Navigating critical valve disease: aortic stenosis, Ebstein Anomaly, and pulmonary stenosis

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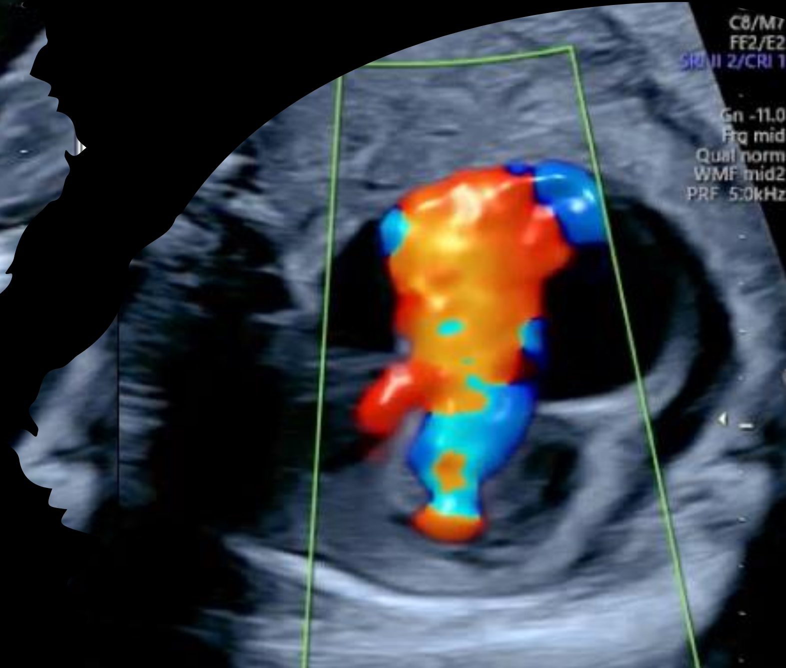


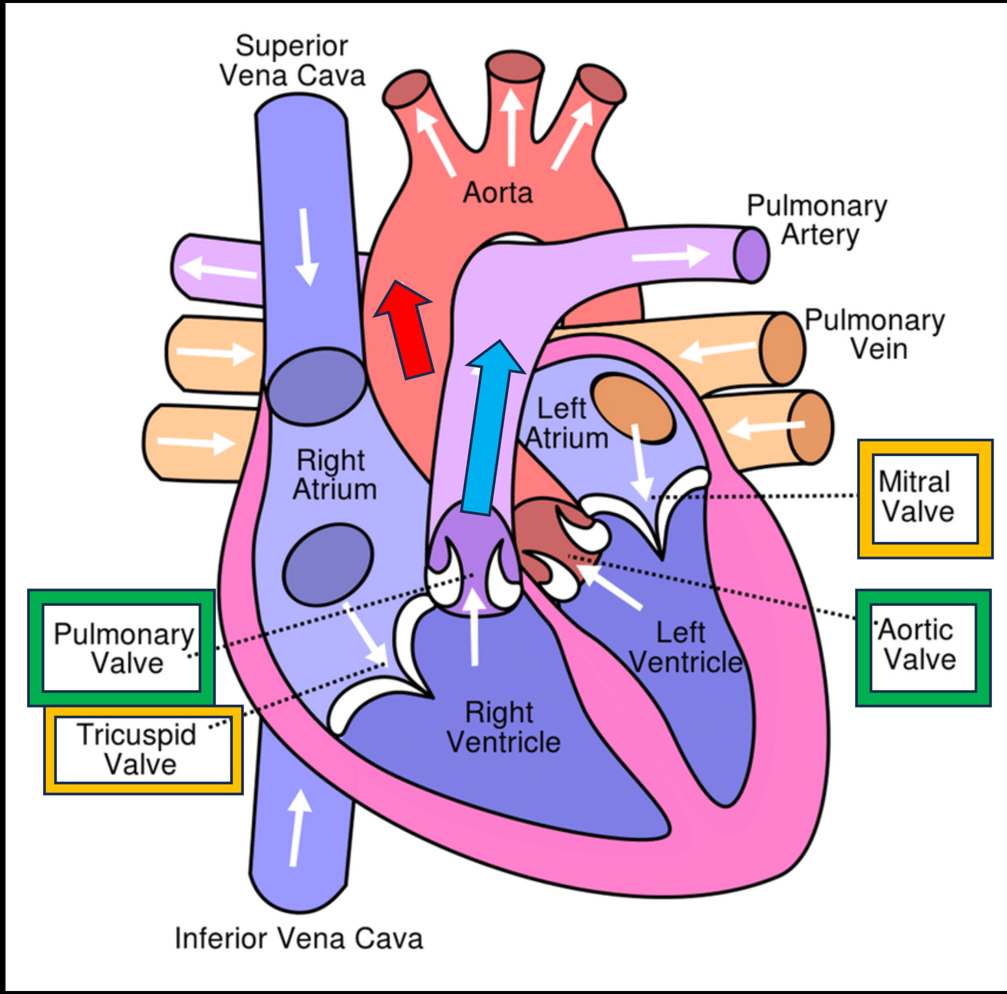
Overview

- Review of atrioventricular (AV) and semilunar (valves) anatomy
- Critical Aortic Stenosis
- Severe Ebstein Anomaly
- Critical Pulmonary Stenosis
- Question and Answer

Disclosures

- I have no financial relationship with any manufacturer of any commercial product and/or provider of commercial services discussed in the conference.
- I do not intend to discuss an unapproved/investigative use of a commercial product or device in my presentation

Cardiac Anatomy Review

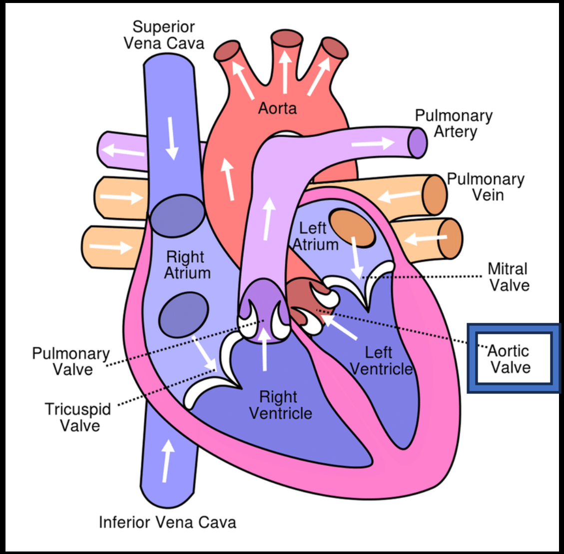


Atrioventricular (AV) valves	Tricuspid valve
	Mitral Valve
Semilunar Valves	Pulmonary valve
	Aortic valve
Great Vessels	Pulmonary artery
	Aorta

Image Source: https://en.wikipedia.org/wiki/Atrium_(heart) #

Aortic valve

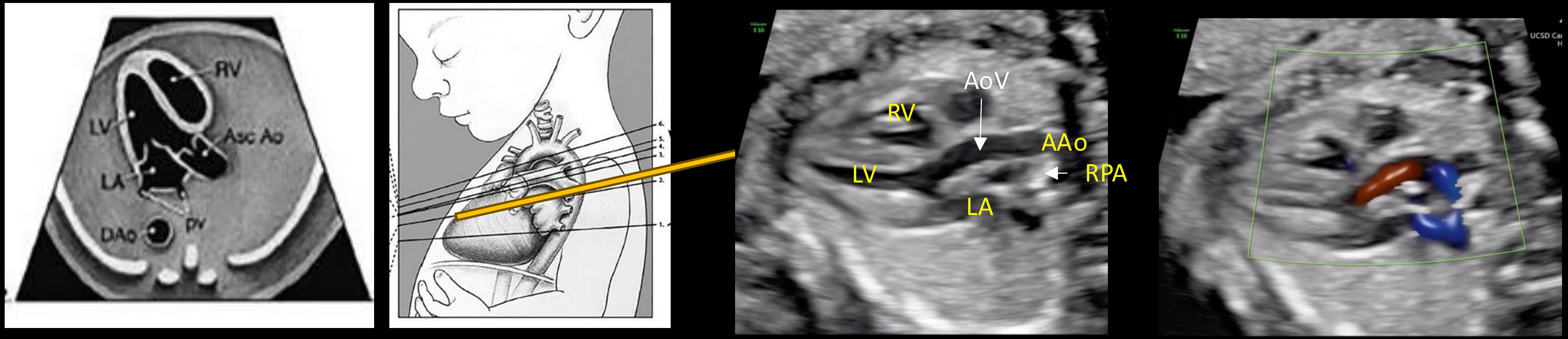
- Normal anatomy consist of 3 leaflet
  - Right, Left, non-coronary cusp
- Connects LV to aorta



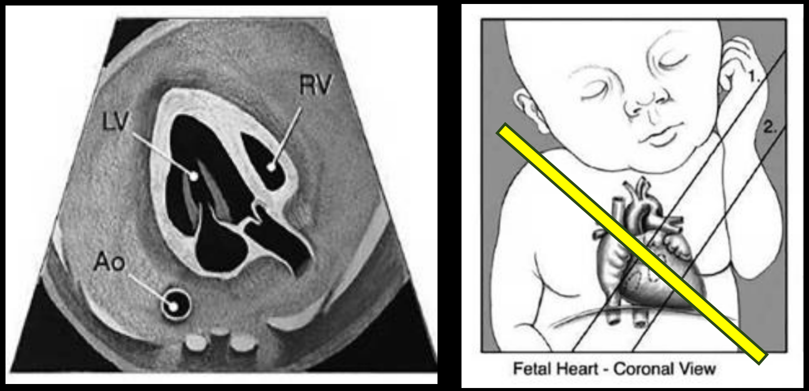
Images: Gotteiner, N.L. (2023). Fetal Echocardiography. In: Abdulla, Ri., *et al*. Pediatric Cardiology. Springer, Cham. https://doi.org/10.1007/978-3-030-42937-9_14-1

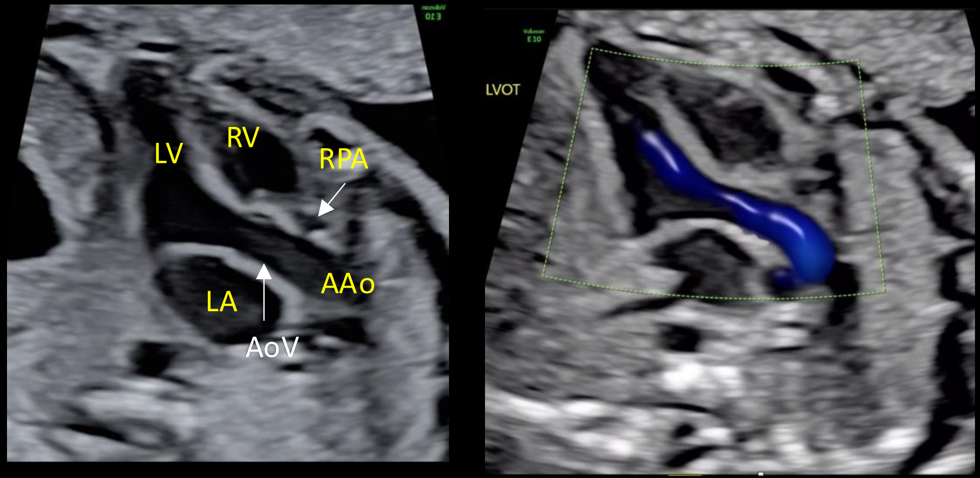
Normal

Apical Long axis

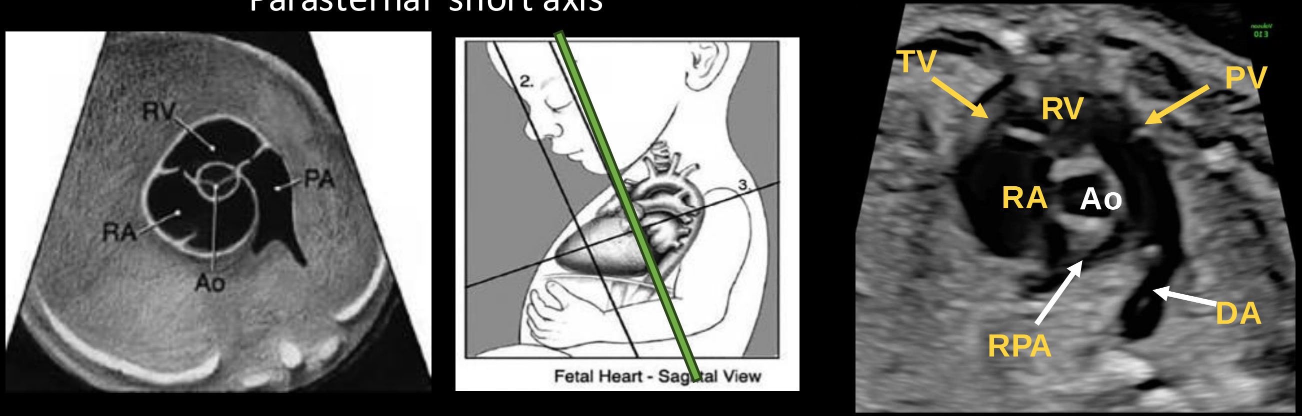


Parasternal Long axis

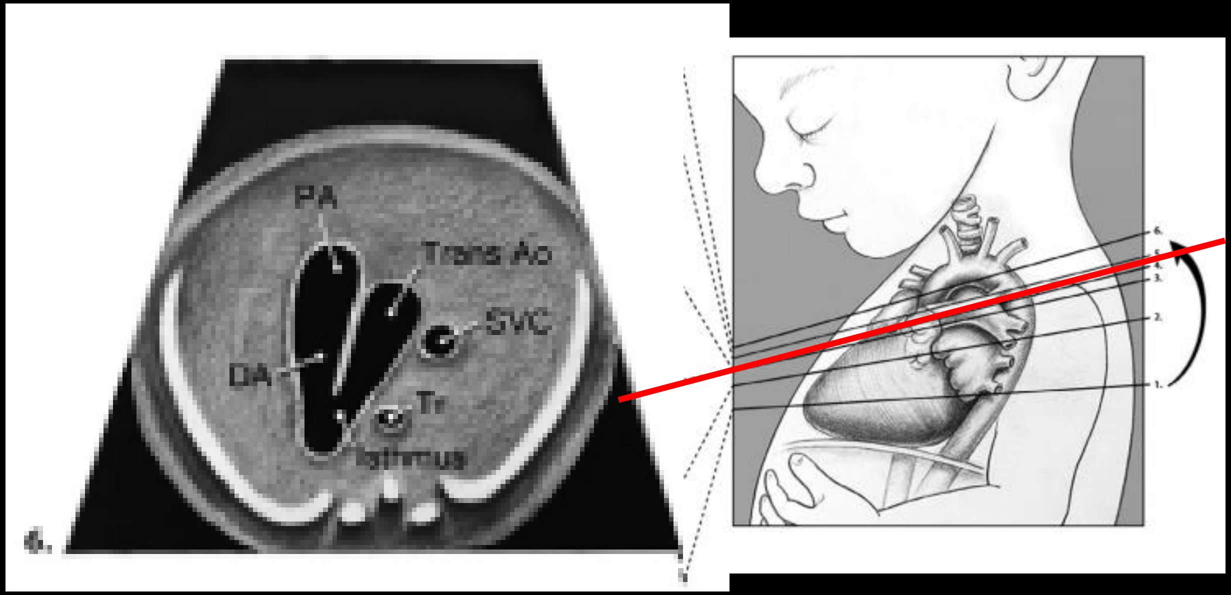




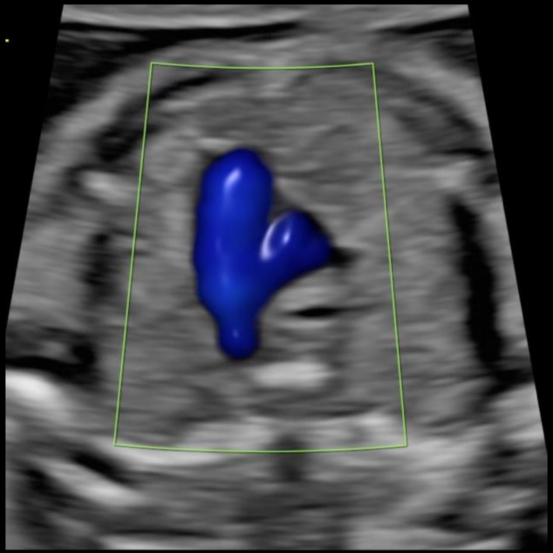
Parasternal short axis



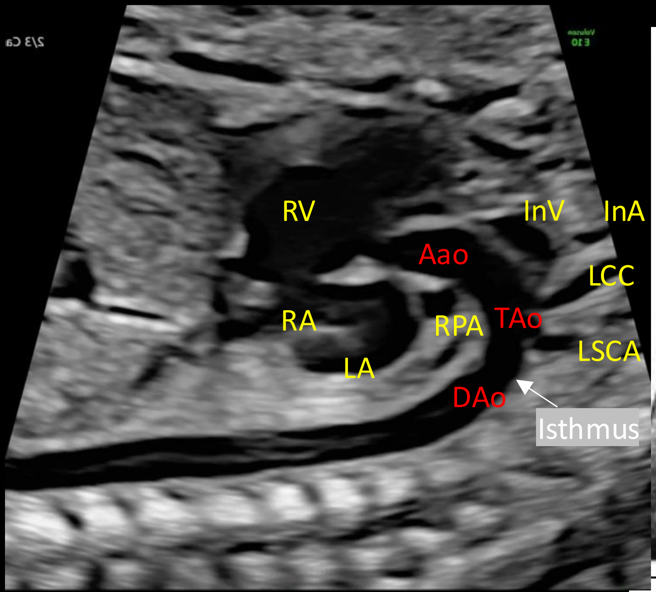
Aortic arch

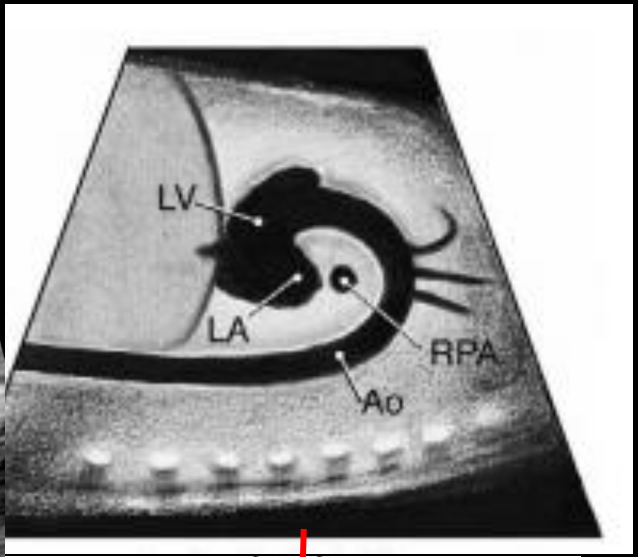


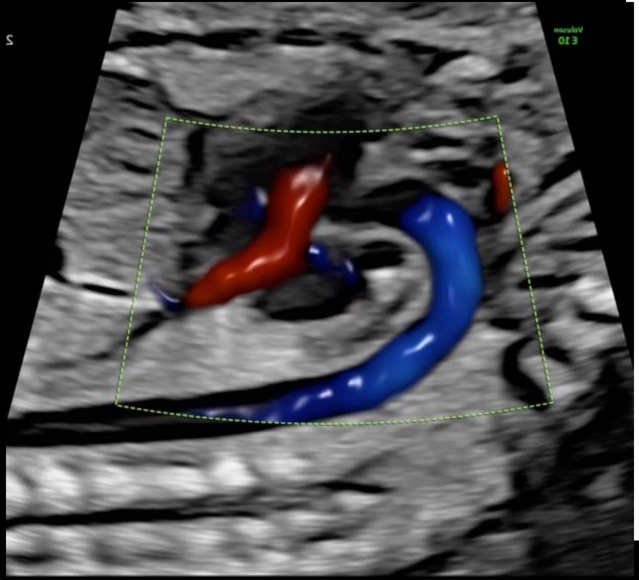
3VV

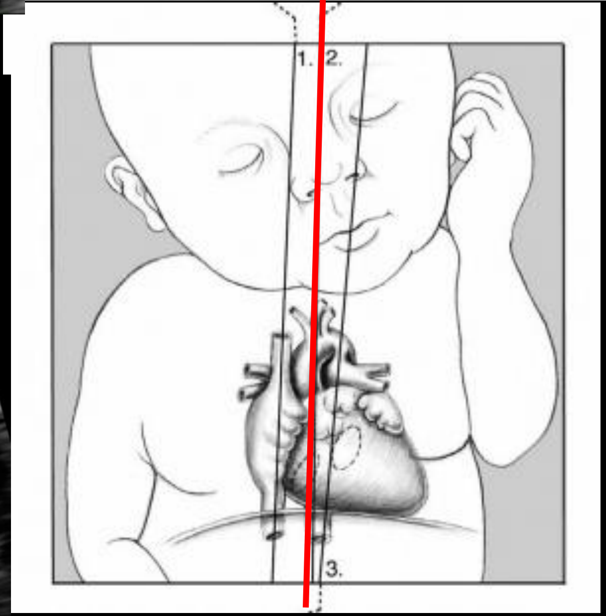


Aortic arch - Saggital









Aortic Stenosis

- Abnormal fusion of leaflets at the commissures resulting in two leaflets (bicuspid)
- Depending on degree of fusion and size of valve, varying degrees of stenosis

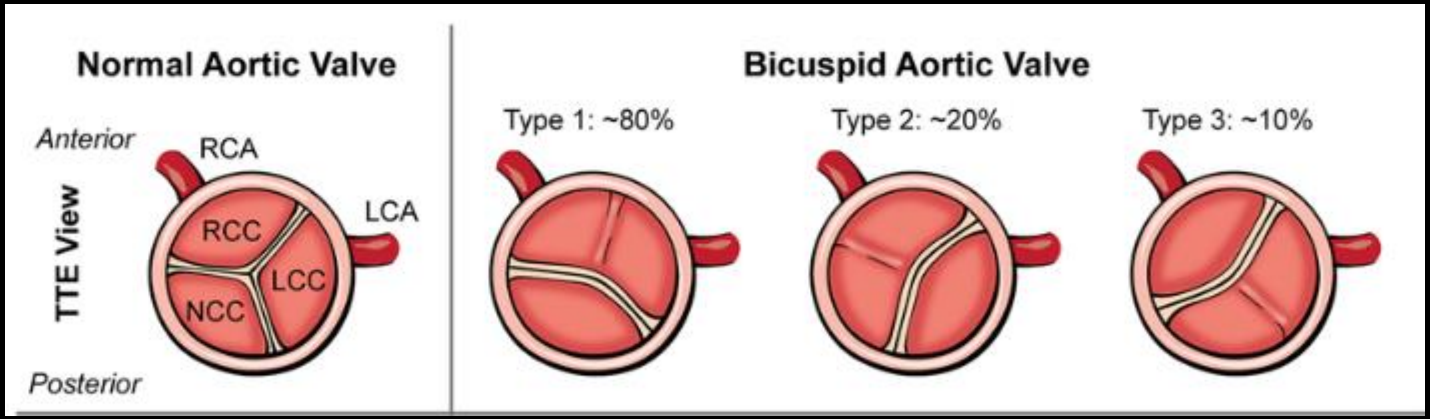
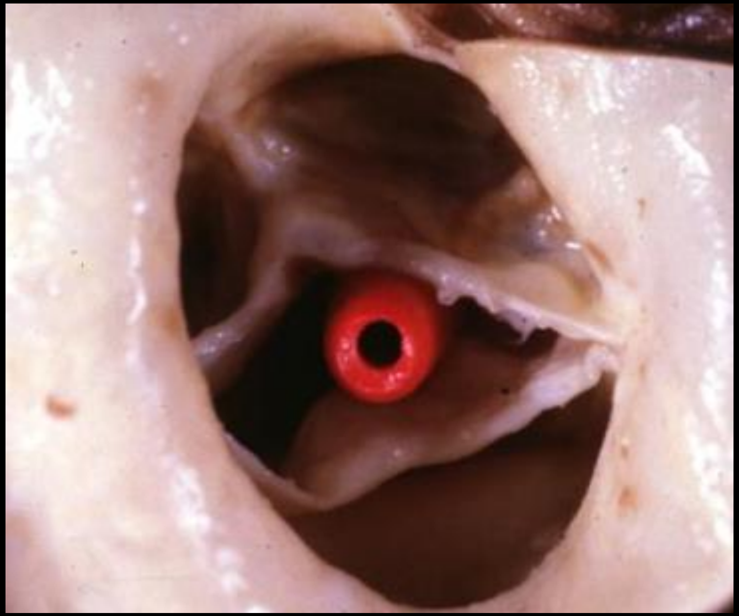
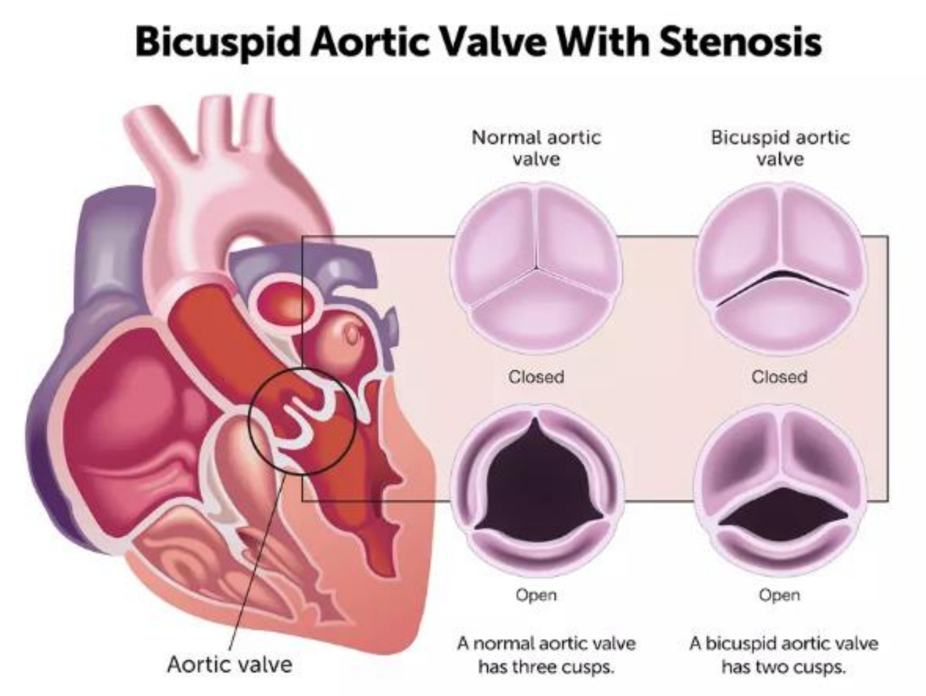


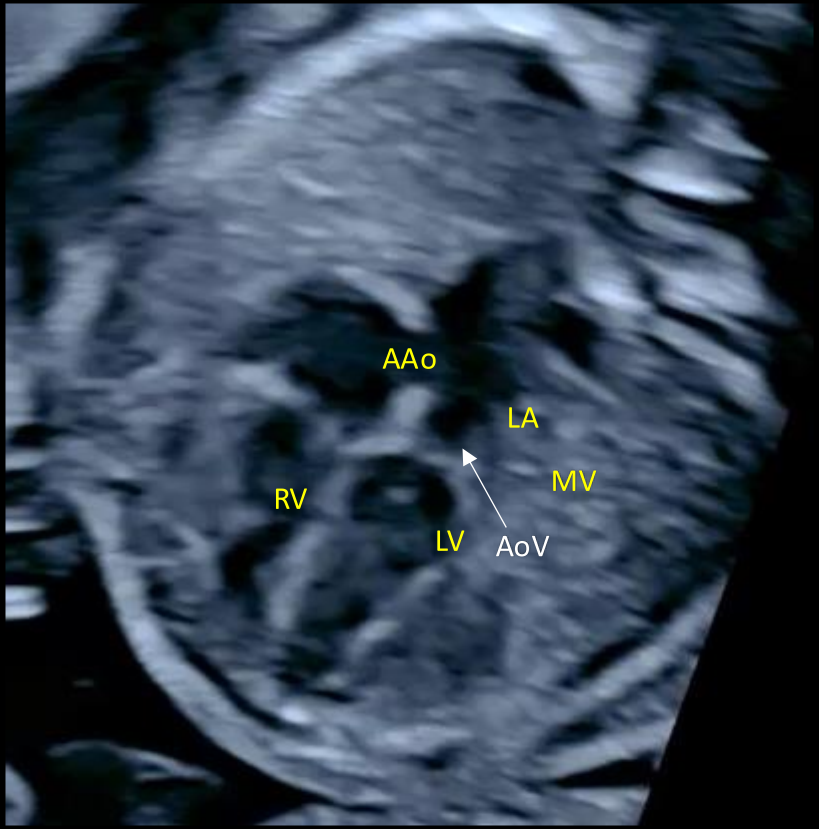
Image source: Rashed. Bicuspid Aortic Valves: an Up-to-Date Review on Genetics, Natural History, and Management. Current Cardiology Reports. 24. 1-10. 10.1007/s11886-022-01716-2.

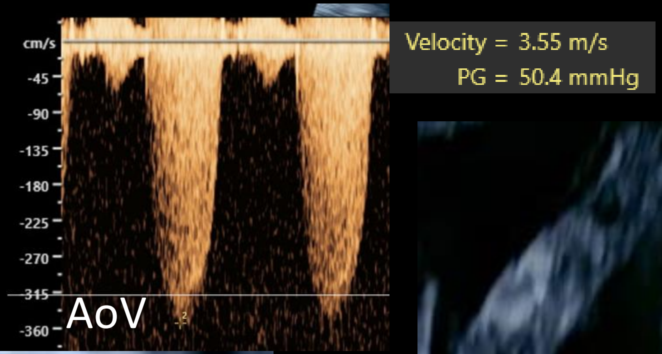


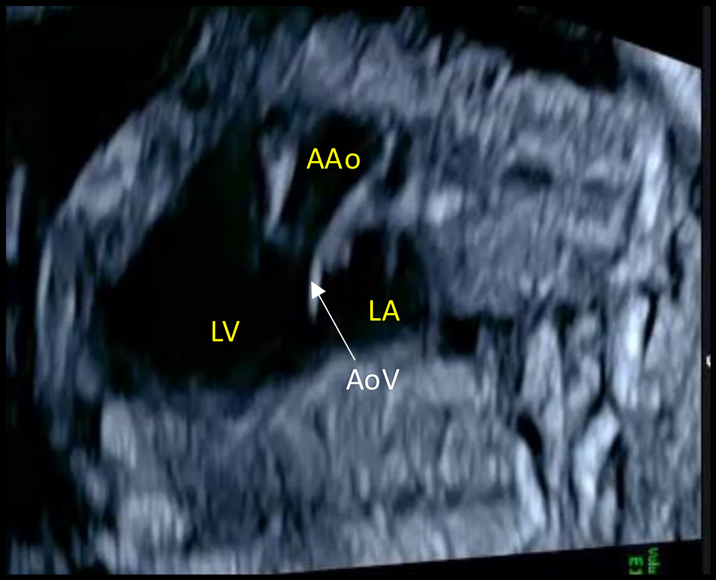


CASE: Critical Aortic Stenosis

Apical Long Axis







EGA: 20 weeks 1 day

Mitral Regurgitation/ Function

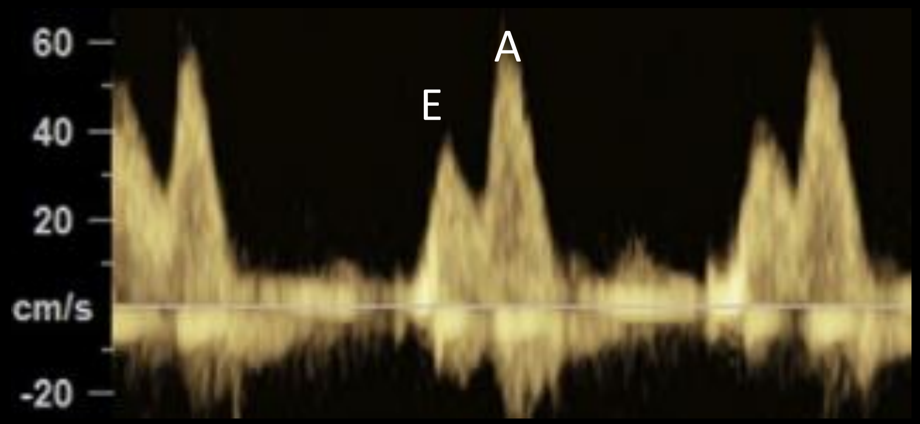
Severe LV dysfunction

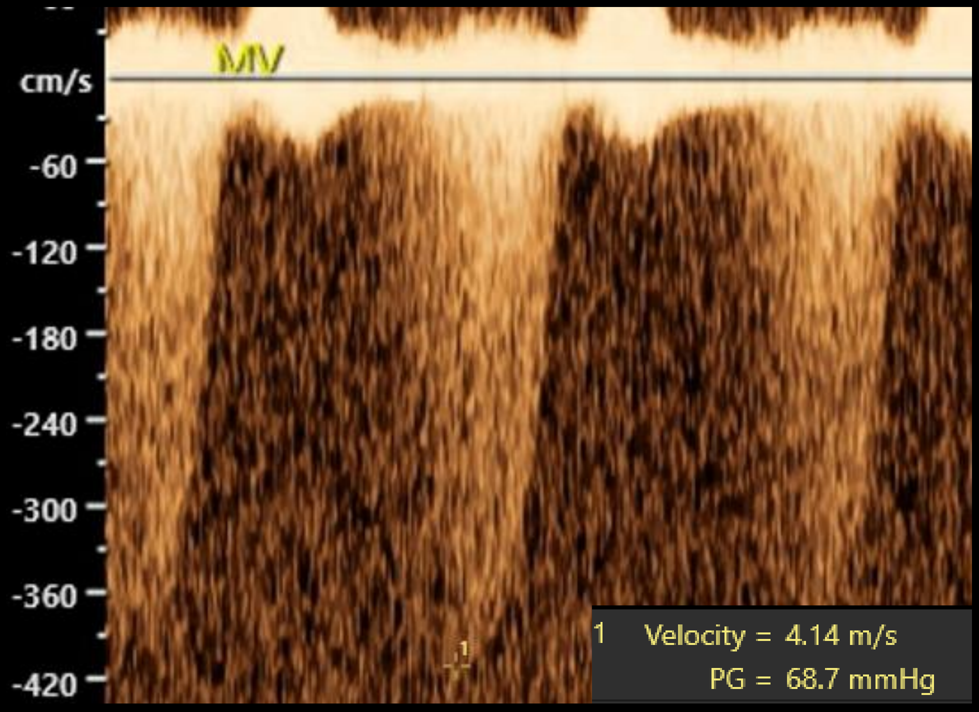
Mild-to-moderate MR

EGA: 20 weeks 1 day

- MR Velocity estimates LA-LV gradient
- Surrogate for LV function
- Able to generate very adequate “force”

Mitral valve inflow: Biphasic

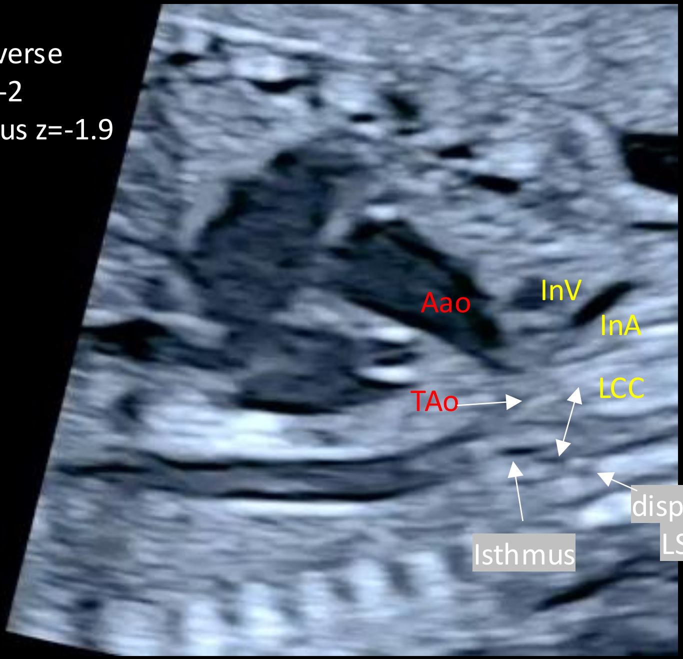




Mitral valve regurgitation

Aortic Arch

Transverse arch=-2
Isthmus z=-1.9



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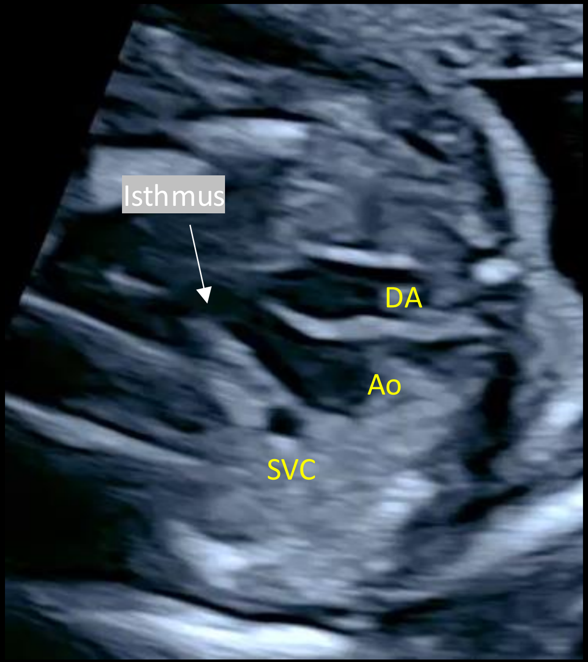
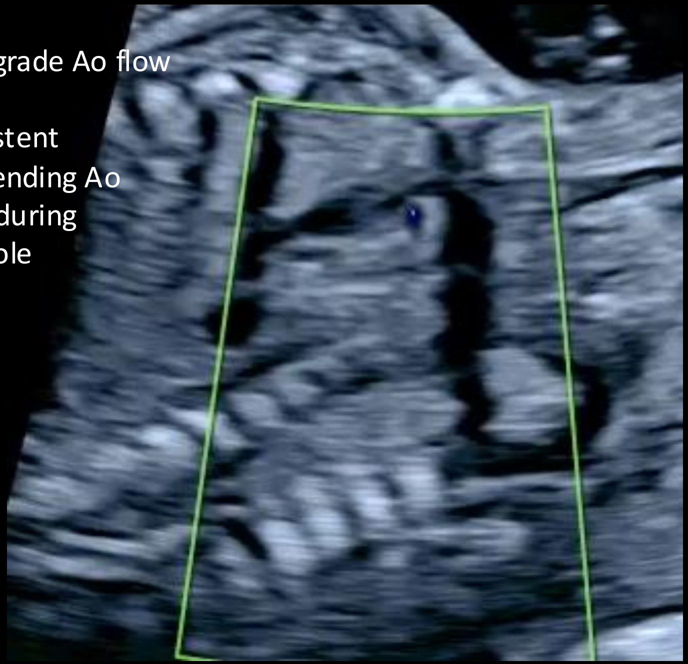


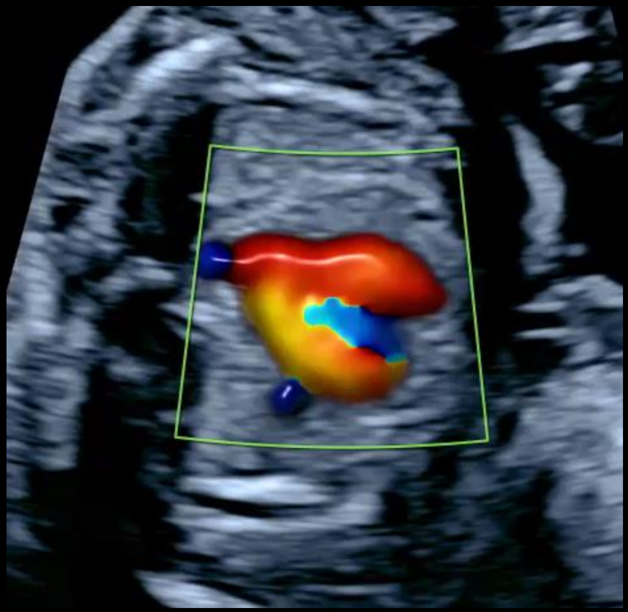
EGA: 20 weeks 1 day

- Aortic stenosis has high correlation with coarctation of the aorta
- Suspect coarctation with hypoplastic transverse arch/isthmus displaced left subclavian artery in sagittal view
- Disproportionate Ao:DA sizes in 3VV (not in this case)

Antegrade Ao flow

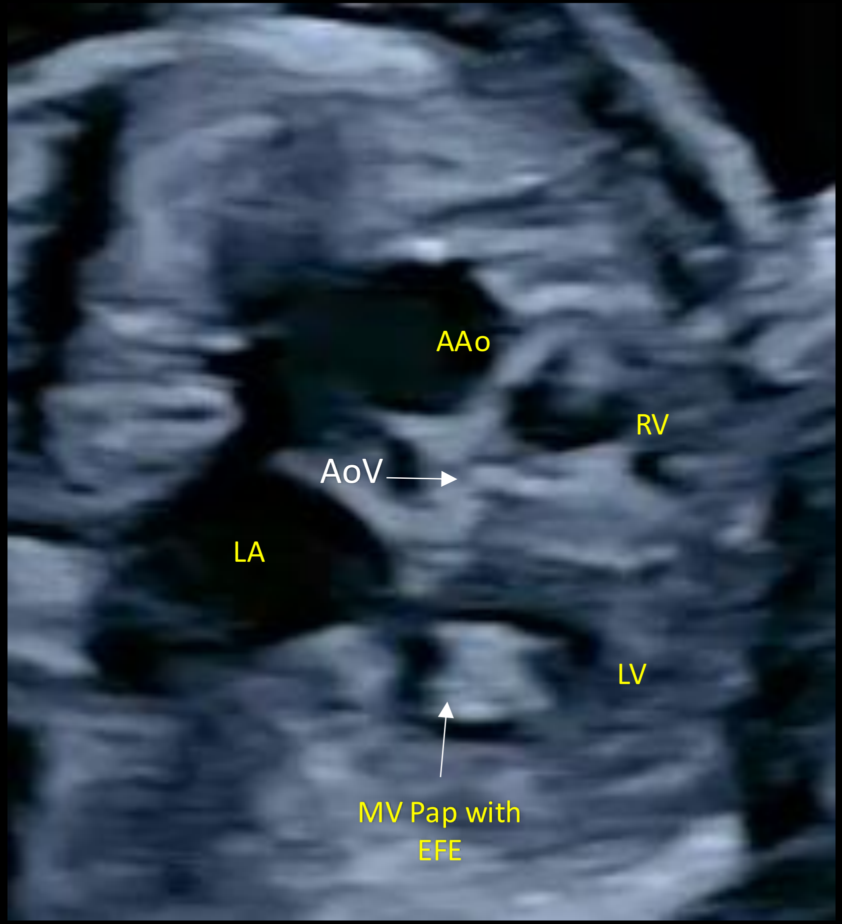
Persistent descending Ao flow during diastole



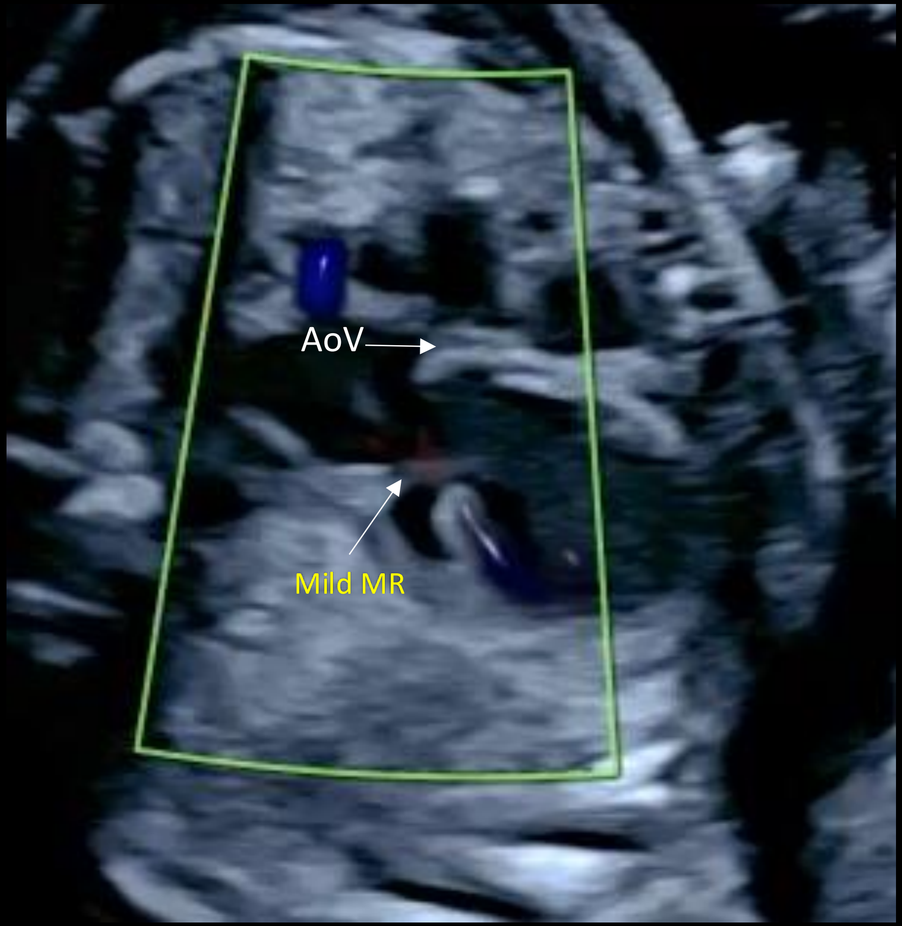


PFO bidirectional with left-to-right shunting

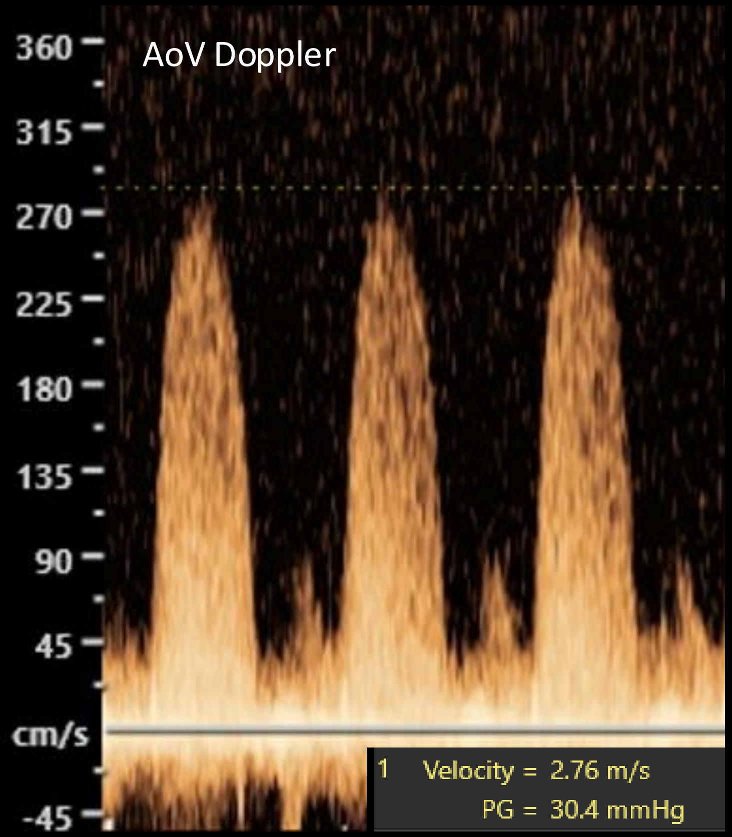
Follow up at EGA: 21 weeks 6 days



Aortic valve with very thickened leaflets/poor mobility
More dilated and "globular" LV under pressure
Dilated LA

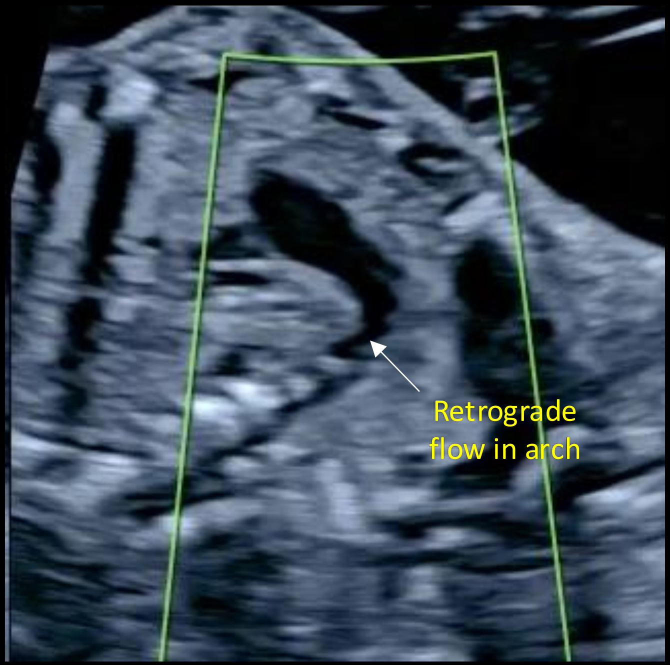


Severe Aortic stenosis by color
Narrowed color jet with aliasing
Mild MR (less than before)



AoV Vmax is less than previous
(Vmax=3.5 m/s; PG=50mmHg)
LV unable to generate as much
force/pressure
Worsening LV function

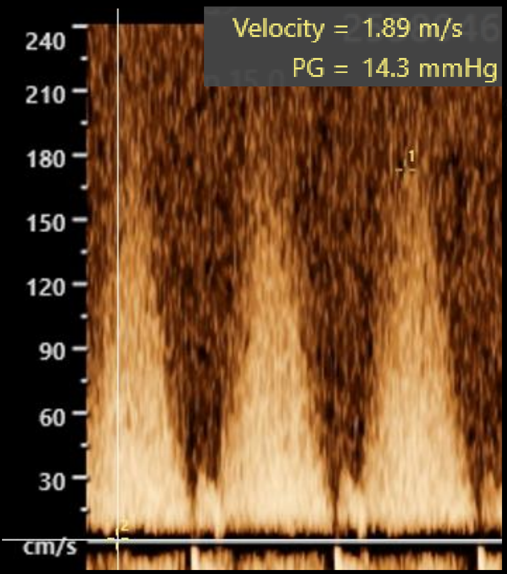
Follow up at EGA: 21 weeks 6 days



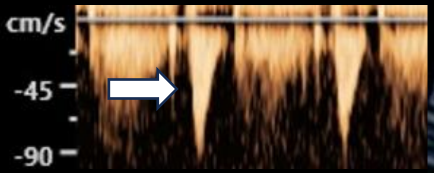
Descending aorta flow reversal due decreased AoV flow AND isthmus obstruction

Transverse arch fed retrograde by DA

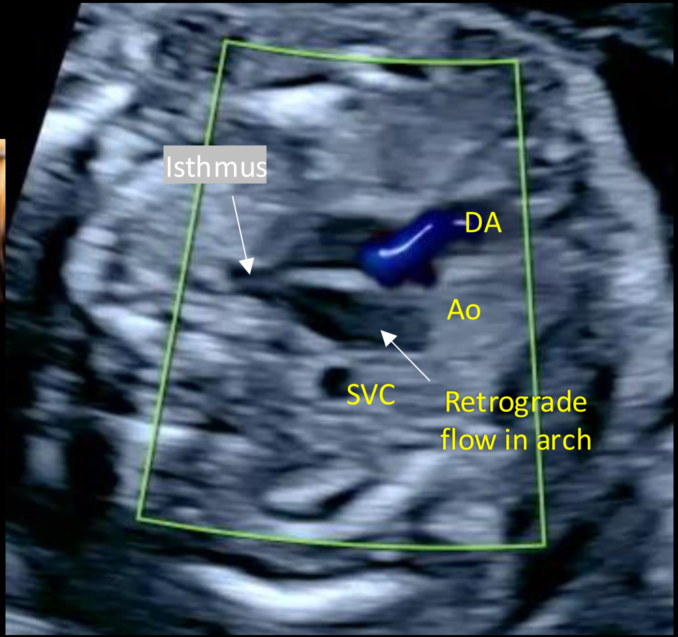
Less MR compared to previous (improved MR)
Sign of worsening LV systolic function
Unable to generate as much LV force



MV inflow monophasic = diastolic dysfunction



MR Vmax is less than previous (Vmax=4.1 m/s; PG=67mmHg)
Unable to generate as much force/pressure



ULTRASOUND in Obstetrics & Gynecology
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Valvuloplasty in 103 fetuses with critical aortic stenosis: outcome and new predictors for postnatal circulation

A. Tulzer, W. Arzt, R. Gitter, E. Sames-Dolzer, M. Kreuzer, R. Mair, G. Tulzer

First published: 04 October 2021 | https://doi.org/10.1002/uog.24792 | Citations: 15

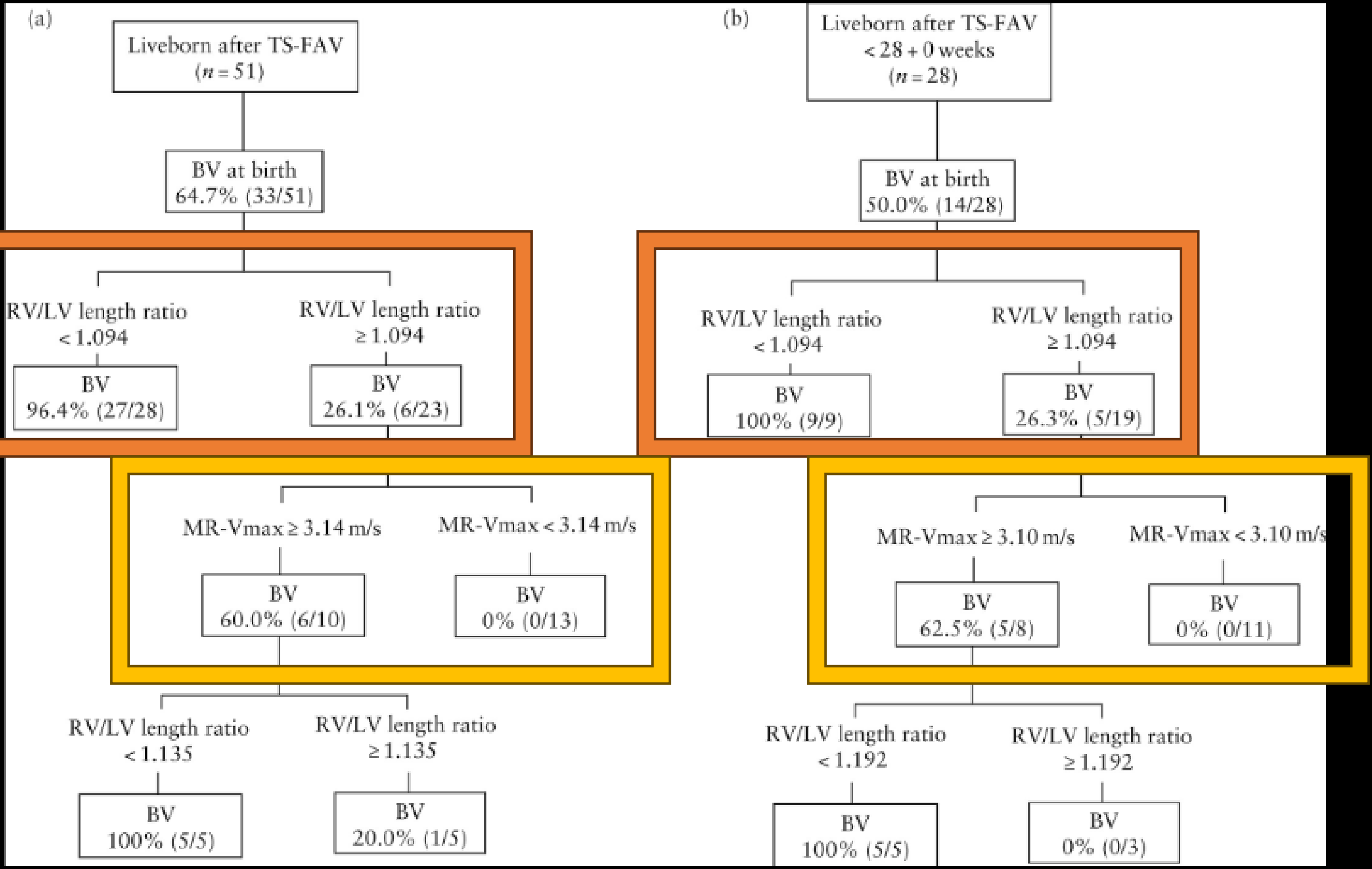

Table 2 Cohort size, procedure-related mortality and biventricular (BV) outcome in published studies on fetal aortic valvuloplasty (FAV)

Study	*Country*	*FAV cases (n)*	*Procedure-related mortality (%)*	*BV outcome (%)*
Friedman (2018)[3]	USA	123	4	58.7
Pedra (2014)[15]	Brazil	14	0	38.5
Debska (2020)[16]	Poland	88	8	No data
Galindo (2017)[18]	Spain	28	32	72.7
Patel (2020)[17]	IFCIR	108	17	42
Kovacevic (2018)[7]	European multicenter	67	10	36

Only first author is given for each study. IFCIR, international fetal cardiac intervention registry.

- Procedure related mortality = 4-32%
- BV outcome = 36-71%

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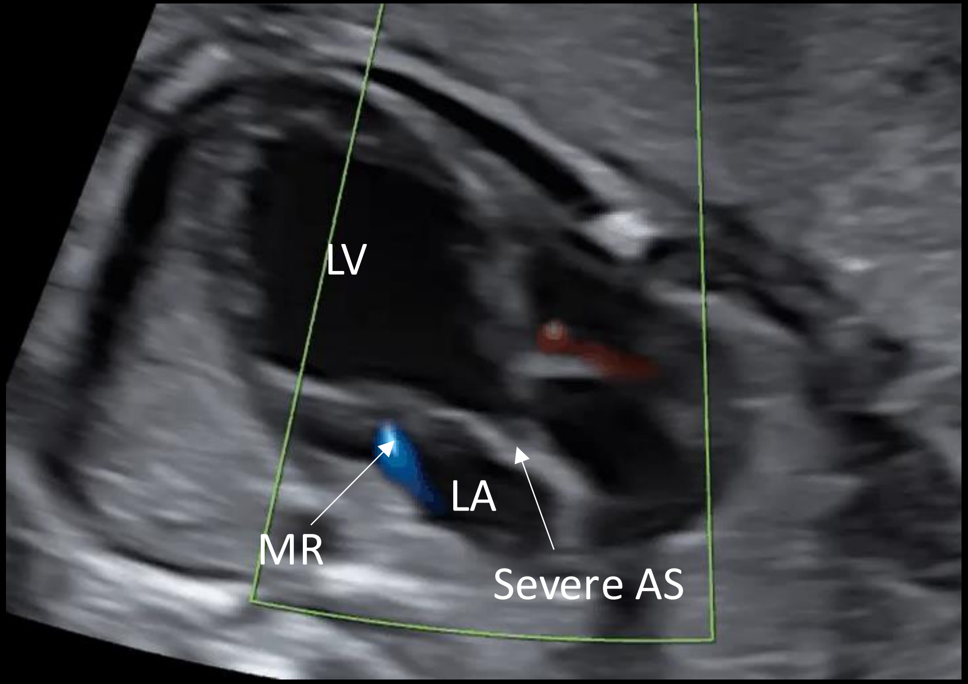
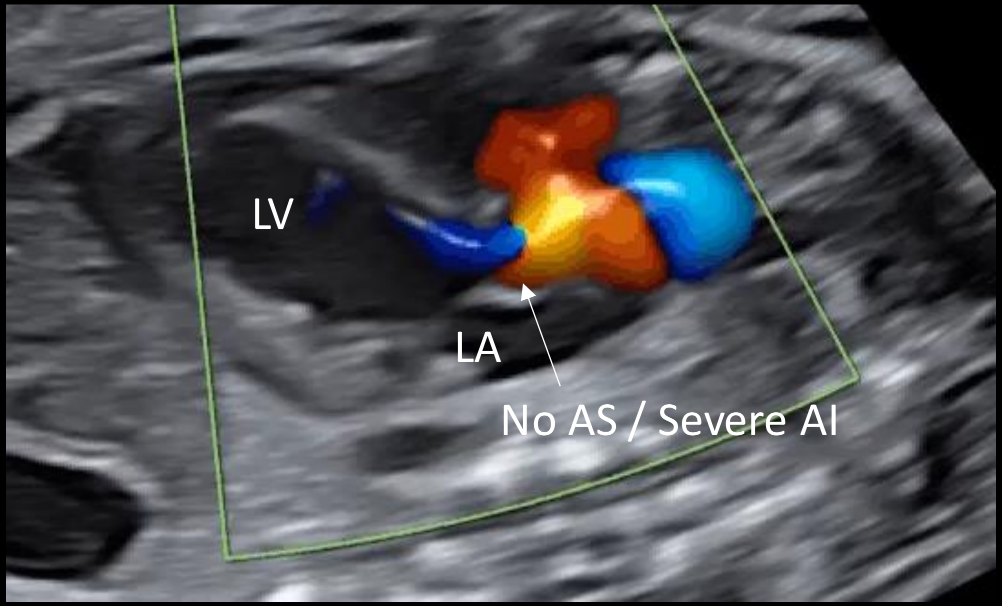
Improved technical success, postnatal outcome and refined predictors of outcome for fetal aortic valvuloplasty

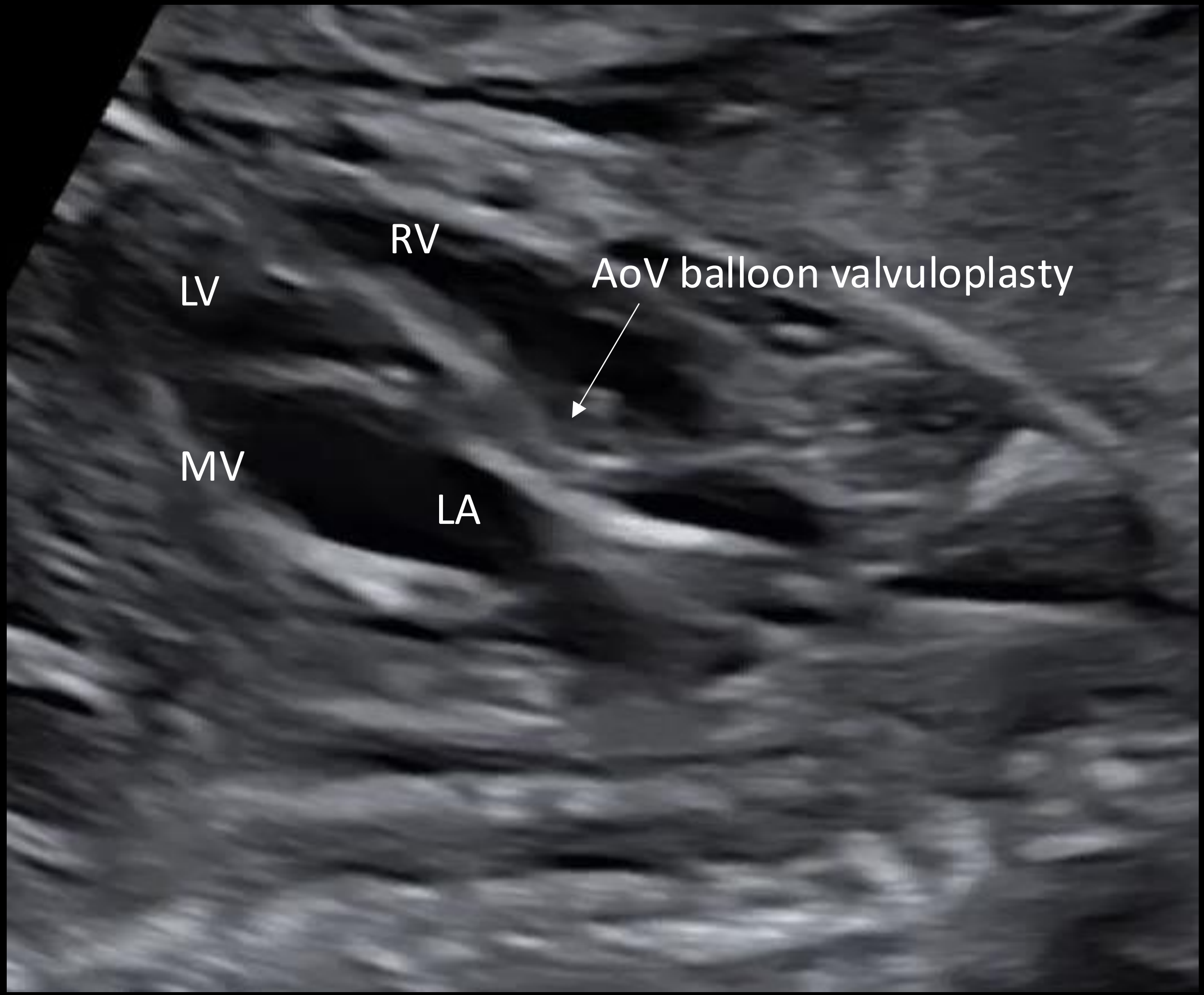
Predicting BiV with FAV
- AAo Z score >0.6
- MV inflow time Z score > -2.6
- MV dimension Z score > 1.5
- LV pressure >47 mm Hg

Fetal aortic valve balloon valvuloplasty

EGA 22 weeks 2 days





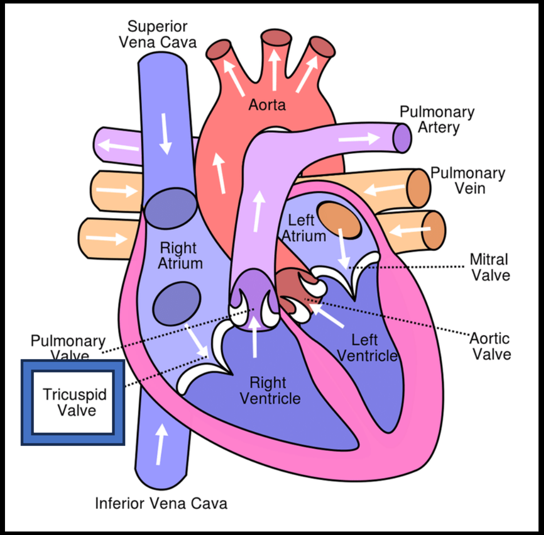


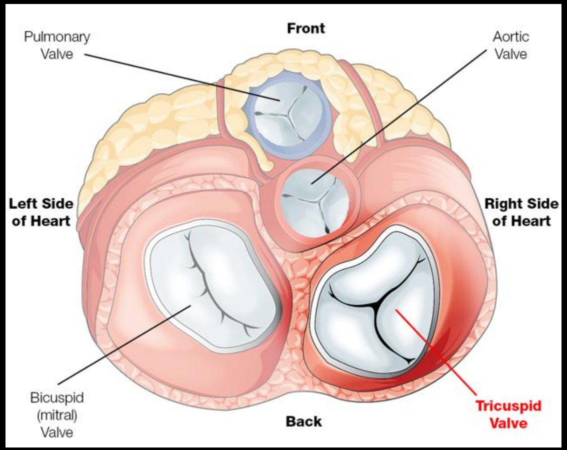
Take up for critical aortic stenosis

- As LV becomes less capable of supporting systemic circulation, pathophysiologic changes occur
  - Monophasic MV inflow
  - Left to right flow at PFO
  - Flow reversal in transverse arch
  - LV dilation, EFE, and LV systolic dysfunction
- These features are **common to those who evolve into HLHS** thus are used to identify potential candidates for Fetal Aortic Valvuloplasty
- Prompt referral to fetal cardiologist to assess for need for intervention at specialized center for certain candidates

Tricuspid Valve Anatomy

- Normal anatomy with three leaflets
  - Anterior, posterior, septal
- Connects right atrium and RV
- TV/RV usually more rightward and anterior compared to MV/LV
- Normally, TV slightly more apically displaced than MV





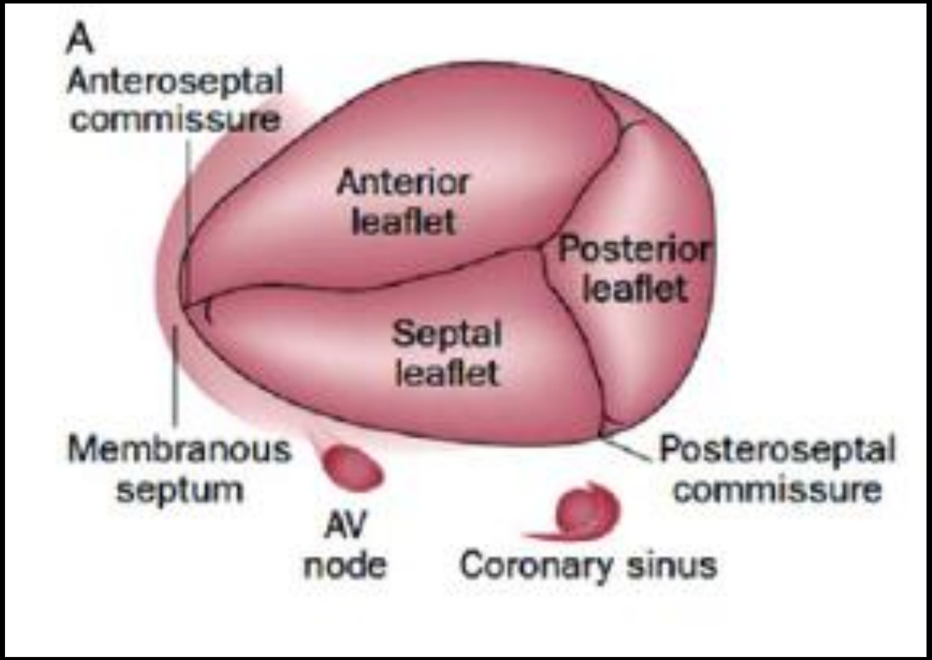
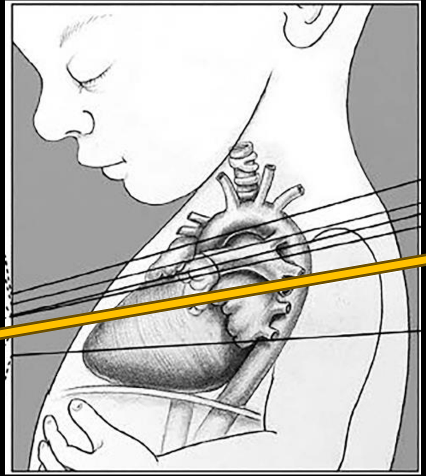
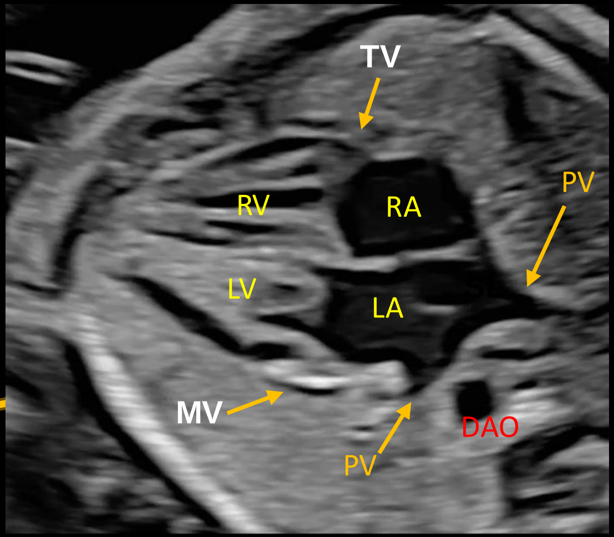


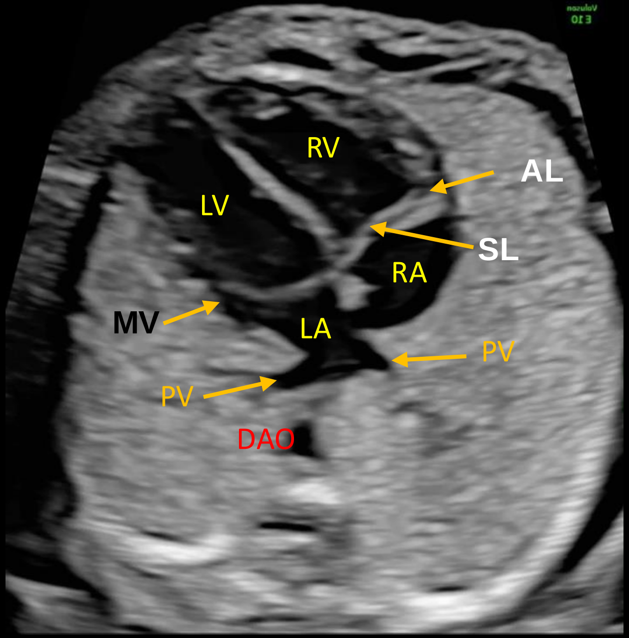
Image source: https://ctsurgerypatients.org/adult-heart-disease/tricuspid-valve-disease

Tricuspid Valve

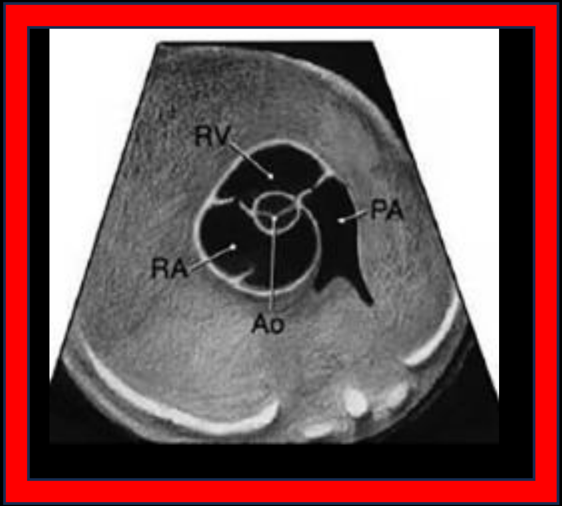
Apical 4 chamber

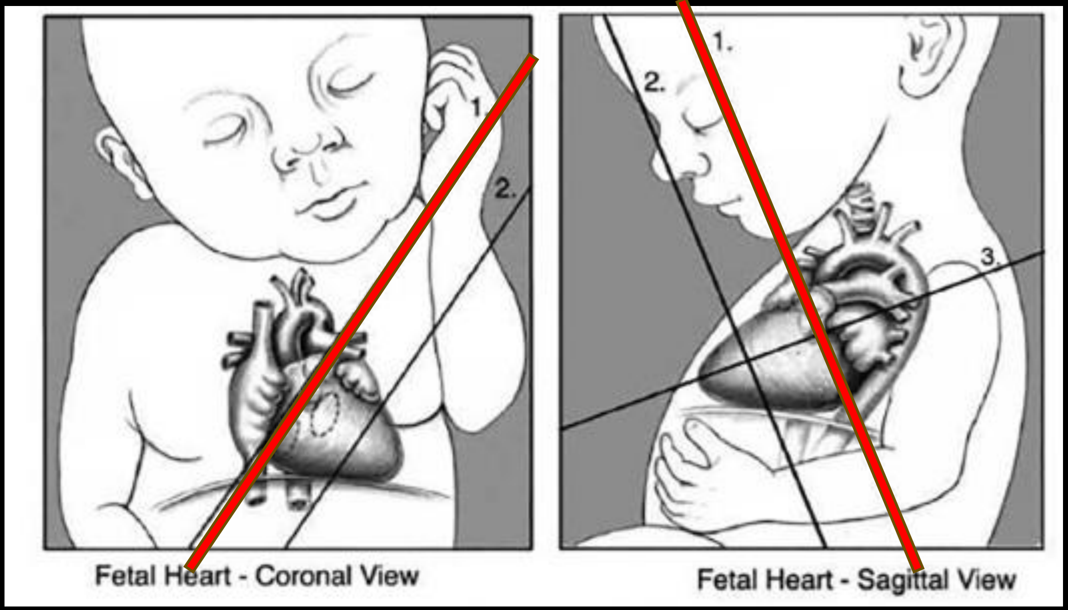






Parasternal Short Axis





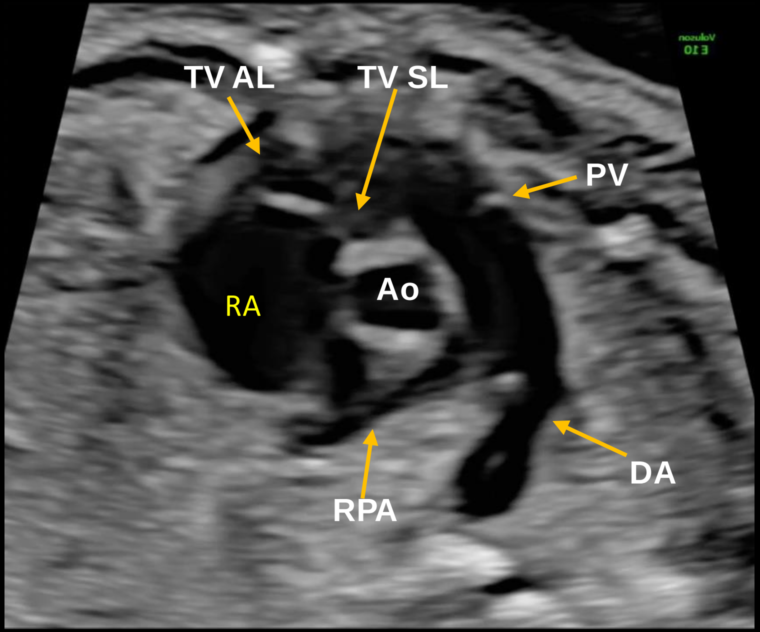


Image Source: Gotteiner, N.L. (2023). Fetal Echocardiography. In: Abdulla, Ri., *et al*. Pediatric Cardiology.

Normal tricuspid valve embryology

Image source: Echocardiography in Pediatric and Congenital Heart Disease: From Fetus to Adult
Editor(s):Wyman W. Lai MD, MPH,, Luc L. Mertens MD, PhD,, Meryl S. Cohen MD,, Tal Geva MD,
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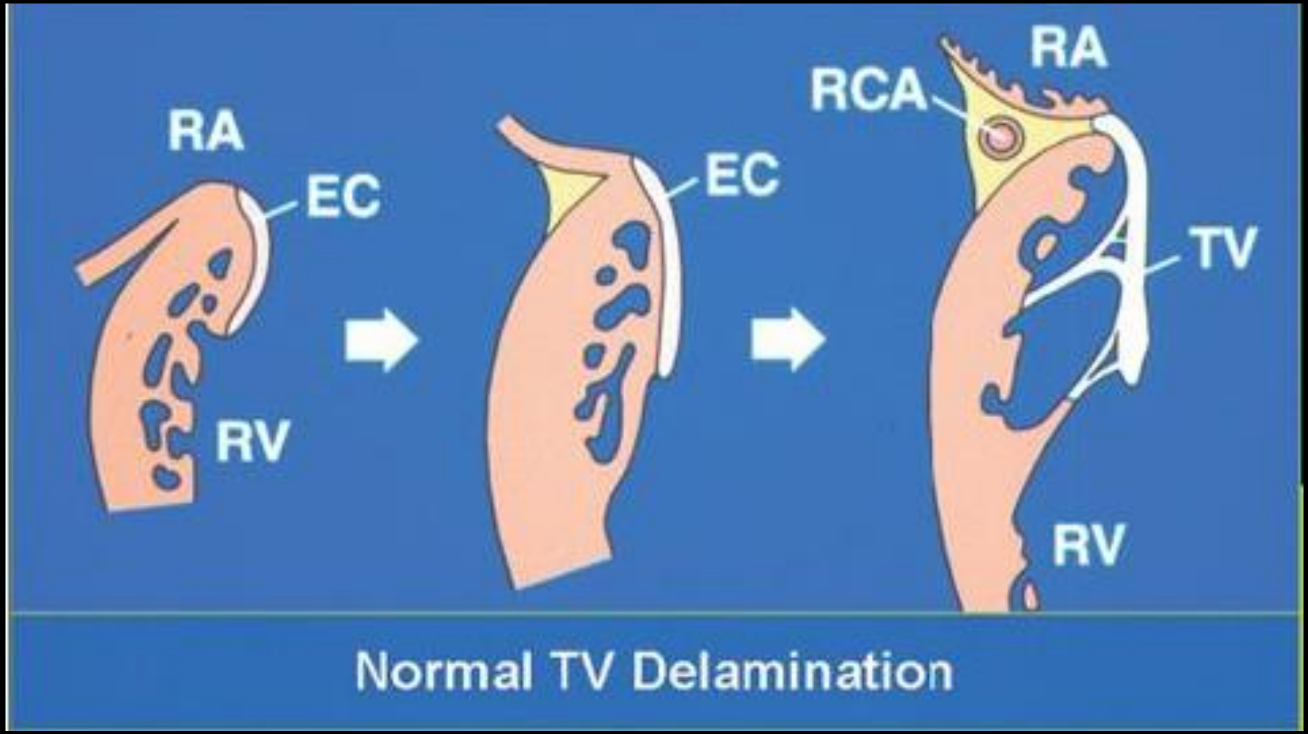
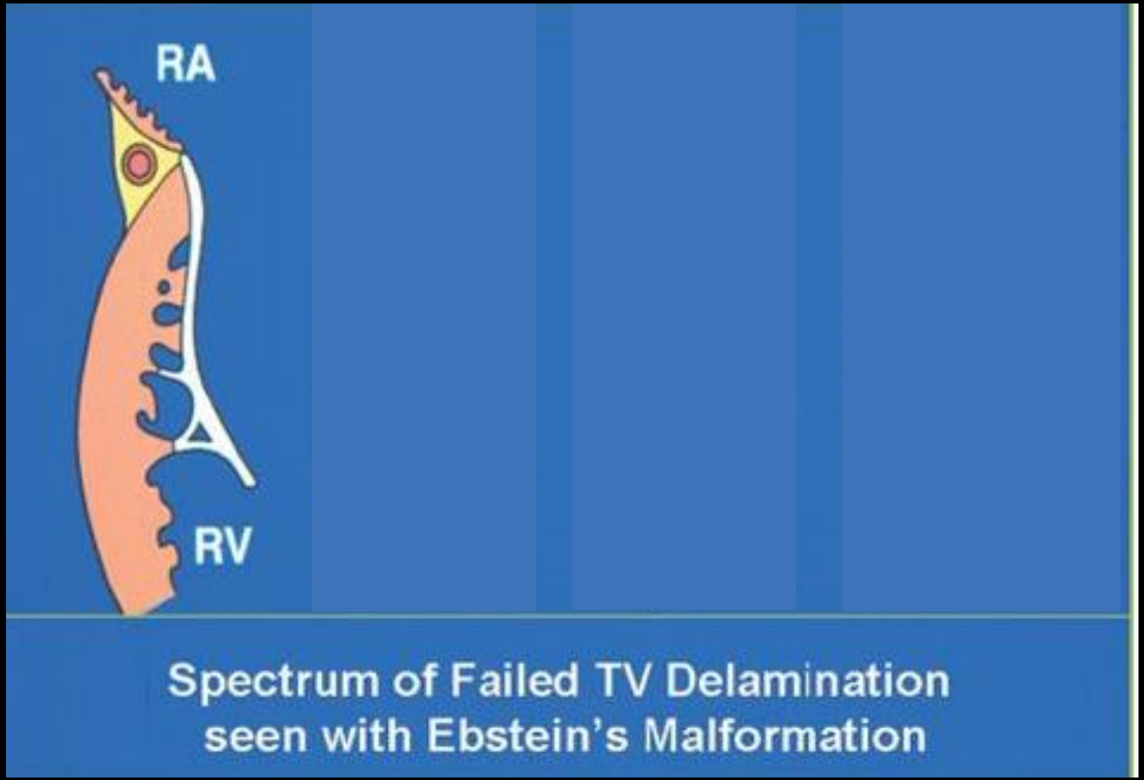
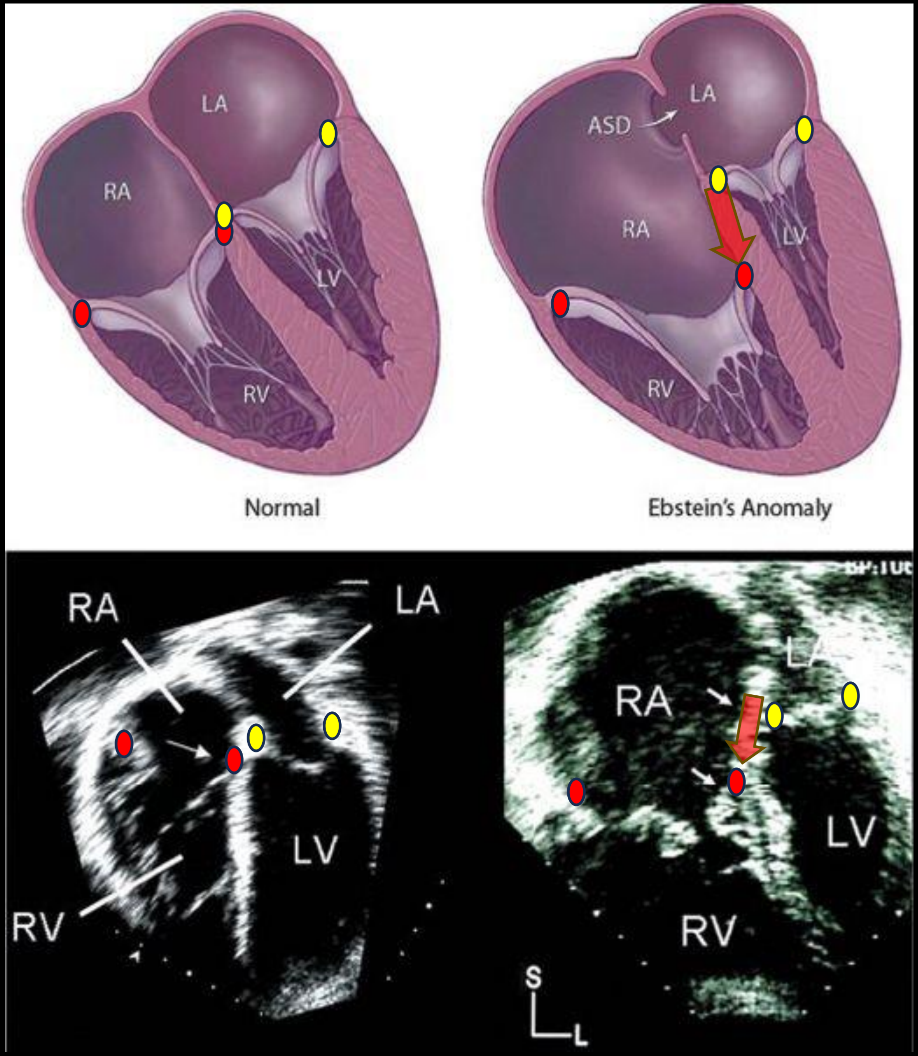


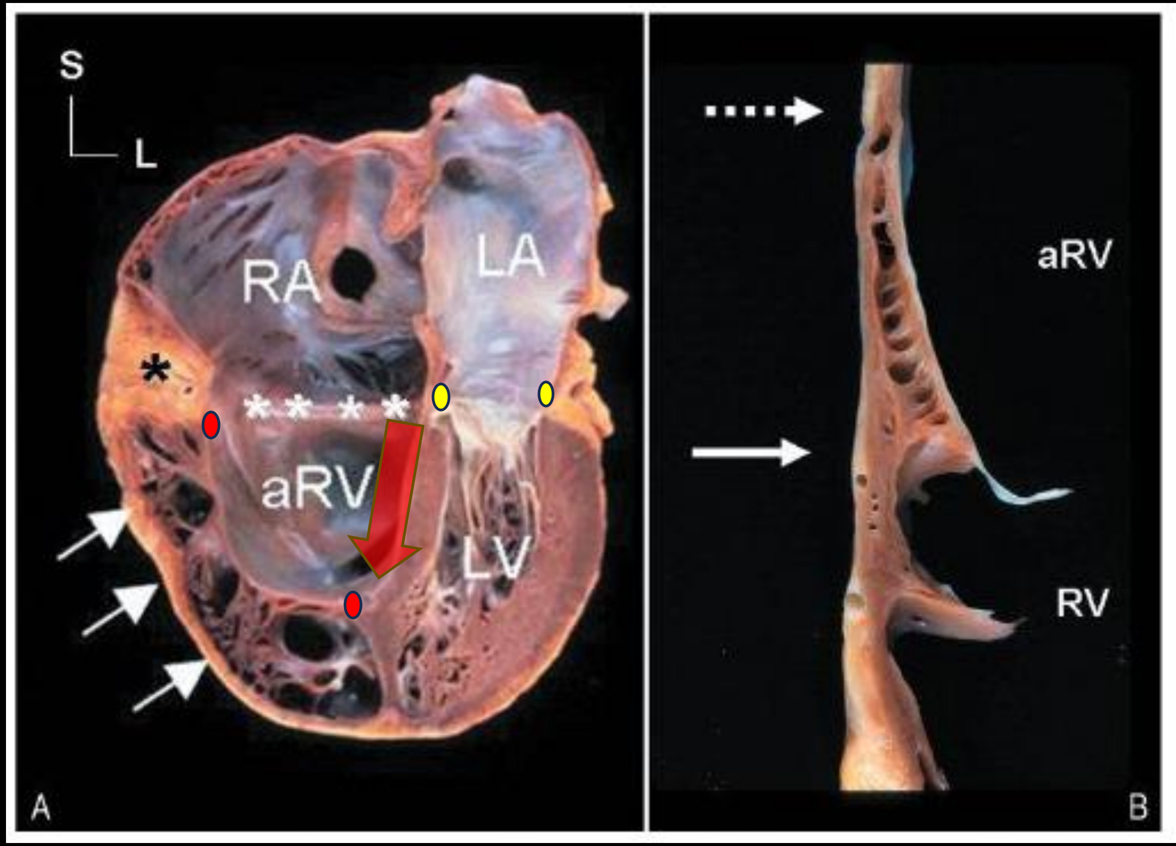


Tricuspid valve anomalies



Ebstein Anomaly

- AV valve leaflets are formed from delamination from ventricular myocardium
- Ebstein anomaly: failure of TV leaflet to delaminate properly.
- SL is most affected and delamination defect = <u>apical displacement of tricuspid valve</u>



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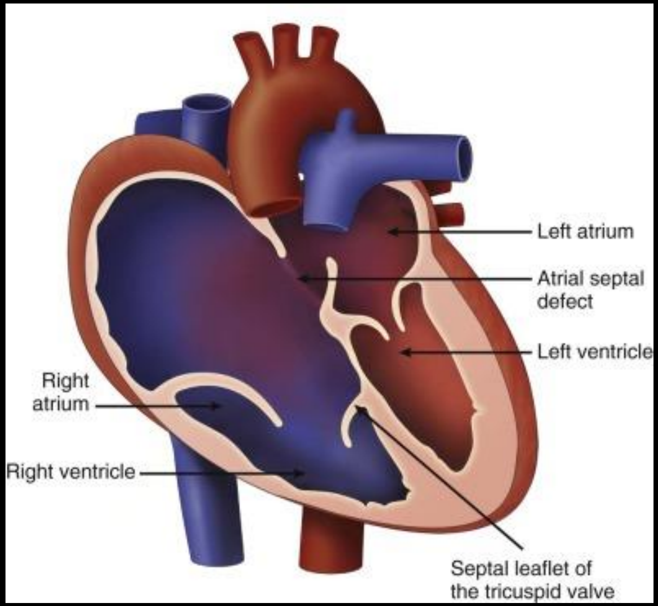
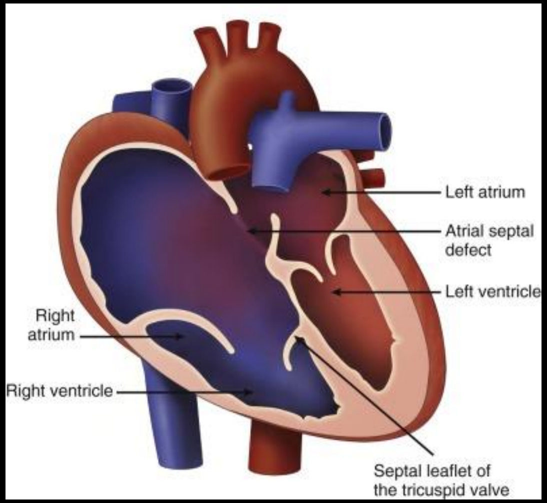


Abnormal tricuspid valve leaflets (sail like anterior leaflets and poor delaminated "tethered" septal leaflet) →poor <u>coaptation</u> → tricuspid regurgitation

Normal

Ebstein Anomaly



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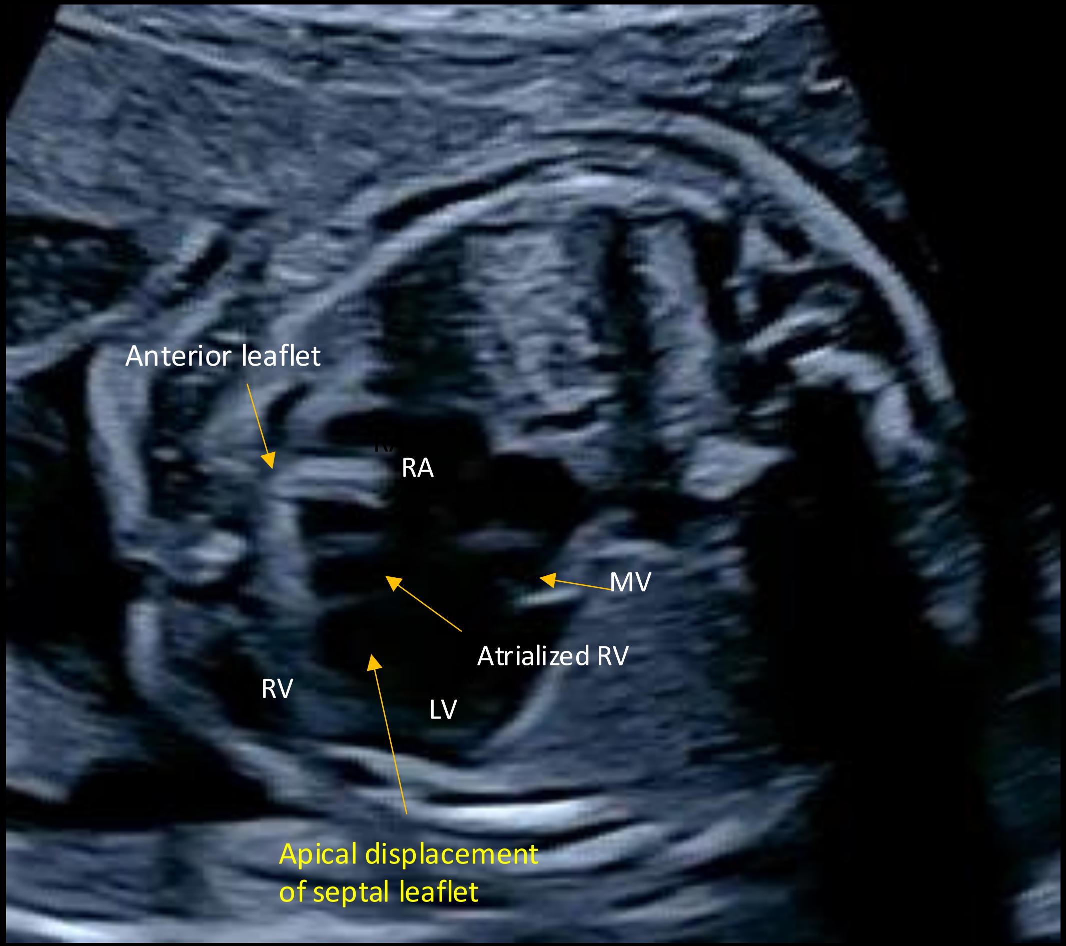
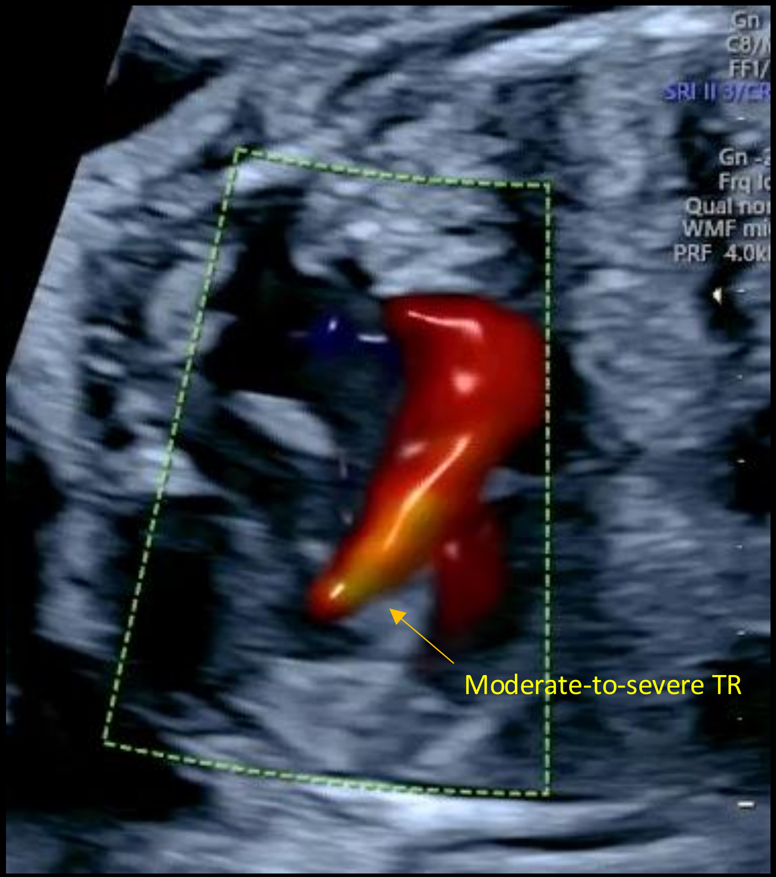
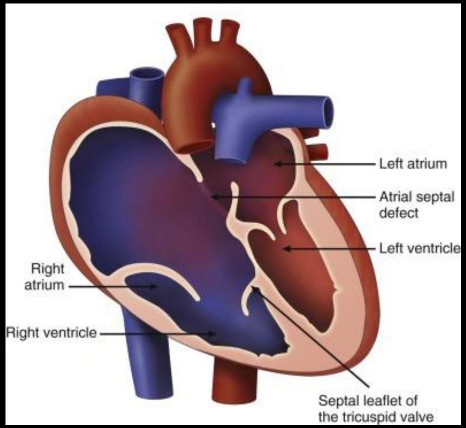


Severe TV annulus dilation
Displacement of SL
Severely dilated RA



TR jet vena contracta starts much more apically

Ebstein Anomaly



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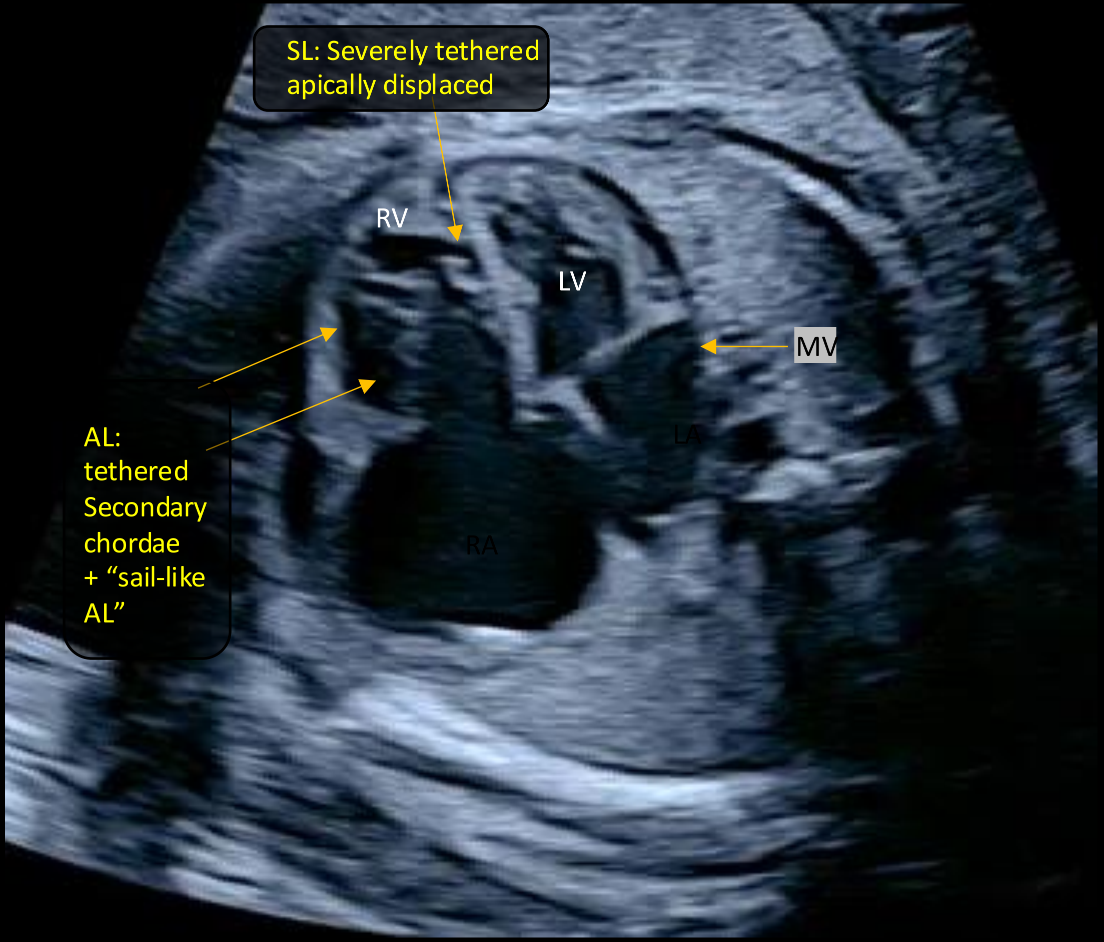
Severe Ebsteins Anomaly



Severe tricuspid regurgitation

Circulation

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RESEARCH ARTICLE | Originally Published 9 June 2015 | Check for updates

Outcomes and Predictors of Perinatal Mortality in Fetuses With Ebstein Anomaly or Tricuspid Valve Dysplasia in the Current Era: A Multicenter Study

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Circulation • Volume 132, Number 6 • https://doi.org/10.1161/CIRCULATIONAHA.115.015839

	Nonsurvivors (n=54)	Survivors (n=106)	Unadjusted UVA OR (95% CI)	Unadjusted UVA *P* Value
GA at last fetal echocardiogram, wk	33.4±2.6	34.6±2.4	0.80 (0.69–0.93)	0.003
CTA ratio‡ (n=152)	0.53±0.1	0.45±0.1	1.9‡ (1.4–2.6)	<0.001
≥ Moderate TR‡ (n=160)	49 (91)	79 (75)	3.2 (1.2–9.0)	0.02
TV annulus diameter z-score	6.5±2.9	4.9±3.0	1.2 (1.1–1.3)	0.002
TR jet velocity,‡ m/s (n=110)	2.3±0.7	3.0±0.7	0.23 (0.12–0.47)	<0.001
No antegrade PV flow‡ (n=159)	39 (74)	49 (46)	3.2 (1.5–6.5)	0.002
Retrograde duct flow‡ (n=157)	47 (89)	62 (60)	5.3 (2.1–13.5)	<0.001
Pulmonary regurgitation	24 (44)	27 (26)	2.4 (1.2–4.7)	0.016
Depressed RV function	33 (61)	36 (34)	3.1 (1.6–6.0)	0.001
Depressed LV function	21 (39)	15 (14)	3.9 (1.8–8.4)	<0.001
Pericardial effusion	24 (44)	26 (25)	2.5 (1.2–4.9)	0.01
Hydrops	12 (22)	7 (7)	4.0 (1.5–11.0)	0.006

Comparative Study > Am J Cardiol. 2008 Apr 1;101(7):1046-50.
doi: 10.1016/j.amjcard.2007.11.049. Epub 2008 Feb 6.

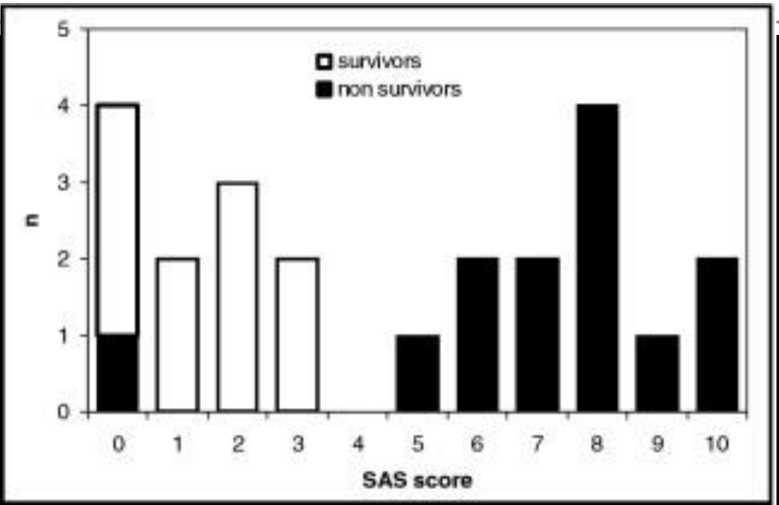
Prediction of outcome of tricuspid valve malformations diagnosed during fetal life

Rachel E Andrews [1], Shane M Tibby, Gurleen K Sharland, John M Simpson

Affiliations + expand
PMID: 18359329 DOI: 10.1016/j.amjcard.2007.11.049

Table 2. Prognostic (SAS) score

	Weighting		
Variable	0	1	2
Cardiothoracic ratio	<0.65	0.65–0.75	>0.75
Celermajer index	<1.0	1.0–1.5	>1.5
Pulmonary valve flow	Normal	Reduced	Absent
Duct flow	Anterograde	Both	Retrograde
Right–left ventricular Ratio	<1.5	1.5–2.0	>2.0

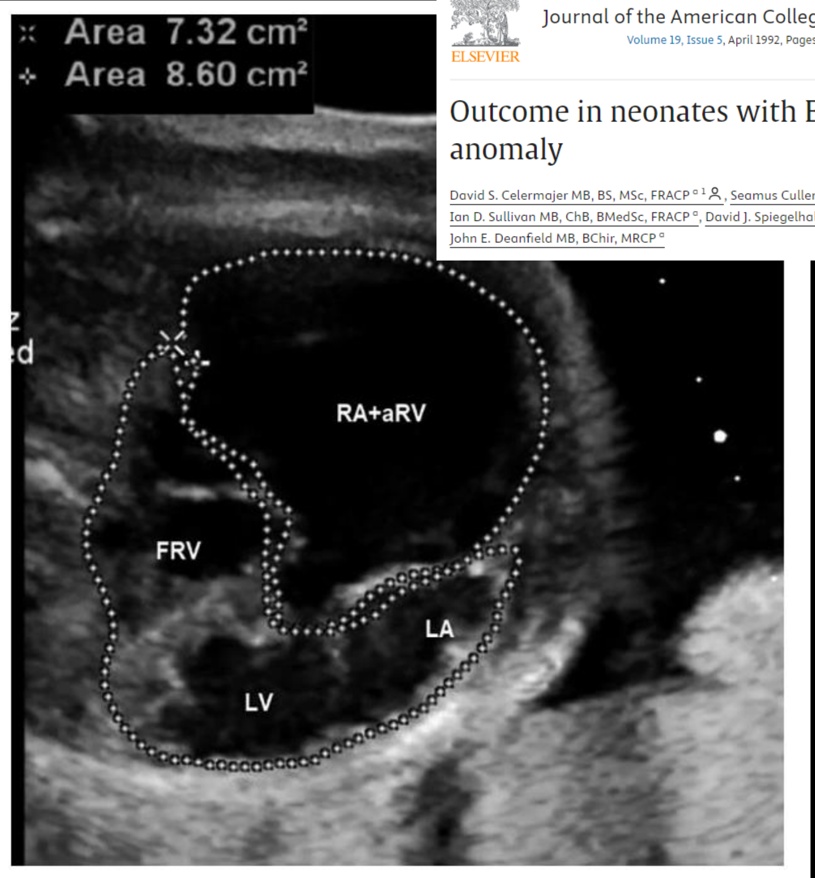


SAS SCORE >4 = 100% mortality rate

ELSEVIER Journal of the American College of Cardiology
Volume 19, Issue 5, April 1992, Pages 1041-1046

Outcome in neonates with Ebstein's anomaly

David S. Celermajer MB, BS, MSc, FRACP [a][1], Seamus Cullen MB, ChB, MRCPI [a], Ian D. Sullivan MB, ChB, BMedSc, FRACP [a], David J. Spiegelhalter PhD [*], Richard K.H. Wyse PhD [a], John E. Deanfield MB, BChir, MRCP [a]

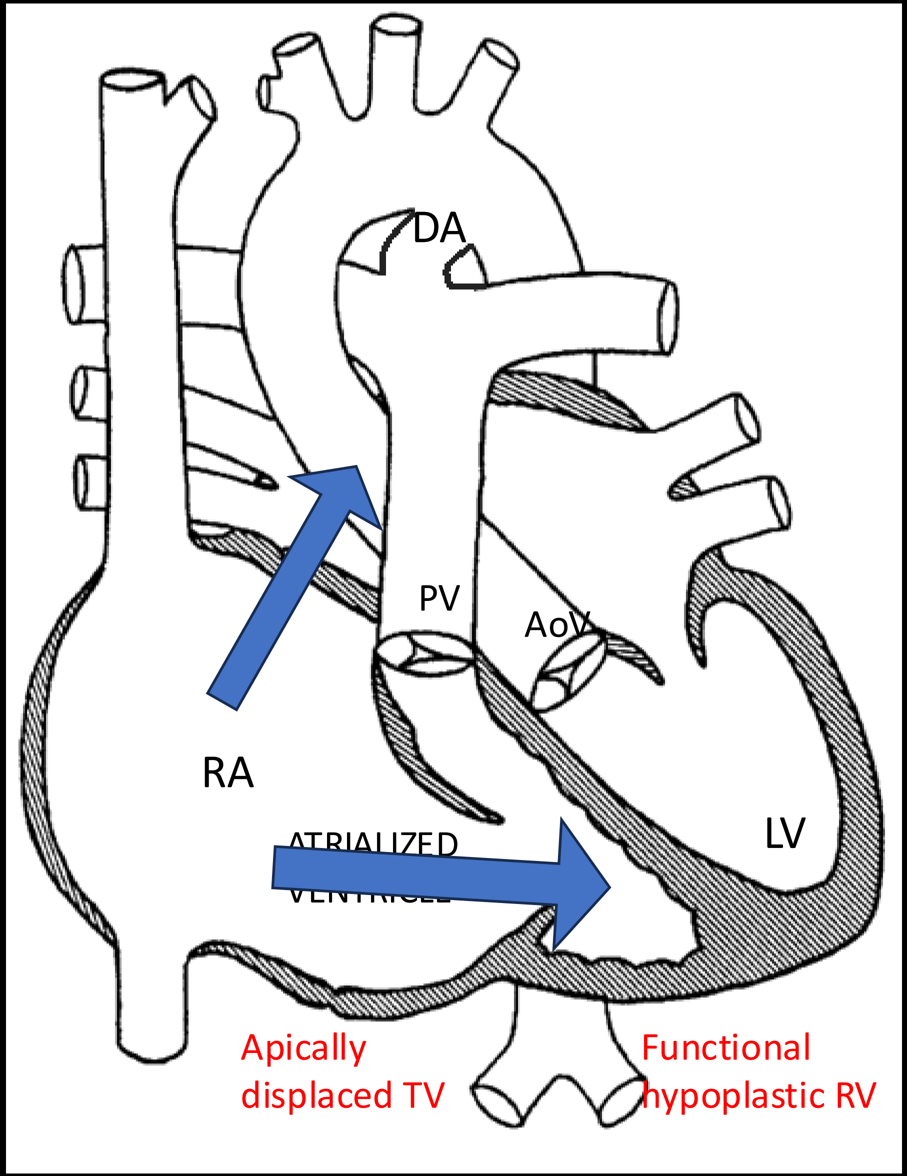


Celermajer index at end-diastole: combined area of the right atrium (RA) and atrialized right ventricle (aRV)/the combined area of the functional right ventricle (FRV) + left atrium (LA) + LV (left ventricle). This fetus had an index of 1.17

Table 3. Echocardiographic Features in 28 Neonates With Ebstein's Anomaly

Grade	RA + aRV Ratio*	No. of Patients	Cardiac Deaths
1	<0.5	4	0†
2	0.5 to 0.99	10	1 (10%)
3	1 to 1.49	9	4 (44%)
4	≥1.5	5	5 (100%)

Ebstein Anomaly physiology

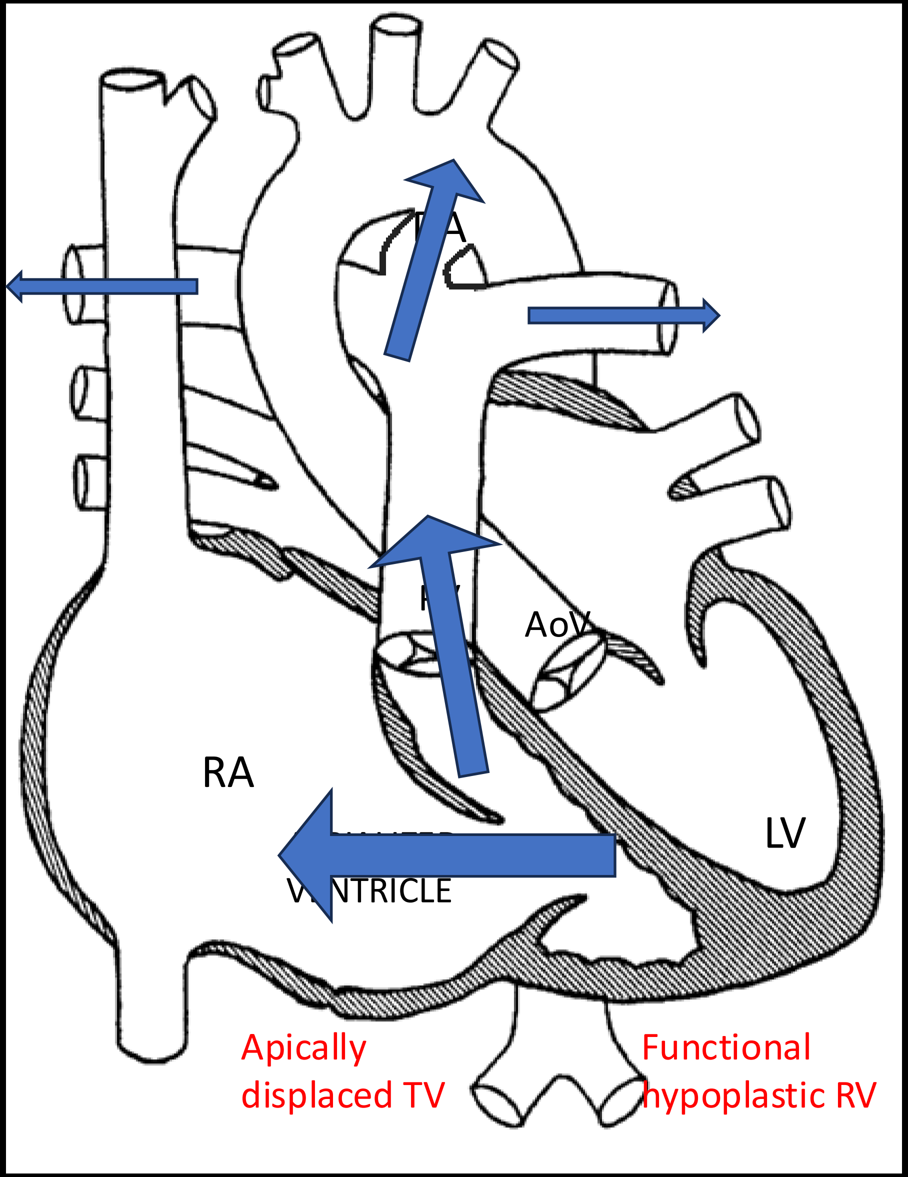


<u>Diastole</u>

Antegrade flow to TV

PFO with right to left shunting

Ebstein Anomaly physiology



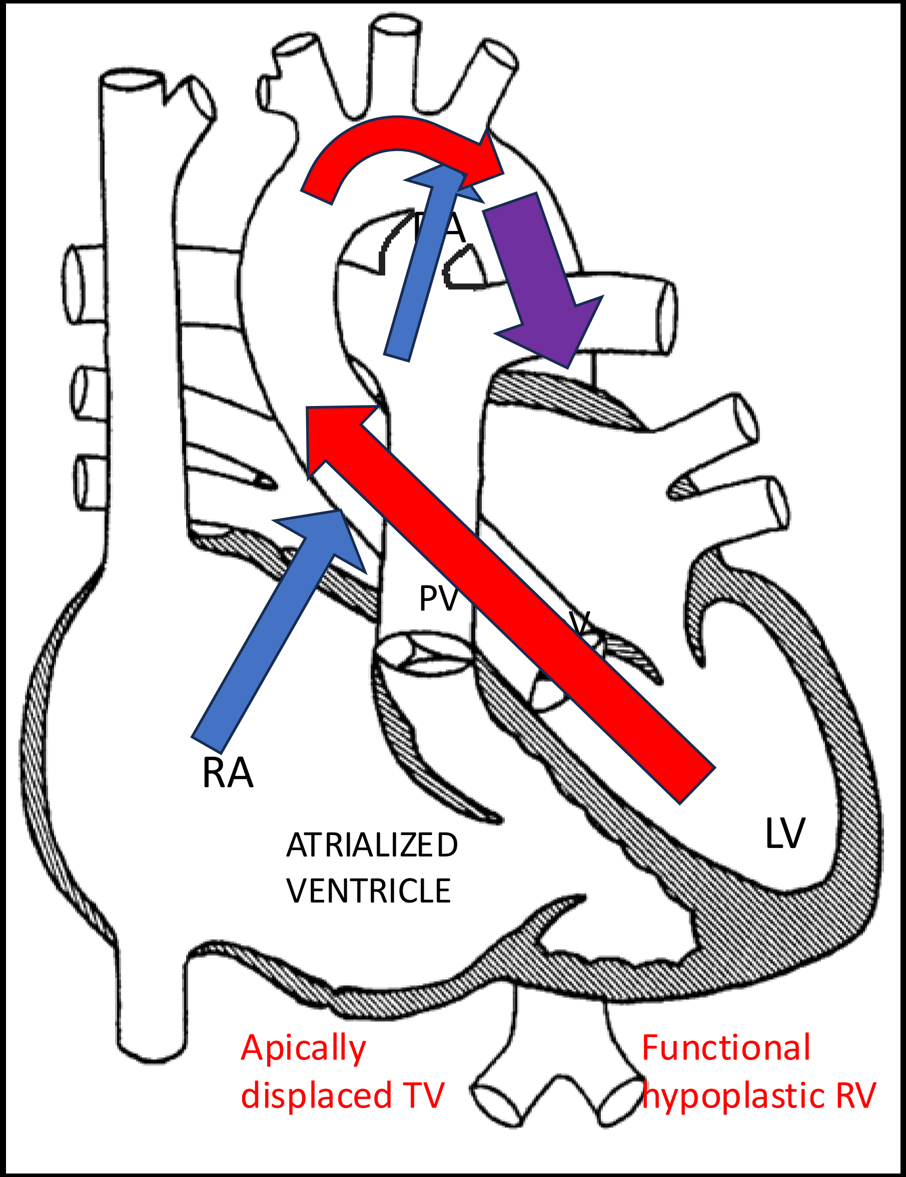
Systole

Severe TR (retrograde flow through TV)

Antegrade flow through PV into branch PA and DA

DA with right to left flow (PA to Ao)

Ebstein Anomaly physiology



<u>Systole</u>

Severe TR (retrograde flow through TV)

Antegrade flow through PV into branch PA and DA

DA with right to left flow (PA to Ao)

Antegrade flow through aortic valve

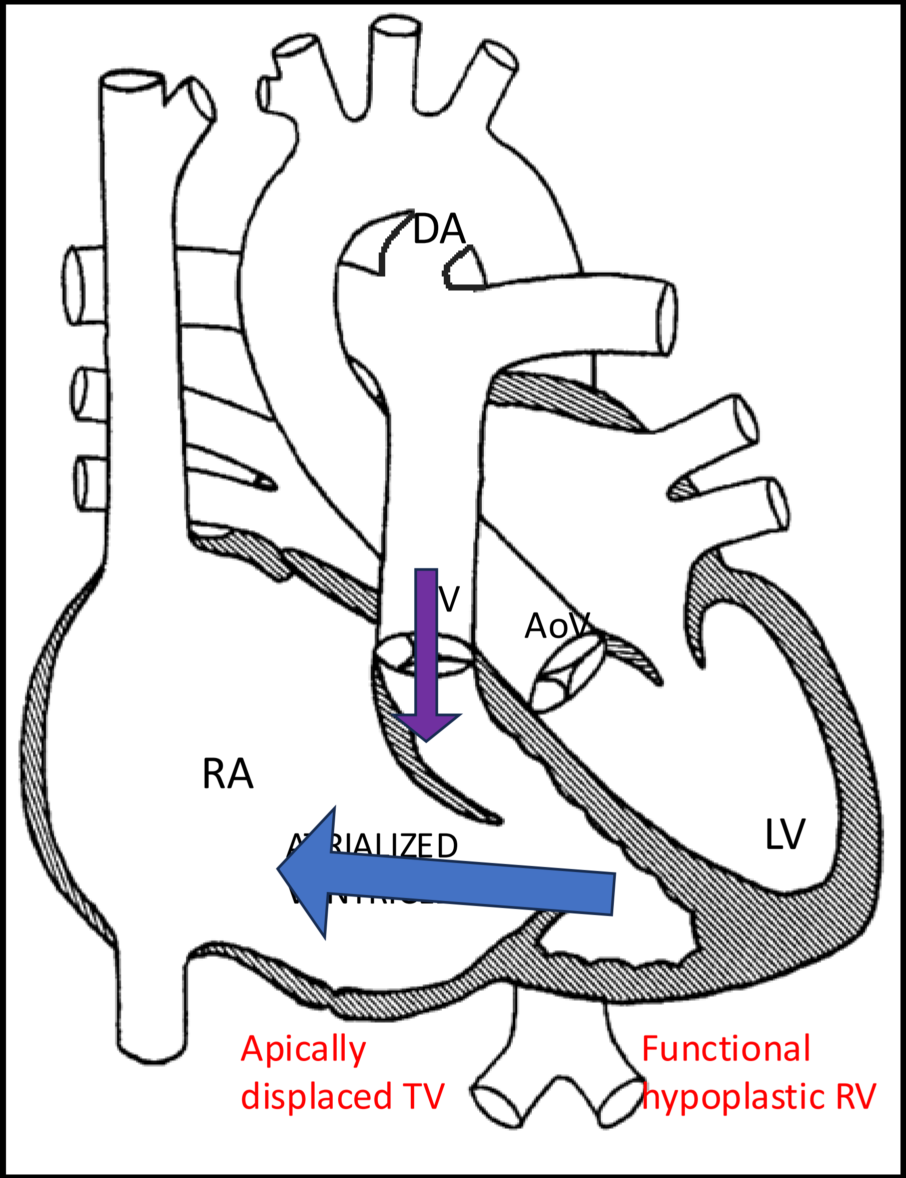
DA + Aorta flow enters systemic circulation

Adequate Cardiac Output

Ebstein Anomaly physiology: circular shunt

Key components to circular shunt physiology:

1. Severe TR
2. Pulmonary regurgitation



Ebstein Anomaly has very high association with abnormal pulmonary valve due to abnormal flow

Leads to :

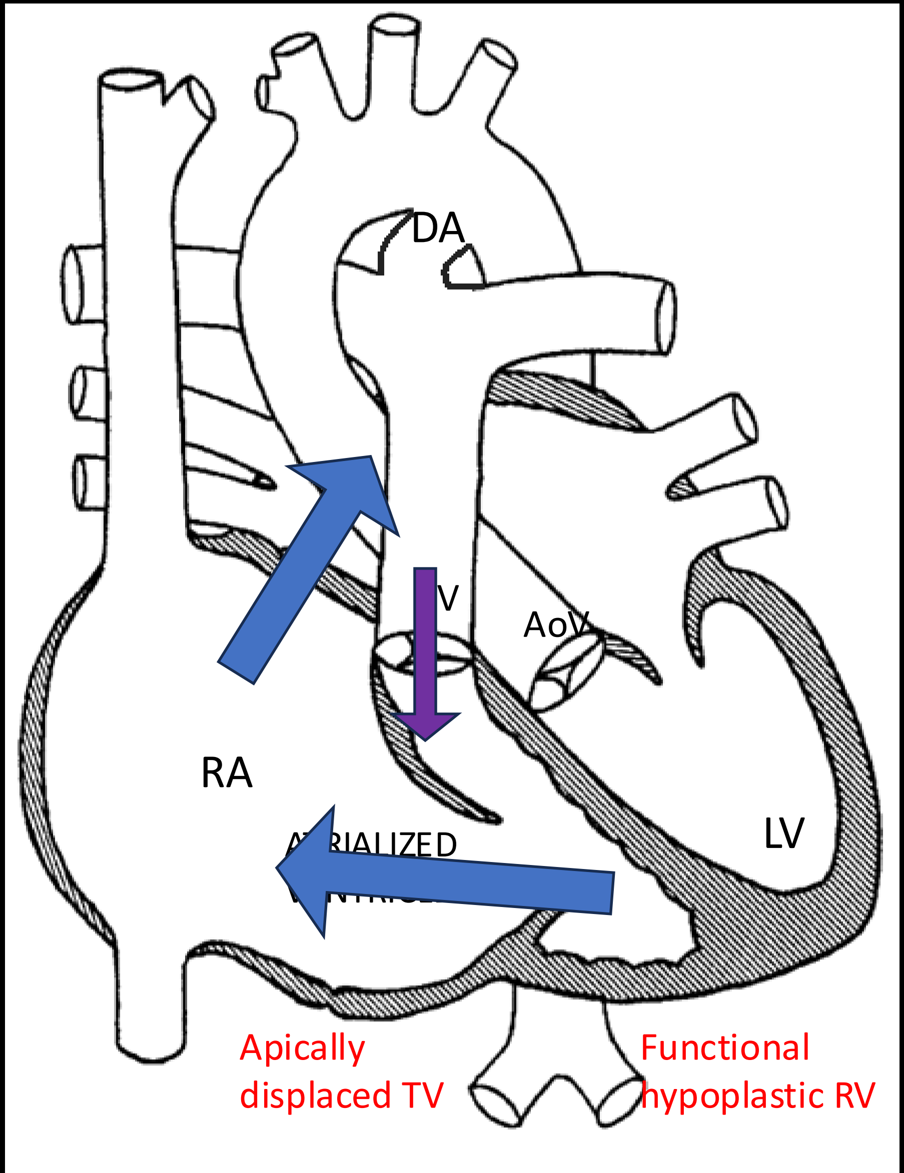
- pulmonary stenosis and/or
- pulmonary regurgitation

With significant pulmonary regurgitation → circular shunt

Ebstein Anomaly physiology: circular shunt

Key components to circular shunt physiology:

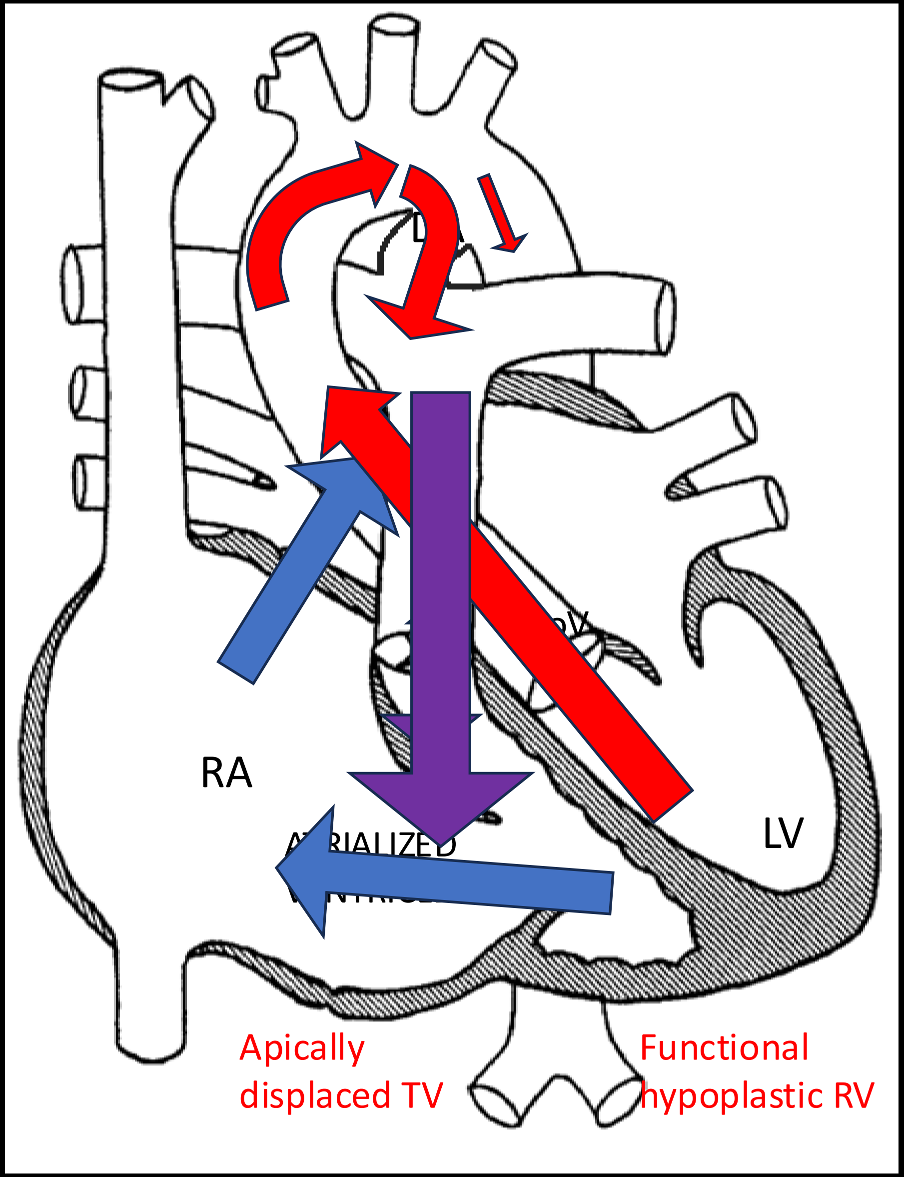
1. Severe TR
2. Pulmonary regurgitation
3. Foramen ovale right-to-left shunt



Ebstein Anomaly physiology: circular shunt

Key components to circular shunt physiology:

1. Severe TR
2. Pulmonary regurgitation
3. Foramen ovale right-to-left shunt
4. Retrograde flow in DA (reversal)



LV ejects through Aorta in systole

There may be little antegrade PV flow or no flow

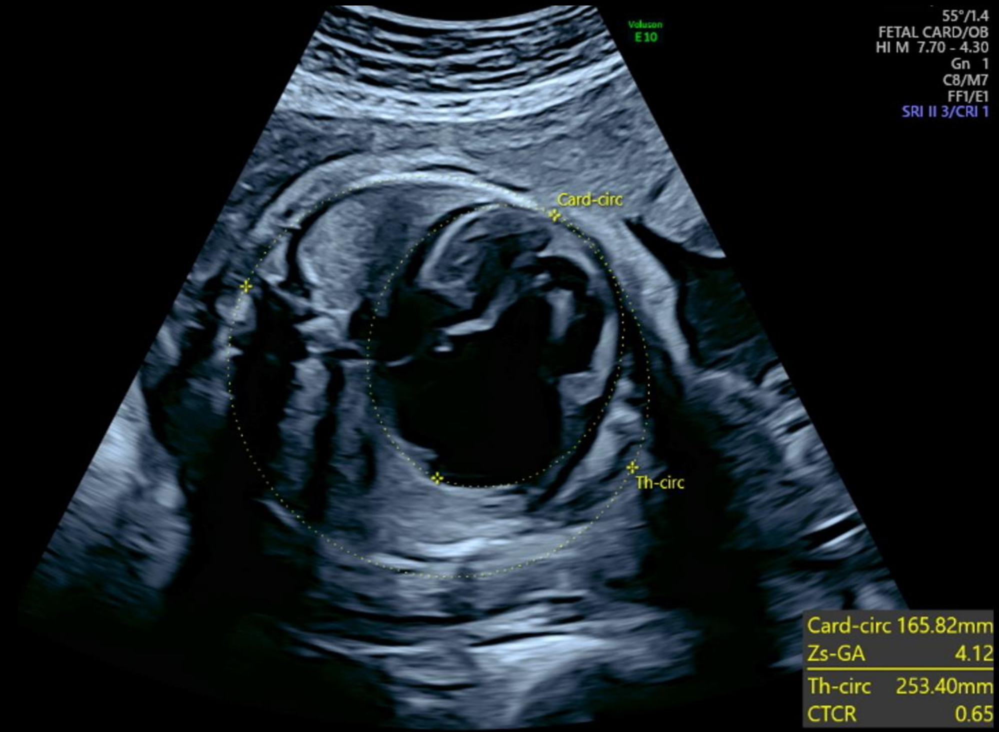
When there is significant pulmonary regurgitation, there is reversal of low in the DA

Results in significantly decreased cardiac output

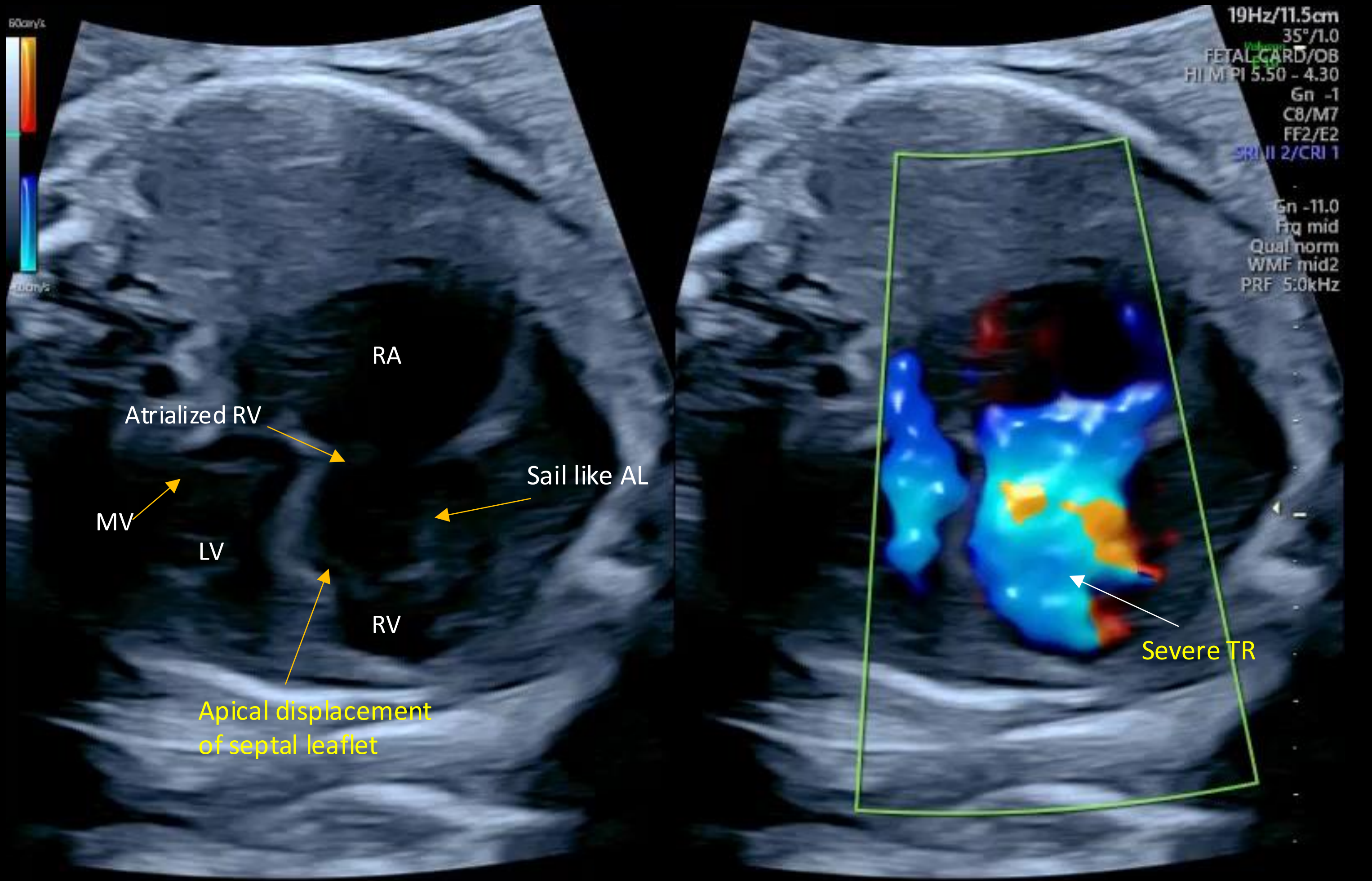
High Risk for Fetal Dimise

TV annulus/ TR jet/RA dilation

CTA



CTA: 065

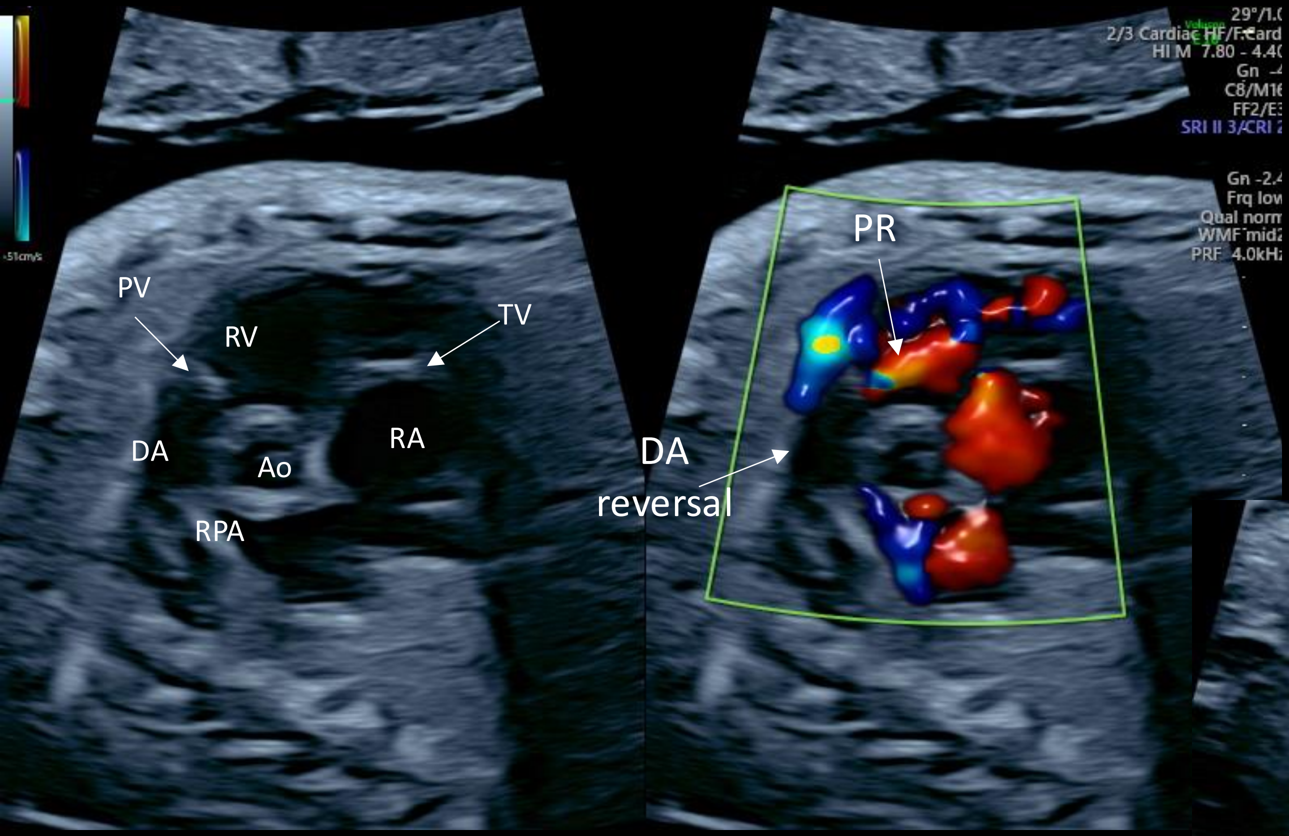


Severe TR

Severely dilated TV annulus (z=+10)

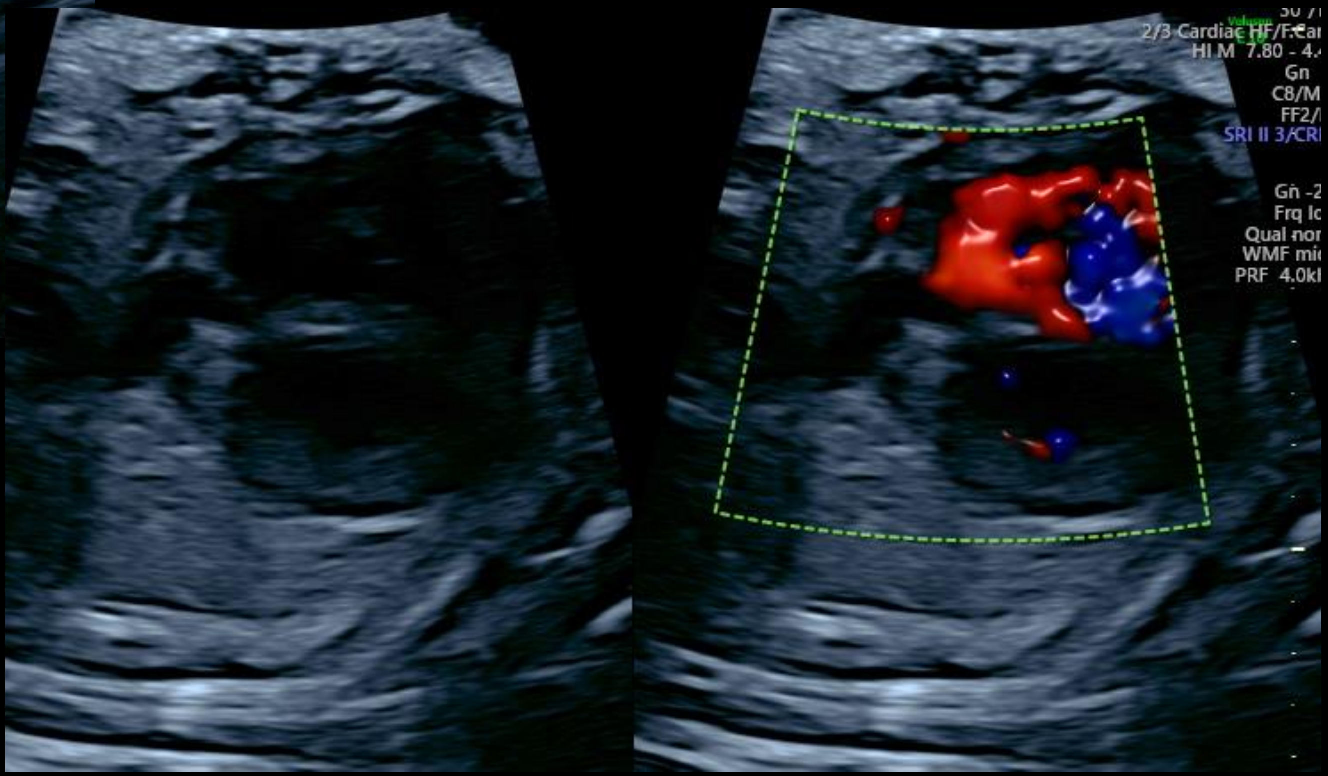
Severe RA dilation

PV flow

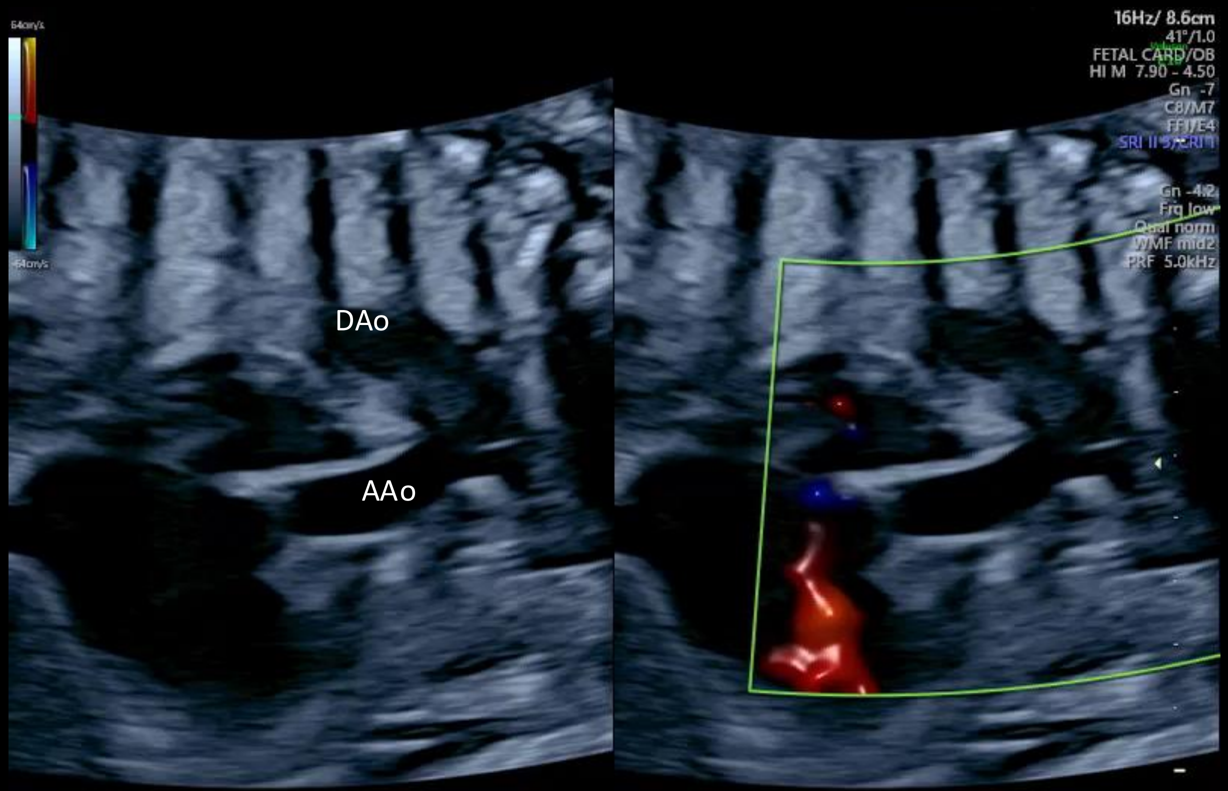


Moderate-to-severe pulmonary regurgitation
DA flow reversal
Thickened PV with abnormal mobility

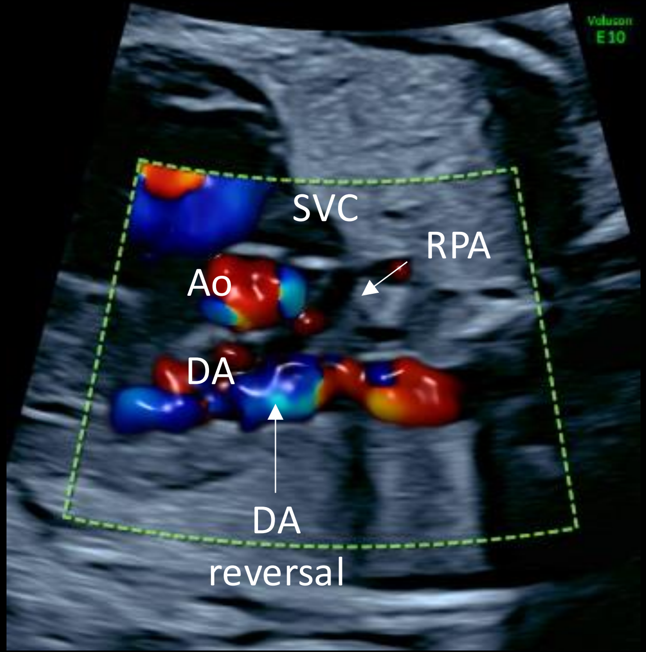
Moderate-to-severe pulmonary regurgitation



Blood flow in DA



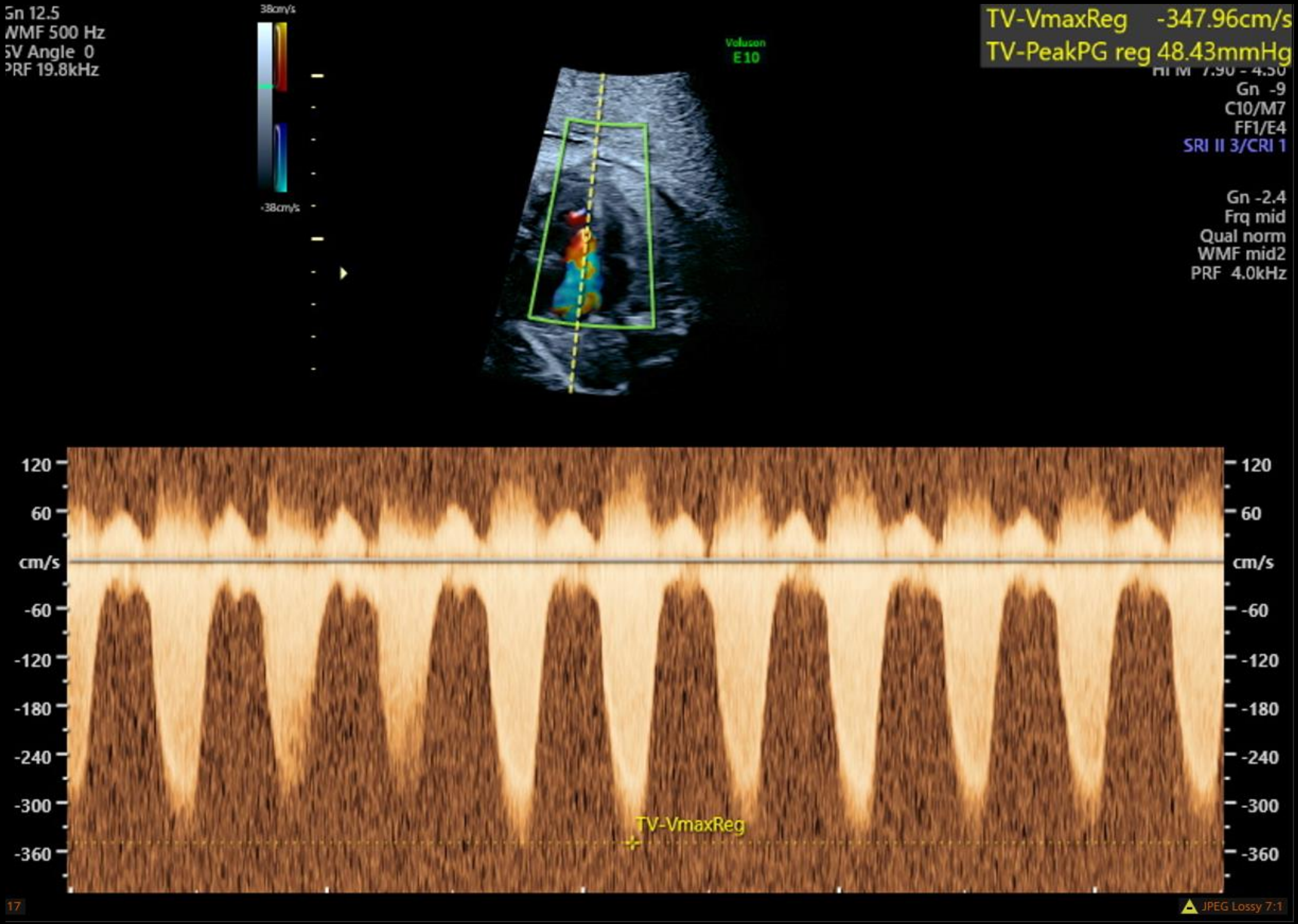
DA flow reversal
Normal aortic arch flow



3VV View
DA flow reversal
Large DA

- Using TR jet to estimate RV pressure as a surrogate for RV function
- Worse prognosis with TR vmax ≤2.5 m/s
- Half of the neonates with TR jet or RV pressure ≤2.5 m/s die ie 50% mortality
- All those ≥3.0 m/s survived.

Freud et al. JAMA. Risk Factors for Mortality and Circulatory Outcome Among Neonates Prenatally Diagnosed With Ebstein Anomaly or Tricuspid Valve Dysplasia: A Multicenter Study. J Am Heart Assoc. 2020 Nov 3;9(21)



ULTRASOUND
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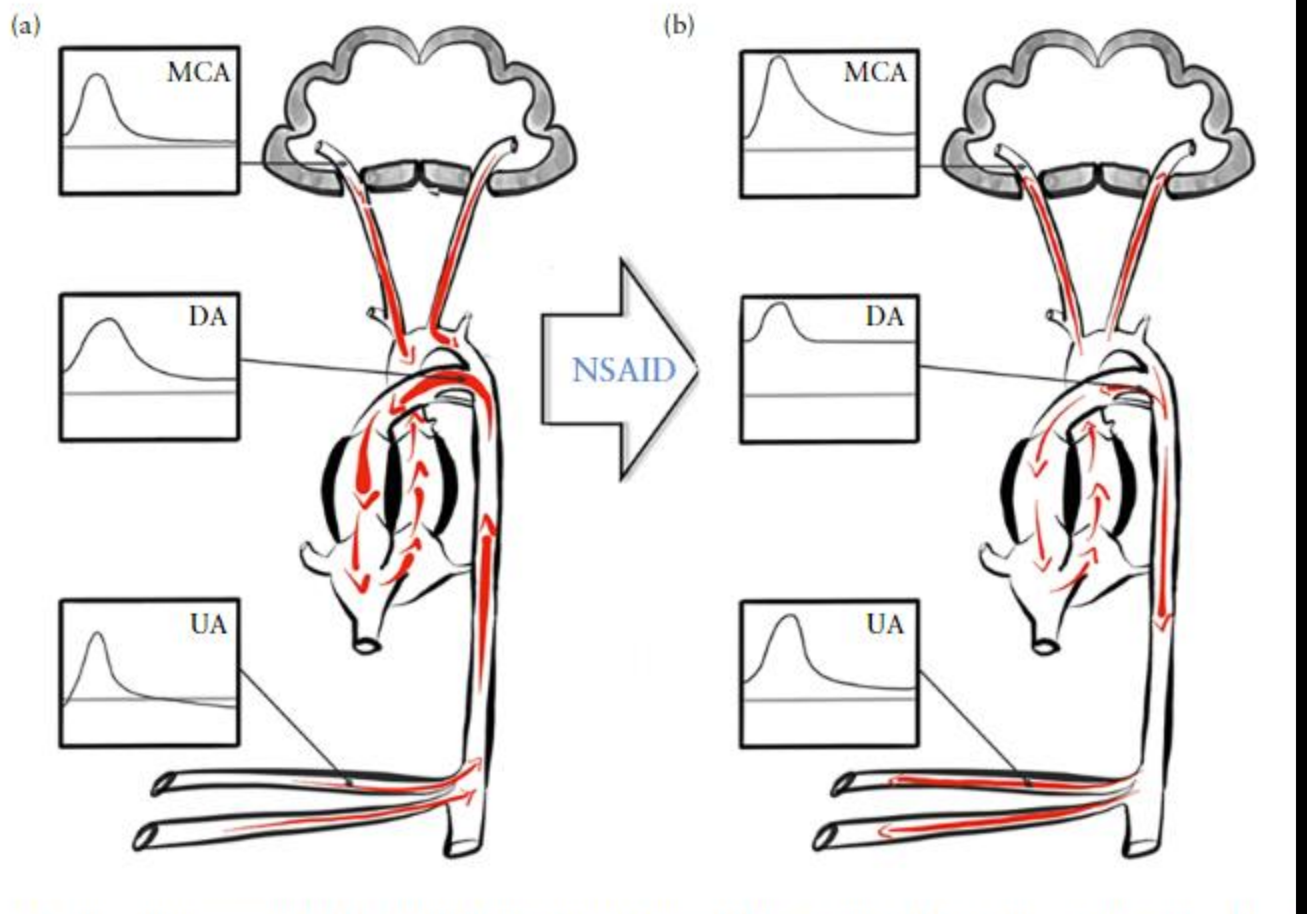
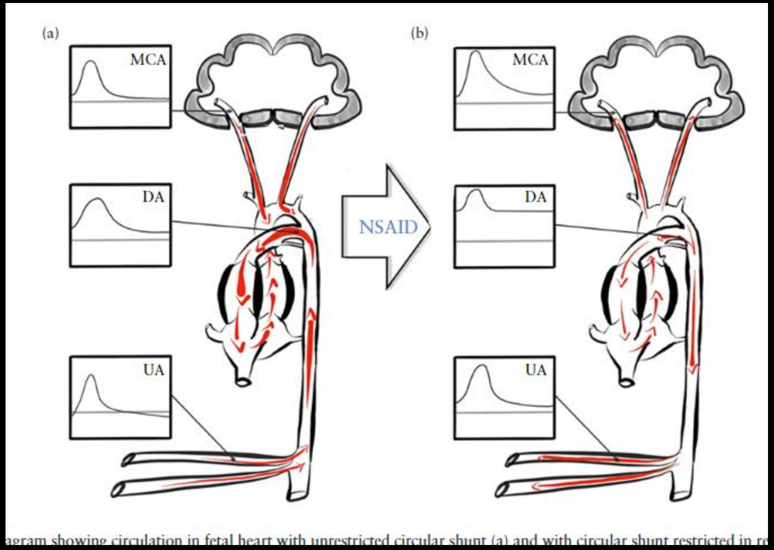
Treatment of fetal circular shunt with non-steroidal anti-inflammatory drugs

T. Torigoe, W. Mawad, M. Seed, G. Ryan, D. Marini, F. Golding, T. VAN Mieghem, E. Jaeggi

- Use of NSAIDs caused ductal constriction
- Decreased steal from circular shunt by reducing PDA size resulting in:
  - Improved hemodynamic function
  - Continuation of pregnancy 3-7 weeks
  - Potential improved survival
  - Improved cardiac output

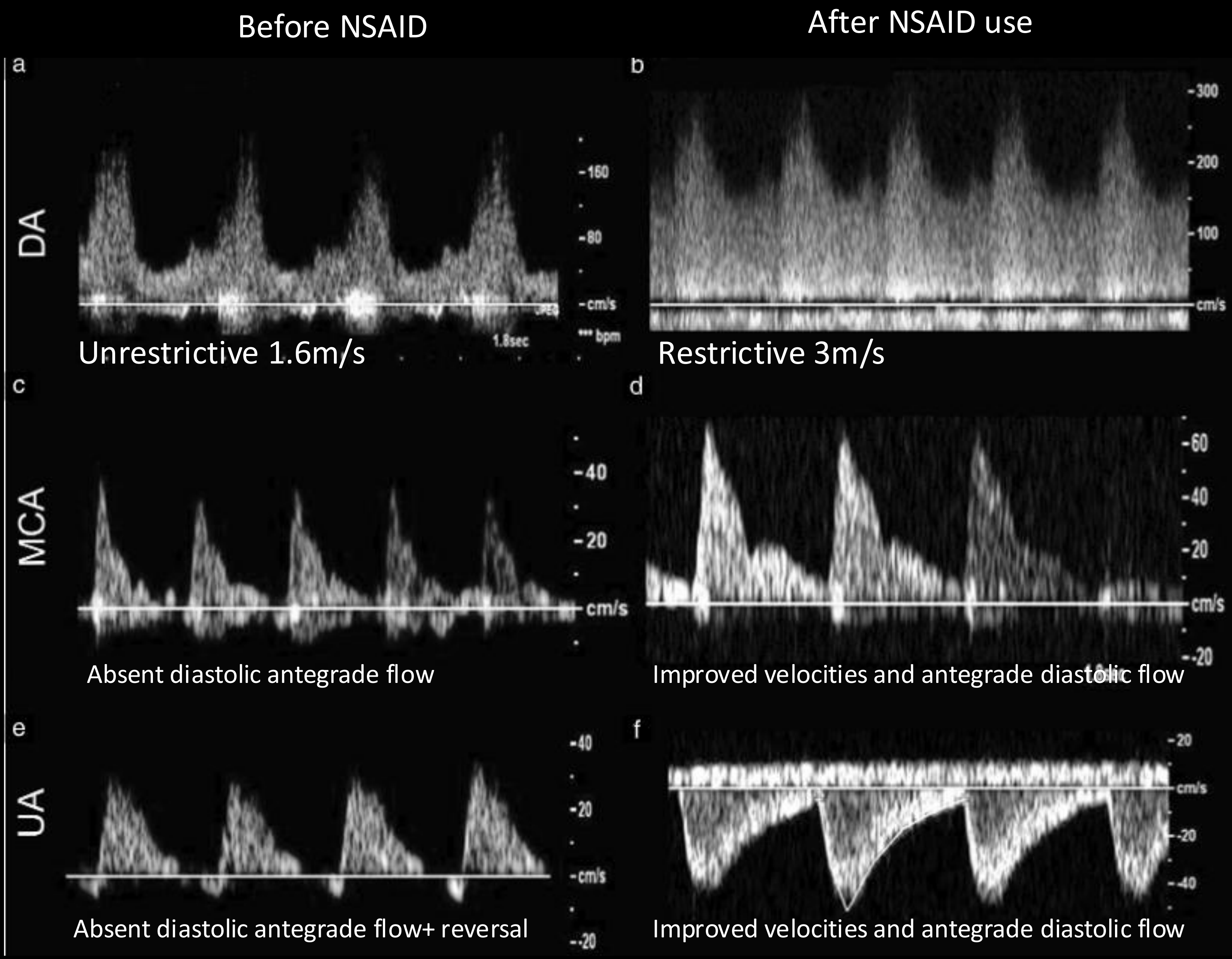


agram showing circulation in fetal heart with unrestricted circular shunt (a) and with circular shunt restricted in re

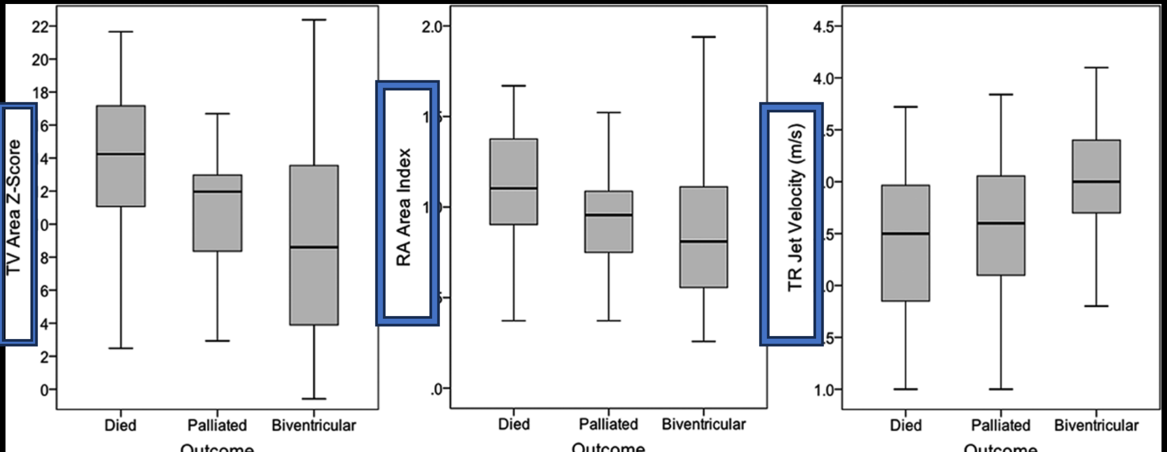


After NSAID use:

- Restrictive DA flow
- UA and MCA with restoration of antegrade diastolic flow and increased velocities
- Overall decrease in systemic steal and improved cardiac output



Variable	Survived (n=116)	Died (n=38)	*P* Value
Gestational age at diagnosis, wk	28.2±6.0	26.1±5.5	0.059
Gestational age at birth, wk*	37.5±2.7	36.3±2.2	0.005
Birth weight, kg	3.0±0.6	2.6±0.5	0.001
Delivery by caesarean section	51 (48)	20 (59)	0.26
Apgar scores			
1 min	6.7±2.3	4.5±2.8	<0.001
5 min	8.0±1.2	6.3±2.4	<0.001
Delivery room intubation	32 (28)	26 (70)	<0.001
Mechanical ventilation in ICU	63 (54)	38 (100)	<0.001
Prostaglandin therapy	69 (59)	30 (79)	0.03
Inotropic support	41 (35)	32 (84)	<0.001
ECMO	3 (3)	15 (39)	<0.001
Any neonatal intervention	50 (43)	21 (53)	0.19
Neonatal catheter intervention	13 (11)	5 (13)	0.74
Neonatal cardiac surgery	40 (35)	19 (50)	0.088
Multiple neonatal surgeries	1 (1)	6 (16)	0.001



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Risk Factors for Mortality and Circulatory Outcome Among Neonates Prenatally Diagnosed With Ebstein Anomaly or Tricuspid Valve Dysplasia: A Multicenter Study

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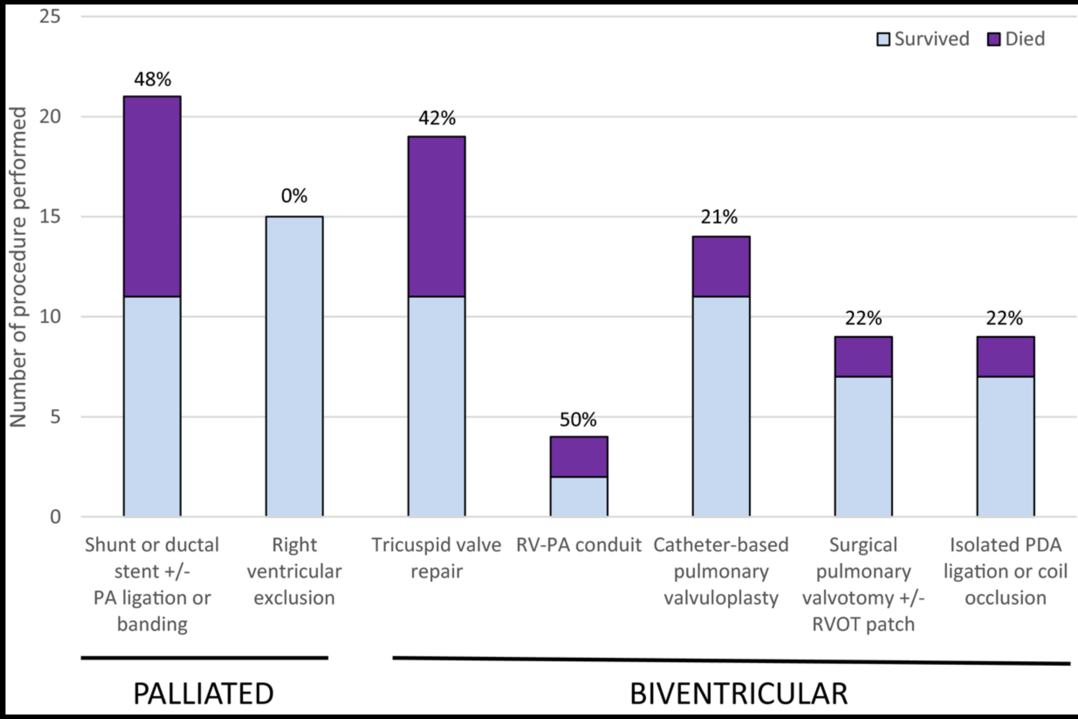
Journal of the American Heart Association • Volume 9, Number 21 • https://doi.org/10.1161/JAHA.120.016684

Among prenatally diagnosed neonates with severe EA/TVD who survived >24 hours and were intended to be treated, mortality remained high at 25%.

Notable risk factors for neonatal mortality included:

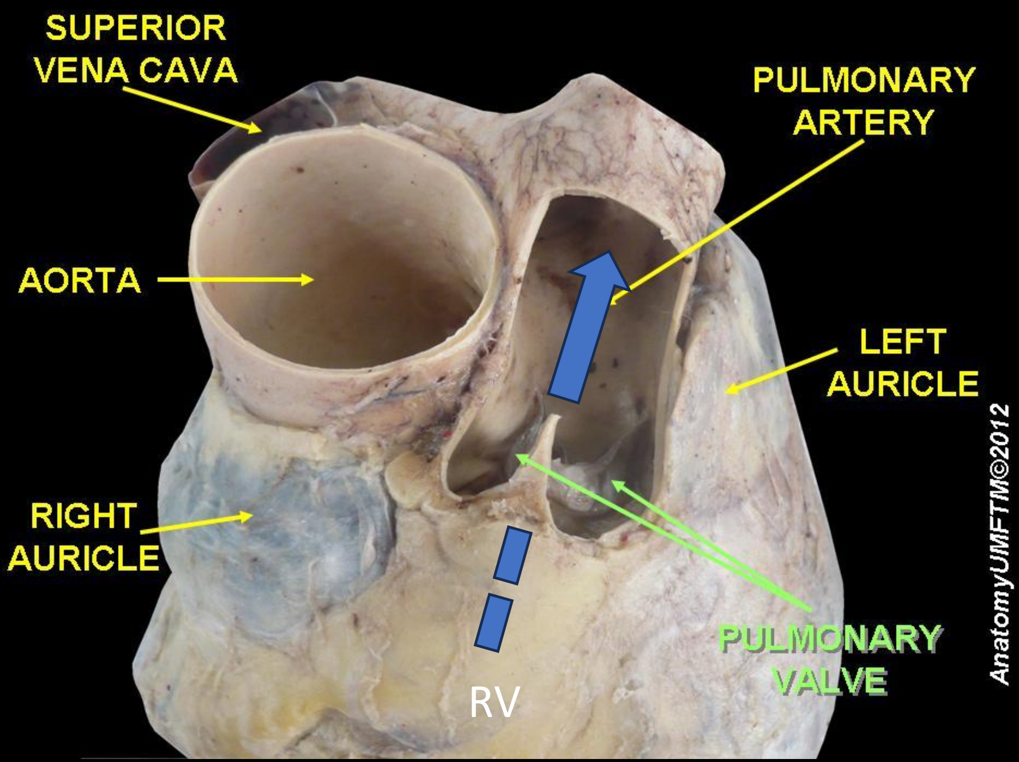
- lower birth weight
- lower TR jet velocity
- lack of antegrade pulmonary blood flow
- TV annulus size

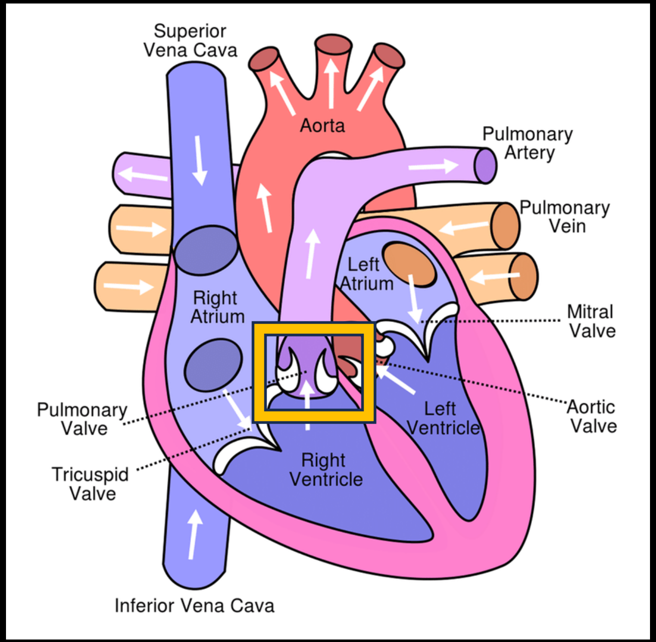


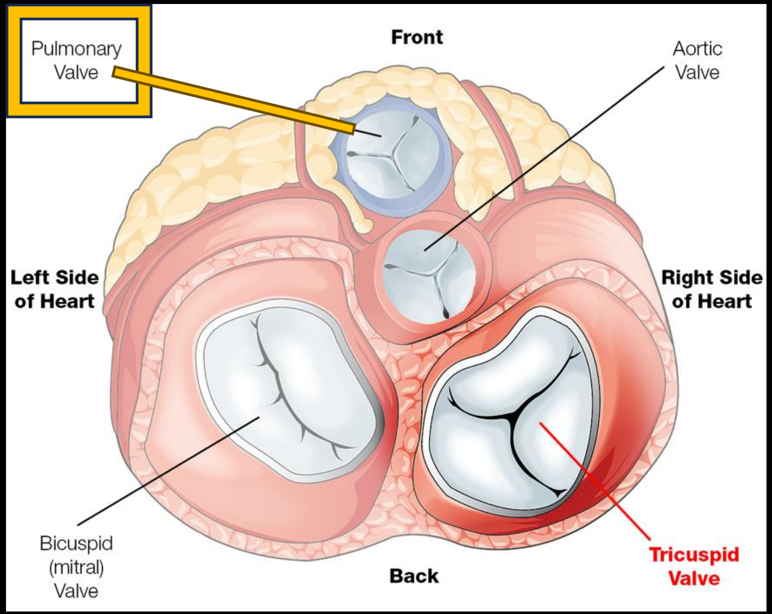
Freud, L et al. Risk Factors for Mortality and Circulatory Outcome Among Neonates Prenatally Diagnosed With Ebstein Anomaly or Tricuspid Valve Dysplasia: A Multicenter Study. JAMA. 2020

Pulmonary valve

- Semilunar valve
- Formed with 3 leaflets
- Connects right ventricle to main pulmonary artery, branch PA, and ductus arteriosus (DA)

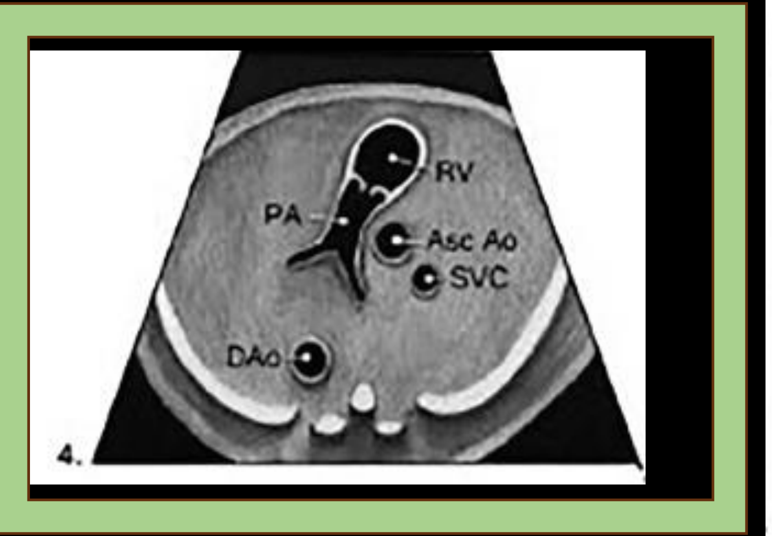


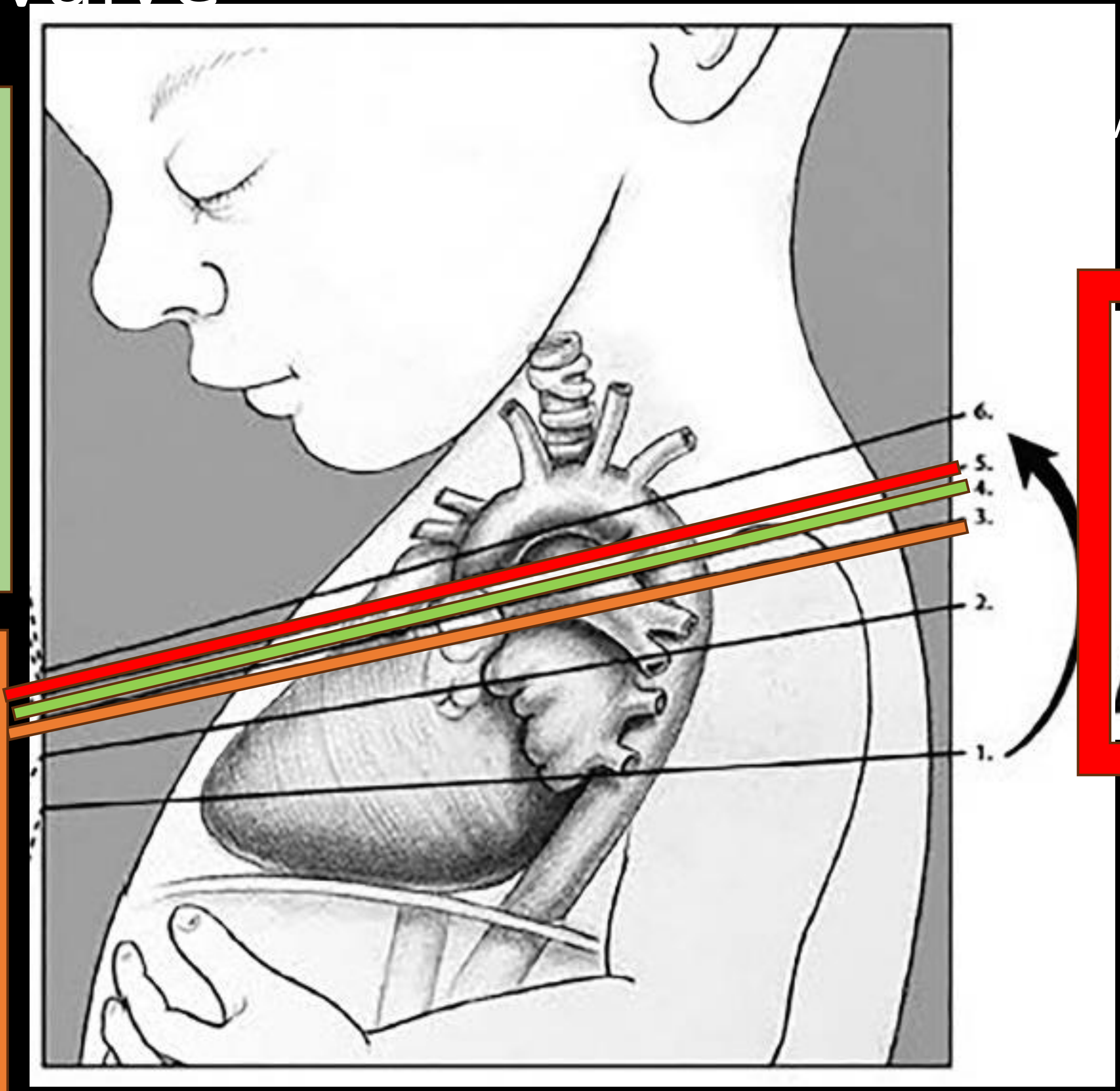


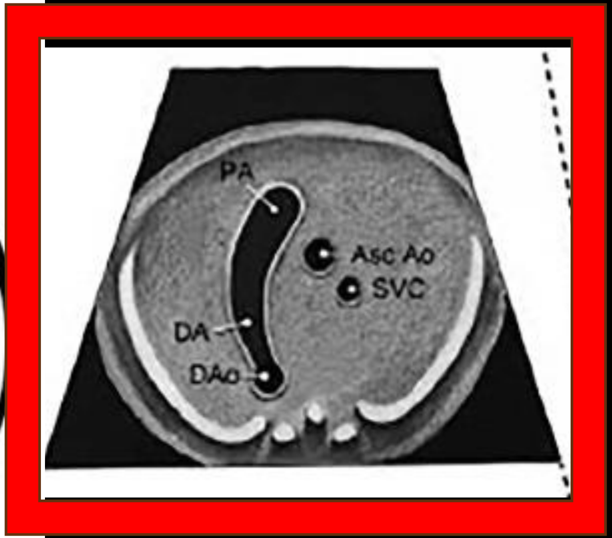


Pulmonary valve

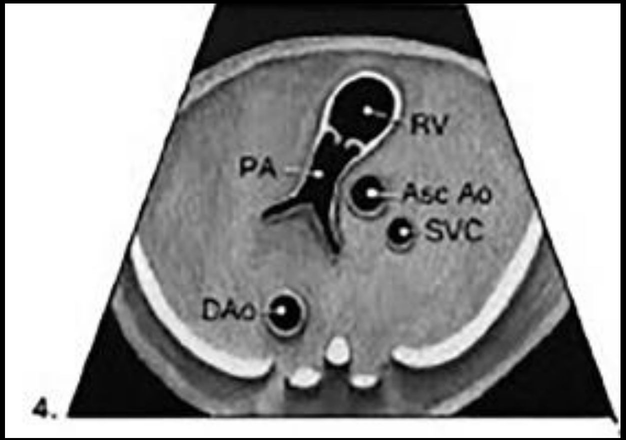
verse views





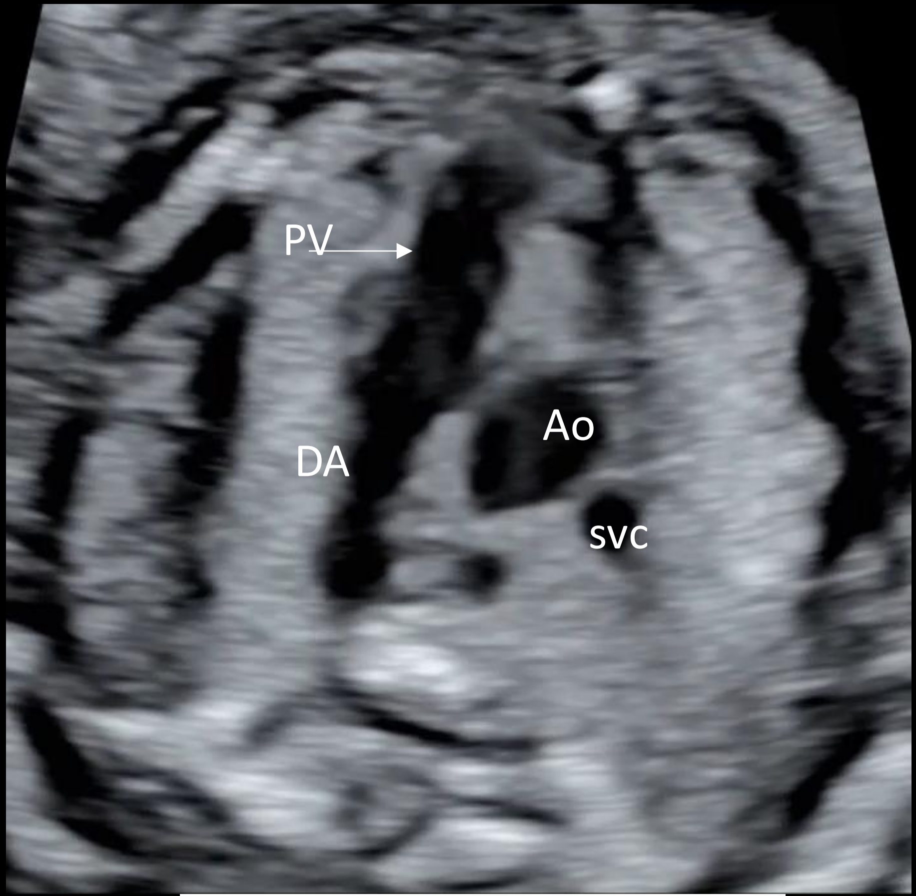


Pulmonary valve



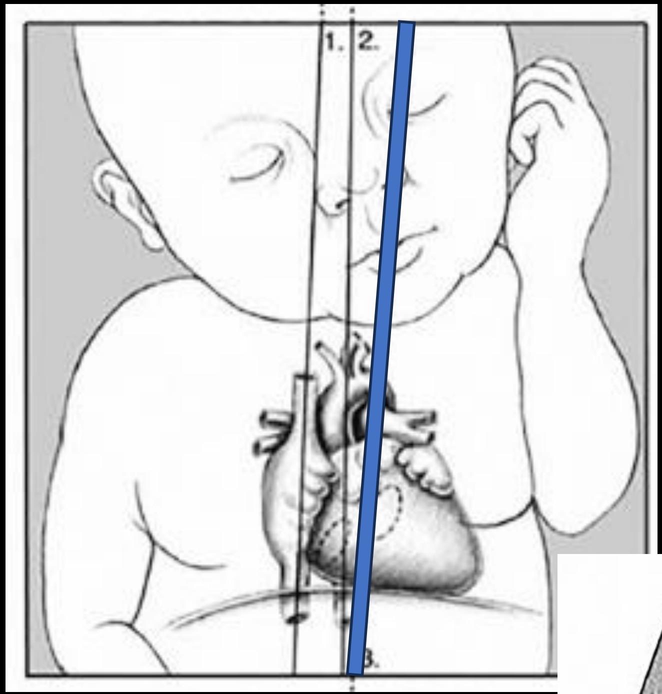
Branch PA view
(inferior to 3VV)

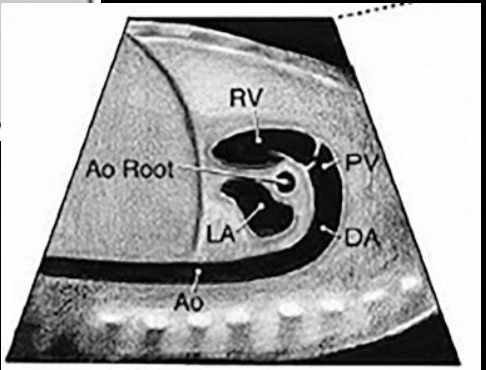
3VV (slightly inferior)



Pulmonary valve

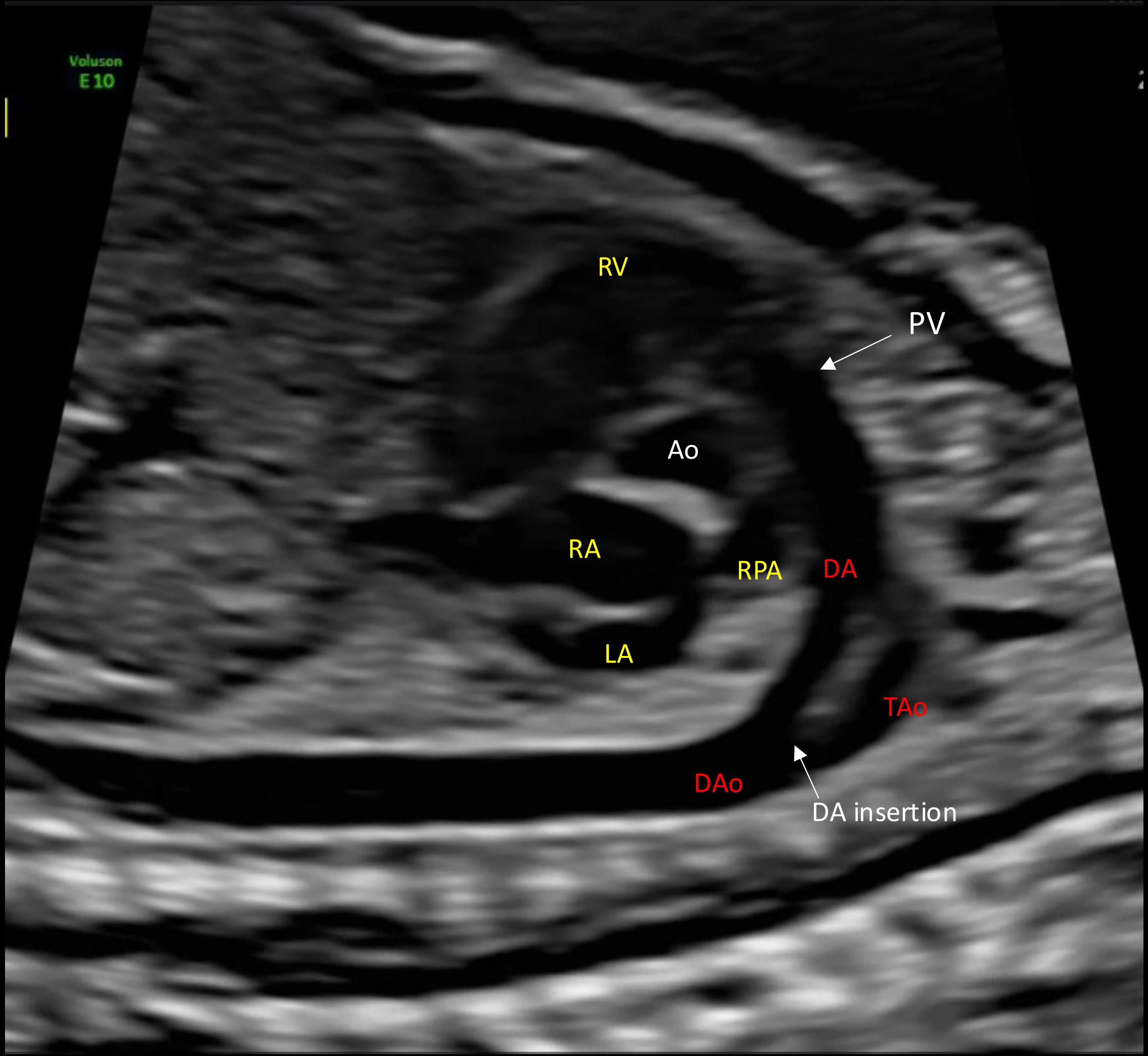
Sagittal view





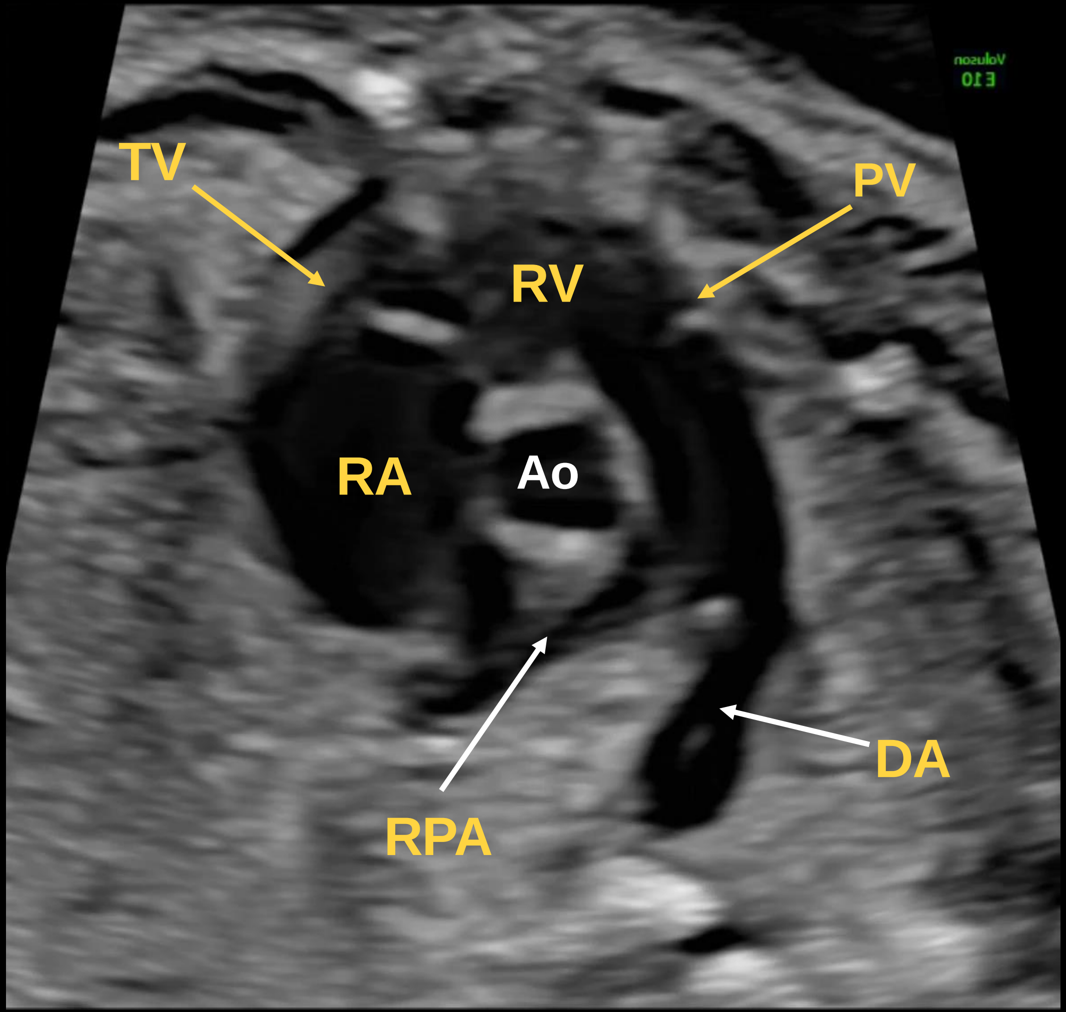
3. Ductal Arch View

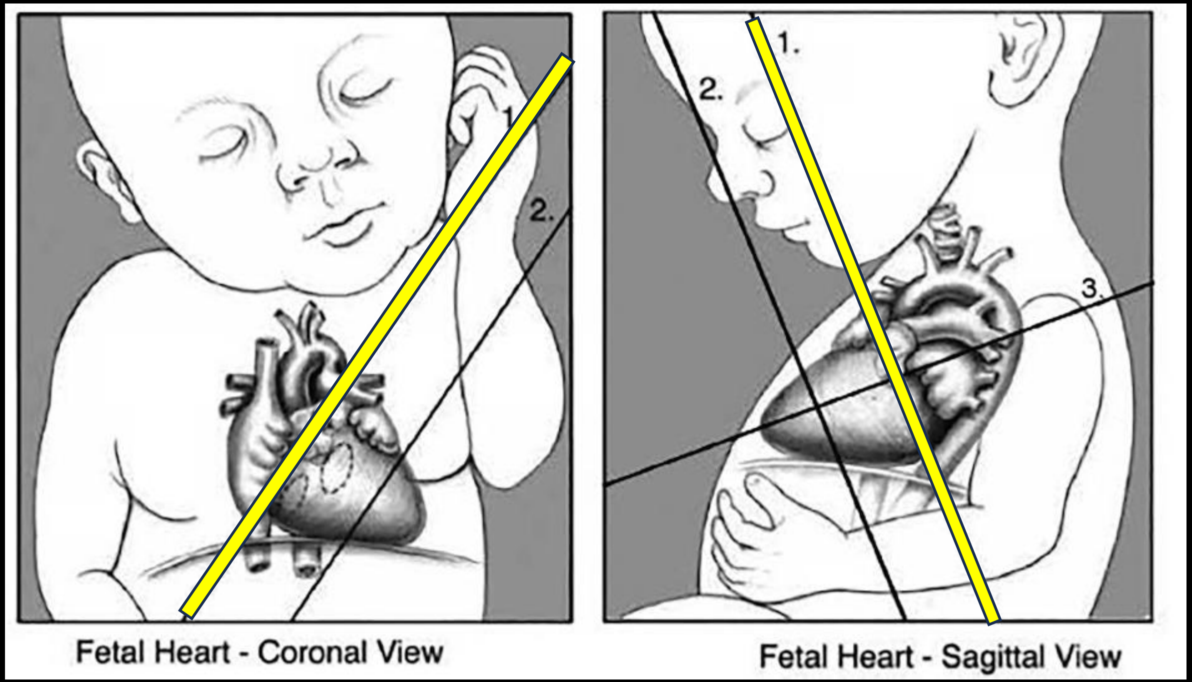
Ductal Arch View

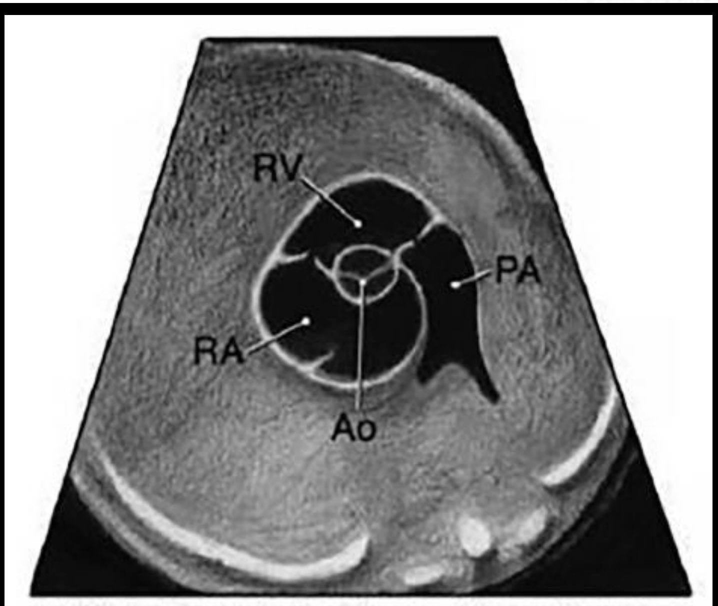


Pulmonary valve

Short Axis

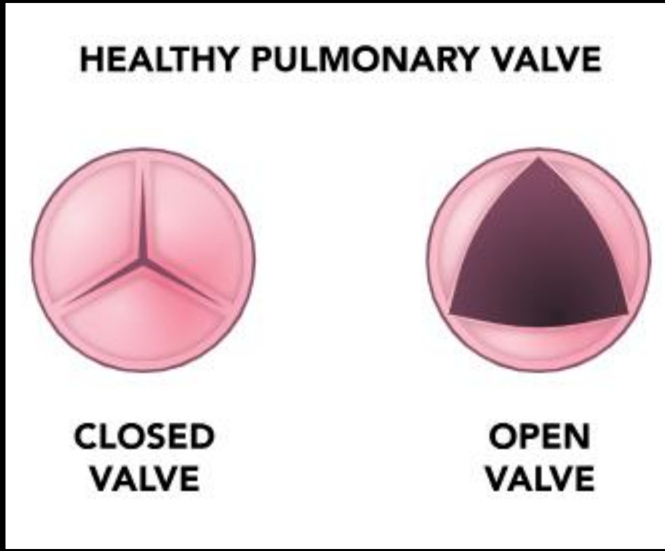






1. High Short Axis View - Great Arteries

Pulmonary stenosis



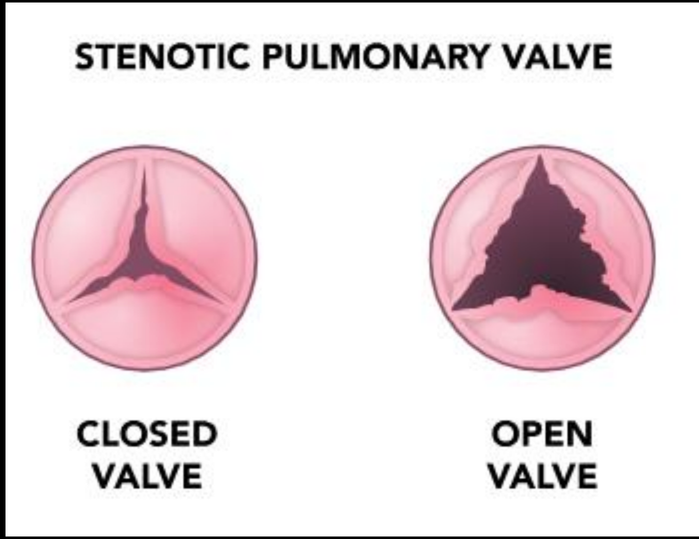


Image source: SCAI secondscount.org

- Pulmonary valve leaflets are thickened
- May also have fused leaflets / fused commissures
- Pulmonary valve annulus may be hypoplastic
- Effective orifice is smaller resulting in increased resistance
- Obstruction to blood flow to lungs
- Can be valvar, subvalvar, supravalvar, or mixed
- Can cause increased afterload for right ventricle resulting in hypertrophy, dilation, and/or dysfunction

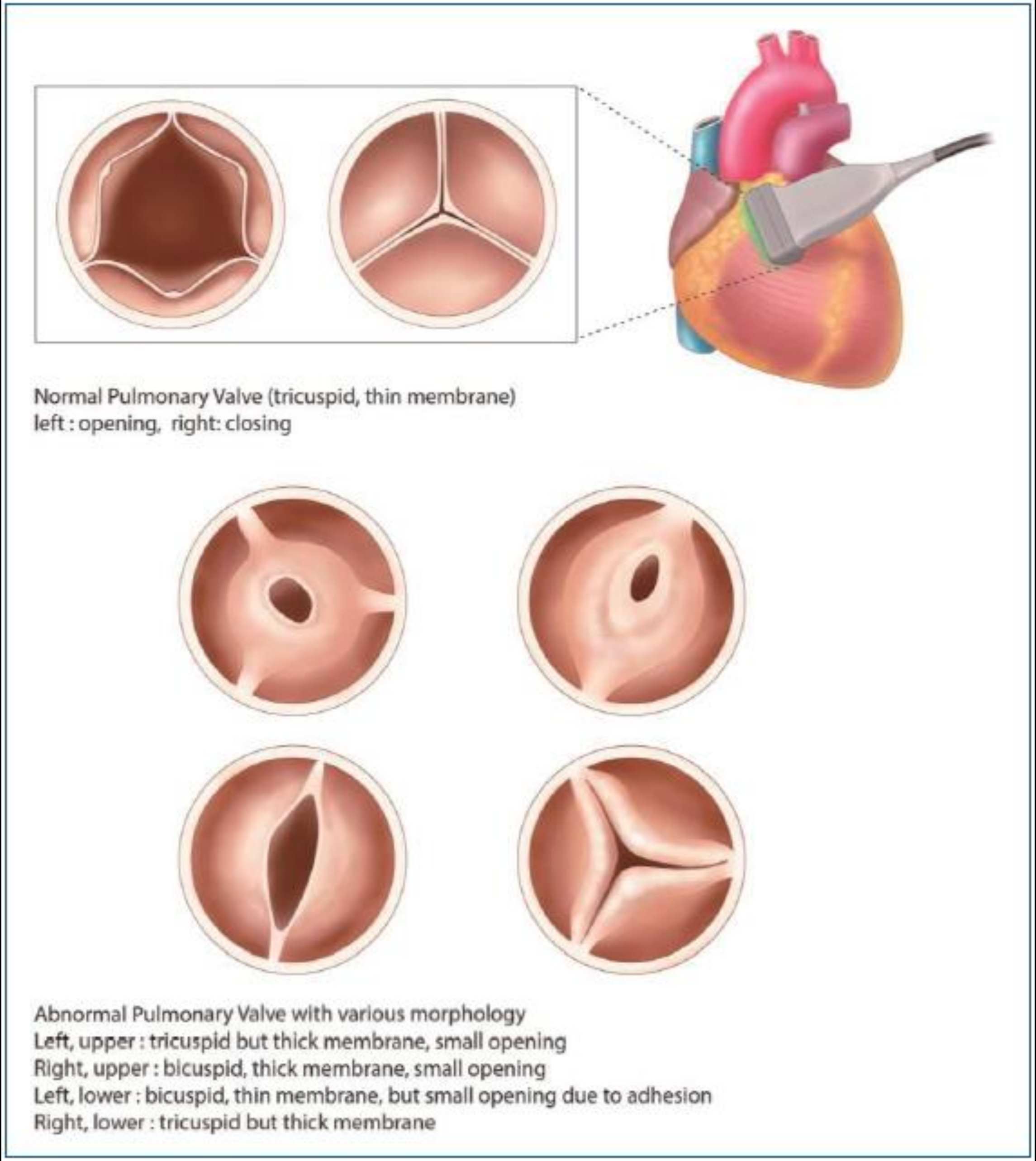
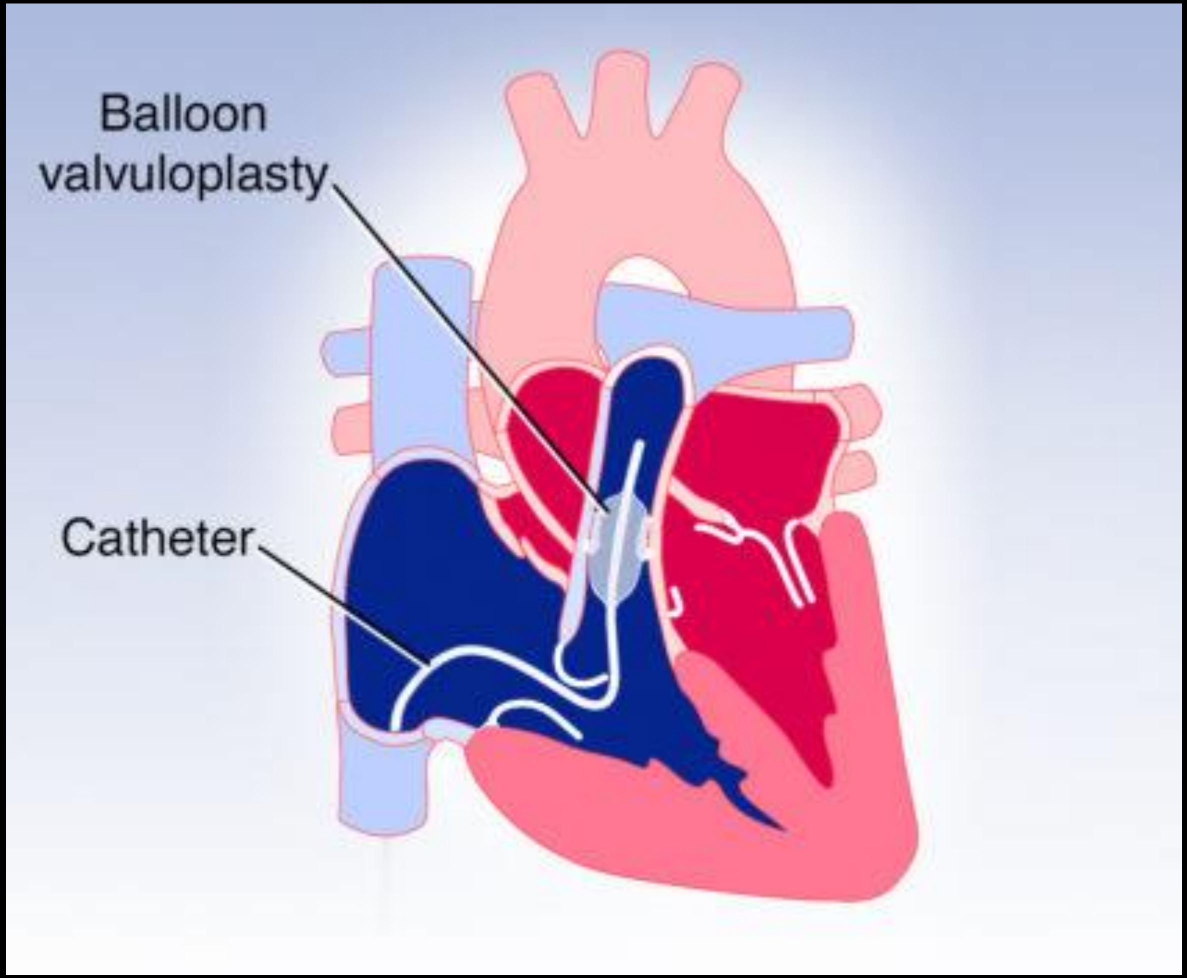


Image source: Su Jin Choi et al. Clinical Exp Pediatrics. 2020

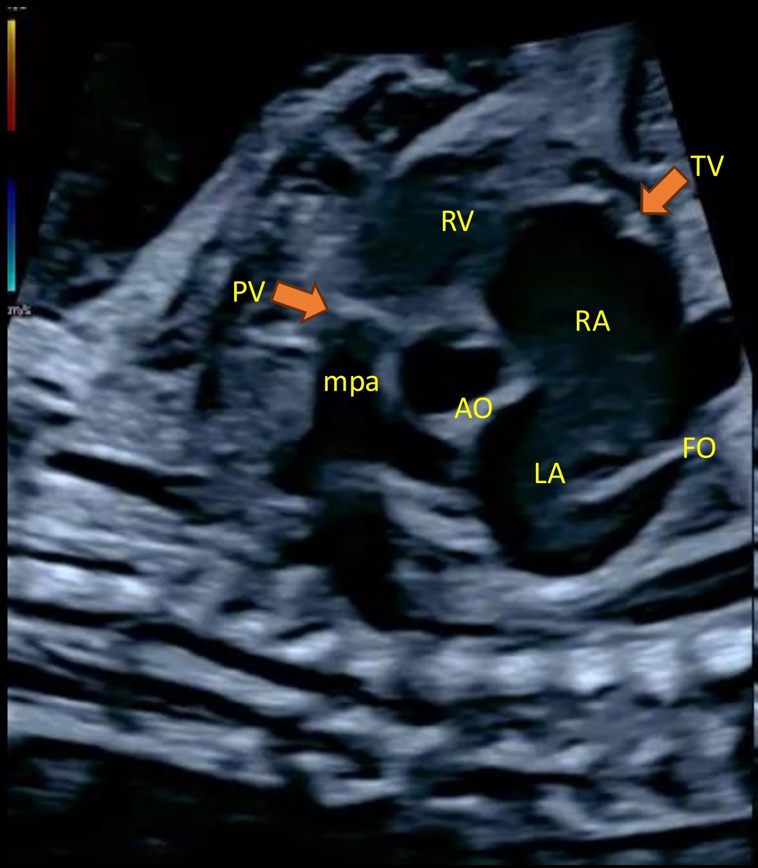
Critical Pulmonary stenosis

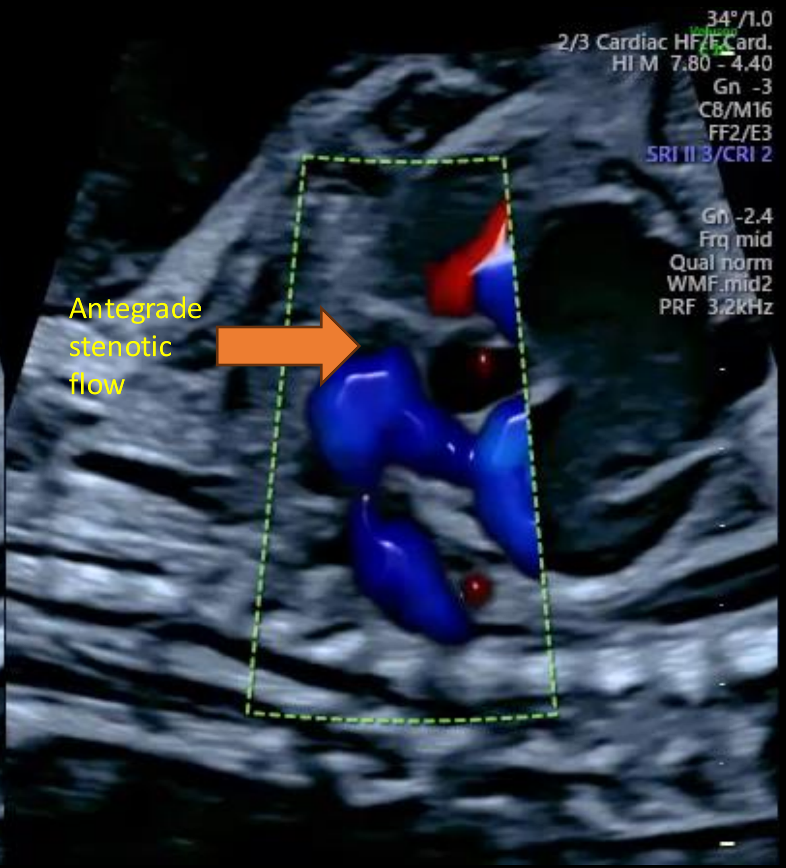
- Not enough pulmonary blood flow→ductal dependent pulmonary flow
- Will need PGE after birth to keep ductus arteriosus open
- Balloon valvuloplasty to open pulmonary valve and improve pulmonary blood flow after birth

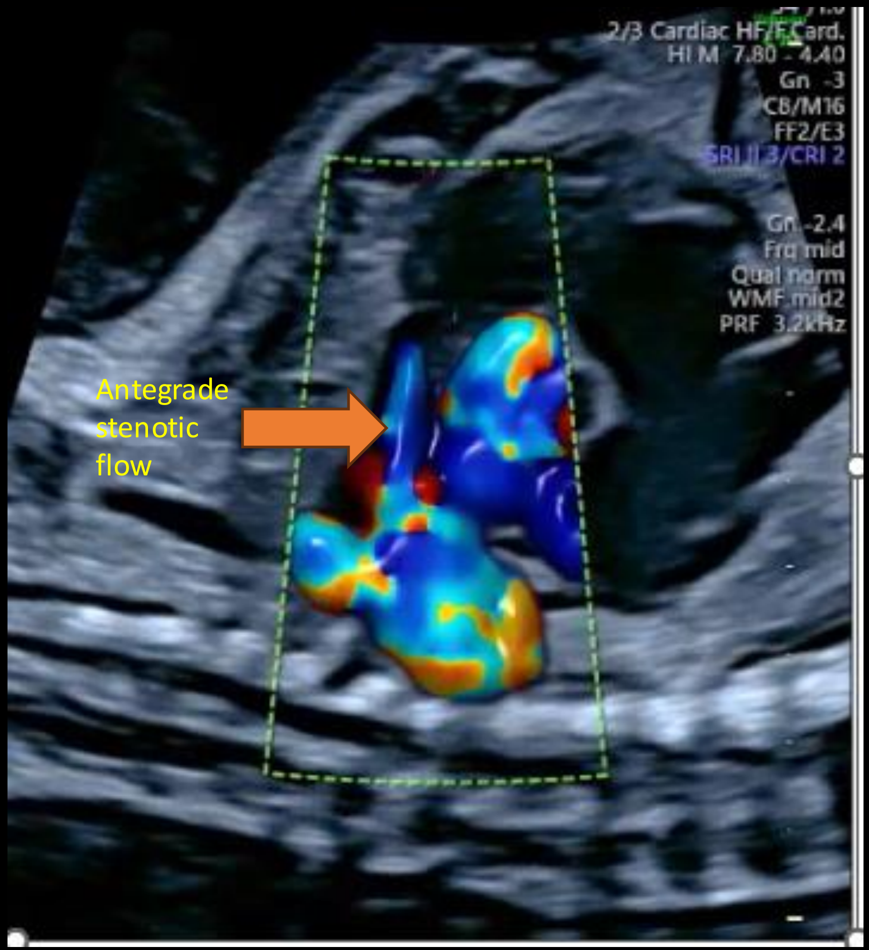


Critical Pulmonary stenosis

Parasternal short axis





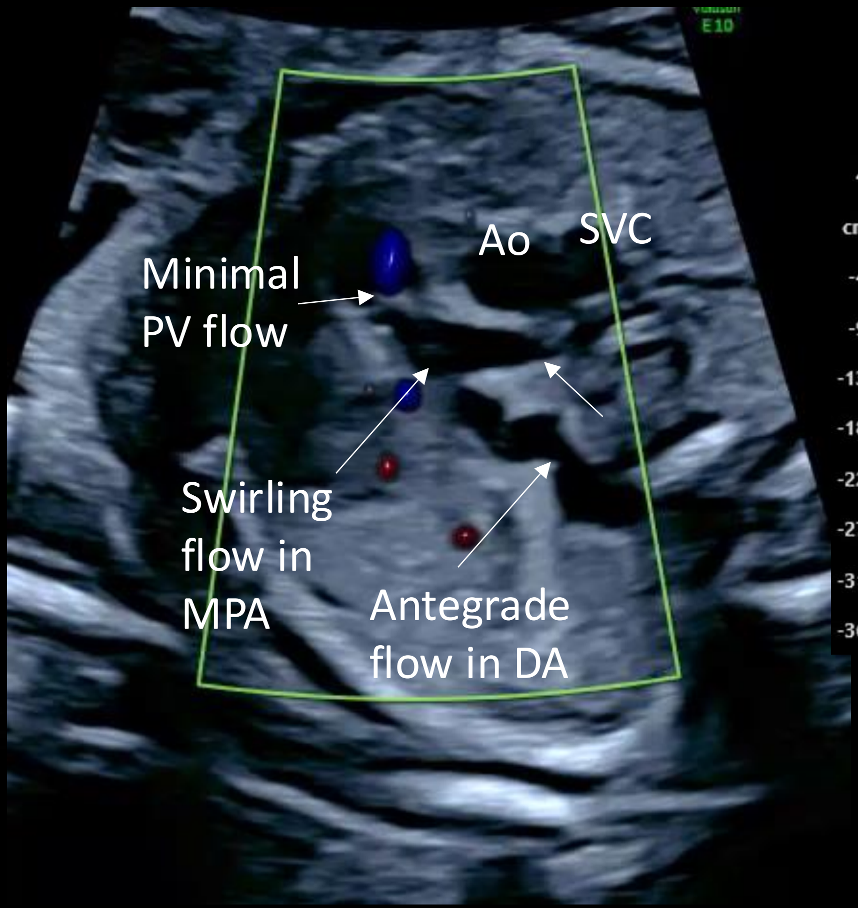


PV Thickened leaflet with limited excursion
Decreased PV flow by Color

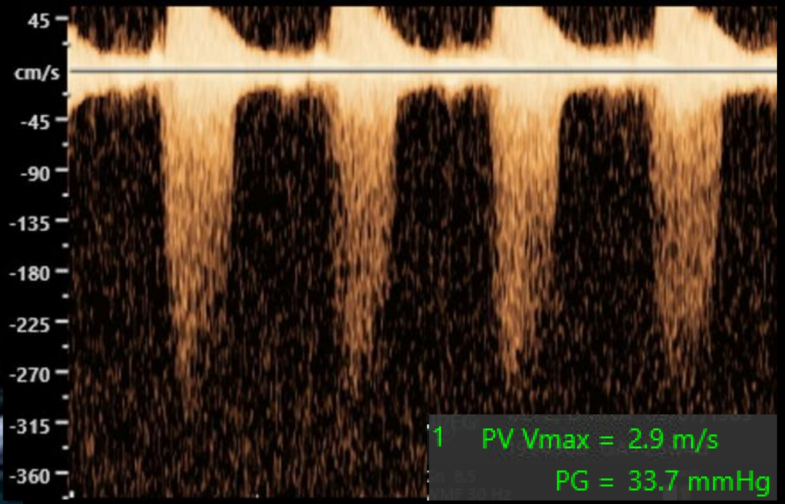
EGA 22 weeks and 3 days

3VV

Thickening of PV leaflets
Poor PV leaflet mobility
DA normal size



Tortuous PDA
Narrowed and minimal PV antegrade flow
Antegrade flow through DA

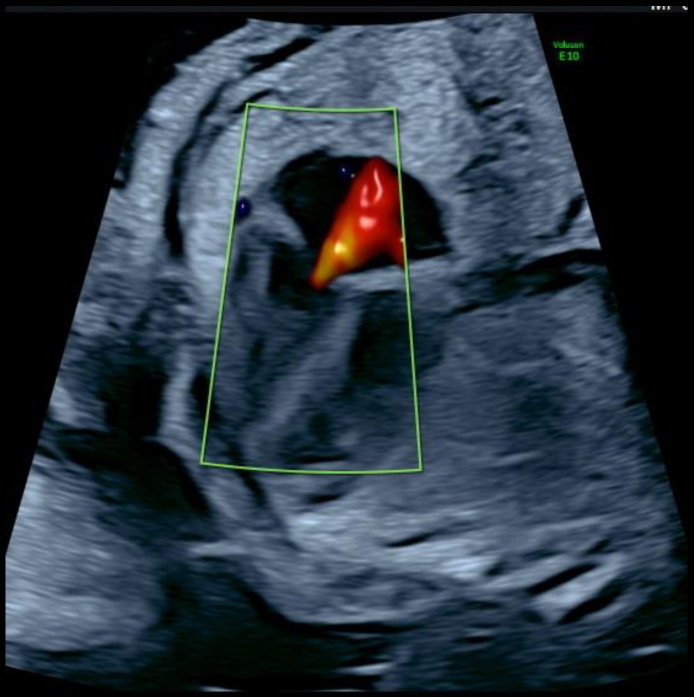


PV doppler
2.9 m/s, peak gradient 33 mmHg

EGA 22 weeks and 3 days

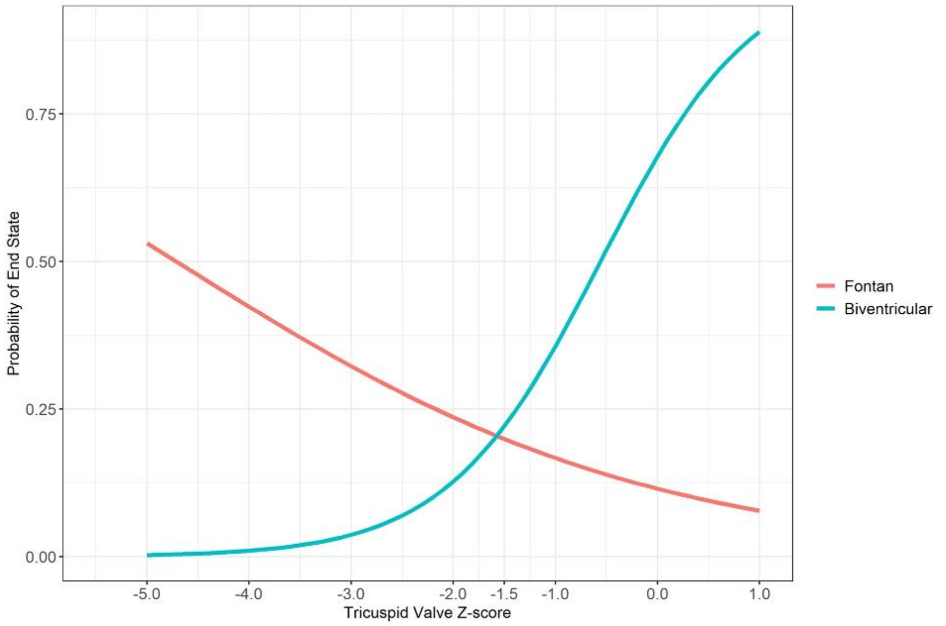
RV hypertrophy
Severe RV dysfunction
TV annulus z=-0.71

TV annulus size by z-score predicts biventricular repair vs. single ventricle pathway for similar physiology



Moderate tricuspid regurgitation

From: Pulmonary Atresia with Intact Ventricular Septum: Midterm Outcomes from a Multicenter Cohort



Probability of biventricular and Fontan end-state according to TV Z-score: A logistic regression of biventricular repair on TV Z-score was fitted and the conditional effect plot of TV Z-score generated. TV Z-score is significantly associated with increased probabilities of biventricular repair [odds ratio = 26.90; 95% confidence interval = (9.43–76.74), *p* value < 0.001]. A similar analysis for Fontan end-state was performed and the two regression lines were interposed

- Iliopoulos, I., Mastropietro, C.W., Flores, S. *et al.* Pulmonary Atresia with Intact Ventricular Septum: Midterm Outcomes from a Multicenter Cohort. *Pediatr Cardiol* **45**, 847–857 (2024). https://doi.org/10.1007/s00246-022-02954-5

Prediction of postnatal circulation in pulmonary atresia/critical stenosis with intact ventricular septum: systematic review and external validation of models

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Table 1 Prenatal models and reported performance (if available)

Study	*Model type*	*Outcome*	*Included parameters*	*Reported diagnostic performance*
Peterson (2006)[15]	Individual parameters	UV	TV Z-score ≤ −3 (21–23 weeks) or ≤ −4 (23–30 weeks); TV < 5 mm (> 30 weeks) RV/LV length or width ratio < 0.5 Mild to moderate TR	NR
Salvin (2006)[3]	Individual parameters	Non-BV and RVDCC *vs* non-RVDCC	TV Z-score at diagnosis and at last scan ≤ −3 TV growth	NR
Roman (2007)[9]	Multiparametric score	Non-BV	RV/LV length ratio < 0.6 TV/MV ratio < 0.7 TID/CCD < 31.5% VCC	Presence of three of four parameters predicts non-BV with Sn of 100% and Sp of 75%
Gardiner (2008)[16]	Multiparametric score or individual parameters	BV *vs* non-BV	< 23 weeks: PV Z-score ≤ −1 and TV Z-score ≤ 3.4 < 26 weeks: median TV Z-score ≤ −3.95 26–31 weeks: median PV Z-score ≤ −2.8 and median TV/MV ratio ≤ 0.7 Right atrial pressure model (score 0–6): TR, waveform of ductus venosus and restriction of foramen ovale	100% prediction of BV and 80% of non-BV 85.7% prediction of BV and 66.7% of UV 100% prediction of postnatal circulation AUC of 0.833 when considered alone; Sn of 92% and Sp of 100% when combined with TV Z-score and used at < 26 weeks
Gómez-Montes (2011)[10]	Multiparametric score	BV *vs* non-BV	TV/MV ratio ≤ 0.83 PV/AV ratio ≤ 0.75 TID/CCD ≤ 36.5% RV/LV length ratio ≤ 0.64	Three of four criteria: Sn, 100%; Sp, 75%. Four of four criteria: Sn, 100%; Sp, 100%
Lowenthal (2014)[17]	Individual parameters	Neonatal TV Z-score > −3	TV/MV ratio; cut-off, 0.63 TV Z-score; cut-off, −4 TID/CCD; cut-off, 0.31 RV/LV length ratio; cut-off, 0.54 Antegrade PV flow, moderate TR (predictors of BV)	Sn, 78%; Sp, 100% Sn, 90%; Sp, 83% Sn, 83%; Sp, 80% Sn, 89%; Sp, 83% NR
Cao (2017)[18]	Individual parameters	BV	TV Z-score > −3 Presence of significant TR Absence of visualization of VCC Lack of subaortic stenosis	NR
Liu (2019)[19]	Individual parameters	UV *vs* BV	TV Z-score; cut-off, −3.28 TV/MV ratio; cut-off, 0.71 RV/LV length ratio; cut-off, 0.62 TID/CCD; cut-off, 33.95% Absent/mild TR Presence of VCC	Sn, 100%; Sp, 94% Sn, 77%; Sp, 100% Sn, 85%; Sp, 100% Sn, 92%; Sp, 94% NR NR
Cohen (2019)[21]	Individual parameters	RVDCC and/or type of surgery	LV- and RV-GLS TV Z-score TV/MV ratio RV end-diastolic length Z-score RV/LV length ratio	NR
Gottschalk (2020)[20]	Multiparametric score	UV *vs* BV	Absent or mild TR < 2 m/s Presence of VCC Presence of RVH (defined as RV/LV ratio ≤ 0.6)	BV if ≤ 1 criterion is fulfilled; UV if > 1 criterion is fulfilled (Sn, 100%; Sp, 100%)
Wolter (2021)[22]	Multiparametric score	Non-BV	TV/MV ratio < 0.62 Presence of VCC TR < 2.5 m/s	BV if ≤ 1 criterion is fulfilled; non-BV if > 1 criterion is fulfilled (Sn, 100%; Sp, 83%)

Only first author is given for each study. AUC, area under the receiver-operating-characteristics curve; AV, aortic valve diameter; BV, biventricular; CCD, cardiac cycle duration; GLS, global longitudinal strain; LV, left ventricle; MV, mitral valve diameter; NR, not reported; PV, pulmonary valve diameter; RV, right ventricle; RVDCC, RV-dependent coronary circulation; RVH, RV hypoplasia; Sn, sensitivity; Sp, specificity; TID, tricuspid inflow duration; TR, tricuspid regurgitation; TV, tricuspid valve diameter; UV, univentricular; VCC, ventriculocoronary connections.

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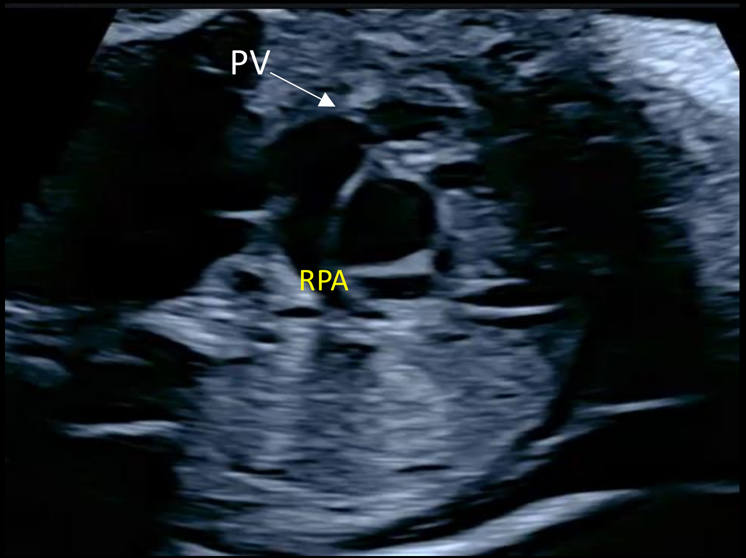
Important variables to assess Biventricular repair vs. univentricular repair

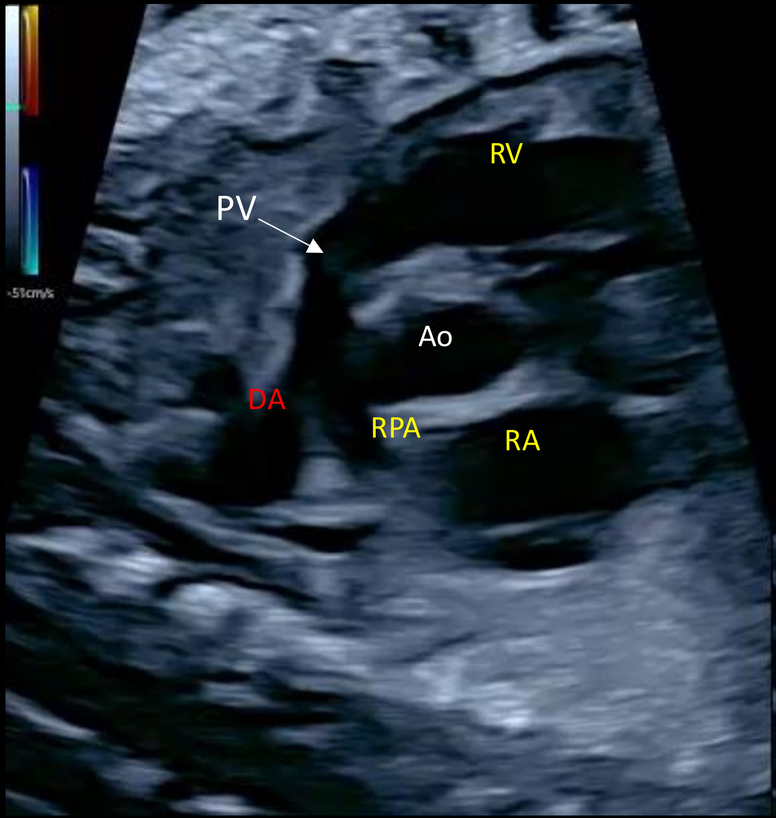
- TV z-score (strongest determinant)
- RV/LV length
- TV/MV ratio (smaller the ratio; more likely single V)
- TR jet Vmax
- Degree of TR
- RV size

Pulmonary stenosis--->Pulmonary atresia/intact ventricular septum

MPA mild dilated z+3



Follow up EGA 32 weeks 6 days



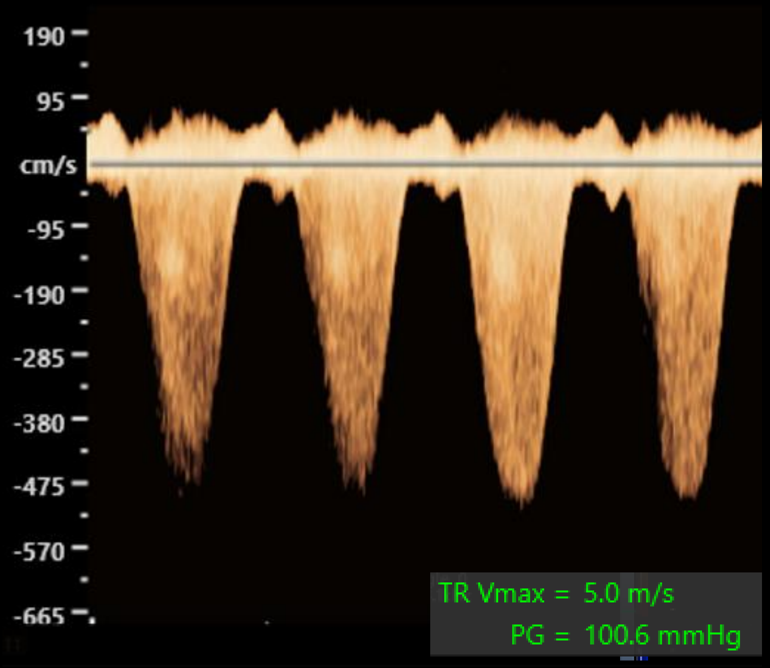
Minimal flow /functional atresia – PV z=-3.7

Pulmonary stenosis--->Pulmonary atresia/intact ventricular septum

Follow up EGA 32 weeks 6 days

Severely Dilated RV
Severe RV dysfunction
RV Hypertrophy
TV annulus z=0.21

Severe tricuspid regurgitation

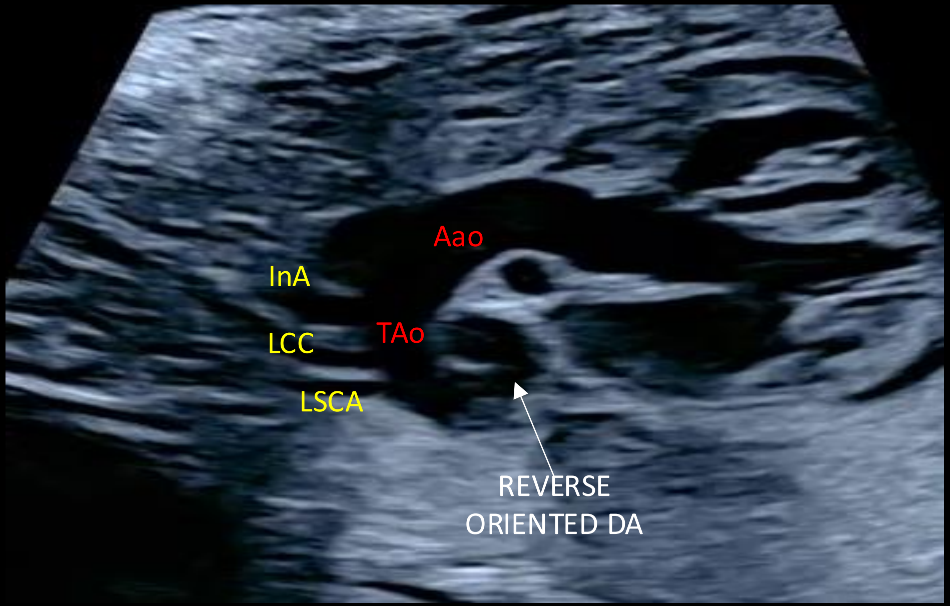


TR Doppler
TR Vmax=5 m/s, PG 100mmHg

Pulmonary stenosis--->Pulmonary atresia/intact ventricular septum

Follow up EGA 32 weeks 6 days

Aortic Arch – Sagittal View

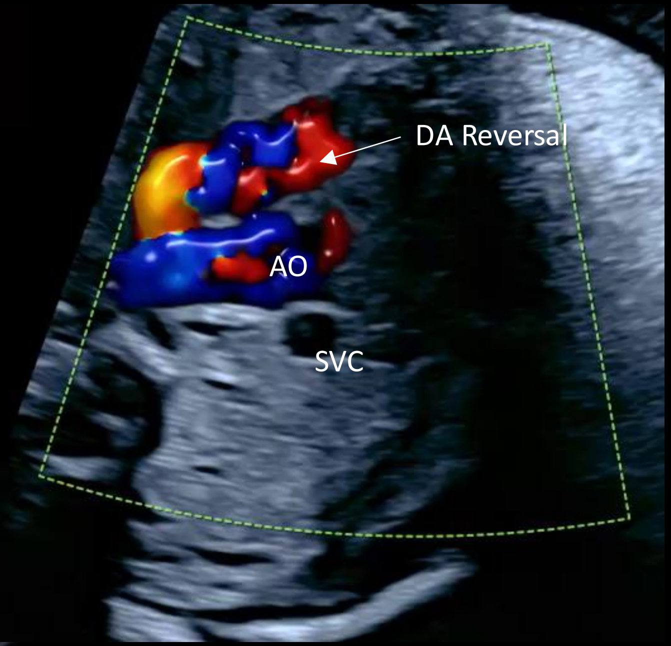


Reverse oriented DA = abnormal curvature
DA arises from underside of Ao
Indicative of ductal dependent pulmonary blood flow (Start PGE!)

Aortic Arch – Sagittal View

Flow reversal in DA
Pulmonary blood flow is ductal dependent
Ie. Not enough antegrade PV flow to supply lungs

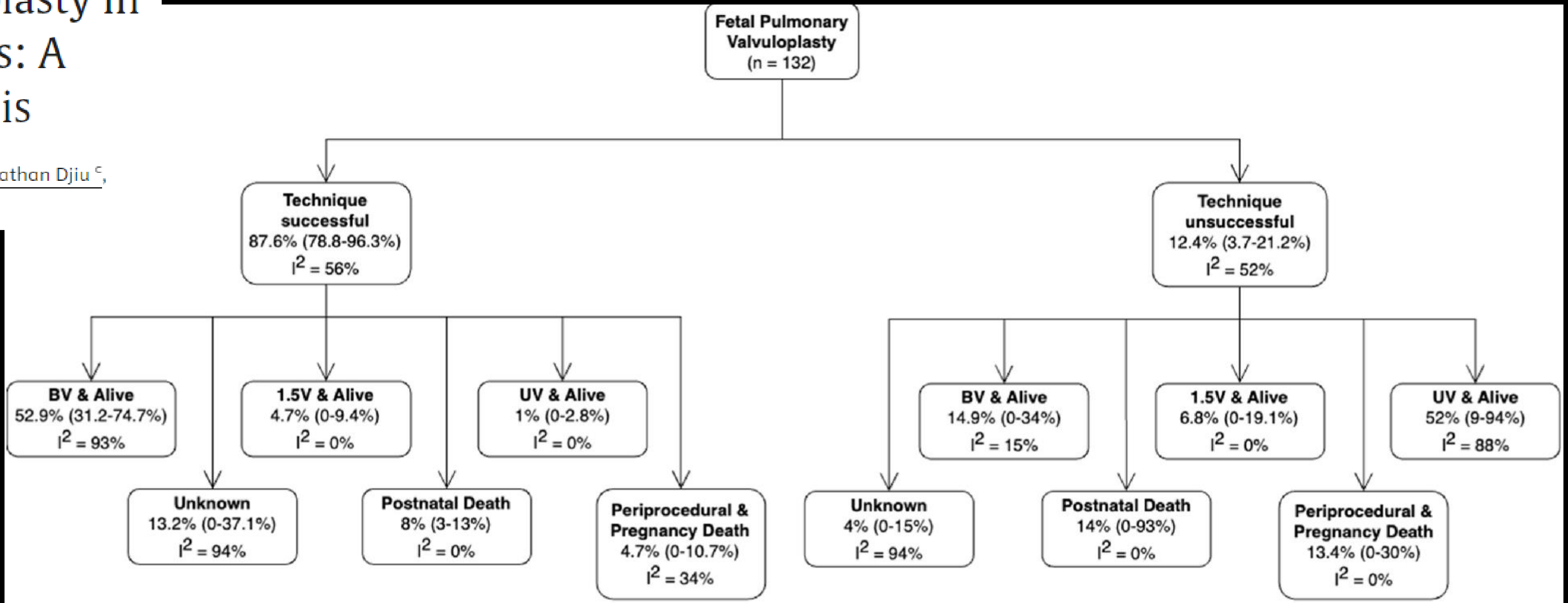
3VV



Flow reversal in DA

Impact of fetal pulmonary valvuloplasty in in-utero critical pulmonary stenosis: A systematic review and meta-analysis

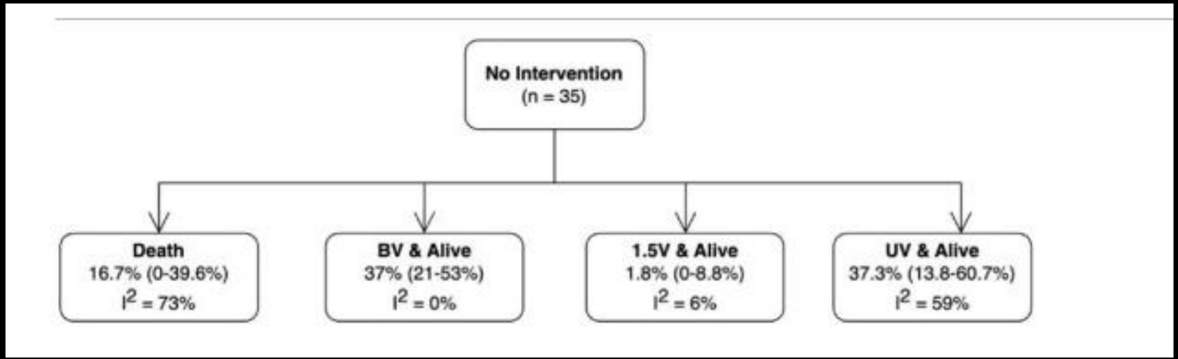
Brian Mendel [a] [b], Kelvin Kohar [c], Defin Allevia Yumnanisha [c], Richie Jonathan Djiu [c], Justin Winarta [c], Radityo Prakoso [a], Sisca Natalia Siagian [a]



Study aims: Meta-anlsyis of PA-IVS and potential intervention candidate.

Results:

- FPV successful at 97.6%
- FPV: 52.9 % patients attained biventricular circulation postnatally
- Successful FPV was associated with a slightly higher overall mortality rate [periprocedural death 4.7 % (95%CI: 0–10.7 %) and postnatal death 8 % (95%CI: 3–13 %)] compared to the three currently available definitive therapies



Brian Mendel, Kelvin Kohar, Defin Allevia Yumnanisha, Richie Jonathan Djiu, Justin Winarta, Radityo Prakoso, Sisca Natalia Siagian, Impact of fetal pulmonary valvuloplasty in in-utero critical pulmonary stenosis: A systematic review and meta-analysis, International Journal of Cardiology Congenital Heart Disease, Volume 15, 2024, 100485, ISSN 2666-6685, https://doi.org/10.1016/j.ijcchd.2023.100485.

Fetal pulmonary valvuloplasty is uncommon practice with current outcomes

Conclusions

In Summary

- severe Ebsteins anomaly, critical aortic stenosis with worsening function, and critical PS may require very urgent referral for fetal intervention
- Recognizing these defects and evolving physiology can alter course for child with timely intervention
- Prenatal diagnosis can change the delivery and postnatal immediate management
- Knowing the degree of severity will help aid in counseling and expectations

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Phoenix Children's

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Fetal Cardiology Symposium 2024

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- 4th Annual Advanced Fetal Imaging: Ultrasound & MRI Course
- Pathologic Specimen and Fetal Echo Review Course
- Nurse Coordinator Collaborative
- Hands-on Fetal Echo Learning Lab
- 4th Annual Fetal Heart Society Scientific Session

Co directors

Chris Lindblade, MD
Anita Moon-Grady, MD, FAAP, FAAC, FASE
Julia Solomon, MD, FACOG, MDCM
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- **Placental Influences on CHD and Neurodevelopment**
- **Fetal AVSD: Isolated and Complex Variants**
- **Management and Prenatal Counseling of Tricuspid Valve Dysplasia and Ebstein's Anomaly**
- **Aortic Stenosis: Early Detection, Management and Intervention**
- **PA-IVS: Future Circulation and Role of Intervention**
- **Anomalies of the Systemic Veins**
- **Prenatal Evaluation of Vascular Rings**
- **Evolution of Echo Findings in Aortic Arch Obstruction**
- **Predicting the Need for Urgent BAS in D-TGA**
  Tachycardia Resistant to Treatment
- **Fetal Atrial Septal Intervention: Who Do I Put on a Plane?**
- **Uncommon Presentations of Tetralogy of Fallot and Clinically Relevant Variants**

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Thank you

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References

1. Rashed, Eman & Dembar, Alexandra & Riasat, Maria & Zaidi, Ali. (2022). Bicuspid Aortic Valves: an Up-to-Date Review on Genetics, Natural History, and Management. Current Cardiology Reports. 24. 1-10. 10.1007/s11886-022-01716-2.
2. https://www.secondscount.org/condition/pulmonary-valve-stenosis
3. https://ctsurgerypatients.org/adult-heart-disease/tricuspid-valve-disease
4. **:** Topilsky Y (2020) Mitral Regurgitation: Anatomy, Physiology, and Pathophysiology—Lessons Learned From Surgery and Cardiac Imaging. *Front. Cardiovasc. Med.* 7:84. doi: 10.3389/fcvm.2020.00084
5. 1. Rychik J., Rome J., Collins M., DeCampli W., Spray T. The hypoplastic left heart syndrome with intact atrial septum: atrial morphololgy, pulmonary vascular histopathology, and outcome. *J Am Coll Cardiol.* 1999;34:554–560..
6. Torigoe T, Mawad W, Seed M, Ryan G, Marini D, Golding F, VAN Mieghem T, Jaeggi E. Treatment of fetal circular shunt with non-steroidal anti-inflammatory drugs. Ultrasound Obstet Gynecol. 2019 Jun;53(6):841-846. doi: 10.1002/uog.20169. PMID: 30381862.
7. Su Jin Choi et al. Importance of pulmonary valve morphology for pulmonary valve preservation in tetralogy of Fallot surgery: comparison of the echocardiographic parameters. Clin Exp Pediatr. 2020;63(5):189-194. Published online November 8, 2019
8. Andrews RE, Tibby SM, Sharland GK, Simpson JM. Prediction of outcome of tricuspid valve malformations diagnosed during fetal life. Am J Cardiol. 2008 Apr 1;101(7):1046-50. doi: 10.1016/j.amjcard.2007.11.049. Epub 2008 Feb 6. PMID: 18359329.
9. Villalaín C, Moon-Grady AJ, Herberg U, Strainic J, Cohen JL, Shah A, Levi DS, Gómez-Montes E, Herraiz I, Galindo A. Prediction of postnatal circulation in pulmonary atresia/critical stenosis with intact ventricular septum: systematic review and external validation of models. Ultrasound Obstet Gynecol. 2023 Jul;62(1):14-22. doi: 10.1002/uog.26176. Epub 2023 Jun 5. PMID: 36776132.
10. Brian Mendel, Kelvin Kohar, Defin Allevia Yumnanisha, Richie Jonathan Djiu, Justin Winarta, Radityo Prakoso, Sisca Natalia Siagian, Impact of fetal pulmonary valvuloplasty in in-utero critical pulmonary stenosis: A systematic review and meta-analysis, International Journal of Cardiology Congenital Heart Disease, Volume 15, 2024, 100485, ISSN 2666-6685, https://doi.org/10.1016/j.ijcchd.2023.100485.
11. Freud, L. R., McElhinney, D. B., Kalish, B. T., Escobar-Diaz, M. C., Komarlu, R., Puchalski, M. D., Jaeggi, E. T., Szwast, A. L., Freire, G., Levasseur, S. M., Kavanaugh-McHugh, A., Michelfelder, E. C., Moon-Grady, A. J., Donofrio, M. T., Howley, L. W., Selamet Tierney, E. S., Cuneo, B. F., Morris, S. A., Pruetz, J. D., … Tworetzky, W. (2020). Risk Factors for Mortality and Circulatory Outcome Among Neonates Prenatally Diagnosed With Ebstein Anomaly or Tricuspid Valve Dysplasia: A Multicenter Study. In Journal of the American Heart Association (Vol. 9, Issue 21). Ovid Technologies (Wolters Kluwer Health). https://doi.org/10.1161/jaha.120.016684
12. Freud LR, McElhinney DB, Kalish BT, Escobar-Diaz MC, Komarlu R, Puchalski MD, Jaeggi ET, Szwast AL, Freire G, Levasseur SM, Kavanaugh-McHugh A, Michelfelder EC, Moon-Grady AJ, Donofrio MT, Howley LW, Selamet Tierney ES, Cuneo BF, Morris SA, Pruetz JD, van der Velde ME, Kovalchin JP, Ikemba CM, Vernon MM, Samai C, Satou GM, Gotteiner NL, Phoon CK, Silverman NH, Tworetzky W. Risk Factors for Mortality and Circulatory Outcome Among Neonates Prenatally Diagnosed With Ebstein Anomaly or Tricuspid Valve Dysplasia: A Multicenter Study. J Am Heart Assoc. 2020 Nov 3;9(21):e016684. doi: 10.1161/JAHA.120.016684. Epub 2020 Oct 20. PMID: 33076749; PMCID: PMC7763426.