



Tetralogy of Fallot

Damien Bonnet

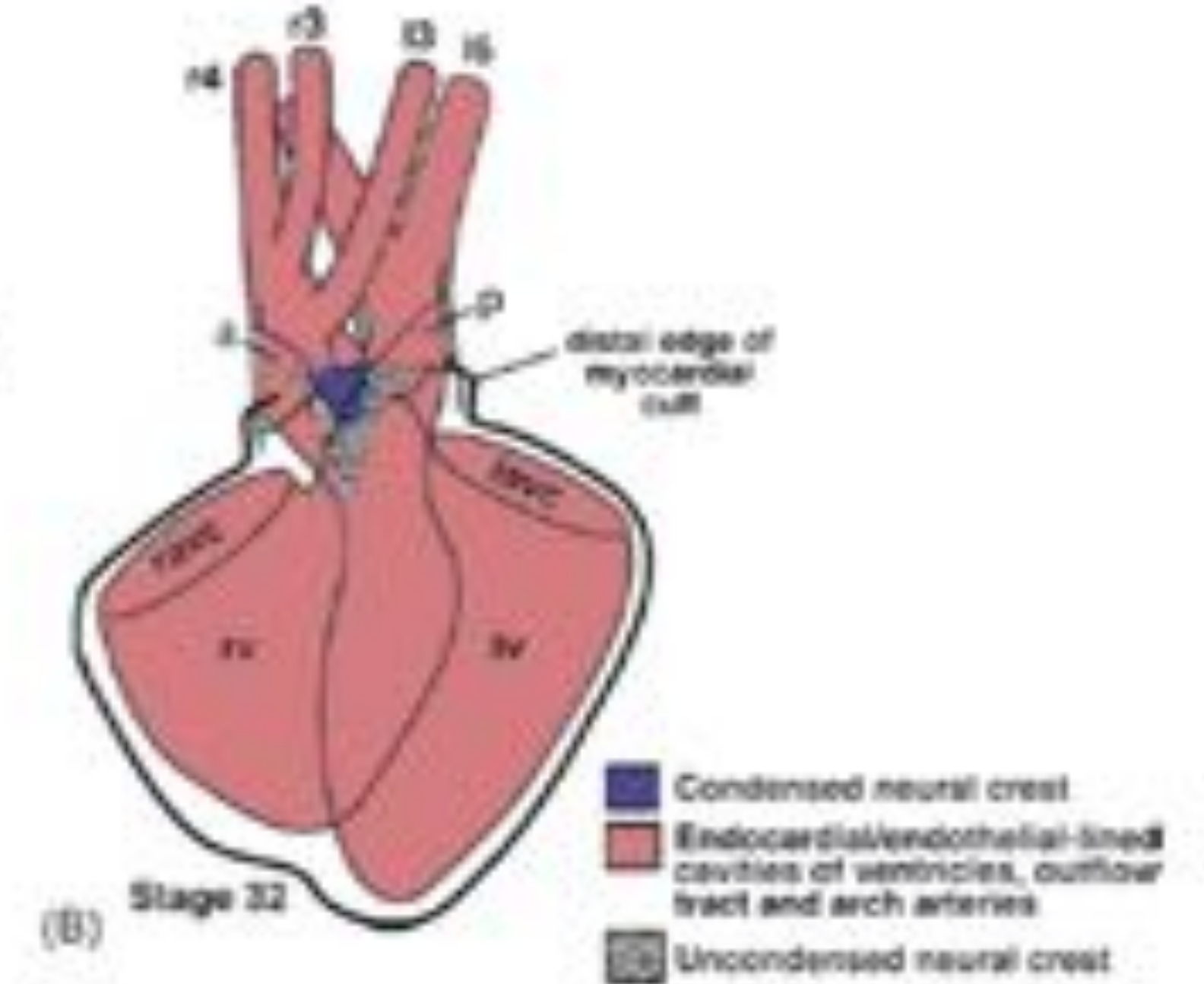
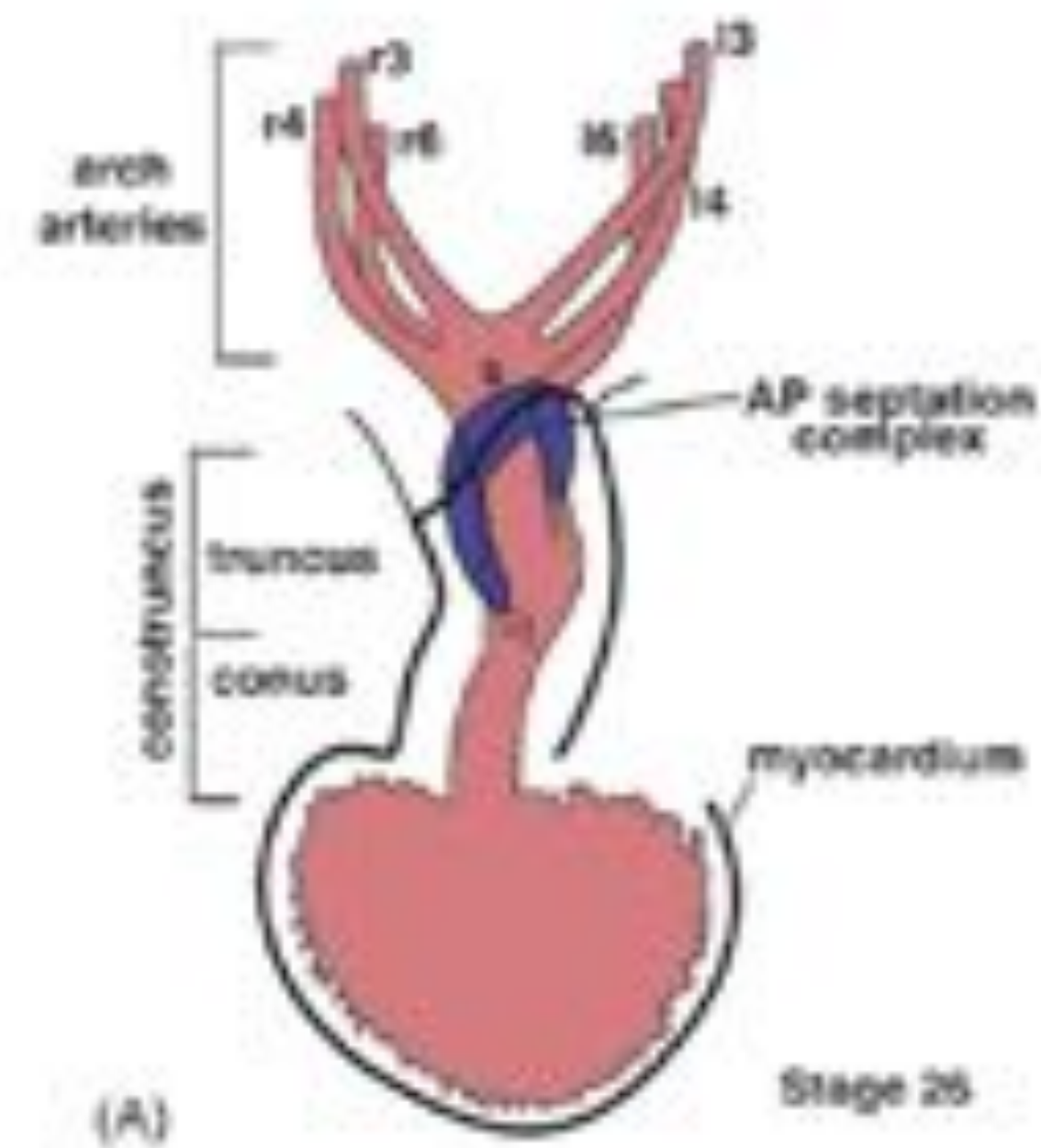
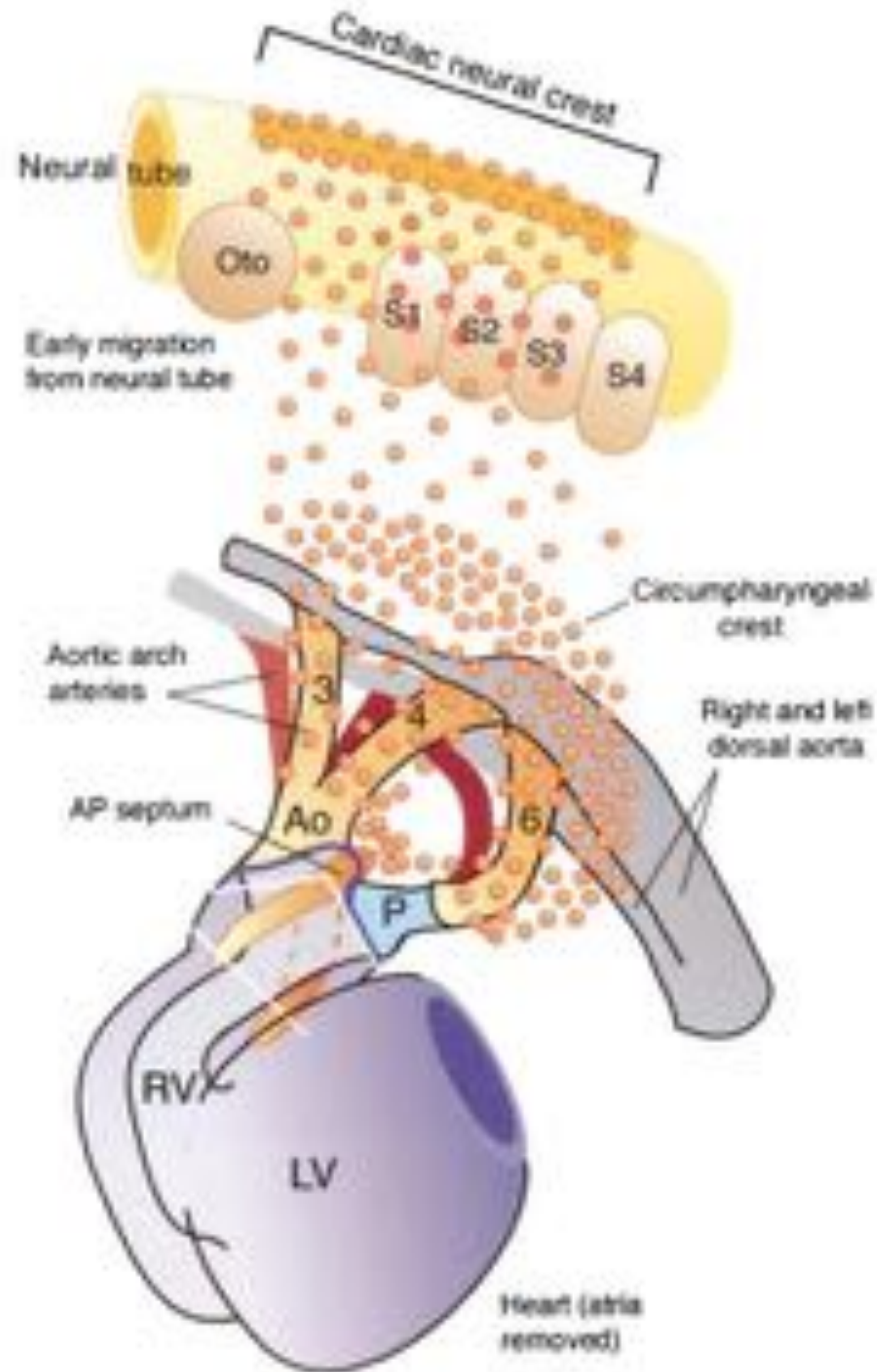
Unité médico-chirurgicale de Cardiologie Congénitale et Pédiatrique
Hôpital Universitaire Necker Enfants malades – APHP, Université Paris Descartes, Sorbonne Paris Cité
IcarP Cardiology, Institut Hospitalo-Universitaire IMAGINE

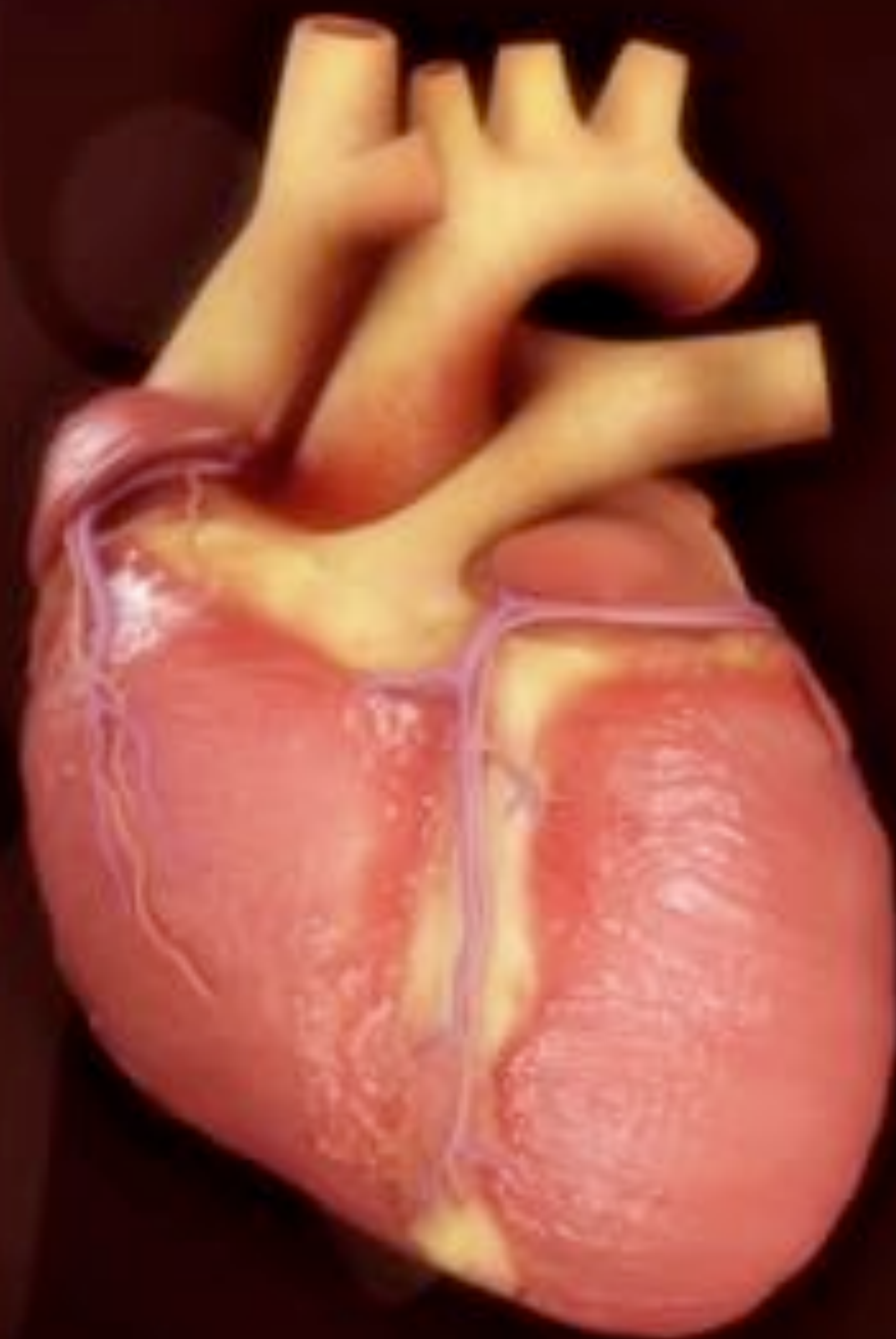
Centre de Référence Maladies Rares
Malformations Cardiaques Congénitales Complexes-M3C

Centre de Référence Maladies Rares
Maladies Cardiaques Héréditaires- CARDIOGEN



Migration of neural crest cells into the outflow tract





Subpulmonary
conus

PA

Septal
band

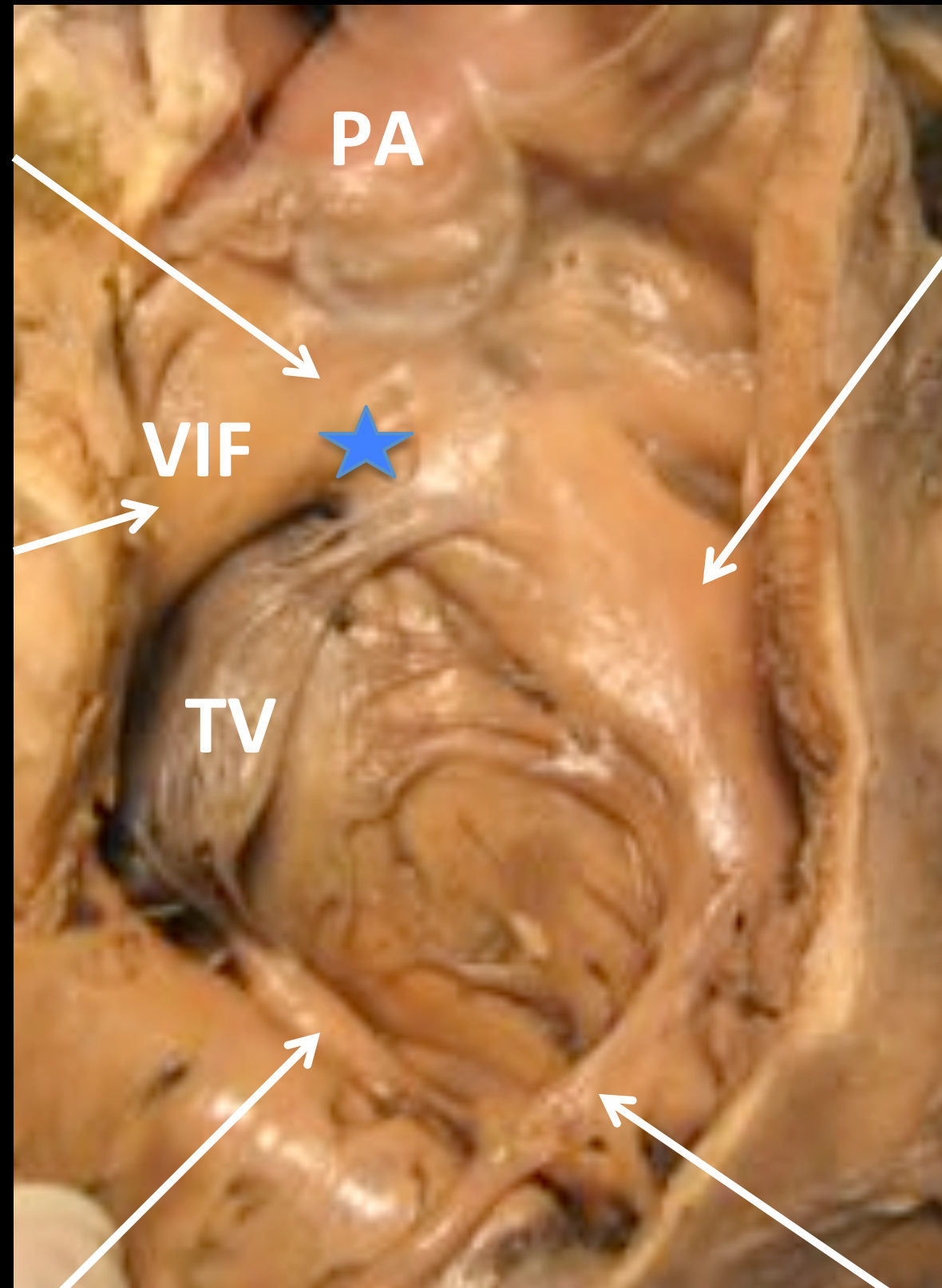
Ventriculo-
infundibular
fold

VIF

TV

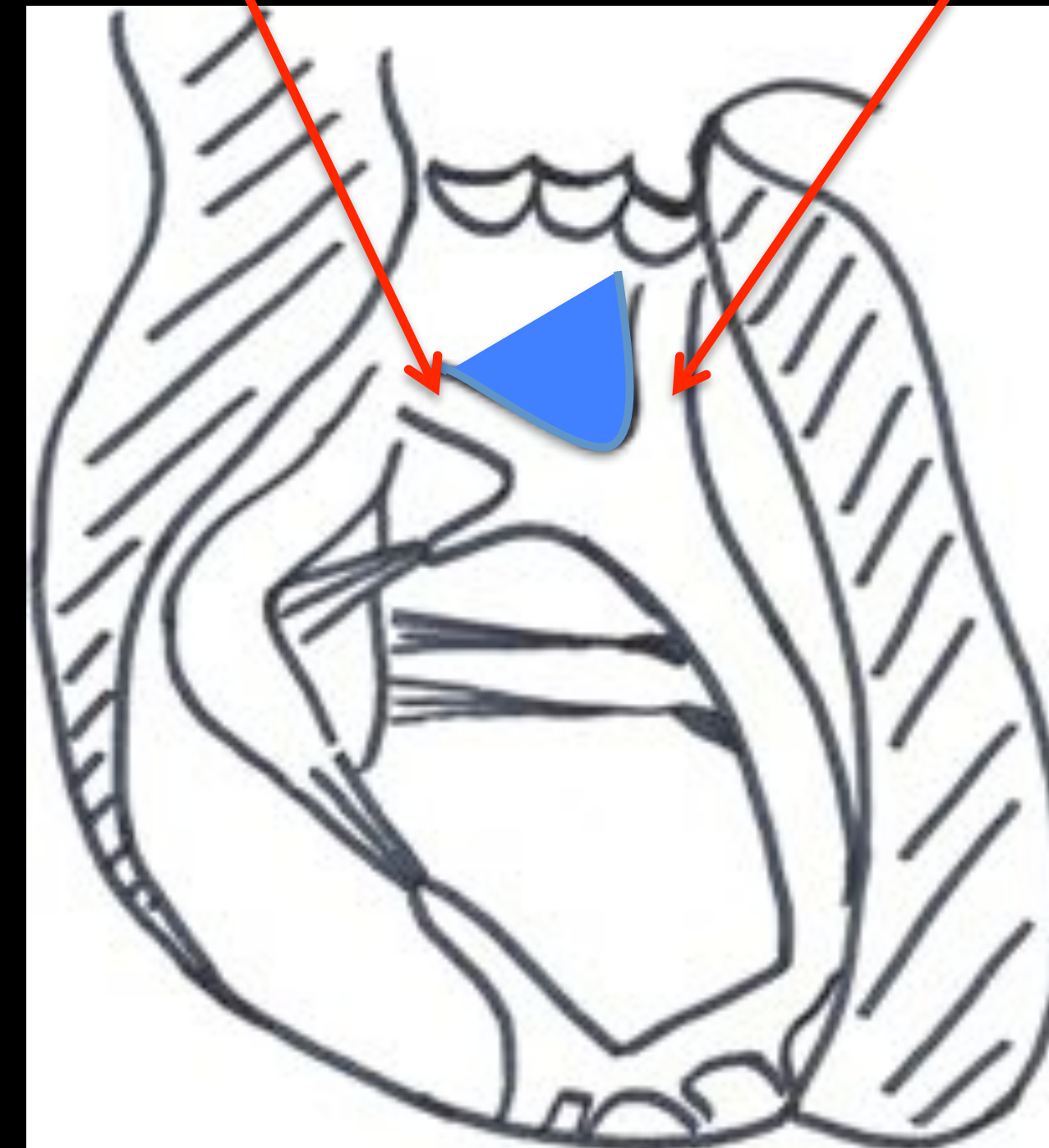
Anterior papillary muscle of the tricuspid valve

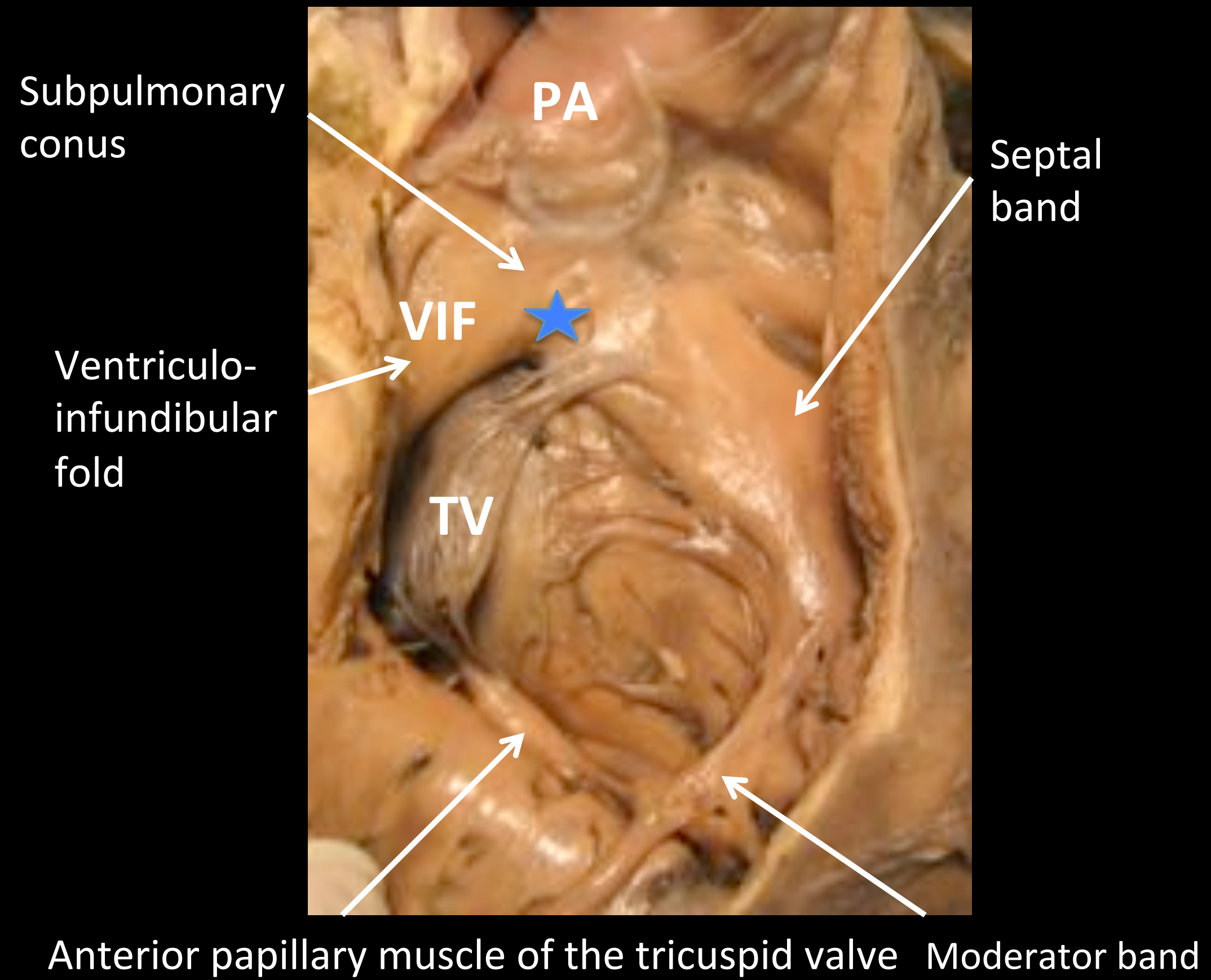
Moderator band



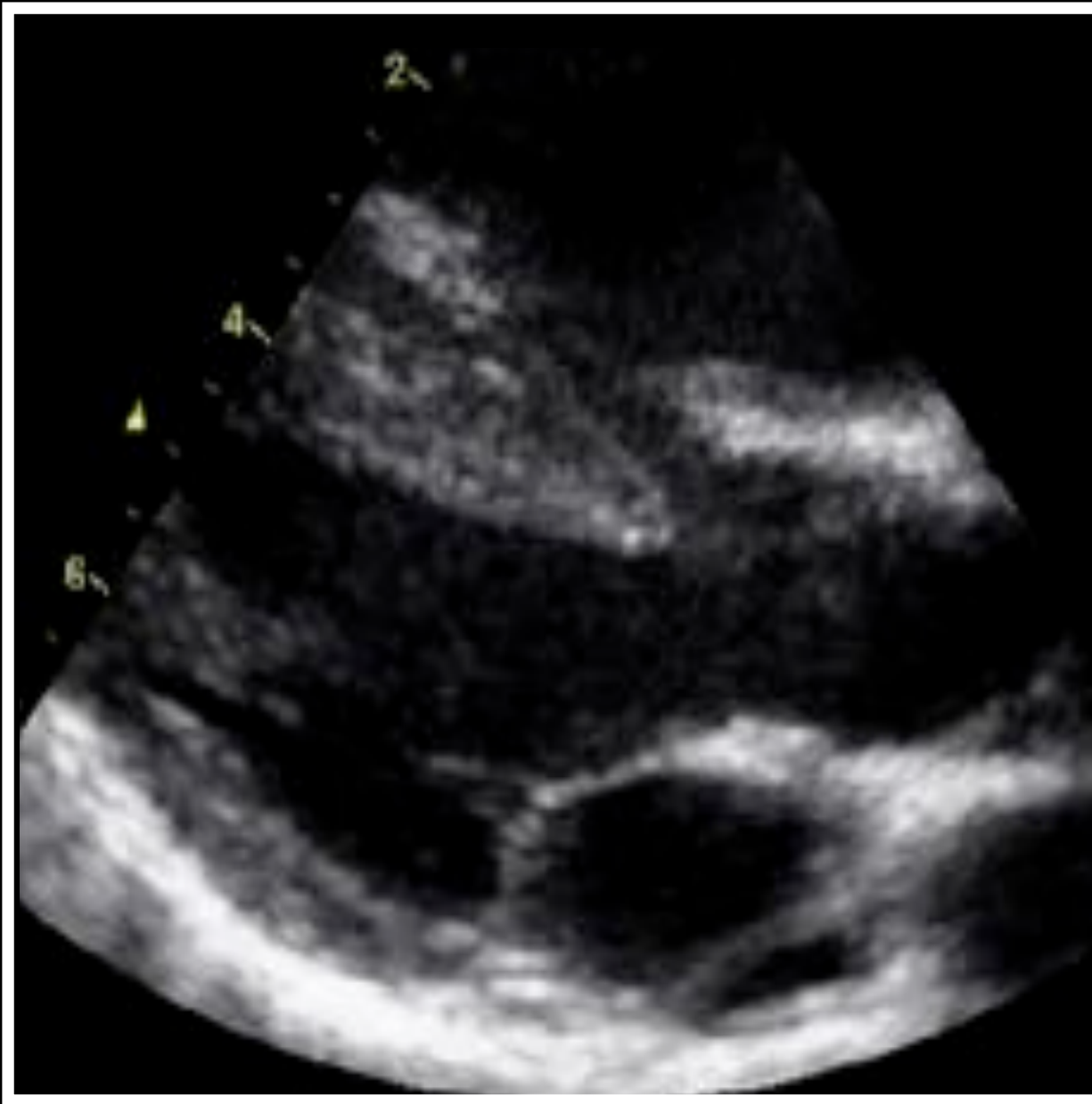
Postero-inferior limb
of the septal band

Anterior limb
of the septal band





Simple Fallot



Main topics in tetralogy of Fallot

- Prenatal diagnosis
- Perinatal management
- Strategy for repair
- Late outcomes

Prenatal diagnosis of tetralogy of Fallot

What are the main issues ?

- 1. Associated cytogenetic and extra-cardiac anomalies**

Trisomie 21



Délétion 22q11



Alagille

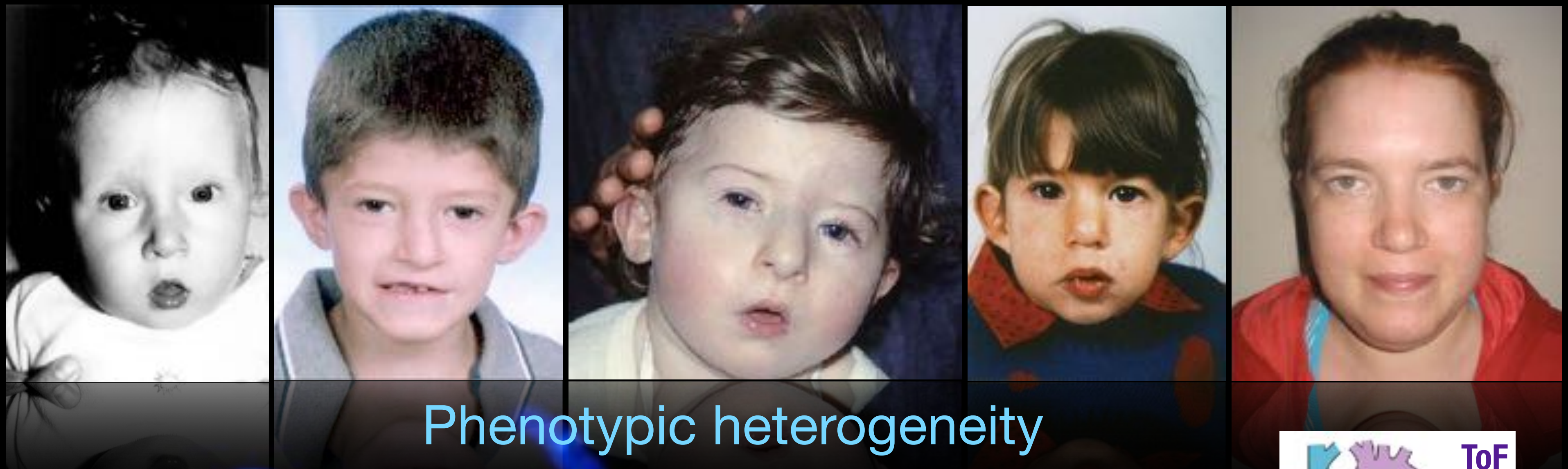


CHARGE

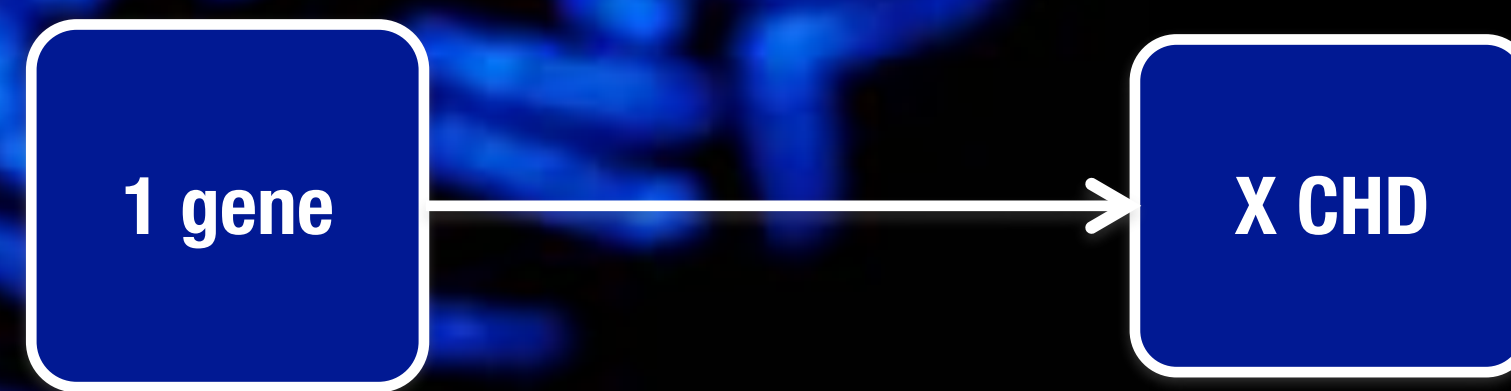
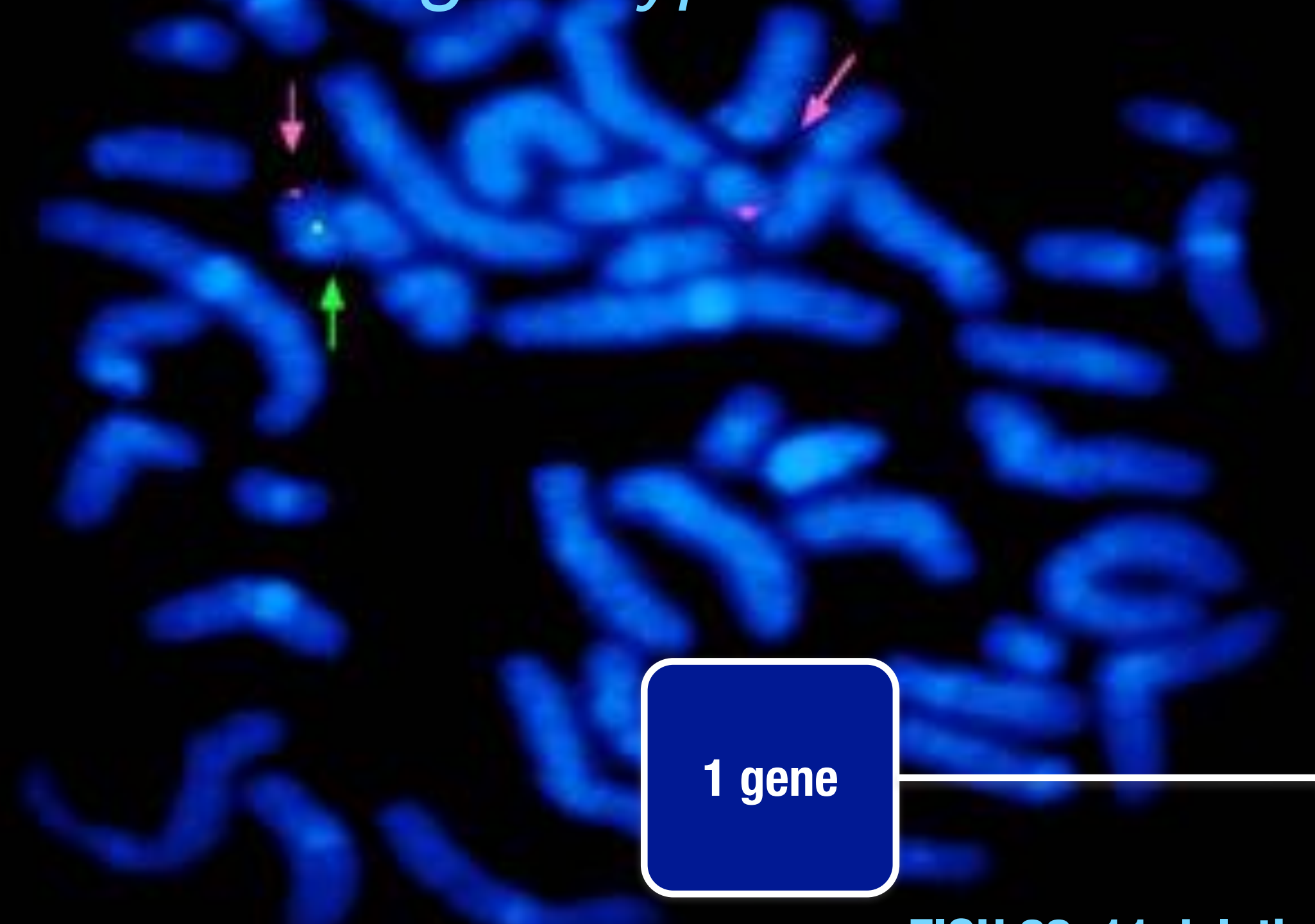


Waardenburg

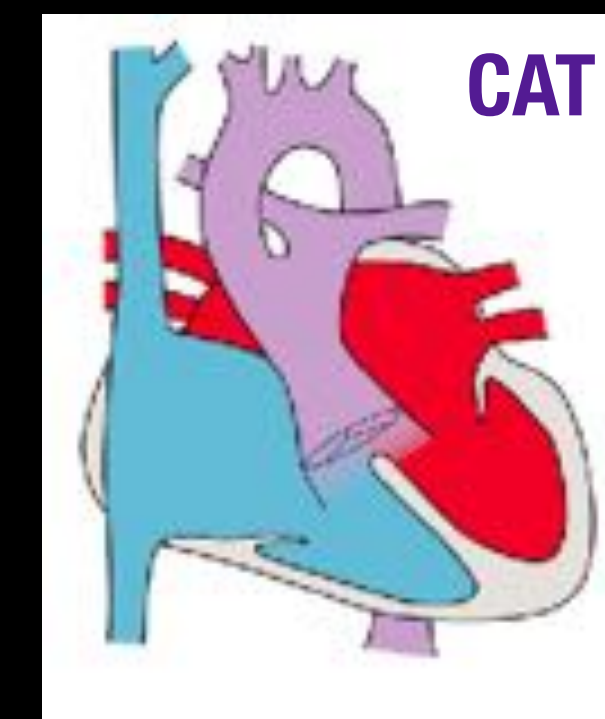
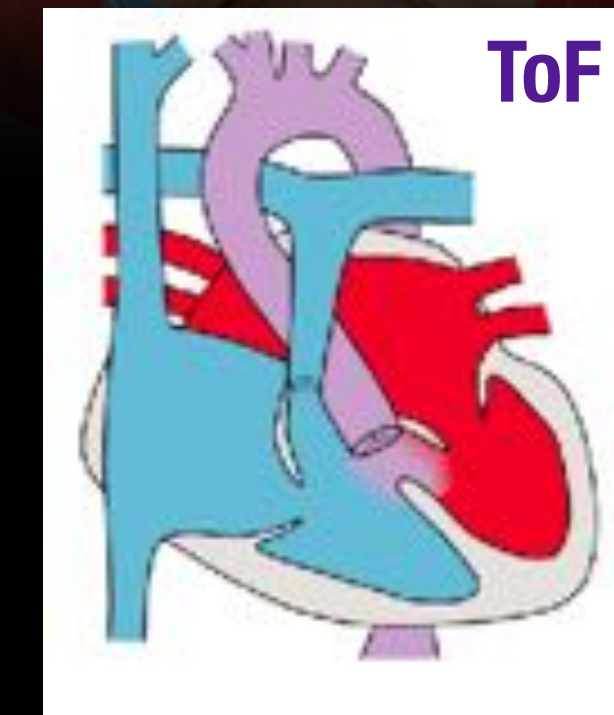
10 % karyotypic anomalies on standard analysis
18% 22q11 deletion : 15% in ToF-PS, 26% in ToF-PA

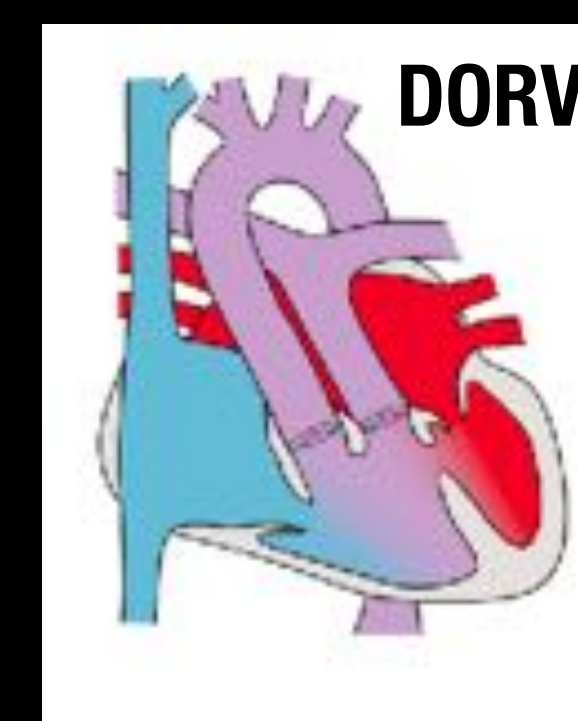
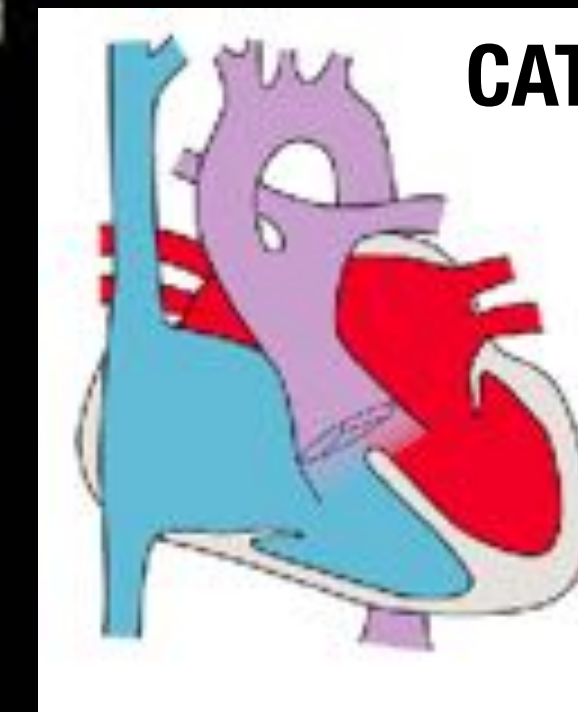
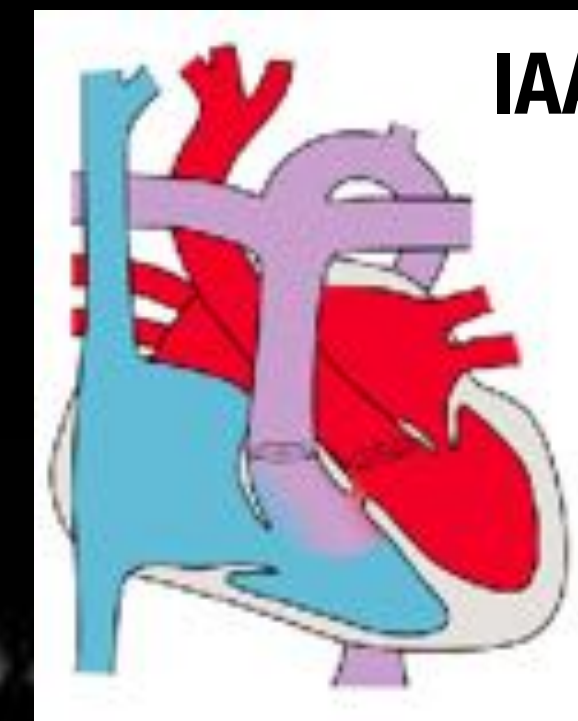
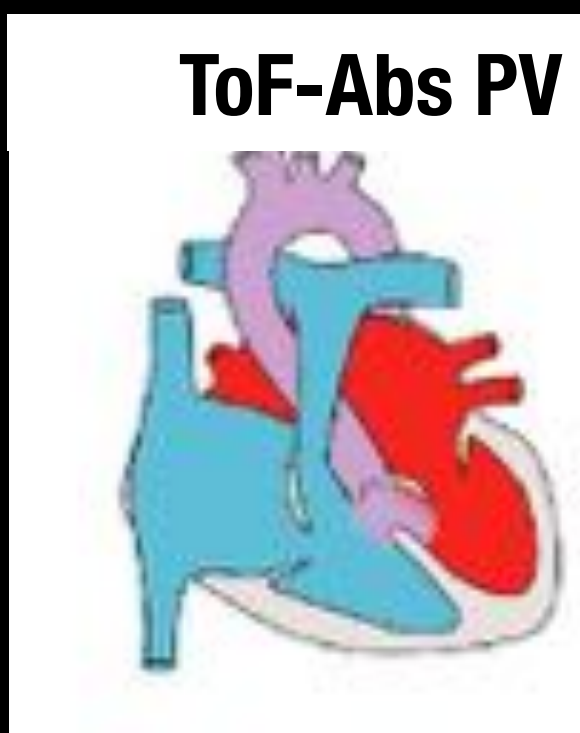
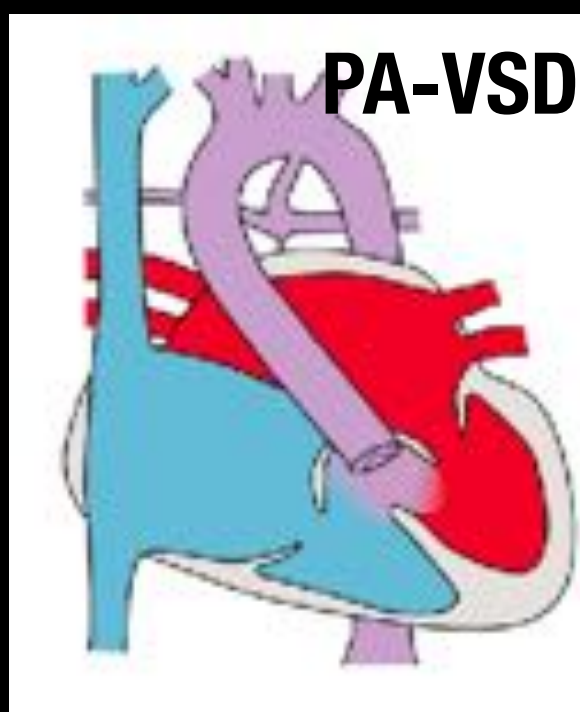
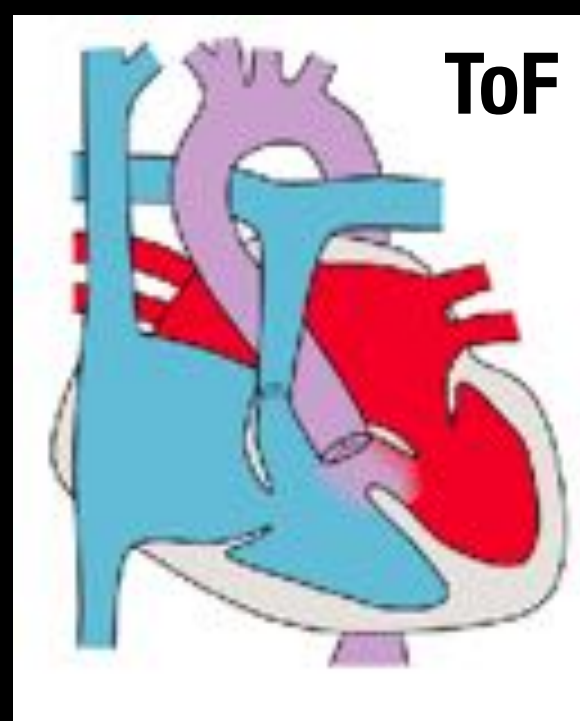


Phenotypic heterogeneity
One genotype-Different cardiac phenotypes



FISH 22q11 deletion





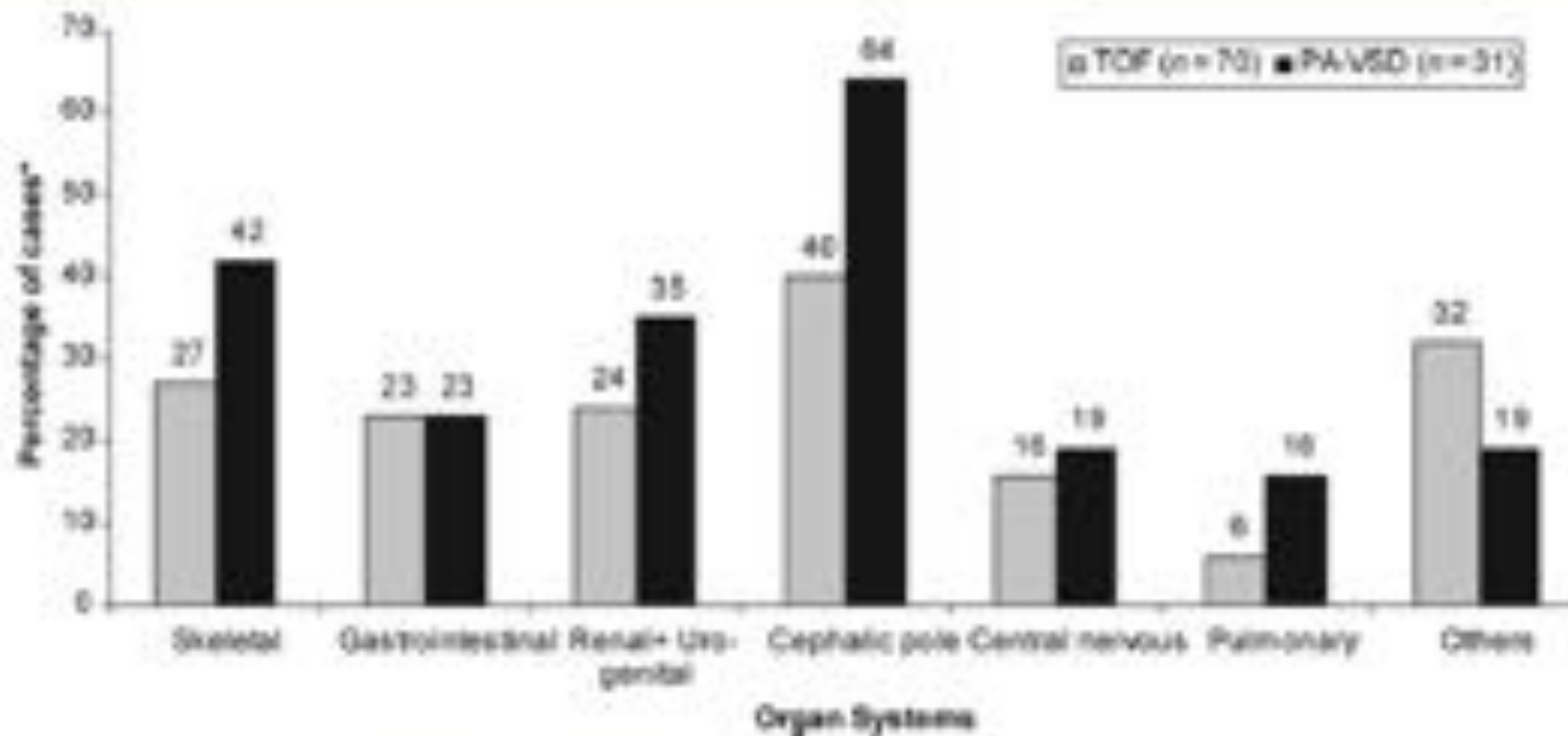


Figure 1 Details on extracardiac anomaly in foetal TOF and PA-VSD. Others, growth and endocrinological abnormalities, mental retardation, ophthalmological anomalies, unic umbilical artery, cystic hygroma; TOF, tetralogy of Fallot; PA-VSD, pulmonary atresia with ventricular septal defect; the asterisk indicates the number of abnormalities by system/number of fetuses with associated extracardiac malformations per type of CHD (TOF or PA-VSD).

One third of fetuses with ToF had extra cardiac anomalies
15% had intra-uterine growth retardation


Prenatal diagnosis of tetralogy of Fallot

What are the main issues ?

1. Associated cytogenetic and extra-cardiac anomalies
- 2. Accuracy of diagnosis and decision for in utero transfer**

Prenatal diagnosis, pregnancy termination, perinatal and early neonatal mortality for selected (**isolated**) congenital heart anomalies

Paris Registry of Congenital Malformations, 1983-2010



ToF	83-88 %	89-94 %	95-00 %	00-10 %	p
Prenatal diagnosis	20.0	37.5	69.7	74	<0.005
Pregnancy termination	10.0	12.5	0	1.8	0.07
First week mortality	0	0	0	0.3	-
Perinatal mortality	0	7.1	2.9	2.0	0.63



Recent studies show that prenatal diagnosis DOES NOT impact neonatal CHD mortality

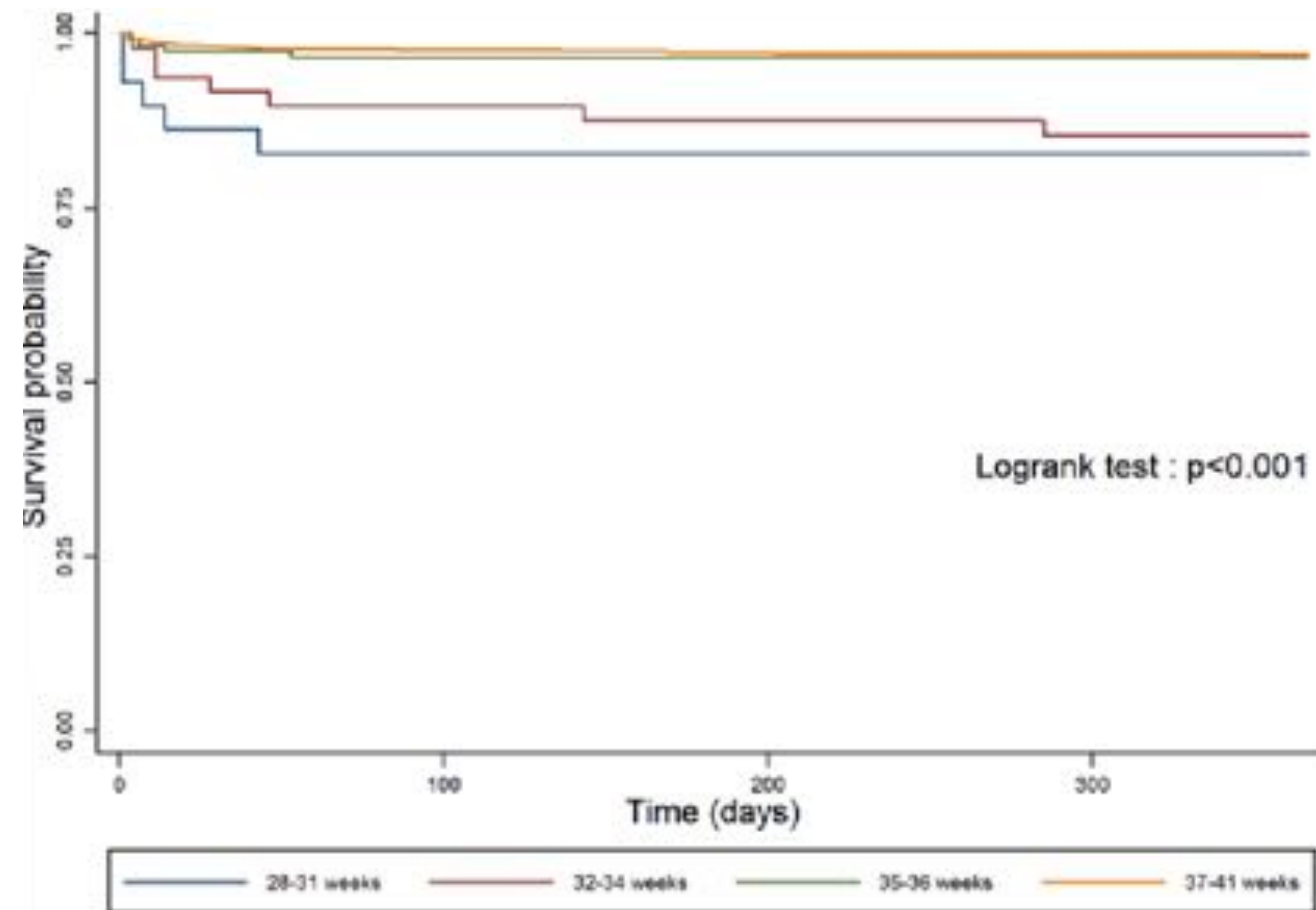
Table 3 Association between prenatal diagnosis and risk of infant mortality for four specific congenital heart defects (CHDs), EPIdémiologie des CARDiopathies congénitales (EPICARD) Population-Based Cohort Study

CHD	Prenatal diagnosis		Infant mortality		Risk ratio	95% CI
		n*	n†	%		
Functionally univentricular heart‡	No	7	3	42.9	9.9 to 81.6	
	Yes	32	17	53.1	34.7 to 70.9	1.2 0.5 to 3.1
d-Transposition of the great arteries‡	No	24	1	4.2	0.1 to 21.1	
	Yes	57	5	8.8	2.9 to 19.3	2.1 0.3 to 17.1
Tetralogy of Fallot‡	No	18	2	11.1	1.4 to 34.7	
	Yes	36	1	2.8	0.07 to 14.5	0.3 0.02 to 2.6
Coarctation of the aorta‡	No	44	3	6.8	1.4 to 18.7	
	Yes	29	2	6.9	0.8 to 22.8	1.0 0.2 to 5.7

*N = number of live births (denominator data).
†n= number of deaths (numerator data).
‡Cases with the specific International Paediatric and Congenital Cardiac Code for the given CHD; whether or not other CHD codes were also included, all cases with chromosomal or others anomalies were excluded.

Impact of preterm birth on infant mortality for newborns with congenital heart defects

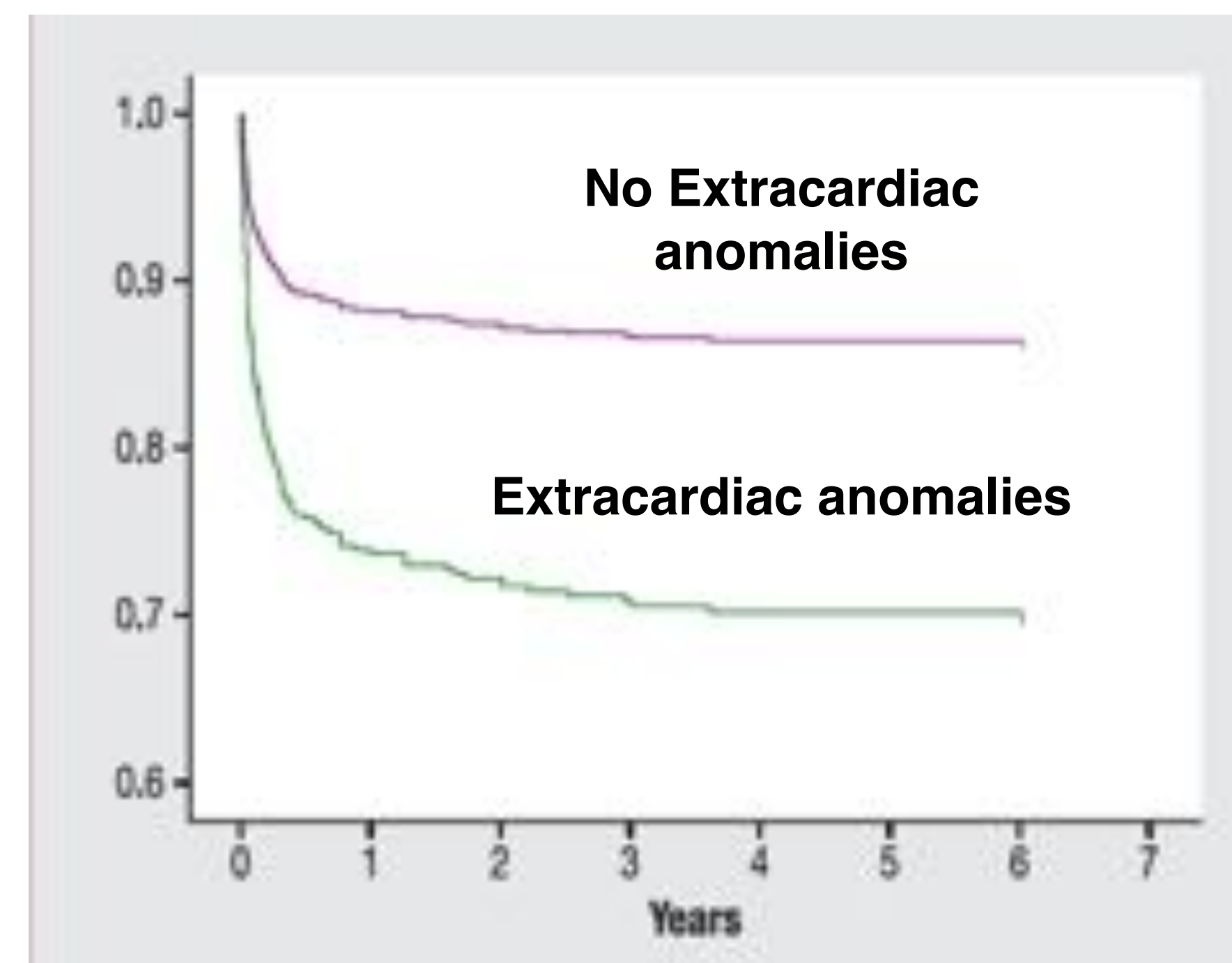
The EPICARD Study Group



- Preterm birth is associated with an approximately **four-fold higher risk** of infant mortality for newborns with CHD.
- This excess risk appears to be mostly limited to newborns **< 35 weeks of gestation** and is disproportionately **due to early deaths**.

Death before hospital discharge in prenatally diagnosed « in-born » CCHD

Type of CHD/predicted physiology	Mortality before discharge n (%)
at risk for Rashkind	8 (2.3)
ductal-dependent pulmonary flow	13 (12.1)
potentially ductal-dependent pulmonary flow	3 (2.1)
ductal-dependent systemic flow	25 (39.6)
potentially ductal-dependent systemic flow	16 (5.2)
TAPVR	1 (12.5)
AV block with CHD	0 (0)
a priori at no risk of early intervention	7 (6.5)
ALL	73 (6.7)



Prenatal diagnosis anticipates and prevents early demise

Is in utero transfer a valid option ?

Common indications for in utero transfer

- Life threatening CHDs
 - *Ex: TGA, TAPVR, HLHS*
- Evolutive defects
 - *Ex: Coarctation of the aorta*
- Uncertain perinatal physiology
 - *Ex: Tetralogy of Fallot*
- Highly variable/unpredictable postnatal outcome
 - *Ex: Ebstein*

Interventions in prenatally diagnosed « in-born » CHD

2543 in-born

TGA

748 in born

21% early demise

87% intervention

Suspected coarctation

486 in born

35% intervention

ToF

287 in born

4% intervention

Prenatal diagnosis of tetralogy of Fallot

What are the main issues ?

1. Associated cytogenetic and extra-cardiac anomalies
2. Accuracy of diagnosis and decision for in utero transfer
- 3. Prediction of repair**

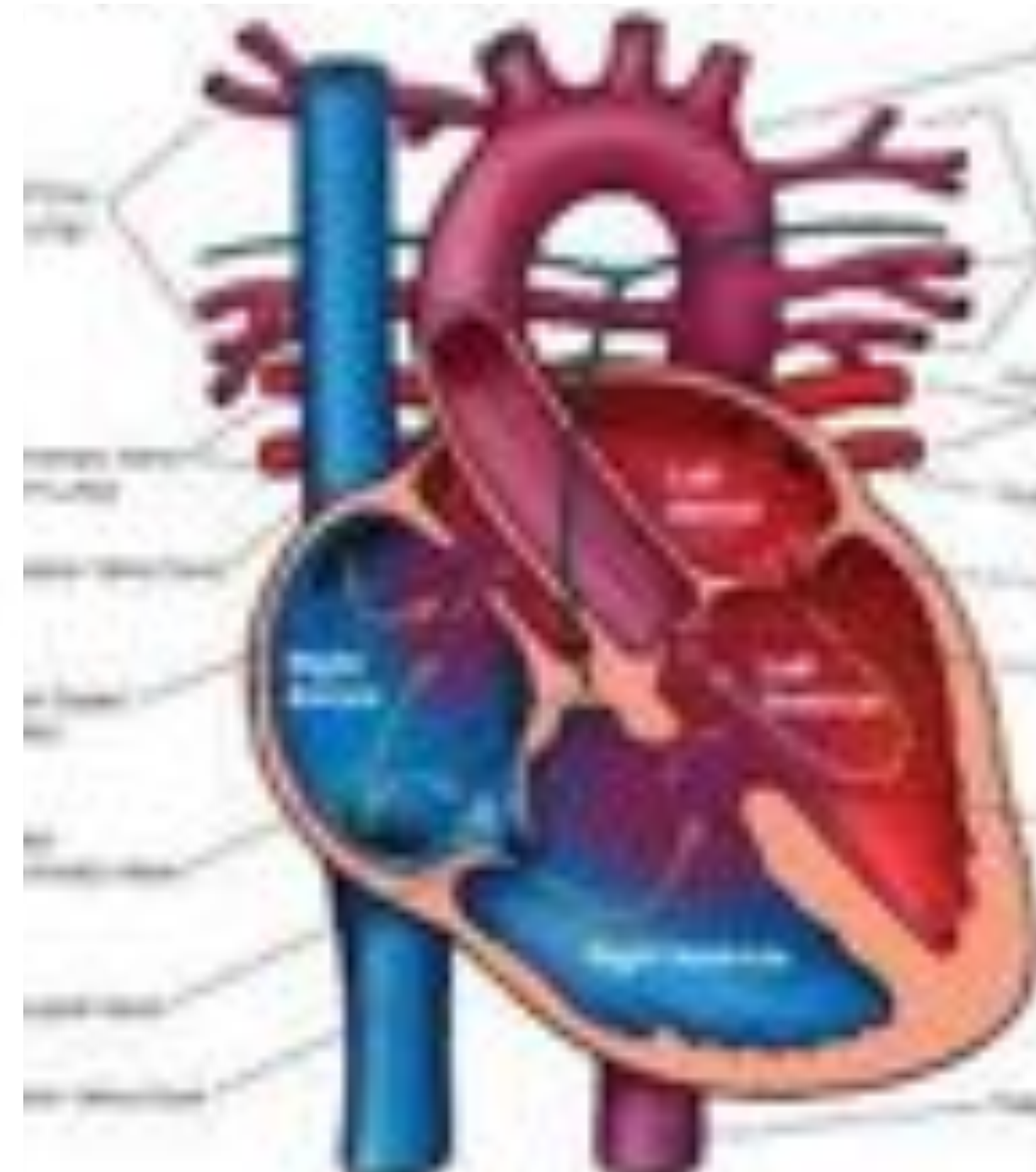
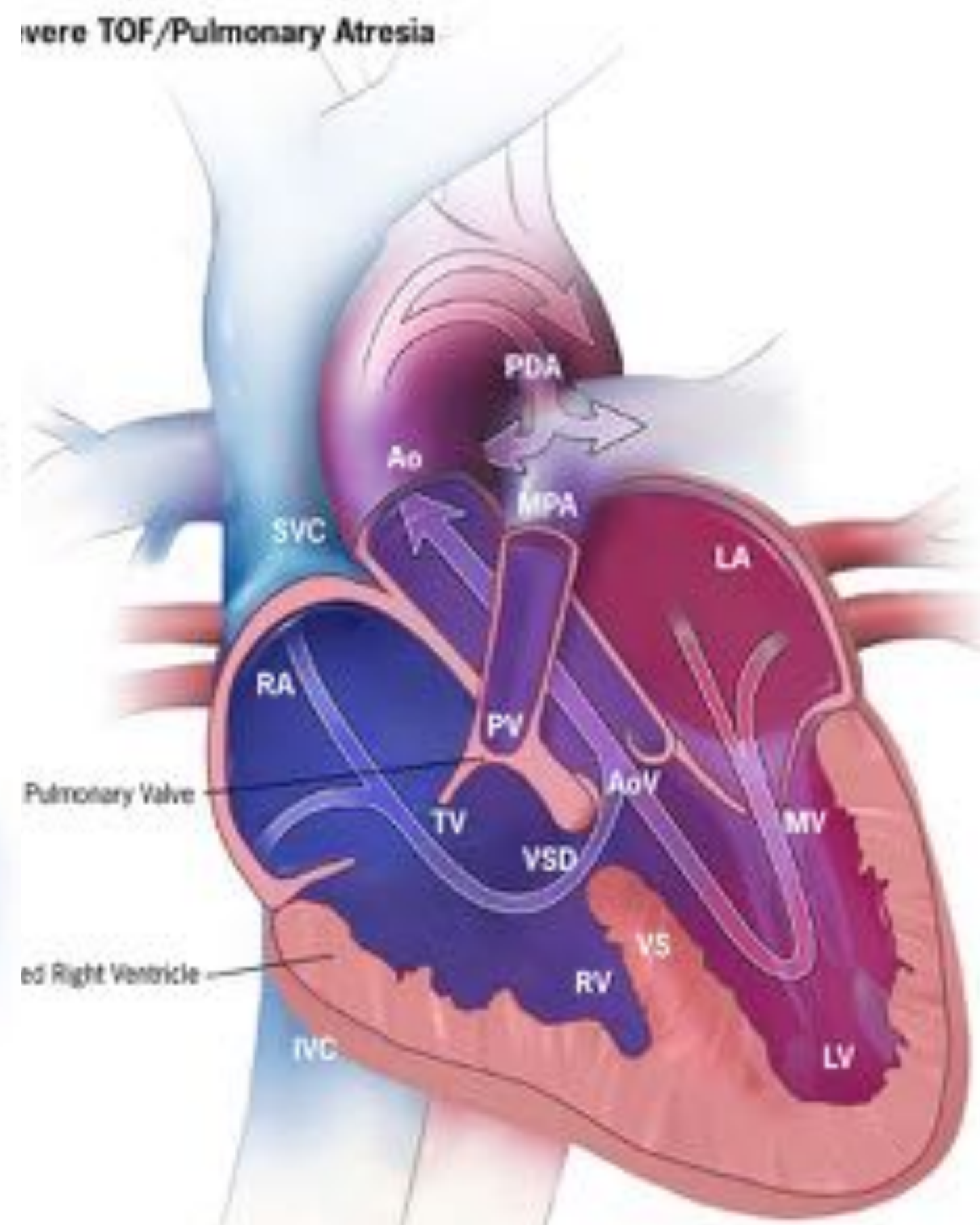
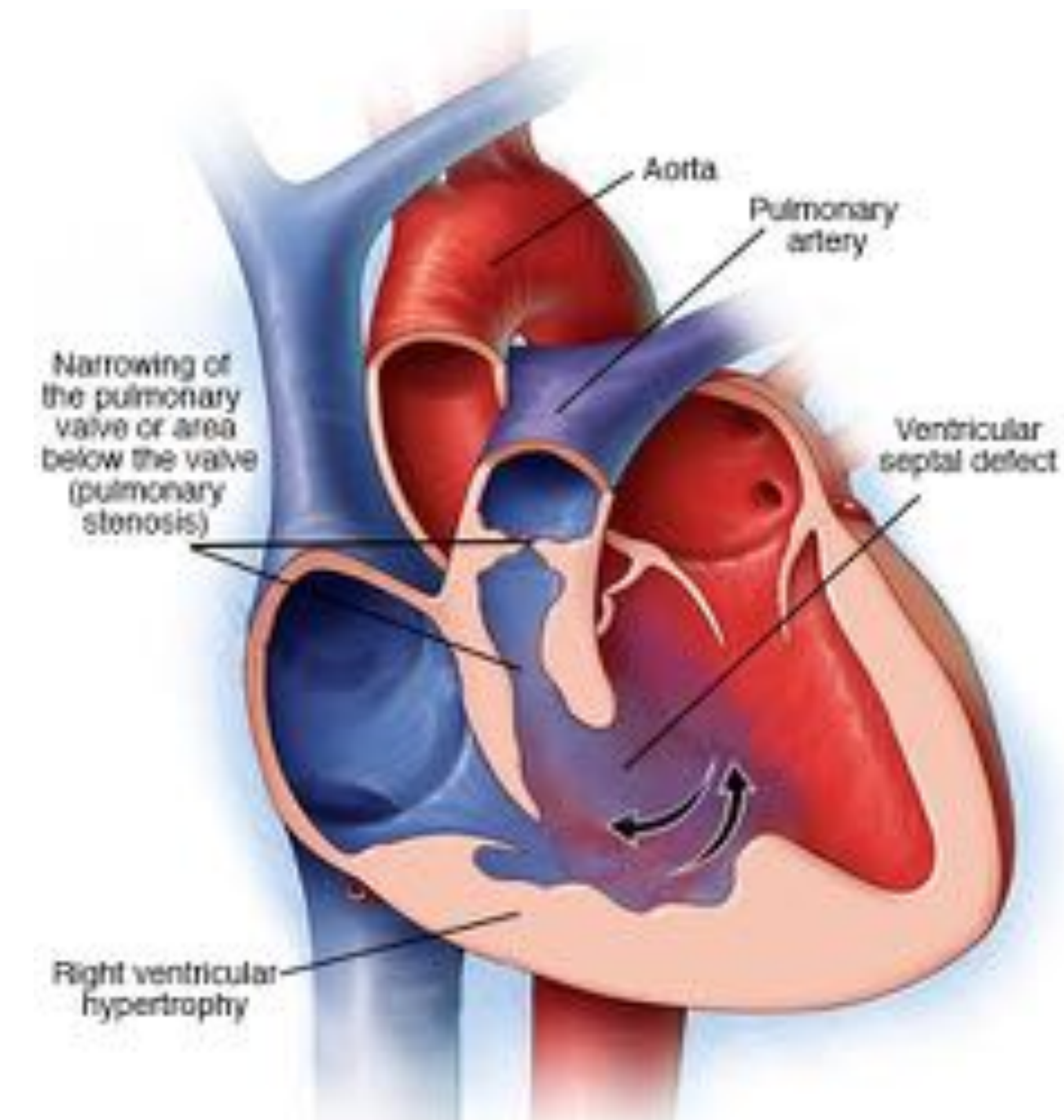
Is information on probability of complete repair individualized ?

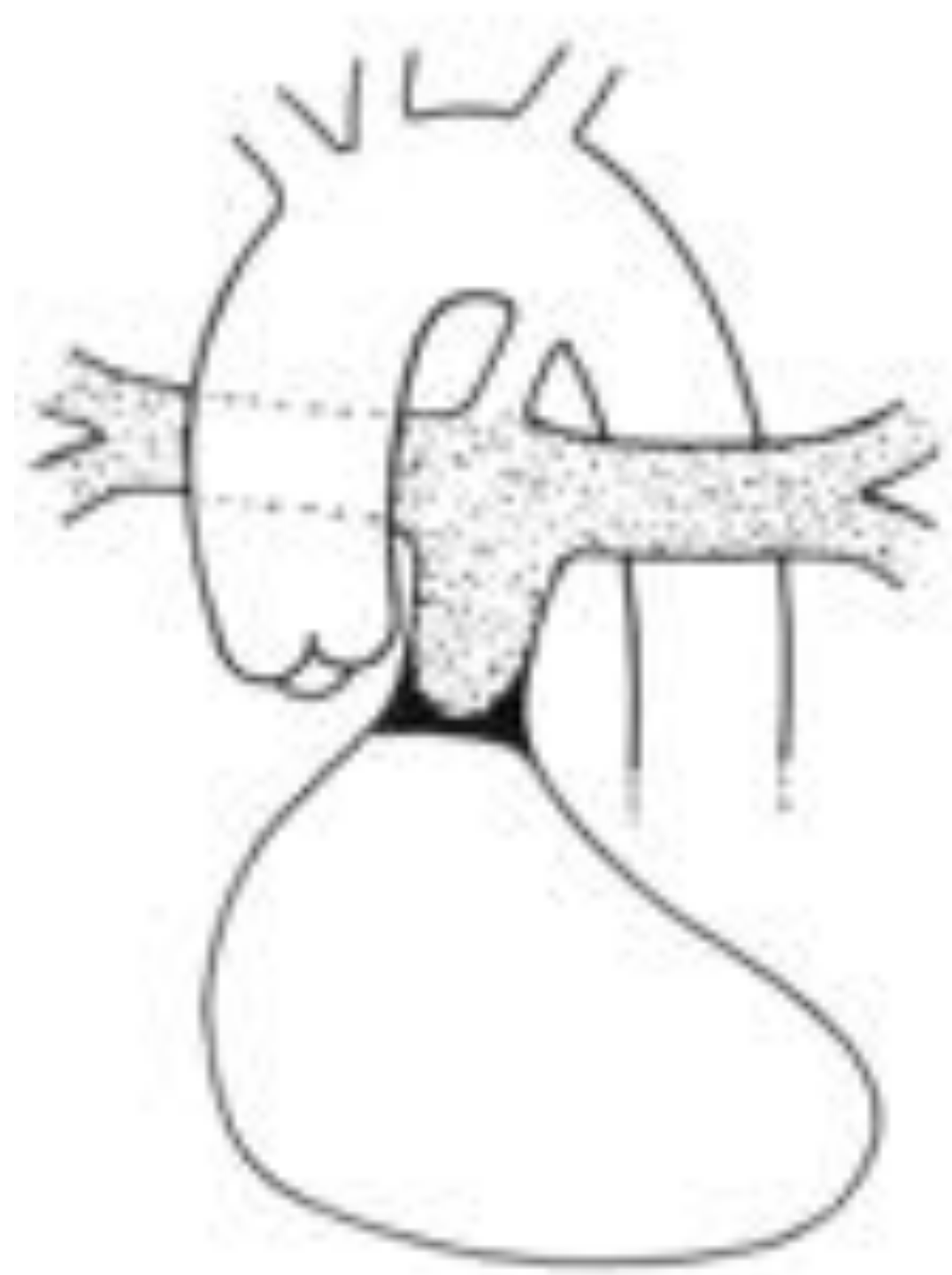
**Repair of TOF & PA-VSD at one year
is closely related to size of pulmonary artery branches**

	Repair < 1y %	p
PA branches Normal vs. absent/hypoplastic	86 vs. 55	<0.001
PA trunk present vs. absent	79 vs. 16	0,003
MAPCAs present vs. absent	76 vs. 50	0.17

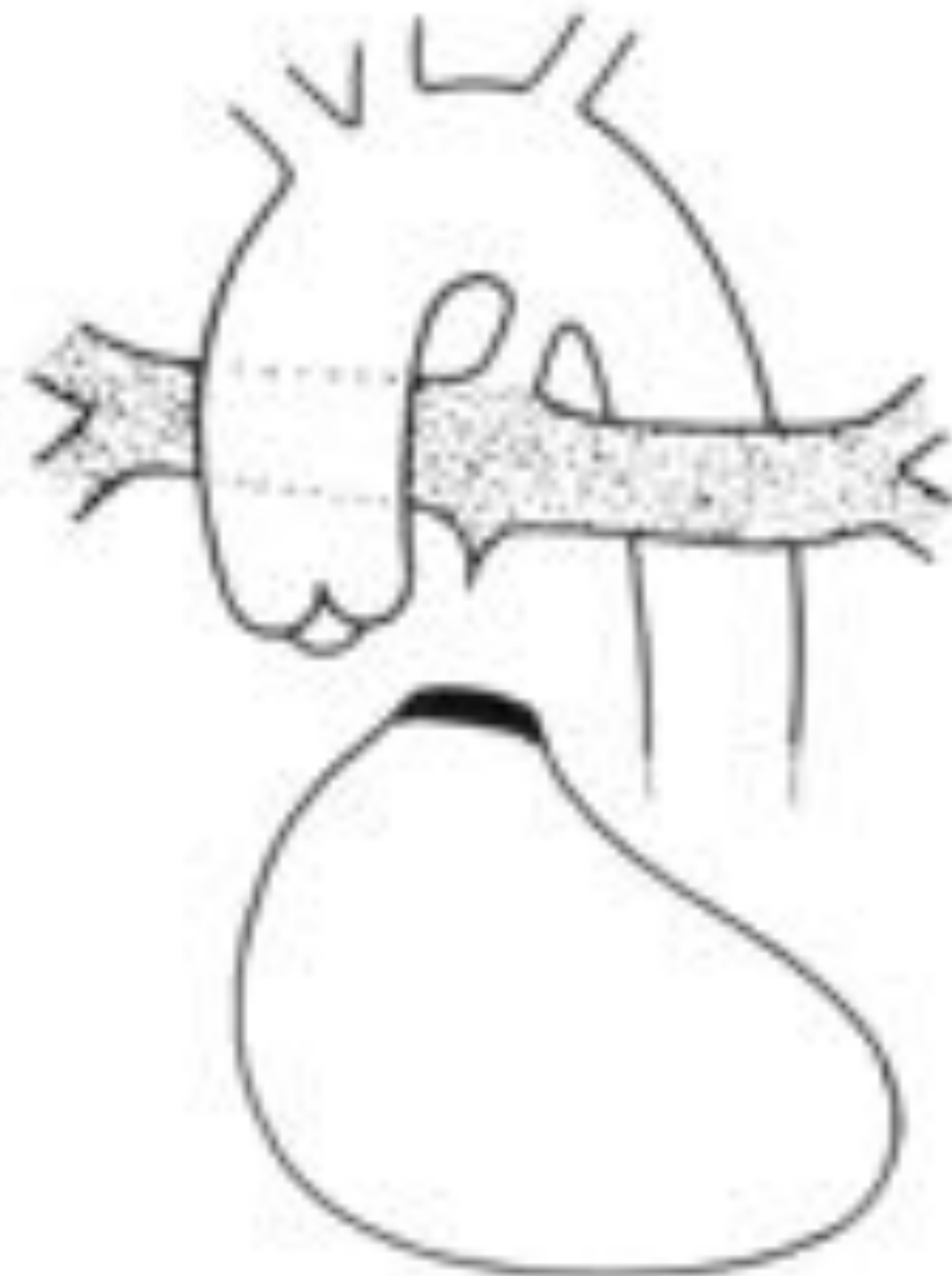
Perinatal management

1. Ducto-dependent defect ?

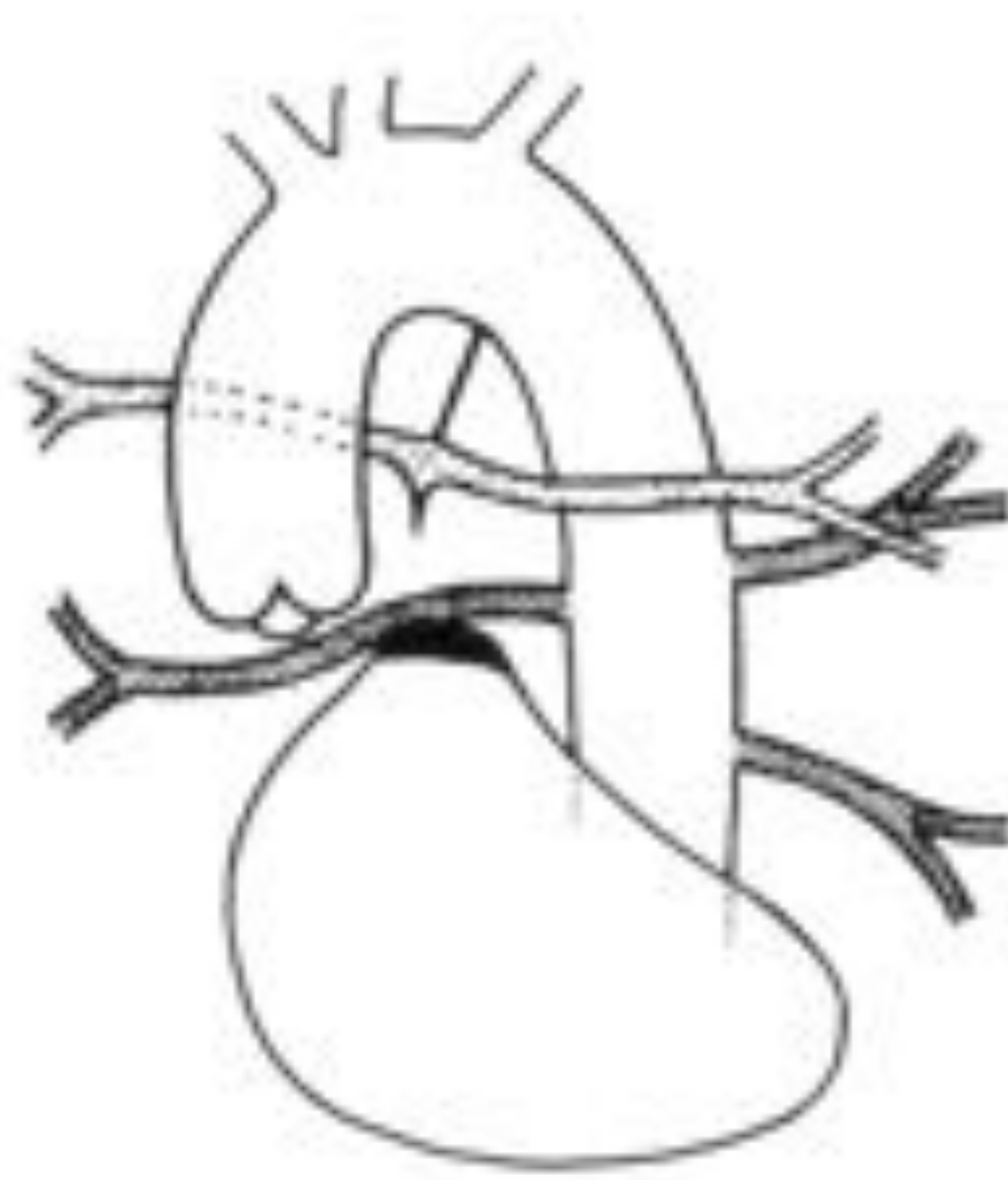




I



II



III

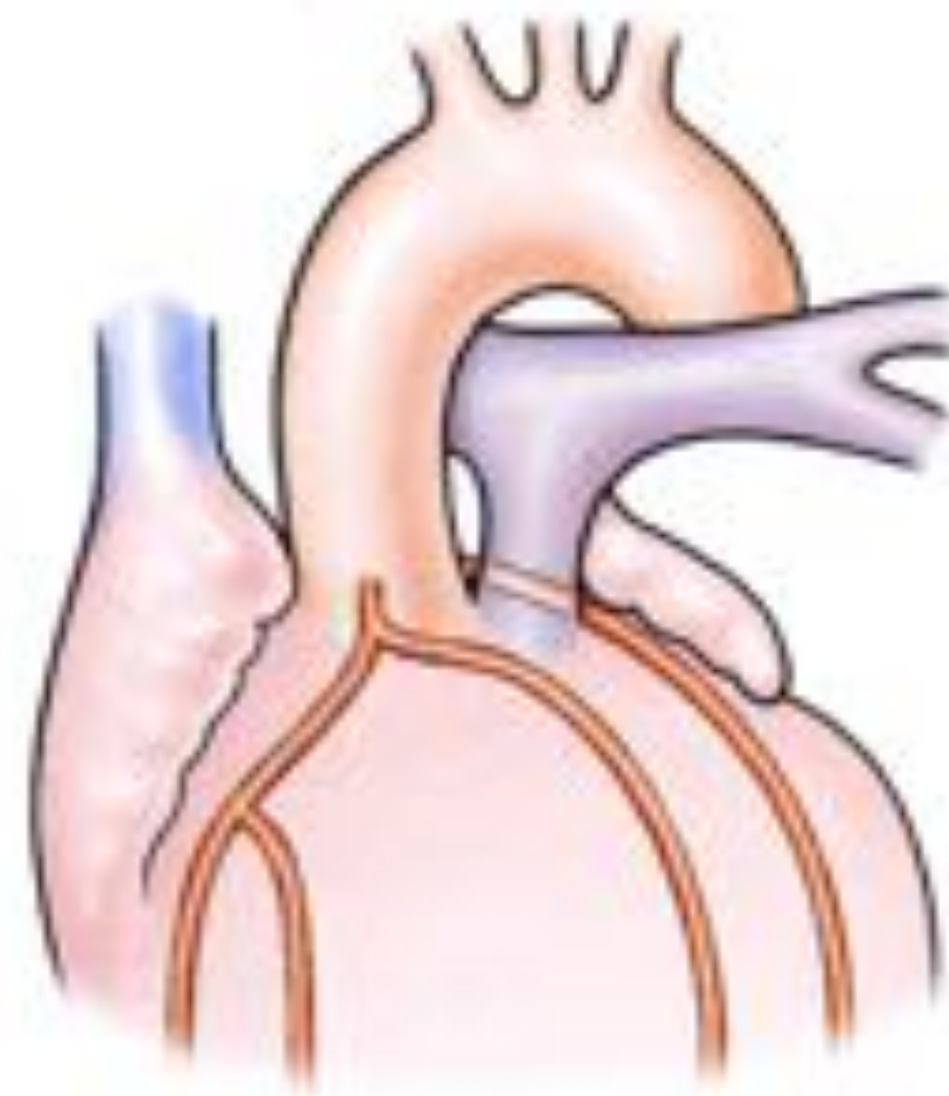
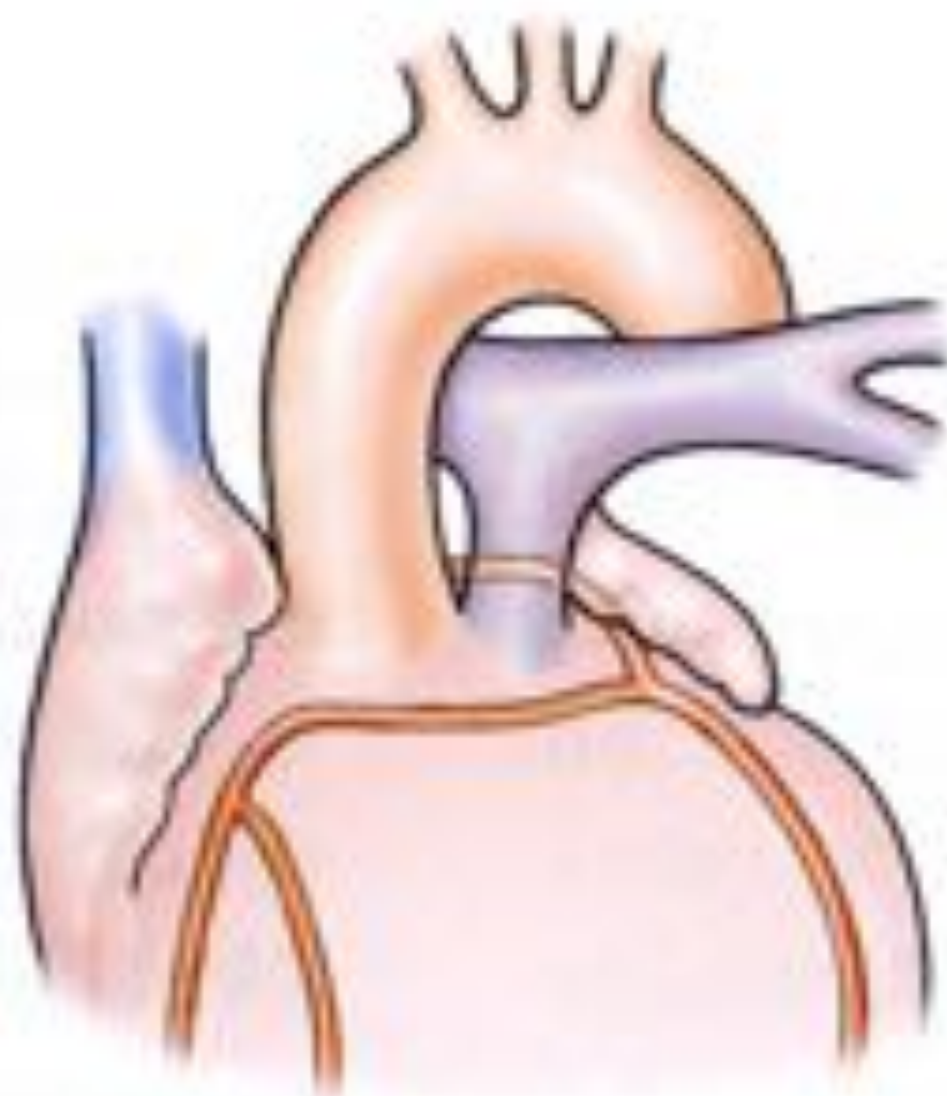
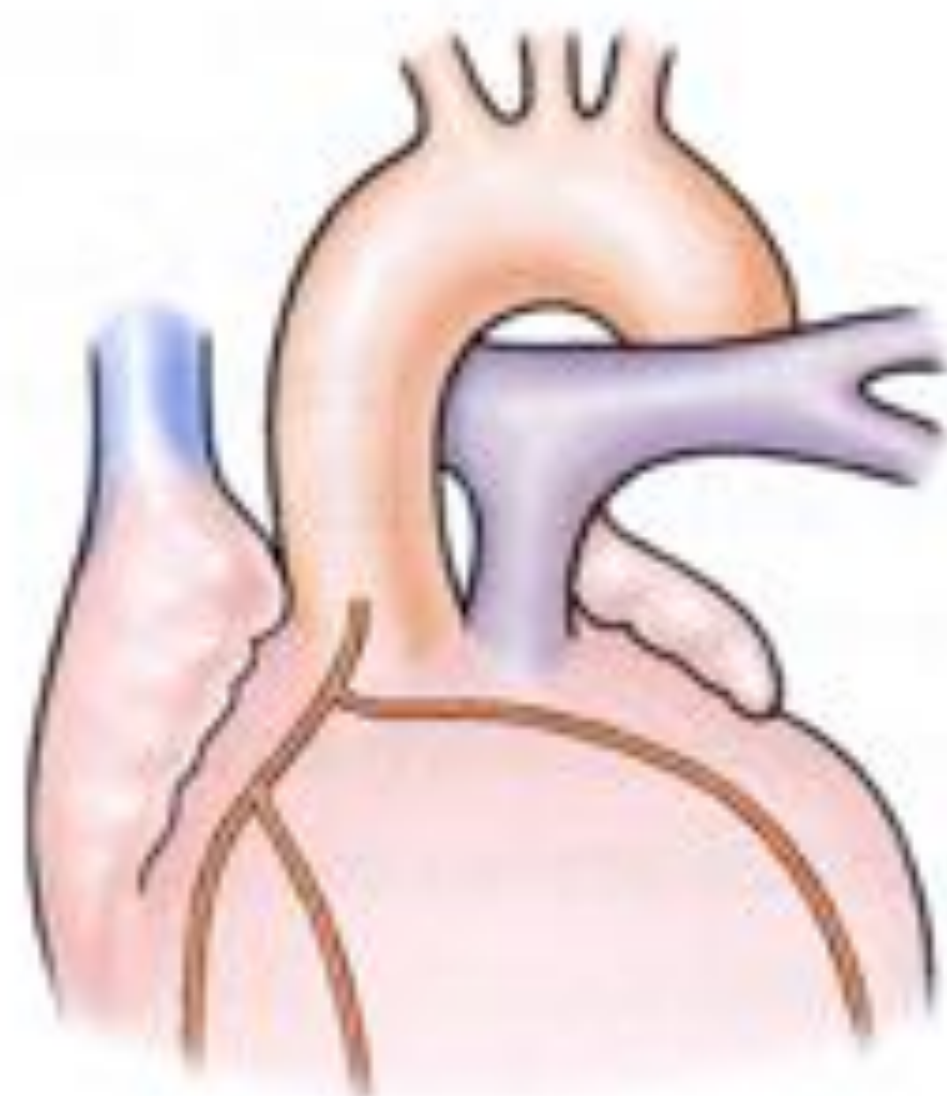
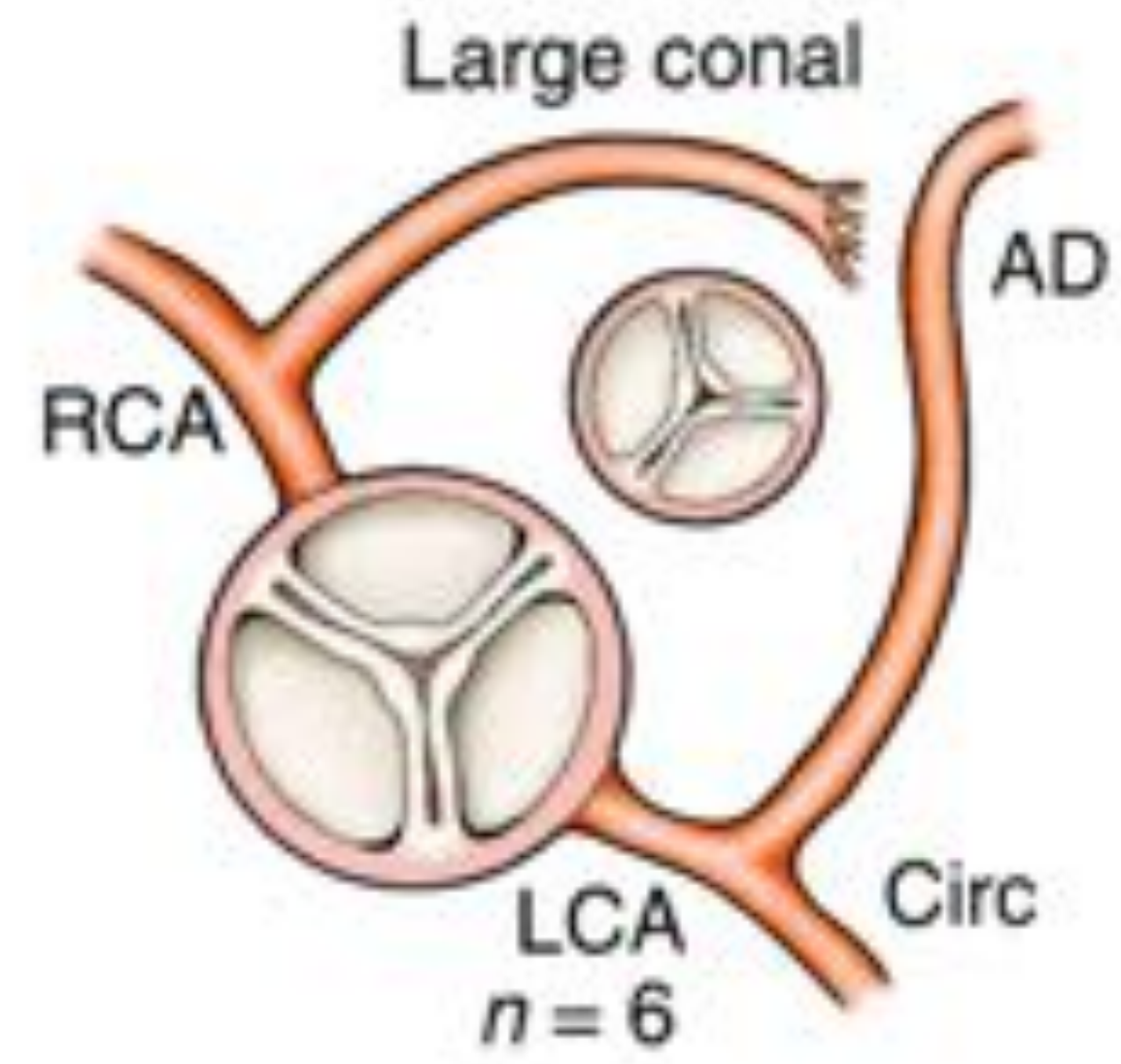
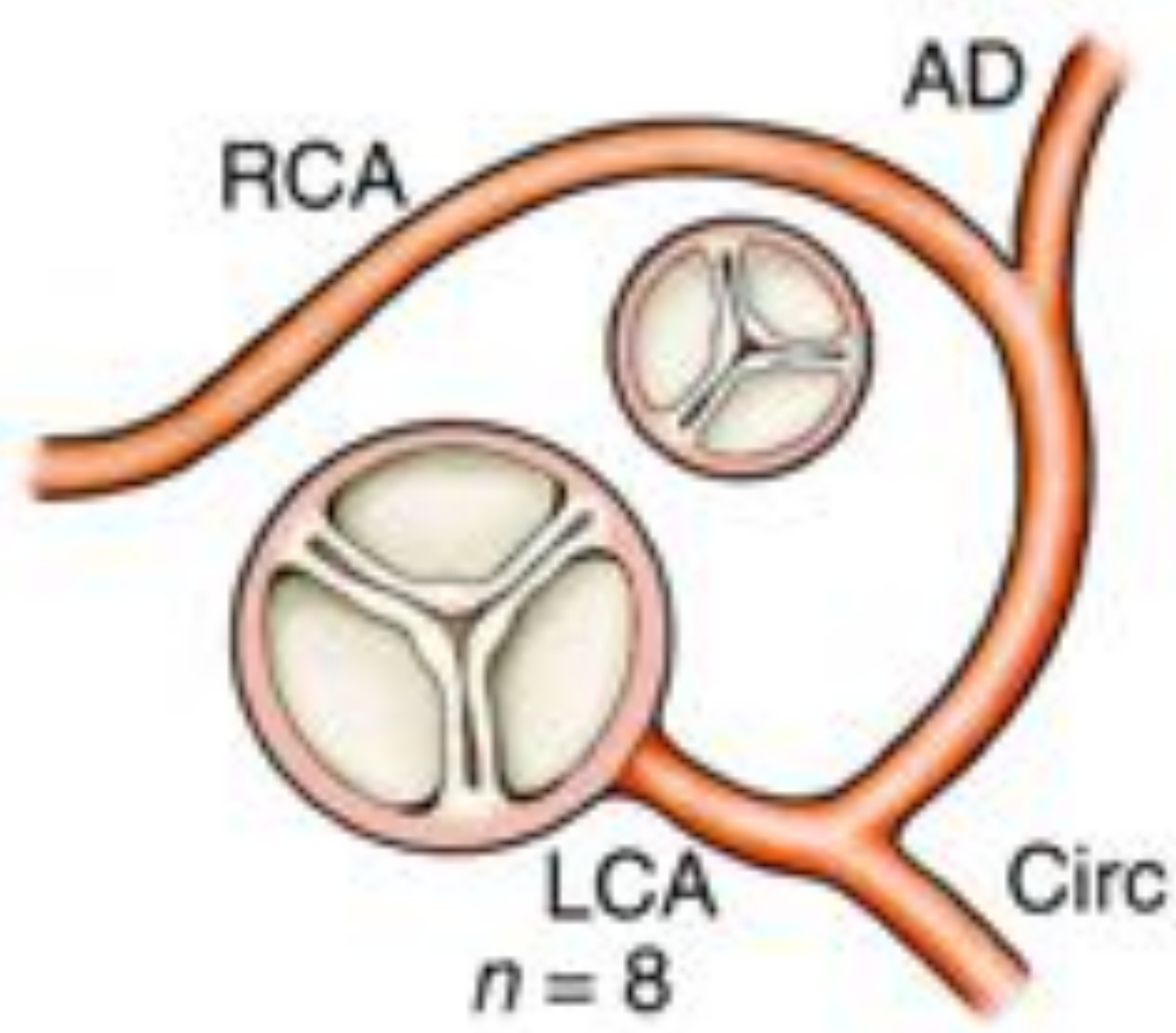
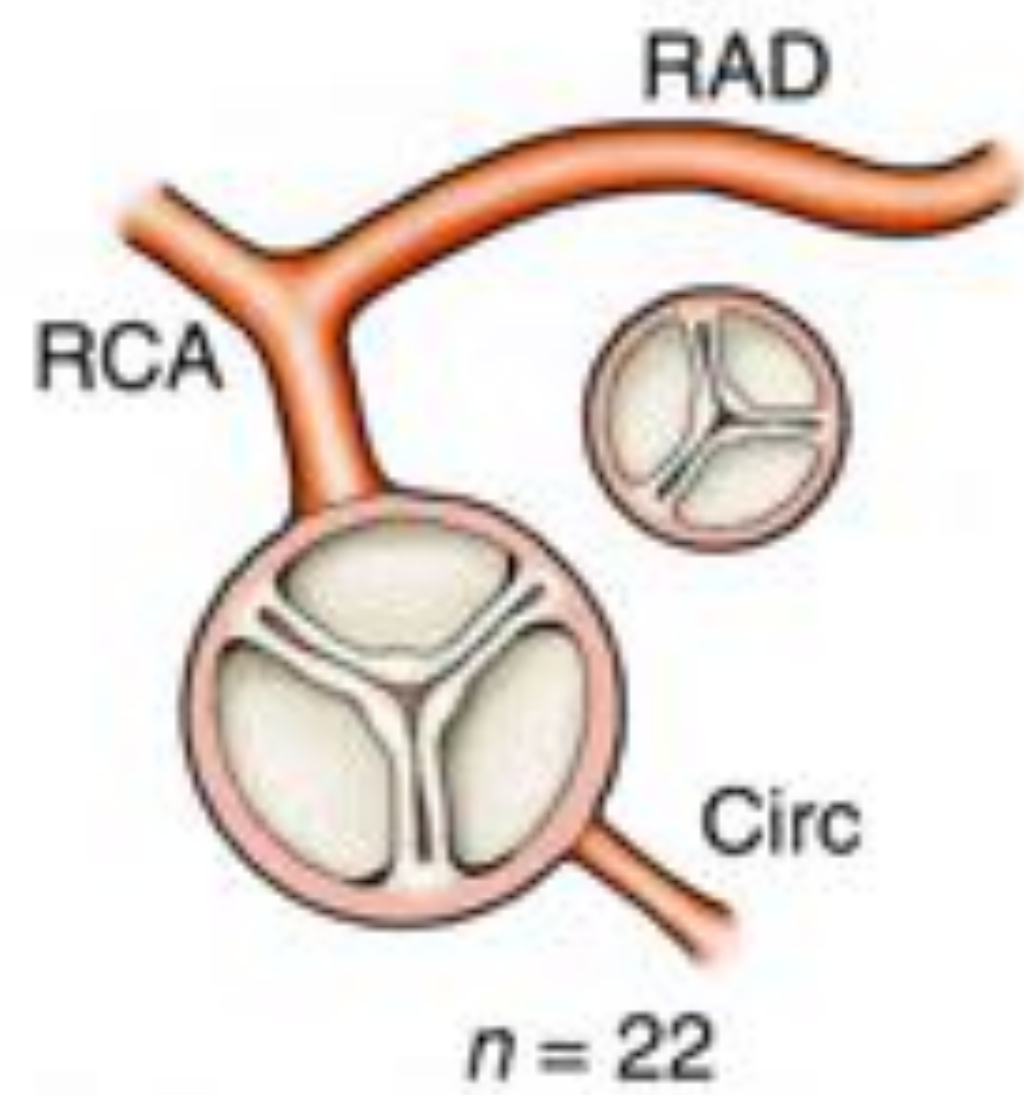


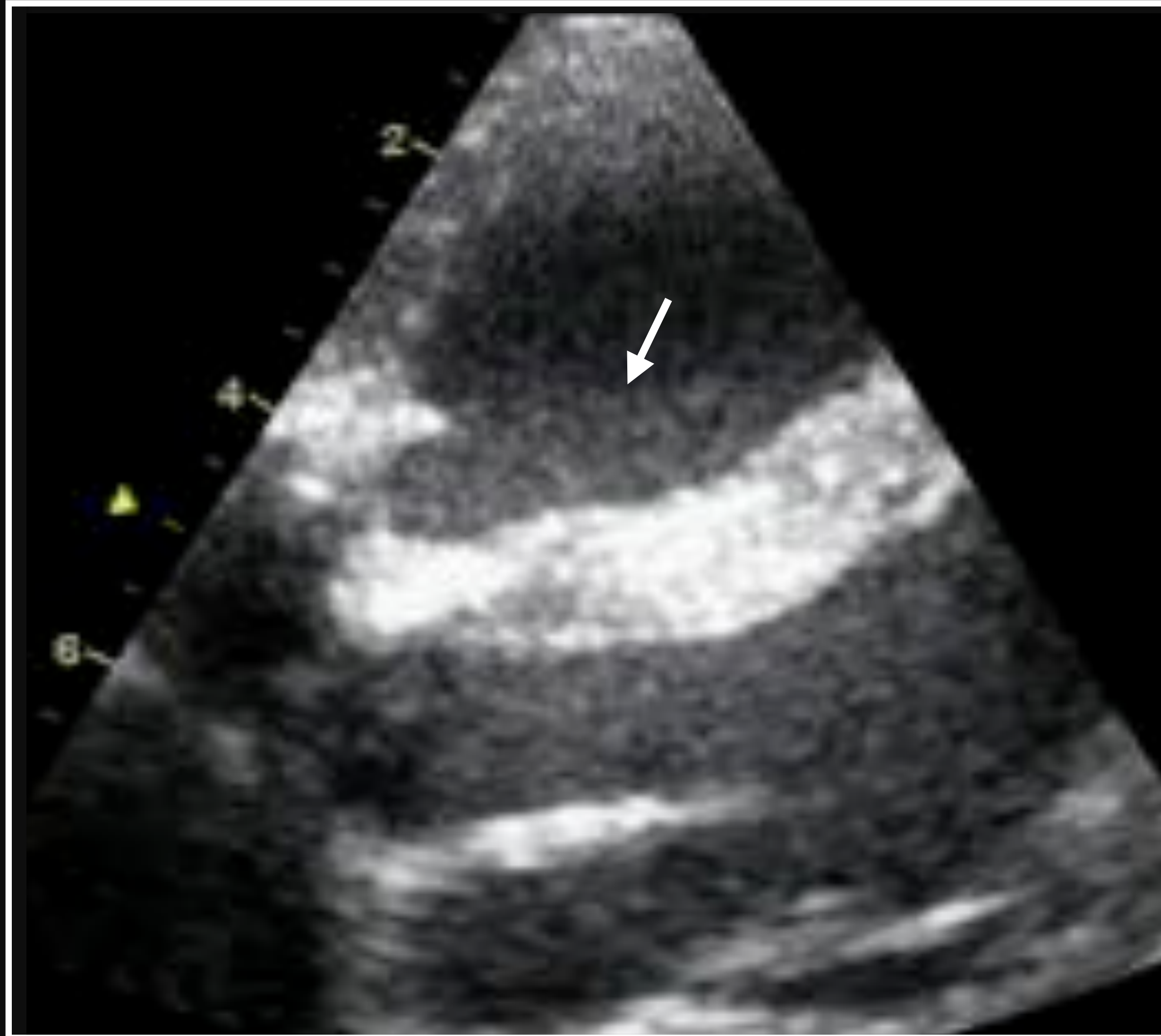
IV

Perinatal management

1. Ducto-dependent defect ?

2. Associated cardiac anomalies



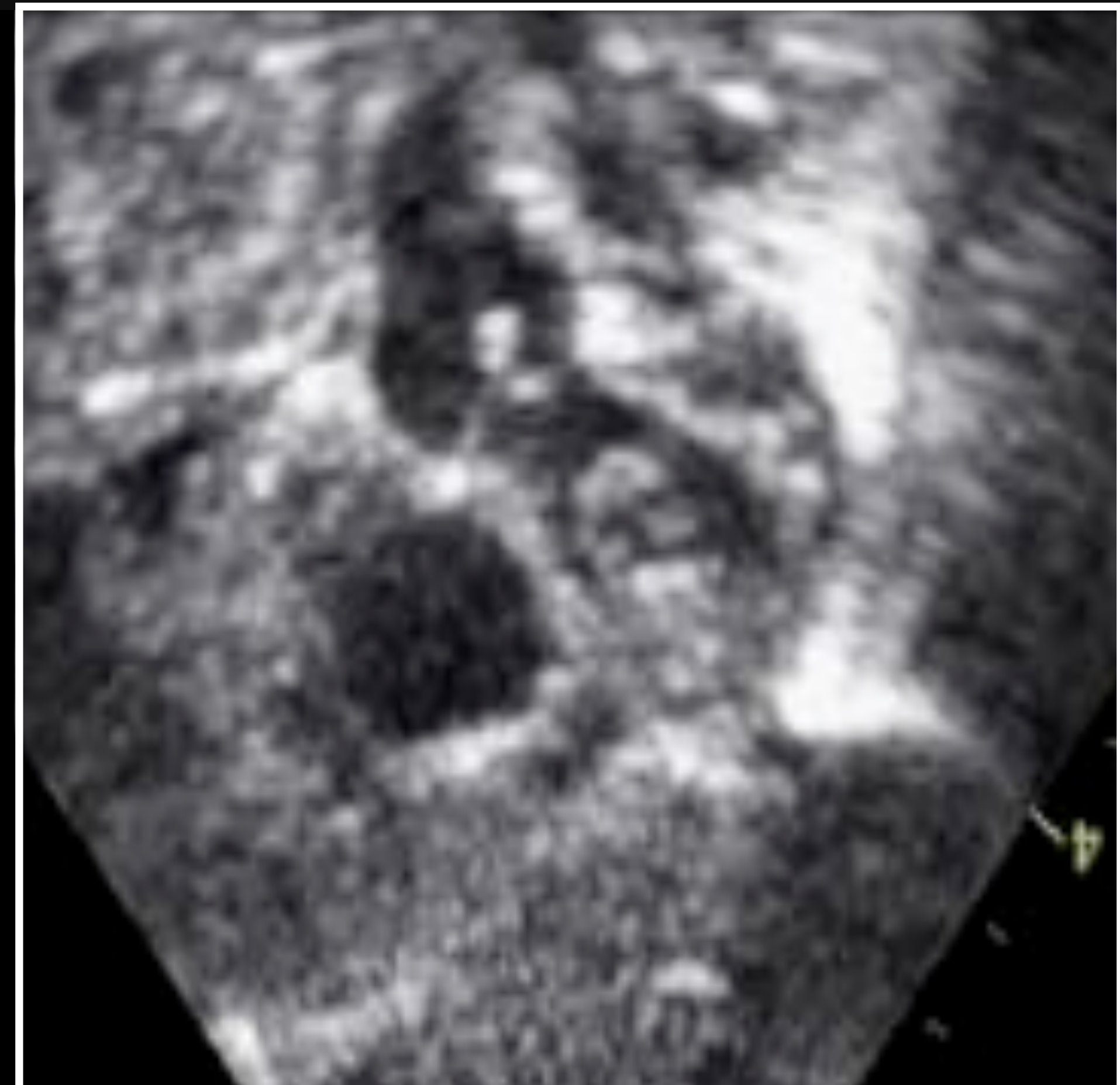


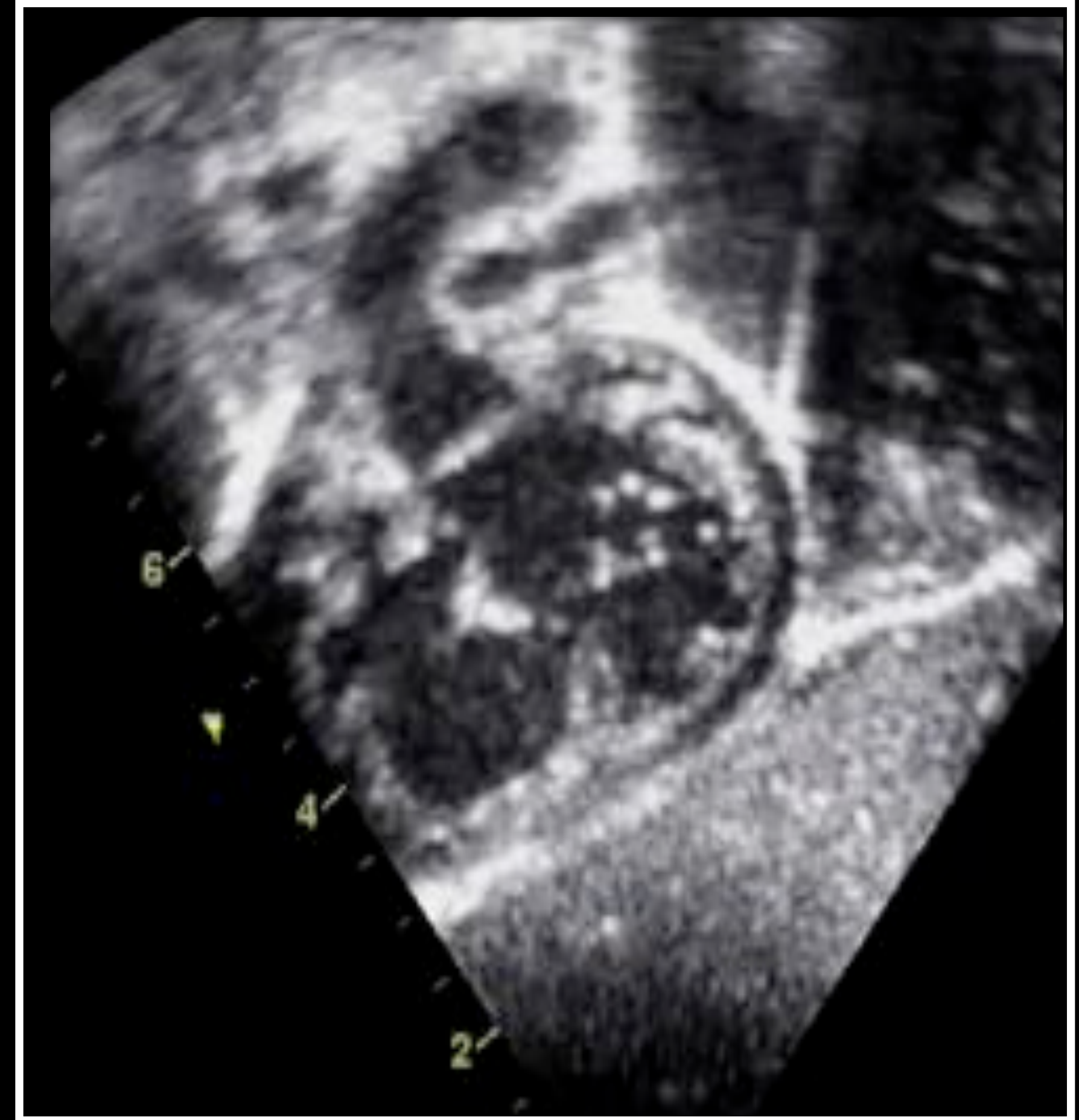
Fallot with LAD from the RCA with anterior course

Pulmonary branches stenosis

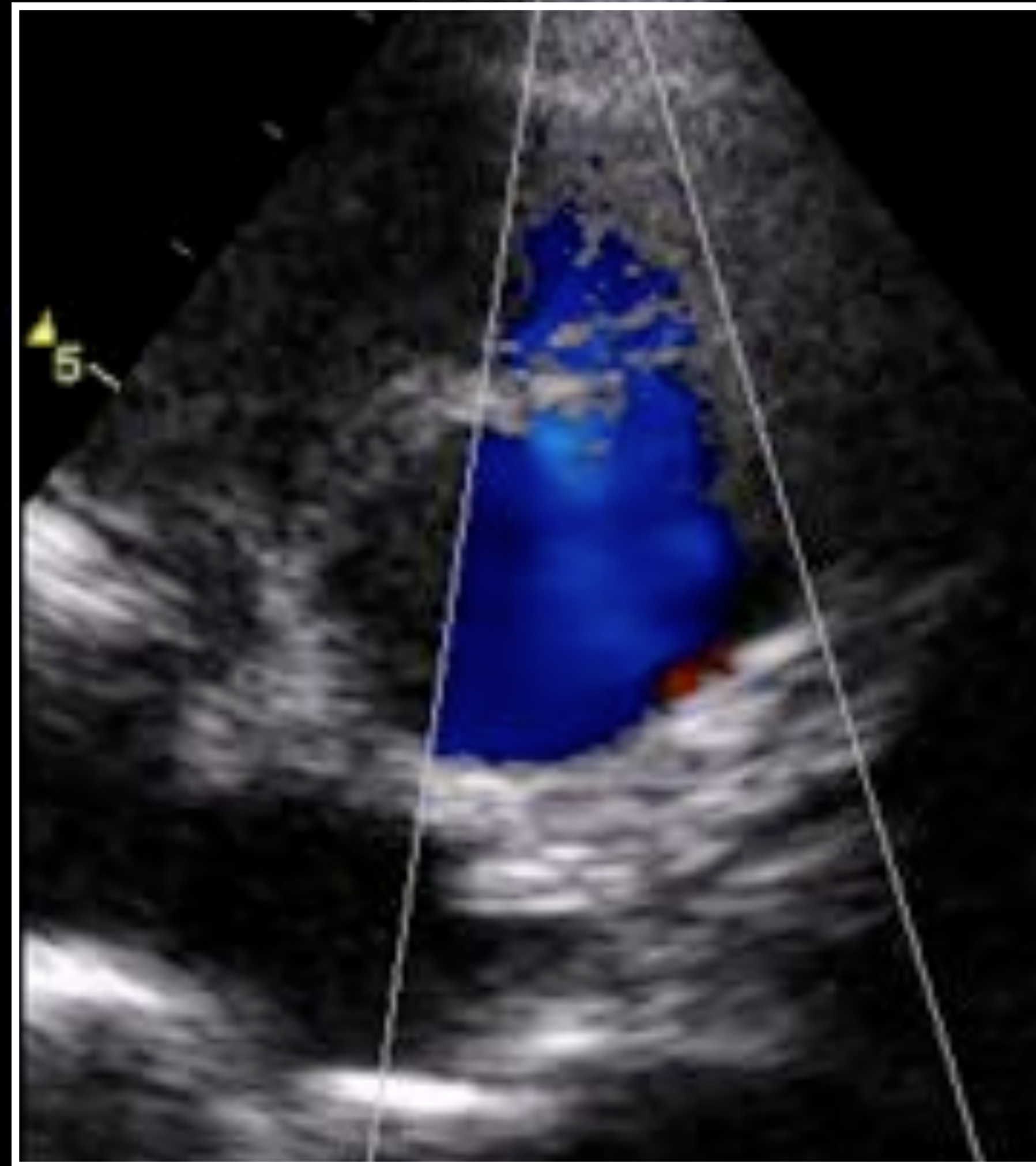


Multiple VSDs



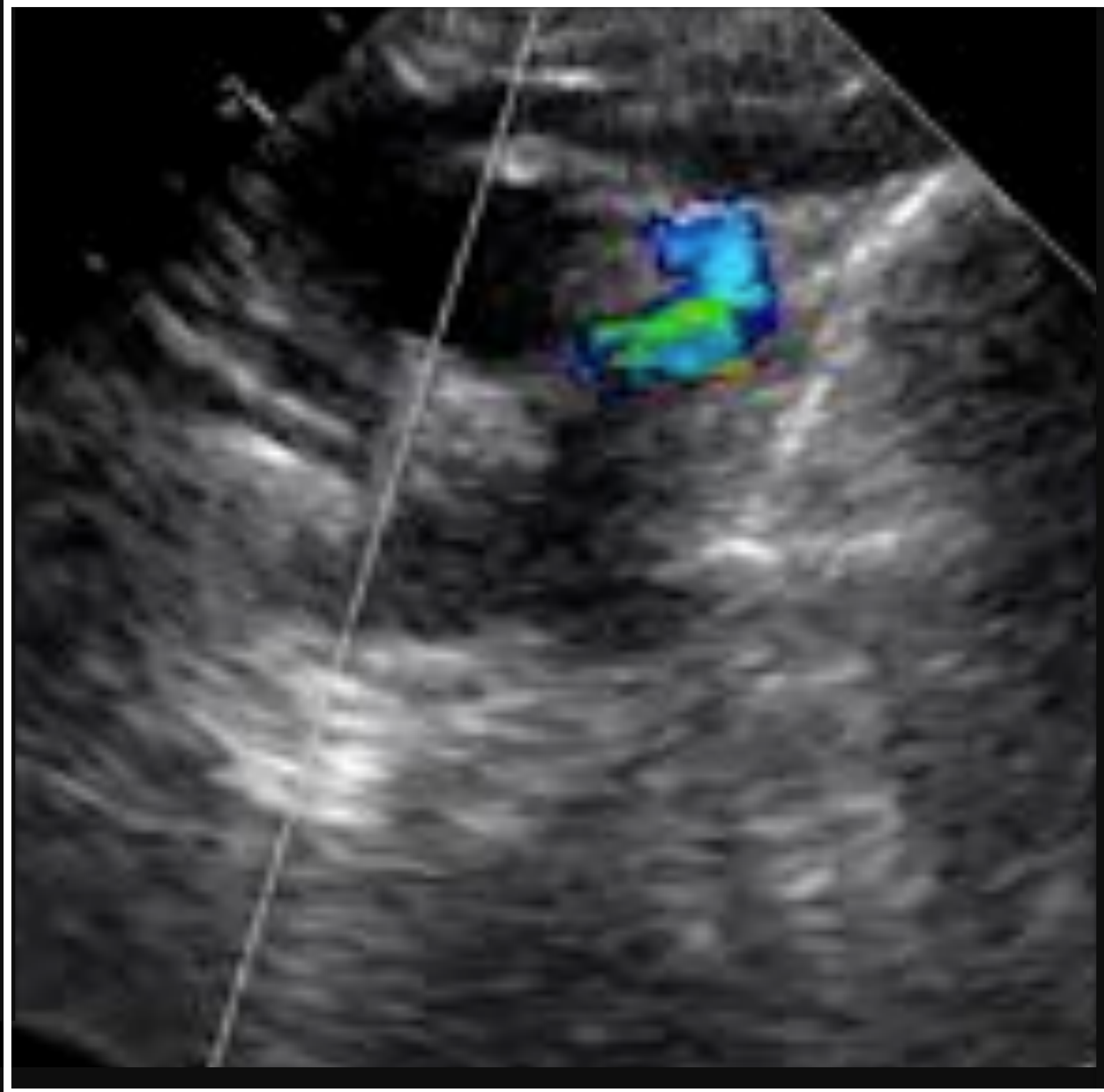


AVSD Fallot



Fallot with outlet VSD and absent conal septum

Patent arterial duct from brachiocephalic trunk



Perinatal management

1. Ducto-dependent defect ?
2. Associated cardiac anomalies
- 3. Strategy in neonates and infants**

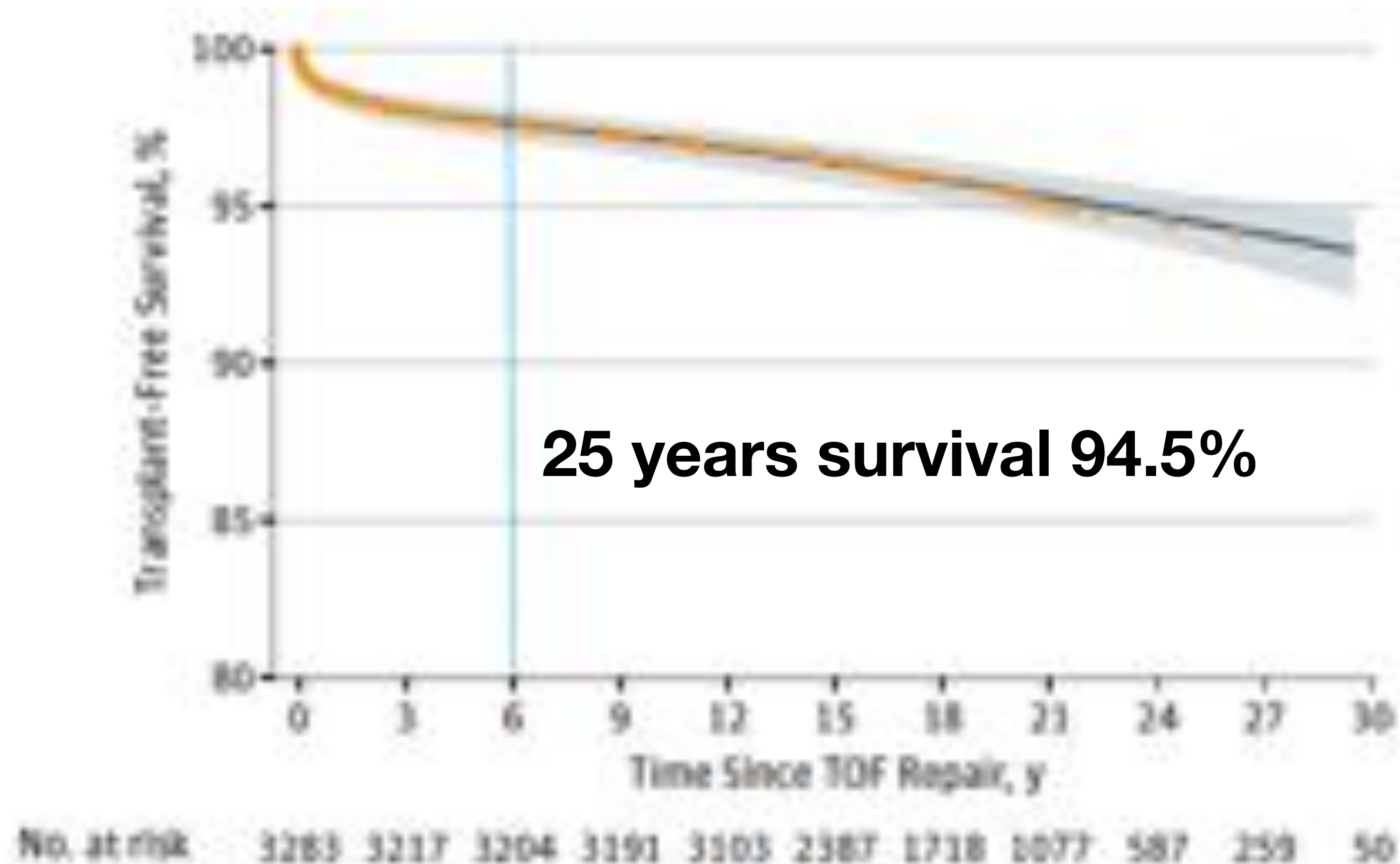
Predictors of long term outcome

Pediatric Cardiac Care Consortium

3283 patients with simple TOF

Follow-up 18.5 years (maximum, 33 years; IQR, 14.6-22.4 years),

The median age at death was 1.0 years (IQR, 0.6-2.1 years), with range 3 days to 19.7 years.



Predictors of long term outcome

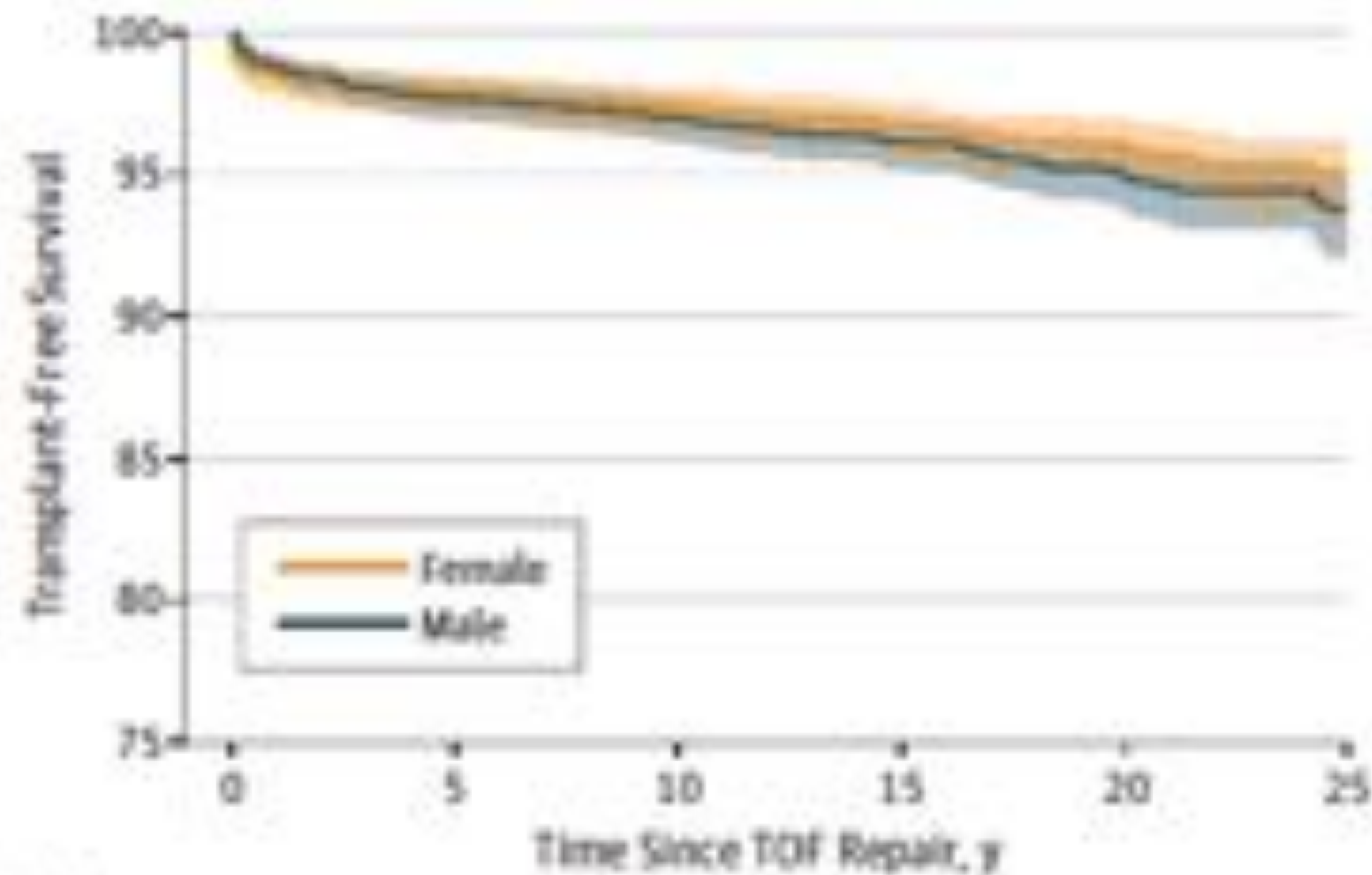
Pediatric Cardiac Care Consortium

3283 patients with simple TOF

Follow-up 18.5 years (maximum, 33 years; IQR, 14.6-22.4 years),

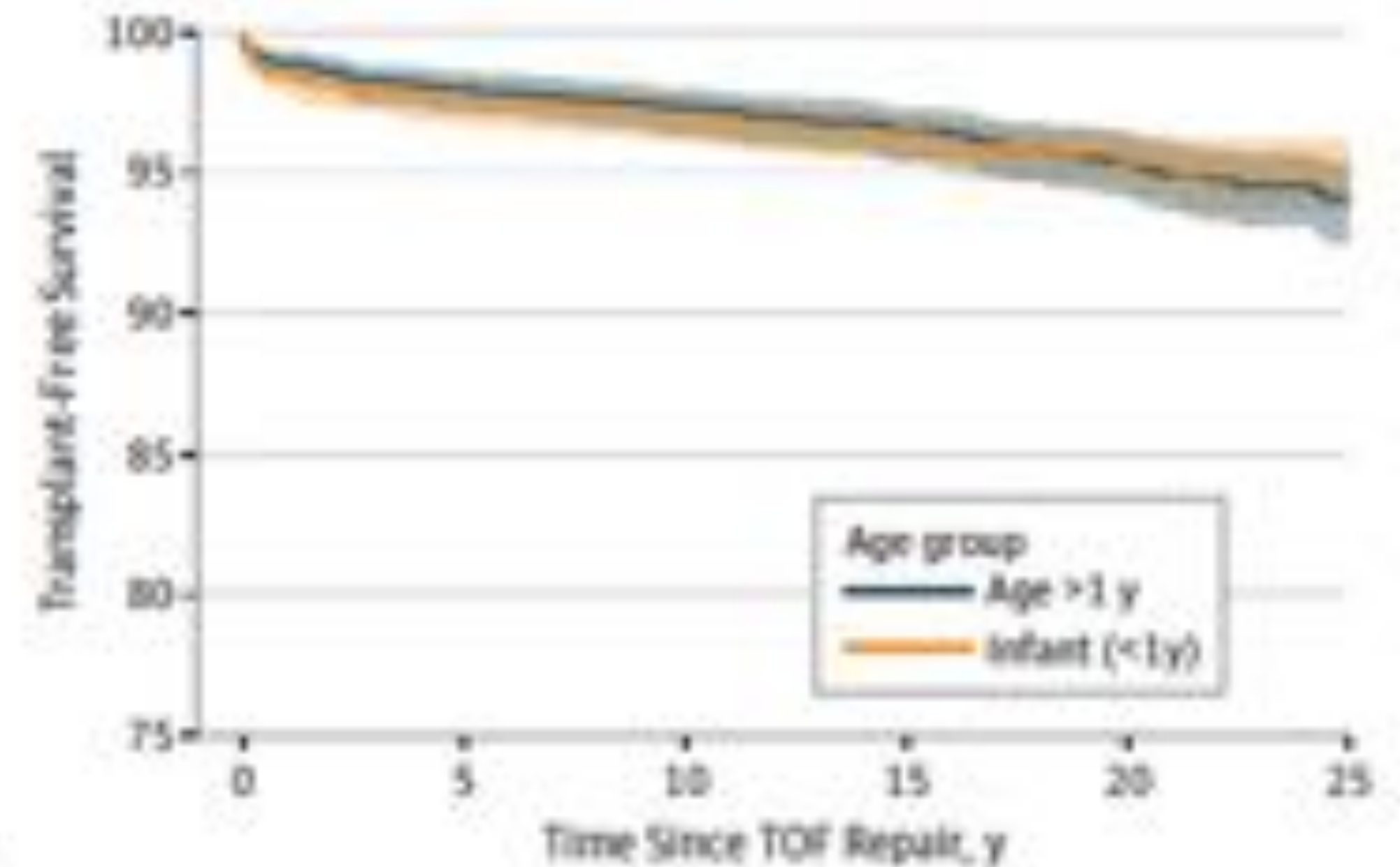
The median age at death was 1.0 years (IQR, 0.6-2.1 years), with range 3 days to 19.7 years.

SEX



No. at risk						
Female	1434	1403	1393	1073	582	209
Male	1849	1806	1793	1314	722	252

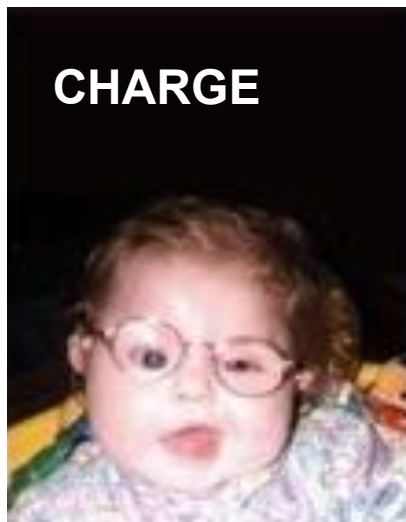
AGE GROUP



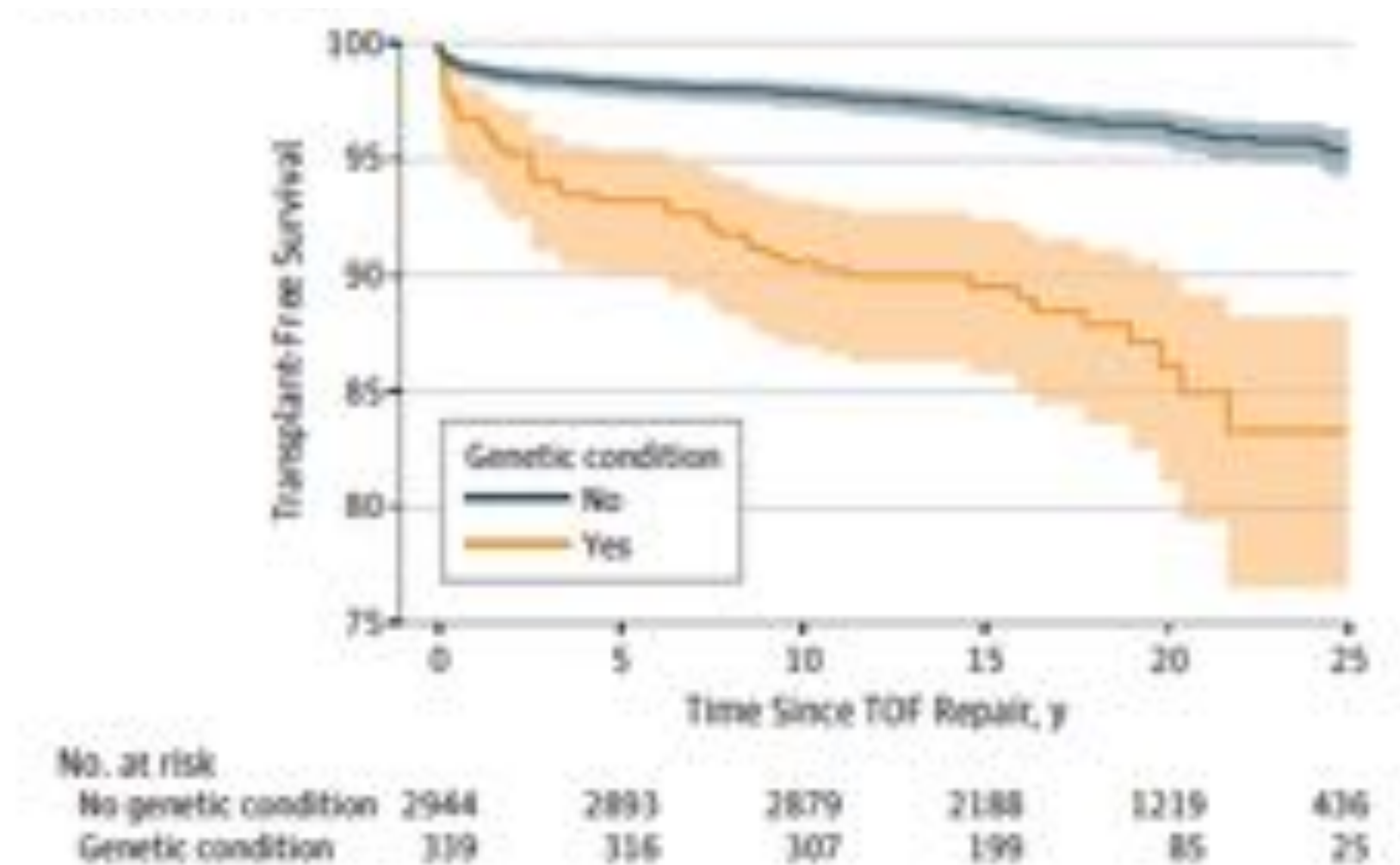
No. at risk						
Older than 1 y	1489	1459	1446	1208	834	358
Infant	1794	1750	1740	1179	470	103

Predictors of long term outcome

Pediatric Cardiac Care Consortium



Non modifiable factor : genetic condition

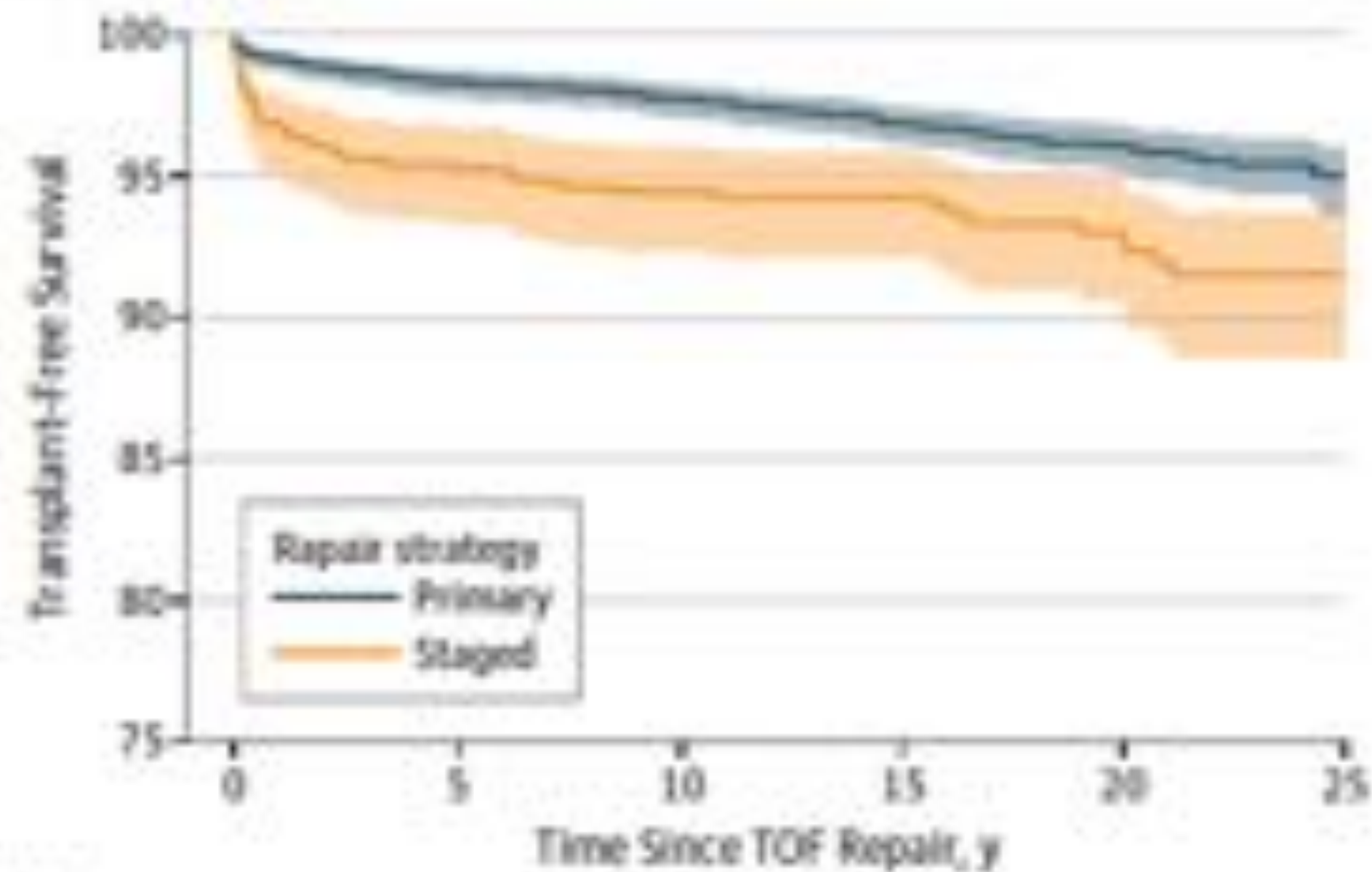


HR 3.64

Predictors of long term outcome

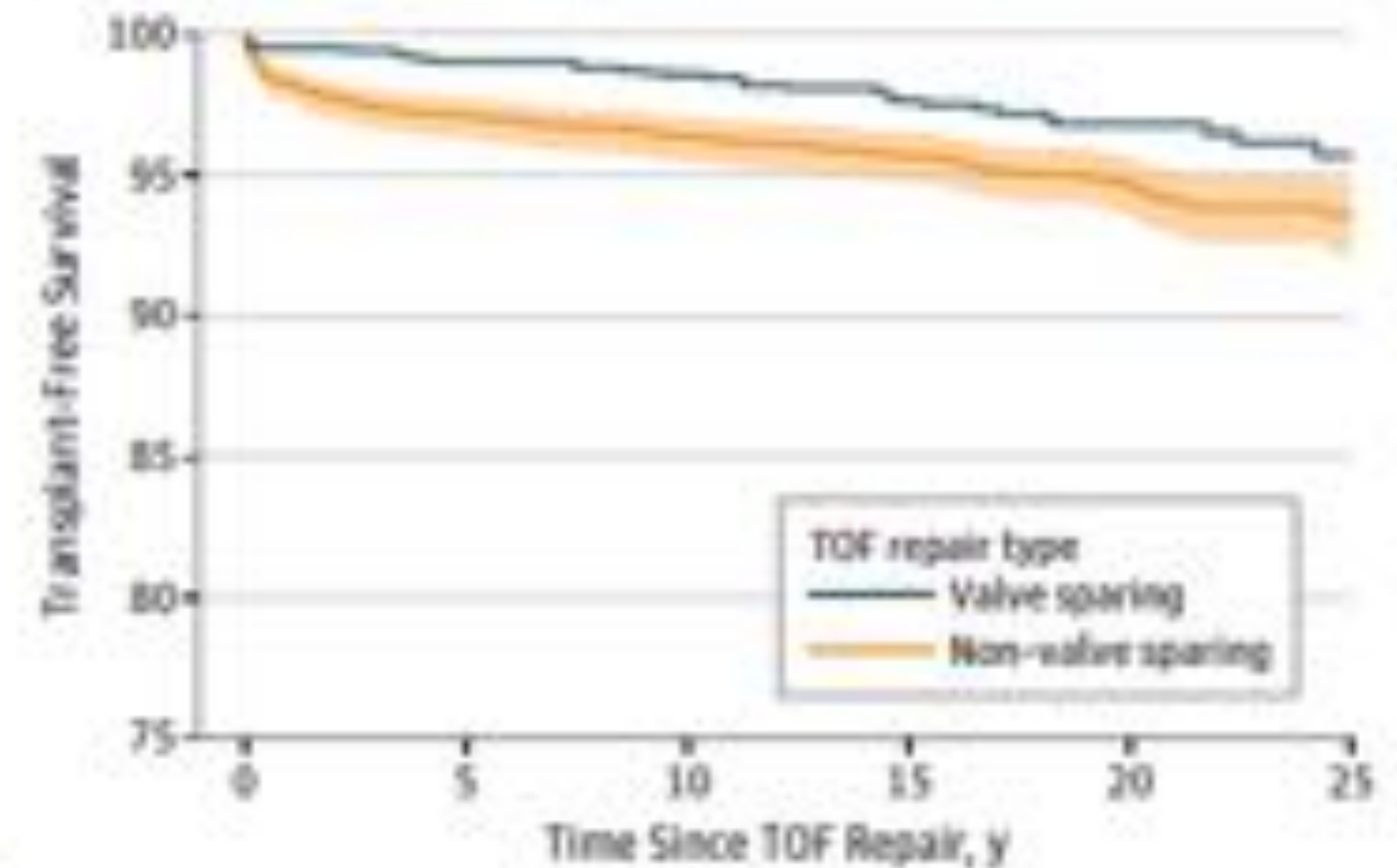
Pediatric Cardiac Care Consortium

Repair strategy



No. at risk						
Primary	2672	2627	2610	1952	1041	365
Staged	611	582	576	435	263	96

TOF Repair type



No. at risk						
Valve sparing	1058	1048	1043	778	424	155
Non-valve sparing	2201	2137	2119	1587	866	301

Perinatal strategy in simple ToF

What is the plan during infancy ?

ToF is a **progressive disease** with a potential increase in severity with time.

Optimizing the pulmonary blood flow in the most physiologic fashion may halt this process,

With the objective to **normalize growth of the pulmonary arteries** during infancy.

Thus, **early repair** is thought to be the **optimal** management approach.

Preserving the pulmonary valve predicts a better long-term outcome.

Patients vs. Strategies & Alternative techniques



Patients characteristics

Different categories



Non modifiable

- underlying genetic conditions

Time-dependent

- age and weight
- symptoms

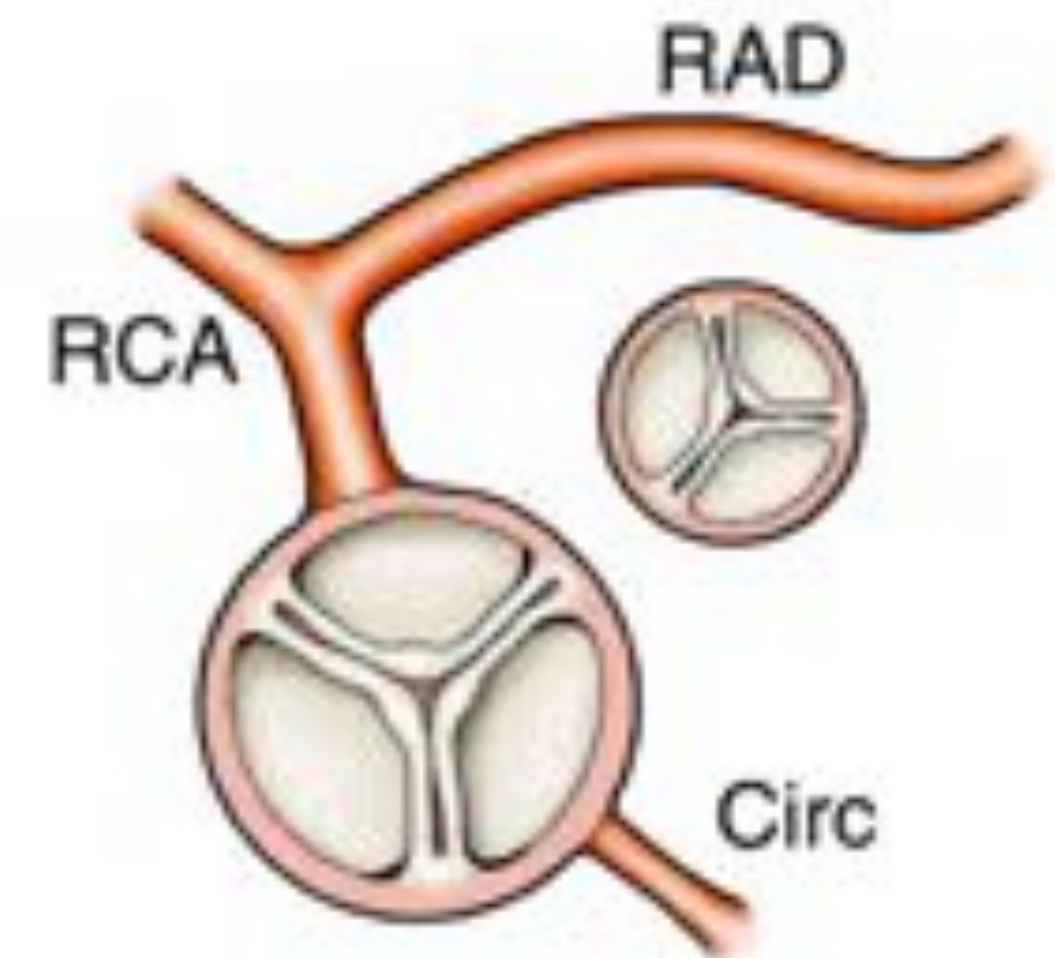
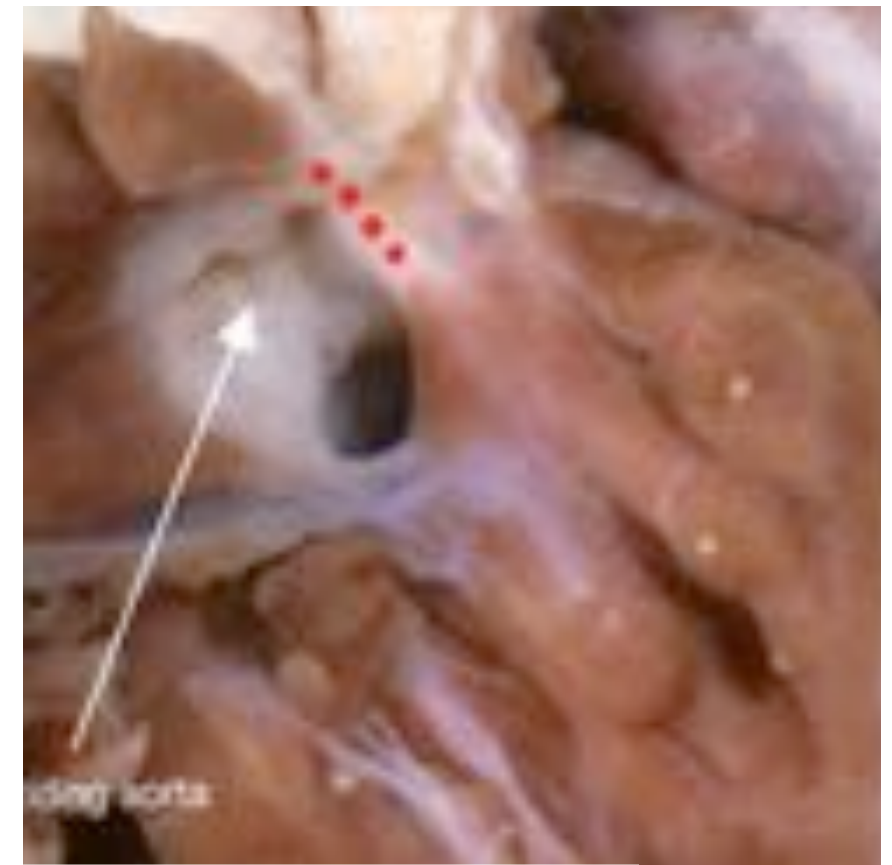
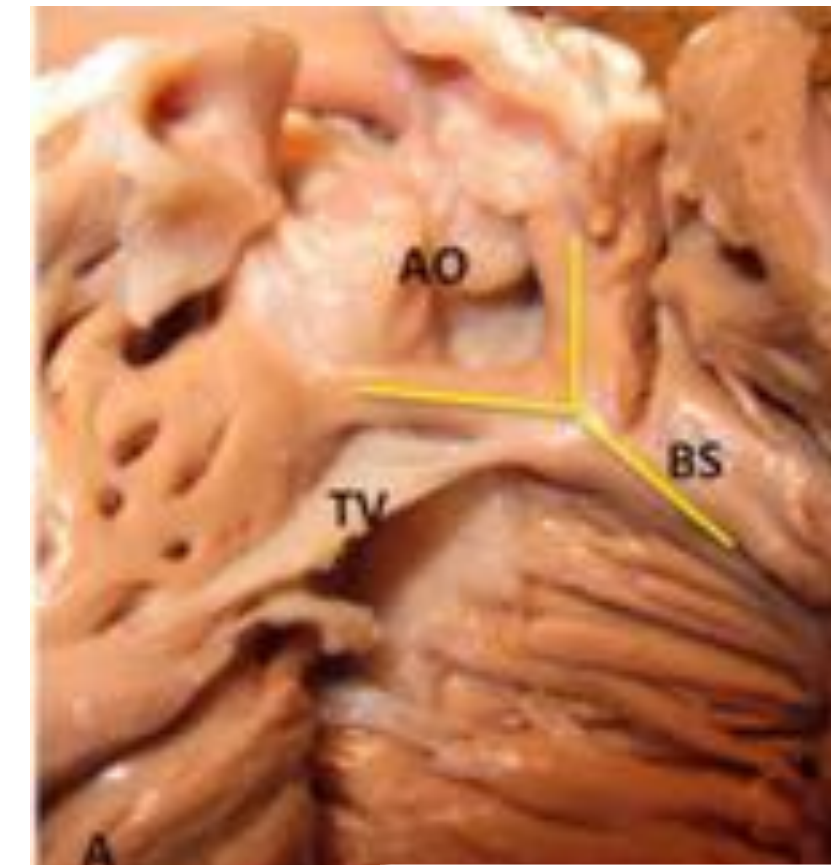
Anatomical characteristics

Non modifiable

- location of the VSD
- coronary artery anatomy

Time-dependent/modifiable

- pulmonary valve and annulus
- pulmonary artery branches (size, contiguity)
- anatomy of the arterial duct



Strategy

Different options

Goal: closed VSD, preserved pulmonary valve without obstruction or regurgitation, normal growth of pulmonary artery branches, normal RV function, no aortic regurgitation



Make plan : elective repair or patient's dependent repair (staged or one step)

Get to work: when ? and how ?

Reach goal: initial strategy and long-term outcomes

Alternative techniques

Palliate:

Blalock

or Stenting the arterial duct

or surgical right ventricle to pulmonary connection

or stenting the right outflow tract

Repair:

Trans-annular patch

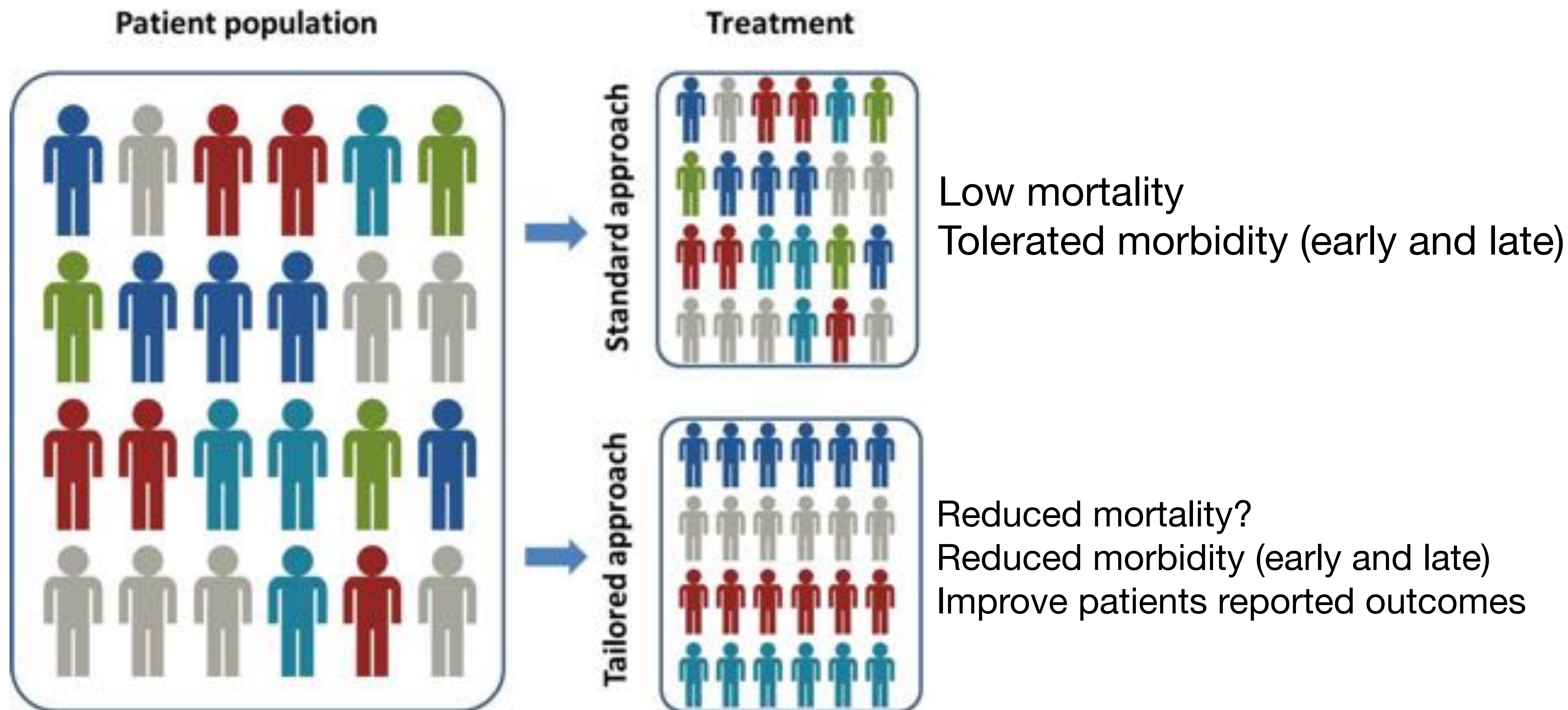
Preserve pulmonary valve

RV-PA conduit

Limit right ventriculotomy



Simple ToF(s) or one patient/one ToF





Helen Taussig

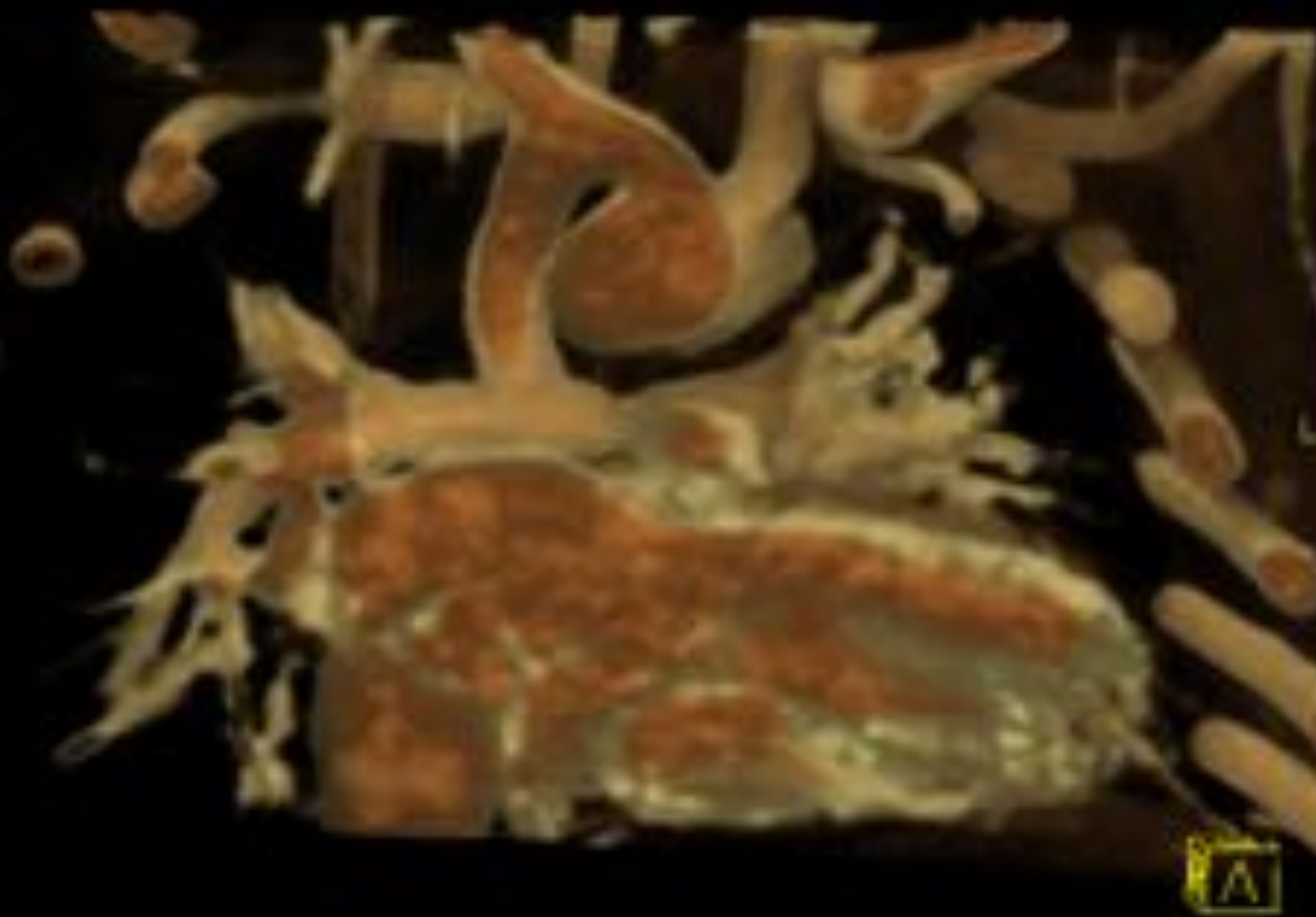
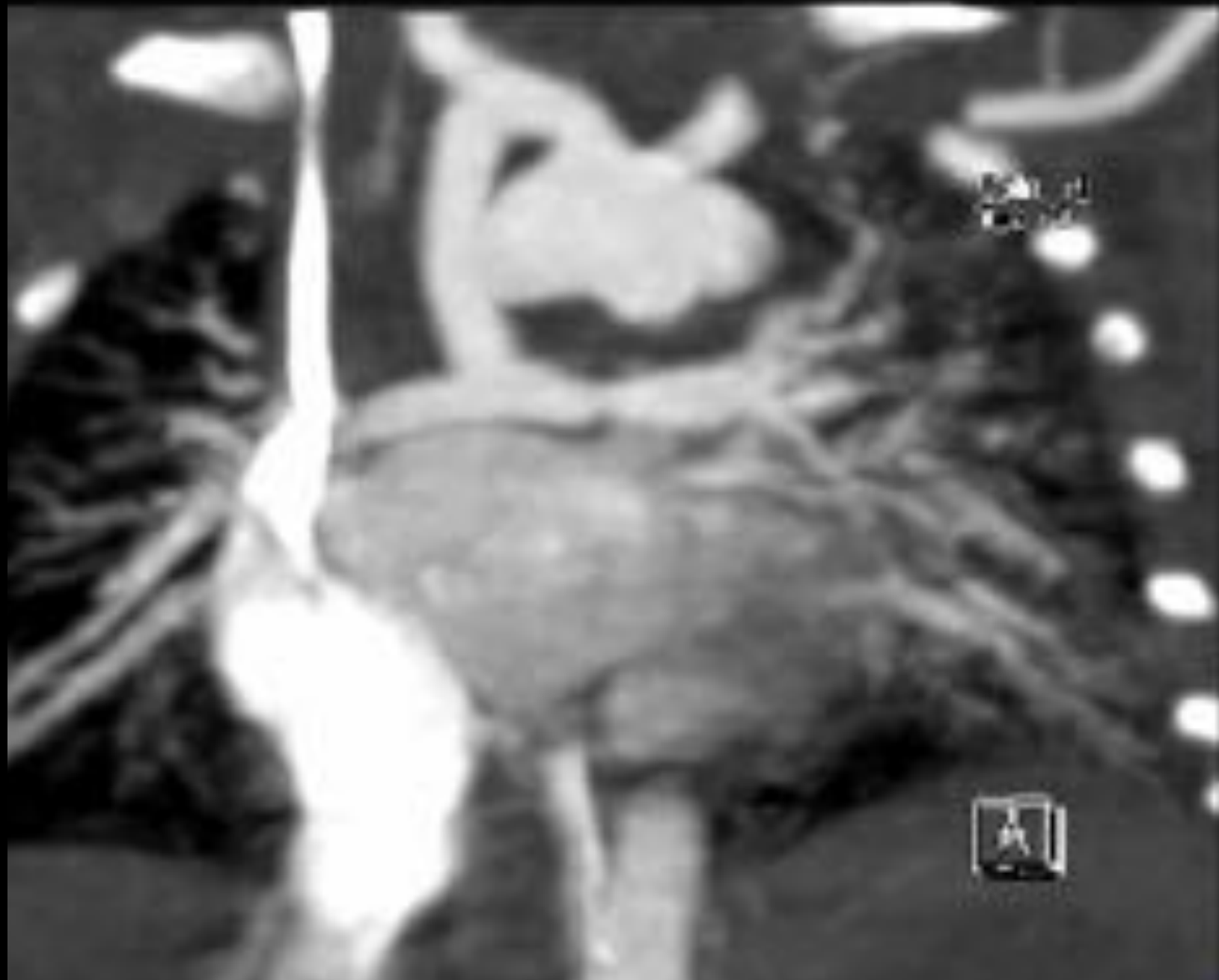
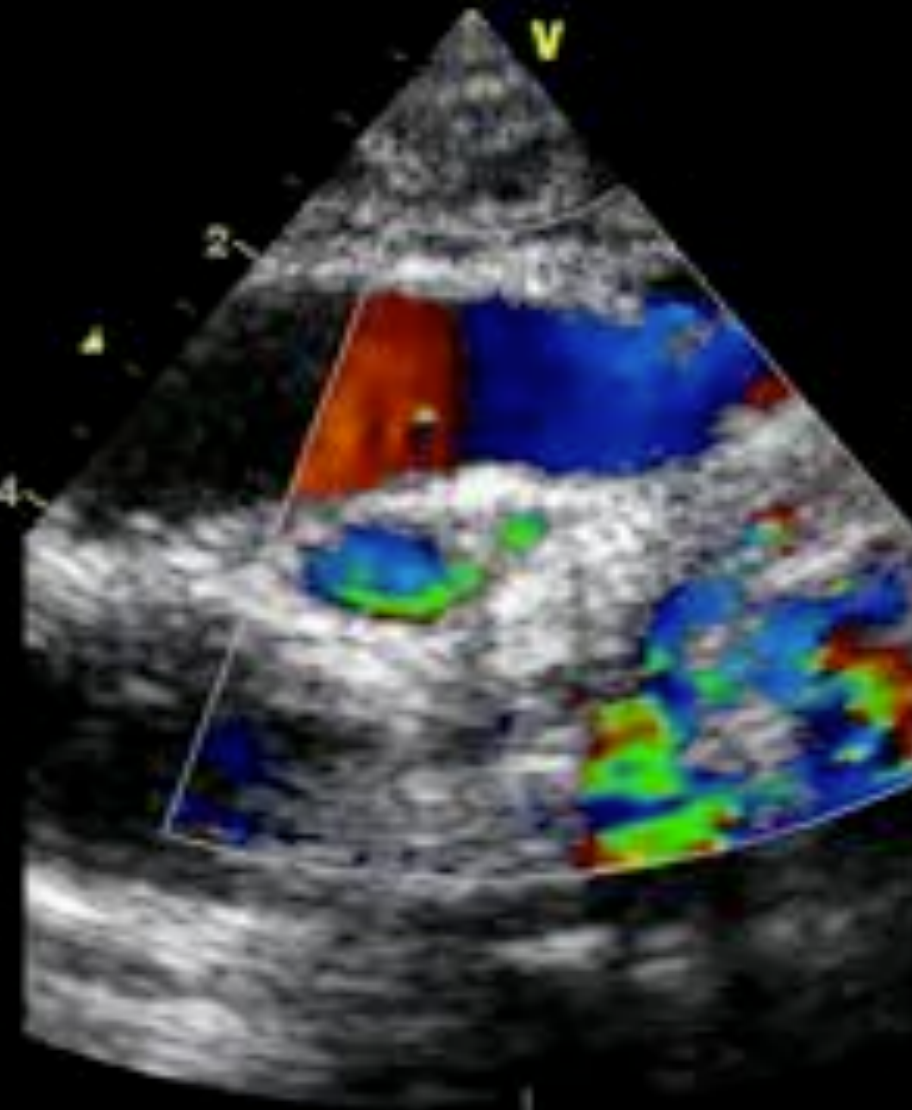
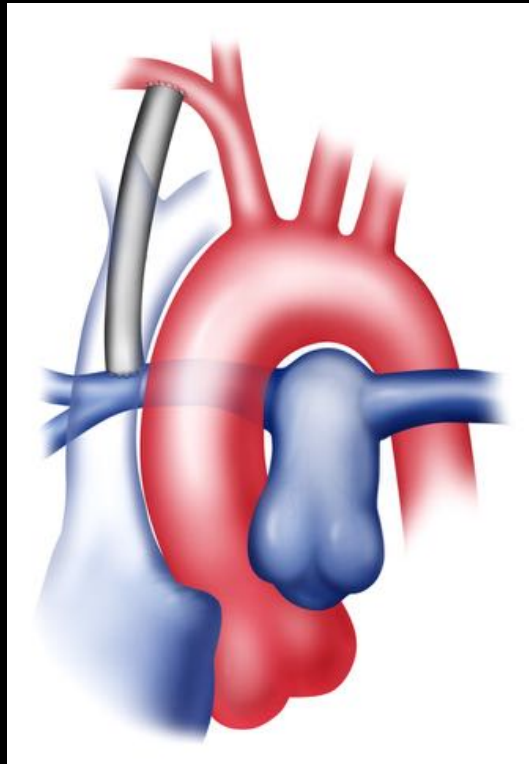


Alfred Blalock and Eileen Saxon



Vivien Thomas

Blalock-Taussig-Thomas shunt



Initial strategy in symptomatic neonates with ToF

Non elective intervention

Outcomes of BT shunts

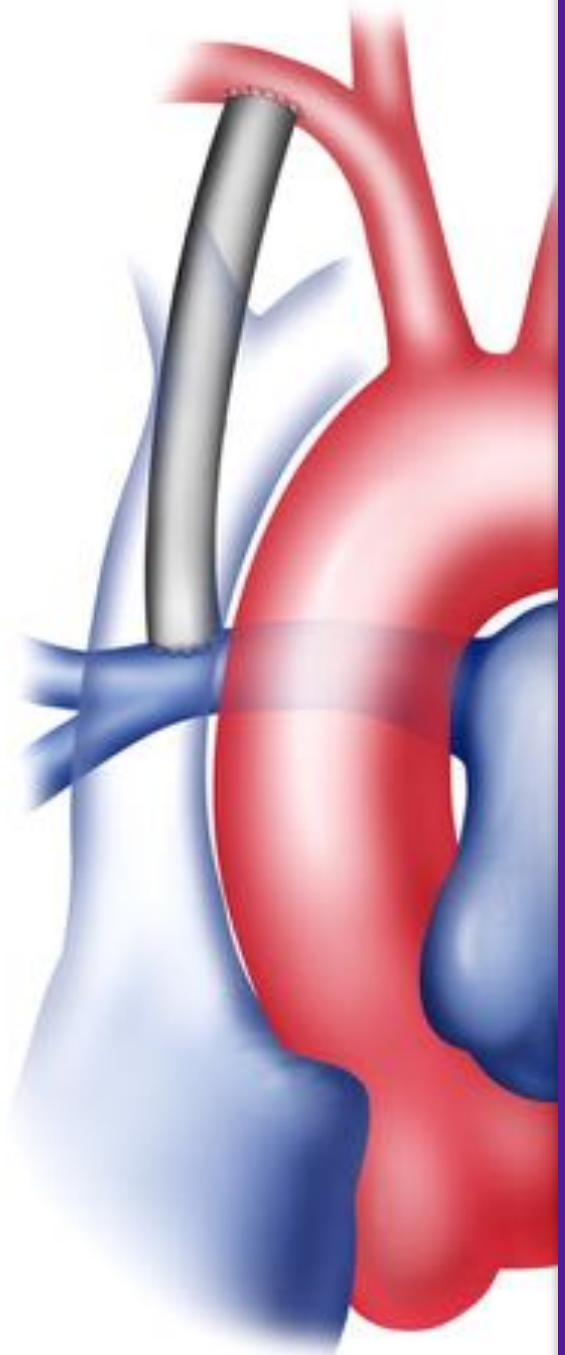
In hospital mortality (4-5%)

Inter-stage mortality (3.6%)

24% of acute post-operative events including shunt thrombosis, pulmonary overcirculation, shunt stenosis, and pulmonary artery stenosis

Hobbes B et al. Ann Thorac Surg 2017;104:1365–70

-vs. complete repair in neonatal period



Initial strategy in symptomatic neonates with ToF

Non elective intervention

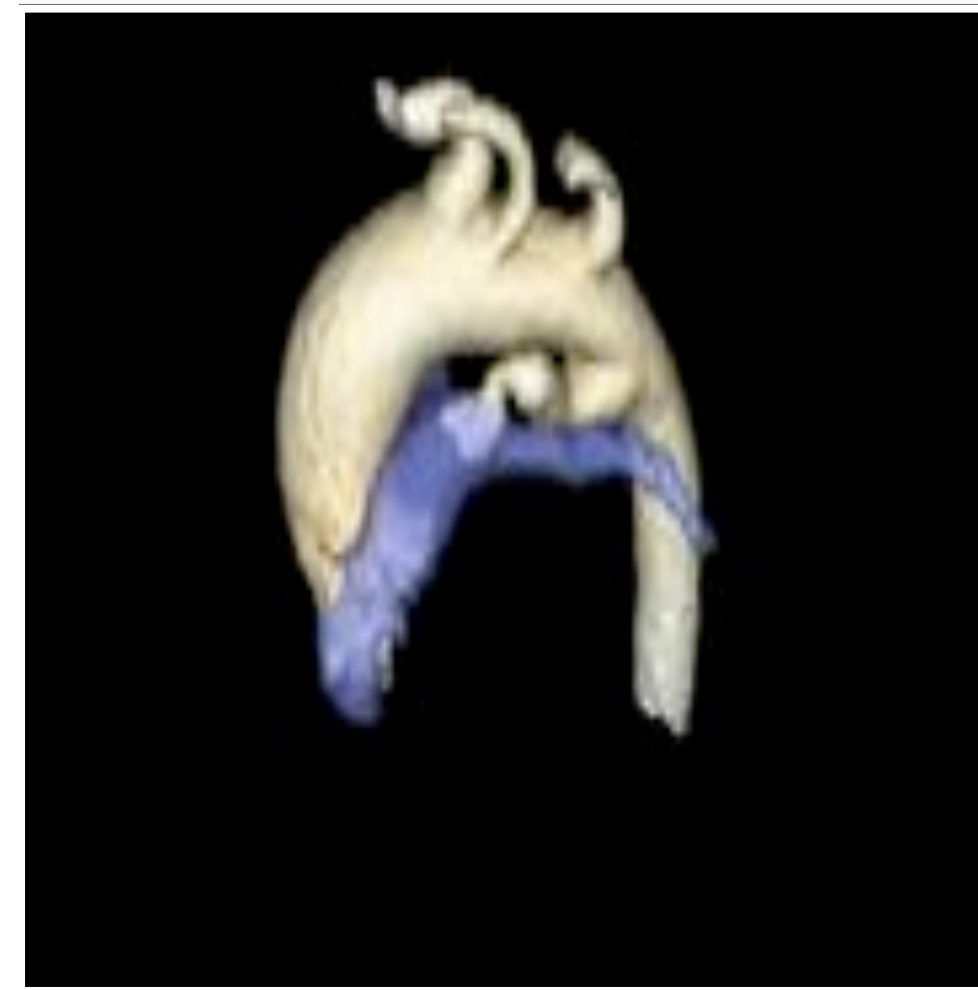
Stenting of arterial duct

1-Patients characteristics

- Tendency for complex PDA–pulmonary artery morphology.



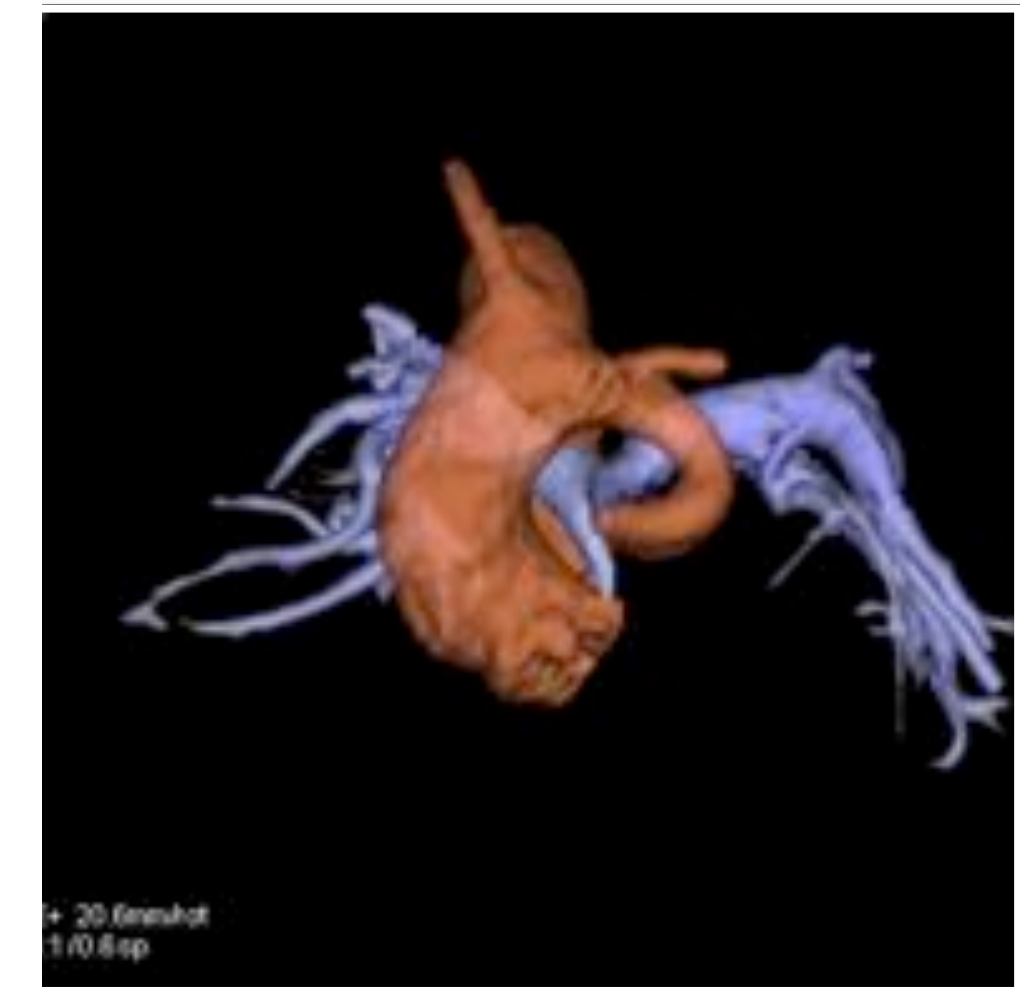
LPA coarctation



Tortuous



Underneath
the aortic arch



From innominate artery
Right aortic arch

Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting 2-Strategy

-avoid surgery

Outcomes of PDA stenting in ToF

Aggravation of PA branch stenosis

Poor growth of vessel 'jailed » by stent

Shorter duration of palliation vs. BT shunt

Acute stent thrombosis

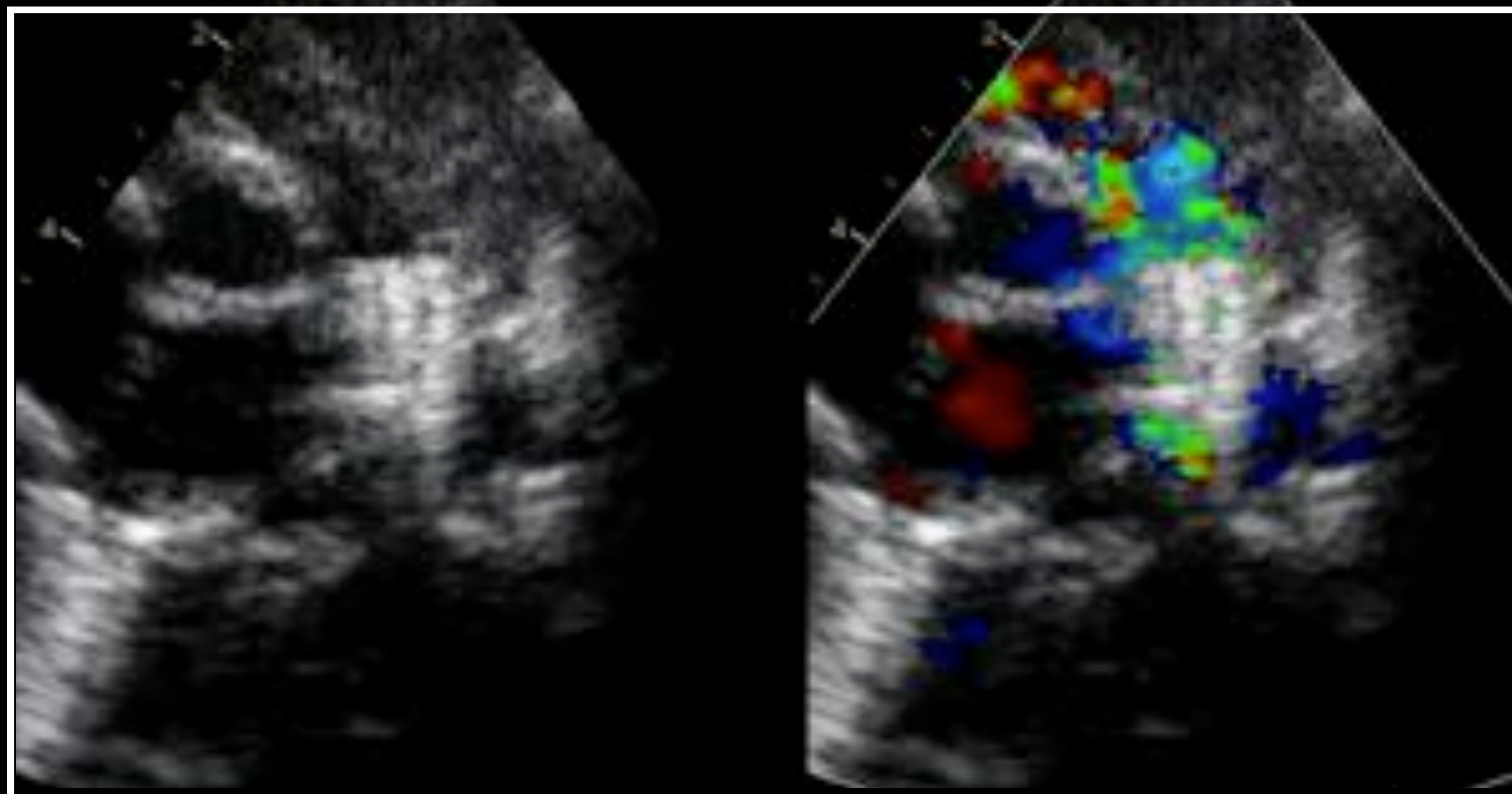
Tortuous PDA with multiple bends is NOT an indication

Rehman R et al. Future Cardiol 2018



cess





Initial strategy in symptomatic neonates with ToF

Non elective intervention

Surgical right ventricle to pulmonary connection

1-Patients characteristics

- small sized pulmonary arteries or LPA stenosis or disconnected PA
- with very diminutive RVOT

2-Strategy

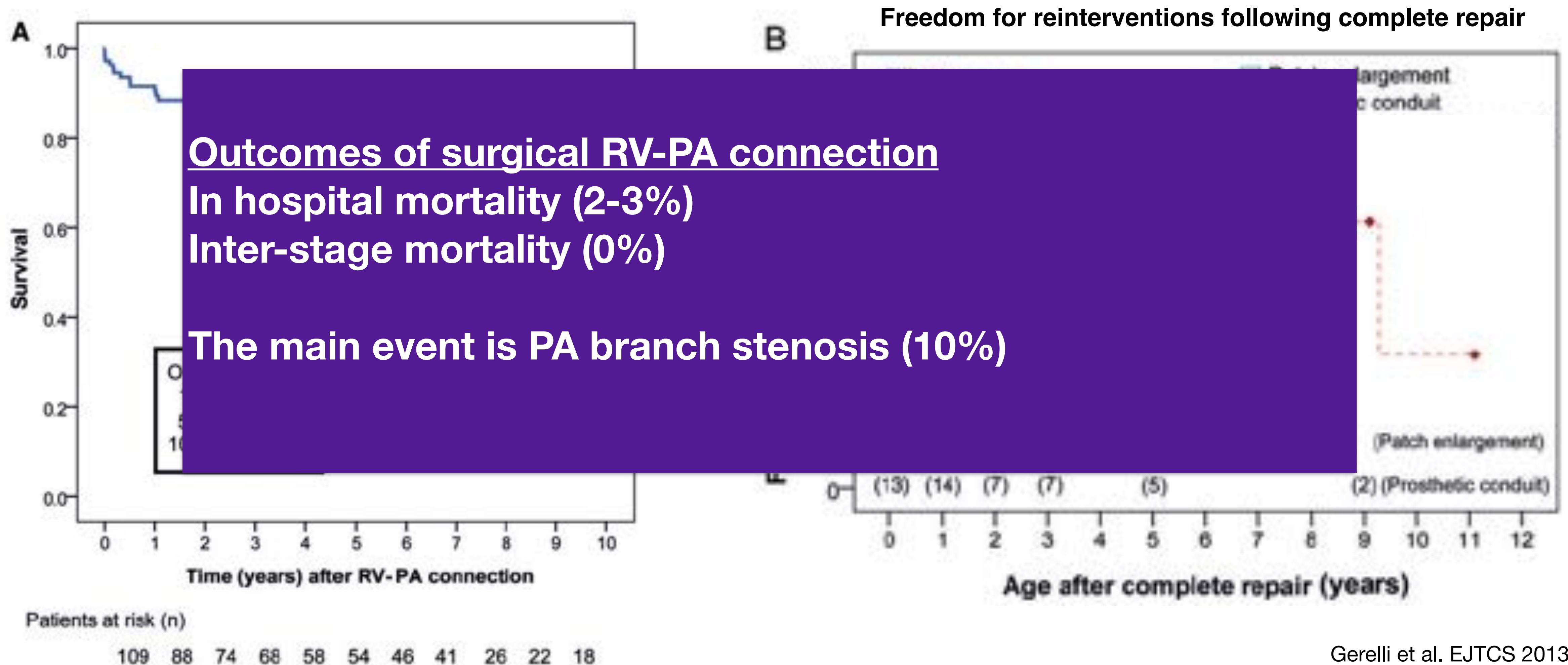
- promote symmetrical growth of PA
- more physiological than shunt

3-Alternative techniques

- vs. stenting of the RVOT
- vs. complete repair in neonatal period

Initial strategy in symptomatic neonates with ToF
Non elective intervention

Neonatal right ventricle to pulmonary connection



Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of right ventricle outflow tract

1-Patients characteristics

- small sized pulmonary arteries
- with very diminutive RVOT

2-Strategy

- promote symmetrical growth of PA
- more physiological than shunt

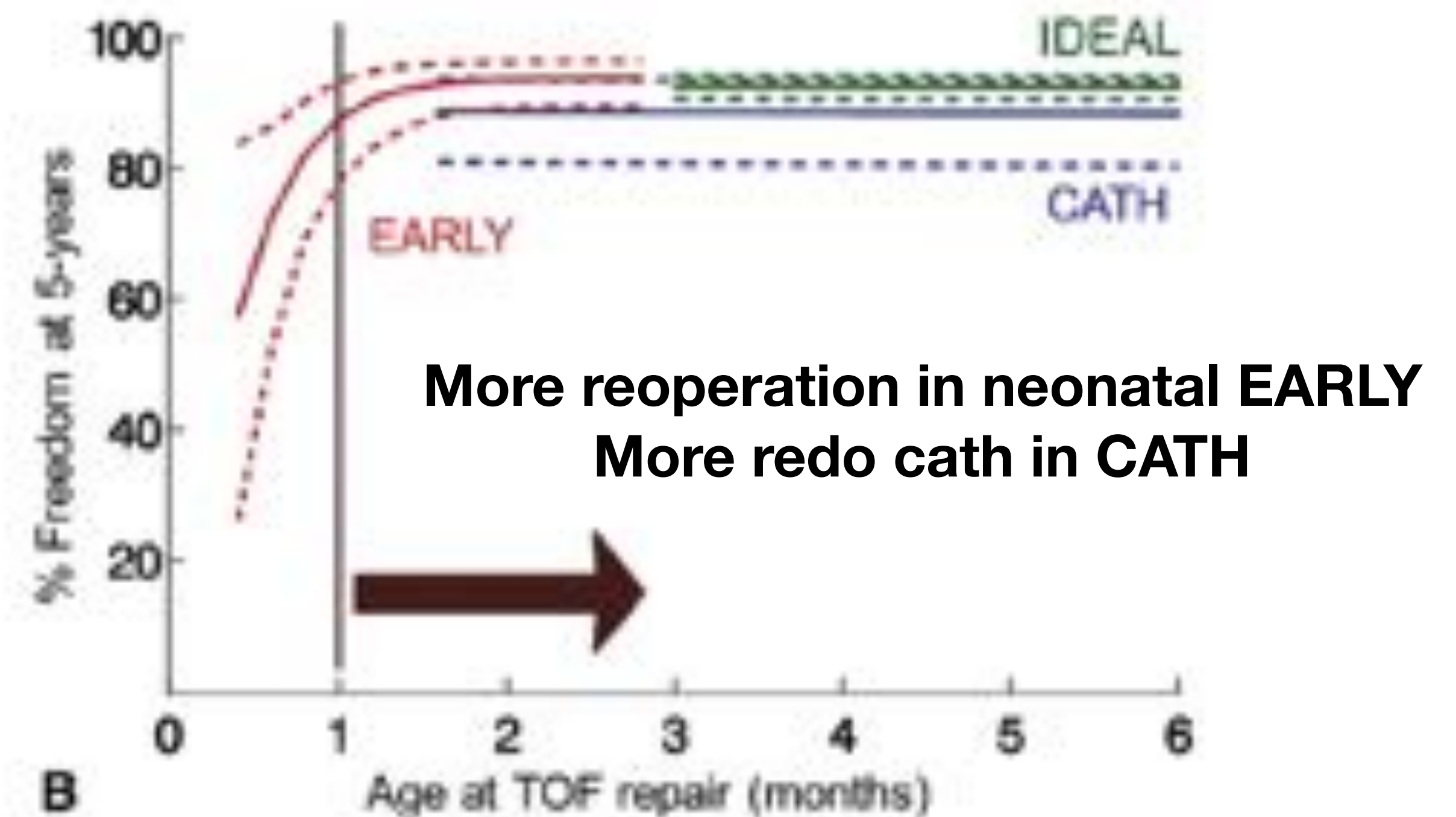
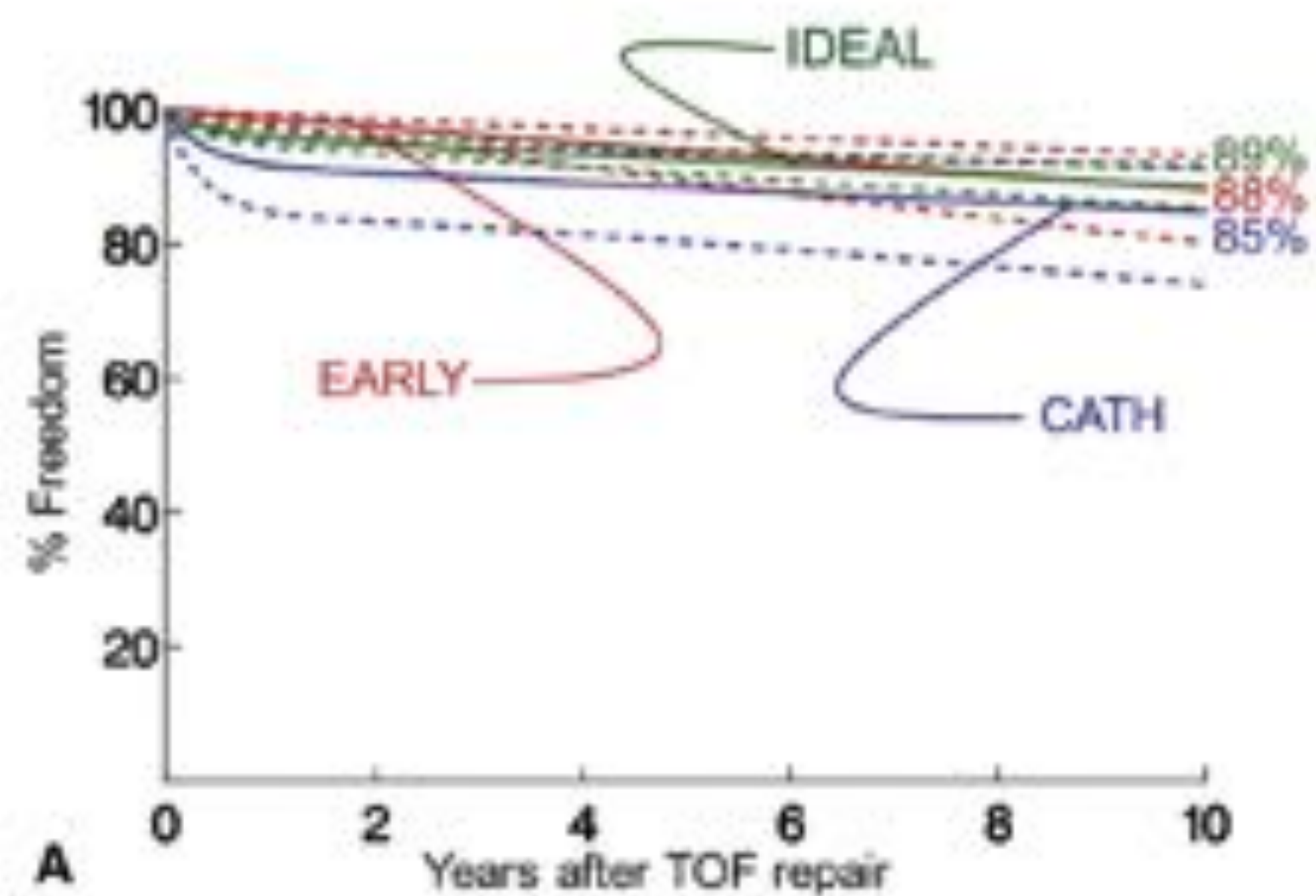
3-Alternative techniques

- vs. complete repair in neonatal period

Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of right ventricle outflow tract



IDEAL : elective repair > 3 months

CATH: Stenting

EARLY: repair before 3 months

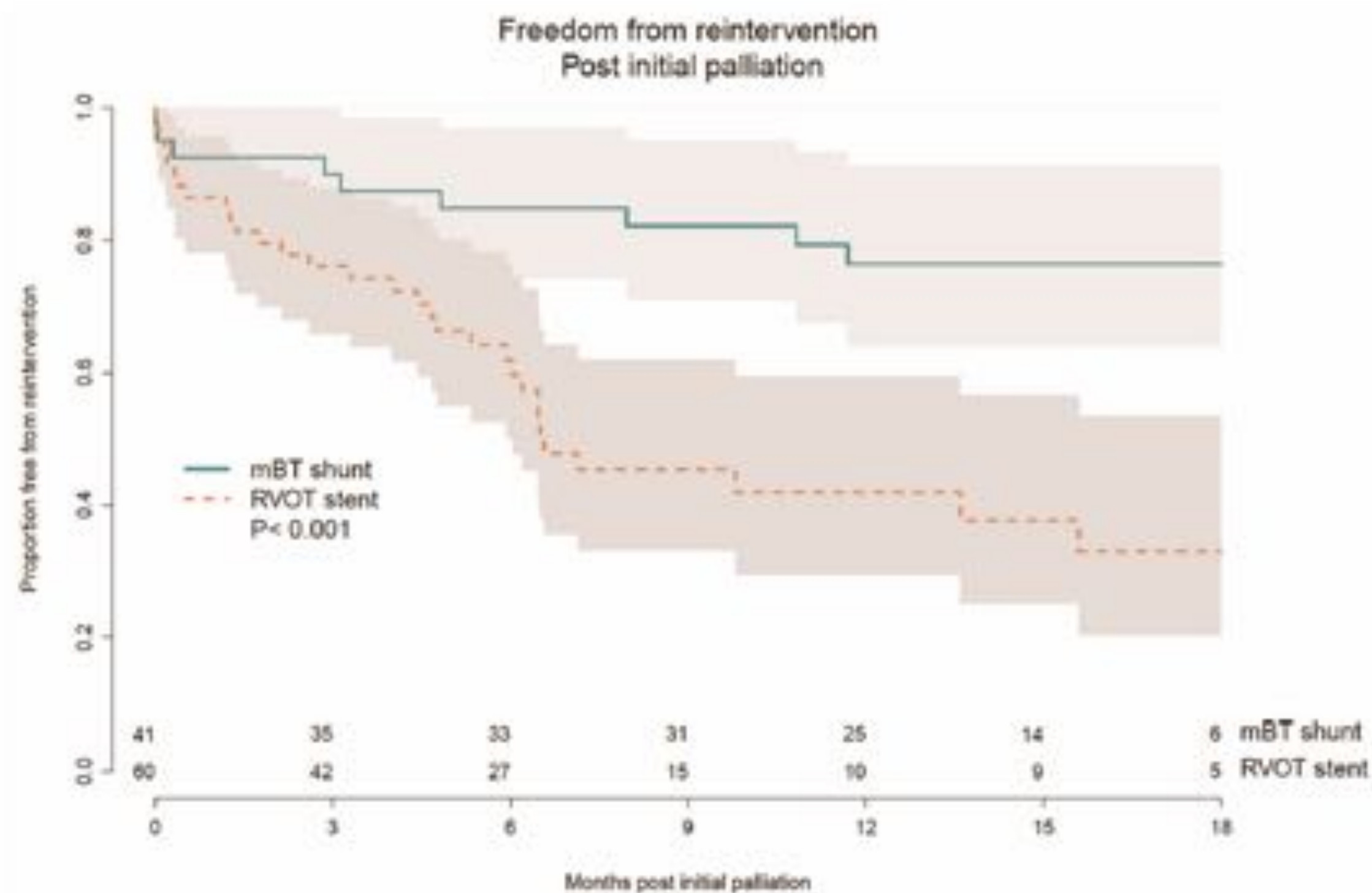
Wilder TJ et al. JTCVS 2017

Sandoval JP et al. Circ Cardiovasc Interv 2016

Initial strategy in symptomatic neonates with ToF

Non elective intervention

Stenting of right ventricle outflow tract vs. BT shunt



- More reinterventions in stent**
- No mortality**
- Severe complications in 4-5%**
- No difference in late survival**
- Reduced ICU LOS**
- Better oxygenation?**
- Better growth of PA branches**

Quandt D et al. J Am Coll Cardiol Interv 2017;10:1774–84)
Quandt D et al. Heart 2017;103:1985–1991

Initial strategy in symptomatic neonates with ToF

Non elective intervention

Non elective primary repair vs. shunt in infants < 3 months

BT patients were significantly younger (14 vs 25 days, $P < .0001$), had a higher incidence of extracardiac congenital abnormalities (41% vs 33%, $P .02$), had a higher rate of prematurity (17% vs 12%, $P .04$), and more frequently received PGE1

No difference in mortality between the two techniques

Irrespective of the surgical approach, younger patients (OR 1.03, $P .007$), patients with noncardiac congenital anomalies (OR 2.48, $P .016$), and those with prematurity (OR 3.28, $P .007$) had a higher risk of mortality.

Initial strategy in **Asymptomatic** neonates with ToF

Elective neonatal repair

Metanalysis

3858 patients in 8 studies with 724 (19%) having undergone neonatal repair (6-20 days) and 3134 (81%) having undergone non-neonatal repair (60-220 days).



Strategy in Asymptomatic infants > 3 months with ToF

Elective repair

Elective repair 6 kgs/3 months

1-Patients characteristics

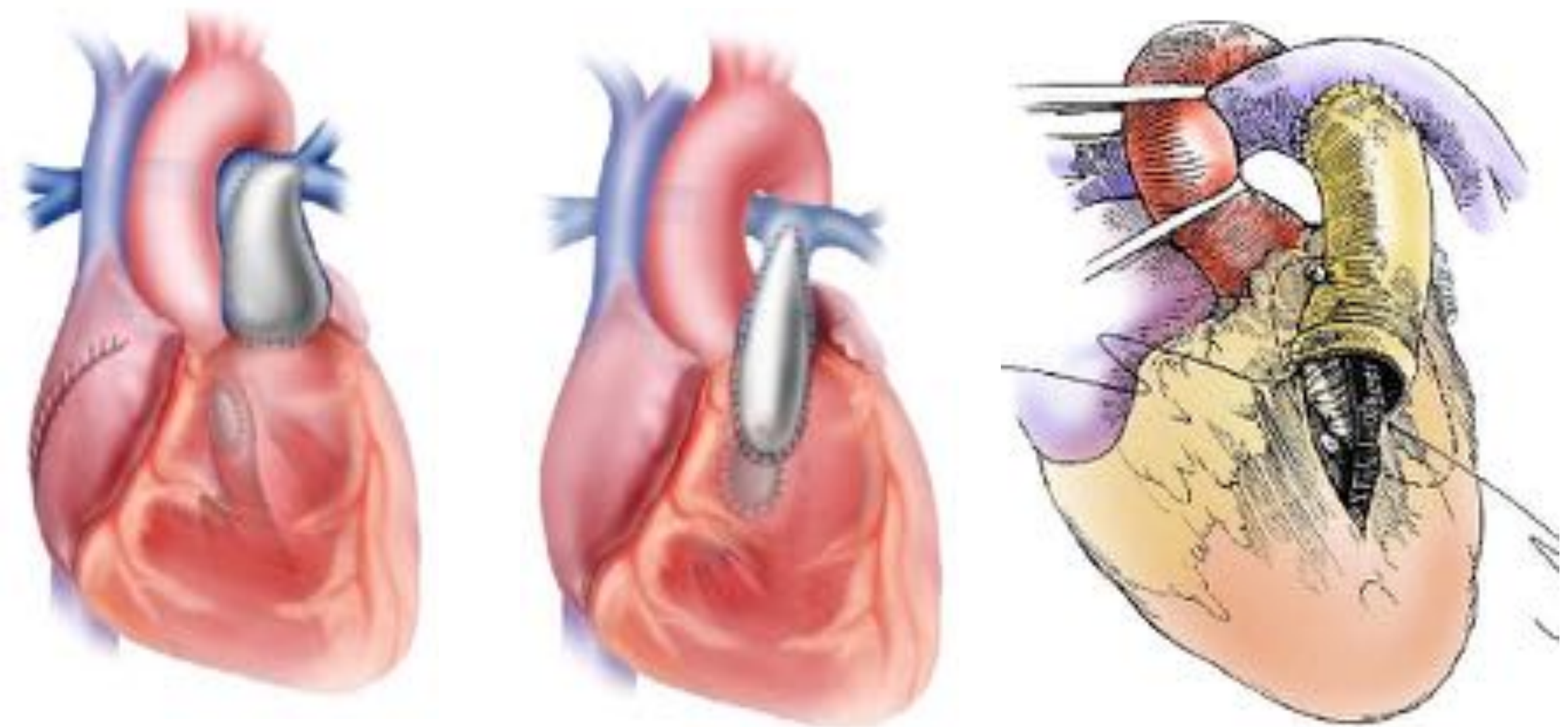
- acceptable sized pulmonary arteries
- pulmonary valve ?
- coronary artery epicardial course ?
- multiple VSD ?

2-Strategy

- limit late complications

3-Alternative techniques

- None



Outcomes ToF

Parisian experience (07-17): 923 ToF (PA-VSD excluded)



46%



Risk factors for reintervention (surgical or cath) after repair

Initial staged strategy

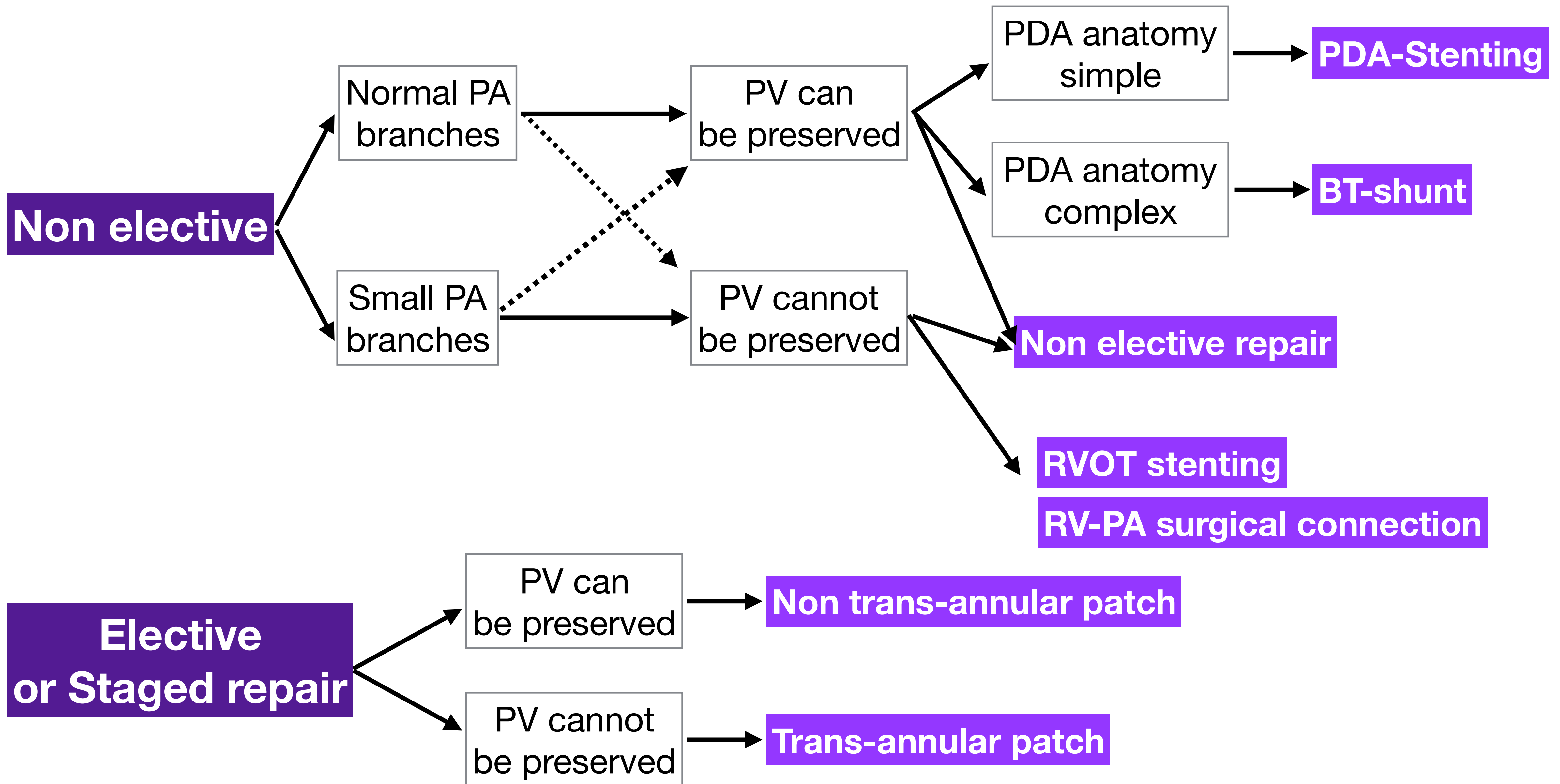
Trans-annular patch and conduit

Pulmonary branch stenosis

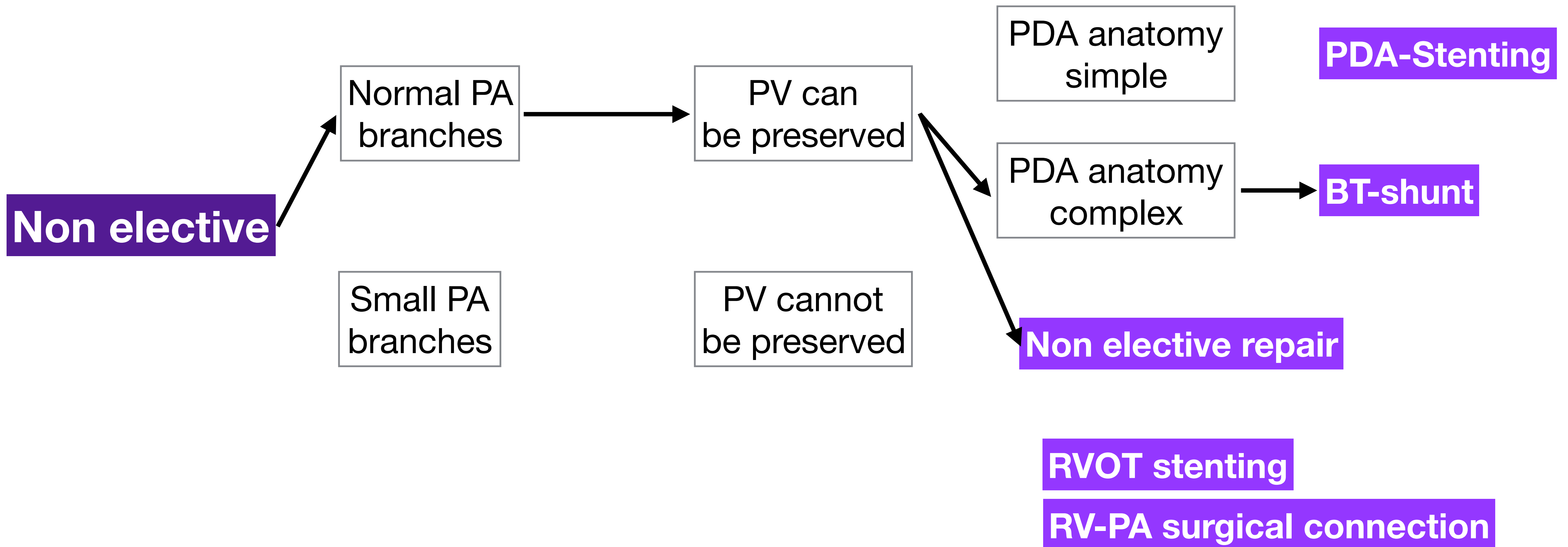
001

atch
lar patch

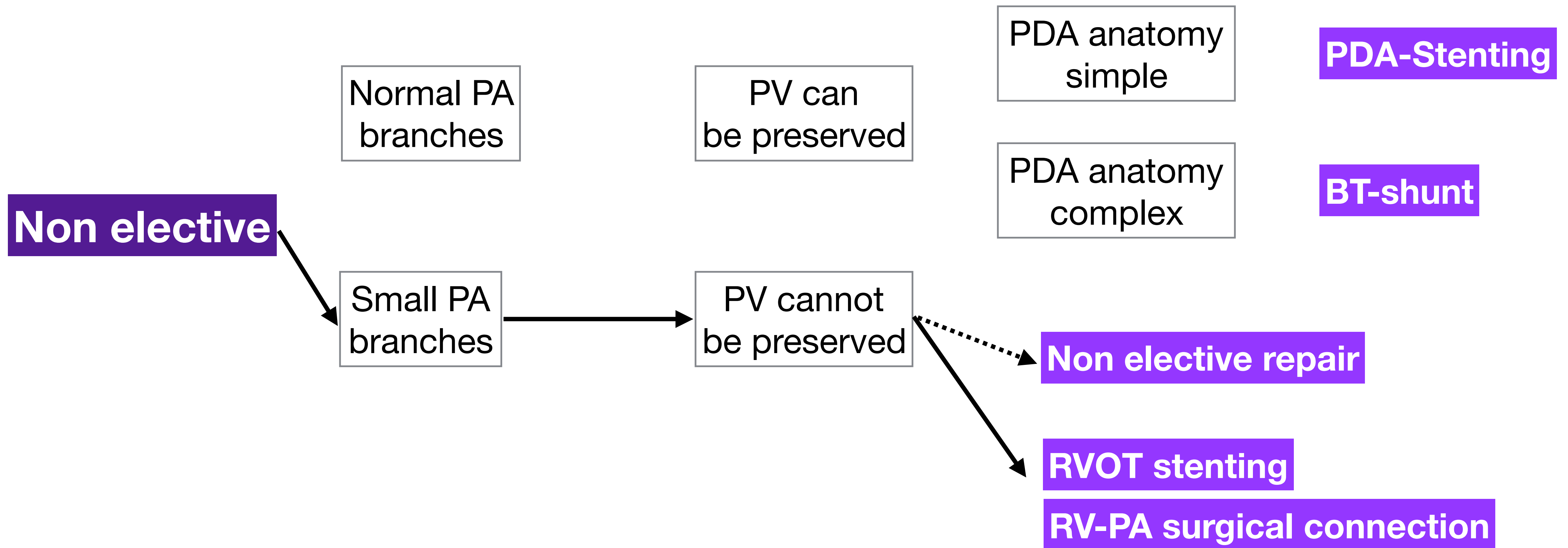
Can we have an algorithm in simple ToF ?



Can we have an algorithm in simple ToF ?

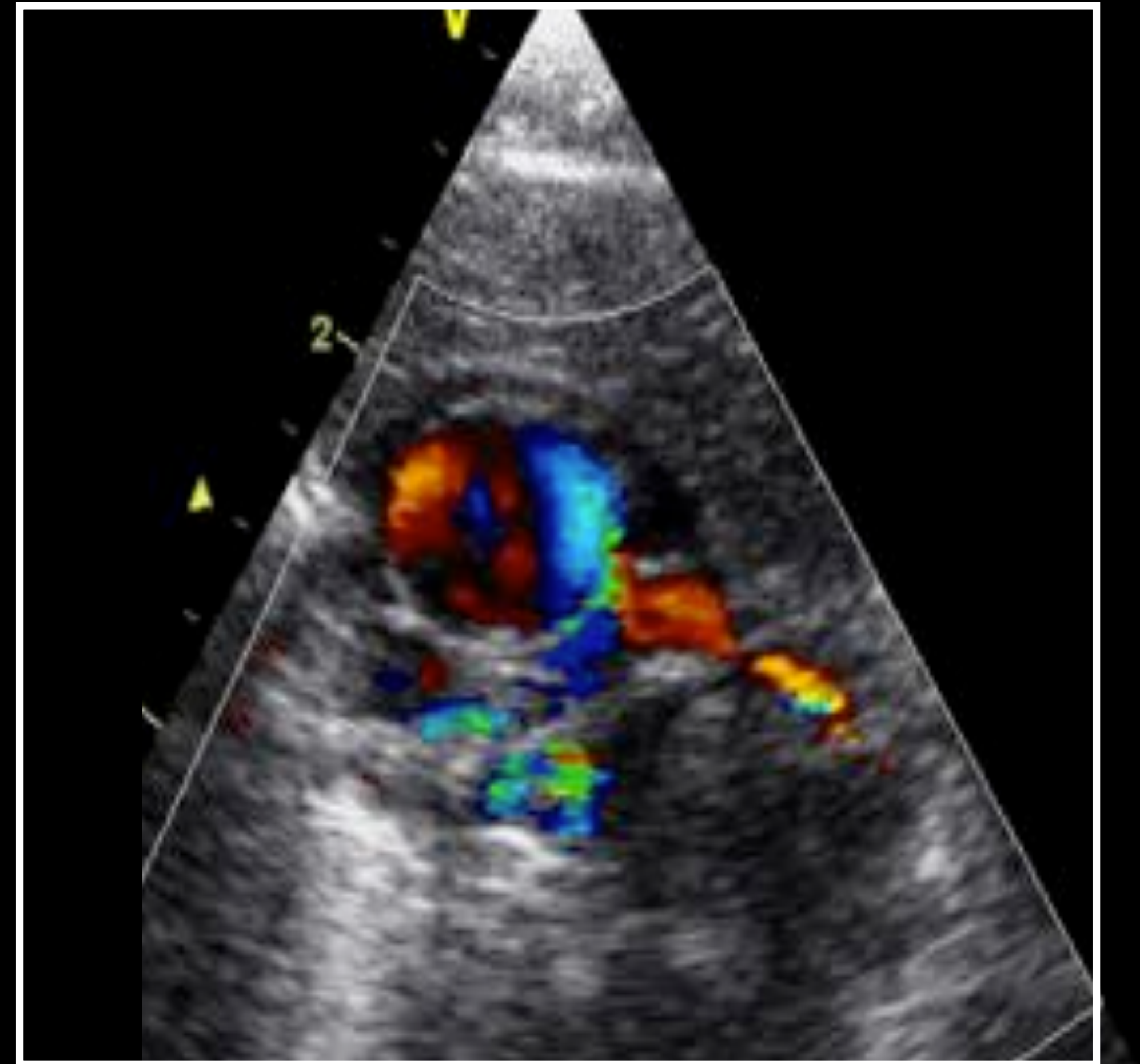
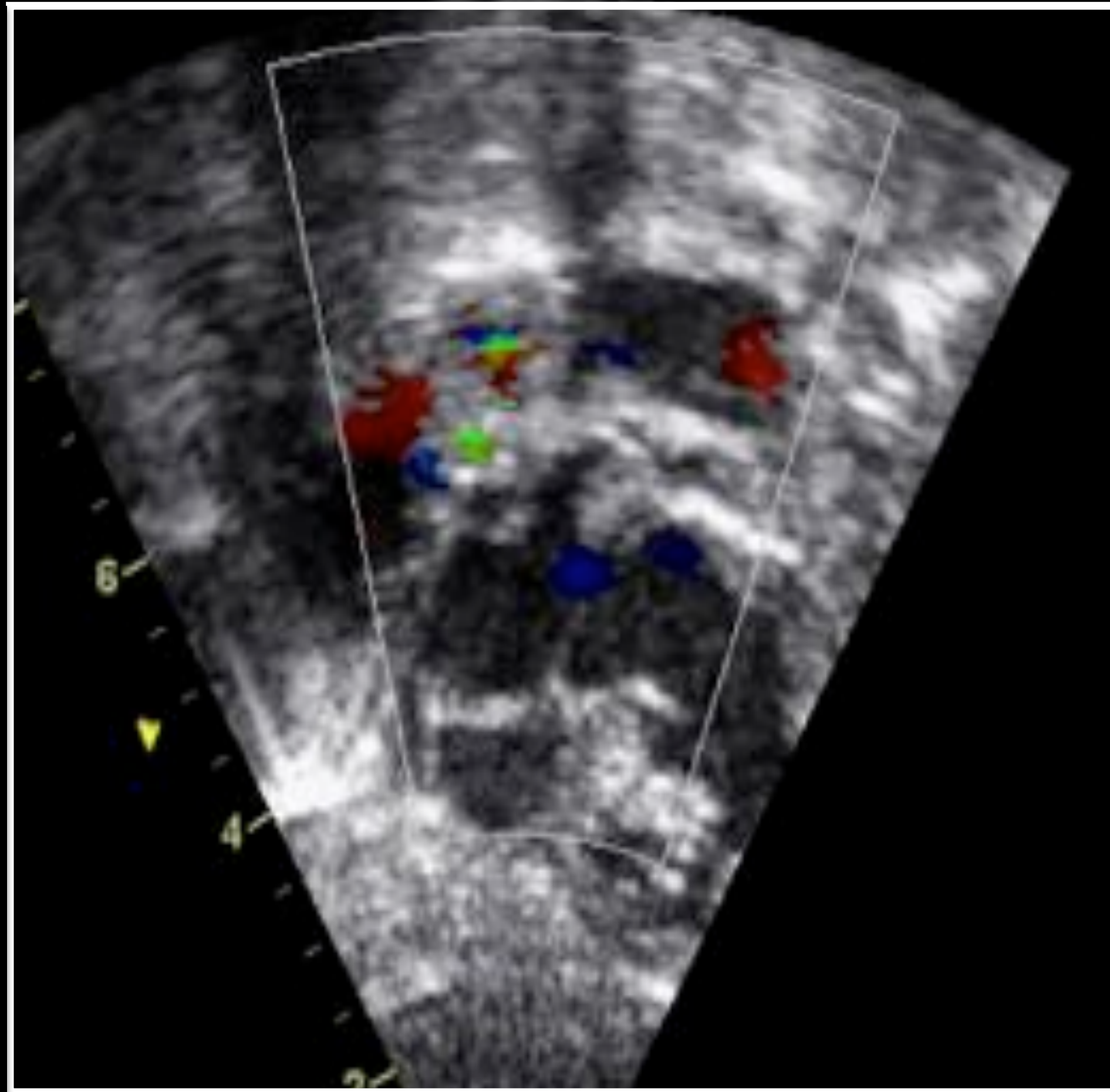


Can we have an algorithm in simple ToF ?

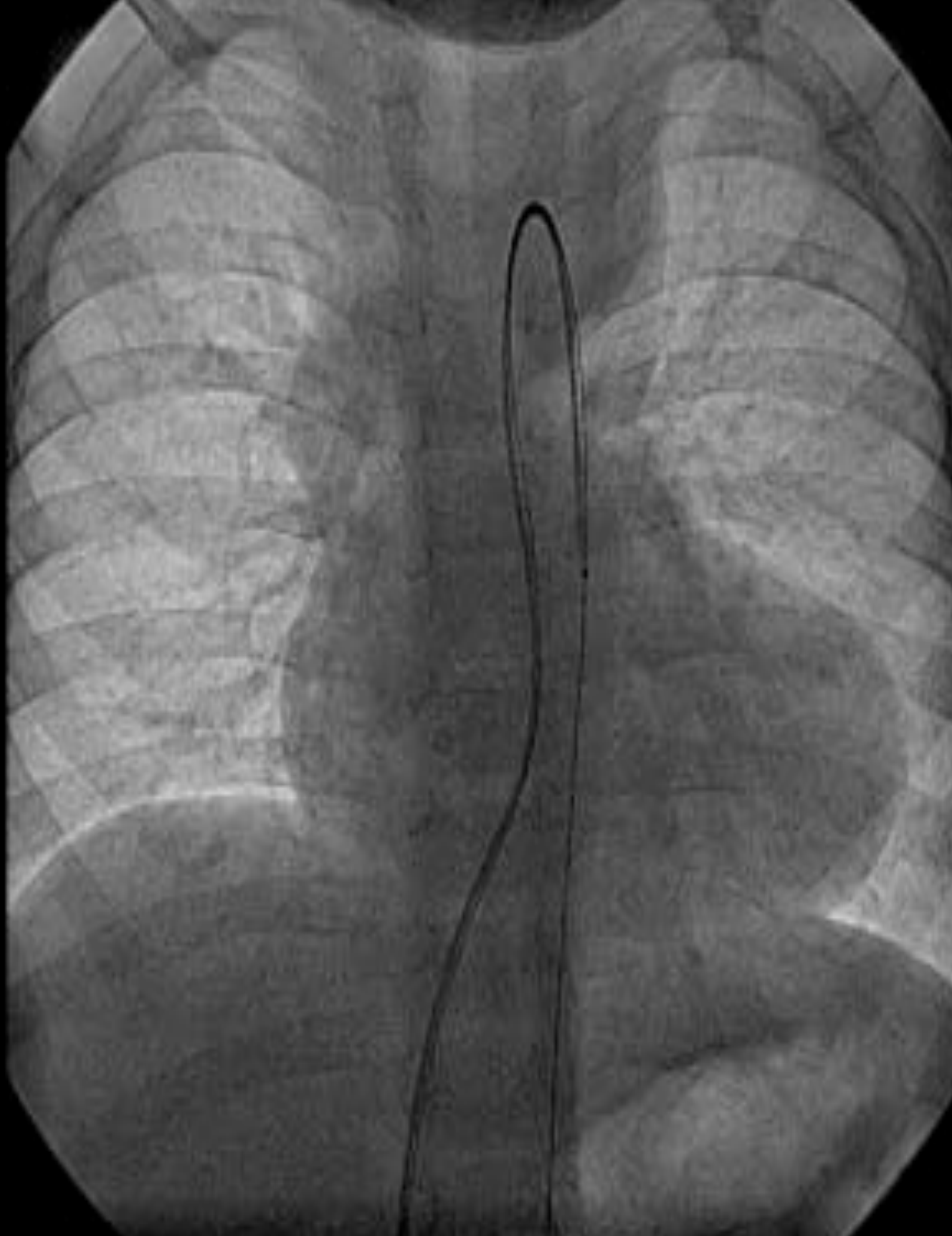


Tetralogy of Fallot with pulmonary atresia
or
Pulmonary atresia with VSD

MAPCAs in ToF-PA



MAPCAs in ToF-PA

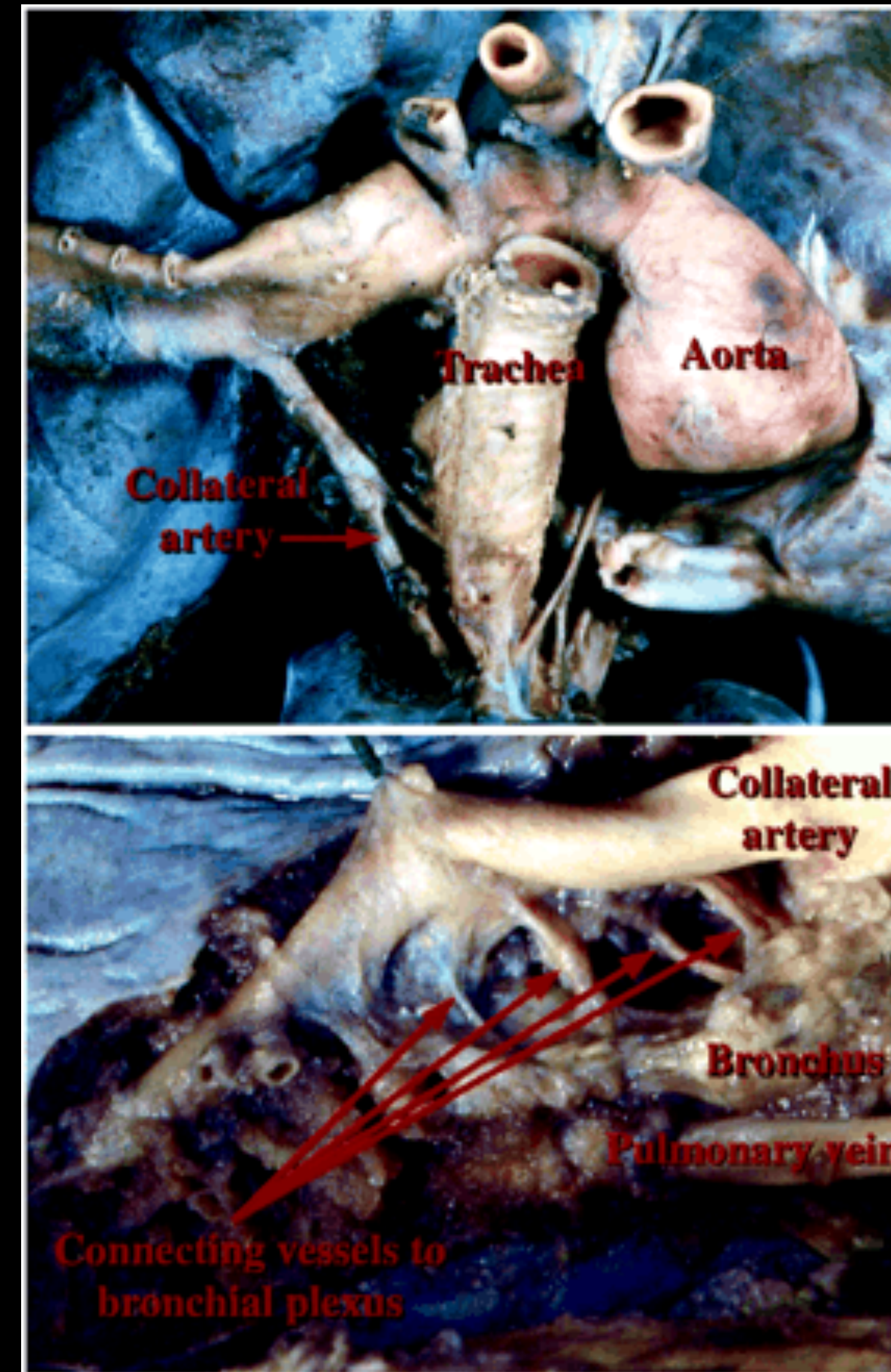


Left main coronary to pulmonary artery fistula in ToF-PA

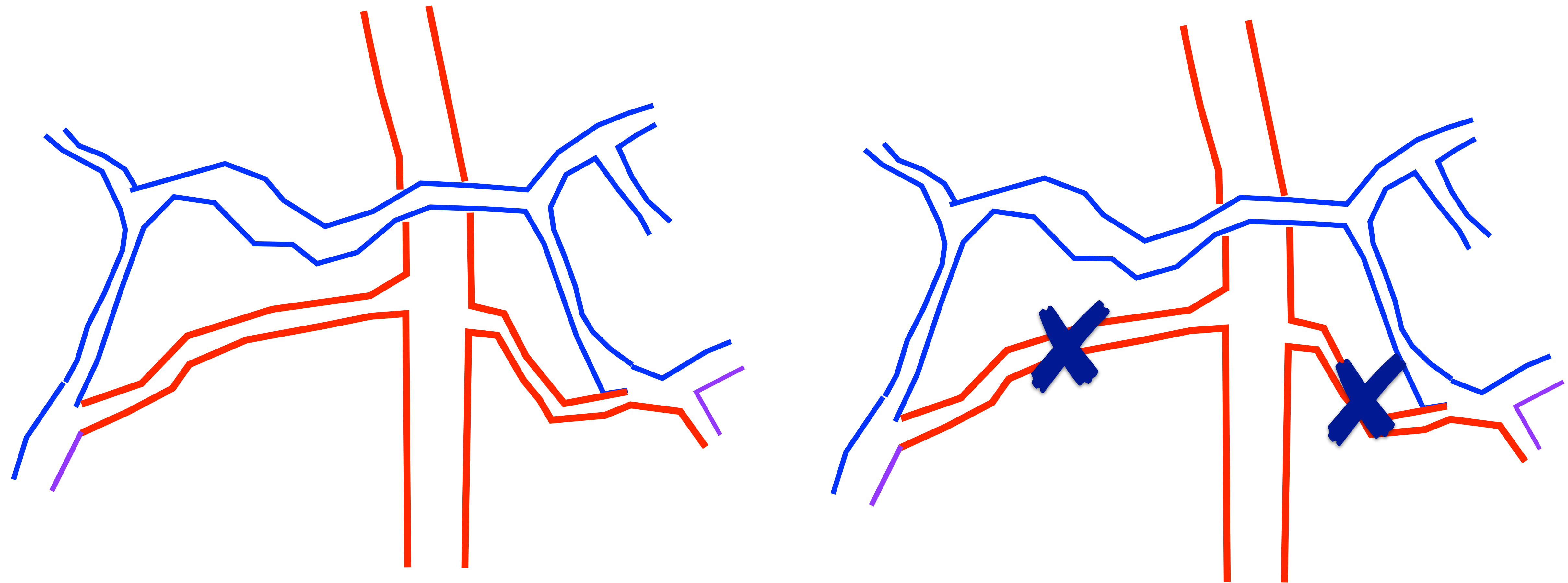


MAPCAs in ToF-PA

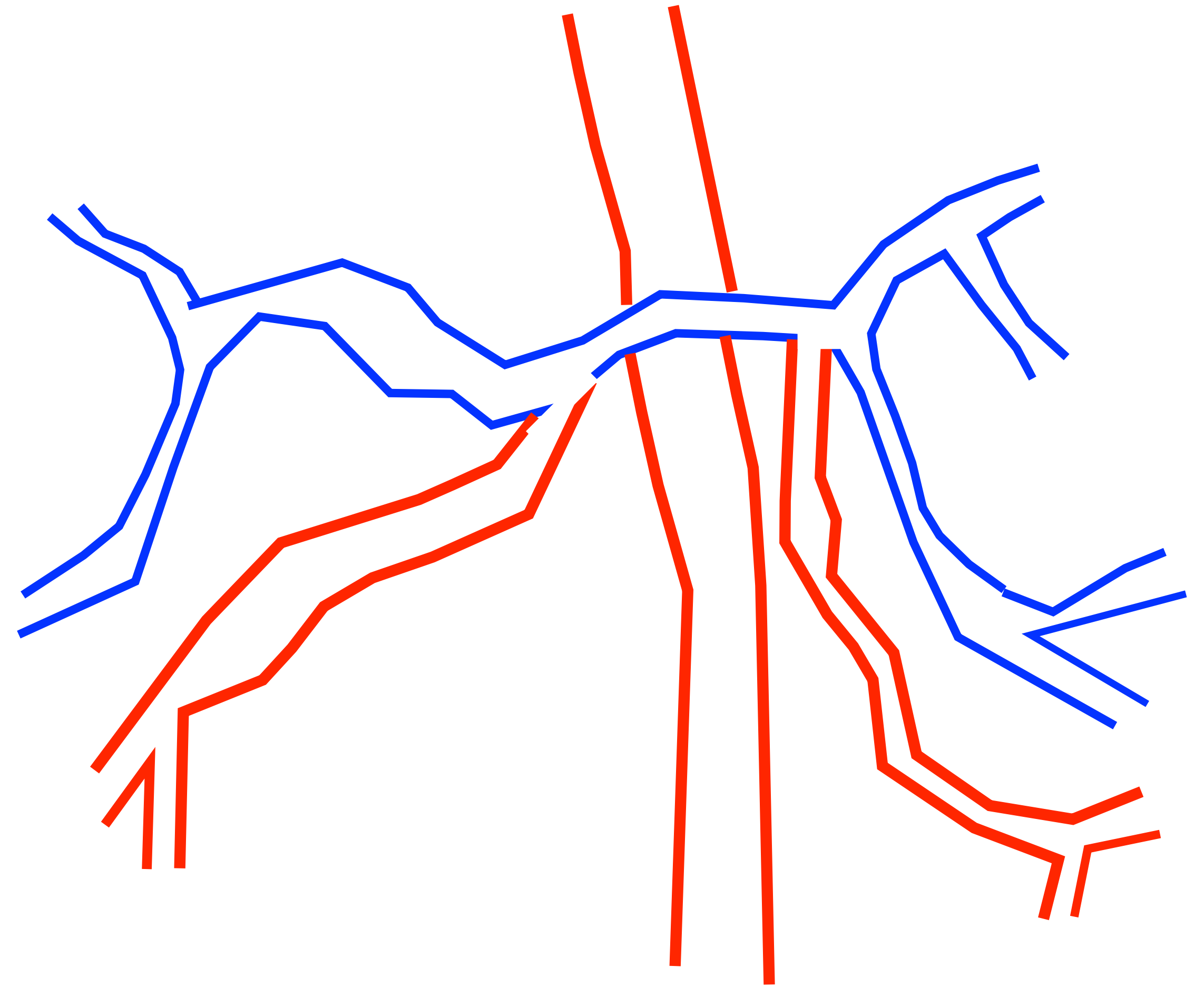
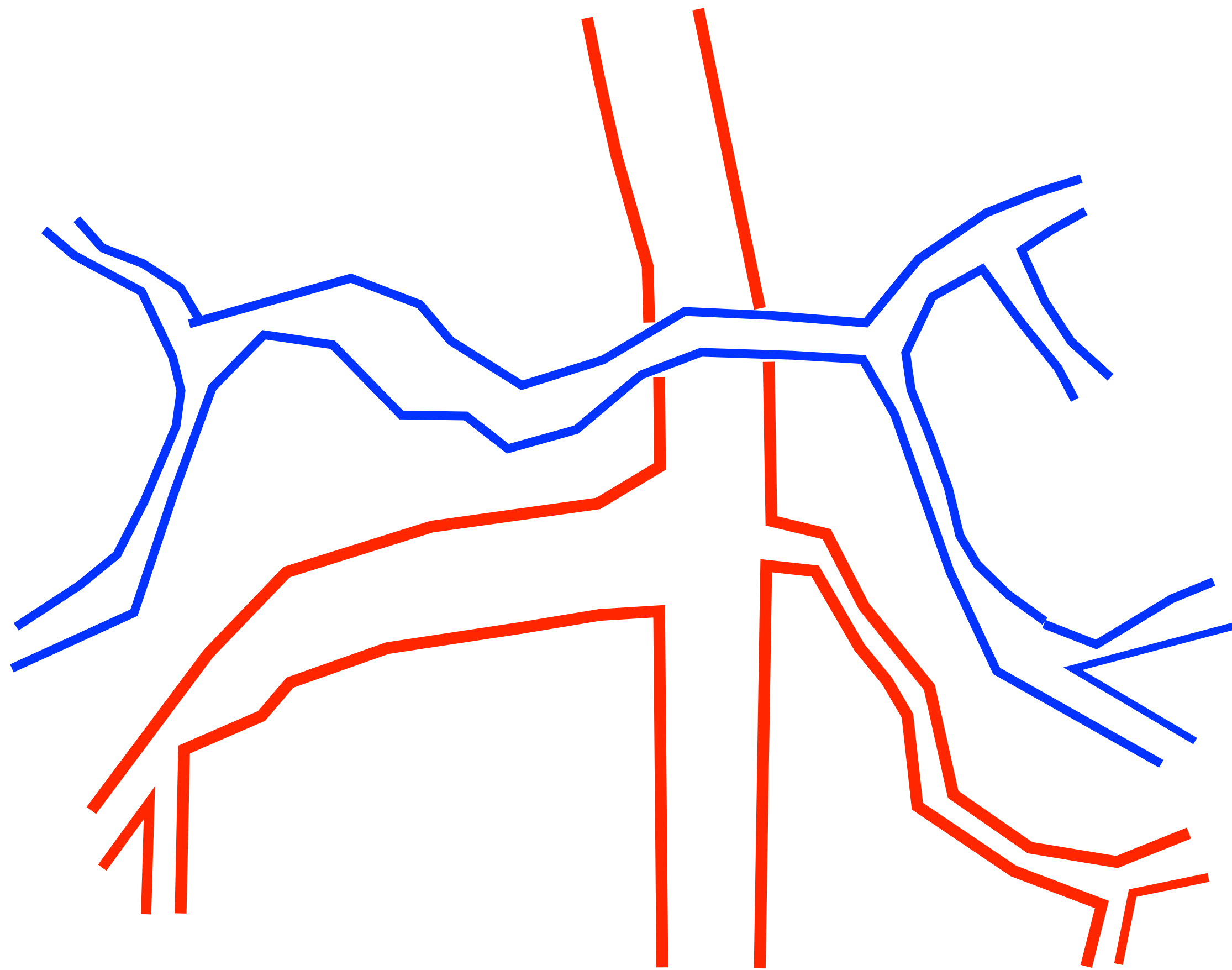
Vicinity with bronchi



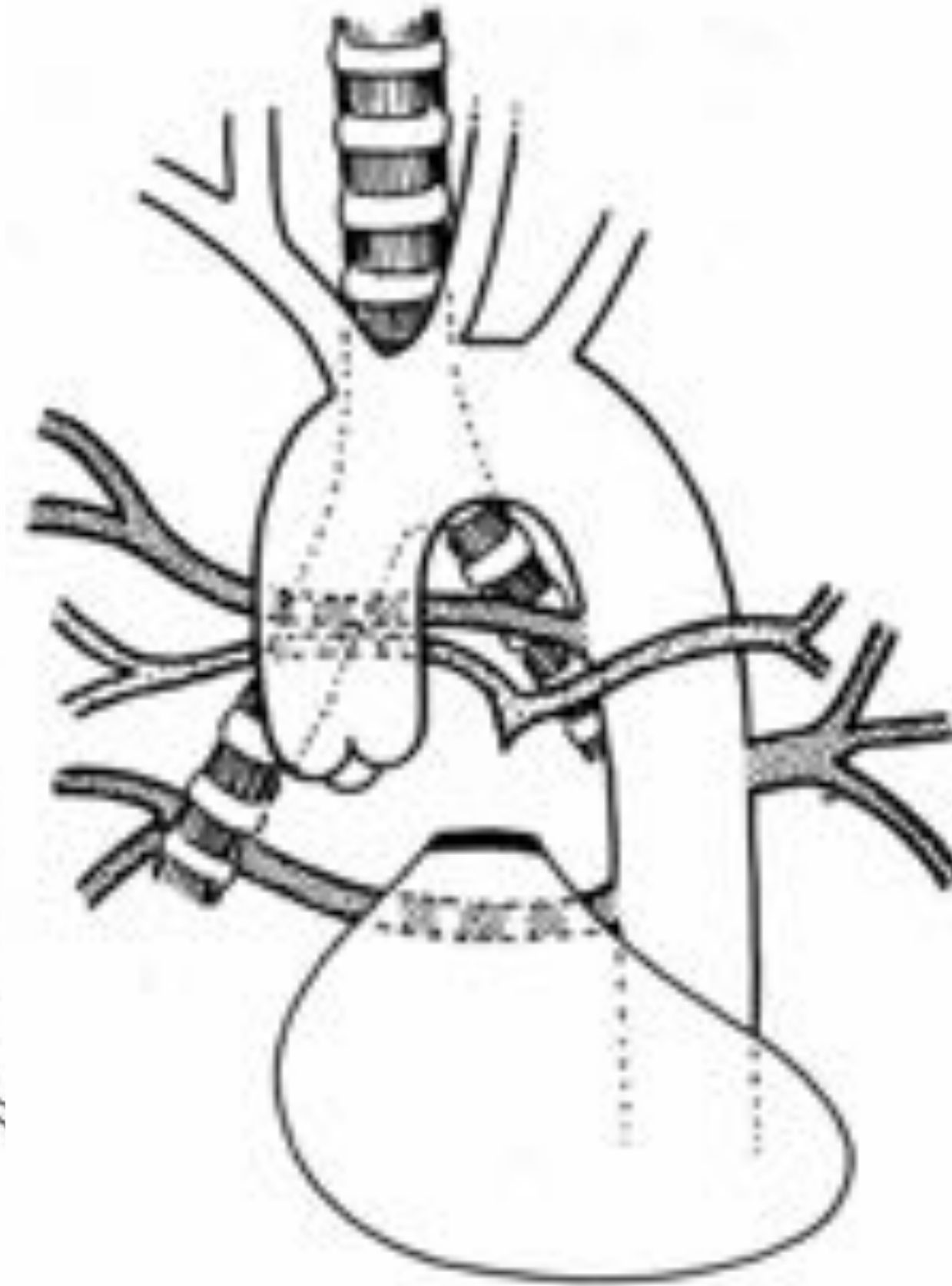
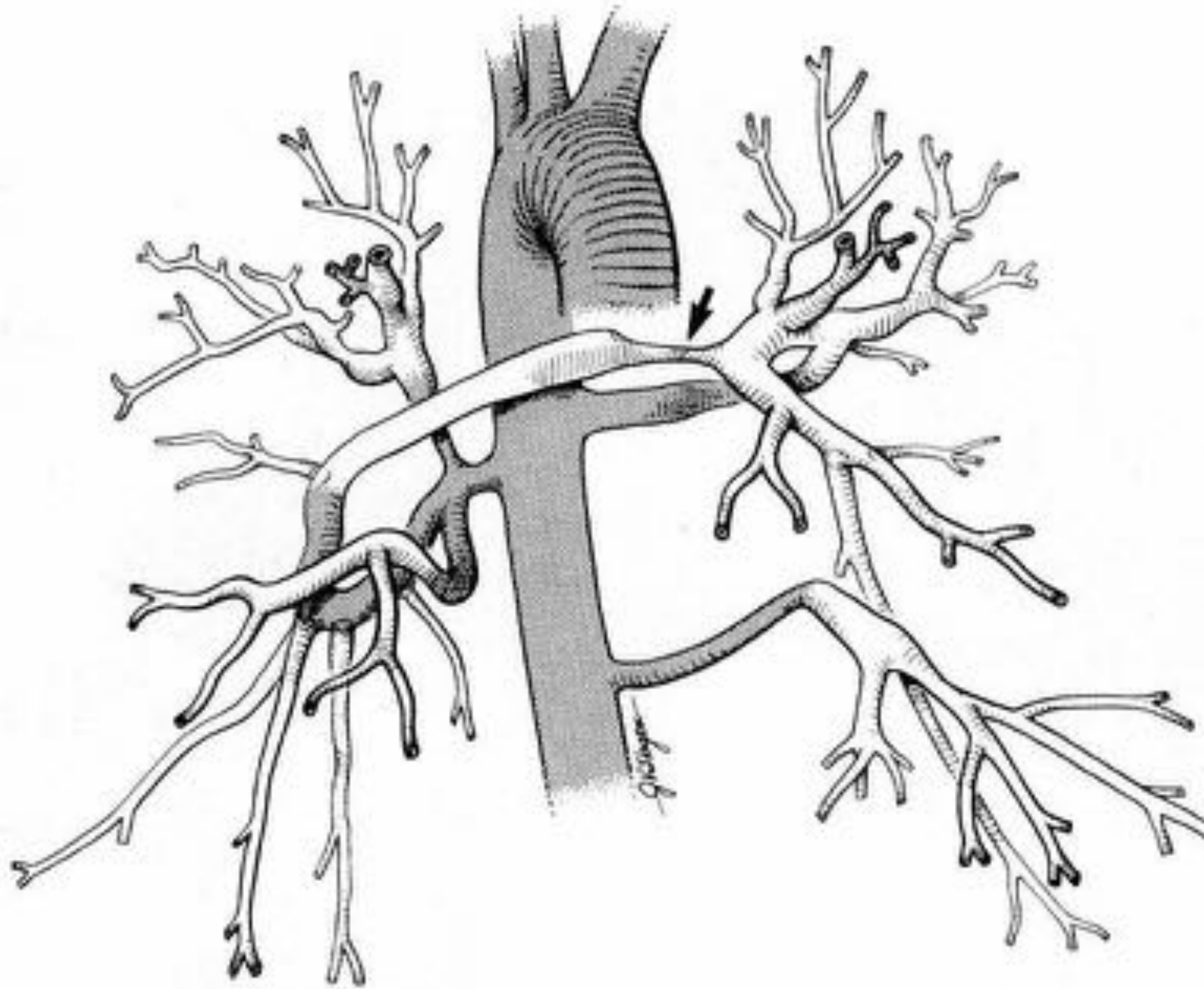
MAPCAs with or without communication with the pulmonary arteries



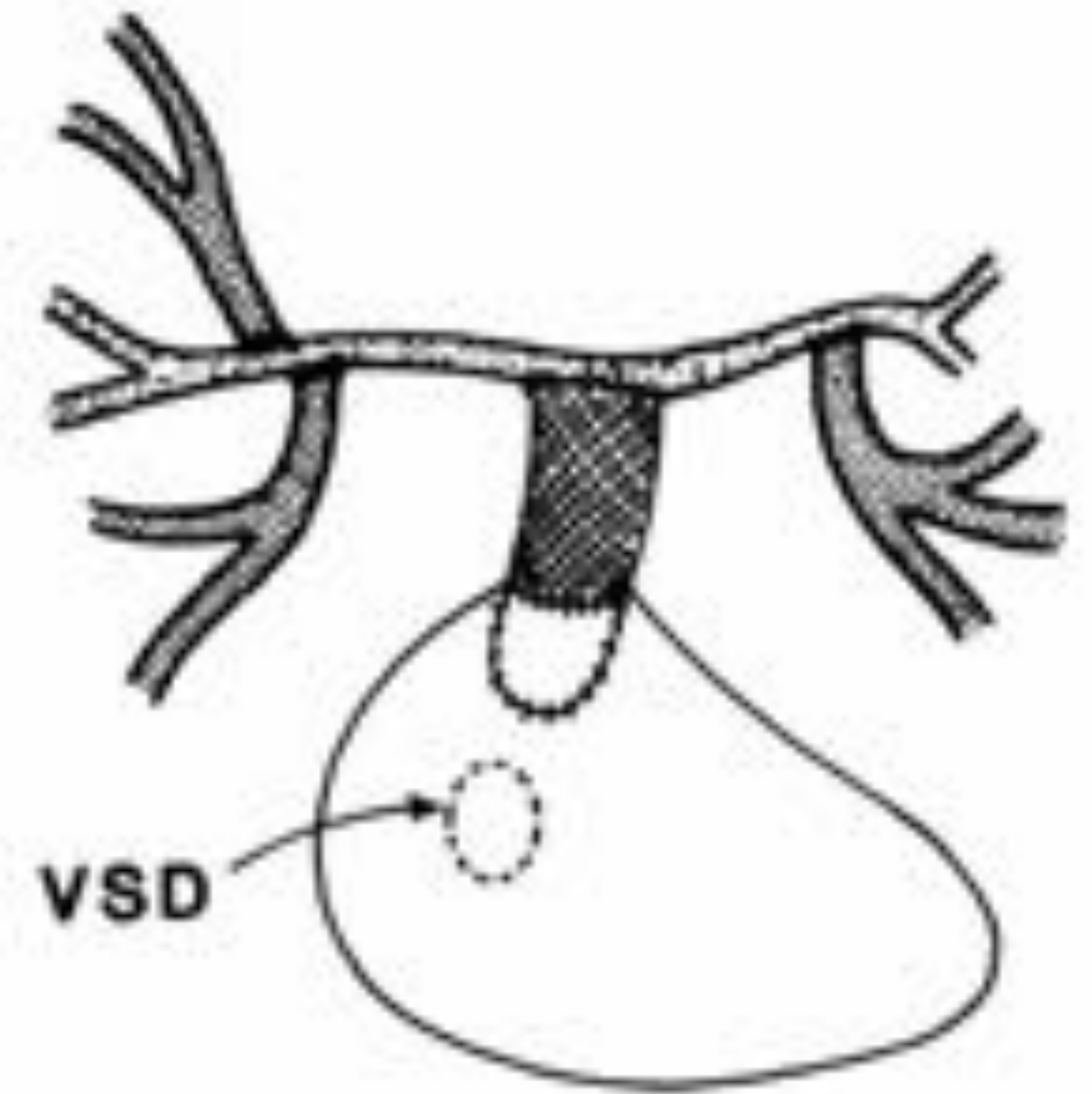
MAPCAs with or without communication with the pulmonary arteries



Unifocalisation



TOF/PA, MAPC
(PAi 50 mm²/M²)



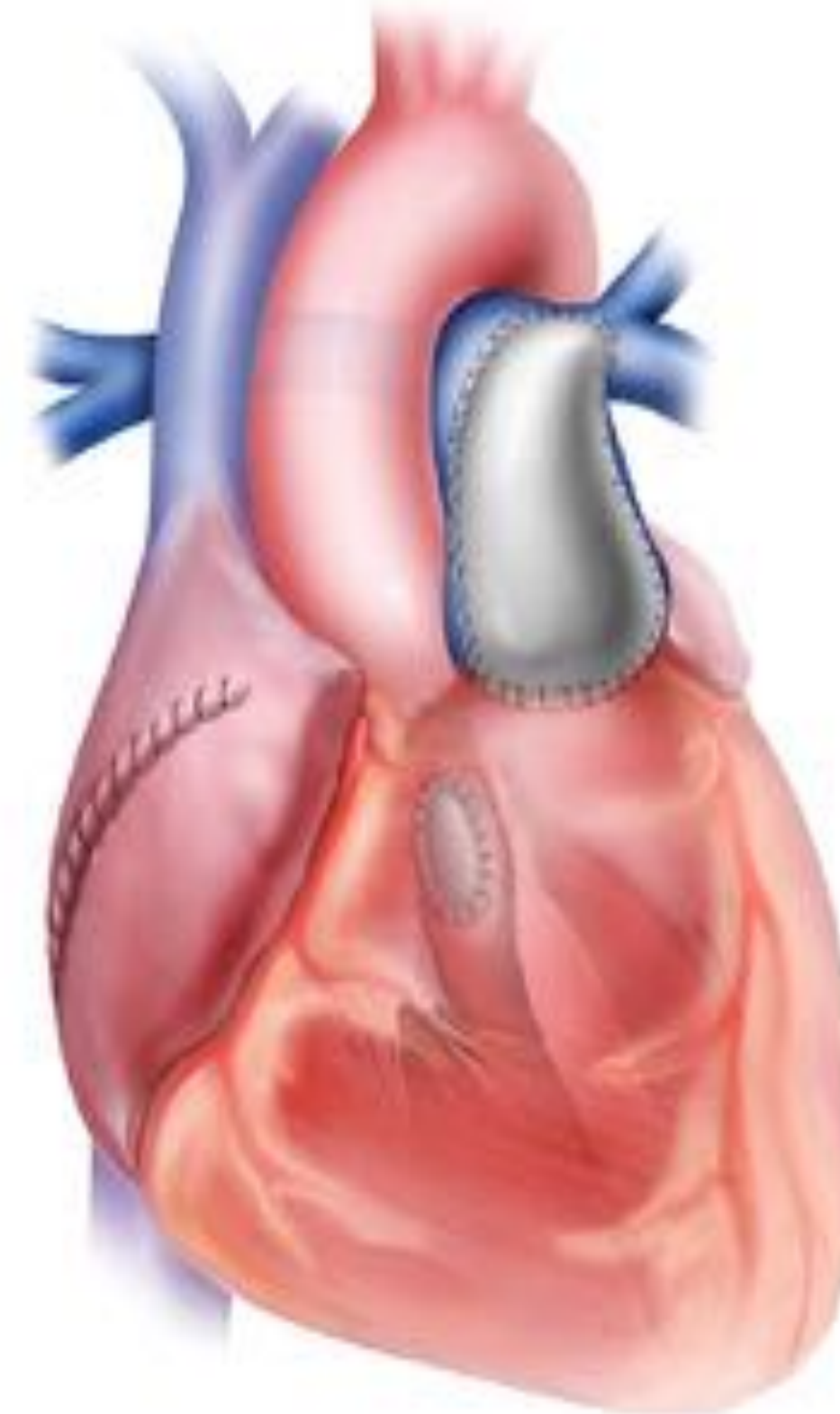
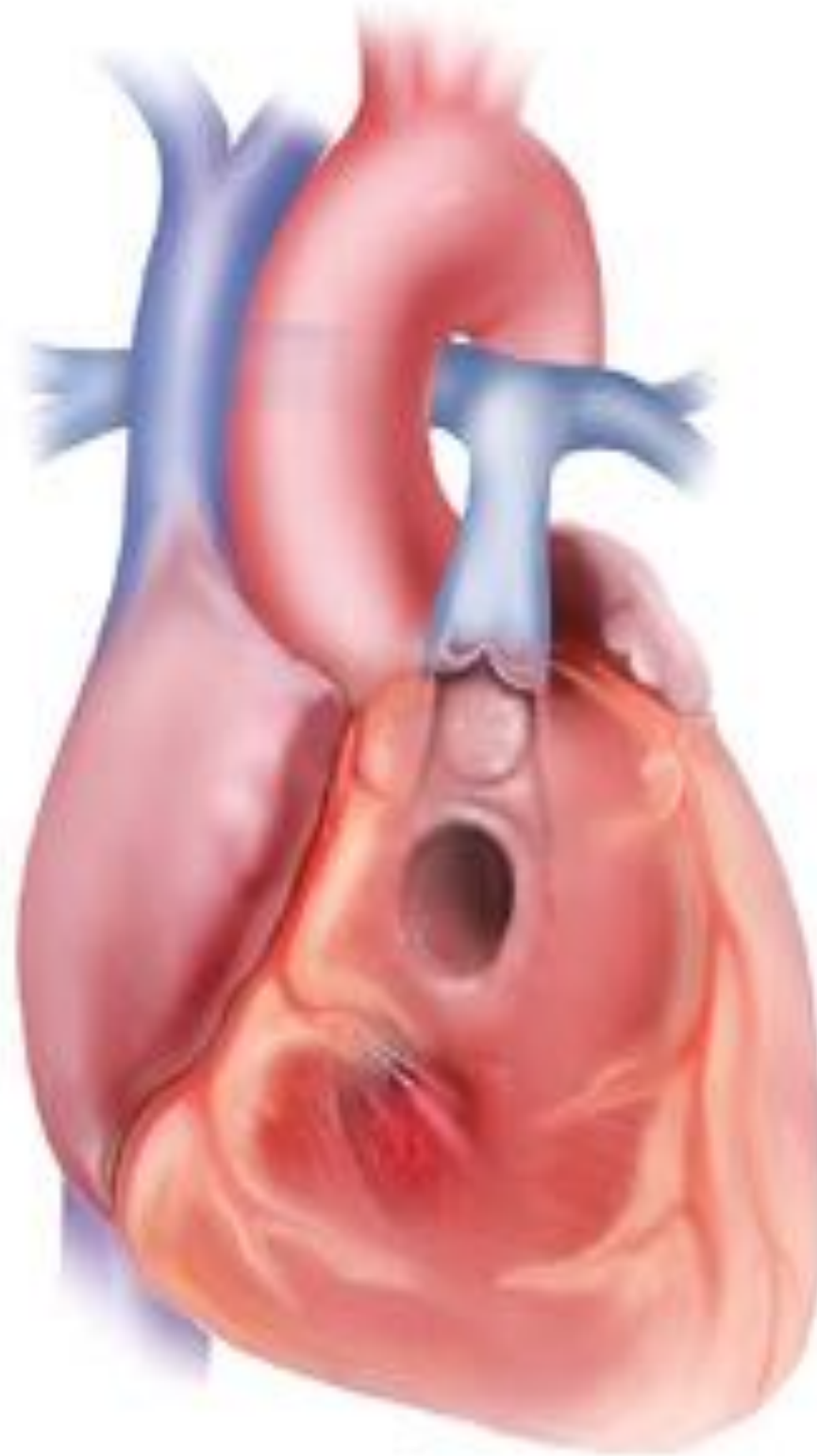
RV-PA homograft
and bilateral
unifocalization

Strategy for repair

What are the main issues ?

- Neonatal repair should not be performed
 - closure of VSD is difficult
 - pulmonary arteries size and PVR do not allow repair without conduit
- Repair with closure of the VSD in children > 6 kgs
 - If closure of VSD is possible : multiple VSD
 - Without conduit : coronary artery anatomy
 - Without valve : size/stenosis of pulmonary artery branches

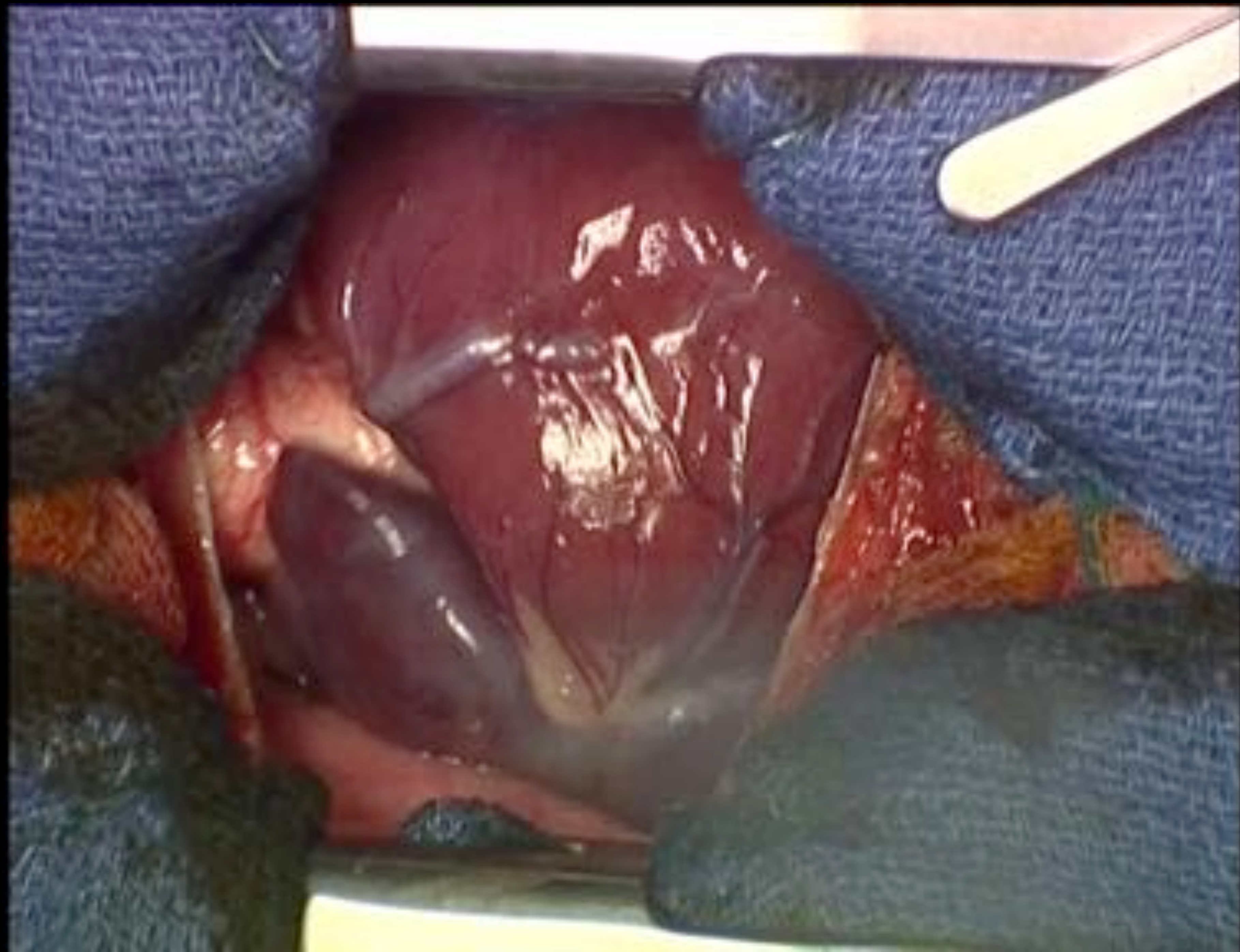
Surgical repair of tetralogy of Fallot

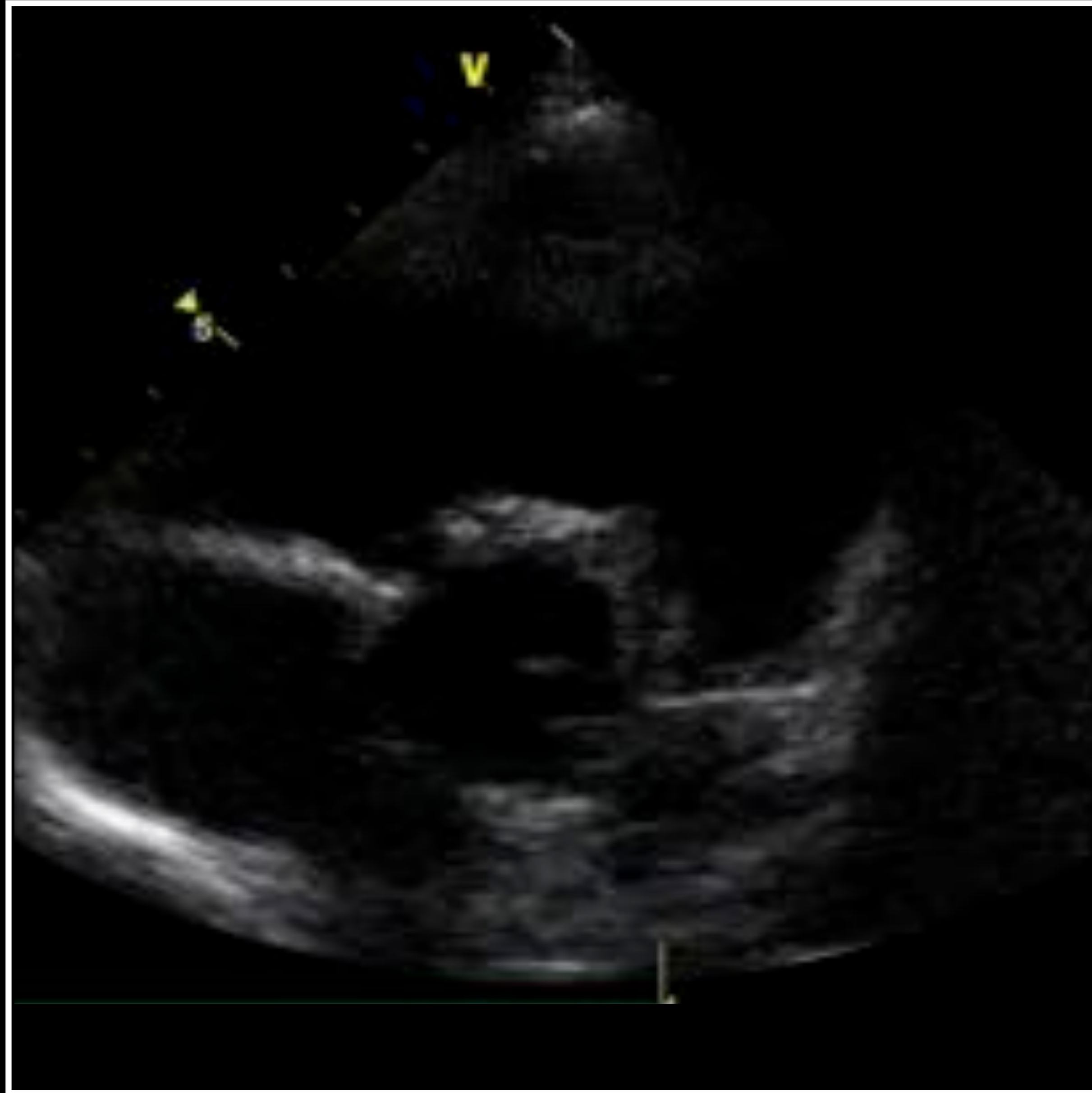


Atrial route



Trans-annular patch



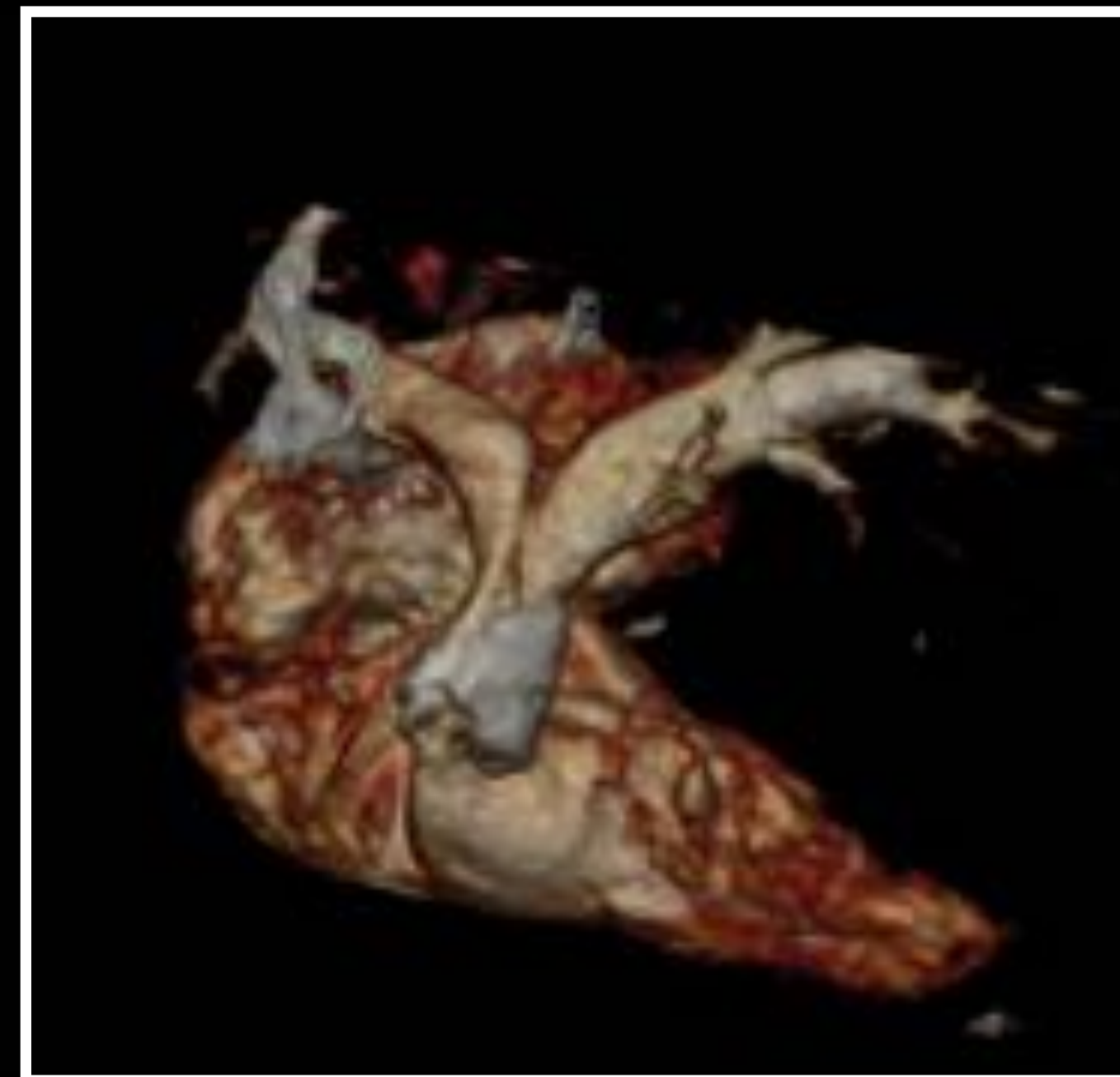
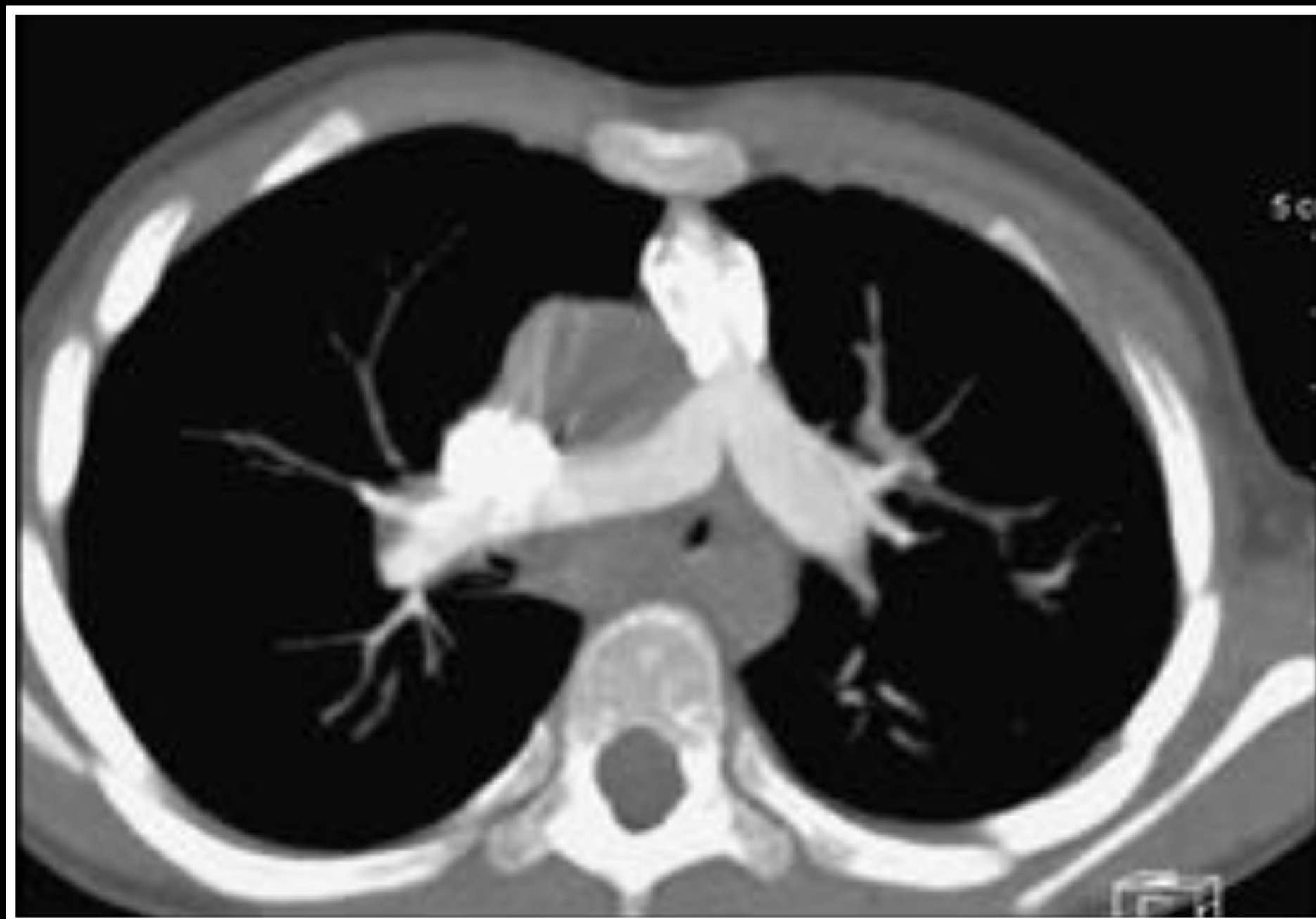


Fallot after repair with preserved annulus

Late outcome

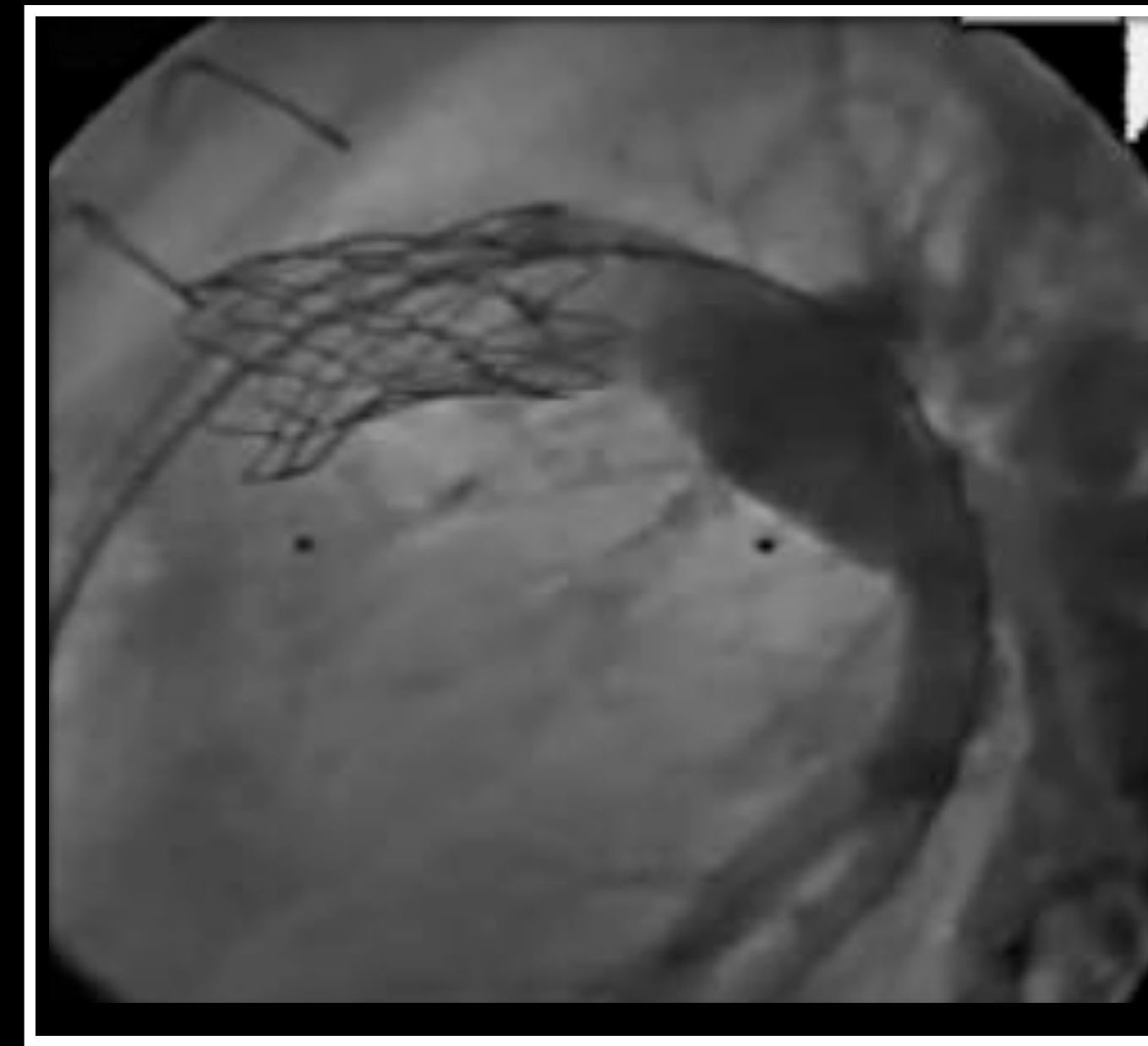
What are the issues ?

- **Right outflow tract obstructions**
- **Pulmonary branches stenoses**
- **Chronic pulmonary regurgitation**
- **Ventricular tachycardia, other arrhythmias and sudden death**

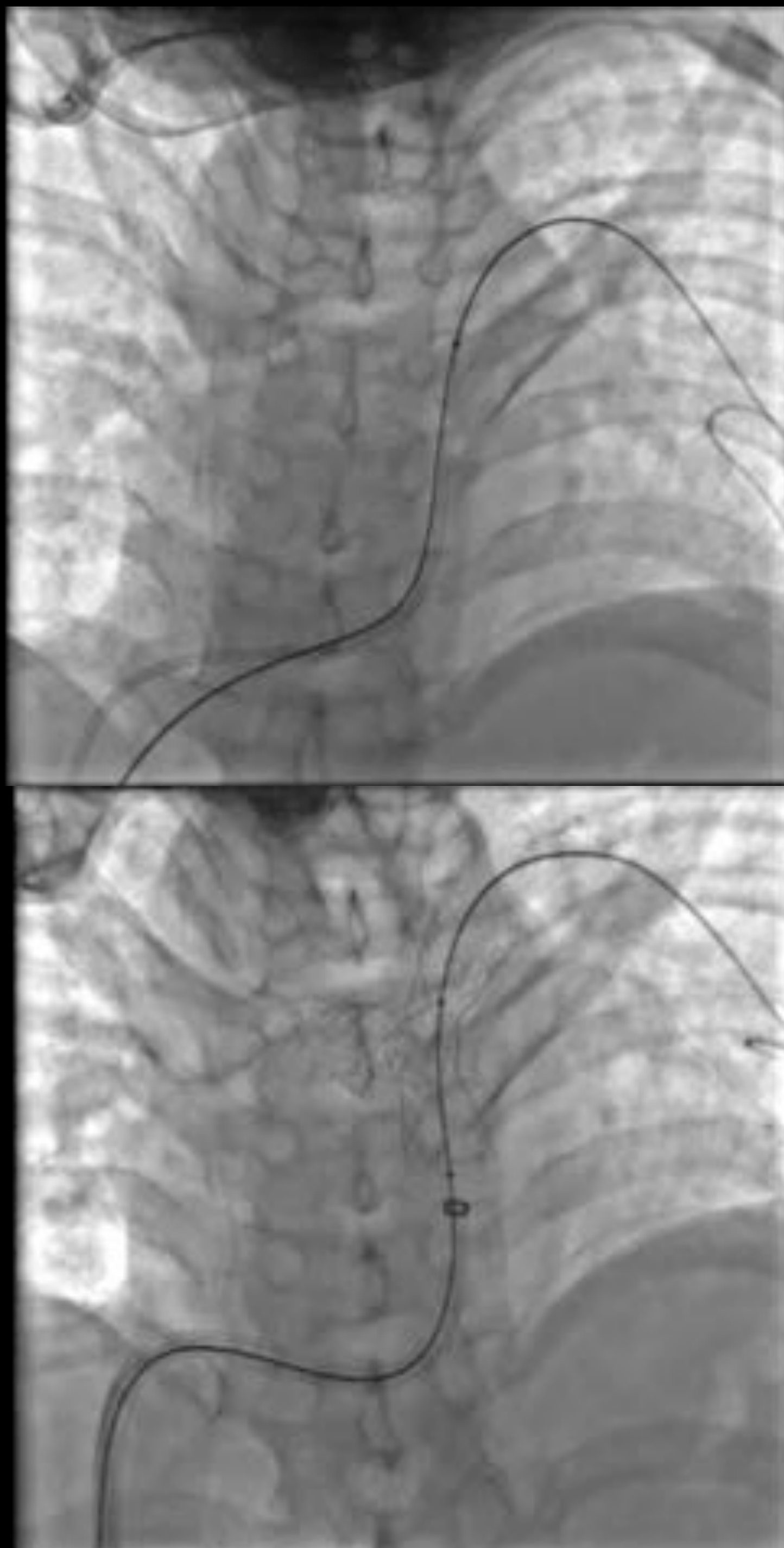


**Calcification of RVOT
Dysfunctioning RVOT**

Stenting of the RVOT



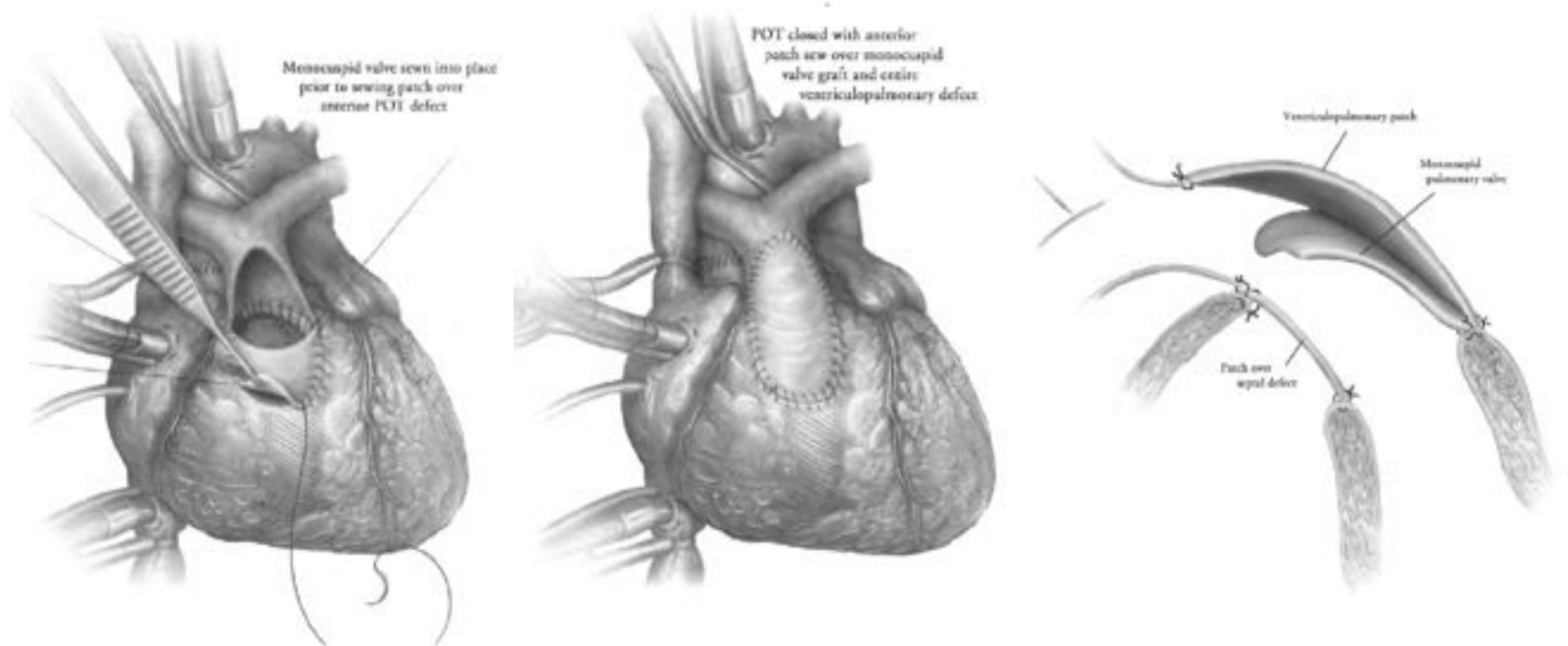
Stenting of pulmonary artery bifurcation



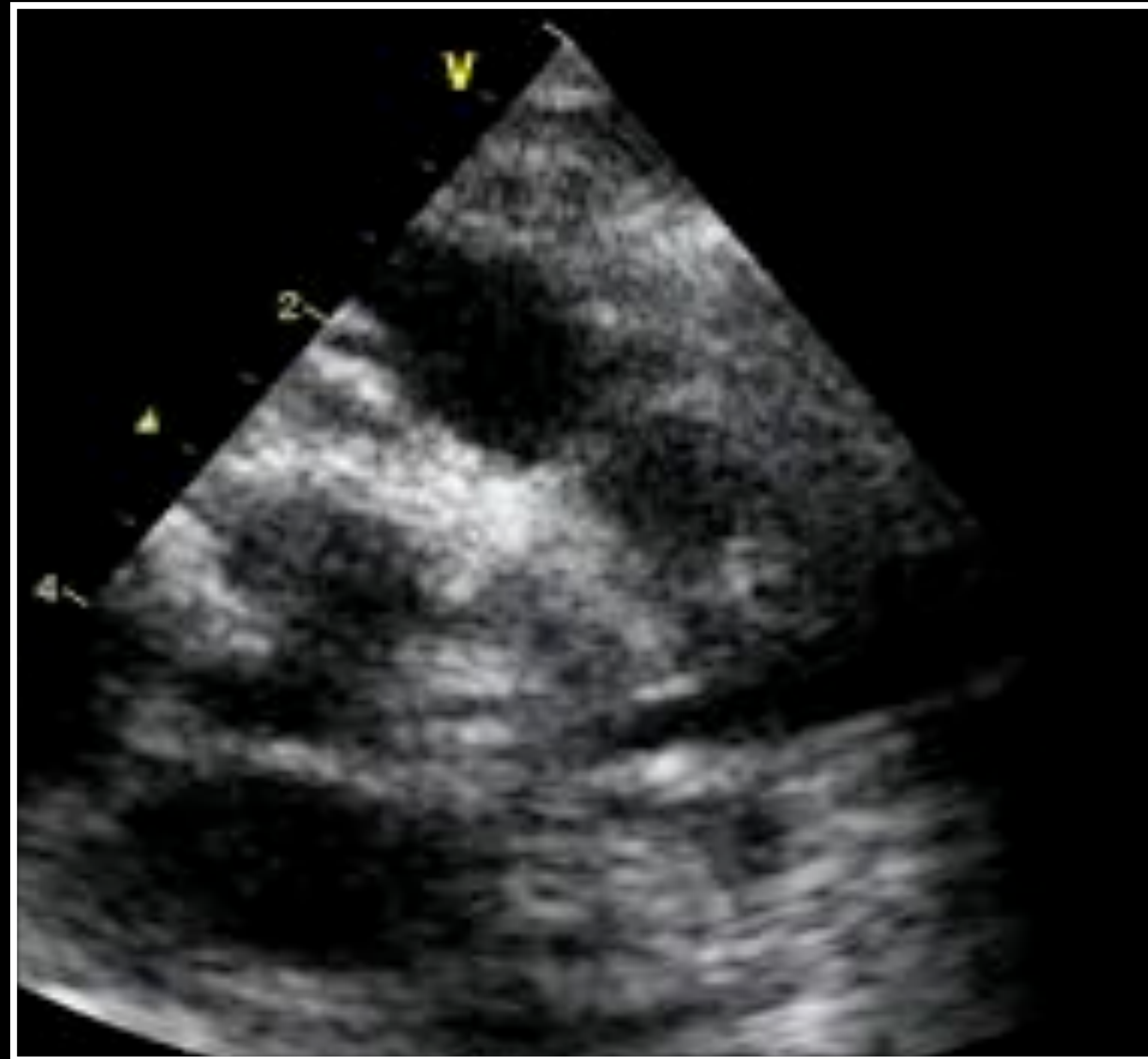
RVOT conduits



Monocusp in tetralogy of Fallot



Monocusp in ToF



Pulmonary homograft



Contegra - Venpro conduit





Labcor

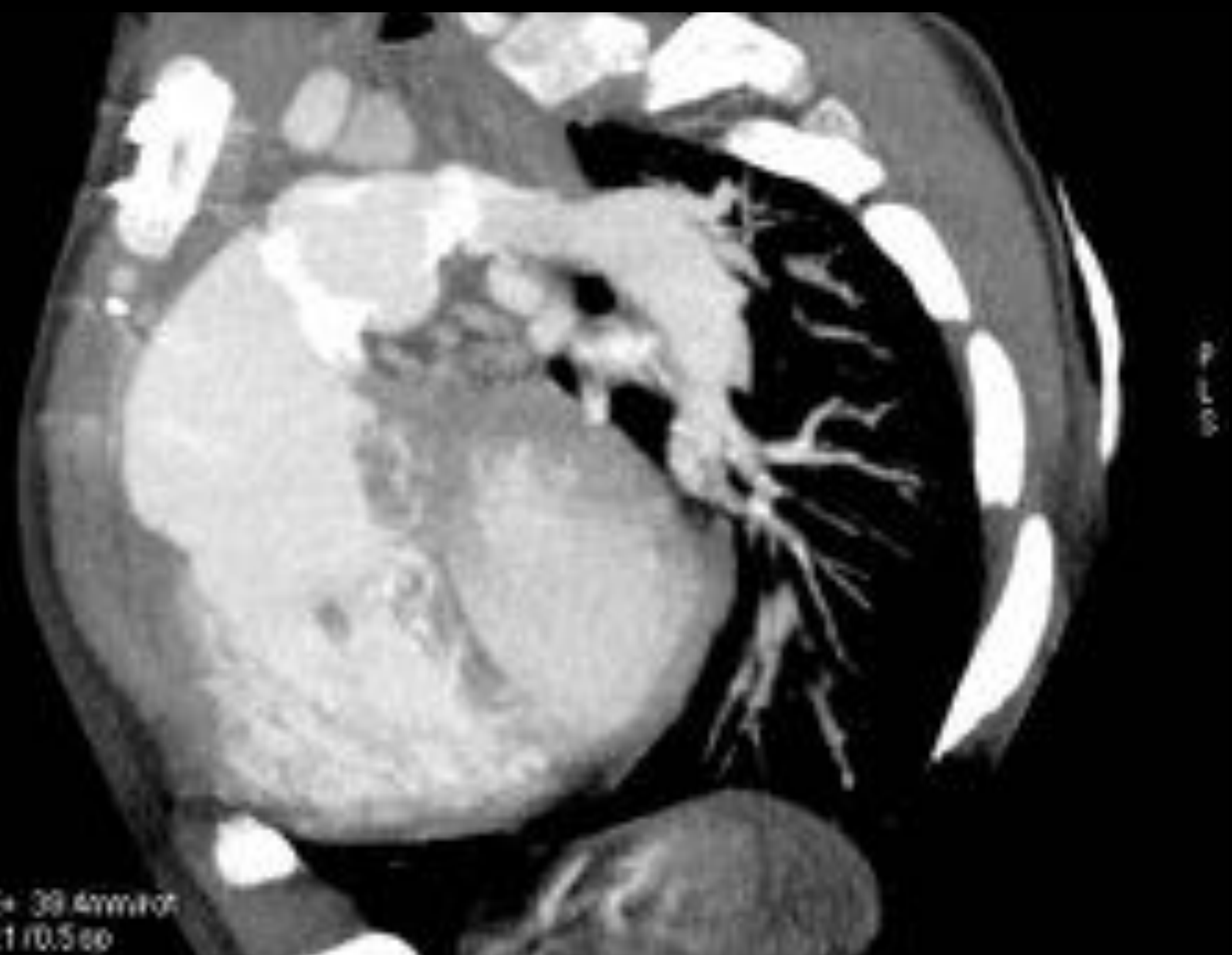


VenPro

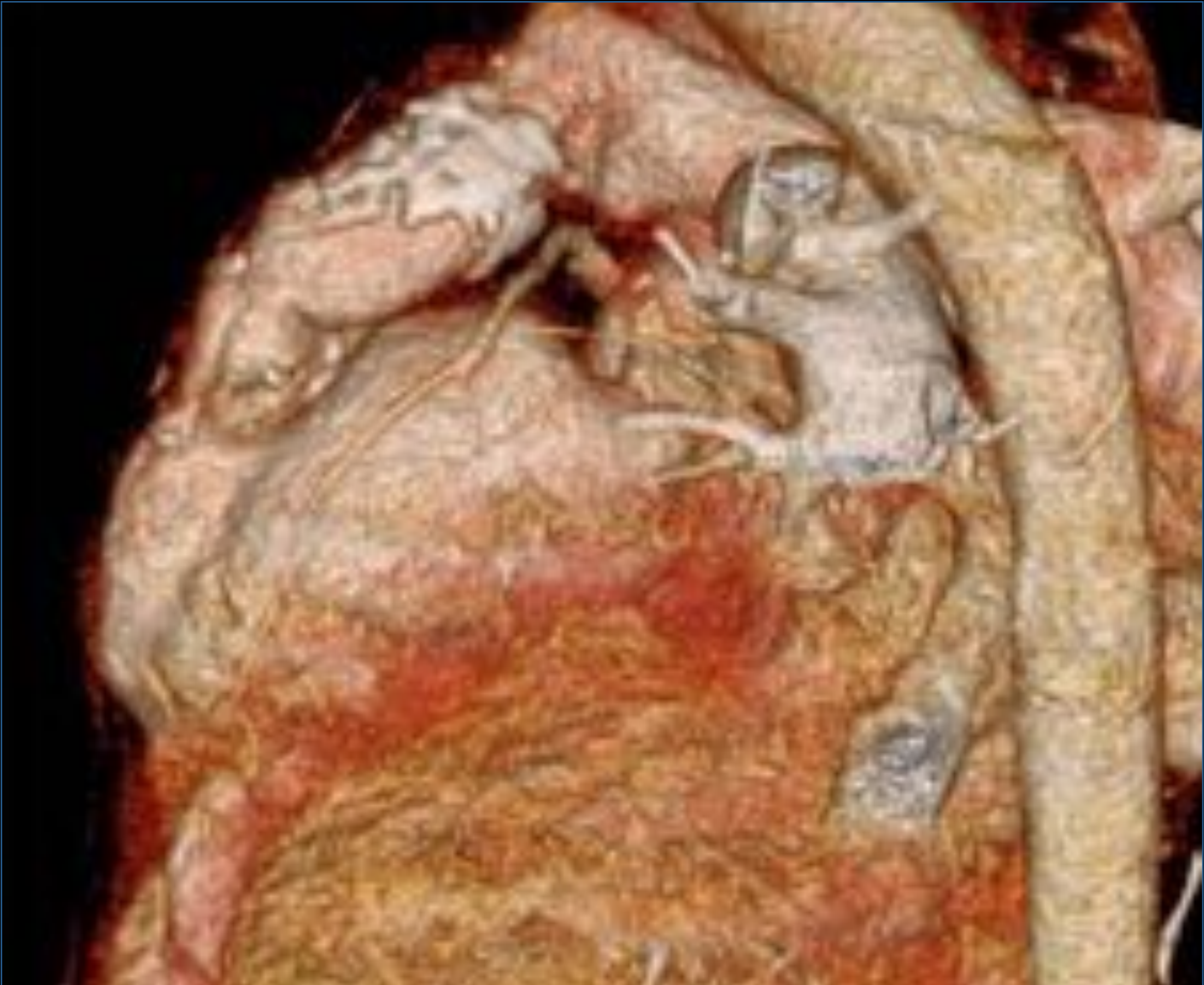
Calcified RV-PA conduit



Calcified RV-PA conduit



Calcified RV-PA conduit

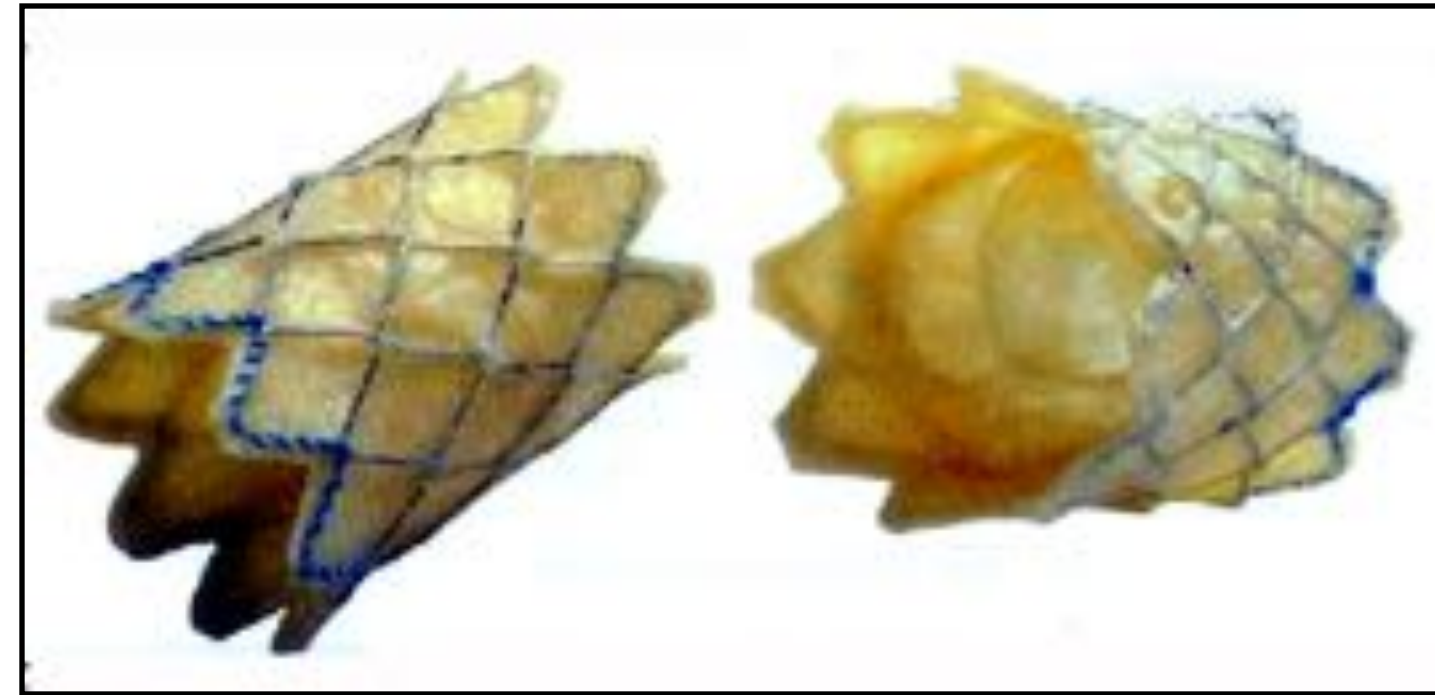


Calcified RV-PA conduit



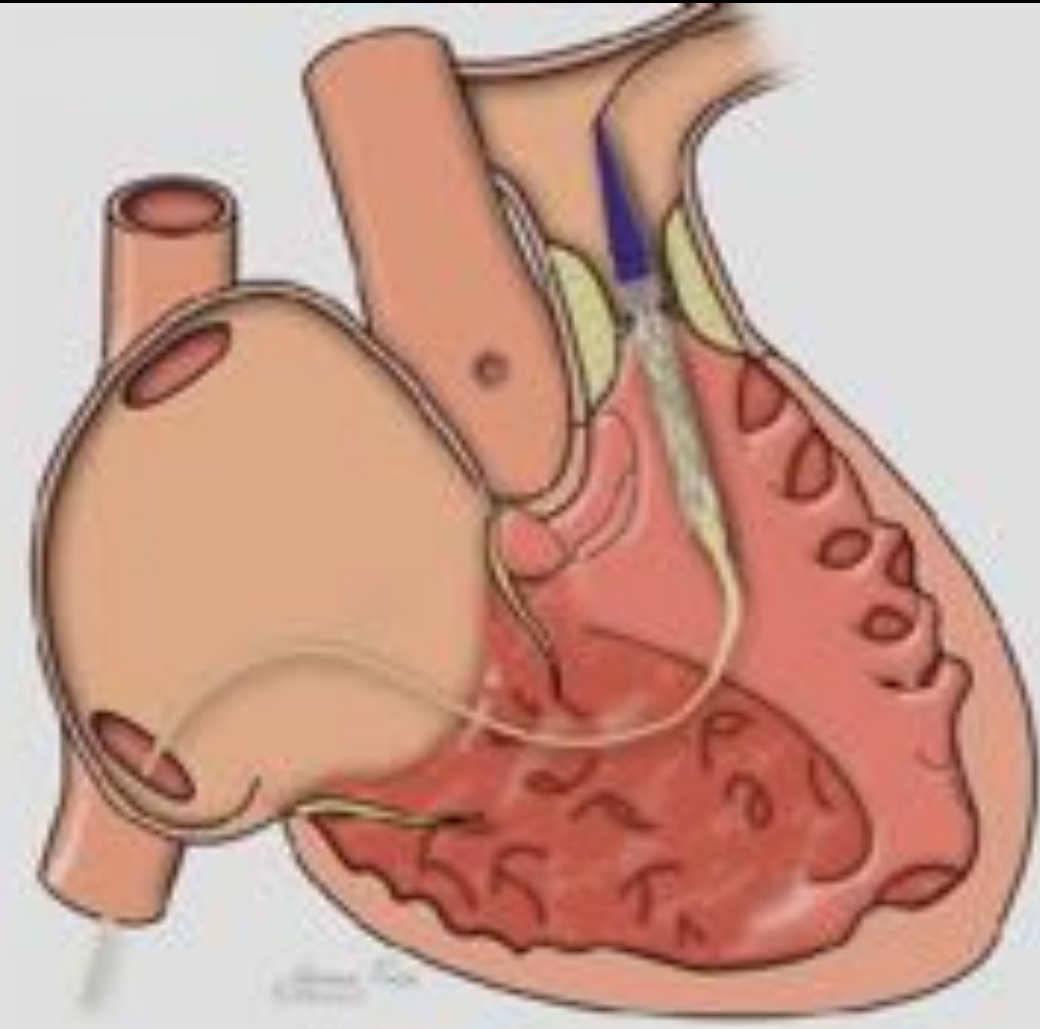
Percutaneous pulmonary valves

«Melody»

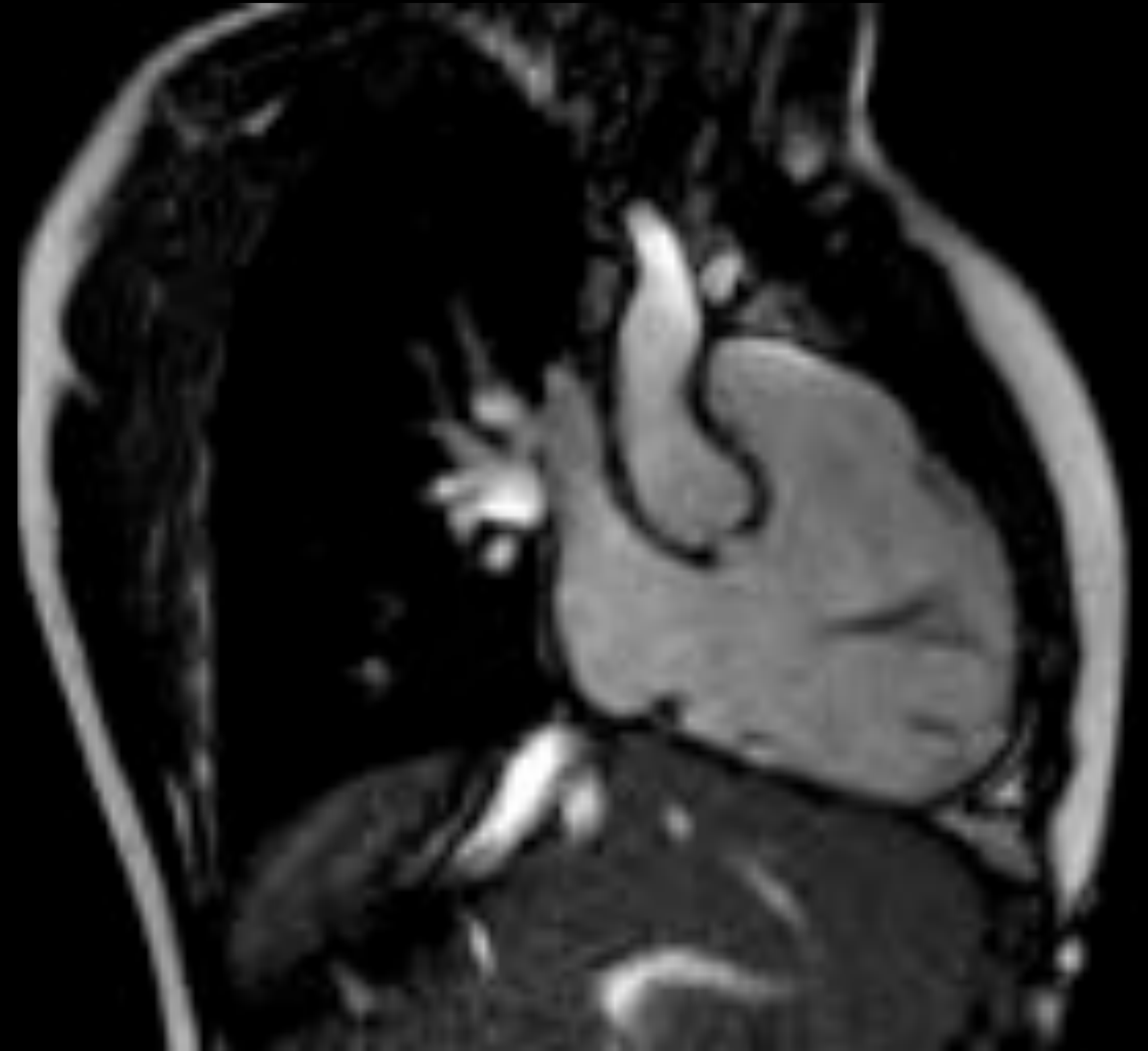
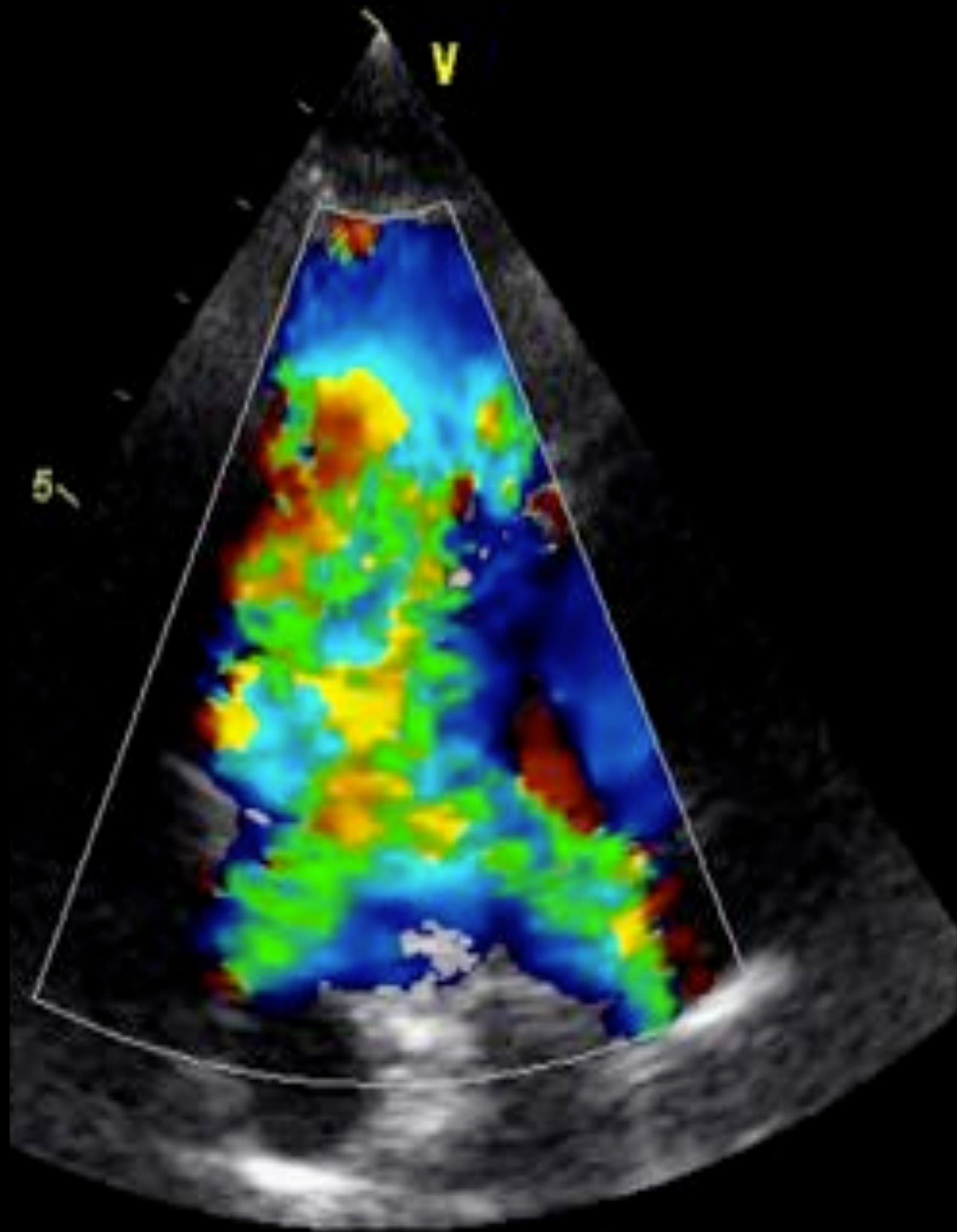


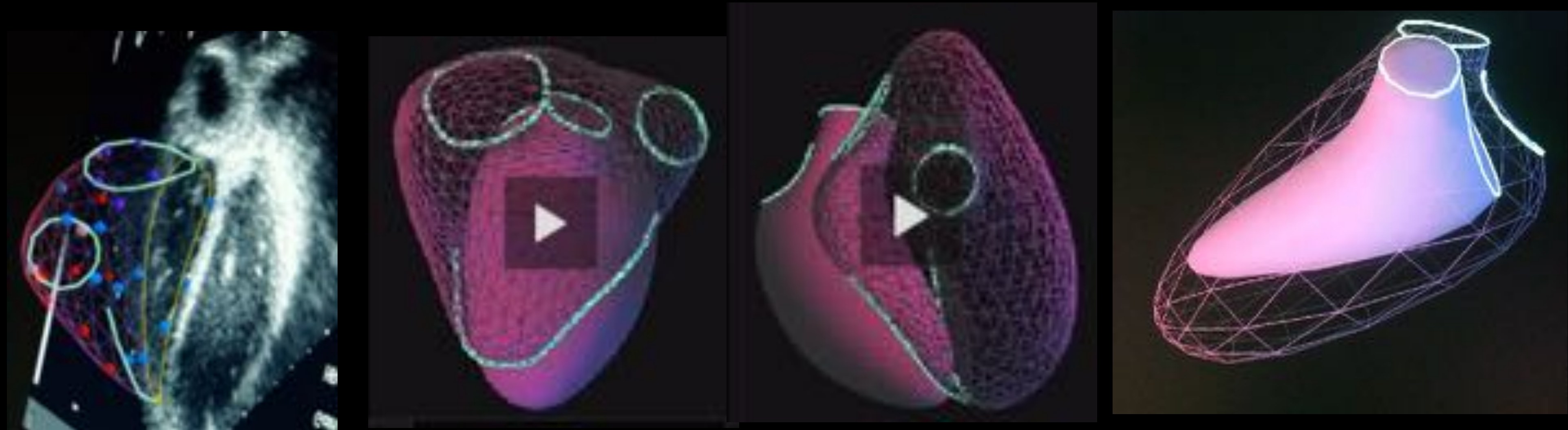
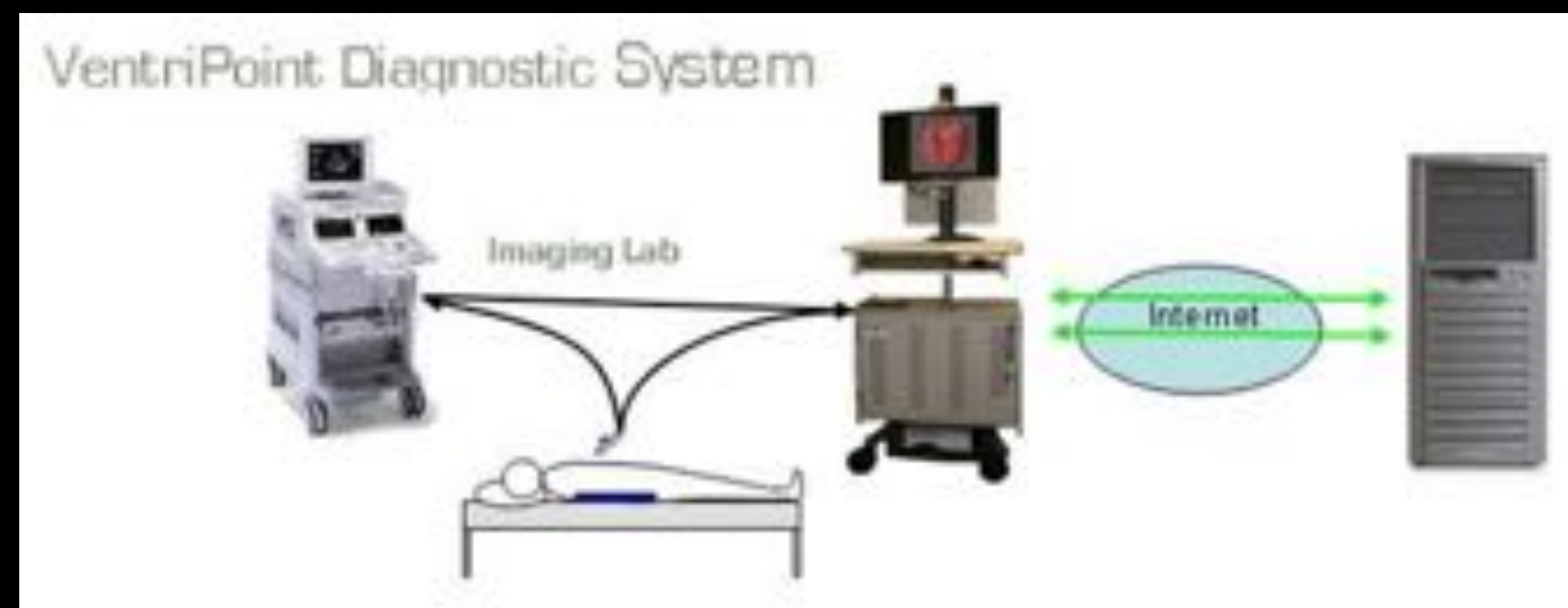
«Shelhigh»



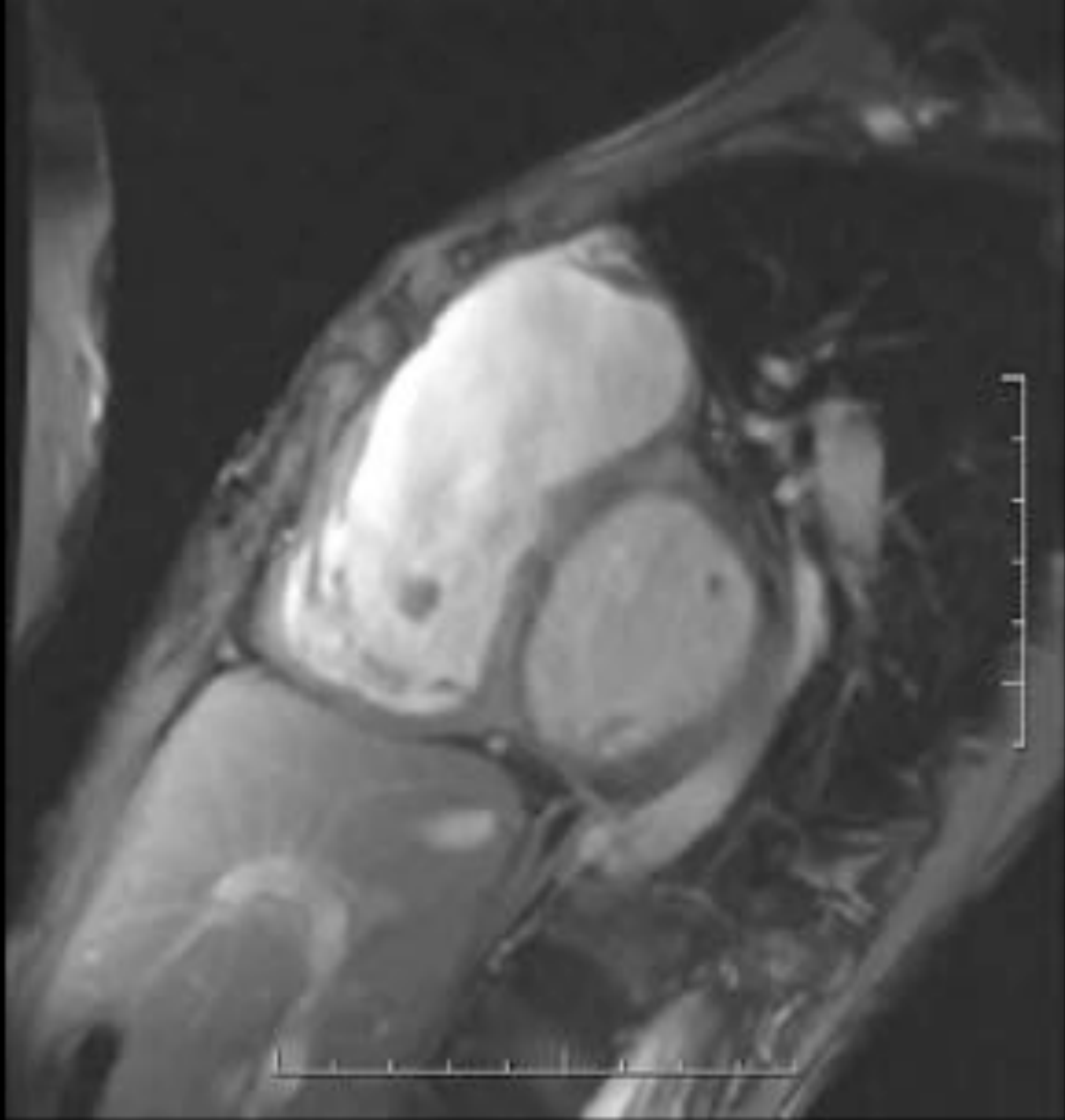


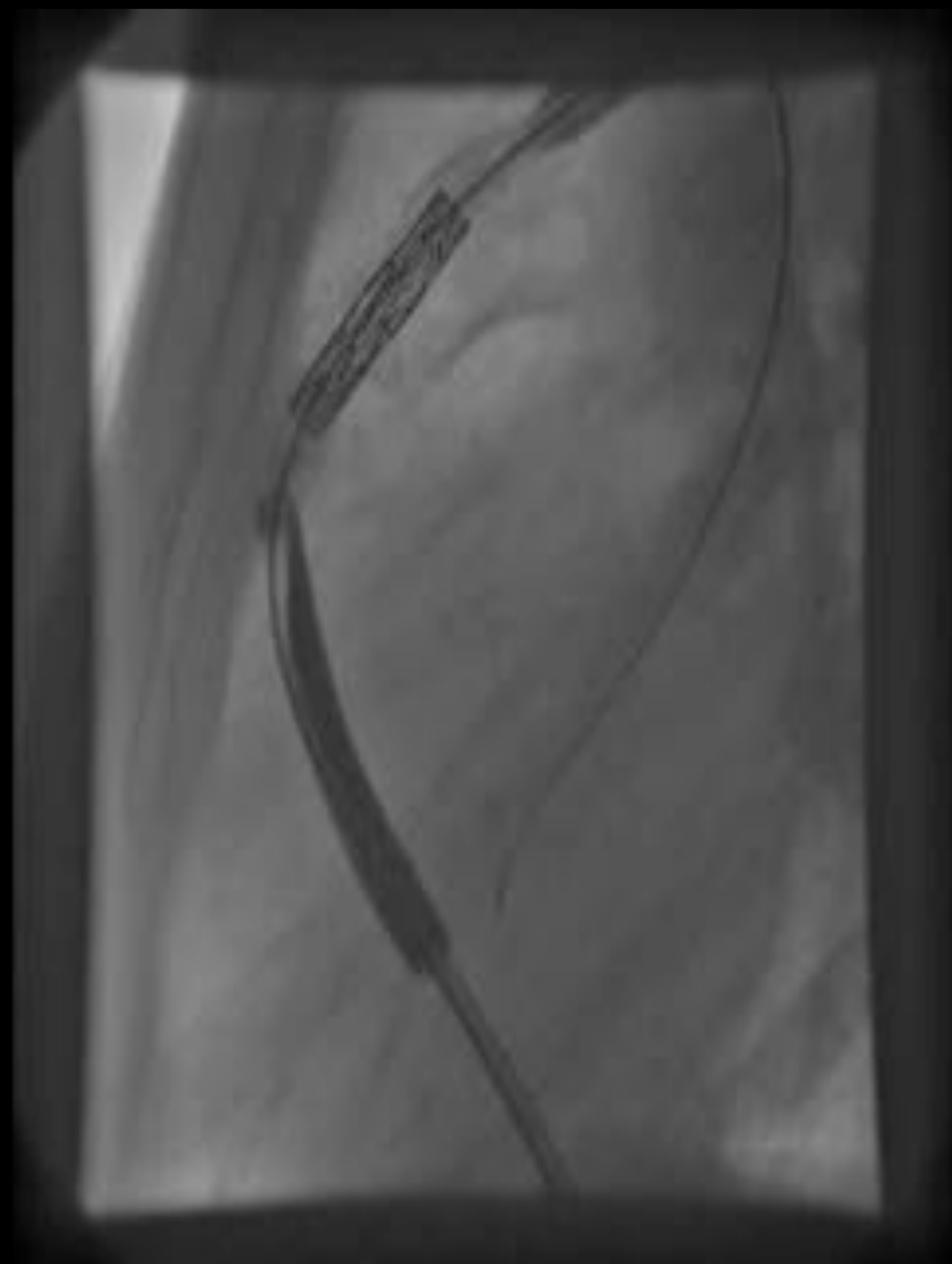
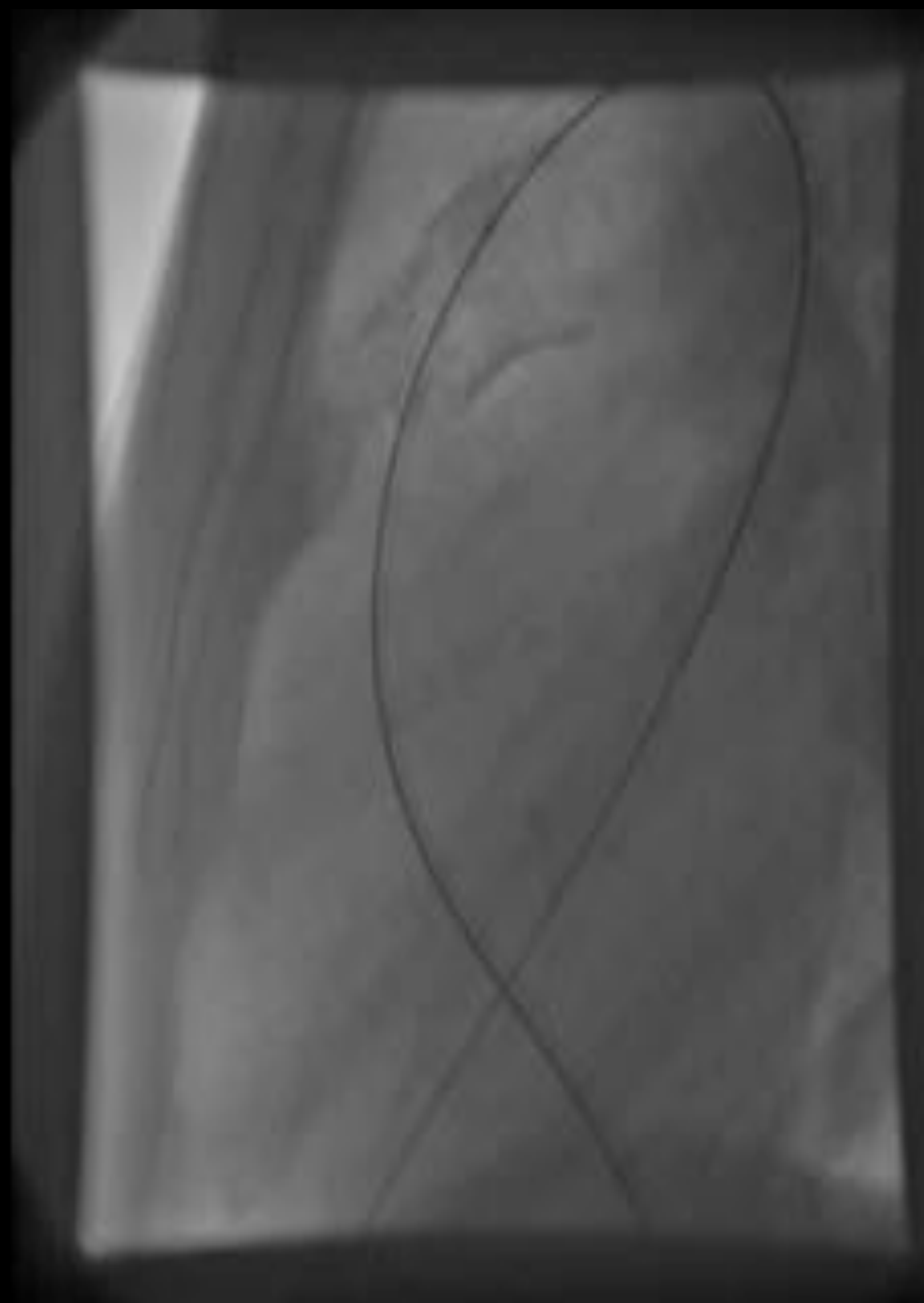
Pulmonary regurgitation in after ToF repair with trans-annular patch

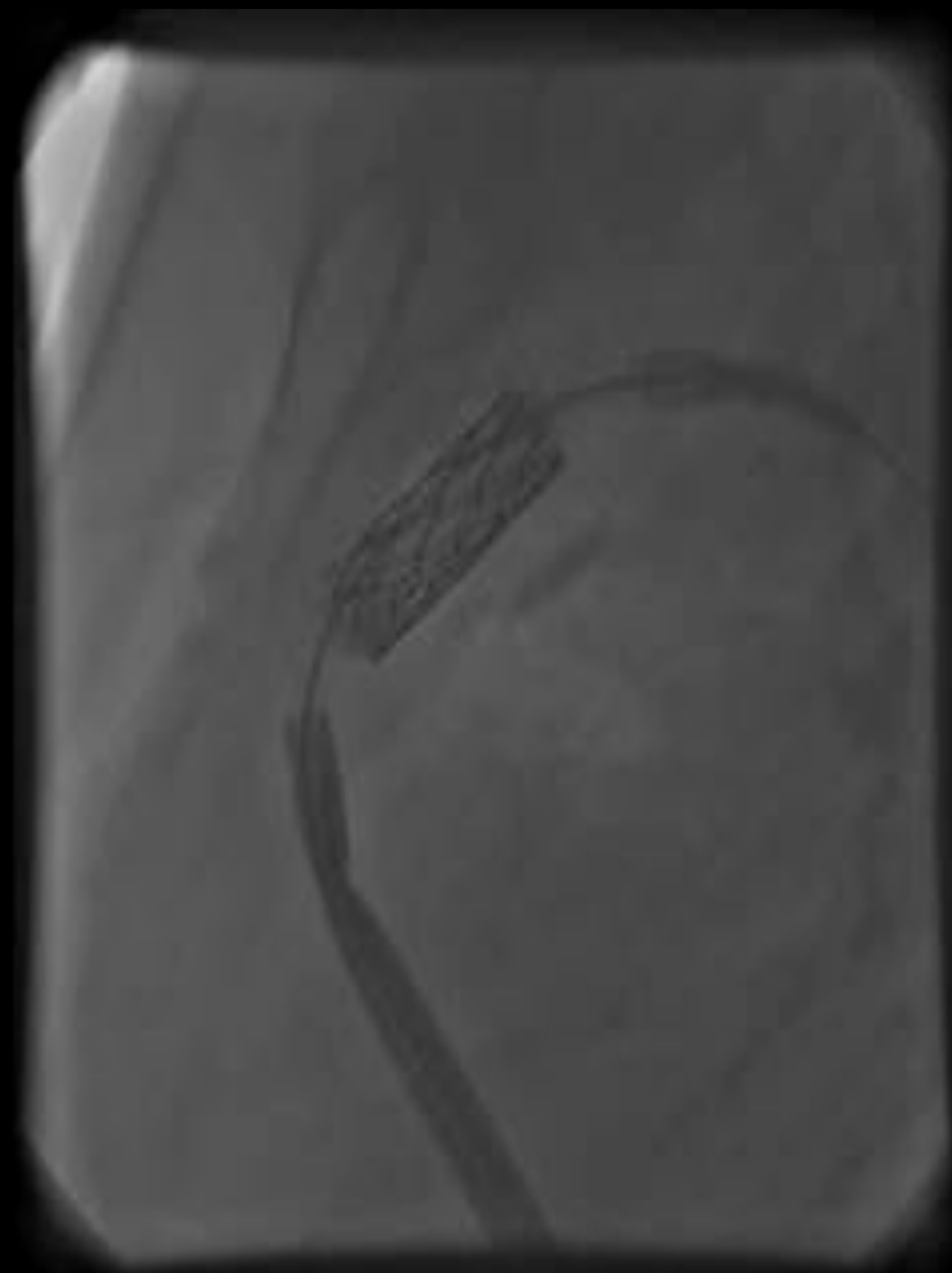


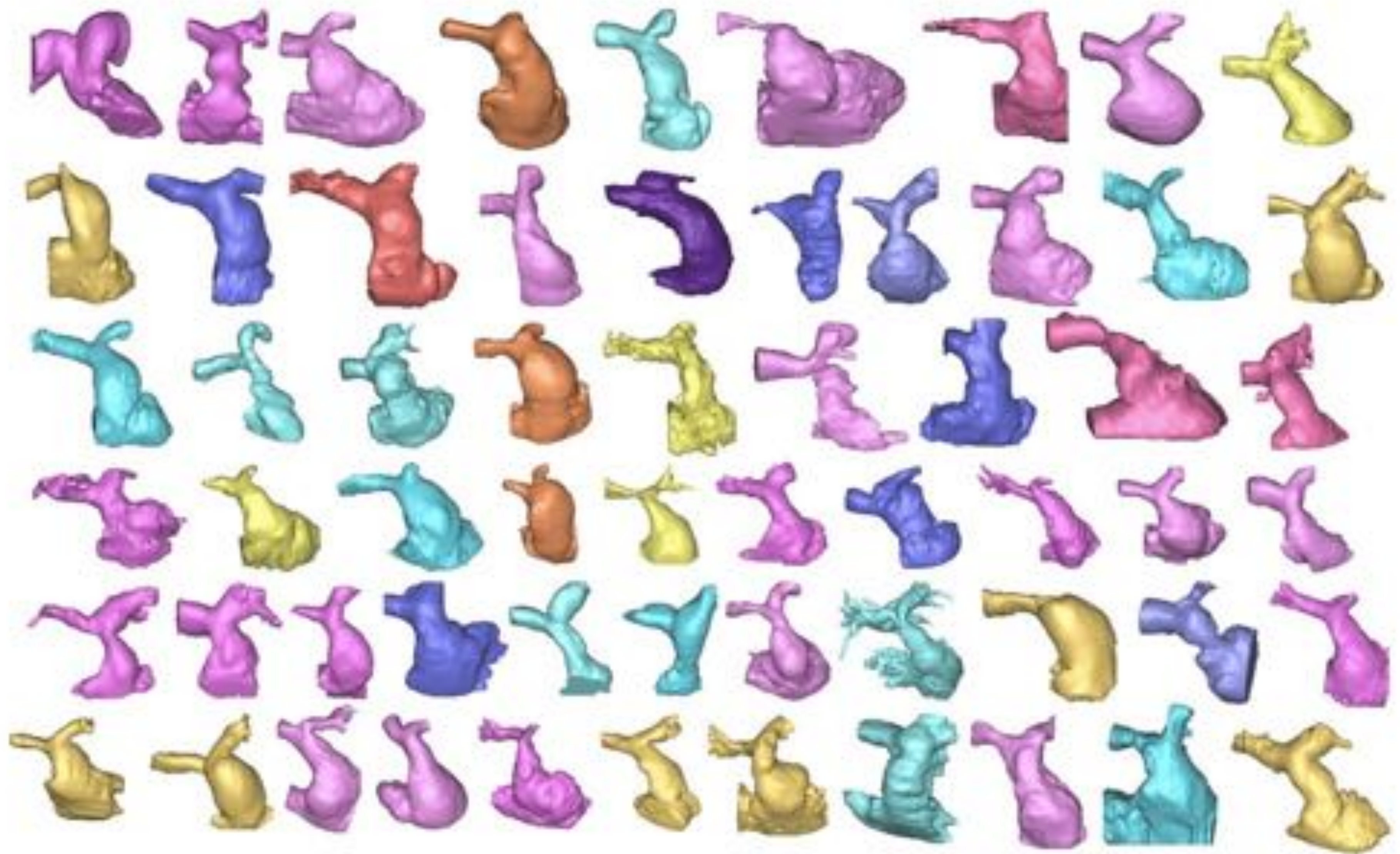


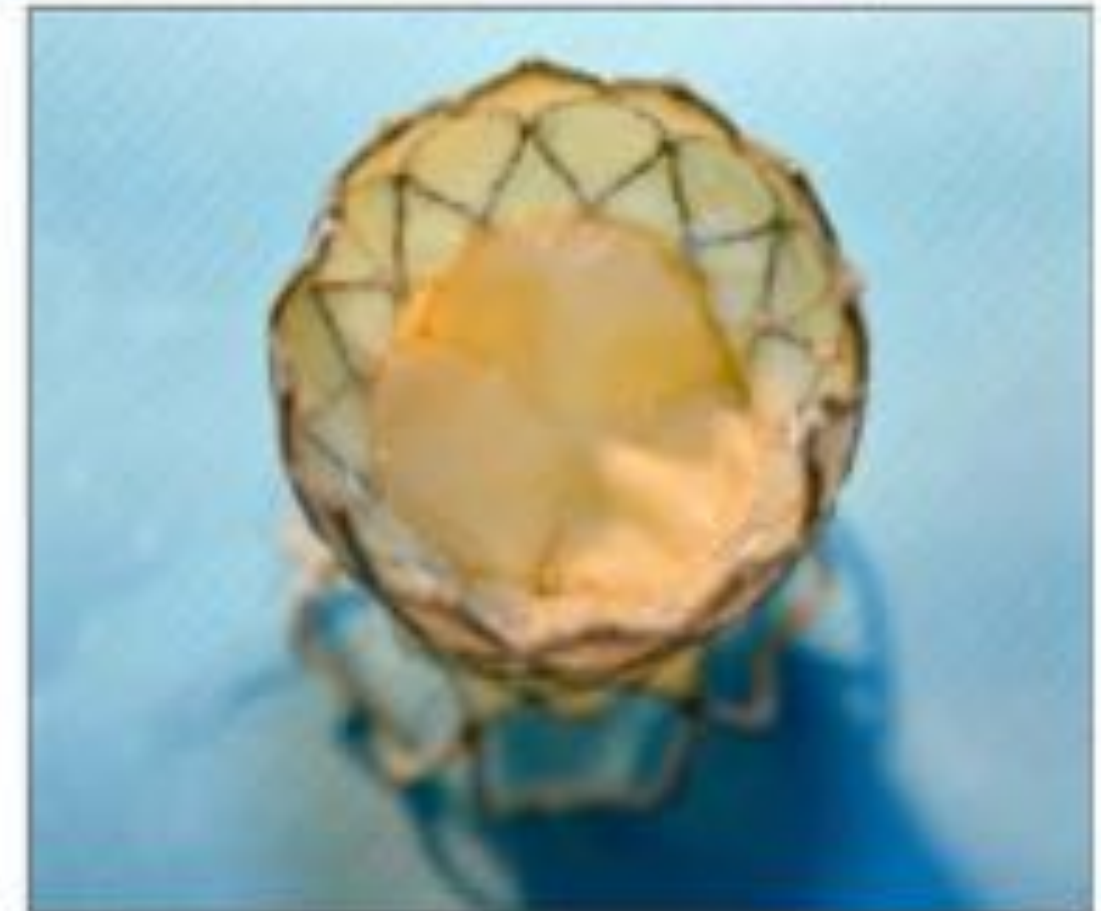
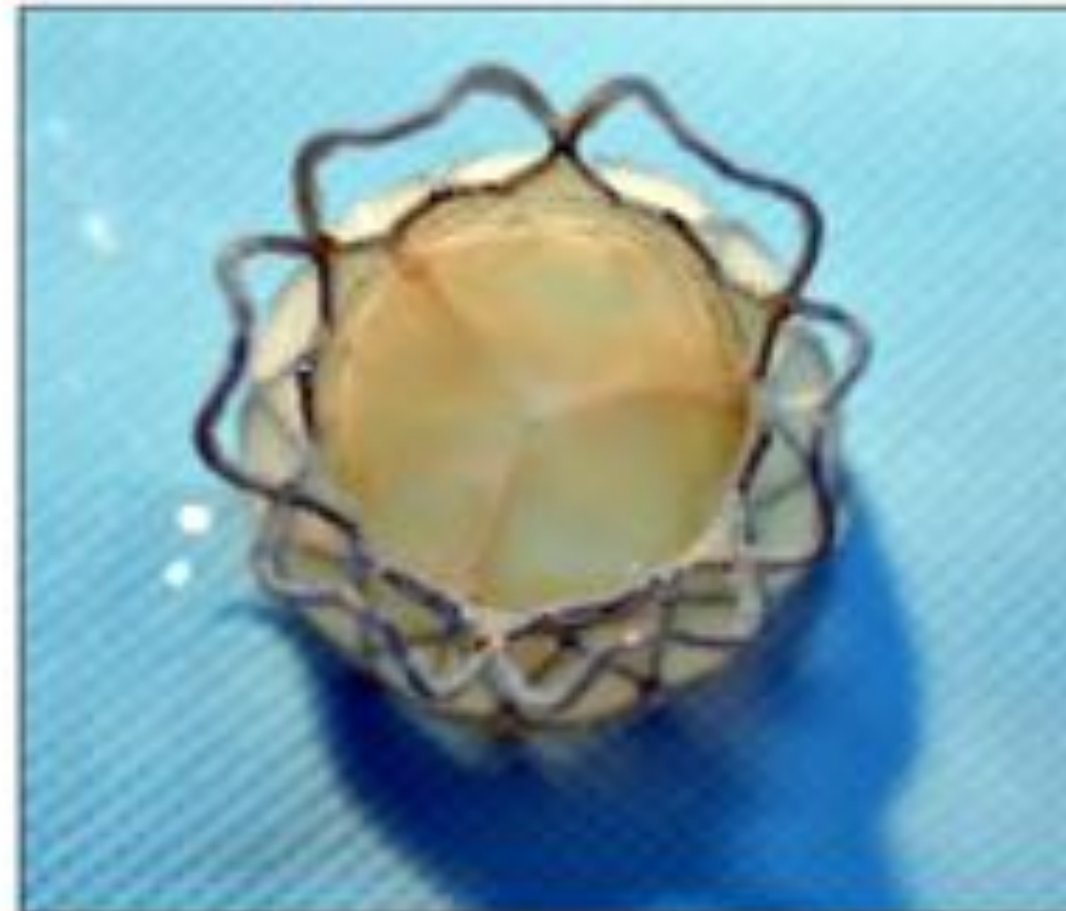
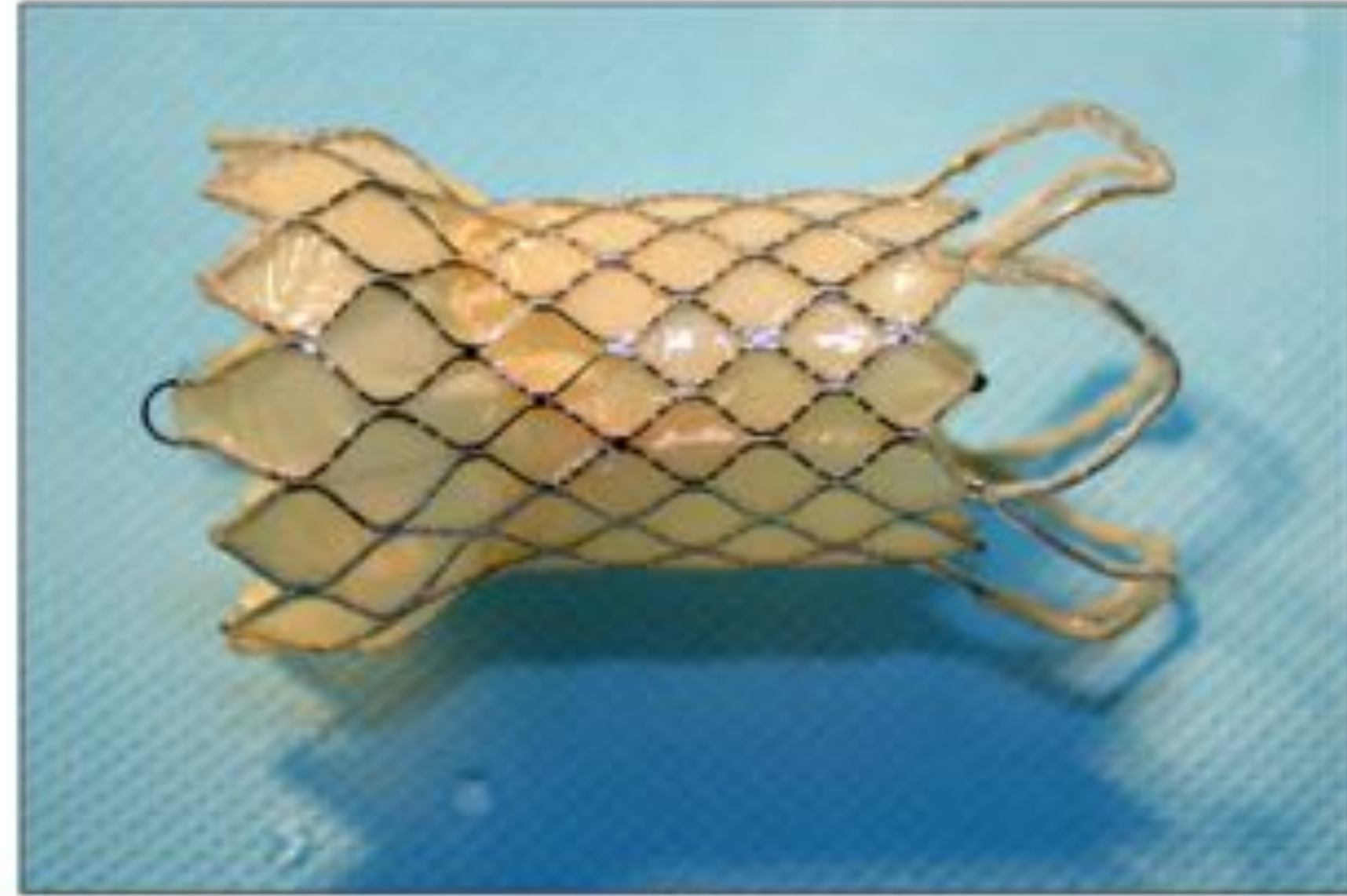
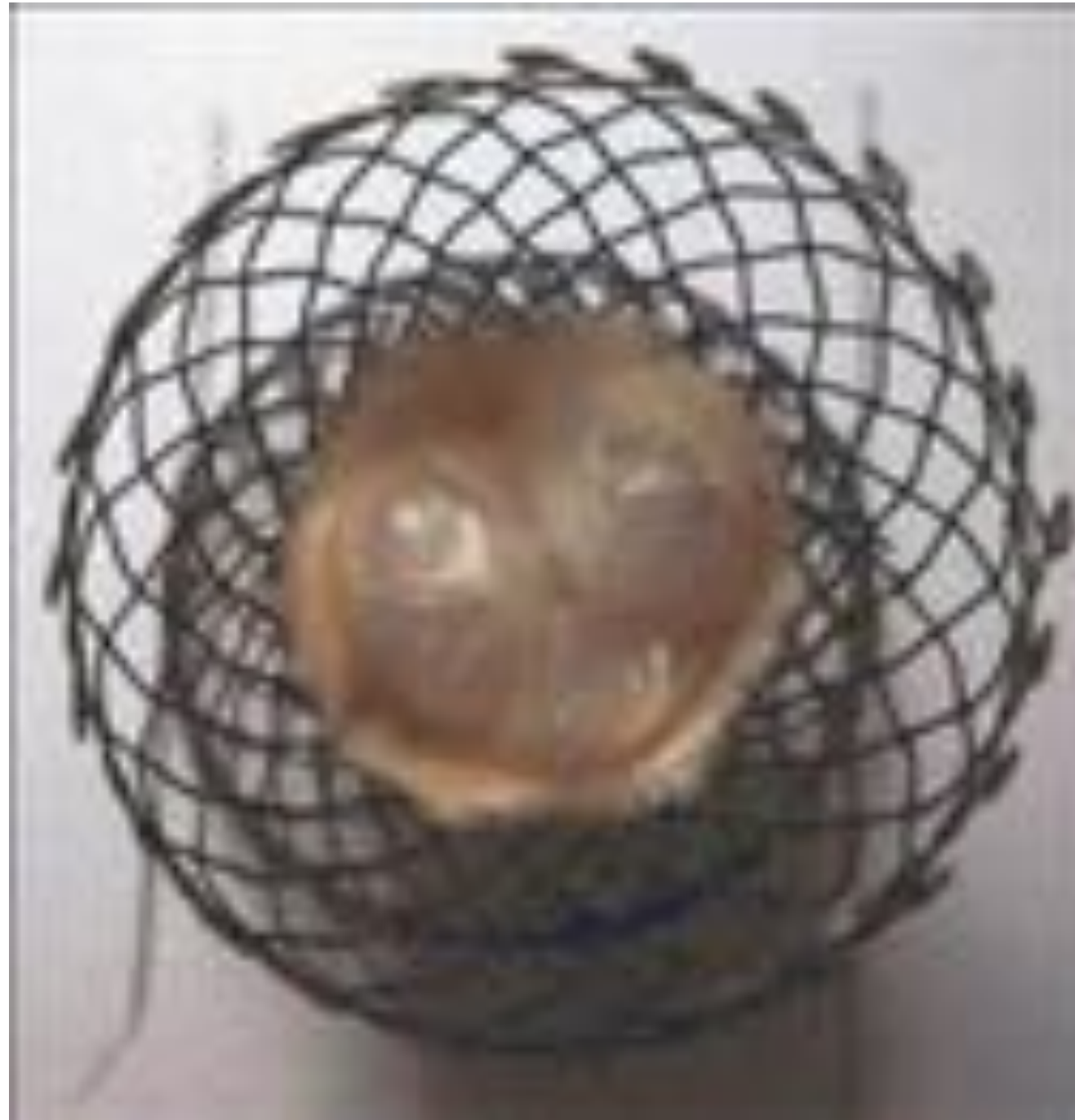
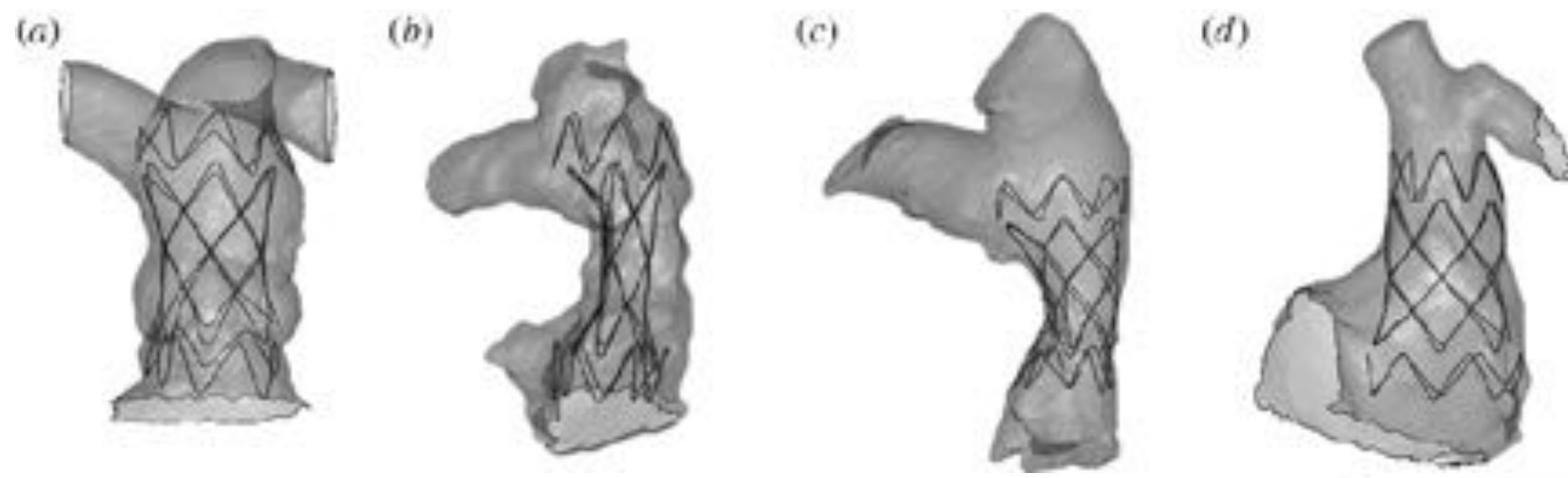
3D Knowledge system





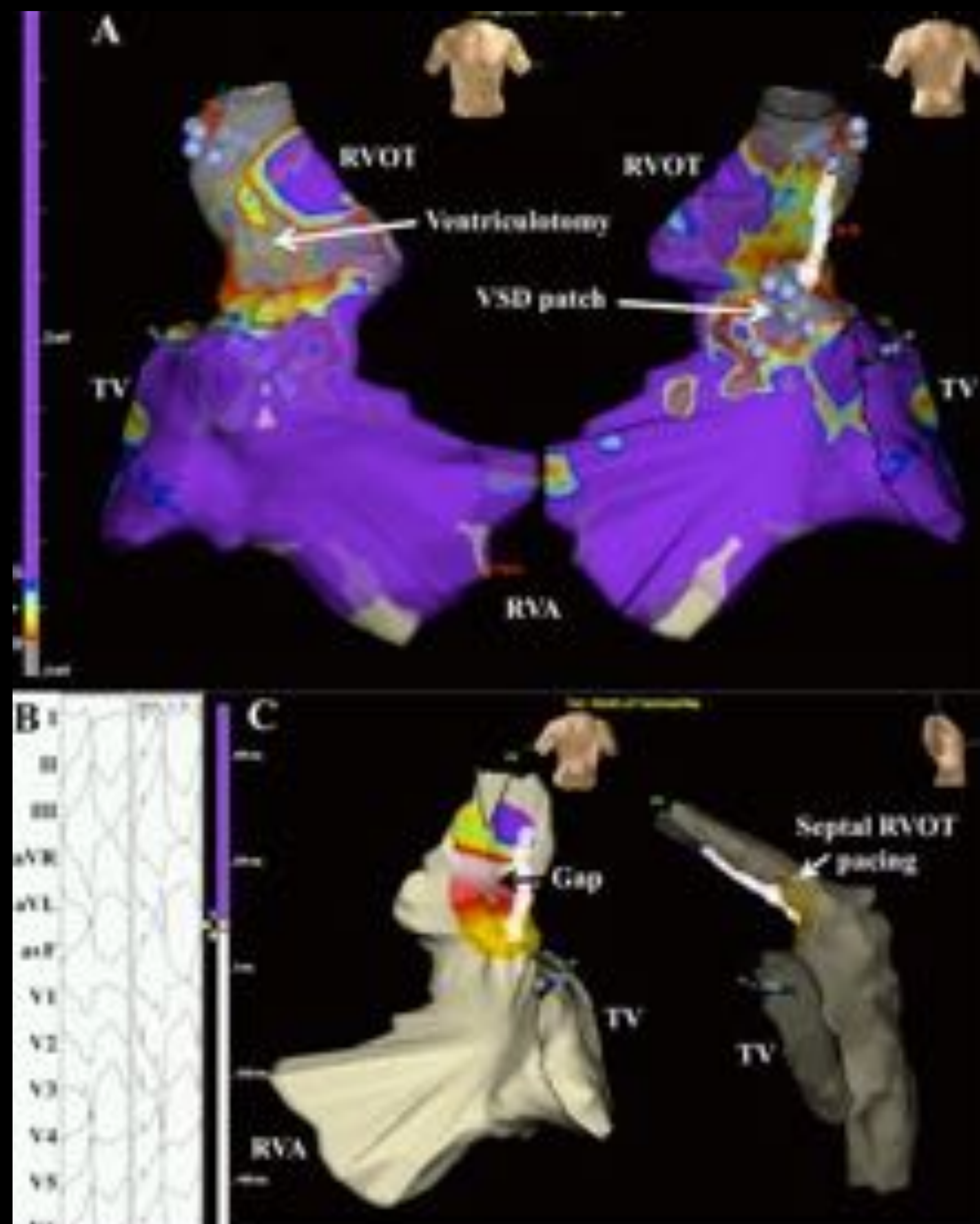






Indications	Class ^a	Level ^b
Aortic valve replacement should be performed in patients with severe AR with symptoms or signs of LV dysfunction	I	C
PVRep should be performed in symptomatic patients with severe PR and/or stenosis (RV systolic pressure >60 mmHg, TR velocity >3.5 m/s)	I	C
PVRep should be considered in asymptomatic patients with severe PR and/or PS when at least one of the following criteria is present: <ul style="list-style-type: none"> • Decrease in objective exercise capacity • Progressive RV dilation • Progressive RV systolic dysfunction • Progressive TR (at least moderate) • RVOTD with RV systolic pressure >80 mmHg (TR velocity >4.3 m/s) • Sustained atrial/ventricular arrhythmias 	IIa	C
VSD closure should be considered in patients with residual VSD and significant LV volume overload or if the patient is undergoing pulmonary valve surgery	IIa	C

Voltage and pace mapping of ventricular tachycardia in tetralogy of Fallot



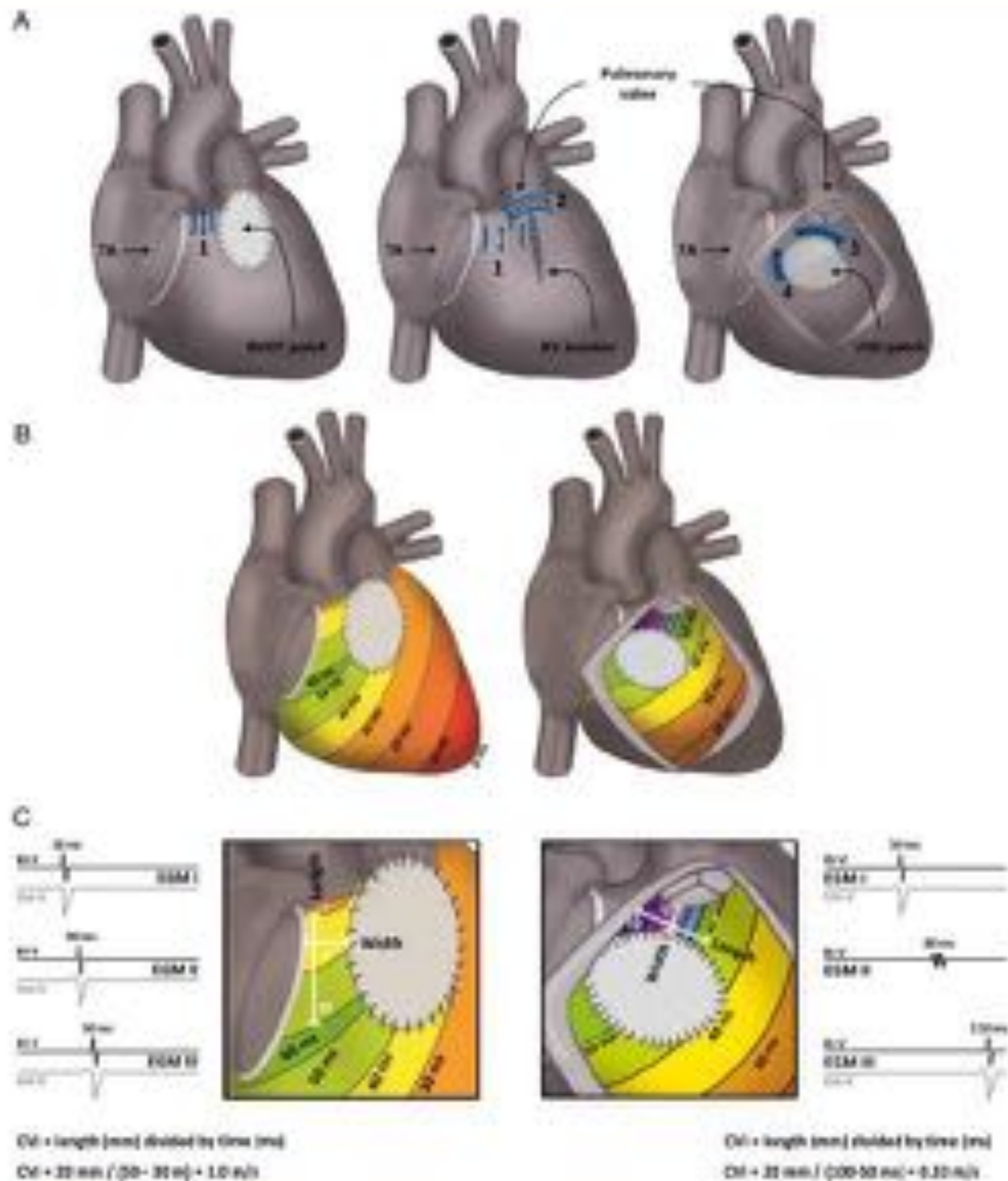
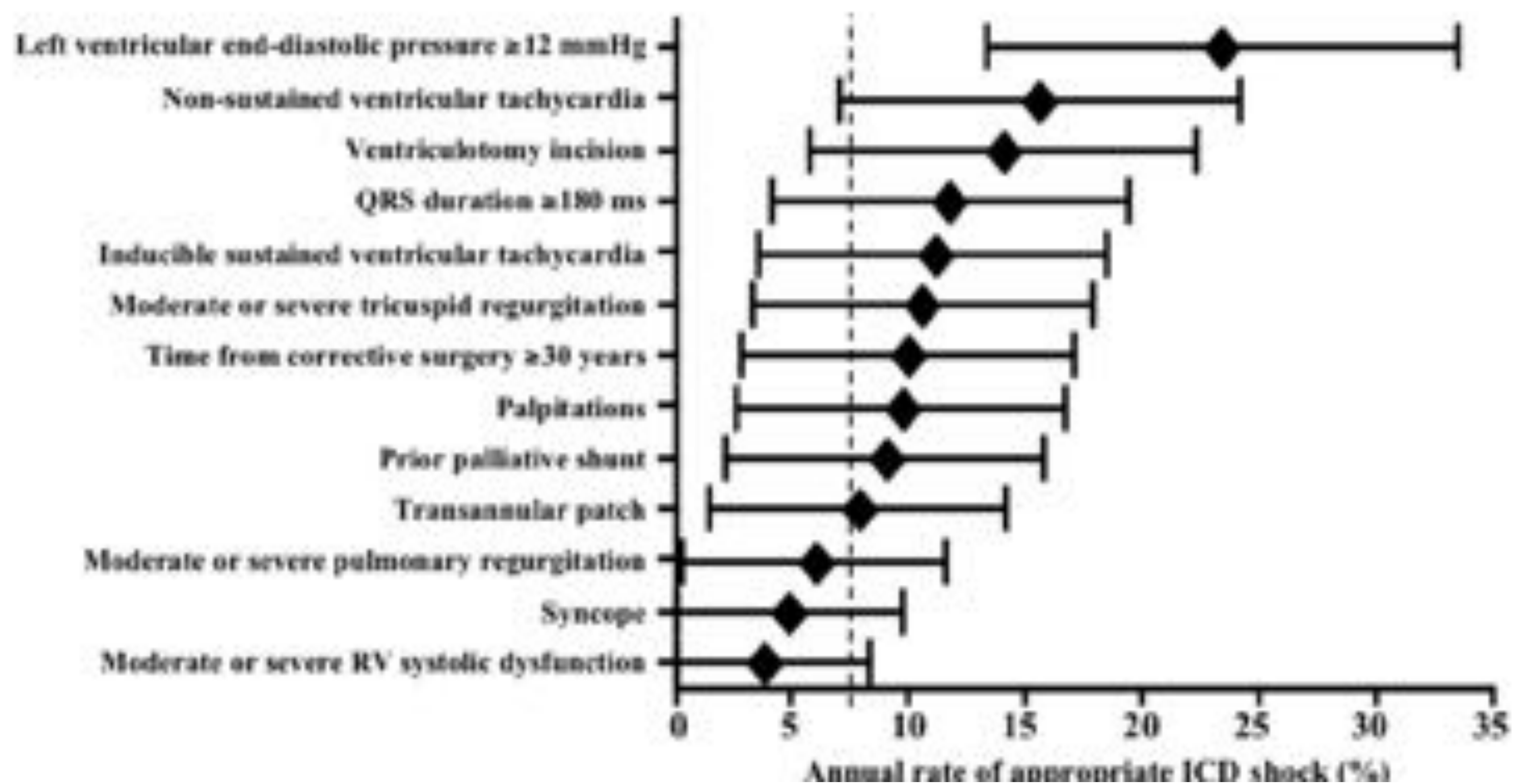


Figure 1 (A) Schematic overview of the four potential anatomical isthmuses (blue brackets), isthmus I bordered by tricuspid annulus and right ventricular outflow tract patch/right ventricular incision, isthmus II by right ventricular incision and pulmonary valve, isthmus III by pulmonary valve and ventricular septal defect patch, isthmus IV by ventricular septal defect patch and tricuspid annulus. (B) Schematic activation of the right ventricle during SR displayed as colour-coded isochronal (10 ms) map from red (early activation) to purple (late activation). (C) Enlarged views of anatomical isthmus I (left) and III (right) with corresponding electrograms recorded from sites I-I and II-II, as indicated. Isthmus width, distance between unexcitable anatomical boundaries; Isthmus length, distance between normal electrograms (I and II) recorded at entrance and exit site of the anatomical isthmus. Conduction time through the anatomical isthmus, difference in local activation time between the entrance and exit of the anatomical isthmus. Conduction velocity index calculated as indicated. ECG, electrogram; RVOT, right ventricular outflow tract; RV, right ventricle; VSD, ventricular septal defect.



Resynchronization for failing right ventricle after repair of tetralogy of Fallot

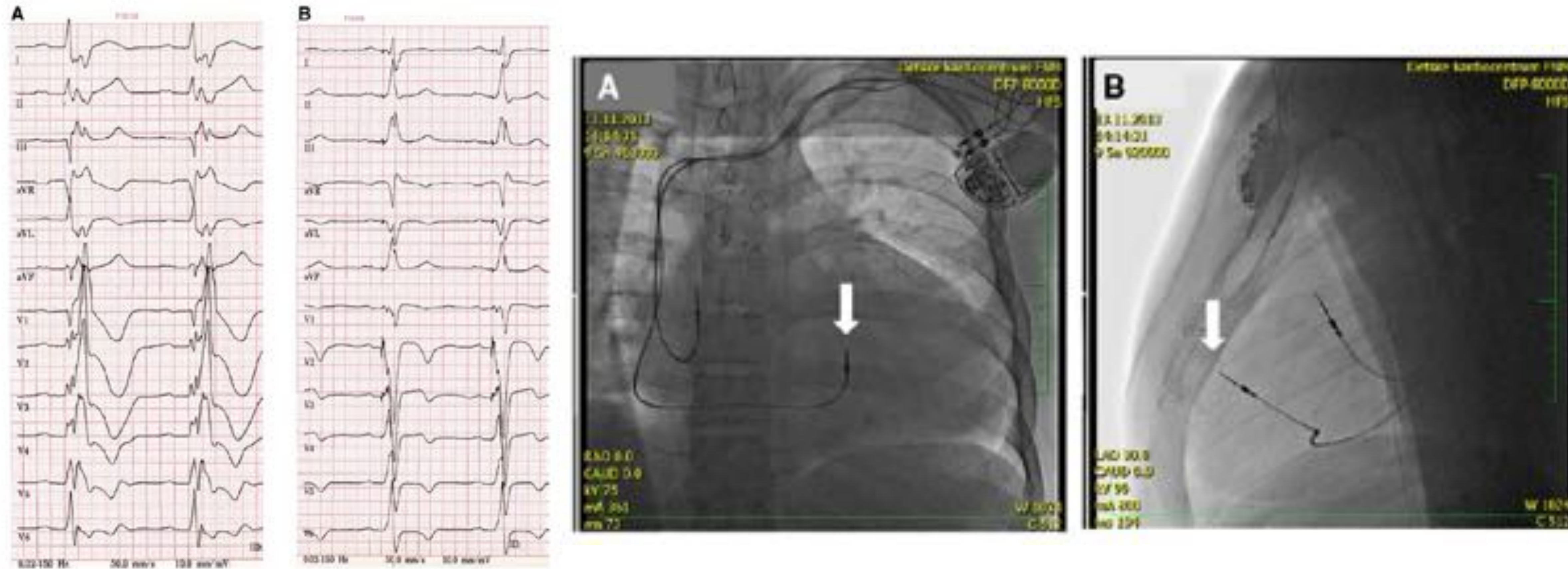
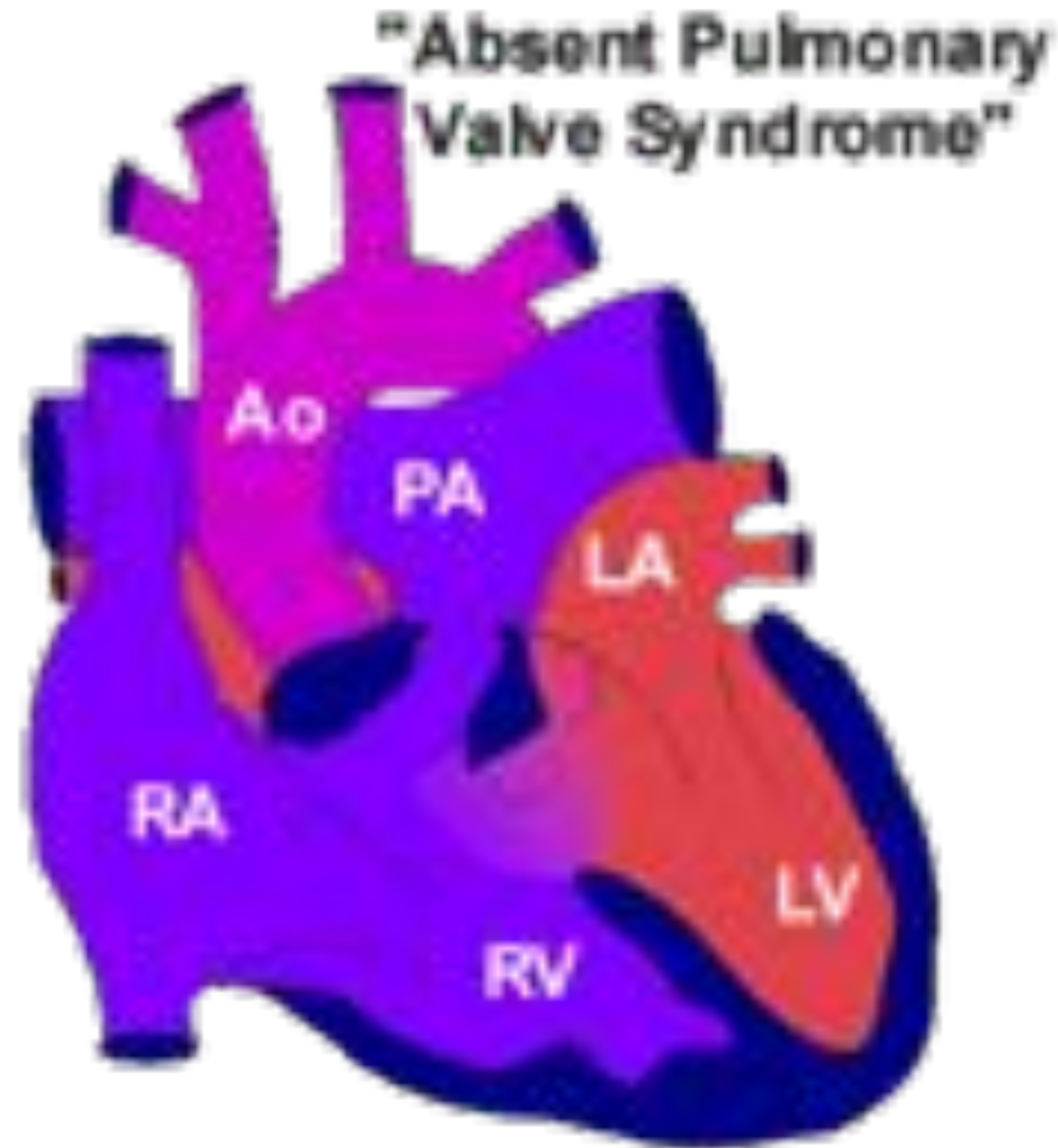
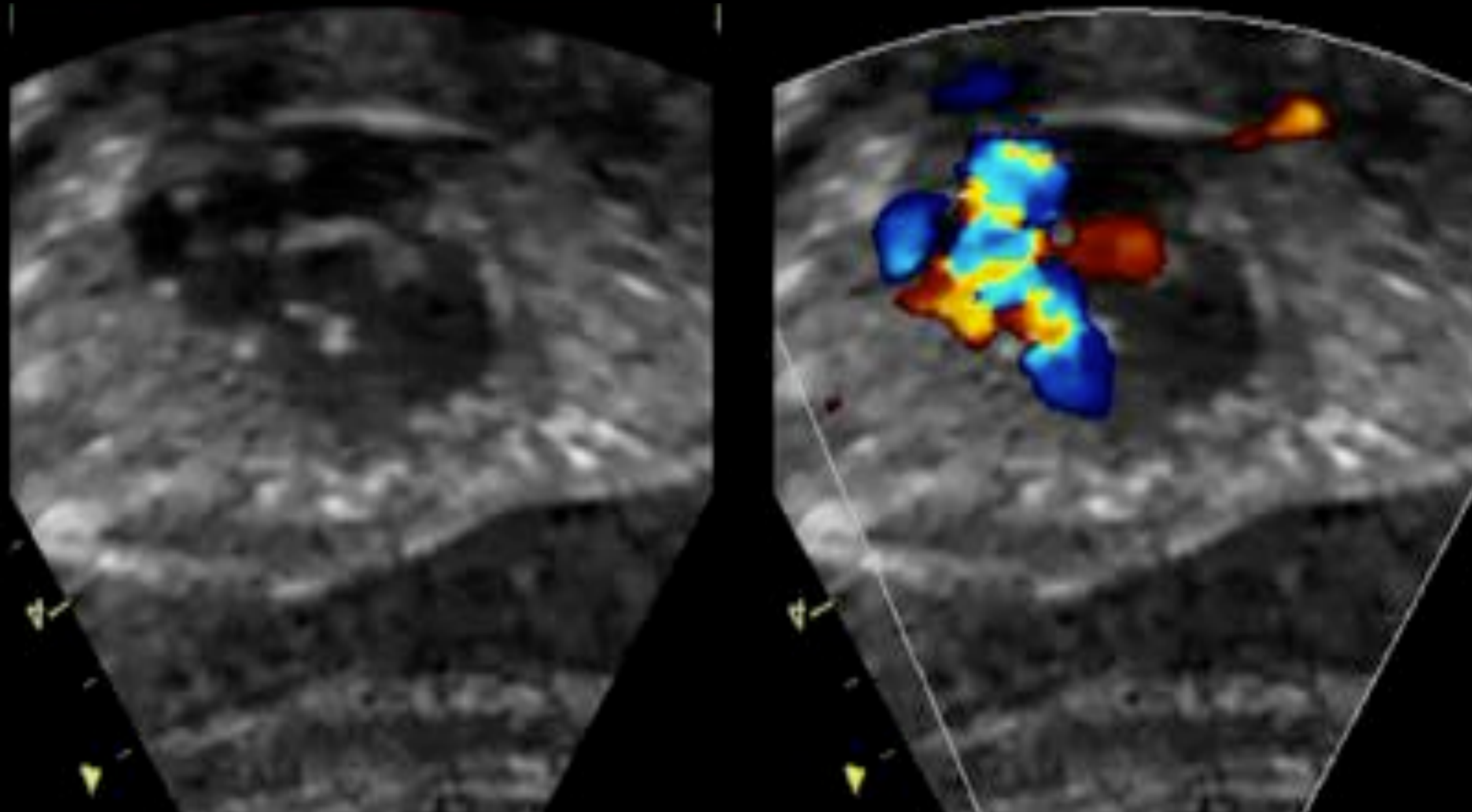


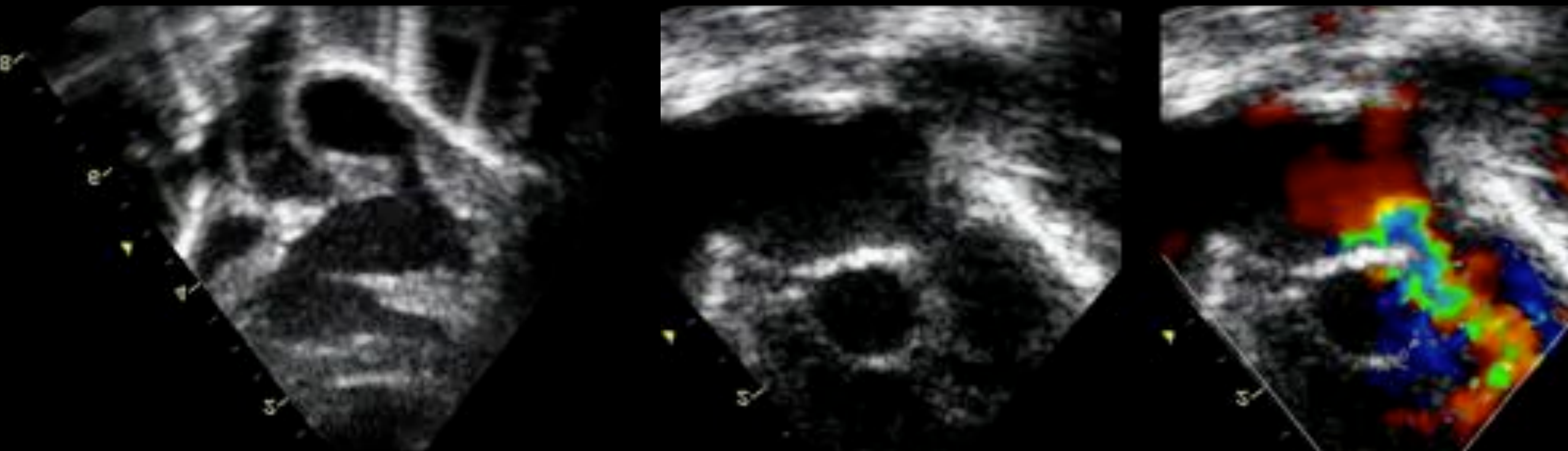
Figure 2. Twelve-lead ECG. **A**, Before pacing: sinus rhythm, spontaneous ventricular activation with complete right bundle-branch block morphology. **B**, After resynchronization: major decrease in QRS complex duration during dual mode, dual chamber, dual sensing (DDD) pacing with an atrio-ventricular delay adjusted to achieve complete fusion with spontaneous ventricular depolarization. Leads aVR, aVL and aVF indicates augmented limb leads.

Tetralogy of Fallot with absent pulmonary valve



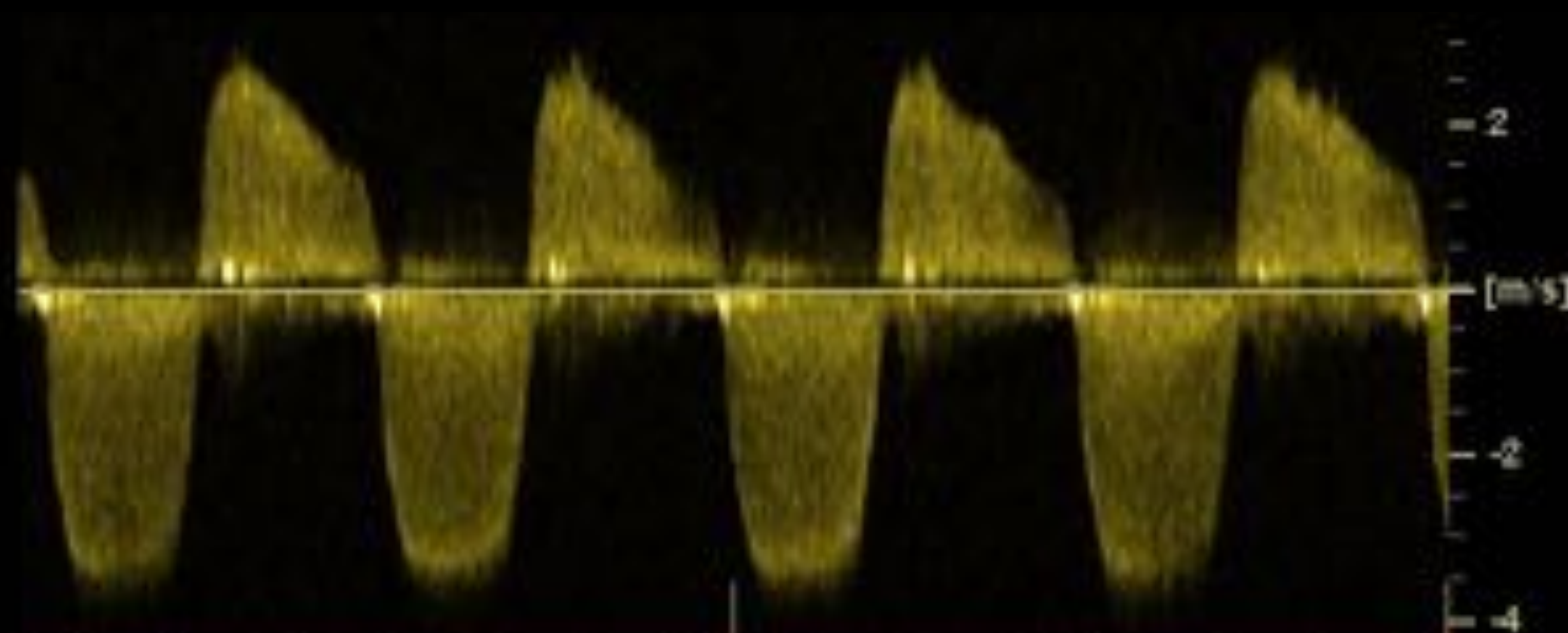
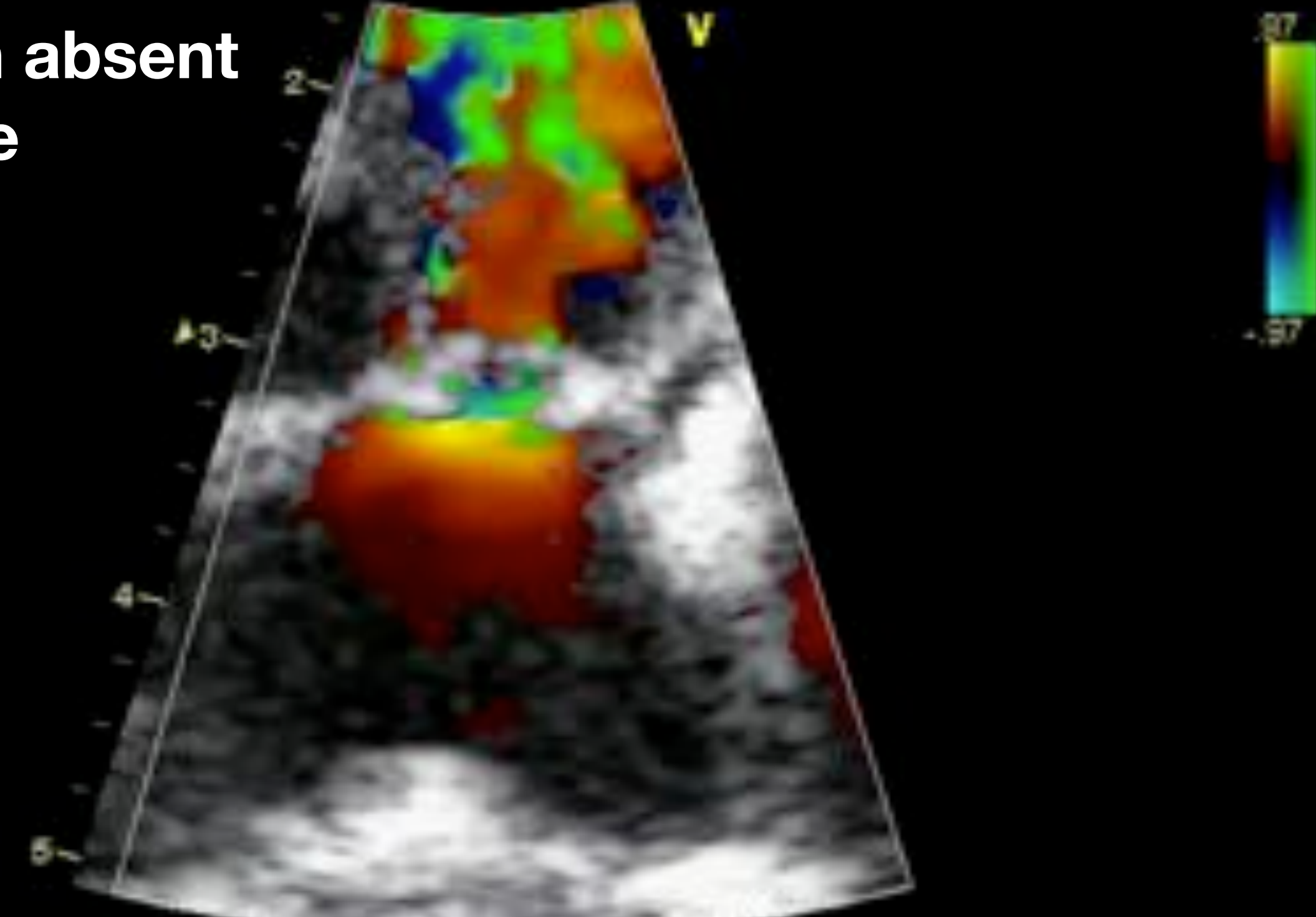
Tetralogy of Fallot with absent pulmonary valve

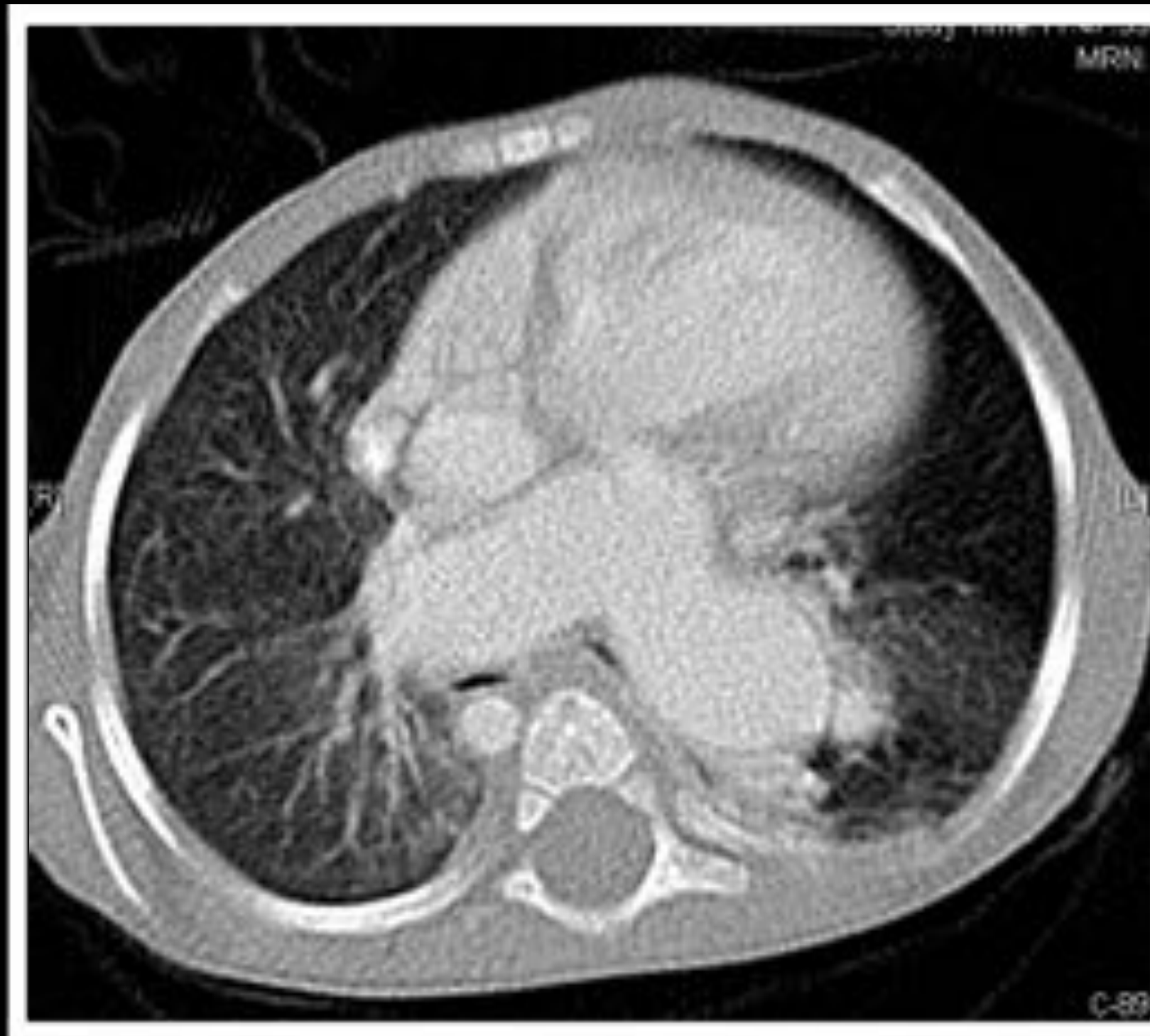
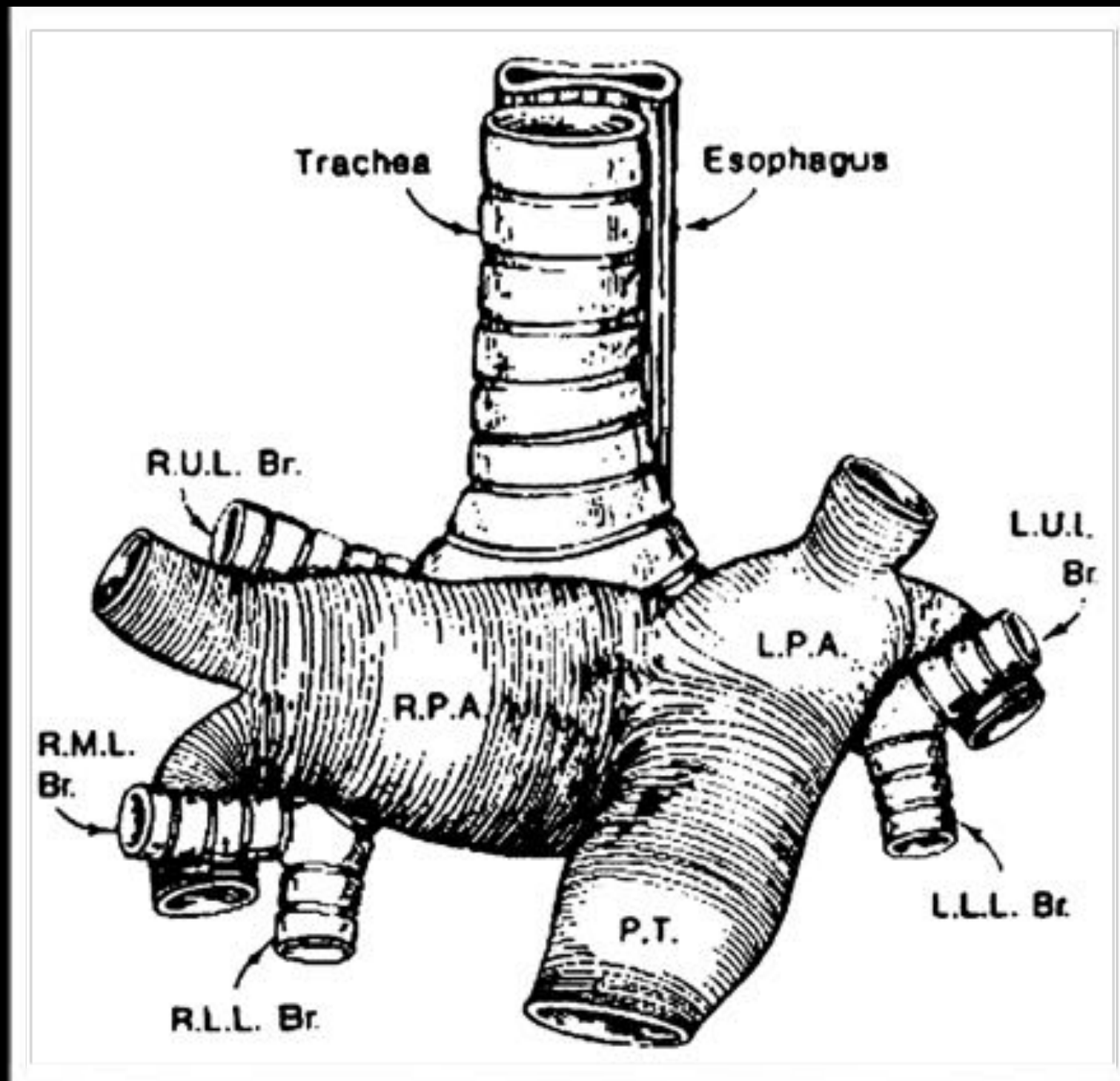




Tetralogy of Fallot with absent pulmonary valve

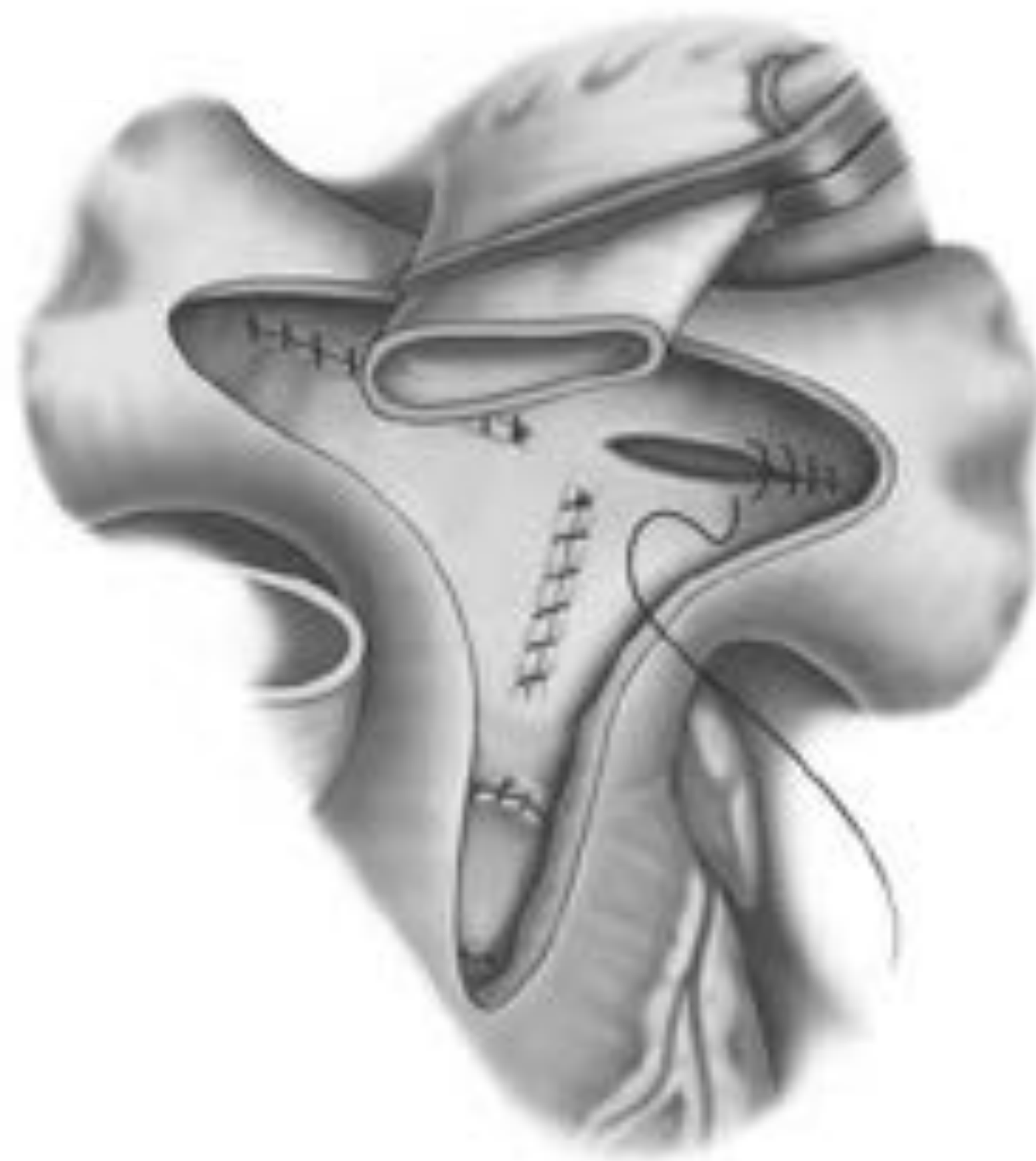
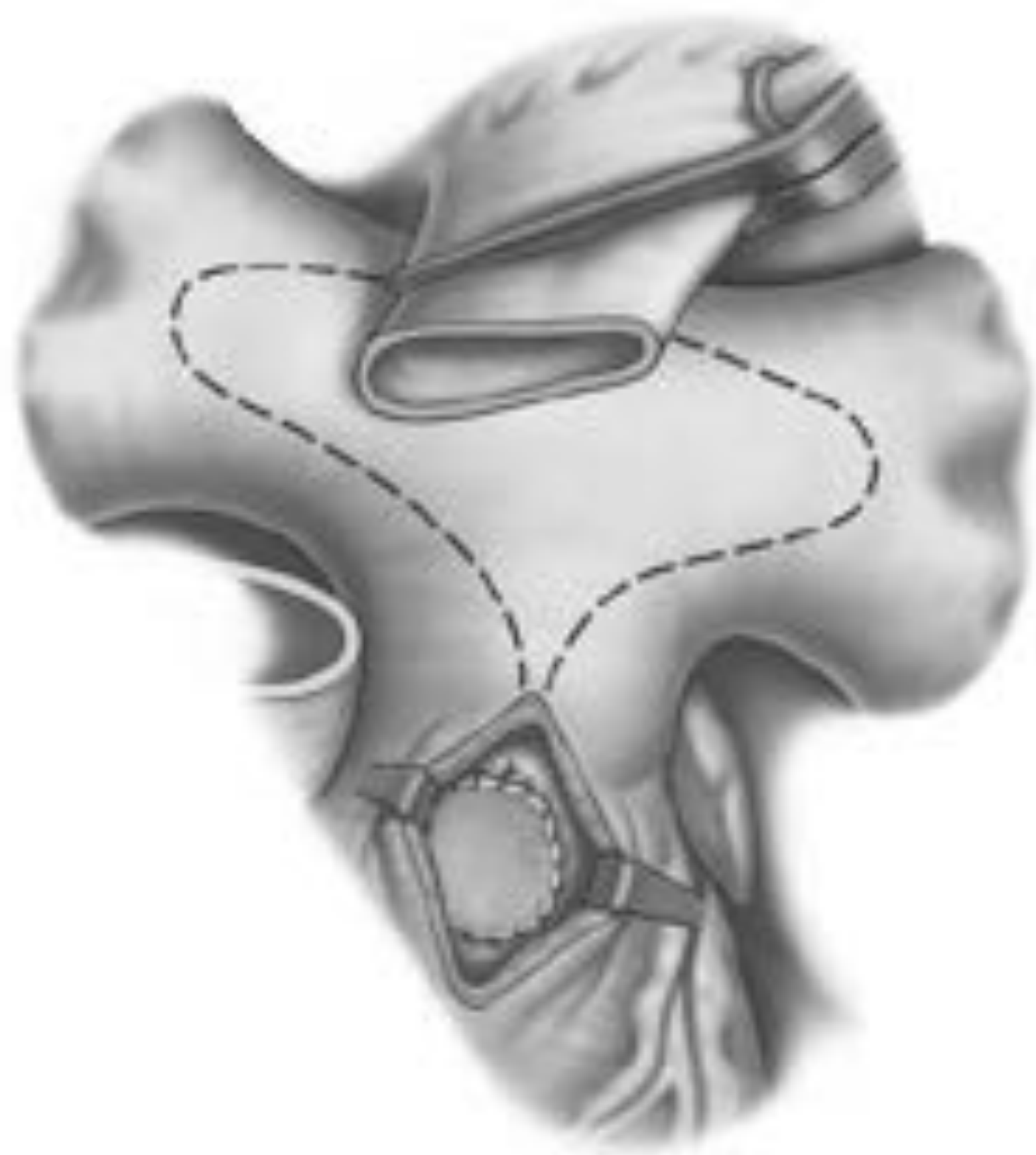
Tetralogy of Fallot with absent pulmonary valve





Tetralogy of Fallot with absent pulmonary valve

Tetralogy of Fallot-Absent pulmonary valve: repair



preoperative

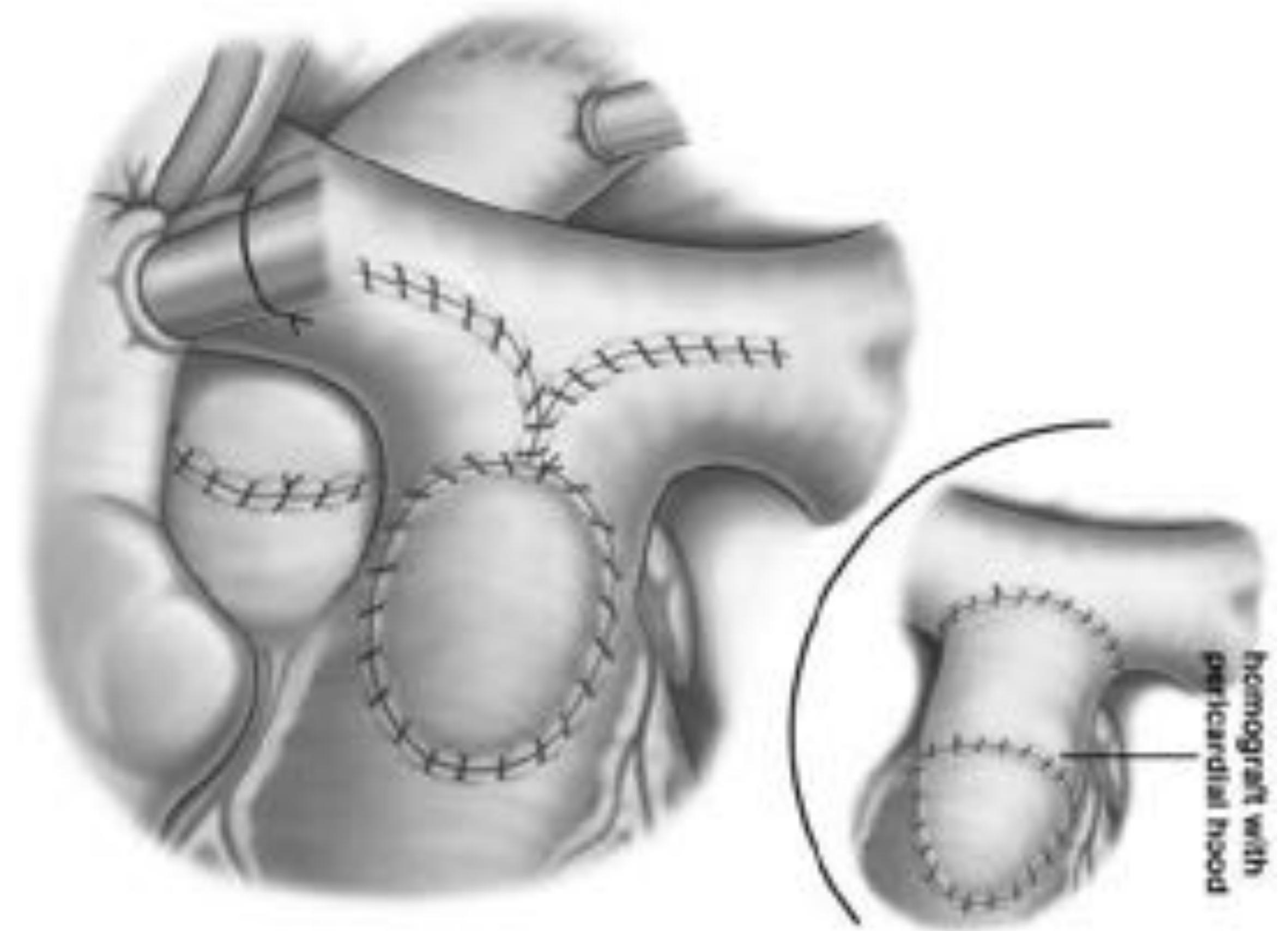


postoperative

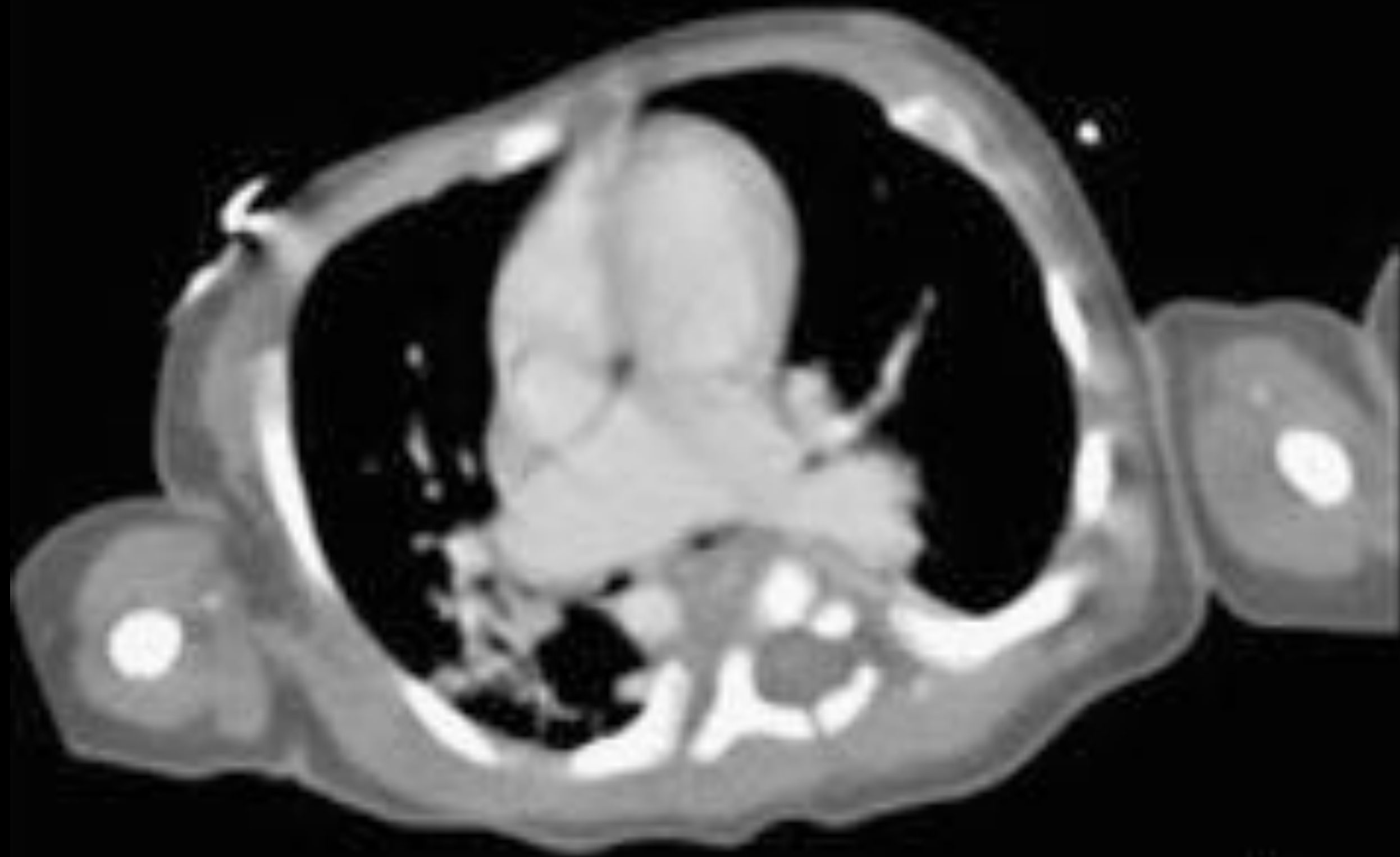


**Tetralogy of Fallot with absent
pulmonary valve**

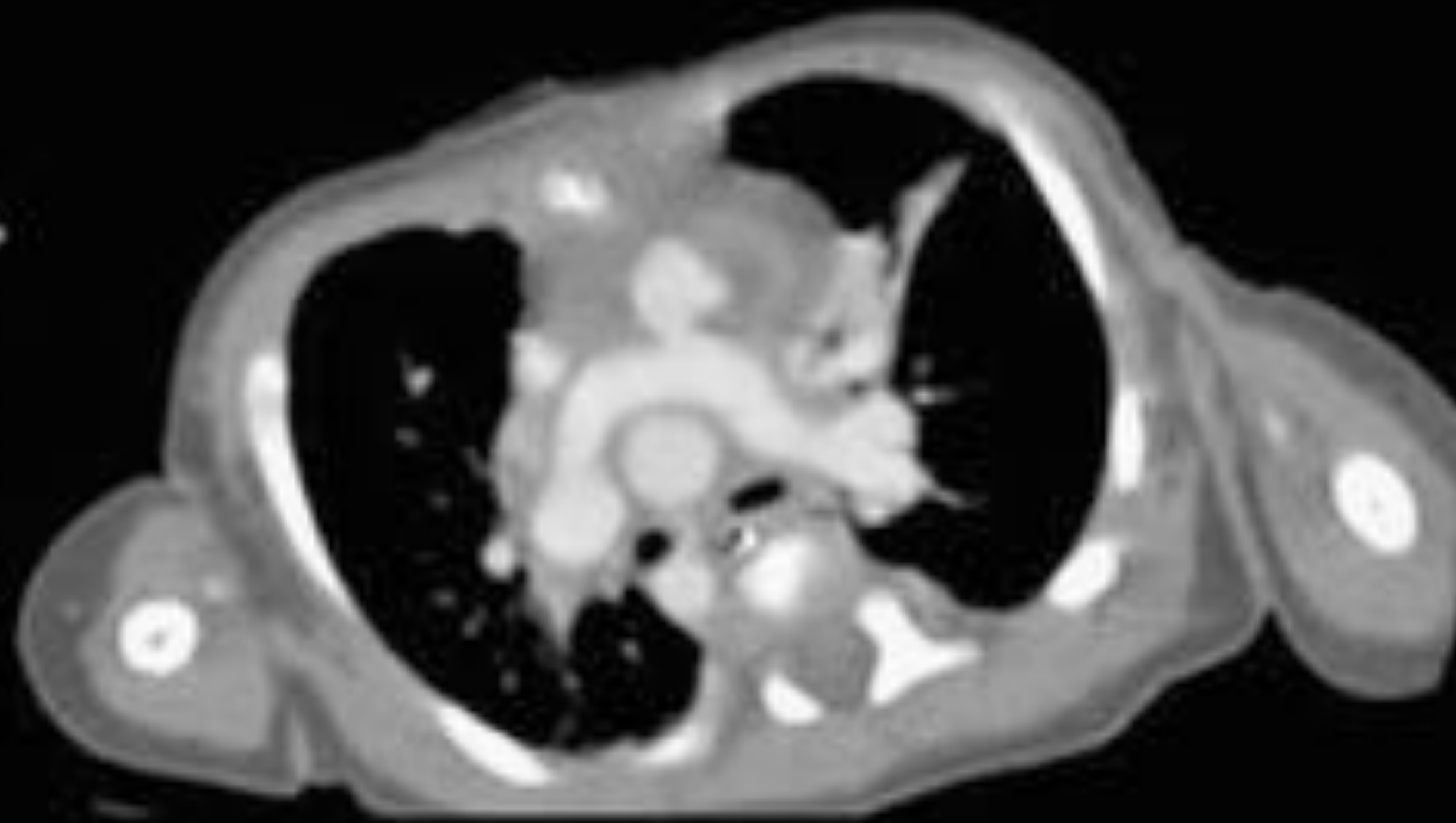
Tetralogy of Fallot-Absent pulmonary valve: repair *With Lecompte manoeuvre*



preoperative



postoperative



**Tetralogy of Fallot with absent
pulmonary valve**



« Tetralogy of Fallot »

Thank you