Transposition of the great arteries

Damien Bonnet

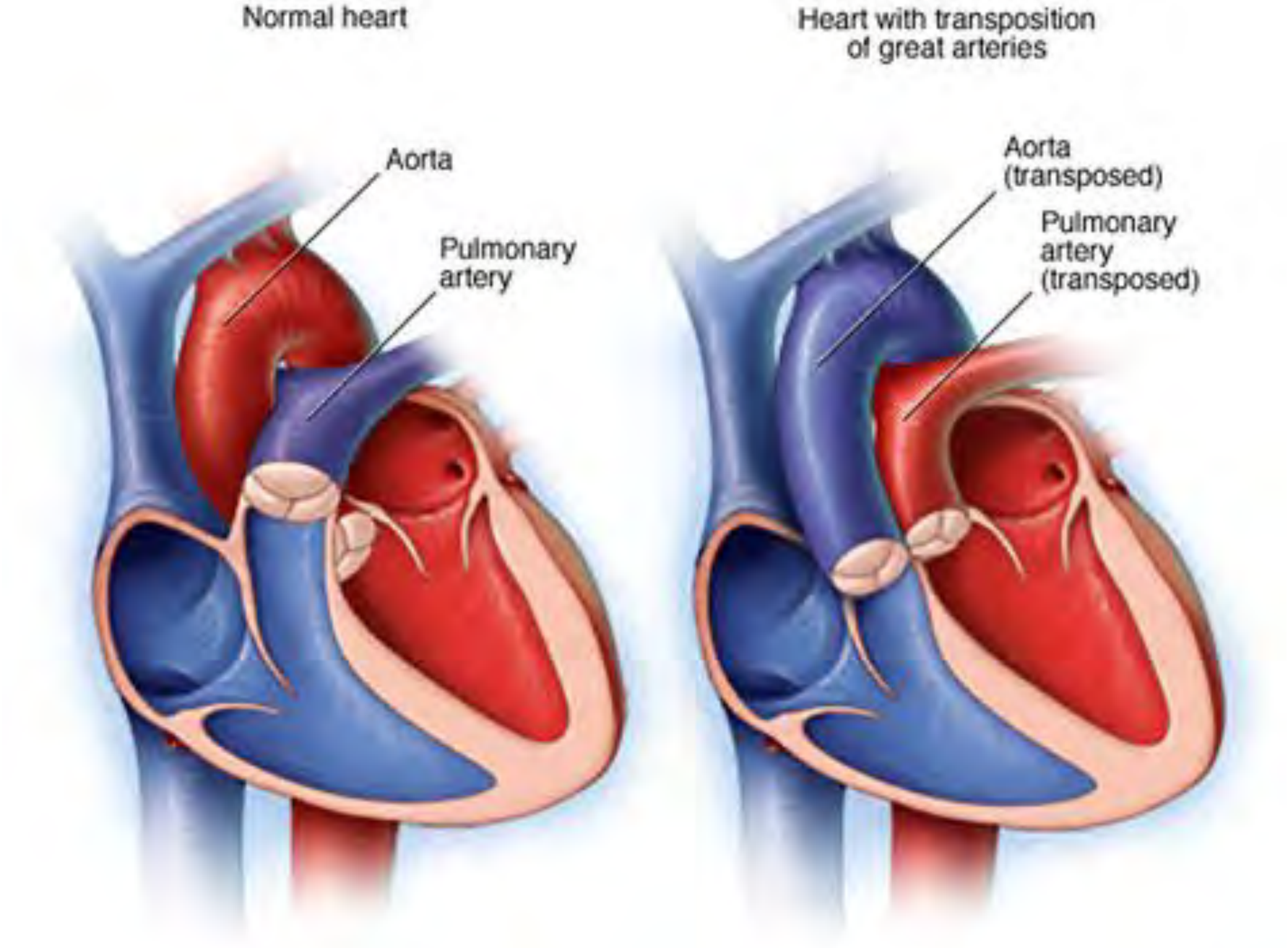
Service de Cardiologie Congénitale et Pédiatrique
Hôpital Universitaire Necker Enfants malades – APHP
Université de Paris
IcarP Cardiology, Institut Hospitalo-Universitaire IMAGINE

Centre de Référence Maladies Rares
Malformations Cardiaques Congénitales Complexes-M3C
Centre de Référence Maladies Rares
Maladies Cardiaques Héréditaires- CARDIOGEN

« **Malpositions** » **of the great arteries**

4 categories

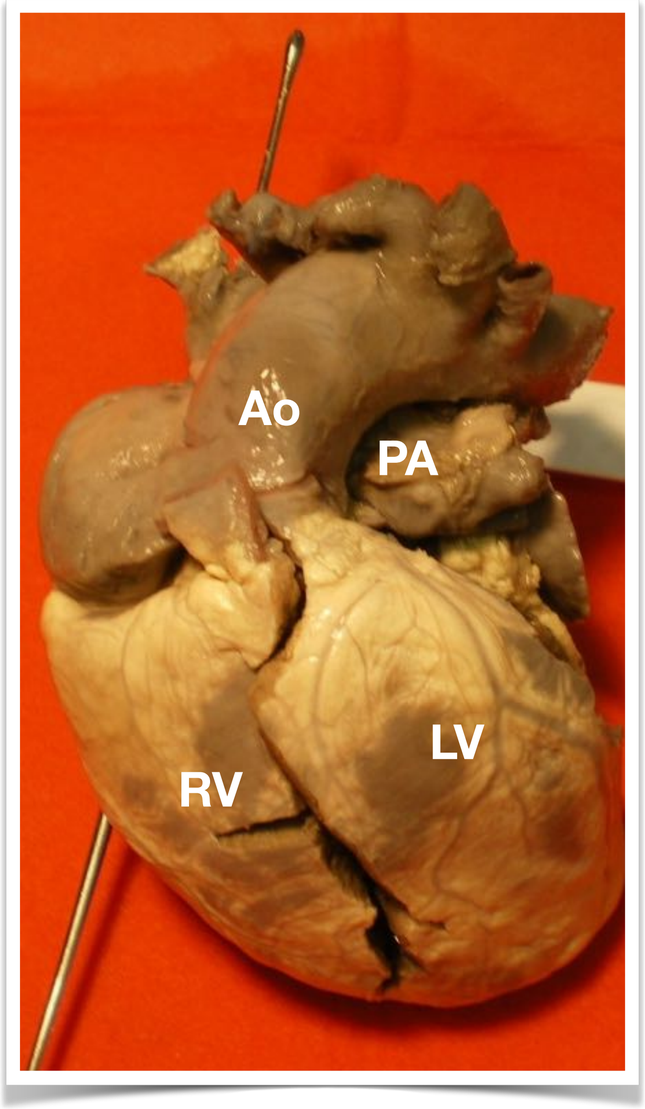
- Transposition of the great arteries
- Double outlet right ventricle
- Double outlet left ventricle
- Anatomically corrected malposition of the great arteries


Normal heart
Aorta
Pulmonary artery
Heart with transposition of great arteries
Aorta (transposed)
Pulmonary artery (transposed)

Anatomy of transpositions of the great arteries

TGA or Ventricle-Arterial Discordance

- Great vessels have parallel course
- Sub-aortic conus
- Fibrous continuity mitral and pulmonary valve
- D-transposition with Aorta anterior and right
- Segment analysis
  - most frequently {S,D,D}
  - sometimes {I,L,L} (mirror image)
  - rarely exception to the looping rule {S,D,L} or {I,L,D}

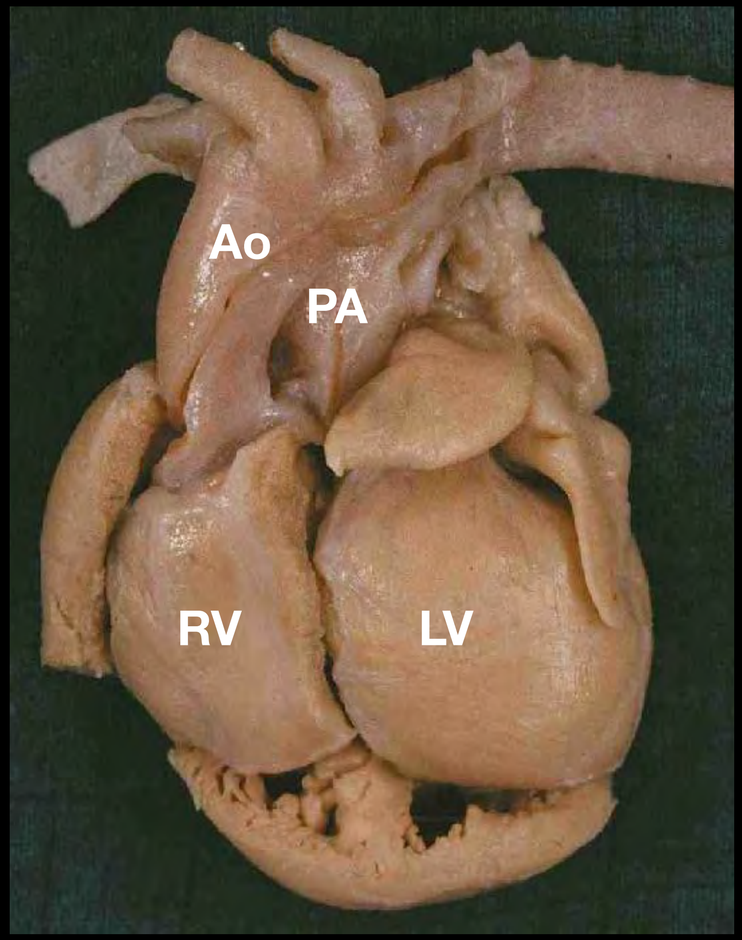


Anatomical variation of TGA

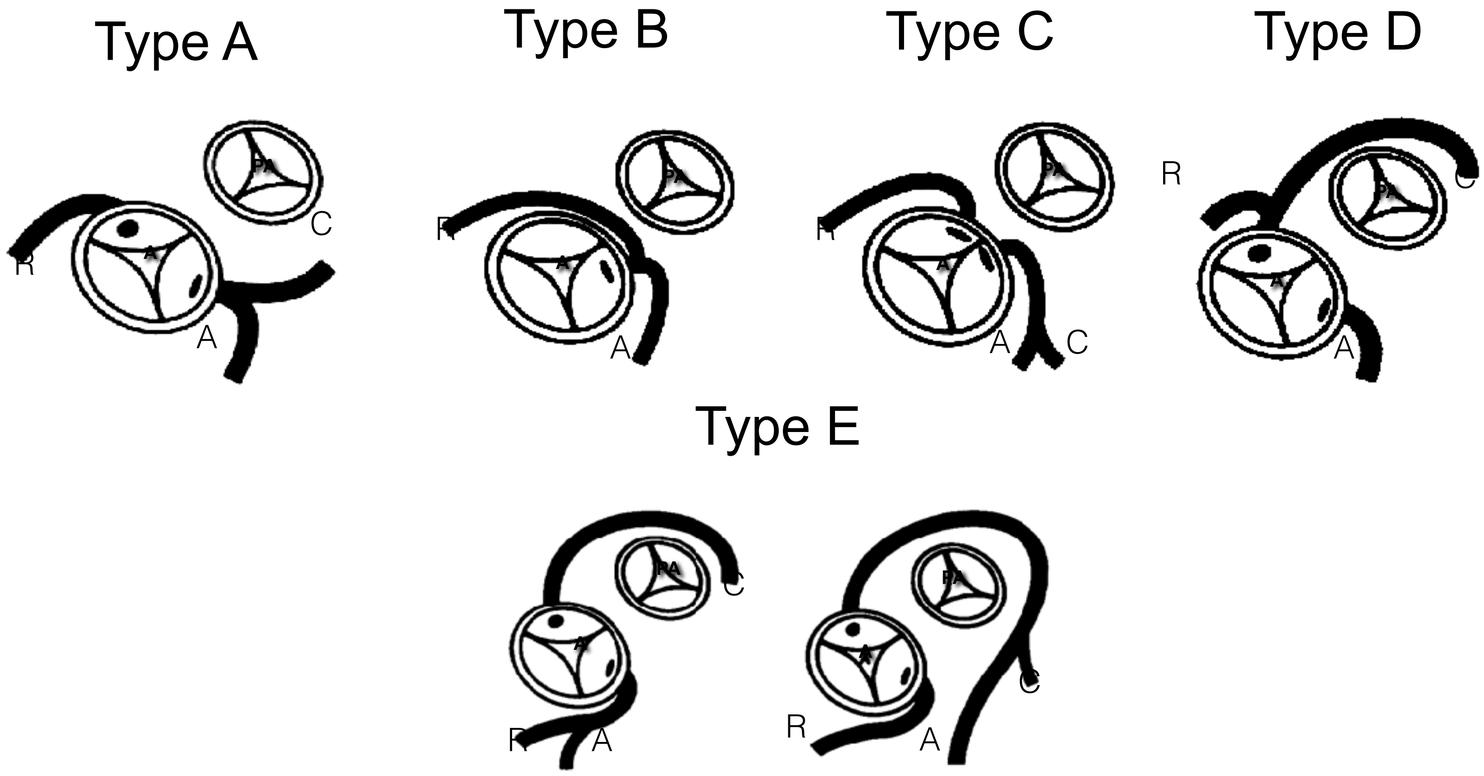
- Variants of simple TGA
  - Relative sizes of the conus
  - Relative position of great vessels
  - Variants in coronary anatomy
- Associated anomalies
  - VSD
  - LVOT obstructions
  - RVOT obstructions
  - AV valves anomalies : straddling and clefts

Left juxtaposition of the atrial appendages

- 2 to 5% of cases
- Frequently associated with other anomalies : dextrocardia, hypoplasia of right ventricle, bilateral conus



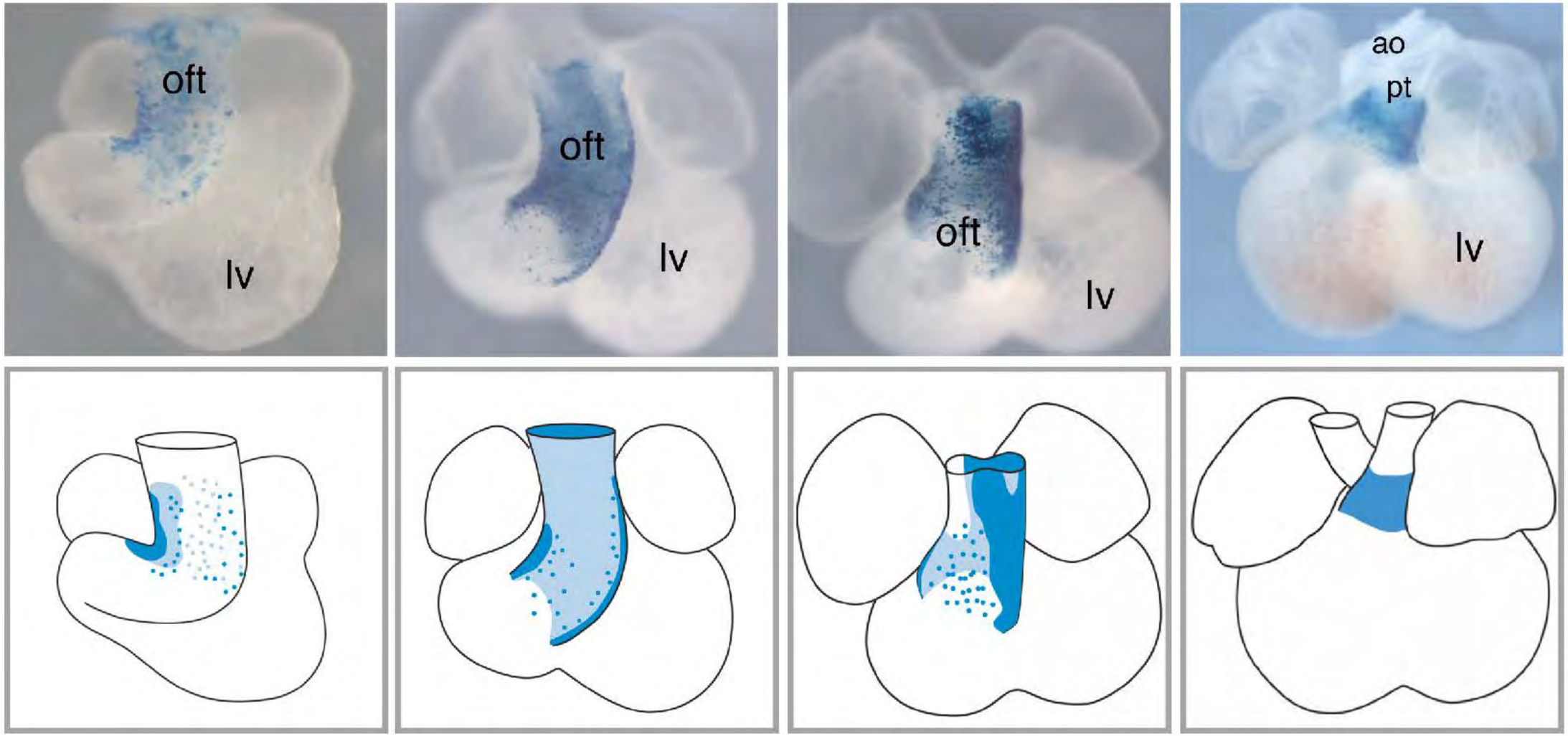
Coronary arteries in TGA



Yacoub and Radley-Smith classification

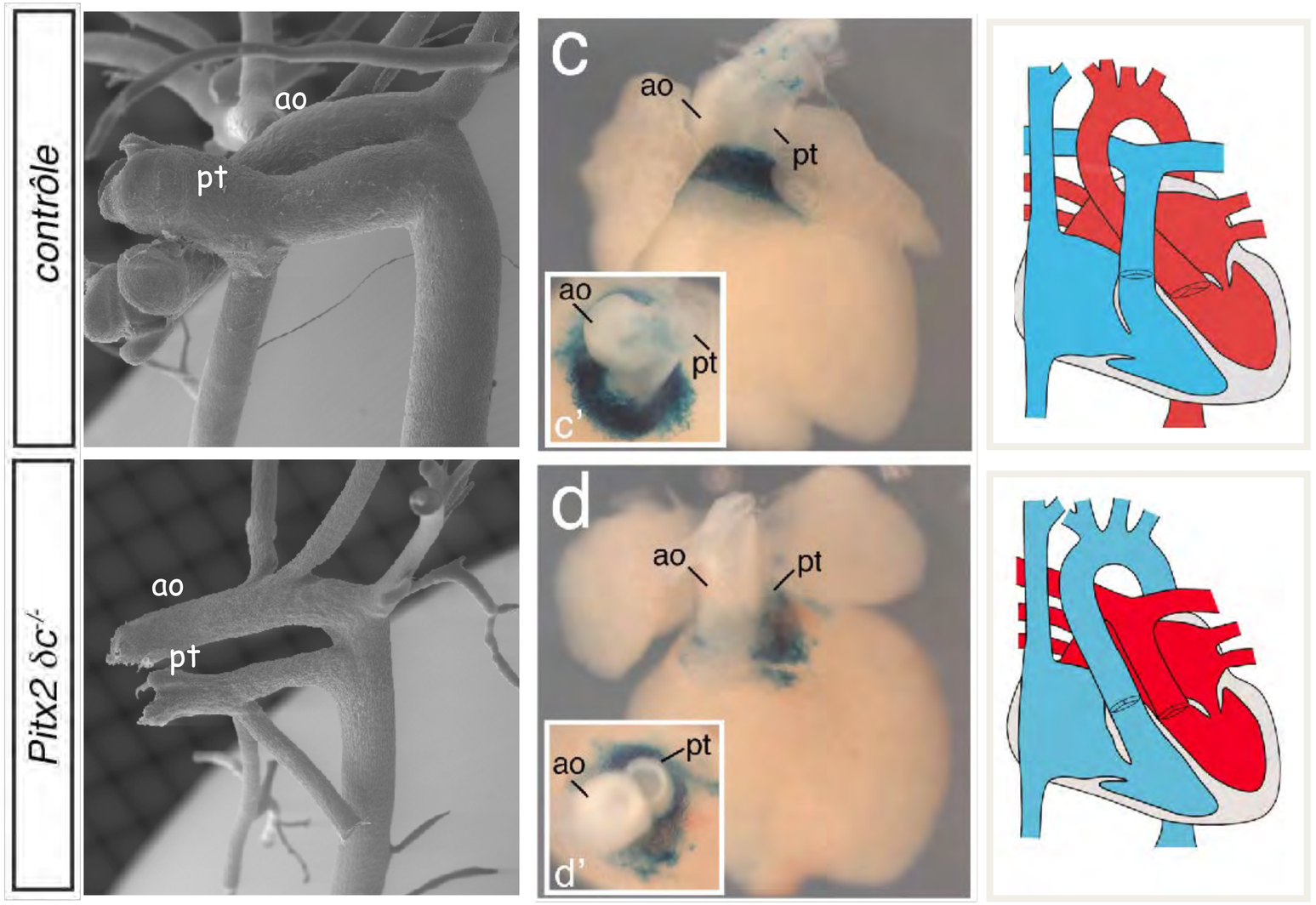
What causes transposition of the great arteries ?

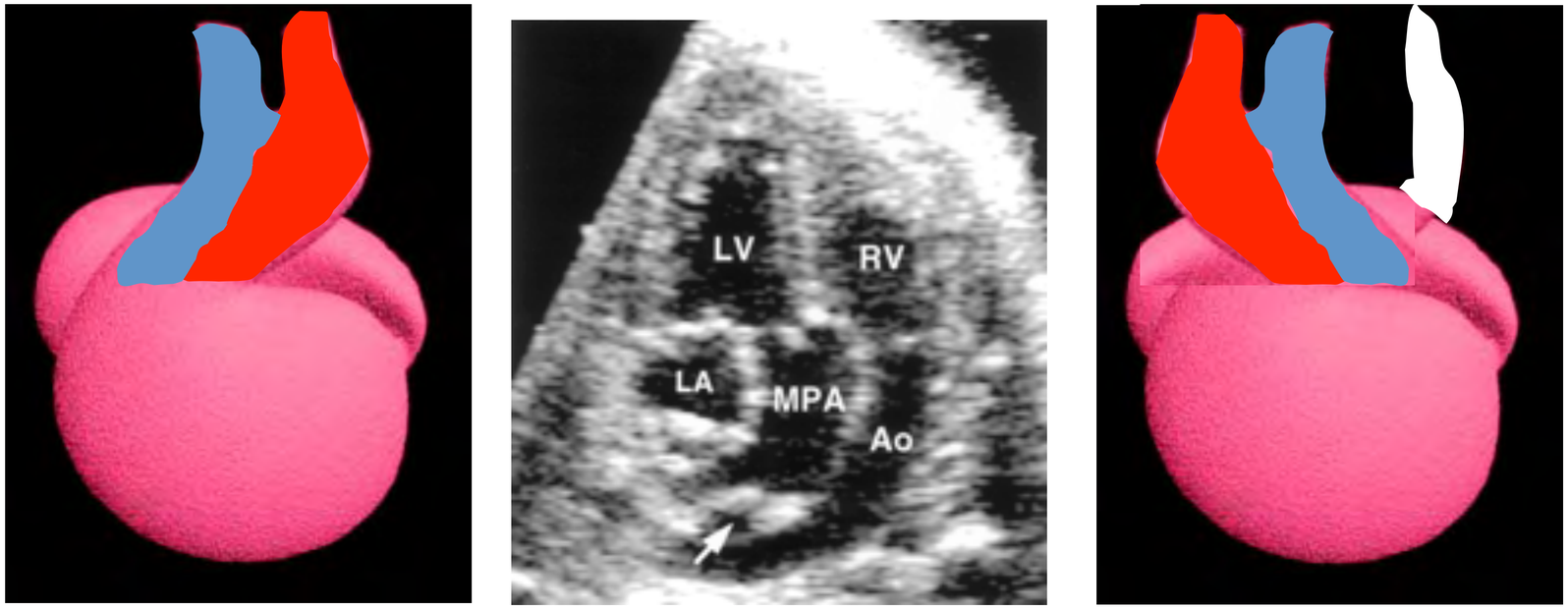
96-16 provides direct evidence for rotation of outflow tract myocardium

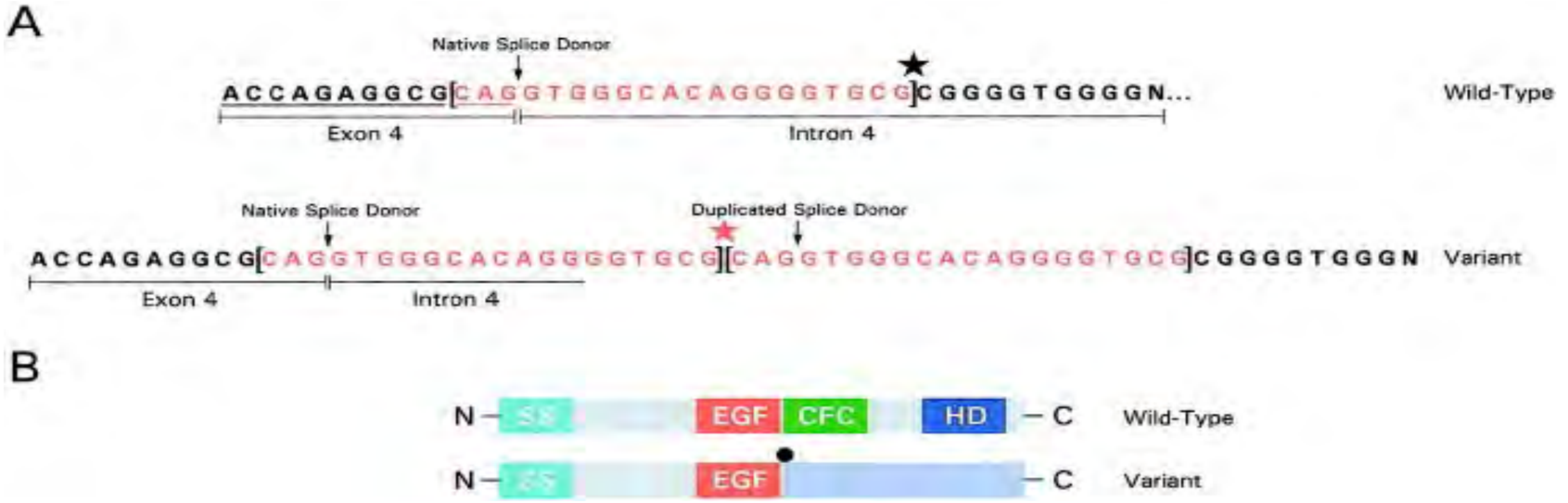


96-16 expression in Pitx2δc heart with TGA

- Transposition of the great arteries with a rotation defect
- Normal septation and normal neural crest cell migration
- Defect of left-right signalling







CFC1 mutations and TGA/DORV

ZIC3 mutations in TGA

Foetal TGA

The French system during pregnancy

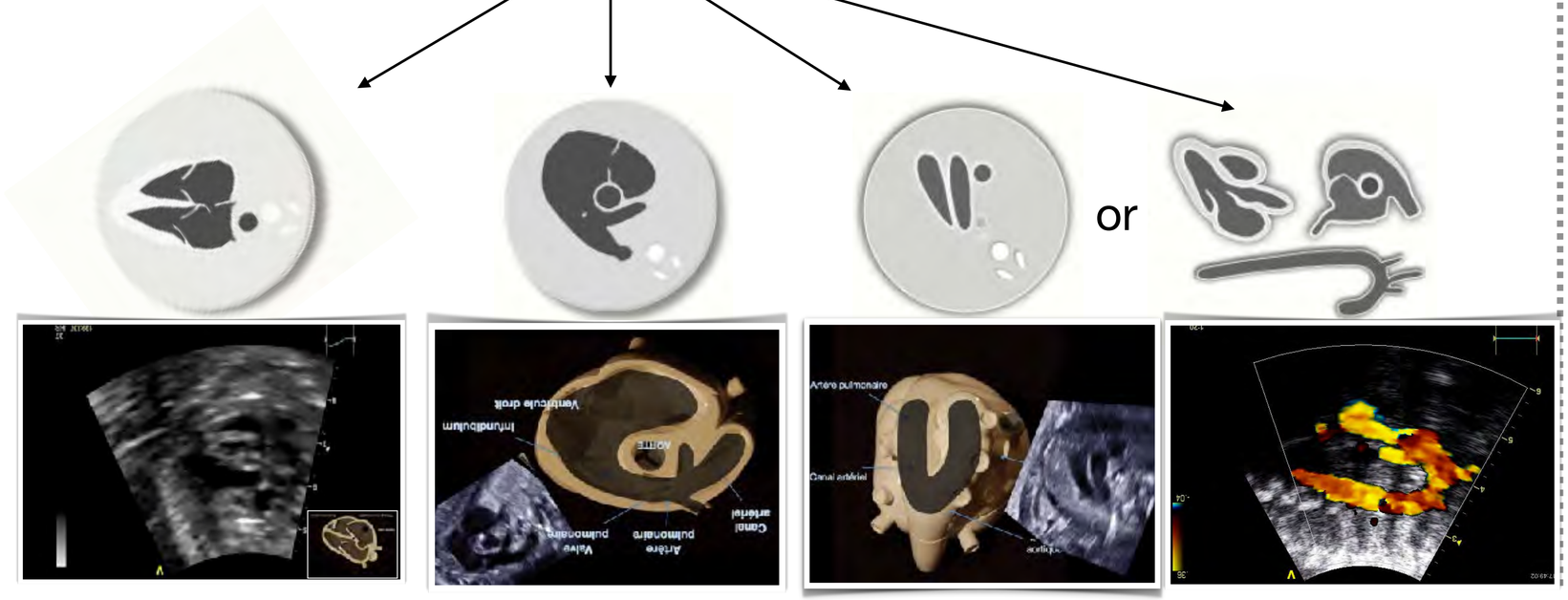
3 systematic foetal echographies - Level 1

11 Weeks — 18-22 Weeks — 32-34 Weeks

Nuchal translucency
Term
Number fetuses

Morphology

Growth
Malformations



In case of anomaly
or difficulty in assessing
normality

Level 2

Expert foetal
echography

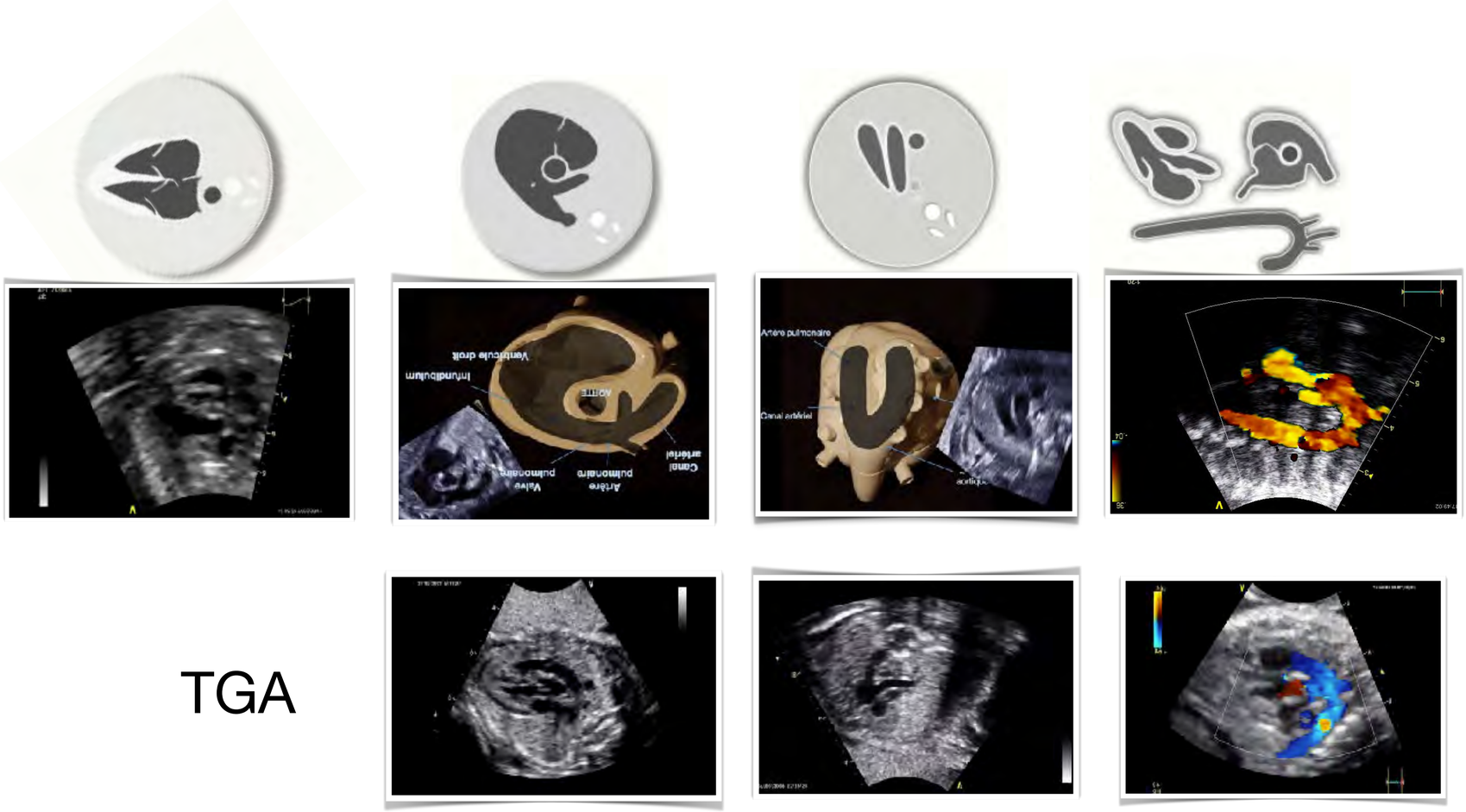
If heart anomaly is confirmed

↓

Level 3

Fetal echocardiography
by expert

Prenatal diagnosis of TGA



TGA

Preoperative mortality in TGA = 4-6%
(*vs./+)* Surgical mortality = 1-2%

Comparison of Characteristics of Patients in the Prenatal and Postnatal Groups

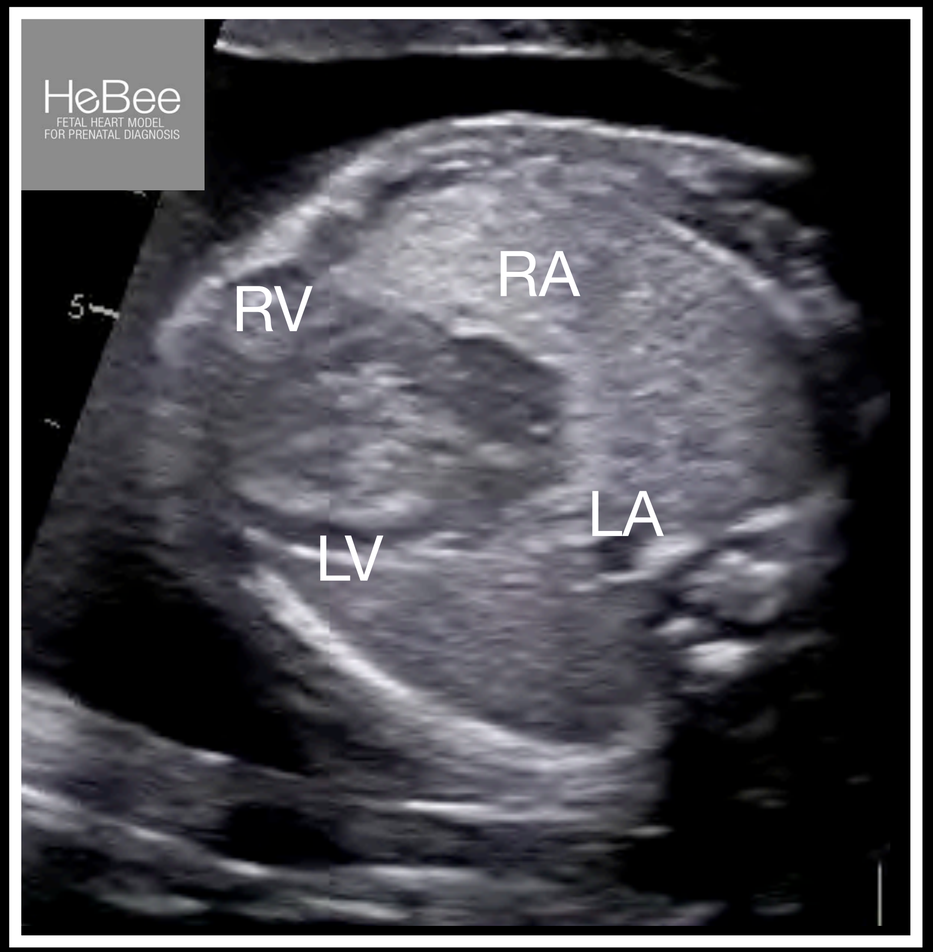
	Postnatal Group	Prenatal Group	*P*
Isolated TGA	204	57	NS
Associated defects	46	11	NS
VSD	31	8	NS
VSD+CoA	14	3	NS
CoA	1	1	NS
Age at admission, h	73±210	2.2±2.8	<0.01
Mechanical ventilation	95 (38)	12 (17.6)	<0.01
Metabolic acidosis±MOF	56	8	<0.05
PGE_1 infusion	95	32	NS
BAS	168	54	NS
Preoperative mortality	15	0	<0.05
Coronary artery pattern	233 ASO	68 ASO	
Normal	168	47	NS
Abnormal	65	21	NS
Postoperative mortality	20	0	<0.01
Hospital stay, d	30±17	24±11	<0.01

VSD indicates ventricular septal defect; CoA, coarctation; MOF, multiorgan failure; PGE_1, prostaglandin E_1; BAS, balloon atrioseptotomy; and ASO, arterial switch operation. Values are n (%).

Bonnet D et al. Circulation 1997

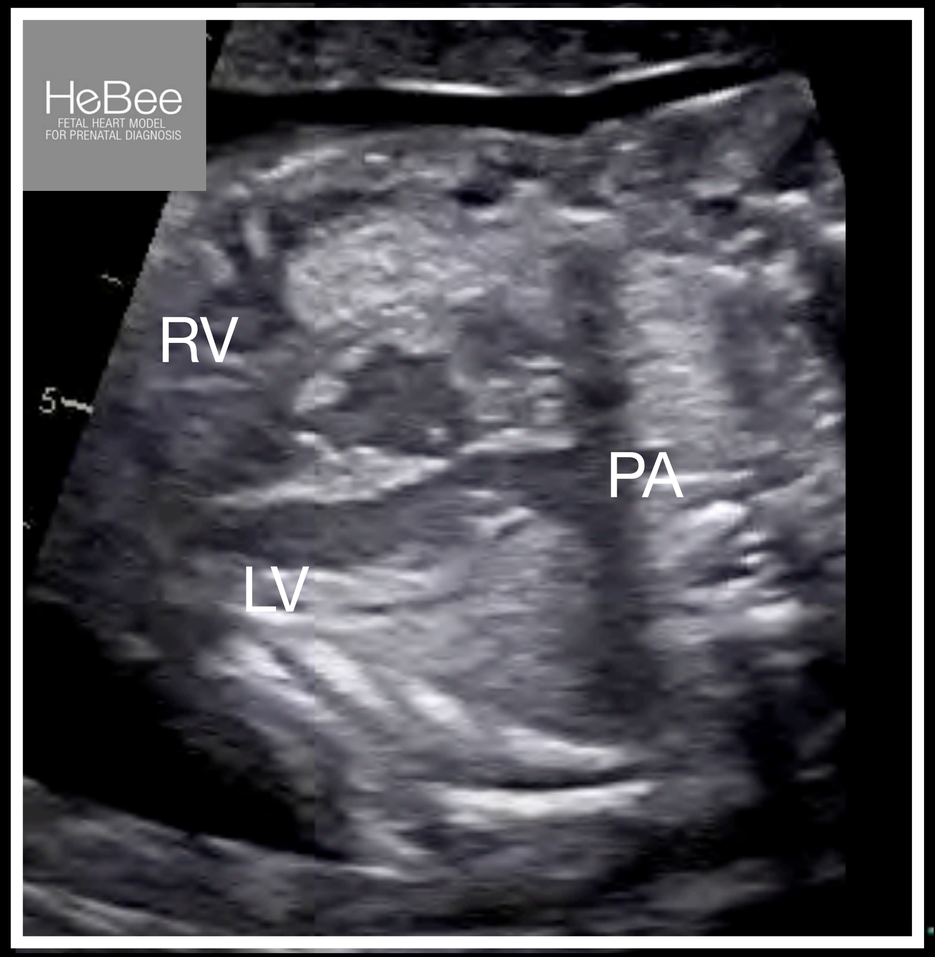
TGA

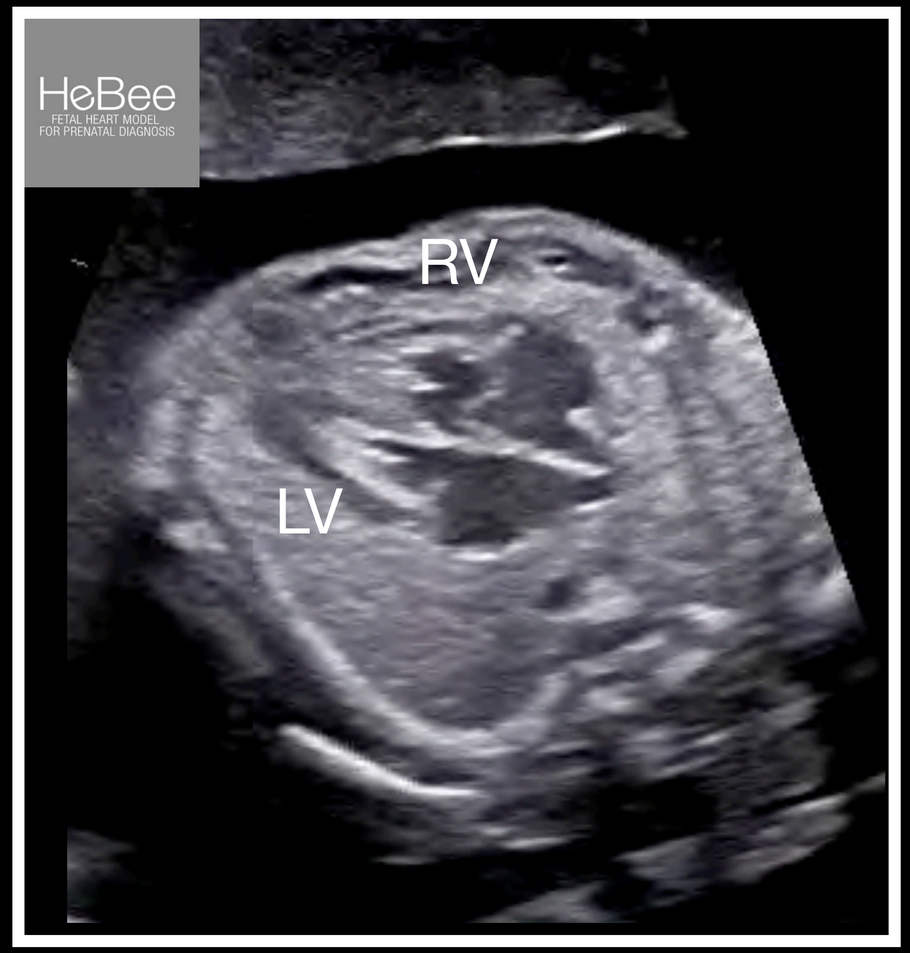
situs & 4 chamber view



Courtesy Bertrand Stos - HeBee

TGA
LVOT view

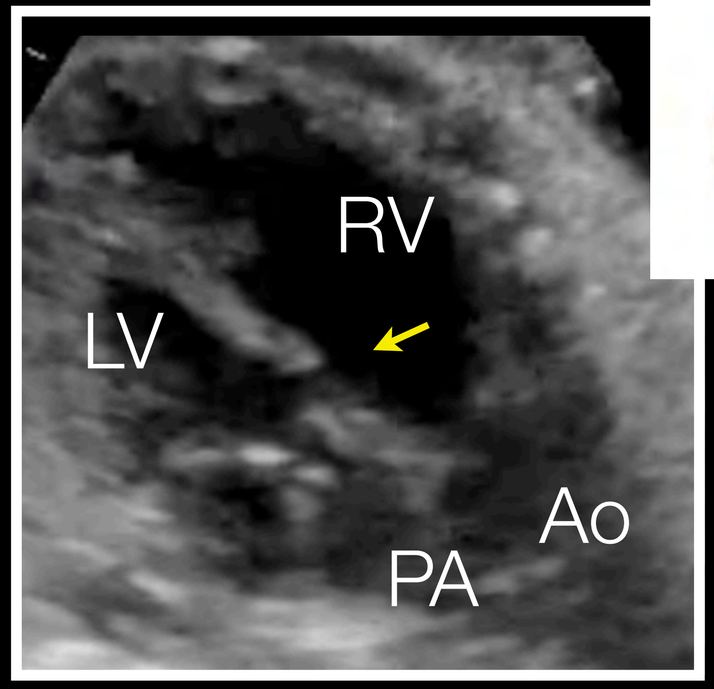


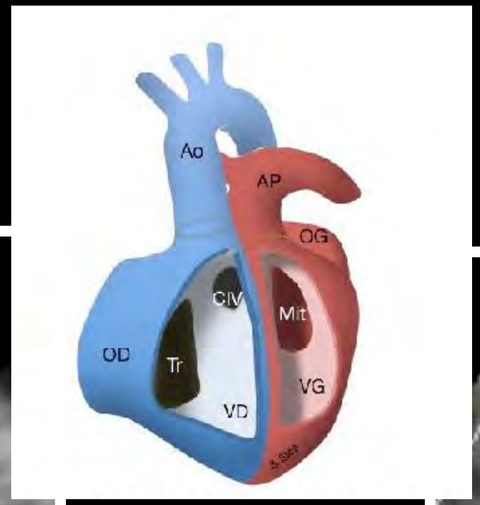


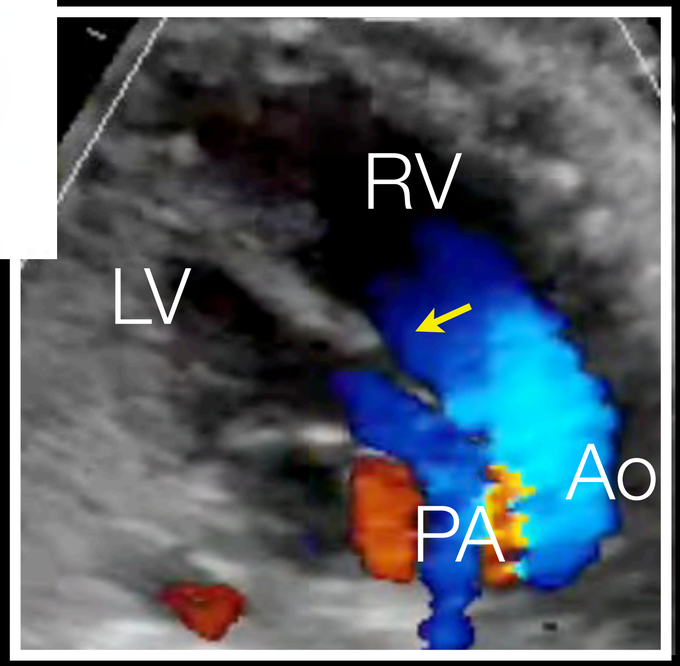
Courtesy Bertrand Stos - HeBee

TGA

Complex forms



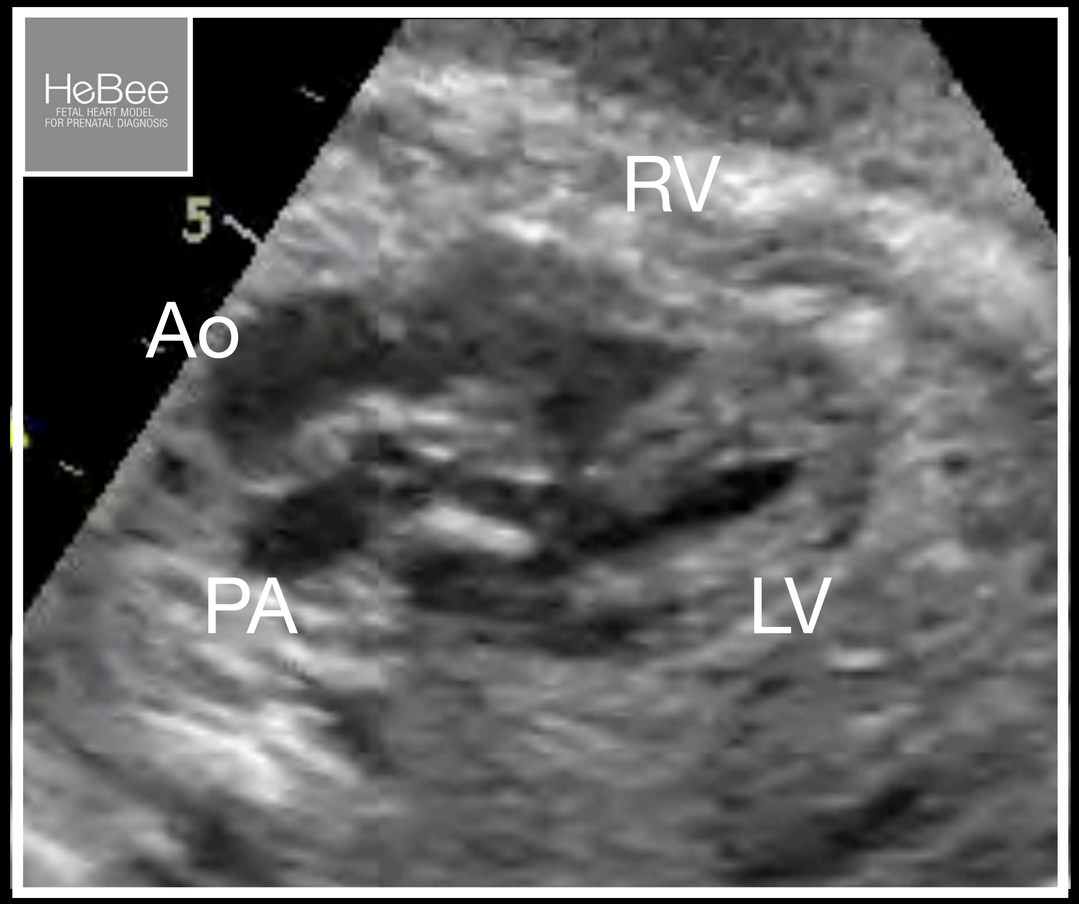




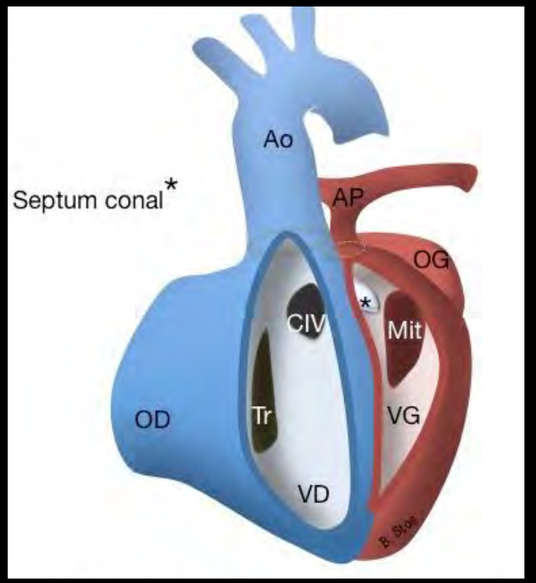
TGA-membranous VSD

TGA

Complex forms



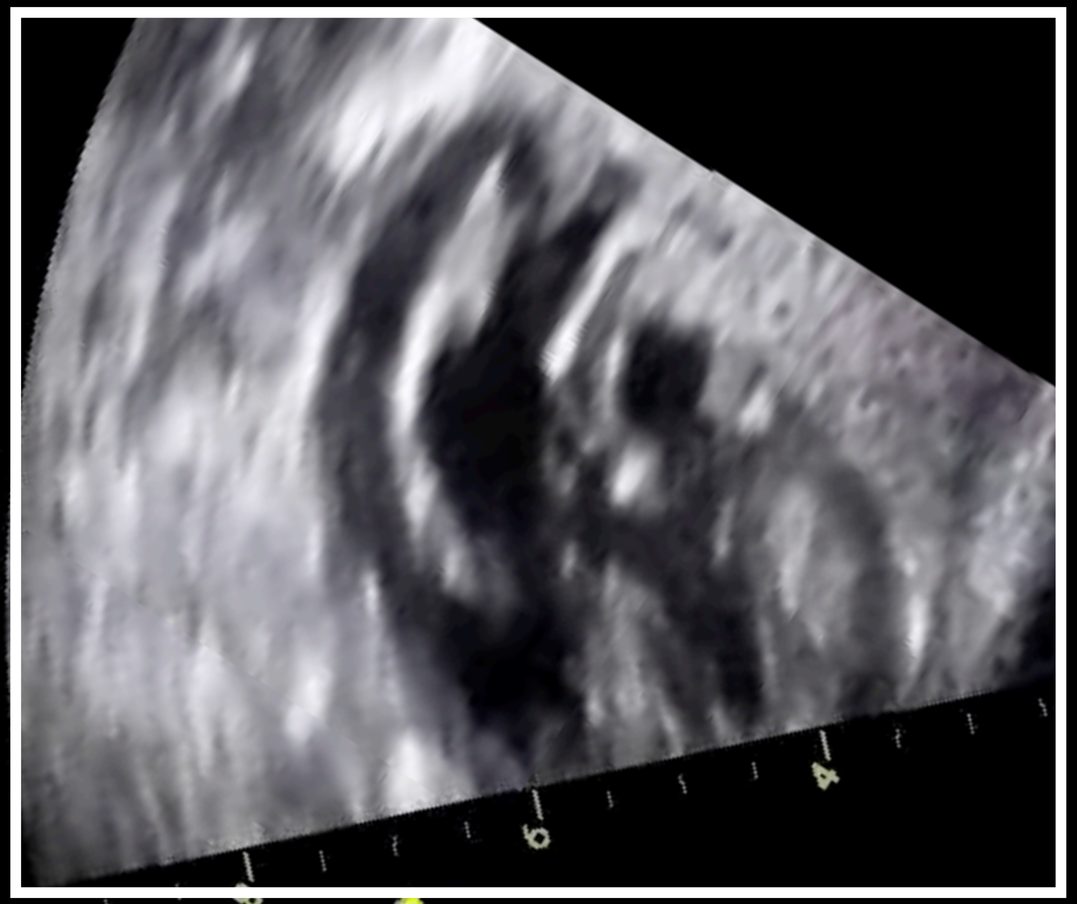
TGA-VSD-PS



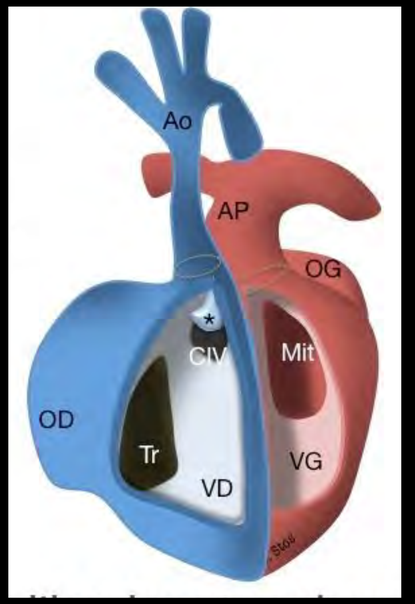
Courtesy Bertrand Stos - HeBee

TGA

Complex forms



TGA-VSD-Coa



Chromosomal anomalies in fetal CHD

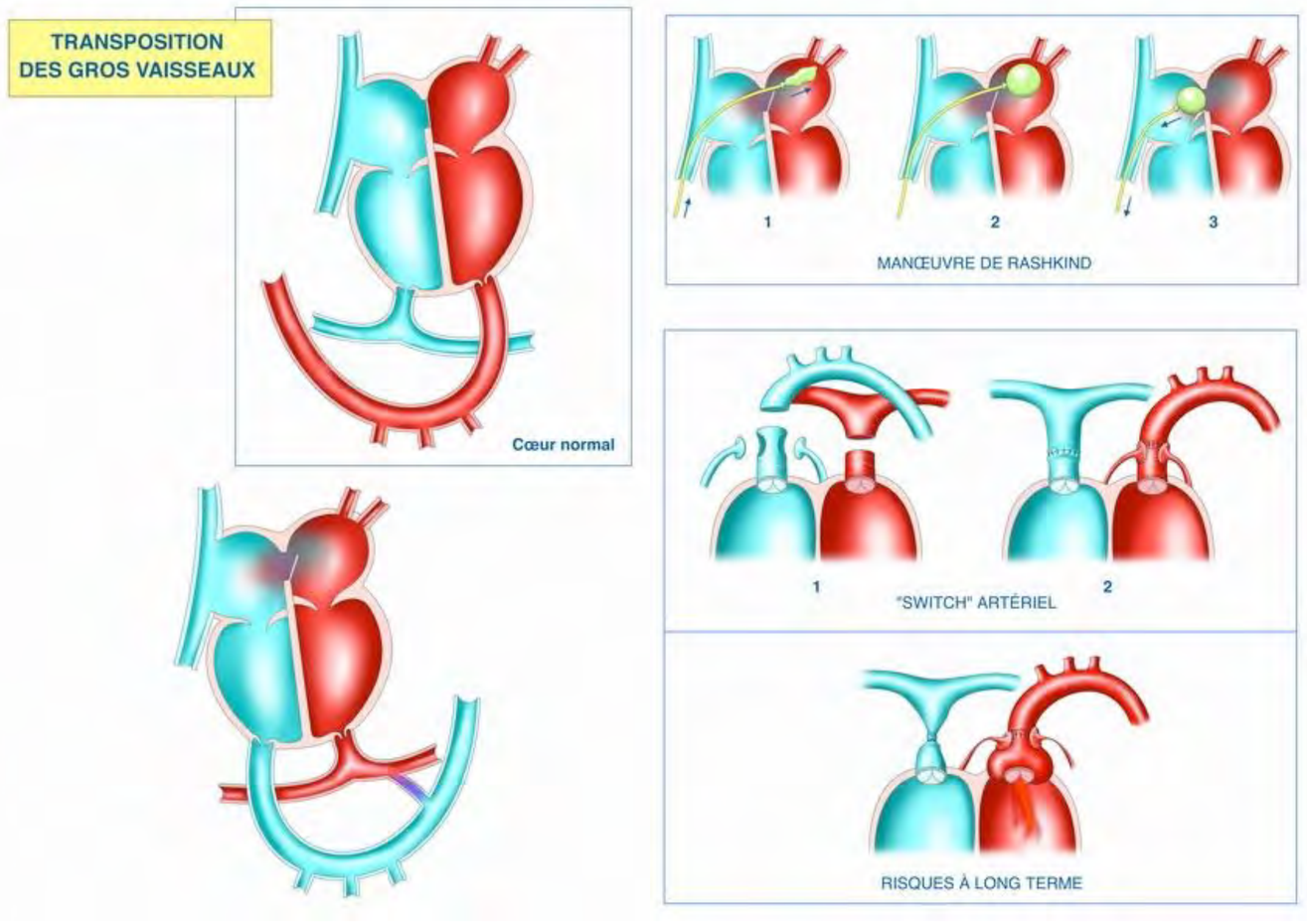
548 CHD-18.5%

PA-IVS and PS	0	0
Left heart obstruction	12/130	9.2%
6 XO; 3 T18; 3 translocations		
Conotruncal defects	23/91	25%
20 del22q11; 1 T21; 2 translocations		
AVSD	32/68	47%
28 T21; 3 T18; 1 XXX		
VSD	12/74	16%
9 trisomies, 2 del22q11, 1 del5		
Transposition of the great vessels	0	0
DORV	7/38	18%
Univentricular heart	2/24	8%
2 T18		

Prenatal diagnosis of transposition of the great arteries

Perinatal organization in Paris

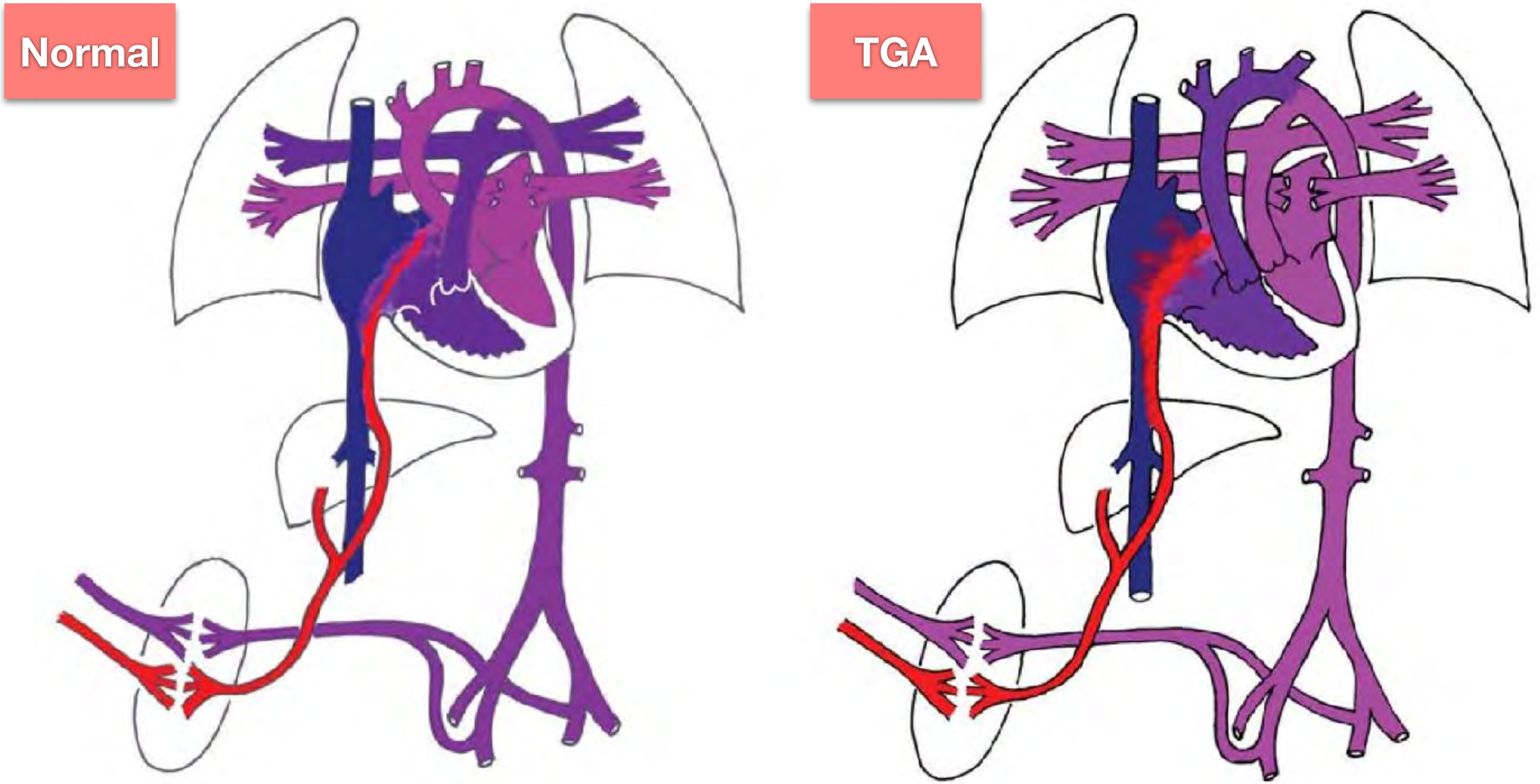
- Organisation of foetal cardiac growth surveillance
  - Foramen ovale and arterial duct
- *In utero* transfer organisation
- Organisation of perinatal management
- Prevention of early neonatal demise
- Prepare the parents to the future even
- Post-natal management and follow-up



Bonnet et al. Circulation 1997; Maeno YV et al. Circulation 1999; Jouannic et al. Circulation 2004; Van Velzen C et al. Ultrasound Obstet Gynecol 2015; 45: 320–325
Escobar-Diaz MC et al. Ultrasound Obstet Gynecol. 2015 June ; 45(6): 678–682.

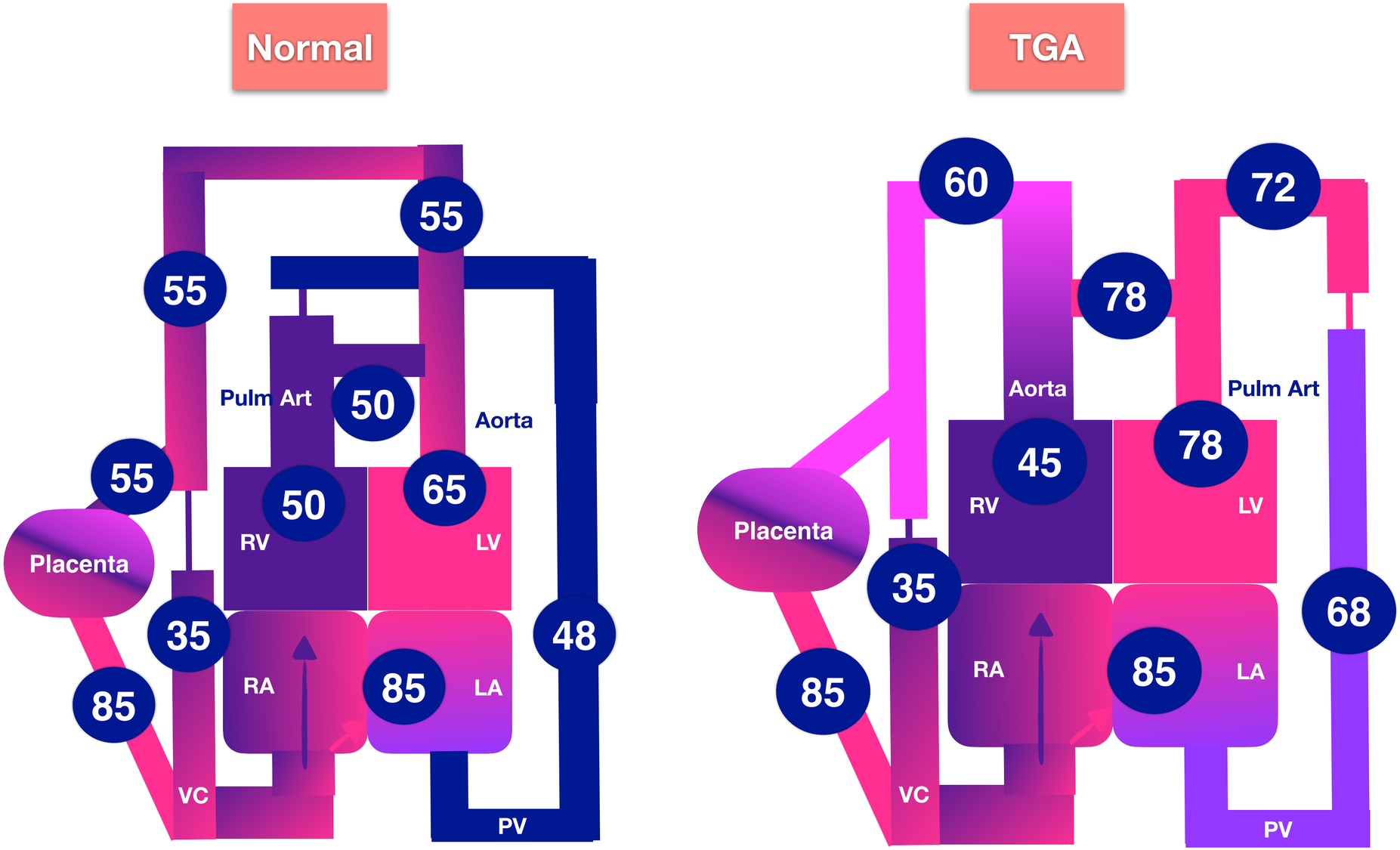
Physiology of TGA

Morphological and physiological consequences of the fetal circulation in TGA



Sun L et al. Circulation. 2015;131:1313-1323.

Morphological and physiological consequences of the fetal circulation in TGA

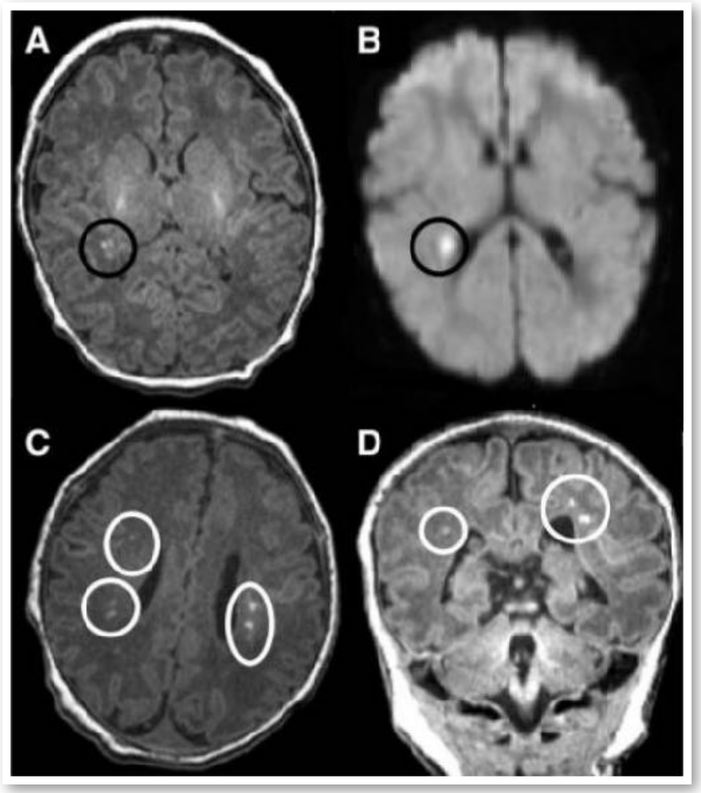


Rudolph A. Ped Res 2007;61:375-80
Prsa M et al. Circ Cardiovas Imaging 2014;7:663-70

Prenatal white matter MRI anomalies in children with cyanotic congenital heart diseases

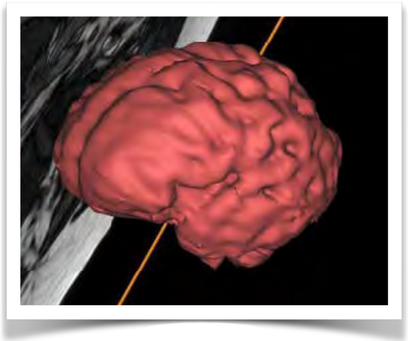
- **White matter lesions in** 30 to 40% of newborns with TGA (Miller et al., 2004; Licht et al., 2009)

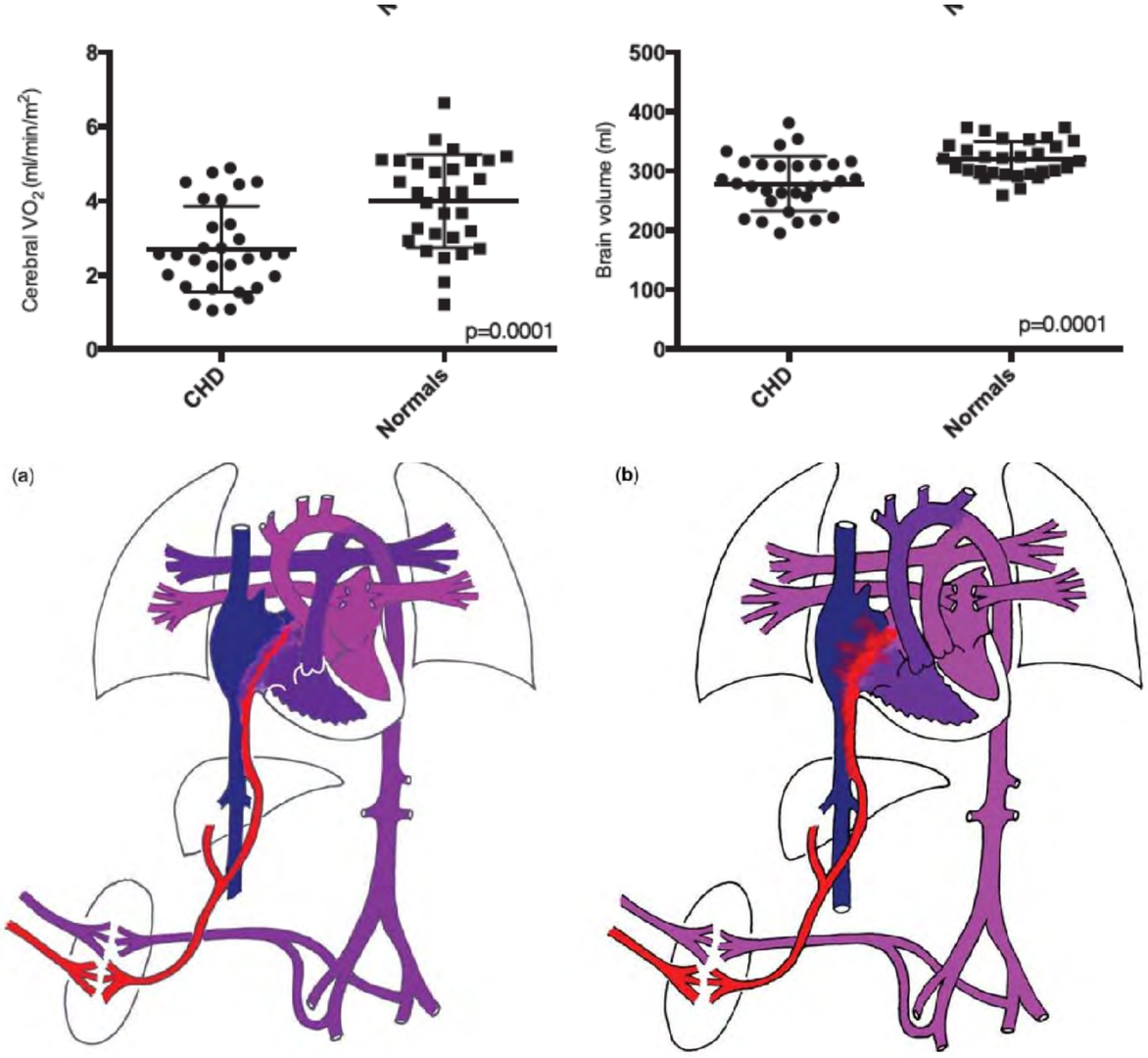
- Same type of anomalies but more severe in complex CHDs such as HLHS (Mahle et al., 2002).



Periventricular white matter lesions in a child with TGA **before** the arterial swicth.
Petit et al., 2009 *in Circulation*

Type of CHD and prenatal brain perfusion

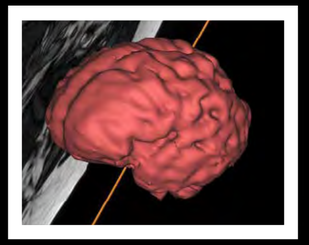




Mechanisms for reduced cerebral oxygenation and impaired brain growth in fetuses with CHD

1-In TGA, streaming results in well oxygenated blood being directed to the pulmonary circulation, whereas the blood supplied to brain is derived largely from more deoxygenated blood returning from the caval veins.
2-Reduction in Umbilical Vein Sao2, which is suggestive of abnormal placental function and results in lower fetal O2 delivery even in the setting of normal CVO and UV flow.

Sun L et al. Circulation. 2015;131:1313-1323.

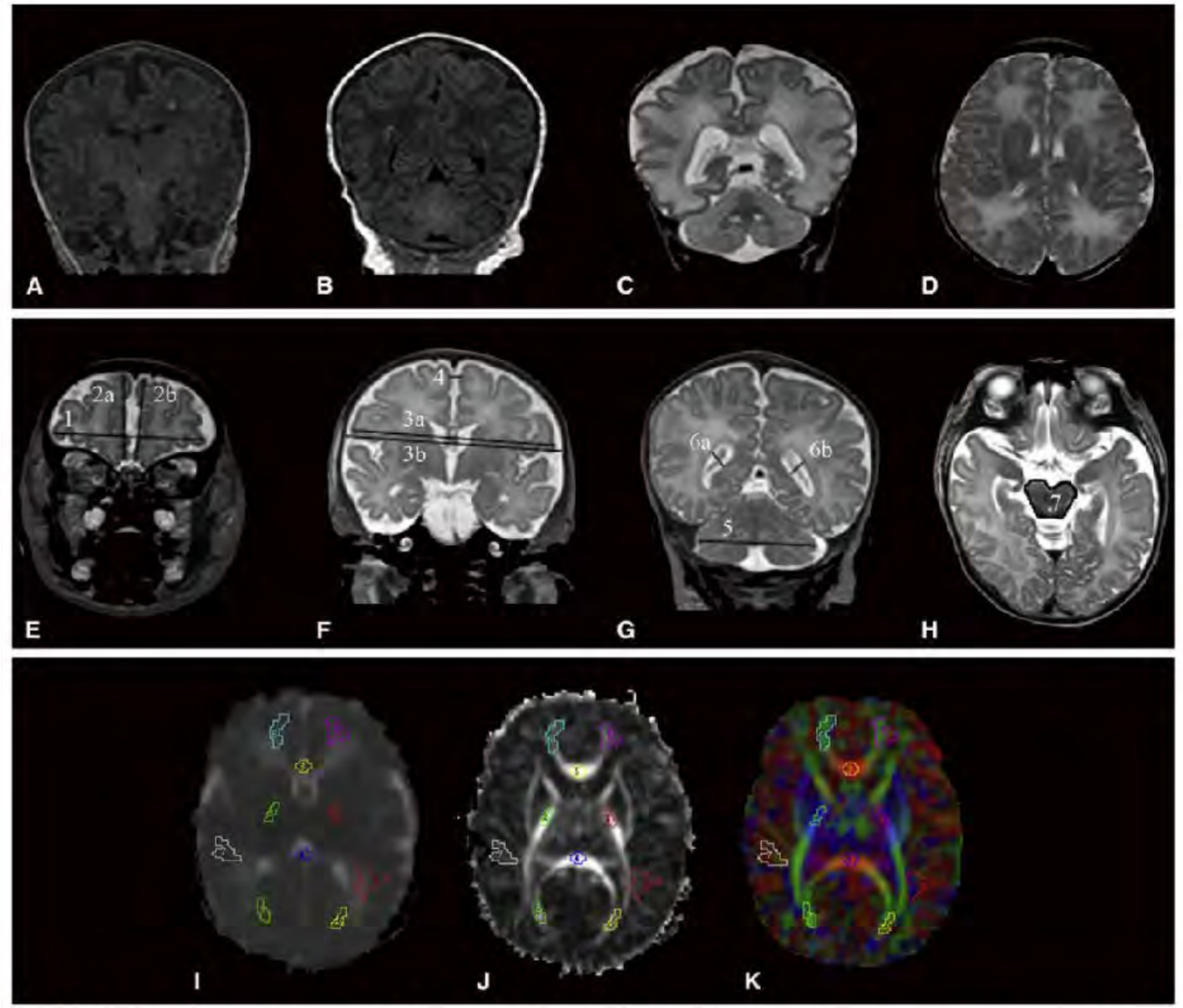


Brain dysmaturation observed in CHD appears to confer increased susceptibility to white matter injury in the perioperative period and neurodevelopmental deficits at 2 years.

The identification of fetal hypoxia as a potentially modifiable cause of delayed fetal brain development
may be clinically significant.

Oxygen saturations in the fetal sheep and human fetuses circulation can be augmented through increases in the oxygen concentration of maternal inhaled air.

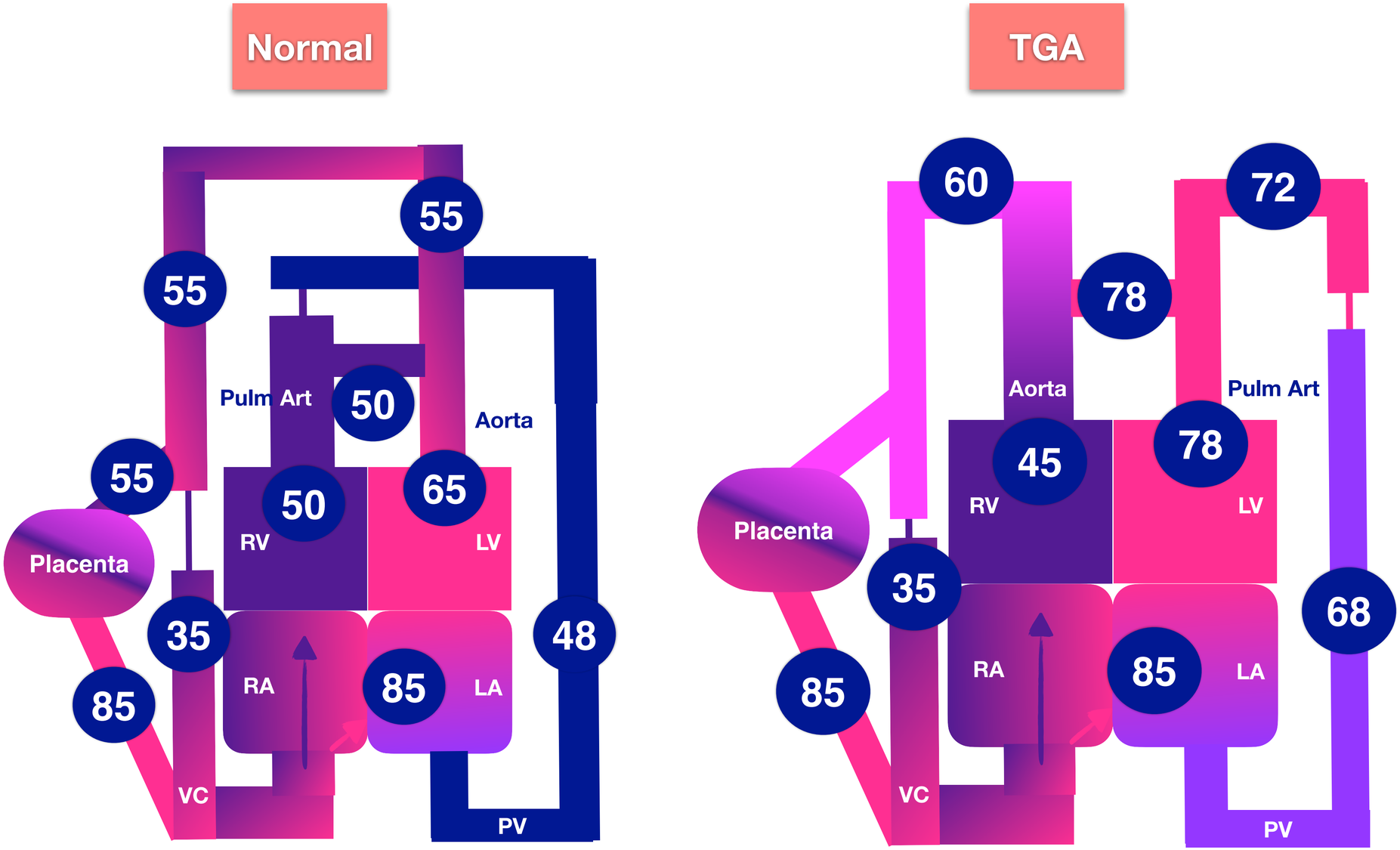
Maternal hyperoxygenation could be a method to improve brain development in utero



IGURE 1. A–D, Qualitative scoring abnormalities. A, T_1-weighted image with abnormalities that included focal signal abnormality, delayed myelination posterior limb of the internal capsule, increased extra-axial space, and delayed gyrification. B, T_1-weighted image with bilateral focal signal abnormalities nd delayed gyrification. C, T_2-weighed image with ventriculomegaly, diffuse excessive high-signal intensity *(DEHSI)*, increased extra-axial space, and oderate-to-severe delay in gyrification. D, T_2-weighted image with DEHSI. E–H, Subset of brain metrics. 1, Bifrontal diameter; 2a, right frontal height; b, left frontal height; 3a, brain biparietal diameter; 3b, bone biparietal diameter; 4, interhemispheric distance; 5, transverse cerebellar diameter; 6a, right entricular diameter; 6b, left ventricular diameter; and 7, brainstem area. I–K, Diffusion imaging: I, mean diffusivity; J, fractional anisotropy; K, red, green, lue color plot. Regions of interest were the same for each image (from top to bottom): left and right frontal white matter, genu of the corpus collosum, left nd right posterior limb of the internal capsule, splenium of the corpus collosum, left and right subcortical white matter, and left and right optic radiation.

J Thorac Cardiovasc Surg 2012;143:1264-70

Morphological and physiological consequences of the fetal circulation in TGA



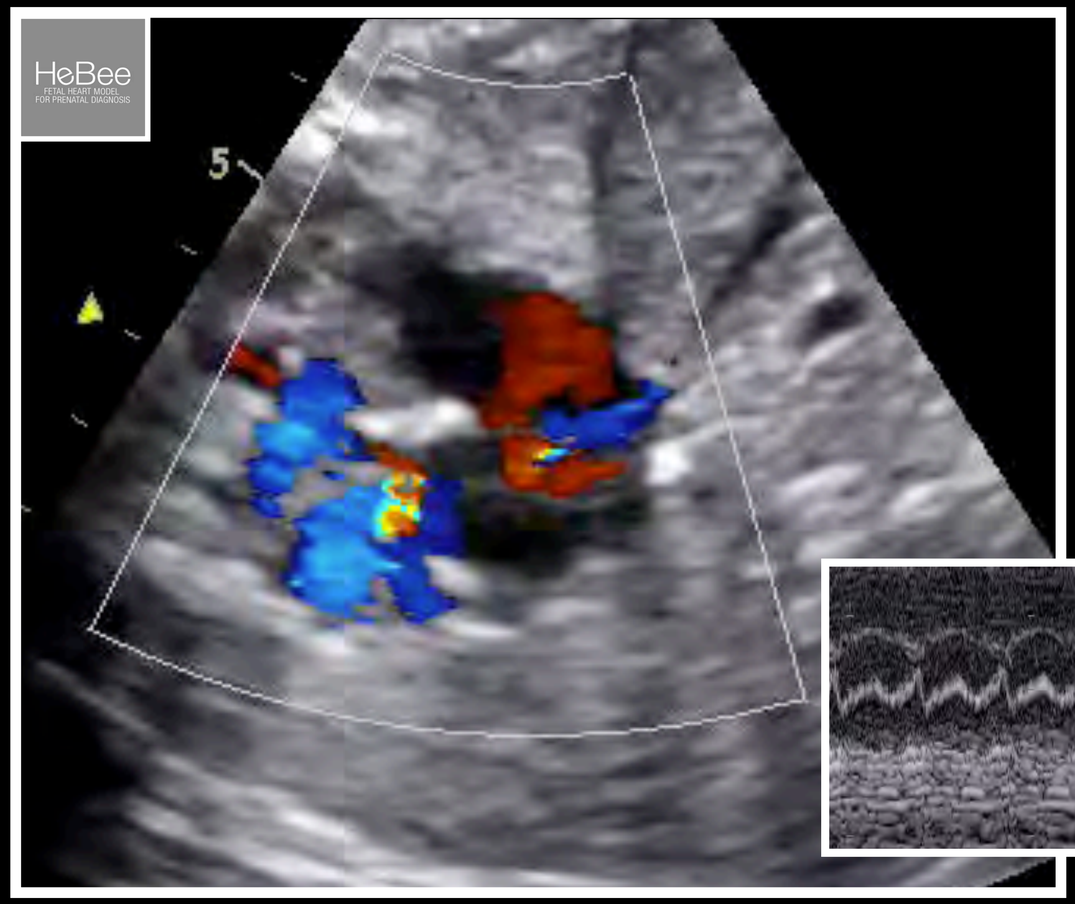
Rudolph A. Ped Res 2007;61:375-80
Prsa M et al. Circ Cardiovas Imaging 2014;7:663-70

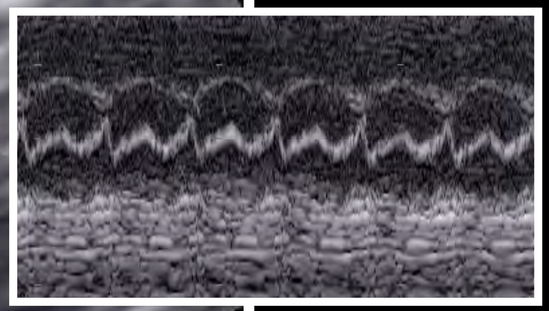
TGA

Foramen Ovale

TGA

Foramen Ovale

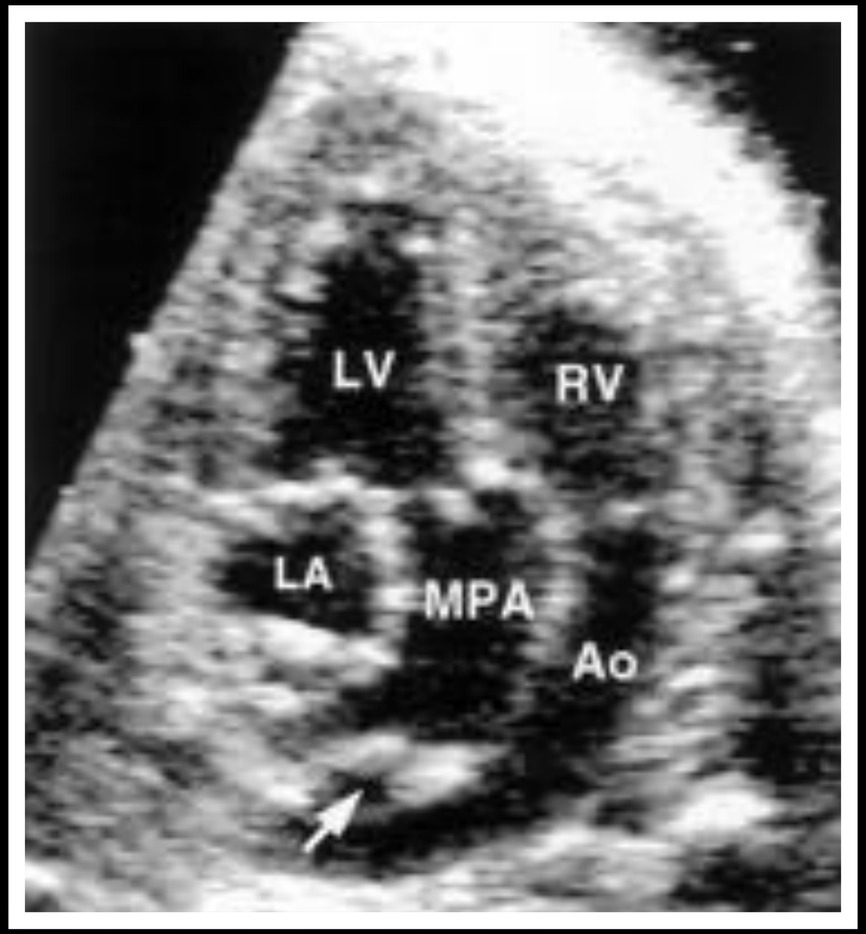




-Floppy Mb
-Small FO
-Small septal length
-pulmonary veins velocity > 0,41 m/s

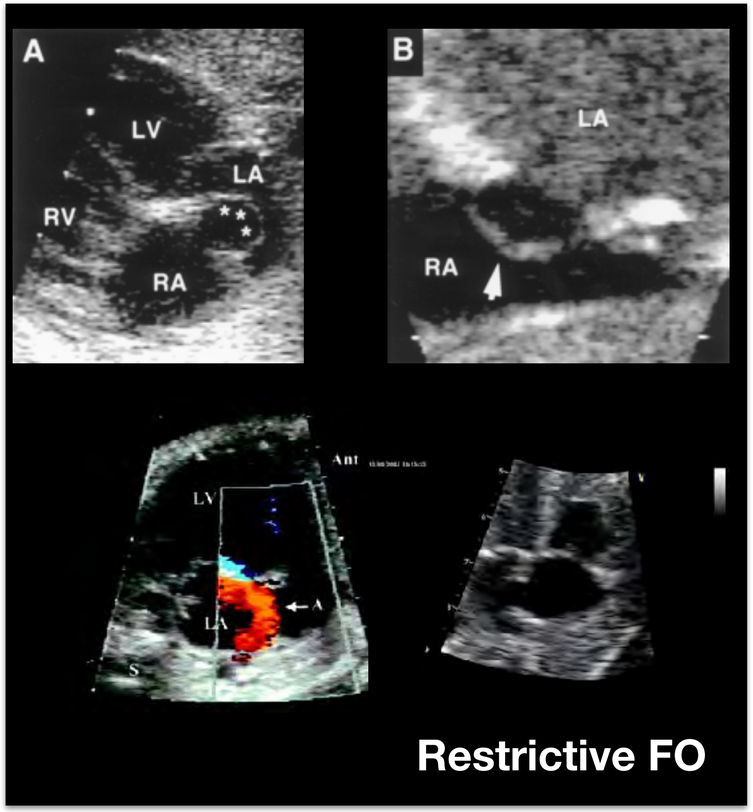
TGA

Arterial duct

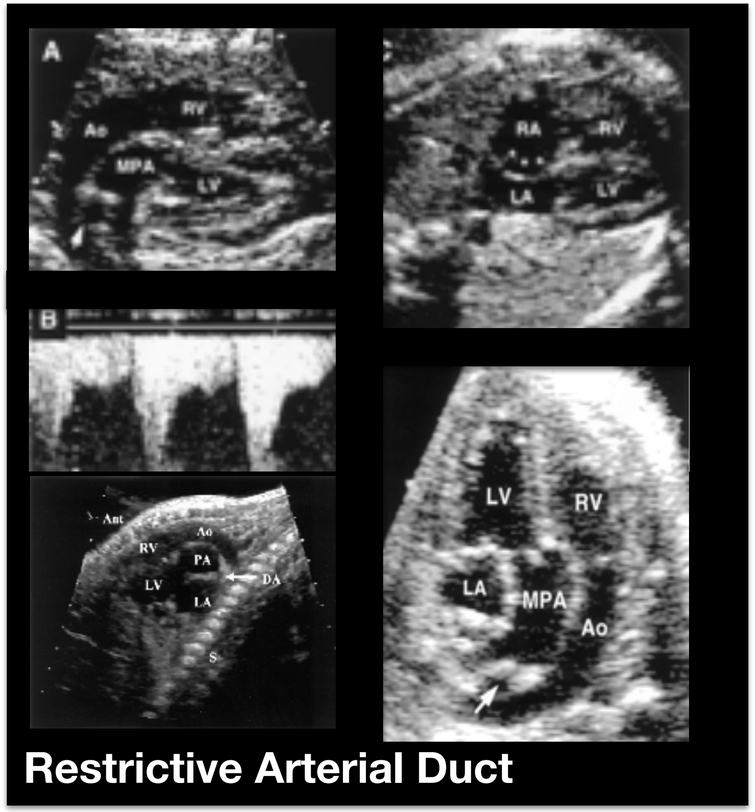


Neonatal management of TGA

Prevention of early neonatal demise



Restrictive FO



Restrictive Arterial Duct

Abnormal Prenatal Shunts and Neonatal Condition

	Abnormal (N=24)		
	FO and DA	FO or DA*	Normal (N=95)
N total	4	20 (19 FO; 1 DA)	96
Critical condition (n=7)	4	3 (2 FO; 1 DA)	6
Stable condition (n=17)	0	17	89

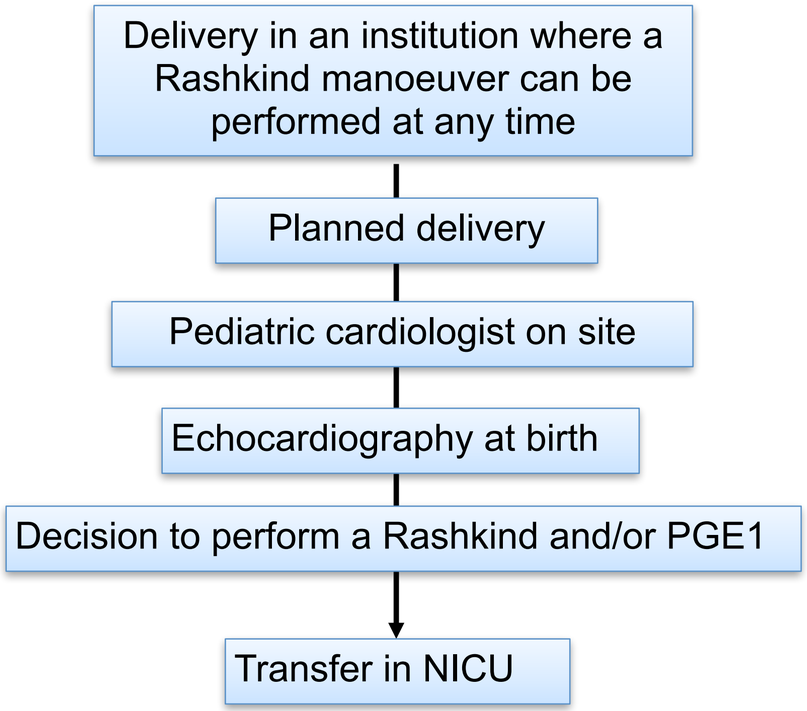
FO indicates foramen ovale; DA, ductus arteriosus.
*This subgroup included 1 fetus in whom the FO was restrictive but the DA could not be analyzed.

Additional criteria [2]
A hypermobile septum and reverse diastolic patent ductus arteriosus

Finally, we do not care
All TGA are delivered on site with the same protocol

Maeno YV et al. Circulation 1999
Jouannic JM et al. Circulation 2004;110:1743-6
2-Punn R, Silvermann N. JASE 2011;24:425-30
Mary T. Donofrio Circulation. 2002;105:e65-e66

Perinatal organization



From 1992 to 217
717 prenatally diagnosed TGA (IVS or complex)
6 had congenitally corrected TGA
3 deaths immediately after birth in the delivery room
3 additional preoperative deaths

1 extra cardiac malformation in a CHARGE syndrome,
1 necrotizing enterocolitis
1 during the Rashkind procedure (perforation of the left atrium in left juxtaposition of the atrial appendages)

Surgical mortality 1.7 % : 693 survivors at discharge

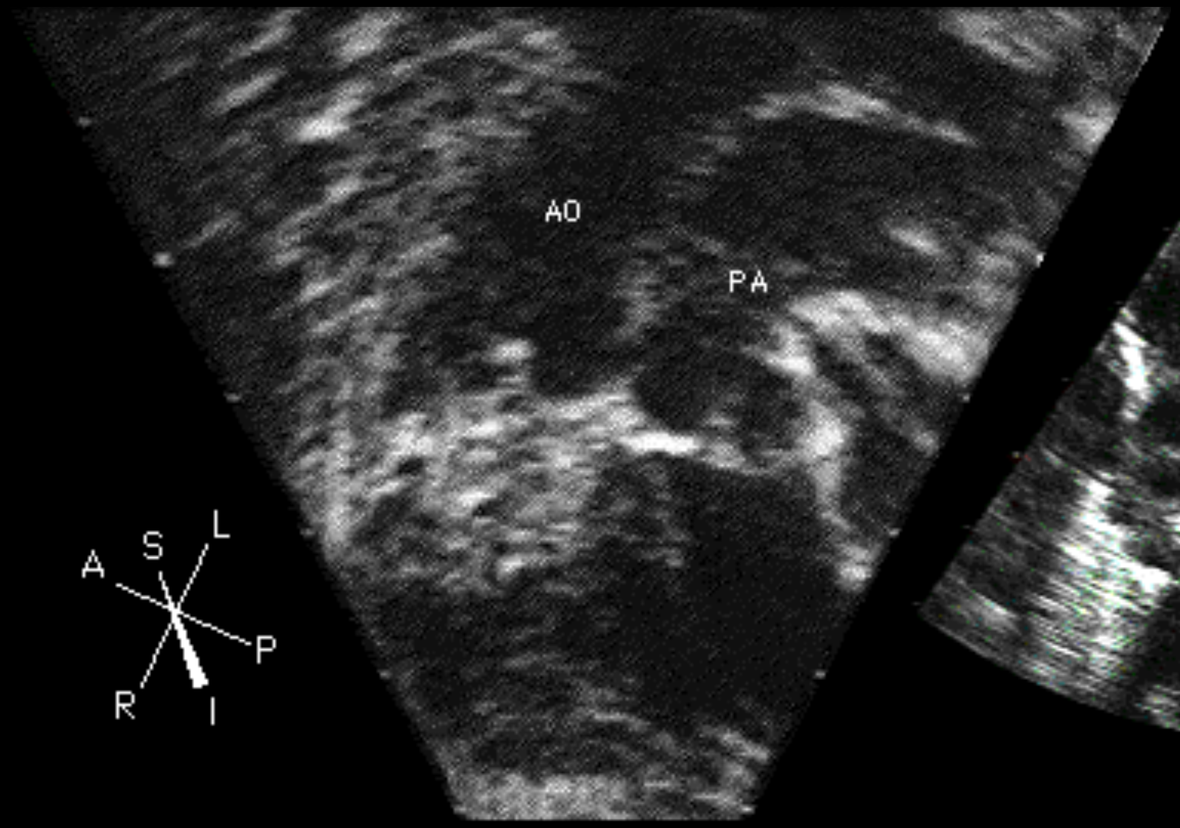
Neonatal diagnosis of TGA

Isolated cyanosis

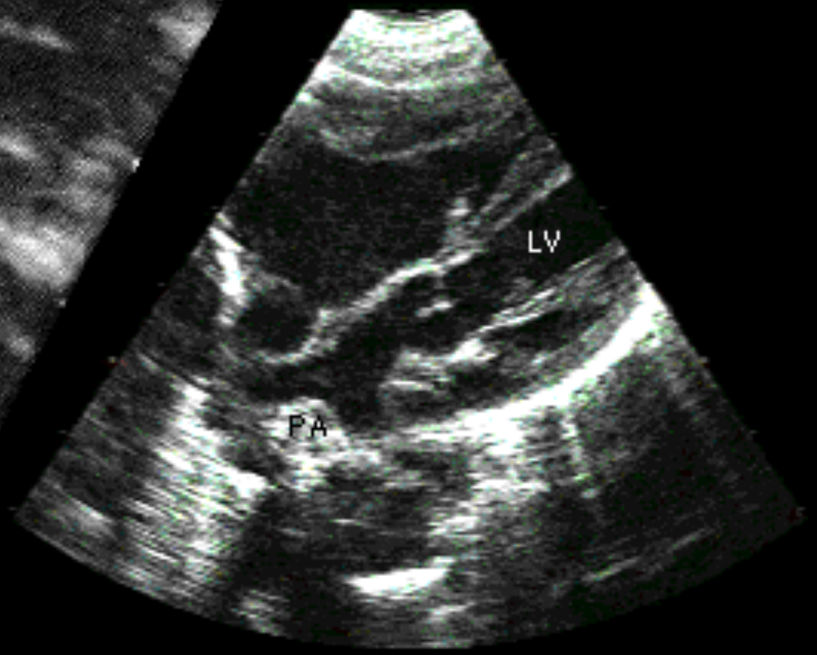
TGA

Rapid diagnosis

Parallel course of great vessels

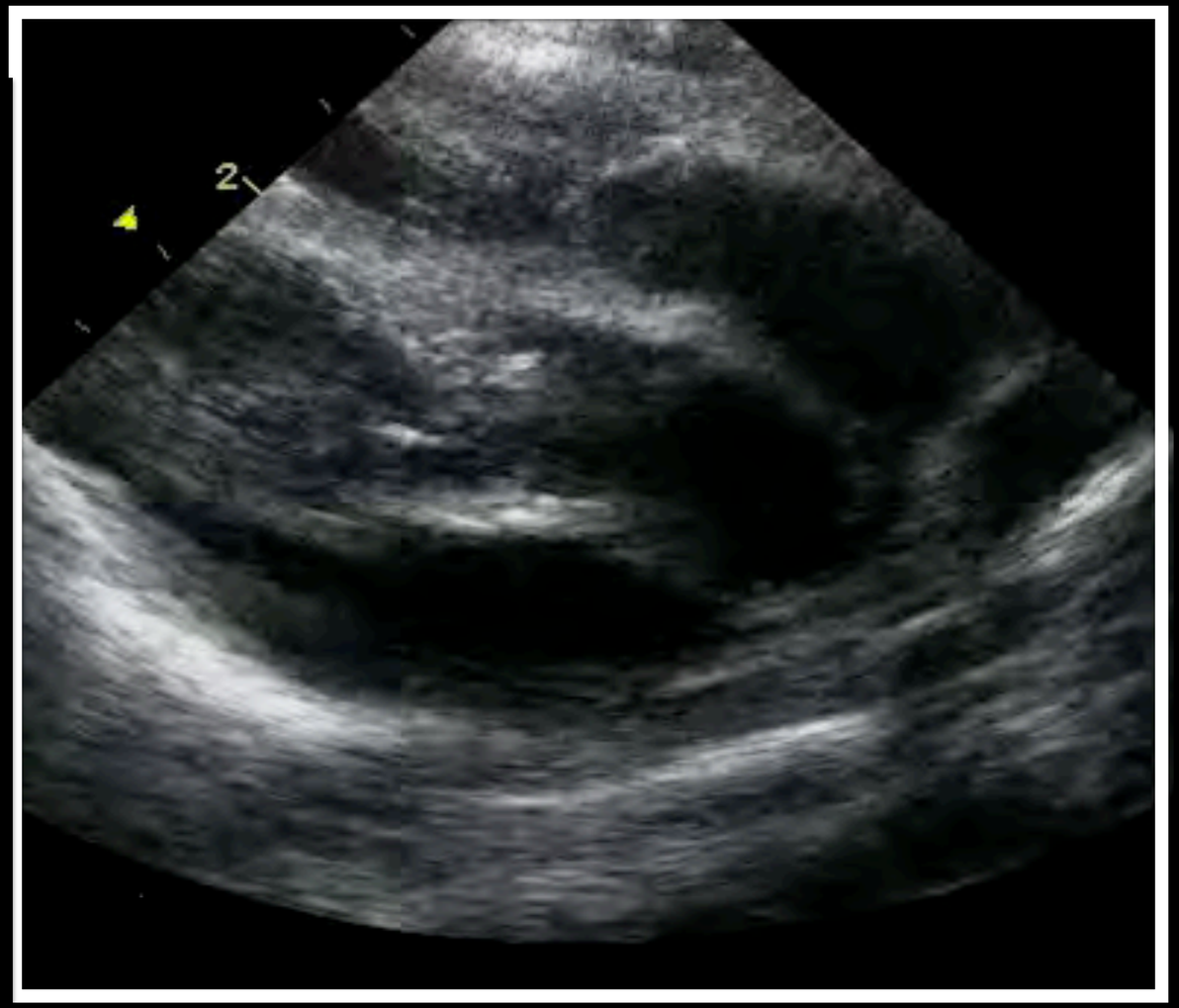


Pulmonary artery from LV



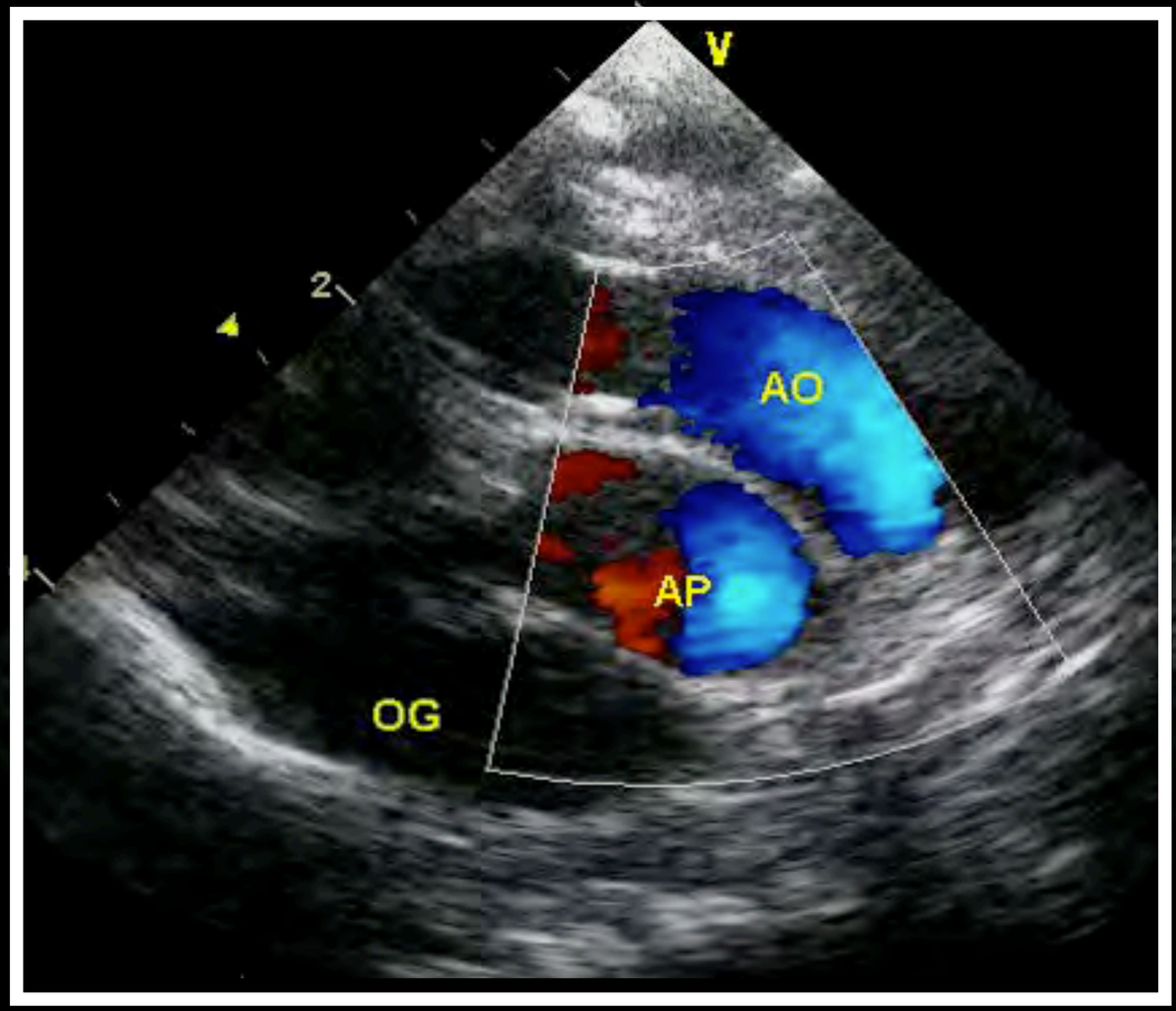
TGA

Rapid diagnosis



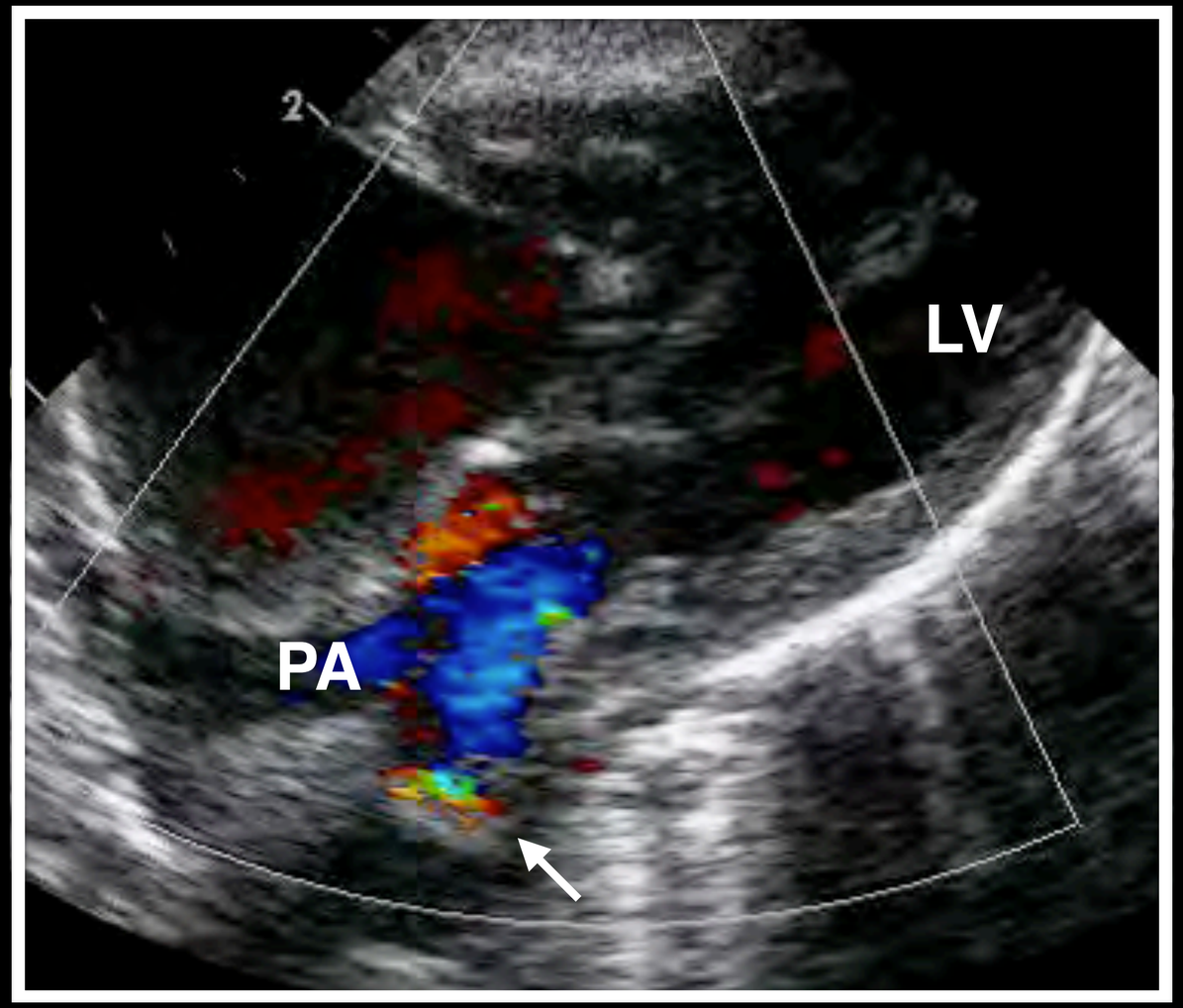
TGA

Rapid diagnosis



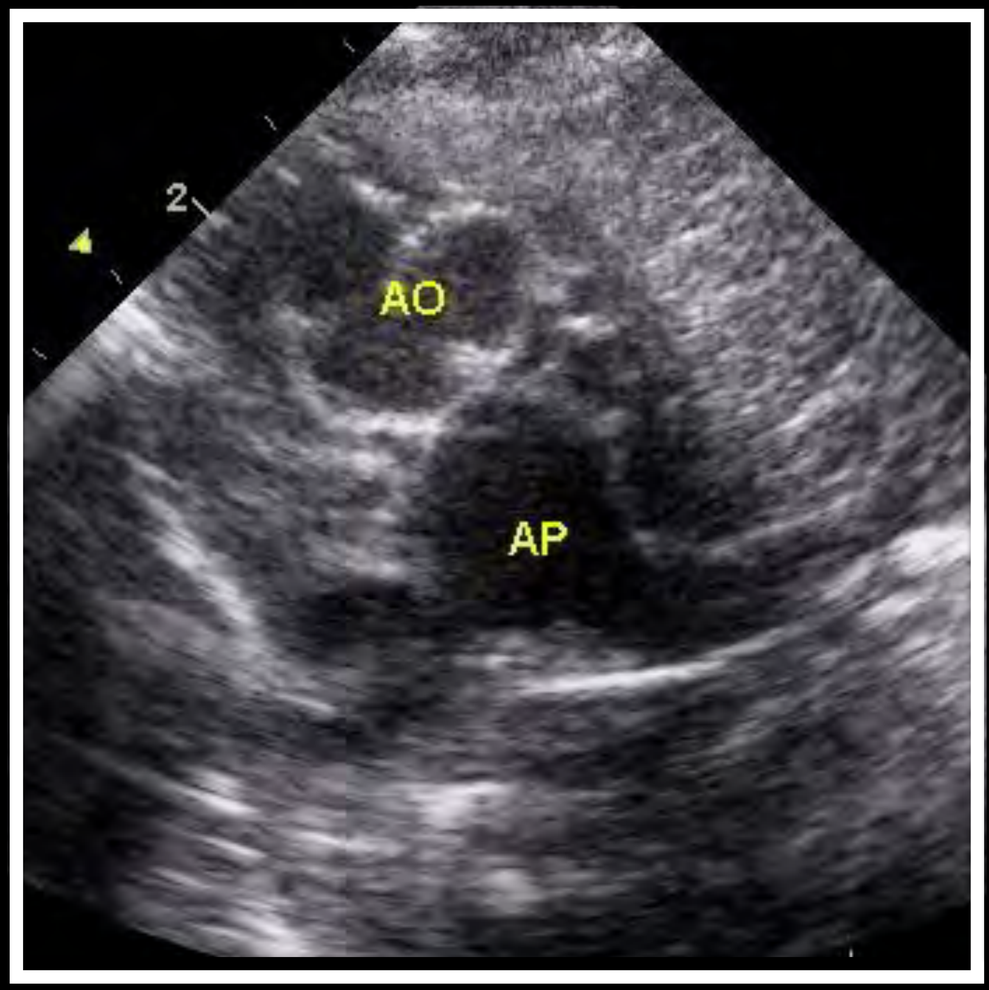
TGA

Rapid diagnosis

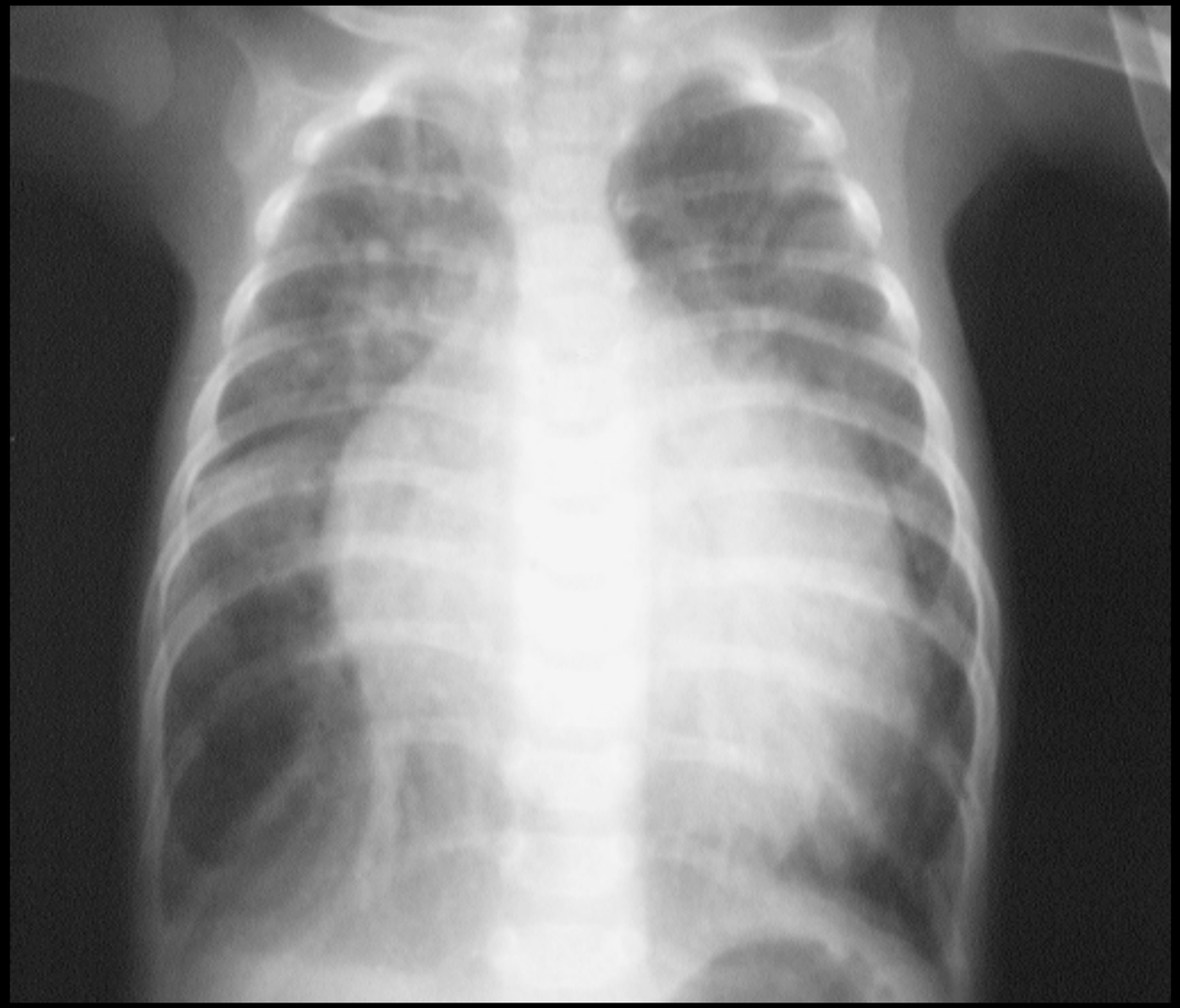


TGA

D-TGA

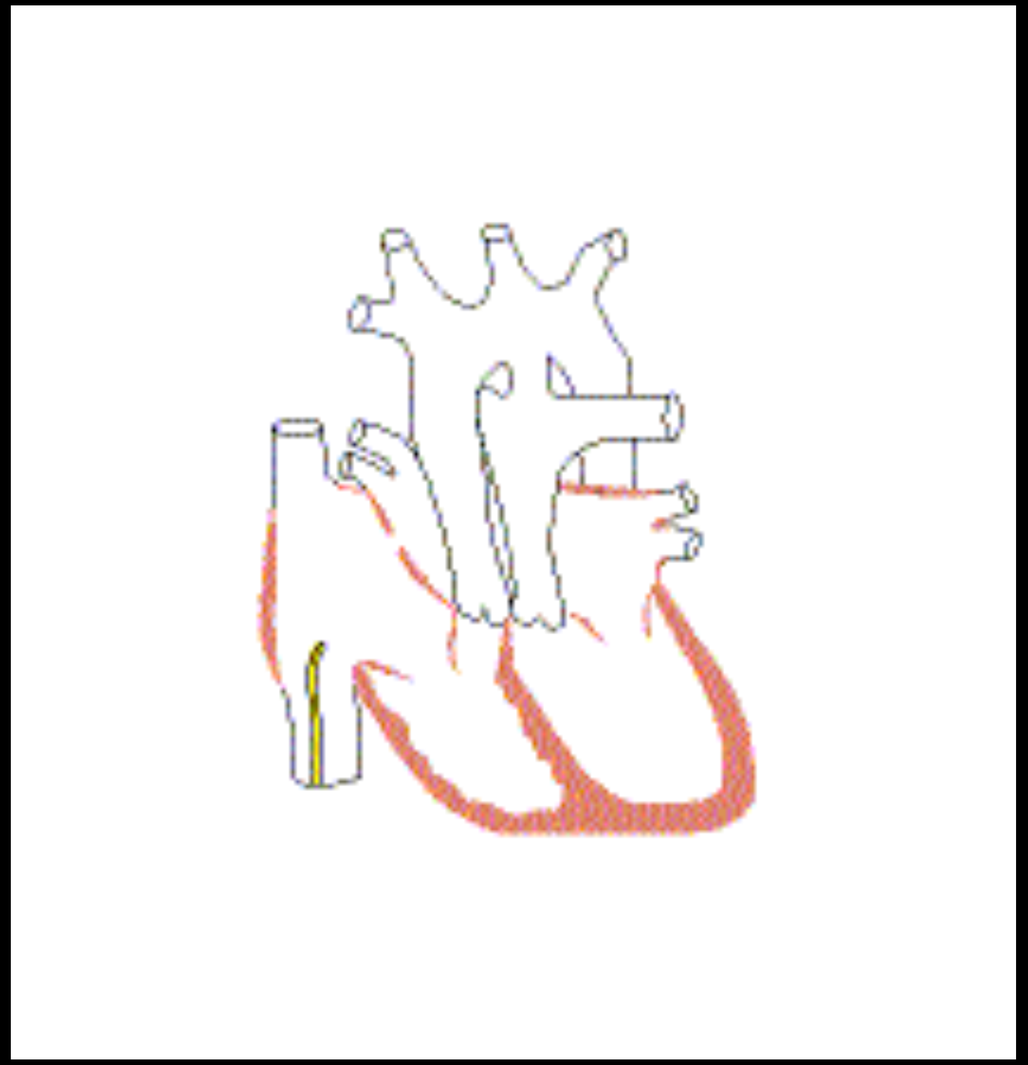


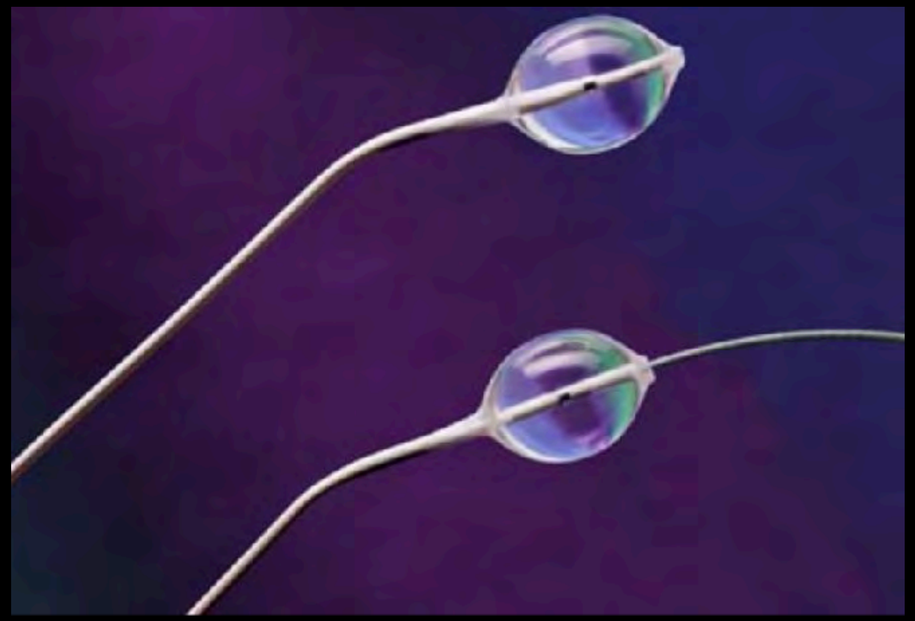
D-TGA

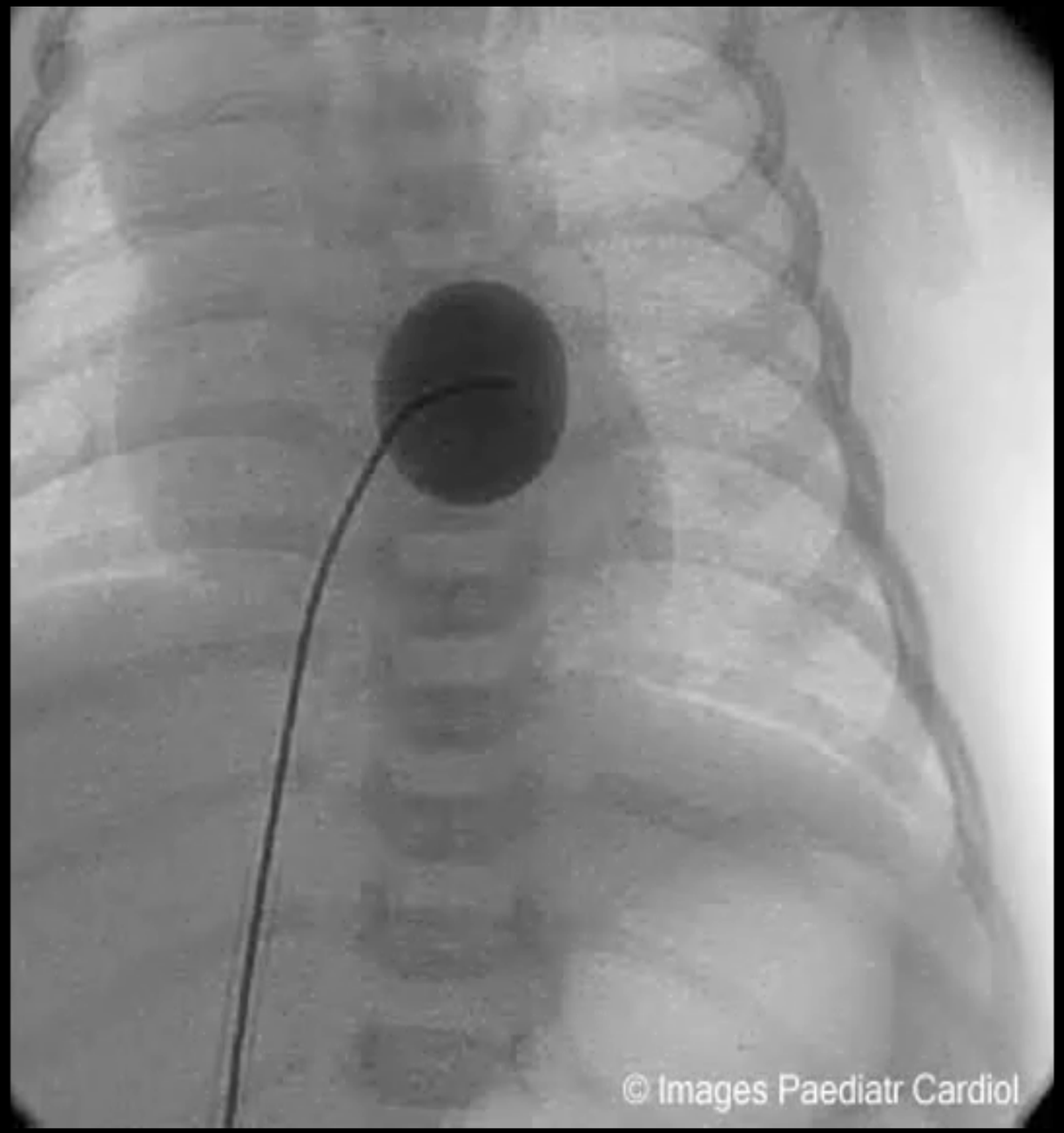


TGA with heart failure and restrictive PFO

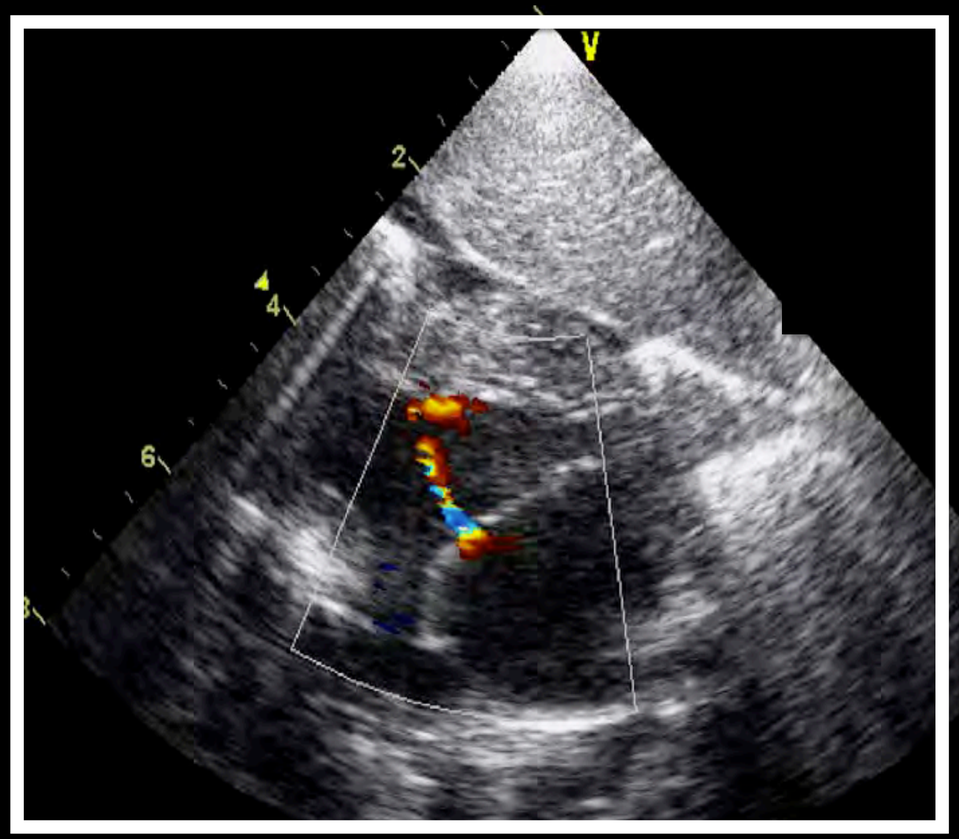
William Rashkind

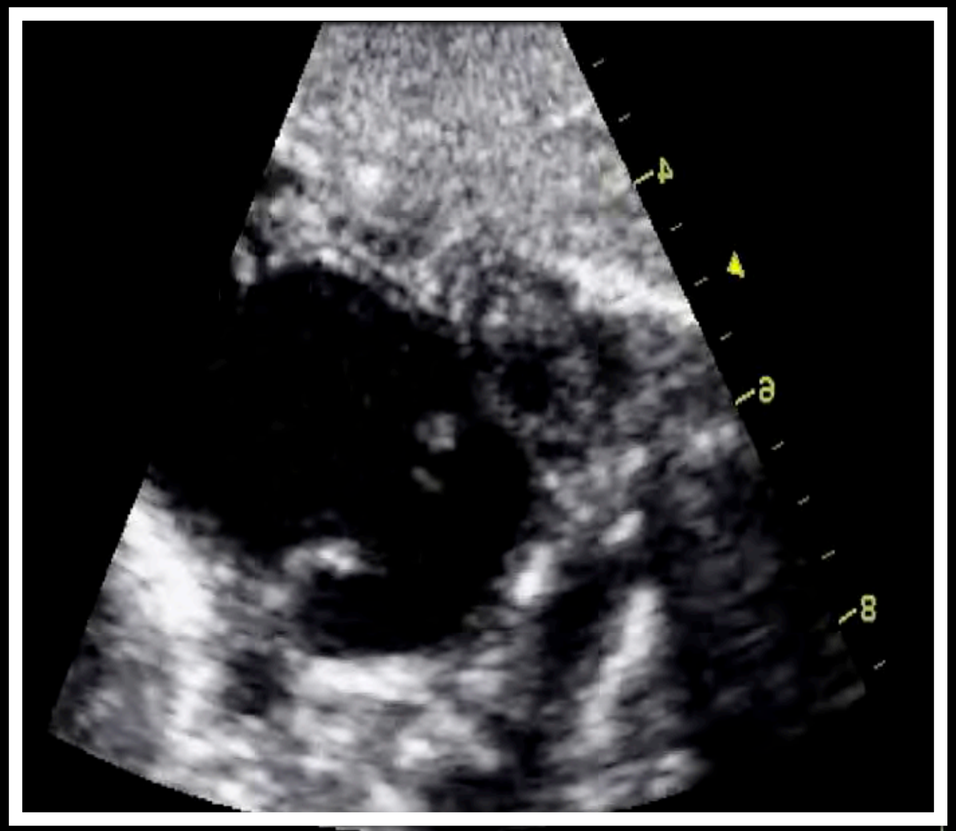




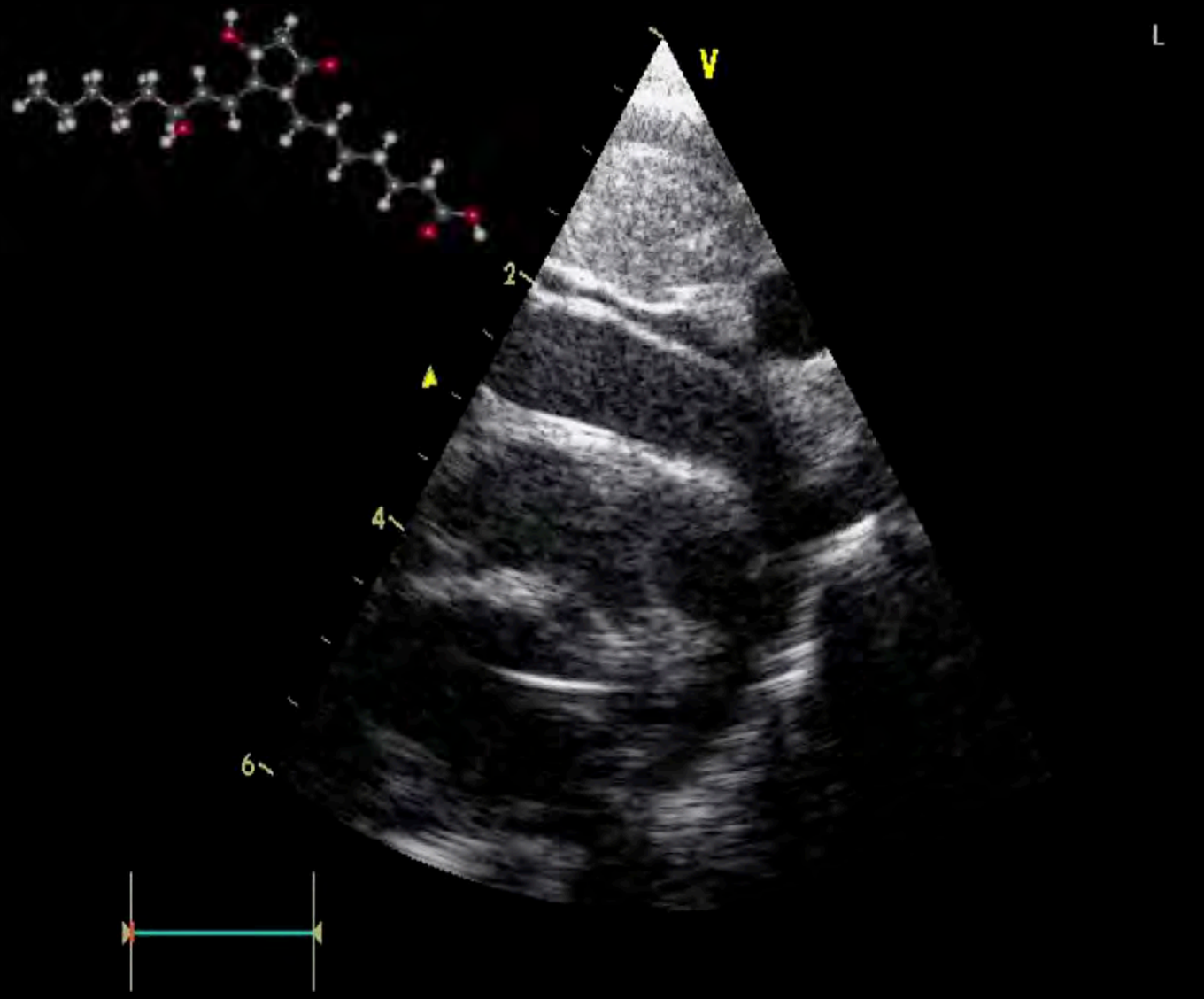

© Images Paediatr Cardiol

TGA Rashkind





PGE1 and arterial duct



Echographic evaluation in TGA

Echocardiographic evaluation of TGA

1. Foramen ovale and arterial duct
2. Size of the ventricles
   Small RV : check aorta
   Small LV : check pulmonary artery
3. Atrioventricular valves anomalies
4. Coronary arteries

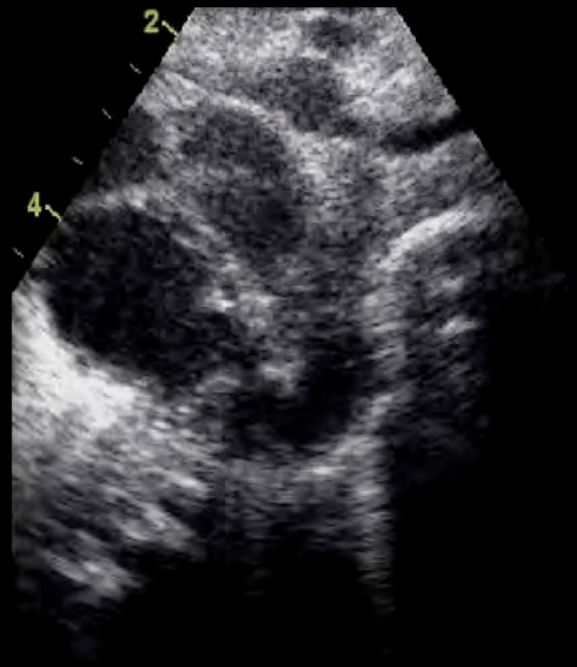
Peroperative analysis

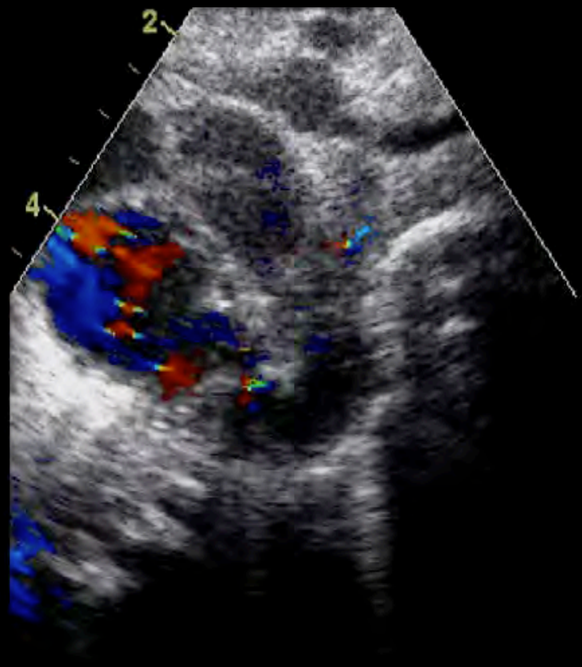
Anything different from the basic form

Expected surgical difficulties

- « Abnormal » coronaries
- Hypoplastic aortic arch/coarctation
- VSD
- Difficult LV to PA routing
- Side by side vessels
- Aorto-pulmonary discrepancy
- Commissural mal-alignement

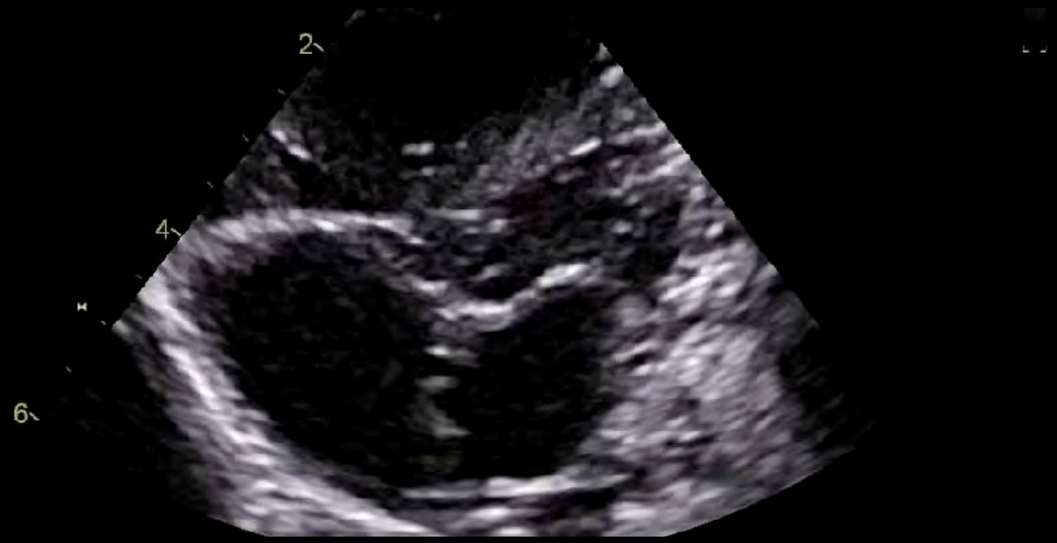
Subarterial conus
Anterior (sub-aortic) deviation





TGA VSD Coarctation

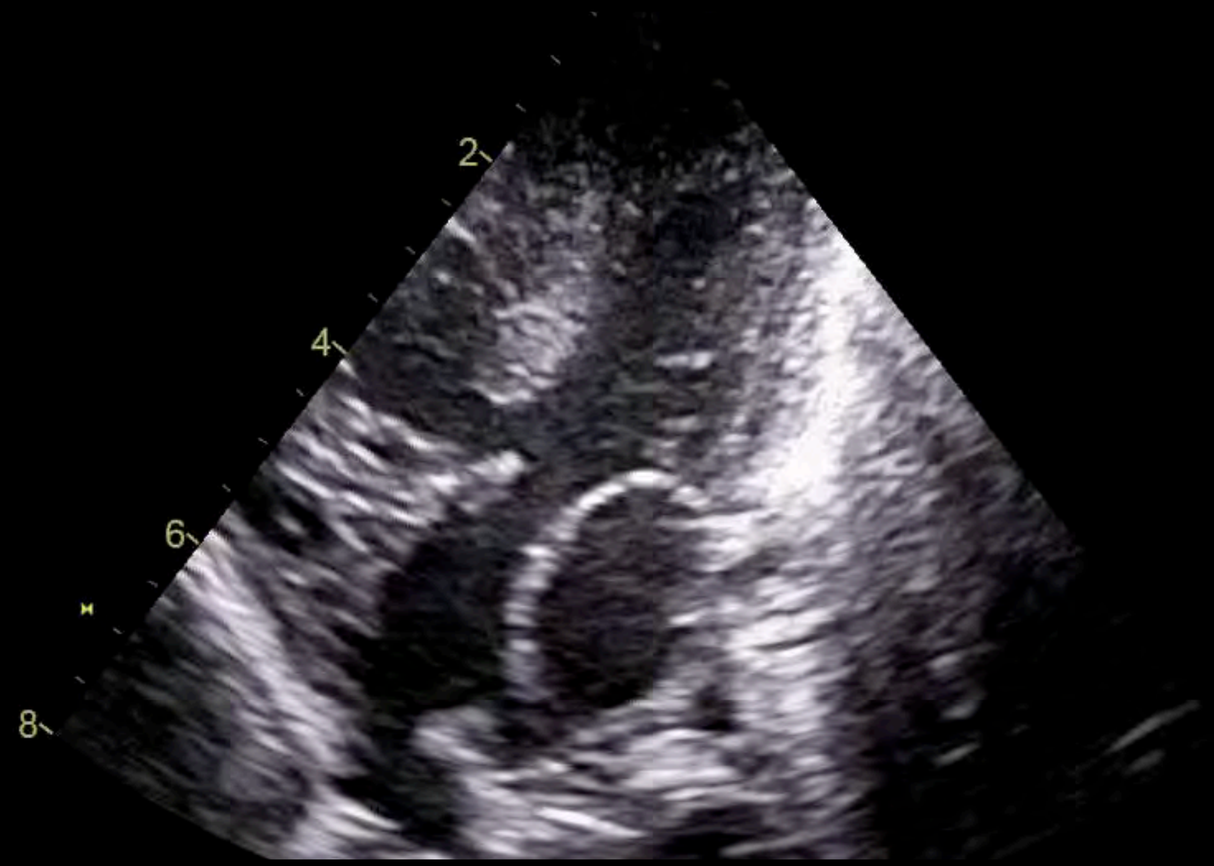
Aorto pulmonary discrepancy



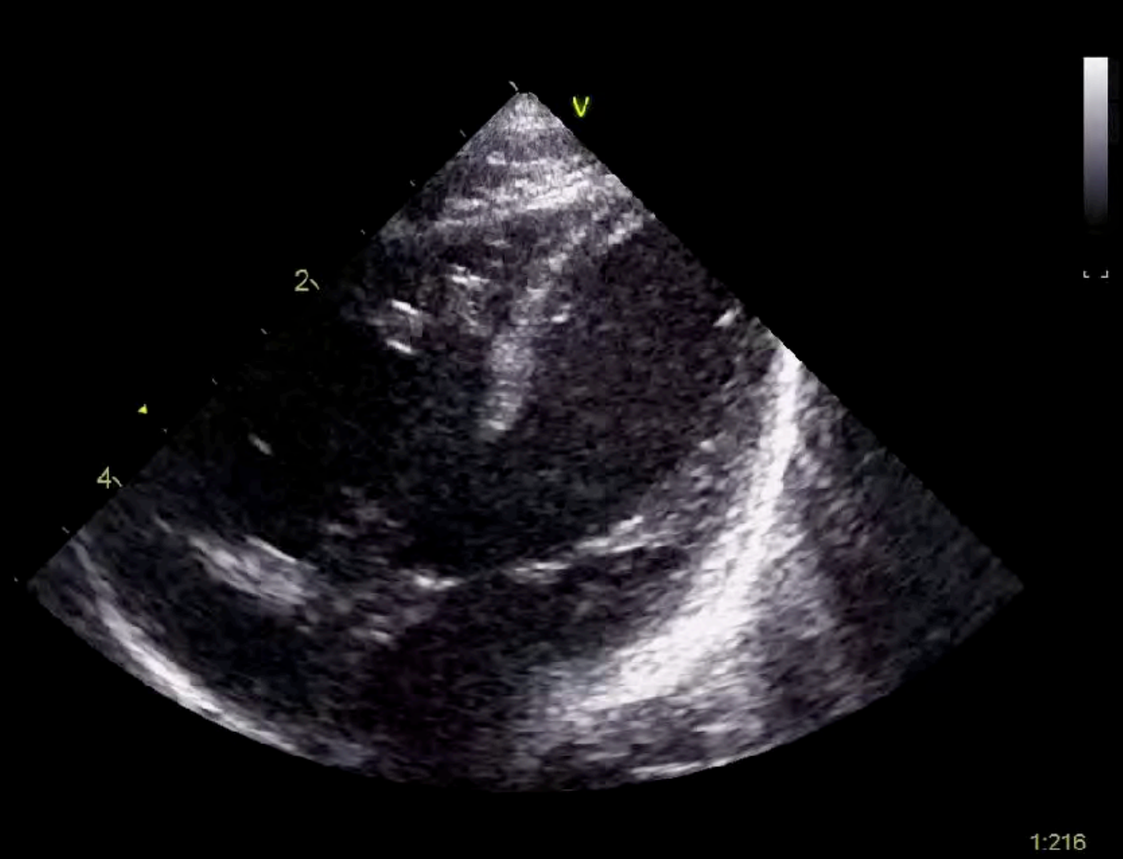
Impact for the type of repair

Subarterial conus

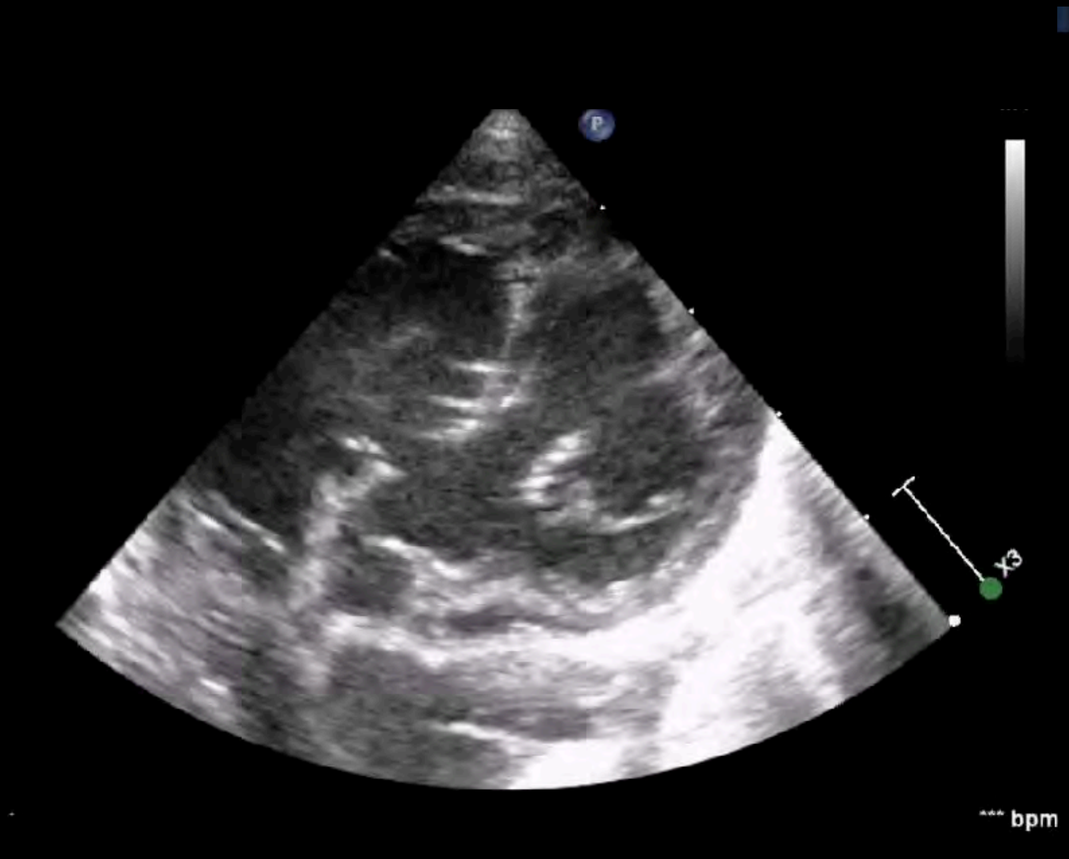
Posterior (sub-pulmonary) deviation



VSD: localization and size



Inlet VSD

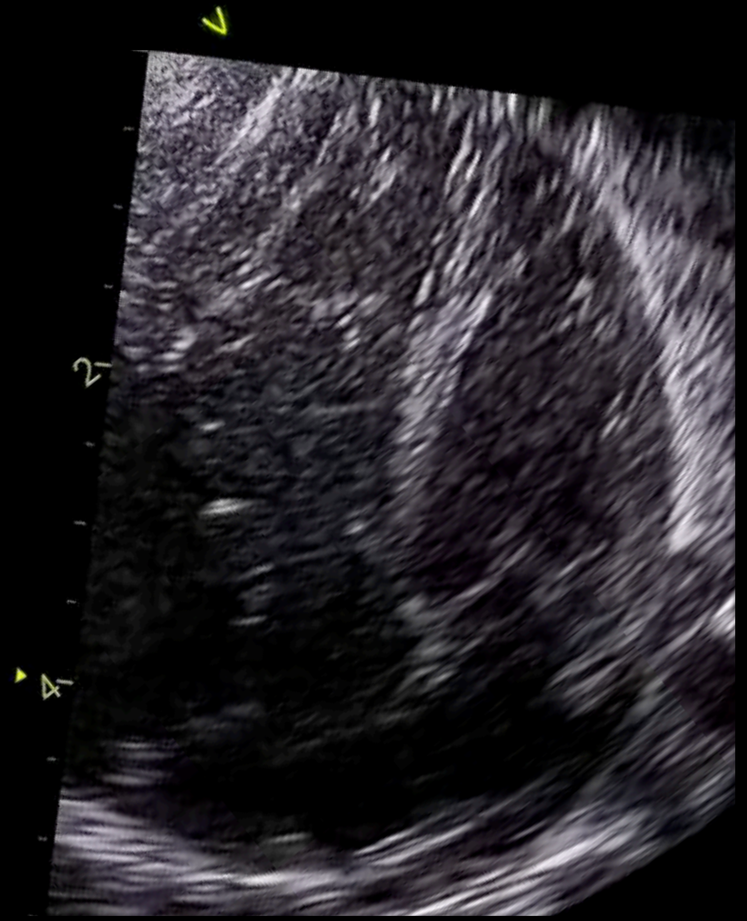


Outlet VSD

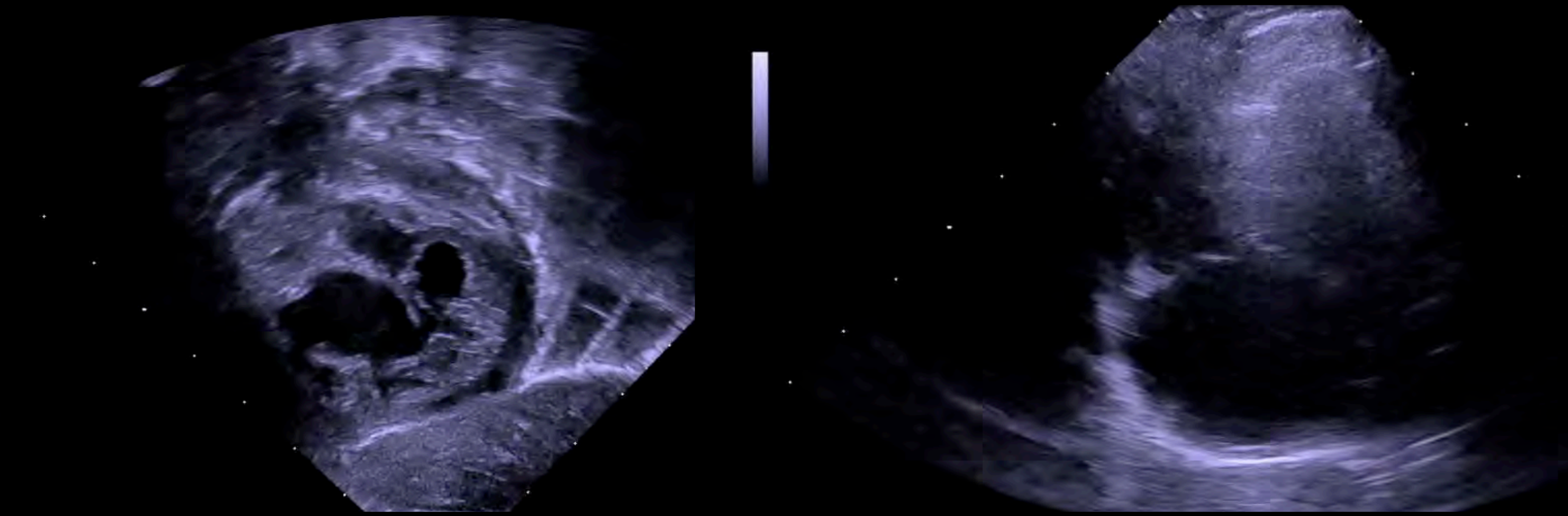
Unbalanced ventricles

« Small » RV

« Small » LV

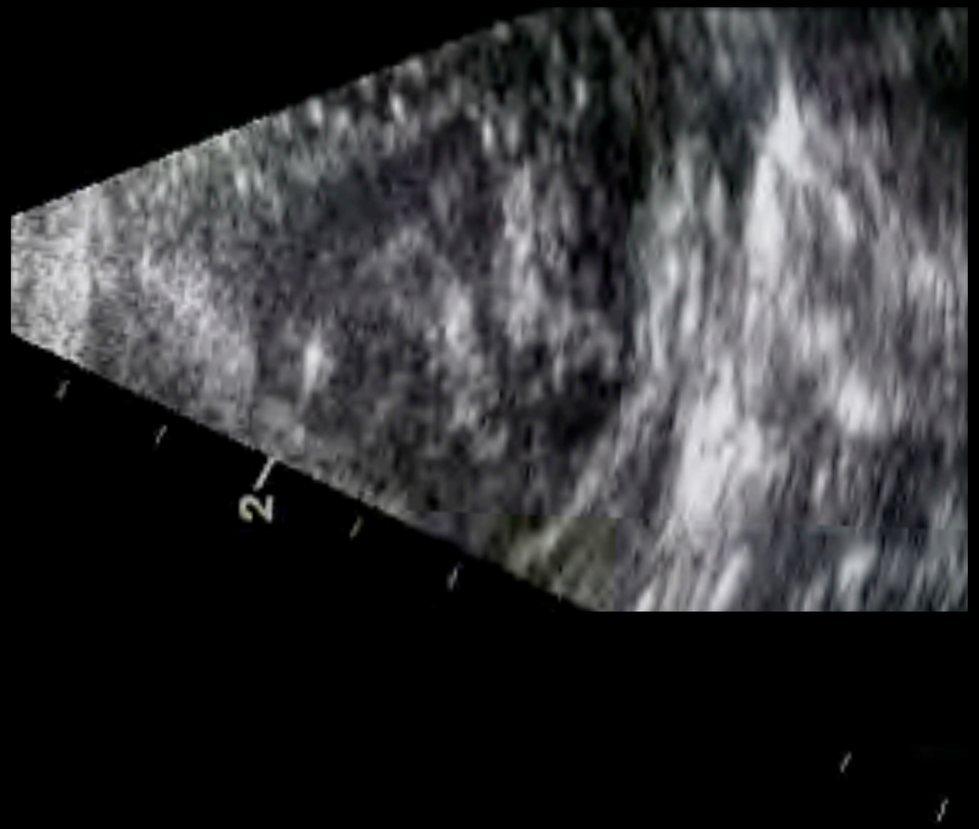


AV valves abnormalities
Straddling and over-riding



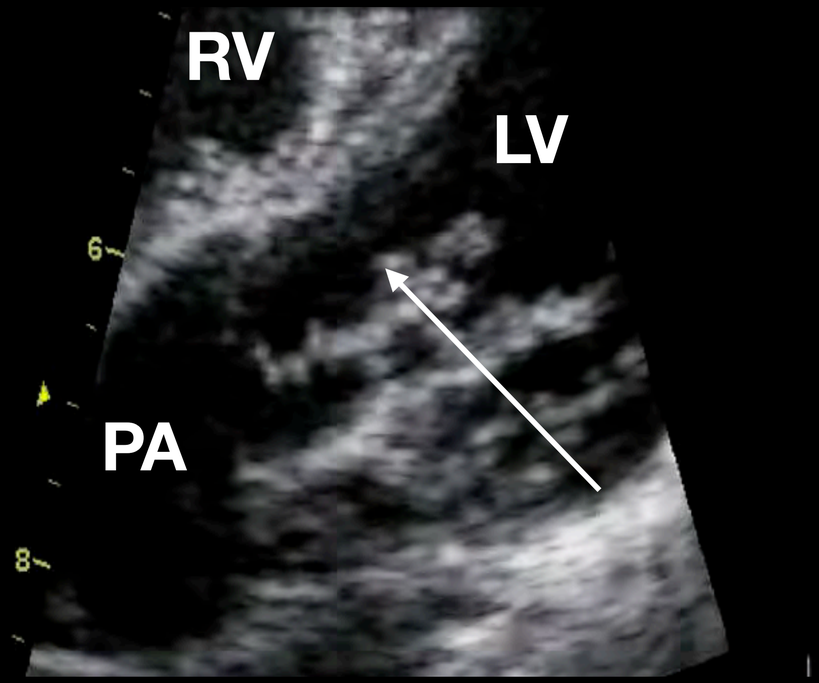
Straddling of tricuspid valve

AV valves abnormalities
Mitral cleft

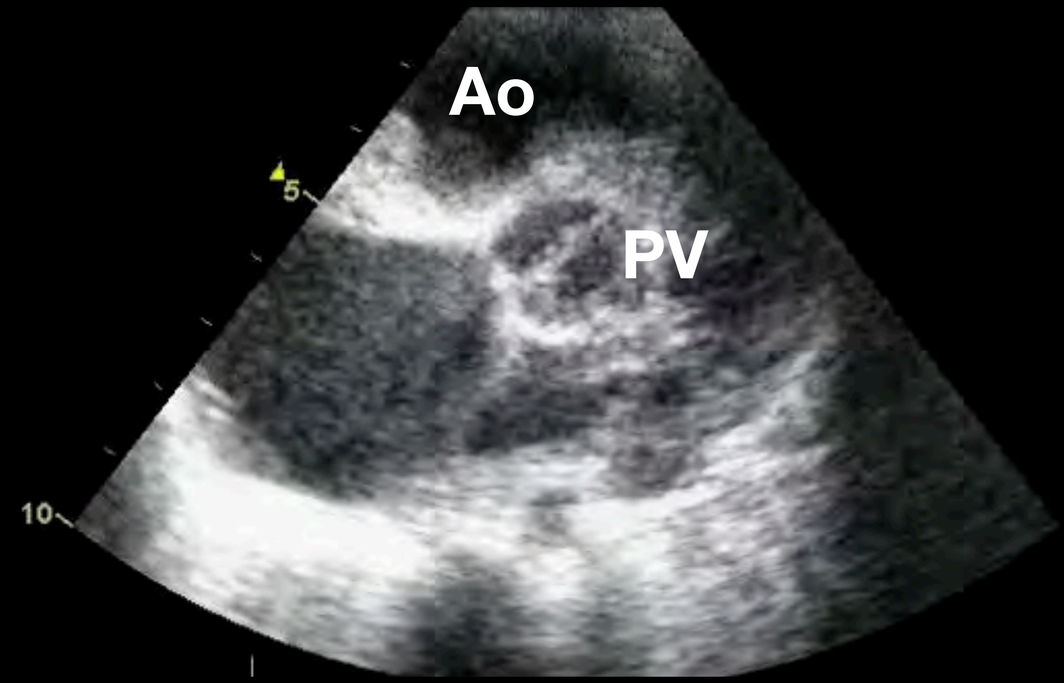


Mitral cleft

TGA left outflow tract obstruction

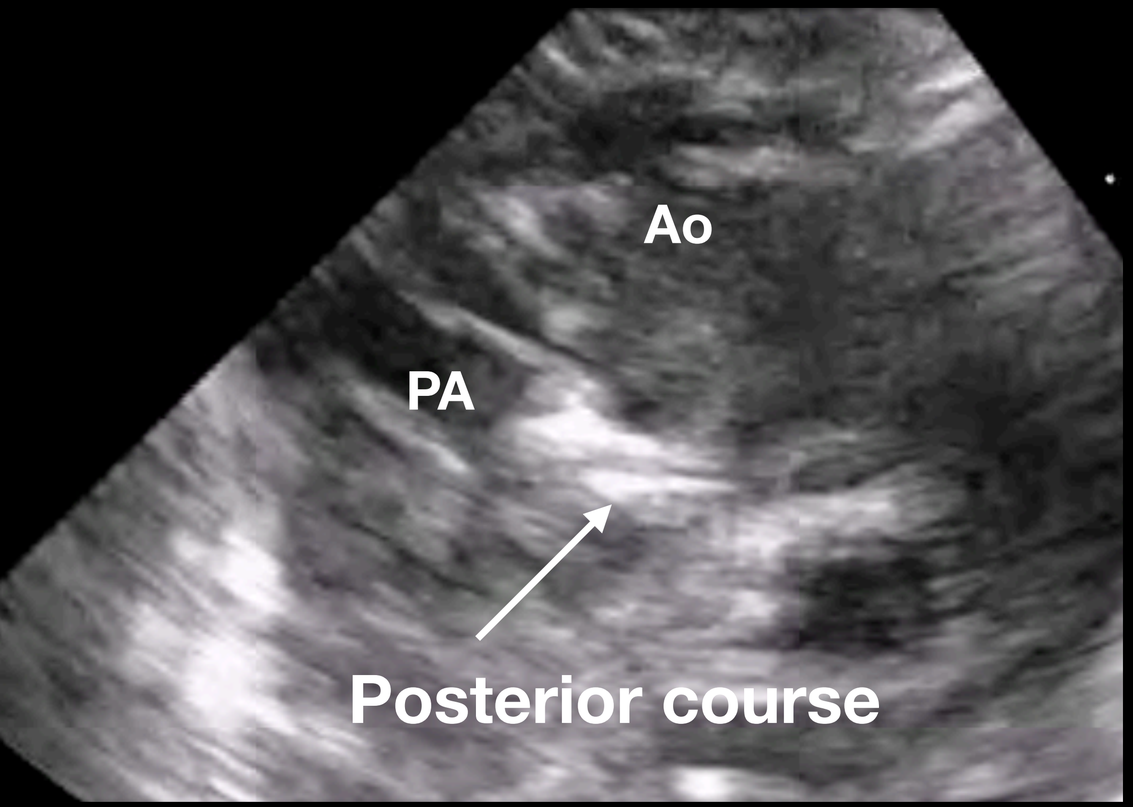


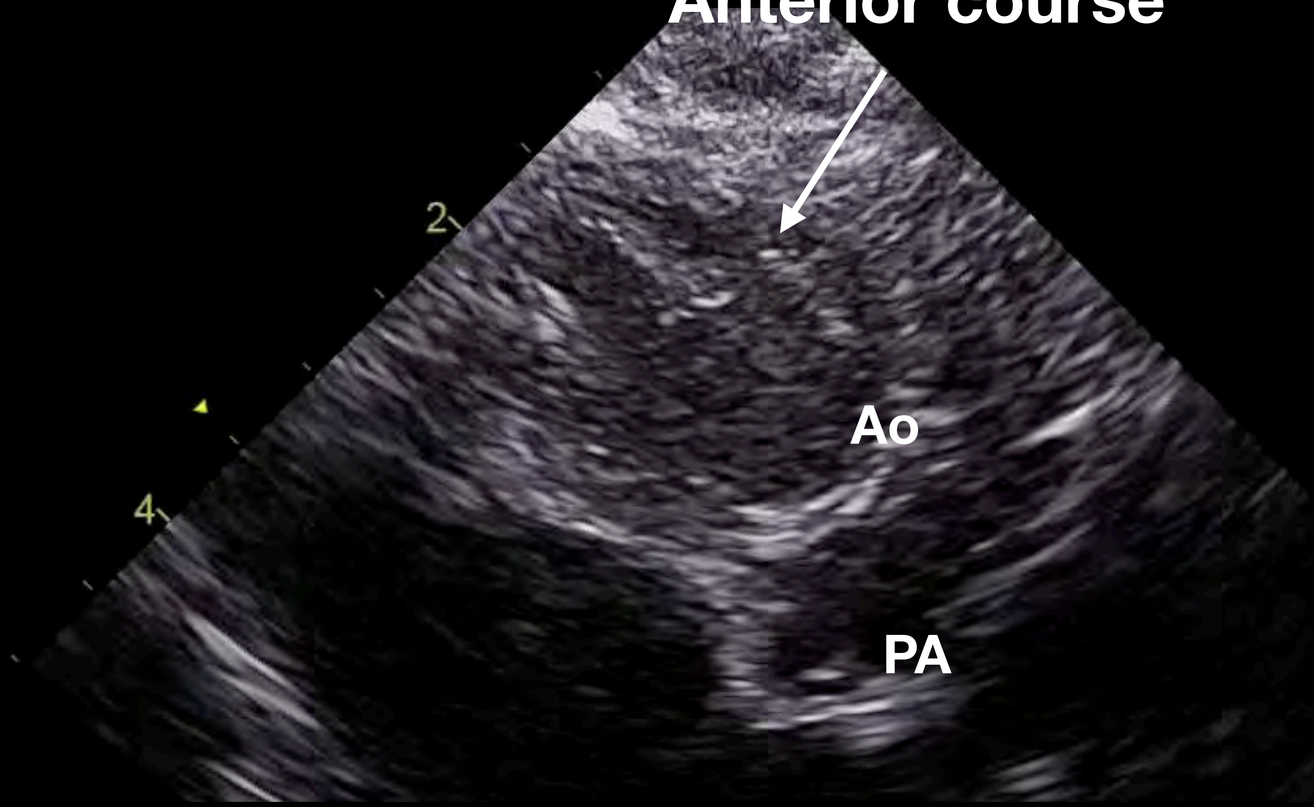
Accessory tissue on mitral valve



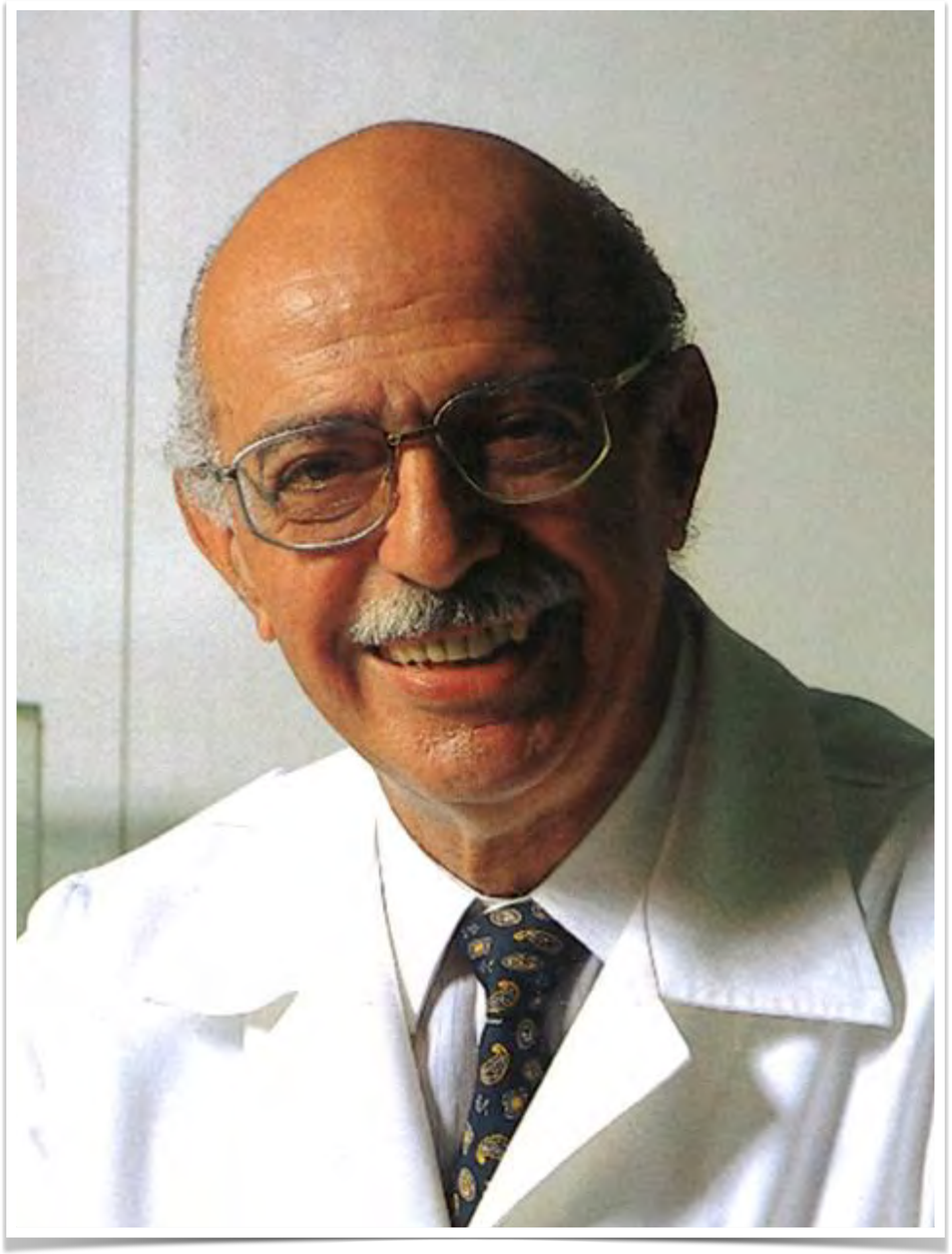
Bicuspid pulmonary valve

Coronary evaluation



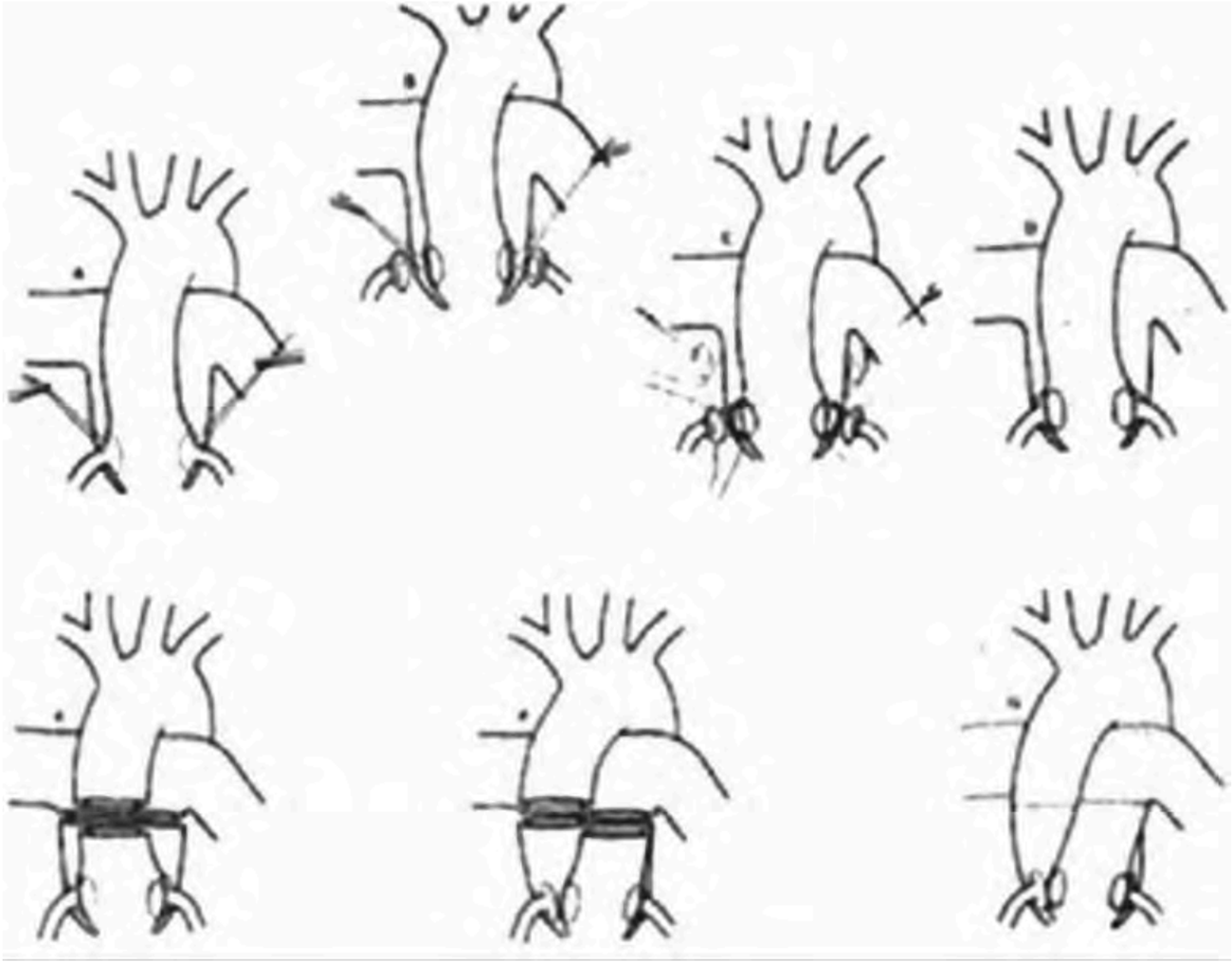


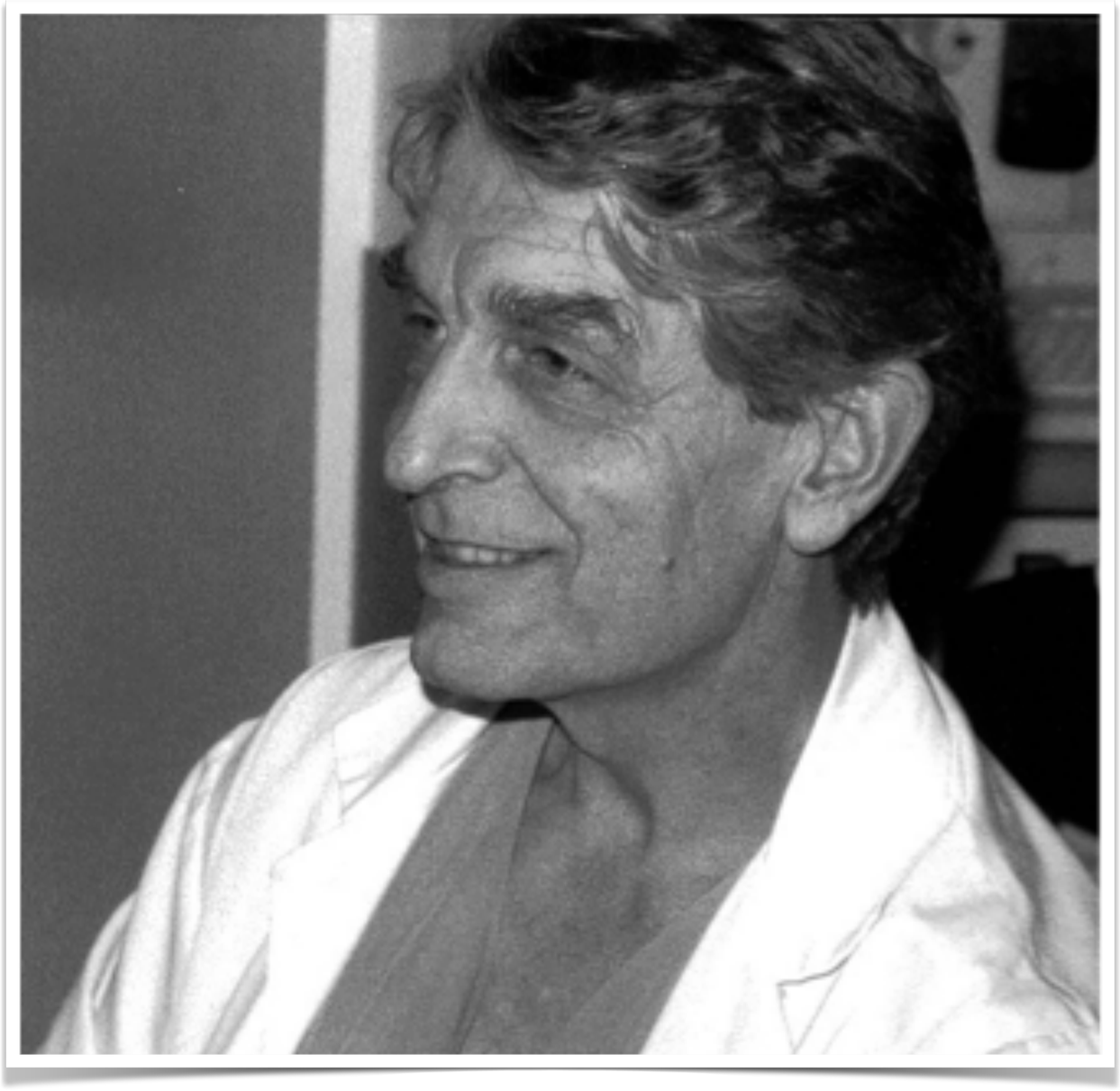
The arterial switch operation



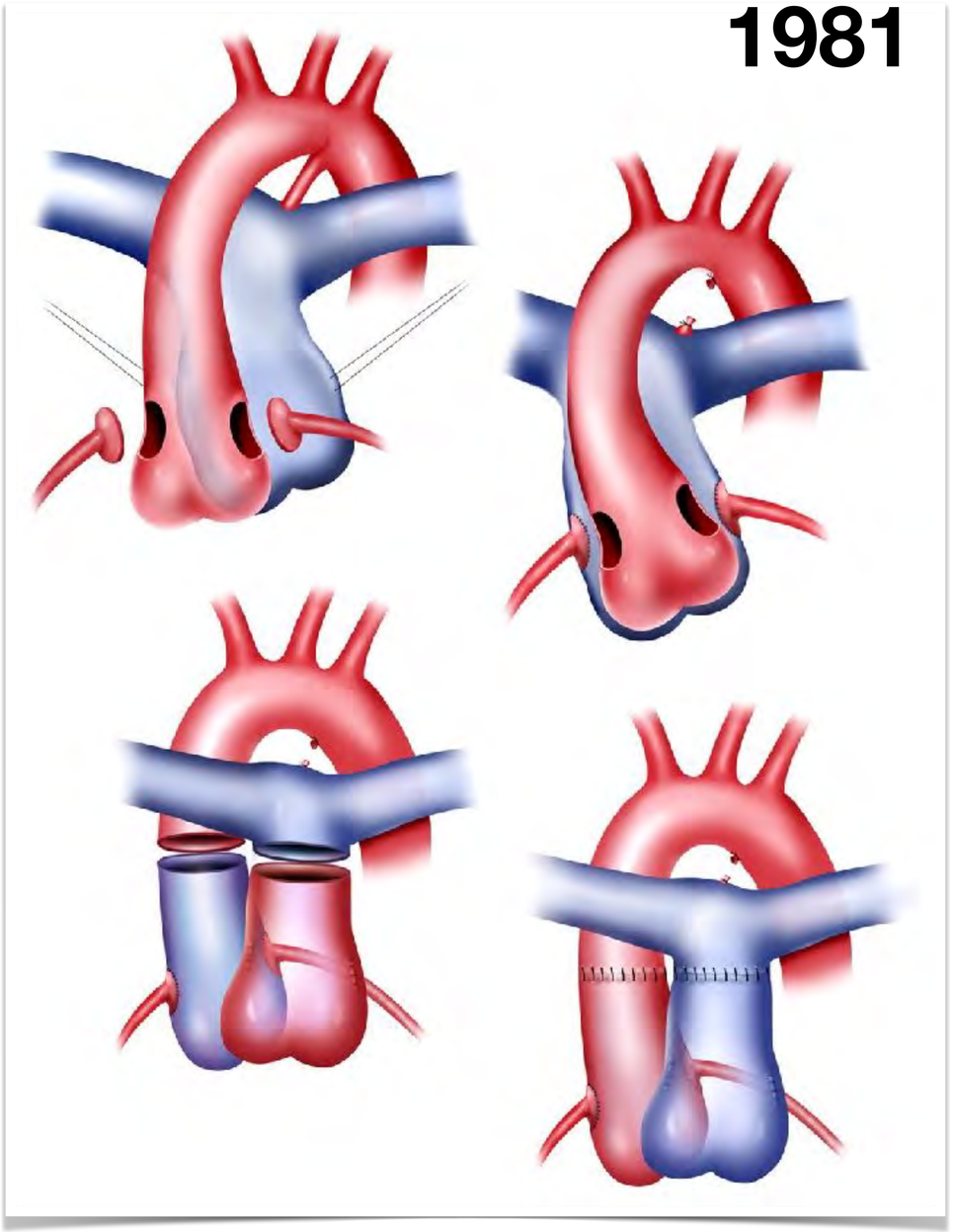
Adib Domingo Jatene

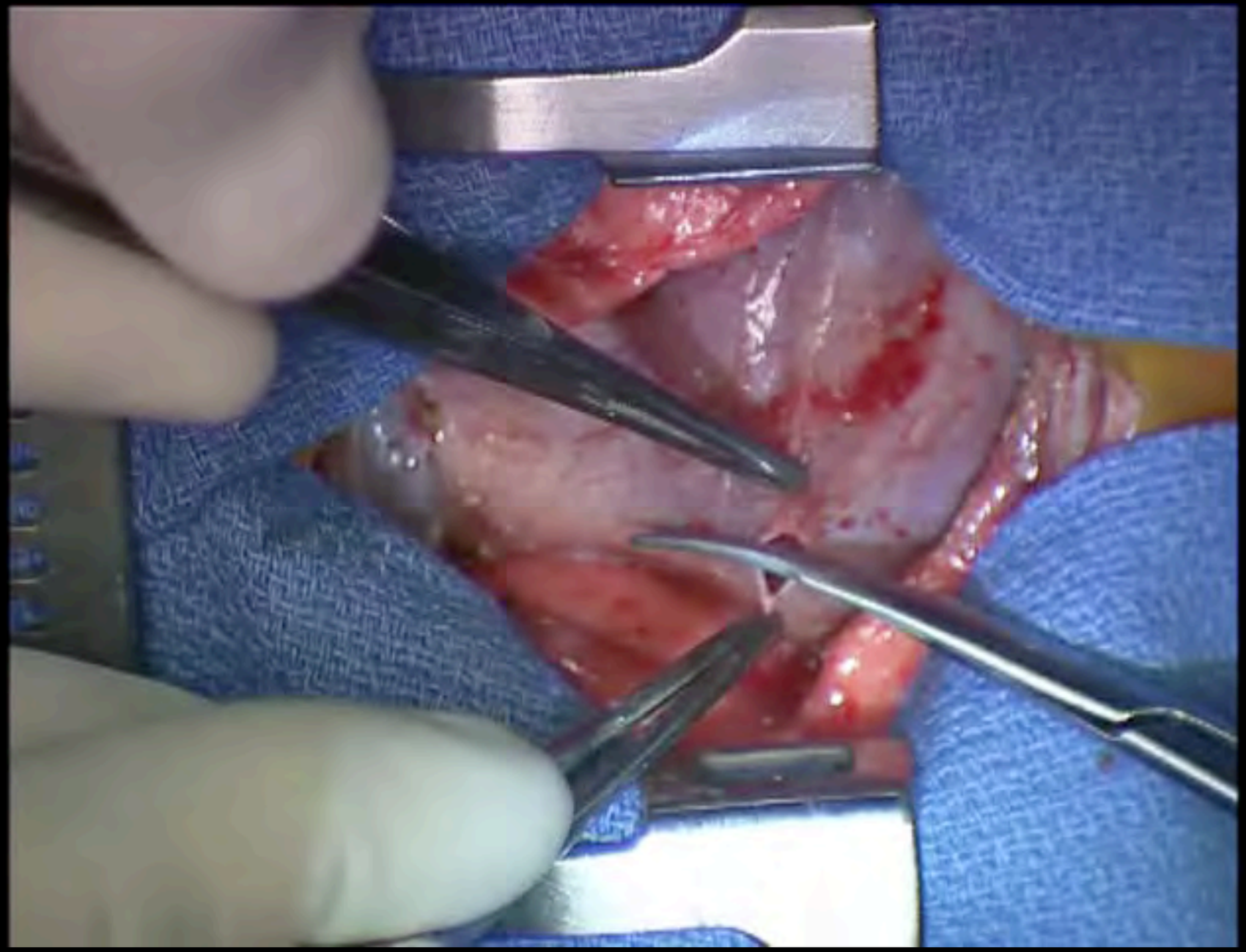
1975

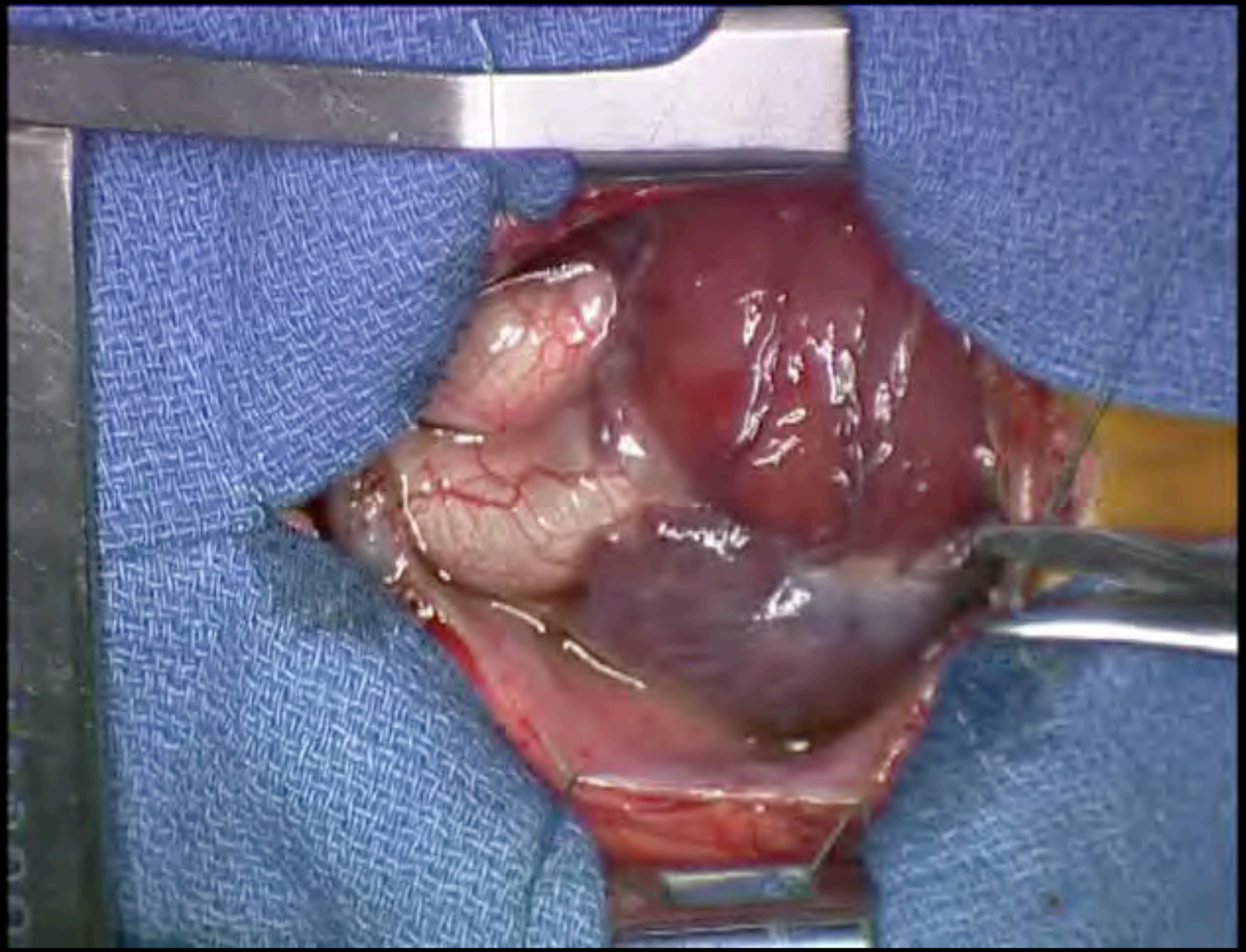


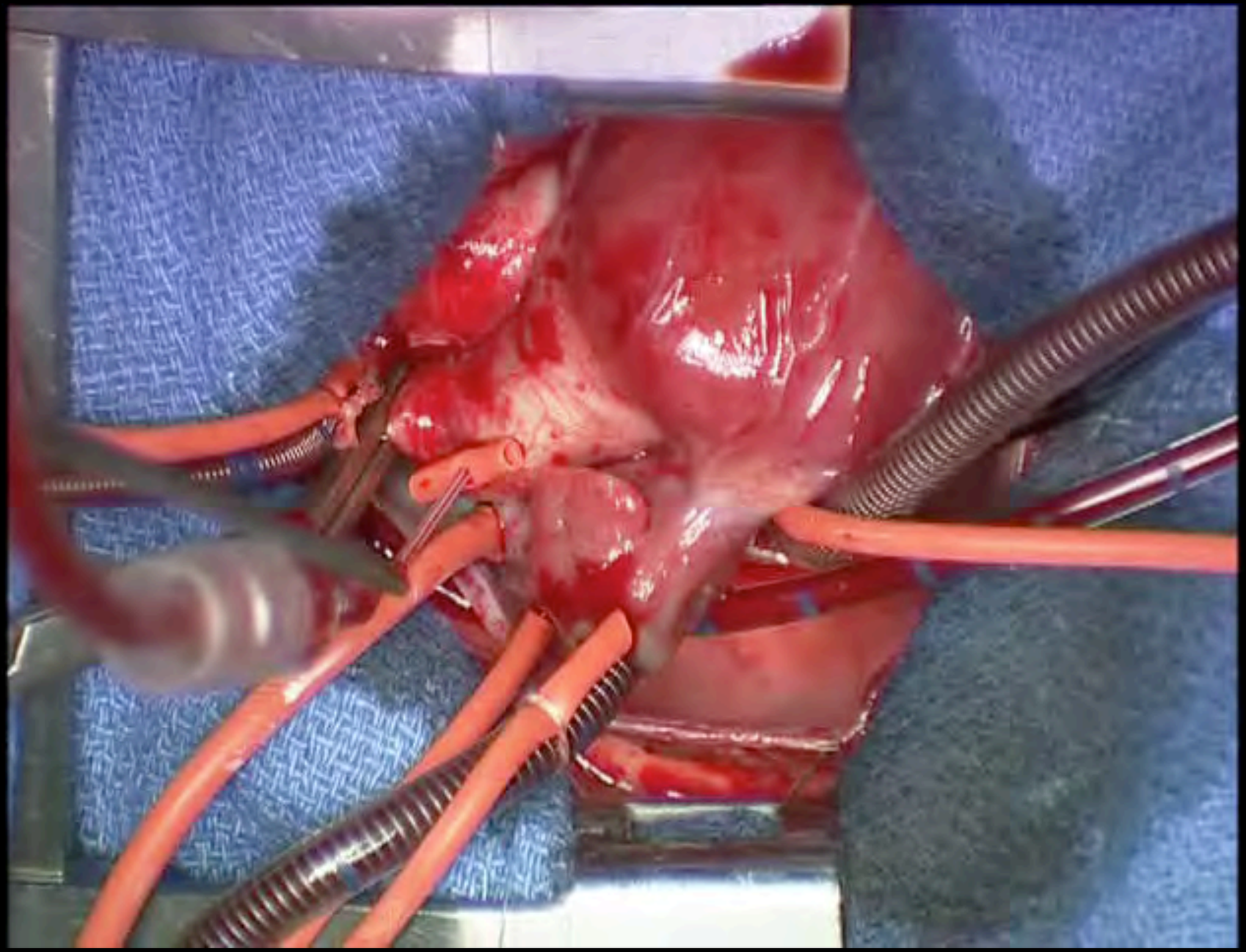


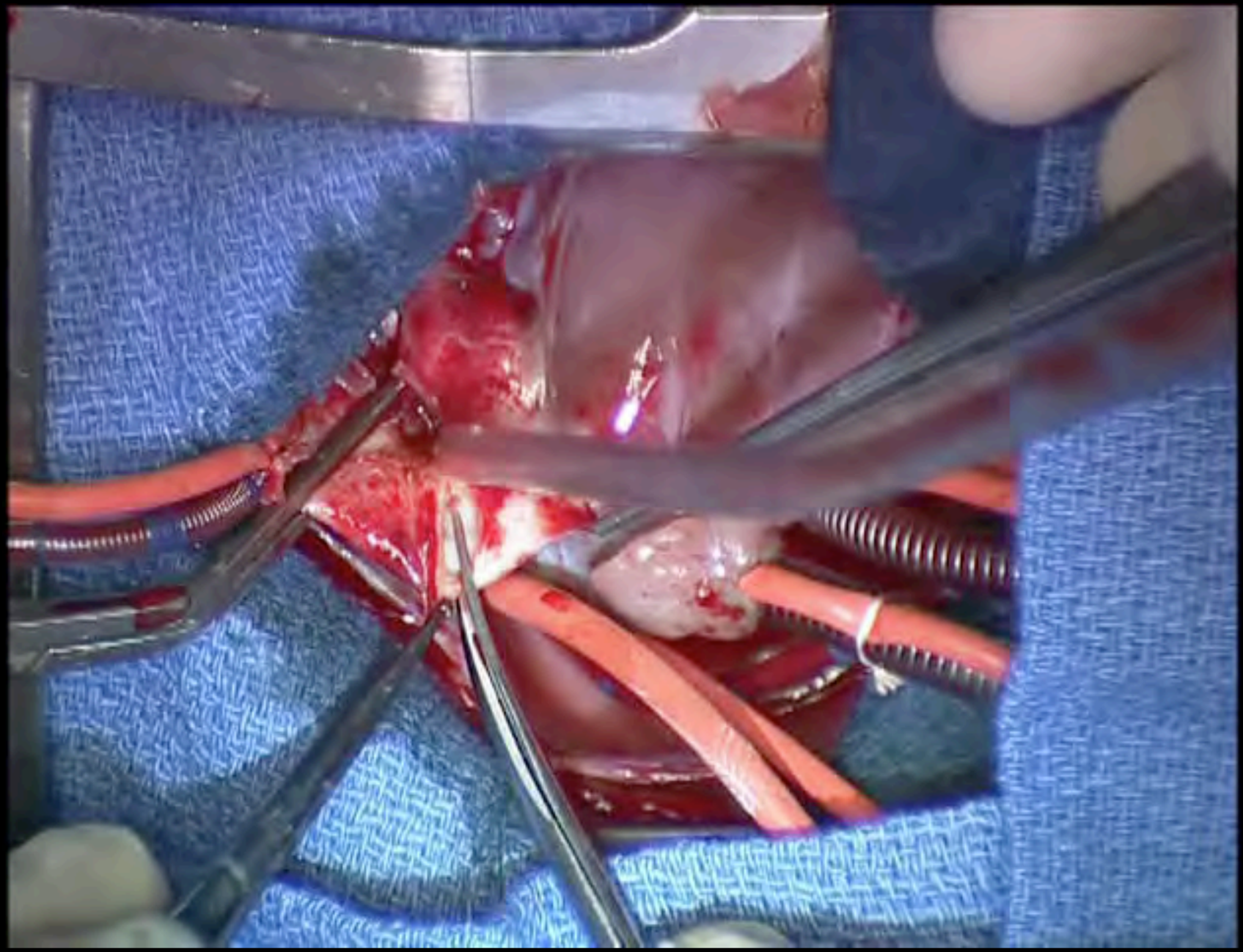
Yves Lecompte

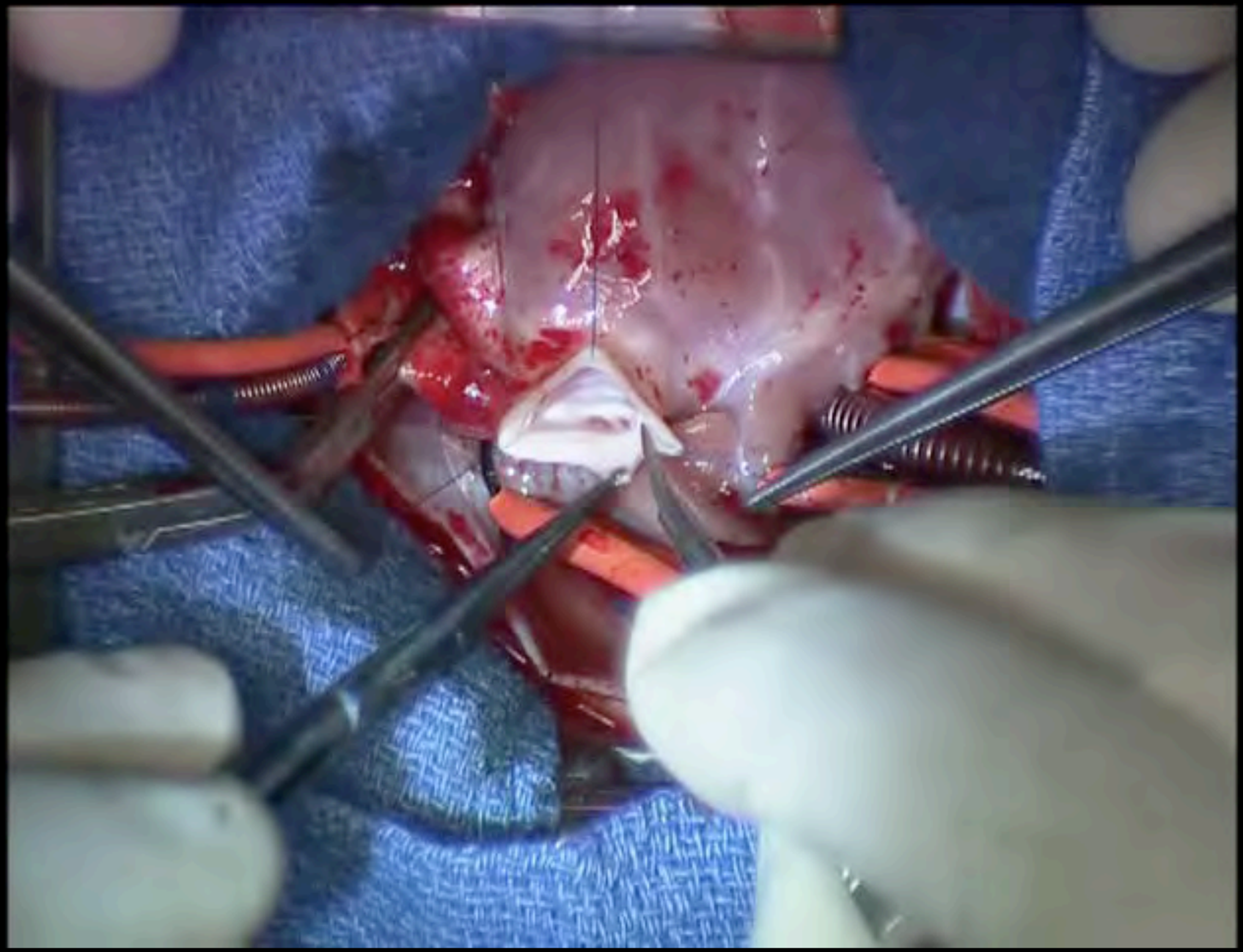


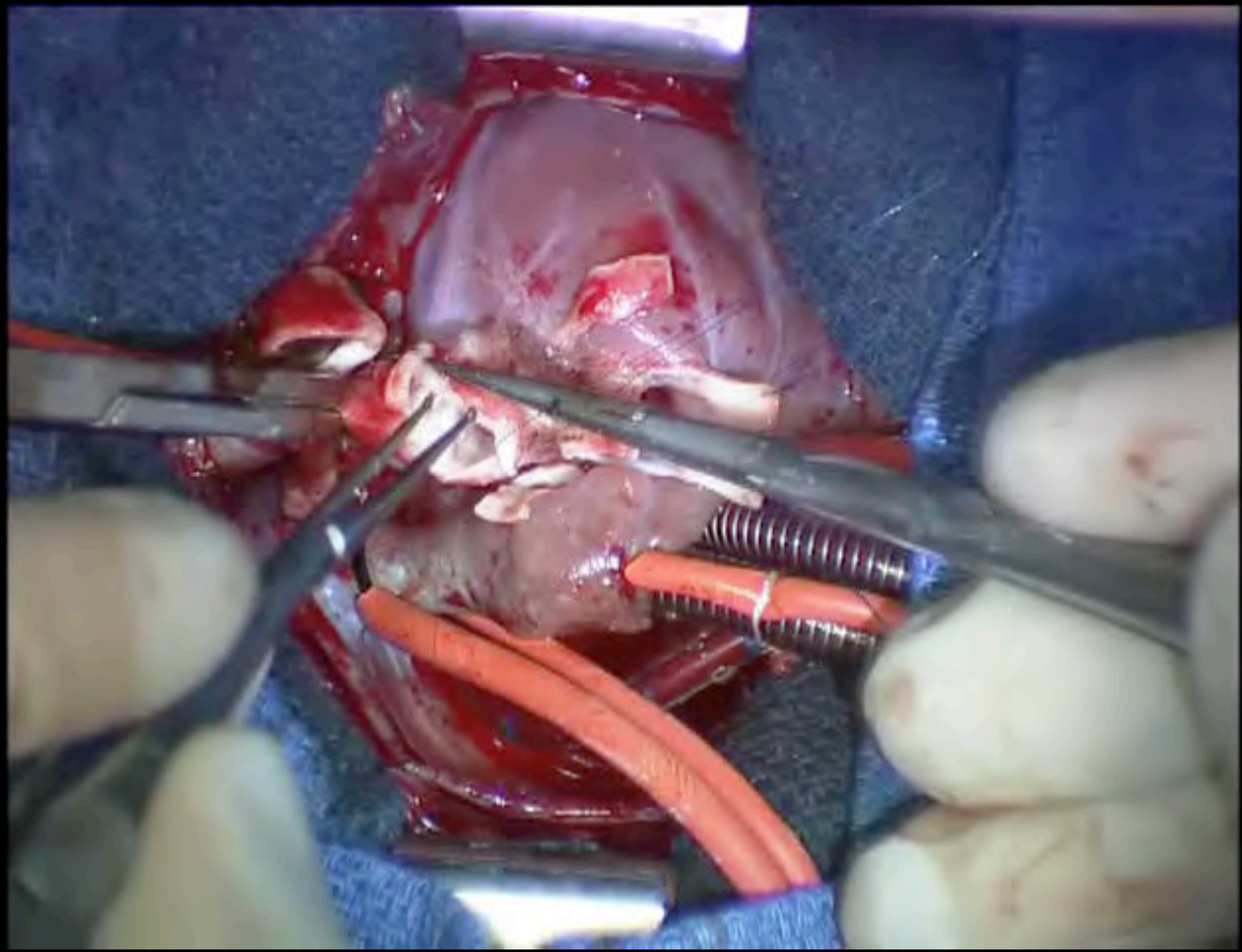


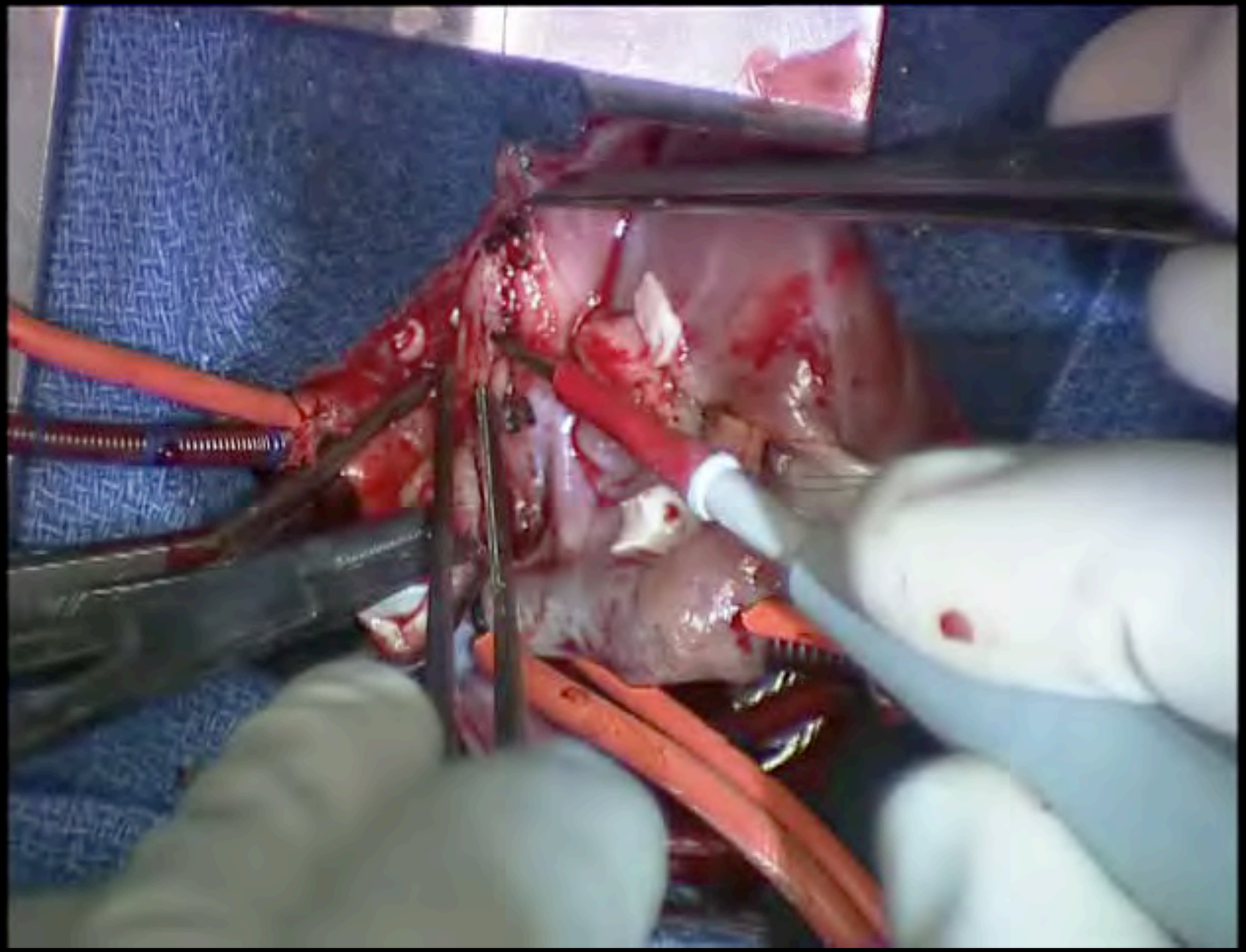


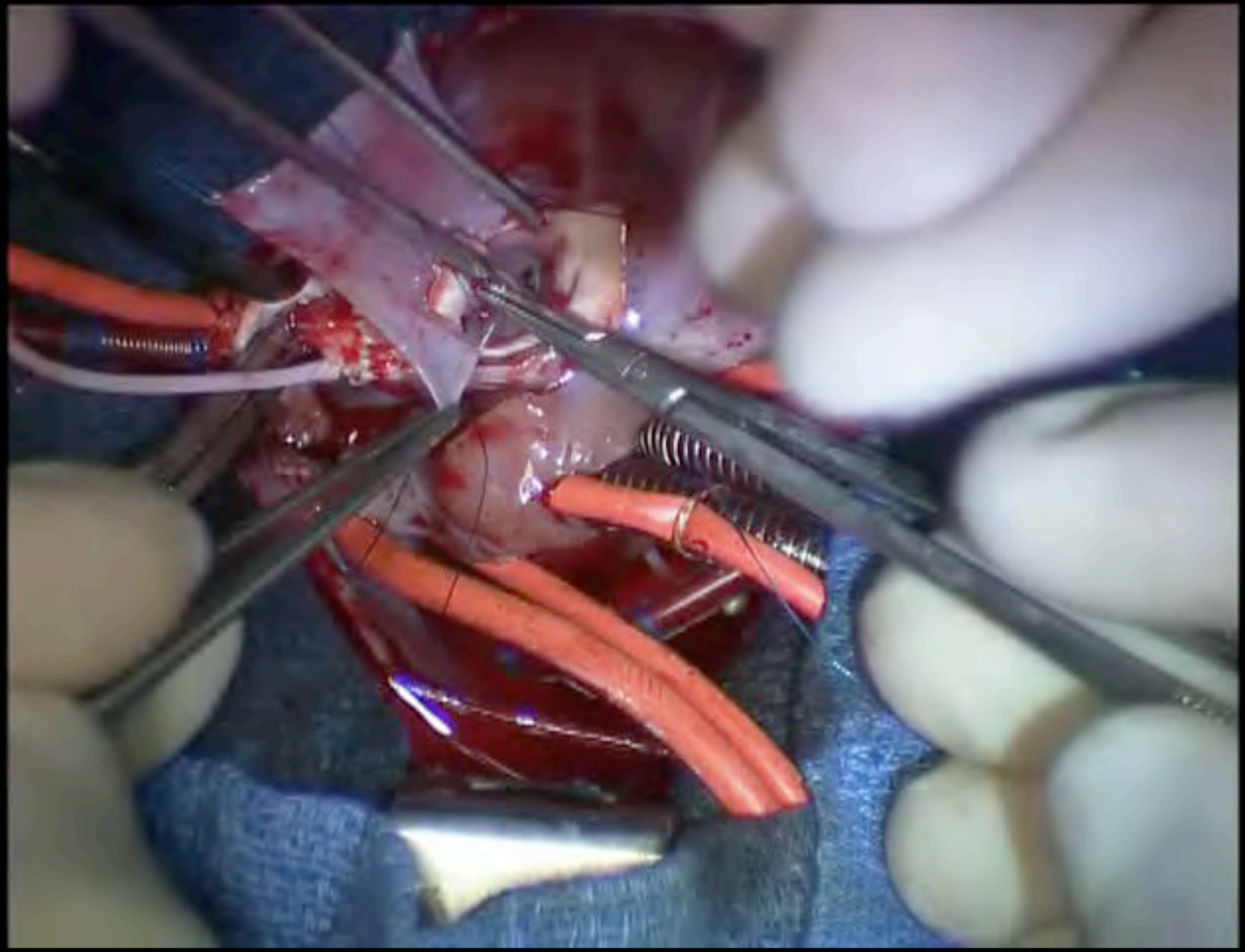


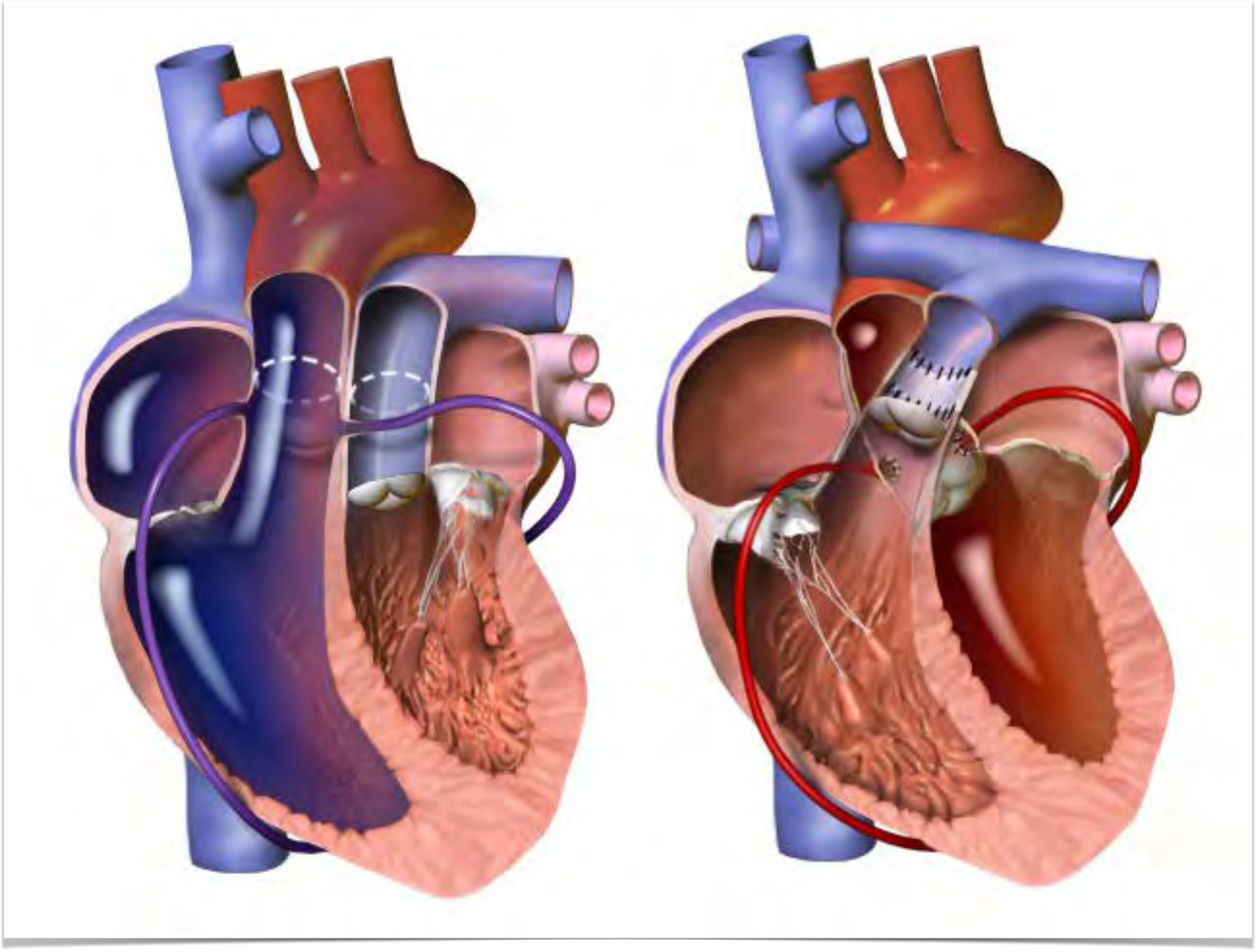




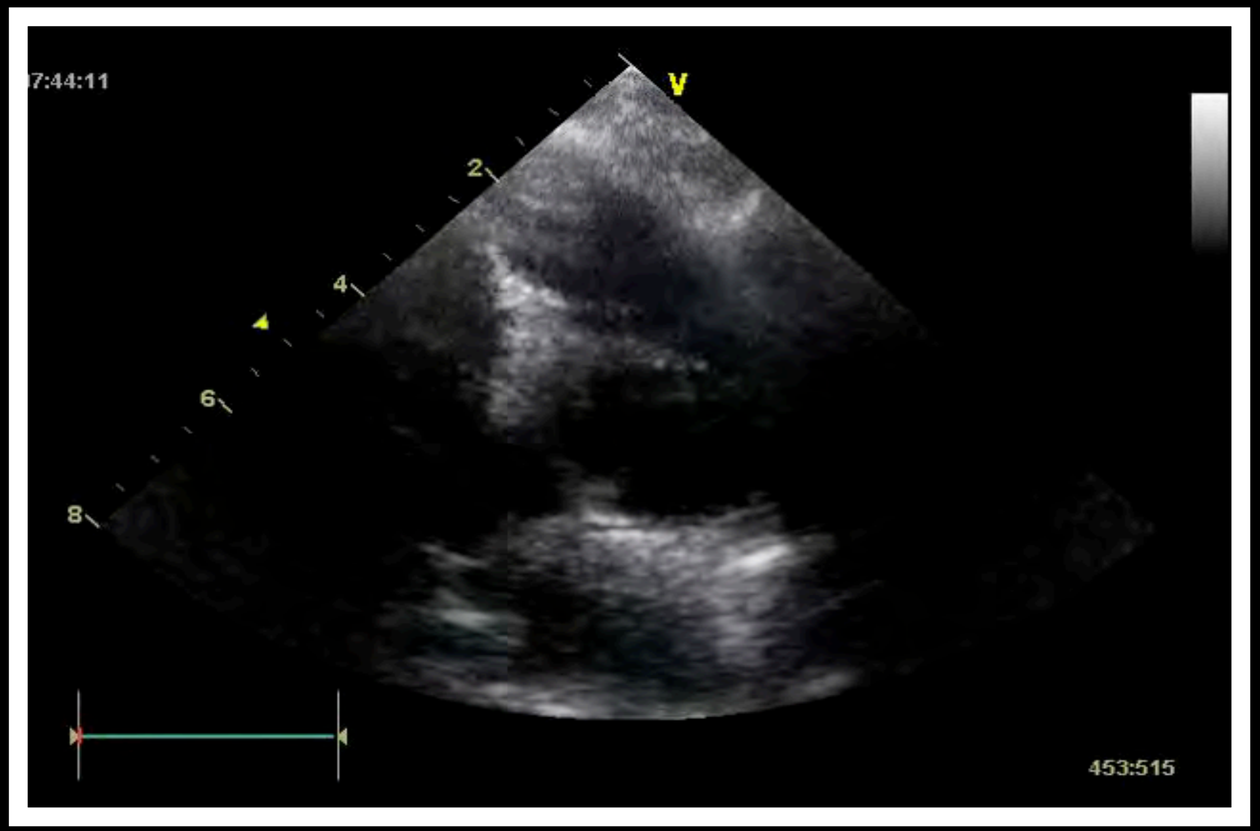


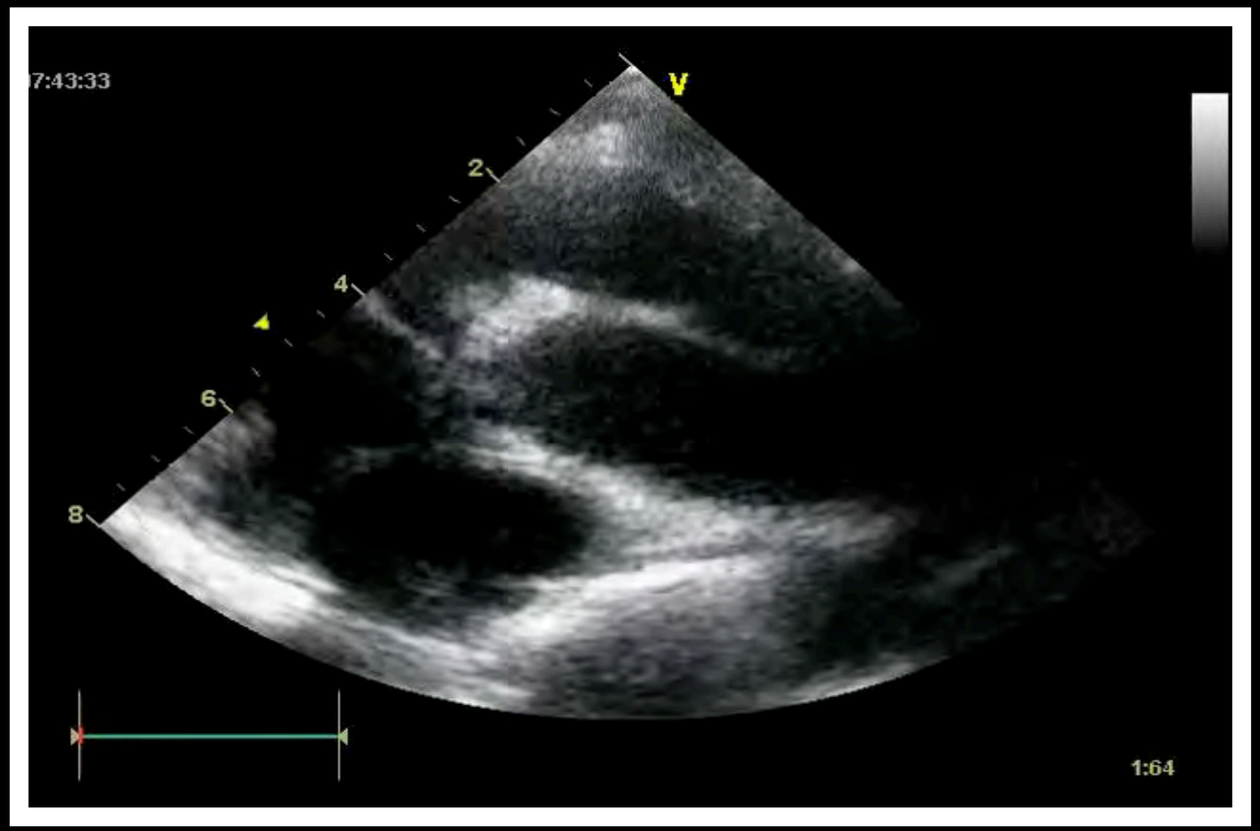




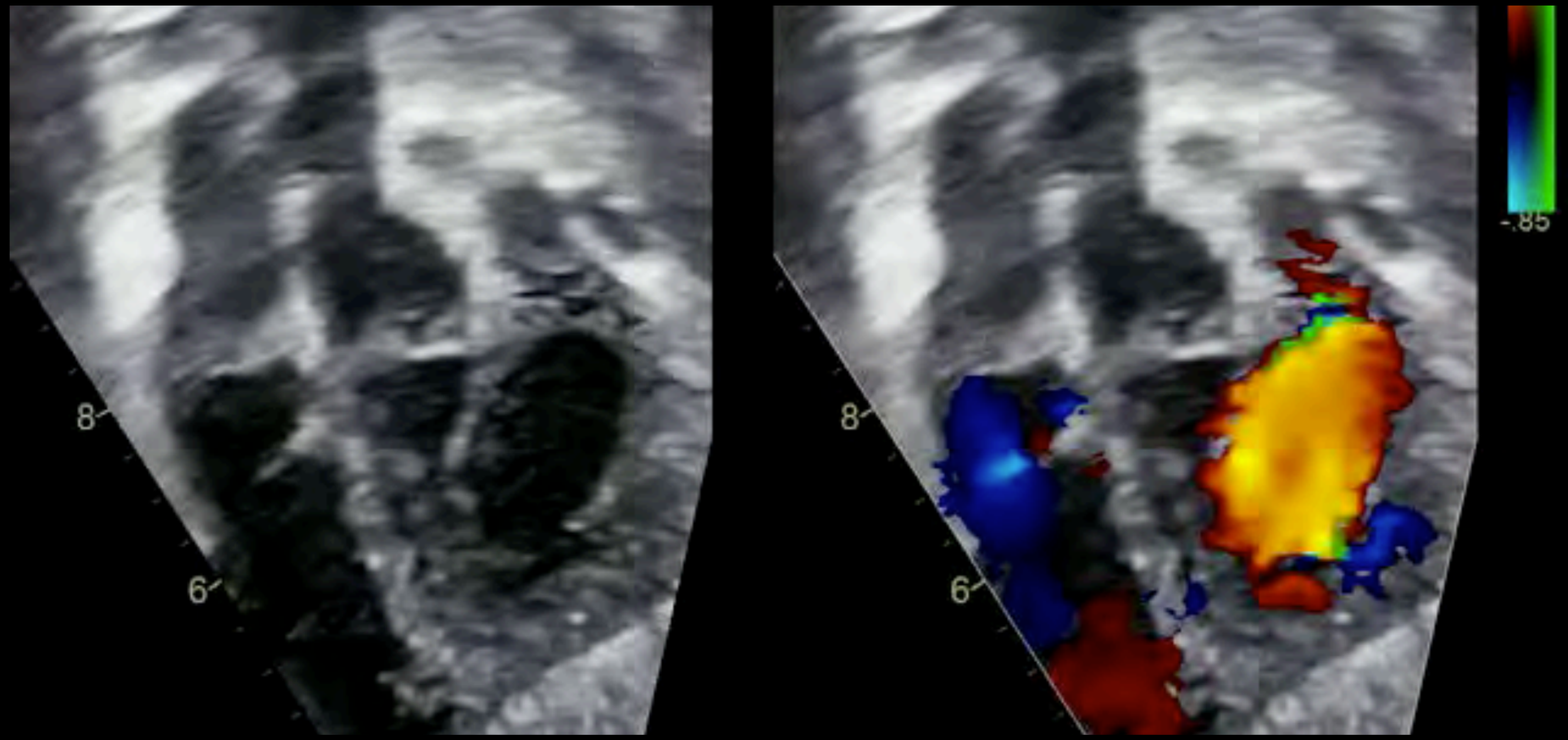


Outflow tracts after the arterial switch for TGA

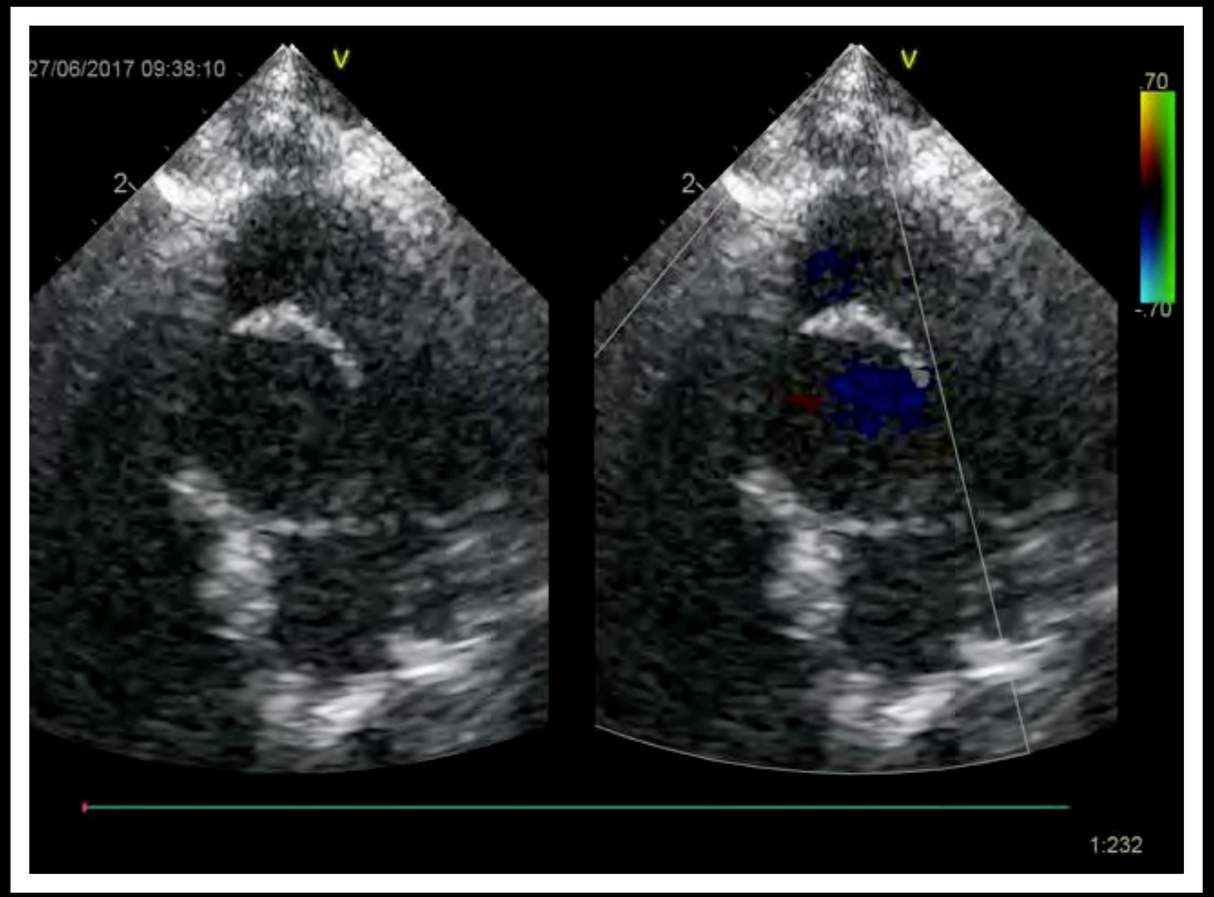


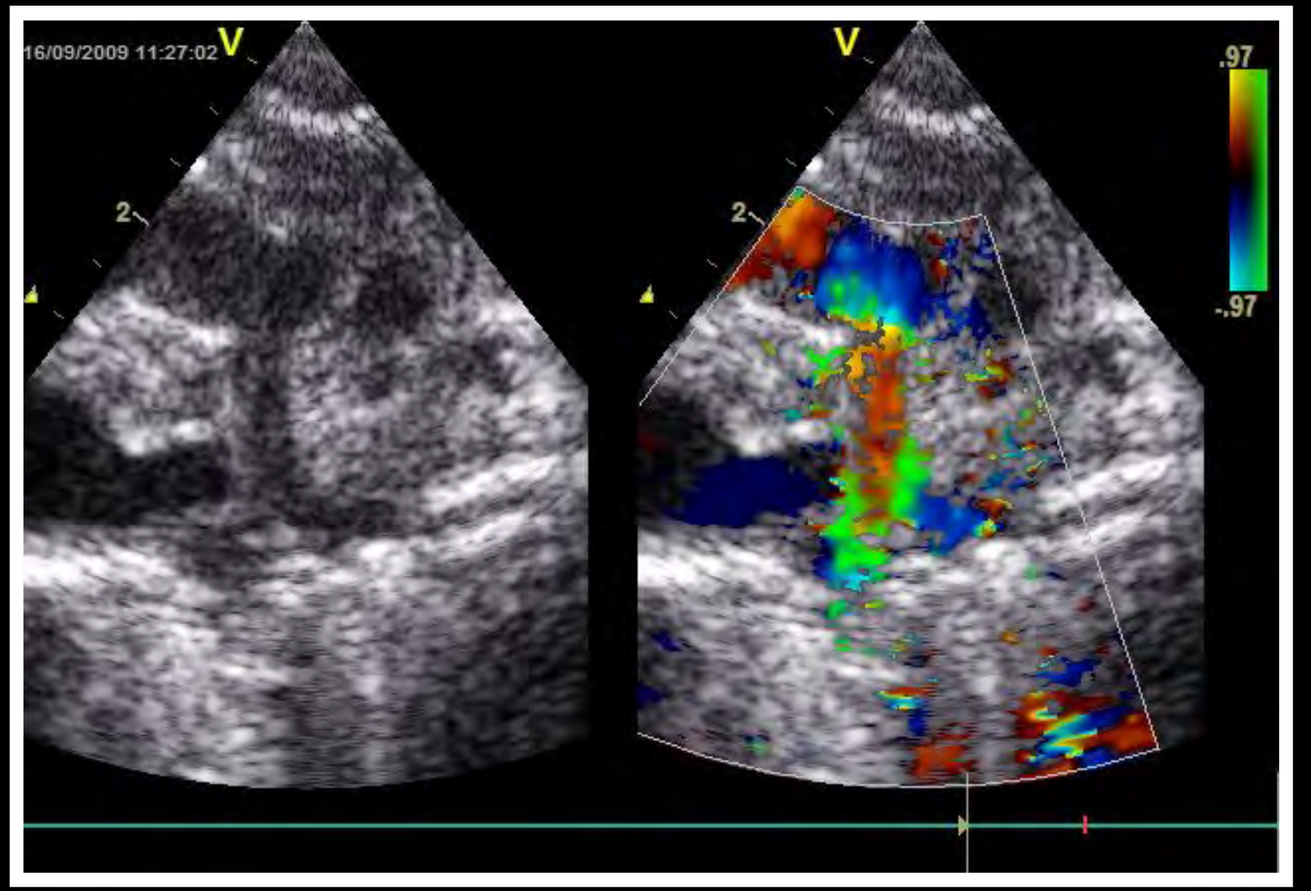


Outflow tracts after the arterial switch for TGA

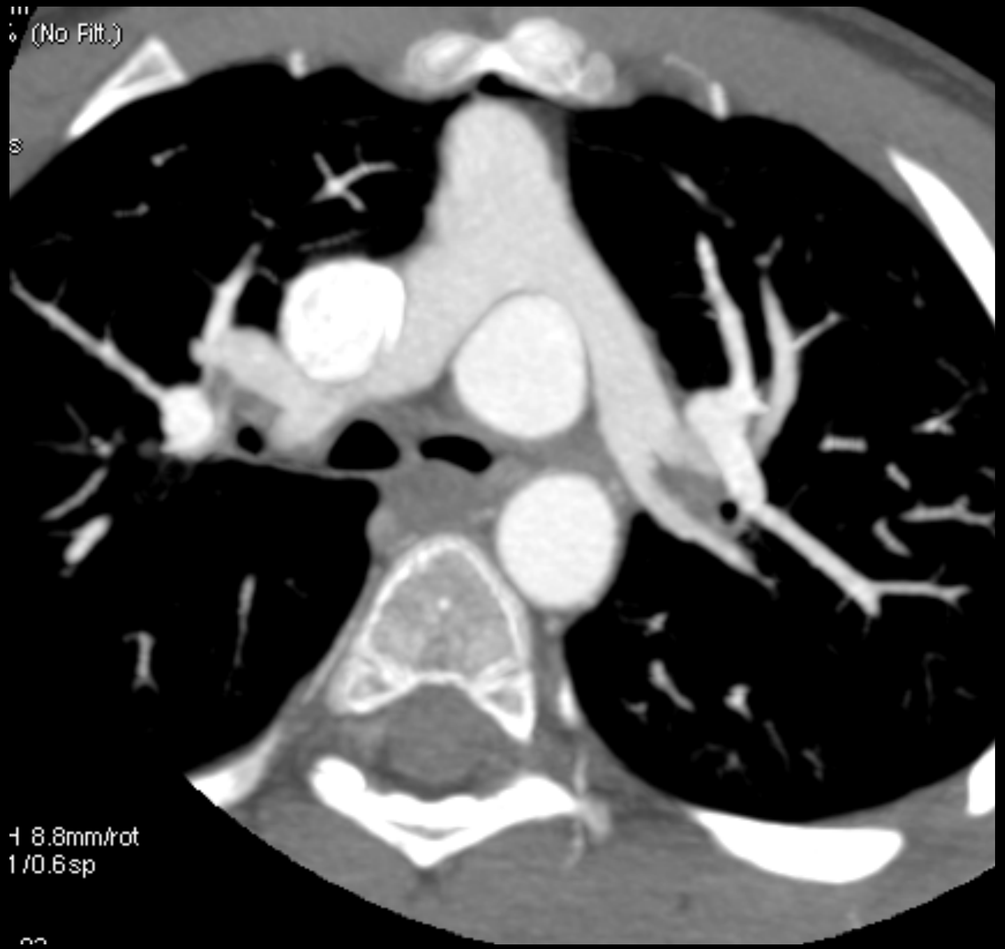


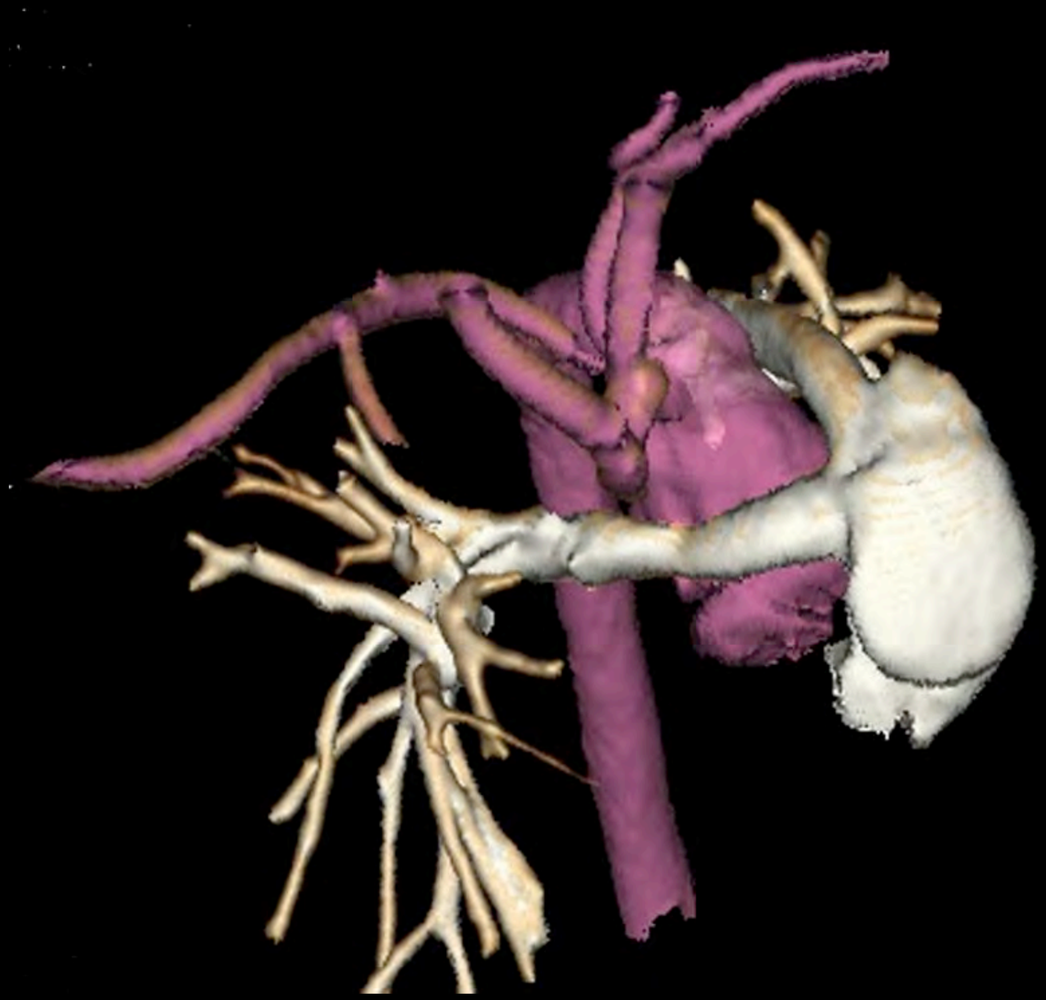
Outflow tracts after the arterial switch for TGA
The Lecompte manoeuver





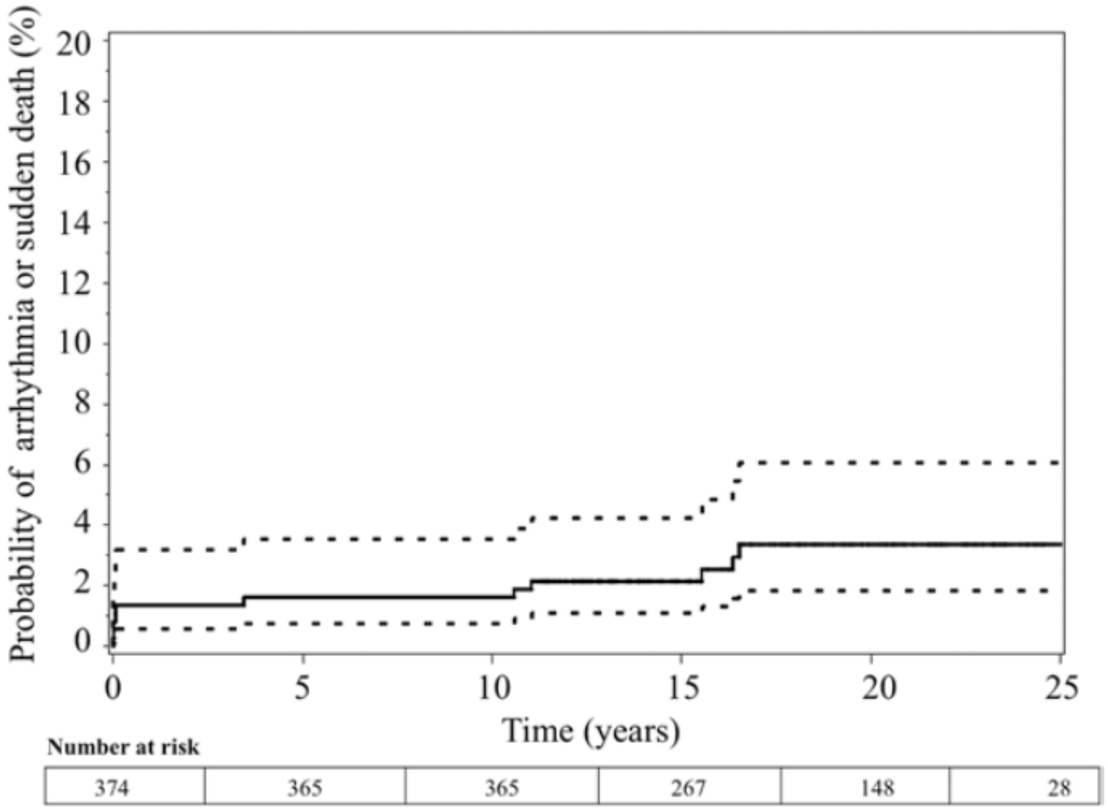
Outflow tracts after the arterial switch for TGA
The Lecompte manoeuver



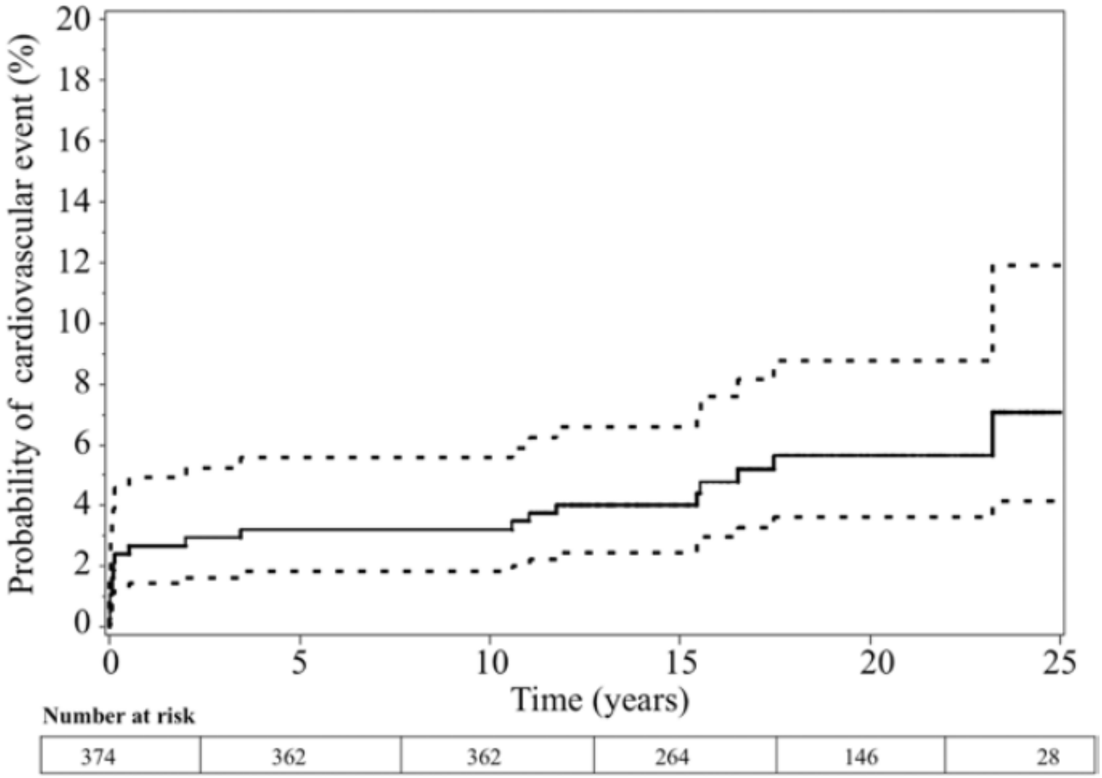


Long term outcomes after the arterial switch operation

Cardiovascular events in the long term

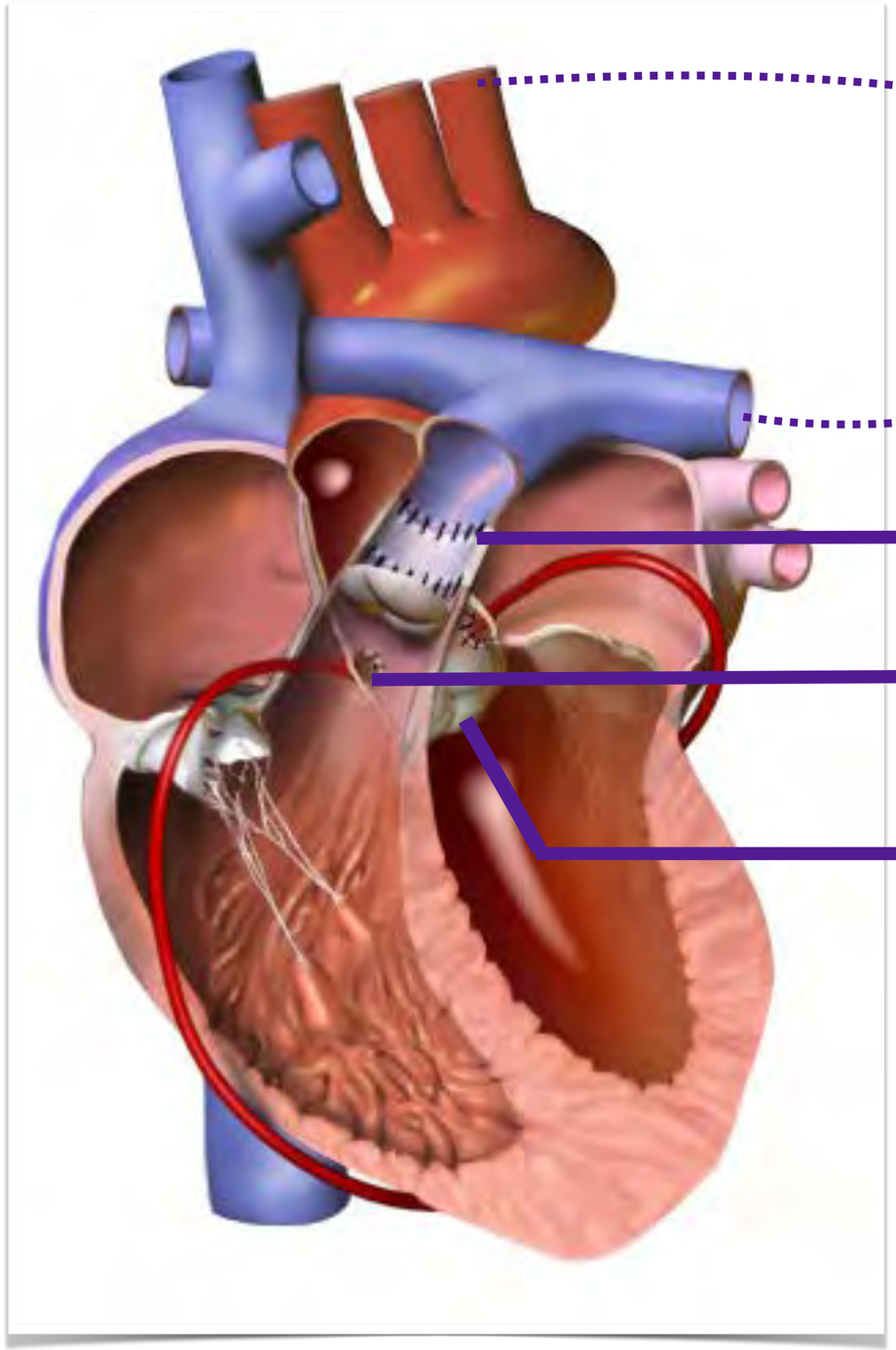


Cumulative probability of arrhythmia or sudden death



Cumulative probability of the combined cardiovascular outcome

Khairy P et al. *Circulation*. 2013;127:331–339.



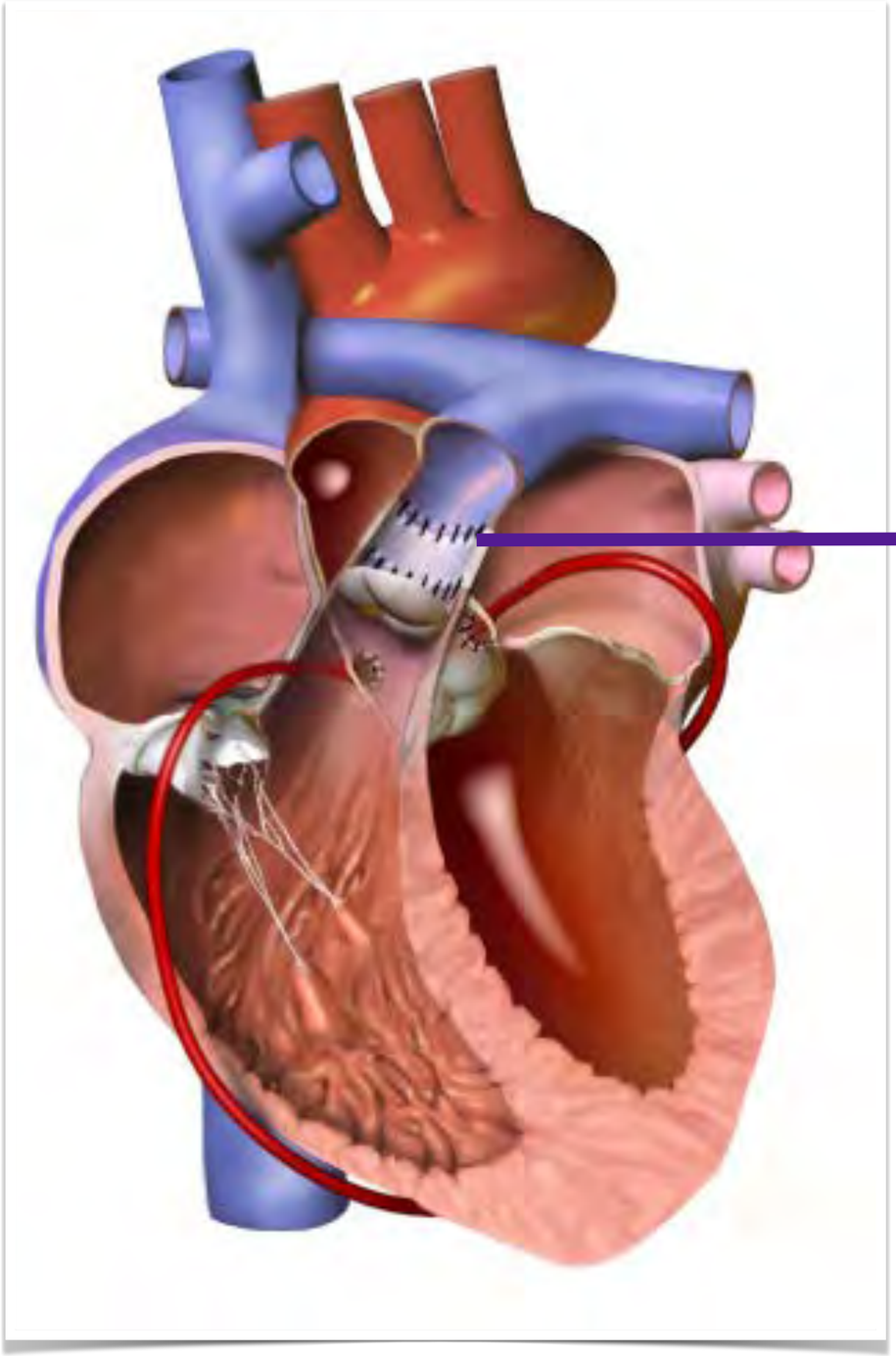
Neurodevelopmental outcomes

Pulmonary arterial hypertension

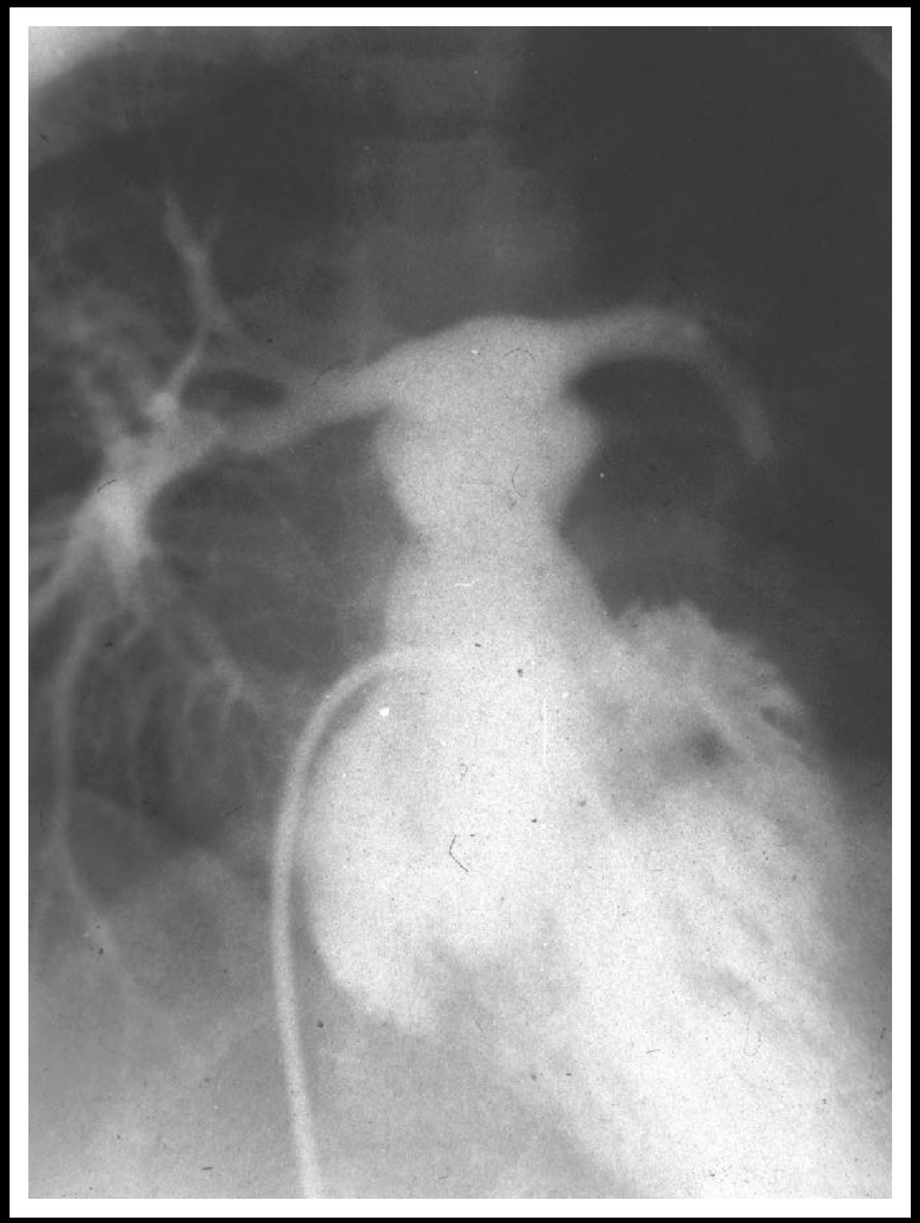
Pulmonary artery stenosis

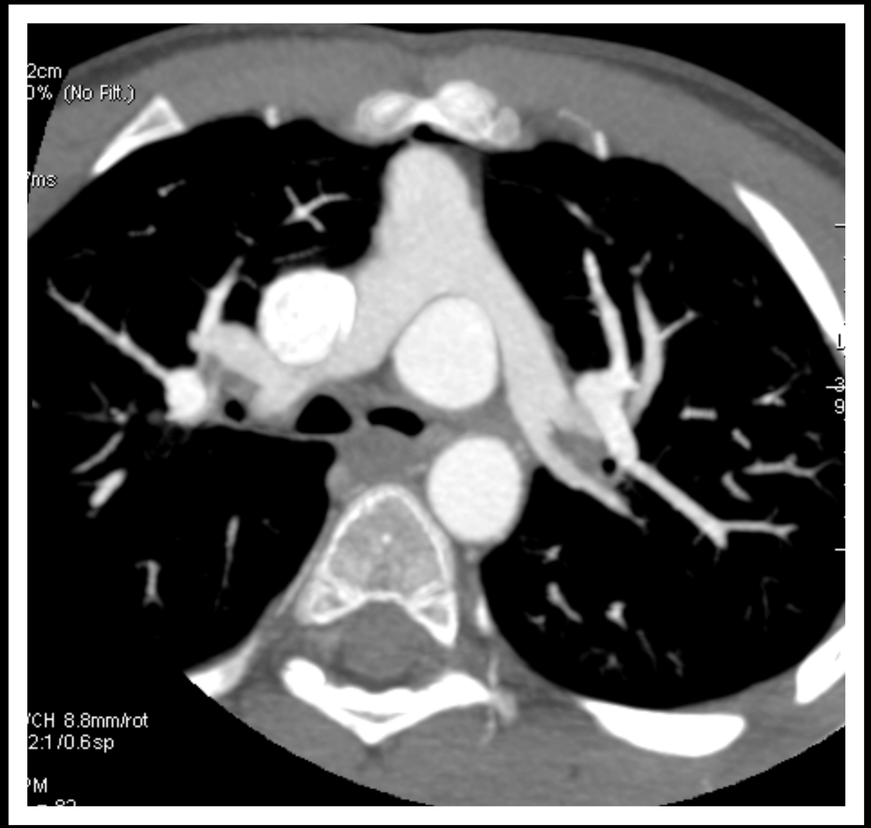
Coronary artery obstruction

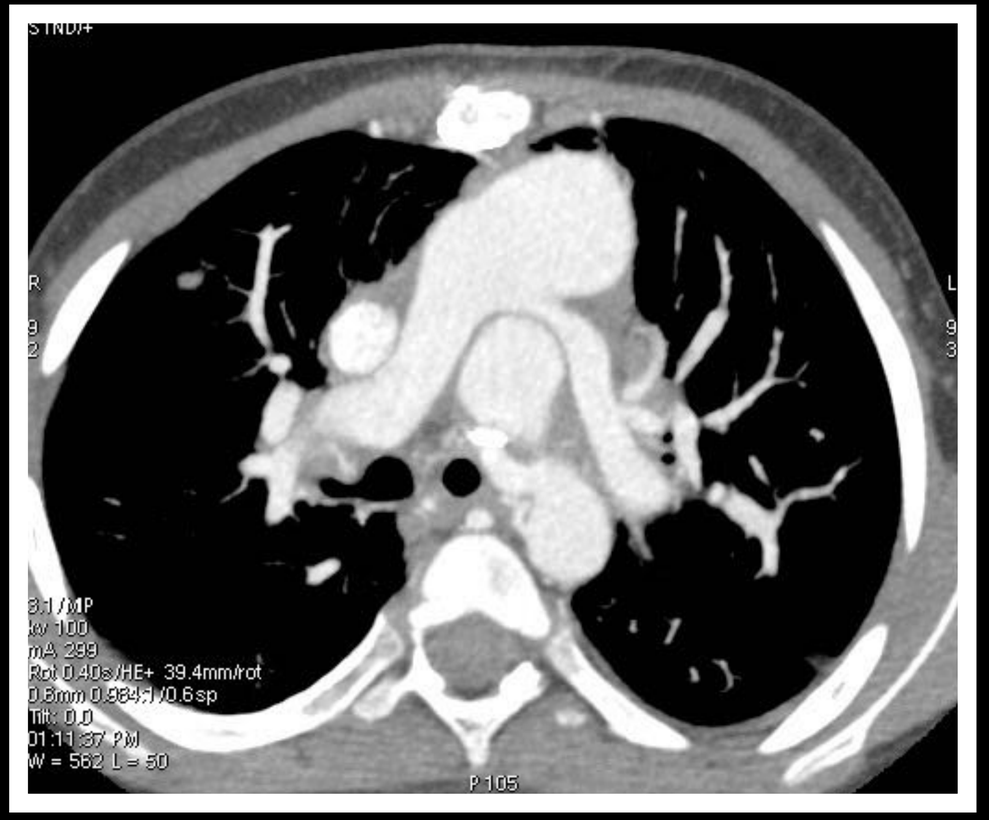
Aortic valve regurgitation

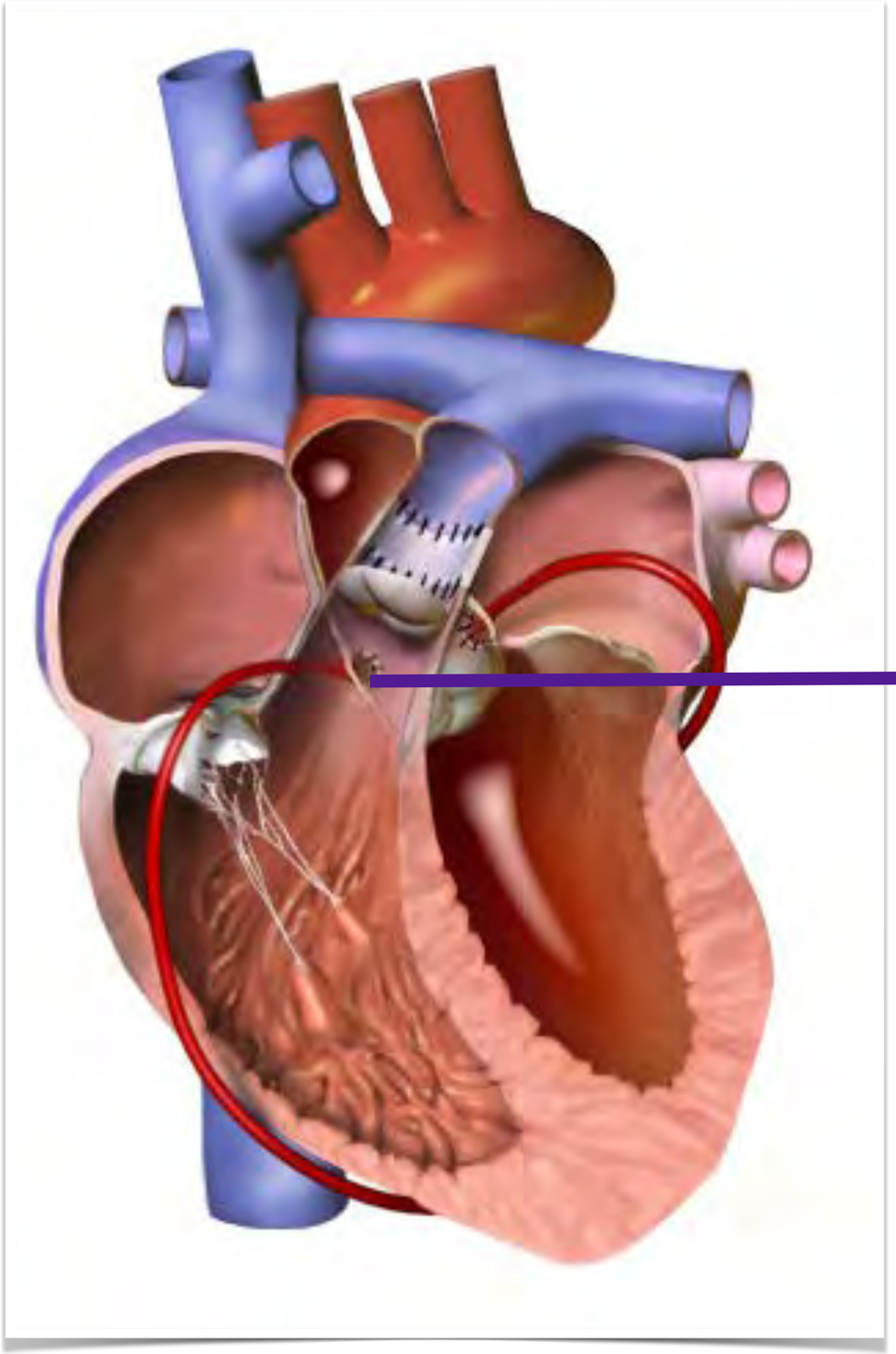


Pulmonary artery stenosis




2cm
0% (No Filt.)
7ms
CH 8.8mm/rot
2:1/0.6sp
PM

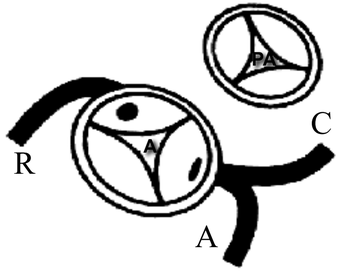

STND+
R
L
3:1/MP
kV 100
mA 299
Rot 0.40s/HE+ 39.4mm/rot
0.6mm 0.984:1/0.6sp
Tilt: 0.0
01:11:37 PM
W = 562 L = 50
P 105



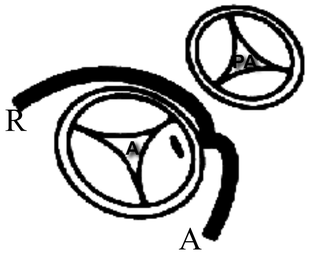
Coronary artery obstruction

Big variations in coronary anatomy (origin, loops, epicardial, intramural)

Type A



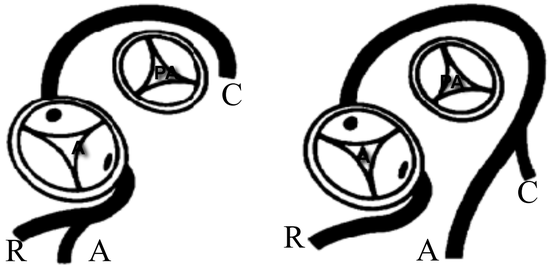
Type B

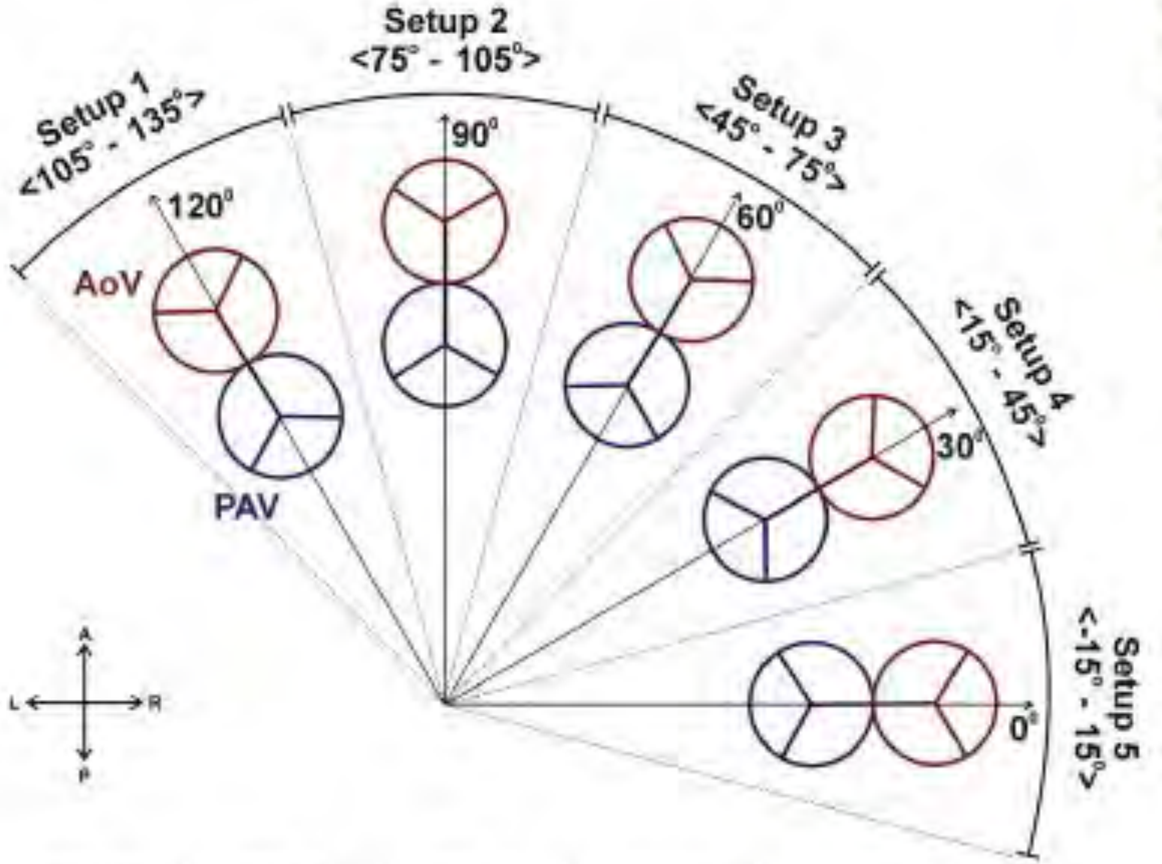


Type C

Type D

Type E



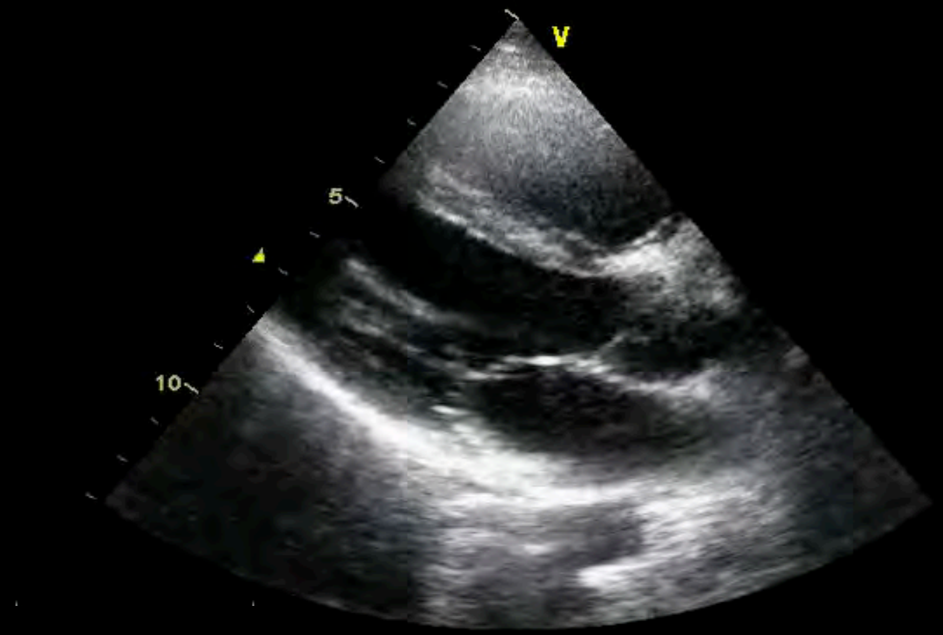


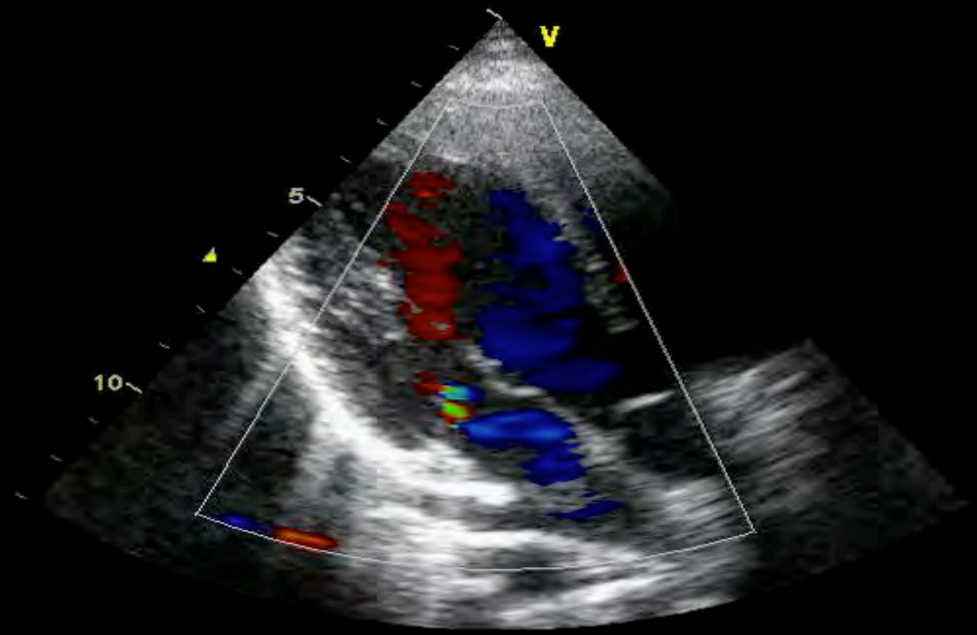
Coronary configuration	Setup 1 (n=83)	Setup 2 (n=246)	Setup 3 (n=263)	Setup 4 (n=56)	Setup 5 (n=65)
usual (n=474)	65 (78.3%)	198 (80.5%)	178 (67.7%)	21 (36.2%)	14 (21.5%)
anomalies (n=241)	18 (21.7%)	48 (19.5%)	85 (32.3%)	37 (63.8%)	51 (78.5%)

Outcomes and predictors of early mortality of the ASO for TGA with IVS

First Author (Ref. #), Year	Inclusive Years	N	% IVS	Early Survival for TGA IVS, %	5-Year Survival, %	10-Year Survival, %	Coronary Anatomic Risk Factors	Other Predictors of Early Mortality
Sarris (43), 2006*	1998-2000	613	70	97	NA	NA	Single coronary (univariate analysis only)	Open sternum
Lalezari (51), 2011	1977-2007	332	60.8	88.6	85.8†	85.2†	Not a risk factor for early mortality	Technical problems with coronary transfer
Fricke (85), 2012	1983-2009	618	64	98.2	98	97	Not a risk factor for early mortality	Weight <2.5 kg ECMO
Khairy (41), 2013	1983-1999	400	59.5	93.5†	NA	92.7†	Single right coronary artery	Post-operative heart failure
Cain (52), 2014	2000-2011	70	100	98.6	NA	NA	None identified	No predictors of early mortality, but earlier repair <4 days of age was associated with decreased resource utilization
Anderson (24), 2014	2003-2012	140	75	98.6	NA	NA	None identified	No predictors of early mortality, but earlier repair <4 days of age was associated with decreased resource utilization

Myocardial ischemia after the arterial switch for TGA

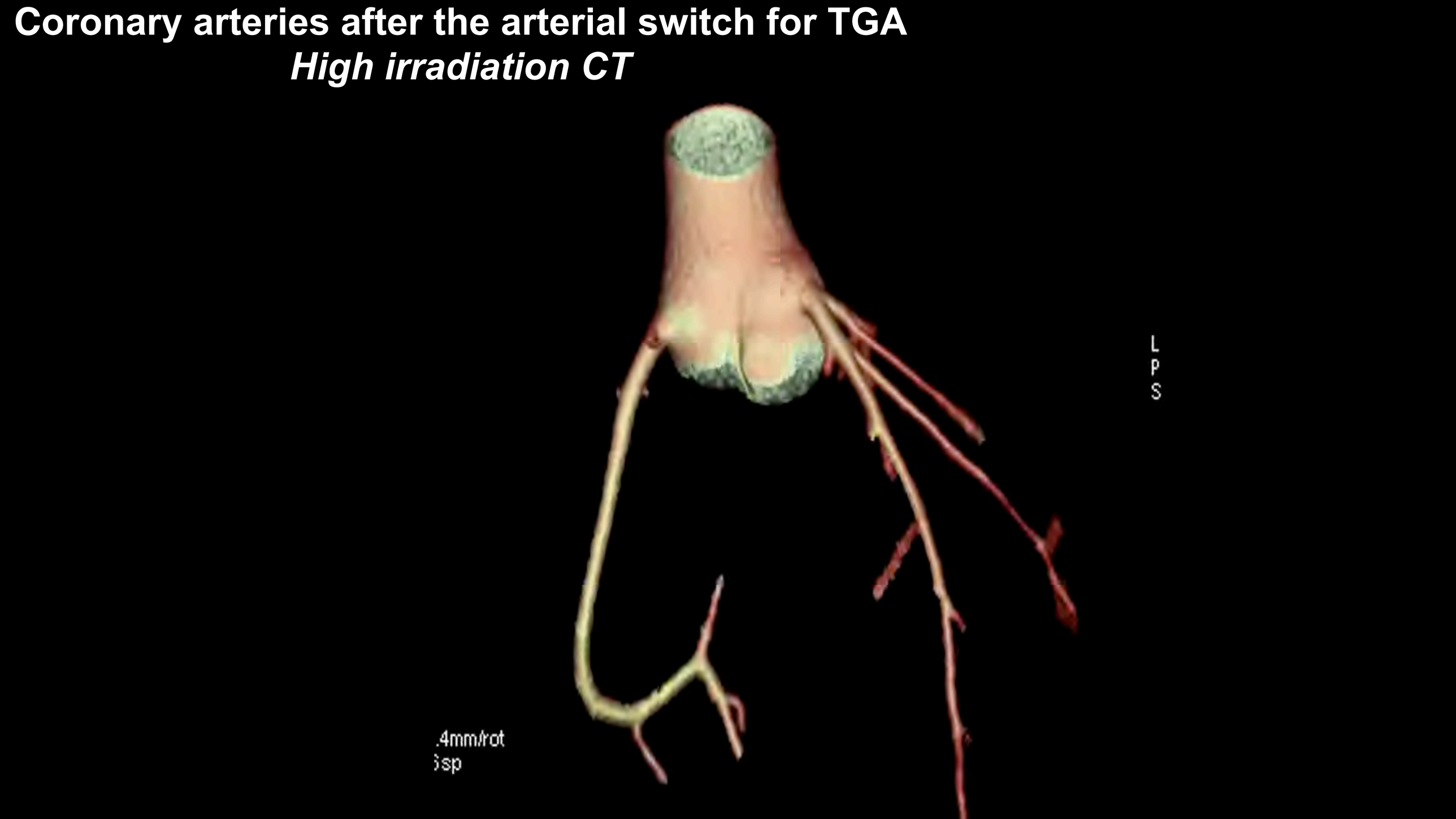




Type D coronary arteries after the arterial switch for TGA

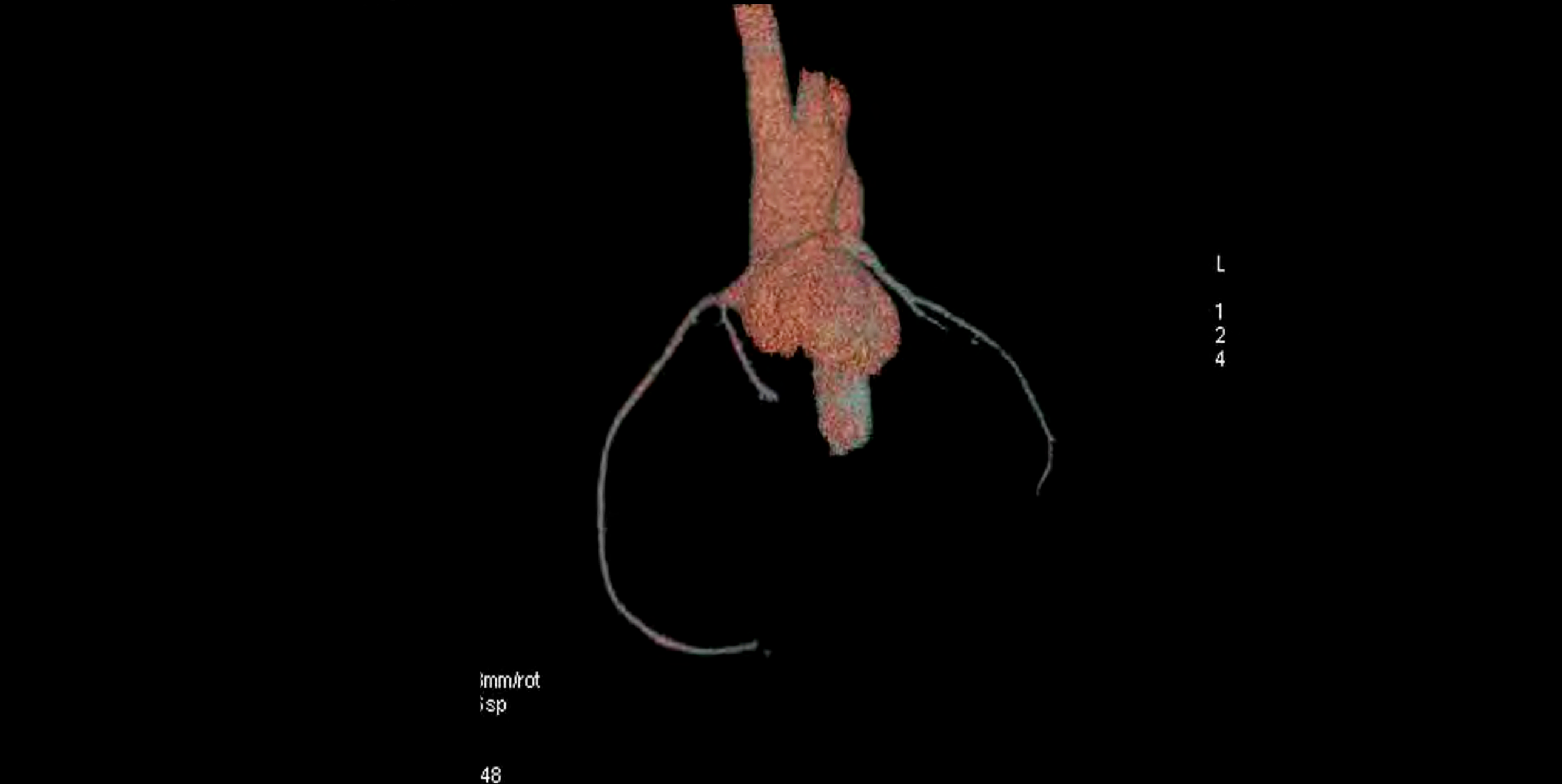
Coronary arteries after the arterial switch for TGA

High irradiation CT



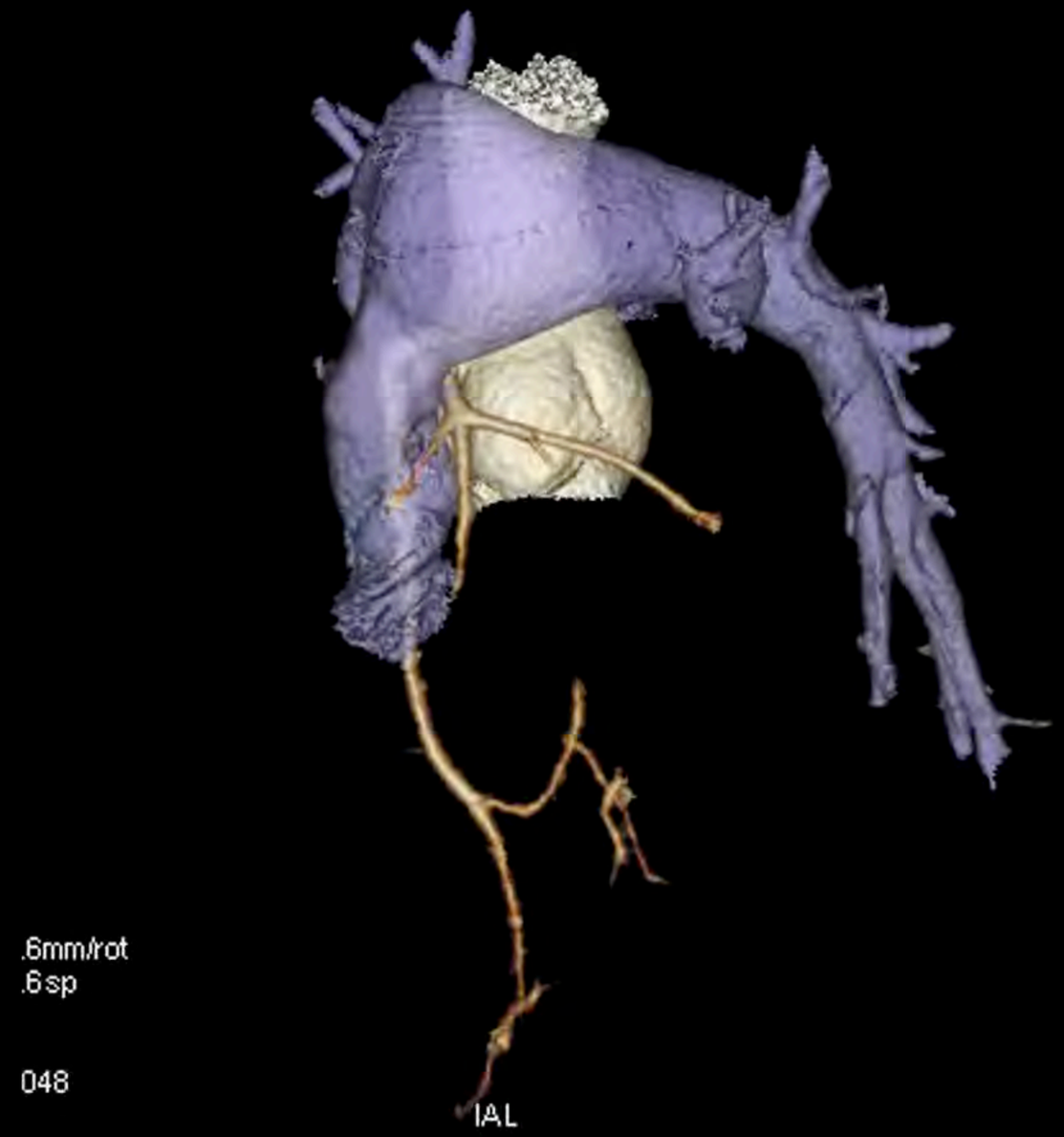
Coronary arteries after the arterial switch for TGA

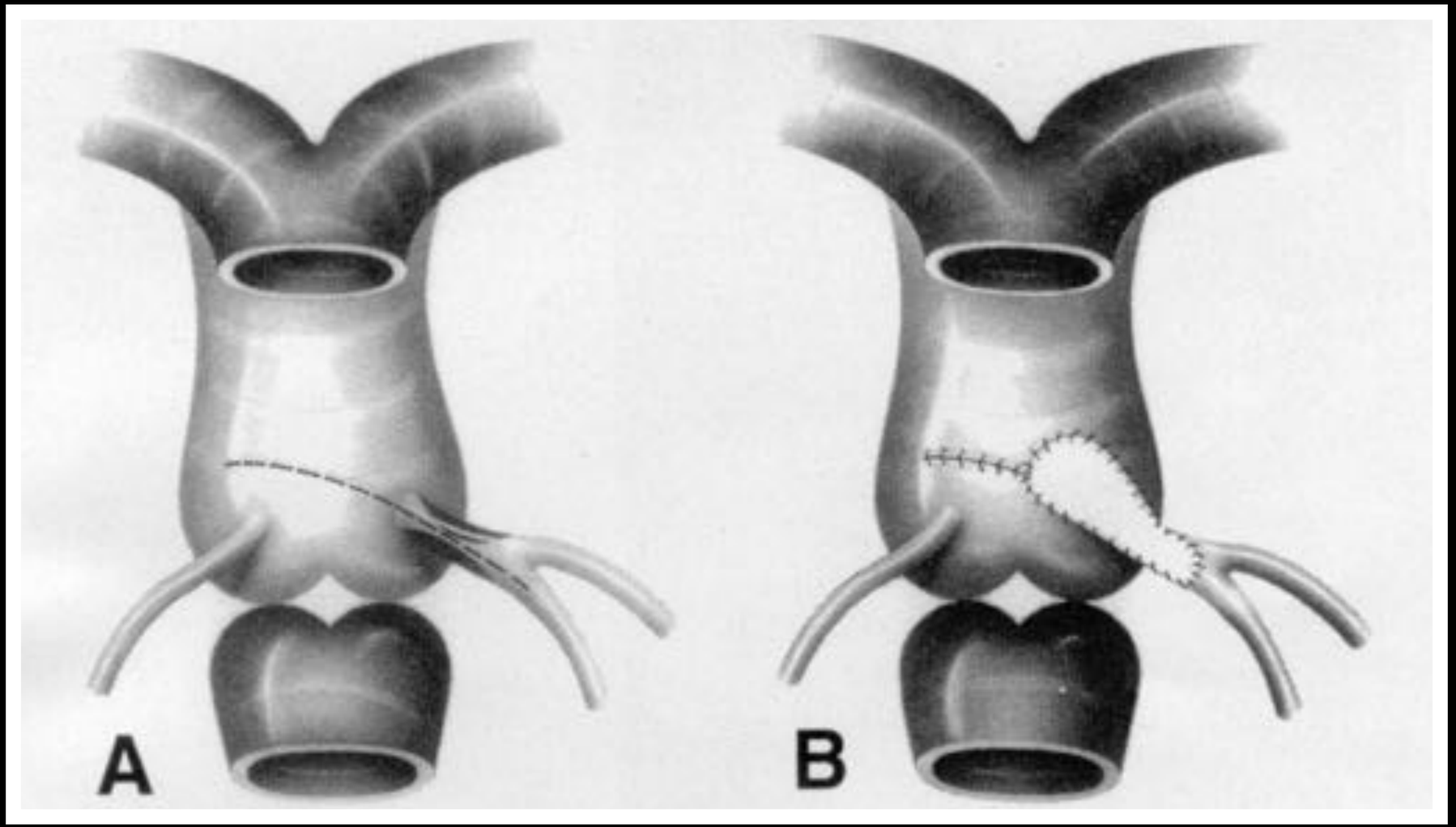
Very low dose CT

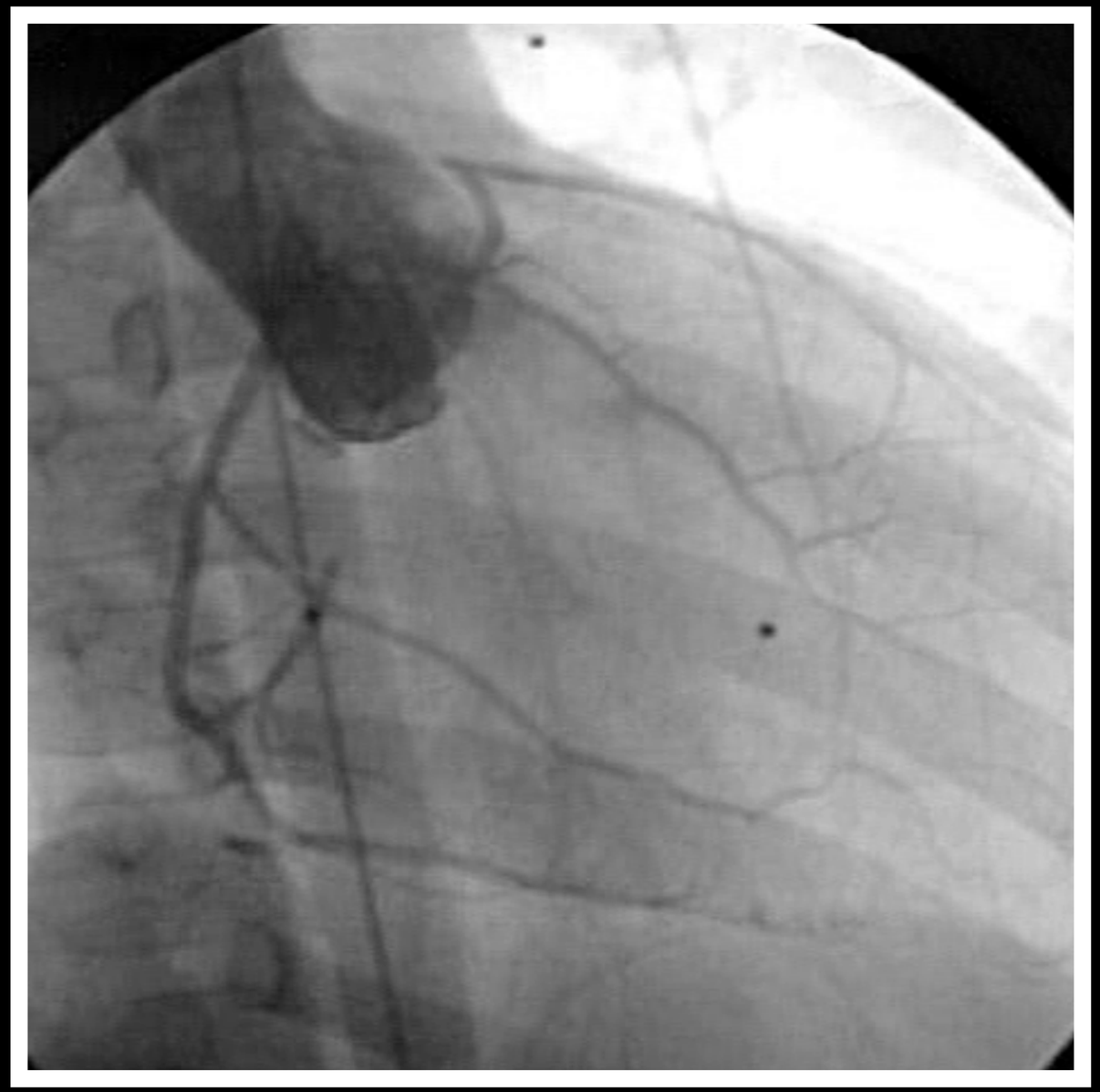


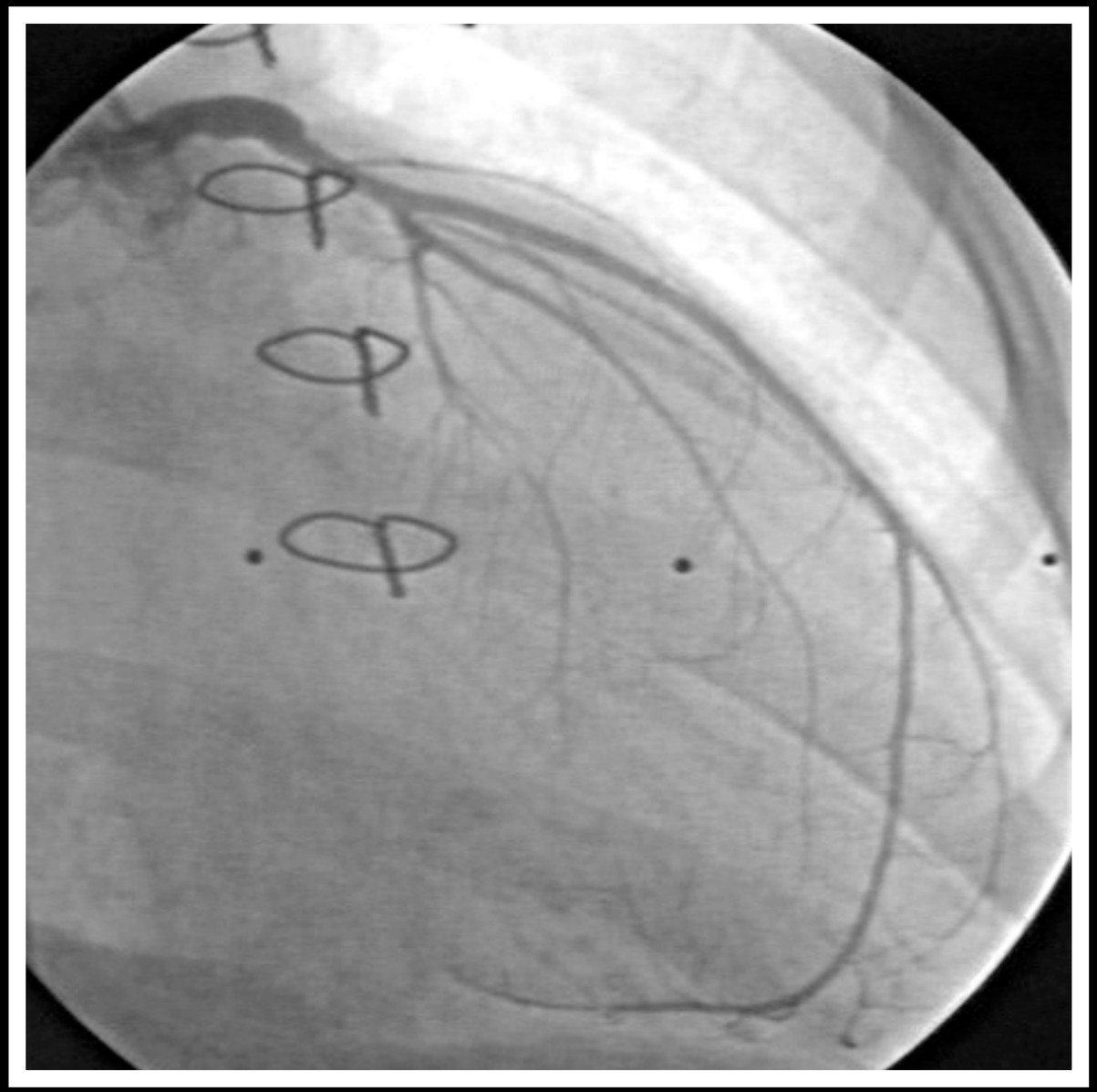
Coronary arteries after the arterial switch for TGA

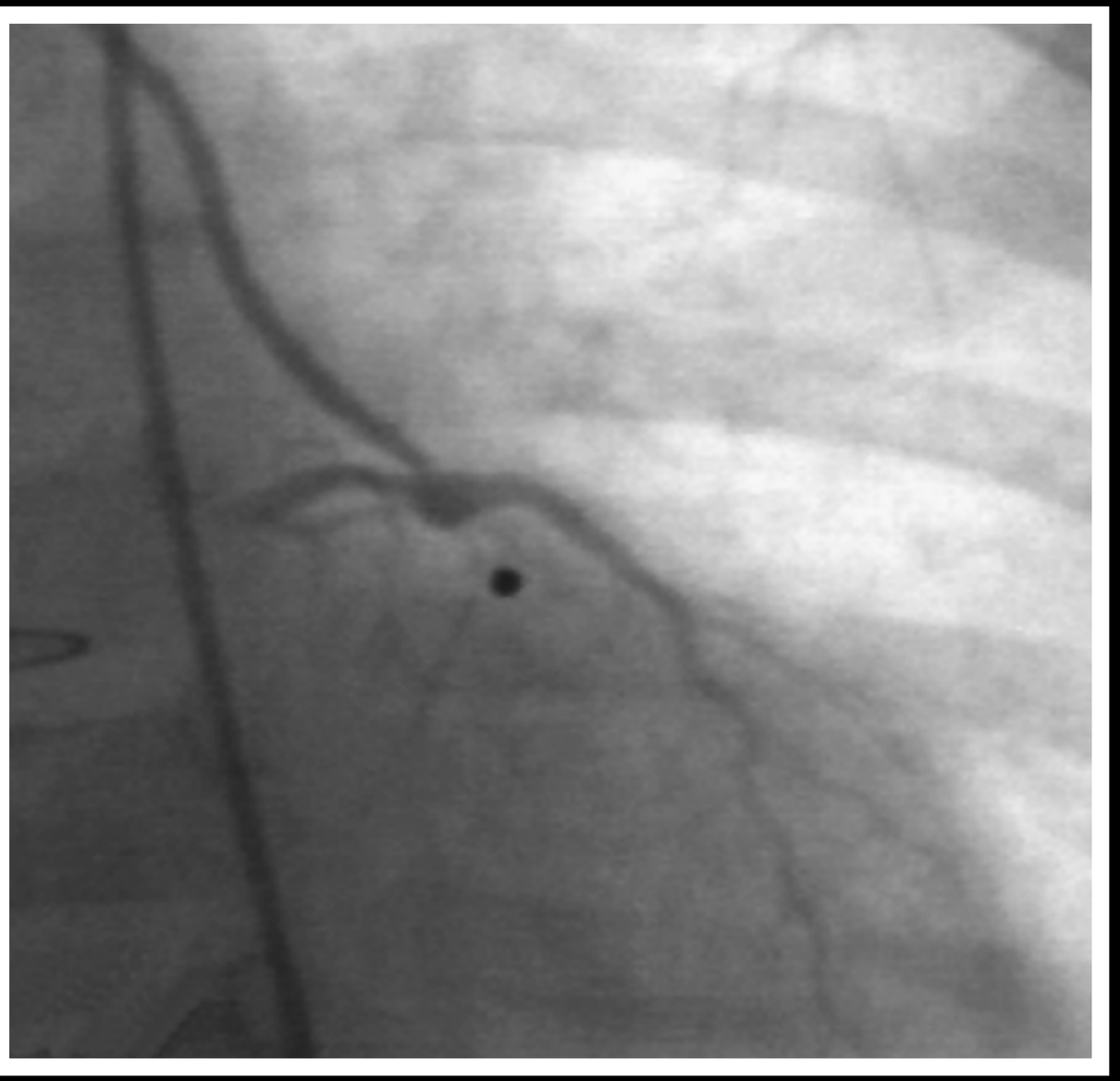
Intervascular course fo left CA



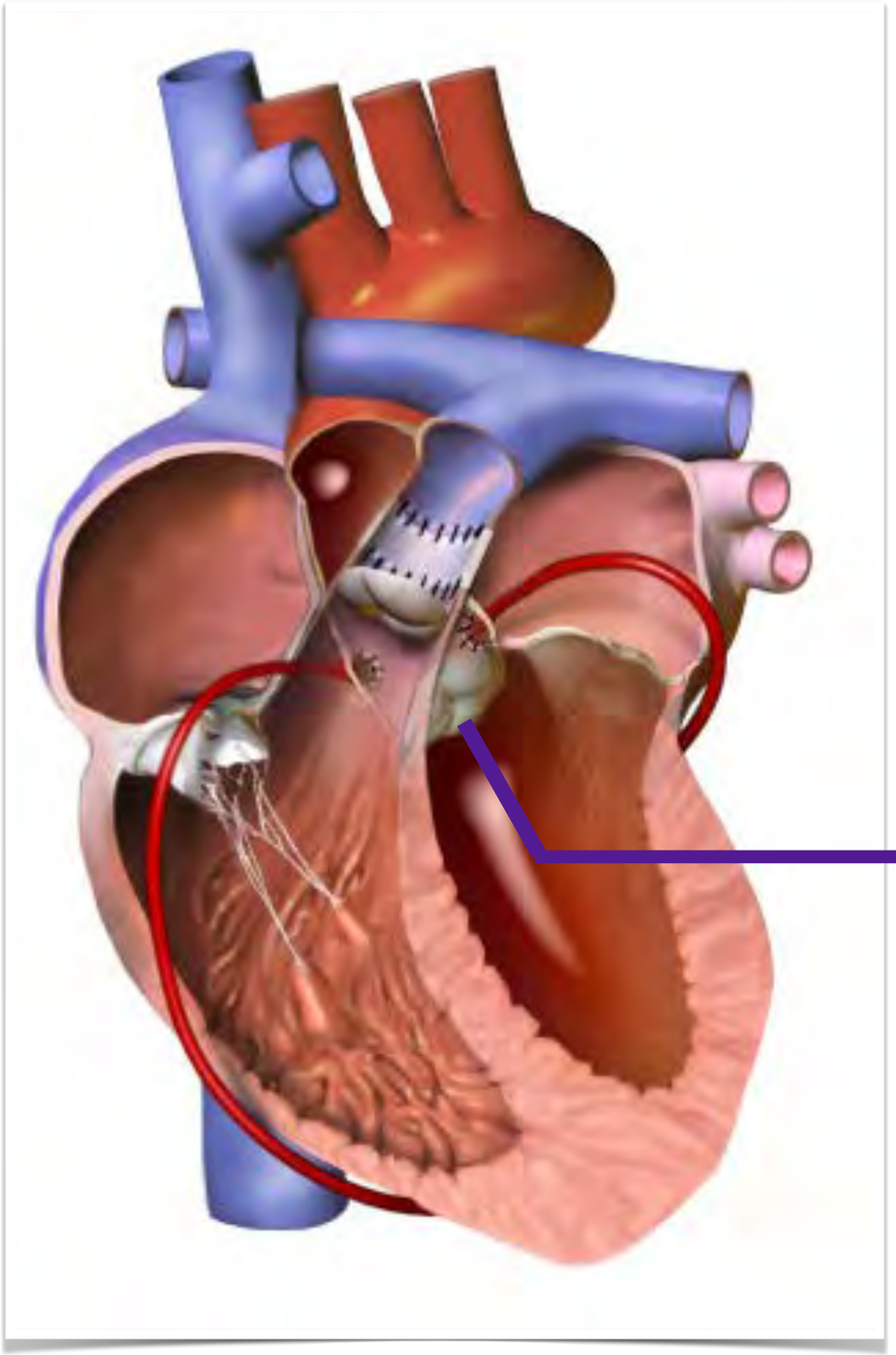

A
B





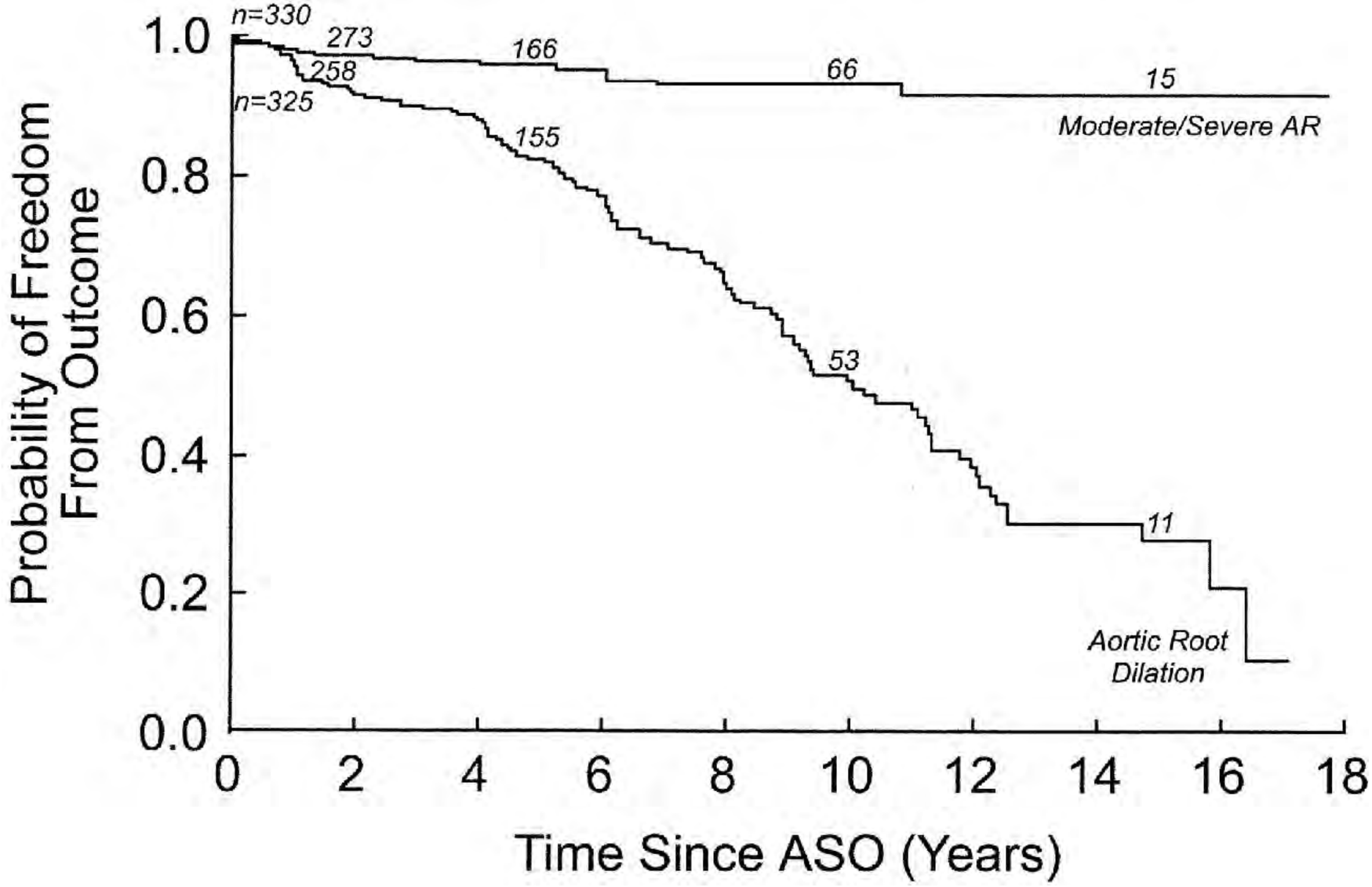


Pontage mammaire interne-IVA post-switch

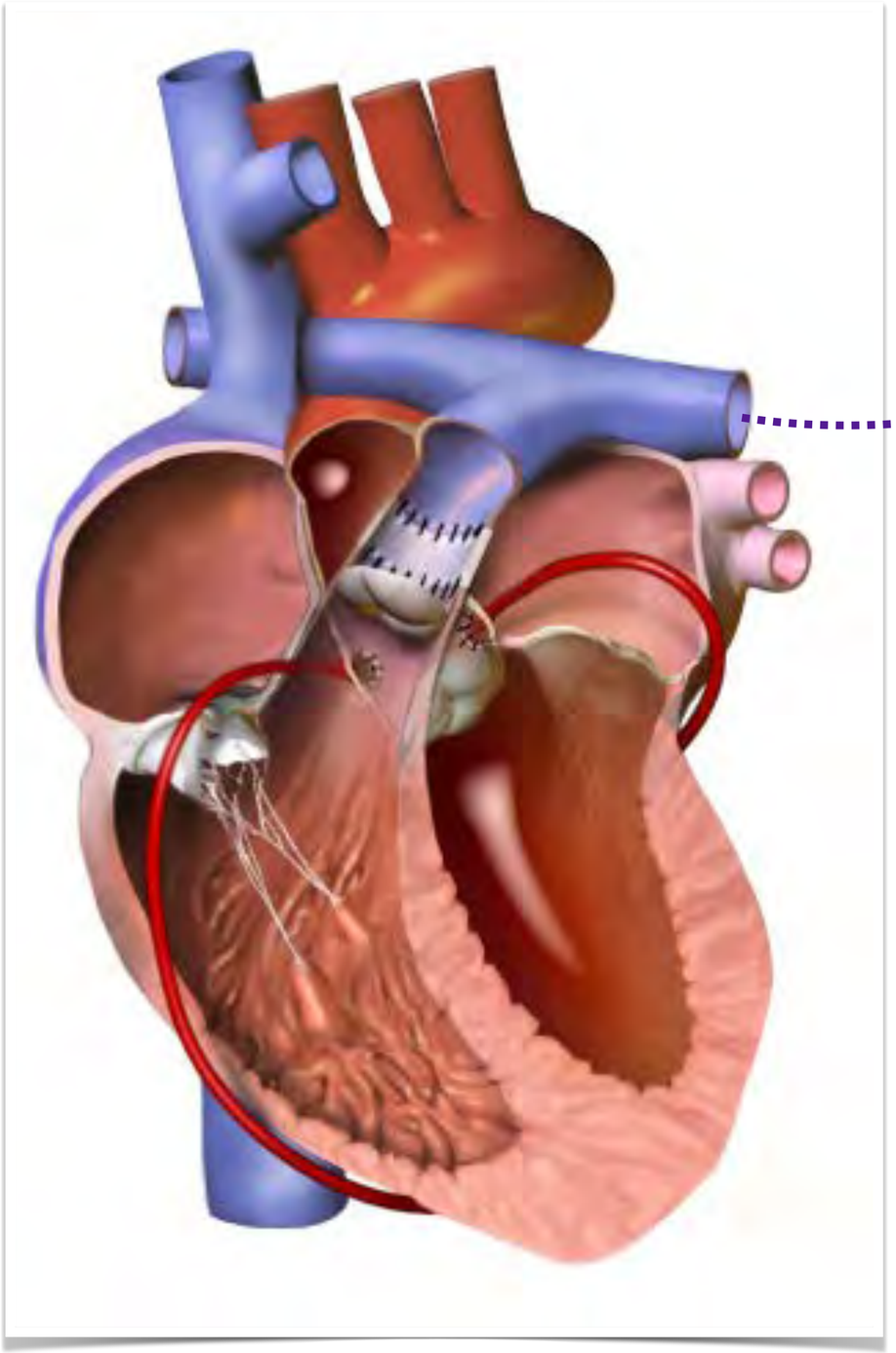


Aortic valve regurgitation

Freedom from neo-aortic root dilation (neo-aortic root z-score >=3.0) and probability from at least moderate neo-aortic regurgitation



Schwartz, M. L. et al. Circulation 2004;110:II-128-II-132



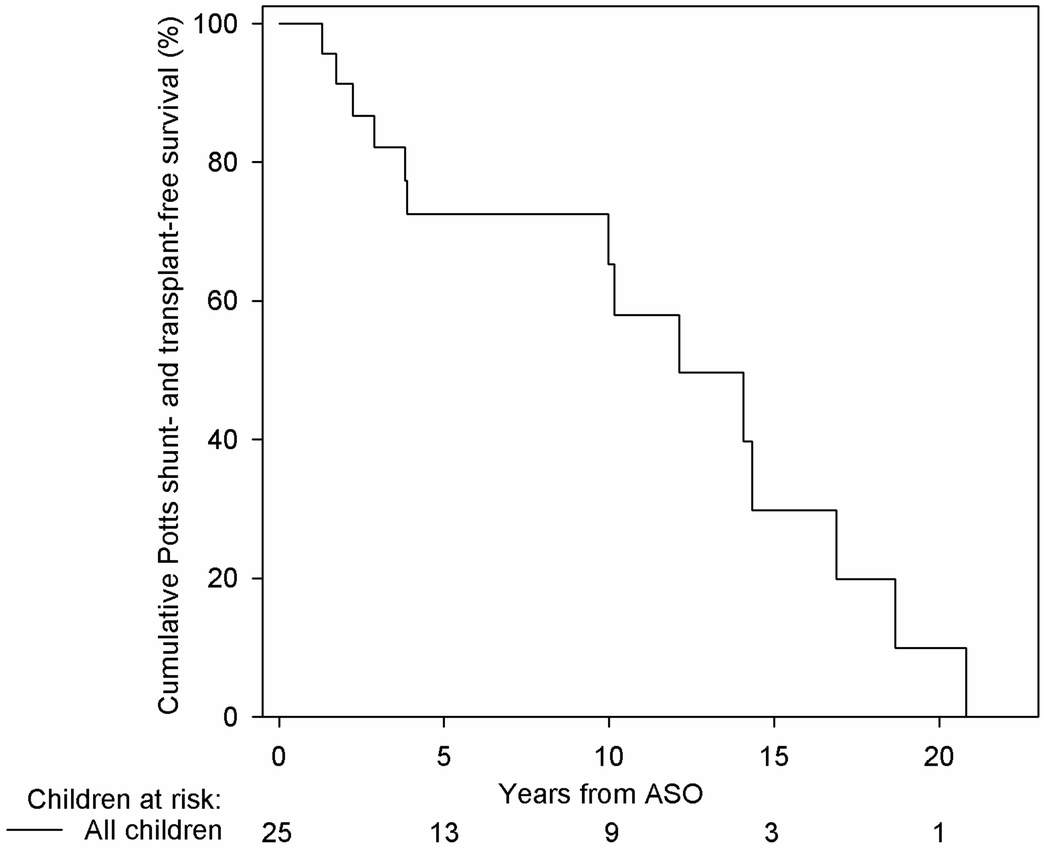
Pulmonary arterial hypertension

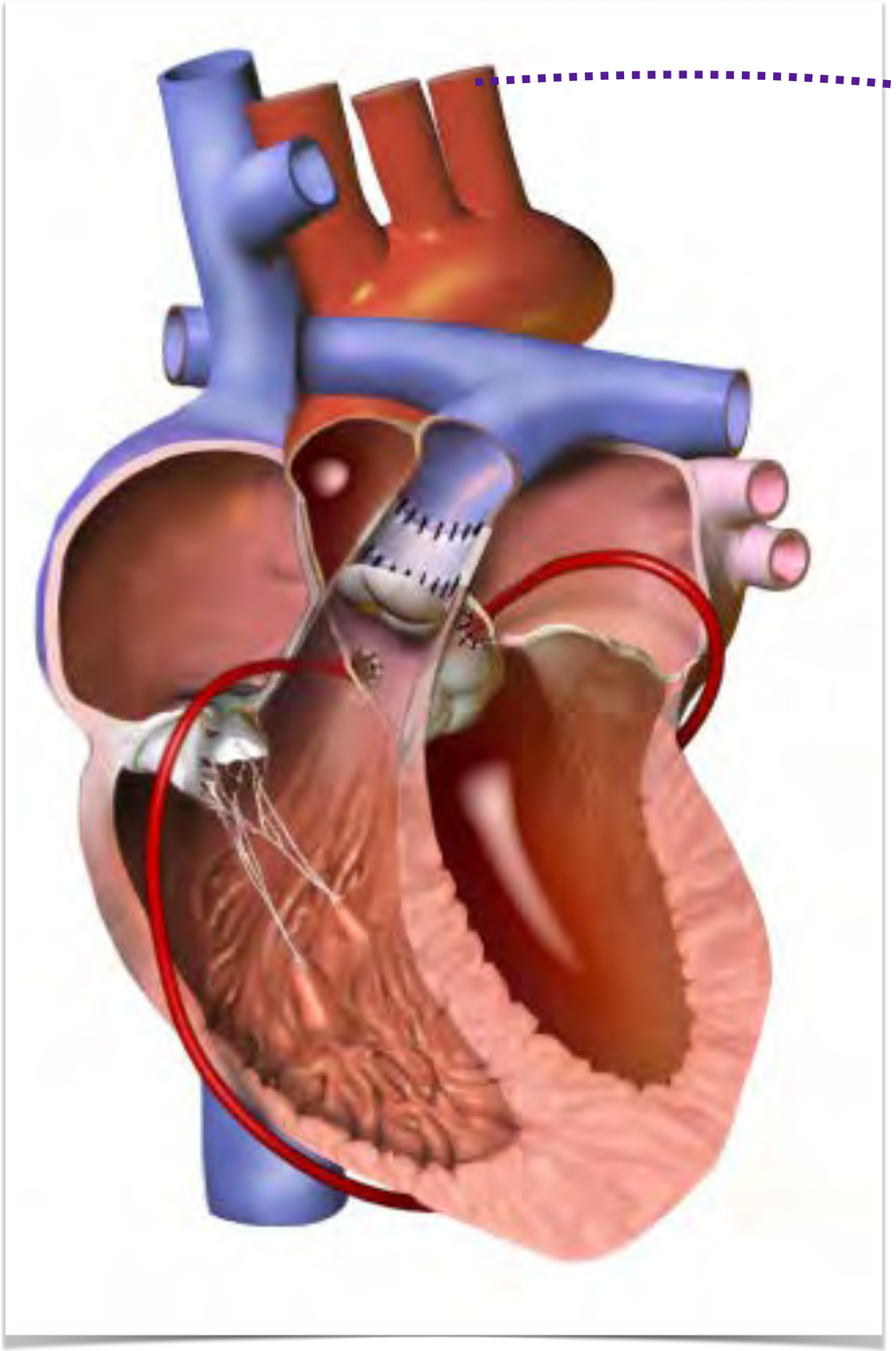
PAH characteristics after ASO for TGA

	Value
Age first PAH detection (months)	4 (1, 25)
PAH detection within one year after ASO	16 (64)
Age first detection (months)	2 (1, 4)
PAH detection more than one year after	9 (36)
Age first detection (months)	40 (25, 93)
Age first RHC (months)	10 (2, 30)
mPAP (mmHg)	48 (37, 55)
mSAP (mmHg)	62 (51, 65)
mPAP/mSAP	0.82 (0.71, 1.07)
mPCWP (mmHg)	10 (8, 12)
PVRi (WU.m²)	11.5 (8.7, 13.0)
PAH therapy at endpoint	
CCB monotherapy	1 (4)
PAH-targeted mono therapy	6 (24)
PAH-targeted dual therapy	8 (32)
PAH-targeted triple therapy	10 (40)

Ziljstra W et al. Heart 2017

Survival in PAH after ASO for TGA





Neurodevelopmental outcomes

ToM tests in TGA vs controls

Cognitive domain	Test	TGA (n=45)	Controls (n=45)	*p*
IQ	CMMS	113 (8.3)	116 (8.85)	*ns*
Receptive Language	NEPSY - Comprehension	12.4 (0.80)	12.5 (0.81)	*ns*
Motor Inhibition	NEPSY – Knock and tap	24.25 (3.81)	25.97 (2.12)	0.01
Cognitive Inhibition	Stroop test (errors)	3.08 (3.02)	1.42 (1.48)	0.001
	Stroop test (Reaction time)	82.42 (31.61)	61.03 (20.53)	0.0002
Verbal working memory	Digit span WISC IV	2.84 (2.49)	3.64 (2.55)	*ns*
Spatial working memory	BEM-144 blocks	3.06 (2.12)	4 (2.03)	0.03
Cognitive flexibility	DCST	7.28 (2.86)	8.66 (2.09)	0.01
Social cognition	Theory of mind tests	0.95 (1.27)	2.15 (1.24)	0.0009

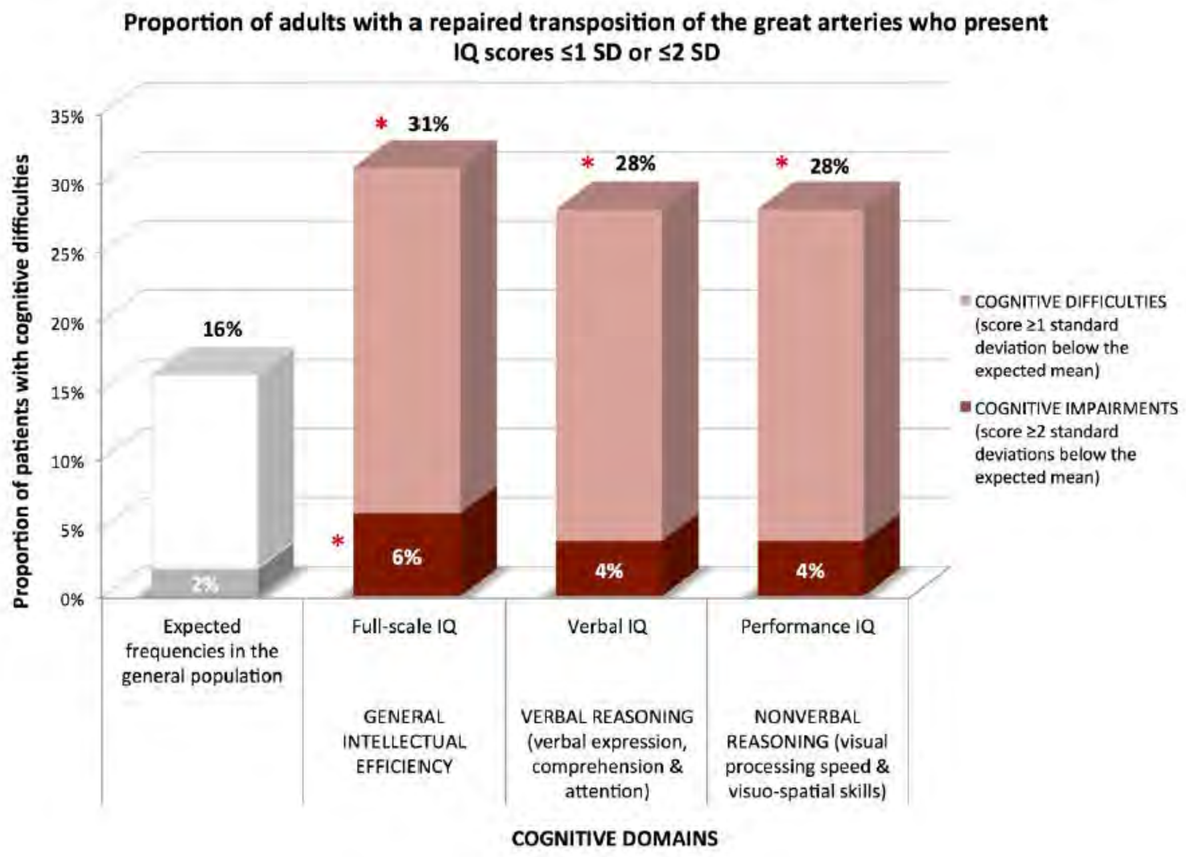
Calderon J et al. J Pediatr 2012

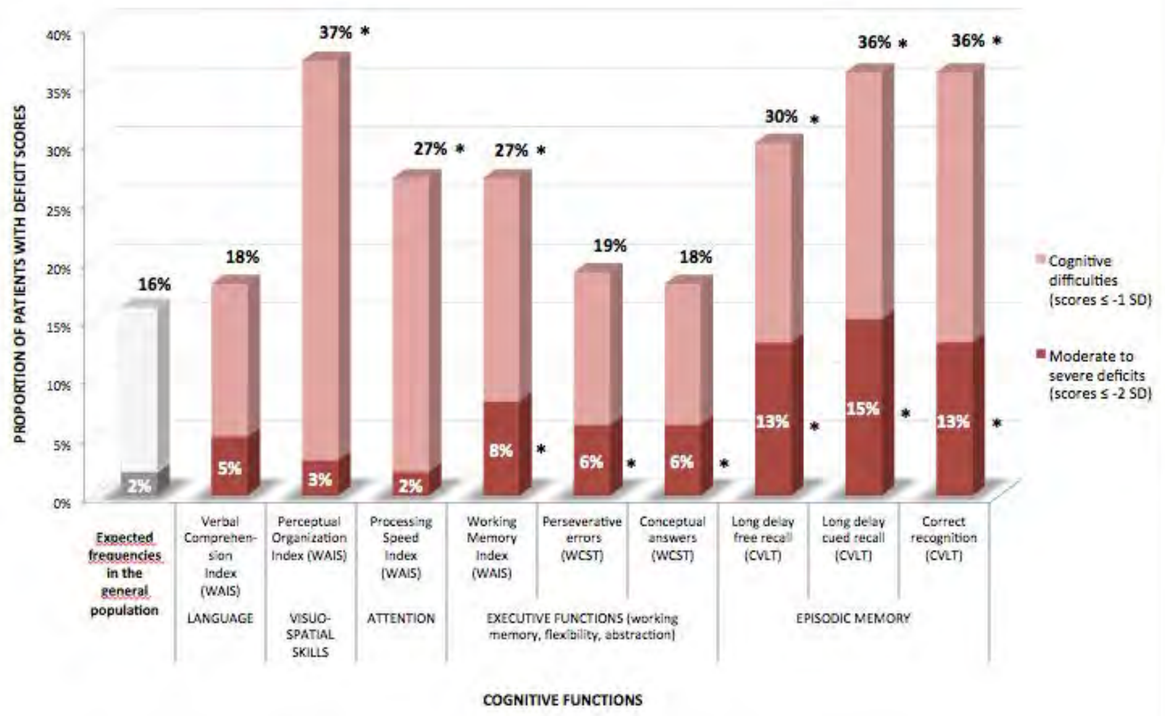
ToM tests in TGA vs controls
role of prenatal diagnosis

Cognitive Domain	Test	Prenatal (n=29)	Postnatal (n=16)	*p*
IQ	CMMS	114.5 (8.50)	112.4 (8.06)	0.4
Receptive Language	NEPSY - Comprehension	12.65 (0.55)	12.25 (1.12)	0.11
Response motor control	NEPSY – Knock and tap	24.31 (2.46)	24.14 (5.82)	0.89
Cognitive control	Stroop test (Number of errors)	2.41 (2.48)	4.31 (3.59)	0.04
	Stroop test (Reaction Time)	77.82 (28.05)	90.74 (36.71)	0.19
Verbal working memory	Digit span WISC IV	2.96 (2.48)	2.62 (2.57)	0.66
Spatial working memory	BEM-144 blocks	3.62 (2.0)	2.06 (2.01)	0.01
Cognitive flexibility	DCST	8.10 (2.65)	5.64 (2.61)	0.006
Social cognition	Theory of mind	1.31 (1.33)	0.31 (0.87)	0.01

Calderon J et al. J Pediatr 2012

Neurodevelopmental outcomes after ASO in adults



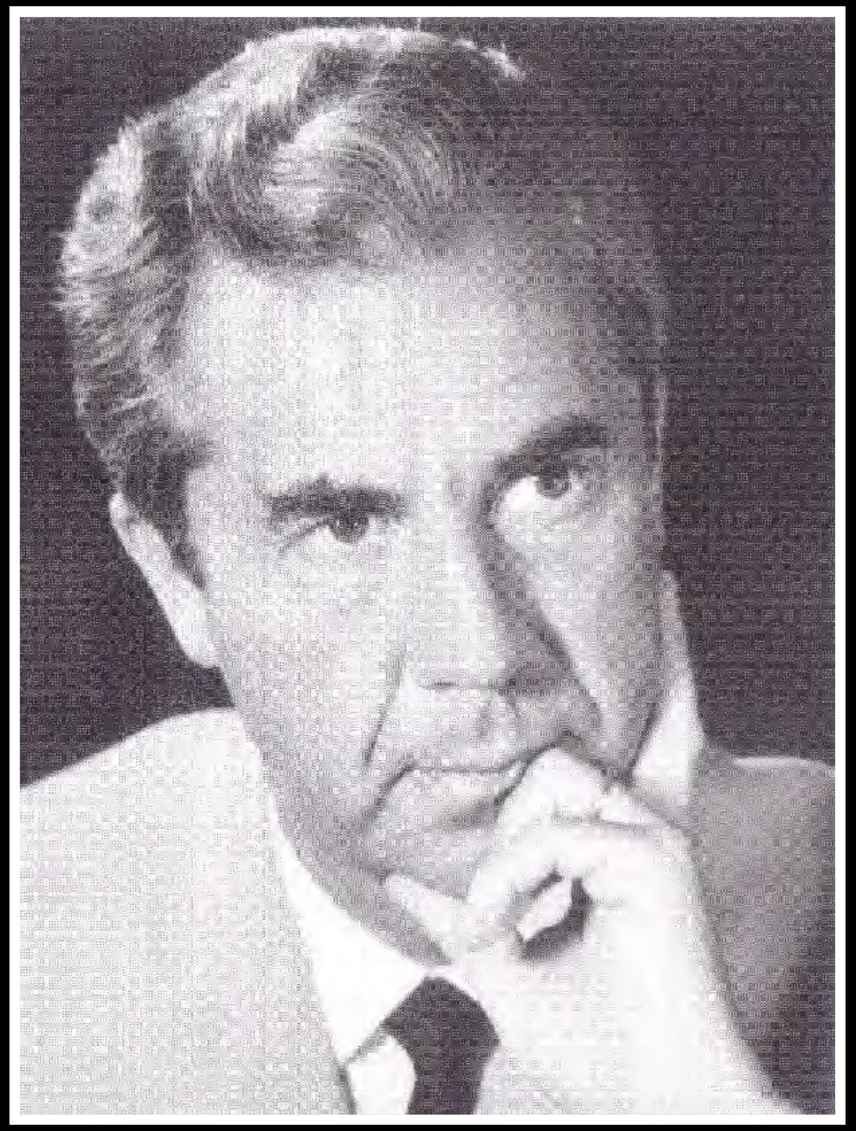


Kasmi L et al. J Thorac Cardiovasc Surg 2017; Ann Thorac Surg 2017

Atrial repair of TGA

The Senning and Mustard operations

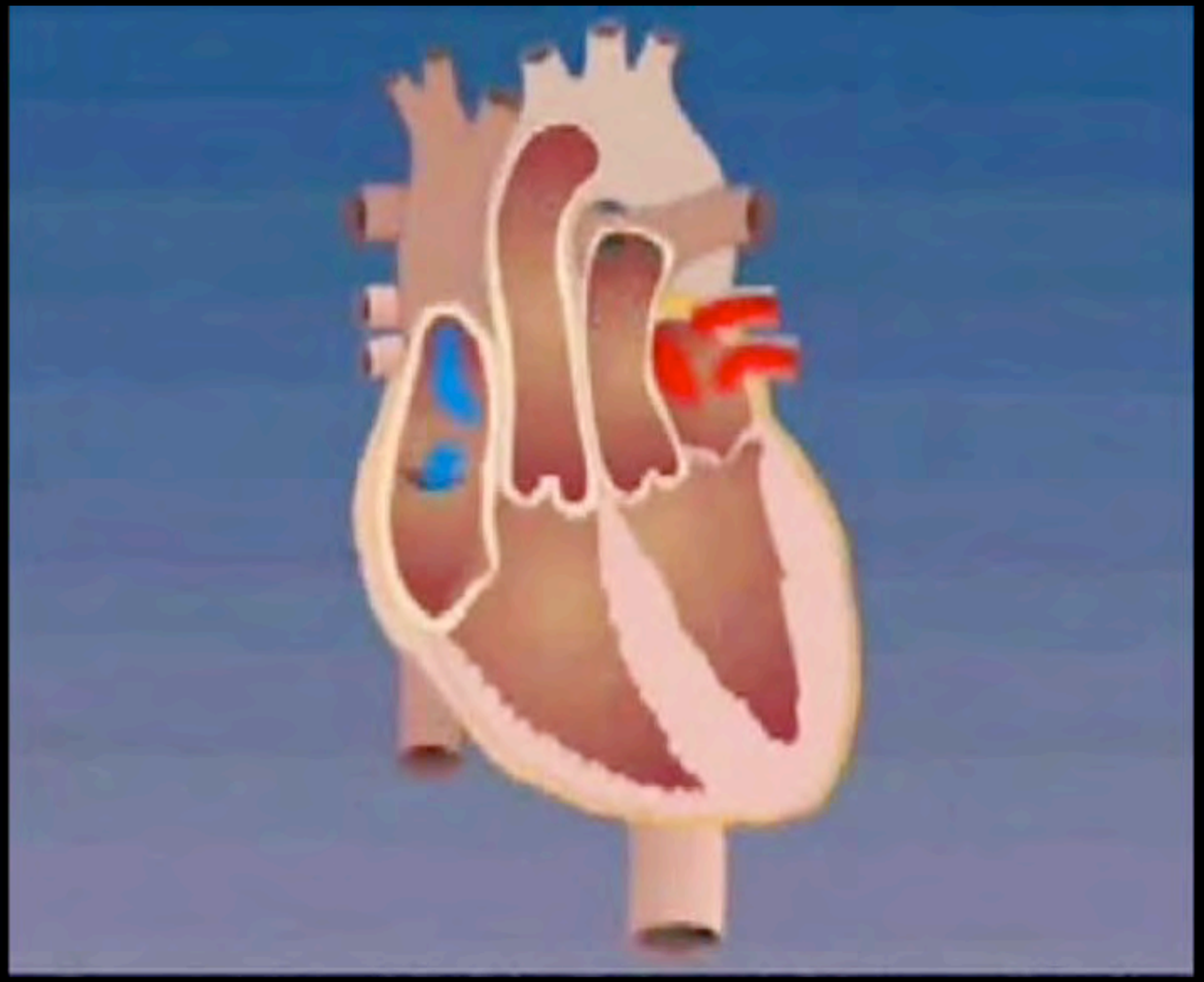
Atrial correction of TGA



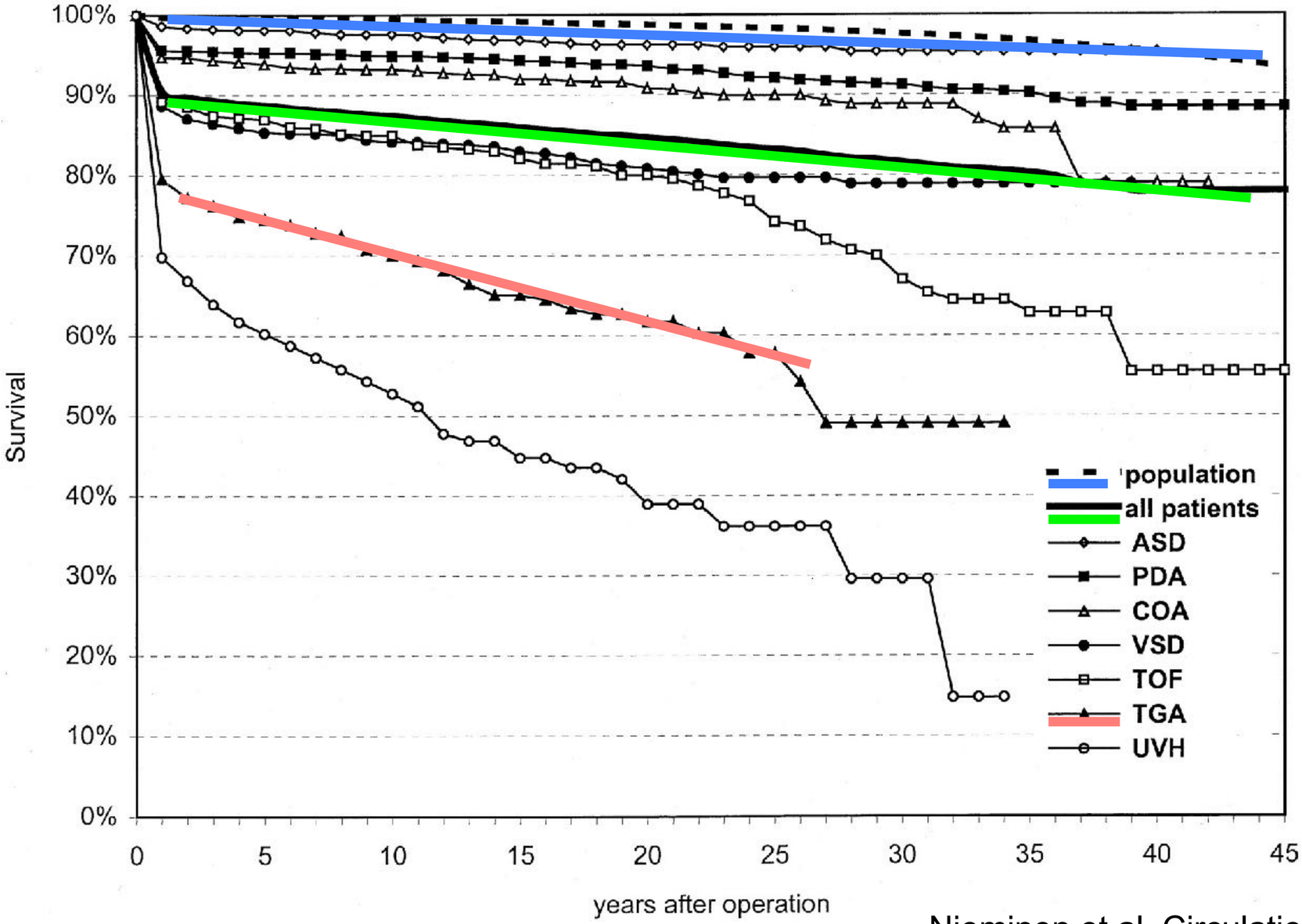
Ake Senning

William Thornton Mustard

Mustard operation

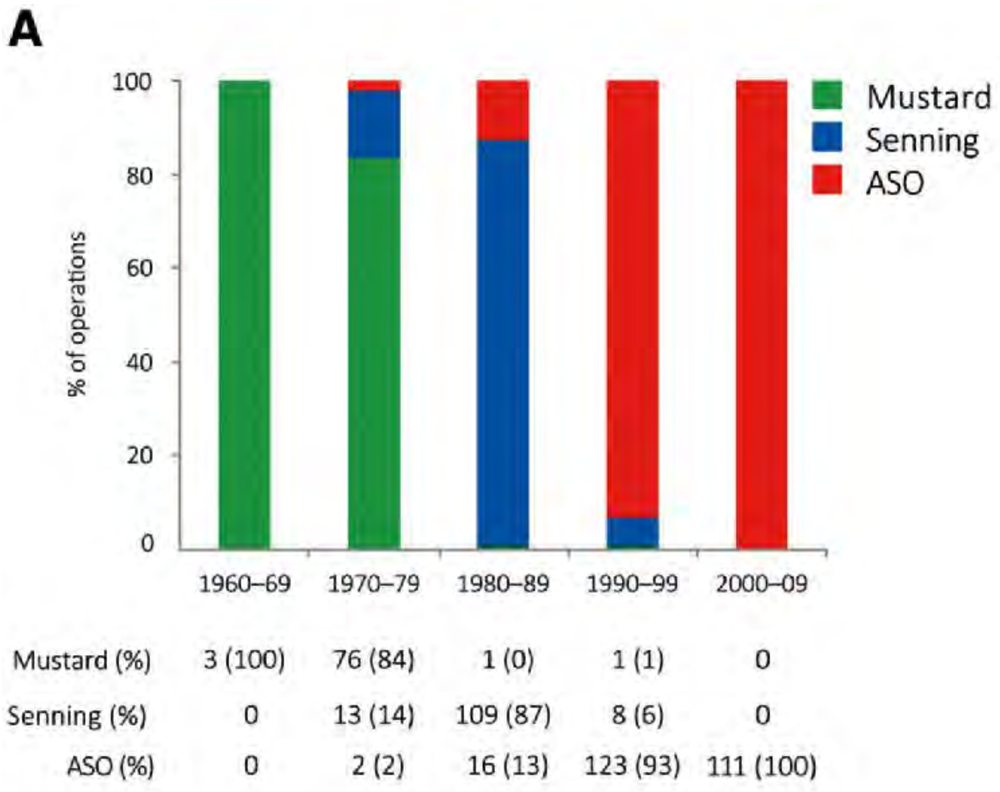


Survival of all patients, separate diagnostic groups, and general population

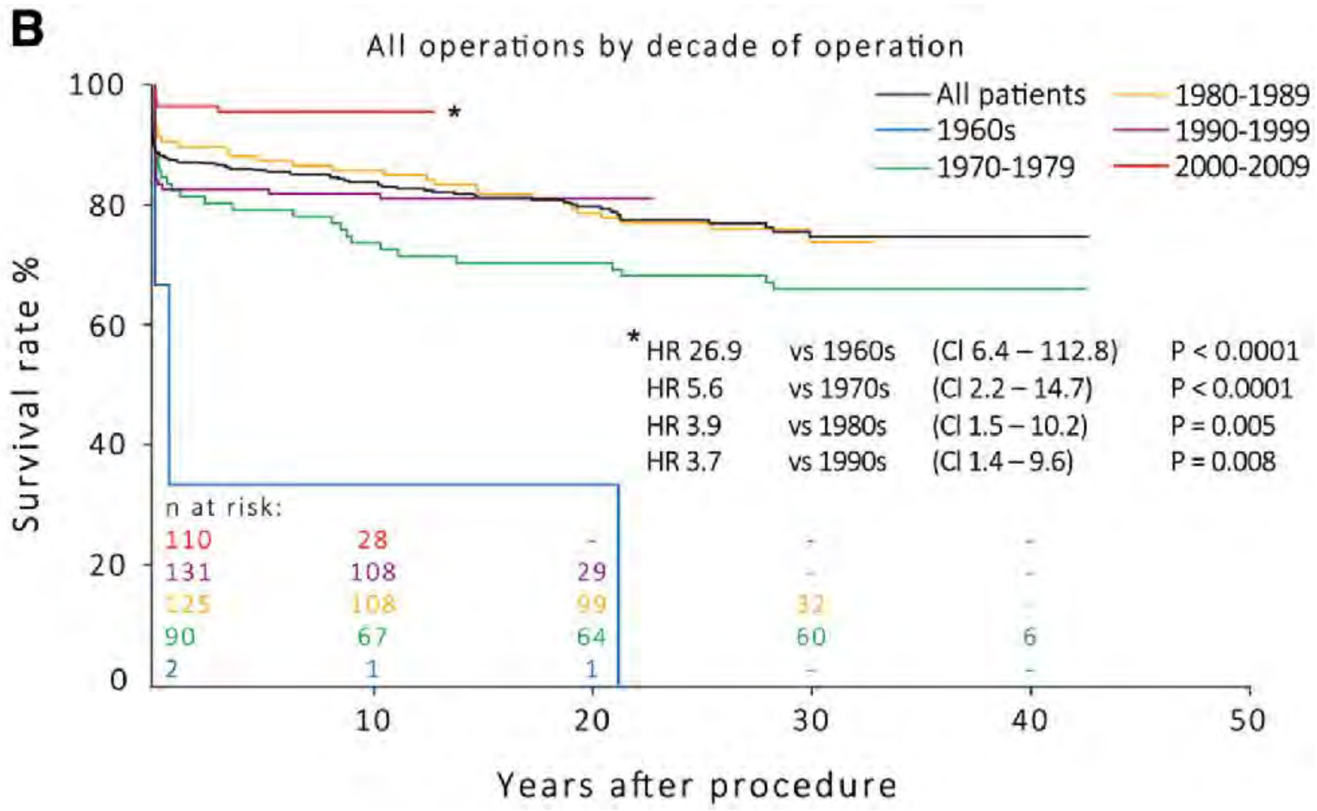


Nieminen et al, Circulation 2001

Outcomes after the Mustard, Senning and arterial switch operation for treatment of transposition of the great arteries in Finland: a nationwide 4-decade perspective

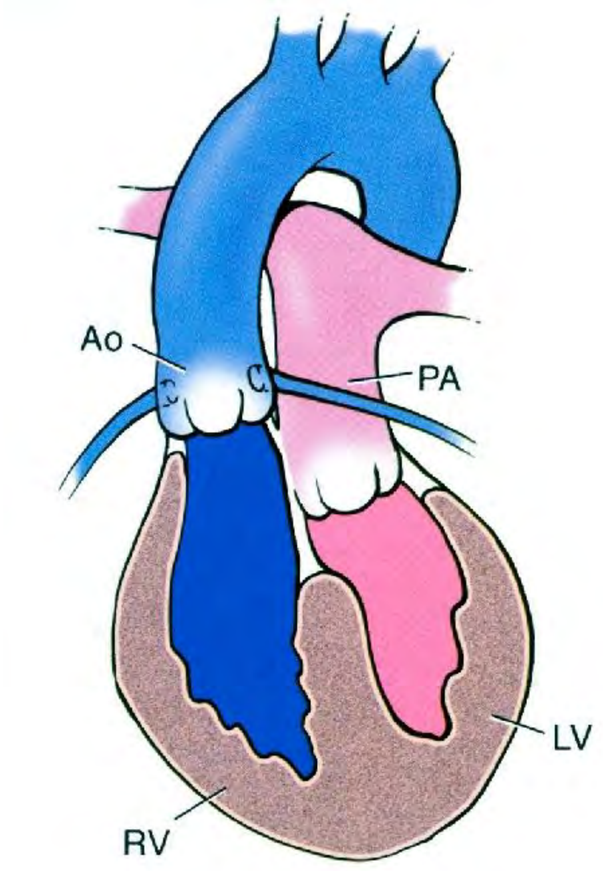


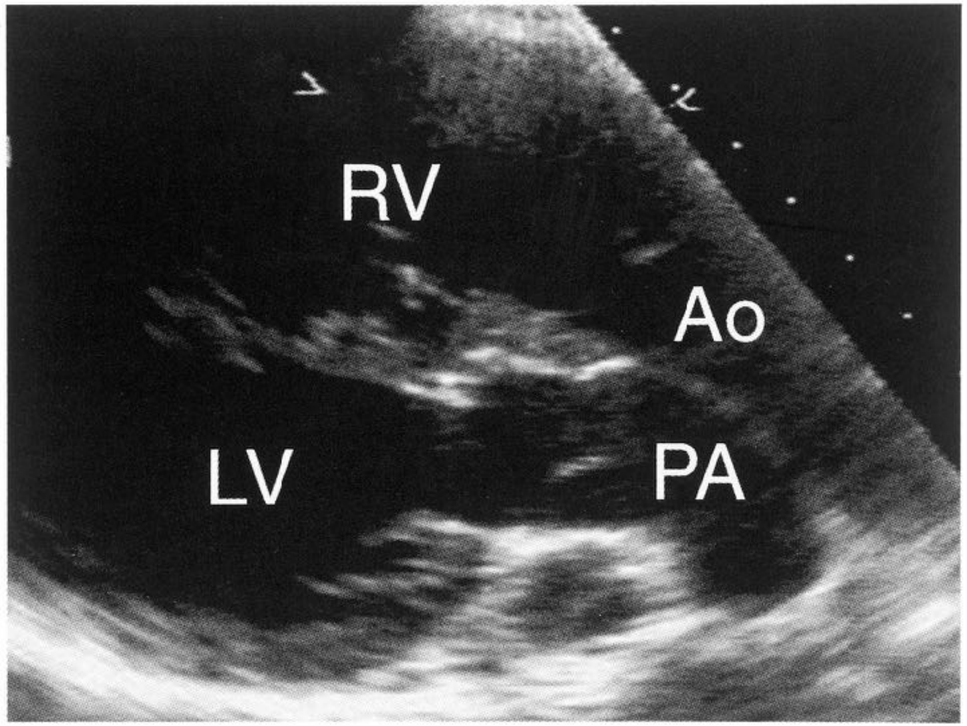
	1960–69	1970–79	1980–89	1990–99	2000–09
Mustard (%)	3 (100)	76 (84)	1 (0)	1 (1)	0
Senning (%)	0	13 (14)	109 (87)	8 (6)	0
ASO (%)	0	2 (2)	16 (13)	123 (93)	111 (100)



Eur J Cardiothorac Surg. 2017;52(3):573-580.

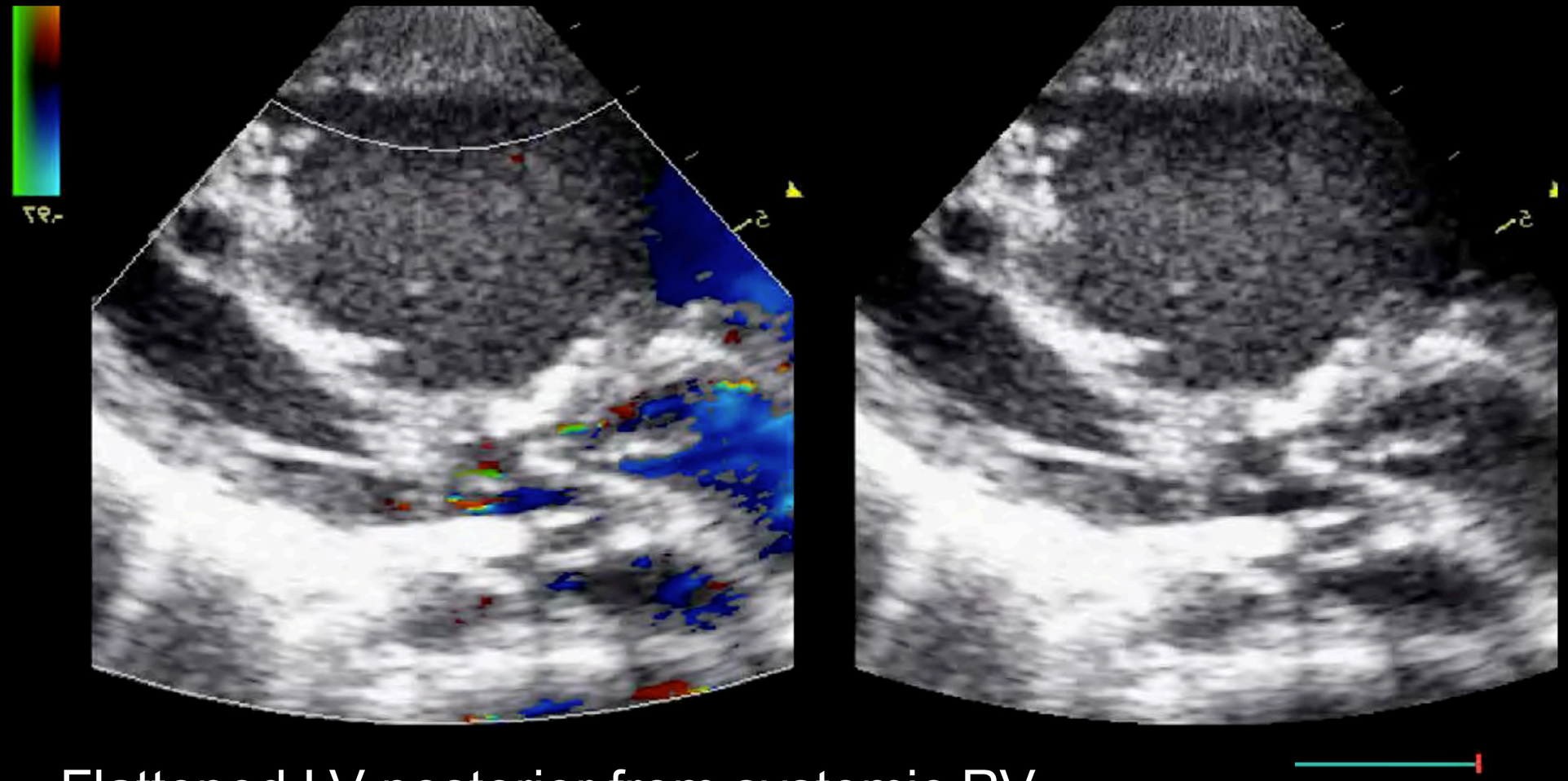
Echocardiogram long axis view





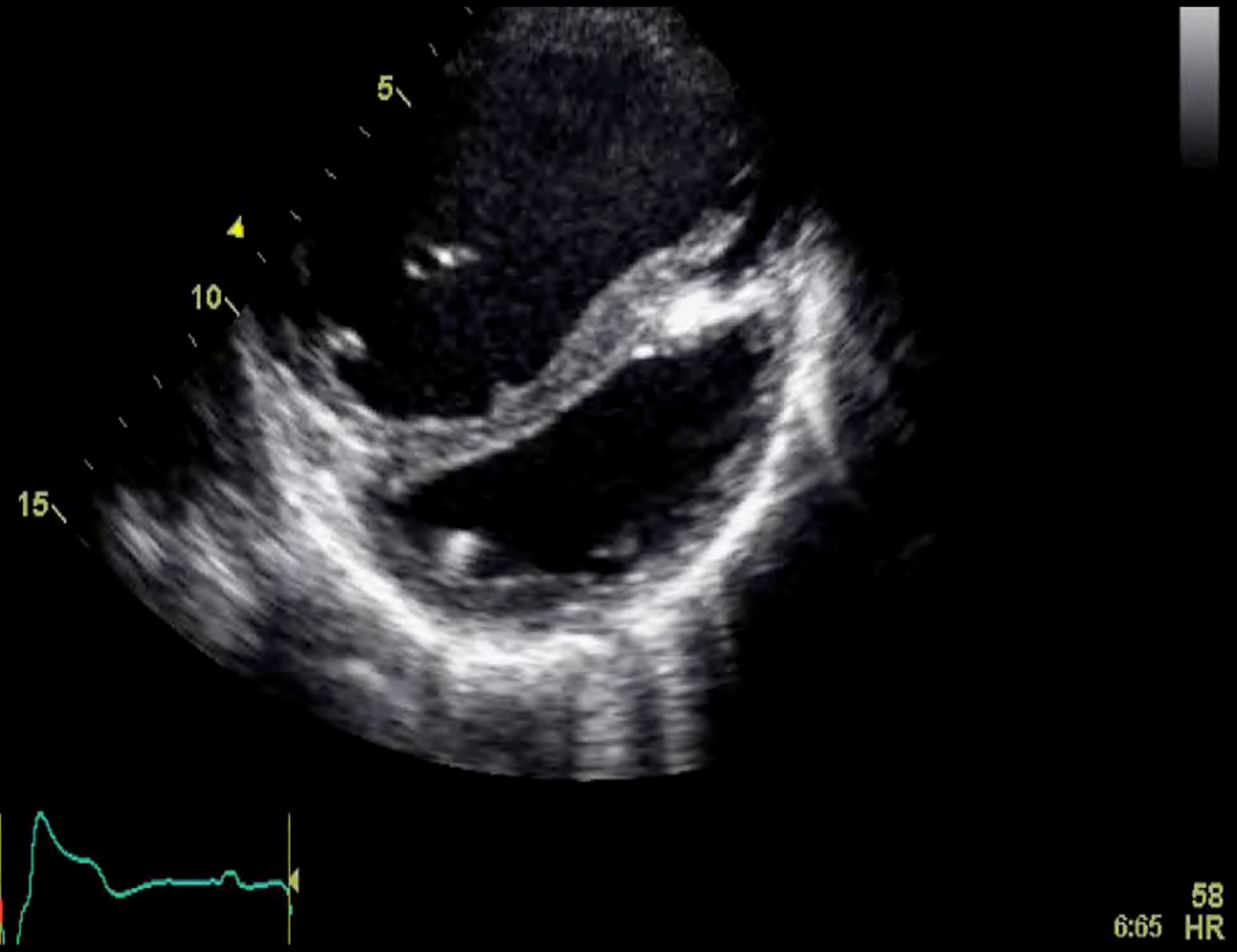
Aorta anterior, PA posterior

Long axis view after atrial correction of TGA



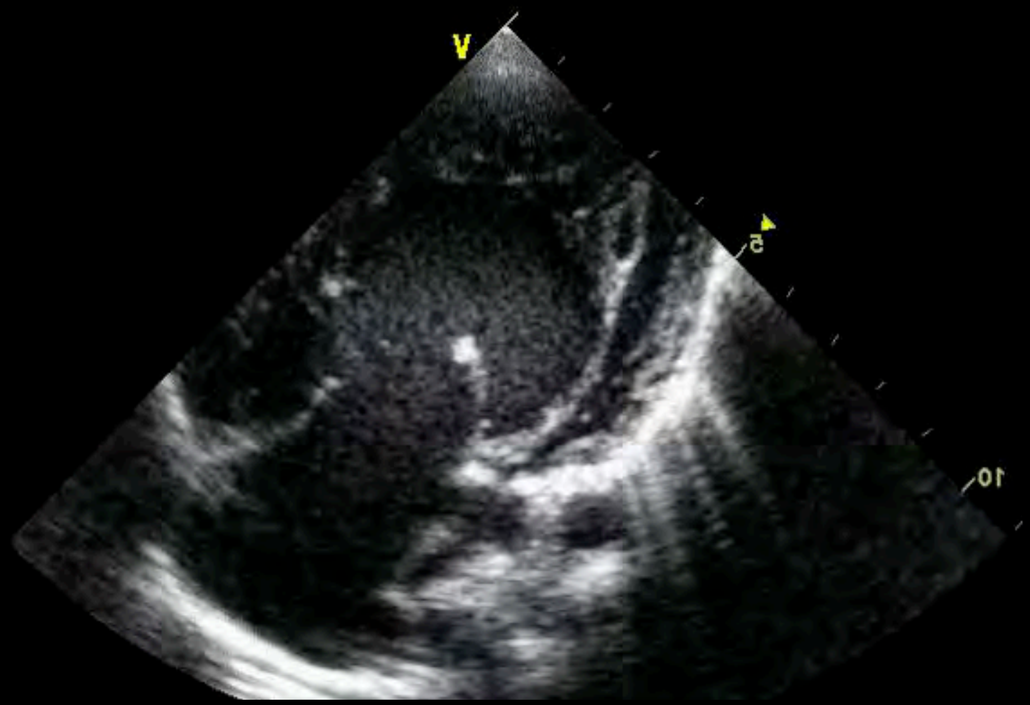
Flattened LV posterior from systemic RV

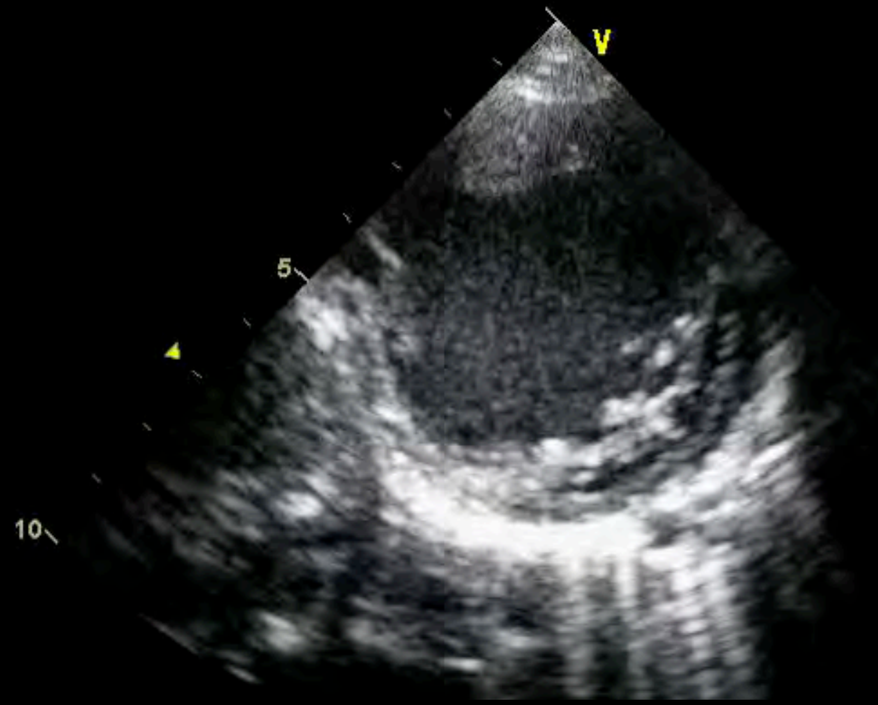
Short axis view after atrial correction of TGA



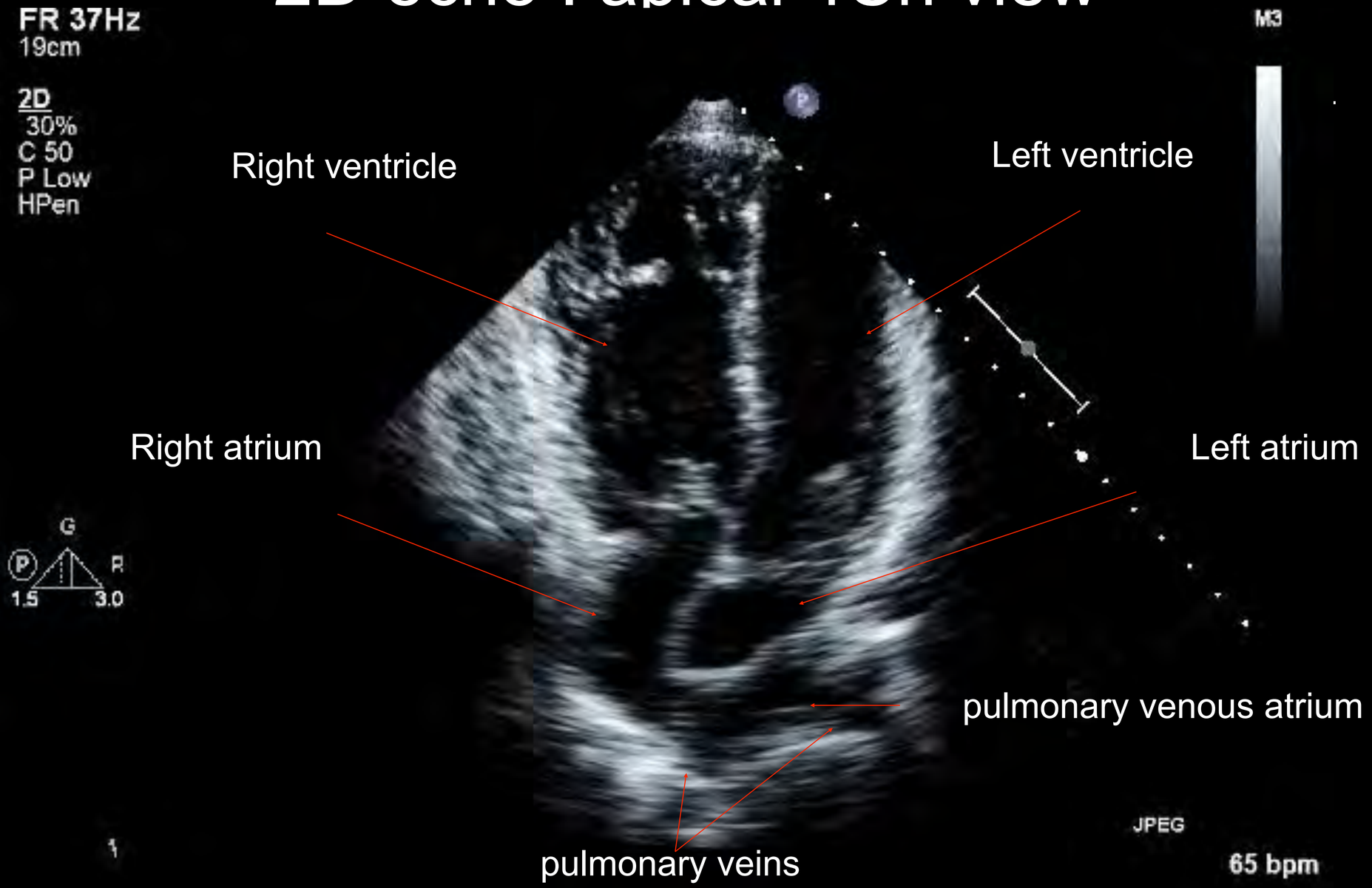
Flattened LV posterior from systemic RV

Right ventricle after atrial correction of TGA



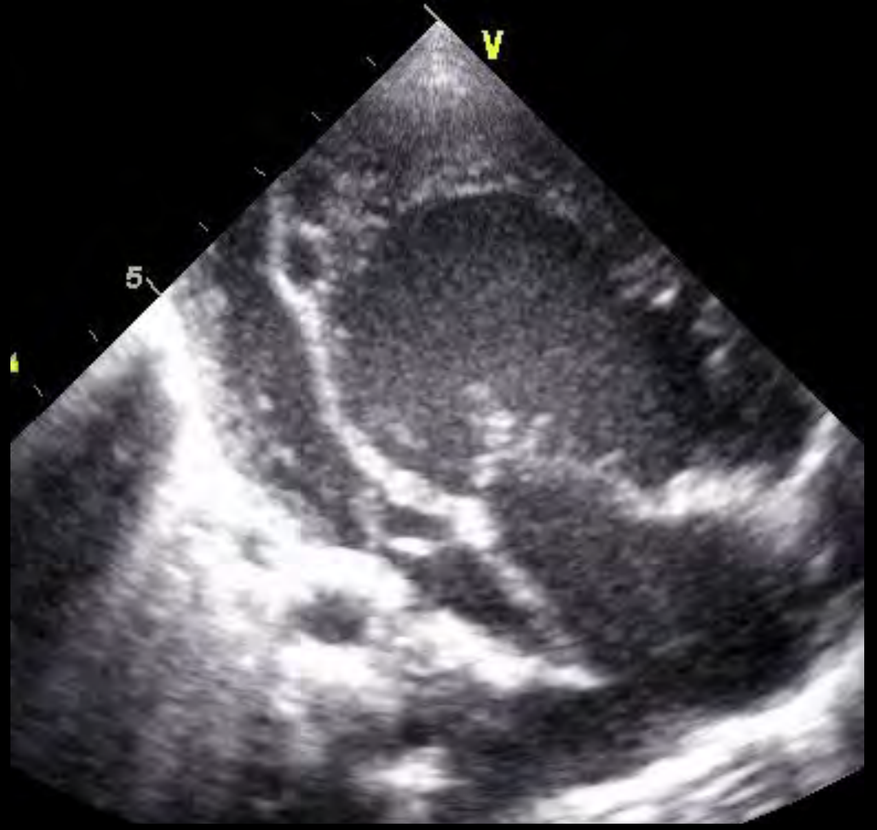


2D echo : apical 4Ch view



Caval baffle

Pulmonary veins baffle

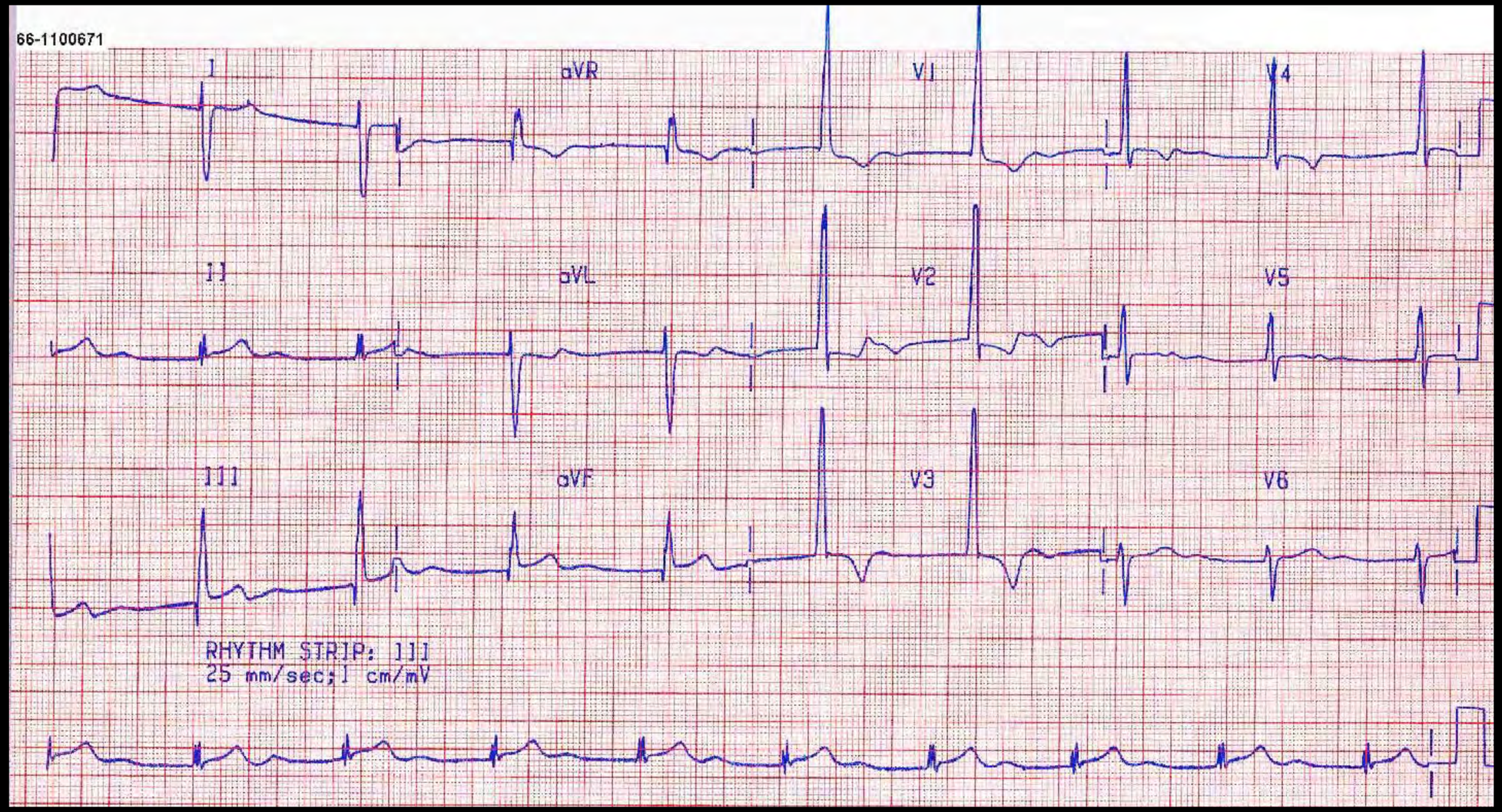


Mortality after atrial switch

- Late yearly mortality 0.5%, due to arrhythmias and heart failure
- Sudden death (42%) most common mode of death
- Independent predictors for mortality:
  - (Atrial)Tachyarrhythmias
  - Advanced functional class

Kammeraad, et al, JACC 2004

ECG after atrial switch



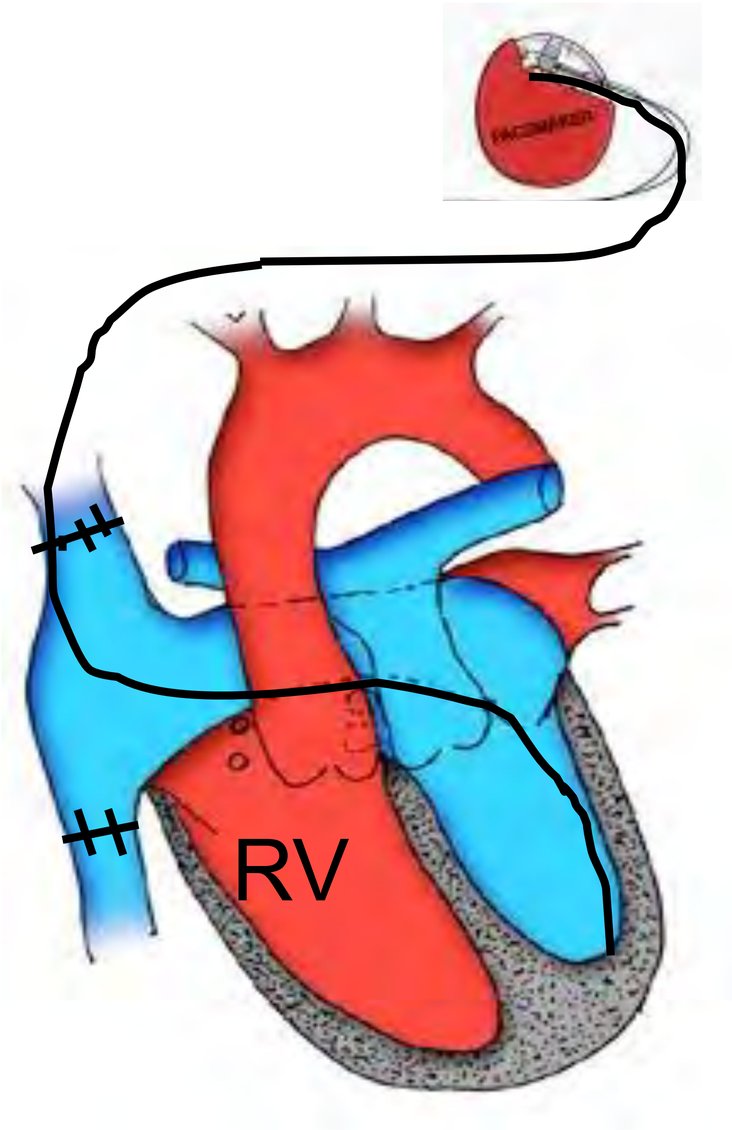
RVH

Right heart axis

Junctional rhythm

Only 40% of patients has SR at age 20

20% of young adults with atrial switch needs PM for sick sinus syndrome



Be aware of altered venous connection:

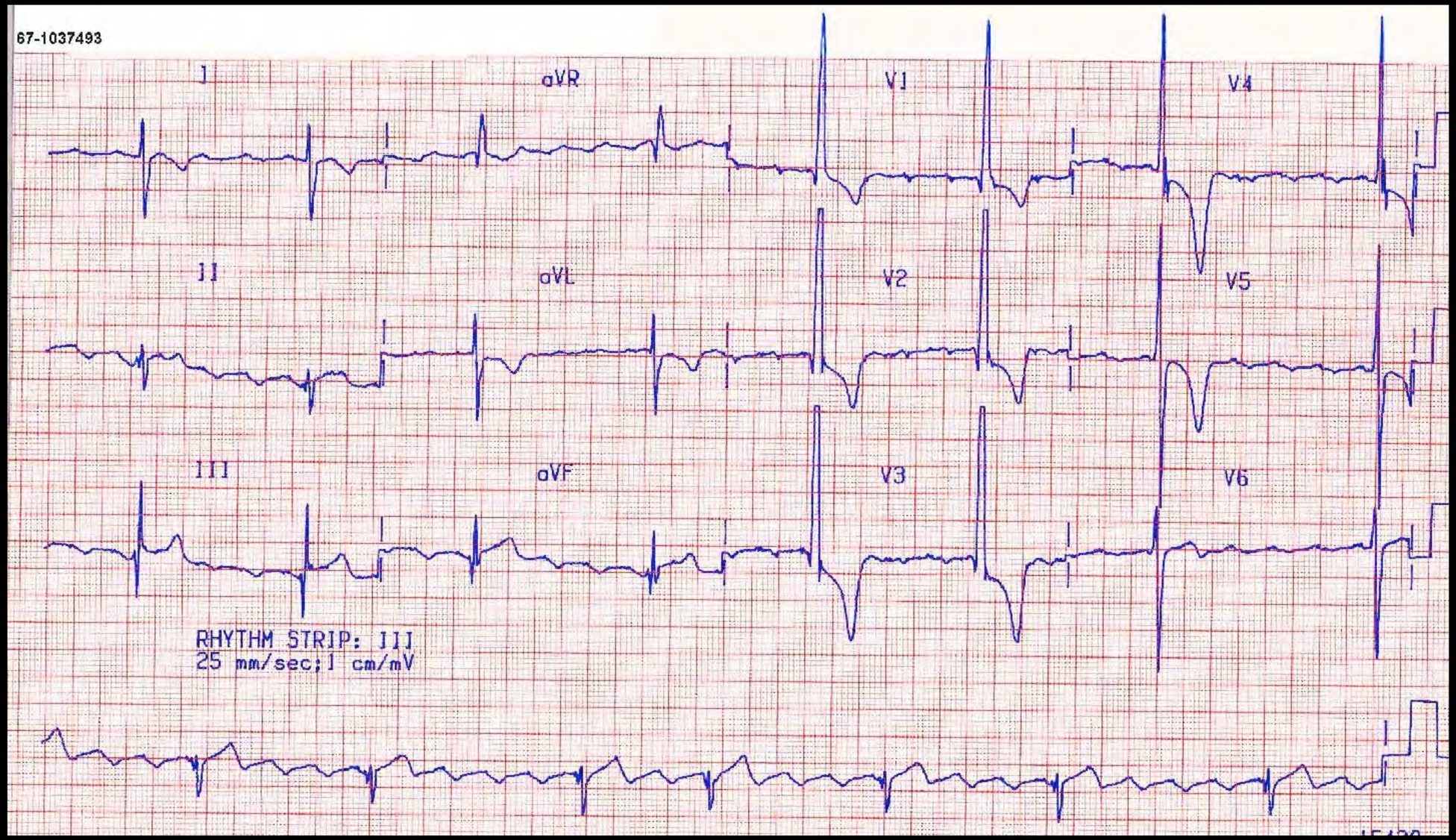
Ventricular lead will end up,

after some unusual loops,

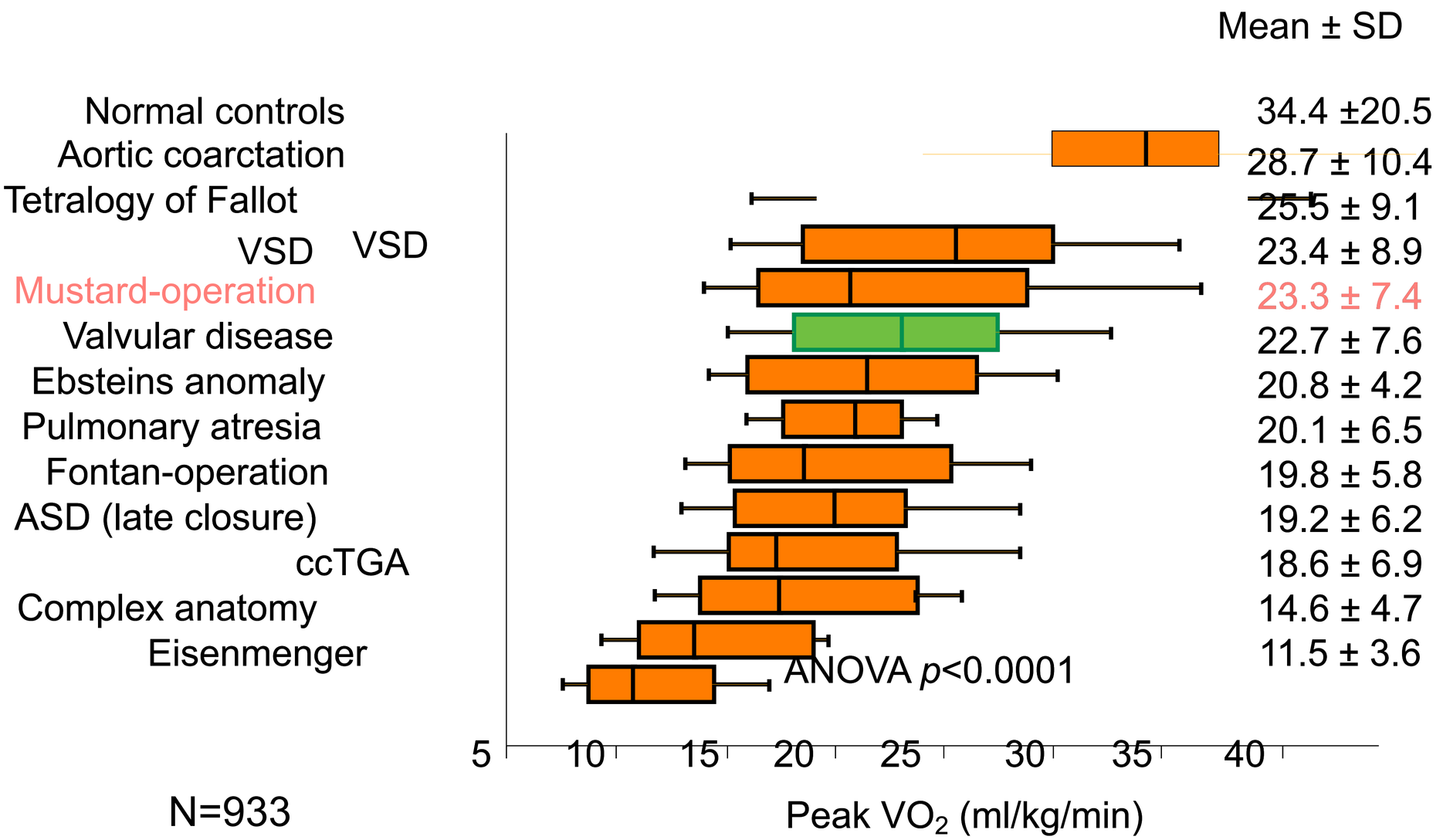
in a smooth-walled LV

Atrial flutter after atrial switch

Atrial arrhythmias may lead to hemodynamic instability and sudden death



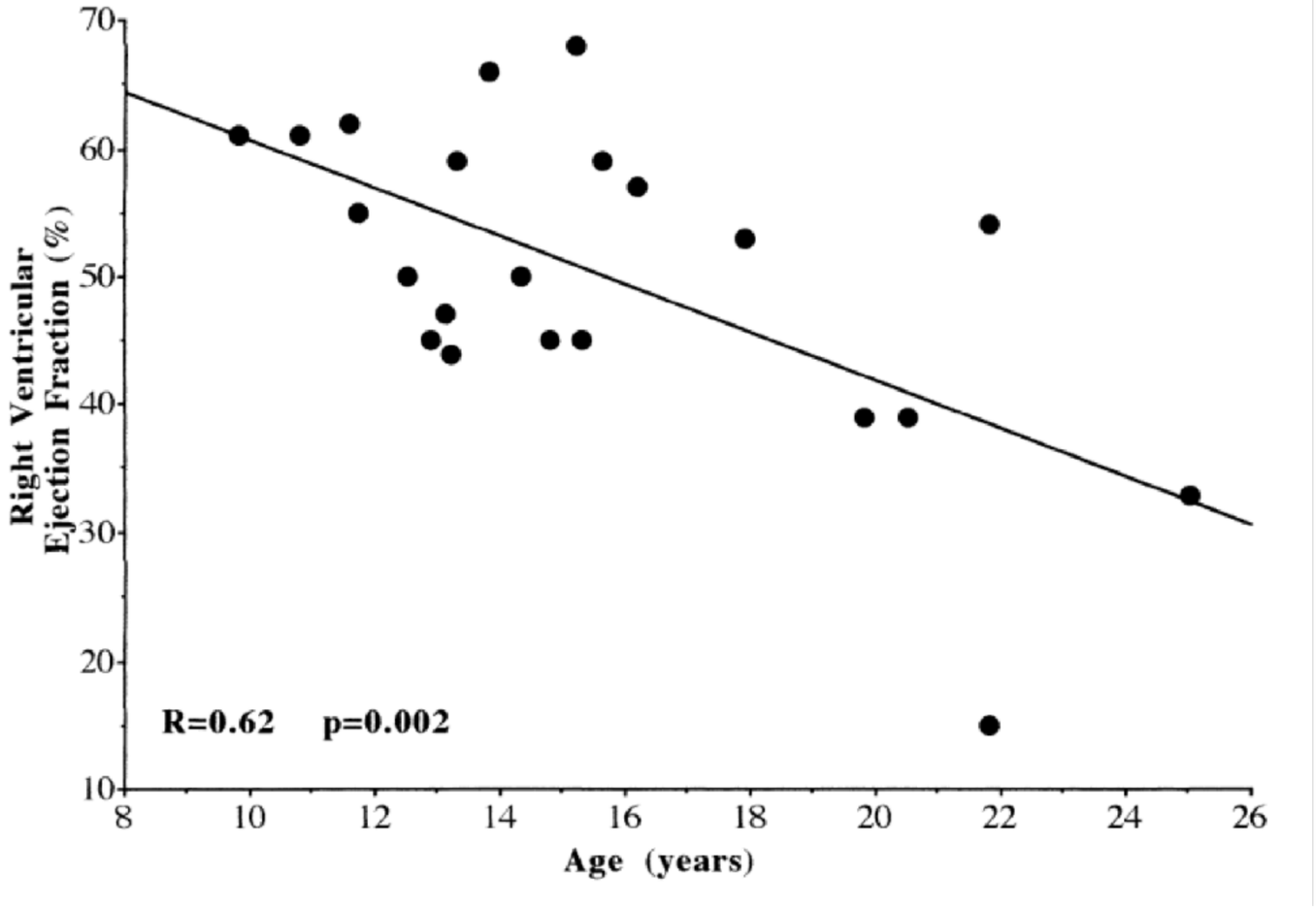
Exercise capacity in CHD



N=933

Diller GP, et al. Circulation 2005;

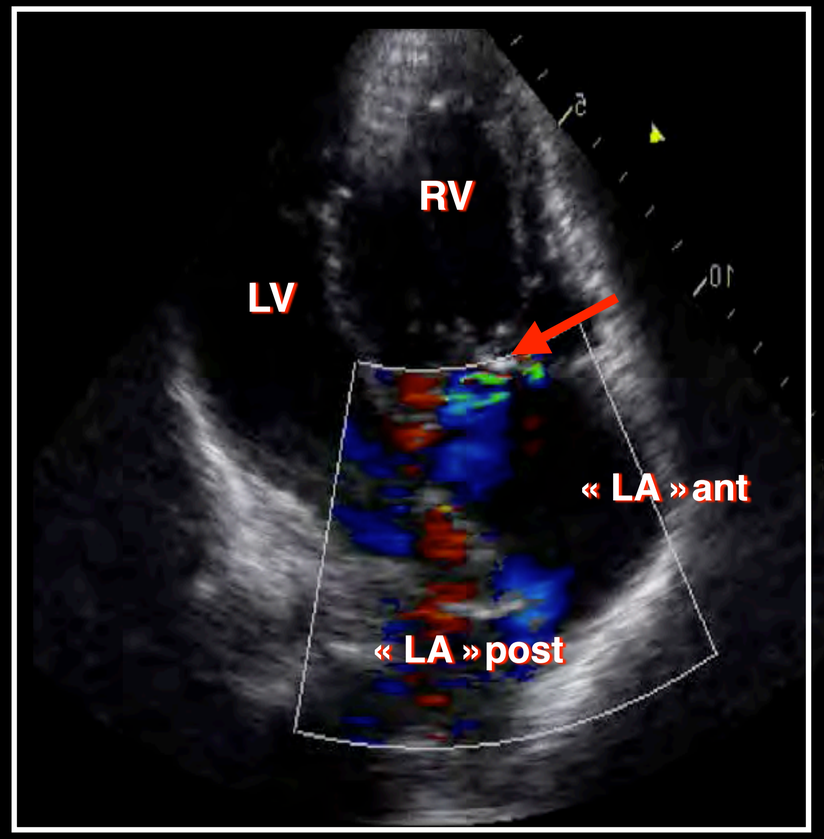
Decline of RV function after atrial switch



Milane et al. , JACC 2000.

Late complications atrial switch

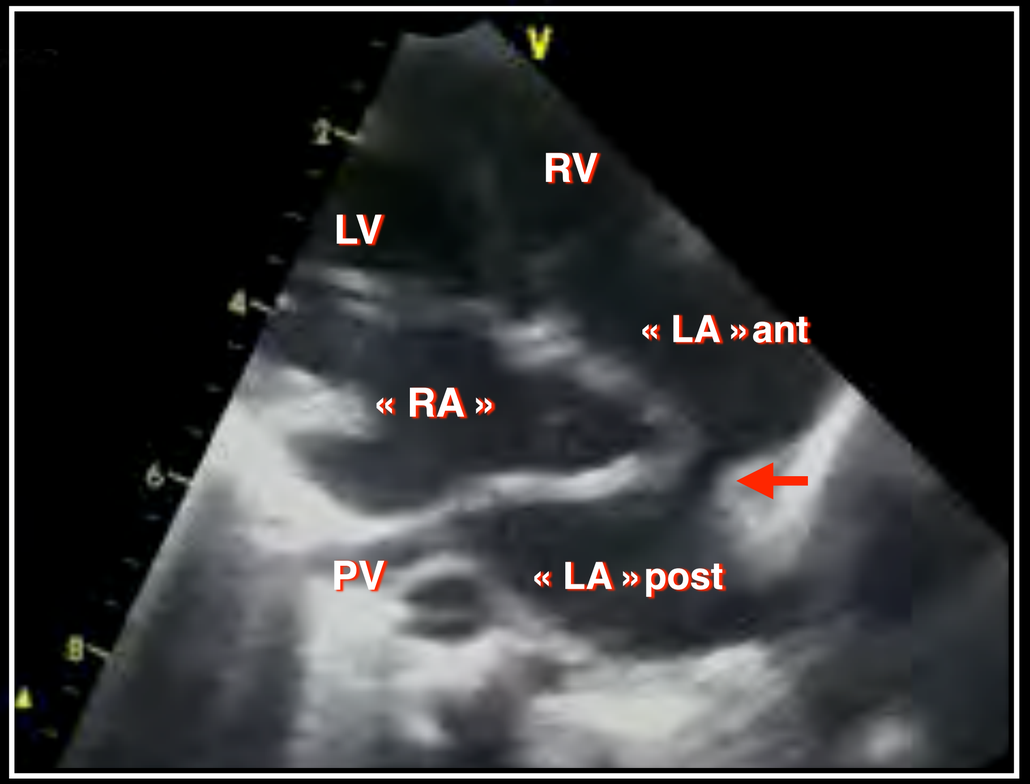
- Early death
- Arrhythmias
- Exercise capacity
- RV dysfunction
- Tricuspid regurgitation

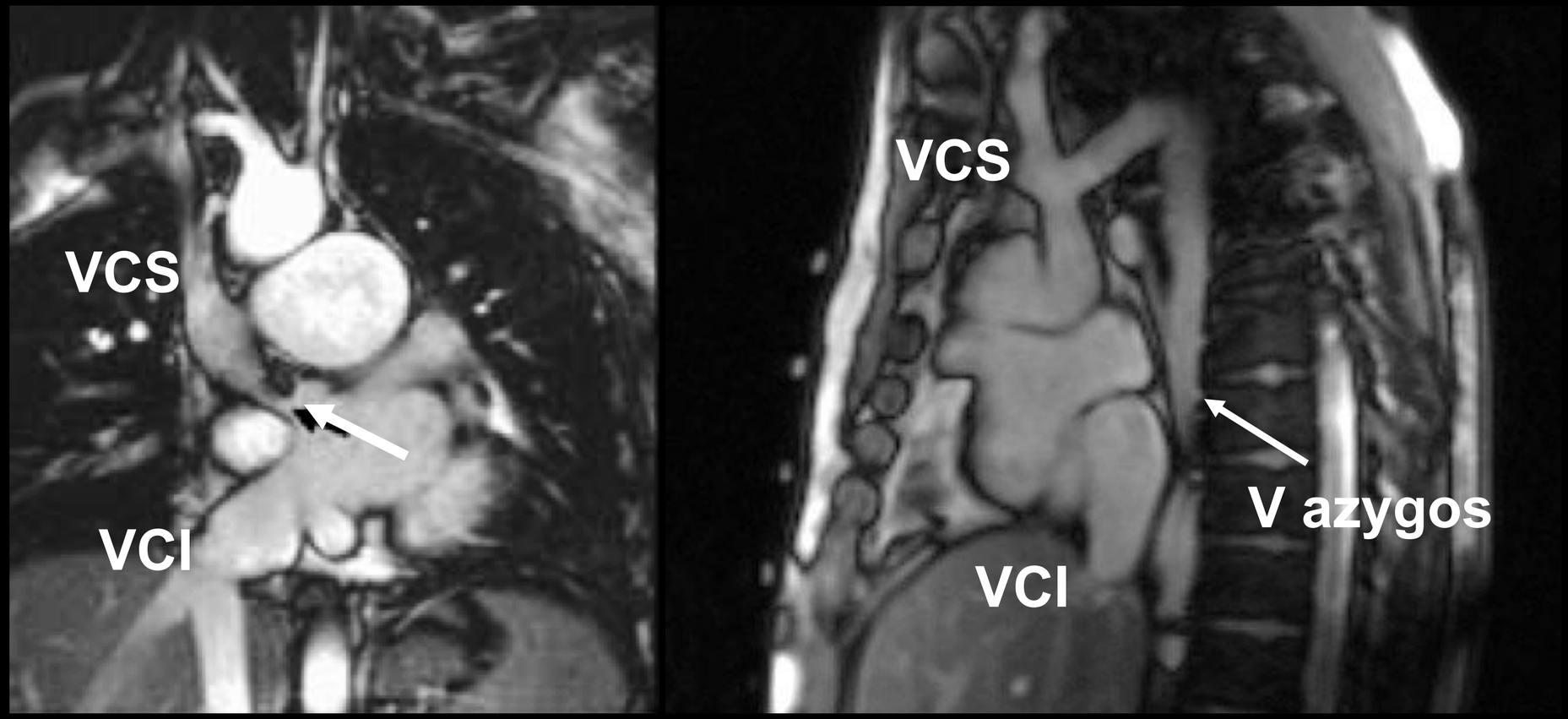


Abnormal septal configuration
RV dilation

Late complications atrial switch

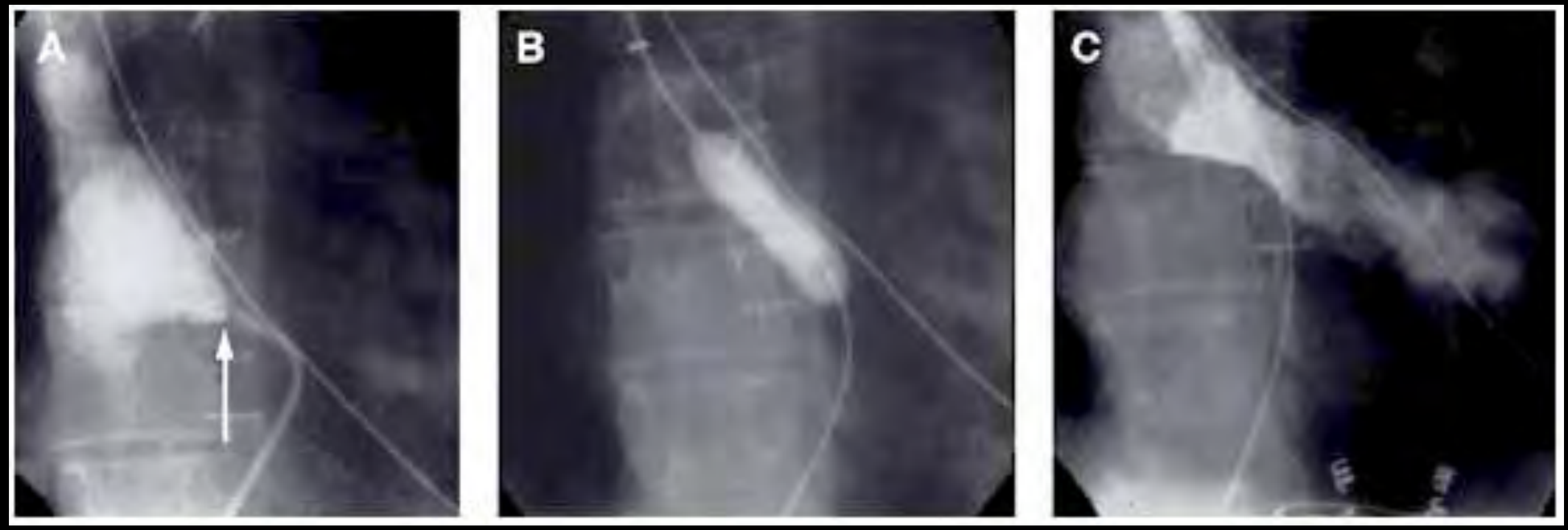
- Early death
- Arrhythmias
- Exercise capacity
- RV dysfunction
- Tricuspid regurgitation
- **Baffle obstructions**





Baffle obstruction with increased azygos flow

Superior baffle-limb stenosis in TGA after atrial switch and following PM implantation



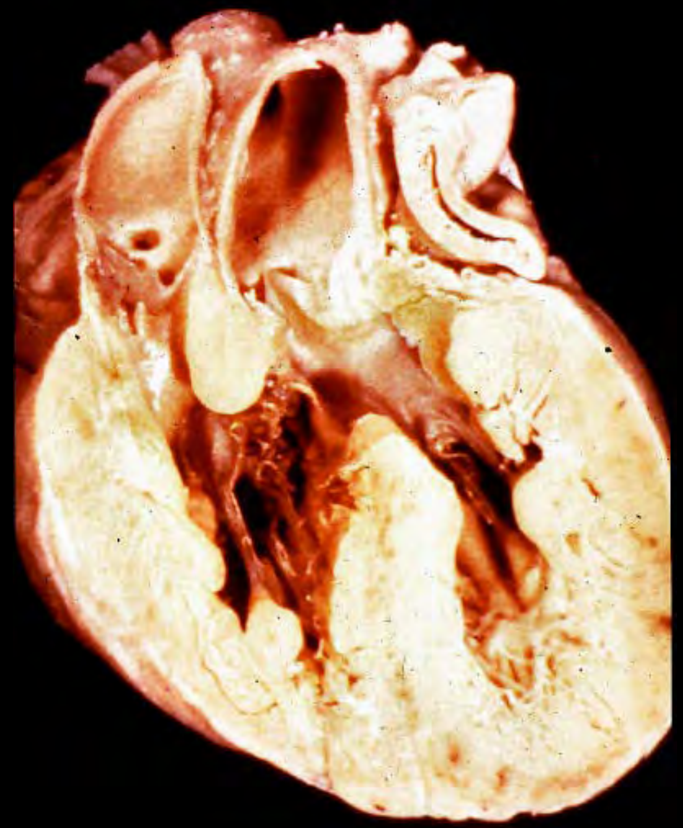
obstruction Radiofrequency + Stent

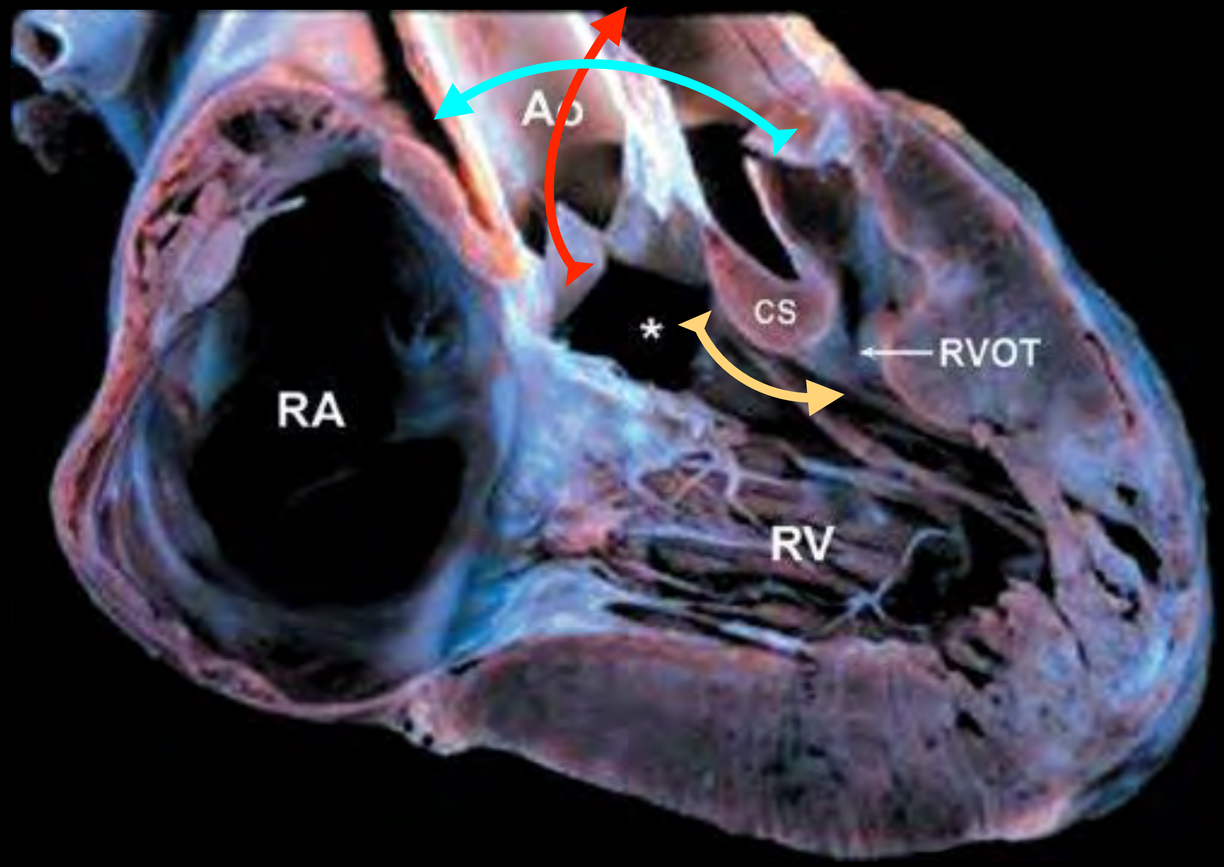
Love BA et al., Nat Clin Pract Cardiovasc Med 2008

TGA-VSD and Pulmonary stenosis

TGA

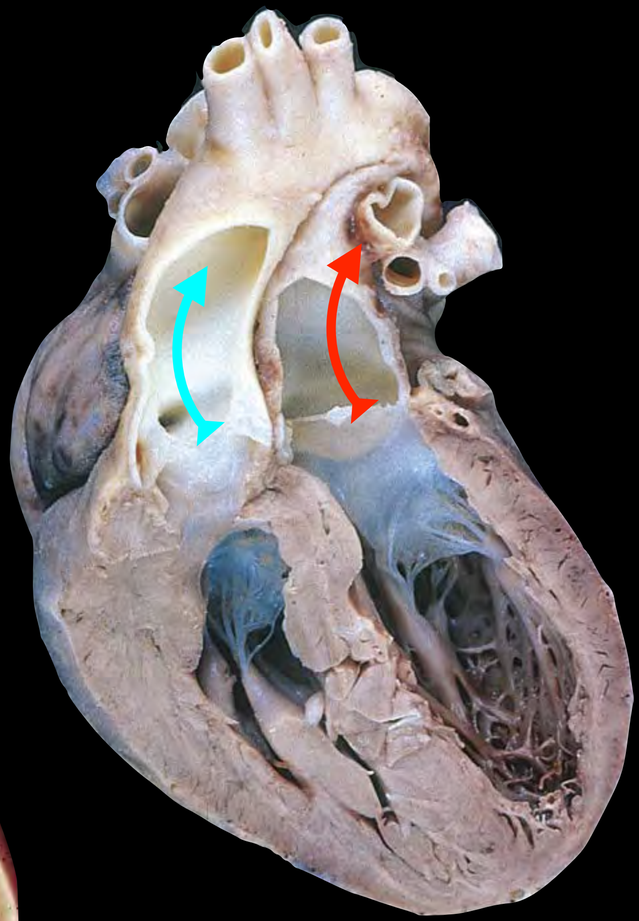
TGA - VSD - Pulmonary stenosis





ToF

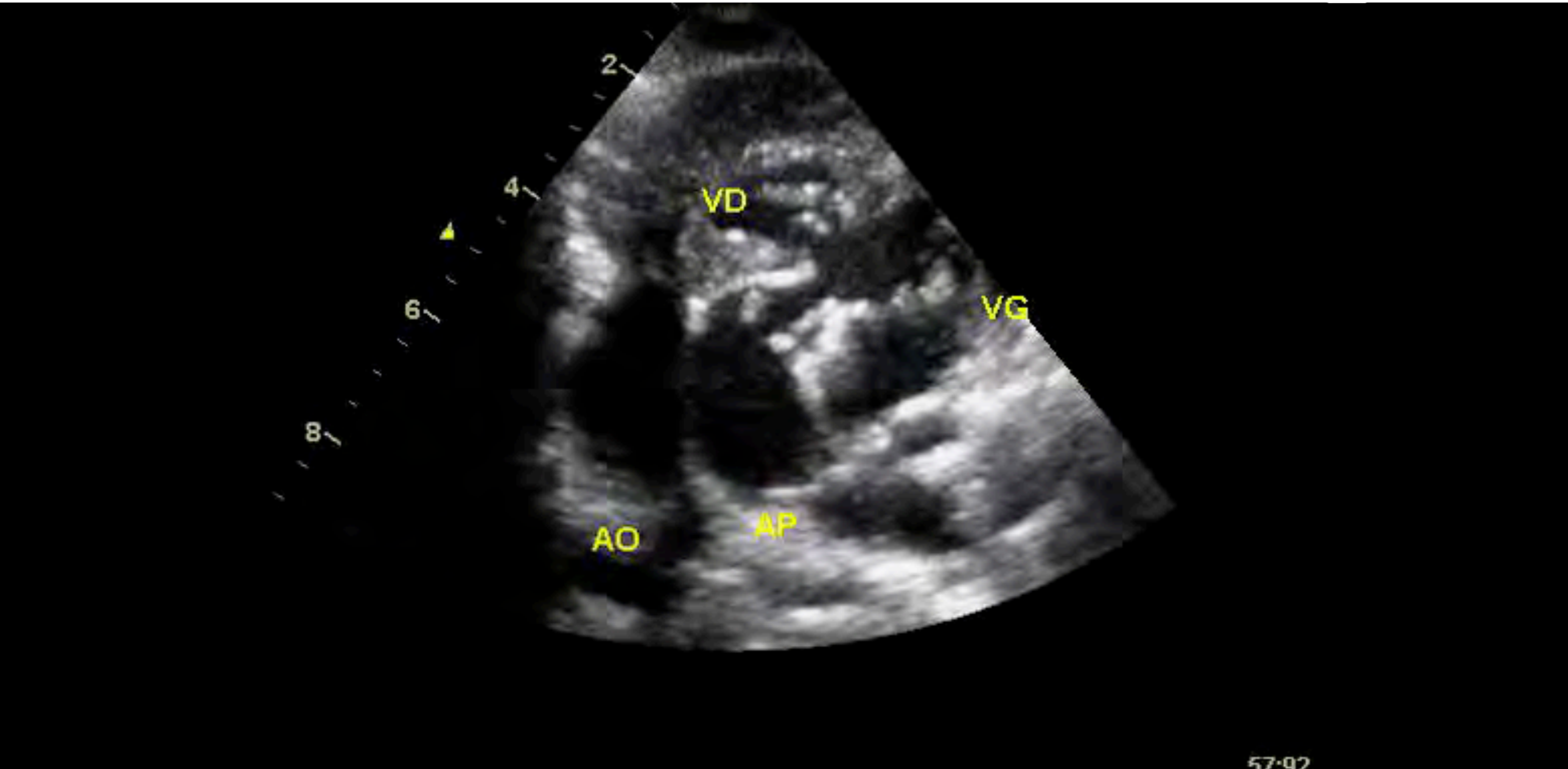
TGA-VSD-PS



TGA

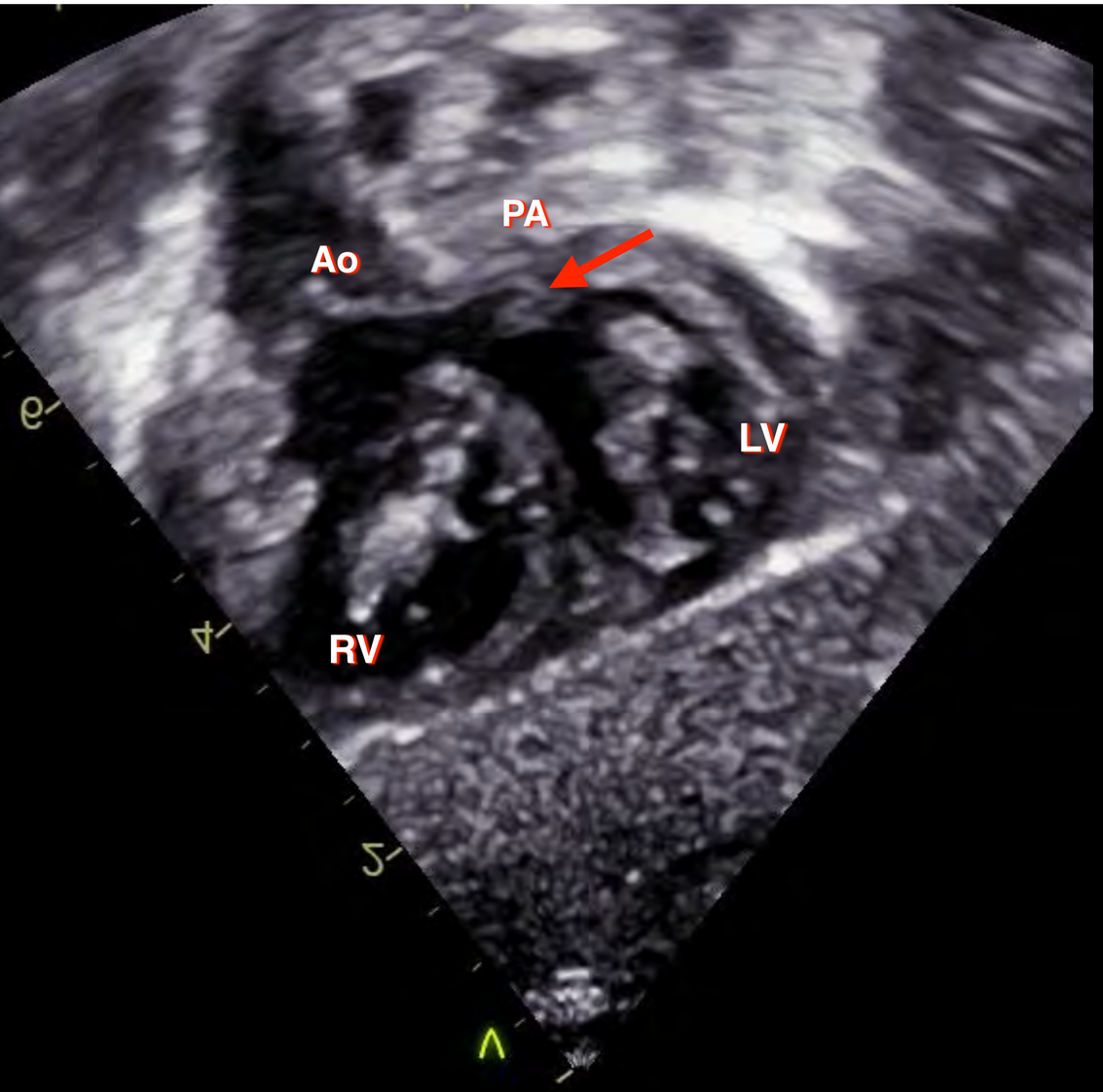
TGA

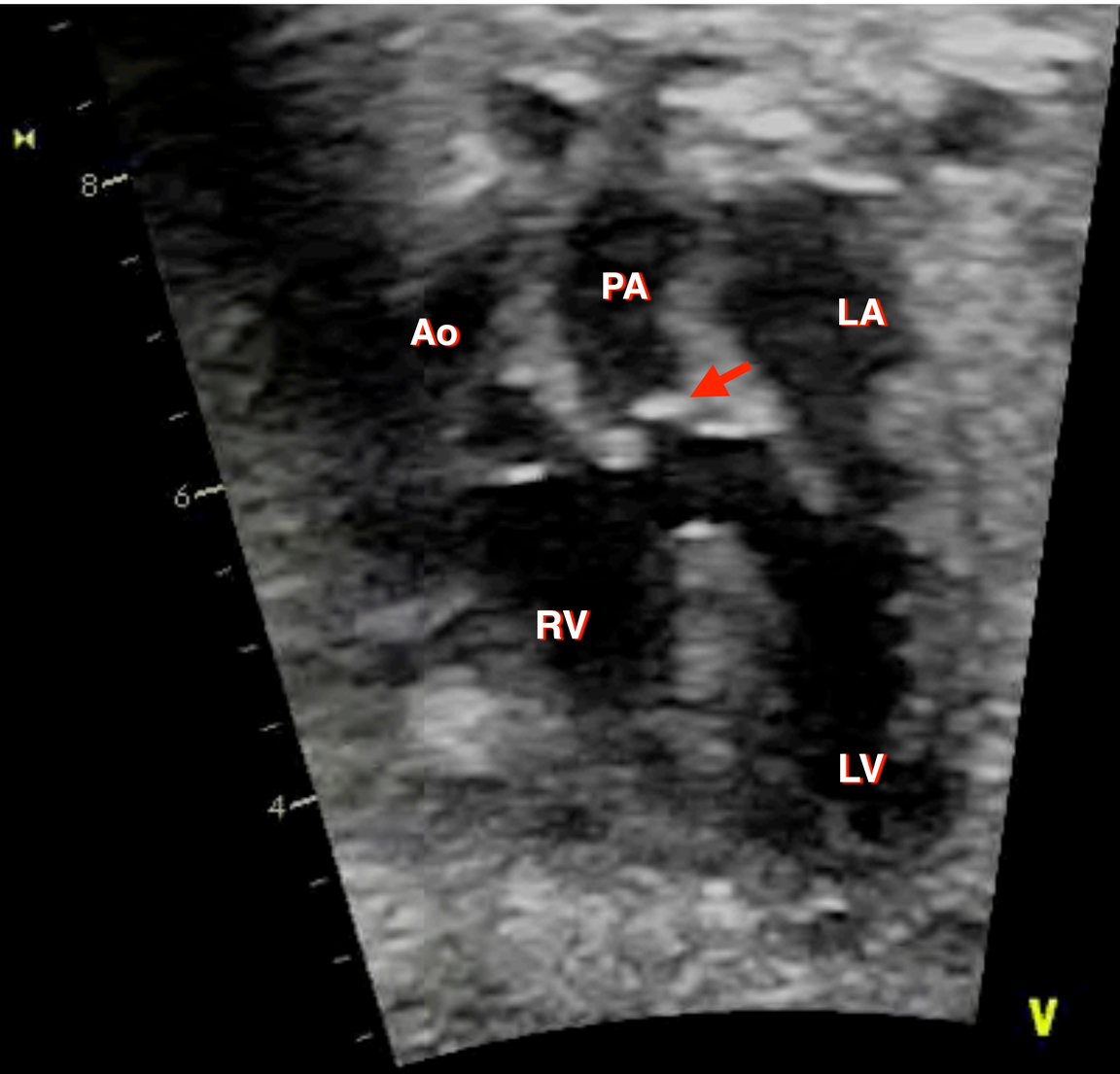
TGA - VSD - Pulmonary stenosis



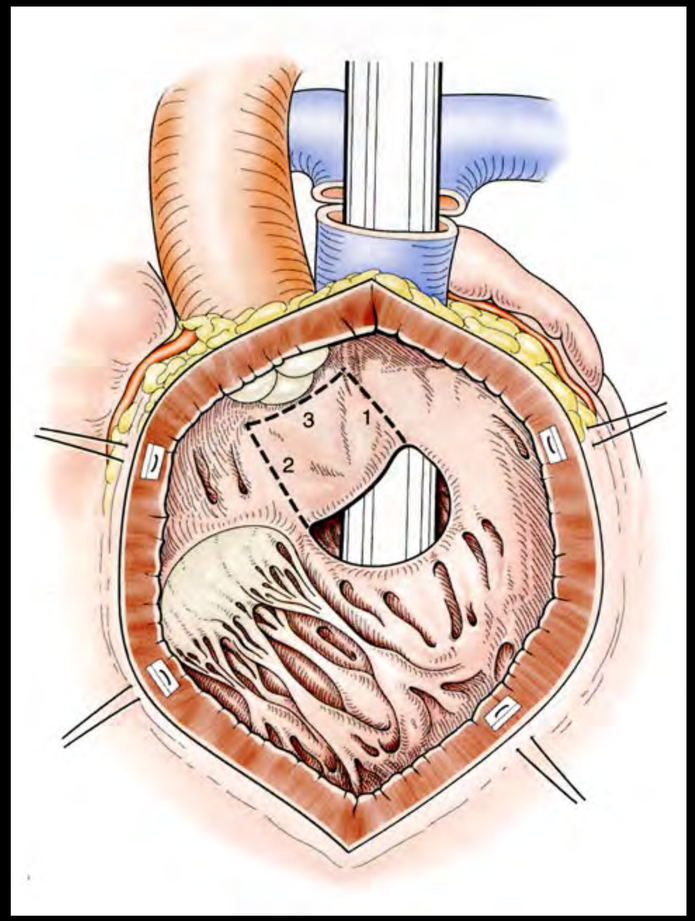
TGA

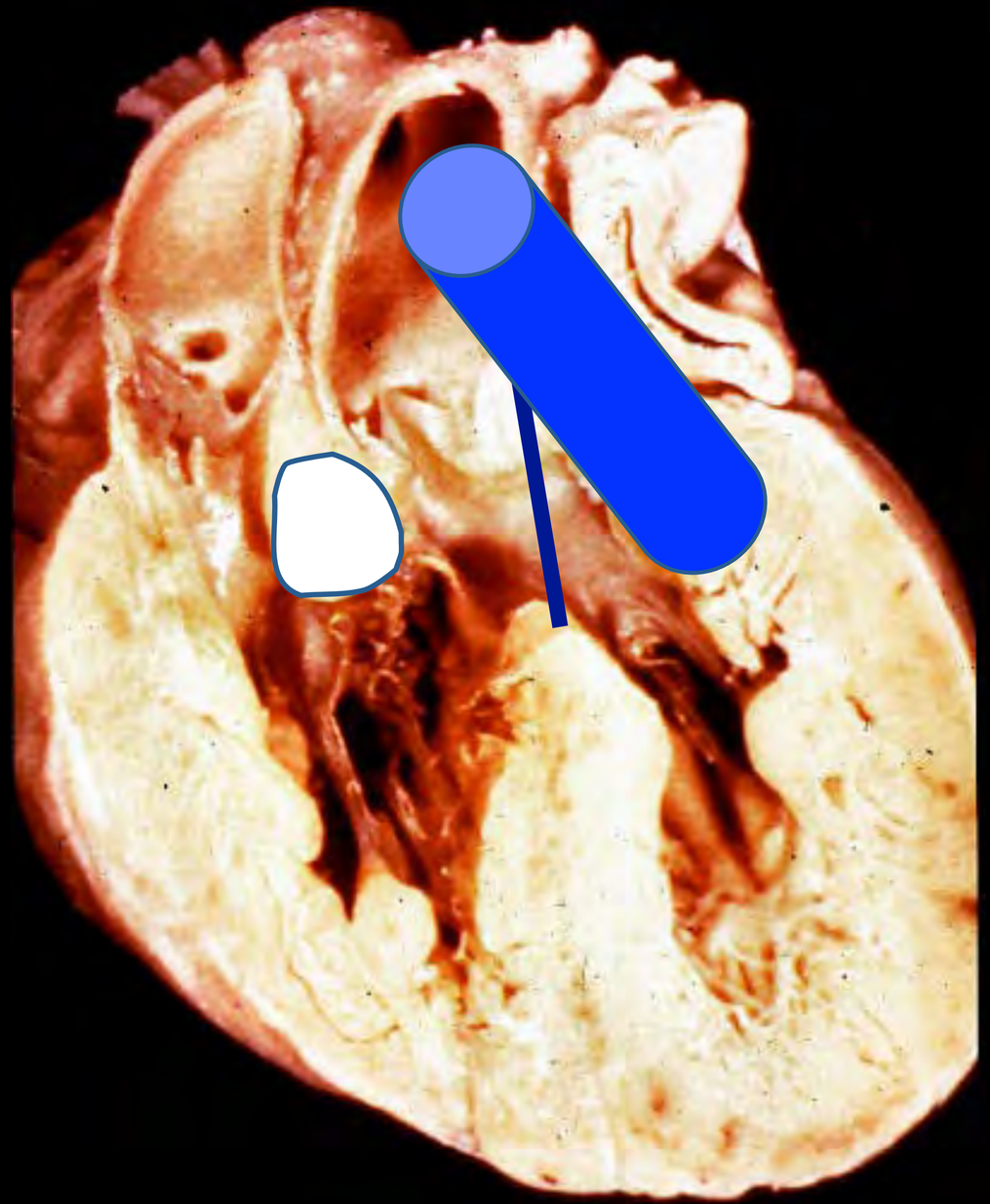
TGA - VSD - Pulmonary stenosis



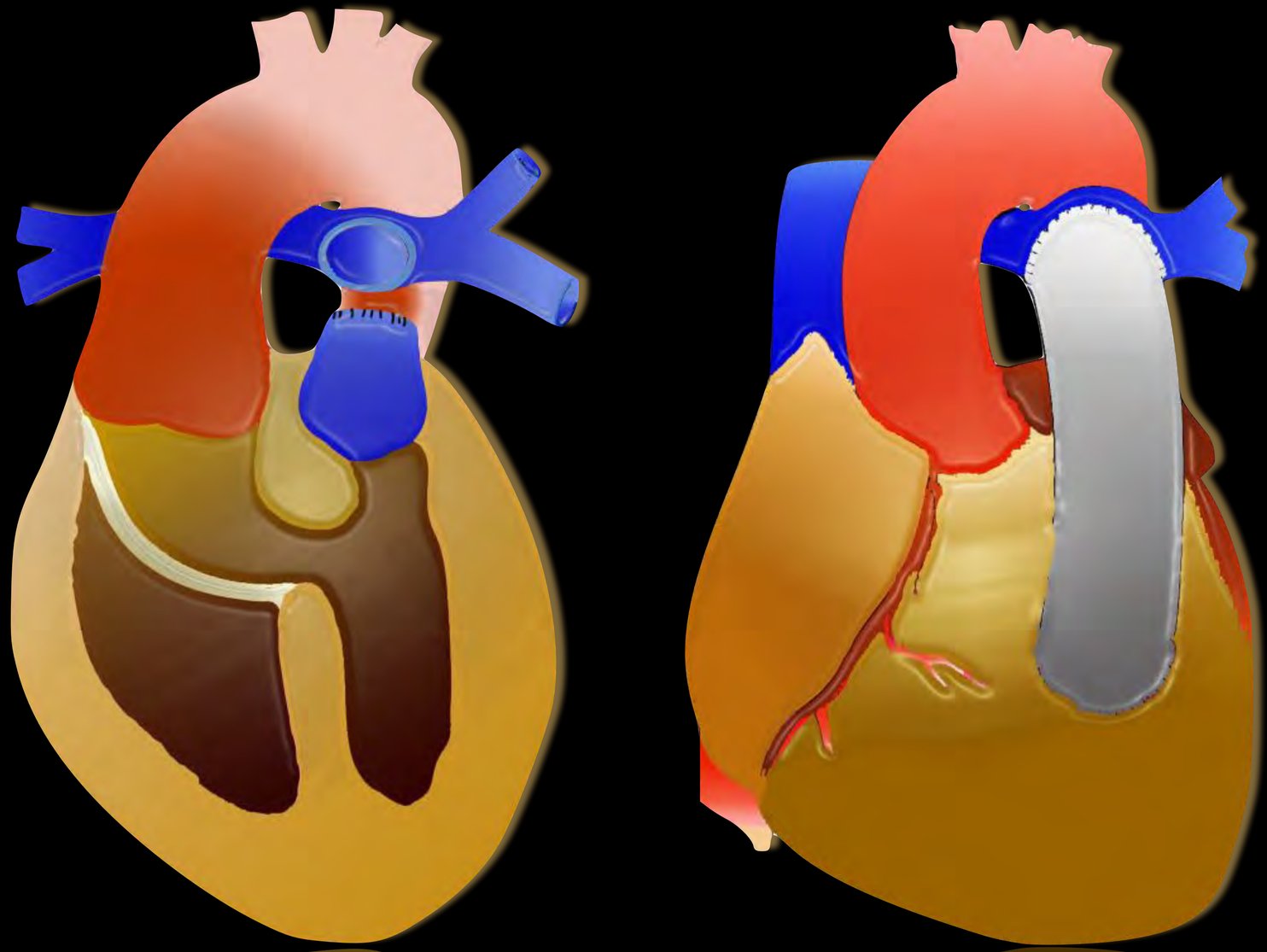


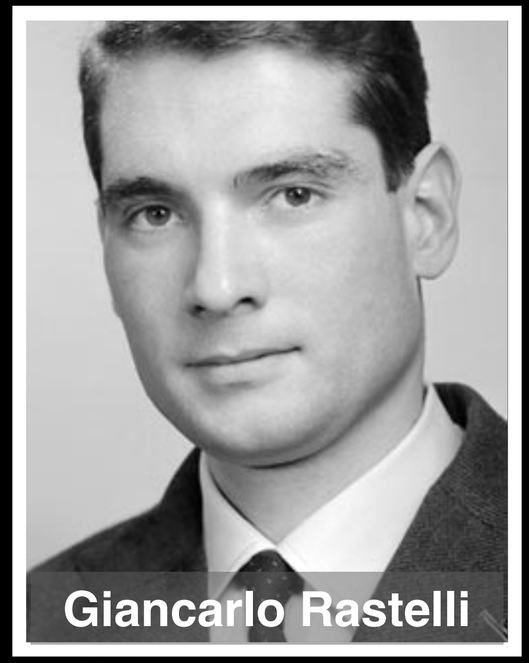
The Rastelli operation



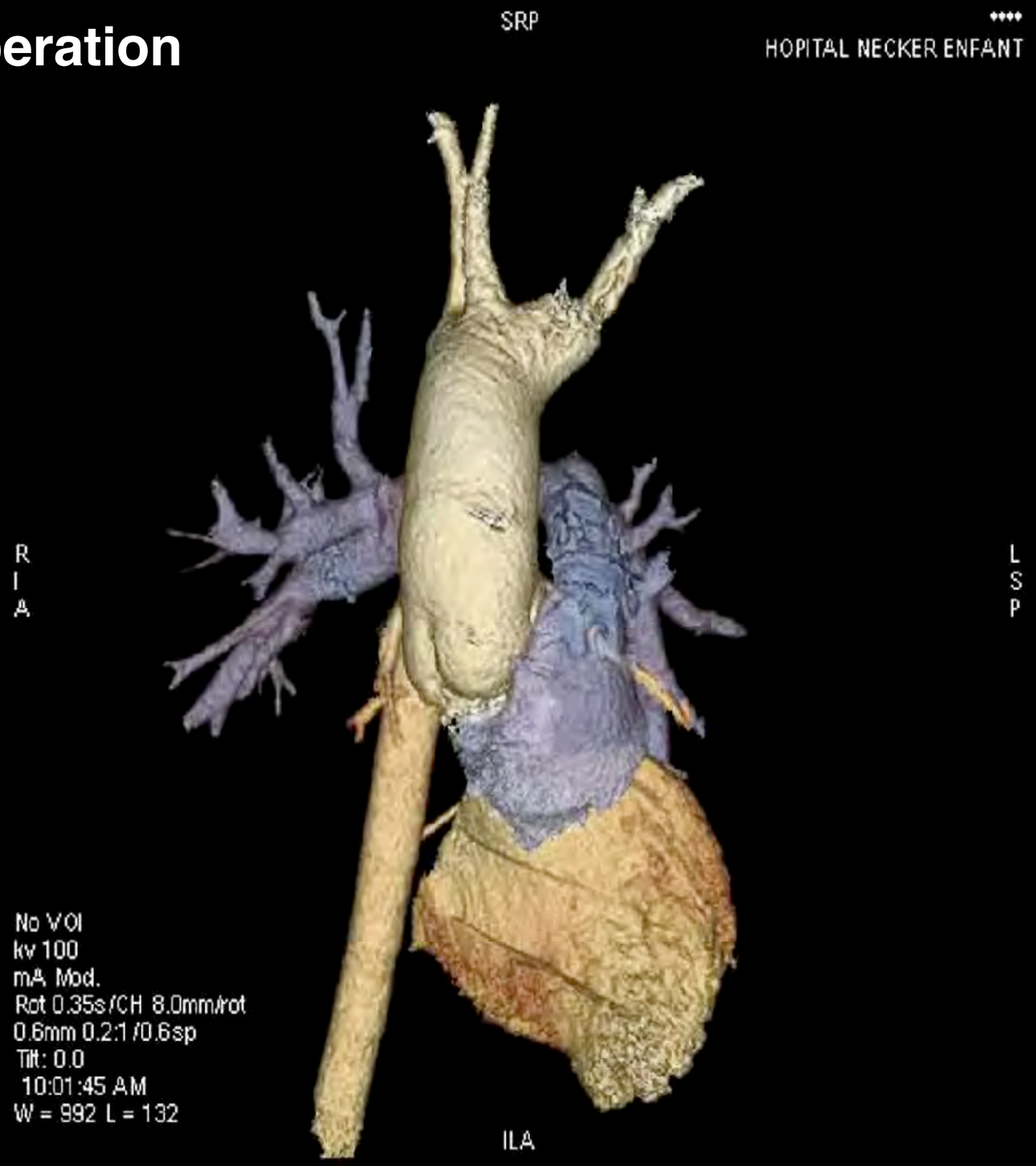


Rastelli procedure

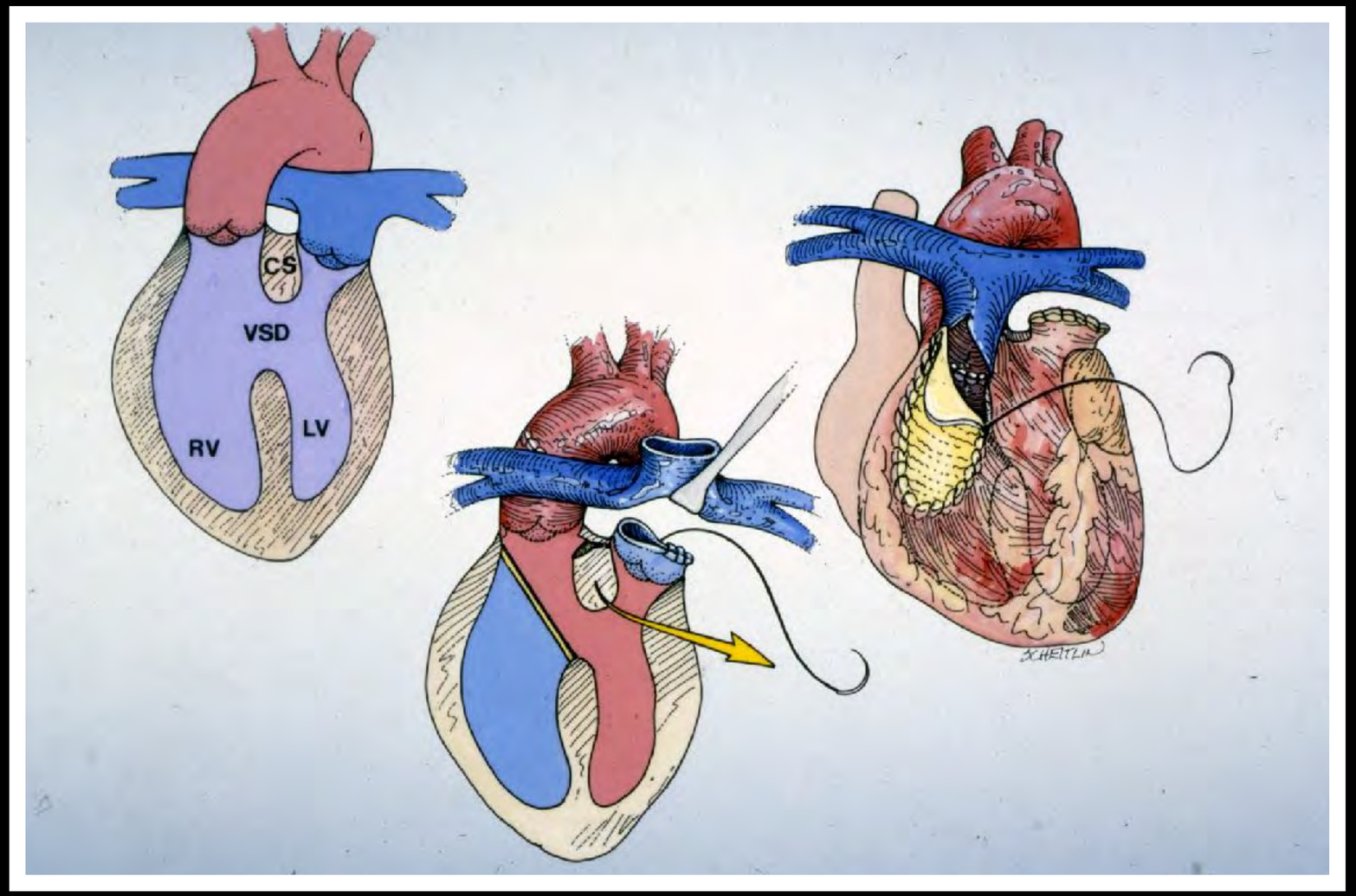




CT after Rastelli operation

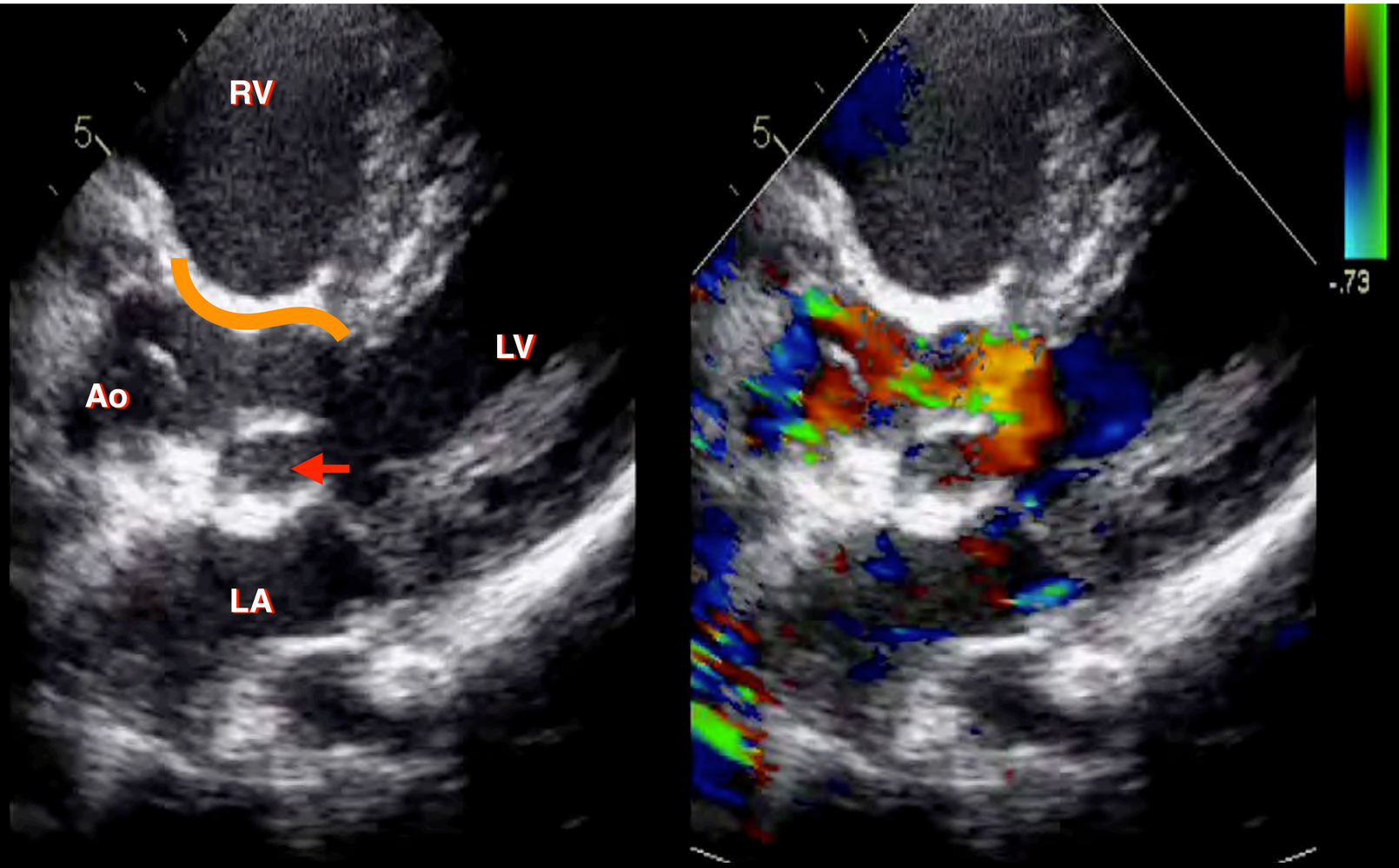


REV operation
(Réparation à l'Etage Ventriculaire)



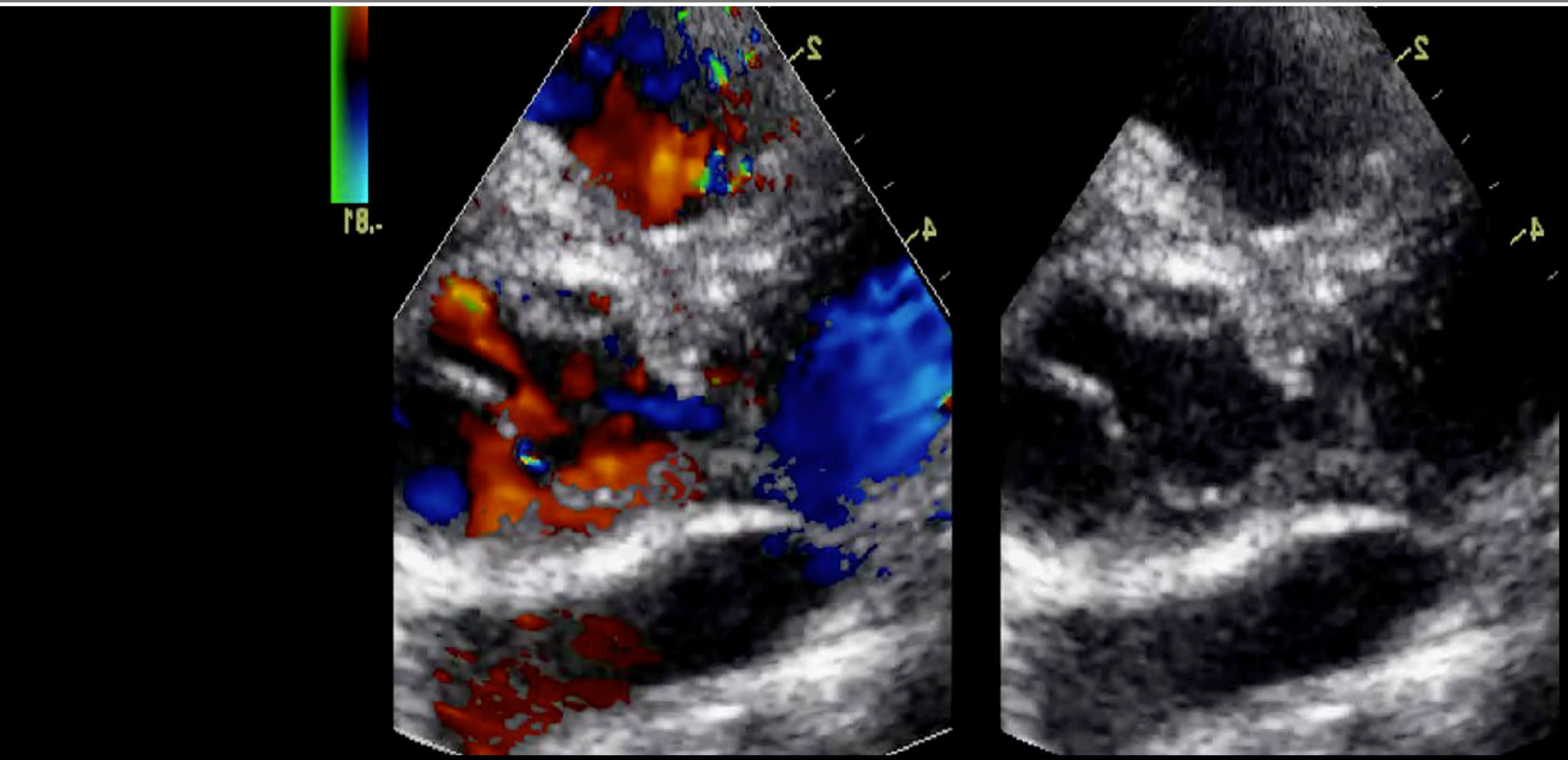
TGA

TGA - VSD - Pulmonary stenosis: tunnel from LV to aorta

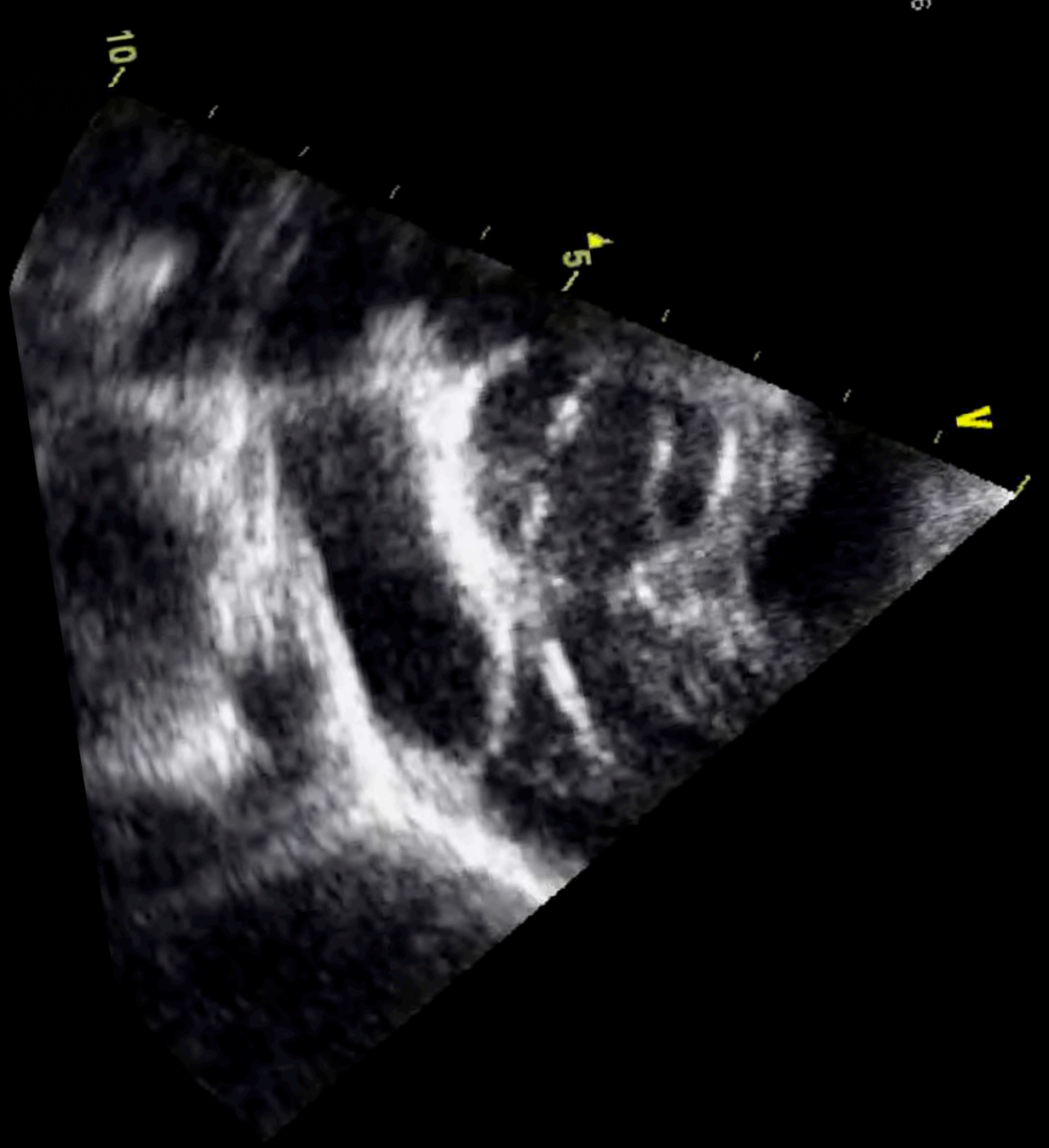


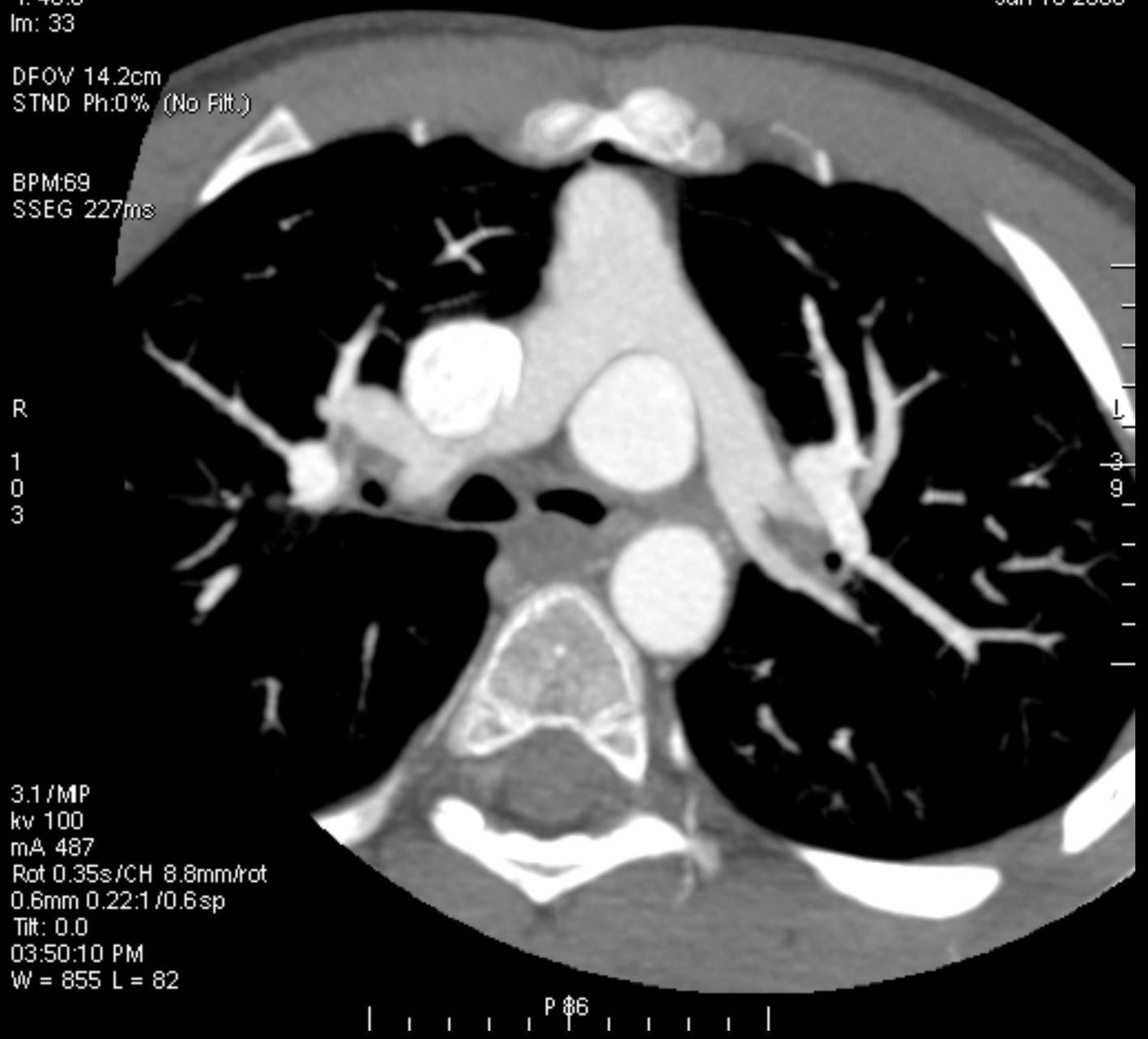
TGA

Sub-aortic obstruction after tunnel from LV to aorta



Rastelli/REV procedure
Sub aortic stenosis




Axial phase 0%
Ex: 3536
Se: 502
I: 48.0
Im: 33
DFOV 14.2cm
STND Ph:0% (No Filt.)
BPM:69
SSEG 227ms
R
1
0
3
3.1/MP
kv 100
mA 487
Rot 0.35s/CH 8.8mm/rot
0.6mm 0.22:1/0.6sp
Tilt: 0.0
03:50:10 PM
W = 855 L = 82
A 56
HOPITAL NECKER ENFANT
Jan 18 2006
P 86