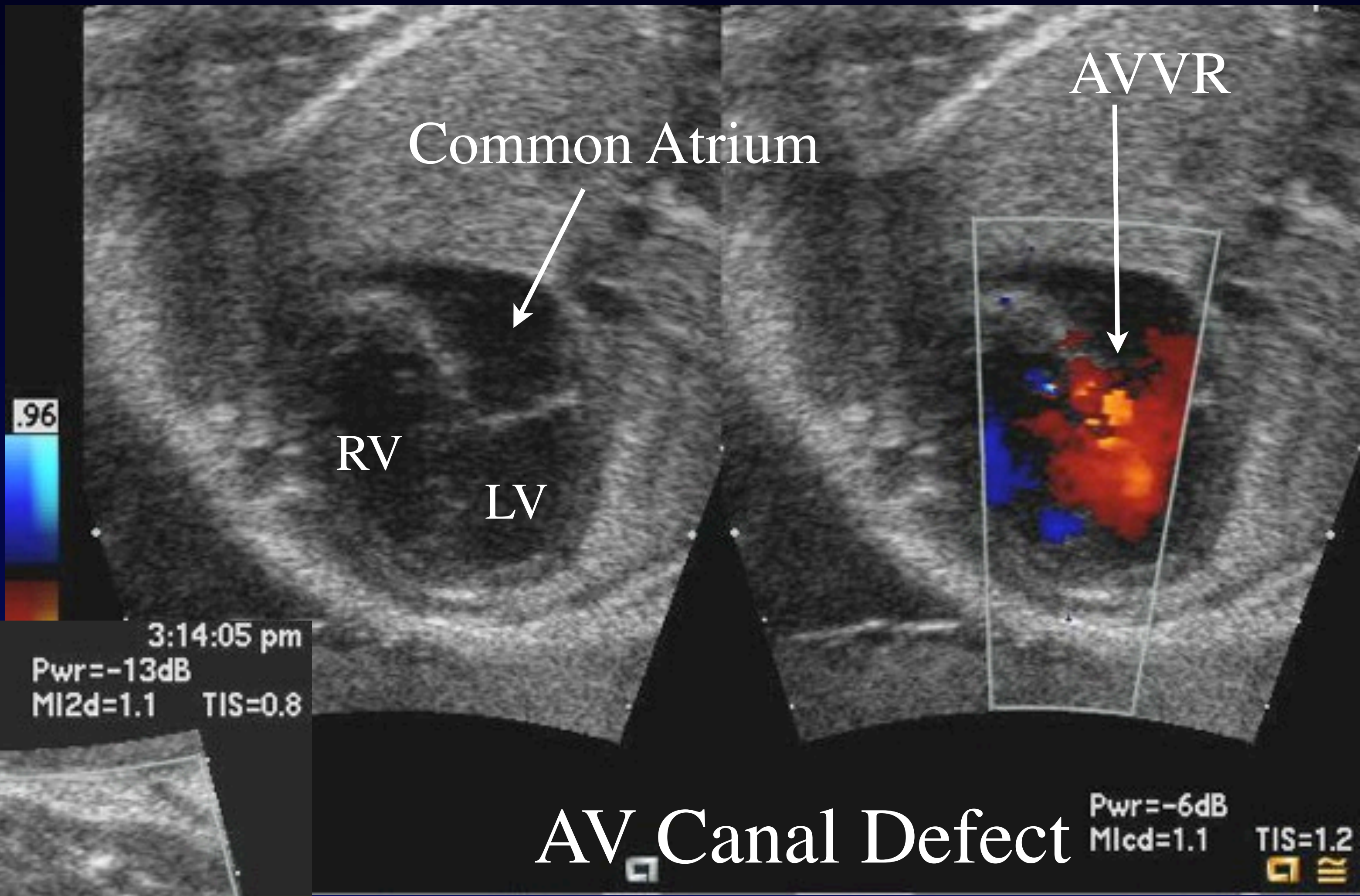


Descending Vertical Vein in TAPVR III

Normal

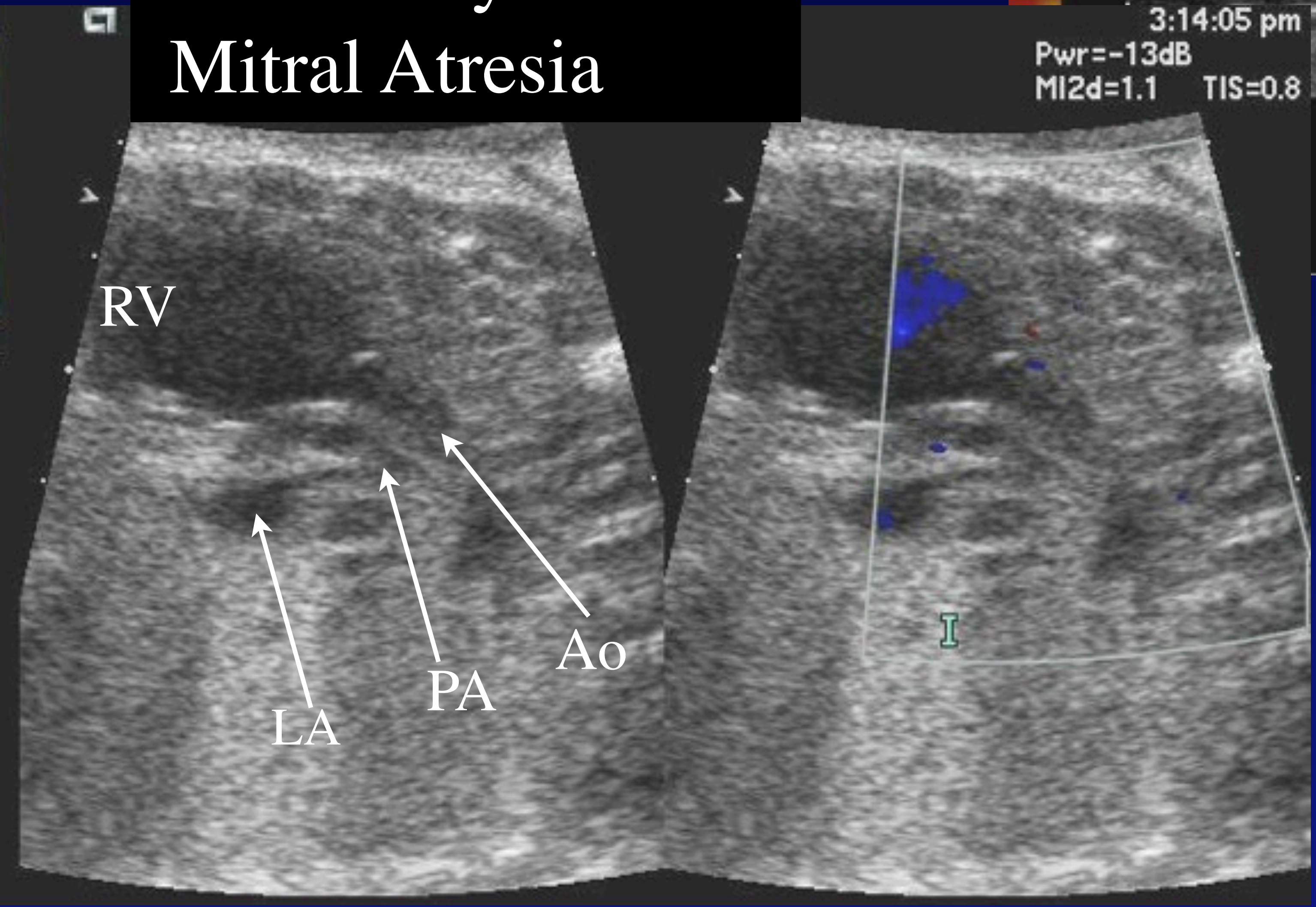
Abnormal

Accompanying Features in Isomerism

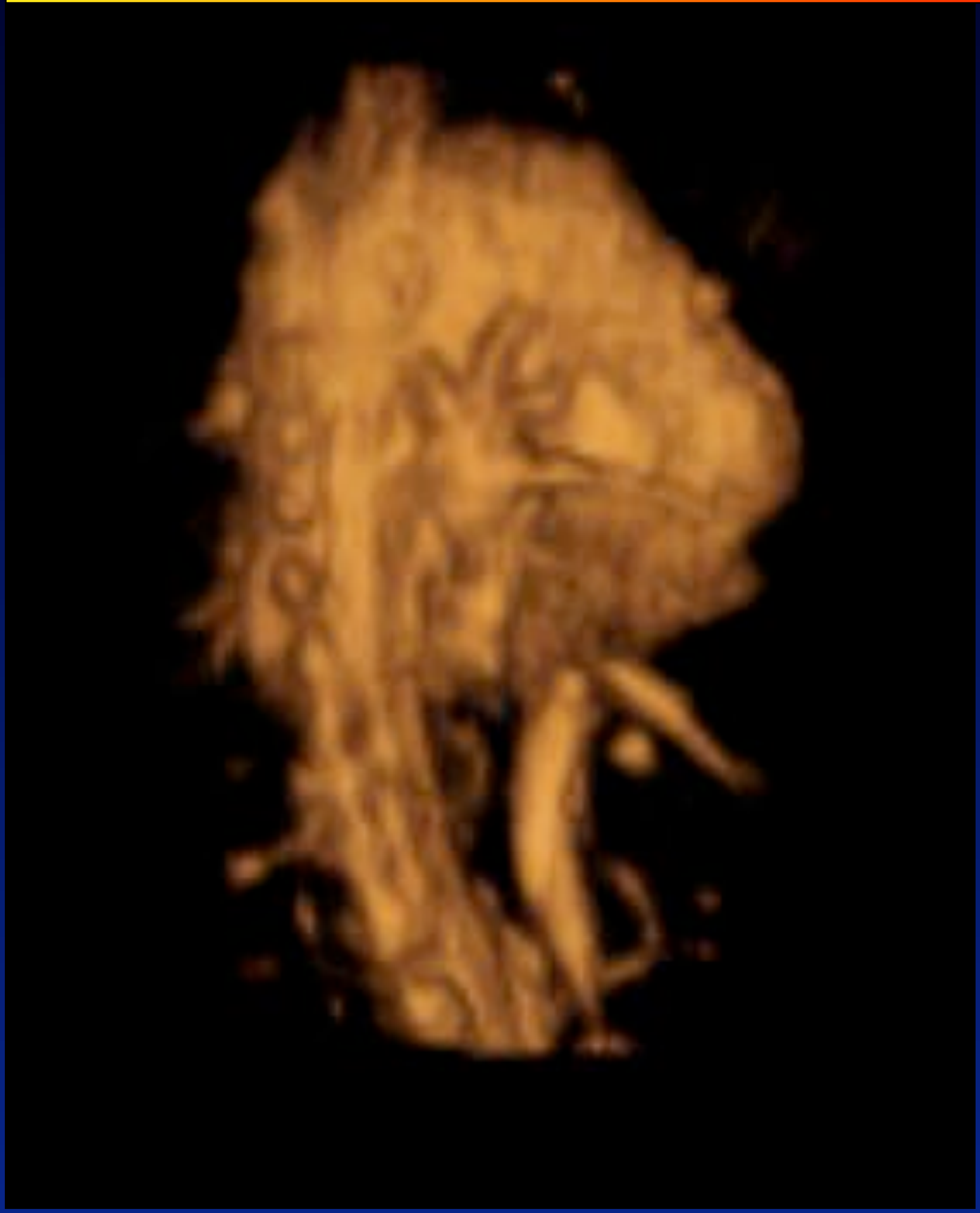


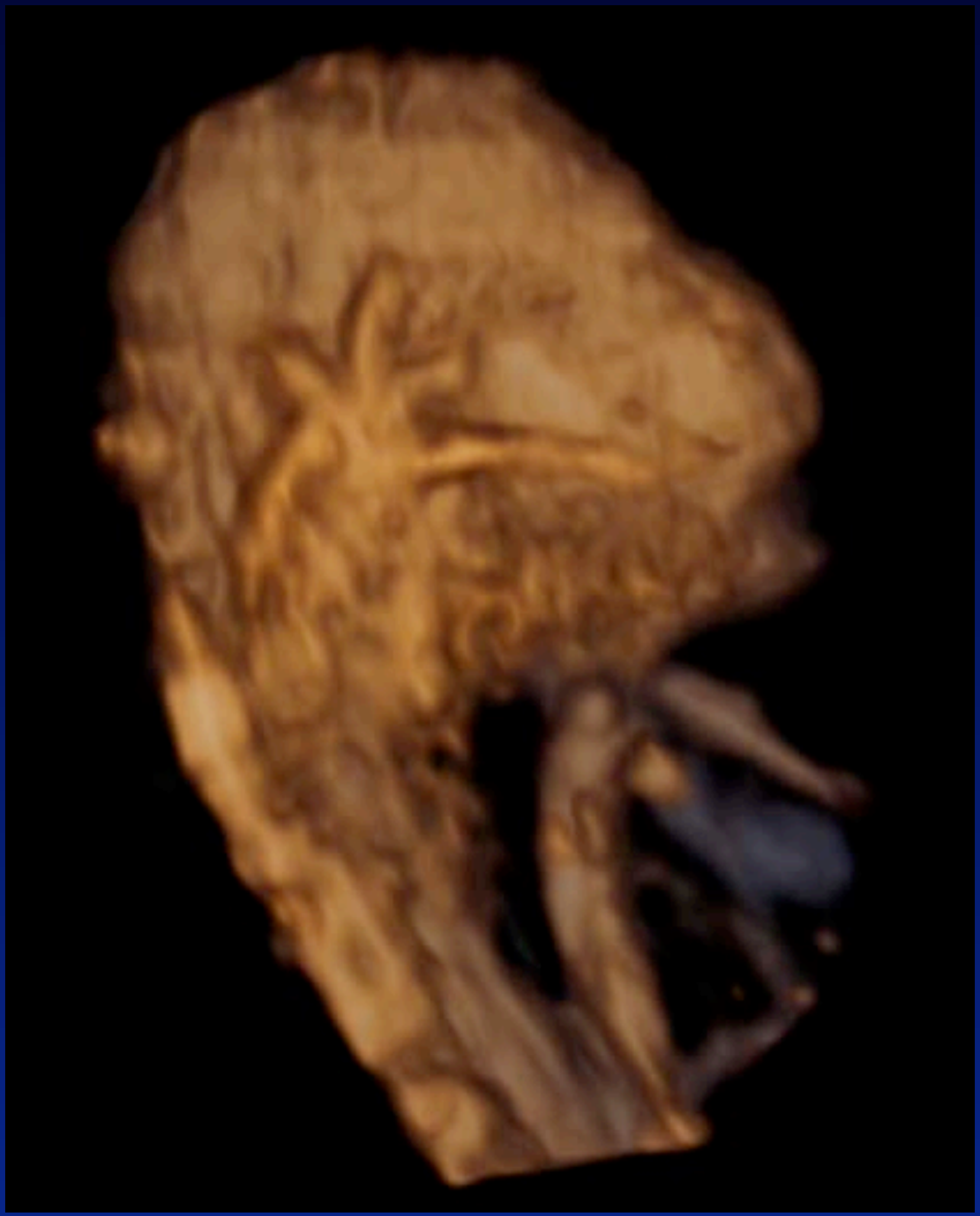
AV Canal Defect

Double outlet RV
Pulmonary Stenosis
Mitral Atresia



Anomalous Pulmonary Venous Return



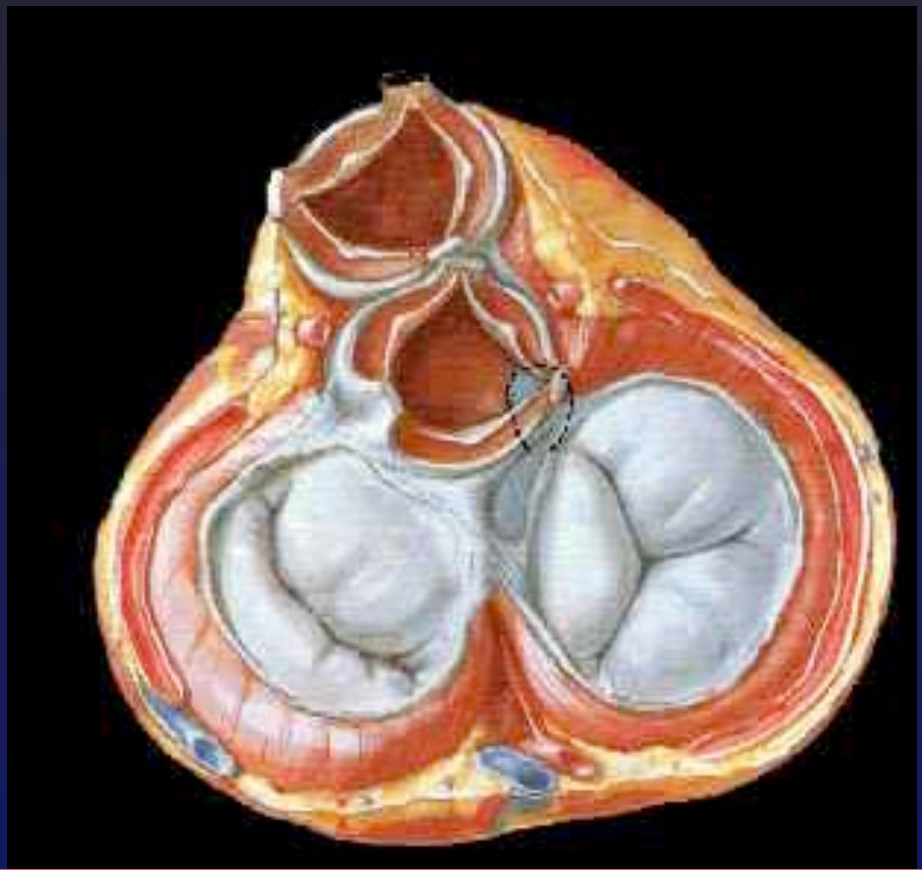


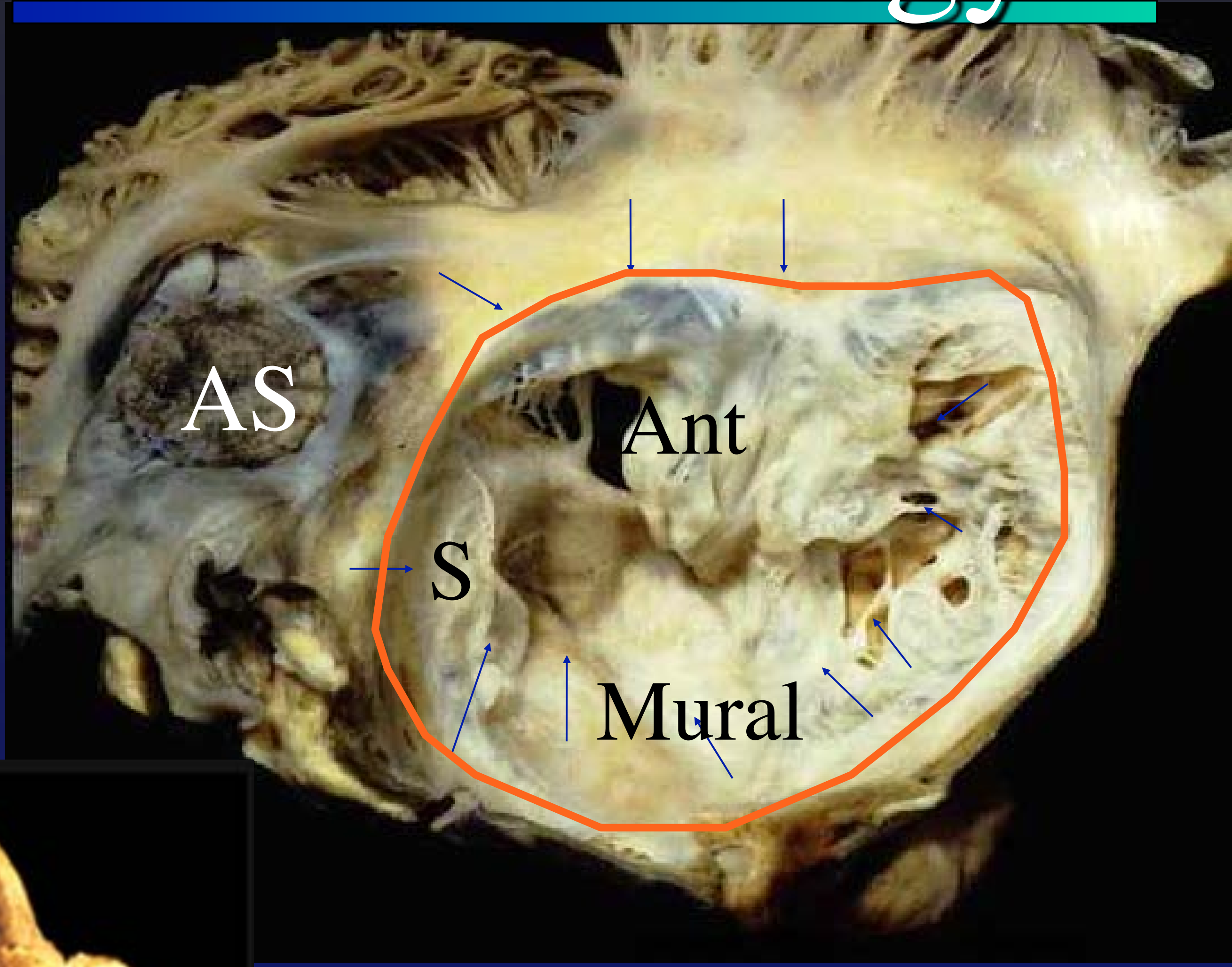
Summary: How not to miss TAPVR

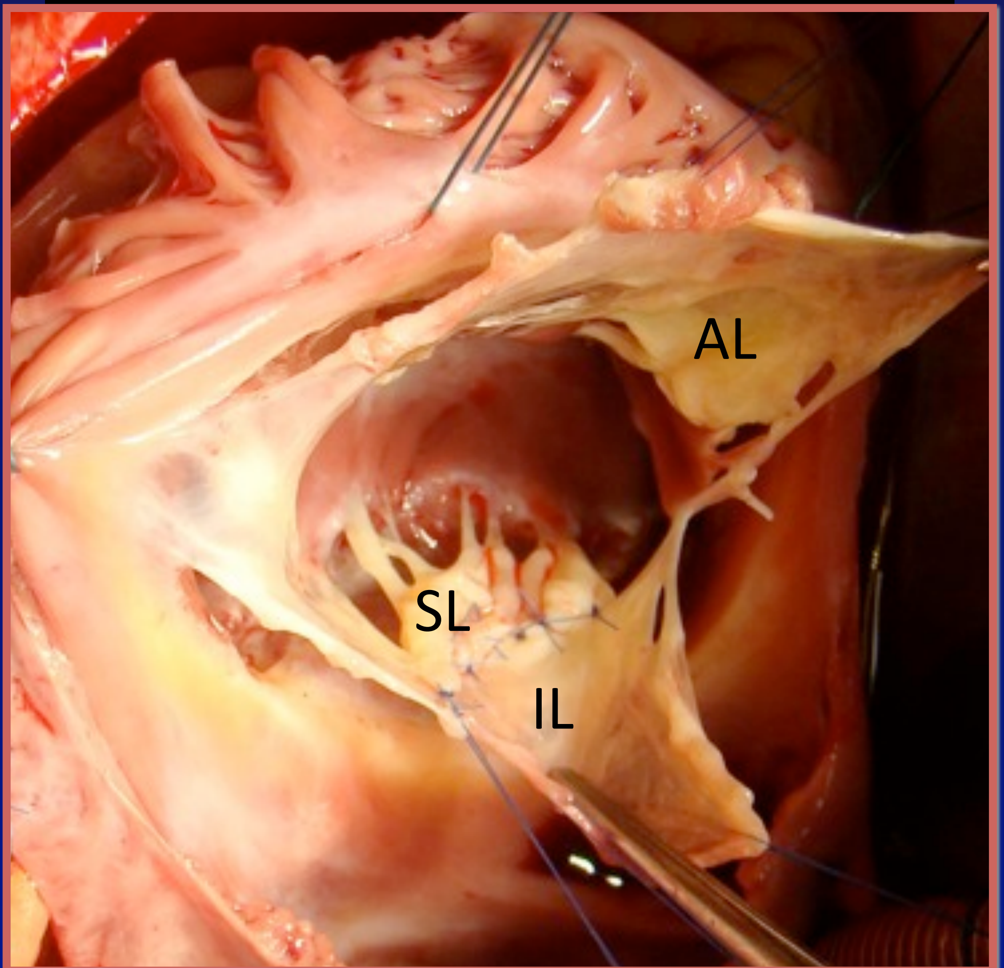
- Have a high index of suspicion.
- Get a good 4 chamber view and then look for the pulmonary veins entering the left atrium. This requires not only good imaging but Doppler color flow with the Nyquist limit held low!
- Obtain good Doppler signals in the pulmonary vein to define flow pattern of obstruction.
- Look for vertical veins and coronary sinus enlargement
- Check for abnormal pulmonary venous Doppler signals
- Look for associated heart disease:- right isomerism (Asplenia)

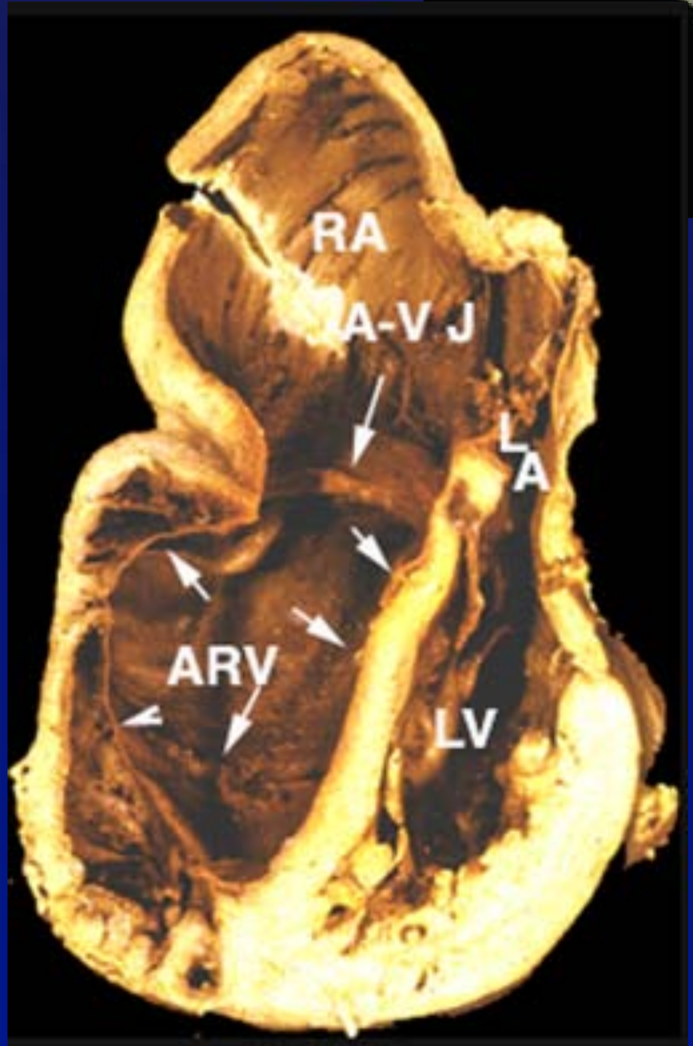
Ebstein's malformation in the fetus: Physiology, Pathology and new treatments

Ebstein's Malformation: Pathology

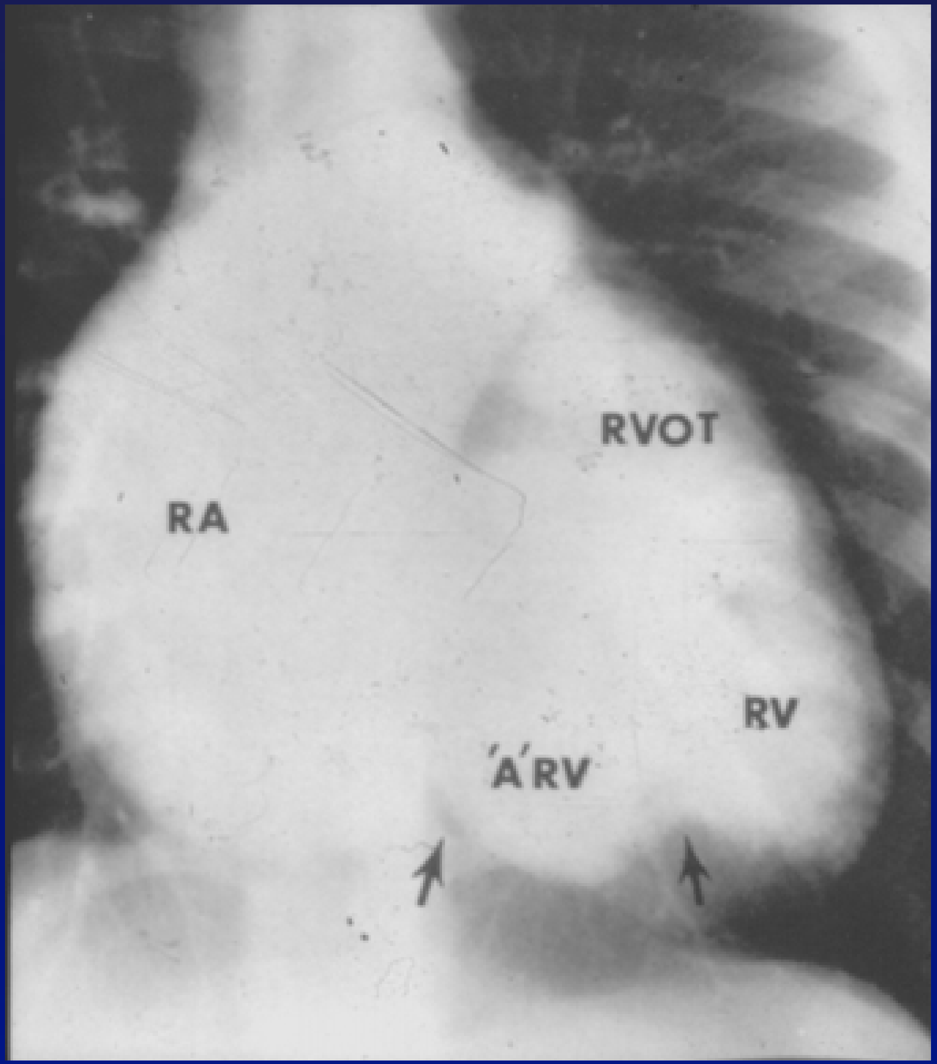


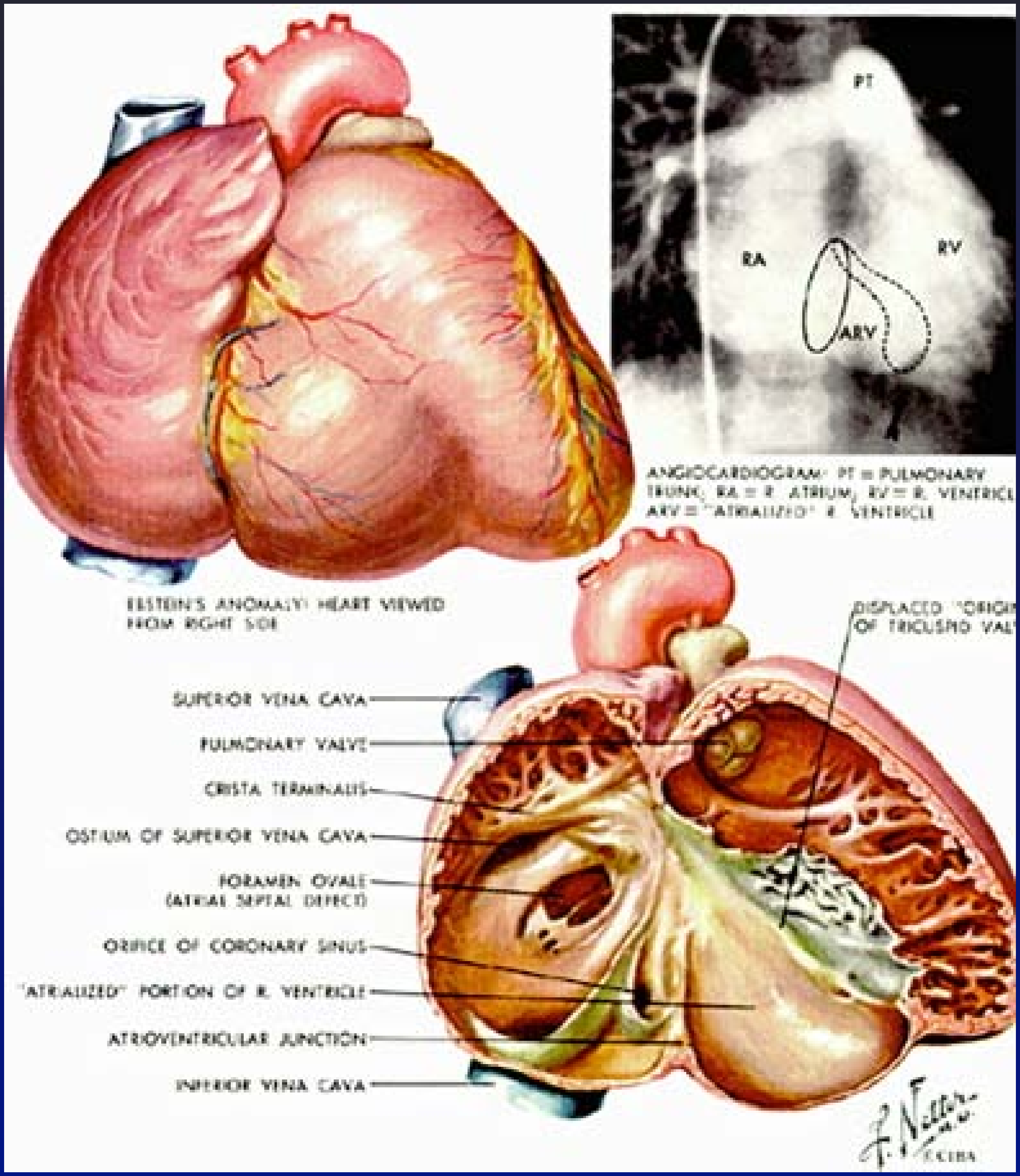




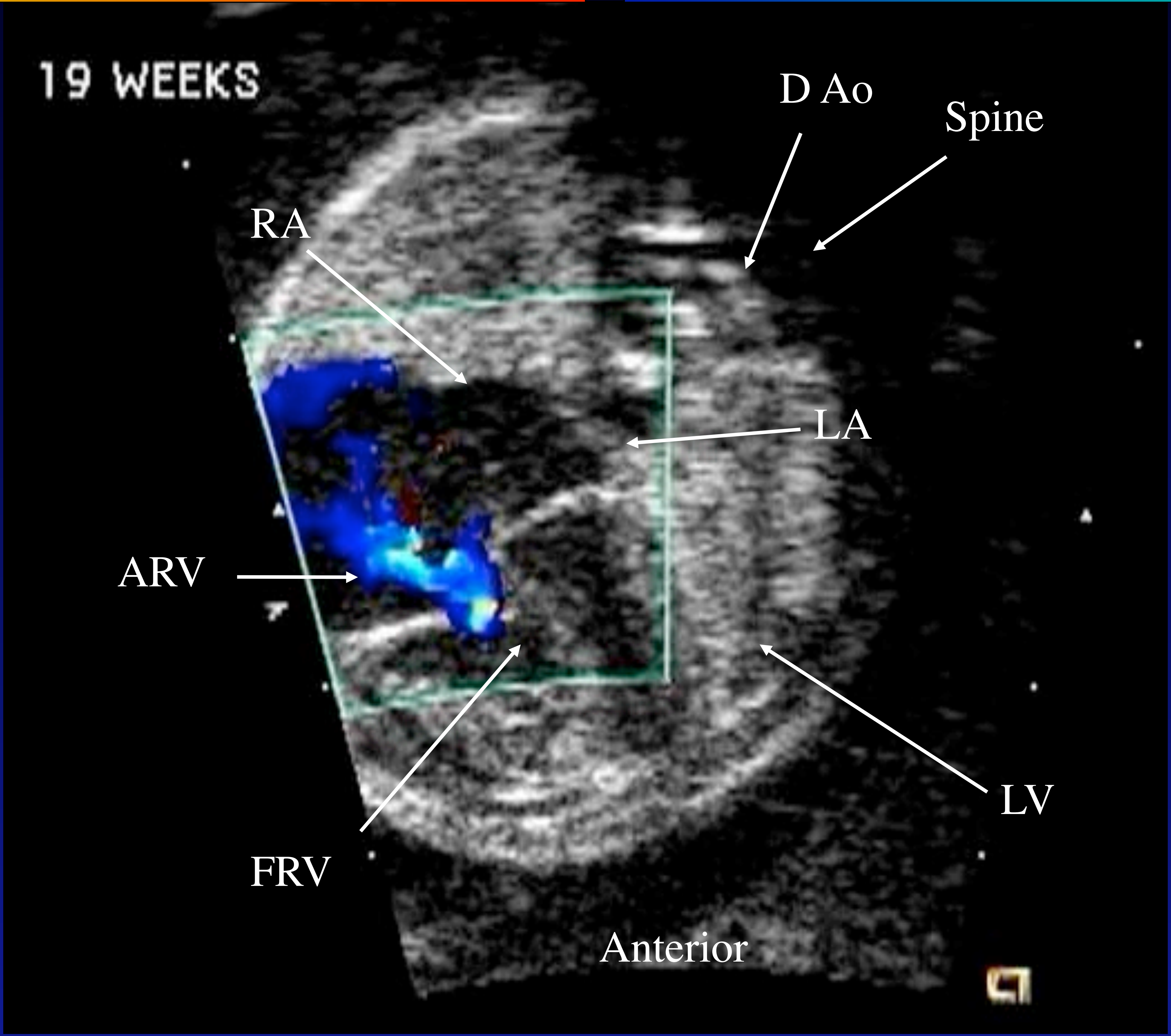


Displacement



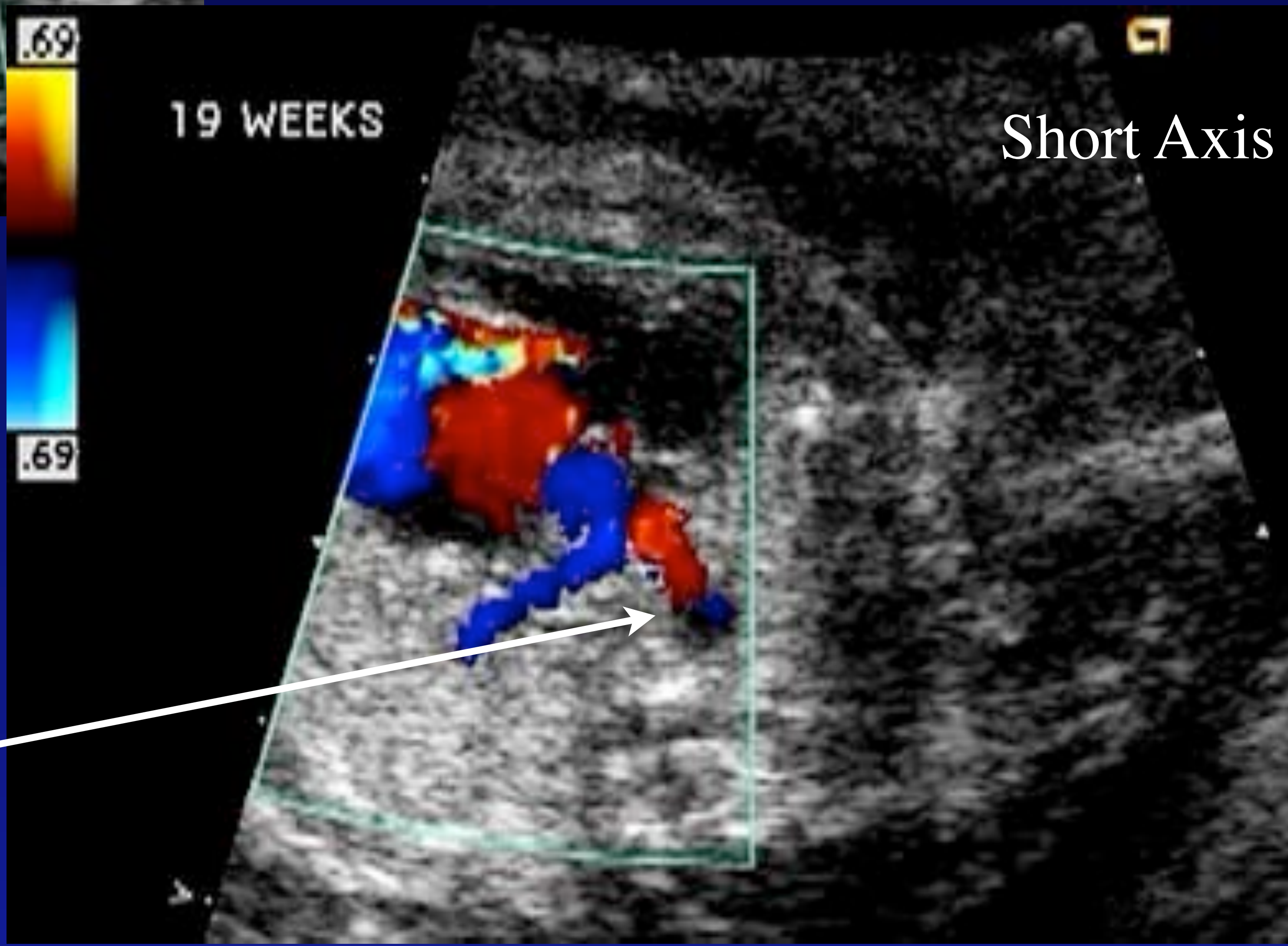


Ebstein's Malformation : Fetal Presentation



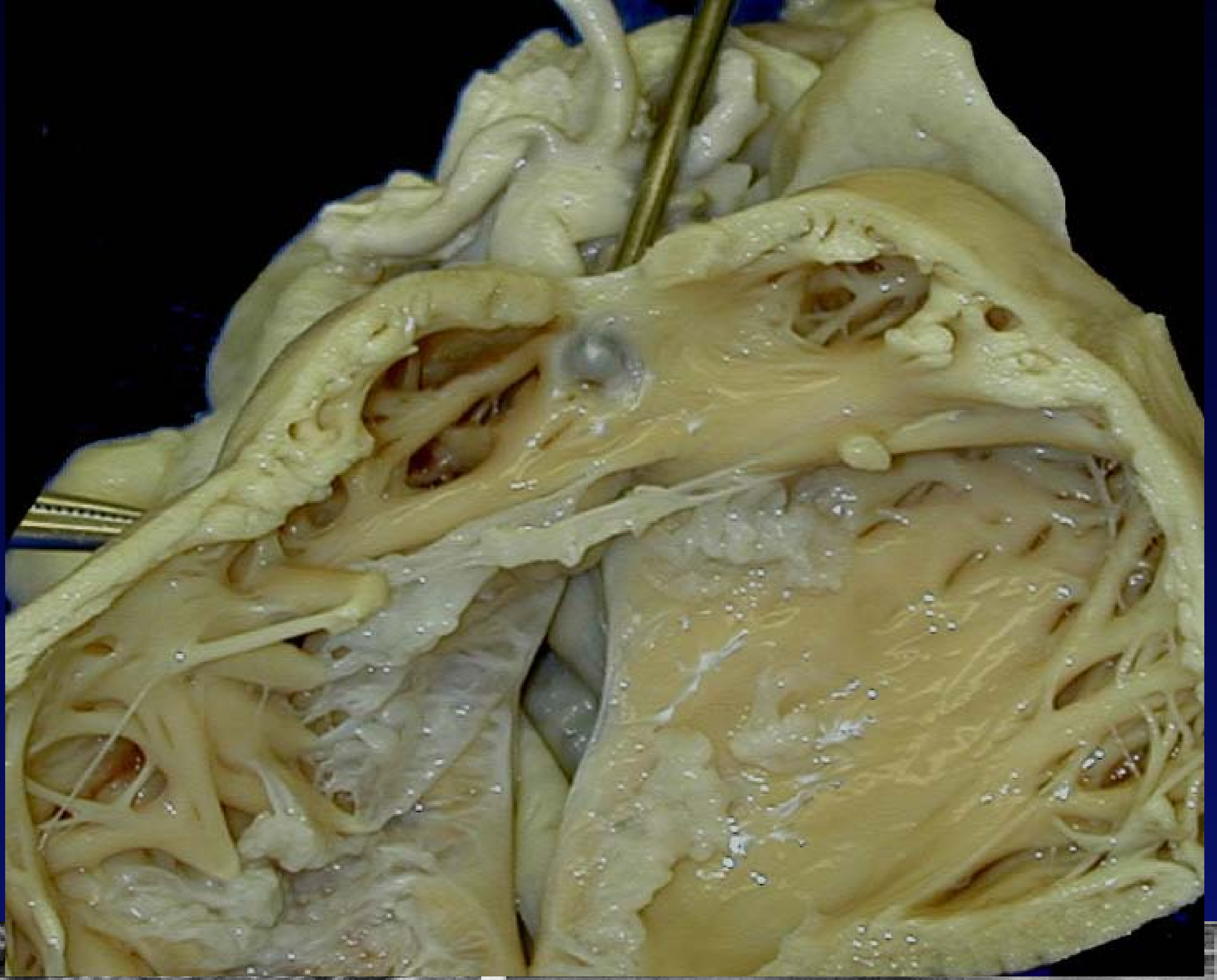
Ebstein's Malformation : Fetal Presentation

Left to right ductus shunt

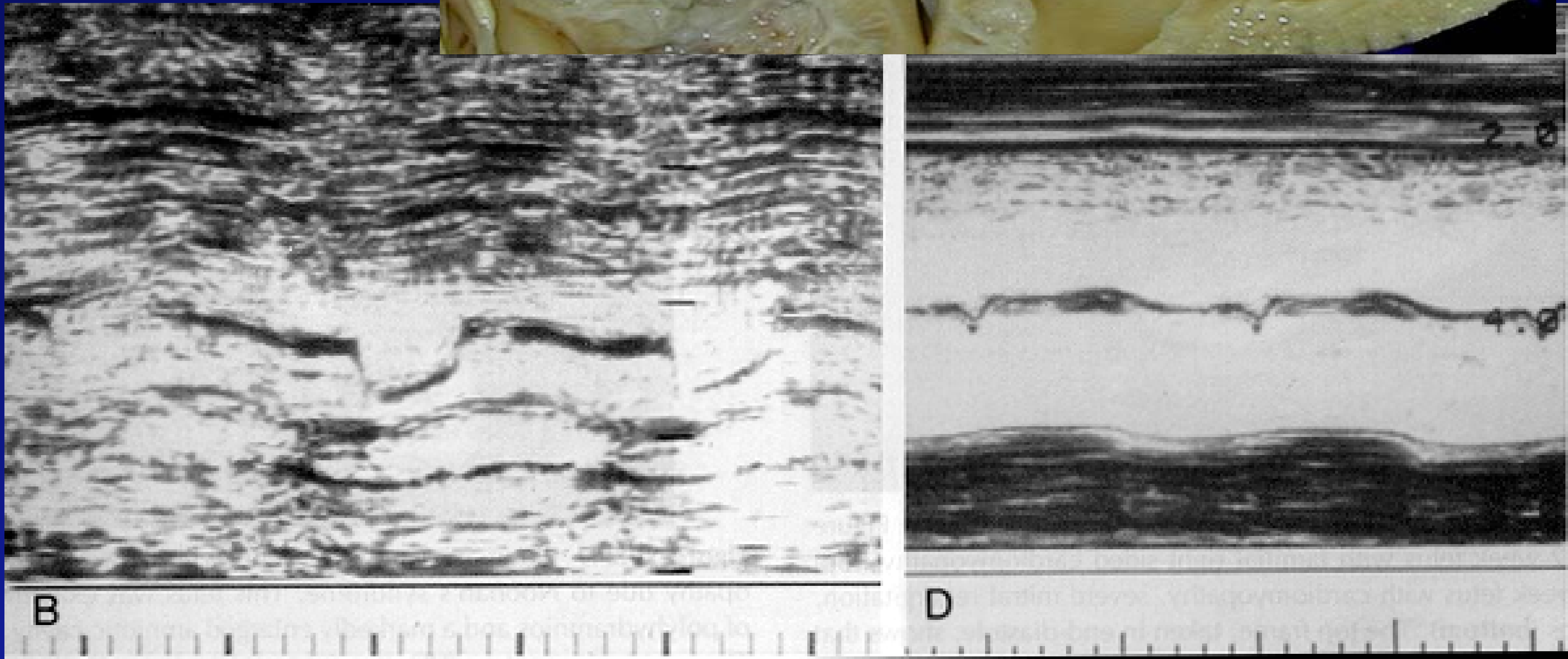


Duct

Consequence of pulmonary pressure holding the valve in the closed position



M-Mode@
20 & 36 weeks



Fetal Findings: Chamber Enlargement

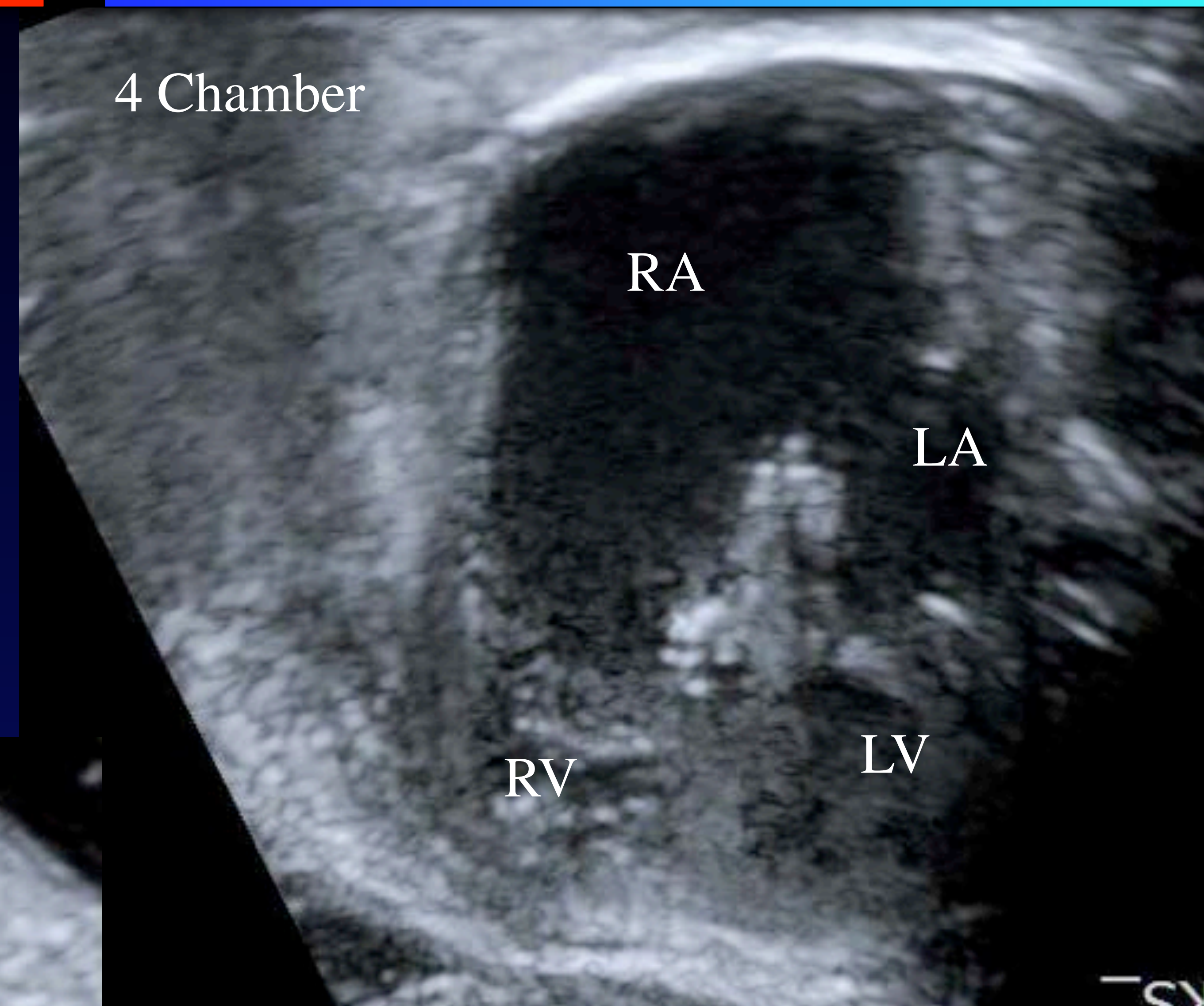
Cellermeyer
JACC

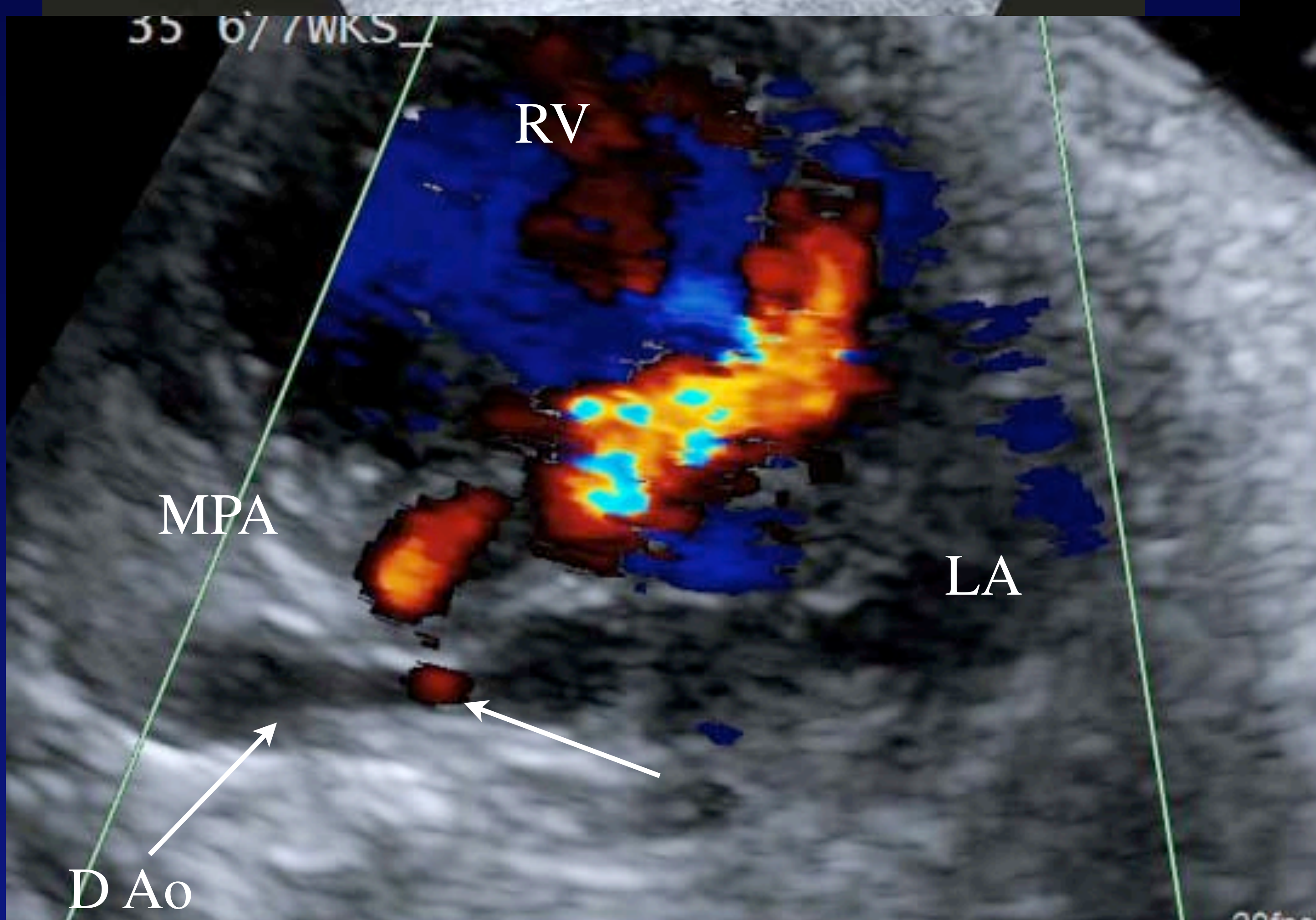
Roberson DA, **Silverman NH**: Ebstein's anomalyin the fetus and neonate. *J Am Coll Card* 14:1300–1307, 1989.

Physiology of Ebstein's Malformation and Related Conditions, such as Dysplastic Tricuspid Valve.

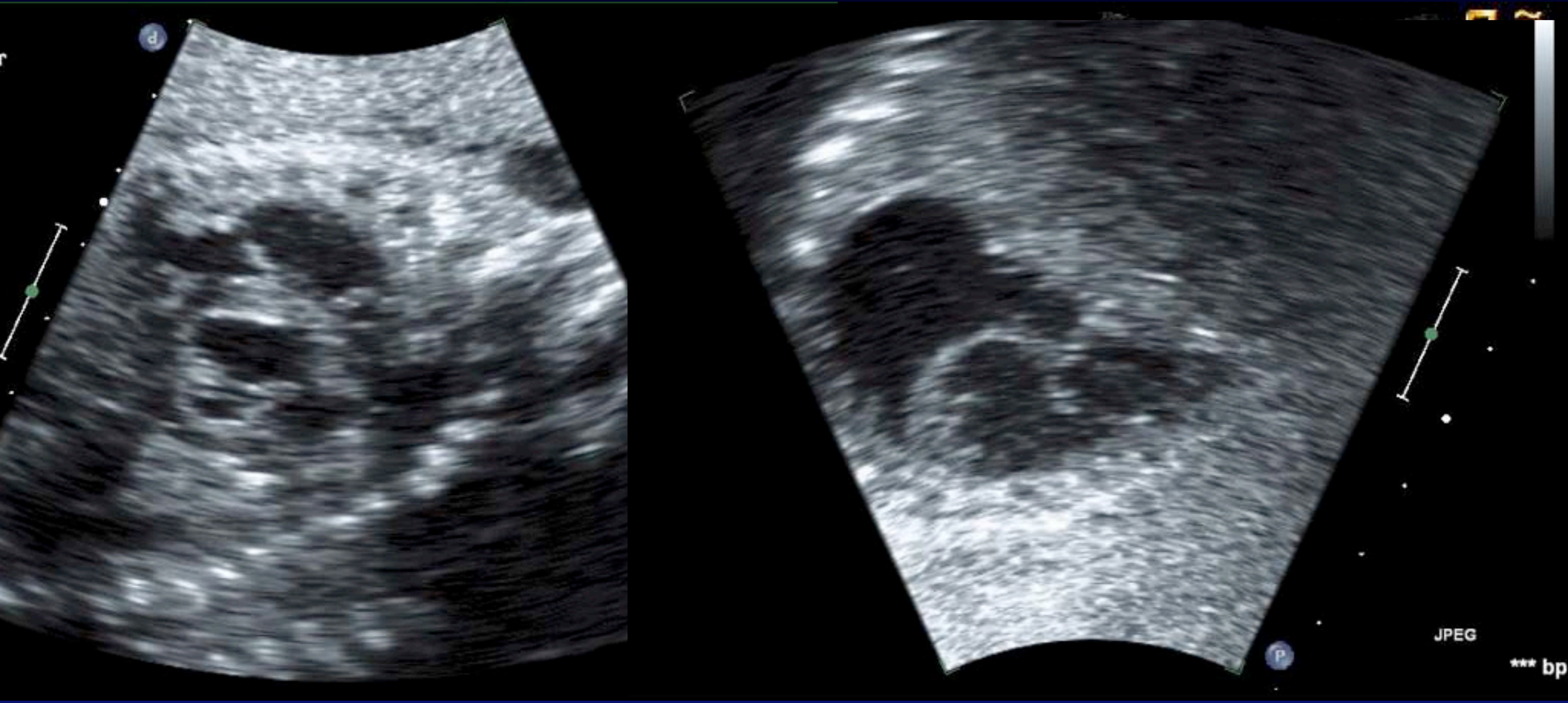
- It's the tricuspid regurgitation that's done 'em in!
- Tricuspid valvar insufficiency, leads to a lack of forward flow into the pulmonary artery.
- Flow into the pulmonary arteries increases during gestation and as the ductus sees the systemic pressure from the aorta, ductus contibution flow into the pulmonary arteries may be partial or complete.
- As blood pressure rises during gestation, the force of contraction of the right ventricle has to increase, but fails.
- The pulmonary valve may be held in the closed position interfering with its development. The valve may become regurgitant and set up a circular Shunt otherwise known as "the circle of death".

The Circular Shunt

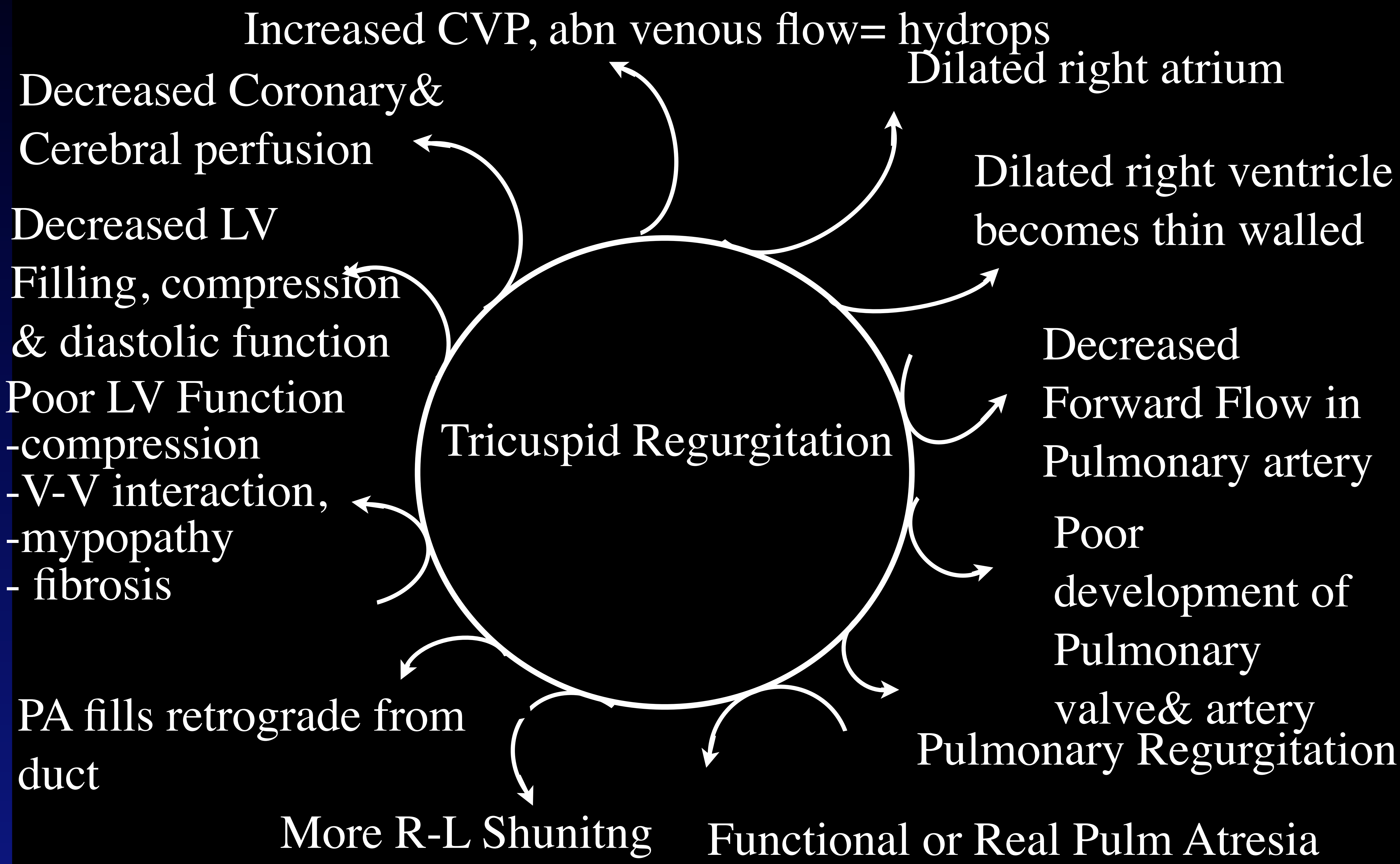




The Circular Shunt Continued



The Ebstein's Cycle.



Perinatal Outcomes after Fetal Diagnosis of Ebstein Anomaly or Tricuspid Valve Dysplasia in the Current Era: A Multi-Center Study

Lindsay Freud, MD; M Escobar-Diaz, MD; B Kalish, MD; R Komarlu, MD; E Jaeggi, MD; M Puchalski, MD; A Szwast, MD; S Morris, MD, MPH; S Levasseur, MD; J Huhta, MD; A Kavanaugh-McHugh, MD; A Moon-Grady, MD; M Donofrio, MD; E Michelfelder, MD; J Pruetz, MD; L Howley, MD; M van der Velde, MD; B Cuneo, MD; M Vernon, MD; C Ikemba, MD; J Kovalchin, MD; C Samai, MD; G Satou, MD; C Phoon, MD; N Silverman, MD; D McElhinney, MD; Wayne Tworetzky, MD

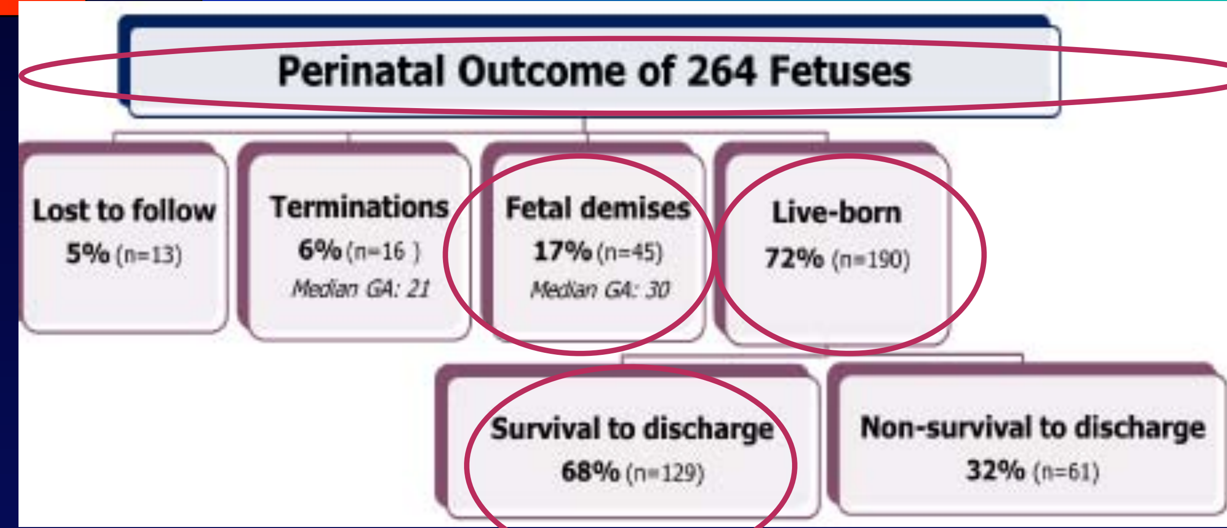
Introduction

- Ebstein anomaly and tricuspid valve dysplasia (EA/TVD) are rare congenital tricuspid valve malformations with high perinatal mortality
  - -40% fetal demise and 35% neonatal mortality among live-born
  - -Improved neonatal mortality has been suggested in recent era
- However, current literature is comprised of small, single-center case series often spanning several decades
- Several, potentially important hemodynamic predictors of perinatal outcome have been unable to be studied, such as the presence of pulmonary regurgitation and ventricular dysfunction

- To report the perinatal outcomes of EA/TVD in a large cohort of fetuses across multiple institutions in the contemporary era
- To enhance our understanding of the natural history in utero
- To better define clinical and echocardiographic predictors of mortality

Baseline Characteristics of Cohort *(n=264)*

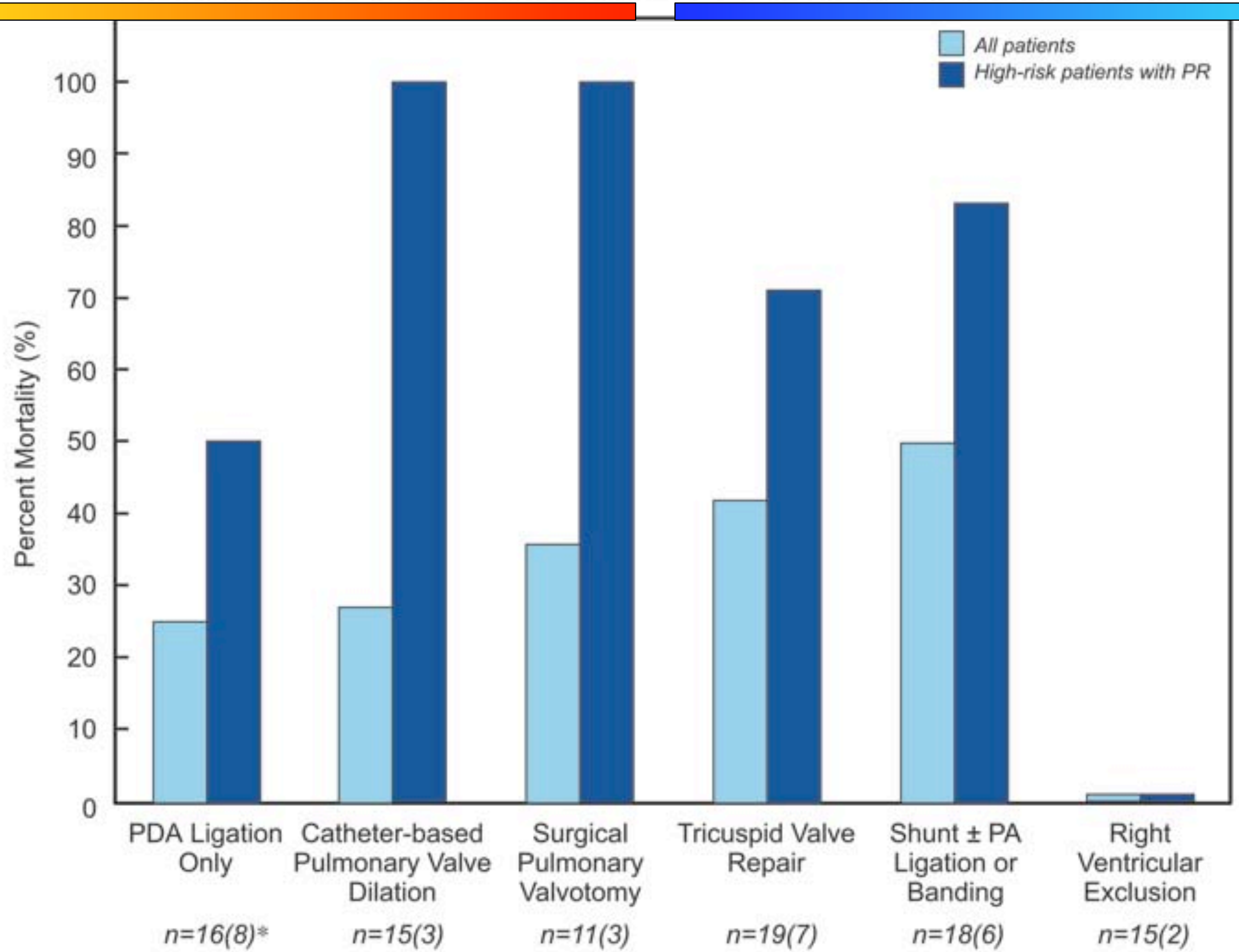
Characteristic	Median (range) or frequency
Gestational age at diagnosis (weeks)	25 (13.5 – 40)
Known genetic diagnosis	22%
Extracardiac anomaly	26.3%
Arrhythmia	6%
Hydrops	28.2%



Clinical Predictors of Neonatal Mortality among Live-Born Patients *(n=190)*

Variable	Survivors (n=129)	Non-survivors (n=61)	p-value
Gestational age at birth (wks)	37.5 ± 2.2	35.6 ± 2.9	<0.001
Birth weight (kg)	3.0 ± 0.6	2.4 ± 0.6	<0.001
Delivery room resuscitation	26%	71%	<0.001
Intubation	55%	89%	<0.001
Inotropic support	36%	76%	<0.001
ECMO	3%	32%	<0.001
Cath/surgical intervention	42%	43%	NS

Mortality in All Patients and High-Risk Patients by Neonatal Procedure



*(n)=number of high-risk patients with PR, PA=pulmonary artery, PDA=patent ductus arteriosus, PR=pulmonary regurgitation.

Poor prognostic signs in 2015

CT ratio (echo) >66%
RVOT obstruction
RVOT insufficiency
Low RV pressure
Marked RA/RV dilation
Hydrops
Atrial arrhythmia
Prematurity
Decreased LV function

Hyperoxia Test

They were requested to wear a rebreathing oxygen mask.

The oxygen flow was adjusted to a maternal arterial PO2 between 250 and 300 mm Hg by ultrasound-guided puncture of the maternal femoral artery using a 26-gauge needle.

A total between 8 and 33 days (mean 15.5 and median 14), the women underwent 3 - 4 h HO/d until delivery.

Options for *in utero* treatment - Hyperoxia

Effects of maternal–fetal hyperoxygenation on aortic arch flow in a late-gestation human fetus with closed oval foramen at risk for coarctation

Thomas Kohl, MD, Giessen-Marburg, Germany

Over 14 days, 45% of oxygen was administered to the mother via a face mask in 3 daily sessions of 3 to 4 hours' duration. This regimen has been found useful in previous cases to improve hypoplastic left heart dimensions by increasing pulmonary venous return to the left side of the heart in human fetuses.[2] The effect of the approach on fetal

Pediatr Cardiol (2010) 31:250–263
DOI 10.1007/s00246-009-9600-5

ORIGINAL ARTICLE

Chronic Intermittent Materno-Fetal Hyperoxygenation in Late Gestation May Improve on Hypoplastic Cardiovascular Structures Associated with Cardiac Malformations in Human Fetuses

Thomas Kohl

Options for *in utero* treatment -

Close the Duct With CxO Inhibitors

A novel approach to the management of critically ill neonatal Ebstein's anomaly: Veno-venous extracorporeal membrane oxygenation to promote right ventricular recovery

Holly Bauser-Heaton, Charles Nguyen, Theresa Tacy, David Axelrod
Annals of Pediatric Cardiology 2015 Vol 8 Issue 1
Department of Pediatric Cardiology, Lucile Packard Children's Hospital at Stanford University, Palo Alto, California, United States

ABSTRACT

This is the first report of the use of veno-venous extracorporeal membrane oxygenation in a neonate with severe Ebstein's anomaly. The report suggests the use of veno-venous extracorporeal membrane oxygenation in the immediate neonatal period may be a useful therapy in severe Ebstein's anomaly. By providing adequate oxygenation independent of the patient's native pulmonary blood flow, veno-venous extracorporeal membrane oxygenation allows the pulmonary vascular resistance to decrease and may promote right ventricular recovery.

25 weeks and 5 days

Cardiothoracic ratio of 0.8, TR Jet of 16 Hg.

Maternal treatment with indomethacin was initiated at 28 weeks and 4 days gestation.

The maximum flow velocity achieved across the patent ductus arteriosus was 2.9 m/sec, with a dosing regimen of indomethacin of 300 mg/day at 37 weeks gestation.

Future Options

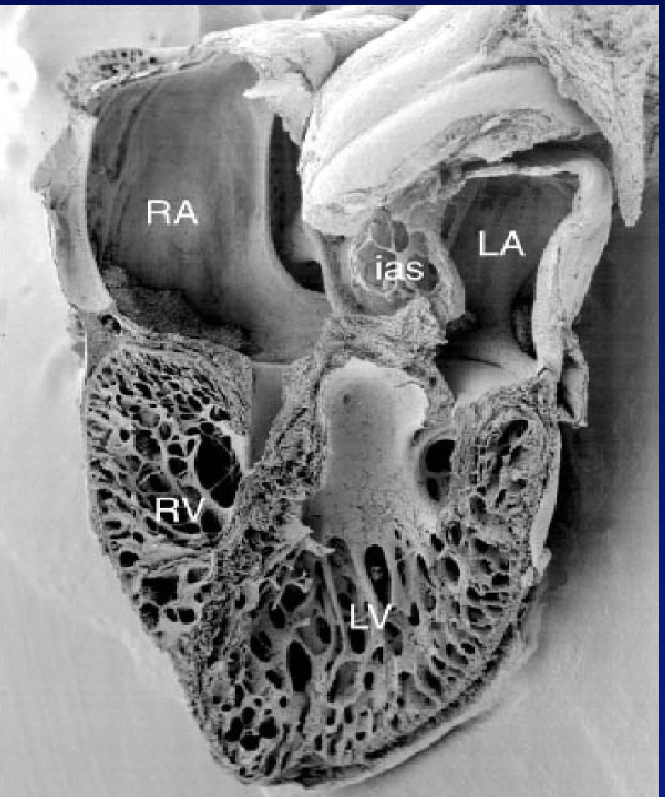
- No intervention
- Delivery + surgery
- Ductal occlusion with Cyclooxygenase inhibitors- Indomenthacin 300-600 Gm a day, plus Ibuprophen
- Hyperoxia

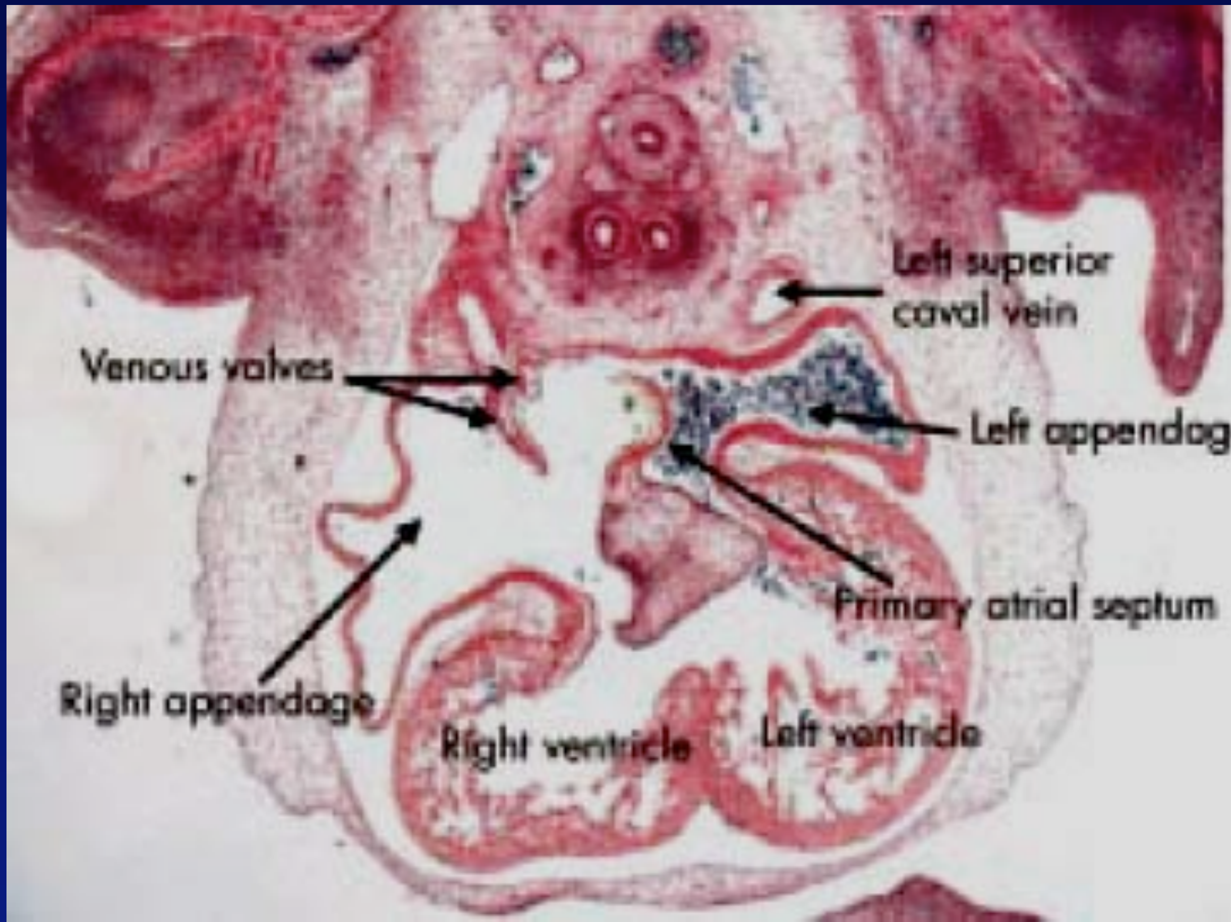
Isolated Non-Compaction (LVNC).
Or,
Spongy Myocardium
Or,
Hypertrabecular Syndrome.

Hypertabeculation Syndrome, Songy Myocardium, Isolated Non-Compaction

"The hearts of primitive vertebrates, such as the hagfish, are formed of interlacing muscle fibers bathed in the same pool of blood that they pump. In the early embryonic life of the higher vertebrates, a similar condition exists, in which the heart wall is a loose meshwork of developing myocardial fibers. Relatively large spaces between the muscle trabeculations contain blood which circulates back and forth from the cavities with the heart beat. With gradual condensation of the myocardium, most of these spaces become flattened sinusoids, while some remain as deep clefts continuous with the ventricular cavities."

Lurie, *Moss & Adams*, 1968.

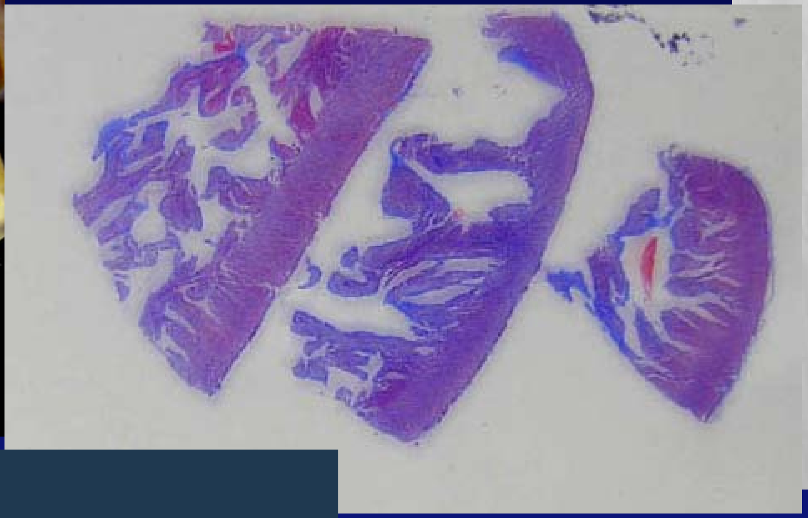


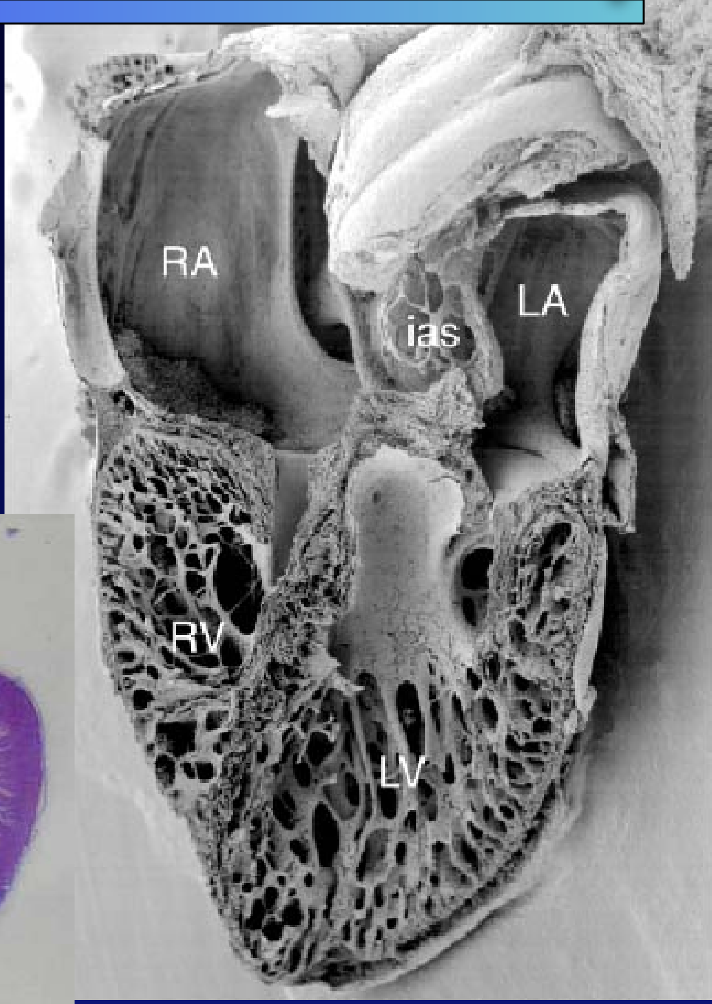


Recent Pathologial Cases

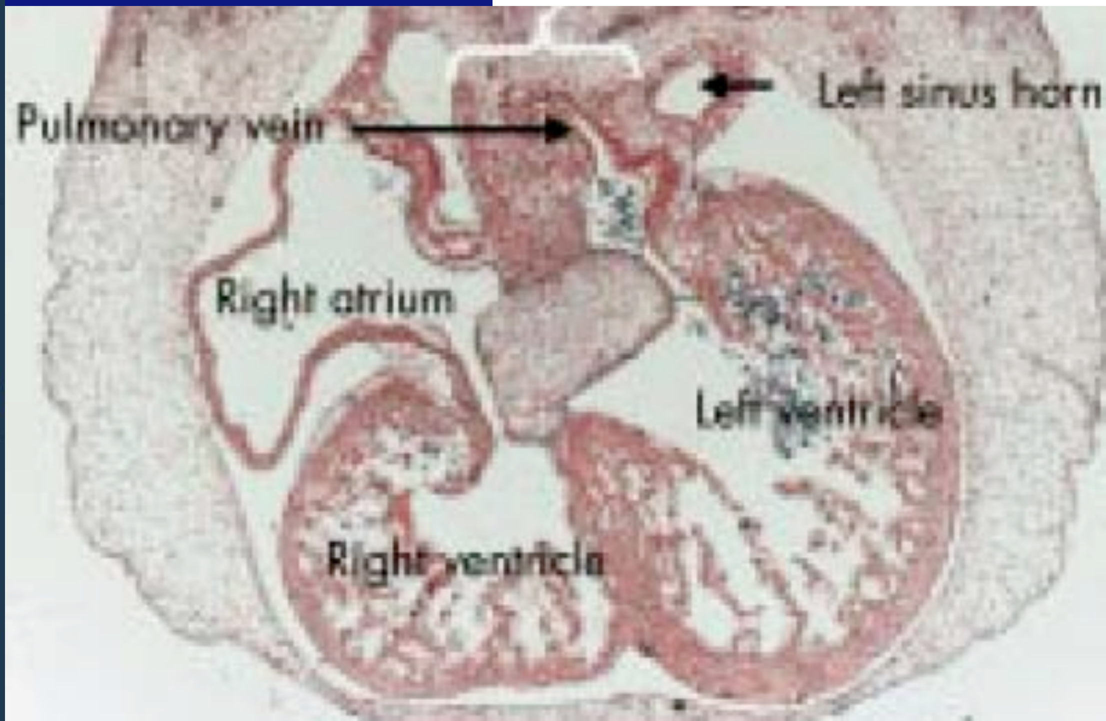
From Sedmera et al
1mm Mouse Embryo

Recent UCSF
Pathology
Collection
Specimen

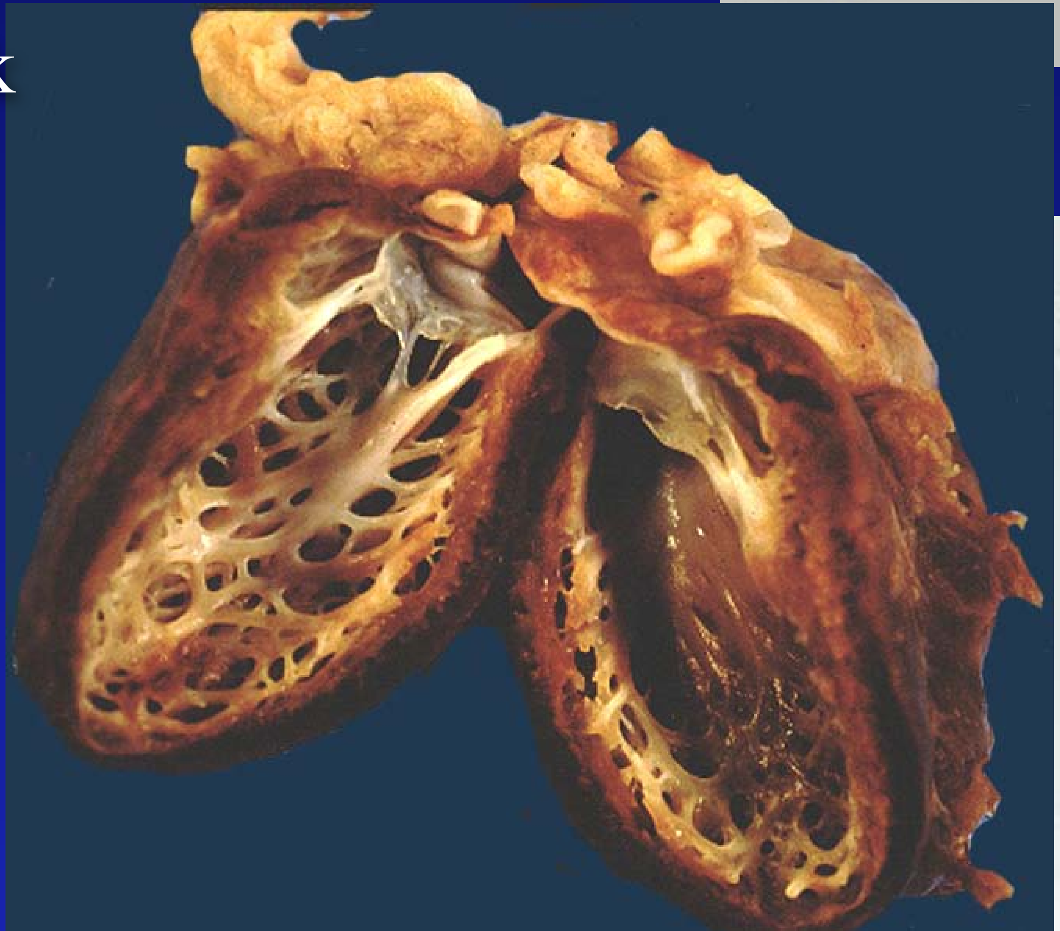




Cardiol Young 2005; 15: 56–72
ISSN 1047-9511
© Cambridge University Press

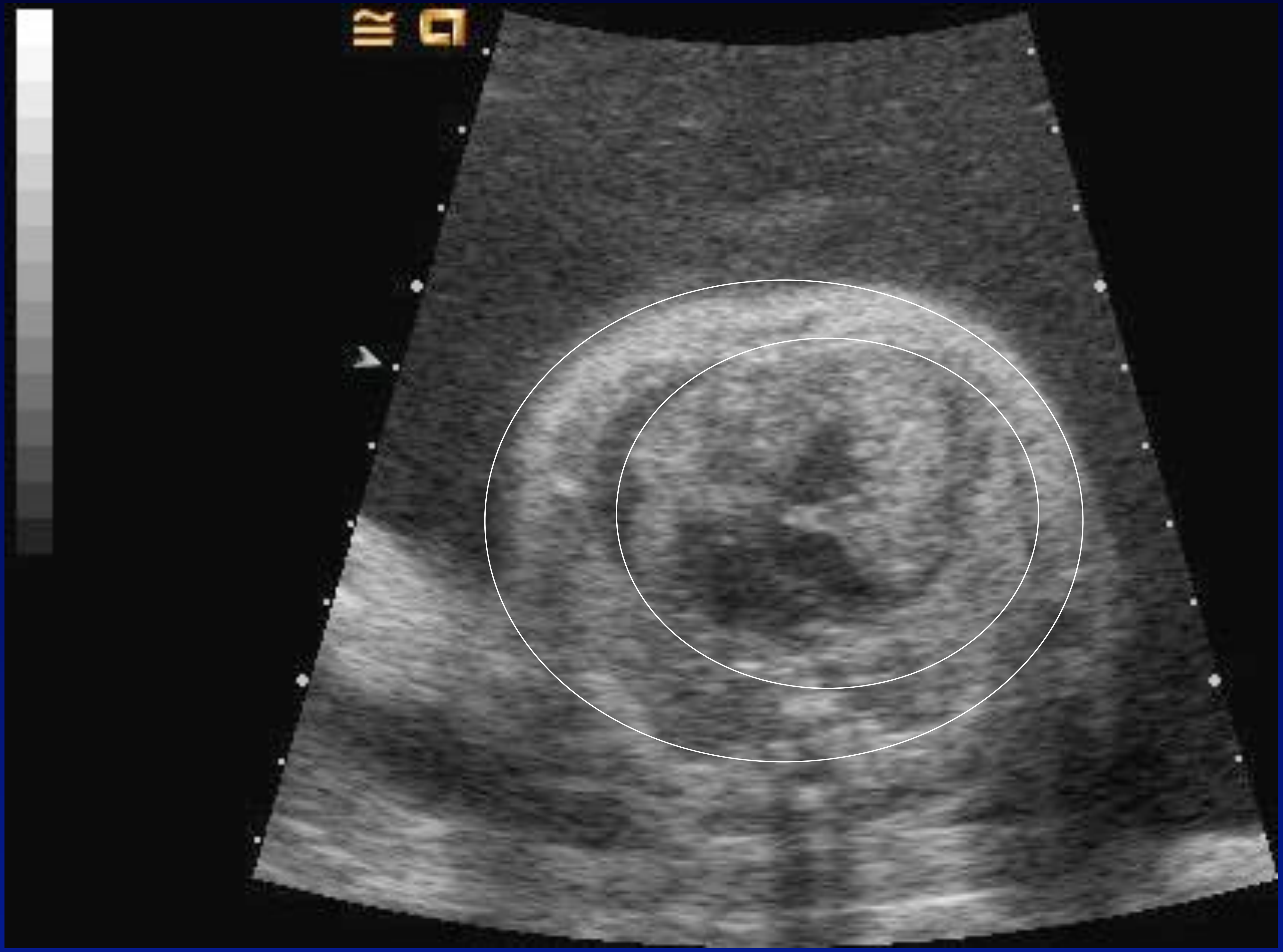


Fetal Heart Block
Hydrops,
Sent for Fetal
Pacemaker.
Patient
succumbed



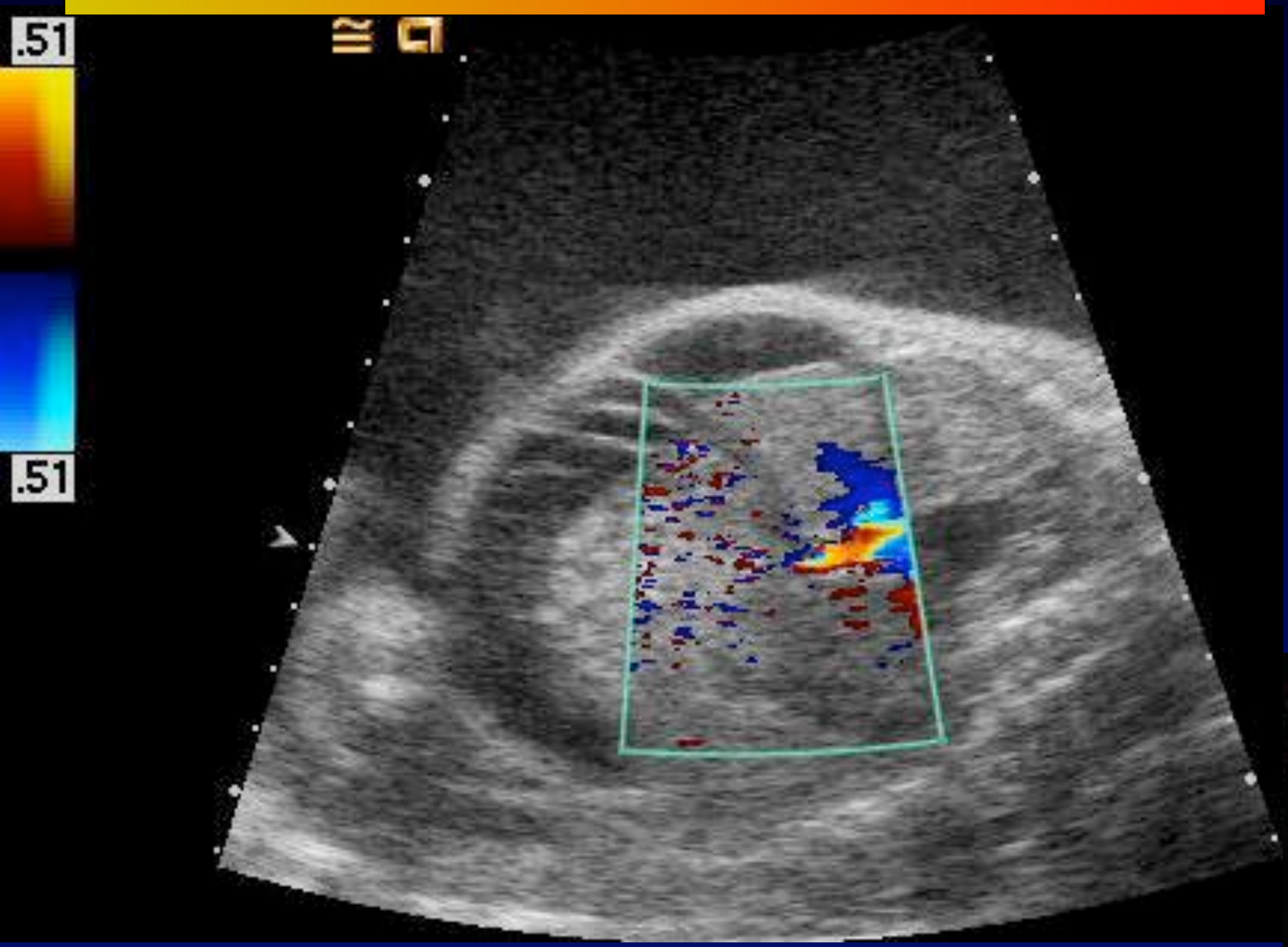
NHS.

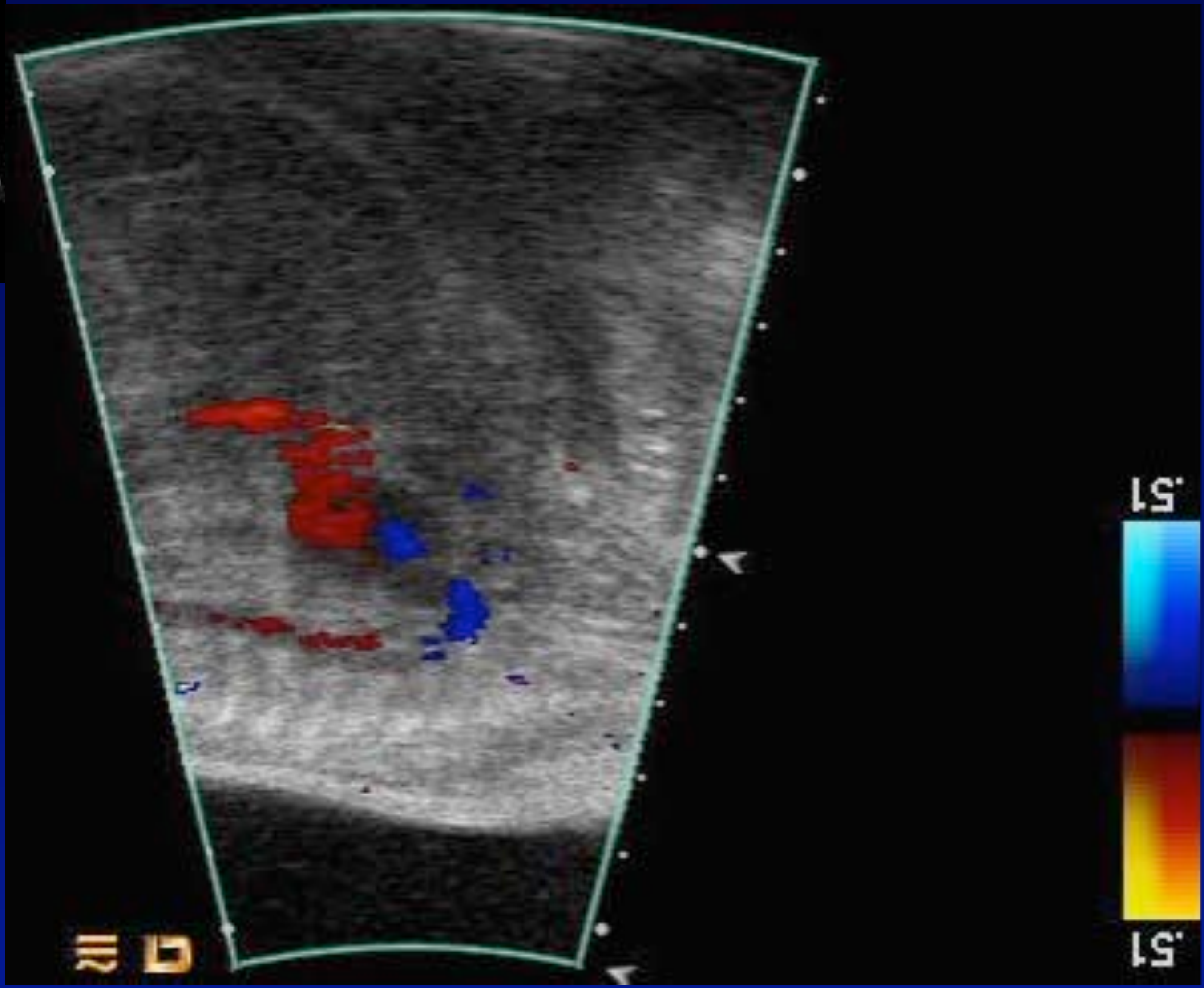
Heart Block & Massive Cardiomegaly.



NHS.

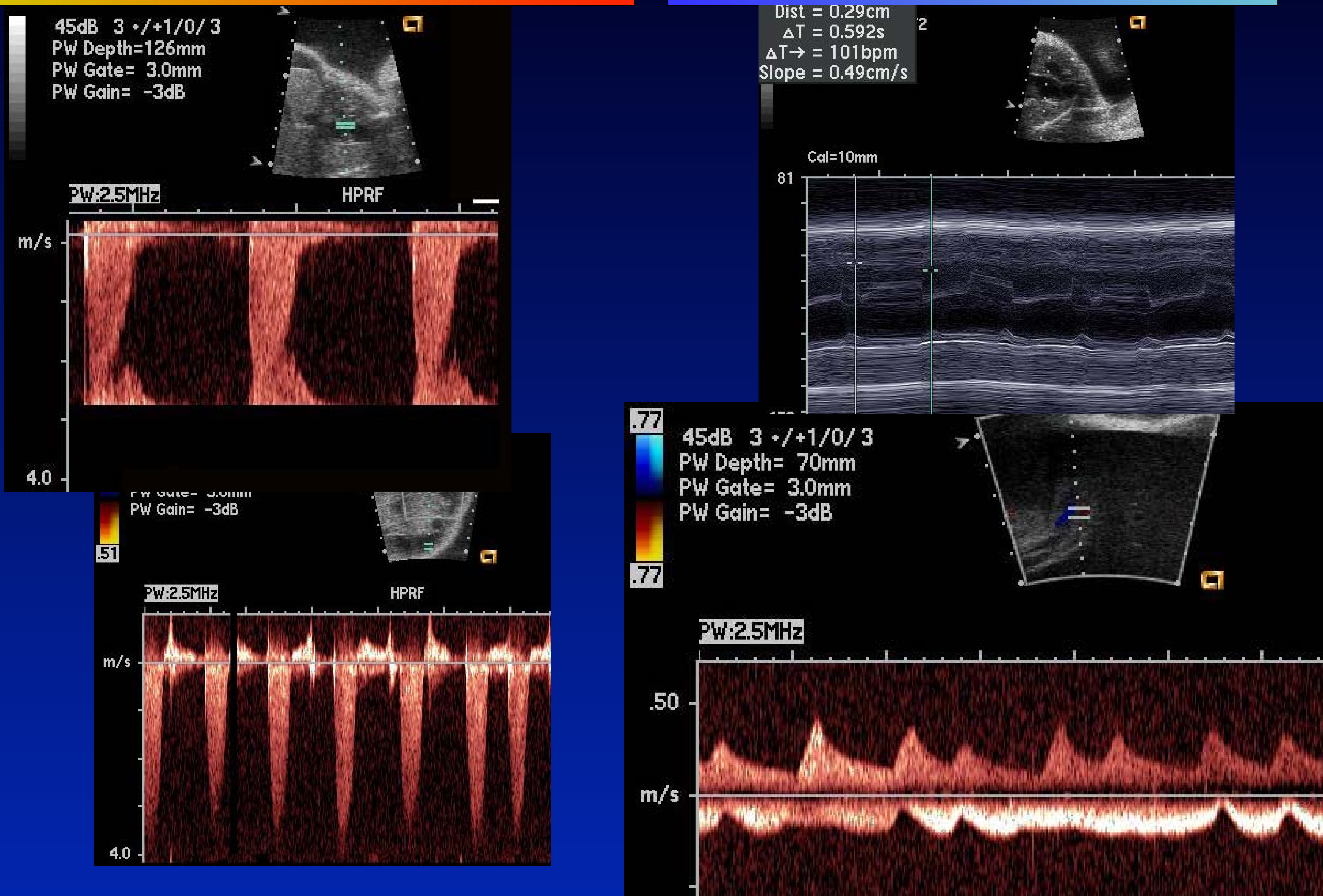
Left Isomerism (Polysplenia):Interrupted IVC& Azygos Continuation





NHS.

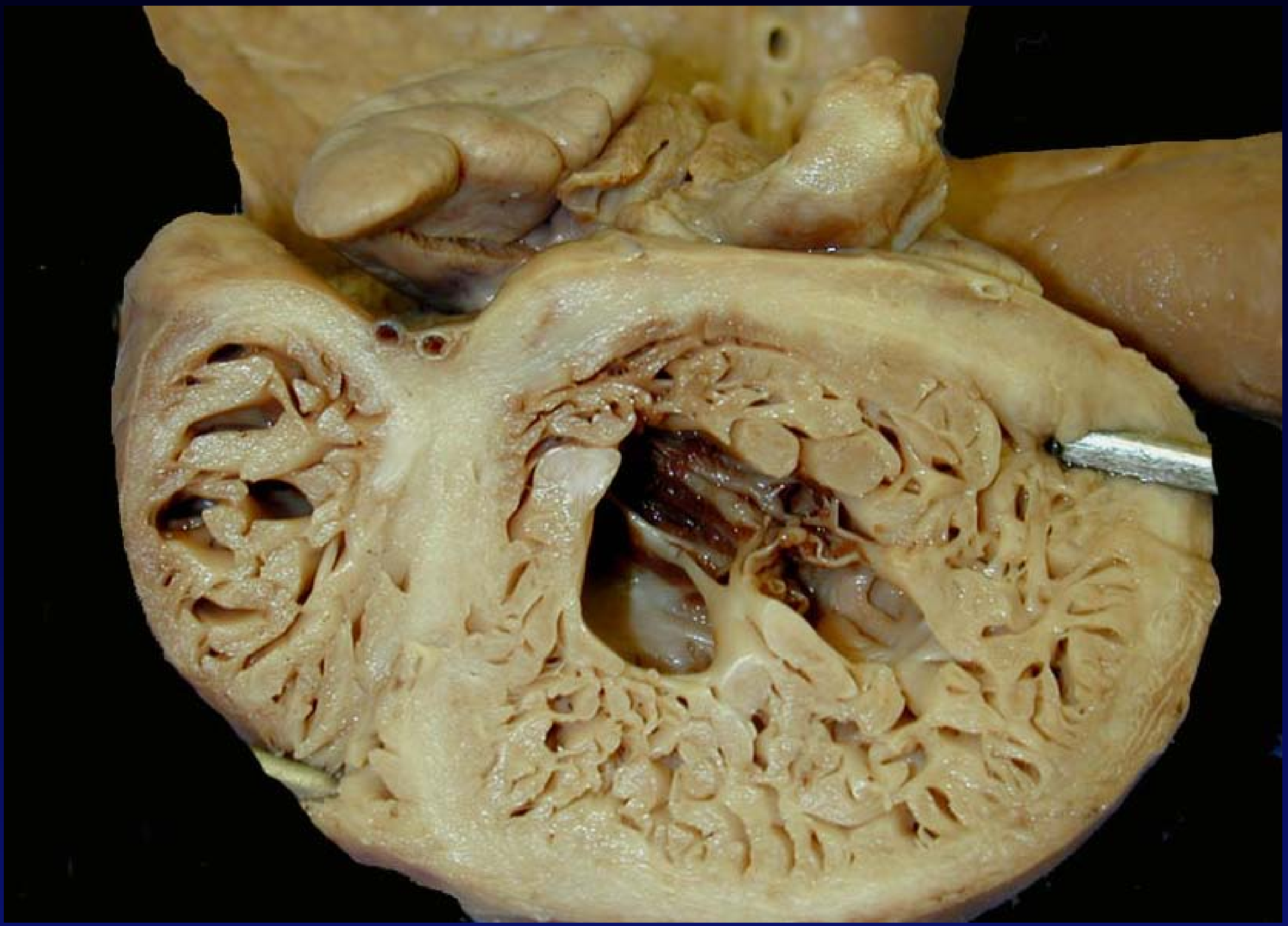
Heart Block Aortic Valve Doppler

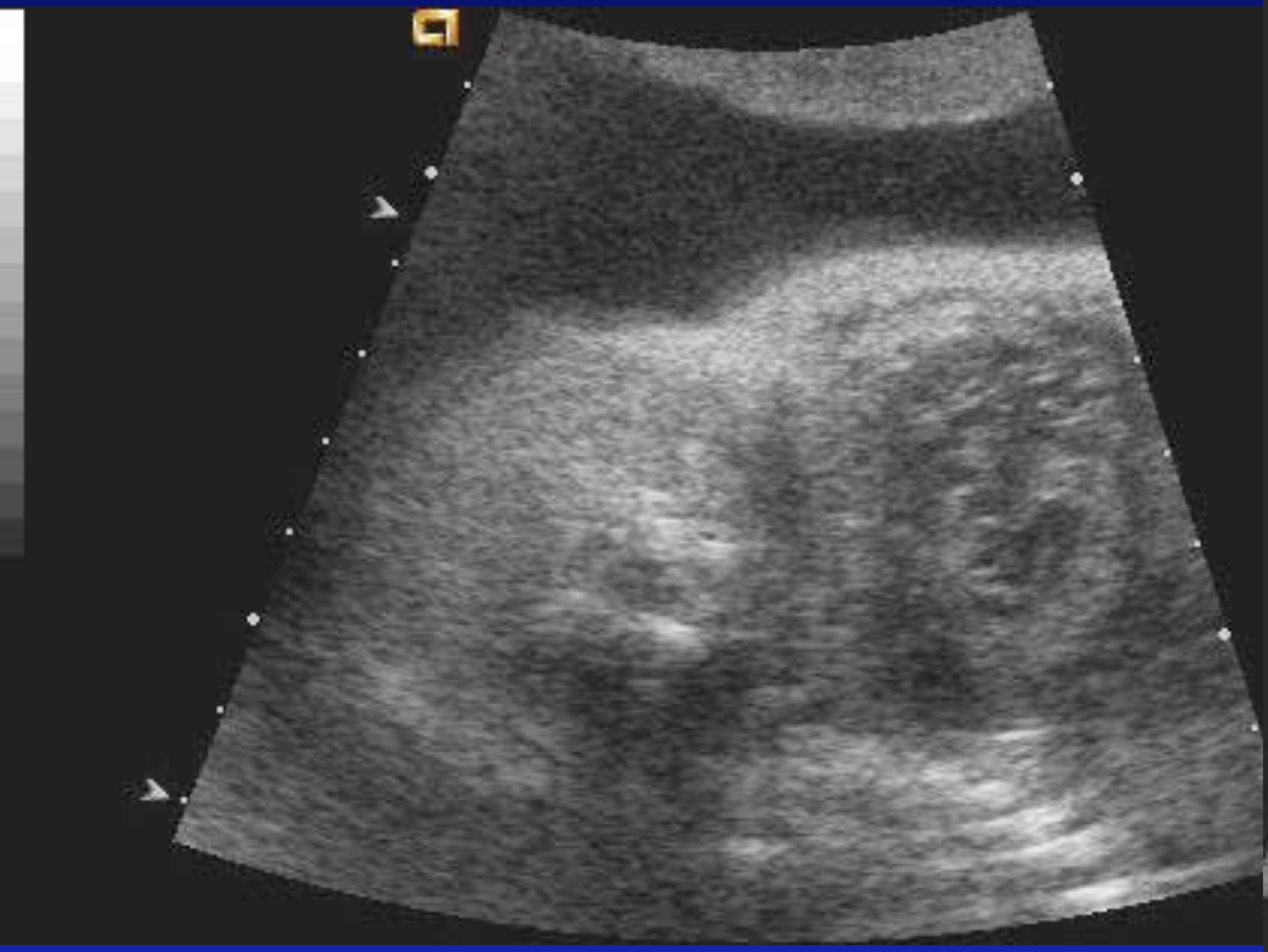


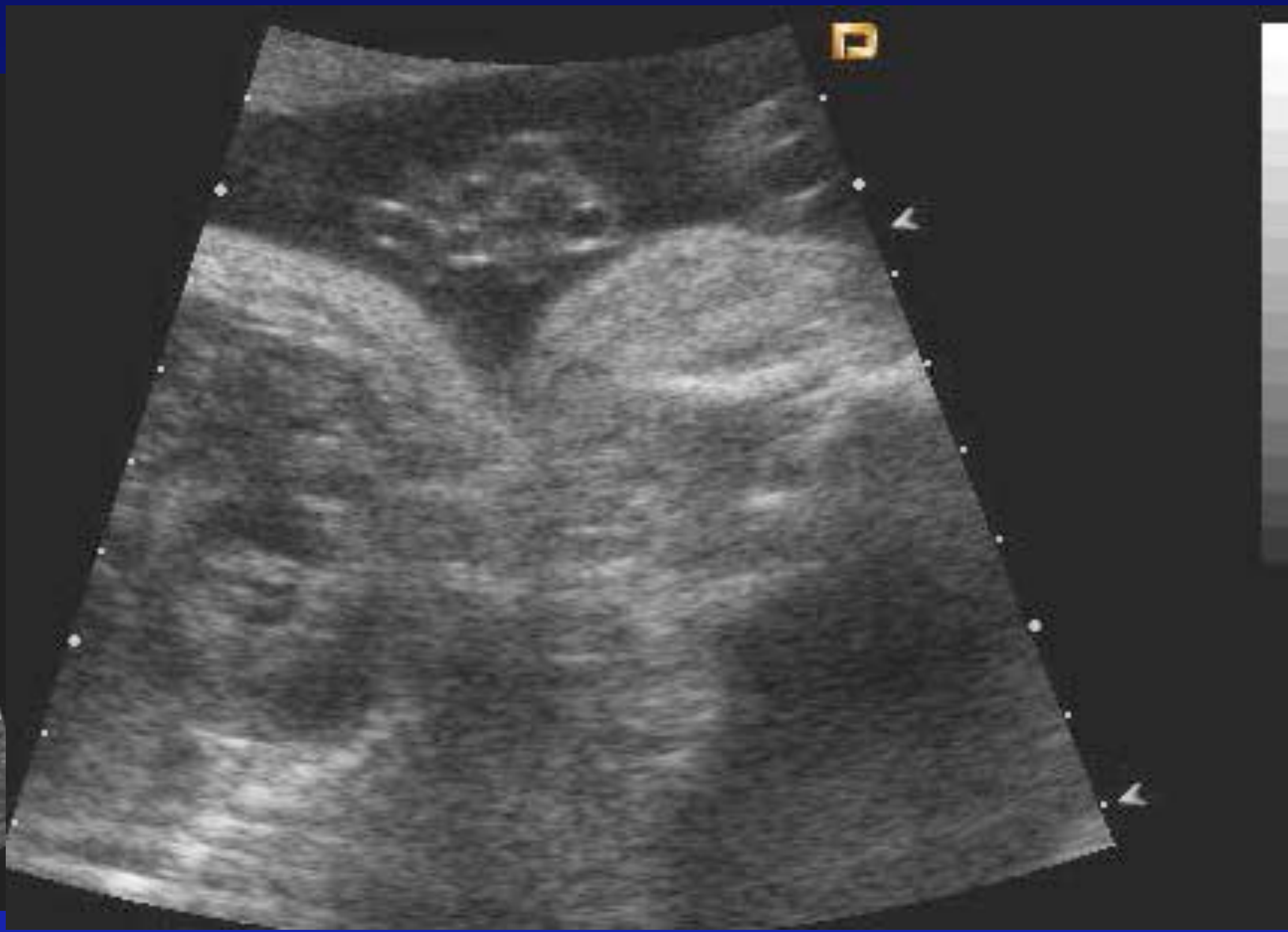
Short Axis View

Spongy Myocardium

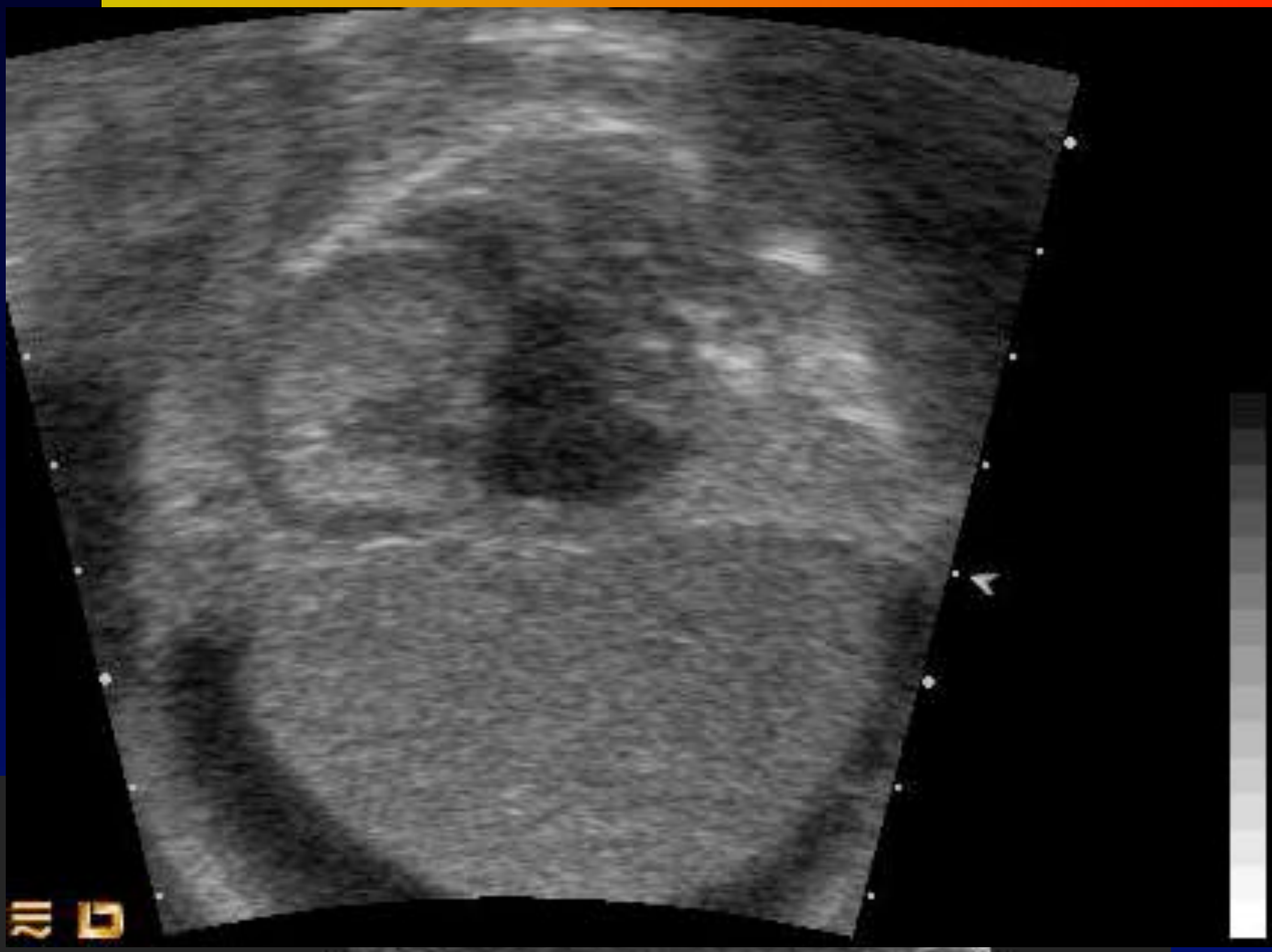
"Single Ventricle"
& Atrioventricular Valve

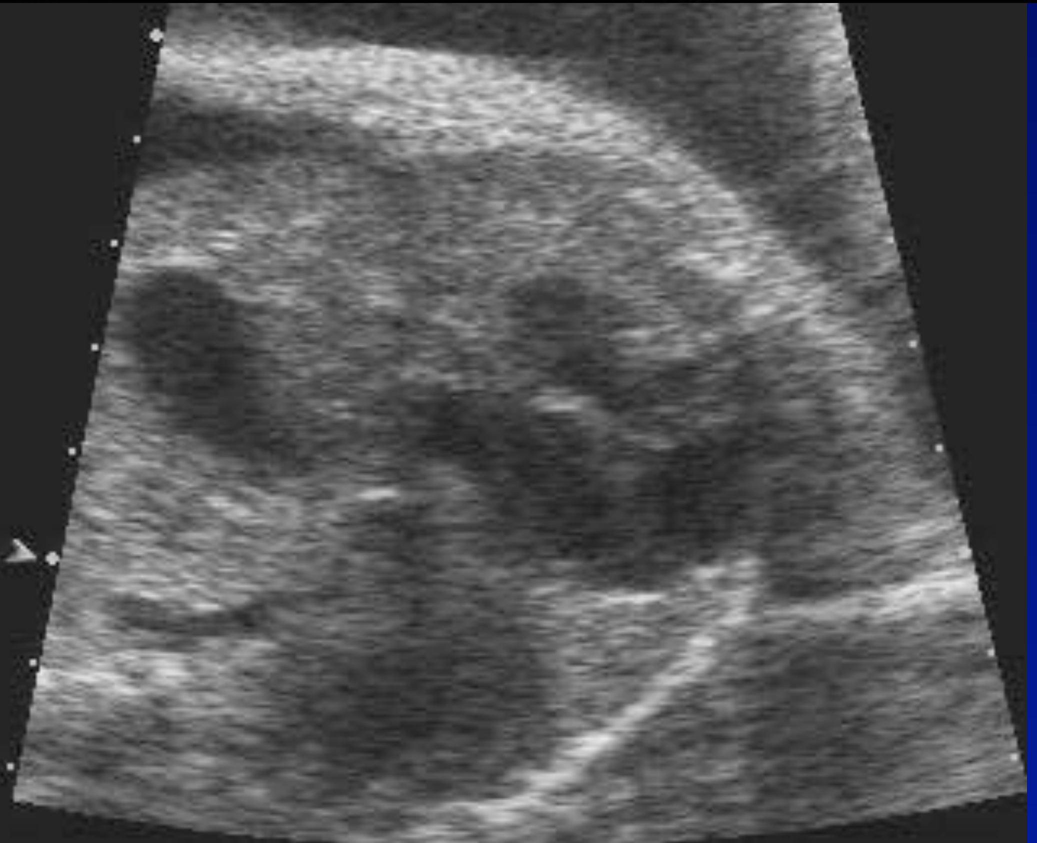


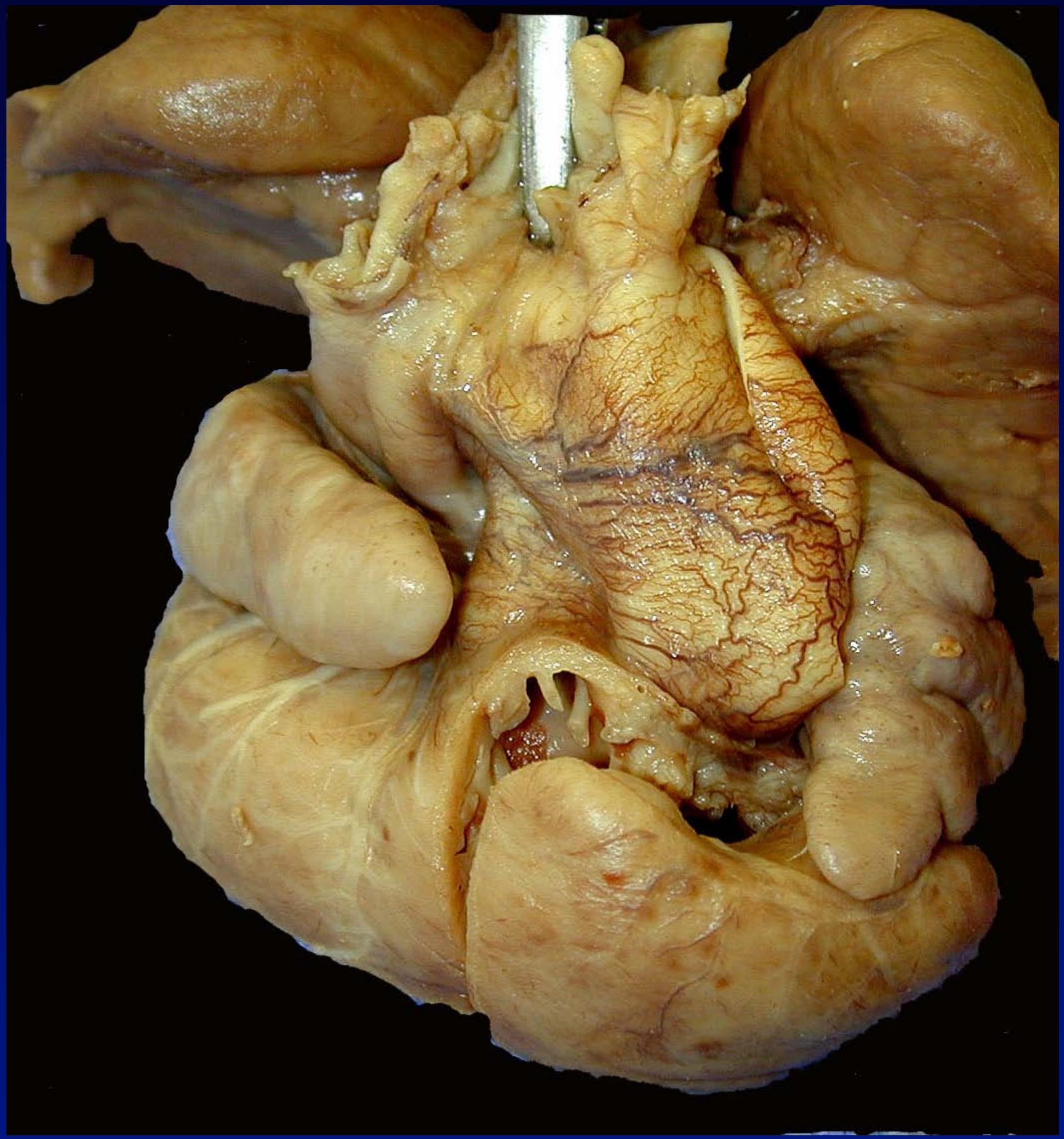




Dominant Right Sided Left Ventricle & Heart Block







Dextrocardia
Cardiac Hypertprophy

NHS.

Common Left-Dominant Atrioventricular Canal Defect

Pericardial effusion

Spongy Myocardium

Spongy Myocardium

Fetal Experience at Stanford/LPCH 2005-2007

Spongy Myocardium	LAI	C Heart Block	Associated Lesions	Outcome	Other
Y	Y	N		D	
Y	Y	Y	TGA PA VSD	D	
Y	Y	Y	DORV AVSD, PA AS	D	
Y	Y	Y	AVSD	TOP	
Y	N	N	ASD	?	
Y	Y	y	AVSD, DORV PS	TOP	
Y	Y	Y	ASD DORV PS Sub AS	D@ 6 Mo	
Y	Y	Y	AVSD DORV PS	NND	
Y	N	Y	PS, TR	_	

Genetics

- Both familial and sporadic cases
- X linked inheritance documented
  - Localized to a mutation in the G4.5 region of the Xq28 locus
  - Similar location to other myopathies with cardiac involvement
    - Barth Syndrome
    - Emery Dreifuss Muscular Dystrophy

Courtesy of Mark Lewin

Epidemiology

- True prevalence unclear
  - Prevalence 0.05% in the general population
  - incidence of left ventricular noncompaction diagnosed at Stanford is estimated to be approximately 0.3% *.
- Male > Female
- Can present at any age
  - "Waxing and waning course"
  - *Over 7 Years At Stanford there were 17,229 patients who had 46,547 echocardiograms at our institution of which, 44 patients had a diagnosis of left ventricular noncompaction based on the echocardiographic criteria and were included in the study.
  - Eight patients (50%) in the group that died and only 5 patients (18%) in group that survived had significant congenital heart disease ($p < 0.05$,

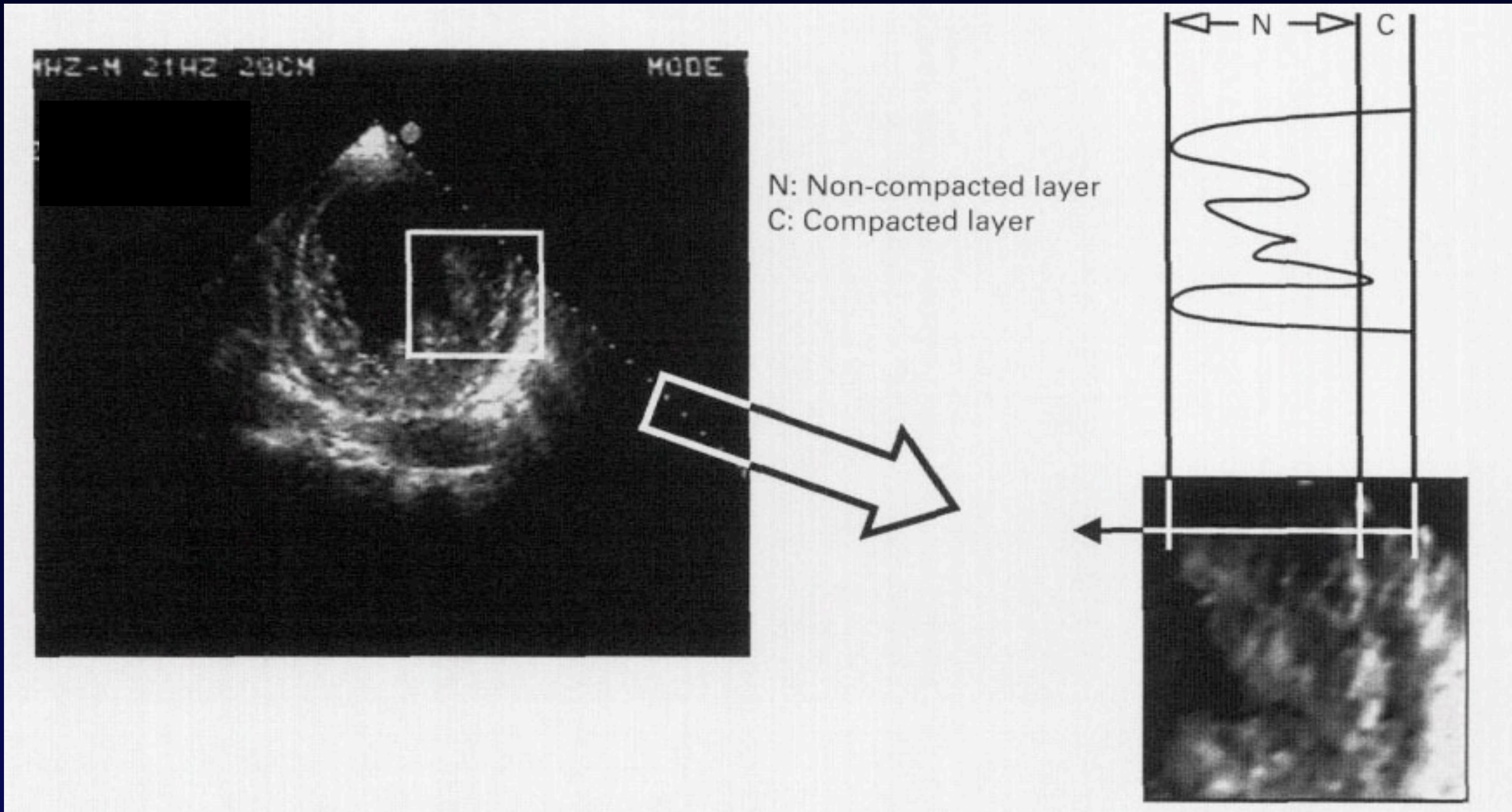
Cardiac Segmental Analysis in Left Ventricular Noncompaction: Experience in a Pediatric Population Punn. Silverman, J Am Soc Echocardiogr *2010; 23(1):46–53.*)

Diagnostic Criteria

Strict criteria were employed to ensure the appropriate diagnosis in that all patients had the following left ventricular findings as described by Oechslin et al and Jenni et al:

1. Multiple trabeculations and recesses
2. Distinct compacted and non-compacted layers
3. Low Nyquist limit color mapping delineating continuity of intertrabecular recesses with ventricular cavity
4. A non-compaction: compaction ratio of at least 2:1 during systole

Cardiac Segmental Analysis in Left Ventricular Noncompaction: Experience in a Pediatric Population
Punn. Silverman, *J Am Soc Echocardiogr. 2010; 23(1):46–53*.)



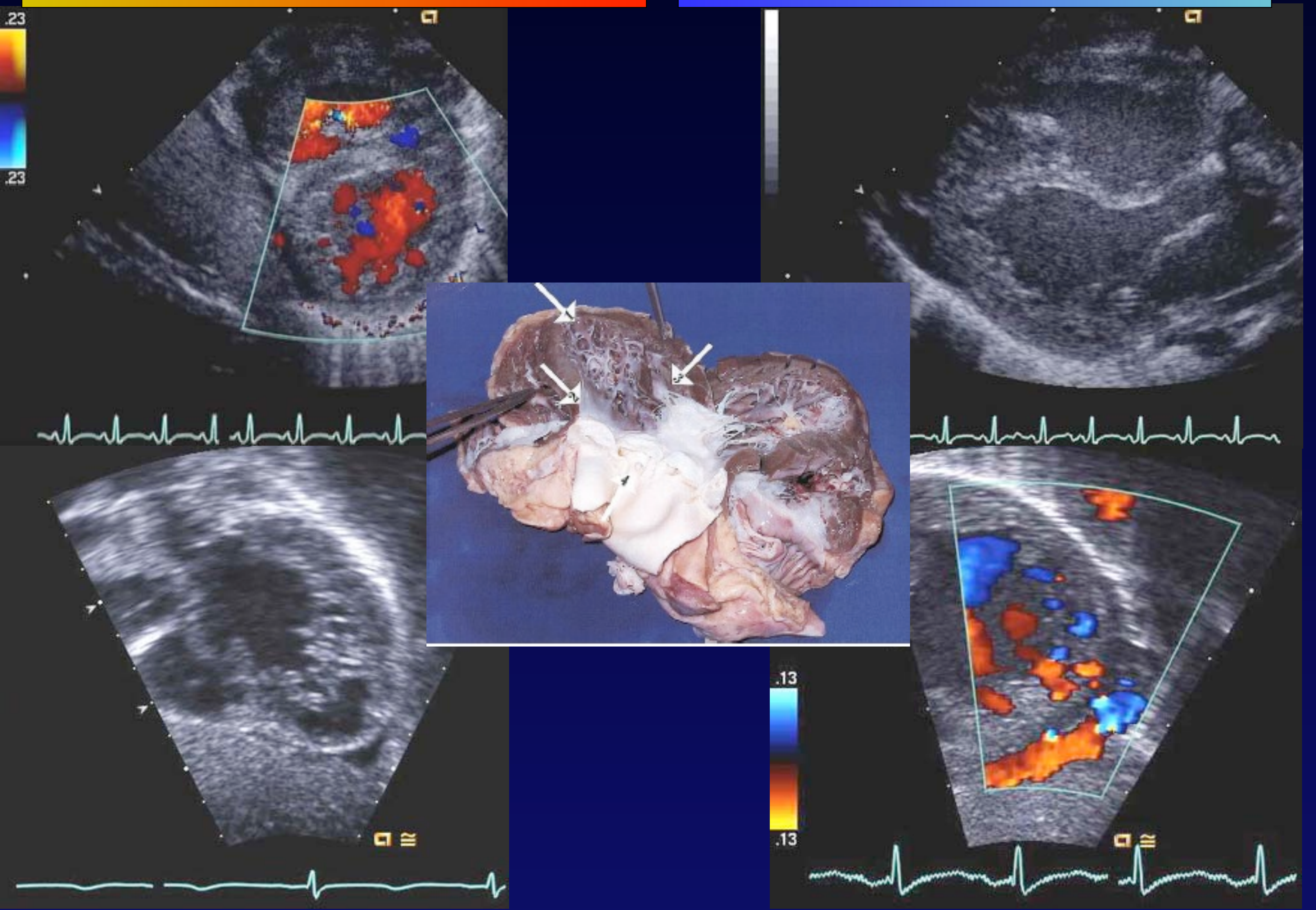
<u>Non-compacted to compacted ratio > 2</u> at end <u>systole</u>

in parasternal short axis

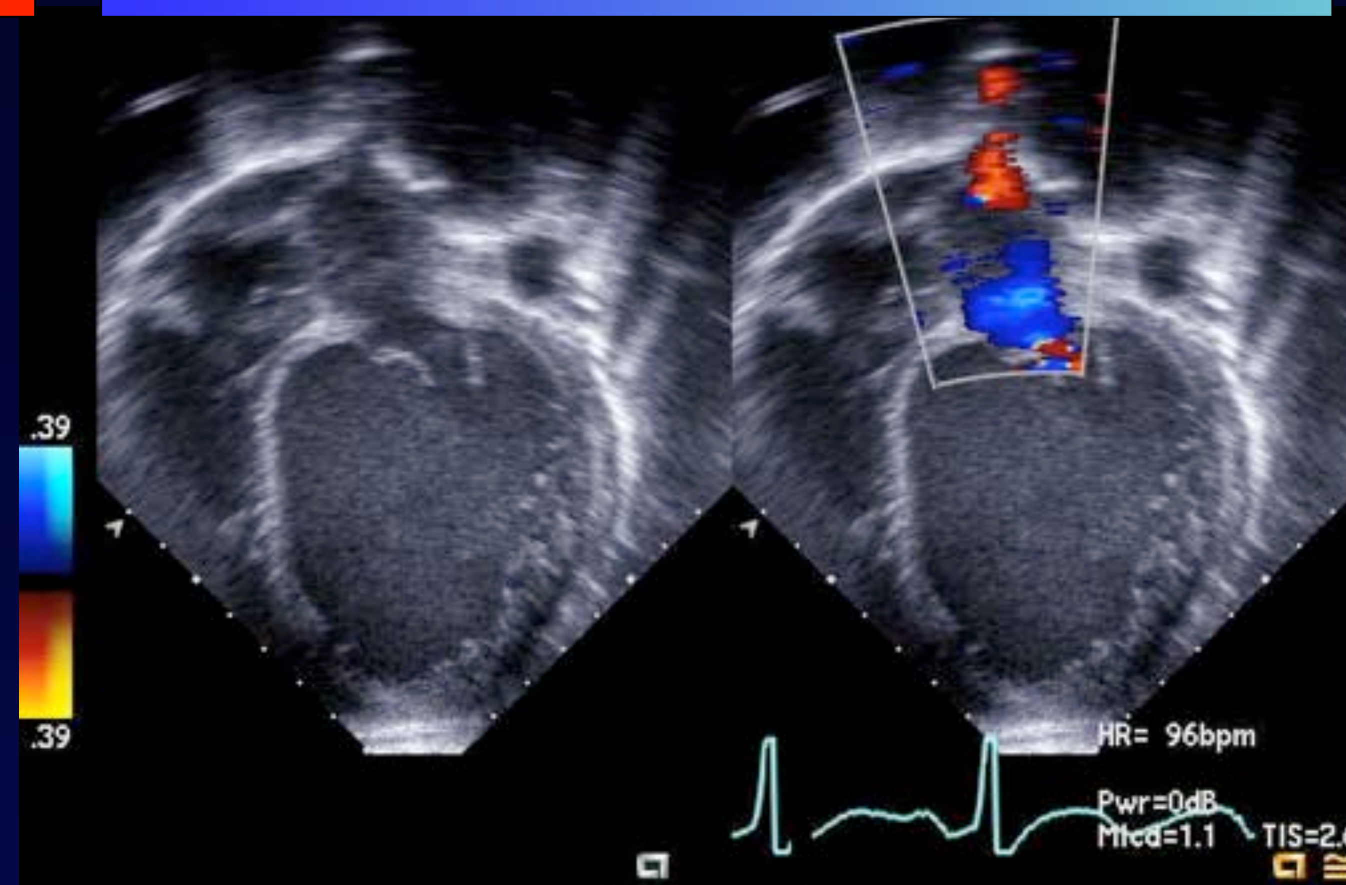
Jenni, *Heart* 2001

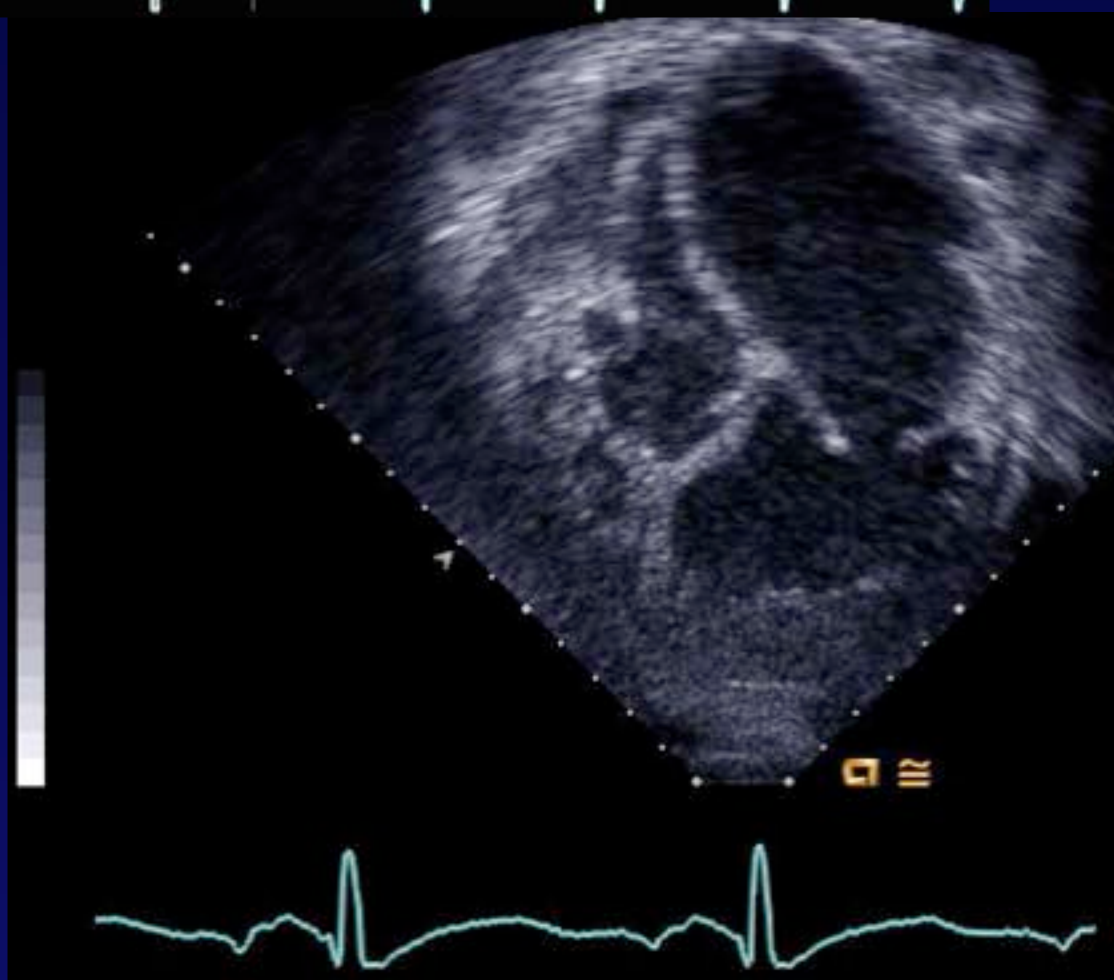
Cardiac Segmental Analysis in Left Ventricular Noncompaction: Experience in a Pediatric Population Punn. Silverman, *J Am Soc Echocardiogr. 2010; 23(1):46–53*.)

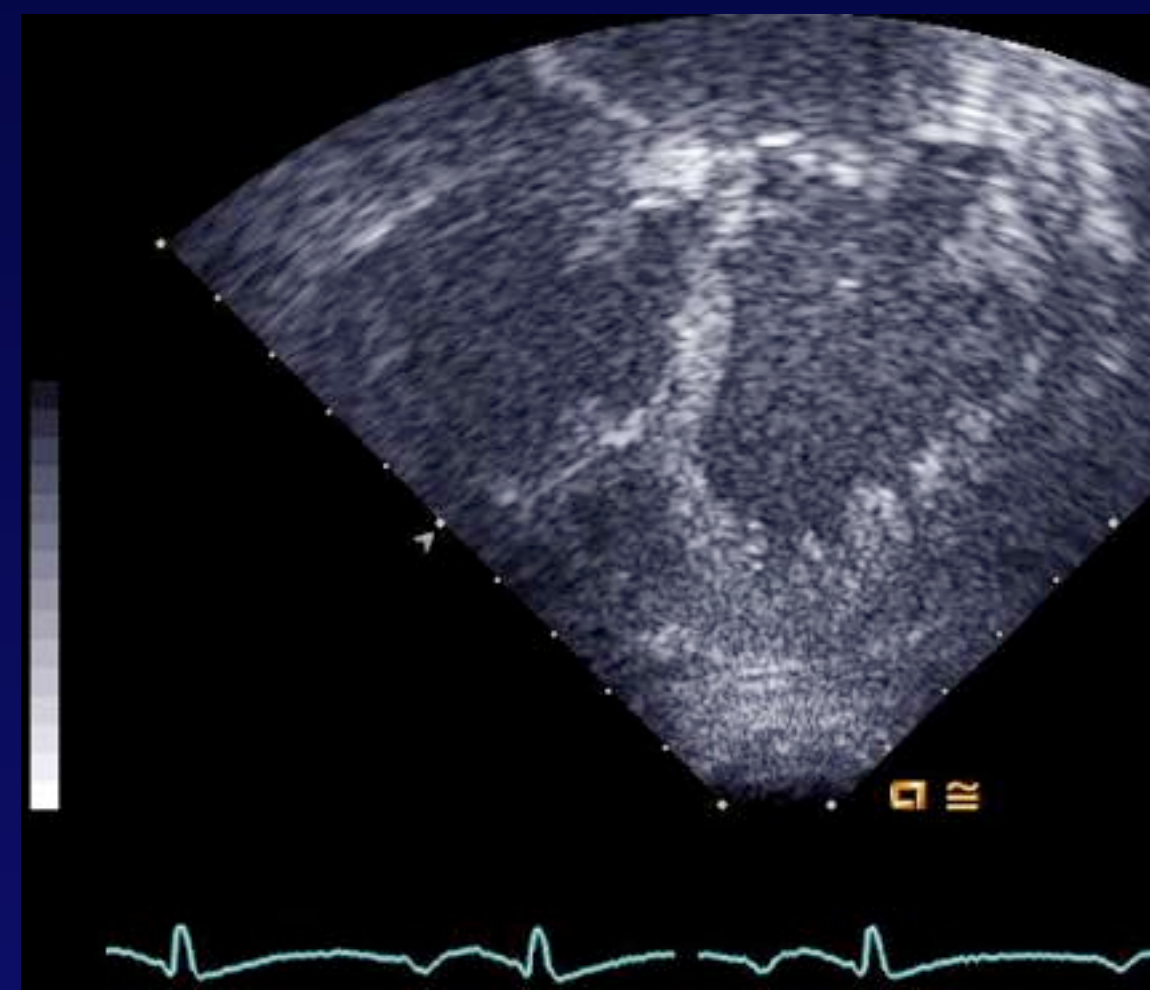
LVNC: Other Views



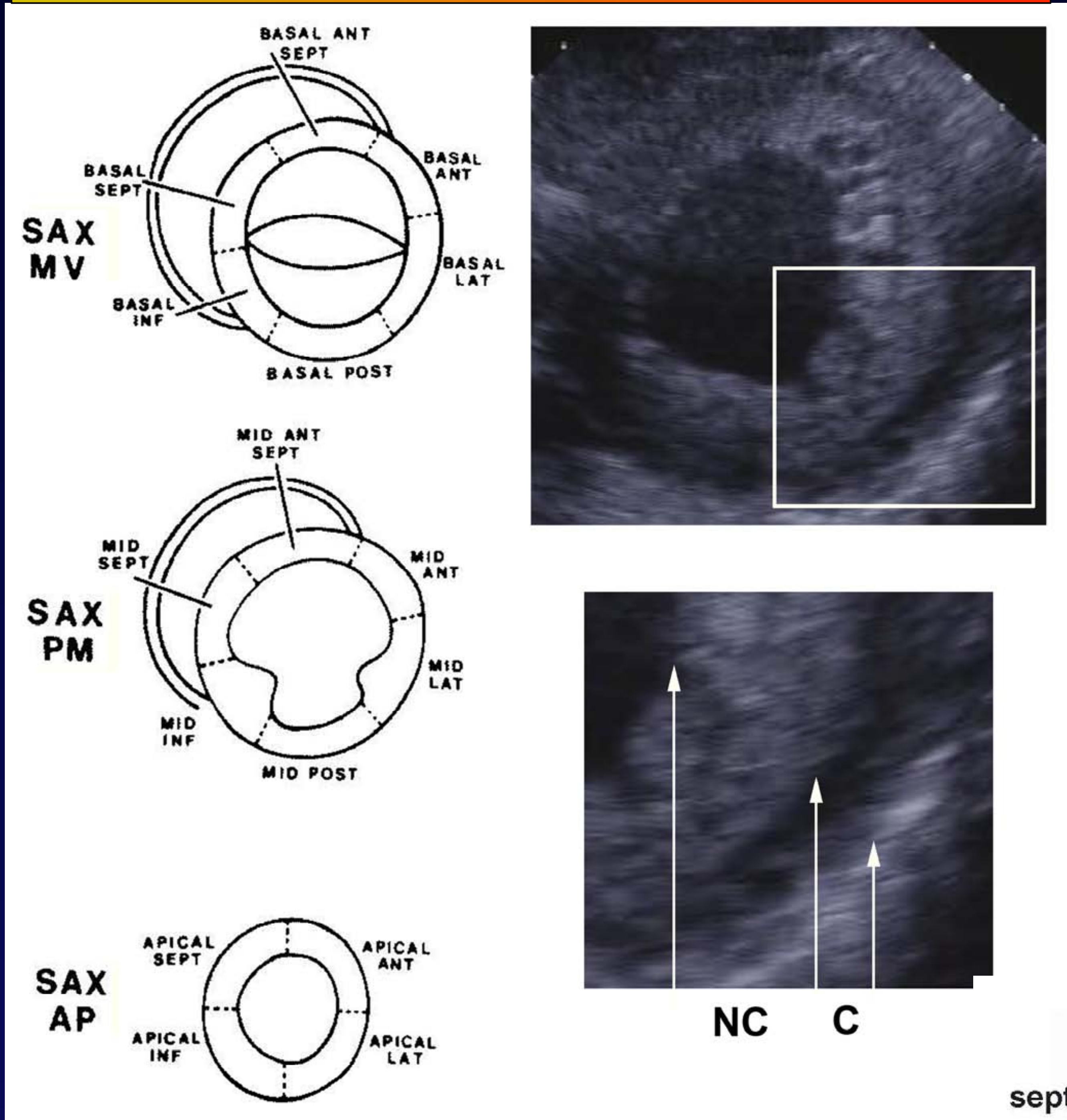
LVNC: 4 Chamber View



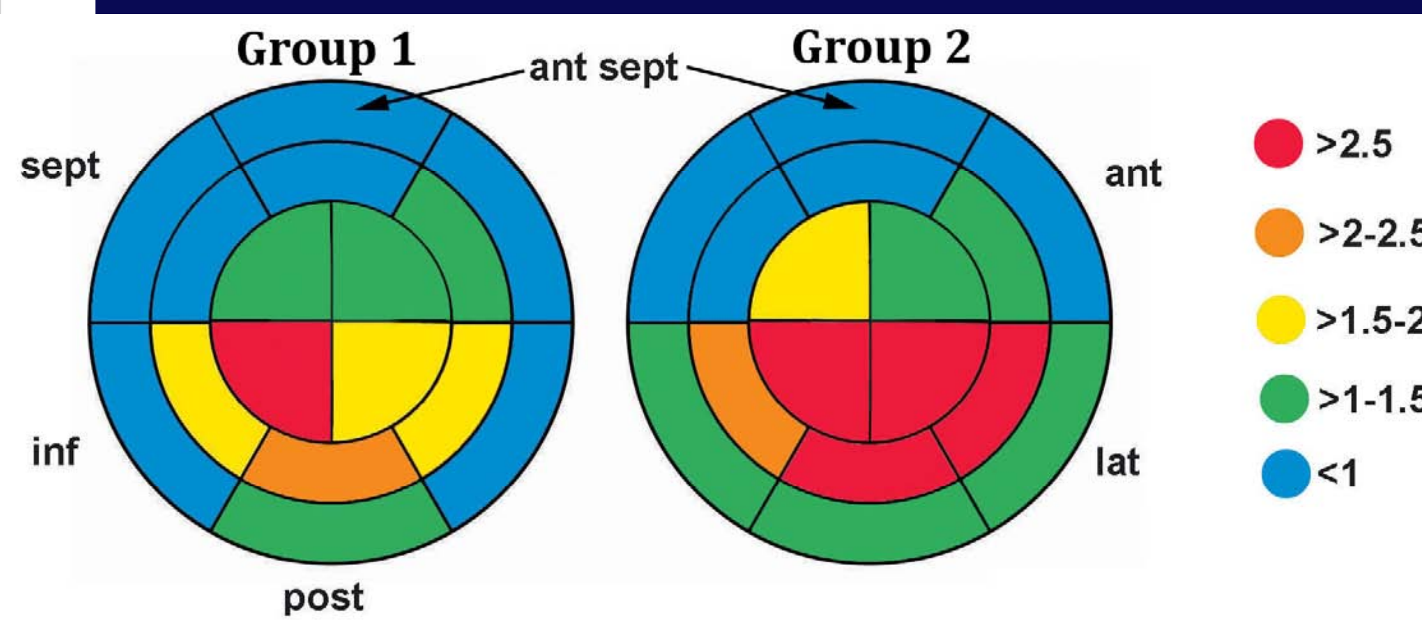


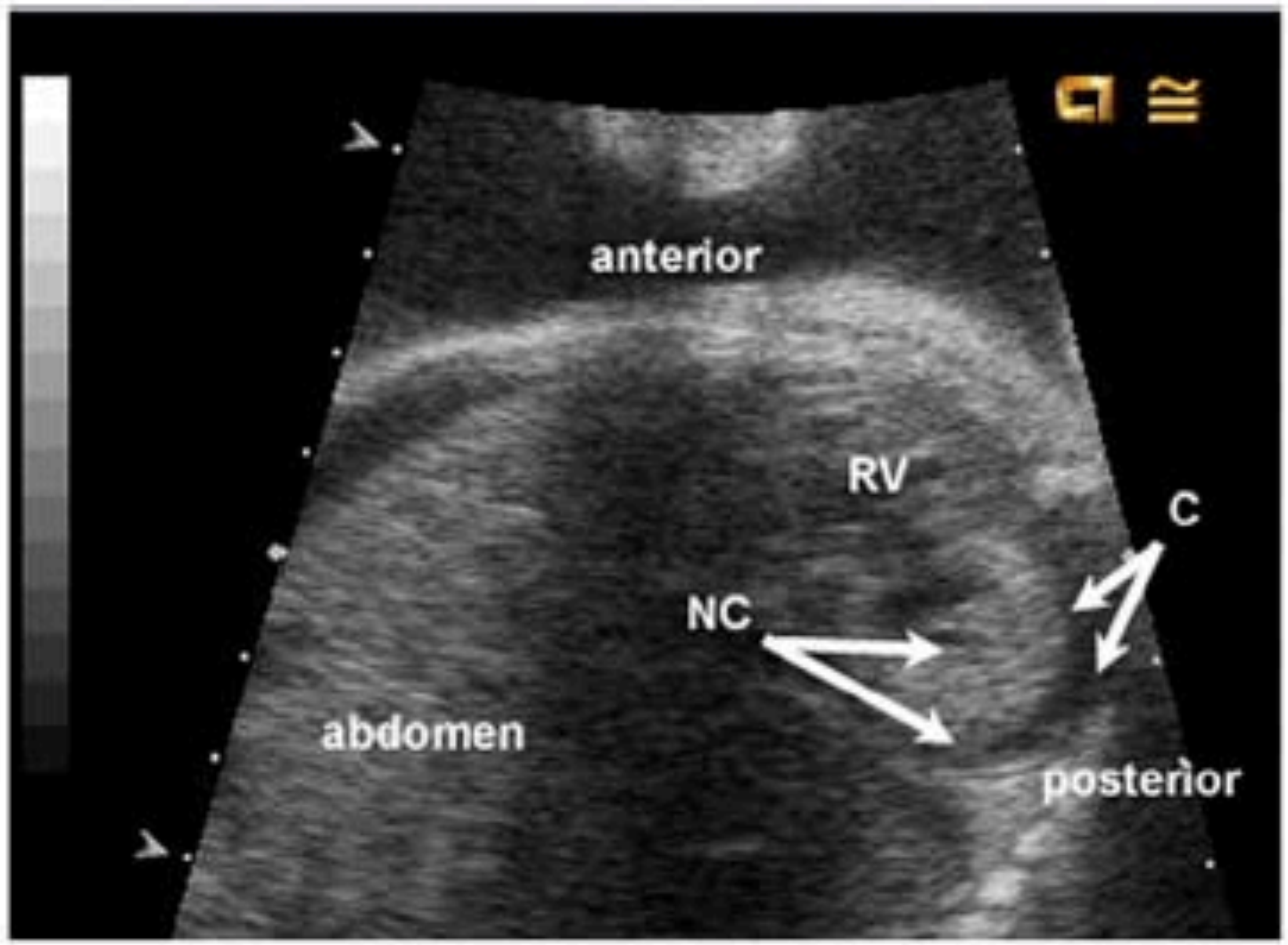


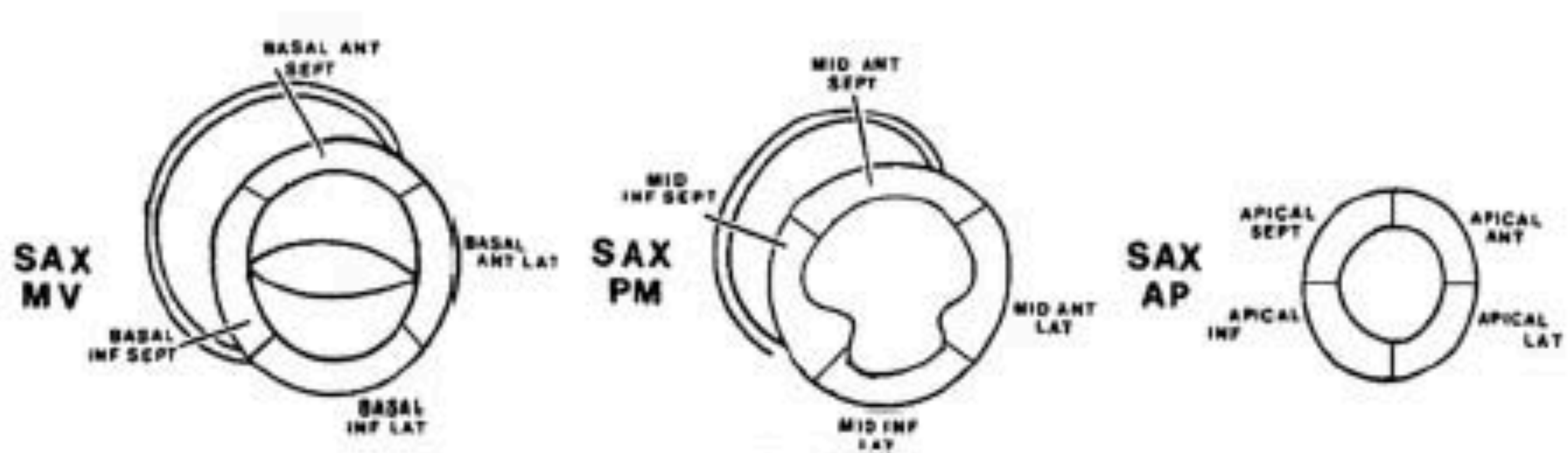
Cardiac Segmental Analysis in LV N-C a Pediatric Population



Cardiac Segmental Analysis in Left Ventricular Noncompaction: Experience in a Pediatric Population Punn. Silverman, *J Am Soc Echocardiogr. 2010; 23(1):46–53.*)

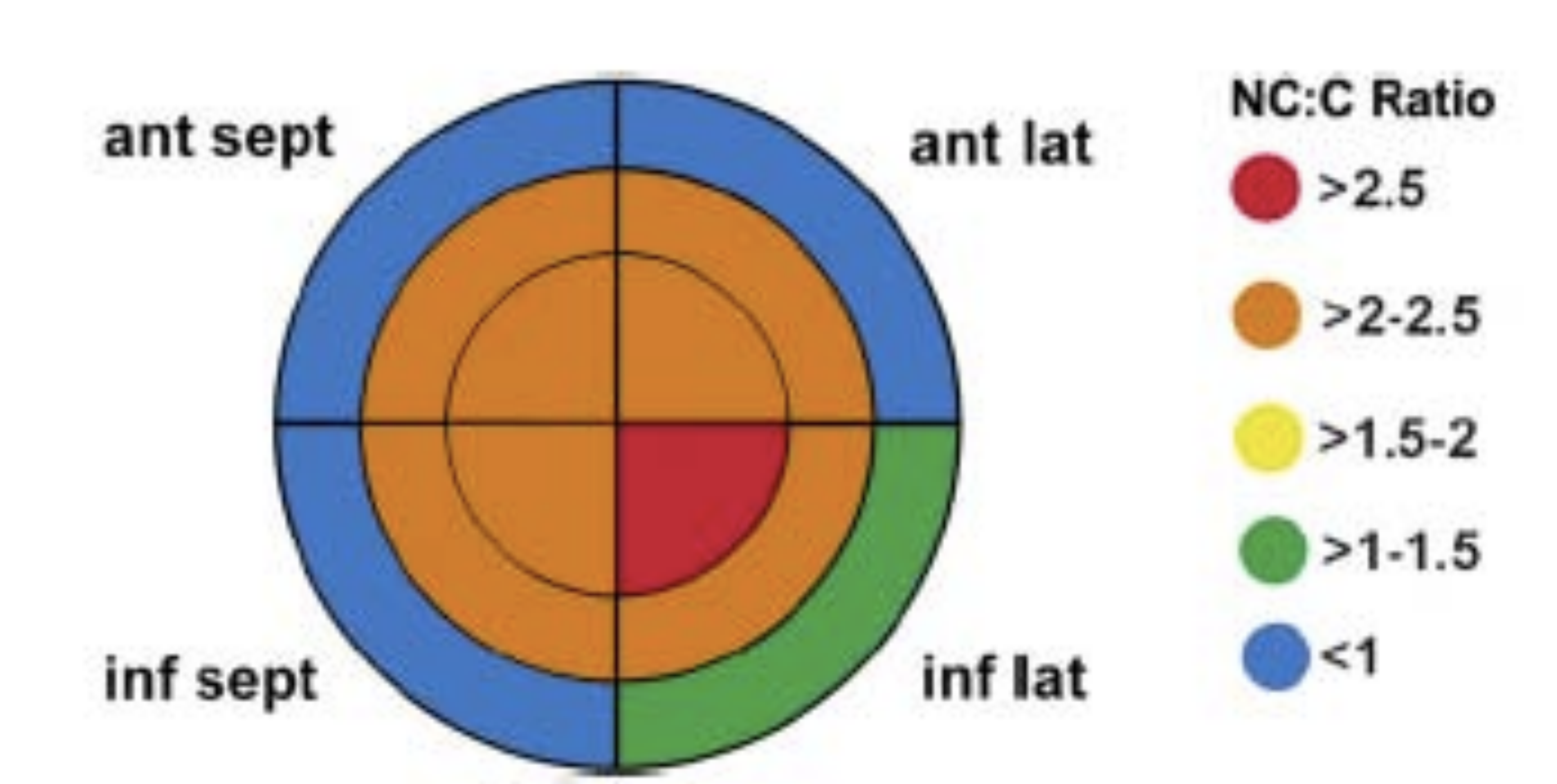


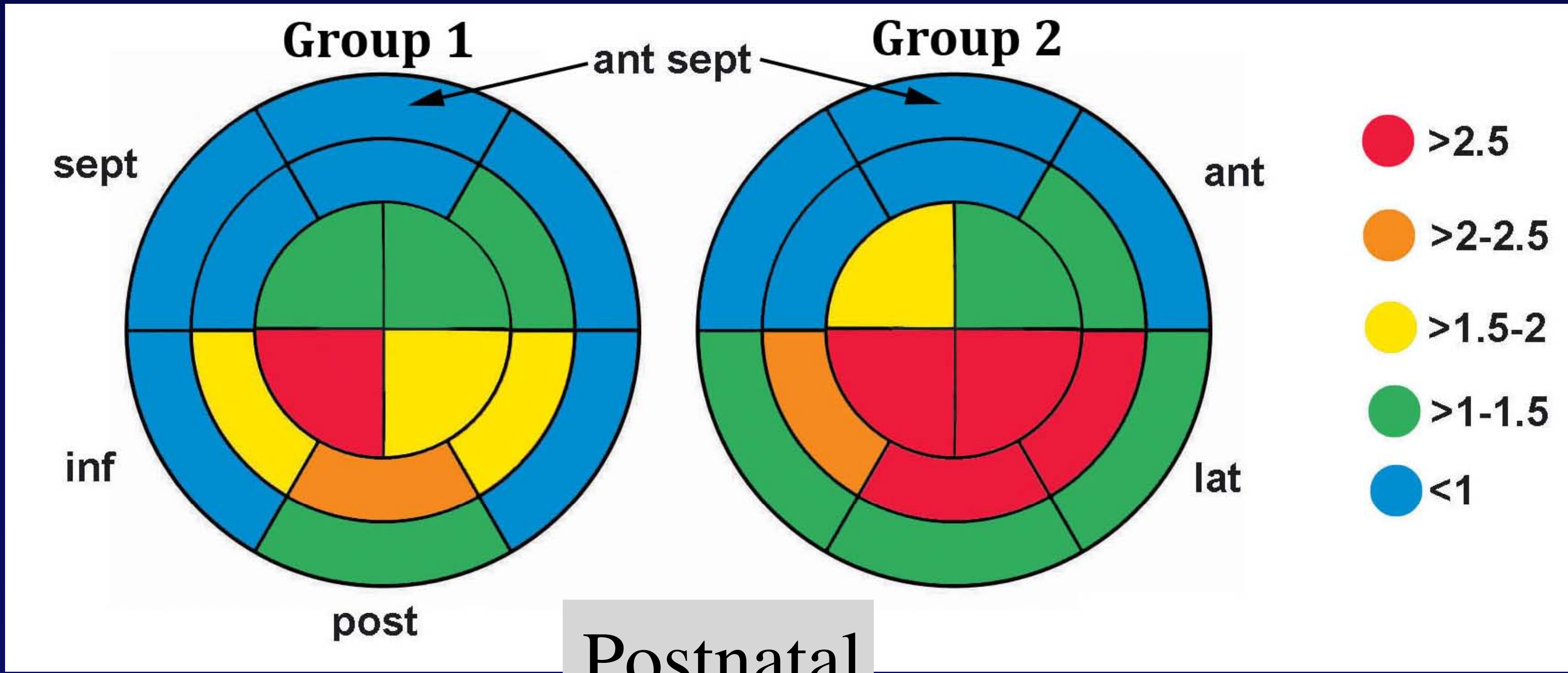

anterior
RV
C
NC
abdomen
posterior


BASAL ANT SEPT
SAX MV
BASAL ANT LAT
BASAL INF SEPT
BASAL INF LAT
MID ANT SEPT
MID INF SEPT
SAX PM
MID ANT LAT
MID INF
APICAL SEPT
APICAL ANT
SAX AP
APICAL INF
APICAL LAT

Segments not compacted

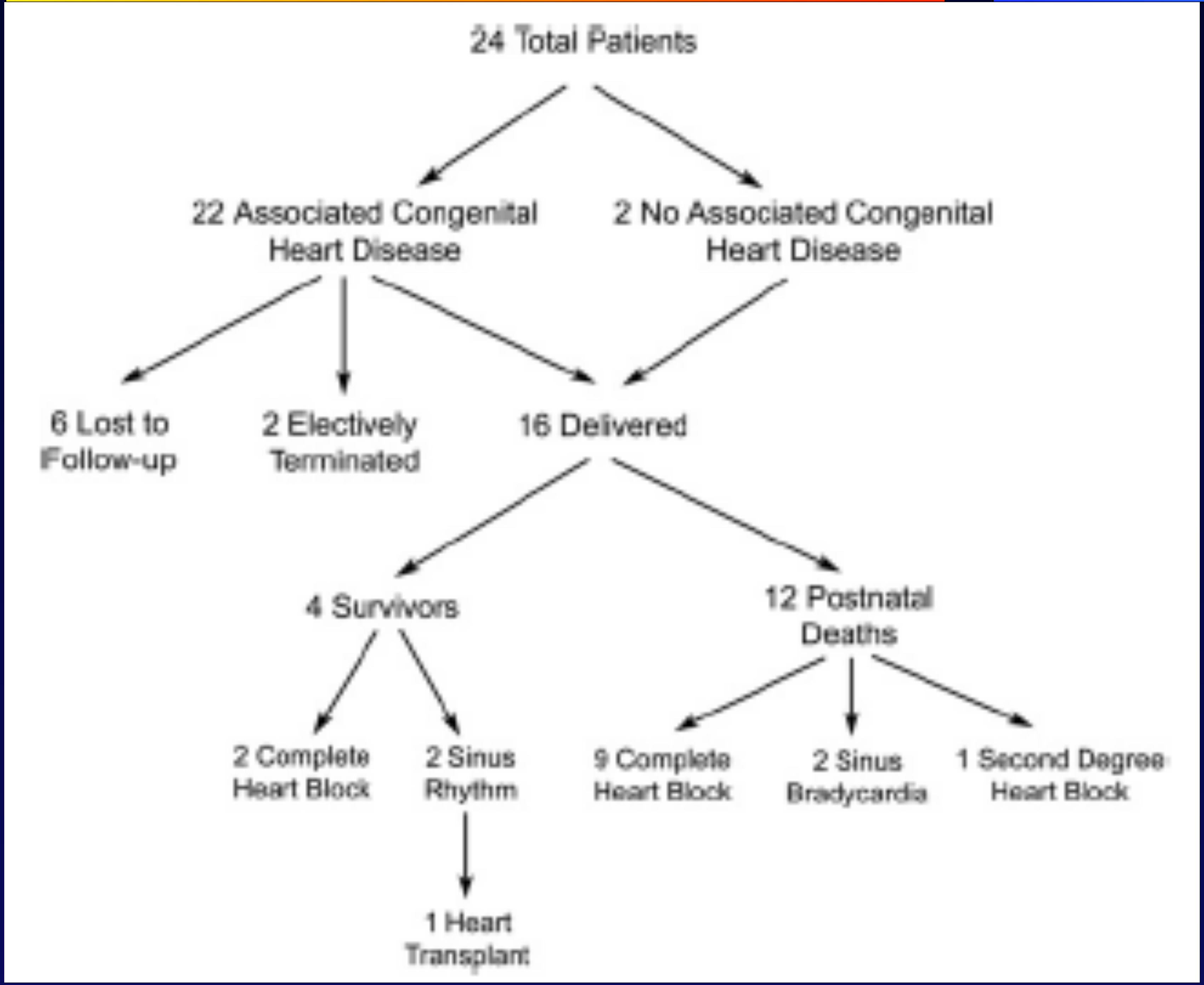
Prenatal





Postnatal

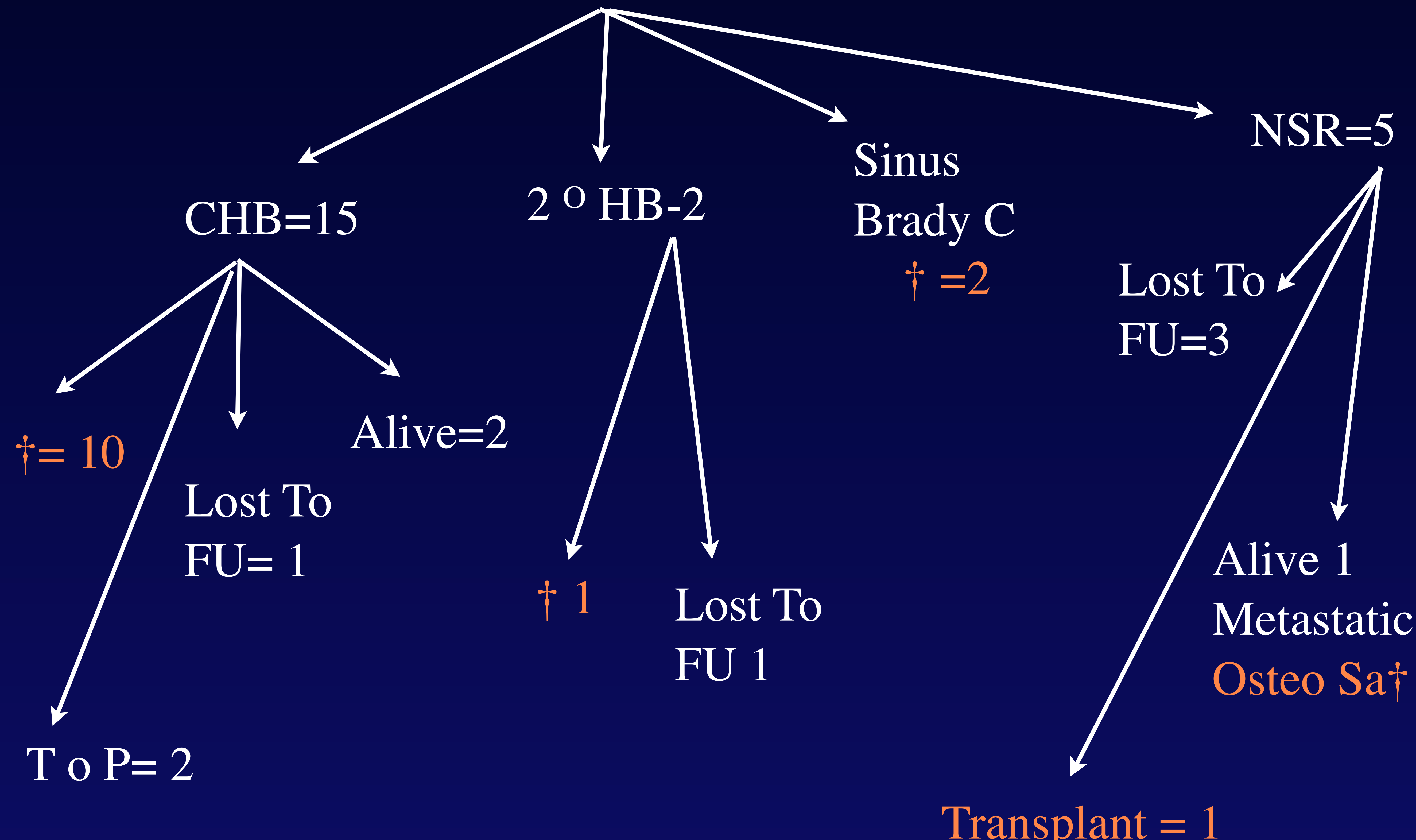
Outcomes



- AVSD 13
- DORV 14
- VSD 11
- TGA 6
- Pulm Atresia 3
- Mitral Atresia 1
- PS 4
- 21 genetics : 0+ve
- Arrhythmias

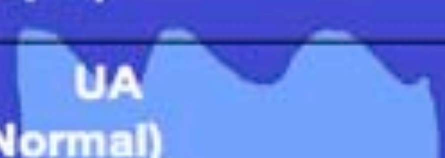
- Mean age @ diagnosis 26 W ± 7

Arrhythmias =19/24

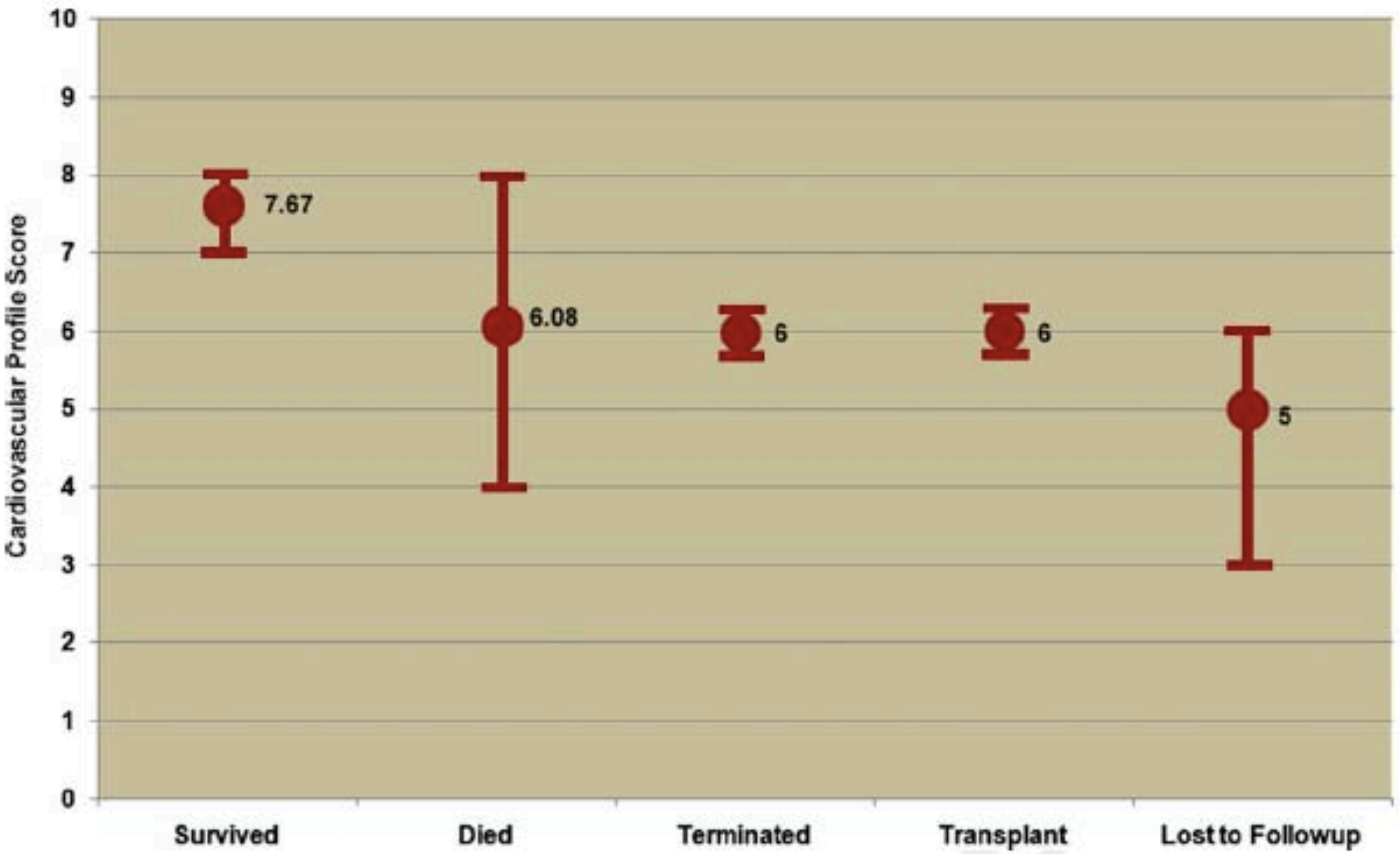


CV Profile

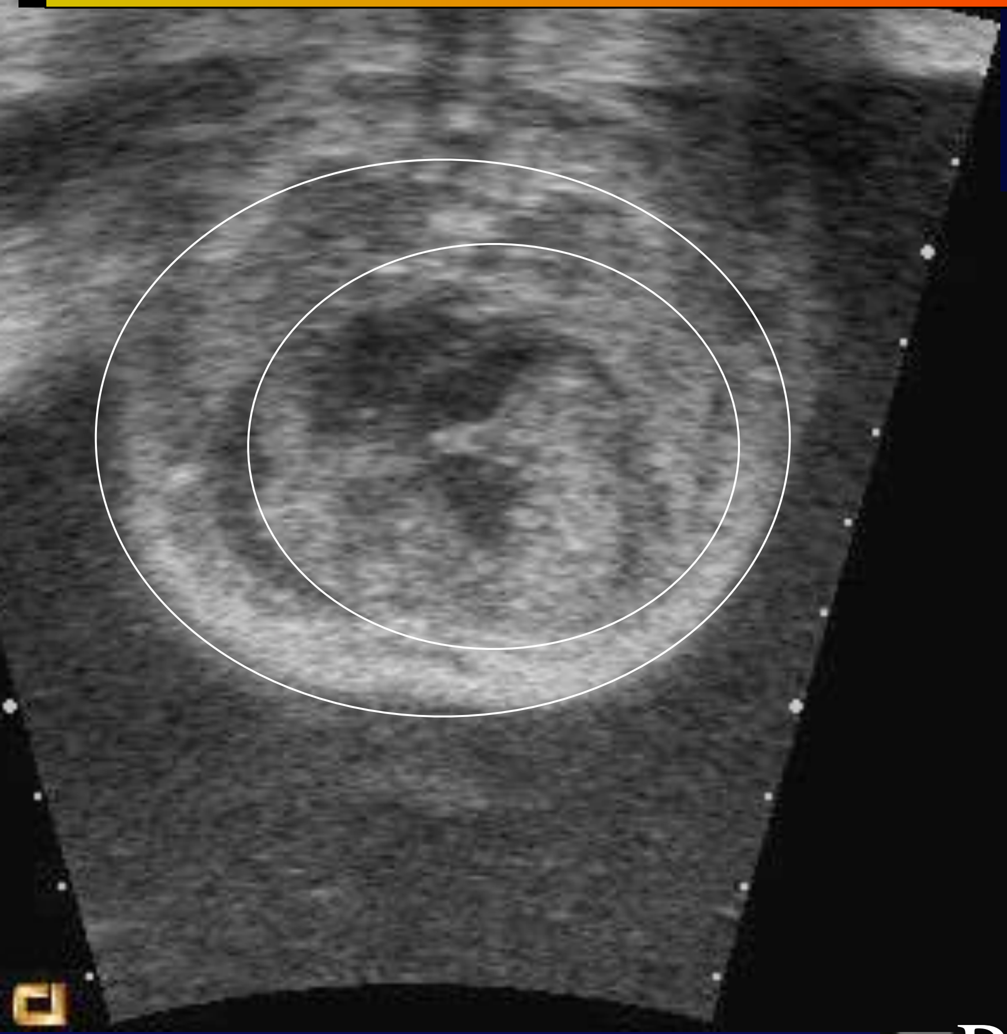
10-point score

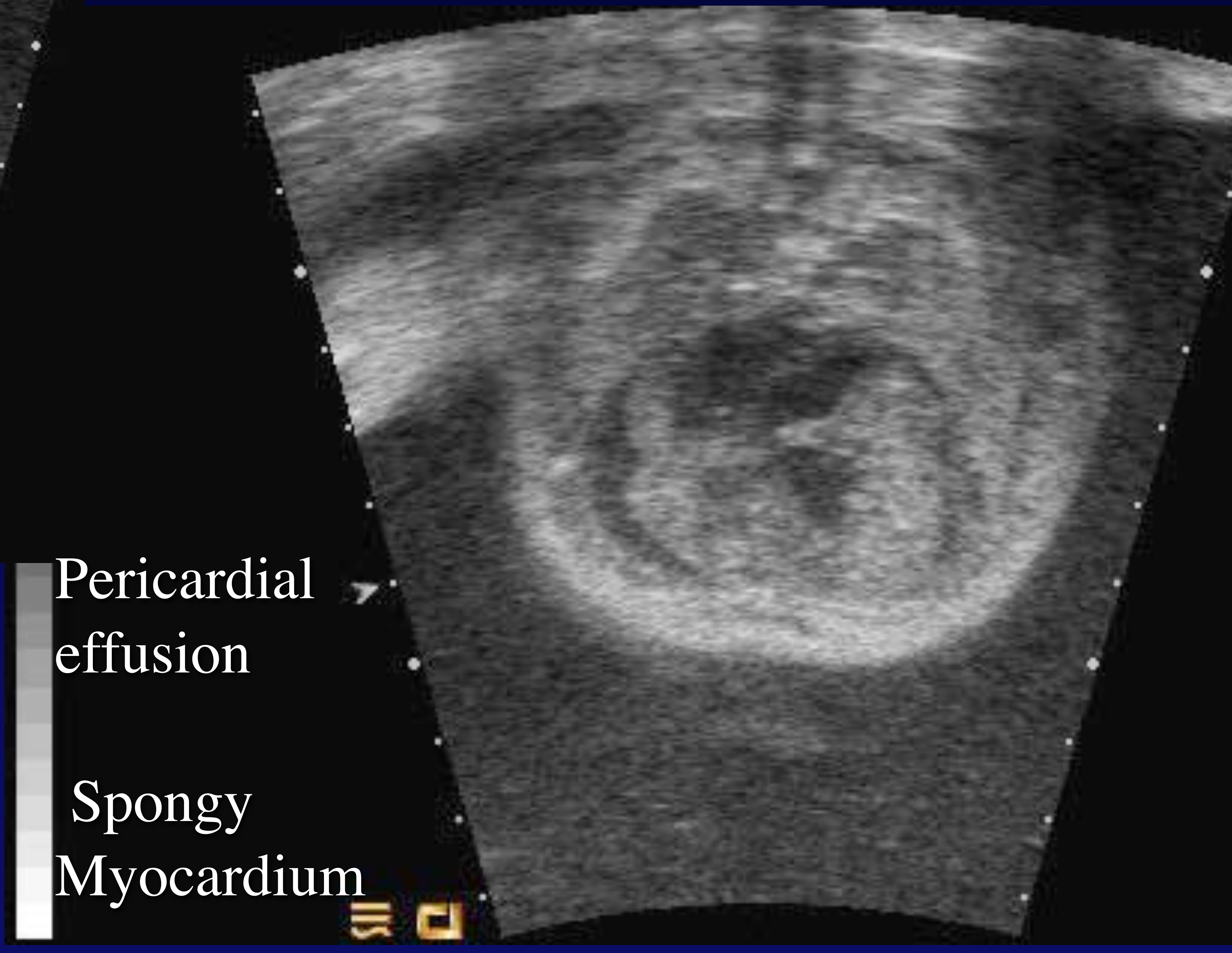
	NORMAL	-1 POINT	-2 POINTS
Hydrops	None (2 pts)	Ascites <u>or</u> Pleural effusion <u>or</u> Pericardial effusion	Skin edema
Venous Doppler (Umbilical Vein) (Ductus Venosus)	DV (2 pts) UV 	DV 	UV pulsations 
Heart Size (Heart/Chest Area)	$\leq$ 0.35 (2 pts)	0.35 - 0.50	>0.50 or <0.25
Cardiac Function	Normal TV & MV RV/LV S.F. > 0.28 Biphasic diastolic filling (2 pts)	Holosystolic TR <u>or</u> RV/LV S.F. < 0.28	Holosystolic MR <u>or</u> TR dP/dt < 400 <u>or</u> Monophasic filling
Arterial Doppler (Umbilical artery)	UA (Normal) (2 pts) 	UA (AEDV) 	UA (REDV) 

Cardiovascular Profile Score

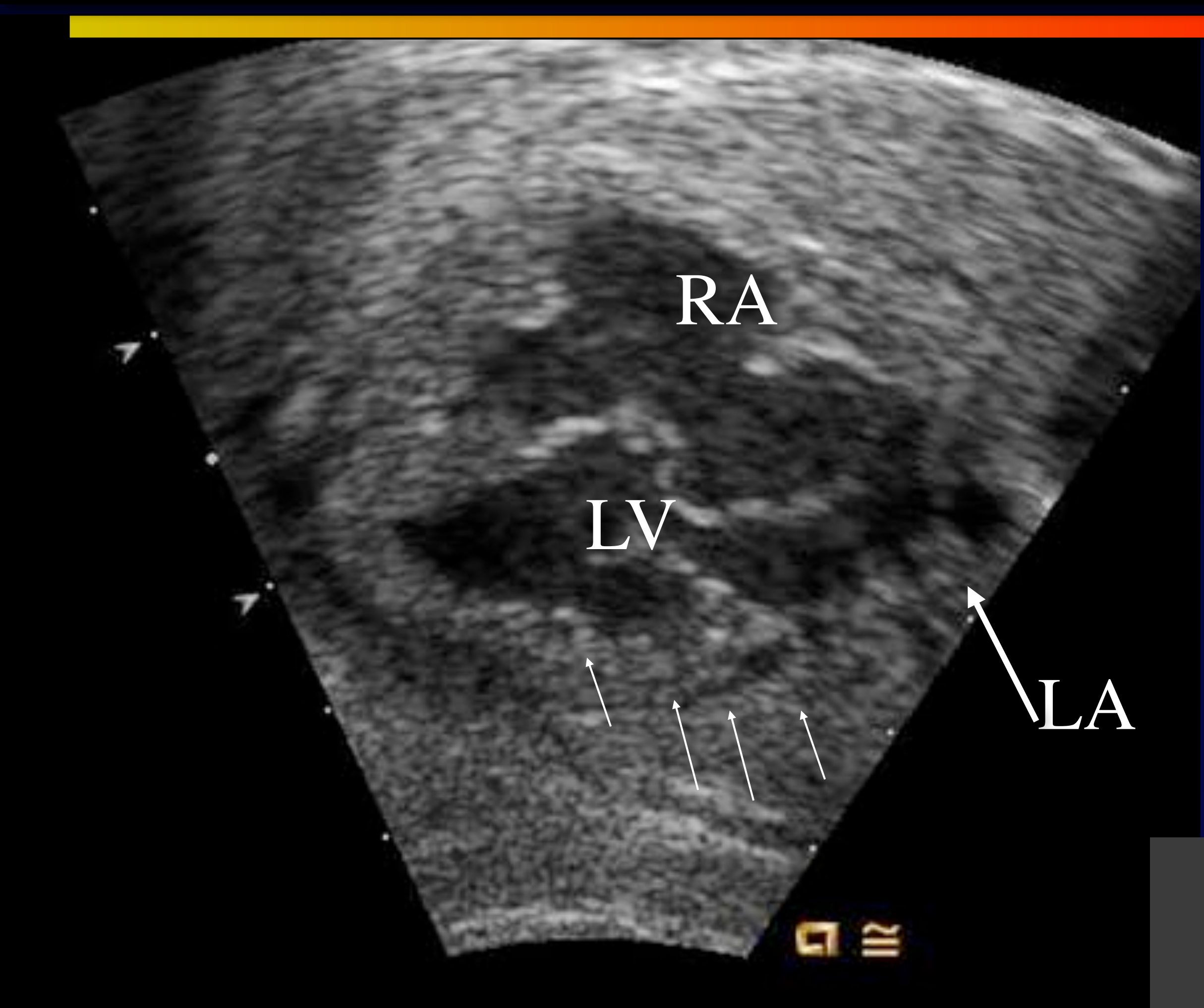


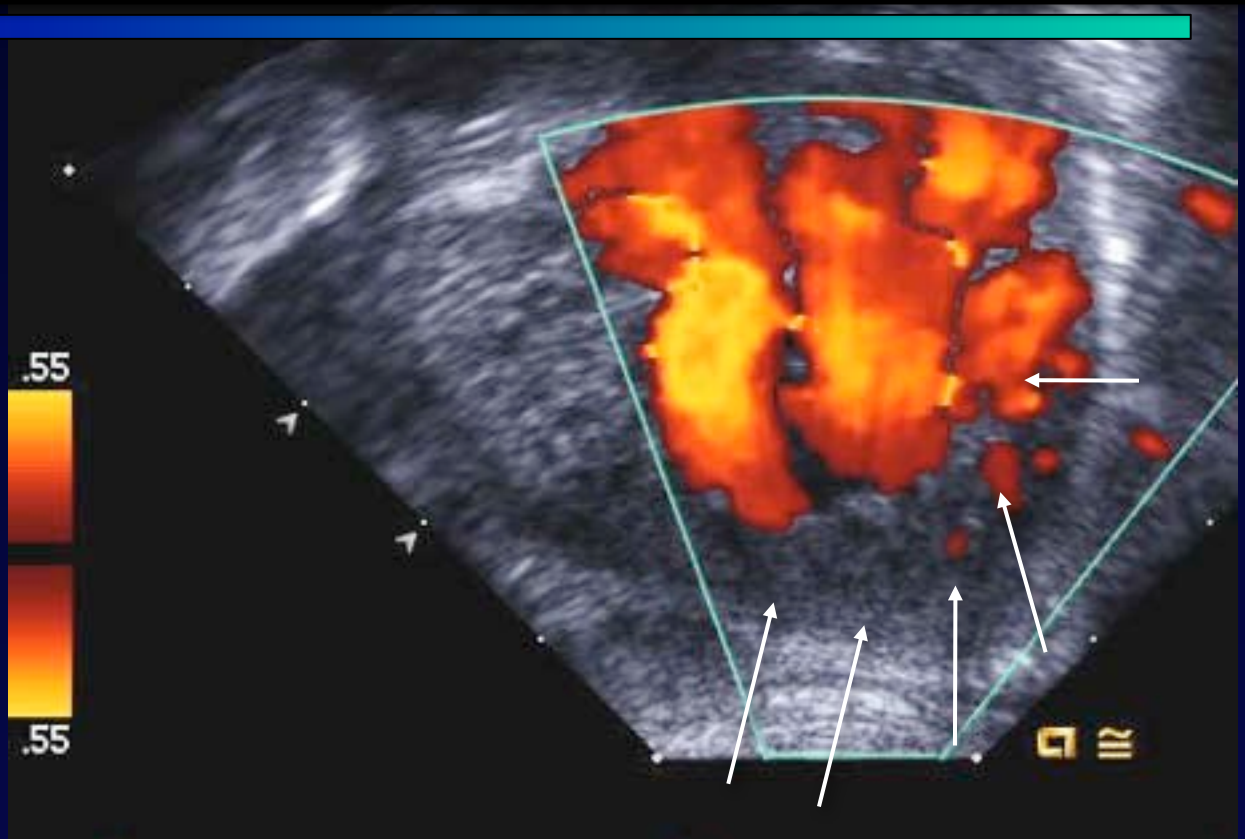
Common Left-Dominant Atrioventricular Canal Defect

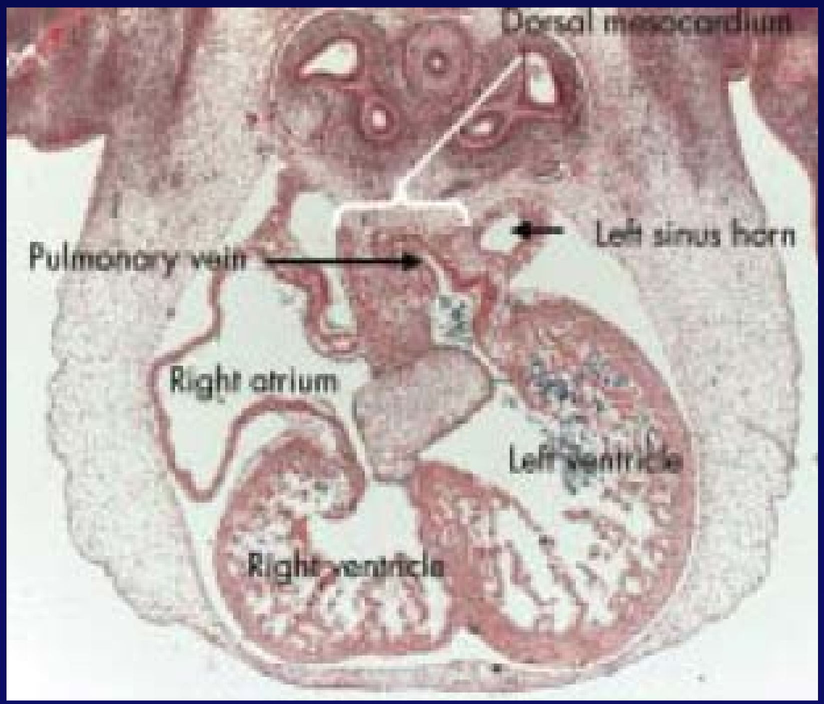


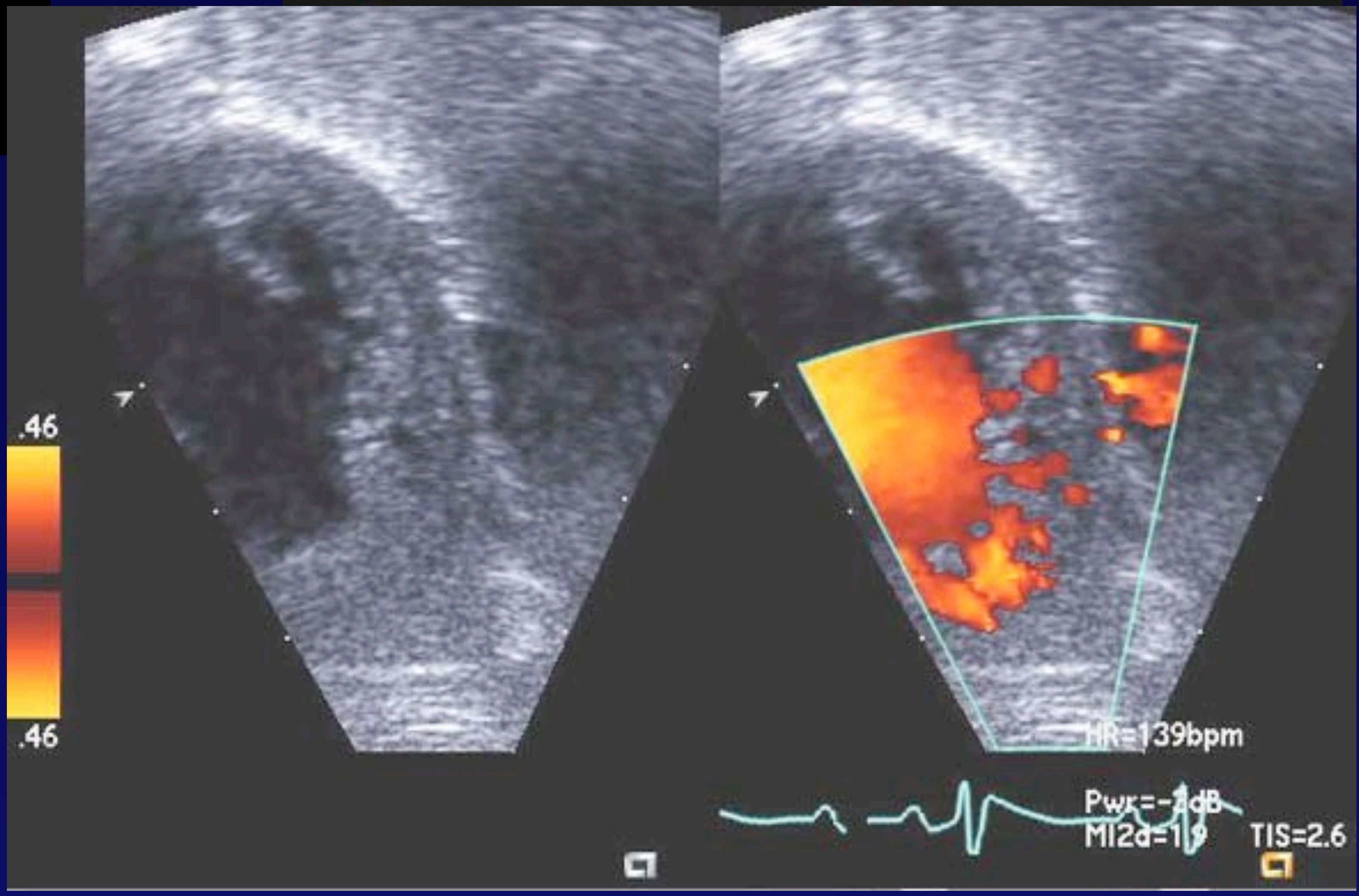


Ebstein's Malformation: Non- Compaction Syndrome



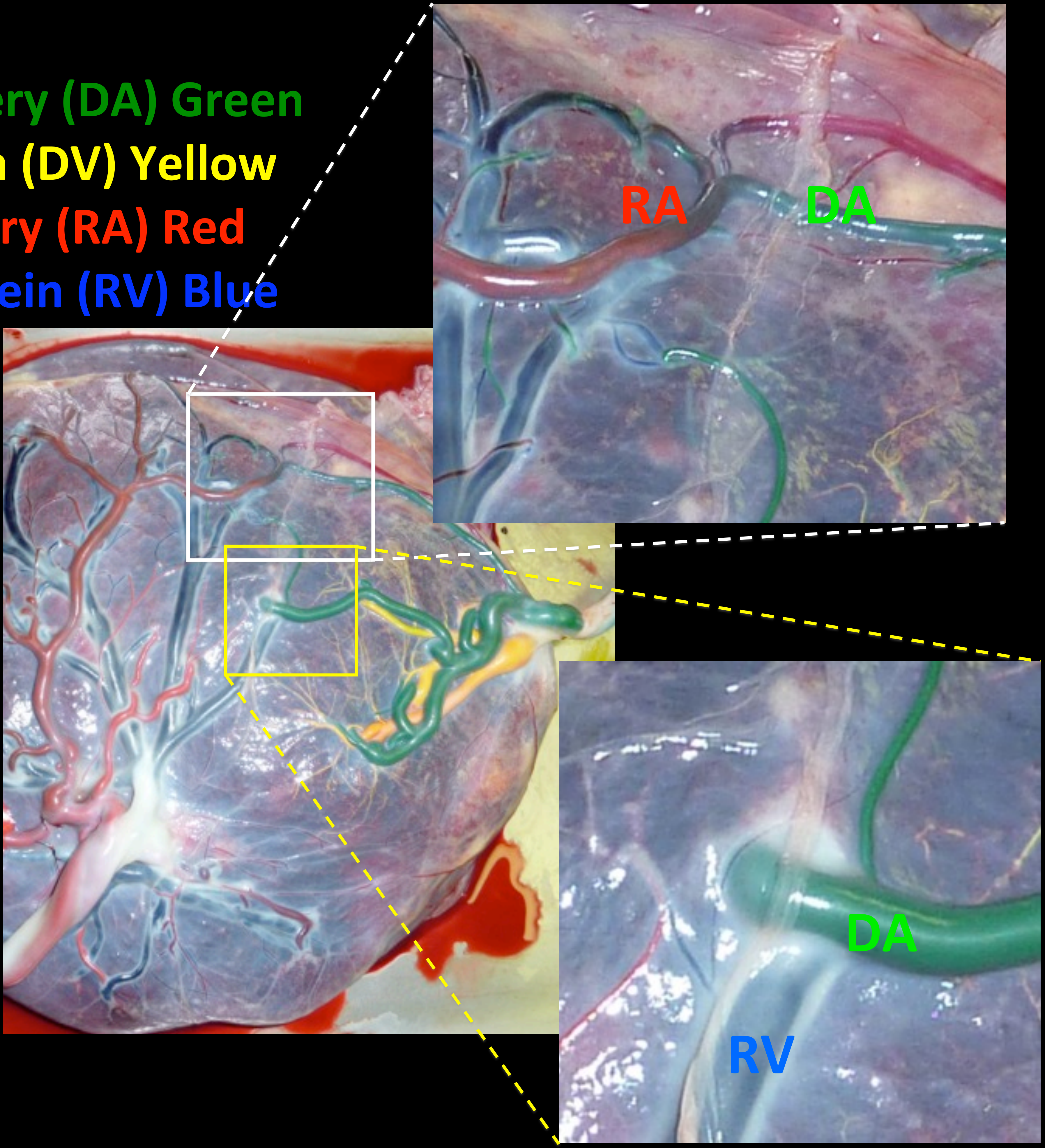


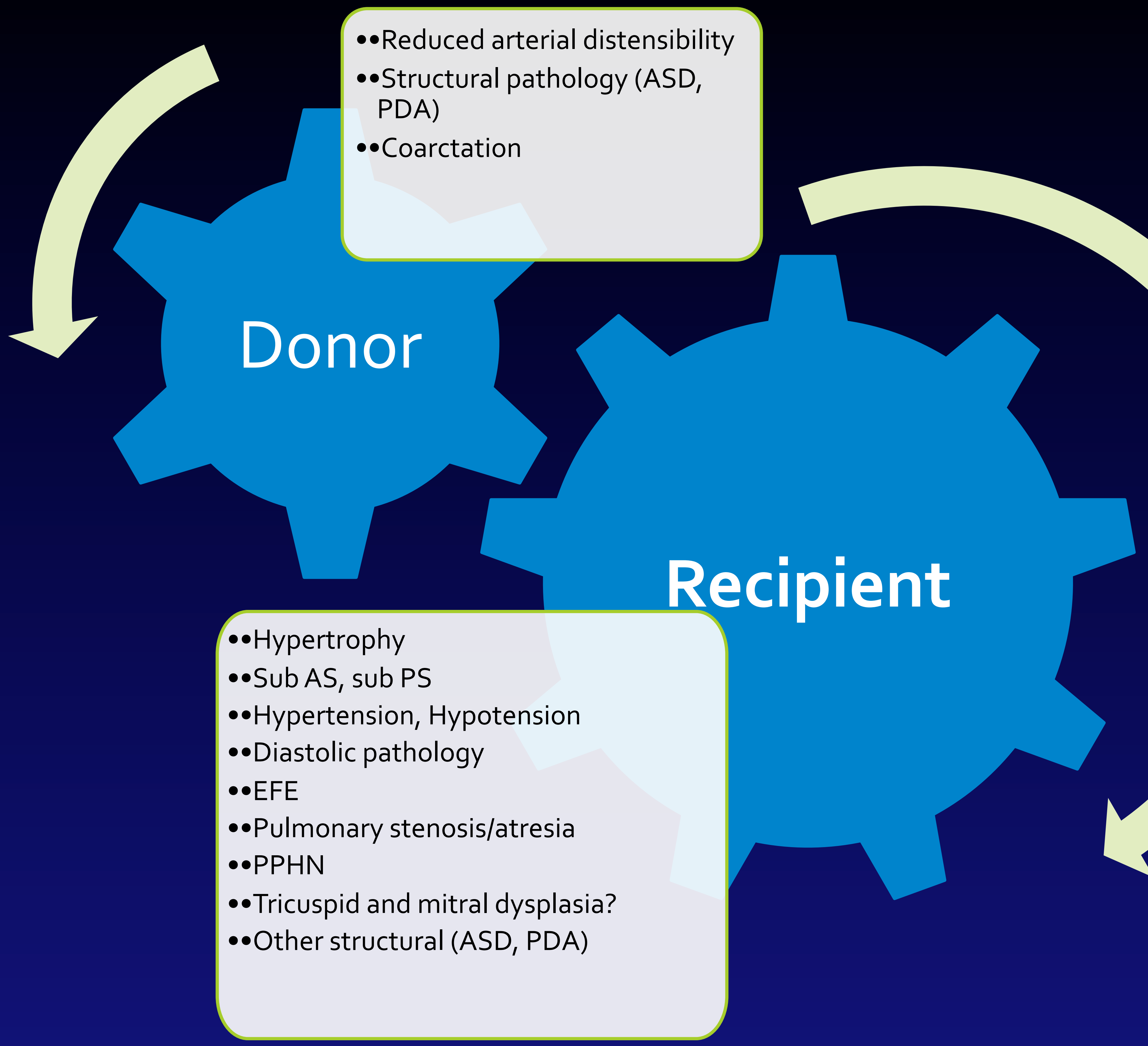


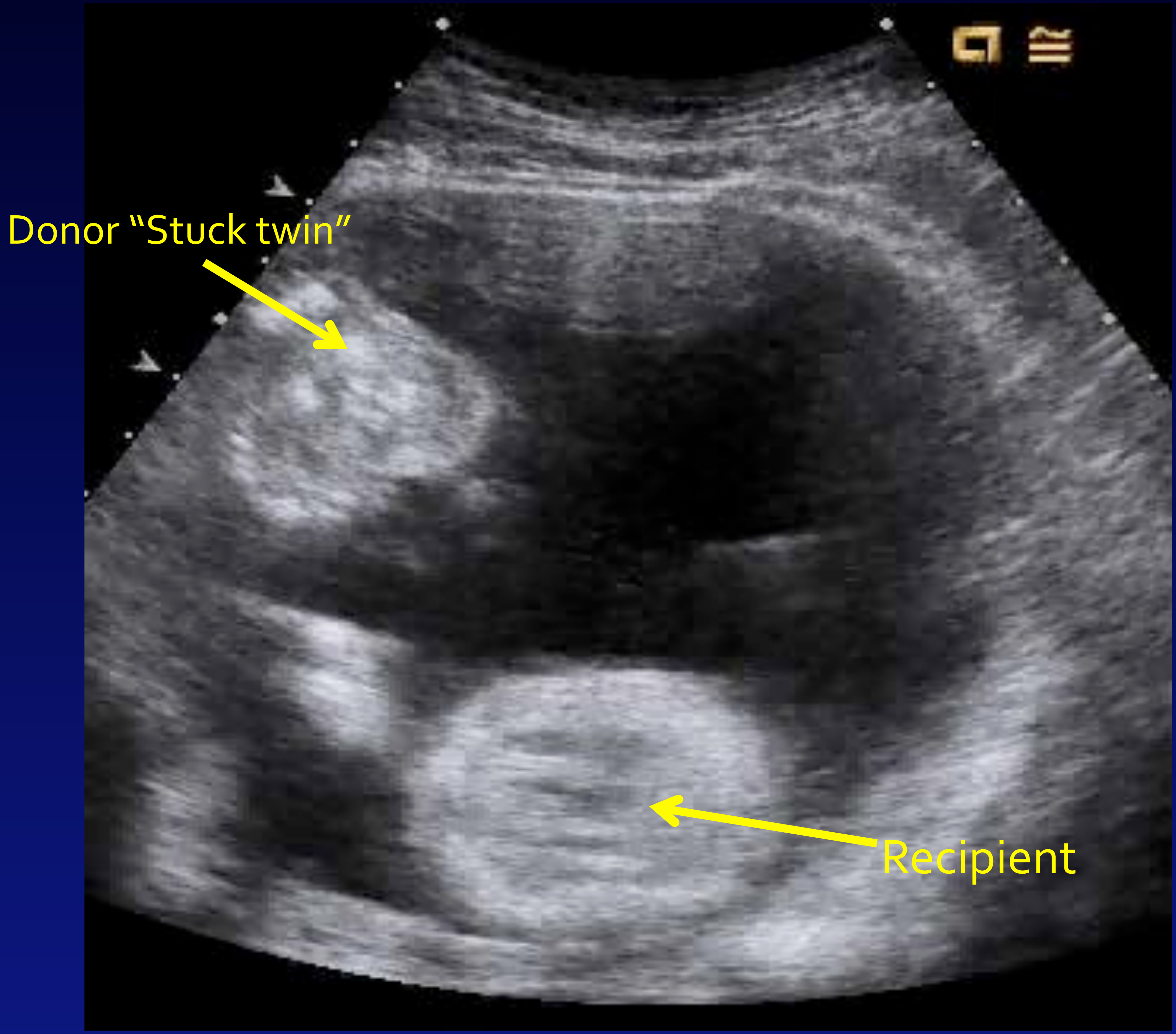


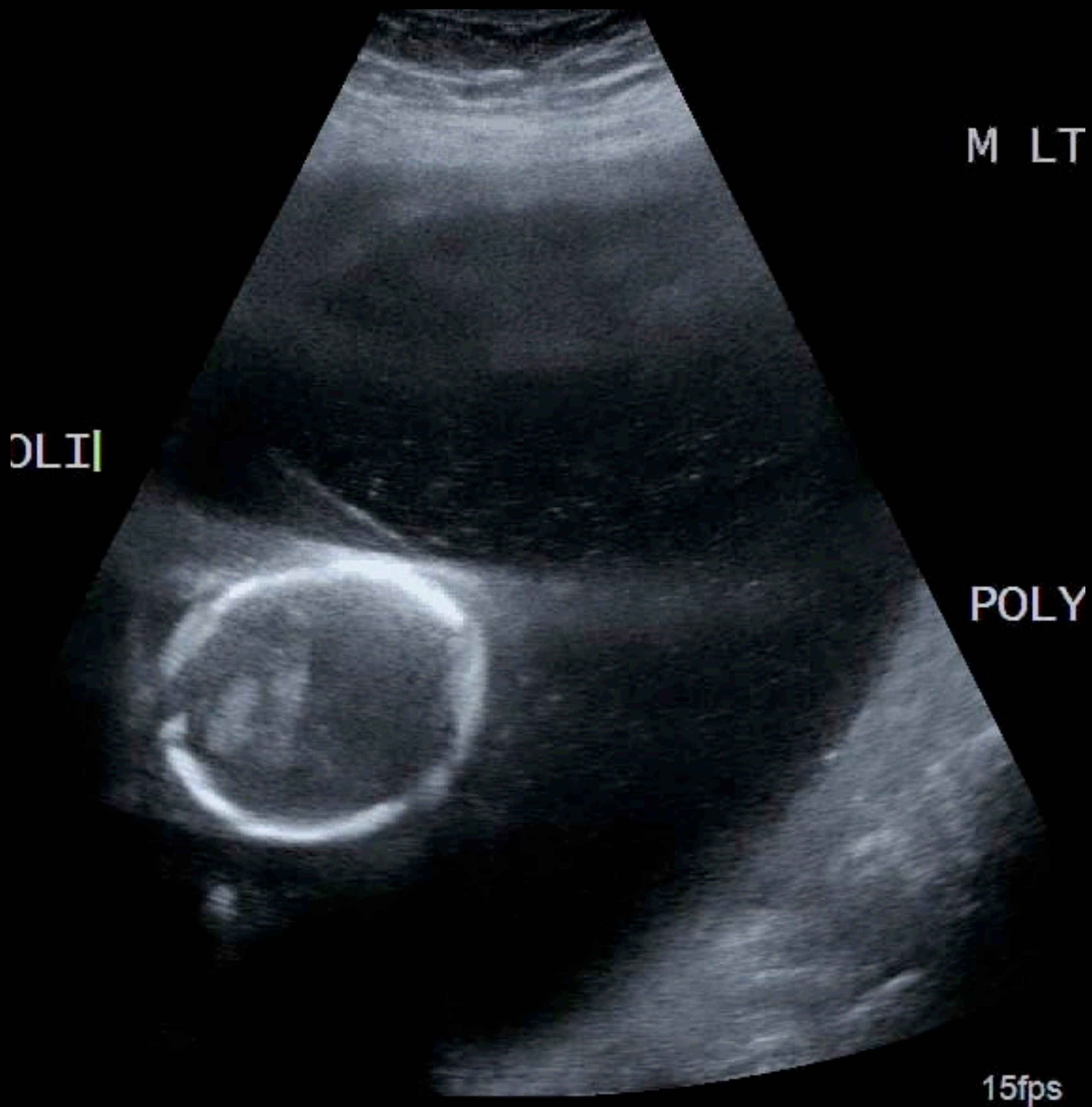
Cardiological Aspects of the twin to twin transfusion syndrome

Donor Artery (DA) Green
Donor Vein (DV) Yellow
Recip Artery (RA) Red
Recipent Vein (RV) Blue

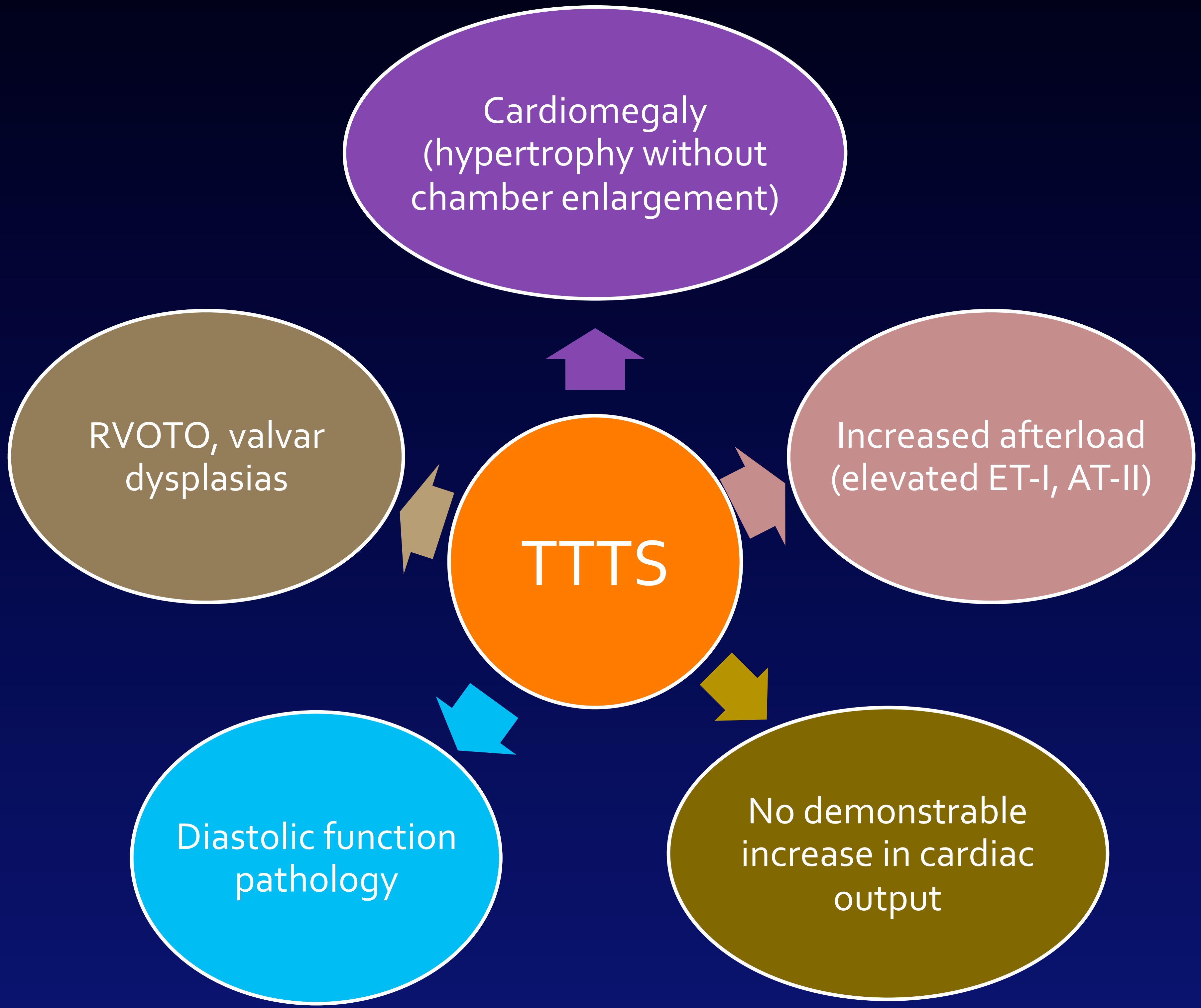


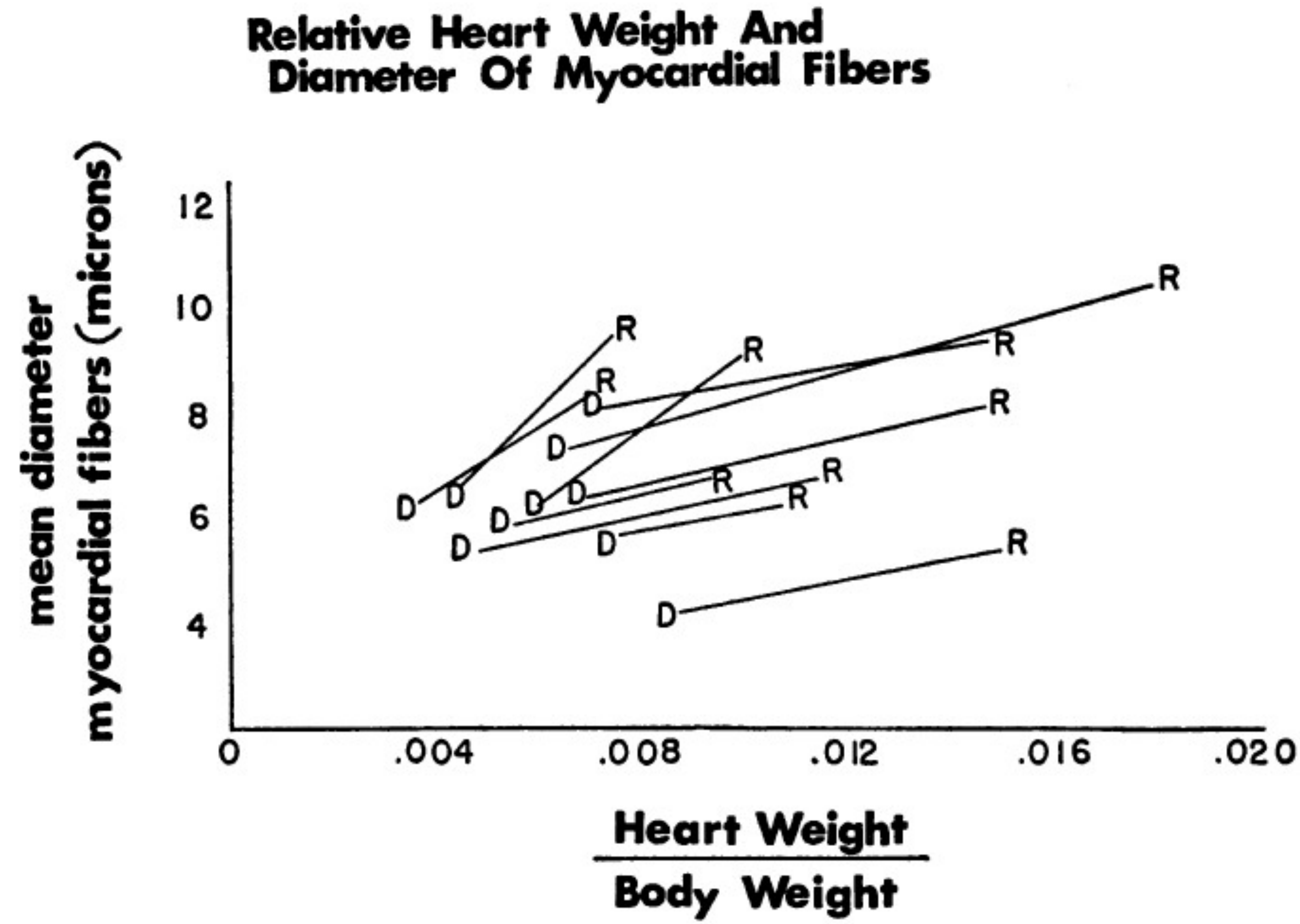

••Reduced arterial distensibility
••Structural pathology (ASD, PDA)
••Coarctation
Donor
Recipient
••Hypertrophy
••Sub AS, sub PS
••Hypertension, Hypotension
••Diastolic pathology
••EFE
••Pulmonary stenosis/atresia
••PPHN
••Tricuspid and mitral dysplasia?
••Other structural (ASD, PDA)


Donor "Stuck twin"
Recipient


M LT
OLI
POLY
15fps

TTTS: Really a Cardiovascular Disease?





TEXT-FIG. 2. Individual myocardial fibers are wider (hypertrophied) in recipient twins (R) than in donor twins (D).

Naeye, NEJM 1963; 268:804-9

TTTS: not a high-output lesion

TTTS

SCT

SMFM PAPERS www.AJOG.org

Diastolic cardiac pathology and clinical twin-twin transfusion syndrome in monochorionic/diamniotic twins

Anita J. Moon-Grady, MD; Larry Rand, MD; Salvador Gallardo, MD; Kristen Gosnell, MSN; Hanmin Lee, MD; Vickie A. Feldstein, MD

OBJECTIVE: We sought to identify differences in echocardiographic profiles of monochorionic (MC)/diamniotic (DA) pregnancies with early or mild twin-twin transfusion syndrome (TTTS), compared to MC/DA twins affected only by discordant growth or discordant fluid.

STUDY DESIGN: This was a retrospective evaluation of sonograms and echocardiograms of twin pregnancies referred for suspected TTTS.

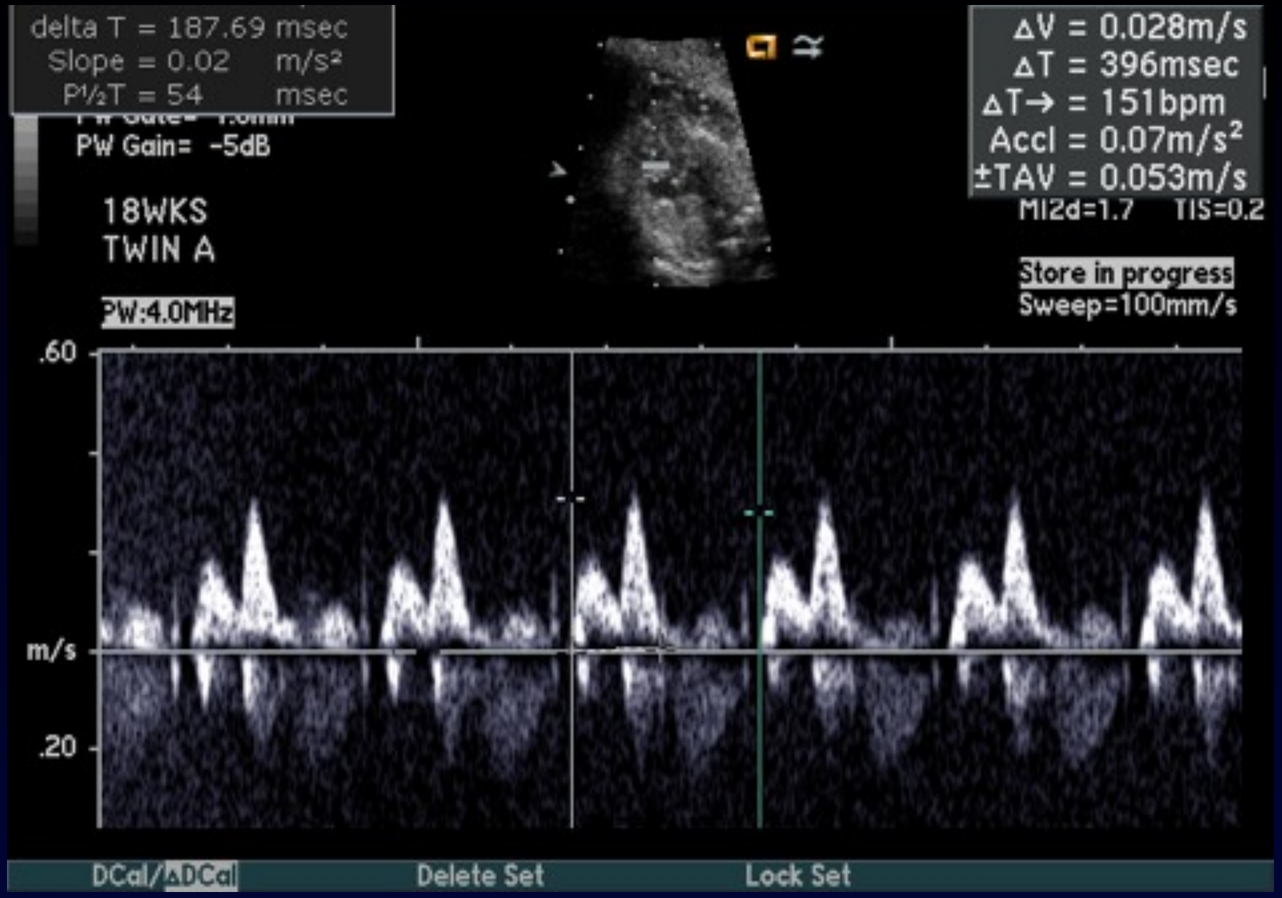
RESULTS: A total of 112 MC/DA pairs were studied. In all, 41 did not have/develop TTTS, and 61 had stage I/II TTTS. Ten developed TTTS after initially not meeting criteria. TTTS recipients had a higher rate of venous Doppler or tricuspid inflow abnormalities than purported recipients in non-TTTS pregnancies (86% vs 37%, $P < .001$). TTTS recipients had shorter tricuspid inflow duration/R-R intervals than non-TTTS fetuses (32 $\pm$ 6% vs 37 $\pm$ 4%, $P < .001$). Logistic regression and recursive partitioning identified shorter tricuspid inflow duration, longer isovolumic relaxation, and ductus venosus abnormality associated with TTTS.

CONCLUSION: Diastolic pathology, specifically shorter tricuspid inflow duration, may be considered a hallmark of TTTS distinguishing these pregnancies from other MC/DA twin complications.

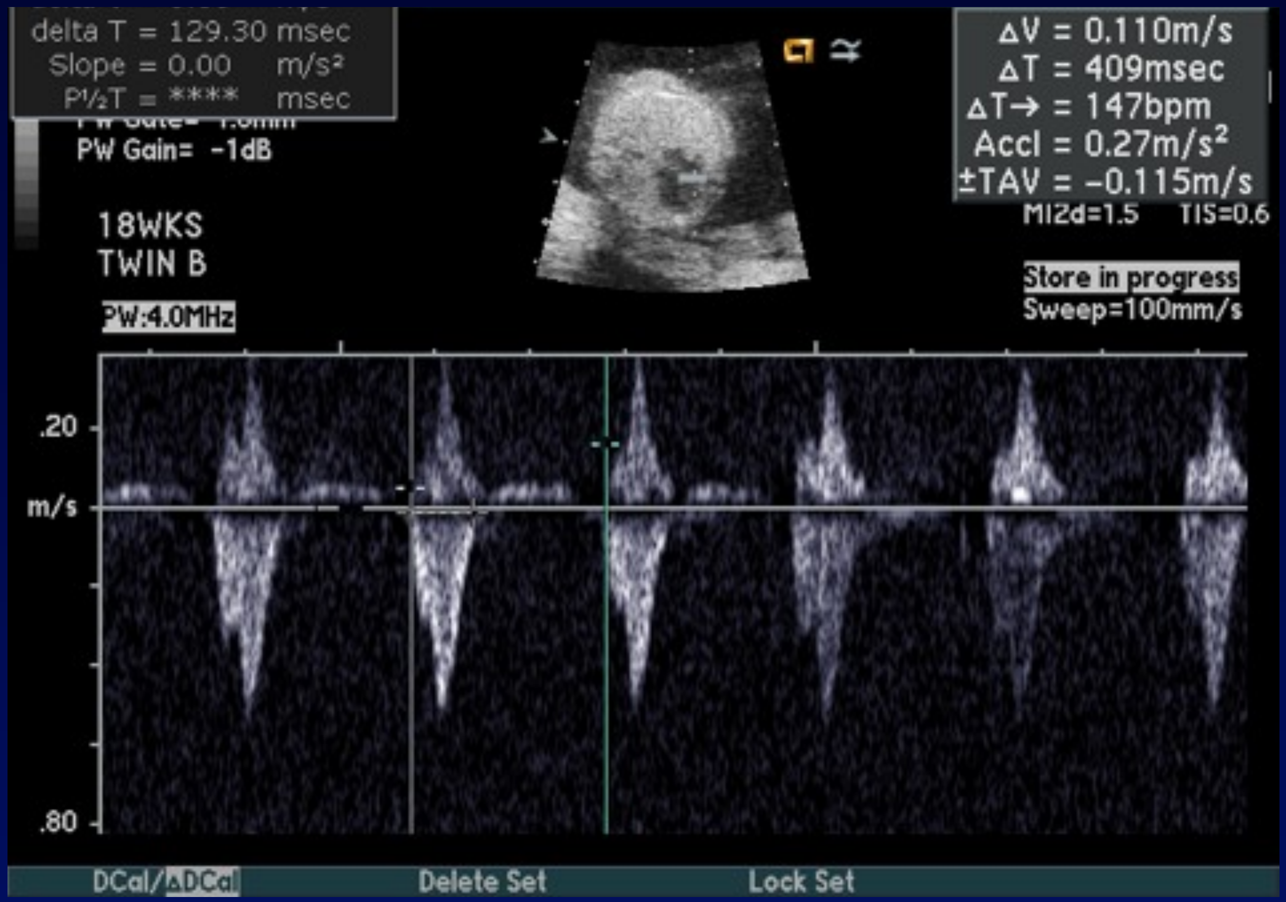
Key words: fetal echocardiography, monochorionic twins, twin-twin transfusion syndrome

Cite this article as: Moon-Grady AJ, Rand L, Gallardo S, et al. Diastolic cardiac pathology and clinical twin-twin transfusion syndrome in monochorionic/diamniotic twins. Am J Obstet Gynecol 2011;205:x.ex-x.ex.

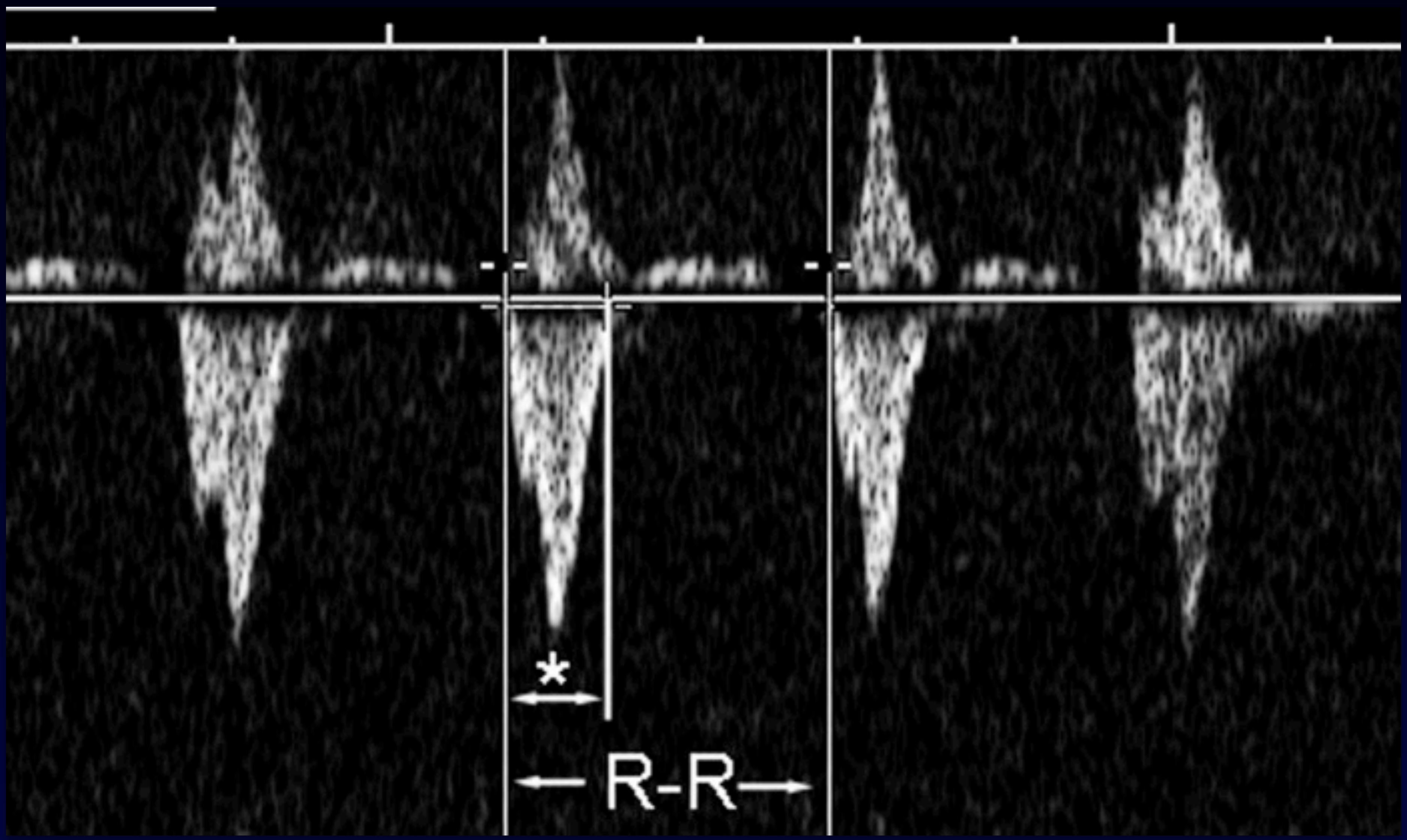
DONOR



RECIPIENT

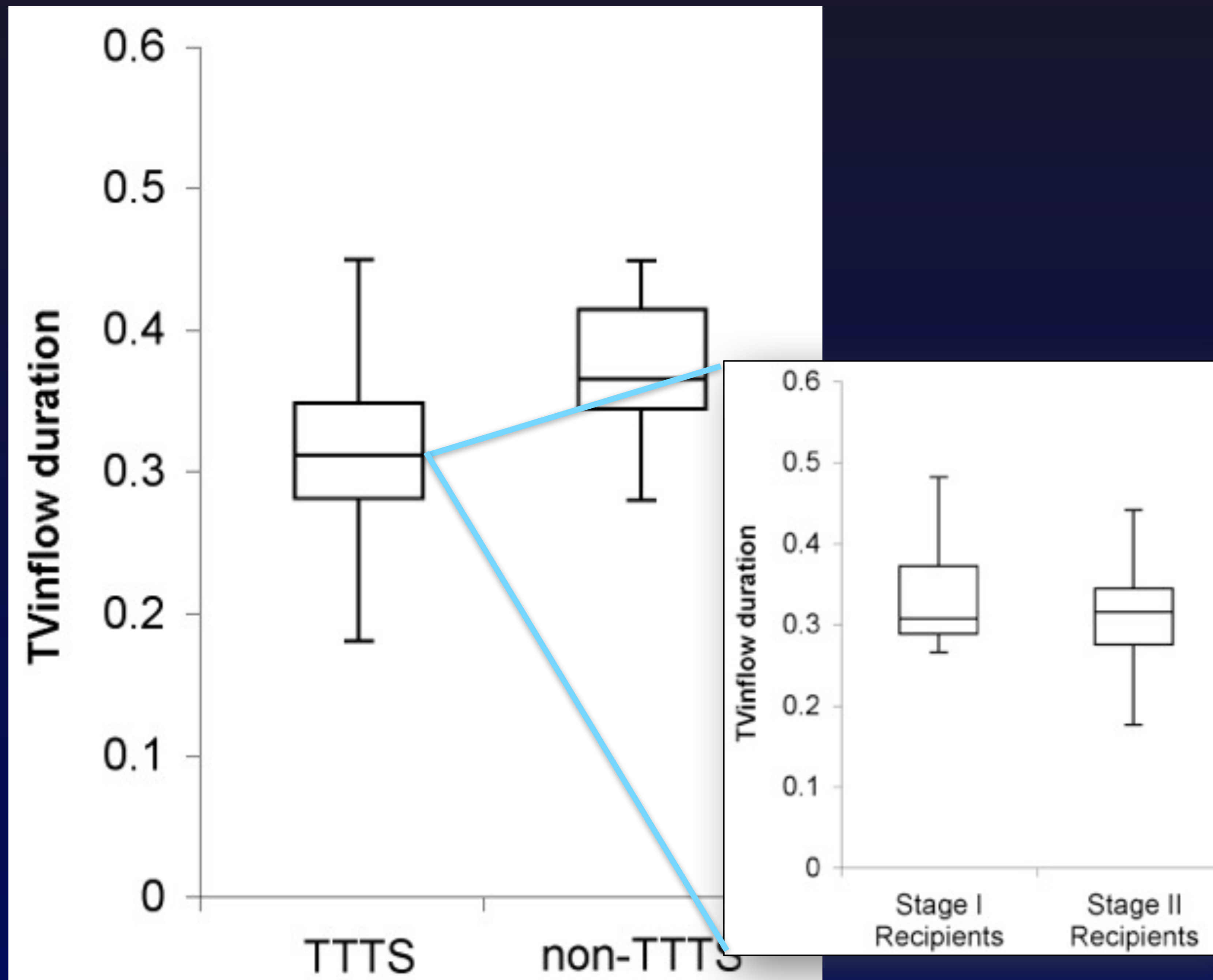


Observation: tricuspid inflow pattern may be only abnormal finding



Measurement of tricuspid inflow duration (TV/RR)

Tricuspid Inflow duration %: Shorter in TTTS



TTTS- prolongation of IVRT

- Difference in IVRT between twins seen in Stage I TTTS but not in discordant twins (Raboisson,Fouron Circ 2004;110:3043-8)

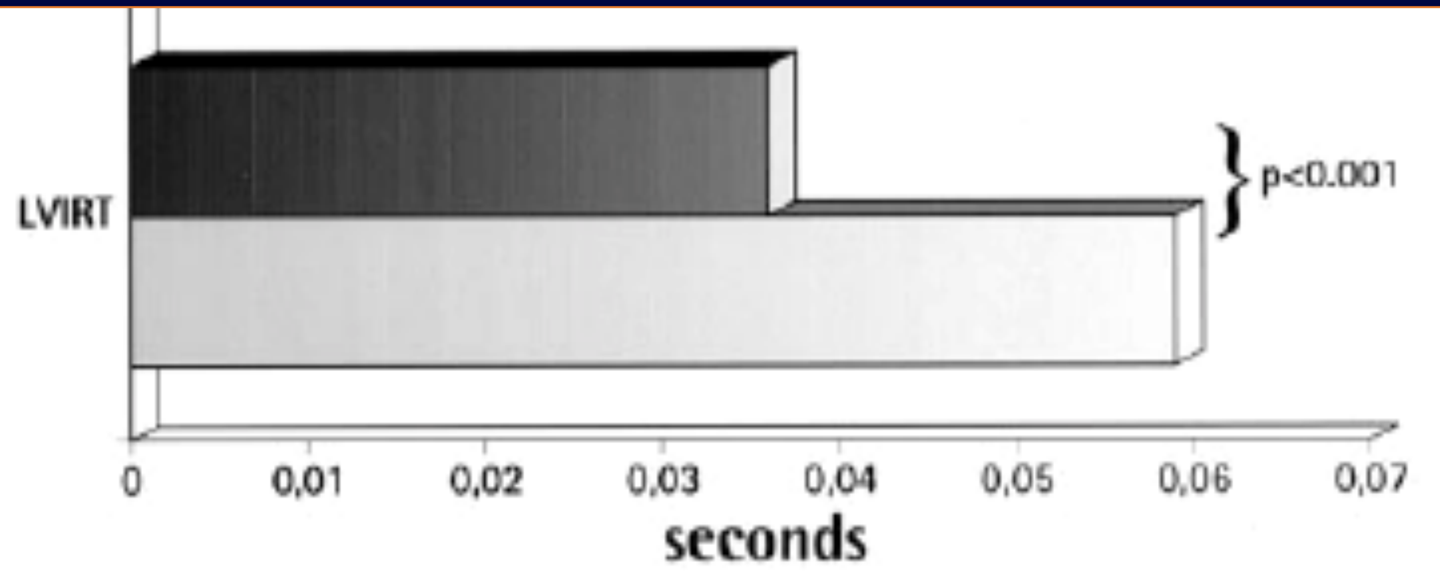
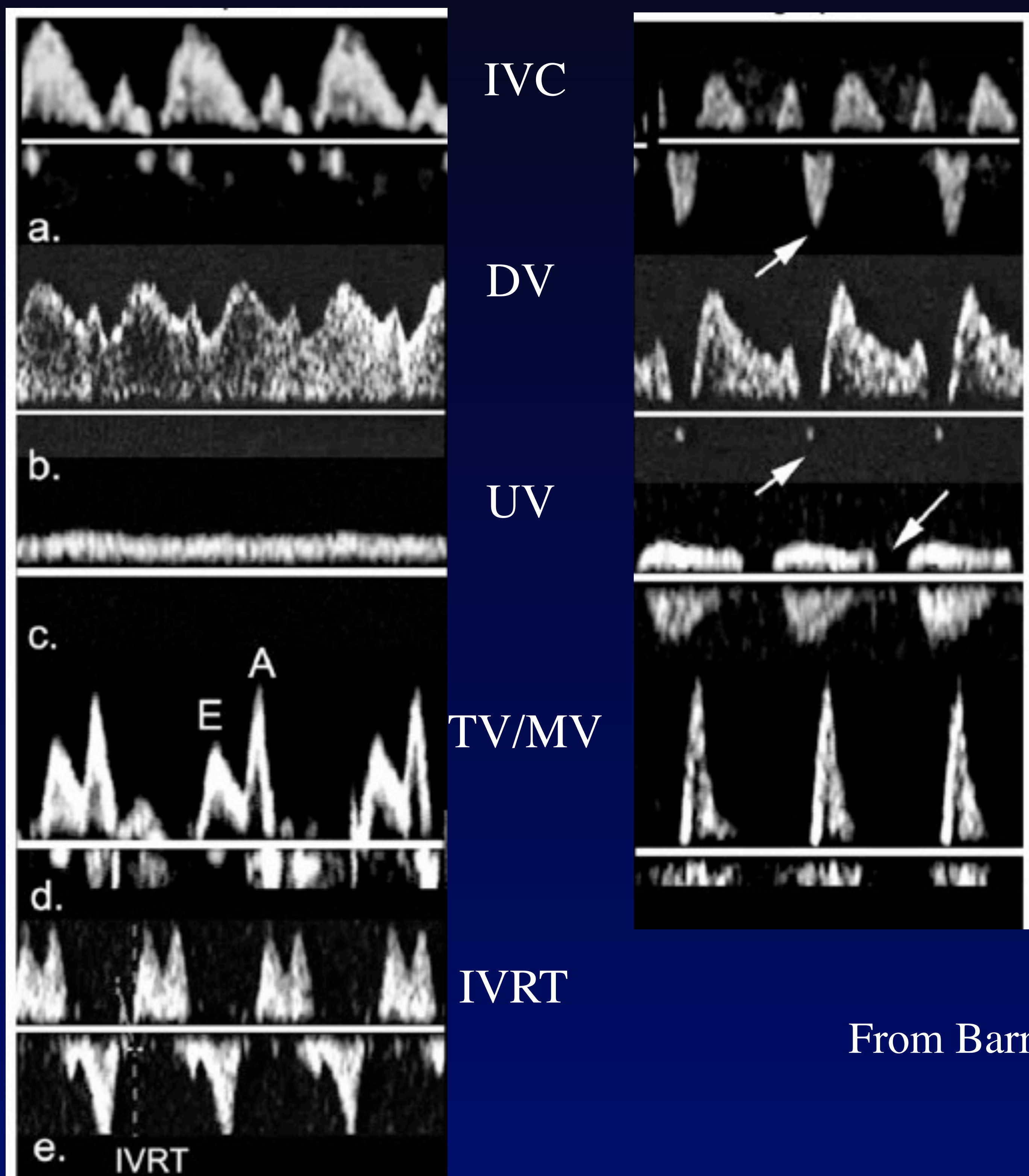


Figure 2. Comparison of LV isometric contraction (LVICT) and relaxation (LVIRT) times in donor and recipient twins.

TTTS case post laser

Doppler assessment of diastolic fn in TTTS



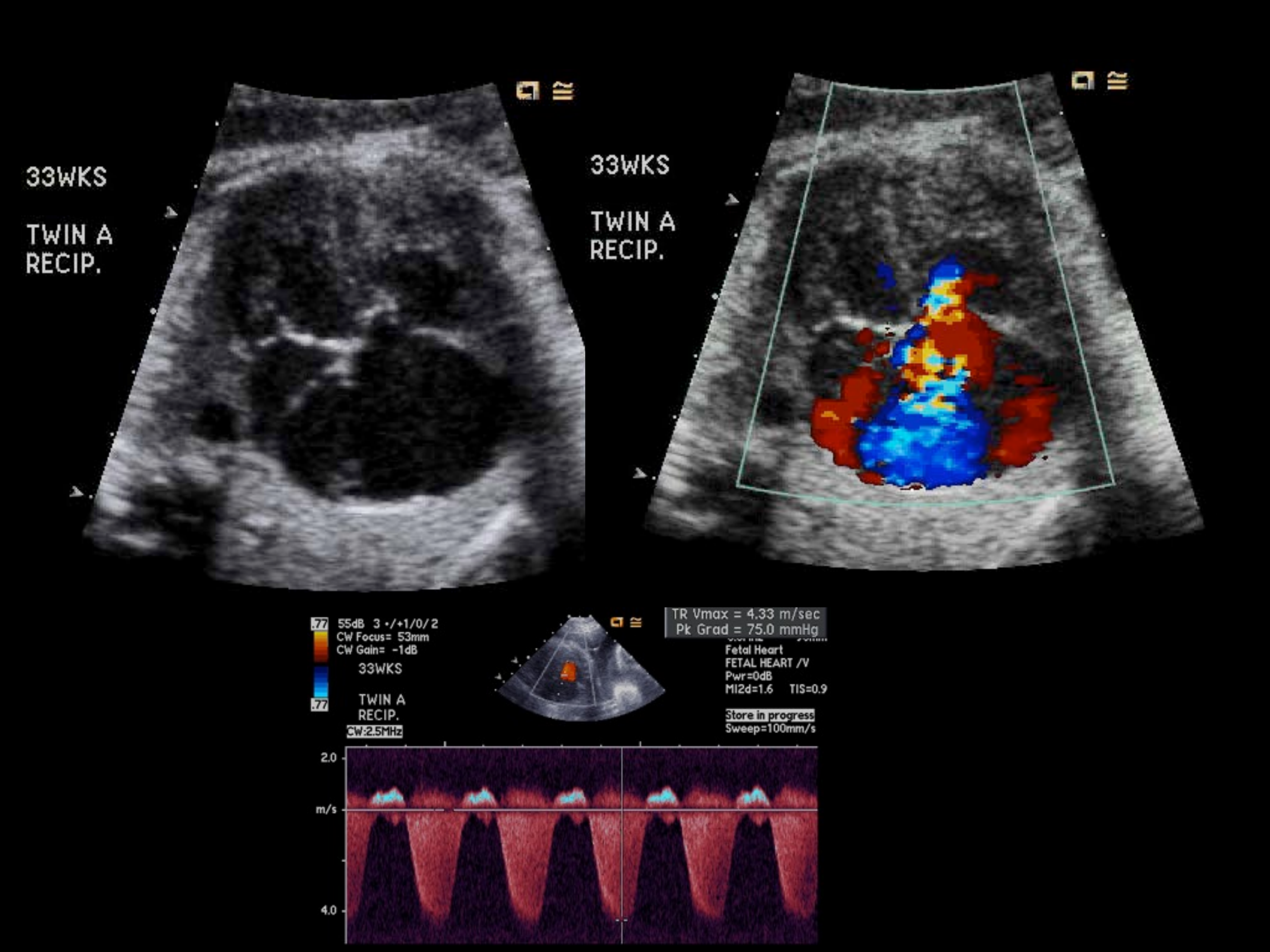
- Characterized by increasing a wave reversal in IVC, reversal in DV, UV pulsations,loss of early diastolic filling (E) wave

- increasing IVRT (>45 msec)

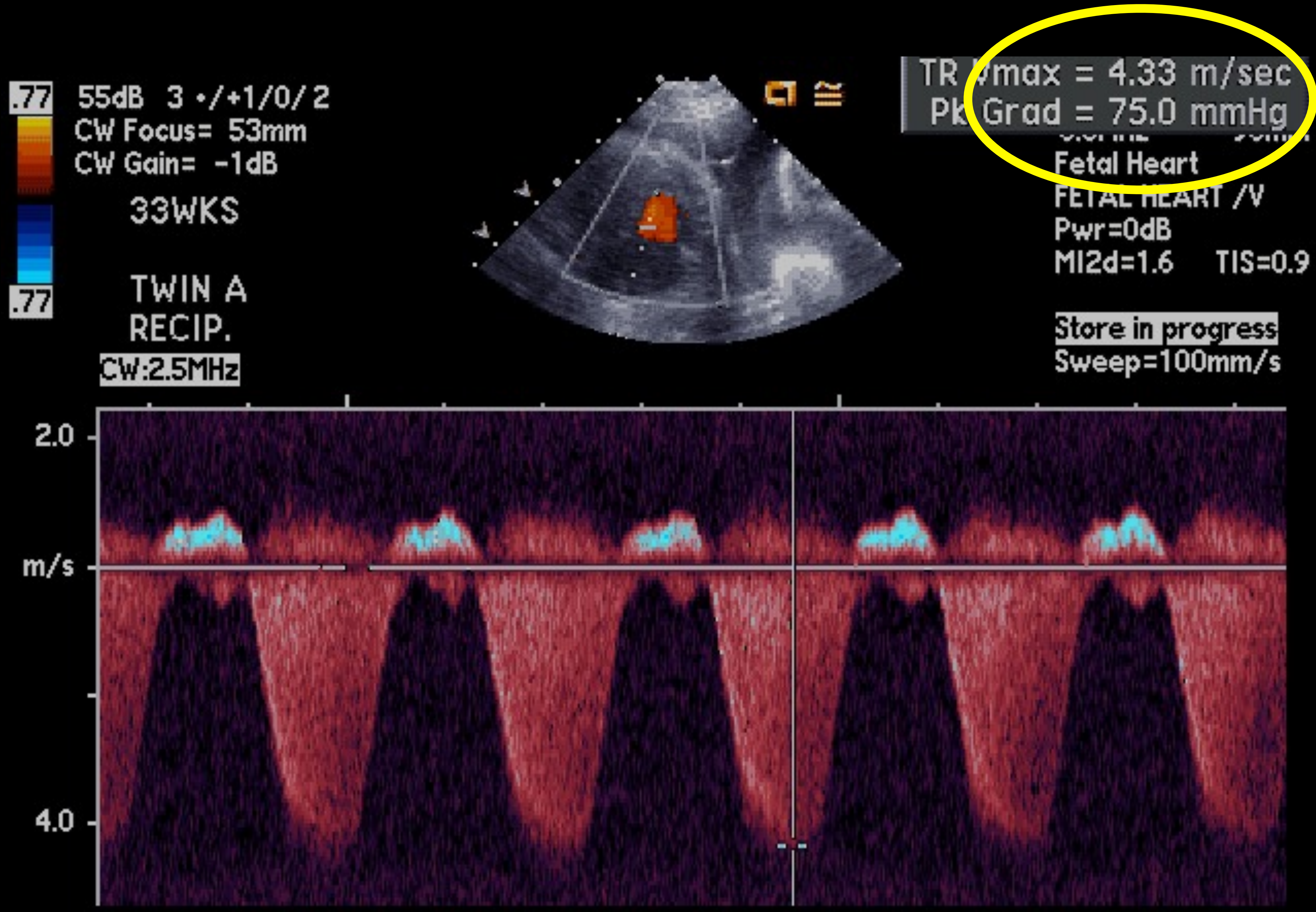
From Barrea et al Am J Ob/Gyn(2005) 192, 892–902

Value of Cardiac Assessment in investigations of disease

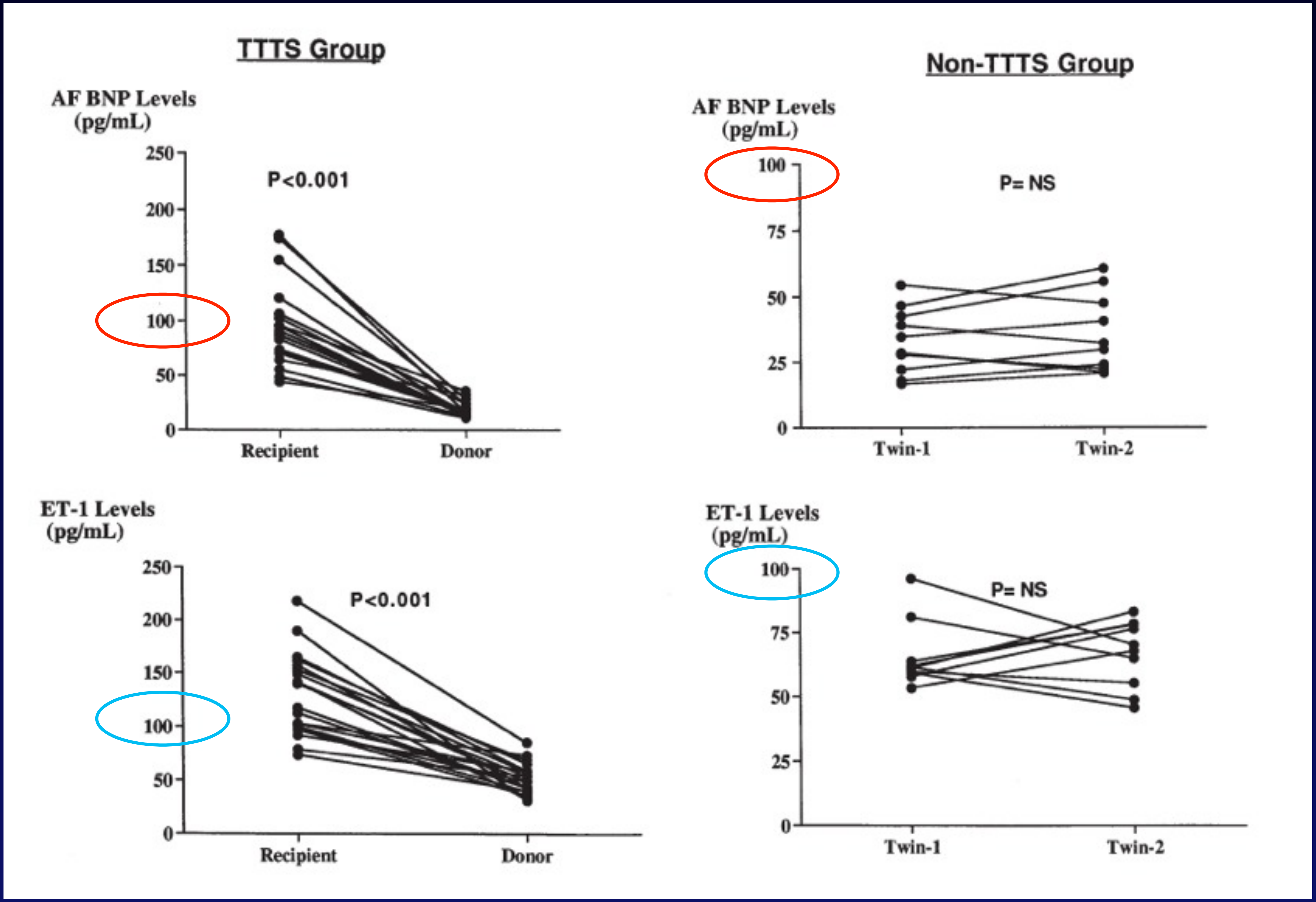
- Cardiomyopathy
- Valvar Dysplasias
- Vascular Programming



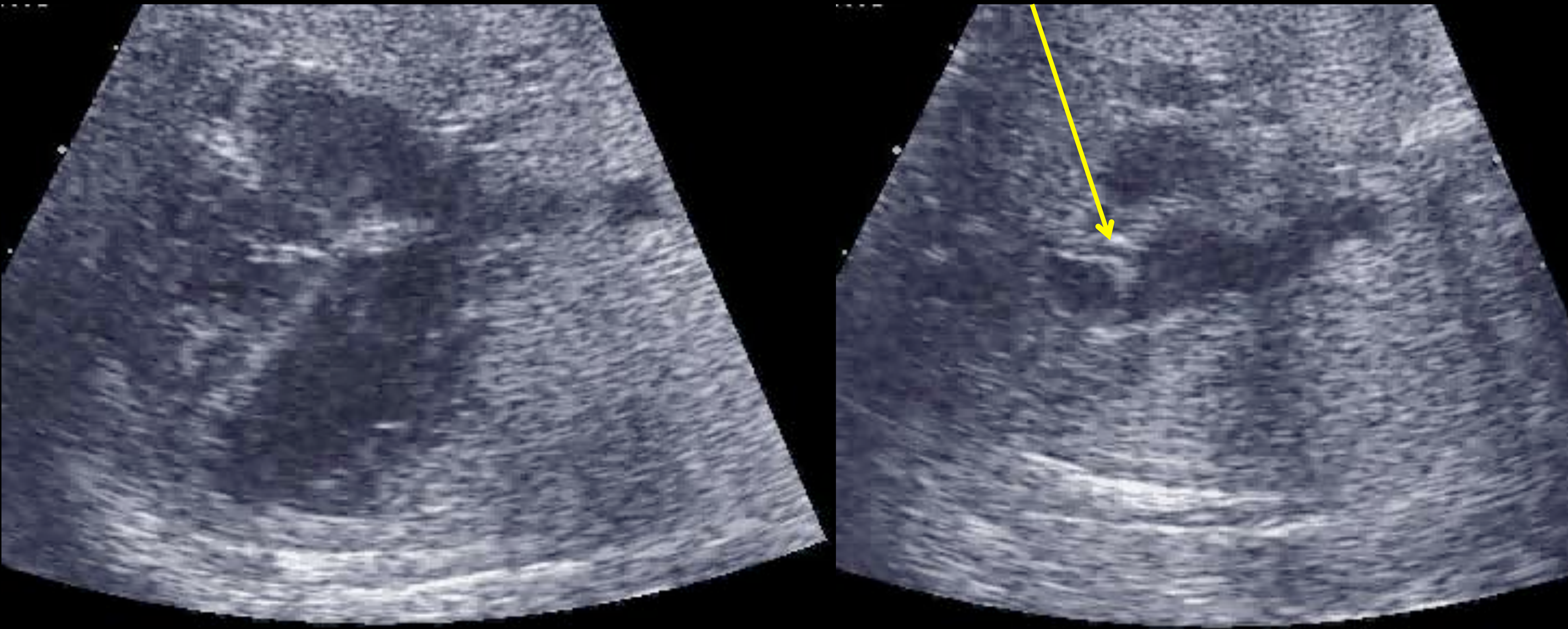
33WKS
TWIN A
RECIP.
33WKS
TWIN A
RECIP.
.77
55dB 3 •/+1/0/2
CW Focus= 53mm
CW Gain= -1dB
33WKS
TWIN A
RECIP.
.77
CW:2.5MHz
TR Vmax = 4.33 m/sec
Pk Grad = 75.0 mmHg
Fetal Heart
FETAL HEART /V
Pwr=0dB
MI2d=1.6 TIS=0.9
Store in progress
Sweep=100mm/s
2.0
m/s
4.0


.77
55dB 3 •/+1/0/2
CW Focus= 53mm
CW Gain= -1dB
33WKS
.77
TWIN A
RECIP.
CW:2.5MHz
TR Vmax = 4.33 m/sec
Pk Grad = 75.0 mmHg
Fetal Heart
FETAL HEART /V
Pwr=0dB
MI2d=1.6 TIS=0.9
Store in progress
Sweep=100mm/s
2.0
m/s
4.0

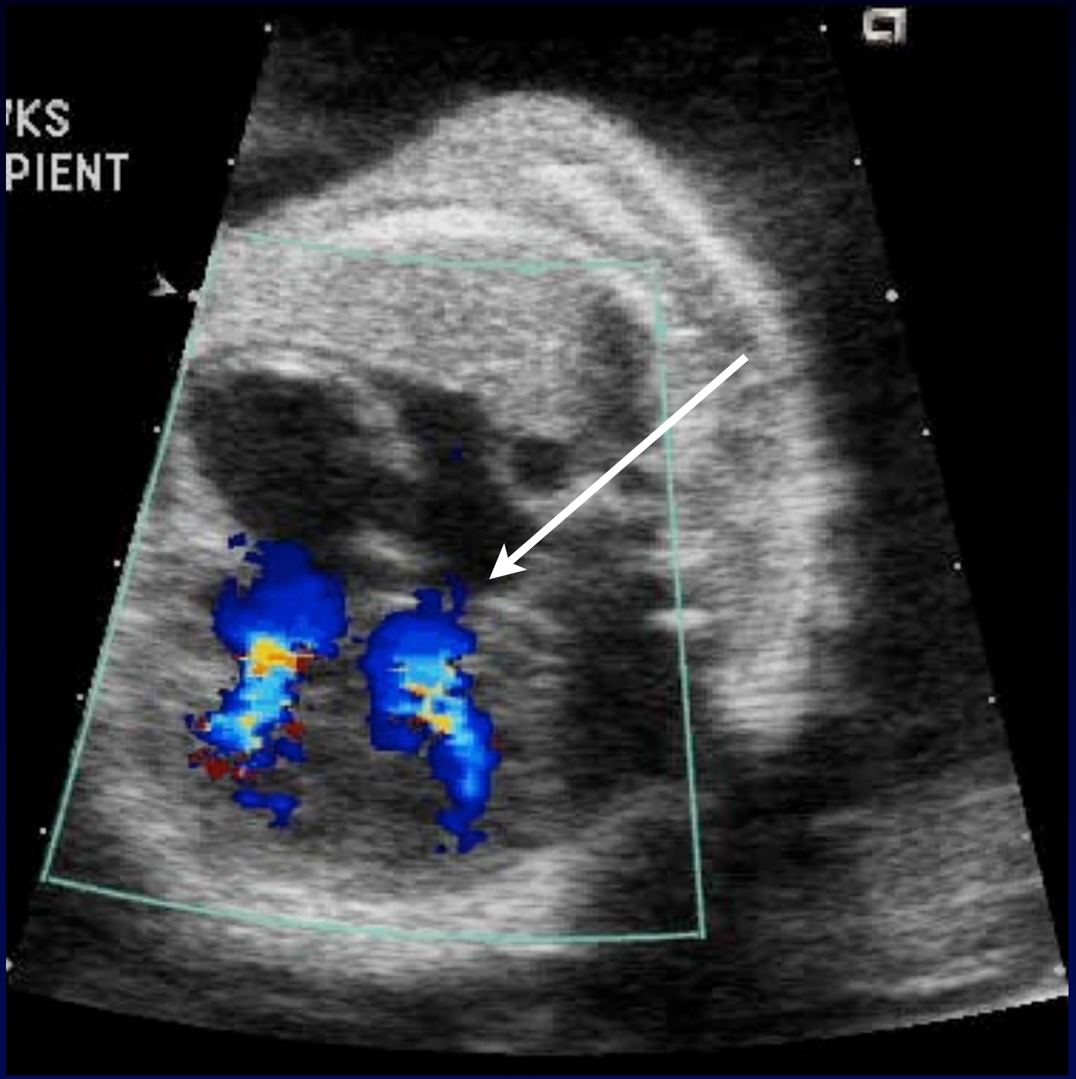
Elevated ET-1 and BNP in recipient



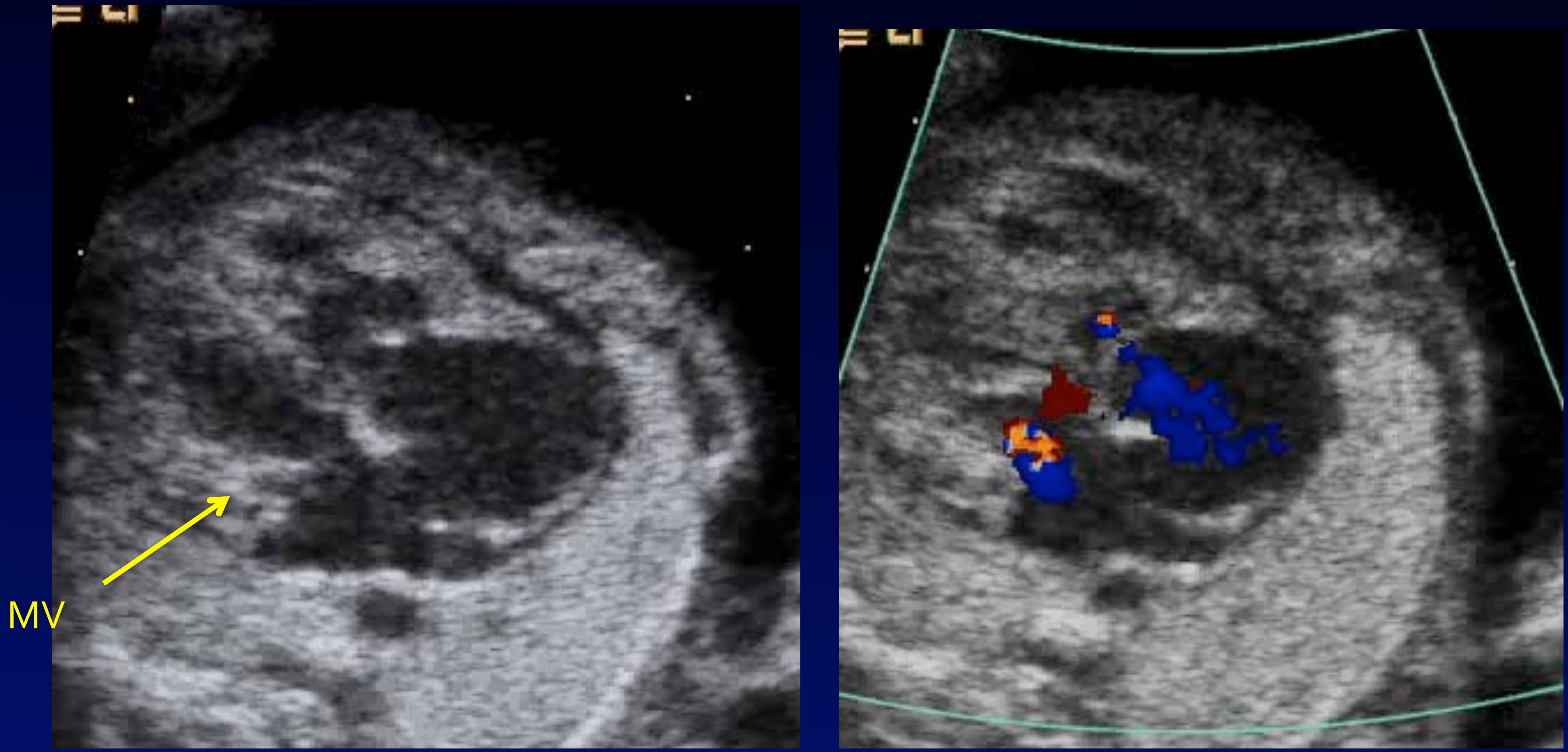
Bajoria et al., Am J Obstet Gynecol 2003;189:189-94.)



23 5/7 weeks



20 4/7 weeks



Effect of selective fetoscopic laser photocoagulation therapy for twin–twin transfusion syndrome on pulmonary valve pathology in recipient twins

A. J. MOON-GRADY*†‡, L. RAND‡§, B. LEMLEY*, K. GOSNELL*†, L. K. HORNBERGER¶ and H. LEE‡**

Ultrasound Obstet Gynecol 2011; **37**: 27–33

Objective *To investigate the impact of selective fetoscopic laser photocoagulation (SFLP) on pre-existing pulmonary valve pathology in the recipient twin in twin–twin transfusion syndrome (TTTS).*

Results *The mean gestational age at SFLP was 21 (range, 18.7–24.3) weeks. Seven of sixteen (44%) recipients with abnormal pulmonary valve prior to SFLP survived. Six of the 16 (37.5%) recipient twins had documented absence of persistent pulmonary valve abnormalities at birth or at autopsy. Two (12.5%) of the 16 recipients (2.6% of the original cohort) had persistent pulmonary valve abnormalities at birth, requiring intervention. Systolic and diastolic function improved or normalized after SFLP in all patients undergoing longitudinal follow-up. There was a tendency for a better cardiovascular profile score (best = 10 points) at initial evaluation in pregnancies with survivors compared with those with no survivors (mean (SD): 5.6 (2.2) vs. 6.75 (1.28)), but this was not statistically significant. Severity of cardiac involvement did not predict persistence of valve pathology or survival.*

Conclusions *SFLP can improve flow through the pulmonary valve of the recipient twin in TTTS, probably as a consequence of improvements in right ventricular systolic and diastolic function. However, pulmonary valve pathology may persist and require postnatal intervention.*

Congenital Heart Disease

Anomalous Mitral Arcade in Twin-Twin Transfusion Syndrome

Elizabeth Losada, MD*; Anita J. Moon-Grady, MD*; William C. Strohsnitter, DSc; Danny Wu, MD; Philip C. Ursell, MD

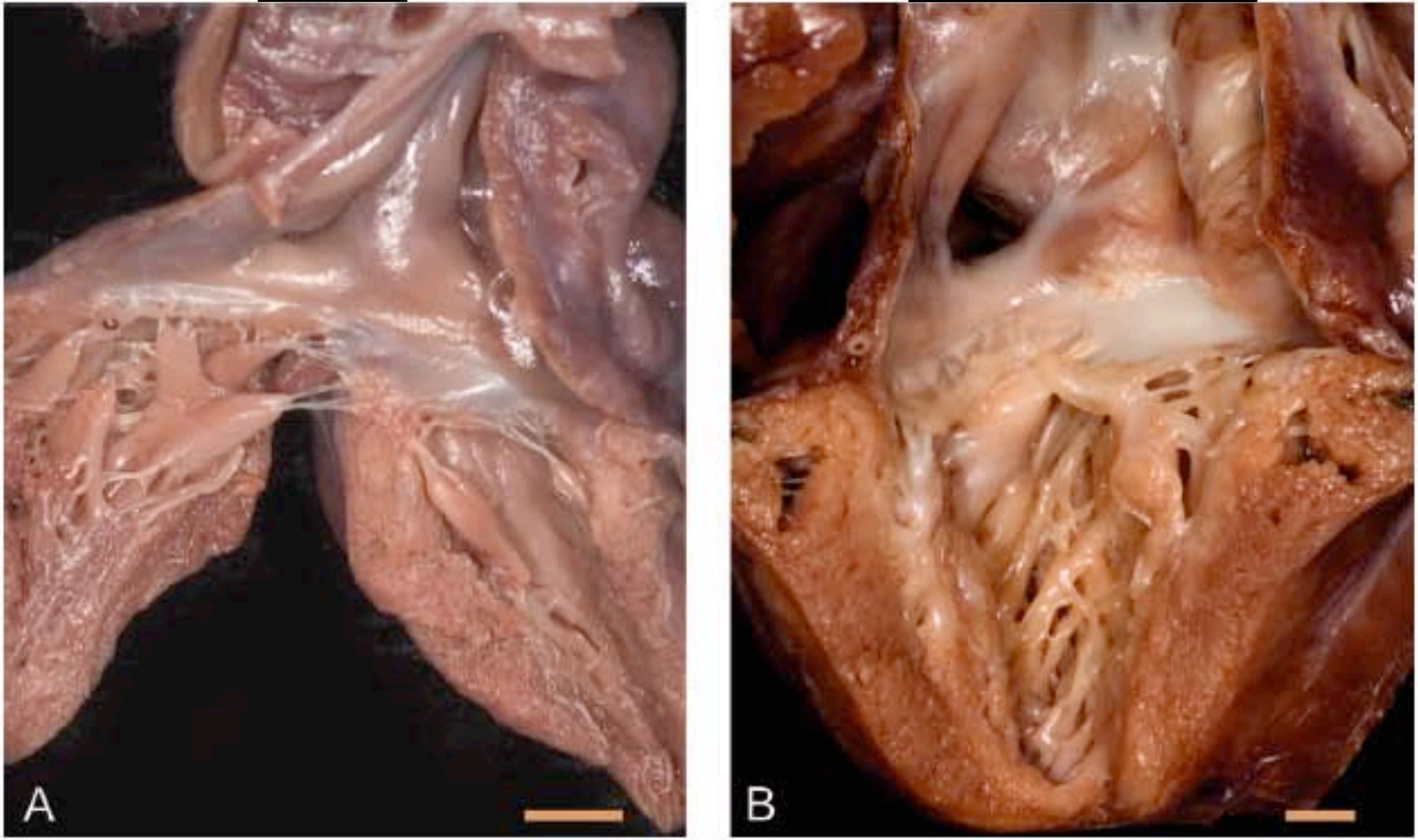
Background—Echocardiography has documented acquired pulmonary stenosis and cardiomyopathy in recipient fetuses in twin-twin transfusion syndrome. At autopsy, we also have identified anomalous mitral arcade, a rare valve deformity associated with mitral regurgitation.

Methods and Results—To identify a profile for anomalous mitral arcade, we compared clinicopathological data from 11 sets of autopsied twin-twin transfusion syndrome fetuses, including 4 twin pairs in whom the recipient had anomalous mitral arcade (affected) and 7 pairs in whom both had structurally normal mitral valves (unaffected). Anomalous mitral arcade was characterized by a thick fibrous band at the free margin of the leaflets tethering papillary muscles and absent/short tendinous cords. One affected recipient also had pulmonary stenosis and tricuspid valve dysplasia. In all 11 sets, recipient hearts were larger than paired donor hearts. All 11 recipients had moderate to severe cardiac dysfunction by echocardiography. Echocardiography disclosed left atrial enlargement in all affected recipients but none of the unaffected recipients. Mitral regurgitation was present before demise in all affected recipients evaluated with color Doppler. Progressive decrease in mitral leaflet mobility was noted in those affected recipients with serial echocardiography.

Conclusions—Previously unreported in twin-twin transfusion syndrome, anomalous mitral arcade was identified in 4 of 11 recipient fetuses (36%) in this autopsy series. Ultrasound or echocardiographic evidence of left atrial dilation, mitral regurgitation, and decreased leaflet mobility in recipients should raise suspicion for anomalous mitral arcade. Development of anomalous mitral arcade in twin-twin transfusion syndrome recipients suggests that the lesion is an acquired valve deformity in this setting, not a malformation. (*Circulation*. **2010;122:1456-1463.**)

Donor

Recipient



Thank you!