Right Ventricular Outflow Tract Obstructive Lesions

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Thursday, March 21, 2024

Disclosures

I have disclosures to present.

Objectives

1. To define and describe the cardiac lesions that cause RVOT obstruction
2. To recognize the clinical signs or RVOT obstruction in neonates
3. Application of proper assessment methods and medical management in RVOT obstructive lesions

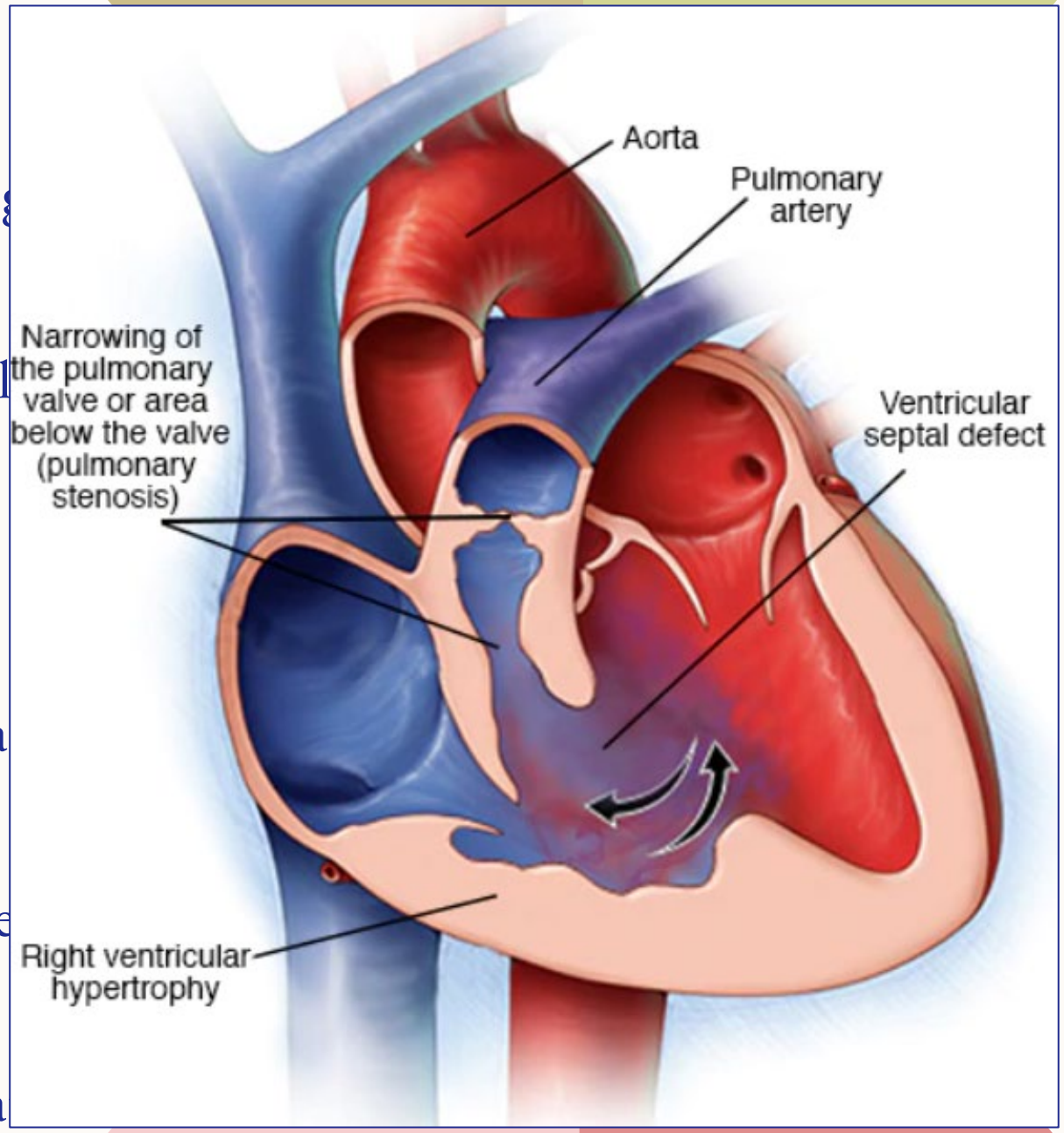
Tetralogy of Fallot

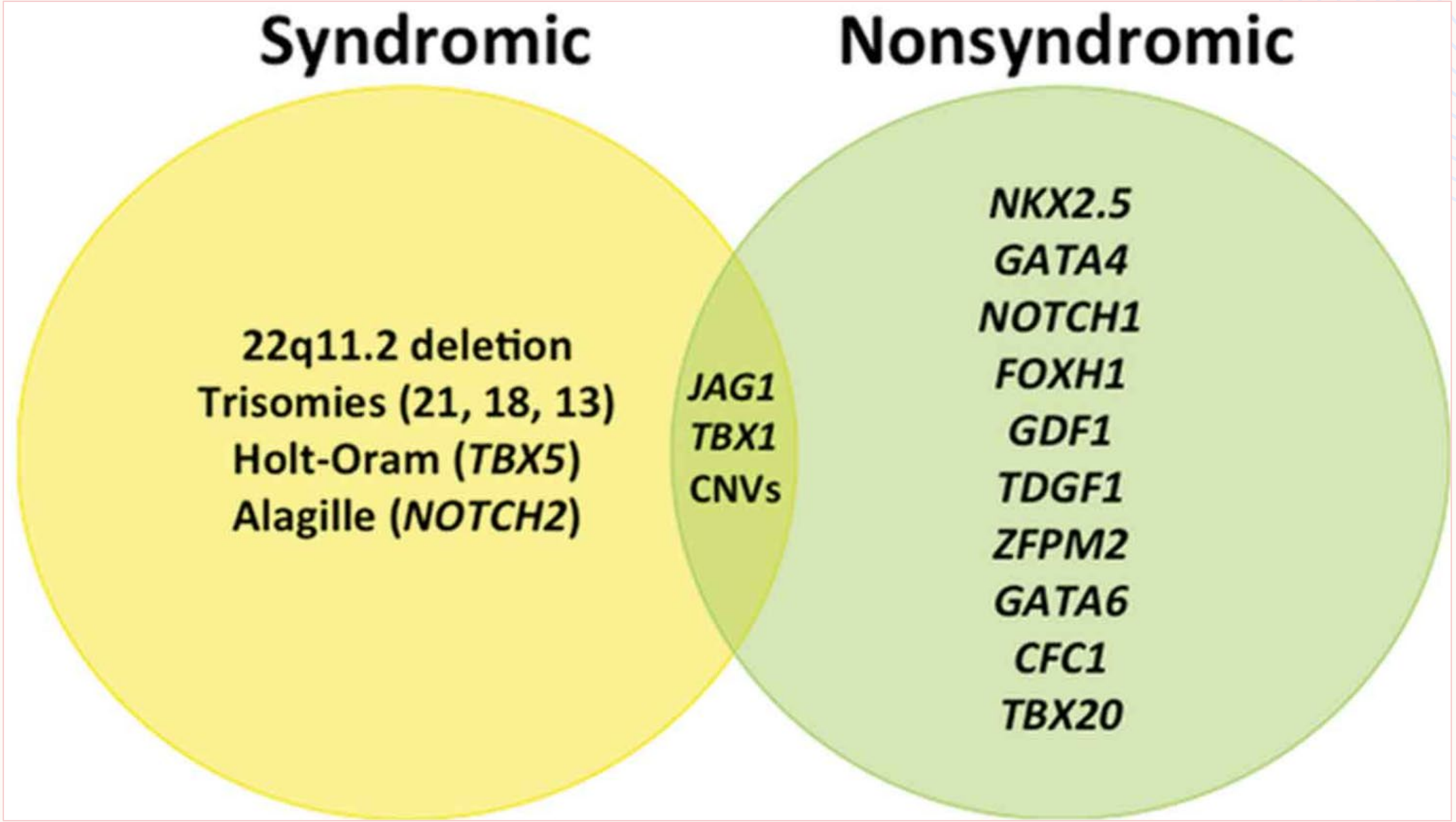
History of Tetralogy of Fallot

- Earliest description was first described by Danish anatomist and Bishop, Niels Stenson in 1671
    - Reported his findings in a fetus with multiple abnormalities
- Eduard Sandifort published clinical and autopsy findings in 1888 of a 12-year-old male with progressive cyanosis and SOB but had been "perfectly normal at birth"
- In the 1800's, 15 cases were described by John Farre and 64 cases referenced by Thomas Peacock
- Etienne-Louis Arthur Fallot went on to define the clustering of 4 distinct anatomic features of a frequent cause of cyanosis, hence a "tetralogy"
    - Acknowledged earlier reported cases in his many papers about this disease
- Dr. Maude Abbott popularized the disease and introduced the name in 1924

TOF Overview

- TOF is the most common form of cyanotic cong heart disease
- Obstruction to pulmonary blood flow is the hal TOF with varying severity
- Prevalence of ~577 cases per million live births
  - Possibly a slight predominance in males
- There's about a 2-3% chance of patient having a with CHD, but not necessarily TOF
- 22q11.2 chromosomal duplication or microdele occurs in ~20% of patients with TOF
- ~60% of cases of TOF have unknown genetic ca




Syndromic
Nonsyndromic
22q11.2 deletion
Trisomies (21, 18, 13)
Holt-Oram (*TBX5*)
Alagille (*NOTCH2*)
JAG1
TBX1
CNVs
NKX2.5
GATA4
NOTCH1
FOXH1
GDF1
TDGF1
ZFPM2
GATA6
CFC1
TBX20

Syndromic TOF

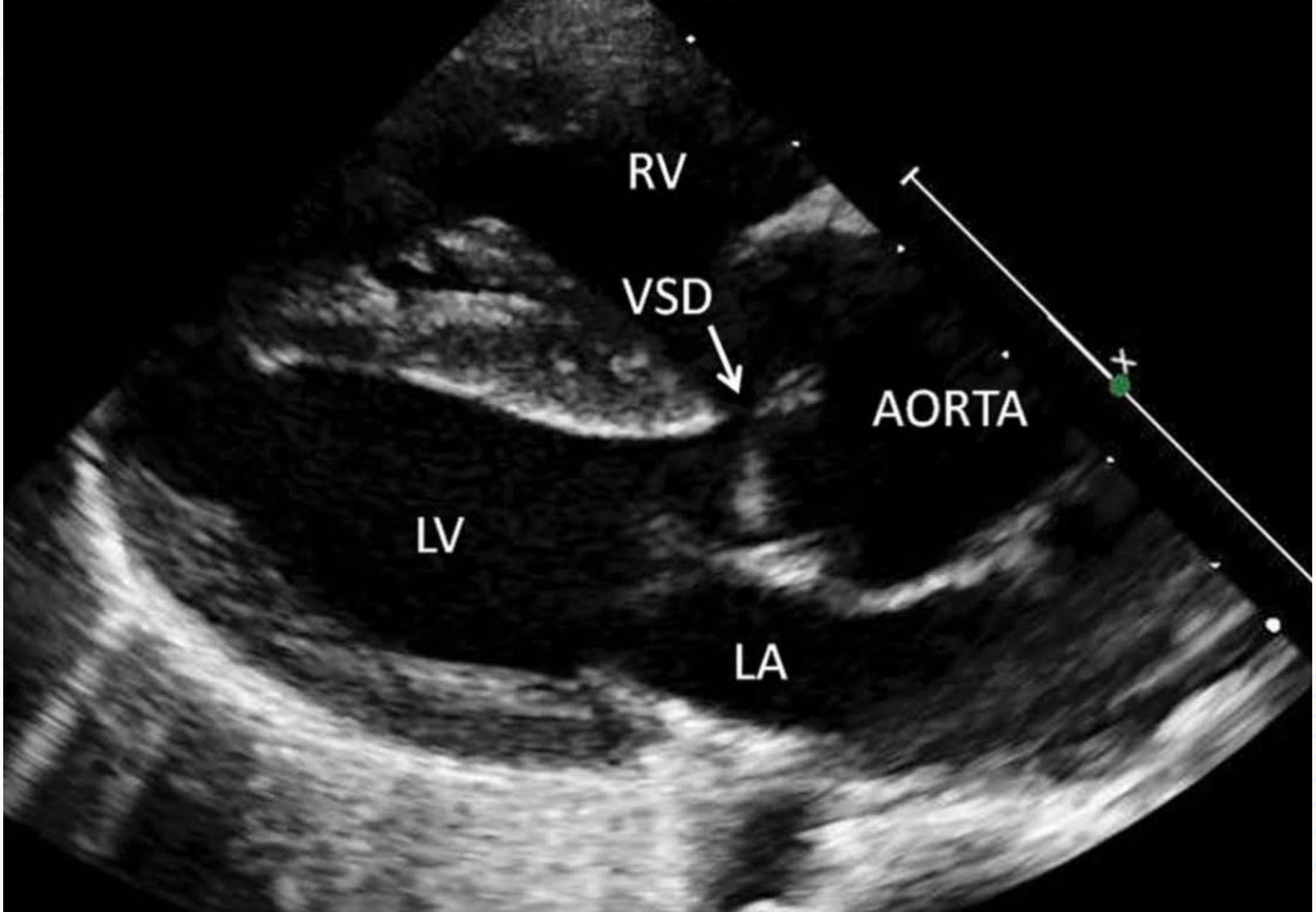
- TOF is associated with 121 entries in OMIM database
  - 32 listed syndromes include TOF as the characteristic feature
- 22q11.2 microdeletion syndrome is the most frequently identified cause of TOF
  - Seen in 16% of TOF patients
  - Occurs in 1 per 3,000-6,000 live births
- Trisomies 13, 18, and 21 cause 5-7% of syndromic TOF cases
  - Trisomy 21 is the most common of these
- Single gene causes are associated with TOF
  - TBX5 causes Holt-Oram syndrome
  - JAG1 and NOTCH2 mutations cause Alagille syndrome

Nonsyndromic TOF

- Mutations in 12 single genes have been associated with nonsyndromic TOF
- Genetic associations with 22q11.2 deletion, JAG1 mutations, and TBX1 mutations are associated with nonsyndromic TOF
- Environmental exposures have been associated with an increased risk of TOF and other conotruncal defects
    - Maternal diabetes
    - Febrile or viral illnesses
    - Vitamin A exposure
    - Exposure to organic solvents

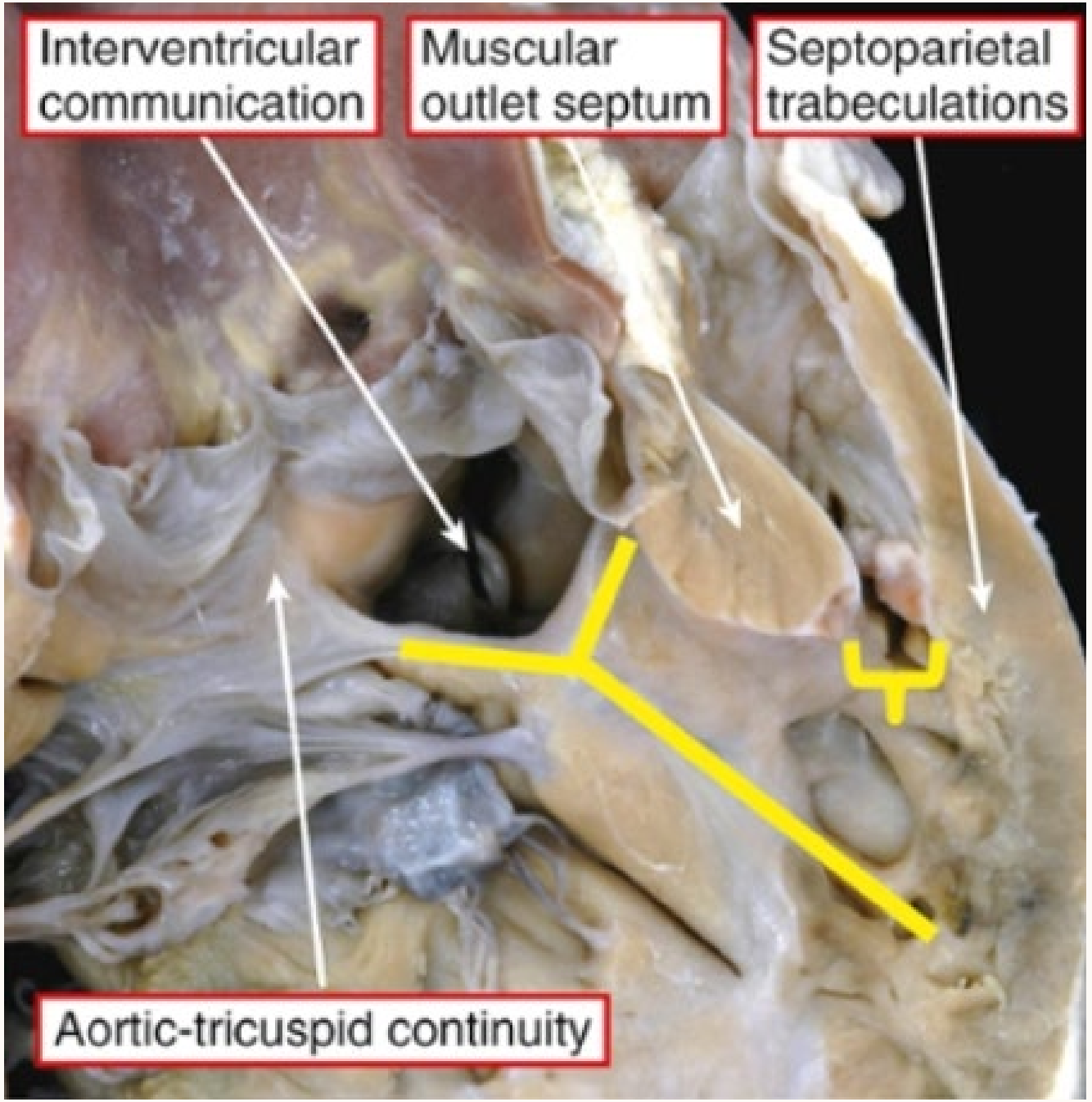
Anatomy of TOF

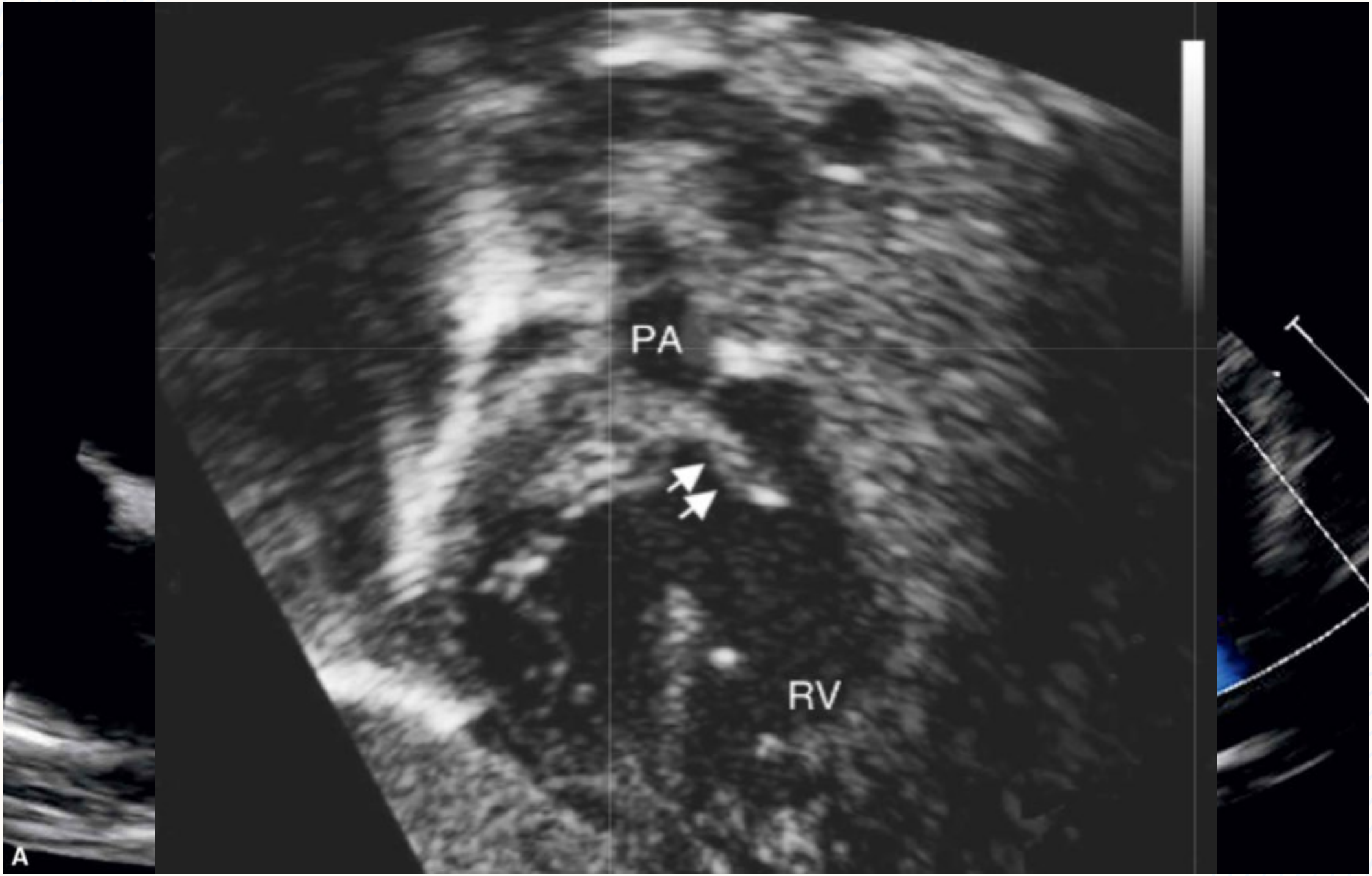
- VSD is beneath the aortic valve
  - Located in the outlet septum
  - Deviated anteriorly
    - Anterior malalignment
  - Types of VSDs
    - Perimembranous (60-70%)
    - Muscular outlet (20-30%)
    - Doubly committed subarterial (rare)
- "Overriding aorta"
  - Overrides the VSD
  - Degree of override varies
- 20-25% of patients have a right-sided aortic arch


RV
VSD
AORTA
LV
LA

Anatomy of TOF

- Pulmonary valve is dysplastic and hypoplastic
- Infundibular narrowing causing narrowing of the RVOT
- Main and branch pulmonary arteries are often hypoplastic
- May also have supravalvular stenosis
- Right ventricular hypertrophy
- 5-7% of TOF patients have coronary artery abnormalities
- Uncommon to have MAPCAs in the absence of pulmonary atresia
- Can be associated with AVSD


Interventricular communication
Muscular outlet septum
Septoparietal trabeculations
Aortic-tricuspid continuity


PA
RV
A

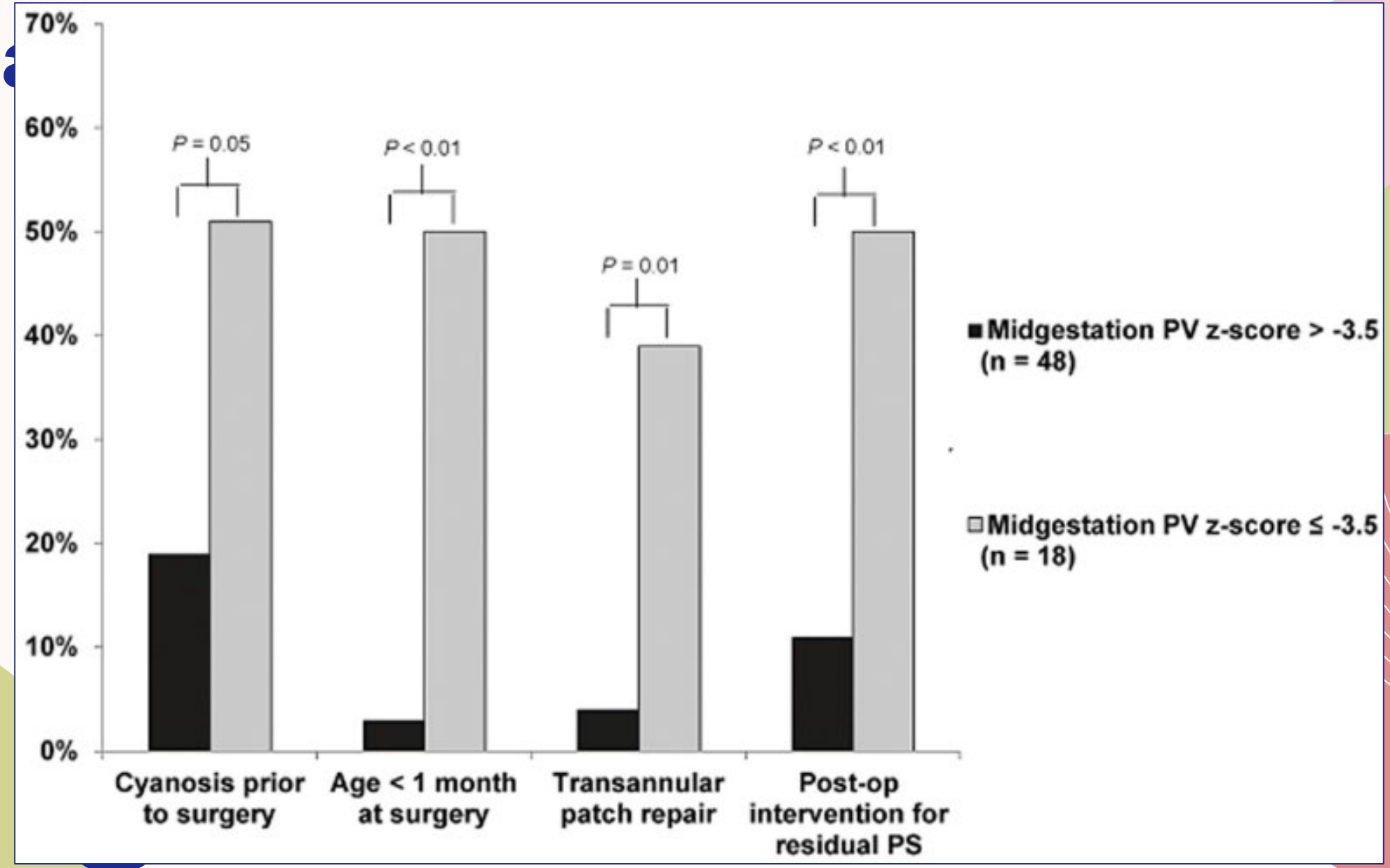
Prenatal Diagnosis

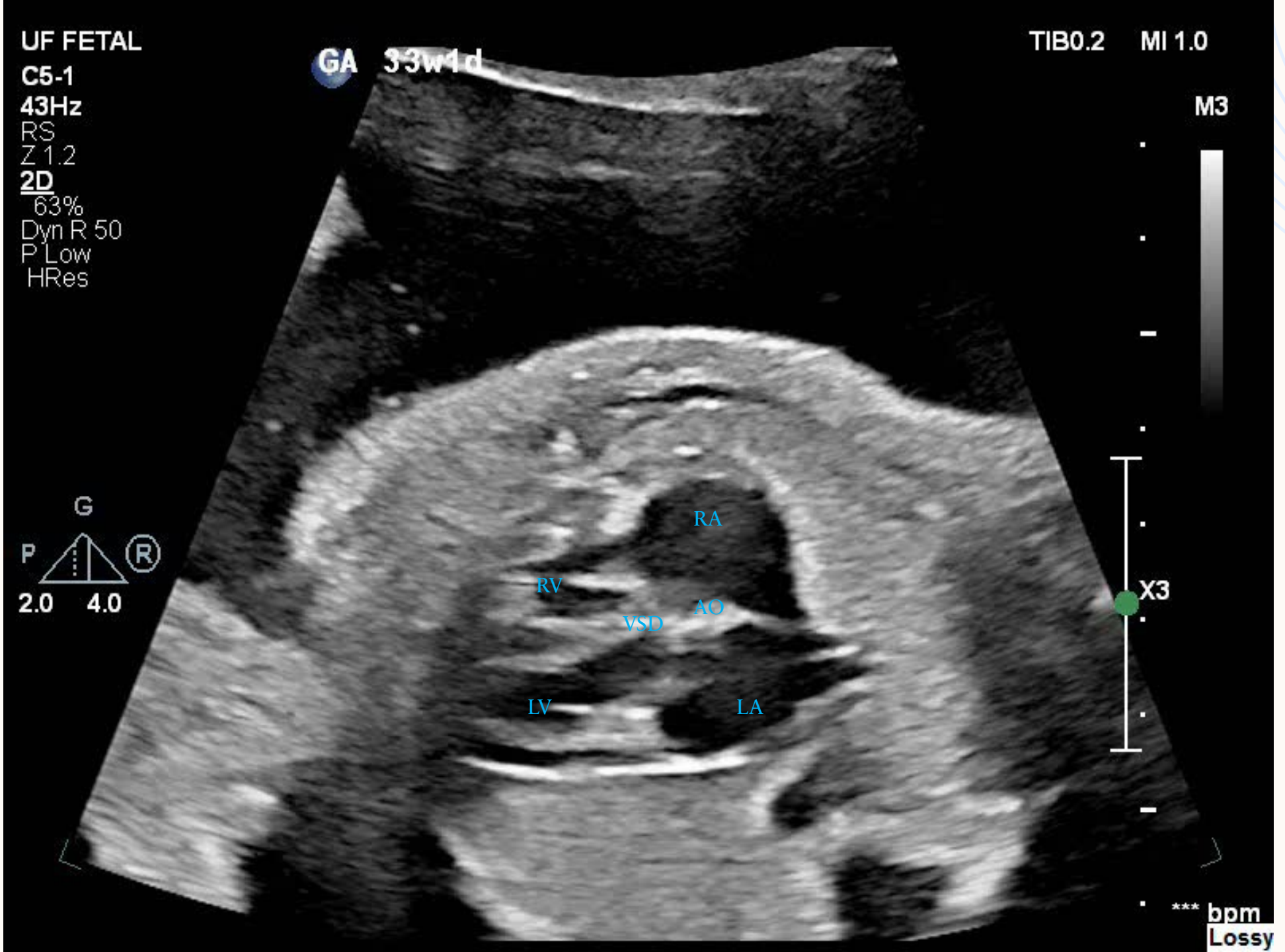
- Prenatal diagnosis rate of TOF is as high as 70%
  - Diagnostic accuracy is up to 90%
    - RVOT obstruction seen in TOF can progress during fetal life in some cases
- Median gestational age at time of fetal diagnosis is 24 weeks
- Optimal timing for fetal echocardiogram is 18-22 weeks gestation
  - Serial assessments are done at 2-to-8-week intervals until 34-36 weeks gestation

Table 1 Potential indications for fetal echocardiography

	ASE 2023 recommendation	AIUM 2020[4]	AHA 2014[2*]
Maternal factors (absolute risk)[†]			
Pre–gestational diabetes (3%-5%)	Is indicated	Is indicated	I (indicated)
Gestational diabetes diagnosed after second trimester (<1%)	Not indicated	Not indicated	III (no benefit)
Phenylketonuria (12%-14%)	Is indicated	Is indicated	I (indicated)
Autoimmune disease: SSA/SSB positive (1%-5%)[‡]	Is indicated	Is indicated	IIa (probably indicated)
In vitro fertilization (1.1%-3.3%)	May be considered[§]	Is indicated	IIa (Probably indicated)
Maternal infection: rubella (3%-4%)	Is indicated	Is indicated	I (indicated)
Family history of CHD: first-degree relative (3%-20%)[¶]	Is indicated	Is indicated	I (indicated)
Family history of CHD: second-degree or more distant relative (<2%)[‖]	Not indicated	May be indicated	IIb (may be indicated)
Obesity (BMI > 30 kg/m^2) (1-2%)	Not indicated	Not indicated	—
Retinoids (8%-20%)	Is indicated	Is indicated	I (indicated)
ACE inhibitors (3%)	May be considered[§]	May be indicated	IIa (probably indicated)
Paroxetine (3%)	May be considered[§]	May be indicated	IIb (may be indicated)
Other selective serotonin reuptake inhibitors (1%-2%)[6,7]	Not indicated	Not indicated	III (no benefit)
Anticonvulsants (1%-2%)	Not indicated	May be indicated	IIb (may be indicated)
Lithium (1%-2%)	Not indicated	May be indicated	IIb (may be indicated)
Warfarin (<1%)[8]	Not indicated	Not indicated	III (no benefit)
Fetal factors identified during screening (absolute risk)			
Fetal hydrops (15%-20%)[9]	Is indicated	Is indicated	I (indicated)
Extracardiac anomaly (20%-45%)[10,11]	Is indicated	Is indicated	I (indicated)
Chromosomal abnormalities (10%-90%)	Is indicated	Is indicated	I (indicated)
Monochorionic twinning (2%-10%)	Is indicated	Is indicated	I (indicated)
Nuchal translucency 3.0-3.4 mm (~3%)	May be considered[§]	May be indicated	IIa (probably indicated)
Nuchal translucency ≥3.5 mm (6%-60%)	Is indicated	Is indicated	I (indicated)
Single umbilical artery in isolation (1.2%-1.8%)[12]	Not indicated	Not indicated	IIb (may be indicated)

Feta


70%
60%
50%
40%
30%
20%
10%
0%
P = 0.05
P < 0.01
P = 0.01
P < 0.01
Cyanosis prior to surgery
Age < 1 month at surgery
Transannular patch repair
Post-op intervention for residual PS
Midgestation PV z-score > -3.5 (n = 48)
Midgestation PV z-score ≤ -3.5 (n = 18)


UF FETAL
C5-1
43Hz
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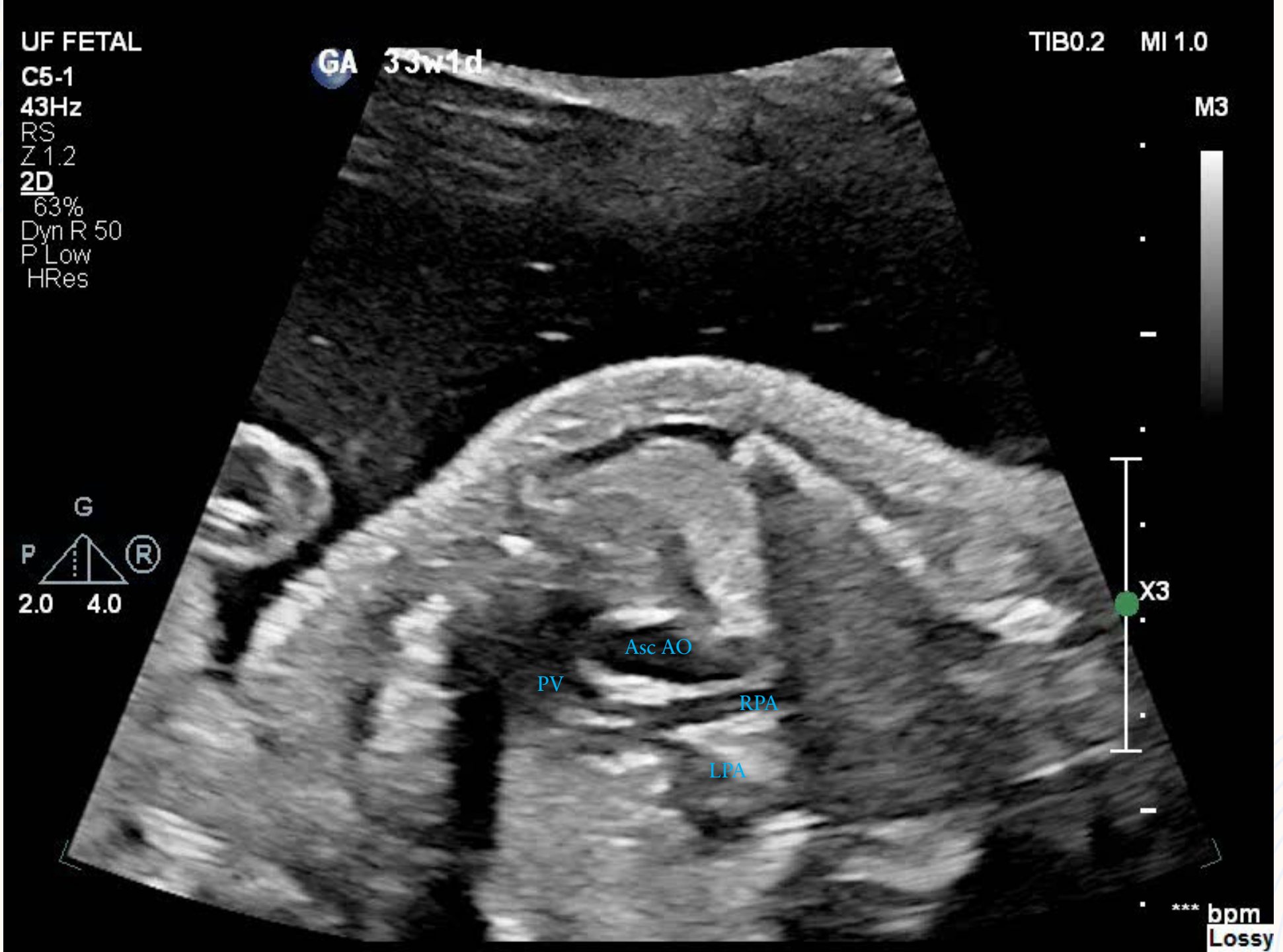
UF FETAL
C5-1
43Hz
RS
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2D
63%
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LPA
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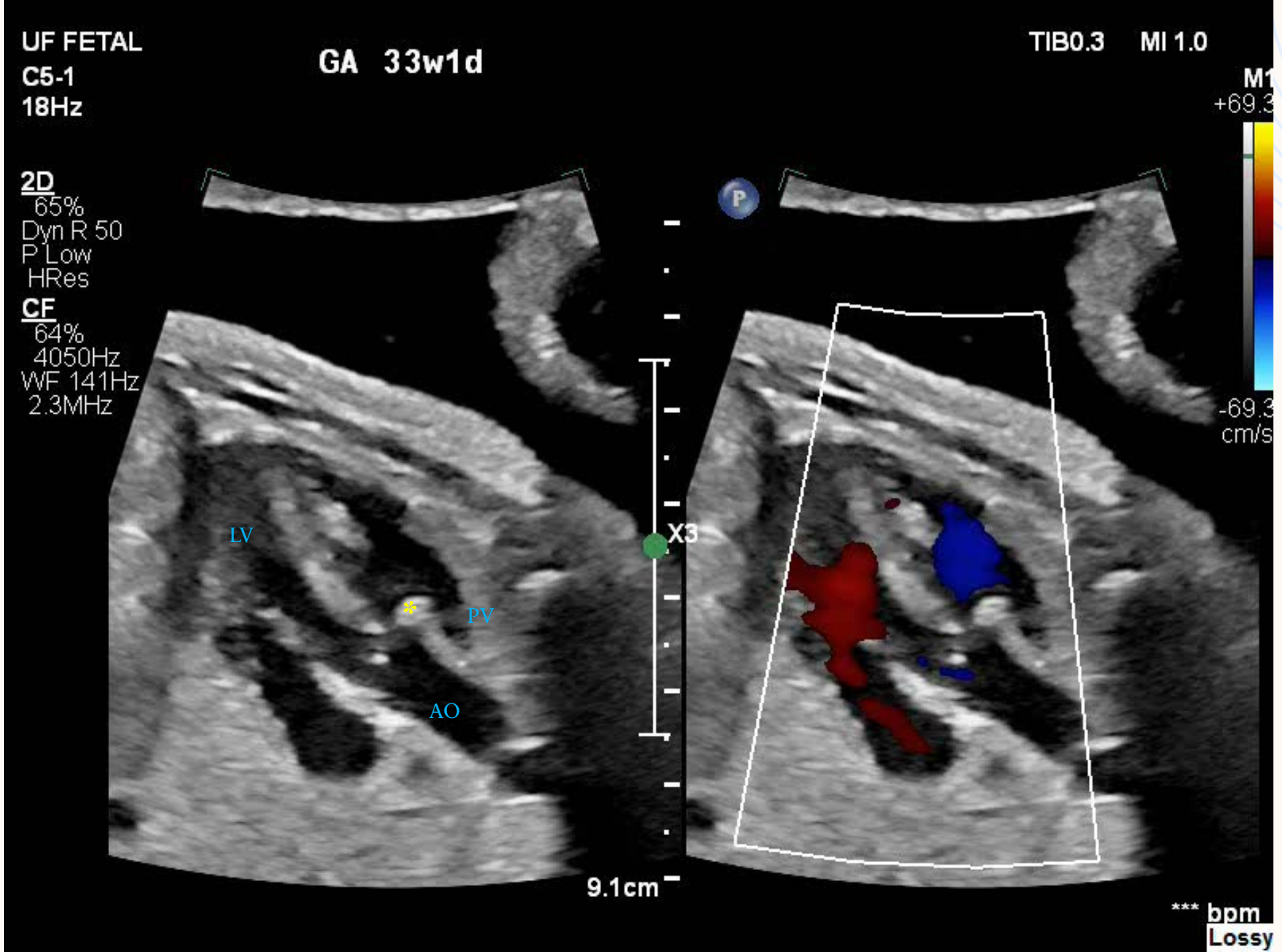
bpm
Lossy


UF FETAL
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2.3MHz
LV
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AO
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9.1cm
*** bpm
Lossy

Clinical Presentation

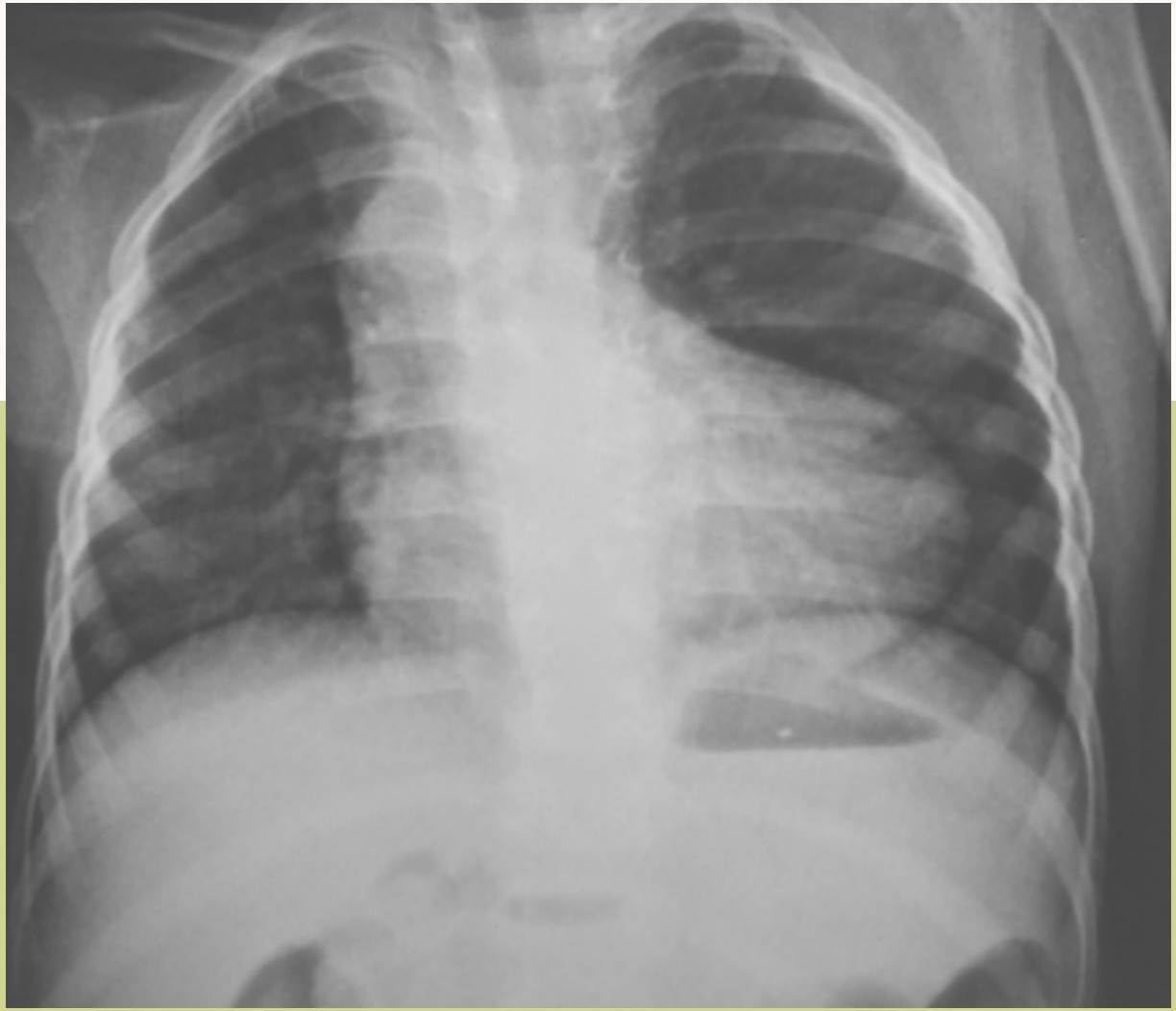
- Clinical symptoms will vary based on degree of RVOT obstruction
- Cyanosis will present within the first few days of life in cases of severe RVOT obstruction
  - Causes right-to-left shunt across the VSD with reduced pulmonary blood flow
- "Pink tets" have minimal RVOT obstruction
  - Typically have normal/near normal oxygen saturations after birth
  - Present with heart failure at 4-6 weeks of age due to increased pulmonary blood flow
- Exam findings
  - Normal S1, single S2
  - Loud systolic ejection murmur at LLSB that radiates to the back (from the RVOTO/PS, **not the VSD**)
    - The louder the and the shorter the murmur, the more severe the RVOT obstruction

Clinical Presentation

- 2/3 of newborns with TOF are acyanotic at birth
  - By 6 months of age, over 50% will have desaturations at rest
  - Desaturations progress as RVOT obstructions progresses and RV hypertrophy worsens, as this reduces pulmonary blood flow and increases right-to-left shunt across the VSD
- "Tet spells" or hypercyanotic episodes
  - Often caused by crying or stressful event
  - Develops worsening cyanosis and inability to catch their breath
  - Can progress to LOC or death in severe cases
  - Caused by increased systemic oxygen consumption due to pain/anxiety and increase in inotropy that ultimately leads to decreased RV preload and decreased pulmonary blood flow

Diagnostic Evaluation

- ECG
  - Sinus rhythm, right axis deviation, RVH
- CXR
  - "Boot-shaped" heart
  - Reduced pulmonary vasculature
- Echocardiogram
- Cardiac catheterization
  - Not commonly used now
  - Can be useful to evaluate coronary arteries or peripheral PAs



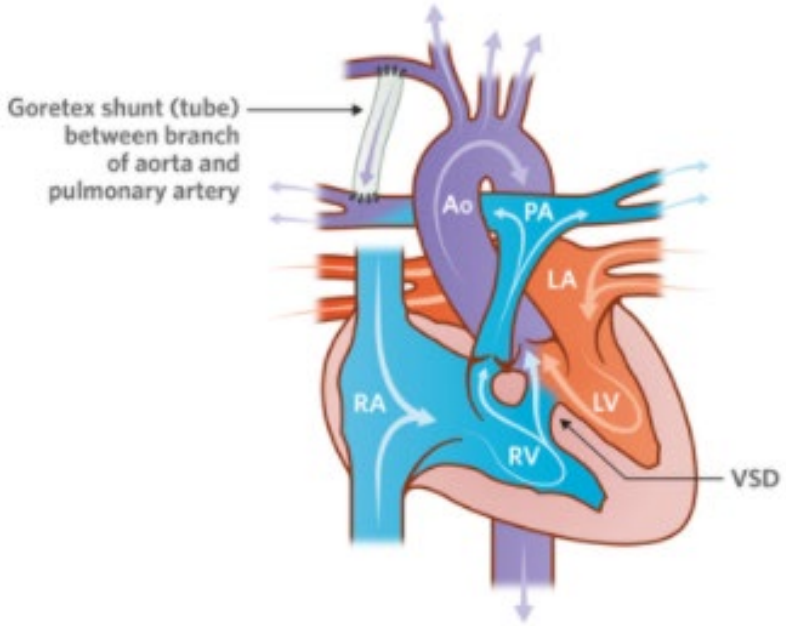
Medical Management

- Caloric supplementation
- Pharmacotherapy
  - Beta blockers (Propranolol 0.5-1 mg/kg/dose Q6H)
- “Tet spells”
  - Comfort (holding infant with flexed knees and hips)
  - Oxygen
  - IV fluid bolus (10-20 mL/kg NS)
  - IV morphine
  - IV beta blockers
    - Propranolol (0.1-0.2 mg/kg/dose)
    - Esmolol (100-500 mcg/kg over 1 minute push, then 25-100 mc/kg/min infusion)
  - IV phenylephrine (5-20 mcg/kg IV push, then 0.1-0.4 mcgk/kg/min infusion)
  - Anesthesia, intubation, mechanical ventilation

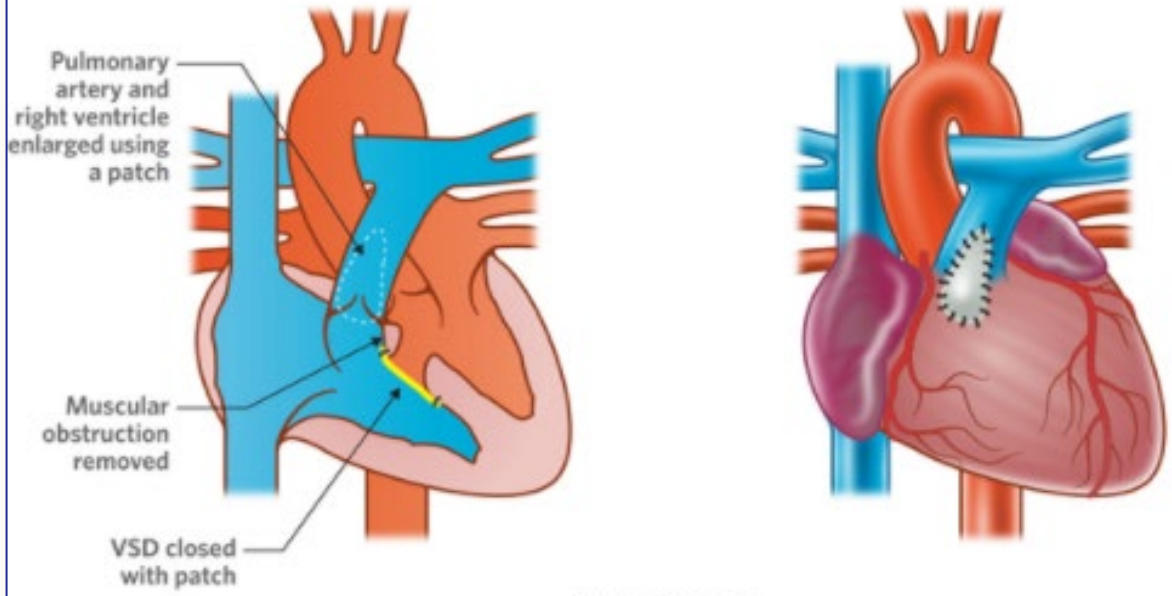
Surgical Management

- Palliative Surgery
  - Systemic-to-PA shunts improve clinical symptoms in the short term
  - Late occurrence of complications including endocarditis, cerebral abscesses, and heart failure
- Complete TOF repair
  - Elective repair in asymptomatic infants between 3-12 months of age
  - Goal of surgery is to close the VSD and relieve the RVOT obstruction
  - ~5% of patients require reoperation
  - 6% require catheter reintervention
  - Complications following surgery include incomplete relief of RVOT obstruction, residual VSD, tricuspid regurgitation, RVOT aneurysms, pulmonary insufficiency, and right bundle branch block

Repair of tetralogy of Fallot



Temporary shunt operation



Complete repair

Tetralogy of Fallot with Pulmonary Atresia

TOF/PA Overview

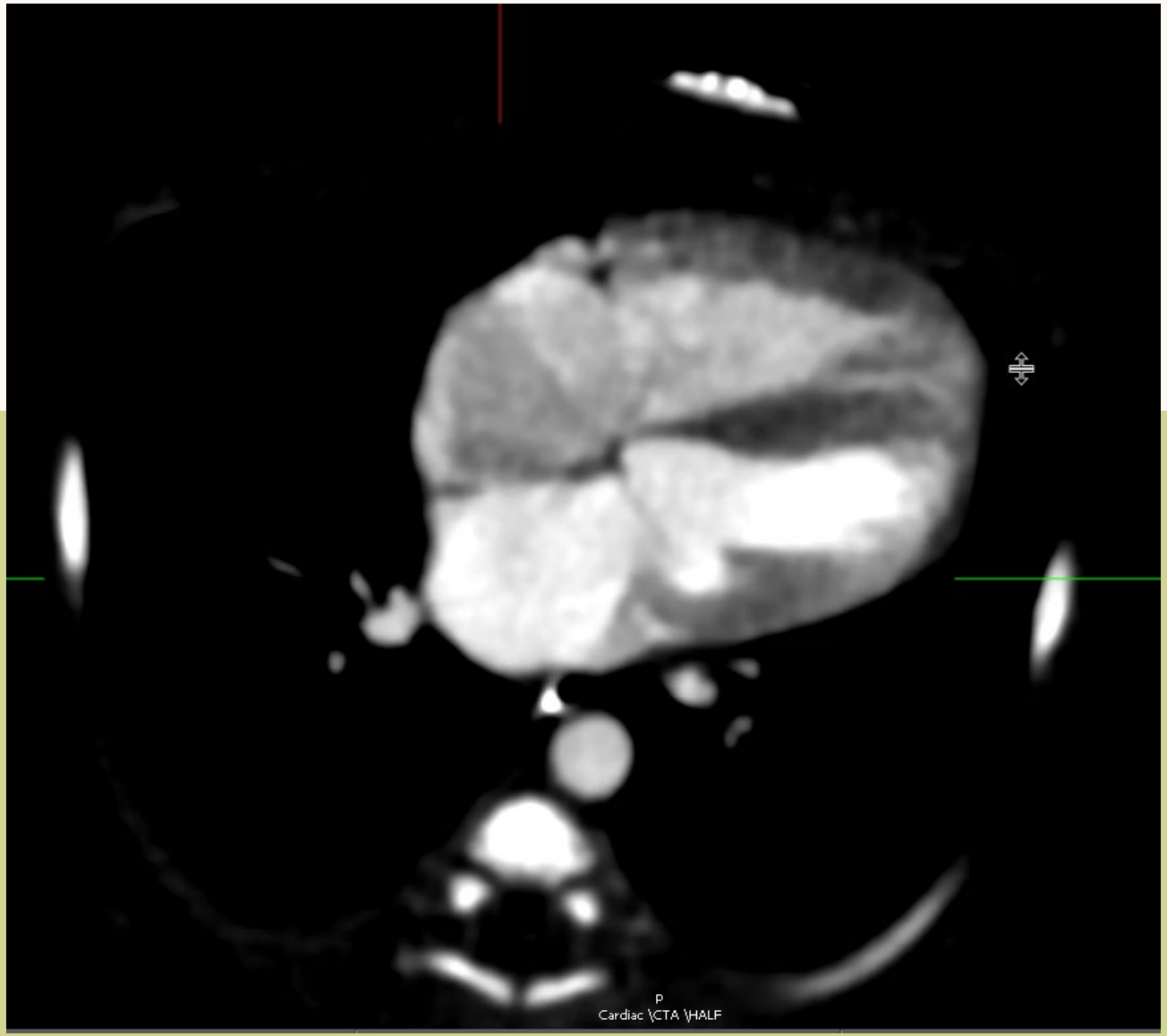
- Likelihood of having 22q11.2 deletion is increased in cases of TOF/PA compared to TOF
    - Clinical outcomes are worse in patients with this syndrome with TOF/PA
- During fetal development, can have progression to TOF/PA
    - Extent is variable and can involve the MPA or the branch PAs
- Branch PA abnormalities is more common
    - Can have MAPCAs
    - Can have nonconfluence of the Pas
- Pulmonary blood flow is supplied by the systemic arterial circulation

Clinical Presentation

- Typically present with cyanosis at birth or within the first few days of life
- Hypoxemia increases as PDA closes
- Cyanosis increases as infant ages as they outgrow the fixed pulmonary blood supply
- Exam findings
  - Normal S1, single S2
  - Patients with MAPCAs can have diffuse, continuous murmurs

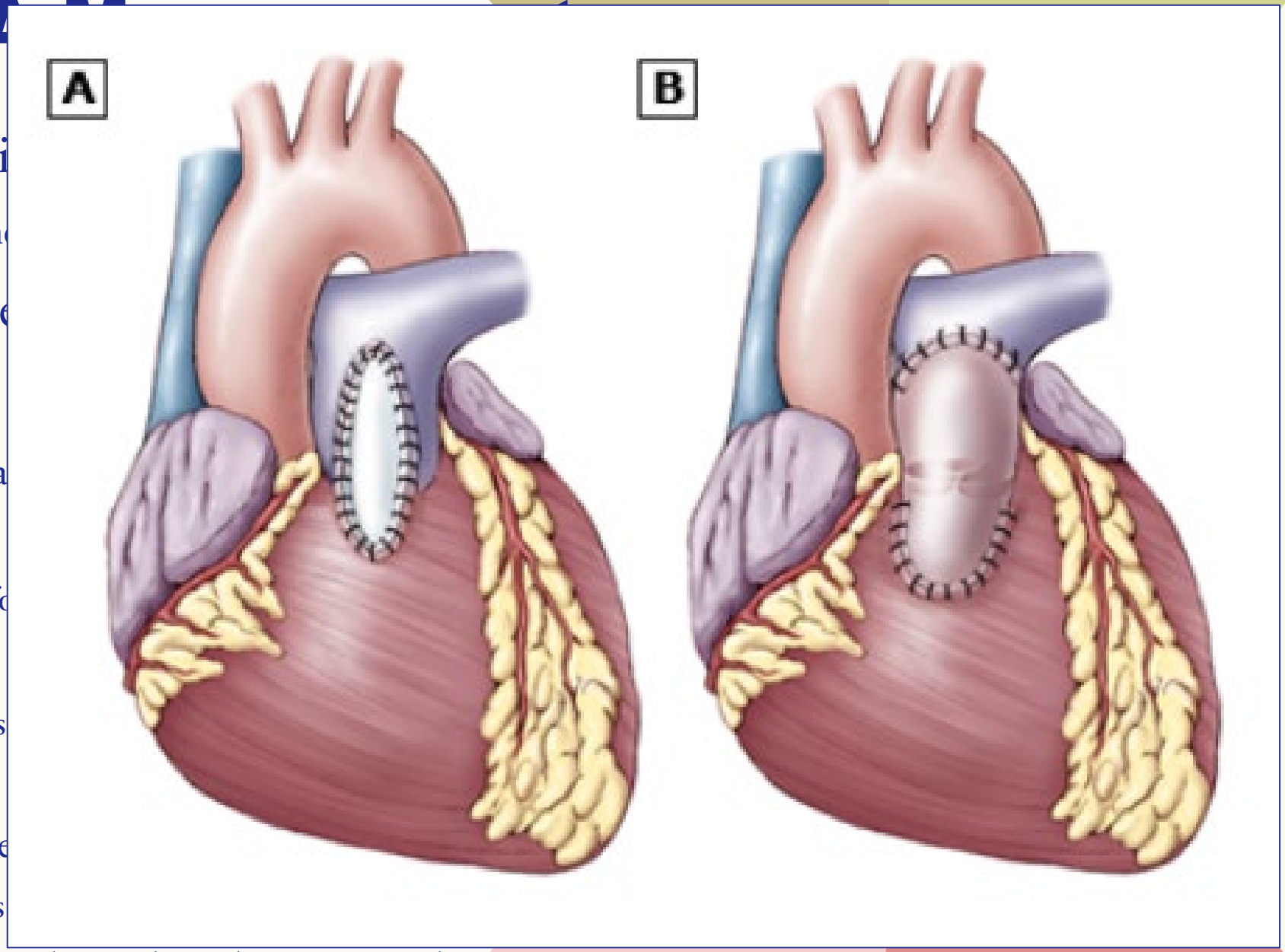
Diagnostic Evaluation

- ECG
  - Sinus rhythm, right axis deviation, RVH
- CXR
  - Reduced pulmonary vasculature
- Echocardiogram
- Cardiac catheterization
  - Further detailed evaluation of PAs and MAPCAs
- CT



TOF/PA

- Initiation of PGE at bi
  - To maintain ductal depen
- Can perform complete repair
  - Initial stage palliation goa pulmonary blood flow
    - Systemic-PA shunts, unifo
  - Complete repair
    - Goals are to perform clos arteriooplasty, and place
  - Unifocalization procedure
    - Disconnect the MAPCAs the heart for connection to the RV through a RV-PA conduit



Congenital Pulmonary Stenosis

sis

monary valve

patients with PS

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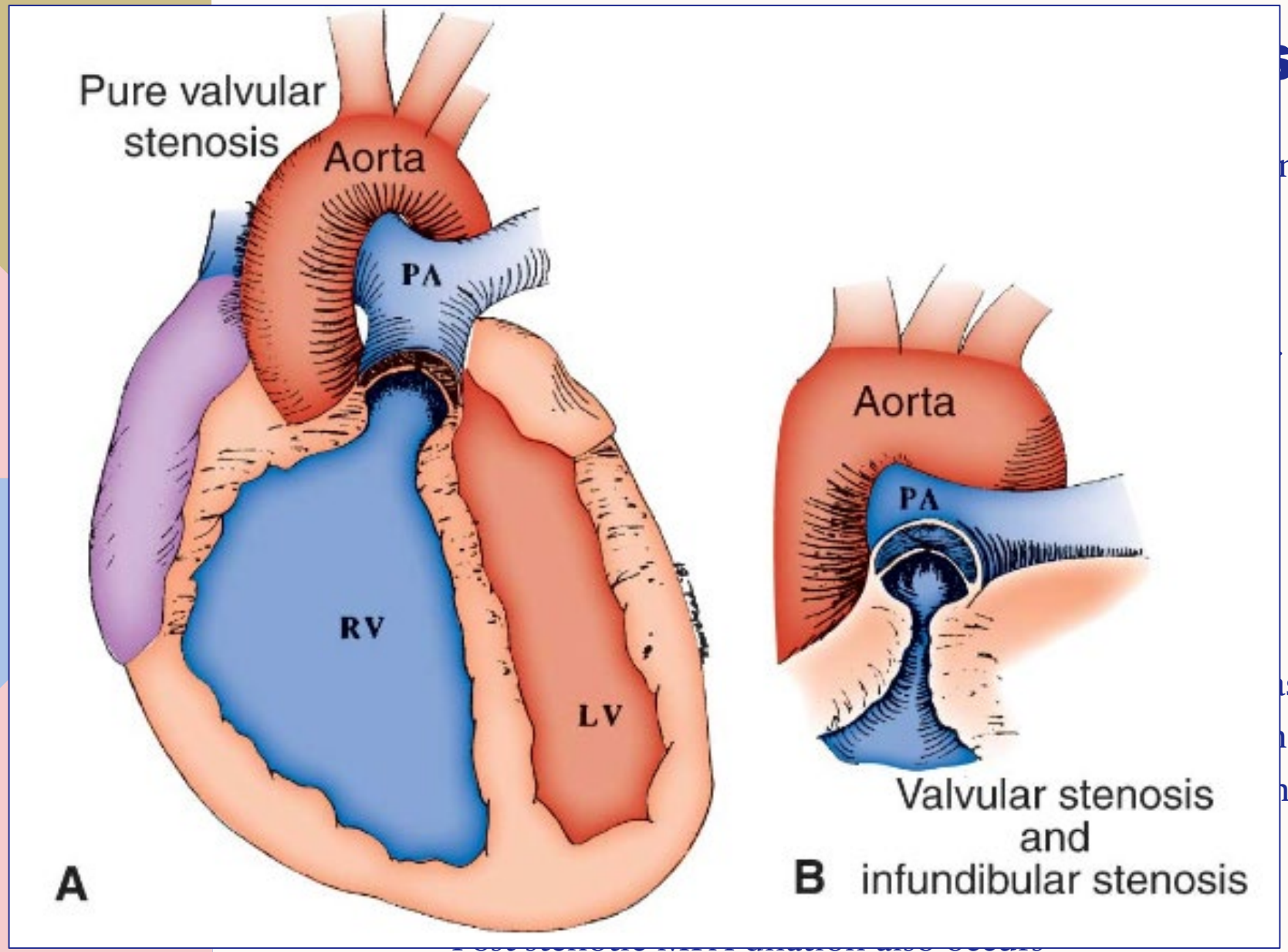


Pulmonary Valve Stenosis

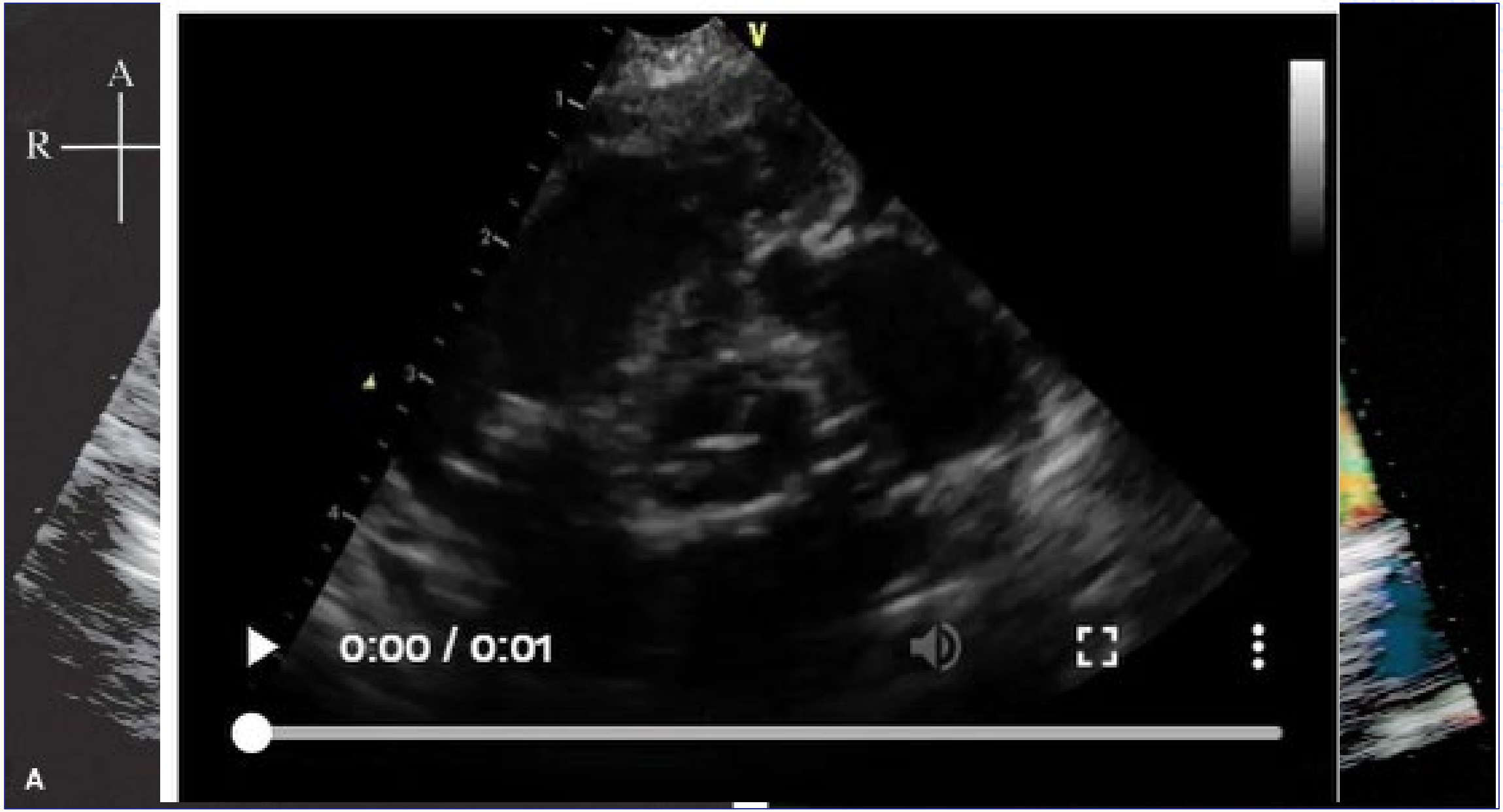
- PS causes an increase in RV pressure
  - Increasing RV pressure is directly related to degree of obstruction
- This leads to increasing RV hypertrophy
  - Normal stroke volume is maintained by the hypertensive RV working against a fixed obstruction
- Can lead to RV dilation and subsequent RV failure
- If a PFO or ASD is present, increased RA pressure leads to right-to-left shunting
- Prenatal PS severity is variable
  - Critical PS in utero results in increased right-to-left atrial shunt
  - RV is typically hypoplastic with significant RV hypertrophy

PS Clinical Features

- Most patients are asymptomatic
  - Murmur is heard in otherwise healthy appearing infant
  - Most patients have normal growth and development
- In less severe cases, symptoms are rare in childhood
  - Symptoms begin to occur in response to age and exertion
    - Exertional dyspnea, fatigue, and cyanosis with exertion
- In cases of critical PS, symptoms present at birth
  - Cyanosis at birth
  - May develop RV failure early in infancy
- Exam findings
  - Normal S1, followed by pulmonary ejection click and then systolic ejection murmur at LUSB
  - Split S2
  - Critical PS in infants – PS murmur may be soft due to decreased PV flow and may have TR or PDA murmur

Diagnostic Evaluation

- ECG
  - Normal in ~50% cases of mild PS
  - Right axis deviation
  - RVH in moderate PS
  - RA enlargement in severe PS
- CXR
  - Prominent MPA segment
  - RA prominence
  - Cardiomegaly
  - Decreased pulmonary vascularity
- Echocardiogram
  - Mild PS – peak gradient 20-40 mmHg
  - Moderate – peak gradient 40-60 mmHg
  - Severe – peak gradient >60 mmHg
- Cardiac catheterization
  - More useful for therapeutic intervention than diagnosis
  - RVSP > 35 mmHg is abnormal
  - PV gradient > 10 mmHg is abnormal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PS Management

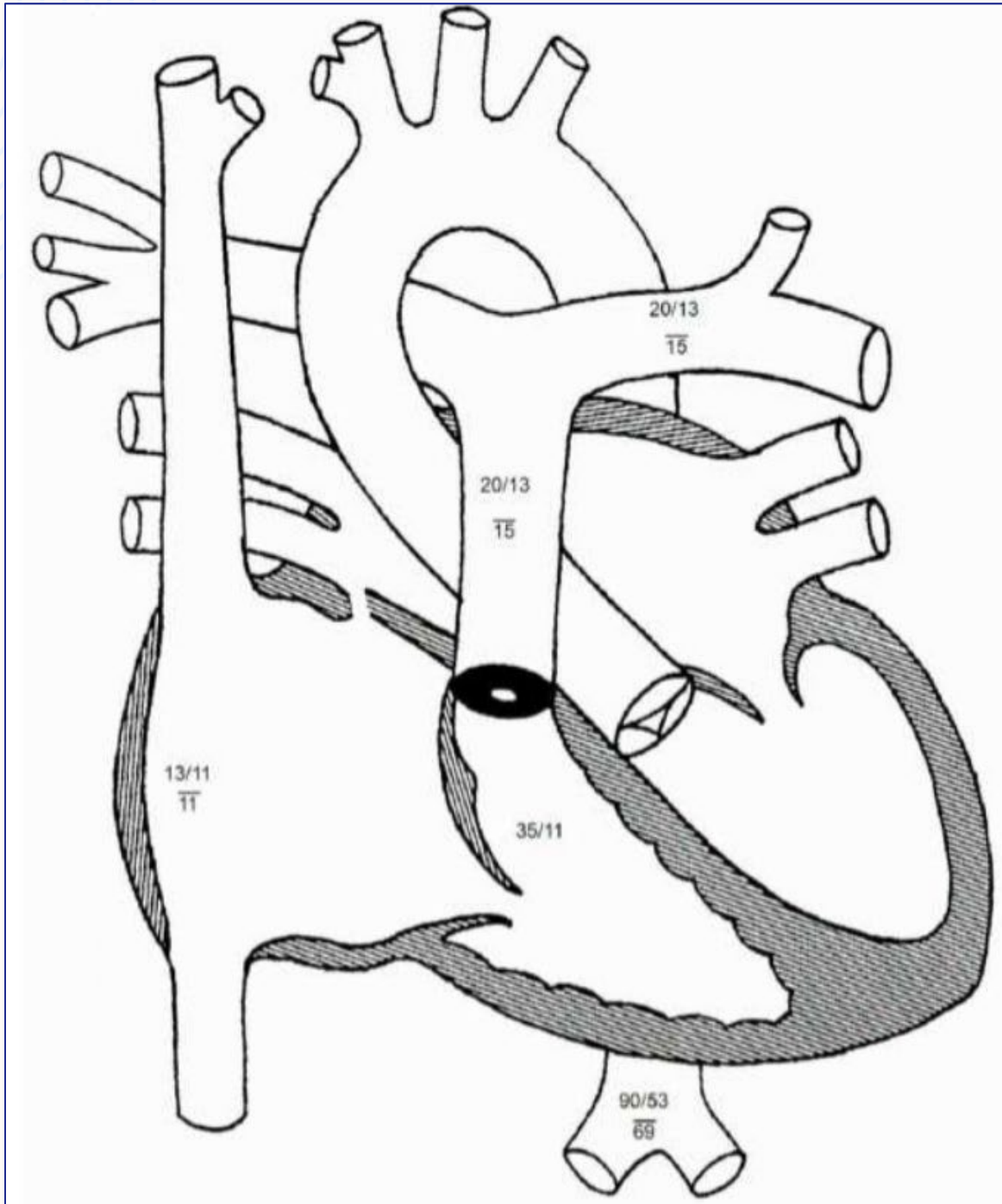
- Mild PS
  - Supportive care and close monitoring
  - Most patients do not usually require intervention
  - Most cases will not worsen, and cases either remain stable or improve over time
- Moderate PS
  - Close surveillance as patients are at risk for progression to severe PS
  - Monitor for RV changes, including RV dysfunction and worsening RV hypertrophy
  - If severity increases, RV changes occur, or patient becomes symptomatic, then proceed with intervention
- Severe PS/Critical PS
  - Initiate PGE at birth to maintain PDA
  - Balloon pulmonary valvuloplasty or surgical pulmonary valvotomy
  - Catheterization intervention is typically pursued first in neonates

Balloon Pulmonary Valvuloplasty

- First line treatment for dome-shaped valvular PS and neonates with critical PS
- BPV is not very effective in subvalular or supravalvular PS
- Complications are relatively uncommon
    - Pulmonary valve perforation or flail leaflet
    - Tricuspid valve injury
    - Femoral vein occlusion
    - Varying degrees of pulmonary insufficiency
- PGE is discontinued after BPV
- In some cases of neonates with critical PS after BPV, there is still insufficiency forward flow across the PV
    - PGE can be maintained with intermittent allowance of ductal constriction to monitor for tolerance

Surgical Pulmonary Valvotomy

- Not usually required for common valvular PS
  - 10-15% of infants with critical PS ultimately undergo surgery
- Complications are very rare
  - Watch for "suicide RV" postoperatively
- More commonly performed in PS due to dysplastic or hypoplastic pulmonary valves
  - Also option of choice if there is MPA or branch PA hypoplasia
  - Indicated in cases of subvalvular or supravalvular PS
- More commonly performed in PS associated with Alagille syndrome, Williams syndrome, and Noonan syndrome



Gender: Male

Attending: Curt Fudge, MD
Fellow: Summer Rye-Buckingham, MD
Referring:

Height: 64.5 cm Weight: 9.1 kg
BSA = 0.38 m²

Fluoro: 9.40 min Contrast: 16.00 mL
Vein: Right femoral 5fr
Artery: Right femoral 22g

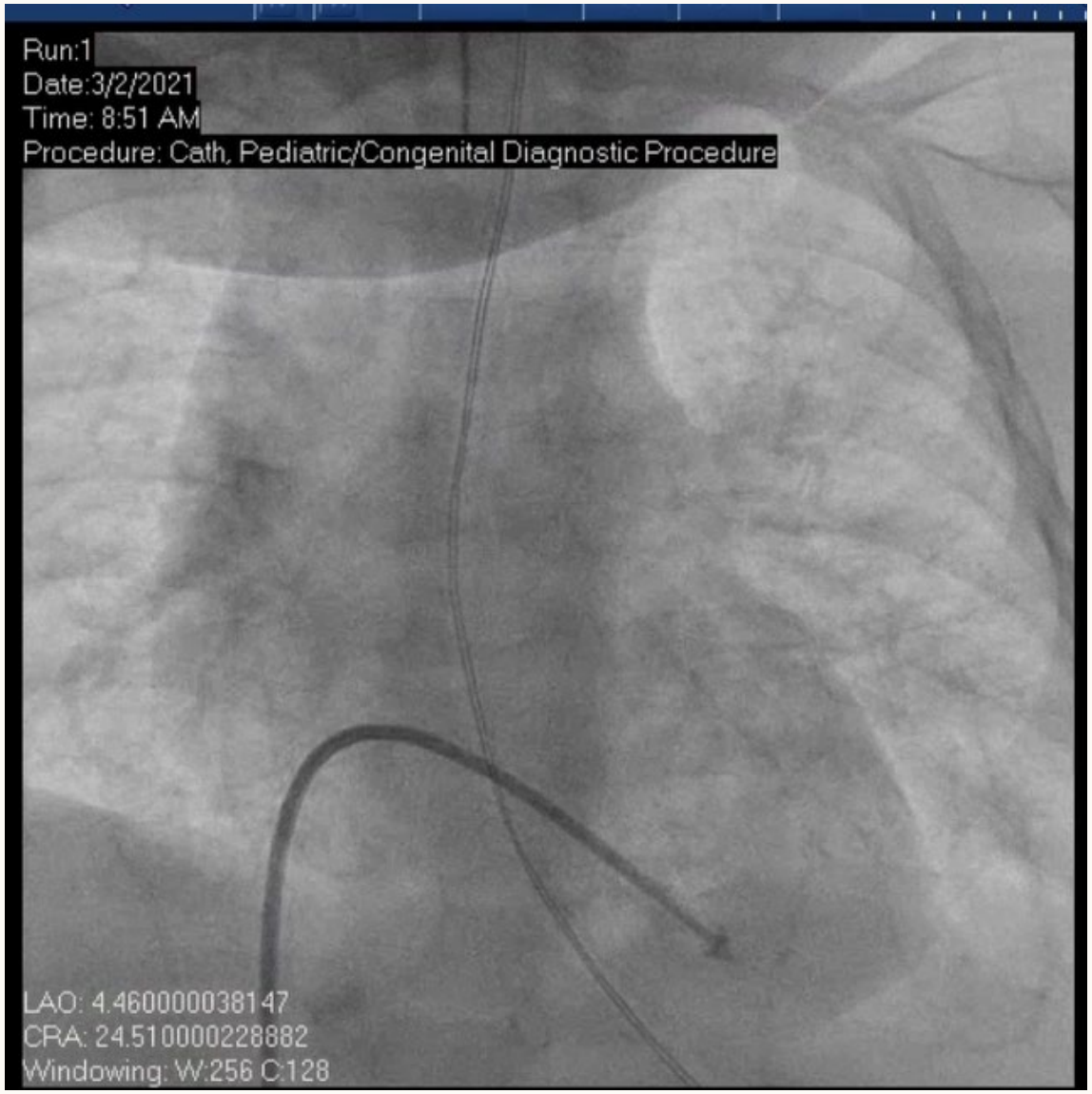
Post 12 mm Balloon

Heart Rate: 145 bpm
VO2:
Hemoglobin:

Inspired O2:
pH:
pCO2:
pO2:
HCO3:

%O2	Site	Sys/A	Dias/V	Mean
	SVC			
	RA	13	11	11
	RV	35.0	11	
	PA	20.0	13	15.0
	RPA			
	LPA	20	13	15

%O2	Site	Sys/A	Dias/V	Mean
	LA			
	LV			
	aAO			
	dAO	90	53	69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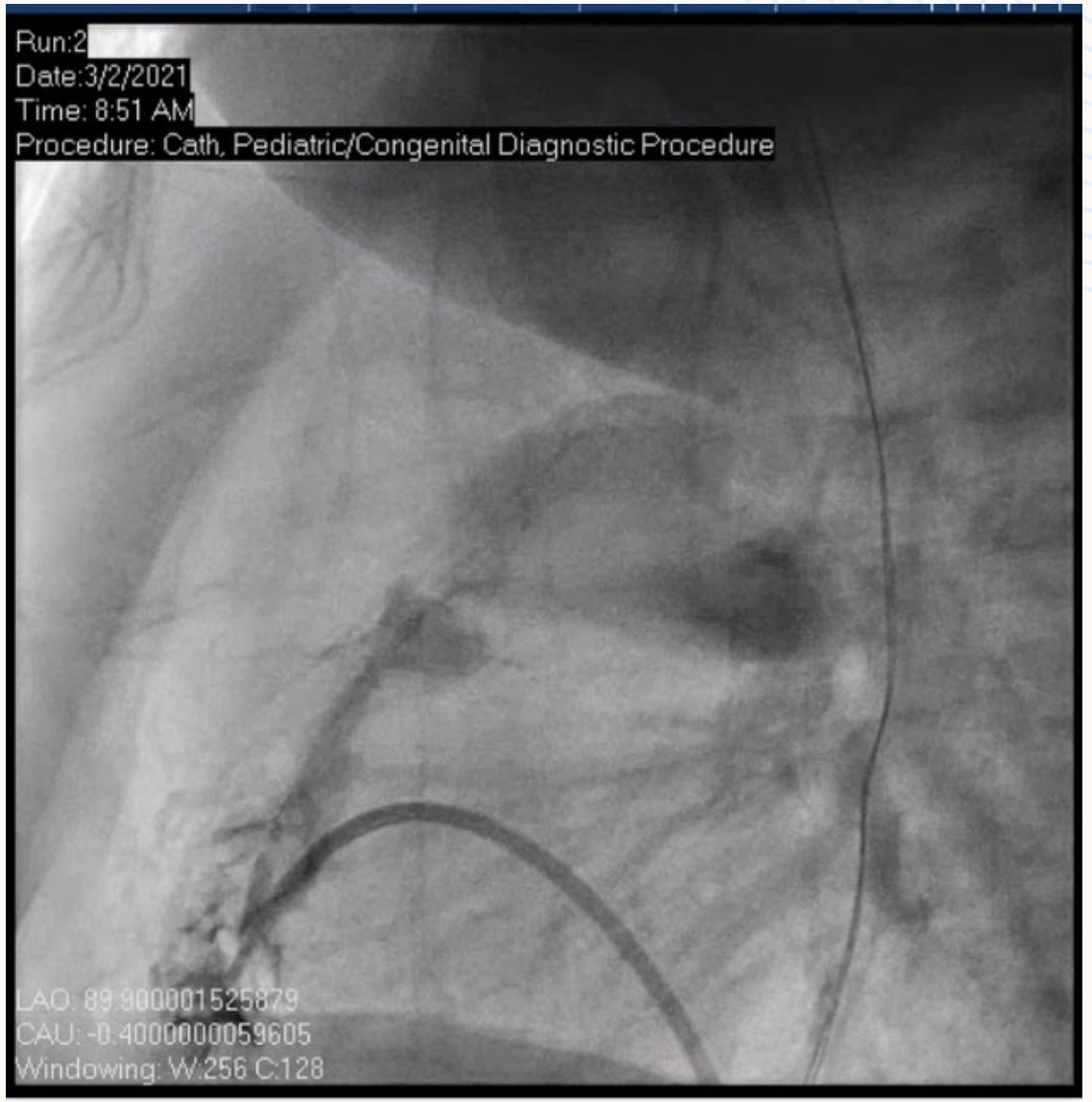
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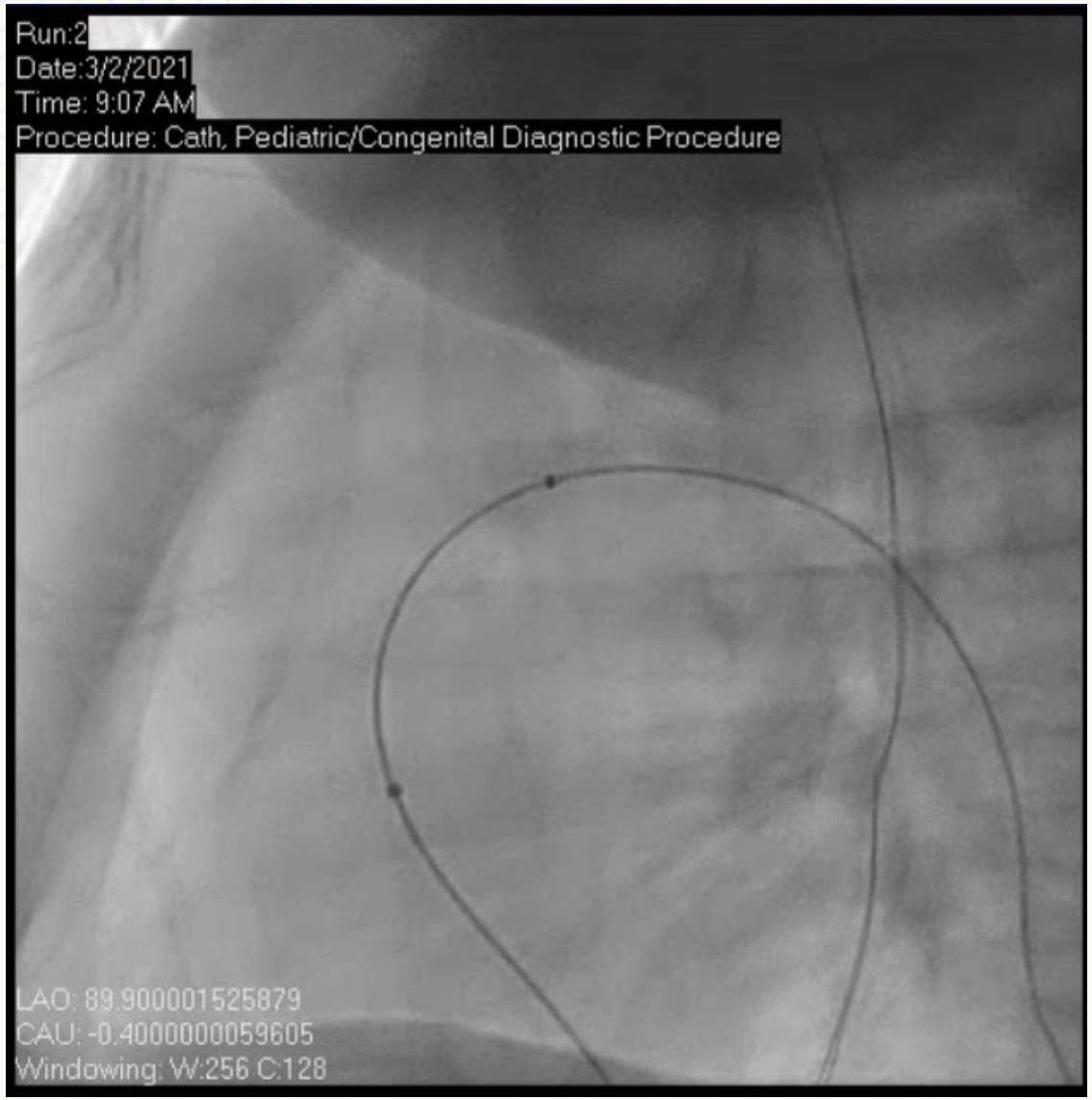
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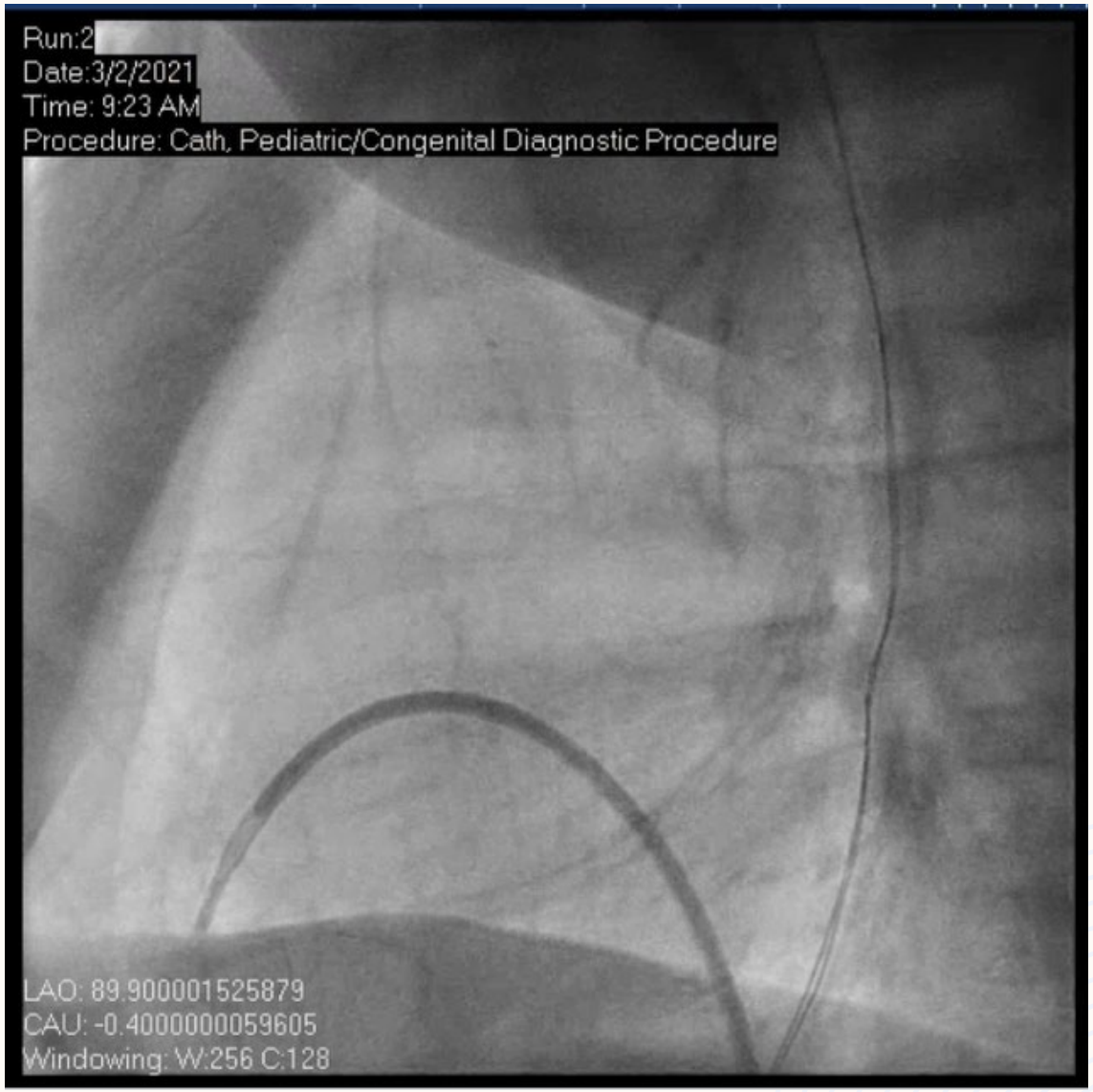
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CAU: -0.4000000059605
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References

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Thank you!

Any questions?