DSMIG-USA®
Down Syndrome Medical Interest Group

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

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FSCAI, FAAP
Advent Health For Children

Assistant Professor, UCF
College of Medicine

ANNUAL symposium

no financial disclosure

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

CARDIOVASCULAR ASSOCIATION

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CONGENITAL HEART DISEASE

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

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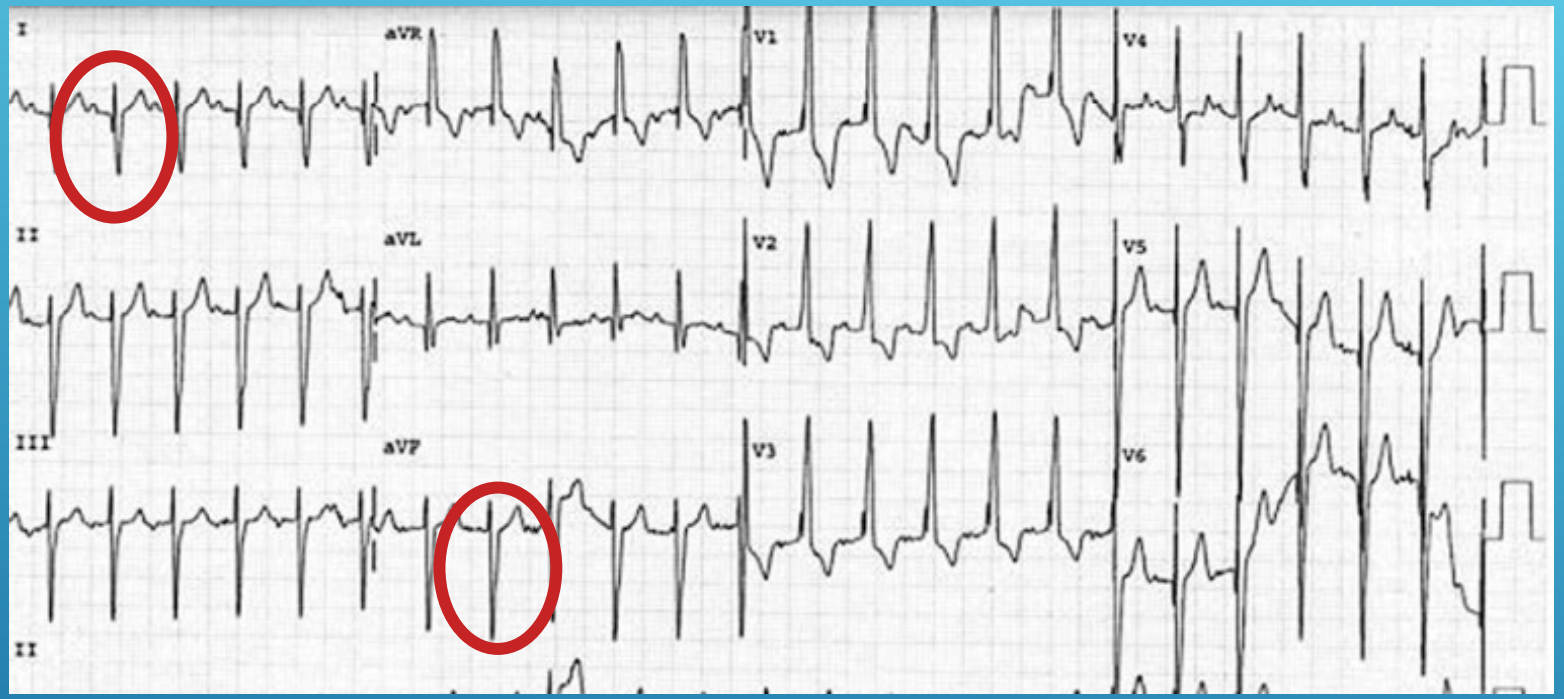
I
aVR
V1
V4
II
aVL
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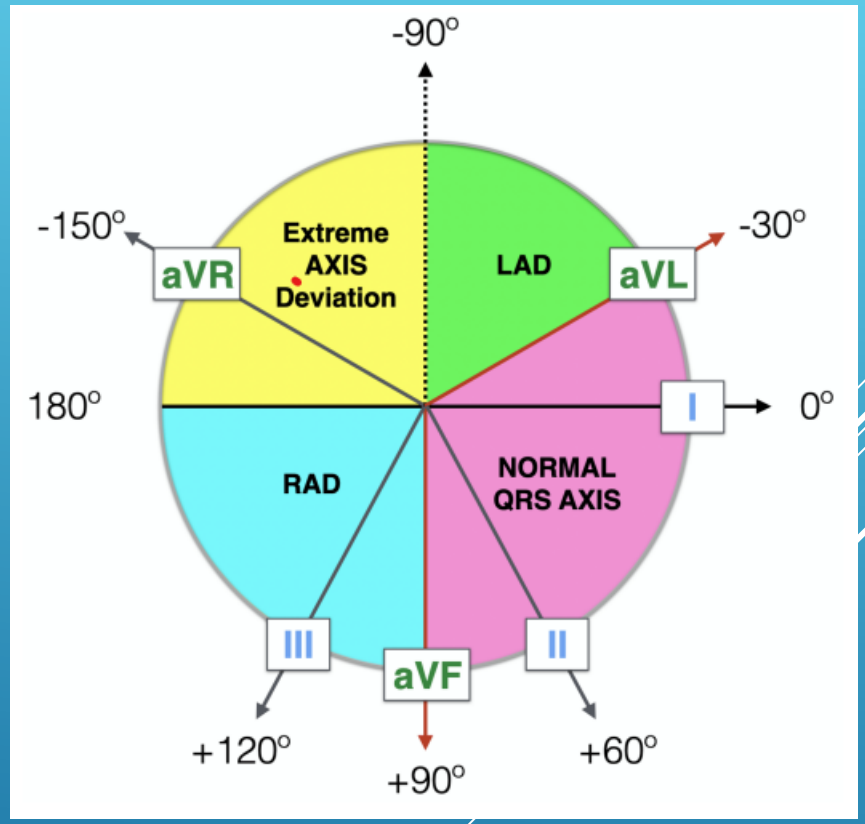
V5
III
aVF
V3
V6
II


-90°
-150°
-30°
aVR
Extreme
AXIS
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LAD
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III
aVF
II
+120°
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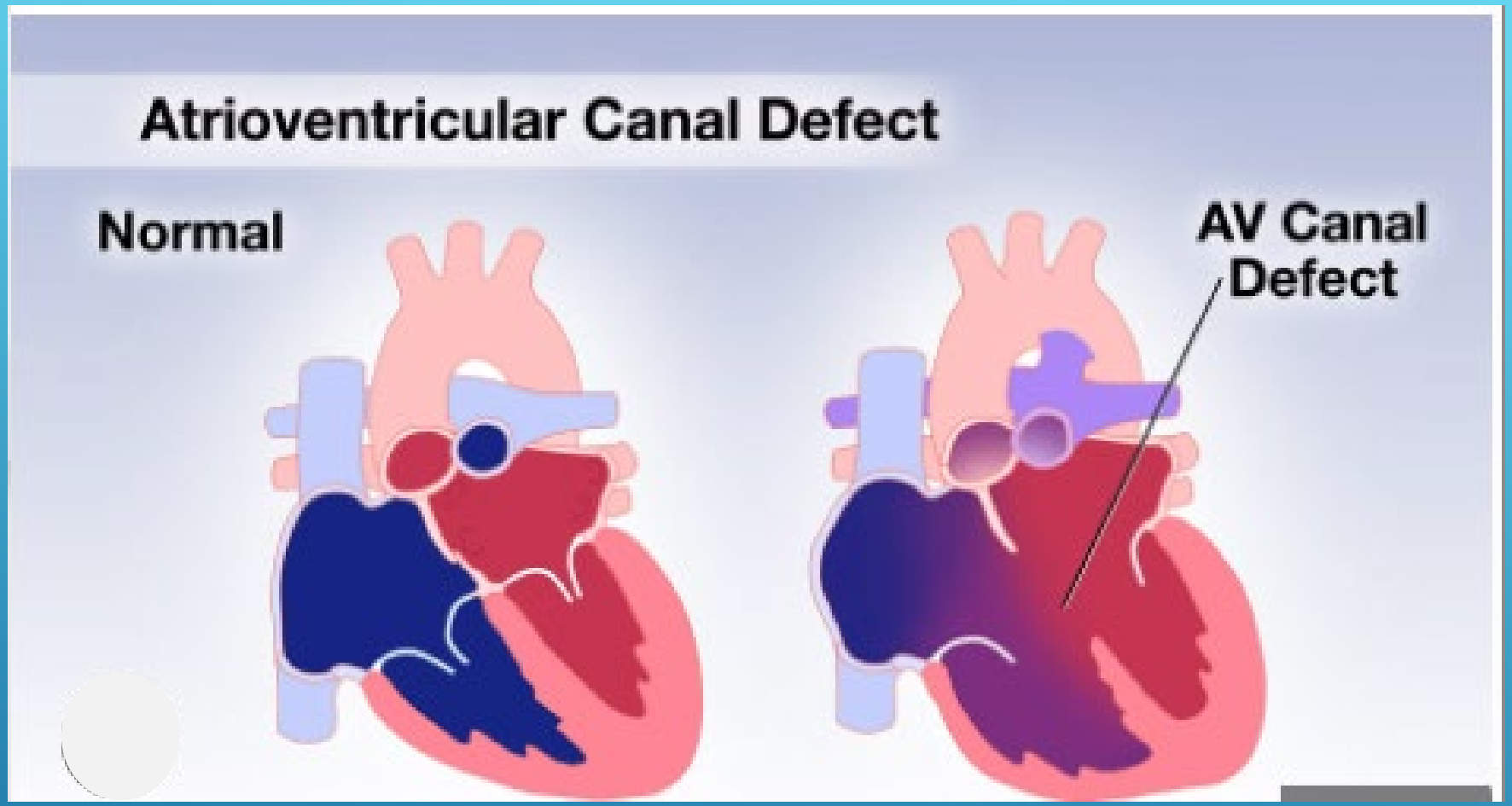
+60°

AV CANAL



CONGENITAL HEART DISEASE

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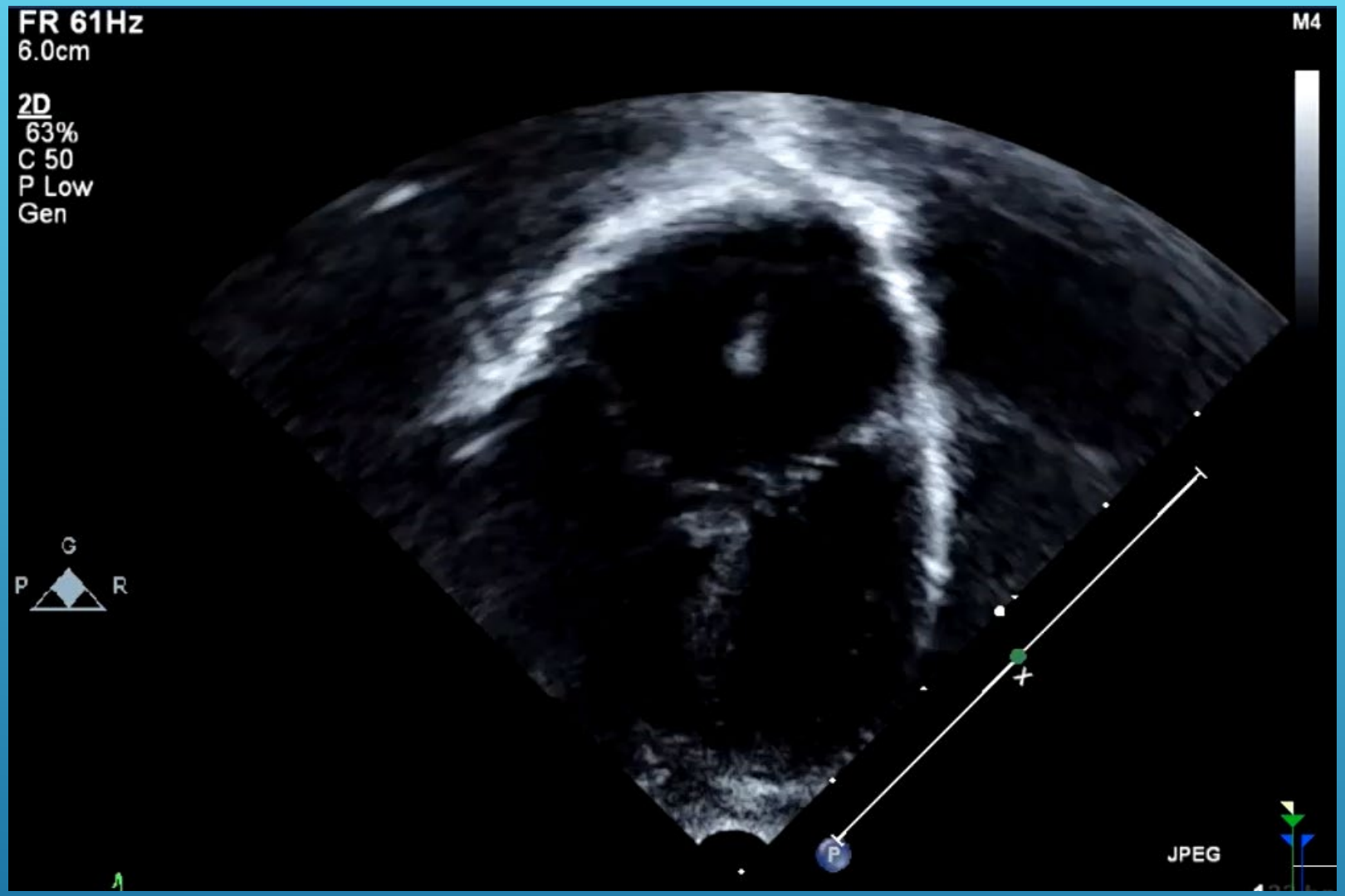
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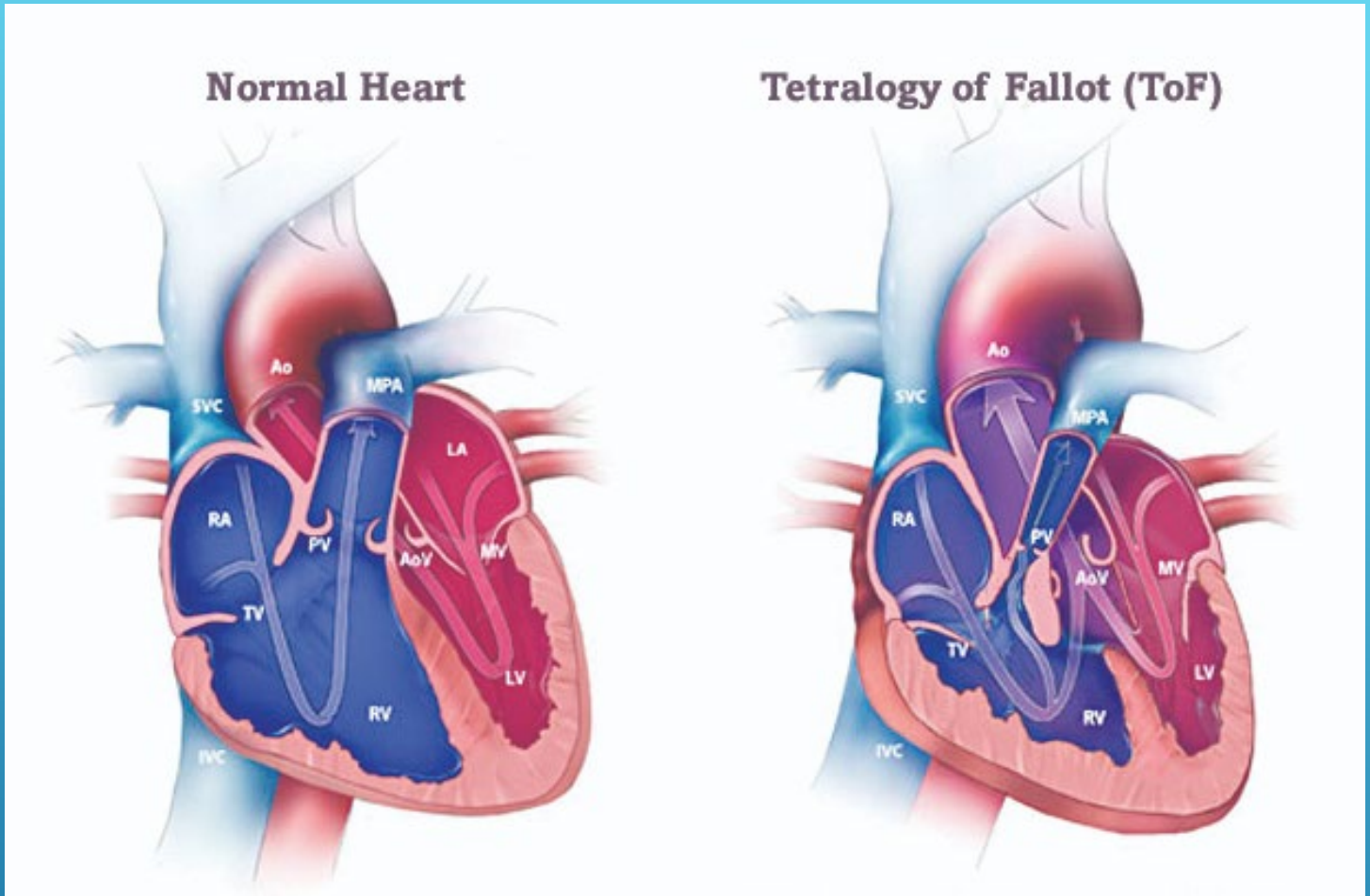

CONGENITAL HEART DISEASE

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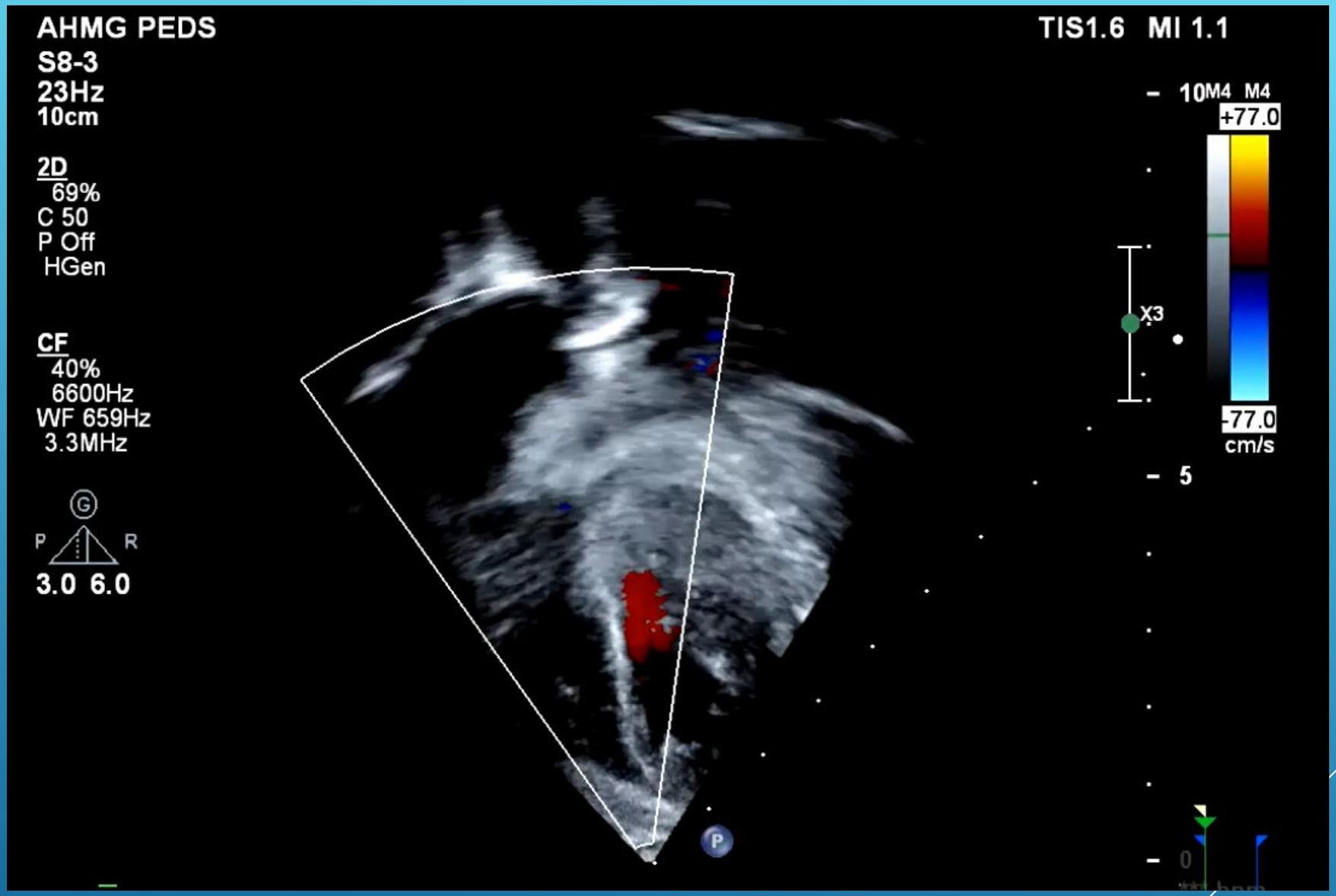
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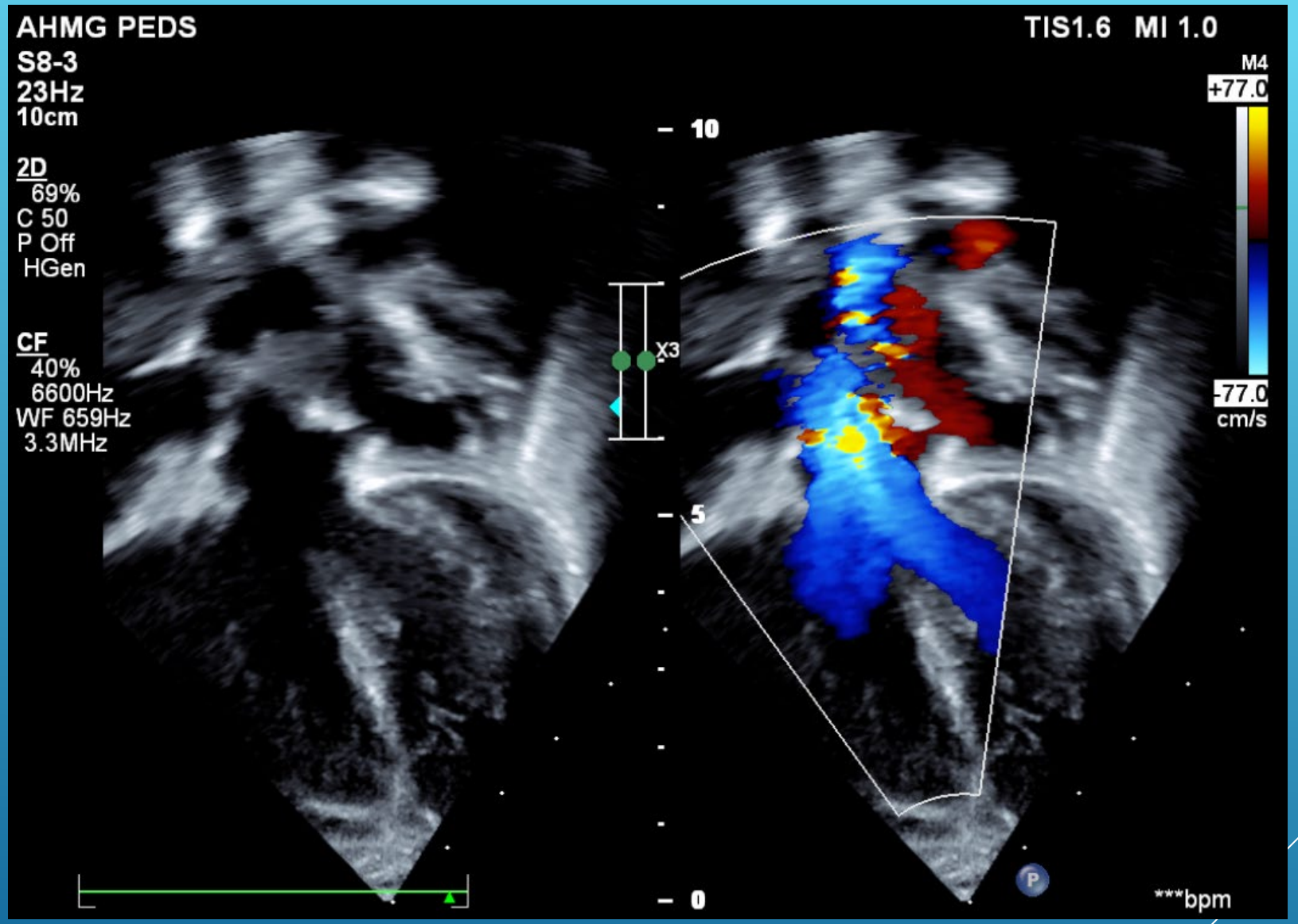
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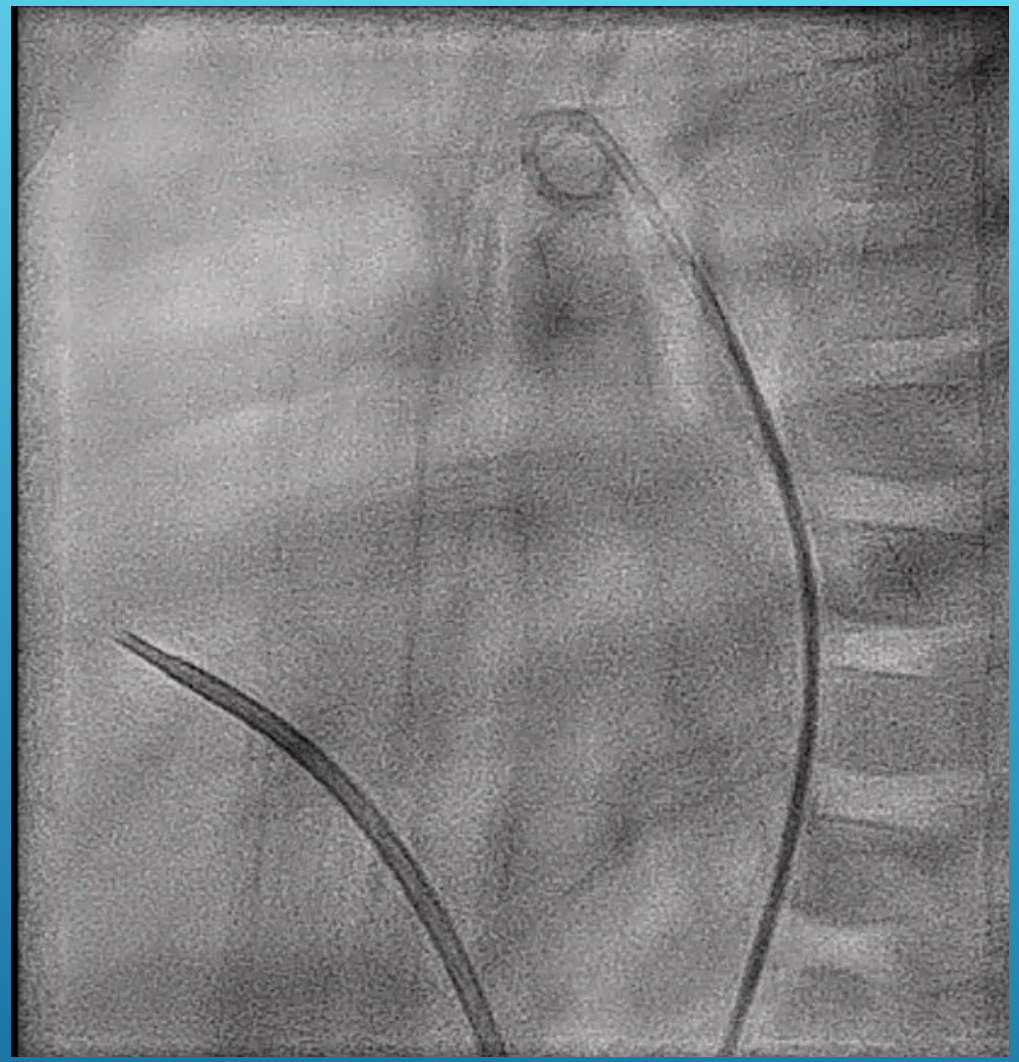

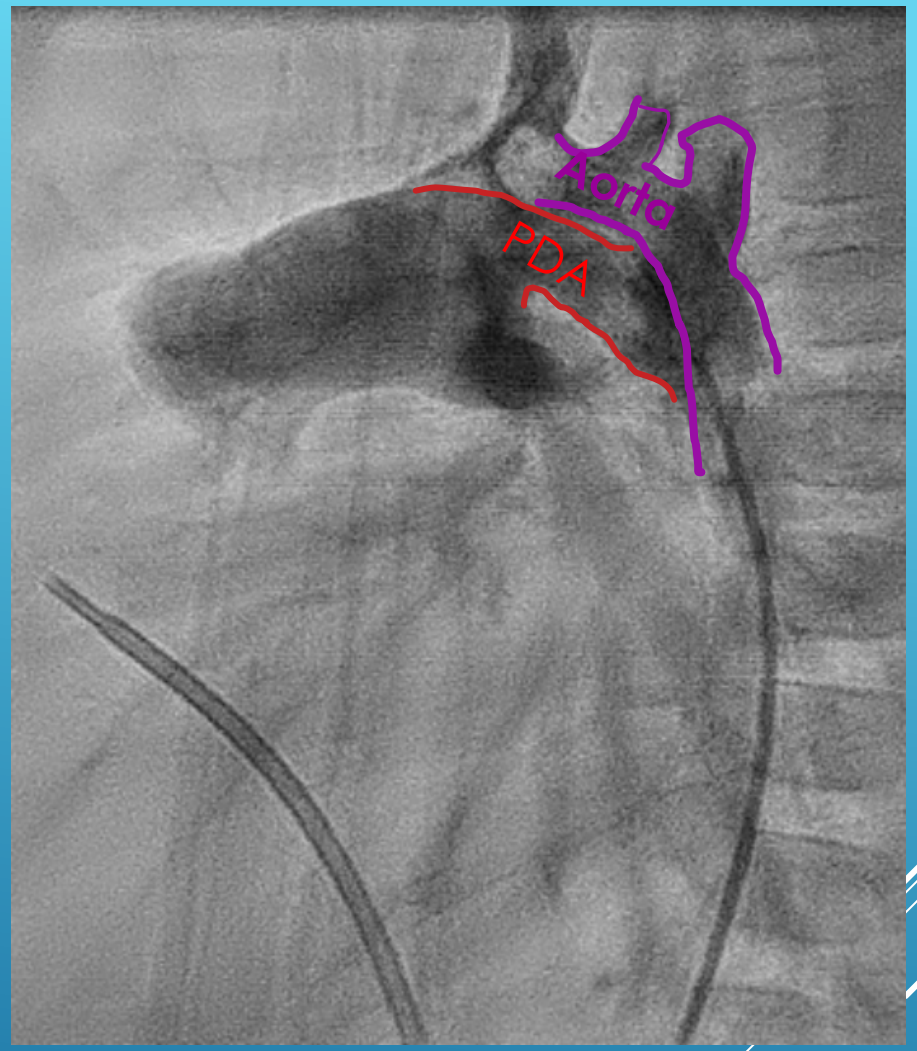

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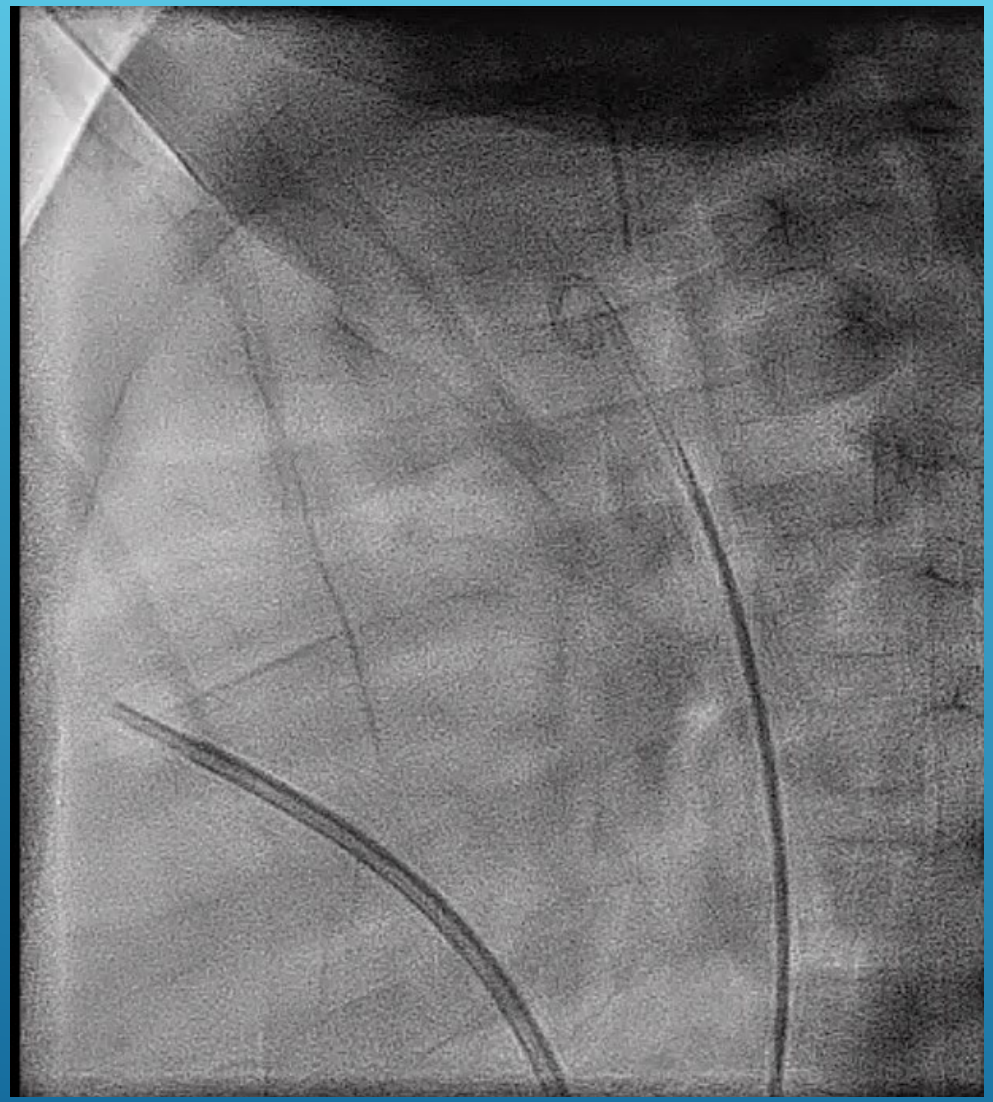

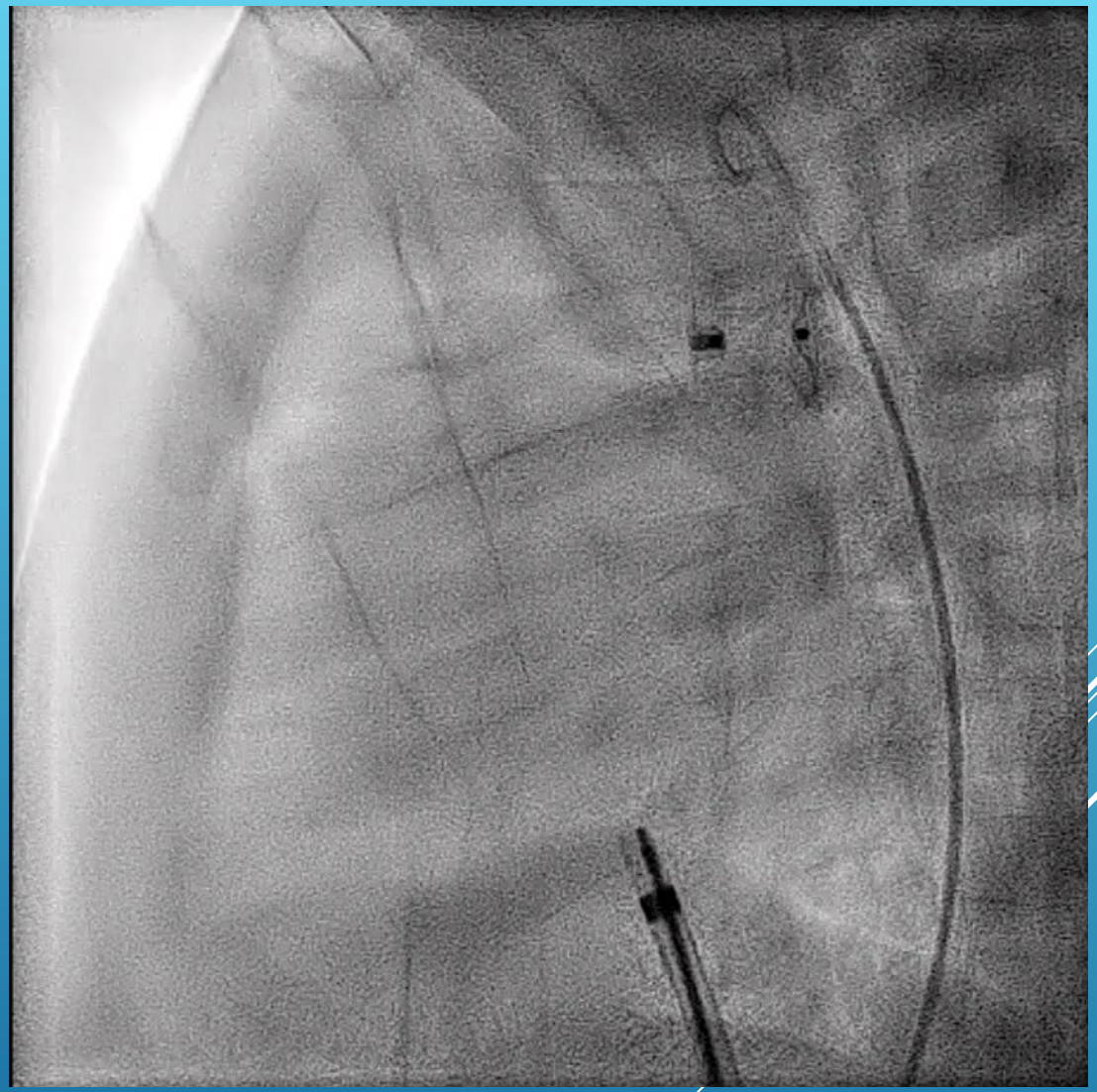

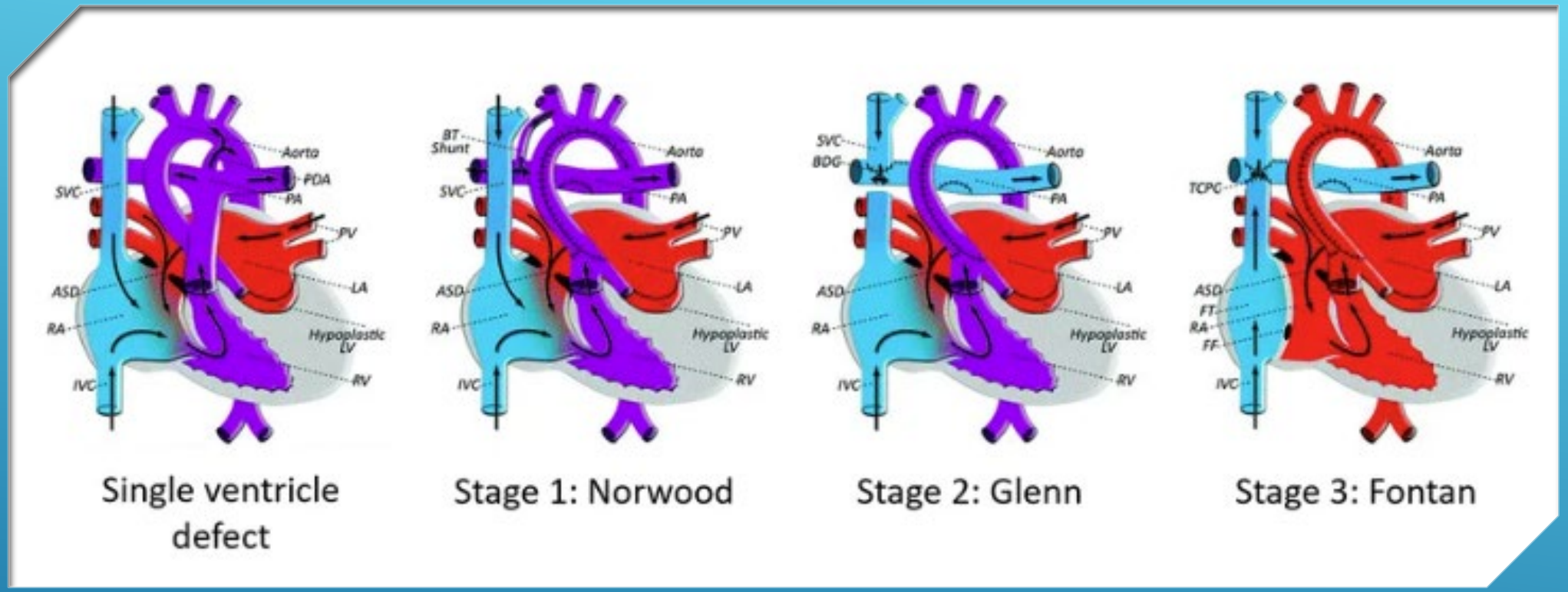

Single ventricle defect

Stage 1: Norwood

Stage 2: Glenn

Stage 3: Fontan

SINGLE V + TRISOMY 21

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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

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SINGLE V + TRISOMY 21

- **High PVR (pulm htn) impedes passive pulmonary blood flow**
- **Historical quality of life bias**

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SINGLE V + TRISOMY 21

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

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CONGENITAL HEART DISEASE-SCREENING

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

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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

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CHD- OUTCOMES

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

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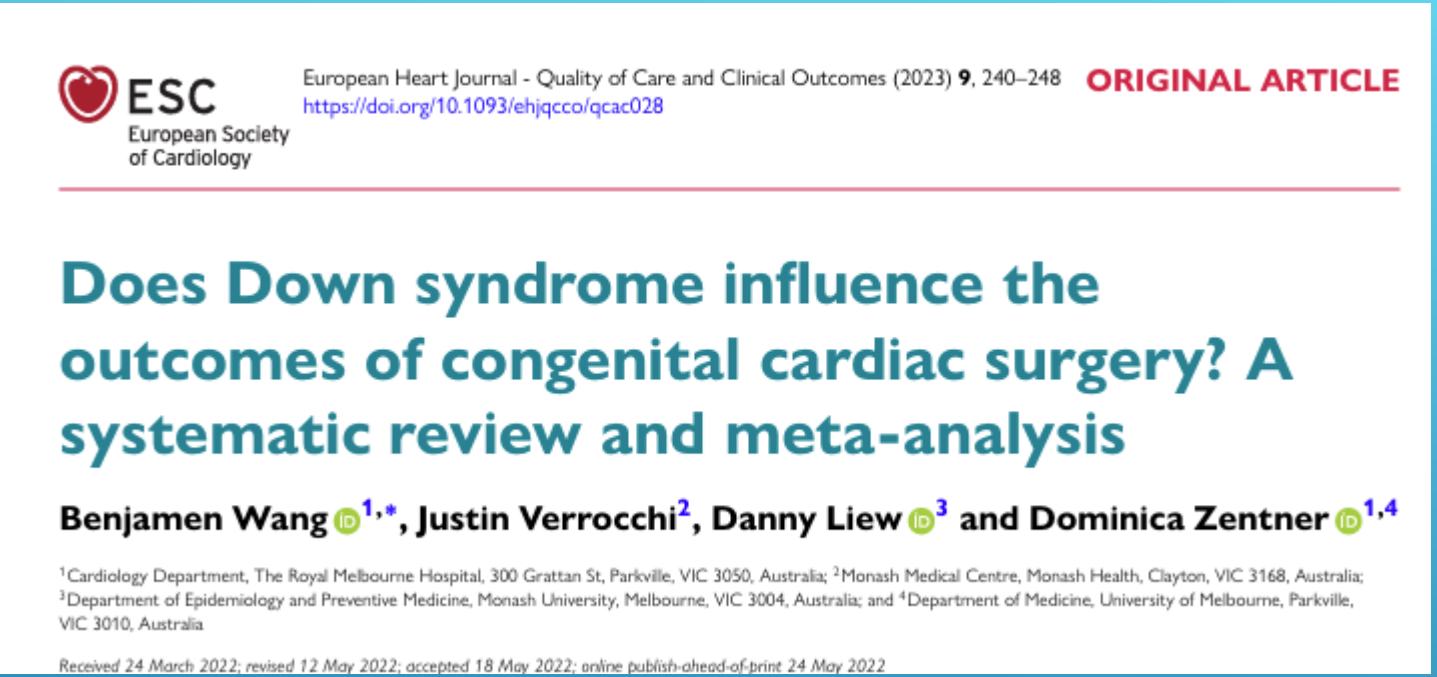

ESC European Society of Cardiology

European Heart Journal - Quality of Care and Clinical Outcomes (2023) **9**, 240–248 **ORIGINAL ARTICLE**
https://doi.org/10.1093/ehjqcco/qcac028

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

Benjamen Wang [1,*], Justin Verrocchi [2], Danny Liew [3] and Dominica Zentner [1,4]

[1]Cardiology Department, The Royal Melbourne Hospital, 300 Grattan St, Parkville, VIC 3050, Australia; [2]Monash Medical Centre, Monash Health, Clayton, VIC 3168, Australia; [3]Department of Epidemiology and Preventive Medicine, Monash University, Melbourne, VIC 3004, Australia; and [4]Department of Medicine, University of Melbourne, Parkville, VIC 3010, Australia

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CHD- OUTCOMES

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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

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CHD- OUTCOMES

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

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CHD- OUTCOMES

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

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CHD- OUTCOMES

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

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CHD- OUTCOMES

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

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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, MS[1], Shaun P. Setty, MD[1,2], Jessica H. Knight, PhD[3], Amanda S. Thomas, MSPH[4], James H. Moller, MD[5], Lazaros K. Kochilas, MD, MSCR[4,6]

SINGLE V OUTCOMES

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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)	

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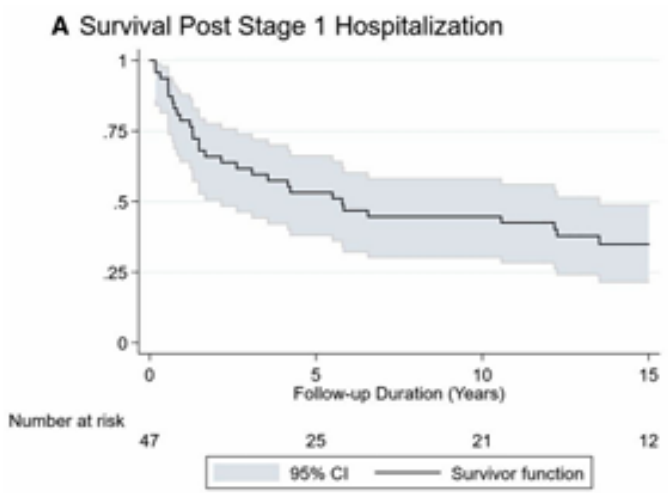
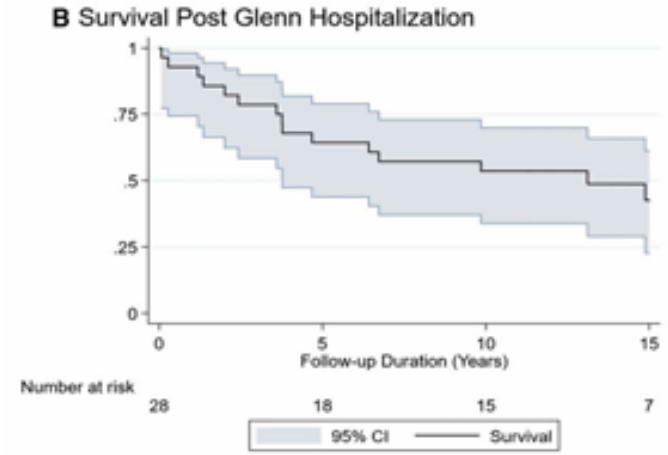
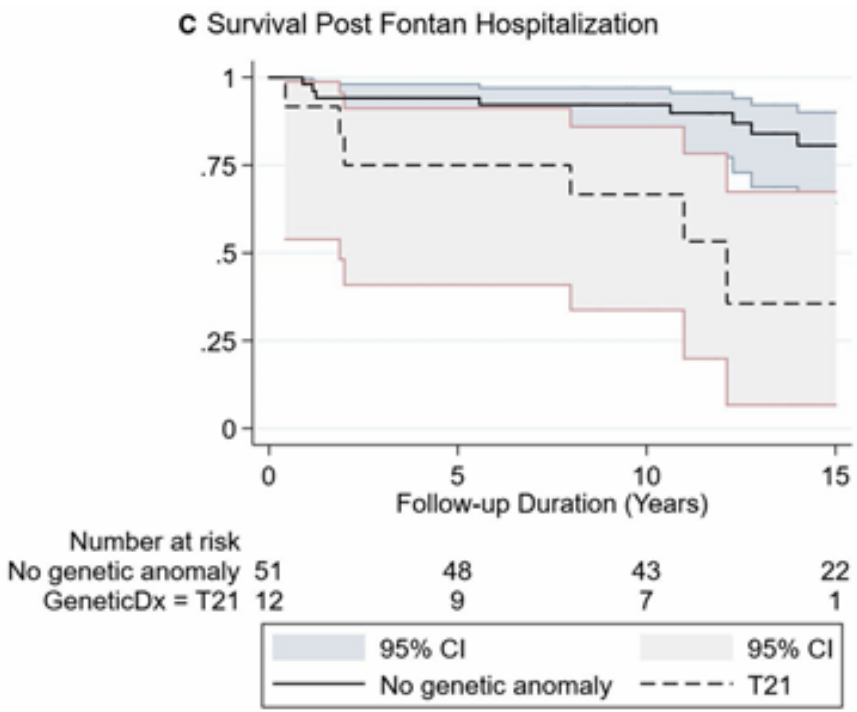

A Survival Post Stage 1 Hospitalization
1
.75
.5
.25
0
0
5
10
15
Follow-up Duration (Years)
Number at risk
47
25
21
12
95% CI
Survivor function


B Survival Post Glenn Hospitalization
1
.75
.5
.25
0
0
5
10
15
Follow-up Duration (Years)
Number at risk
28
18
15
7
95% CI
Survival


C Survival Post Fontan Hospitalization
1
.75
.5
.25
0
0
5
10
15
Follow-up Duration (Years)
Number at risk
No genetic anomaly 51 48 43 22
GeneticDx = T21 12 9 7 1
95% CI
95% CI
No genetic anomaly
T21

- **Pulmonary Hypertension**
- **Decreased exercise tolerance with no known etiology**

DS MINUS CHD = NORMAL???

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PULMONARY HYPERTENSION

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

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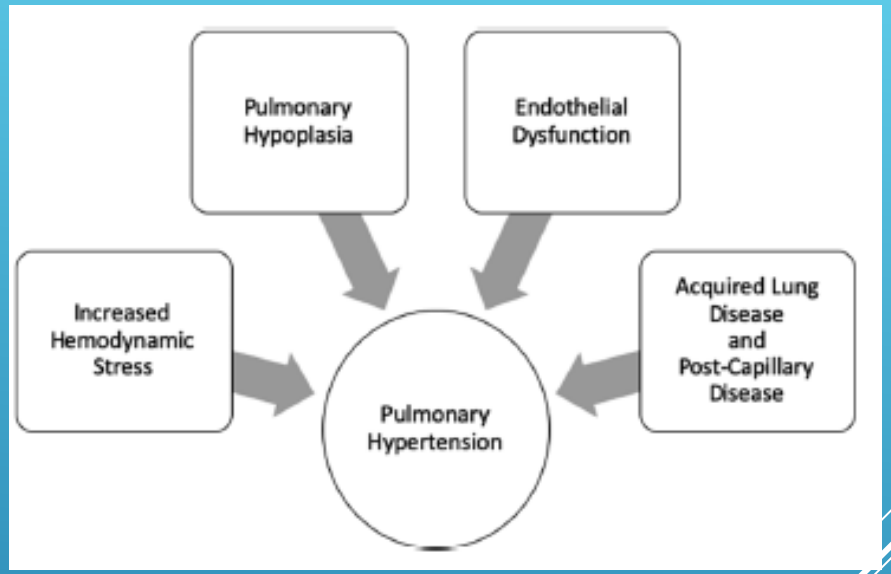
PULMONARY HYPERTENSION-ETIOLOGY

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



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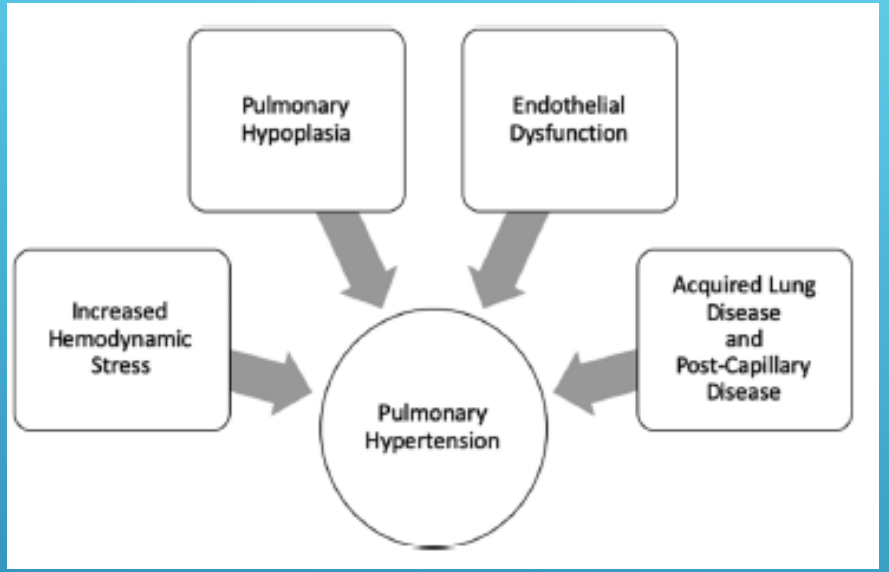
PULMONARY HYPERTENSION-ETIOLOGY

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



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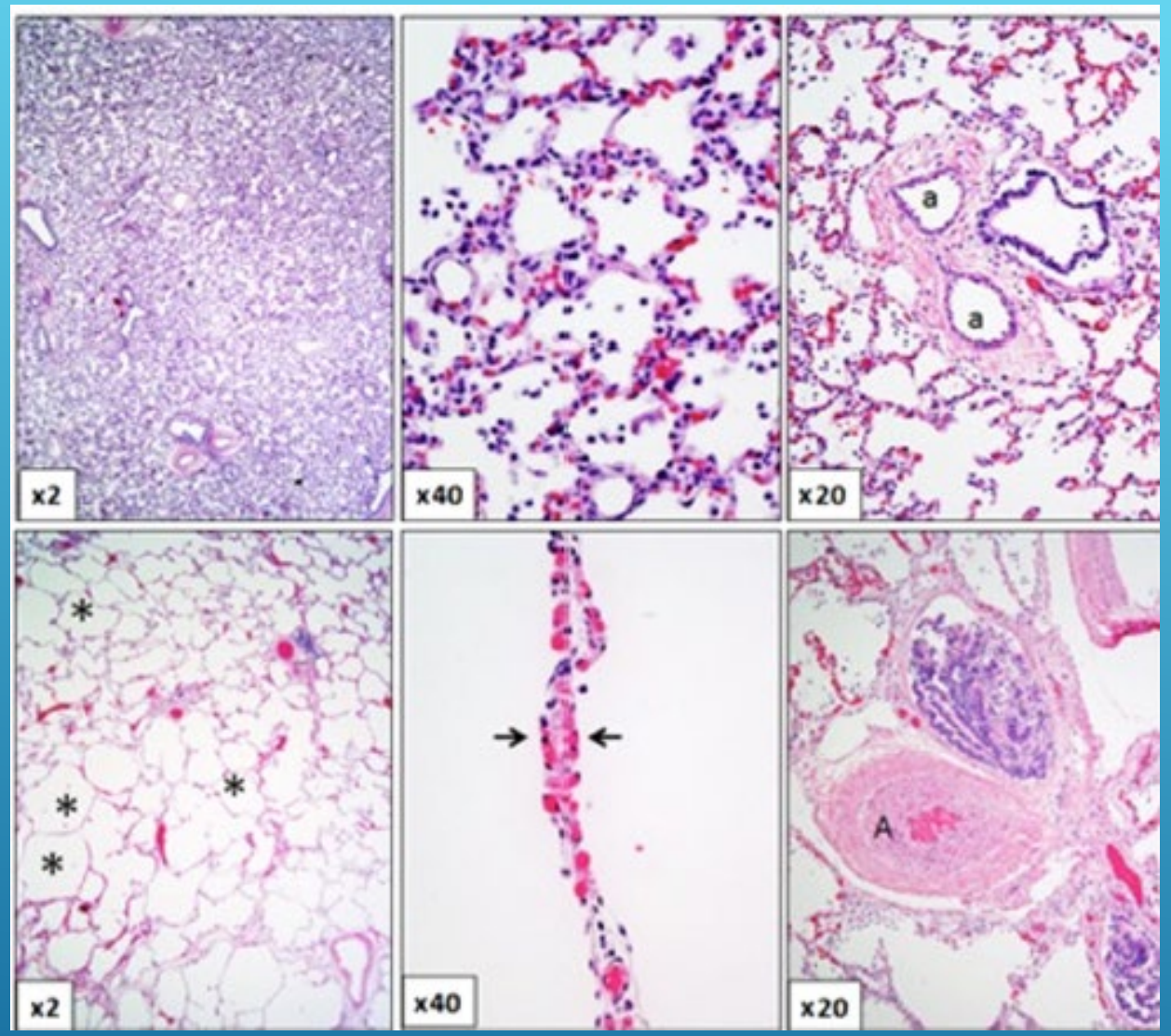

Pulmonary hypertension in children with Down syndrome

Douglas Bush MD[1] | Csaba Galambos MD, PhD[2] | David Dunbar Ivy MD[3]

Pediatric Pulmonology. 2021;56:621–629.

PULMONARY HYPERTENSION

- **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**

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Circulation
Volume 147, Issue 5, 31 January 2023; Pages 425-441
https://doi.org/10.1161/CIRCULATIONAHA.122.059706

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(Paeds), Michele D'Alto, MD, PhD, Francisco J. Gamero, MD, Brian Chicoine, MD, Hong Gu, MD, PhD, Alisa Limsuwan, MD, Tosin Majekodunmi, BSc, PhD, MBBS, Werner Budts, MD, PhD, Gerry Coghlan, MB BCh, BAO, MD, and Craig S. Broberg, MD

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LONG TERM CARE FOR DS+CHD

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

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TRANSITION TO ADULT CARE

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

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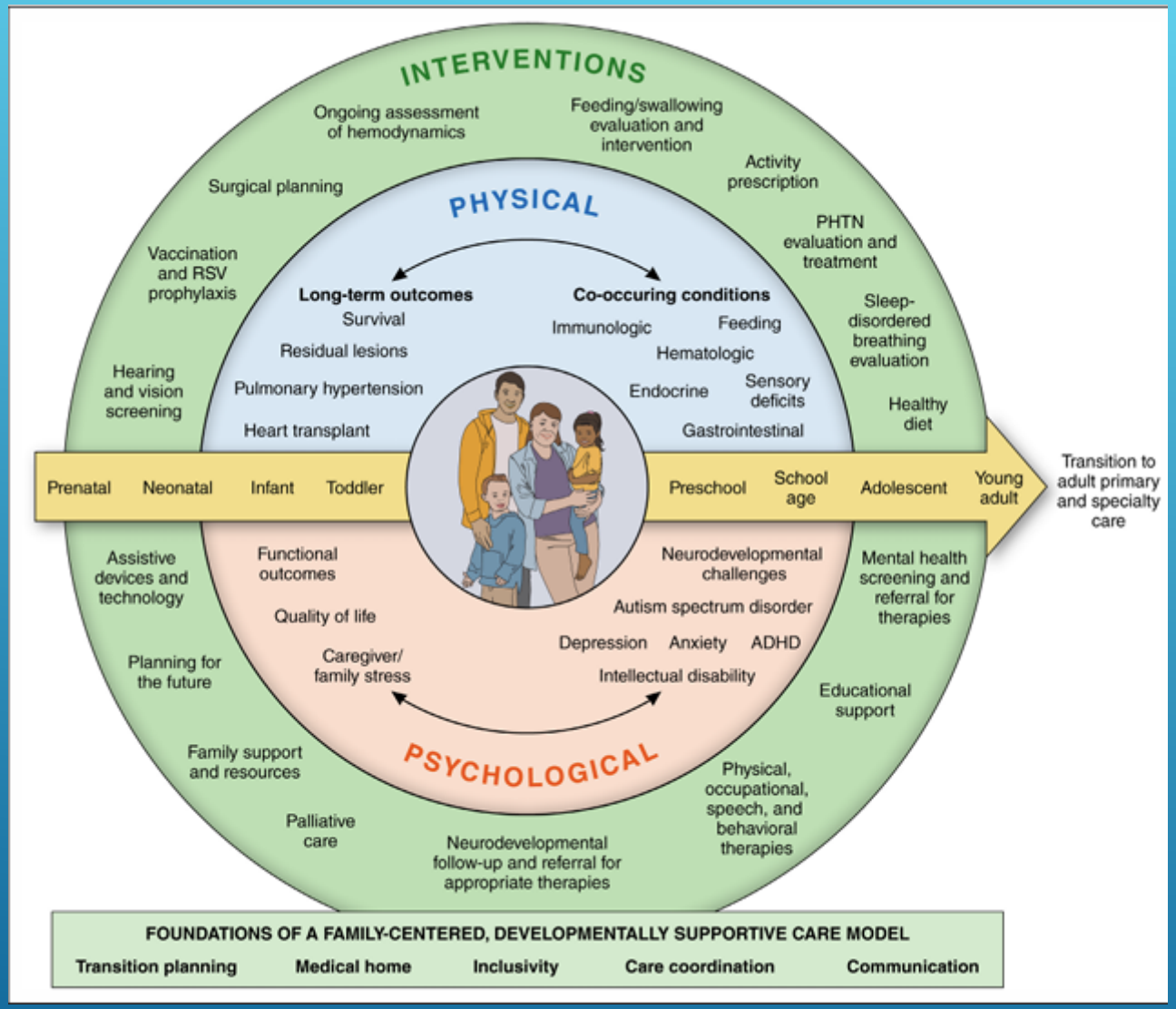

Peterson, J *et al* J Am Heart Assoc. 2024;13:e036214

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

LONG TERM COMPLICATIONS/OUTCOMES

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LONG TERM FOLLOW-UP

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

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ARRHYTHMIA

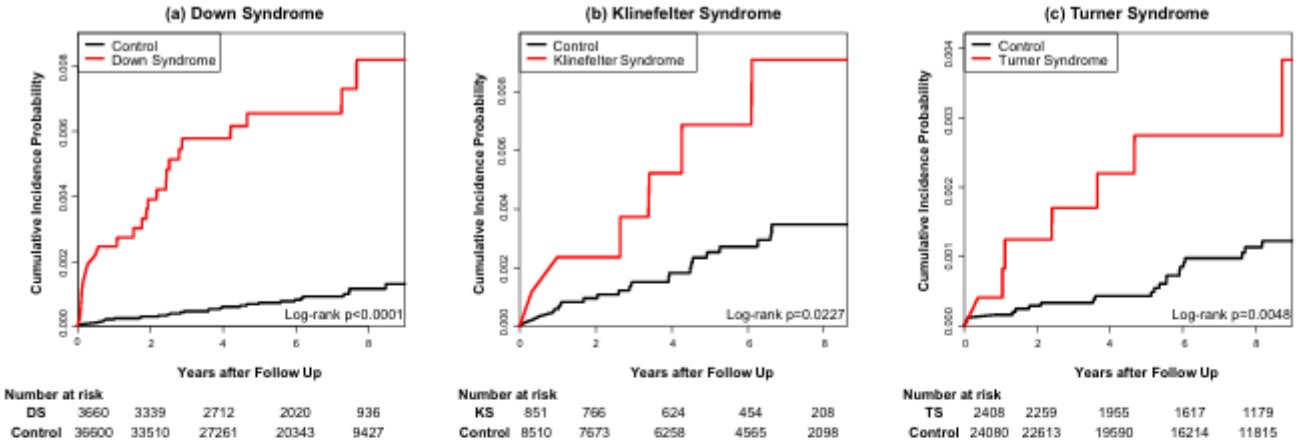

Figure 1. Comparison of cumulative incidence of atrial fibrillation events in chromosomal abnormalities. (**a**) Down Syndrome, (**b**) Klinefelter Syndrome (**c**) Turner Syndrome. *DS* Down Syndrome, *KS* Klinefelter Syndrome, *TS* Turner Syndrome.

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. [a]Incidence rates were calculated per 1000 patient-years. [b]Unadjusted crude hazard ration (HR) and 95% CI. [c]Multivariate Cox regression model adjusted for age, sex, income, diabetes mellitus, hypertension, dyslipidemia, COPD, IHD, CHF, ESRD, and PAD.

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

ARRHYTHMIA

- Sinoatrial node dysfunction
  - Little known
  - Case series

Table 2. Echocardiograph Findings.

	Down Syndrome ($n = 9$)	Control ($n = 10$)	p-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 *at al* **Cardiac Structure and Function in Adults with Down Syndrome**Int. J. Environ. Res. Public Health **2022**, 19, 12310

Table 2. *Cont.*

	Down Syndrome (n = 9)	Control (n = 10)	p-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 *at al* **Cardiac Structure and Function in Adults with Down Syndrome** Int. J. Environ. Res. Public Health **2022**, 19, 12310

LONG TERM FOLLOW-UP

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

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LONG TERM FOLLOW-UP

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

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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

	N	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]

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LONG TERM FOLLOW-UP

- **Heart Failure/Transplant**
  - **DS patients <u>ARE</u> candidates for transplant**

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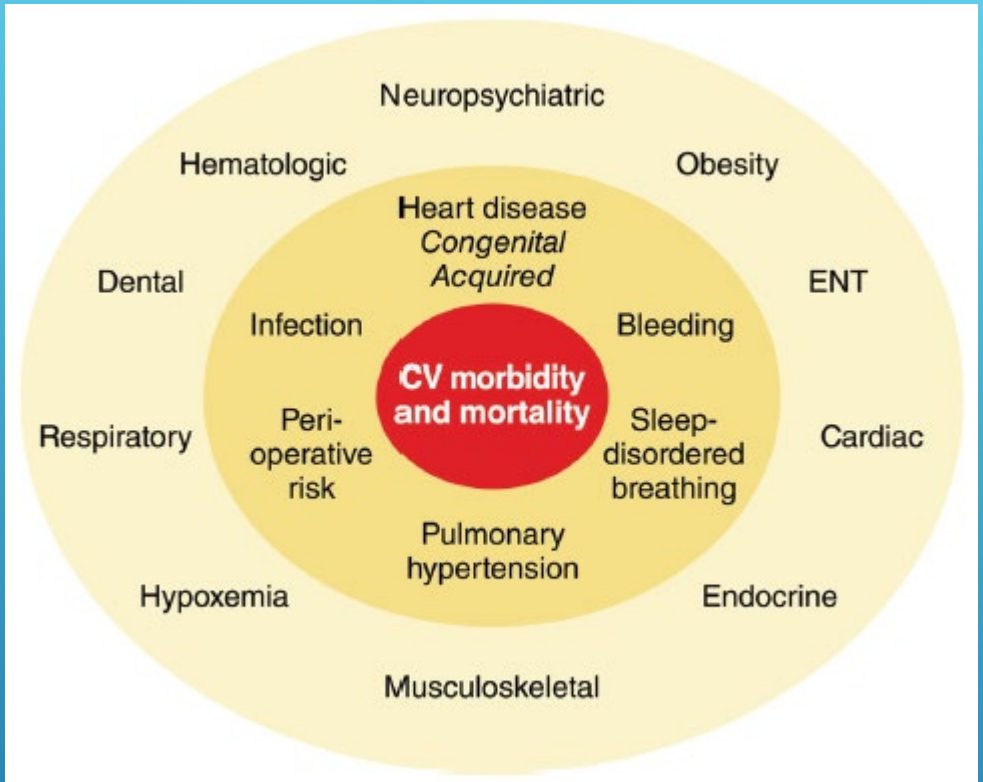
LONG TERM FOLLOW-UP

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




Walt Disney Pavilion
Walt Disney Pavilion at AdventHealth for Children
Thank you!!