

LONG TERM OUTCOMES FOR PATIENTS WITH CONGENITAL HEART DISEASE REPAIR AND DOWN SYNDROME

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 **ANNUAL**
symposium



no financial disclosure

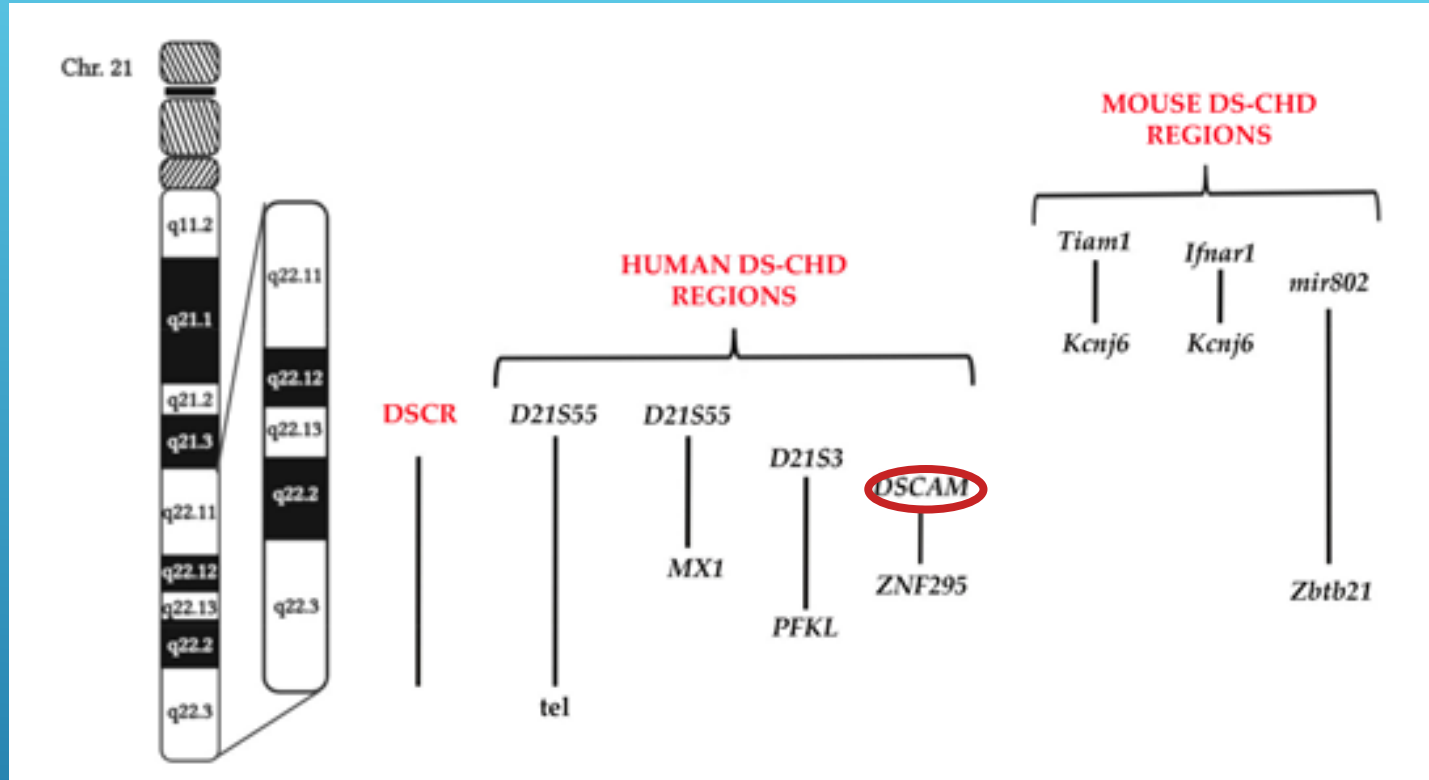


- **Congenital Heart Disease**
- **Pulmonary Hypertension**
- **Secondary cardiovascular complications**
 - **Obesity**
 - **Sleep Apnea**

CARDIOVASCULAR ASSOCIATION

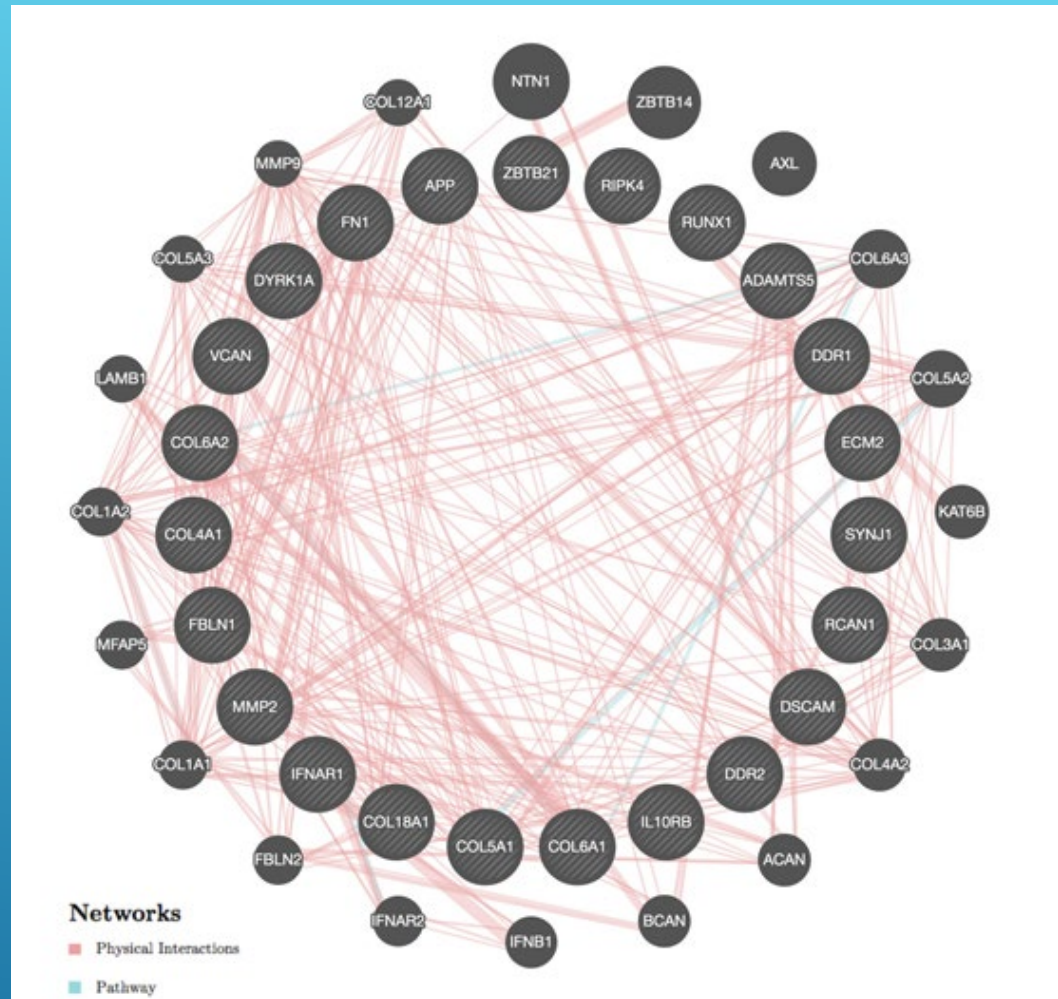
- Approximately 50% in DS
- AV canal is the most common lesion

CONGENITAL HEART DISEASE



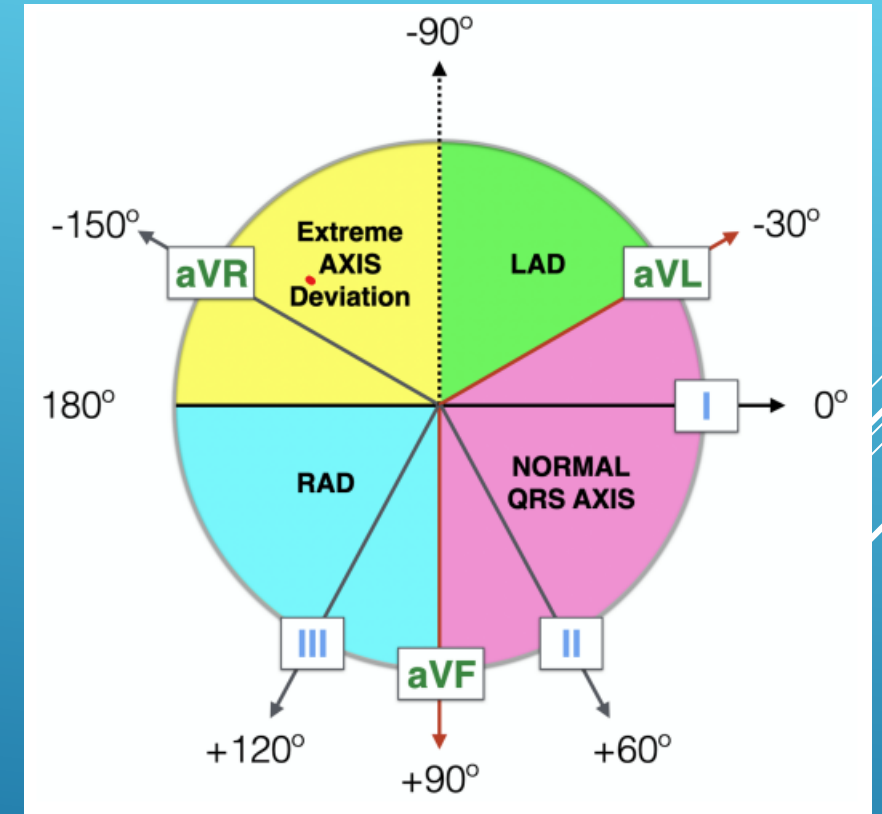
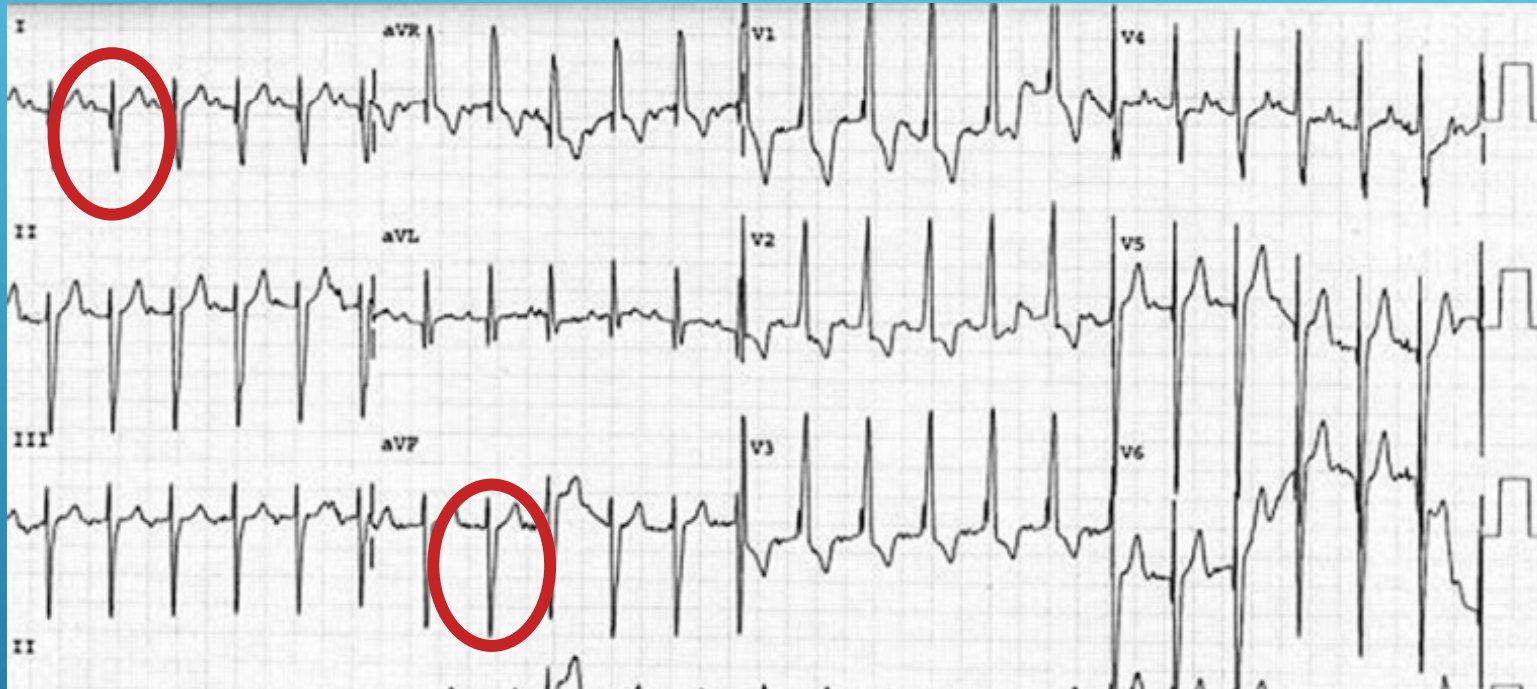
Mollo, N. et al. "Genetics and Molecular Basis of Congenital Heart Defects in Down Syndrome: Role of Extracellular Matrix Regulation" *Int. J. Mol. Sci.* 2023, 24, 2918

CONGENITAL HEART DISEASE



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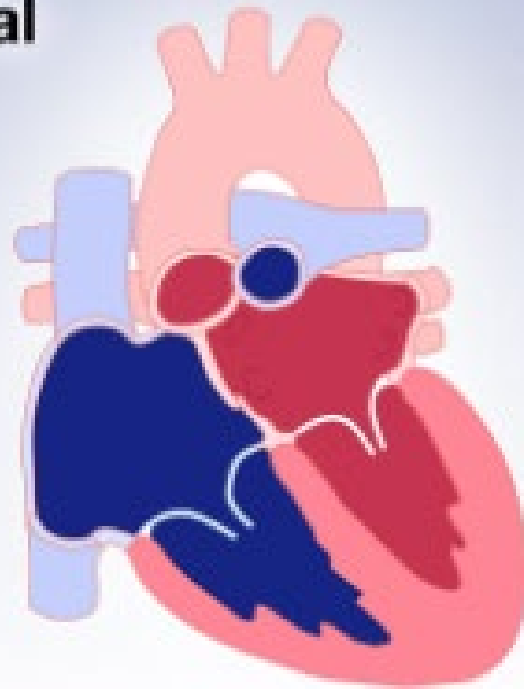
CONGENITAL HEART DISEASE



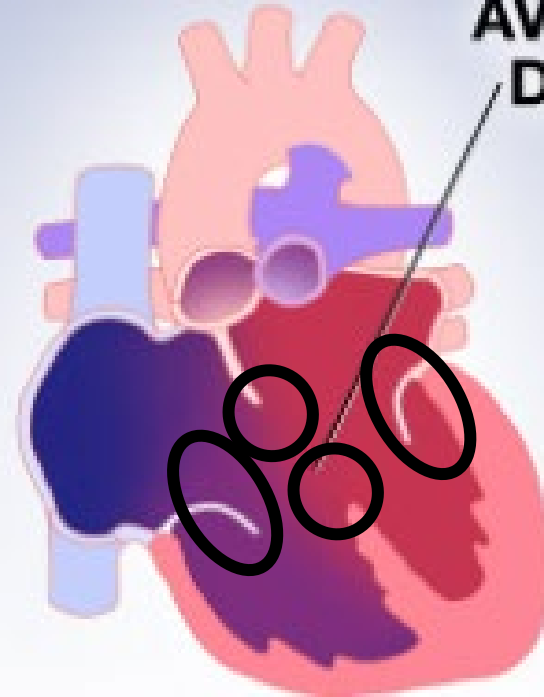
AV CANAL

Atrioventricular Canal Defect

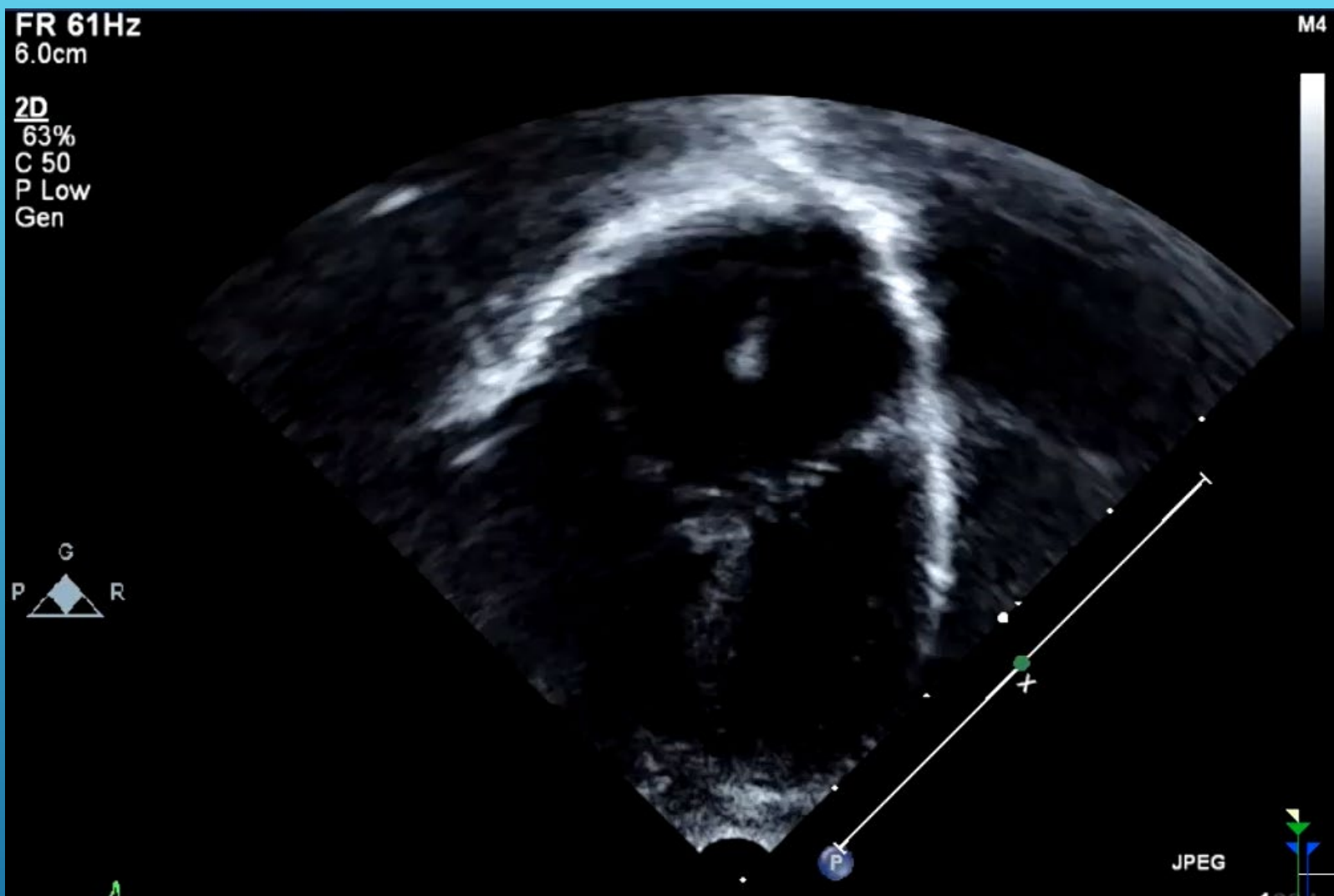
Normal



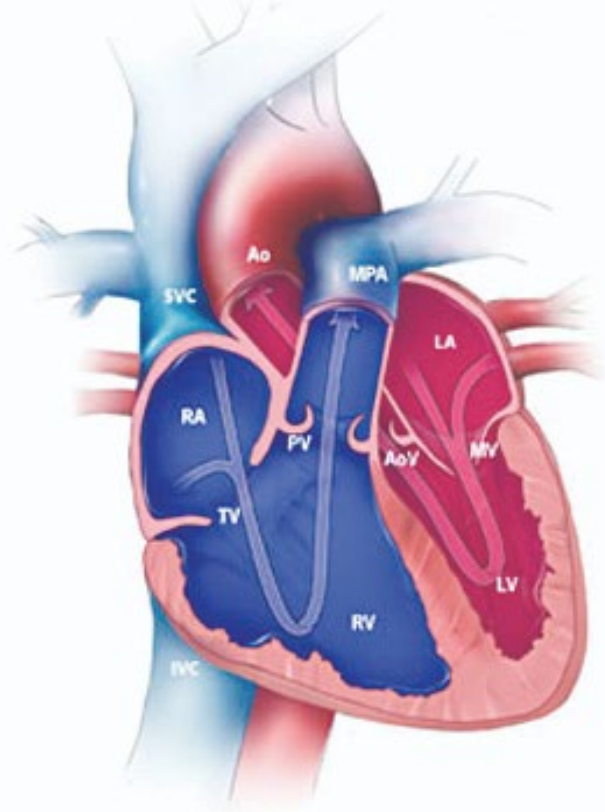
AV Canal Defect



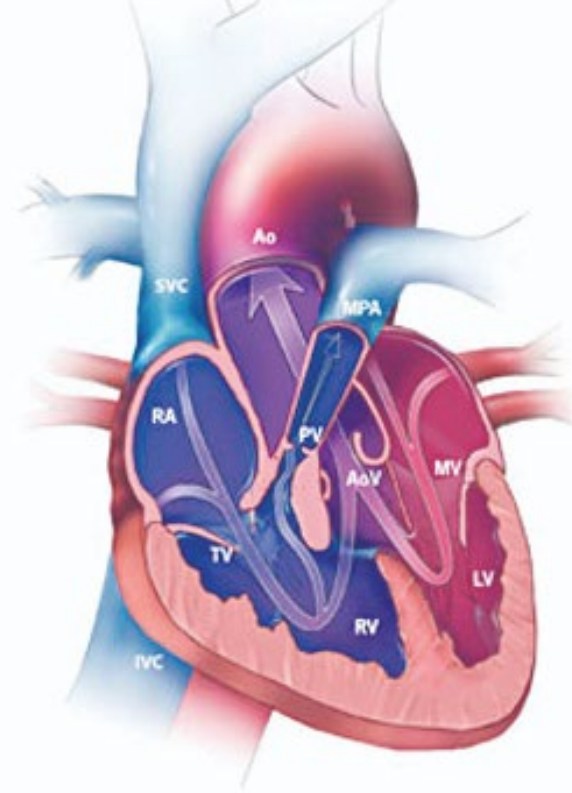
CONGENITAL HEART DISEASE



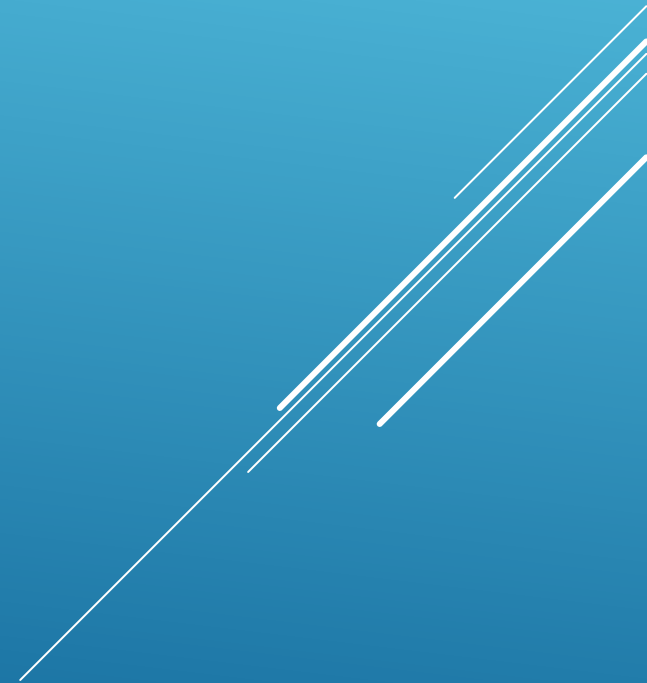
Normal Heart

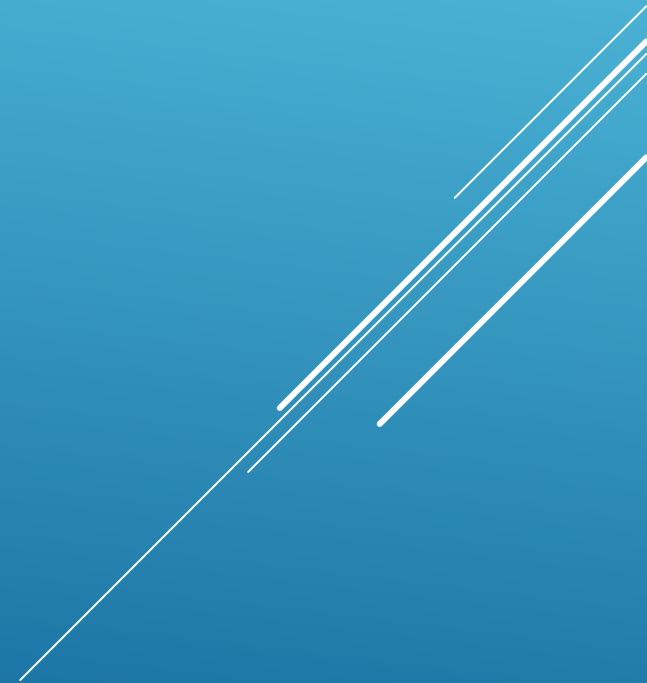
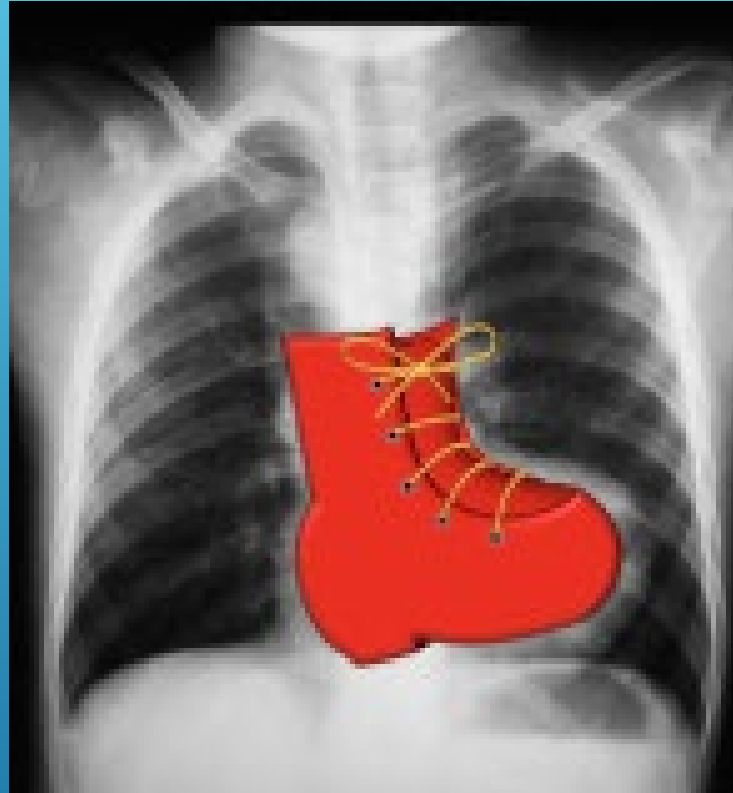


Tetralogy of Fallot (ToF)



CONGENITAL HEART DISEASE





AHMG PEDS

S8-3

23Hz

10cm

2D

69%

C 50

P Off

HGen

CF

40%

6600Hz

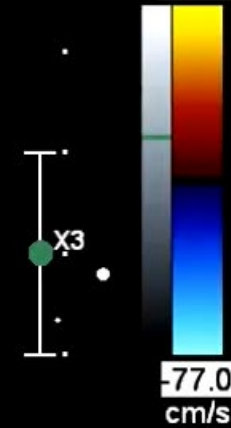
WF 659Hz

3.3MHz



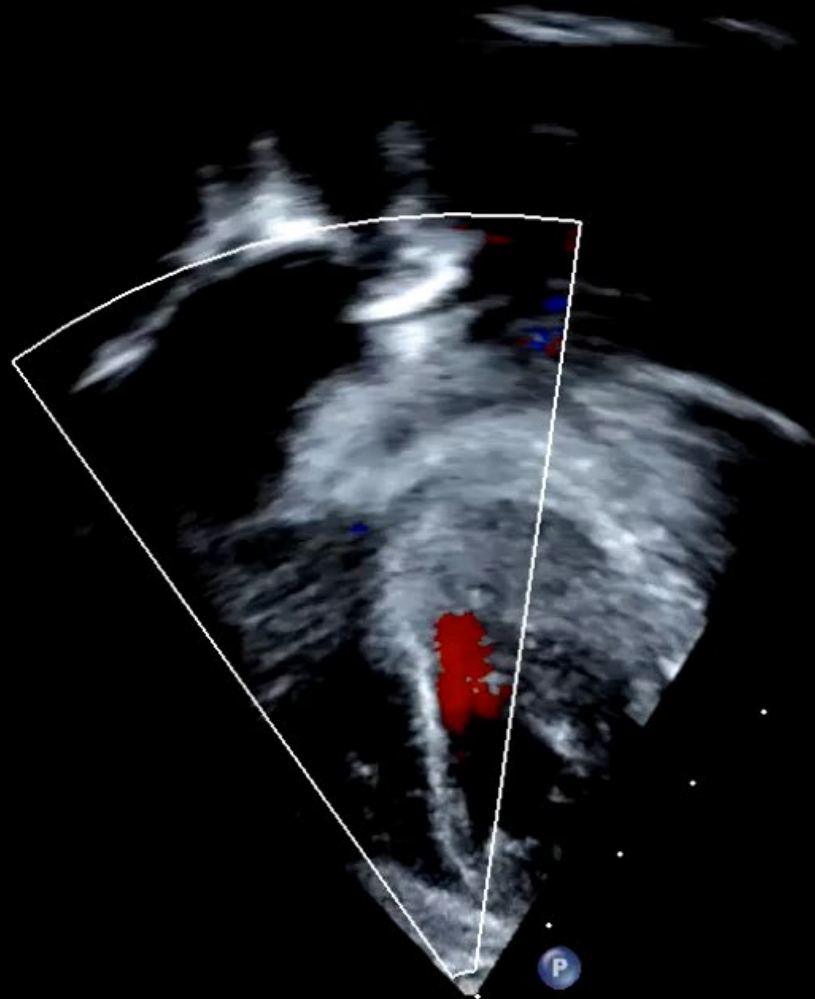
TIS1.6 MI 1.1

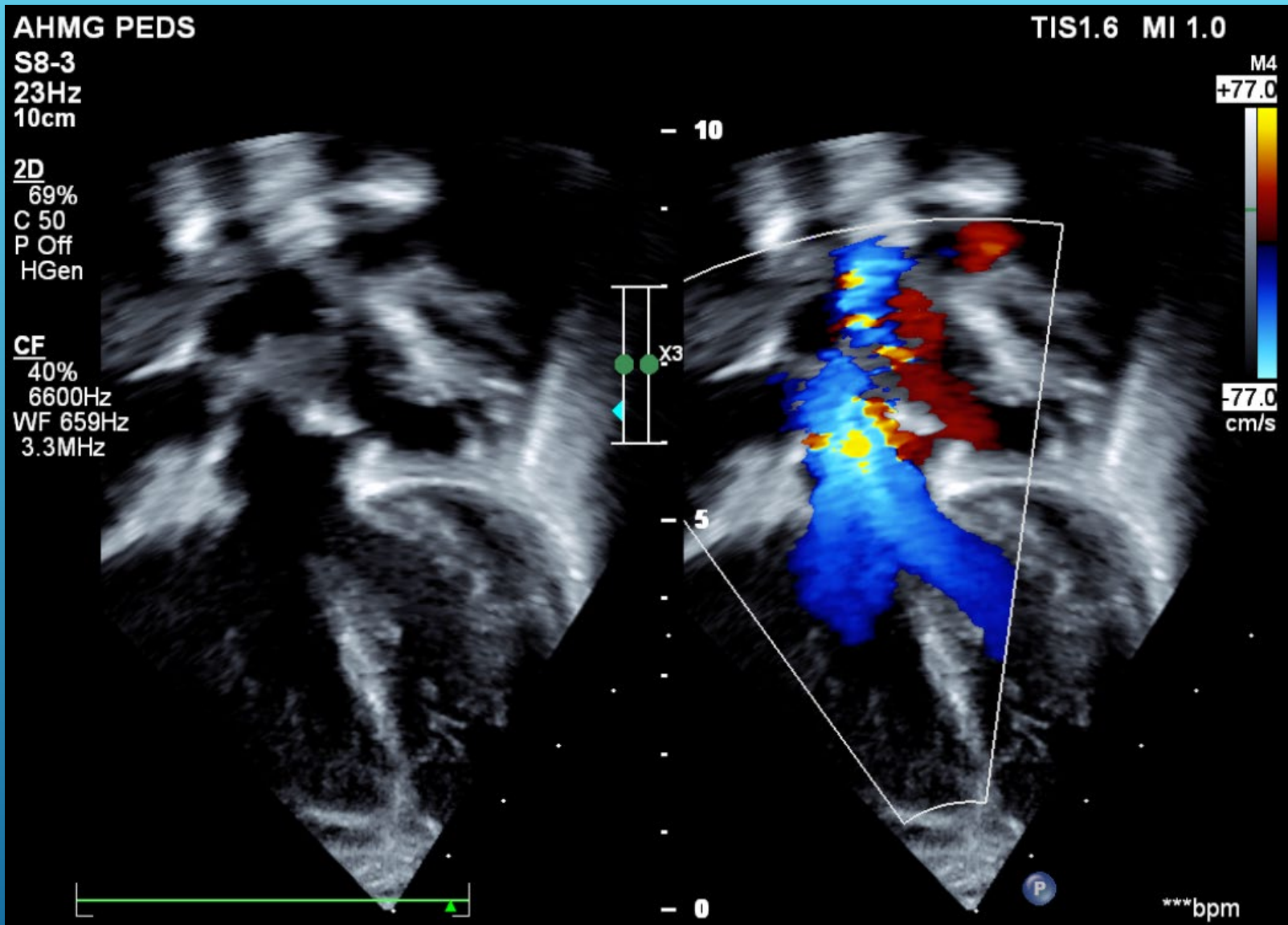
- 10M4 M4
+77.0



- 5

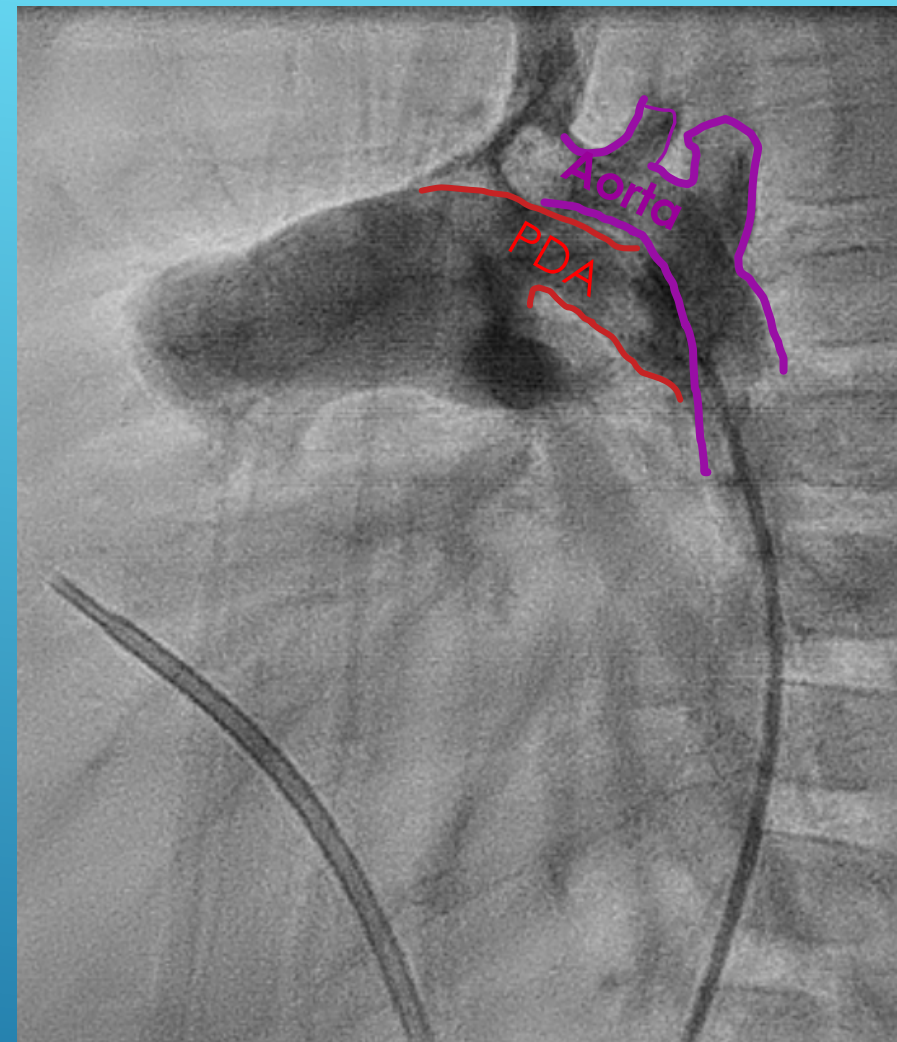
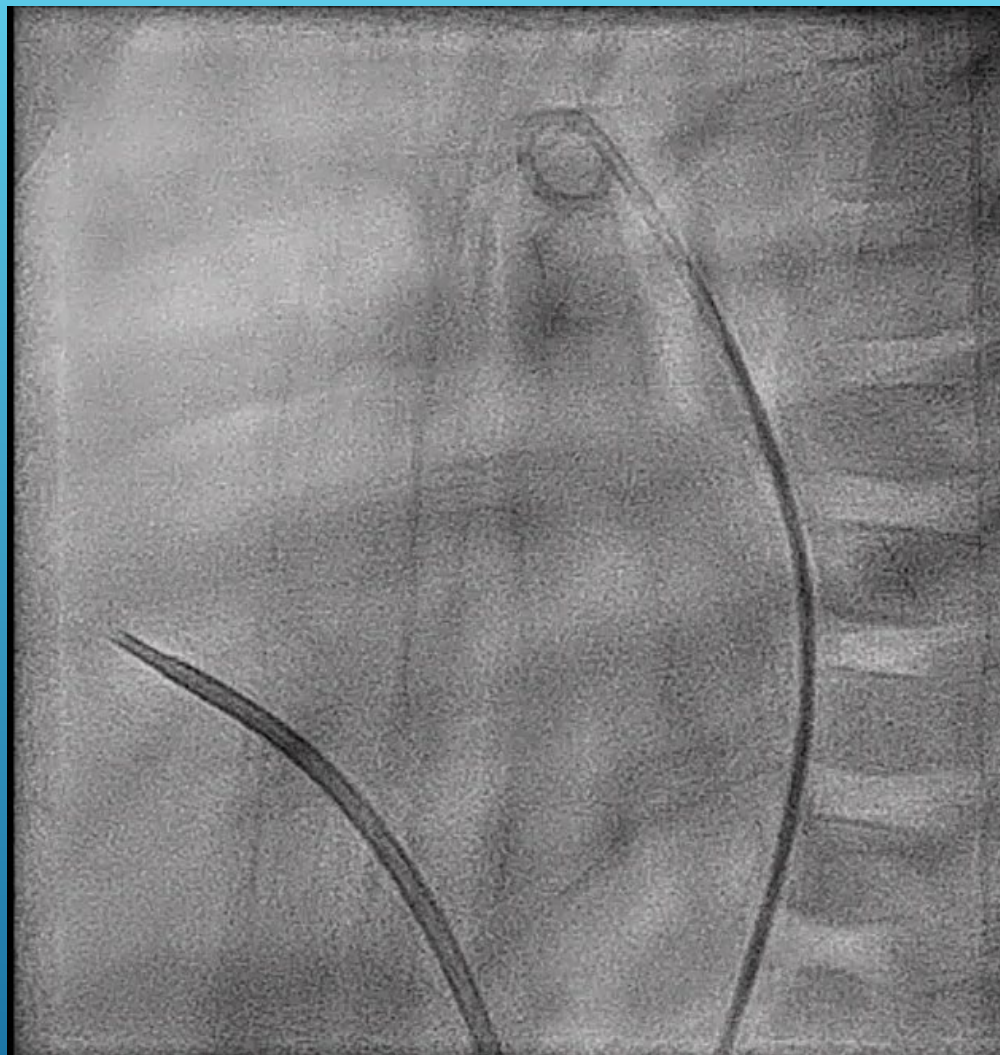
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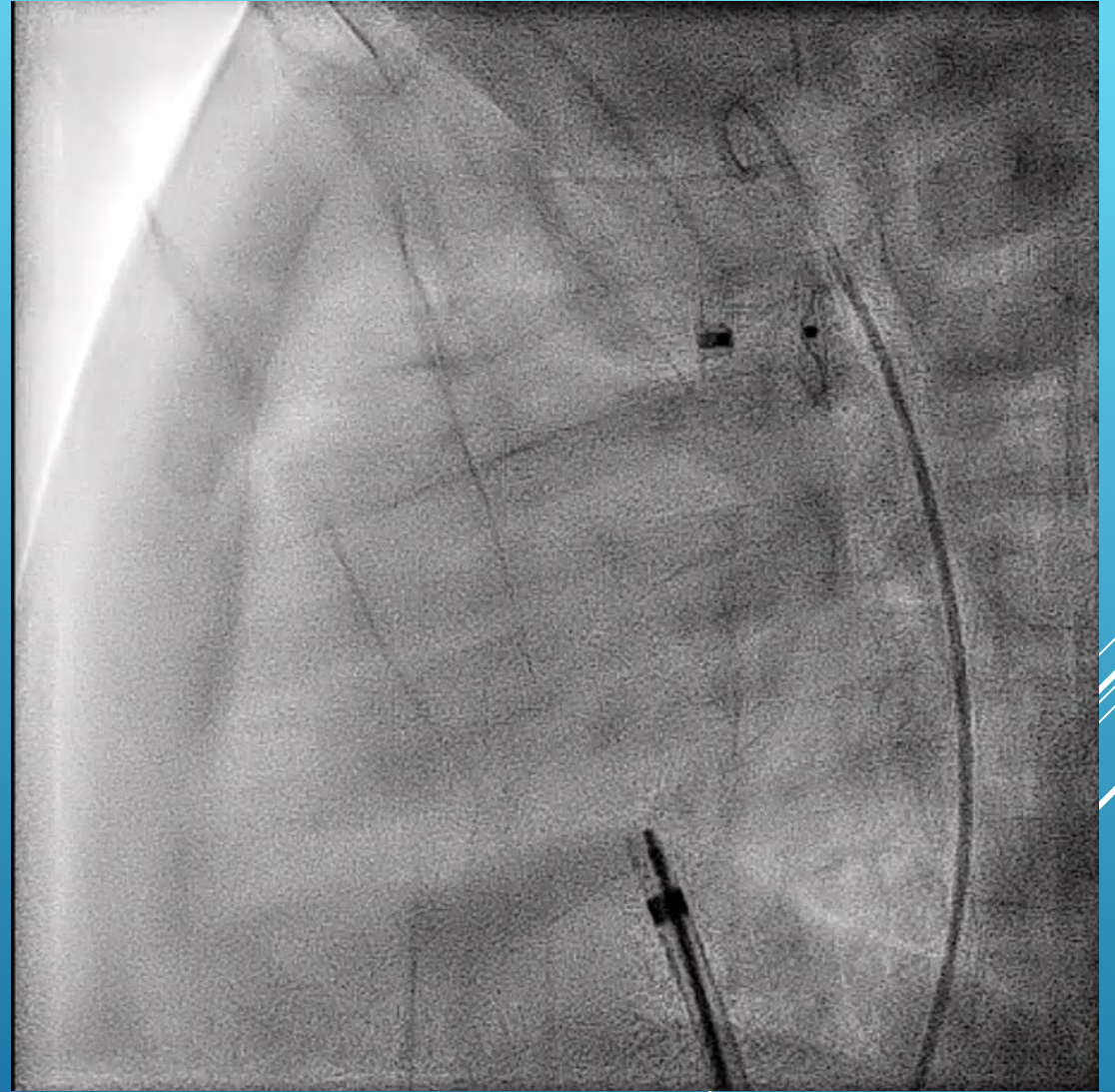
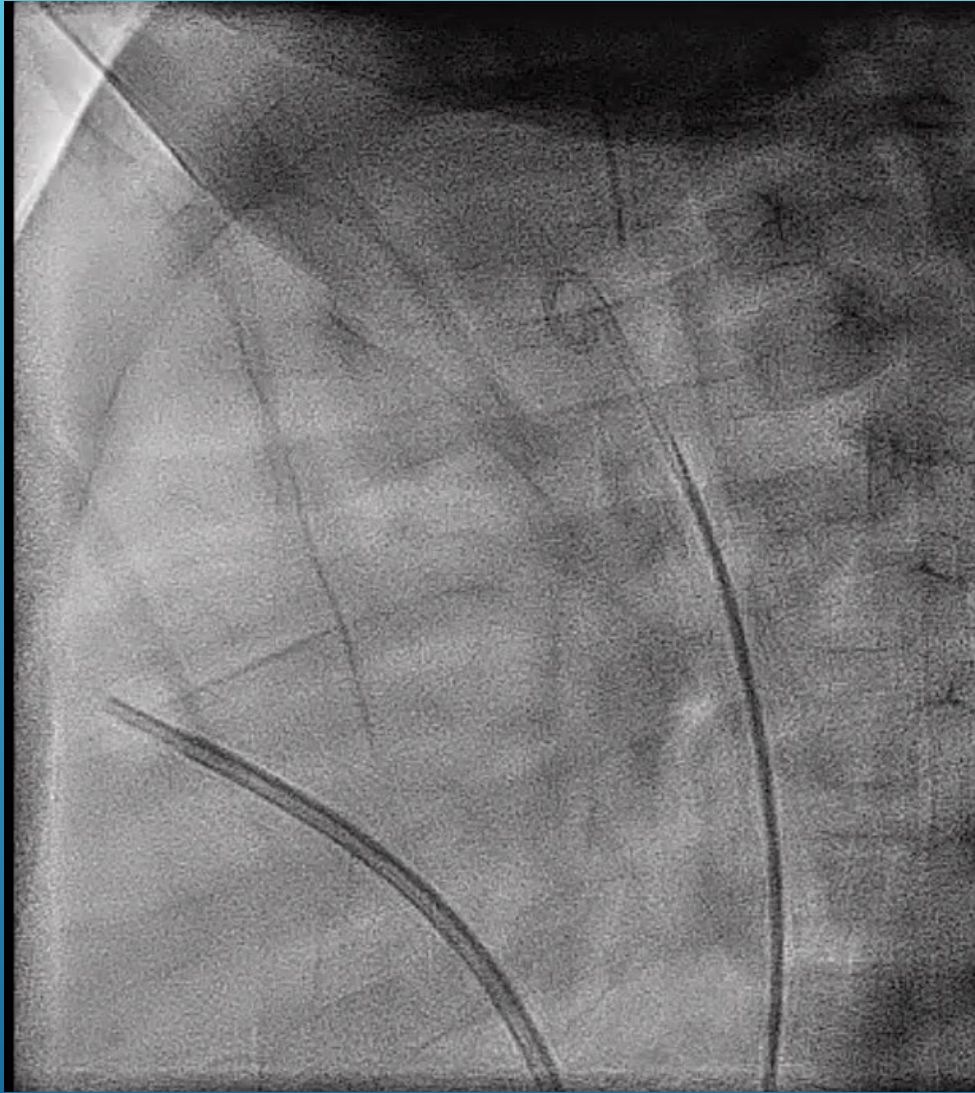


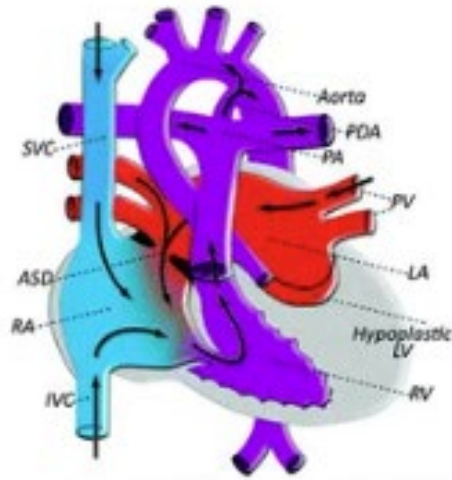


- ▶ Affects between 5 and 18% of down syndrome patients
- ▶ Is an especially important contributor to pulmonary hypertension

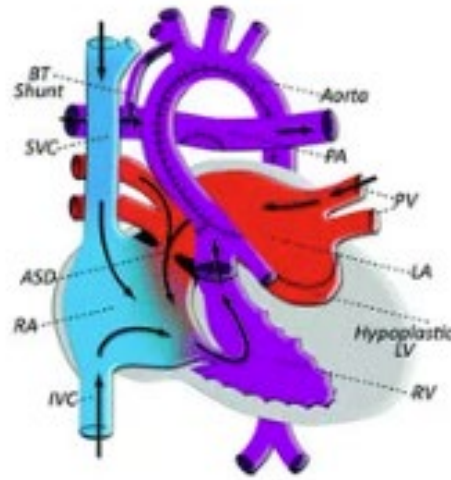
PATENT DUCTUS ARTERIOSUS (PDA)



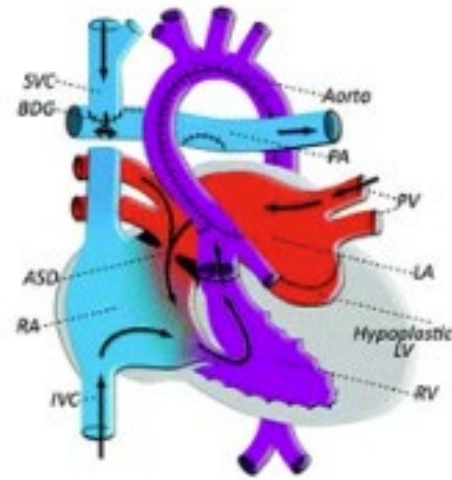




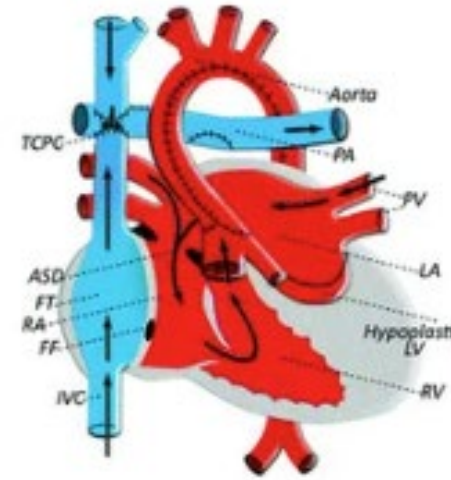
Single ventricle defect



Stage 1: Norwood



Stage 2: Glenn



Stage 3: Fontan

SINGLE V + TRISOMY 21

- For Decades Trisomy 21 patients were not offered Single V palliation
- First Fontan surgery was 1968
- Down syndrome not routinely considered for repair until the mid 1990s

SINGLE V + TRISOMY 21

- Improved surgical techniques
- Better selection criteria
- Use of fenestrations in the Fontan circuit

SINGLE V + TRISOMY 21

- Routine prenatal U/S 18-22 weeks
- Consideration of fetal echocardiogram
- Typically, 100% receive postnatal echo

CONGENITAL HEART DISEASE- SCREENING

Timing of repair

Congenital heart defect	Type of repair	Timing of repair	Potential for pulmonary vascular disease
Atrial septal defect	Interventional/surgical	Early if large	–
Ventricular septal defect	Interventional/surgical	Early if large	++
Atrioventricular septal defect	Surgical	Early	+++
Patent ductus arteriosus	Interventional/surgical	Early if large	++
Tetralogy of Fallot	Surgical	Early	+/-

CONGENITAL HEART DISEASE

Dimopoulos et al, "Cardiovascular Complications of Down Syndrome: Scoping Review and Expert Consensus" *Circ*; Volume 147, Issue 5, 31 January 2023; Pages 425-441

- **Morbidity and Mortality**
- **Neurodevelopmental**
- **Psychological**
- **Functional**

CHD- OUTCOMES

Does Down syndrome influence the outcomes of congenital cardiac surgery? A systematic review and meta-analysis

Benjamin Wang ^{1,*}, **Justin Verrocchi**², **Danny Liew** ³ and **Dominica Zentner** ^{1,4}

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CHD- OUTCOMES

Table 3 Hazard ratios from pooled analyses of individual studies

Outcome	Control	Statistical model type	HR (95% CI)	Participants (N)	Number of studies included (N)	I ² (%)
Mortality	nDS, operated	Unadjusted	0.86 (0.60–1.23)	1946	5	14
Cardiac reoperation	nDS, operated	Unadjusted	0.60 (0.46–0.78)	1681	5	0
		Adjusted	0.54 (0.36–0.81)	971	3	40
LAVV reoperation	nDS, operated	Unadjusted	0.51 (0.34–0.77)	743	3	0
		Adjusted	0.32 (0.13–0.76)	463	2	44

CI, confidence interval; HR, hazard ratio; nDS, non-Down syndrome; and LAVV, left atrioventricular valve.

CHD- OUTCOMES

- **Mortality**
 - Not associated with increased in hospital or short-term mortality
 - Lower mortality in balanced AVC defect

CHD- OUTCOMES

- **Morbidity**
 - Longer length of stay
 - Increased respiratory complications
 - Increased lifelong risk for needing pacemaker

CHD- OUTCOMES

- **Neurodevelopmental/behavioral**
 - **Autism**
 - **Mental Health**
 - **Intellectual Disabilities**

CHD- OUTCOMES

- **Functional outcomes**
 - Early interventions
 - Specialized education program
 - Hold a job as an adult

CHD- OUTCOMES

Congenit Heart Dis. 2019 September ; 14(5): 854–863. doi:10.1111/chd.12823.

Postoperative and long-term outcomes in children with Trisomy 21 and single ventricle palliation

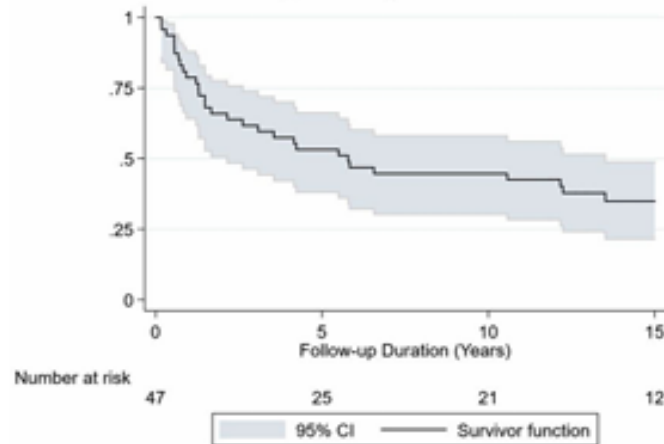
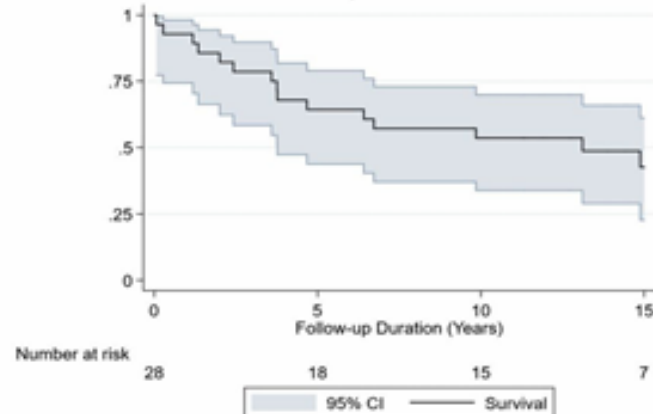
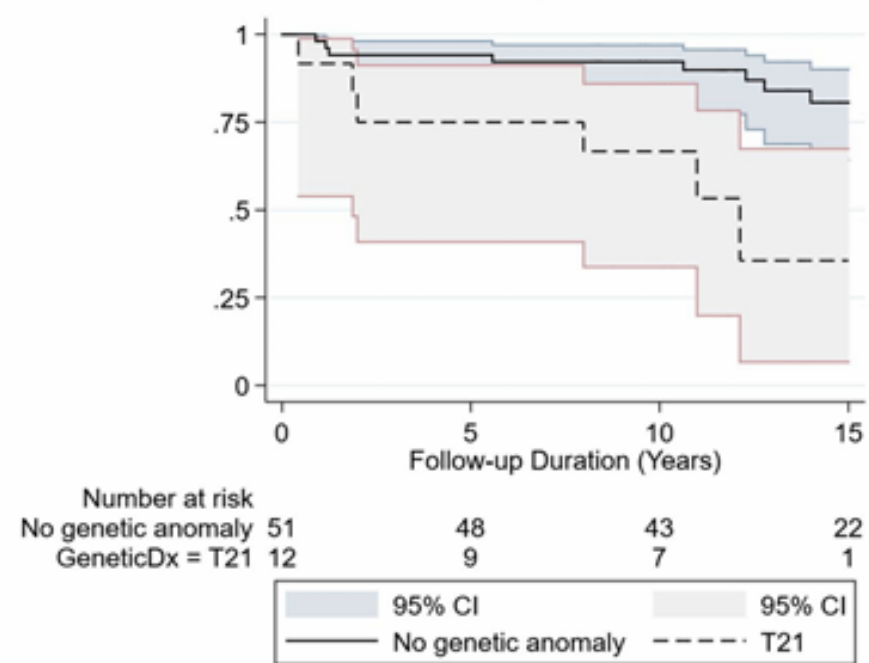
Jennifer K. Peterson, MS¹, Shaun P. Setty, MD^{1,2}, Jessica H. Knight, PhD³, Amanda S. Thomas, MSPH⁴, James H. Moller, MD⁵, Lazaros K. Kochilas, MD, MSCR^{4,6}

SINGLE V OUTCOMES

TABLE 5

Comparison of characteristics between long-term Fontan survivors with T21 vs no known genetic anomaly

	T 21 N= 16	No genetic anomaly N= 55	P value
Clinical features			
Male Sex	7 (43.8)	25 (45.4)	1.00
Birth era (%)			
1990–1999	10 (62.5)	42 (76.4)	.339
2000–2003	6 (37.5)	13 (23.6)	
Systemic ventricle (%)			
Left ventricle	11 (68.7)	16 (29.1)	.020
Right ventricle	5 (31.3)	36 (65.5)	
Undetermined	0 (0)	3 (5.4)	
Single ventricle type (%)			<.001
Unbalanced CAVC	8 (50.0)	4 (7.3)	
Complex unbalanced CAVC ^a	7 (43.7)	48 (87.3)	
Complex tricuspid/pulmonary atresia ^b	0	3 (5.4)	
Hypoplastic left heart syndrome	1 (6.3)	0	
Fontan age (years)	3.0 (2.3–3.9)	3.1 (2.3–4.1)	.665
<2 years	3 (18.8)	7 (12.7)	.847
2–4 years	9 (56.2)	33 (60.0)	
>4 years	4 (25.0)	15 (27.3)	
Fontan type			
Extracardiac	11 (68.7)	34 (61.8)	.771
Lateral tunnel	5 (31.3)	21 (38.2)	
Fenestrated	11 (68.7)	36 (65.4)	1.00
Pre-Fontan hemodynamics			
SVO ₂ (%)	62.0 (58.0–69.0)	64.5 (58.0–69.0)	.74
Missing (%)	1 (6.3)	5 (9.1)	
Mean PAP (mm Hg)	11.0 (10.0–14.0)	11.0 (8.5–13.0)	.62
<15 mm Hg (%)	12 (75.0)	44 (80.0)	.87
≥15 mm Hg	3 (18.7)	8 (14.5)	

A Survival Post Stage 1 Hospitalization**B** Survival Post Glenn Hospitalization**C** Survival Post Fontan Hospitalization

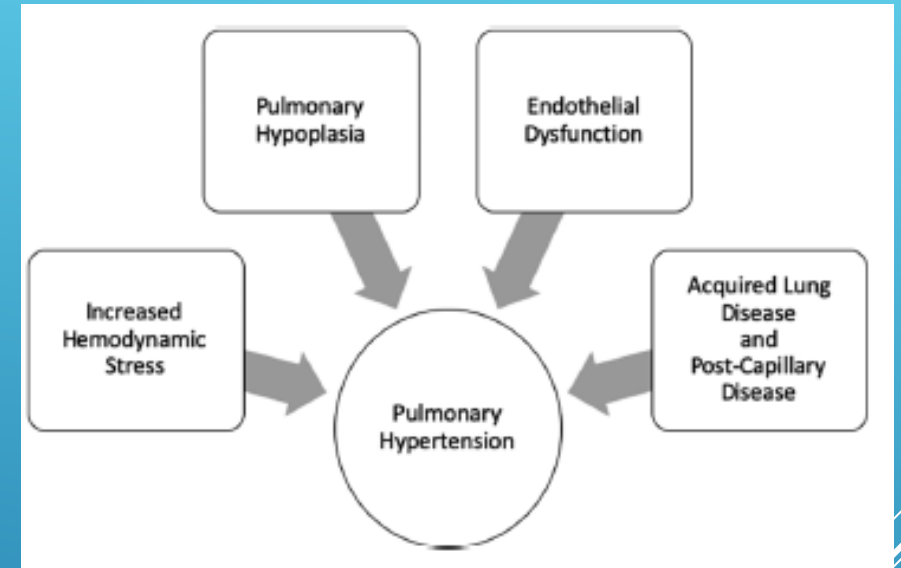
- Pulmonary Hypertension
- Decreased exercise tolerance with no known etiology

DS MINUS CHD = NORMAL???

- Up to 25 % of patients with Trisomy 21
- As high as 45% in those with Trisomy 21 + CHD
- Increases with age

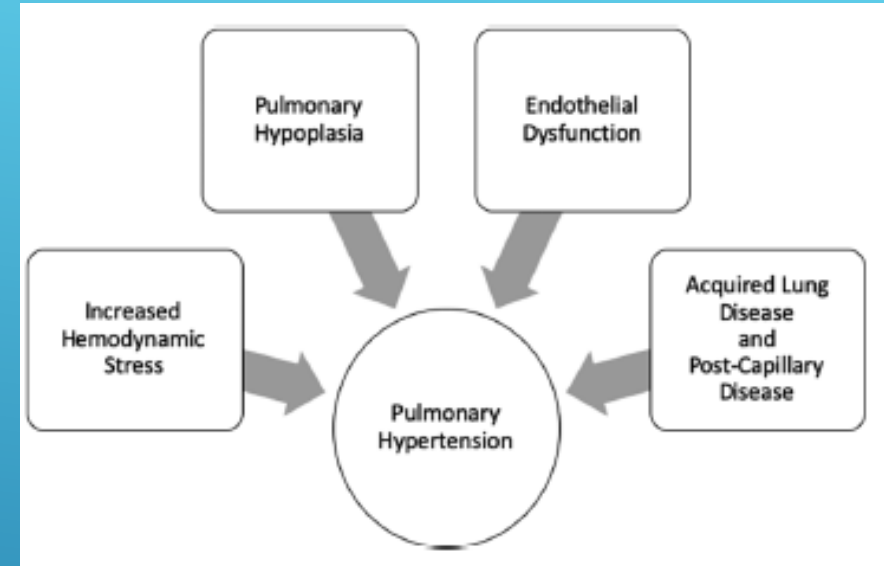
PULMONARY HYPERTENSION

- **Intrinsic lung factors**
 - Decreased alveolarization
 - Pulmonary hyperplasia
 - Pulmonary vascular dysfunction

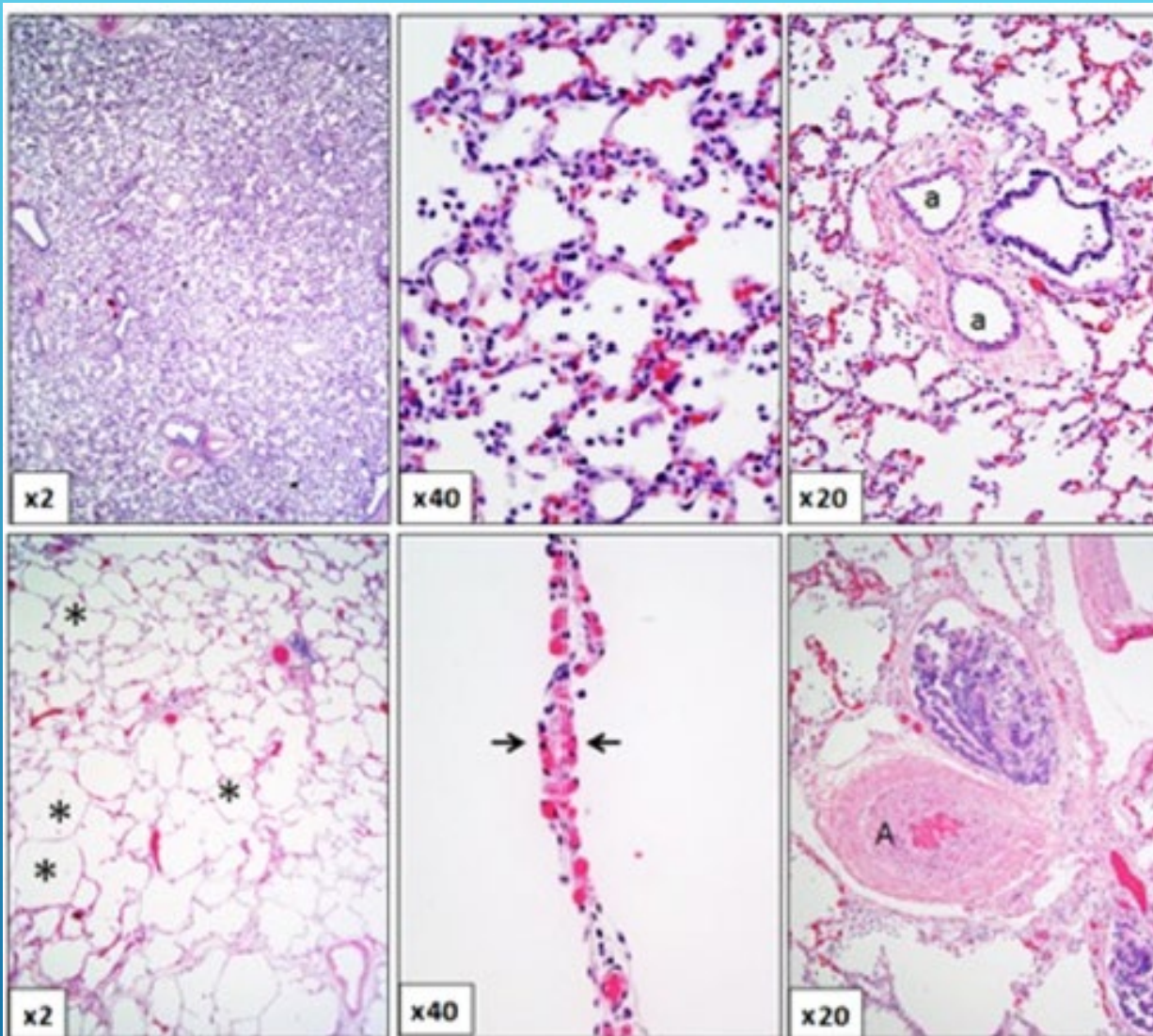


PULMONARY HYPERTENSION- ETIOLOGY

- **Extrinsic lung factors**
 - Congenital heart disease
 - Airway obstruction
 - Chronic aspiration
 - Recurrent pneumonias



PULMONARY HYPERTENSION- ETIOLOGY



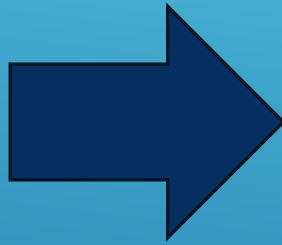
Pulmonary hypertension in children with Down syndrome

Douglas Bush MD¹  | Csaba Galambos MD, PhD² | David Dunbar Ivy MD³ 

Pediatric Pulmonology. 2021;56:621–629.

- Etiologies change with age
 - Younger DS population more likely to be secondary to congenital heart disease or PPHN
 - Older DS population increased risk of secondary PH to left heart dysfunction

PULMONARY HYPERTENSION



FRONTIERS

Cardiovascular Complications of Down Syndrome: Scoping Review and Expert Consensus

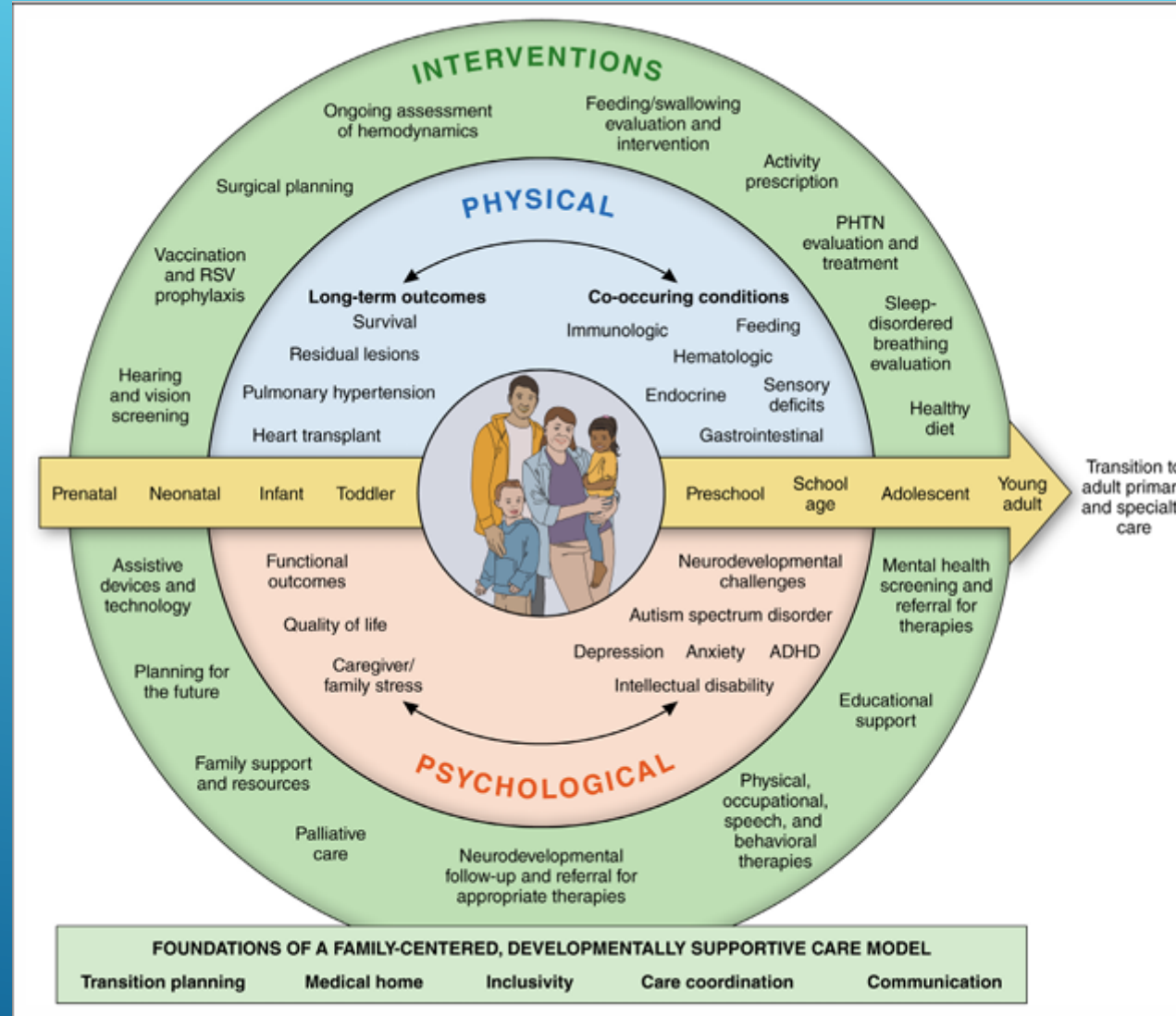
Konstantinos Dimopoulos, MD, PhD, MSc ^{*,†}, Andrew Constantine, MBBS, MA ^{*,†}, Paul Clift, MBBS, MD, BA ^{*}, Robin Condliffe, MD ^{*}, Shahin Moledina, MBChB ^{*}, Katrijn Jansen, MD ^{*}, Ryo Inuzuka, MD, PhD, Gruschen R. Veldtman, MBChB, Clifford L. Cua, MD , Edgar Lik Wui Tay, MBBS, MMed, Alexander R. Opotowsky, MD, MPH, MMSc , George Giannakoulas, MD, PhD , Rafael Alonso-Gonzalez, MD, MSc , Rachael Cordina, MBBS, PhD , George Capone, MD, Judith Namuyonga, MBChB, MMed, Charmaine H. Scott, OD, BSc, MBBS, DCH, DM(Paed), Michele D'Alto, MD, PhD , Francisco J. Gamero, MD, Brian Chicoine, MD , Hong Gu, MD, PhD, Alisa Limswan, MD, Tosin Majekodunmi, BSc, PhD, MBBS, Werner Budts, MD, PhD , Gerry Coghlan, MB ChB, BAO, MD, and Craig S. Broberg, MD 

- **Transition to ACHD**
- **Multidisciplinary team**
- **Special consideration to PAH**

LONG TERM CARE FOR DS+CHD

- **More complex in Trisomy 21 + CHD**
- **More difficulty with transition**
- **Worse outcomes**

TRANSITION TO ADULT CARE



- Lifelong expert care
- Repeat intervention based on risk:benefit
- Using objective measures extremely important in DS

LONG TERM
COMPLICATIONS/OUTCOMES

- **Cong. Heart Disease**
 - Regular life-long follow-up
 - Electrical considerations
 - Exercise Capacity

LONG TERM FOLLOW-UP

ARRHYTHMIA

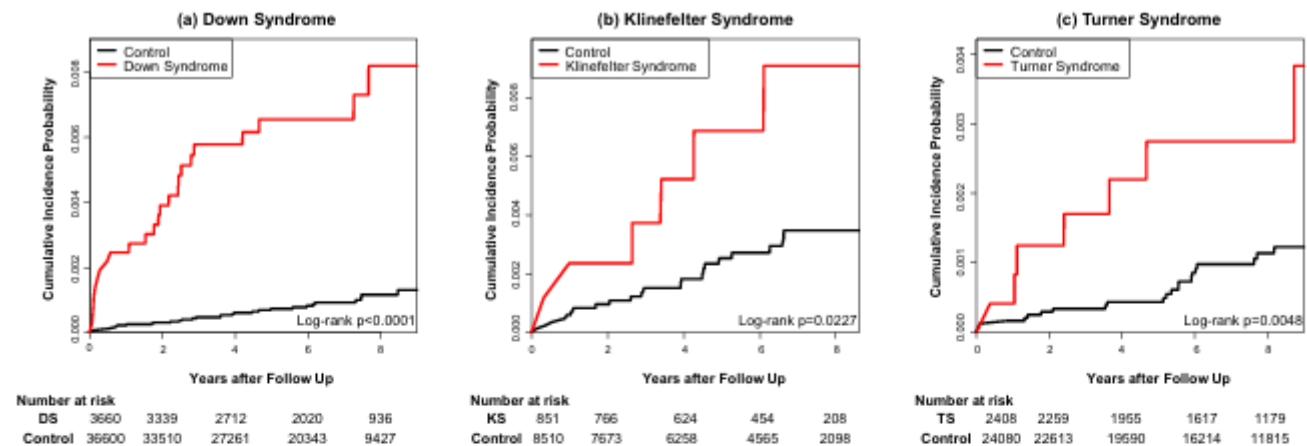


Figure 1. Comparison of cumulative incidence of atrial fibrillation events in chromosomal abnormalities. (a) Down Syndrome, (b) Klinefelter Syndrome (c) Turner Syndrome. DS Down Syndrome, KS Klinefelter Syndrome, TS Turner Syndrome.

Groups	N	No. of events	Incidence rate (IR) ^a	Hazard Ratio (95% CI)	
				Crude HR ^b	Adjusted HR ^c
Down Syndrome					
No	36,600	31	0.143	1 (ref.)	1 (ref.)
Yes	3660	24	1.114	7.77 (4.52–13.20)	6.84 (3.77–12.20)
Klinefelter Syndrome					
No	8510	22	0.450	1 (ref.)	1 (ref.)
Yes	851	6	1.232	2.74 (1.00–6.34)	2.84 (1.01–6.88)
Turner Syndrome					
No	24,080	22	0.135	1 (ref.)	1 (ref.)
Yes	2408	7	0.430	3.19 (1.26–7.10)	2.75 (1.03–6.43)

Table 2. Risk of the atrial fibrillation events in chromosomal abnormalities. HR hazard ratio, CI confidence interval, COPD chronic obstructive pulmonary disease, IHD ischemic heart disease, CHF Chronic heart failure, ESRD End-stage renal disease, PAD peripheral artery disease. ^aIncidence rates were calculated per 1000 patient-years. ^bUnadjusted crude hazard ratio (HR) and 95% CI. ^cMultivariate Cox regression model adjusted for age, sex, income, diabetes mellitus, hypertension, dyslipidemia, COPD, IHD, CHF, ESRD, and PAD.

Cho, J.H., Choi, E.K., Moon, I.K. *et al.* Chromosomal abnormalities and atrial fibrillation and ischemic stroke incidence: a nationwide population-based study. *Sci Rep* 10, 15872 (2020)

- Sinoatrial node dysfunction
 - Little known
 - Case series

ARRHYTHMIA

Table 2. Echocardiograph Findings.

	Down Syndrome (<i>n</i> = 9)	Control (<i>n</i> = 10)	<i>p</i> -Value
Systolic Function			
LVEF	56.00 ± 11.04	58.39 ± 11.88	0.630
FS	25.97 ± 4.87	26.29 ± 7.83	0.917
S' TDI Lateral	0.09 ± 0.03	0.09 ± 0.01	0.657
S' TDI Septal	0.08 ± 0.01	0.09 ± 0.01	0.026 *
Diastolic Function			
E/ A Mitral Flow ^a	2.65 (1.52)	2.24 (0.45)	0.447
E' TDI Lateral	0.13 ± 0.02	0.15 ± 0.02	0.007 *
E' TDI Septal	0.11 ± 0.02	0.13 ± 0.02	0.025 *
A' TDI Lateral	0.06 ± 0.01	0.08 ± 0.02	0.027 *
A' TDI Septal	0.07 ± 0.02	0.08 ± 0.02	0.063
E' / A' TDI Lateral	2.30 ± 0.52	2.11 ± 0.67	0.513
E' / A' TDI Septal ^a	1.81 (0.59)	1.73 (0.69)	0.633
E/ e' TDI Lateral	7.24 ± 1.81	4.66 ± 0.97	0.001 *

HEART FAILURE

Azar *et al* **Cardiac Structure and Function in Adults with Down Syndrome** Int. J. Environ. Res. Public Health **2022**, 19, 12310

Table 2. *Cont.*

	Down Syndrome (<i>n</i> = 9)	Control (<i>n</i> = 10)	<i>p</i> -Value
E/e' TDI Septal ^a	8.24 (2.81)	4.92 (2.16)	0.001 *
Cardiac Structure			
IVSs	1.03 ± 0.15	1.02 ± 0.13	0.937
IVSd ^a	0.80 (0.10)	0.76 (0.16)	0.720
LVPWs	1.42 ± 0.14	1.24 ± 0.12	0.007 *
LVPWd ^a	0.84 (0.13)	0.80 (0.08)	0.133
LVIDs ^a	3.05 (0.69)	2.77 (1.17)	0.447
LVIDd ^a	4.29 (0.76)	4.21 (1.20)	0.604
LVM ^a	104.00 (34.00)	90.50 (82.63)	0.447

HEART FAILURE

Azar *et al* **Cardiac Structure and Function in Adults with Down Syndrome** *Int. J. Environ. Res. Public Health* **2022**, *19*, 12310

- **Pulmonary Hypertension**
 - Lifelong screening recommended
 - Consideration of cardiac catheterization
 - Look for secondary sources

LONG TERM FOLLOW-UP

- **Coronary Artery Disease**
 - Screening needed
 - Unique presentation

LONG TERM FOLLOW-UP

Age-related cardiovascular disease in Down syndrome: A population-based matched cohort study

■ Annie Pedersen^{1,2} , Anna Skarin Nordenvall^{3,4}, Giorgio Tettamanti^{4,5} & Ann Nordgren^{1,2,4,6}

The Journal of Internal Medicine. Journal of Internal Medicine, 2025, 297; 683–692

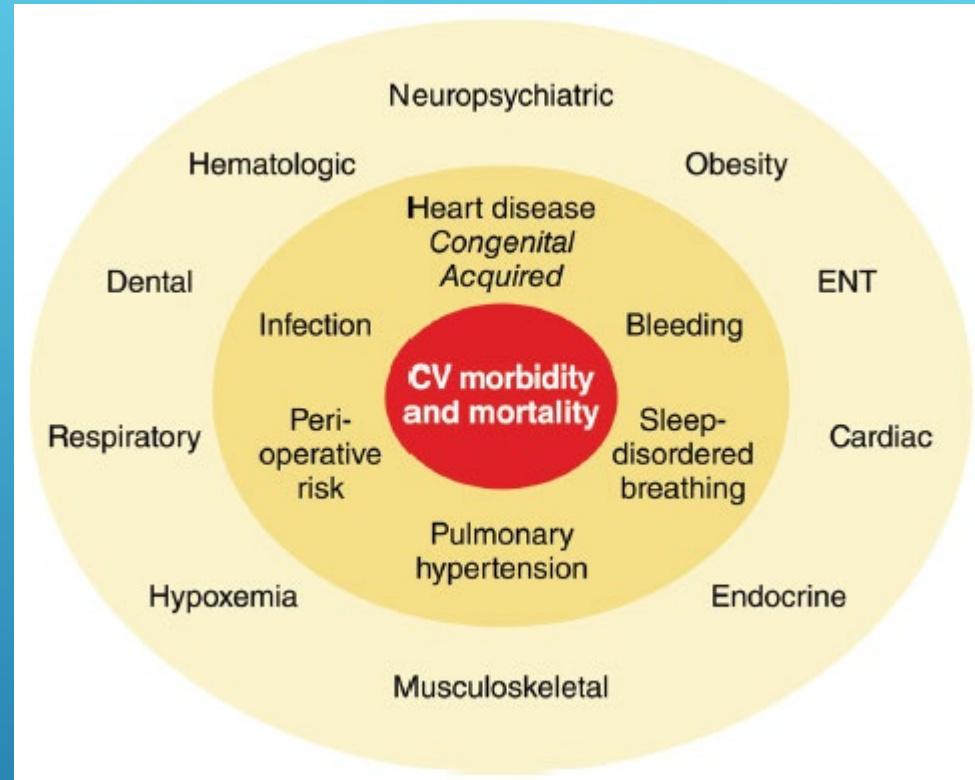
- ▶ Population based matched cohort study
- ▶ Included 5155 individuals with DS

	<i>N</i>	aHR (95% CI)
Intracerebral hemorrhage	62	5.03 (3.67–6.88) ^a
Subarachnoid hemorrhage	11	1.20 (0.59–2.44) ^a
Any hemorrhagic stroke ^b	71	5.14 (3.84–6.89) ^a
Ischemic stroke	121	4.41 (3.53–5.52)
Stroke NOS	21	6.30 (3.59–11.06) ^a
Any stroke ^c	199	4.18 (3.50–4.98) ^a
Acute myocardial infarction	32	0.85 (0.56–1.29)
Any coronary artery surgery	5	0.13 (0.05–0.63) ^a

- Heart Failure/Transplant
 - DS patients ARE candidates for transplant

LONG TERM FOLLOW-UP

- **Whole body care**
 - **Cerebrovascular**
 - **Endocrine**
 - **Respiratory**
 - **ENT**
 - **Dental**
 - **Hematologic**



LONG TERM FOLLOW-UP

WALT Disney Pavilion

WALT Disney Pavilion at Advent Health
for Children



Thank you!!